2022

The evaluation of the reliability of radiographic features using CBCT and periapical radiographs in the differential diagnosis of periapical lesions

BOSTON UNIVERSITY

HENRY M. GOLDMAN SCHOOL OF DENTAL MEDICINE

THESIS

THE EVALUATION OF THE RELIABILITY OF RADIOGRAPHIC FEATURES USING CBCT AND PERIAPICAL RADIOGRAPHS IN THE DIFFERENTIAL DIAGNOSIS OF PERIAPICAL LESIONS.

SKYLAR MONTANA GRIZZLY PENBERTHY

DMD, Oregon Health and Science University School of Dental Medicine, 2019

CAGS in Endodontics, Boston University, 2022

Submitted in partial fulfillment of the requirements for the degree of

Master of Science in Dentistry

In the Department of Endodontics

2022

Approved by:

First Reader _____

Sami Chogle, B.D.S., D.M.D., M.S.D., C.A.G.S.

Associate Professor of Endodontics;

Chair of Endodontics;

Director of Advanced Specialty Education Program in Endodontics;

Herbert Schilder Professor in Endodontics

Second Reader _____

Yanling Jiang B.D.S., D.M.D., D.Sc., C.A.G.S.

Clinical Professor of Endodontics

Approved by:

Department Chairman: _____

Sami Chogle, B.D.S., D.M.D., M.S.D., C.A.G.S.

Associate Professor of Endodontics;

Chair of Endodontics;

Director of Advanced Specialty Education Program in Endodontics;

Herbert Schilder Professor in Endodontics

DEDICATION

To my loving family and co-residents who have always supported and pushed me in my dreams no matter where the journey has taken me. With their love and admiration, I have found the strength to push myself beyond what I thought possible.

ACKNOWLEDGMENTS

I would love to thank Dr. Sami Chogle for his mentorship and knowledge throughout this project. The help he has provided is immeasurable.

I would like to also thank Dr. Yanling Jiang for all her expertise while performing the data collection for the project.

I would like to thank Dr. Ramzi Sarkis for his help and knowledge throughout the project.

I would like to thank Dr. Xiaofei Zhu for his comprehensive understanding and knowledge of the topic and project design.

I would like to thank Ms. Han Nguyen for her continued knowledge and help on all statistics-related work.

I would like to thank Dr. Luke Harden for continual help during the project.

I would like to thank Dr. Dominic Do for help on data collection and project design.

I would like to thank Dr. Jevon Rhule for continual support throughout the project.

I would like to thank Dr. William Richards for encouragement throughout the project.

THE EVALUATION OF THE RELIABILITY OF RADIOGRAPHIC FEATURES USING CBCT AND PERIAPICAL RADIOGRAPHS IN THE DIFFERENTIAL DIAGNOSIS OF PERIAPICAL LESIONS.

SKYLAR PENBERTHY, D.M.D.

Boston University, Henry M. Goldman School of Dental Medicine, 2022

Major Professor: Sami Chogle, B.D.S., D.M.D., M.S.D., C.A.G.S.

Associate Professor of Endodontics;

Chair of Endodontics;

Director of Advanced Specialty Education Program in Endodontics;

Herbert Schilder Professor in Endodontics

ABSTRACT

Introduction: The diagnosis and treatment of endodontic infections is a multi-step fact gathering process, with the gold standard of periapical lesion diagnosis being histological biopsy. With common diagnoses, such as periapical granulomas and radicular cysts, representing the bulk of biopsies, the possibility of a less invasive method of lesion identification ought to be examined. In recent years Cone Beam Computed Tomography (CBCT) imaging has been proposed as a potential diagnostic tool for periapical diagnosis, but this theory requires further testing and data in order to verify its appropriateness.

Objective: The aim of this study was to evaluate six criteria used for assessing periapical lesions of teeth seen on CBCT scan from the textbook *Oral Radiology White and Pharoah* [1].

Materials and Methods: Three blinded endodontists observed radiographic features of oral periapical lesions of teeth previously diagnosed as either radicular cysts or periapical granulomas via histological biopsy. All lesions had previously been scanned via CBCT, and endodontic apical surgery was performed allowing for a pathology sample of the lesion. The observers viewed 40 CBCT and 40 corresponding periapical (PA) radiographic images, all randomized, and reported which of the six criteria (Location- apex of tooth, periphery- corticated border, shape- curved or circular, internal structure- radiolucent, effects on surrounding structures- displace or resorb roots, corticated plate perforation- present) were present in the scans. Data was analyzed using a Logistical Regression Fleiss Kappa statistic with a 95% confidence level.

Results:

CBCT cyst showed no agreement between examiners criteria selected to statistical significance. The most selected criteria by all examiners were shape and internal structure.

PA radiographic Cyst showed moderate agreement for ‘Location’ and ‘Periphery’ and substantial agreement on ‘none’ criteria. The most selected criteria by all examiners were internal structure and location.

CBCT Granuloma showed moderate agreement for ‘location’ and perfect agreement for ‘none’. The most selected criteria by all examiners were shape, location, and internal structure.

PA radiographic Granuloma showed substantial agreement for ‘periphery’ and moderate agreement for internal structure (radiolucency). The most selected criteria by all examiners were location, and occasionally shape and internal structure.

Logistic regression of selected criteria shows with each additional criteria present on each lesion the chance of the lesion being a granuloma decreases 24.9% on PA radiographs and 33.9% on CBCT images.

Conclusion:

The current study shows an inter-examiner agreement of moderate to perfect kappa statistic does not align with the most commonly selected criteria among examiners, showing poor examiner agreement among lesions.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

1. Cone Beam Computed Tomography……..…CBCT

2. Periapical……PA

Chapter 1. INTRODUCTION

The hallmark of a successful endodontic procedure has historically laid upon a singular foundation: eradication of bacterial infection. While the modality of treatment and diagnostic process has evolved over the years, the end result has consistently relied upon resolution of symptoms and an environment for future biologic healing. The specialty of Endodontics, as formed in 1963, has specialized in the management of dental infections pertaining to the dental nerve and supporting structures in cleansing them of bacteria. As stated by the American Academy of Endodontists, the specialty defines itself as:

> "The branch of dentistry concerned with the morphology, physiology and pathology of the human dental pulp and peri radicular tissues. Its study and practice encompass the basic and clinical sciences including the biology of the normal pulp and the etiology, diagnosis, prevention and treatment of diseases and injuries of the pulp and associated peri radicular conditions." (Glossary of Endodontic Terms)

With the pulpal and periapical disease prevention as the focus of an entire specialty, the proper analysis, diagnosis, and treatment planning of the disease in question is of the utmost importance.

1.1 Endodontic periapical lesion formation

The genesis of pulpal and periapical disease relies on the introduction of bacteria [2] into the root canal system of a tooth. Teeth, assuming no genetic defects present, possess a natural barrier to the pulp consisting of enamel, dentin, and cementum. While the mineralized content of these structures varies, their function remains the same, to protect the dental pulp from external threats. These barriers are subject to constant strain from

caries, trauma, bruxism, abrasion and other mechanisms that allow bacteria to inch closer and closer to the pulp. In the events of exposed dentinal tubules [3] and fractures [4,5] , a direct path for bacteria to the dental pulp is created. However, the pulp is a reactive structure and is able to safeguard itself via production of tertiary dentin, which can be either reparative or reactive. The goal is to reduce the permeability of dentinal tubules and facilitate inflammatory changes in the form of increased vascular permeability and vasodilation. [6]

If the progression of the bacterial invasion is not stopped, both bacteria and their endotoxic byproducts will reach the pulp ultimately resulting in pulpal necrosis. The response of pulpal tissue to bacterial irritants was summarized in four zones by Dr. Fish in 1939: [7] infection, contamination, irritation, and stimulation. The active bacteria are infecting the pulpal space and releasing contaminates, such as the endotoxin LPS, which causes irritation of the pulpal tissues and facilitates the stimulation of an inflammatory response. The progression of pulpal necrosis will work in a crown-down direction until reaching the apex of the tooth and the surrounding bone and periodontal ligament. However, the presence of pulpal necrosis is not required at the root apex for a periapical lesion to start developing. As the infection is traversing the canal space towards the apex, the bacterial contaminates and byproducts approach the apex faster than the bacteria themselves resulting in a stimulation process that exceeds the physical radius of the bacteria. [8,9]

As the bacteria and their virulence factors approach the apical terminus of the root canal system, an inflammatory response occurs in the supporting structures, resulting in periodontal ligament (PDL) and bone destruction. The periapical lesion formed from the

loss of PDL and bone maintains its presence thanks to bacterial biofilm, which creates a protective layer, and a decreased defense response from host cells as a result of reduced blood flow in the area. Inflammatory cells such as polymorphonuclear leukocytes (PMNs), monocytes, cytotoxic T-cells, T-helper cells, B-cells, antibodies, and natural killer cells (NKCs) are seen entering the area in varying amounts in response to the bacteria's presence. Their goal is to sequester the bacterial endotoxins in order to limit the area that is damaged. As a part of the body's immune response, bone destruction can be seen around the tooth apex as a function of yet another cell—the osteoclast. [9,10,11]. The osteoclasts attempt to contain the infection via destruction of the bony matrix to create an isolated zone. It is at this point that the true periapical lesions—periapical granulomas and radicular cysts—start to form.

1.2 Periapical Granuloma formation

A periapical granuloma is one of the possible results of long-standing periapical infections, and it is the most common lesion associated with apical periodontitis. Several studies have shown that periapical granulomas range from 48-50% prevalence of all periapical lesions present when excised during surgery [12,13]. Periapical granulomas can be characterized as chronic inflammatory lesions with large amounts of granulation tissue. Also present are a mix of various immune cells such as: macrophages, lymphocytes, plasma cells, PMNs, and foam cells. The periapical granuloma is surrounded by a dense fibrous connective tissue wall with lymphocytic infiltrate and epithelial strands present internally.

1.3 Radicular Cyst Formation

Behind the periapical granuloma and apical abscess, the next plausible result of a long-standing infection is a radicular cyst. Although the prevalence of actual cysts varies from study to study, 45% by Bhaskar [12] to 15% by Nair [13], it is believed cysts make up a large portion of persistent periapical infections. Two types of cysts are routinely identified, a true cyst and bay (or pocket) cyst. Both cysts are characterized by a cavity lined by epithelial cells, frequently stratified squamous epithelium but ciliated columnar epithelium can be present on occasion. The major difference between a true cyst and a bay cyst is the continuity of the epithelial lining. Because bay cysts are still attached to the root canal system at the apical foramen, a completely closed off epithelial lining is hindered from forming. The inside of the epithelial lining contains necrotic tissue and cholesterol crystals surrounded by PMNS, macrophages, and foam cells. On the outside of the epithelial cells, collagen fibers are separate the epithelial cells from bone. [14,15]

The exact pathology of cyst formation is still debated today, with several theories in existence. One commonly accepted idea is the formation of the epithelial cells, which are thought to arise from residual Hertwig's epithelial root sheath (HERS), used in the formation of root dentin are activated and allow for cyst creation. The residual HERS cells are known as the cell rests of Malassez residing in the PDL area. The exact function of the cell rests of Malassez are unknown, but when stimulated during a periapical granuloma they can lead to epithelial proliferation and cyst formation. After the formation of the epithelial lining, there is still debate on the steps which occur next for the formation of the internal lumen. Four theories have been postulated for possible cyst

formation: the Breakdown theory, Abscess theory, Immunologic theory, and the Fusion theory.

The Breakdown theory states: Epithelial strands form islands which will start to grow in a 3-D shape due to inflammatory stimuli. The central cells then undergo necrosis and microcavities form the cystic cavity. [16]

The Abscess Theory: This theory relies on the hypothesis that epithelial cells have an intrinsic want to cover connective tissue surfaces. The theory states pre-existing abscess cavities form, and epithelial cells start to proliferate to cover the exposed connective tissue. [17]

The Immunologic Theory: This theory hypotheses the certain cells of the cell rests of Malassez undergo abnormal growth and an immunologic antigenic response occurs causing the formation of cysts. [18]

The Fusion Theory: This theory states that epithelial strands fuse in all directions creating a 3-D ball ass, the connective tissue residing inside the ball will necrose from decreased vascular support, and a cystic cavity is formed. [19]

No matter the method of cyst formation, a true cyst has now formed as a separate entity from the root canal system which now begs the question of how to treat a lesion that is a separated entity from the infected tooth.

1.4 Periapical Granuloma and Radicular Cyst Treatment options and outcomes

When presented with a lesion of endodontic origin, there are two main approaches for treatment of the infection, orthograde (traditional root canal therapy) or retrograde root canal treatment (a surgical approach). Many factors go into determining which is the best

course of action for each lesion; these include: the size, the location, whether the tooth has been treated previously, the time interval from last treatment, symptoms the patient is experiencing, etc. Taking into account all of these factors, the practitioner decides between primary root canal treatment, retreatment of non-surgical root canal, or retrograde apical surgery. There is a theory that a true radicular cyst will not resolve after non-surgical root canal therapy due to the idea that the true radicular cysts are separate entities from the root canal system [13]. The argument is that a surgical option is needed to physically remove the cyst from the periapical space. Following that logic, a periapical granuloma and a bay cyst will heal from orthograde treatment options as they have a retained attachment to the root canal system and removal of radicular bacteria would allow for the resolution of the surrounding pathology. The issue with this theory is currently there is only one way to accurately determine if a lesion is a cyst or granuloma, from histology via surgery, creating the problem of no way to prove if a healing lesion from orthograde treatment is possibly a cyst.

With cysts ranging from 15-42% [12,13] of periapical lesions, and the theory of true cysts being unable to heal from orthograde root canal therapy, the expected success rate of root canal treatment would purported to be 58-85% when periapical lesions are present. Several studies have shown that the presence of a periapical lesion, as seen on a radiograph, decreases non-surgical success rates to 62-86% [20, 21, 22, 24] and retreatment success rates to 56-71% [20, 22, 23, 24]. The reduction in success when periapical lesions are present may play into the theory of cysts being un-resolved from traditional non-surgical root canal methods, until a method for testing lesions is available beside histology, such as CBCT imaging.

1.5 Evaluation of Periapical Granuloma and Radicular Cyst using CBCT

With the need for less invasive methods of periapical lesion diagnosis, the possibility that CBCT imaging has a higher accuracy rate as compared to a traditional periapical (PA) radiograph when diagnosing radicular cyst or periapical granuloma ought to be explored. Traditionally, PA radiographs were the only way to identify and possibly diagnose a periapical lesion before a surgery was performed. Radiographs were first introduced into endodontics at the turn of the 20th century [25] and revolutionized how root canals were performed. The use of radiographs in endodontics allowed for the visualization of periapical lesions, the extent to which a lesion may be seen was studied by Bender in 1961 [26] when it was reported that at least 6.6% mineral bone loss, or 12.5% volumetric bone loss must be seen for a periapical lesion to be visualized. Bender and Seltzer [27] also concluded for a lesion to be visualized on a radiograph, the buccal or lingual plate must be perforated or compromised to some extent. One of the methods proposed to increase radiographic interpretation and diagnosis of periapical lesions was introducing the method of taking multiple radiographs of various angles [28]. This allows the diagnostic success to increase dramatically which each angle taken. Another improvement proposed for increased interpretation of periapical images is the advent of the paralleling image technique [29]. When taking a periapical radiograph, the sensor is placed along the long axis of the tooth, parallel, and the x-ray beam is aligned perpendicular to the tooth and sensor.

With the advent of radiographs for interpreting periapical lesions there needed to be a criteria for examiners to follow, Brynolf in 1967 [30] was able to list possible features on a

radiographs which were representative of likely signs of a lesion based off of histology. Brynolf listed the features such as a widened PDL and loss of lamina dura as features commonly seen in periapical lesions which could be identified routinely for diagnosis. This foundation allowed for more criteria in the future such as the Periapical Index (PAI) for evaluating apical healing on radiographs [31]. Even with the improvements of both radiographs and radiograph interpretation, the diagnosis of periapical lesions as radicular cysts or periapical granuloma cannot simply rely on PA radiographs alone but may be a supplement along with histology. [32]

With the limited capabilities of strictly conventional radiographs for periapical lesion identification and histological pathology being the only accurate way to diagnose a lesion, methods have been proposed for easier and still accurate diagnosis techniques. One of the major techniques which is being studied is the use of CBCT imaging for lesion diagnosis as either a periapical granuloma or radicular cyst. The largest study known to this author, which was able to examine CBCT vs a periapical radiograph for lesion diagnosis was performed by Estrela et al in 2008 [33]. In this study 1014 images were used for the diagnosis of either cyst or granuloma. The results of this study showed CBCT was more accurate than traditional radiography with 60.9% of CBCT correctly being diagnosed compared to 39.5% of periapical radiographs correctly diagnosing a cyst or granuloma. These results showed promising improvements, but they still failed to confidently rely on CBCT for lesion diagnosis proposing new evaluation criteria are needed.

Research involving the examination of CBCT for diagnosis of periapical pathology is limited; the numbers are few and the cases present in the research are limited. A study

published in 2006 by Simon et al [34] examined the accuracy of CBCT vs biopsy results for the diagnosis of periapical pathology. In this study 17 lesions were examined, and a grey scale was used for diagnosis, via CBCT, of a granuloma or cyst. The basis of these diagnoses was on a grey scale used in the imaging; when viewing lesions at the center of the radiolucency, granulomas will have a narrower grey scale and decreased grey scale value, while cysts, being less dense in matter, will have a negative grey scale [39]. Out of the 17 lesions used in the study, 13 were correctly identified as either a granuloma or cyst for a high accuracy rate. This study showed promising results, 76% accuracy in lesion identification, but the small sample size draws sharp criticism.

Contrastingly, a 2010 study published by Rosenberg et al [35] looked at 45 lesions for the evaluation of CBCT accuracy of periapical diagnosis; however, this study did not conclude the success rate. Two oral radiologists examined the lesions and were given criteria on how to rank the lesions as either: cyst, likely cyst, likely granuloma, granuloma, or other. The accuracy of the oral radiologists resulted in a poor diagnosis rate, and CBCT was not recommended for diagnosis use.

Two follow-up studies took a different approach of how a CBCT can be utilized to diagnose periapical pathology. These two studies used the criteria laid out in the textbook *Oral Radiology: Principles and interpretations* by White and Pharoah [1]. In the first study, performed in 2013 by Guo [36], three endodontists examined 36 periapical lesions using the six criteria from White and Pharoah: location- apex of tooth, periphery- corticated border, shape- curved or circular, internal structure- radiolucent, effect on surrounding structures- displacement or resorption of roots, corticated plate perforation. Using these criteria Guo demonstrated moderate success using CBCT for periapical

lesion diagnosis. The second study, using White and Pharaohs' criteria for diagnosing periapical lesions via CBCT, was performed in 2017 by Chanani [37] in which 45 lesions were examined and compared to histology results. Again, a moderate success was concluded leading to CBCT and the proposed criteria as not being an accurate method to diagnose apical lesions over histology findings.

A current study published by Etoz et al in 2020 [38] went one step further and looked at both the grey scale and the criteria from the Oral Radiology text by White and Pharoah. This study examined 21 teeth and concluded the following: grey scale value was statistically insignificant on cyst and granuloma diagnosis, and the two major criteria points which help with lesion diagnosis were a well-defined cortical border and lesion shape. This study helped to pose the question of refinement of the six criteria for more accurate results. All of the abovementioned studies which previously examined CBCT use for periapical granuloma and radicular cyst identification present a mixed bag of results. One promising method which has presented with moderate to accurate success is the use of the diagnosing criteria from the textbook Oral Pathology [1]. Further studies of these criteria are needed to conclude if these criteria are more accurate than past periapical radiographs and possibly rival the gold standard of histological examination.

1.6 Statement of the problem

With the promising results of current studies, however yet still uncertainty of the accuracy of CBCT scans for the diagnosis of periapical cysts and radicular granulomas in comparison to the gold standard of histological biopsy; this study looks if the protocol criteria listed in the textbook Oral Radiology: Principles and Interpretations [1], currently

being used in previous research studies and taught in dental schools, for radiographic periapical lesion determination is adequate, or in need of further refinement.

1.7 Objectives

The aim of this study is to evaluate the usefulness of six radiographic criteria for assessing apical lesions of teeth seen on CBCT scans, from the textbook Oral Radiology by White and Pharoah [1], to aid in the differential diagnosis of radicular cysts and periapical granulomas.

1.8 Hypothesis

The null hypothesis of this study is that the current protocol criteria listed in the textbook Oral Radiology: Principles and Interpretations 7th edition by White and Pharoah [1] for radiographic periapical lesion determination is not adequate for proper CBCT diagnosis of radicular cysts and a new protocol is needed.

Chapter 2. MATERIALS AND METHODS

2.1 Materials:

- CBCT Software: Sidexis 4.
- CBCT: Sirona Orthophos XG 3D CBCT
- Radiographic Software: MiPacs.
- Radiographic sensors: Sirona Schick 33
- Evaluation Form: Google Forms
- Biopsy report of apicoectomy surgeries performed from 2015-2019 at Boston University School of Dental medicine Endodontic Department, via Boston University Oral pathology department.
- N., Lam Ernest W. "Chapter 23:Cysts." *White and Pharoah's Oral Radiology: Principles and Interpretation*, 8th ed., Elsevier, St. Louis, MO, 2019.

2.2 Methods:

In this study, three blinded observers, all endodontists, were anonymized, and used to evaluate radiographic features of oral periapical lesions of teeth previously diagnosed as either radicular cysts or periapical granulomas via endodontic surgery and subsequent histological biopsy. Endodontists were selected as observers due to the training and experience they possess in evaluating periapical lesions on radiographs and CBCT scans. The selected observers fulfilled the following criteria: completion of an advanced education in endodontics, faculty appointment at Boston University School of Dental

Medicine, a minimum of five years' experience/are eligible for the American Board of Endodontics. IRB Exemption approval on 04/01/2020-03/31/2023, IRB #: H39765. Radiographic data of forty patients, including PA radiographs and CBCTs, prior to apicoectomy and biopsy performed, between the dates of 01/01/2015- 12/31/2019 were selected for this study. All PA radiographs, CBCT scans, and biopsy results, for this study were de-identified and provided via Boston University School of Dentistry IT and Boston University Oral Pathology department. Consents from patients were not acquired. The inclusion criteria for the following scans include patients who had periapical radiographs, CBCT scans, apicoectomy performed, and a biopsy performed on a lesion at the root end of a tooth. Ten lesions were selected from four quadrants of the mouth: maxillary anterior/ posterior and mandibular anterior/ posterior with as equal numbers of radicular cysts and periapical granulomas as possible due to the lesions available from inclusion criteria, totaling 20 cysts and 20 granulomas.

Cyst	Maxillary	Mandibular
Anterior	7	3
Posterior	4	6

Granuloma	Maxillary	Mandibular
Anterior	5	5
Posterior	5	5

Table 1 and Table 2 : Cyst and Granuloma Count- Showing the number of cysts and granuloma selected from the available lesion within the inclusion criteria. Due to a lack of cysts in the maxillary posterior and mandibular anterior, more maxillary anterior and mandibular posterior were selected to allow for 20 cysts.

The three endodontists were provided with both CBCT and periapical radiographs, all randomized, of the selected lesions for evaluation. Radiographs were evaluated by the

observers using the following six Oral Radiology via White and Pharoah textbook Chapter 23: "Cysts" by Erenst Lam [41] criteria:

- Location- apex of tooth
- periphery- corticated border
- shape- curved or circular
- internal structure- radiolucent
- effects on surrounding structures- displace or resorb roots
- corticated plate perforation- present

Observers were allowed to view only periapical radiographs and CBCT scans, no additional patient information was available. Observers were given access to manipulate all CBCTs via Sidexis imaging software used at the Boston University School of Dental Medicine. Observers were given screen shots of periapical radiographs from MiPacs imaging software with the Endodontic filter enhancement activated. Observers were asked to indicate which of the six criteria are present on each radiograph, and a 'none' option was available, using a google forms survey. Observers were asked to select a final diagnosis of Radicular Cyst or Periapical Granuloma based off the criteria and their professional endodontic expertise; the final diagnosis was not used for this project.

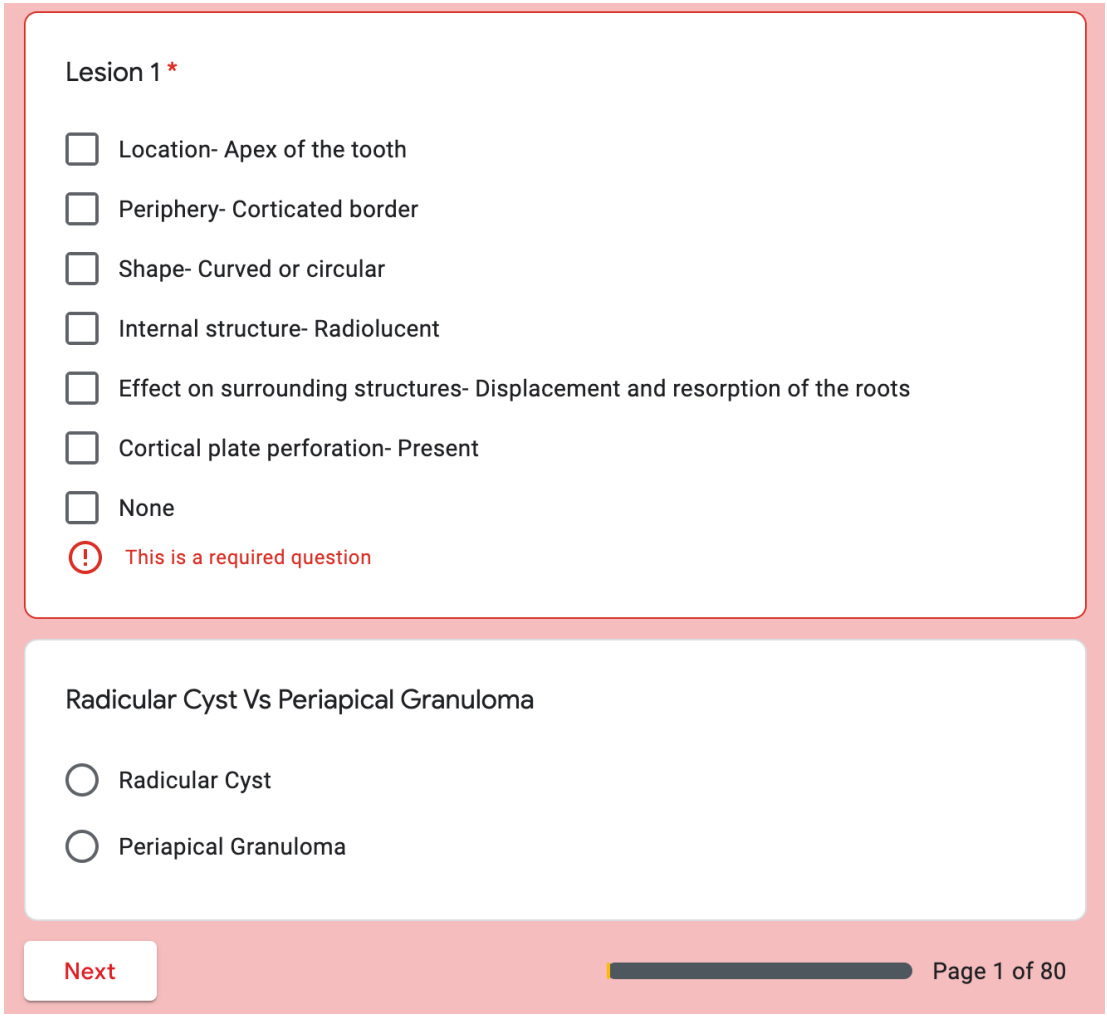

Figure 1: Google Forms Survey layout. - This image represents the layout of the Google Survey Form used for observers to select criteria for participating lesions. Observers were able to select any combination of the answers provided. Observers then gave a final diagnosis of the lesion, which is not used for this project.

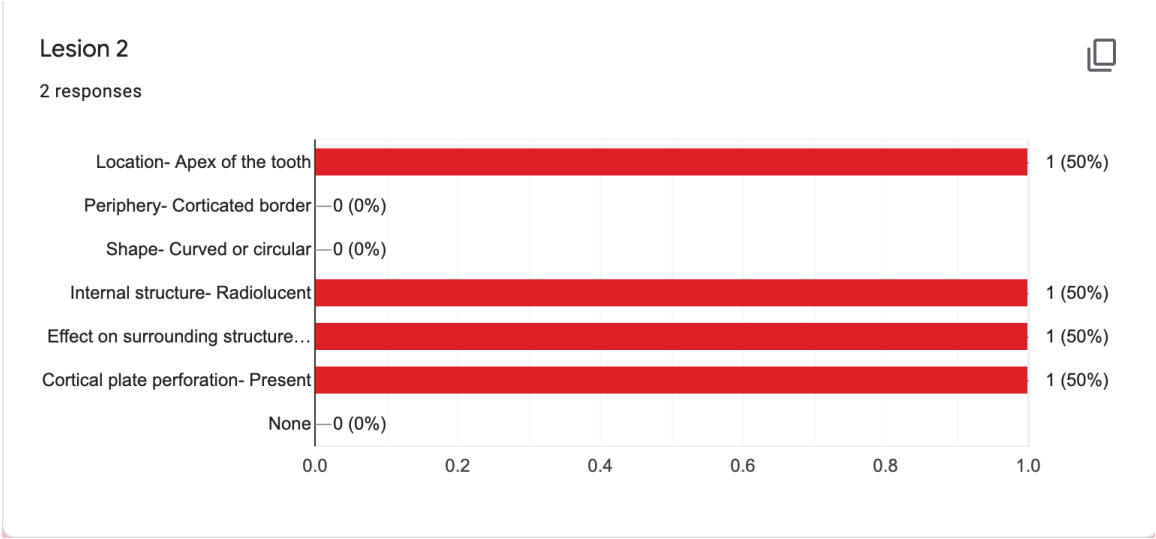

Figure 2: Google Forms results provided by the software indicating which criteria per lesion were selected. See Figure 5 for entire Google Form presented to examiners.

Figure 3: Periapical Lesion Radiograph: This image represents a periapical lesion of tooth #19, an example of a lesion presented to observers.

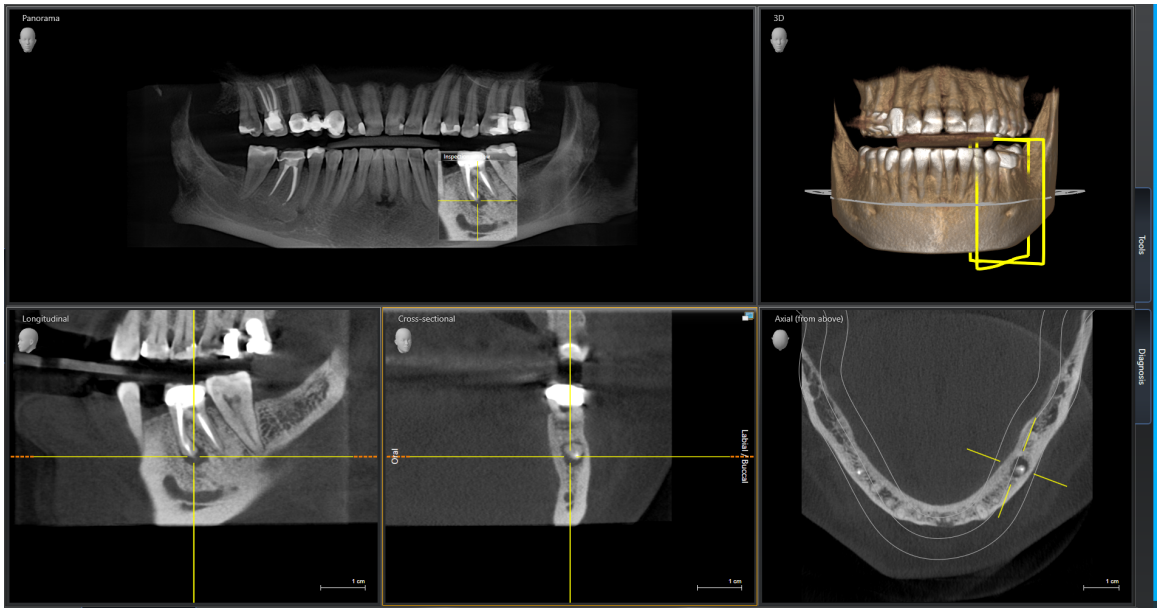

Figure 4: CBCT Lesion Image: This image represents a CBCT lesion of tooth #19, an example of a lesion presented to observers. Observers had full control of all CBCT data and could view all slices of the CBCT.

2.2.1 Inclusion Criteria:

1. Date range of 01/01/2015-12/31/2019

2. Age range: All patients will be 18 years or older

3. Patient is/was a patient of record at the Boston University School of Dental Medicine

4. Radiographic exposure of Periapical lesion and Cone Beam Computer Tomography of associated lesion

5. An apicoectomy surgical procedure performed on patients associated lesion, and tissue sample sent to Boston University Oral Pathology Department

6. Biopsy performed of associated lesion at Boston University School of Dentistry Oral Pathology Department and a diagnosis of Radicular Cyst or Periapical Granuloma given.

7. The following CDT dental codes most be present in the patients Salud Dental Software chart:

CBCT Codes: D0364, D0365, D0366, D0367

Apicoectomy Code: D3410, D3421, D3425

Periodical Radiograph: D0210, D0220, D0230

Biopsy: D7286

8. Observer Calibration:

A. Completion of advanced education of endodontics.

B. Current faculty appointment at the Boston University School of Dental Medicine.

C. A minimum of five years of experience/ or American Board of Endodontics eligible

D. Examiners were calibrated with at least 3 clinical cases

2.3 Statistical Methods:

*Note that all analyses were run with R Studio.

Each data set was divided by result: Cyst or Granuloma. We then further created subsets for each tooth area: maxillary, mandibular, anterior, posterior, maxillary anterior, maxillary posterior, mandibular anterior, mandibular posterior. Further analyses were run on each subset.

Evaluation inter-rater reliability for each criteria

Since there were three examiners, we utilized a Fleiss kappa statistic to determine inter-rater reliability for each criterion for each subset. For each criteria, we tested the hypothesis of whether or not the agreement is the same as chance agreement at an alpha

level of 0.05. To compare criteria with different subsets, we looked at each 95% confidence interval to see if they overlap. If they do, the criteria for the subsets were not significantly different.

Most selected criteria

Counts of criteria clicked by examiner was determined to find the criteria that was most commonly selected. Furthermore, to determine if number of selected criteria was associated with result, we used a logistic regression analysis. The dependent variable was the actual result of the periapical lesion and the independent variable was the average number of selected criteria.

Chapter 3. RESULTS

3.1 Fleiss Kappa Statistic Results

Despite the uncertainty of alternative methods for lesion diagnosis in recent studies, one foundation holds true; if a criterion is developed, it must be subject to rigorous testing before being accepted as accurate and practical. This study aimed to evaluate a current criterion which has been featured in both recent studies and textbooks utilized in dental school curriculum. And with as much weight being placed on this criterion, the validity of it must be verified. The current criteria from the textbook *Oral Radiology by White and Pharoah* uses six features to help aid in the differential diagnosis of periapical granulomas and radicular cysts. This study looked to evaluate how well observers can understand the criteria and evaluate its presence or absence on both CBCT and periapical radiographs of periapical lesions. The observers were instructed to select whichever criteria were present on the images, including a 'none' option if no features were present. Statistical analysis was performed to look for commonly selected traits among cysts and granulomas on both CBCT and periapical images, as well as the inter-agreement of the observers with these traits. For the inter-agreement of the observers, a Fleiss Kappa statistic was performed and only agreements of moderate or higher value were deemed of significance. All statistics were evaluated to 95% confidence level. The following results of the Kappa statistic can be seen below.

Table 3: Fleiss Kappa Statistic

Cohen's Kappa	Interpretation
0	No agreement
0.10-0.20	Slight agreement
0.21-0.40	Fair agreement
0.41-0.60*	Moderate agreement
0.61-0.80*	Substantial agreement
0.81-0.99*	Near perfect agreement
1*	Perfect Agreement

Table 3 shows the interpretation of the Fleiss Kappa Statistic test to portray the examiners agreement.

Tables 4 through 39 show the results for Fleiss' kappa statistic for each criteria for each sub-setted data. The tables include the kappa statistic, z-score, p-value, and 95% confidence interval.

Table 4: *PA Radiograph Cyst*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.508*	3.93	0.0000845	(0.254, 0.761)
Periphery	0.411*	3.18	0.00146	(0.158, 0.664)
Shape	0.343	2.66	0.00782	(0.090, 0.596)
Internal Structure	0.313	2.42	0.0155	(0.06, 0.566)
Effect	-0.181	-1.4	0.162	(-0.434, 0.072)
CPP	0.191	1.48	0.138	(-0.062, 0.444)
None	0.63*	4.88	0.00000108	(0.377, 0.883)

**Represents Moderate to perfect agreement*

Table 4 represents Periapical (PA) radiograph Cyst. We found location (0.508), periphery (0.411), and none (0.63) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the agreement for location, periphery, and none are significantly different from chance agreement.

Table 5: *PA Radiograph Granuloma*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.271	2.1	0.0359	(0.018, 0.524)
Periphery	0.608*	4.71	0.0000025	(0.355, 0.861)
Shape	0.318	2.46	0.0137	(0.065, 0.571)
Internal Structure	0.425*	3.3	0.000983	(0.172, 0.678)
Effect	-0.19	-1.48	0.14	(-0.444, 0.063)
CPP				
None	0.0296	0.23	0.818	(-0.223, 0.283)

**Represents Moderate to perfect agreement*
no examiners chose CPP

Table 5 represents Periapical (PA) radiograph Granuloma. We found periphery (0.608) and internal structure (0.425) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the agreement for periphery and internal structure are significantly different from chance agreement. No examiner chose cortical plate perforation, so no kappa statistic was determined.

Table 6: *CBCT Cyst*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	-0.0458	-0.354	0.723	(-0.299, 0.207)
Periphery	0.067	0.519	0.604	(-0.186, 0.320)
Shape	-0.132	-1.02	0.306	(-0.385, 0.121)
Internal Structure	-0.00962	-0.0745	0.941	(-0.263, 0.243)
Effect	-0.113	-0.877	0.381	(-0.366, 0.14)
CPP	0.314	2.43	0.0149	(0.061, 0.567)
None	-0.0169	-0.131	0.896	(-0.27, 0.236)

Table 6 represents CBCT Cyst. We found no criteria to have a moderate to perfect agreement. The only criteria that was statistically significant was cortical plate perforation with a kappa statistic of 0.314 (fair agreement).

Table 7: *CBCT Granuloma*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.515*	3.99	0.0000667	(0.262, 0.768)
Periphery	0.0625	0.484	0.628	(-0.191, 0.316)
Shape	0.353	2.74	0.00624	(0.100, 0.606)
Internal Structure	0.279	2.16	0.0308	(0.026, 0.532)
Effect	0.04	0.31	0.757	(-0.213, 0.293)
CPP	0.394	3.05	0.00228	(0.141, 0.647)
None	1*	7.75	9.55e-15	(0.747, 1.253)

**Represents Moderate to perfect agreement*

Table 7 represents CBCT Granuloma. We found location (0.515) and none (1) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the agreement for location and none are significantly different from chance agreement.

Table 8: *PA Radiograph Cyst – Maxillary*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.407*	2.44	0.0145	(0.081, 0.734)
Periphery	0.4	2.4	0.0164	(0.073, 0.727)
Shape	0.157	0.943	0.346	(0.169, 0.484)
Internal Structure	0.215	1.29	0.198	(-0.112, 0.541)
Effect	-0.0519	-0.312	0.755	(-0.379, 0.275)
CPP	0.273	1.64	0.102	(-0.054, 0.599)
None	0.768*	4.61	0.0000041	(0.441, 1.094)

**Represents Moderate to perfect agreement*

Table 8 represents Periapical (PA) radiograph Cyst in maxilla teeth. We found location (0.407) and none (0.768) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the agreement for location and none are significantly different from chance agreement.

Table 9: *PA Radiograph Granuloma – Maxillary*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.215	1.29	0.198	(-0.112, 0.541)
Periphery	-0.0588	-0.353	0.724	(-0.385, 0.268)
Shape	0.299	1.79	0.0731	(-0.028, 0.625)
Internal Structure	0.314	1.89	0.0593	(-0.012, 0.641)
Effect	-0.037	-0.222	0.824	(-0.364, 0.29)
CPP				
None	-0.064	-0.384	0.701	(-0.391, 0.263)

**no examiners chose CPP*

Table 9 represents Periapical (PA) radiograph Granuloma in maxilla teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose cortical plate perforation, so no kappa statistic was determined.

Table 10: *CBCT Cyst – Maxillary*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0	0	1	(-0.327, 0.327)
Periphery	-0.0286	-0.171	0.864	(-0.355, 0.298)
Shape	-0.0909	-0.545	0.585	(-0.418, 0.236)
Internal Structure	-0.0909	-0.545	0.585	(-0.418, 0.236)
Effect	-0.161	-0.968	0.333	(-0.488, 0.165)
CPP	0.2	1.2	0.23	(-0.127, 0.527)
None	-0.0286	-0.171	0.864	(-0.355, 0.298)

Table 10 represents CBCT Cyst in maxilla teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant.

Table 11: *CBCT Granuloma – Maxillary*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.273	1.64	0.102	(-0.054, 0.599)
Periphery	-0.037	-0.222	0.824	(-0.364, 0.29)
Shape	-0.125	-0.75	0.453	(-0.452, 0.202)
Internal Structure	-0.125	-0.75	0.453	(-0.452, 0.202)
Effect	0.113	0.68	0.497	(-0.213, 0.44)
CPP	0.0368	0.221	0.825	(-0.29, 0.363)
None				

no examiners chose None

Table 11 represents CBCT Granuloma in maxilla teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose none, so no kappa statistic was determined.

Table 12: *PA Radiograph Cyst – Mandibular*

Criteria	Kappa	Z-score	P-value	95% CI
Location	0.625*	3.06	0.0022	(0.225, 1.025)
Periphery	0.395	1.93	0.053	(-0.005, 0.795)
Shape	0.7*	3.43	0.000605	(0.3, 1.1)
Internal Structure	0.455*	2.23	0.026	(0.054, 0.855)
Effect	-0.371	-1.82	0.0688	(-0.772, 0.029)
CPP	0.1	0.49	0.624	(-0.3, 0.5)
None	-0.0435	-0.213	0.831	(-0.444, 0.357)

**Represents Moderate to perfect agreement*

Table 12 represents Periapical (PA) radiograph Cyst in mandibular teeth. We found location (0.625), shape (0.7), and internal structure (0.455) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the agreement for location, shape, and internal structure are significantly different from chance agreement.

Table 13: *PA Radiograph Granuloma – Mandibular*

Criteria	Kappa	Z-score	P-value	95% CI
Location	-0.0435	-0.213	0.831	(-0.443, 0.357)
Periphery	0.798*	3.91	0.0000919	(0.398, 1.198)
Shape	-0.0909	-0.445	0.656	(-0.491, 0.309)
Internal Structure	0.455*	2.23	0.026	(0.054, 0.855)
Effect	-0.422	-2.07	0.0386	(-0.822, -0.022)
CPP				
None				

**Represents Moderate to perfect agreement*
no examiners chose CPP and None

Table 13 represents Periapical (PA) radiograph Granuloma in mandibular teeth. We found periphery (0.798) and internal structure (0.455) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the agreement for periphery and internal structure are significantly different from chance agreement. No examiner chose cortical plate perforation or none, so no kappa statistic was determined.

Table 14: *CBCT Cyst – Mandibular*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	-0.143	-0.7	0.484	(-0.543, 0.257)
Periphery	0.193	0.947	0.344	(-0.207, 0.593)
Shape	-0.2	-0.98	0.327	(-0.6, 0.2)
Internal Structure	-0.0105	-0.0516	0.959	(-0.411, 0.39)
Effect	-0.111	-0.544	0.586	(-0.511, 0.289)
CPP	0.486*	2.38	0.0173	(0.086, 0.886)
None				

**Represents Moderate to perfect agreement*
no examiners chose None

Table 14 represents CBCT Cyst in mandibular teeth. We found cortical plate perforation (0.486) to have a statistically significant moderate agreement with p-value less than 0.05. Therefore, the agreement for cortical plate perforation is significantly different from chance agreement. No examiner chose none, so no kappa statistic was determined.

Table 15: *CBCT Granuloma – Mandibular*

Criteria	Kappa	Z-score	P-value	95% CI
Location	0.7*	3.43	0.000605	(0.3, 1.1)
Periphery	0.238	1.17	0.243	(-0.162, 0.638)
Shape	1*	4.9	0.000000963	(0.6, 1.4)
Internal Structure	0.7*	3.43	0.000605	(0.3, 1.1)
Effect	-0.143	-0.7	0.484	(-0.543, 0.257)
CPP	0.7*	3.43	0.000605	(0.3, 1.1)
None	1*	4.9	0.000000963	(0.6, 1.4)

Table 15 represents CBCT Granuloma in mandibular teeth. We found location (0.7), shape (1), internal structure (0.7), cortical plate perforation (0.7), and none (1) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the agreement for location, shape, internal structure, cortical plate perforation, and none are significantly different from chance agreement.

Table 16: *PA Radiograph Cyst – Anterior*

Criteria	Kappa	Z-score	P-value	95% CI
Location	0.511*	2.94	0.00332	(0.17, 0.852)
Periphery	0.456*	2.62	0.0088	(0.115, 0.797)
Shape	0.492*	2.83	0.00468	(0.151, 0.833)
Internal Structure	0.389	2.23	0.0255	(0.048, 0.73)
Effect	-0.0476	-0.274	0.784	(-0.389, 0.294)
CPP	0.147	0.842	0.4	(-0.195, 0.488)
None	0.593*	3.4	0.000664	(0.251, 0.934)

Table 16 represents Periapical (PA) radiograph Cyst in anterior teeth. We found location (0.511), periphery (0.456), shape (0.492), and none (0.593) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the

agreement for location, periphery, shape, and none are significantly different from chance agreement.

Table 17: *PA Radiograph Granuloma – Anterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.456*	2.62	0.0088	(0.115, 0.797)
Periphery	1*	5.74	9.22e-09	(0.659, 1.341)
Shape	0.456*	2.62	0.0088	(0.115, 0.797)
Internal Structure	0.456*	2.62	0.0088	(0.115, 0.797)
Effect	-0.31	-1.78	0.0754	(-0.651, 0.032)
CPP				
None	-0.1	-0.574	0.566	(-0.441, 0.241)

**Represents Moderate to perfect agreement*
no examiners chose CPP

Table 17 represents Periapical (PA) radiograph Granuloma in anterior teeth. We found location (0.456), periphery (1), shape (0.456), and internal structure (0.456) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the agreement for location, periphery, shape, and internal structure are significantly different from chance agreement. No examiner chose cortical plate perforation, so no kappa statistic was determined.

Table 18: *CBCT Cyst – Anterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	-0.179	-1.03	0.305	(-0.52, 0.163)
Periphery	0.00752	0.0432	0.966	(-0.334, 0.349)
Shape	-0.1	-0.574	0.566	(-0.441, 0.241)
Internal Structure	0.147	0.842	0.4	(-0.195, 0.488)
Effect	-0.0185	-0.106	0.915	(-0.36, 0.323)
CPP	0.318	1.83	0.0676	(-0.023, 0.659)
None				

no examiners chose none

Table 18 represents CBCT Cyst in anterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose none, so no kappa statistic was determined.

Table 19: *CBCT Granuloma – Anterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.267	1.53	0.126	(-0.075, 0.608)
Periphery	-0.0185	-0.106	0.915	(-0.36, 0.323)
Shape	-0.138	-0.792	0.428	(-0.479, 0.203)
Internal Structure	-0.0645	-0.371	0.711	(-0.406, 0.277)
Effect	0.01	0.0574	0.954	(-0.331, 0.351)
CPP	0.256	1.47	0.142	(-0.086, 0.597)
None				

no examiners chose None

Table 19 represents CBCT Granuloma in anterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose none, so no kappa statistic was determined.

Table 20: *PA Radiograph Cyst – Posterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	-0.08	-0.416	0.678	(-0.457, 0.297)
Periphery	0.357	1.86	0.0635	(-0.02, 0.734)
Shape	-0.174	-0.904	0.366	(-0.551, 0.203)
Internal Structure	0.12	0.621	0.534	(-0.258, 0.497)
Effect	-0.35	-1.82	0.069	(-0.727, 0.027)
CPP	0.25	1.3	0.194	(-0.127, 0.627)
None				

no examiners chose None

Table 20 represents PA Cyst in posterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose none, so no kappa statistic was determined.

Table 21: *PA Radiograph Granuloma – Posterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.0182	0.0945	0.925	(-0.359, 0.395)
Periphery	0.357	1.86	0.0635	(-0.02, 0.734)
Shape	0.167	0.866	0.386	(-0.211, 0.544)
Internal Structure	0.365	1.9	0.0581	(-0.012, 0.742)
Effect	-0.0714	-0.371	0.711	(-0.449, 0.306)
CPP				
None	0.12	0.621	0.534	(-0.258, 0.497)

no examiners chose CPP

Table 21 represents Periapical (PA) radiograph Granuloma in posterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose cortical plate perforation, so no kappa statistic was determined.

Table 22: *CBCT Cyst – Posterior*

Criteria	Kappa	Z-score	P-value	95% CI
Location	0.12	0.621	0.534	(-0.258, 0.497)
Periphery	0.112	0.581	0.561	(-0.265, 0.489)
Shape	-0.174	-0.904	0.366	(-0.551, 0.203)
Internal Structure	-0.174	-0.904	0.366	(-0.551, 0.203)
Effect	-0.227	-1.18	0.238	(-0.604, 0.15)
CPP	0.258	1.34	0.18	(-0.119, 0.635)
None	-0.0385	-0.2	0.842	(-0.416, 0.339)

Table 22 represents CBCT Cyst in posterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant.

Table 23: *CBCT Granuloma – Posterior*

Criteria	Kappa	Z-score	P-value	95% CI
Location	0.707*	3.67	0.000241	(0.329, 1.084)
Periphery	0.143	0.742	0.458	(-0.234, 0.52)
Shape	1*	5.2	0.000000203	(0.623, 1.377)
Internal Structure	0.357	1.86	0.0635	(-0.02, 0.734)
Effect	-0.08	-0.416	0.678	(-0.457, 0.297)
CPP	0.467*	2.43	0.0152	(0.09, 0.944)
None	1*	5.2	0.000000203	(0.623, 1.377)

Table 23 represents CBCT Granuloma in posterior teeth. We found location (0.707), shape (1), cortical plate perforation (0.467), and none (1) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the agreement for location, shape, cortical plate perforation, and none are significantly different from chance agreement.

Table 24: *PA Radiograph Cyst – Maxillary Anterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.357	1.64	0.102	(-0.071, 0.785)
Periphery	0.691*	3.17	0.00154	(0.263, 1.119)
Shape	0.417	1.91	0.0562*	(-0.011, 0.844)
Internal Structure	0.357	1.64	0.102	(-0.071, 0.785)
Effect	0.0667	0.306	0.76	(-0.361, 0.494)
CPP	0.222	1.02	0.309	(-0.205, 0.65)
None	0.737*	3.38	0.000726	(0.31, 1.165)

Table 24 represents Periapical (PA) radiograph Cyst in maxilla anterior teeth. We found periphery (0.691) and none (0.737) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the agreement for periphery and none are significantly different from chance agreement. We also found shape (0.417) to have a moderate agreement, although its p-value was 0.0562. The agreement for shape is not significantly different from chance agreement.

Table 25: *PA Radiograph Granuloma – Maxillary Anterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.395	1.93	0.053	(-0.005, 0.795)
Periphery				
Shape	0.395	1.93	0.053	(-0.005, 0.795)
Internal Structure	0.395	1.93	0.053	(-0.005, 0.795)
Effect	-0.244	-1.2	0.231	(-0.645, 0.156)
CPP				
None	-0.143	-0.7	0.484	(-0.543, 0.257)

no examiners chose Periphery

Table 25 represents Periapical (PA) radiograph Granuloma in maxilla anterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose periphery or cortical plate perforation, so no kappa statistic was determined.

Table 26: *CBCT Cyst – Maxillary Anterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	-0.143	-0.7	0.484	(-0.543, 0.257)
Periphery	-0.0286	-0.14	0.889	(-0.429, 0.372)
Shape	-0.0435	-0.213	0.831	(-0.444, 0.357)
Internal Structure	-0.0435	-0.213	0.831	(-0.444, 0.357)
Effect	-0.143	-0.7	0.484	(-0.543, 0.257)
CPP	0.314	1.54	0.124	(-0.086, 0.714)
None				

**no examiners chose None*

Table 26 represents CBCT Cyst in maxilla anterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose none, so no kappa statistic was determined.

Table 27: *CBCT Granuloma – Maxillary Anterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.238	1.17	0.243	(-0.162, 0.638)
Periphery	-0.0105	-0.0516	0.959	(-0.411, 0.39)
Shape	-0.2	-0.98	0.327	(-0.6, 0.2)
Internal Structure	-0.0909	-0.445	0.656	(-0.491, 0.309)
Effect	-0.0084	-0.0412	0.967	(-0.408, 0.392)
CPP	0.111	0.544	0.586	(-0.289, 0.511)
None				

no examiners chose None

Table 27 represents CBCT Granuloma in maxilla anterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose none, so no kappa statistic was determined.

Table 28: *PA Radiograph Cyst – Mandibular Anterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	1*	3	0.0027	(0.347, 1.653)
Periphery	0.357	1.07	0.284	(-0.296, 1.01)
Shape	0.55	1.65	0.0989*	(-0.103, 1.203)
Internal Structure	0.357	1.07	0.284	(-0.296, 1.01)
Effect	-0.35	-1.05	0.294	(-1.003, 0.303)
CPP	-0.125	-0.375	0.708	(-0.778, 0.528)
None	-0.125	-0.375	0.708	(-0.778, 0.528)

Table 28 represents Periapical (PA) radiograph Cyst in mandibular anterior teeth. We found location (1) to have a statistically significant perfect agreement with a p-value less than 0.05. Therefore, the agreement for location is significantly different from chance agreement. We also found shape (0.55) to have a moderate agreement, although its p-value was 0.0989. The agreement for shape is not significantly different from chance agreement.

Table 29: *PA Radiograph Granuloma – Mandibular Anterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location				
Periphery	1*	3	0.0027	(0.347, 1.653)
Shape				
Internal Structure				
Effect	-0.5	-1.5	0.134	(-1.153, 0.153)
CPP				
None				

**Represents Moderate to perfect agreement*
no examiners chose Location, Shape, Internal Structure, CPP, and None

Table 29 represents Periapical (PA) radiograph Granuloma in mandibular anterior teeth. We found periphery (1) to have a statistically significant perfect agreement with a p-value less than 0.05. Therefore, the agreement for periphery is significantly different from chance agreement. No examiner chose location, shape, internal structure, cortical plate perforation, or none, so no kappa statistic was determined.

Table 30: *CBCT Cyst – Mandibular Anterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	-0.286	-0.857	0.391	(-0.939, 0.368)
Periphery	0.1	0.3	0.764	(-0.553, 0.753)
Shape	-0.268	-0.857	0.391	(-0.939, 0.368)
Internal Structure	0	0	1	(-0.653, 0.653)
Effect	0	0	1	(-0.653, 0.653)
CPP	-0.125	-0.375	0.708	(-0.778, 0.528)
None				

no examiners chose None

Table 30 represents CBCT Cyst in mandibular anterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose none, so no kappa statistic was determined.

Table 31: *CBCT Granuloma – Mandibular Anterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location				
Periphery	-0.125	-0.375	0.708	(-0.778, 0.528)
Shape				
Internal Structure				
Effect	-0.125	-0.375	0.708	(-0.778, 0.528)
CPP	0.55	1.65	0.0989	(-0.103, 1.203)
None				

no examiners chose Location, Shape, Internal Structure, and None

Table 31 represents CBCT Granuloma in mandibular anterior teeth. We found cortical plate perforation (0.55) to have a moderate agreement, although its p-value was 0.0989. The agreement for cortical plate perforation is not significantly different from chance agreement. No examiner chose location, shape, internal structure, or none, so no kappa statistic was determined.

Table 32: *PA Radiograph Cyst – Maxillary Posterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location				
Periphery	-0.0909	-0.315	0.753	(-0.657, 0.475)
Shape	-0.5	-1.73	0.0833	(-1.066, 0.066)
Internal Structure	-0.125	-0.433	0.665	(-0.691, 0.441)
Effect	-0.333	-1.15	0.248	(-0.899, 0.232)
CPP				
None				

no examiners chose Location, CPP, and None

Table 32 represents Periapical (PA) radiograph Cyst in maxilla posterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose location, cortical plate perforation, or none, so no kappa statistic was determined.

Table 33: *PA Radiograph Granuloma – Maxillary Posterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	-0.125	-0.433	0.665	(-0.691, 0.441)
Periphery	-0.2	-0.693	0.488	(-0.766, 0.366)
Shape	-0.0286	-0.099	0.921	(-0.594, 0.537)
Internal Structure	-0.125	-0.433	0.665	(-0.691, 0.441)
Effect				
CPP				
None	-0.125	-0.433	0.655	(-0.691, 0.441)

no examiners chose Effect and CPP

Table 33 represents Periapical (PA) radiograph Granuloma in maxilla posterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically

significant. No examiner chose effect on surrounding structures or cortical plate perforation, so no kappa statistic was determined.

Table 34: *CBCT Cyst – Maxillary Posterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.111	0.385	0.7	(-0.455, 0.677)
Periphery	-0.0286	-0.099	0.921	(-0.594, 0.537)
Shape	-0.2	-0.693	0.488	(-0.766, 0.366)
Internal Structure	-0.2	-0.693	0.488	(-0.766, 0.366)
Effect	-0.2	-0.693	0.488	(-0.766, 0.366)
CPP	-0.0286	-0.099	0.921	(-0.594, 0.537)
None	-0.0909	-0.315	0.753	(-0.657, 0.475)

Table 34 represents CBCT Cyst in maxilla posterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant.

Table 35: *CBCT Granuloma – Maxillary Posterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location				
Periphery	-0.125	-0.433	0.665	(-0.691, 0.441)
Shape				
Internal Structure	-0.2	-0.693	0.488	(-0.766, 0.366)
Effect				
CPP	-0.125	-0.433	0.665	(-0.691, 0.441)
None				

no examiners chose Location, Shape, Effect, and None

Table 35 represents CBCT Granuloma in maxilla posterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No

examiner chose location, shape, effect on surrounding structures, or none, so no kappa statistic was determined.

Table 36: *PA Radiograph Cyst – Mandibular Posterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	-0.154	-0.596	0.551	(-0.66, 0.352)
Periphery	0.4	1.55	0.121	(-0.106, 0.906)
Shape				
Internal Structure				
Effect	-0.389	-1.51	0.132	(-0.895, 0.117)
CPP	0.167	0.645	0.519	(-0.339, 0.673)
None				

no examiners chose Shape, Internal Structure, and None

Table 36 represents Periapical (PA) radiograph Cyst in mandibular posterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose shape, internal structure, or none, so no kappa statistic was determined.

Table 37: *PA Radiograph Granuloma – Mandibular Posterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	-0.0714	-0.277	0.782	(-0.577, 0.435)
Periphery	0.659*	2.55	0.0107	(0.153, 1.165)
Shape	-0.154	-0.596	0.551	(-0.66, 0.352)
Internal Structure	0.423	1.64	0.101	(-0.083, 0.929)
Effect	-0.389	-1.51	0.132	(-0.895, 0.117)
CPP				
None				

**Represents Moderate to perfect agreement*
no examiners chose CPP and None

Table 37 represents Periapical (PA) radiograph Granuloma in mandibular posterior teeth. We found periphery (0.659) to have a statistically significant moderate agreement with a p-value less than 0.05. Therefore, the agreement for periphery is significantly different from chance agreement. We also found internal structure (0.423) to have a moderate agreement, although its p-value was 0.101. The agreement for internal structure is not significantly different from chance agreement. No examiner chose cortical plate perforation or none, so no kappa statistic was determined.

Table 38: *CBCT Cyst – Mandibular Posterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	-0.0909	-0.315	0.753	(-0.657, 0.475)
Periphery	0.111	0.385	0.7	(-0.455, 0.677)
Shape	-0.0909	-0.315	0.753	(-0.657, 0.475)
Internal Structure	-0.0909	-0.315	0.753	(-0.657, 0.475)
Effect	-0.333	-1.15	0.248	(-0.899, 0.232)
CPP	0.333	1.15	0.248	(-0.232, 0.899)
None				

**Represents Moderate to perfect agreement*
no examiners chose None

Table 38 represents CBCT Cyst in mandibular posterior teeth. We found no criteria to have a moderate to perfect agreement. No criteria were statistically significant. No examiner chose none, so no kappa statistic was determined.

Table 39: *CBCT Granuloma – Mandibular Posterior*

Criteria	**Kappa**	**Z-score**	**P-value**	**95% CI**
Location	0.659*	2.55	0.0107	(0.153, 1.165)
Periphery	0.423	1.64	0.101	(-0.083, 0.929)
Shape	1*	3.87	0.000108	(0.494, 1.506)
Internal Structure	0.659*	2.55	0.0107	(0.153, 1.165)
Effect	-0.154	-0.596	0.551	(-0.66, 0.352)
CPP				
None	1*	3.87	0.000108	(0.494, 1.506)

**Represents Moderate to perfect agreement*
no examiners chose CPP

Table 39 represents CBCT Granuloma in mandibular posterior teeth. We found location (0.659), shape (1), internal structure (0.659), and none (1) to have a statistically significant moderate to perfect agreement with p-values less than 0.05. Therefore, the agreement for location, shape, internal structure, and none are significantly different from chance agreement. No examiner chose cortical plate perforation, so no kappa statistic was determined.

3.2 Examiner Most Commonly Selected Criteria

With the known agreement among criteria selected on lesions via the Kappa statistic, an examination of the actual counts of the criteria selected may also play a role in the evaluation of the criteria. Just because agreement among certain criterion were high, that does not necessarily mean that these criteria are the most prevalent when examining the lesions. Personal interpretation of the criteria may lead to examiner bias, which may lead to some observers to select more criteria than others. The following tables represent the actual counts of criteria which were selected per lesion type and area.

Table 40: *PA Radiograph Cyst Counts*

	Location	Periphery	Shape	Internal Structure	Effect	CPP	None
PA Cyst (N=60)	43	13	43	47*	24	7	6
Maxilla (N=33)	27*	6	23	25	14	3	5
Mandibular (N=27)	16	7	20	22*	10	4	1
Anterior (N=30)	18	7	20	24*	12	4	6
Posterior (N=30)	25*	6	23	23	12	3	0
Maxilla Anterior (N=21)	14	4	12	14*	6	3	5
Mandibular Anterior (N=9)	3	2	5	7*	4	1	1
Maxilla Posterior (N=12)	12*	1	8	8	6	0	0
Mandibular Posterior (N=18)	13	5	15*	15*	6	3	0

**Represents most selected criteria*

Table 41: *PA Radiograph Granuloma Counts*

	Location	Periphery	Shape	Internal Structure	Effect	CPP	None
PA Granuloma (N=60)	48*	9	44	43	18	0	7
Maxilla (N=30)	25*	2	22	21	9	0	7
Mandibular (N=30)	23*	7	22	22	9	0	0
Anterior (N=30)	26*	3	26*	26*	12	0	3
Posterior (N=30)	22*	6	18	17	6	0	4
Maxilla Anterior (N=15)	17*	0	17*	17*	9	0	3
Mandibular Anterior (N=15)	9*	3	9*	9*	3	0	0
Maxilla Posterior (N=15)	8*	2	5	4	0	0	4
Mandibular Posterior (N=15)	14*	4	13	13	6	0	0

**Represents most selected criteria*

Table 42: *CBCT Cyst Counts*

	Location	Periphery	Shape	Internal Structure	Effect	CPP	None
CBCT Cyst (N=60)	51	22	53*	52	11	35	1
Maxilla (N=33)	30	15	33*	33*	5	21	1
Mandibular (N=27)	21*	7	20	19	6	14	0
Anterior (N=30)	28	14	30*	29	6	22	0
Posterior (N=30)	23*	8	23*	23*	5	13	1
Maxilla Anterior (N=21)	21	10	23*	23*	3	14	0
Mandibular Anterior (N=9)	7	4	7	6	3	8*	0
Maxilla Posterior (N=12)	9	5	10*	10*	2	7	1
Mandibular Posterior (N=18)	11*	3	11*	11*	3	6	0

**Represents most selected criteria*

Table 43: *CBCT Granuloma Counts*

	Location	Periphery	Shape	Internal Structure	Effect	CPP	None
CBCT Granuloma (N=60)	53*	12	53*	52	10	27	3
Maxilla (N=30)	33*	9	32	32	7	23	0
Mandibular (N=30)	20	3	21*	20	3	4	3
Anterior (N=30)	30	6	29	31*	8	19	0
Posterior (N=30)	23	6	24*	21	2	8	3
Maxilla Anterior (N=15)	21	5	20	22*	7	15	0
Mandibular Anterior (N=15)	9*	1	9*	9*	1	4	0
Maxilla Posterior (N=15)	12*	4	12*	10	0	8	0
Mandibular Posterior (N=15)	11	2	12*	11	2	0	3

**Represents most selected criteria*

Number of selected criteria is shown in tables 40 through 43. For Periapical (PA) radiograph Cyst (Table 40), the criteria most selected in all areas of teeth were internal structure and location. For Periapical (PA) radiograph Granuloma (Table 41), the criteria most selected in all areas of teeth was location, and occasionally shape or internal structure. For CBCT Cyst (Table 42), the criteria most selected in all areas of teeth were shape and internal structure. For CBCT Granuloma (Table 43), the criteria most selected in all areas of teeth was shape, as well as location and internal structure.

3.3 Examiner Criteria Count Logistic Regression

One interpretation of the textbook criteria is perhaps that no specific criterion needs to be present on a lesion for a diagnosis to be made; it is possible that just a certain number of criteria need to be present. Past studies have used this methodology for assessing the criteria and had moderate results. To evaluate if the number of criteria present allows for a diagnosis to be made, a logistical regression was performed. The logistical regression results can be seen below.

Table 44: **PA Radiograph Logistic Regression**

	Estimate	**Std. Error**	**z-value**	**p-value**
(Intercept)	0.8420	1.0625	0.792	0.428
Avg. count	-0.2860	0.3437	-0.832	0.405

Table 44 shows the logistic regression analysis for average criteria count on results for Periapical (PA) radiographs. The estimate for average count was -0.2860. For a 1 unit increase in criteria count, the odds of granuloma are 0.249 less likely compared to cyst, although this effect is statistically insignificant (p-value = 0.405). Therefore, we conclude that there is no significant association between criteria count and results for Periapical (PA) radiograph.

Table 45: **CBCT Logistic Regression**

	Estimate	**Std. Error**	**z-value**	**p-value**
(Intercept)	1.5004	1.5704	0.955	0.339
Avg. count	-0.4133	0.4223	-0.979	0.328

Table 45 shows the logistic regression analysis for average criteria count on results for CBCT. The estimate for average count was -0.4133. For a 1 unit increase in criteria count, the odds of granuloma are 0.339 less likely compared to cyst, although this effect

is statistically insignificant (p-value = 0.328). Therefore, we conclude that there is no significant association between criteria count and results for CBCT.

Chapter 4: DISCUSSION

Methods for an efficient and prompt periapical lesion diagnosis have been studied for decades. Understandably, histopathology via biopsy has remained the gold standard as it provides diagnostic information on a cellular level. But such precise information comes with the drawback of requiring surgical intervention in order to obtain a specimen; a procedure requiring both patient and provider cooperation. A minimally invasive method for lesion diagnoses would facilitate quicker treatment planning as well as reduced stress for the patient. The aim of this study is to evaluate CBCT scan analysis as one method for periapical lesion diagnosis—particularly in cases of periapical granulomas and radicular cysts. A methodology used frequently in papers and presented in dental schools comes from the textbook, *Oral Radiology by White and Pharoah* [1]. The textbook presents six criteria which may be used to help differentiate between cysts or granulomas based off radiologic images. The six criteria presented are: location of the lesion, periphery of the lesion (cortical border appearance), shape of the lesion (circular or curved), internal structure of the lesion (radiolucent), effect of surrounding structures (resorption or displacement of root structures), and cortical plate perforation. With the abovementioned criteria, if periapical lesions can be diagnosed correctly based off radiological images, the sole reliance on histopathology decreases. An analysis of the current criteria is needed to assess if further refinement is needed before widespread use in studies and dental offices.

This study evaluated the six textbook criteria using three endodontic examiners to assess 40 periapical lesions. An even number of periapical granulomas (20) and radicular cysts

(20) were evaluated using both CBCT imaging and Periapical (PA) radiographs of the corresponding tooth. All images were randomized, and the observers were blinded. Observers were given full control of all CBCT images for viewing and standard endodontic filters were applied to all periapical radiographs. The three examiners were asked to select, from the six criteria, which ones were present on the images, with the option of 'none'. Upon completion, both a logistical regression and Fleiss Kappa Statistic to a 95% confidence level were used for analysis of all data.

The three endodontic examiners concluded the following results while using the six criteria for evaluating both the CBCT images and PA radiographs for radicular cysts and periapical granulomas:

The most commonly selected criteria for each category were: PA radiograph Cyst- Internal structure (47), PA radiograph granuloma- location (48), CBCT Cyst- shape (53), and CBCT granuloma- Location (53) and Shape (53). The lesions were then broken down into regions of the mouth including anterior, posterior, maxilla, and mandible.

Periapical Radiographs, Cysts, most common selected criteria per region are as follows: Maxilla: Location (27), Mandible: Internal Structure (22), Anterior: Internal structure (24), Posterior: Location (25), Maxilla Anterior: Location (14), Mandibular Anterior: Internal Structure (7), Maxilla Posterior: Location (12) and Mandibular Posterior: Shape (15) and Internal Structure (1).

Periapical Radiographs, Granuloma, most common selected criteria per region are as follows: Maxilla: Location (25), Mandible: Location (23), Anterior: Location (26), Shape

(26) and Internal structure (26), Posterior: Location (22), Maxilla Anterior: Location (17), Shape (17), and Internal Structure (17) Mandibular Anterior: Location (9), Shape (9), and Internal Structure (9), Maxilla Posterior: Location (8) and Mandibular Posterior: Location(14).

CBCT, Cysts, most common selected criteria per region are as follows: Maxilla: Shape (53), Mandible: Location (21), Anterior: Shape (30), Posterior: Location (23), Shape (23), and Internal Structure (23), Maxilla Anterior: Shape (23), and Internal Structure (23), Mandibular Anterior: CPP (8), Maxilla Posterior: Shape (10) and Internal Structure (10), and Mandibular Posterior: Location(11), Shape (11), and Internal Structure (11).

CBCT, Granuloma, most common selected criteria per region are as followed: Maxilla: Location (53) Shape (53), Mandible: Location (33), Anterior: Internal Structure (31), Posterior: Shape (24), Maxilla Anterior: Internal Structure (22), Mandibular Anterior: Location (9), Shape (9), and Internal Structure (9), Maxilla Posterior: Location (12) and Shape (12), and Mandibular Posterior: Shape (12).

With the core criteria instituted, the key and differentiating presentations of granulomas and cysts could be compared. When examining the observers' selections for periapical radiograph (cysts), the most commonly selected criteria for all locations were internal structure and location. This suggests that a relationship may exist between a lesion at the apex of the tooth and having a radiolucent internal structure being identified as a radicular cyst. However, a complication in this argument is the lack of diversity among the selected criteria by examiners between all the lesions. The most common trend for periapical radiograph (granuloma) was strongly location, followed by shape and internal

structure. This begets the possibility that a lesion at the apex of a root that has a radiolucent internal structure, and a circular shape is a periapical granuloma. While looking at a periapical radiograph based off the abovementioned parameters, the only difference between a cyst and granuloma would be the shape of the lesion. When the criteria applied to CBCT images, complications arise for both cysts and granulomas, as the most selected criteria are the same. Generically, most lesions are located at the apex of a tooth, radiolucent in internal structure, and have a possibly circular shape. To the author's knowledge, only one other study, which also used the textbook criteria, examined the individual criteria for possible links between a descriptive factor being present and the actual diagnosis. Etoz et al [38] had two examiners select individual criteria seen on 21 CBCT images (a known histopathological diagnosis was present for each lesion). Etoz et al. [38] found a statistical significance of well-defined/partial cortical border and a lesion shape as circular for cystic lesions, which does not match the current findings of location, shape, and internal structure being predictive. Based off the results seen, however not analyzed for statistical significance, in this study we cannot conclude any pattern of the criteria possible leading to a cyst or granuloma aid in diagnosis based off CBCT or periapical radiographs based off criteria counts alone. In this study a pattern of differentiation between the periapical granuloma and radicular cyst based off of the core criteria cannot predict that there will

When looking at the data set, certain criteria were picked more frequently, as seen above, but this does not consider if all the examiners were selecting the criteria evenly or if possibly one outlying examiner is skewing the selection counts. To further evaluate the data set, a Fleiss kappa statistic was used to evaluate the inter-observer agreement for

selecting criteria. The kappa statistic was run to a 95% confidence level (P=.05). The Kappa statistic was run for all regions of the mouth: maxilla, mandible, anterior, posterior, maxilla anterior, mandible anterior, maxilla posterior, and mandible posterior. When evaluating Kappa statistics, scores are reports on a scale of 0 to 1, with 1 being perfect agreement and 0 being no agreement at all. For this study the agreement level of moderate (0.41-.060) to perfect (1) agreement was used to assess if the evaluates agreed upon a criteria. Any Kappa statistic below a value of 0.41 was deemed no examiner agreement for the selected criteria.

Table 46: Kappa Statistics showing observer agreement for moderate (0.41-0.60) to Perfect (1.0) agreement.

Criteria	Location	Periphery	Shape	Internal Structure	Effect	CPP	None
PA Cyst	Moderate	Moderate					Substantial
Maxilla	Moderate*						Substantial
Mandibular	Substantial		Substantial	Moderate*			
Anterior	Moderate	Moderate	Moderate				Moderate
Posterior							
Maxilla Anterior		Substantial					Substantial
Mandibular Anterior	Perfect						
Maxilla Posterior							
mandibular Posterior							
Criteria	Location	Periphery	Shape	Internal Structure	Effect	CPP	None
PA Granuloma		Substantial		Moderate			
Maxilla							
Mandibular		Substantial		Moderate			
Anterior	Moderate*	Perfect	Moderate*	Moderate*			
Posterior							
Maxilla Anterior							
Mandibular Anterior		Perfect					
Maxilla Posterior							
mandibular Posterior		Substantial					
Criteria	Location	Periphery	Shape	Internal Structure	Effect	CPP	None
CBCT Cyst							
Maxilla							
Mandibular							
Anterior							
Posterior							
Maxilla Anterior							
Mandibular Anterior							
Maxilla Posterior							
mandibular Posterior							
Criteria	Location	Periphery	Shape	Internal Structure	Effect	CPP	None
CBCT Granuloma	Moderate*						Perfect
Maxilla							
Mandibular	Substantial		Perfect*	Substantial		Substantial	Perfect
Anterior							
Posterior	Substantial		Perfect*			Substantial	Perfect
Maxilla Anterior							
Mandibular Anterior							
Maxilla Posterior							
mandibular Posterior	Substantial		Perfect*	Perfect			

**Representing agreement with the kappa statistic and most commonly selected criteria from examiners.*

With a moderate to perfect agreement selected criteria for examiner agreement to be deemed meaningful, the following results were concluded (see table 46). Periapical radiograph (cyst) had agreement on location, periphery, and 'none'. Periapical radiograph (granuloma) had agreement on periphery and internal structure. CBCT (cyst) had no agreement between examiners on any criteria. CBCT (granuloma) has agreement on location and 'none'. Comparing these results to the most selected criteria reveals the only crossover of the results is CBCT (granuloma), where the most selected criteria was location which had a moderate agreement. It is apparent that even though a criteria is commonly appearing, it may not be able to be reproduced when multiple examiners view the corresponding image.

When breaking the data set down further into regions of the mouth, the Kappa statistic did show moderate to perfect agreement on most commonly selected criteria. These criteria include:

- Periapical radiograph Cyst: maxilla had moderate agreement with location, mandible had moderate agreement with internal structure.
- Periapical radiograph Granuloma: Anterior had moderate agreement at location, shape, and internal structure.
- CBCT Cyst: no locations showed any agreement to the Kappa statistic and most selected.
- CBCT Granuloma: Mandible showed perfect agreement at shape, posterior showed perfect agreement at shape, and mandibular posterior showed perfect agreement at shape.

Based upon the above-mentioned results, the author concludes the textbook criteria has various interpretations among examiners. Just because six criteria are described for observers to use, that does not mean that each observer will use the criteria in the same

way. The only exception for this could possibly be CBCT, granulomas; observers can repeatedly see moderate agreement at location matching the most selected criteria; Leading to conclude if a lesion is located at the apex of a root on a CBCT, it is possible that the chance of it being a granuloma increase. Shape may also play a factor in CBCT, granulomas, when looking at the mandible and posterior. Further studies are needed to investigate this idea before use in actual practice.

Three previous studies have looked at the interobserver success of this criteria and results have varied. The first two studies examined the same textbook criteria, but they did not have examiners select specific criteria, just the number of criteria present. If a lesion had 4 or more criteria present it was concluded to be a cyst. Though the methodology is different, the examiner inter-reliability can be compared to the above results from this study. The first by Guo et al. [36] in which three evaluators, all endodontists, examined 36 lesions using CBCT imaging and concluded a 0.87 kappa statistic, showing excellent agreement, as reported in the article. The next study by Chanani et al. [37] in which two evaluators examined 45 lesions using CBCT imaging and concluded an excellent agreement of a 0.94 kappa statistic. The final study which examined the same textbook criteria had examiners select criteria present on lesions, the same as the current study. Etoz et al [39] examined 21 lesions using CBCT imaging with two observers, with over seven years of CBCT experience, and showed no significance agreement between the interobserver relationship. The previous studies prompt the issue of when examiners are asked to select specific criteria, they show poor inter-reliability, but they will commonly select a similar number of criteria per lesion, as seen by Guo et al [36] and Chanani et al [37]. With limited reliability among examiners, the validity of the textbook criteria appears

questionable. To further compare the current study with the studies in which high inter-rater reliability was found, a logistic regression of the data was run for the number of criteria selected per lesion.

The number of criteria selected per lesion varied greatly, however does this number play into any chance of diagnosis association. To find answer this question a logistic regression (See tables 44 ad 45) was performed and the following results were concluded. For a Periapical radiograph the estimate of the logistic regression for average criteria selected was -0.2860, leading to the odds of a lesion being a granuloma decreasing by 24.9% with each increase in criteria selected per lesion; However, these results were statistically insignificant. For a CBCT image the estimate of the logistic regression for average criteria selected was -0.4133, leading to the odds of a lesion being a granuloma decreasing by 33.9% with each increase in criteria selected per lesion; however, these results were also statistically insignificant. These results are promising, showing as the number of selected criteria increases, the likelihood of a cyst diagnosis increases, matching previous studies. In the studies listed previously [36, 37] it was concluded if 4/6 criteria were selected the odds of the lesion being a cyst were high using a Receiver Operating Characteristic (ROC) Curve. As the number of selected criteria increases there is a possibility the diagnosis leans more towards cyst than granuloma, however not seen statistically significant in this study. One drawback seen in this study is the variability of criteria selected by examiners, leading to maybe the type of criteria does not play into the diagnosis but possible just a numerical number of criteria present may aid in lesion diagnosis. Further studies are needed to investigate the number of criteria in comparison to the actual criteria selected to aid in observer accuracy.

Comparing the results of the examiners' observations, it is concluded that the current criteria listed in the textbook, *Oral Radiology by White and Pharoah* [1], in its current state, is not a viable source for periapical lesion diagnosis based off CBCT images or Periapical radiographs. Further refinement of the guidelines is needed before the criteria may be used in a clinical setting. The criteria in its current state may aid in helping examiners view periapical lesions, but histological biopsy is still needed for accurate lesion diagnosis.

Future study improvements, which may lead to refinement of the textbook criteria, include increased number of lesions examined, increased number in observers, and examiner background. One of the major drawbacks of the current study is the small sample size of lesions when broken down into sub-categories. Due to the number of lesions, which fulfilled the selection criteria and the burden of examining the lesions by the observers, a population size of 40 was selected; similar to previous studies examining the criteria ranging from 21 to 45 lesions [35, 36, 37, 38]. An attempt to have an even distribution of the lesions in each quadrant of the mouth was made; however, this was not totally possible due to the inclusion criteria. With 40 lesions (20 periapical granuloma and 20 radicular cysts), when breaking down the lesions into the specific quadrant of the mouth the sample size limitation allows for weaker statistics. An increase in sample size in all quadrants of the mouth, may allow for better observer agreement. To help increase the accuracy of the results, an increase in number of observers was made, a flaw noted in past studies such as Simon et al [34] in which only one examiner was used (they then claimed CBCT was accurate for diagnosis). Three observers were selected to allow for a total 120 CBCT images and 120 Periapical Radiographs reports (three observers viewed

all 40 images). An increase in population size may lead to better observer inter-reliability and significance in logistical regression, particularly when viewing each quadrant of the mouth.

With the small sample sizes in this study and other studies before it, a possible improvement could be an increase in examiners to help improve inter-observer agreement. One of the major issues is obtaining accurate inter-examiner reliability in any study when viewing radiographic images. This can be seen as early as 1974, in which Goldman et al [40] examined the inter- and intra -examiner reliability of interpreting radiographs and concluded poor results in both. In the study six examiners were asked to interpret 253 cases with results of intra-observer accuracy of 72-88% and inter-observer accuracy of <50%. With the known challenge of examiners agreeing with each other, it becomes hard to have numerous examiners conclude a singular criterion is accurate. With an increased number of observers, the likelihood that the examiners agreed by chance decreases, and more accurate results may be attained. Ideally, the increased population of the observers would be both in number and in background diversity, leading to possibly more accurate observer results.

Another possible improvement to the current study is diversity among the examiners. In the current study three endodontists were used for all observations. Endodontists were selected due to their experience and knowledge of periapical lesions and viewing CBCT images and Periapical Radiographs. All examiners being of one background plays into a bias since there is only one mindset being utilized. Increased examiner background allows for possibly more accurate use of the criteria. In no study known to the author has

multiple specialties been used to examine the textbook criteria. Rosenberg et al [35] reported two radiologists were used for evaluating CBCT accuracy for cyst and granuloma diagnosis; however, they did not use the same criteria, and a result of poor accuracy was reported. A future study of both an increase in examiner size and background diversity, such as three endodontists and three oral radiologists, would help to evaluate the current criteria as either successful or inaccurate.

Even with all flaws of the current study, as reflected in past studies as well, it is concluded the current criteria from *Oral Radiology by White and Pharoah*[1] is not accurate for lesion diagnosis, for both CBCT and PA radiology, alone and may only be used as a supplement to aid in lesion viewing. The current gold standard of histological biopsy should remain the primary source for lesion diagnosis until further studies and criteria refinement has been completed.

Chapter 5: CONCLUSION

The aim of this study is to evaluate the usefulness of the six radiographic criteria, from the textbook *Oral Radiology by White and Pharoah* [1], for diagnosing periapical lesions via CBCT scans as either periapical granuloma or radicular cysts. The null hypothesis of the study is that further refinement of the criteria is needed before suitable application may be performed for accurate diagnosis of periapical lesions as cysts or granulomas from CBCT scans. Based off the Fleiss Kappa statistic of examiners, only moderate agreement (0.41-0.60) to perfect agreement (1.0) were reported as meaningful to the study. In Periapical radiographic cysts, three criteria had a moderate or higher agreement: location, periphery, and none. These criteria represent a lesion being present at the apex of the root, the border of the lesion being corticated, and the examiner not finding any of the criteria present on the periapical radiograph of cysts. In Periapical radiographic granuloma, two criteria had a moderate or higher agreement: periphery and internal structure. These criteria represent the periphery of the lesion possessing a corticated border and the internal structure of the lesion being radiolucent being present on a periapical radiograph granuloma. CBCT cysts had no criteria which were of moderate or higher agreement. CBCT granuloma's two criteria had a moderate or higher agreement: location and none. These criteria represent the location of the lesion being at the apex of the root and the examiner not finding any criteria present on the CBCT scans of cysts.

The most selected criteria by all three examiners for each type of lesion on a CBCT and periapical radiographic were: PA radiograph Cyst- Internal structure (47), PA radiograph

granuloma- location (48), CBCT Cyst- shape (53), and CBCT granuloma- Location (53) and Shape (53).

Logistic regression of the selected criteria for each lesion showed as the number of selected criteria increased from the minimum of one to the maximum of 6 criteria, the likelihood of a cyst occurring increased. In periapical radiographs with each addition of criteria selected, the odds of the lesion being a granuloma reduced by 24.9%, however to an insignificant level. In CBCT images with each addition of selected criteria the odds of the lesion being a granuloma reduced by 33.9%, however statistically insignificant.

With all the portrayed results, the author concludes the null hypothesis is accepted, further refinement of the selected criteria for this study must occur before reliable application in the diagnosis of periapical lesions.

List of Abbreviated Journal Titles

Crit Rev Oral Biol Med……...Journal of Critical Reviews in Oral Biology & Medicine

Dent Radiogr Photogr……Dental Radiography and Photography

Endod Dent Traumatol…….Journal of Endodontics dental traumatology

Int Endod J……International Endodontic Journal

Int J Oral Surg…….International Journal of Oral Surgery

JAmDentAssoc……..Journal of American Dental Association

J Calif Dent Assoc…….Journal of California Dental Association

J Conserv Dent…….Journal of Conservative Dentistry

J Dent Res……...Journal of Dental Research

J Endod……..Journal of endodontics

Oral Radiol……..Journal of Oral Radiology

Oral Surg Oral Med Oral Pathol…Journal of Oral Surgery Oral Medicine, Oral pathology

Oral Surg Oral Med Oral Pathol Oral Radiol…….Journal of Oral Surgery Oral Medicine, Oral pathology, and Oral Radiology

Scand J Dent Res……...Scandinavia Journal of Dental Research

Swed Dent J…….Swedish Dental Journal

References

1. N., Lam Ernest W. “Chapter 23:Cysts.” *White and Pharoah's Oral Radiology: Principles and Interpretation*, 8th ed., Elsevier, St. Louis, MO, 2019.

2. Kakehashi S, Stanley HR, Fitzgerald RJ. The effects of surgical exposures of dental pulps in germ-free and conventional laboratory rats.Oral Surg Oral Med Oral Pathol. 1965 Sep;20:340-9.

3. Love RM, Jenkinson HF. Invasion of dentinal tubules by oral bacteria. Crit Rev Oral Biol Med. 2002;13(2):171-83.

4. Tronstad L, Langeland K. Effect of attrition on subjacent dentin and pulp. J Dent Res. 1971 Jan-Feb;50(1):1-30.

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

6. Langeland K. Tissue response to dental caries. Endod Dent Traumatol. 1987 Aug;3(4):149-71.

7. E. Wilfred Fish. Bone Infection. JAmDentAssoc. 1939;26(5):691-712.

8. Ricucci D, Pascon EA, Ford TR, Langeland K. Epithelium and bacteria in periapical lesions. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006 Feb;101(2):239-49.

9. Molven O, Olsen I, Kerekes K. Scanning electron microscopy of bacteria in the apical part of root canals in permanent teeth with periapical lesions. Endod Dent Traumatol. 1991 Oct;7(5):226-9.

10. Ricucci D, Russo J, Rutberg M, Burleson JA, Spångberg LS. A prospective cohort study of endodontic treatments of 1,369 root canals: results after 5 years. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2011 Dec;112(6):825-42.

11. Happonen RP. Periapical actinomycosis: a follow-up study of 16 surgically treated cases. Endod Dent Traumatol. 1986 Oct;2(5):205-9.

12. Bhaskar SN. Oral surgery--oral pathology conference No. 17, Walter Reed Army Medical Center. Periapical lesions--types, incidence, and clinical features. Oral Surg Oral Med Oral Pathol. 1966 May;21(5):657-71.

13. Nair PN. New perspectives on radicular cysts: do they heal? Int Endod J. 1998 May;31(3):155-60.

14. Rotstein, Ilan, and John I. Ingle. *Ingle's Endodontics 7*., 2019. Print.

15. Neville, Brad W. *Oral and Maxillofacial Pathology*. St. Louis, Mo: Saunders/Elsevier, 2009. Print.

16. Ten Cate AR. The epithelial cell rests of Malassez and the genesis of the dental cyst. Oral Surg Oral Med Oral Pathol. 1972 Dec;34(6):956-64.

17. Nair PN, Sundqvist G, Sjögren U. Experimental evidence supports the abscess theory of development of radicular cysts. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008 Aug;106(2):294-303.

18. Torabinejad M. The rôle of immunological reactions in apical cyst formation and the fate of epithelial cells after root canal therapy: a theory. Int J Oral Surg. 1983 Feb;12(1):14-22.

19. Lin LM, Ricucci D, Lin J, Rosenberg PA. Nonsurgical root canal therapy of large cyst-like inflammatory periapical lesions and inflammatory apical cysts. J Endod. 2009 May;35(5):607-15.

20. Molven O, Halse A. Success rates for gutta-percha and Kloroperka N-0 root fillings made by undergraduate students: radiographic findings after 10-17 years. Int Endod J. 1988 Jul;21(4):243-50.

21. Akerblom A, Rohlin M, Hasselgren G. Individualised restricted intraoral radiography versus full-mouth radiography in the detection of periradicular lesions. Swed Dent J. 1988;12(4):151-9.

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

23. Friedman S, Mor C. The success of endodontic therapy--healing and functionality. J Calif Dent Assoc. 2004 Jun;32(6):493-503.

24. Friedman S, Löst C, Zarrabian M, Trope M. Evaluation of success and failure after endodontic therapy using a glass ionomer cement sealer. J Endod. 1995 Jul;21(7):384-90.

25. Price, Weston A. "The science of dental radiology." *Dental Cosmos*. 1901; 43: 483-503.

26. Bender IB. Factors influencing the radiographic appearance of bony lesions. J Endod. 1982 Apr;8(4):161-70.

27. Bender IB, Seltzer S. Roentgenographic and direct observation of experimental lesions in bone: II. 1961. J Endod. 2003 Nov;29(11):707-12; discussion 701.

28. Brynolf I. Radiography of the periapical region as a diagnostic aid. I. Diagnosis of marginal changes. Dent Radiogr Photogr. 1978;51(2):21-39.

29. Forsberg J, Halse A. Radiographic simulation of a periapical lesion comparing the paralleling and the bisecting-angle techniques. Int Endod J. 1994 May;27(3):133-8.

30. Brynolf, Ingrid. *A histological and roentgenological study of the periapical region of human upper incisors*. Almqvist & Wiksell, 1967;11.

31. Orstavik D. Reliability of the periapical index scoring system. Scand J Dent Res. 1988 Apr;96(2):108-11.

32. Priebe WA, LaZansky JP, Wuehrmann AH.The value of the roentgenographic film in the differential diagnosis of periapical lesions. Oral Surg Oral Med Oral Pathol. 1954 Sep;7(9):979-83.

33. Estrela C, Bueno MR, Azevedo BC, Azevedo JR, Pécora JD. A new periapical index based on cone beam computed tomography. J Endod. 2008 Nov;34(11):1325-1331.

34. Simon JH, Enciso R, Malfaz JM, Roges R, Bailey-Perry M, Patel A. Differential diagnosis of large periapical lesions using cone-beam computed tomography measurements and biopsy. J Endod. 2006 Sep;32(9):833-7.

35. Rosenberg PA, Frisbie J, Lee J, Lee K, Frommer H, Kottal S, Phelan J, Lin L, Fisch G. Evaluation of pathologists (histopathology) and radiologists (cone beam computed tomography) differentiating radicular cysts from granulomas. J Endod. 2010 Mar;36(3):423-8.

36. Guo J, Simon JH, Sedghizadeh P, Soliman ON, Chapman T, Enciso R. Evaluation of the reliability and accuracy of using cone-beam computed tomography for diagnosing periapical cysts from granulomas. J Endod. 2013 Dec;39(12):1485-90.

37. Chanani A, Adhikari HD. Reliability of cone beam computed tomography as a biopsy-independent tool in differential diagnosis of periapical cysts and granulomas: An *In vivo* Study. J Conserv Dent. 2017 Sep-Oct;20(5):326-331.

38. Etöz M, Amuk M, Avcı F, Yabacı A. Investigation of the effectiveness of CBCT and gray scale values in the differential diagnosis of apical cysts and granulomas. Oral Radiol. 2021 Jan;37(1):109-117.

39. Shrout MK, Hall JM, Hildebolt CE. Differentiation of periapical granulomas and radicular cysts by digital radiometric analysis. Oral Surg Oral Med Oral Pathol. 1993 Sep;76(3):356-61.

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

Curriculum Vitae