# FREQUENCY AND CHARACTERISTICS OF INCIDENTAL FINDINGS USING CONE-BEAM COMPUTED TOMOGRAPHY IN AN ORTHODONTIC POPULATION

by

Ryan James Edwards

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## Abstract

**Objectives**: To explore the nature and frequency of incidental findings in large field of view cone-beam computed tomography (CBCT). Additionally, to assess the agreement among orthodontic clinicians in the assessment of the impact of maxillofacial findings identified in CBCT imaging. **Methods**: A total of 427 consecutive CBCT radiologic reports obtained for orthodontic purposes were retrospectively reviewed. All findings were categorized into six anatomic categories for descriptive purposes. Additionally, using a sub-sample of these findings, the agreement between 3 orthodontists was assessed with respect to need for further follow-up and potential impact of the findings on orthodontic treatment. **Results**: A total of 842 incidental findings were reported in the 427 CBCT scans (1.97 findings/scan). The most prevalent findings were those located in the airway (42.3%), followed by the paranasal sinuses (30.9%), dentoalveolar (14.7%), TMJ (6.4%), surrounding hard/soft tissues (4.0%), and cervical vertebrae (1.3%) regions. Non-odontogenic findings represented 718 of the 842 (85.3%) findings. In terms of agreement when assessing clinical significance of the findings, subjects demonstrated “fair-to-good” inter-rater agreement regarding CBCT findings in terms of the need for further follow-up and the potential impact on future orthodontic treatment. Subjects demonstrated “excellent” intra-rater agreement in the assessment of CBCT findings regarding both need for follow-up and potential impact on future orthodontic treatment. **Conclusions:** This study demonstrates the high occurrence of incidental findings in large field of view CBCT scans in a sample of orthodontically referred cases. The majority are extragnathic findings, which can be normally considered outside the regions of interest of many dental clinicians, but which

may still require follow-up and/or management. Specifically, incidental findings in the nasal-oral-pharyngeal and paranasal air sinuses are the most frequent. Subjects demonstrated higher levels of agreement for dentoalveolar findings compared with all other extragnathic regions when assessing clinical significance.

## Preface

This thesis is an original work by Ryan James Edwards. The research project received ethics approval from the University of Alberta Research Ethics Board under 2 separate applications:

1) "Frequency and characteristics of incidental findings using CBCT in an orthodontic population upon imaging for preliminary orthodontic records", Pro00032248, December 12th 2012.

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# Chapter 1: Introduction and Literature Review

## 1.1 Cone-Beam Computed Tomography

Accurate diagnostic imaging is often a critical adjunct to the derivation of the correct orthodontic diagnosis and optimum treatment plan, as well as in the monitoring and documentation of treatment progress and outcome. Traditionally, planar 2-dimensional (2-D) images (i.e. panoramic, lateral and posterior-anterior cephalogram, periapical) have been used in orthodontics to aid in the diagnostic process. Although these forms of 2-D imaging have been used successfully since their introduction, they unfortunately suffer from inherent limitations during analysis: magnification, geometric distortion, projective displacements, superimposition and misrepresentation of anatomic structures (1).

With the development of cone-beam computed tomography (CBCT), a shift from 2-D to 3-D imaging is occurring. Although the principles of CBCT technology have been in use for approximately 2 decades, it was the development of compact high-quality flat-panel detector arrays, inexpensive x-ray tubes capable of continuous exposure and improved computer processing that has facilitated CBCT scanners to be used commercially (2). Since their commercial introduction, continuous development of CBCT technology has led to a large number of available devices (3,4).

CBCT was initially developed as an alternative to conventional fan beam helical computed tomography (CT) machines to provide more rapid acquisition of a dataset of the entire field of view at a reduced radiation dose (4), and has been in use in the medical field since 1982 (2), in which it was initially used for angiography (5). Recent medical applications in radiology include otolaryngology (6), musculoskeletal (7), mammography (8) and interventional radiology (9). Despite these reported medical uses, it is in the field of dentistry in which CBCT technology is rapidly being utilized as it is well suited for evaluating highly contrasted hard tissue structures of the craniofacial complex (10).

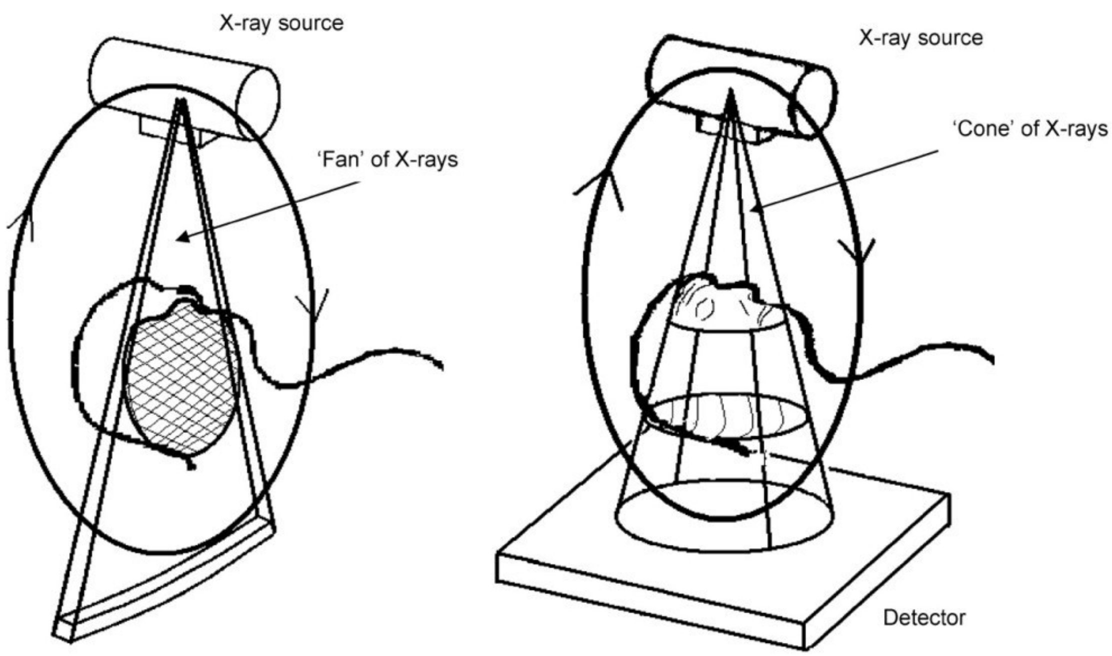
### 1.1.1 CBCT Image Acquisition

Current CBCT devices are capable of scanning patients in sitting, supine, or standing positions (4). Most commonly, CBCT units utilize the sitting or standing position (3), because those requiring a supine position occupy a larger physical footprint, and may pose difficulties for patients with physical disabilities (4). Depending on the machine, standing units may not be able to accommodate patients in wheelchairs, as there are limitations in the extent of their height adjustment (4).

The cone beam technique involves a rotating gantry to which both an x-ray source and detector are fixed, and synchronously rotate between 180-360 degrees around the patient's head during imaging. Head position is stabilized with a head restraint to minimize unwanted movement during imaging. The x-ray source produces a divergent cone-shaped beam of ionizing radiation through the region(s) of interest, onto the x-ray detector located on the opposite side. Thus, during the scan, the x-ray source and the sensor only make one revolution around the subject, in which multiple - 150 to 600 - sequential planar images are acquired at fixed intervals, each slightly offset from one another. The complete set of basis images are known as projection data. This is different than conventional medical CT, which uses a fan shaped beam in a helical progression to acquire individual image slices of the field of view

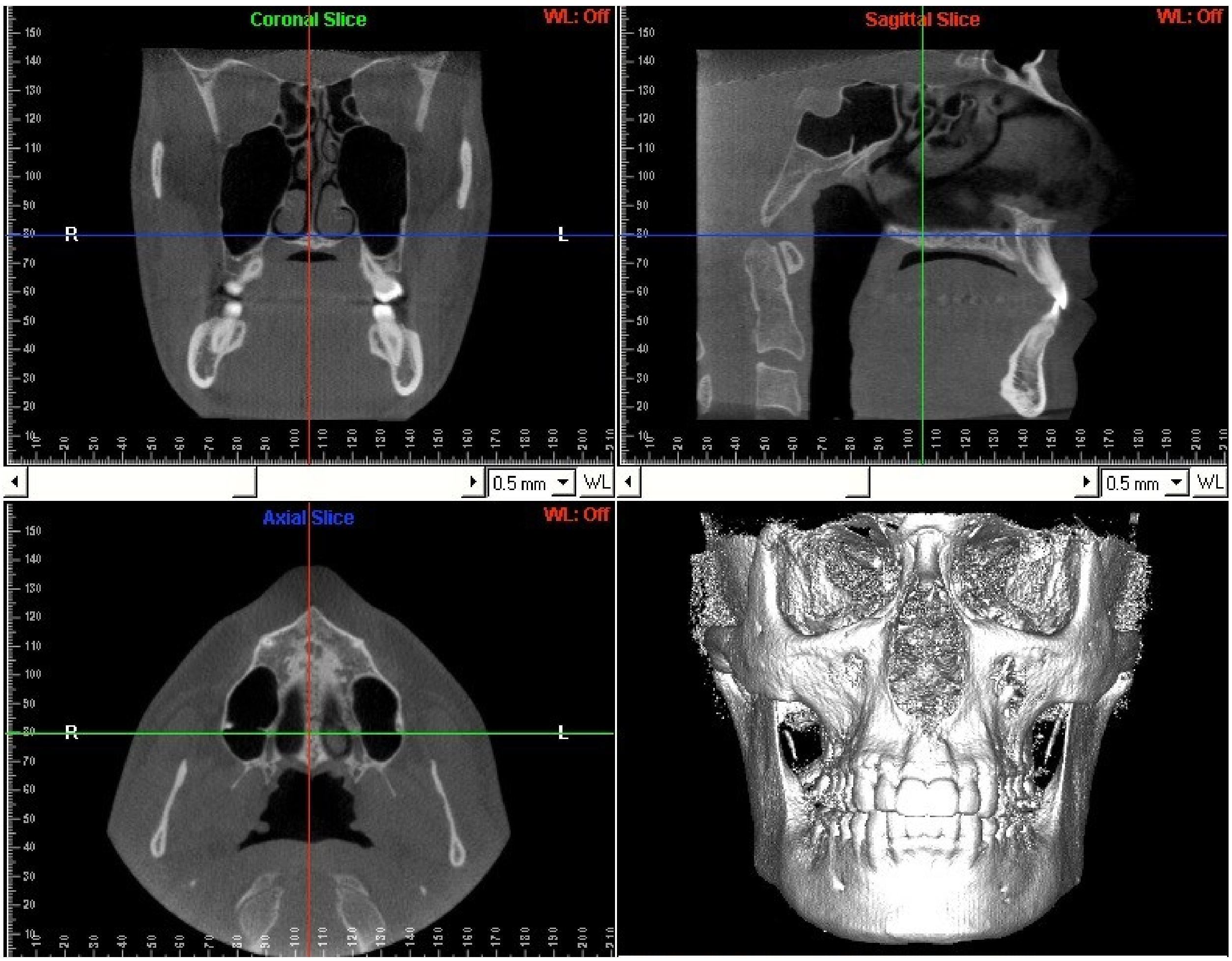
(FOV), requiring a separate scan and 2-D reconstruction for each slice (4). With CBCT, because each exposure incorporates the entire region of interest, only a single rotational sequence is necessary for image reconstruction (Figure 1-1).

Figure 1-1: Image capture technique of CT and CBCT devices. (11)




Once the CBCT basis projection frames have been acquired, various software programs apply complex algorithms to the projection data to create a 3-dimensional volumetric data set by the process of reconstruction, where the planar images are combined into a single volume. This allows the volumetric data set to be presented to the clinician on screen in two formats: a multi-planar reformation allowing scrolling through three orthogonal planes (coronal, axial and sagittal) and a 3-dimensional volume rendering (12) (Figure 1-2).

Figure 1-2: CBCT multi-planar (coronal-top left, sagittal-top right, axial-bottom left) and 3-dimensional reconstructed views (Dolphin Imaging 11.5- Dolphin 3-D).




CBCT uses a tightly collimated x-ray beam, resulting in a scan range with a more restricted FOV in the axial dimension than conventional CT (4,13). Scanners using flat panel detectors describe the dimensions using cylindrical FOVs as defined by height multiplied by width (h x w). While scanners using image intensifiers and charge coupled device sensors as their detectors describe the dimensions using spherical FOVs as $cm^3$. The FOV is primarily dependent on the beam projection geometry, beam collimation and the detector size and shape (12). CBCT machine FOVs can be generally categorized according to the available scan volume heights. Based on volume height, Scarfe and Farman (4) recommended a five-point classification:

- 5 cm height or less: localized/dentoalveolar;
- 5-7 cm height: single arch;
- 7-10 cm height: interarch;
- 10-15 cm height: maxillofacial;
- >15 cm height: craniofacial

A simplified classification scheme is suggested in the SEDENTEXT guidelines (14), which divides field of view sizes into:

- <10 cm height: small and medium: dentoalveolar;
- >10 cm height: large: craniofacial

However, despite these general FOV size guidelines, both the diameter and height of the cone-shaped x-ray beam can be modified, thus allowing some customization of FOV or scan volume depending on the anatomic region(s) of interest. Certain CBCT units offer pre-set FOV sizes for various uses, while others offer full FOV customization (3).

### 1.1.2 Craniofacial and Dentally Related Applications of CBCT

The use of CBCT has many reported applications in the field of dentistry. In recent years, stated uses include pre-operative implant planning (15), pre-surgical planning of orthognathic surgery (16), localization and management of impacted teeth (17,18), upper airway analysis (19) and temporomandibular joint (TMJ) evaluation (20,21). Additionally, the assessment of alveolar bone height and volume (22), and evaluation of bone for signs of pathology has been exhibited (23,24) . Recently, a variety of endodontic applications have been demonstrated (25-27).

Specifically in orthodontics, CBCT is being utilized in the assessment of tooth position and localization (28), resorption related to impacted teeth (29), bone dimensions for mini-implant assessment (30-32), rapid maxillary expansion (33,34) and in routine orthodontic diagnosis and treatment planning (35). In addition, CBCT has potential benefits in the assessment and management of patients with craniofacial deformities or orofacial clefts (36,37). Methods of 3-D cephalometry and superimpositioning are being developed (38) with the potential benefits of accuracy of linear measurements and for perhaps improved assessment of growth and development.

### 1.1.3 Advantages and Disadvantages of Cone-beam Computed Tomography

Compared with conventional CT, cone-beam computed tomography has a number of features that make its use suitable for a variety of dental applications. CBCT has a greatly reduced physical footprint and is approximately one fourth to one fifth the cost of conventional CT (4), allowing for its incorporation into some dental offices. The scanning time is substantially reduced from conventional CT due to all projection images being acquired in a single rotation. The majority of CBCT units can complete a large FOV scan in less than 30 seconds (3), which can contribute to a reduction in motion artifacts as the patient is required to be still for less amount of time during image acquisition. The size of the voxels contributes to determining the resolution of the image. In conventional CT, the voxels are anisotropic or rectangular in shape.

In CBCT imaging, the voxels are isotropic, or equal in all three dimensions (2). As a result, CBCT units are able to provide superb sub-millimeter isotropic voxel resolution of the component basis projection images ranging from 0.4 mm to as low as 0.076mm (3). Thus, CBCT images demonstrate an excellent spatial resolution adequate for maxillofacial applications. Collimation of the primary x-ray beam allows for an optimum FOV to be selected, depending on the region of interest. Published reports indicate an effective dose from CBCT imaging ranging from 18-70 µSv for small-to-medium FOVs and 64.7-216 µSv for large FOVs (39,40). This effective radiation dose is lower when compared with conventional CT used for maxillo-mandibular imaging (280-1410 µSv) (41-45), but higher when compared with a digital panoramic radiograph (2.7-24.3 µSv) (41,42,46-48) or digital lateral cephalogram (4.5-6 µSv) (40,46). However, the CBCT effective doses can vary and are dependent on image parameters implemented, field of view and type/model of machine (40,49).

Table 1-1: Comparison of effective radiation dosages produced by various maxillo-mandibular imaging techniques.

| **Imaging Modality** | **Effective Dose (µSv)** |
|---|---|
| **Helical Medical CT** | 280-1410 µSv (41-45) |
| **CBCT** | Small-to-Medium FOV: 18-70 µSv (39,40) |
| | Large FOV: 64.7-216 µSv (39,40) |
| **Digital Panoramic** | 2.7-24.3 µSv (41,42,46-48) |
| **Digital Lateral Cephalogram** | 4.5-6 µSv (40,46) |

Despite these advantages, there are some limitations with CBCT use. One major disadvantage of CBCT is that it can only demonstrate limited contrast resolution (50). This is mainly due to high scatter radiation and inherent flat panel related artifacts. Although CBCT is excellent for delineating intrinsically high contrast structures such as osseous tissue and the dentition, the soft tissue contrast is poor. Soft tissue outlines can be silhouetted by the air-filled space outside and within them; however, differences within the soft tissues cannot be resolved (51). Additionally, the CBCT acquisition geometry results in a large volume being irradiated with every basis image projection. By way of attenuation, large portions of the photons engage in interactions, resulting in scattered radiation. This additional recorded x-ray attenuation is called noise, and contributes to image degradation (12). Another limitation with CBCT, and conventional fan CT, is partial volume averaging (52). This occurs when the chosen voxel size of the scan is greater than the spatial resolution of the object being imaged (12). This occurs most often along the margin of an object or at the boundary of two substances of differing densities (i.e. bone and soft tissue). A voxel can only display 1 shade of gray at a time, and as a result, the voxel will display an average of the densities present (53). As a simplified example, if a voxel represents an area of 30% lucent soft tissue and 70% opaque cortical bone, the voxel will display a shade of gray that is more opaque than lucent. This process can make boundaries between densities more difficult to accurately distinguish, and results in lower spatial resolution. Reducing the voxel size can decrease the influence of partial volume averaging; however, the trade-off is that smaller voxel sizes require increasing radiation and are more prone to image noise (54).

### 1.1.4 Current Guidelines and Principles of CBCT Use

Despite the rapidly accumulating literature on CBCT, there has been debate regarding guidelines outlining CBCT usage in dentistry. Basic principles for the use of dental CBCT have been published as consensus guidelines by the American Academy of Oral and Maxillofacial Radiology (AAOMR) (55) and more recently by the American Dental Association Council on Scientific Affairs (56). These consensus guidelines outline the basic protocols on dental cone beam CT use, but lack necessary evidence-based recommendations.

The SEDENTEXCT project was an initiative put forth in 2008 by the European Commission Directives, receiving support from the European Academy of Dental and Maxillofacial Radiology (EADMFR), with the specific objective of developing comprehensive, evidence-based guidelines and recommendations on CBCT use. A diverse multi-disciplinary team was assembled to search the literature to identify previously existing guidelines and examine the volume of literature on CBCT. The results of the assessment process were used to develop evidence tables, which were then used to identify gaps in the literature and develop recommendations using the best available evidence for the following: radiation dose and risk, basic principles of use, justification and referral criteria, factors in the reduction of radiation risk, quality assurance, training and staff protection. In May of 2012, a formal document outlining these detailed evidence-based guidelines on CBCT use was released in Europe (57). As part of this process, a set of 20 “Basic Principles” was also established by the EADMFR (Table 1-2). These principles were developed by consensus rather than by an evidence-based process used elsewhere in the document, and were finalized 2 years prior to the other guidelines (58). It must be noted that since the regulatory bodies of Canada did not develop these CBCT guidelines discussed, they technically do not apply to the various practice jurisdictions across the country. However, they do serve as global guidelines to follow until the Canadian governing bodies either develop their own CBCT standards or choose to officially adopt those established by other regions.

Table 1-2: Set of 20 Basic Principles Outlining Cone beam Computed Tomography Use Established by the European Academy of Dental and Maxillofacial Radiology (58).

| | |
|---|---|
| 1 | CBCT examinations must not be carried out unless a history and clinical examination have been performed |
| 2 | CBCT examinations must be justified for each patient to demonstrate that the benefits outweigh the risks |
| 3 | CBCT examinations should potentially add new information to aid the patient's management |
| 4 | CBCT should not be repeated routinely on a patient without a new risk/benefit assessment having been performed |
| 5 | When accepting referrals from other dentists for CBCT examinations, the referring dentist must supply sufficient clinical information (results of a history and examination) to allow the CBCT Practitioner to perform the justification process |
| 6 | CBCT should only be used when the question for which imaging is required cannot be answered adequately by lower dose conventional (traditional) radiography |
| 7 | CBCT images must undergo a thorough clinical evaluation (“radiological report”) of the entire image dataset |
| 8 | Where it is likely that evaluation of soft tissues will be required as part of the patient's radiological assessment, the appropriate imaging should be conventional medical CT or MR, rather than CBCT |
| 9 | CBCT equipment should offer a choice of volume sizes and examinations must use the smallest that is compatible with the clinical situation if this provides less radiation dose to the patient |
| 10 | Where CBCT equipment offers a choice of resolution, the resolution compatible with adequate diagnosis and the lowest achievable dose should be used |
| 11 | A quality assurance program must be established and implemented for each CBCT facility, including equipment, techniques and quality control procedures |
| 12 | Aids to accurate positioning (light beam markers) must always be used |

| | |
|---|---|
| 13 | All new installations of CBCT equipment should undergo a critical examination and detailed acceptance tests before use to ensure that radiation protection for staff, members of the public and patient are optimal |
| 14 | CBCT equipment should undergo regular routine tests to ensure that radiation protection, for both practice/facility users and patients, has not significantly deteriorated |
| 15 | For staff protection from CBCT equipment, the guidelines detailed in Section 6 of the European Commission document *'Radiation Protection 136. European Guidelines on Radiation Protection in Dental Radiology'* should be followed |
| 16 | All those involved with CBCT must have received adequate theoretical and practical training for the purpose of radiological practices and relevant competence in radiation protection |
| 17 | Continuing education and training after qualification are required, particularly when new CBCT equipment or techniques are adopted |
| 18 | Dentists responsible for CBCT facilities who have not previously received adequate theoretical and practical training' should undergo a period of additional theoretical and practical training that has been validated by an academic institution (University or equivalent). Where national specialist qualifications in DMFR exist, the design and delivery of CBCT training programs should involve a DMF Radiologist |
| 19 | For dento-alveolar CBCT images of the teeth, their supporting structures, the mandible and the maxilla up to the floor of the nose (e.g. 8cm x 8cm or smaller fields of view), clinical evaluation ('radiological report') should be made by a specially trained DMF Radiologist or, where this is impracticable, an adequately trained general dental practitioner |
| 20 | For non-dento-alveolar small fields of view (e.g. temporal bone) and all craniofacial CBCT images (fields of view extending beyond the teeth, their supporting structures, the mandible, including the TMJ, and the maxilla up to the floor of the nose), clinical evaluation ('radiological report') should be made by especially trained DMF Radiologist or by a Clinical Radiologist (Medical Radiologist) |

### 1.1.5 Medico-legal Issues with CBCT Use

Certain medico-legal concerns have arisen regarding CBCT use such as issues of ownership, indications of use, training requirements and responsibilities in interpretation of the volume (59).

The major issue relates to the responsibility of image interpretation. Particularly, it is the issue of who is liable for examining the data volume once it is captured, as many clinicians are concerned that they will assume liability for reading the scan. This issue should not be controversial, as it is clearly indicated in the EADMFR's principles, that the ordering clinician is not only professionally responsible for reviewing the anatomic regions related to the indication of the scan, but also for interpretation of the entire image volume (58). Thus, a CBCT image is considered to be no different than any other image obtained by the clinician. Also outlined by the EADMFR, if the clinician is not adequately trained, then the clinician must arrange to have the volume reviewed by another competent practitioner (58). Current guidelines suggest that small FOV dentoalveolar scans of the dentition, mandible and maxilla extending to the floor of the nose (8 x 8 cm or smaller), could be interpreted by an oral and maxillofacial radiologist (OMFR) or an adequately trained dental practitioner. However, for non-dentoalveolar small FOVs (ie. temporal bone) and all large FOV craniofacial scans, interpretation should be from an OMFR or medical radiologist (58). In addition, as a pathology report accompanies a biopsy, an imaging report must accompany a CBCT scan (55).

As mentioned above, the clinician is responsible for interpretation of the entire data volume, and not just selected regions of interest. Failure to read the entire data volume is considered negligence (60). Thus, a clinician cannot have a patient sign a waiver dissolving any interpretation responsibility of the clinician outside the specified purpose. This "waiver of liability" carries no legal weight because the profession as a whole, not the individual clinician, sets the standard of care (59).

Another concern is the FOV size, or specifically which anatomic region(s) of the head the neck should be included in the scan. The basic principles outlined by the EADMFR state that CBCT equipment should offer choices in the FOV, and that the volume size should be reduced to the smallest possible field while still ensuring compatibility with the clinical indication, to protect the patient from unnecessary radiation (58). Thus, the FOV should be reduced when only a localized anatomic region is to be imaged. However, CBCT machines are being marketed to practitioners that may lack sufficient training to interpret anatomic regions beyond their specialty. Thus, one potential strategy to overcome the issue of interpretation is to reduce FOV as much as possible. However, with this strategy there is a potential risk of over-collimation or excessively reducing the FOV, either accidentally or intentionally. The concern with over-collimation is that potentially important diagnostic information related to the indication for imaging may be omitted, such as a supernumerary tooth causing a canine impaction. Thus, as part of the risk-benefit assessment, the FOV should be appropriately sized based on the indication for imaging.

**1.2 Incidental Findings (IFs)**

As diagnostic imaging becomes more sophisticated and more widely applied, there is a likelihood of increased frequency in the detection of incidental findings, which are defined as "any and all discovered findings, detected by CT, MRI, CBCT or any other imaging modality that are unrelated to the clinical indication for the imaging being performed" (61). More important than the definition is the action that each unexpected finding invokes, in terms of deciding the necessity for further evaluation and/or management (62). Underscoring concern among clinicians is the fear that the failure to report IFs will place them in jeopardy for malpractice litigation, should an unexpected or non-reported finding lead to a life-threatening health problem.

### 1.2.1 Incidental Findings in Medical Diagnostic Imaging

In the medical field, incidental findings are often referred to as “incidentalomas”, and often present difficulty to both the physician and the patient in the decision of further investigation or management (61). It is known from the literature, that most IFs are likely to be benign and have little to no clinical significance. Despite this, there is an inclination for further evaluation, even given the rare possibility of an important diagnosis. The most common objective for further evaluation of IFs is to differentiate benign from potentially serious (malignant) findings. However, further evaluation of unexpected findings can trigger additional medical care including additional testing and diagnostic procedures. This is known as the “cascade effect” (63), and may often place further costs on the healthcare system, unnecessarily expose patients to further radiation, provoke anxiety or cause morbidity (61,64).

The frequency of incidental findings has been investigated in various imaging modalities for a variety of anatomic regions. In a literature review of CT colonography, Siddiki et al (65) determined that slightly more than half (52%) of screening or asymptomatic patients had any type of extracolonic finding, with 8% of these findings necessitating further investigation. In studies examining symptomatic subjects, or those with known colorectal disease, extracolonic findings were identified in 69%, with 16% necessitating further evaluation. Hara et al (66) also examined the frequency and clinical significance of extracolonic findings in CT colonography. They demonstrated 151 incidental extracolonic findings in 109 of 264 (41%) patients, with 34 of 151 (23%) findings considered to be of high importance. Investigating CT of the chest, Jacobs et al (67) demonstrated that 7.7% of patients undergoing coronary artery disease screening and

14.2% of patients undergoing lung cancer screening had clinically significant incidental findings requiring further investigations.

Incidental findings are often identified when reviewing spiral-computed tomography in the emergency department and in trauma situations. It has been demonstrated that identification of incidental findings in these situations ranges from 29.1-43.0% of SCT's (68-72). Specifically in the head and neck region, investigators have examined the frequency of IFs using traditional CT. Thompson et al (71) and Munk et al (69) demonstrated IF rates of 23.7% and 8.8% respectively, in patients undergoing CT scanning of the head for trauma investigation. In patients undergoing head CT examination for various reasons, Lumbreras et al (63) demonstrated an IF rate of 5.9%.

In whole-body magnetic resonance imaging (MRI), Morin et al (73) identified incidental findings in 29.1% of scans, with 12.8% having clinical significance, and significantly higher rates in subjects of advanced age and higher body mass index (BMI). Morris et al (74) examined the rate of incidental findings in brain MRI. They demonstrated that 2.4% of subjects had non-neoplastic IFs, while 0.7% of subjects had neoplastic IFs.

Lumbreras et al (63) provided a comprehensive summary of available evidence on the frequency and management of IFs in imaging diagnostic tests, including CT, MRI, ultrasound, positron emission tomography and radiographs. The mean frequency of IFs was 23.6%, with neoplasm being the most the most frequently reported unexpected finding. The mean frequency of follow-up was 64.5%. Localization of findings was related to the characteristics of the findings: findings in musculoskeletal system, skin and head and neck were more likely to be of minor importance. They concluded that a high percentage of IFs can be identified in diagnostic imaging, especially in CT examinations and patients with non-specific initial diagnoses.

### 1.2.2 Incidental Findings in Dental Diagnostic Imaging

Incidental findings have also been investigated in traditional 2-D dental imaging (Table 1-3). Specifically, in orthodontics, panoramic, lateral and postero-anterior (PA) cephalometry and traditional intra-oral radiographs (bitewing, periapical) are used in the diagnostic process. Granlund et al (75) investigated panoramic radiographs obtained for orthodontic purposes, and found that IFs were identified in 43% of the patients. The most common of which were hypodontia (40.7%) and external root resorption (9.2%). They found that only 13% of identified IFs were extragnathic, that is, outside of tooth-bearing regions. Bondemark et al (76), in a similar study, found that IFs in panoramic imaging were identified in only 8.7% of patients, with idiopathic sclerosis (39.3%) and thickening of the mucosal lining of the maxillary sinus (26.8%) being the most common. In reviewing lateral cephalograms, posteroanterior cephalograms, hand/wrist films and intra-oral full mouth series of 325 consecutive patients, Tetradis et al (77) reported 431 findings (1.3 IFs per patient), with 15 findings (3.5%) requiring further inquiry. Of the 431 findings, the most common were enlarged lymphoid tissue (28.5%), ligamentous calcification (26.7%) and intra-cranial calcifications (13.7%). In another study (78), pathologic findings were identified in 6.2% of patients when assessing a variety of orthodontic radiographic images, with mucous retention cysts being the most frequent finding (39.3%).

The frequency of IFs in craniofacial CBCT imaging has also been described. The availability and interpretation of what we know in this regard will be undertaken in Chapters 2 and 3.

Table 1-3: Incidental findings reported in the literature for 2-D dental imaging.

| | Granlund et al. (75) | Bondemark et al. (76) | Tetradis and Kantor (77) | Kuhlberg and Norton (78) |
|---|---|---|---|---|
| **Imaging Assessed** | Panoramic | Panoramic | Lateral Ceph<br>PA Ceph<br>45 degree Ceph<br>Hand/Wrist<br>Full mouth series | Lateral Ceph<br>PA Ceph<br>45 degree Ceph<br>Panoramic<br>Hand/Wrist<br>Full mouth series |
| **IF Frequency** | 43% of patients | 8.7% of patients | 431 findings in 325 patients (1.3 IFs/patient) | 6.2% of patients |
| **Most Common IFs (% of all IFs identified)** | • hypodontia (40.7%)<br>• external root resorption (9.2%) | • idiopathic sclerosis (39.3%)<br>• maxillary sinus mucositis (26.8%) | • enlarged lymphoid tissue (28.5%)<br>• ligamentous calcifications (26.7%) | • mucous retention cysts (39.3%) |

**1.3 Statement of the Problem**

Currently, in many jurisdictions, the dental clinician is not required to demonstrate formal training or competency in CBCT interpretation. This can potentially result in the clinician failing to provide a self-generated radiologic report, filing an incorrect or incomplete report, not examining the entire data volume or potentially missing incidental or possibly pathologic findings. According to the SEDENTEXCT guidelines on CBCT usage (14), upon taking a large FOV craniofacial CBCT image, it is advised that an OMFR or Medical Radiologist be sought to provide a detailed radiologic report of all radiographic findings (57). This recommendation is due to the much larger FOV, and thus data volume, captured CBCT imaging. There is a high potential for some of the reported findings to be located beyond the normal anatomic region(s) within the clinician's training. Even when these advised guidelines are followed, the clinician receives a formal radiologic report, and may be faced with decisions regarding clinical significance and what actions, if any, are to be made regarding patient management as a result of the reported findings.

**1.4 Research Questions**

1. What are the frequency, location and characteristics of incidental findings in CBCT imaging in an orthodontic population being imaged for preliminary orthodontic records?
2. For any given age, are the odds of identifying an incidental finding in CBCT imaging greater for either gender, for any of individual anatomic regions?
3. What is the intra-rater and inter-rater reliability of orthodontic clinicians in the determination of the need for further follow-up and potential impact on future orthodontic management of findings in CBCT imaging?

**1.5 Hypotheses**

1. When controlling for age, there is no greater odds of having an incidental finding based on sex for any anatomic category.
2. There is no more agreement than what might occur by chance by orthodontic clinicians in the determination of clinical significance and management of findings in CBCT imaging.

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## Chapter 2: The frequency and nature of incidental findings in cone-beam computed tomographic scans of the head and neck region: A systematic review

(This chapter has been adapted for this thesis as it was previously published in: Edwards R, Altalibi M, Flores-Mir C. The frequency and nature of incidental findings in cone-beam computed tomographic scans of the head and neck region: A systematic review. Journal of the American Dental Association. 2013; 144(2):161-170)

### 2.1 Introduction

Imaging techniques play a principal role in diagnosis and in medical management of patient care. In the past 20 years, both the quality of and access to imaging techniques have improved considerably. However, as imaging techniques continue to improve, the possibility of identifying incidental findings (IFs) increases. An IF detected on a radiographic image can be defined as any abnormal or pathological finding that is unrelated to the original purpose of the imaging test or tests being performed; it may be a variant that is normal or benign or is of pathological concern. The failure to identify, report or provide follow- up care related to the IF can have adverse effects on the patient and potential medico- legal ramifications for the clinician. In addition, the possibility of inadvertent false- positive findings may lead to increased health care costs and increased patient anxiety.(1)

The use of computed tomographic (CT) technology is increasing in the dental field with the development of cone-beam computed tomography (CBCT). Suggested dental applications include localization of impacted teeth, planning of orthognathic surgery, temporomandibular joint (TMJ) analysis, upper airway assessment, implant placement, and routine orthodontic diagnosis and treatment planning.(2) Although various diagnostic advantages of CBCT have been demonstrated in some specific areas in dentistry, using CBCT is not considered the reference standard (3) and guidelines regarding CBCT use in dentistry are emerging in different parts of the world.(4-6)

During CBCT image acquisition, the desired field of view (FOV) can be modified, as determined by the region of interest. Small-FOV images are used to view a limited anatomical region of the maxillofacial complex, whereas large-FOV images can include paranasal sinuses, cervical spine, neck, airway, intracranial and cranial base structures. However, it remains the responsibility of the clinician to analyze the entire volume of data, and not just the region of interest, to avoid missing a significant finding regardless of the imaging modality used or the image size generated.(4-6)

IFs routinely are detected in other forms of diagnostic imaging, including, in the medical field, traditional CT and magnetic resonance imaging (7-10). Research also has shown that when traditional two-dimensional (2-D) dental images are interpreted, IFs are identified in 6 to 43 percent of patients (11-13). Given that CBCT scans contain more information than do 2-D radiographs, it is probable that CBCT images could demonstrate considerably higher rates of IFs.

Therefore, we undertook a critical analysis of the literature to determine the frequency and nature of IFs in the head and neck region that were found during CBCT use. In addition, we will hypothesize as to the clinical significance of such findings. Quantifying the frequency of IFs discovered in three-dimensional radiography may affect evolving CBCT guidelines and has significant considerations for both the doctor, in medico-legal terms, and the patient, in terms of the potential diagnosis of as-yet-undetected disease.

## 2.2 Methods

We conducted the reporting of this systematic review, as much as was feasible, in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement checklist (14).

### Information Sources and Search

With the assistance of a senior health-sciences librarian, we conducted a computerized search of various electronic databases. We systematically searched MEDLINE via OvidSP, Embase via OvidSP, PubMed, Scopus via Elsevier, Web of Science via Thomson Reuters and the Cochrane Library electronic databases from their earliest records to literature published at the end of the second week of July 2012. We also hand-searched bibliographies of the relevant articles for additional relevant publications that may have been missed in the electronic database searches, and we conducted manual gray- literature searches with Google Scholar.

We developed detailed search strategies for each database. We based them on the search strategy developed for MEDLINE (Table 2-1) but modified the strategy appropriately for each database to take into account differences in controlled terminology. The general search terms we used were “cone beam computed tomography” and “incidental findings”. Specific words, truncations and their combinations used for each database are found in Appendix 1 in the supplemental data to the online version of this article (found at http://jada.ada.org).

Table 2-1: Search strategy for MEDLINE via OVID SP.*

| SEARCH GROUP | KEY WORD OR MeSH† TERM |
|---|---|
| 1 | cone-beam computed tomography [MeSH] OR cone beam computed tomography OR CBCT OR cone beam OR 3D cone beam OR cone-beam OR digital volumetric tomography OR volumetric computed tomography OR digital volumetric reconstruction OR cone beam computer assisted tomography OR cone beam computerized tomography OR spiral cone-beam computed tomography |
| 2 | incidental findings [MeSH] OR incidental finding‡ OR occult finding OR abnormal finding OR unexpected finding |
| 3 | skull base [MeSH] OR skull [MeSH] OR cervical vertebrae [MeSH] OR head [MeSH] OR neck [MeSH] OR brain [MeSH] OR skull base OR skull OR cervical vertebrae OR cervical spine OR (maxillofacial region) OR (head and neck) OR (paranasal sinus‡) OR dental OR orthodontic‡ OR face OR brain OR intracranial OR trauma OR mandible OR maxilla |
| 4 | 1 AND 2 AND 3 |
| * Limits: None.<br>† MeSH: Medical Subject Headings.<br>‡ Truncation symbols. | |

**Eligibility Criteria**

The studies included in this systematic review fulfilled the following criteria. In phase 1, in which we reviewed titles and abstracts, we included articles describing studies that involved human participants of all ages, were published in any language, and contained reports of IFs from CBCT scans of the head and neck region (large FOV). We excluded case reports and studies involving participants with craniofacial syndromes.

In phase 2, in which we evaluated complete articles, we included studies that involved categorization of IFs into discrete head and neck anatomical locations, studies in which the authors reviewed randomized or consecutive images and articles including descriptions of imaging parameters. We excluded articles about studies in which investigators reported IFs from only a select region of a large-FOV CT scan (for instance, maxillary sinuses only).

**Search Selection**

Using the previously described inclusion and exclusion criteria, we conducted a two-phase search. In the first phase, as noted above, two reviewers (R.E., M.A.) independently reviewed titles and abstracts of articles to determine if they described IFs in the head and neck region discovered by means of CBCT. We defined IFs as apparently asymptomatic abnormalities and included both clinically significant and non-significant findings. Before proceeding to phase 2, the researchers resolved any disagreements by discussing them until both researchers were satisfied with the choices. They obtained full-text versions of the articles that met the initial selection criteria, then examined them critically in the more rigorous and specific selection phase 2. The same two reviewers applied the remaining inclusion criteria to the full articles in the second phase of selection (Figure 2-1). Again, they resolved disagreements by means of discussion until they achieved consensus. If they deemed any article in phase 2 to be ambiguous, they contacted the authors for clarification.

**Data Items and Collection**

The same two reviewers extracted data in duplicate. The data included information regarding study design, population characteristics, sample size, overall frequency of IF identification and primary indication for imaging, among other data. The reviewers determined clinical significance according to whether the authors stated it directly or issued a recommendation for follow-up. The reviewers resolved discrepancies by re-examining the literature as a team until they achieved a consensus. When possible, they extracted the frequency of IFs as the absolute number of IFs detected, as opposed to the number of CBCT scans that contained IFs, because it is highly likely for multiple IFs to be detected in a single scan.

### Risk of Bias in Individual Studies

The reviewers evaluated the methodology described in the selected articles according to applicable criteria derived from the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for cross-sectional studies (15), as outlined in Appendix 2 in the supplemental data to the online version of this article (found at http://jada.ada.org). We made no attempt to validate the selected criteria.

### Data synthesis

If we found the available collected information to be adequate, we planned to consider conducting a meta-analysis.

## 2.3 Results

### Study selection

Searches of electronic databases yielded 66 articles (125 before removal of duplicates), and the gray-literature search (Google Scholar) yielded one relevant article. Of the 67 articles, eight (16-23) satisfied phase 1-selection criteria, and we retrieved them in full for further analysis and hand searched their bibliographies as well. We included no additional articles as a result of hand searching. After a thorough phase 2-review process, only five articles satisfied the selection criteria. Table 2-2 provides a summary of key methodological data and the results from the selected studies (16-20). Three articles (21-23) failed to satisfy the second set of selection criteria; thus, we excluded them (Table 2-3).

**Study Characteristics**

All five of the included articles (16-20) were written in English; they were published during the period from 2007 through 2012. All five of the studies had a retrospective single-center study design. The sizes of the samples in the included studies ranged from 194 to 500. The mean age of the participants ranged from 13.0 to 64.7 years. We made multiple unsuccessful attempts to contact the various authors for information not provided.

**Risk of Bias**

We found that the quality of reported methodology ranged from moderate bias to low bias according to the STROBE statement (15) for cross-sectional studies (Table 4). Common weaknesses identified were failure to justify or calculate sample sizes, failure to report inter-rater or intra-rater reliability, failure to identify limitations in study design and failure to describe in detail any and all statistical methods.

Figure 2-1: Methodology flowchart.

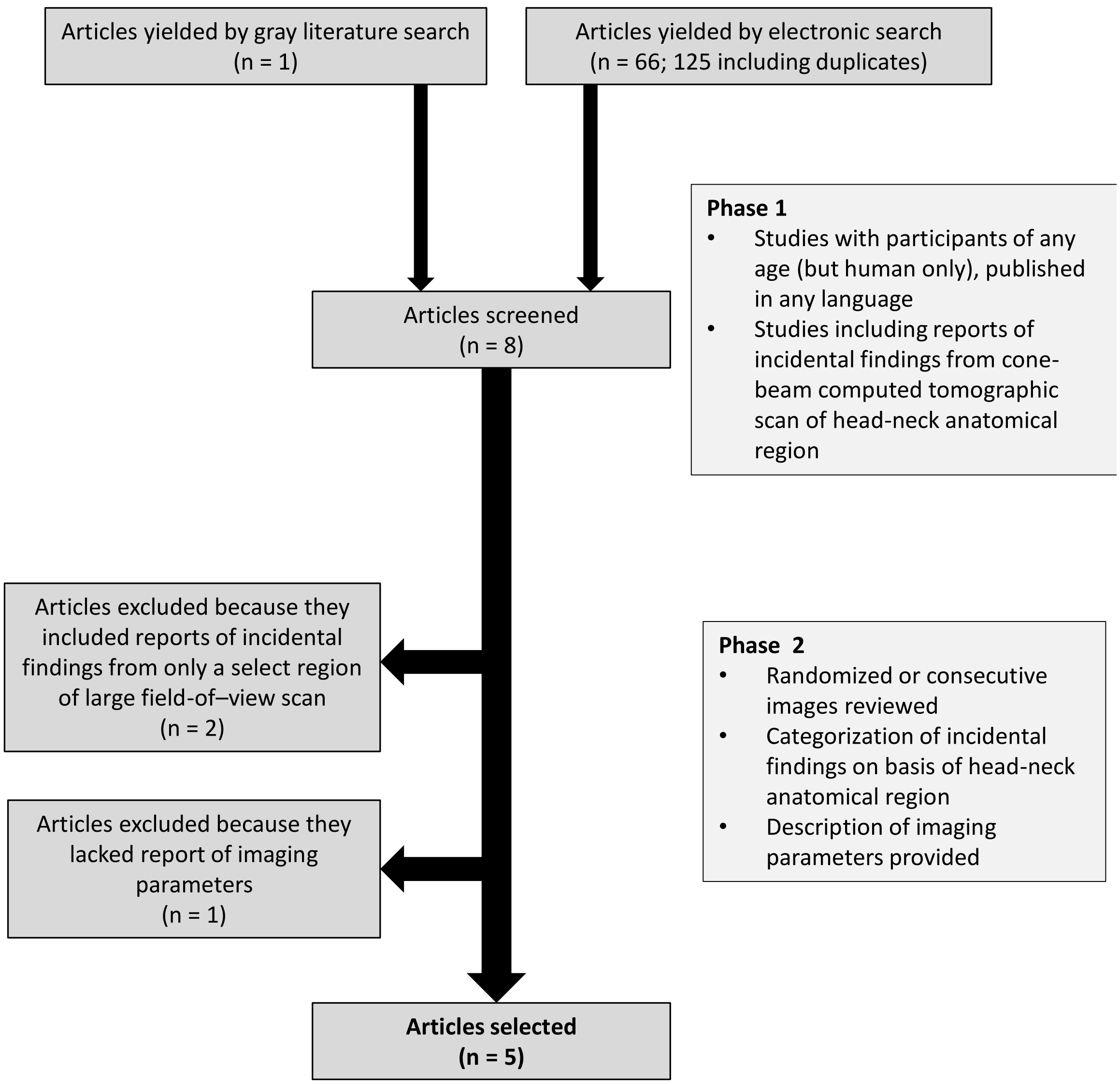

Table 2-2: Summary of included studies.

| CHARACTERISTIC | STUDY | | | | |
|---|---|---|---|---|---|
| | **Caglayan and Tozoglu[16] (2012)** | **Cha and Colleagues[17] (2007)** | **Pette and Colleagues[18] (2012)** | **Pliska and Colleagues[19] (2011)** | **Price and Colleagues[20] (2011)** |
| **Indication for Imaging** | Temporomandibular joint (TMJ) evaluation, paranasal evaluation, sleep apnea, dental implants, other | Orthodontic, TMJ evaluation, endodontic, dental implants | Evaluation for dental implant placement | Orthodontic diagnostic purposes | Dental implants, TMJ evaluation, pathology, orthodontic applications |
| **Sample Size** | 207 | 500 | 318 | 194 | 300 |
| **Mean (Range) Age in Years** | 30.3 (9-74) | 39.3 (not specified) | Male, 64.7; female 62.3 (16-91) | 13.0 (8-63) | 49.3 (9-80) |
| **Male, Percentage** | 38 | 45 | Not specified | 43 | 44 |
| **Frequency (Percentage) of Incidental Findings (IFs) in the Head-Neck Region** | 192 of 207 scans (92.8) | 123 of 500 scans (24.6) | 297 of 318 scans (93.4) 779 IFs in 318 scans (2.5 IFs per scan) | 127 of 194 scans (65.5) 247 IFs in 194 scans (1.3 IFs per scan) | 272 of 300 scans (90.7) 881 IFs in 300 scans (2.9IFs per scan) |
| **Cone-Beam Computed Tomography Machine** | NewTom 3G (Quantitative Radiology, Verona, Italy) | NewTom QR 9000 (Asperio, Sarasota, FL) | i-CAT (Imaging Sciences International, Hatfield, PE) | i-CAT Next Generation (Imaging Sciences International) | • NewTom 3G (AFP Imaging, Elmsford, N.Y.)<br>• Sirona Galileos 3D Comfort (Sirona Dental Systems, Charlotte, N.C.) |
| **Size of Field of View** | Large (exact size not specified) | Large (exact size not specified) | 13 centimeters | Large (exact size not specified) | 15-22 cm |
| **Imaging Parameters** | 5.4 seconds, 0.16 voxel, 110 kilovolts, 15 milliamperes | 0.25 voxel, 100 kV, 3.5mA | 20 seconds, 0.3 voxel, 120 kV, 5 mA | 17.8 seconds, 120 kV, 37.1 mA | • NewTom 3G: 100 kV, 1-15 mA<br>• Sirona Galileos: 85 |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | kV, 5-7 mA |
| **Reviewer(s) of Images** | Independent review of each image by two oral and maxillofacial radiologists (OMFRs) | Review by single OMFR | Each scan reviewed by only one of 13 masked OMFRs | Review of each image by one of two OMFRs | Each scan reviewed by a single third-year OMFR resident, with consultation from a single board certified OMFR for questionable cases |

Table 2-3: Articles excluded during phase 2 review.

| STUDY | INDICATION FOR IMAGING | REASON FOR EXCLUSION |
|---|---|---|
| Miles[21] (2006) | Primarily for evaluation of dental implant placement | Did not provide image parameters for cone-beam computed tomography (CBCT) |
| Pazera and Colleagues [22] (2010) | Orthodontic diagnostic purposes | Reported incidental findings (IFs) from only a limited region (maxillary sinuses) of a large field-of-view CBCT scan without providing information about IFs from other regions of the CBCT scan |
| Ritter and Colleagues[23] (2011) | Primarily for evaluation of dental implant placement | Reported incidental findings (IFs) from only a limited region (maxillary sinuses) of a large field-of-view CBCT scan without providing information about IFs from other regions of the CBCT scan |

Table 2-4: Methodological scores for selected articles.

| CRITERION† | STUDY | | | | |
|---|---|---|---|---|---|
| | Caglayan and Tozoglu[16] (2012) | Cha and Colleagues [17] (2007) | Pette and Colleagues[18] (2012) | Pliska and Colleagues[19] (2011) | Price and Colleagues[20] (2011) |
| **Objectives: Clearly Formatted (√)** | √ | √ | √ | √ | √ |
| **Study Design: Described in Detail (√)** | √ | √ | √ | √ | √ |
| **Setting: Described in Terms of Setting, Locations and Relevant Dates (√)** | X | √ | √ | √ | √ |
| **Participants: Eligibility Criteria and Methods of Selection Described (√)** | √ | √ | √ | √ | √ |
| **Bias: Any Efforts to Address Potential Sources of Bias Described (√)** | X | X | √ | X | X |
| **Sample Size: Explanation of Derivation (√); Adequate (√)** | X;√ | X;√ | X;√ | X;√ | X;√ |
| **Statistical Methods: Described (√); Appropriate for Data (√)** | X;√ | X;√ | √;√ | √;√ | X;√ |
| **Population: Described (√)** | √ | √ | √ | √ | √ |
| **Outcome Data: Numbers of Outcome Events Reported (√)** | √ | √ | √ | √ | √ |
| **Other Analyses: Any Other Analyses Conducted Reported (√)** | X | √ | √ | √ | X |
| **Limitations: Limitations of the Study and Any Potential Bias Discussed (√)** | X | √ | √ | X | √ |
| **Interpretation: Overall Interpretation of the Results Provided (√)** | √ | √ | √ | √ | √ |
| **External Validity: Generalizability of the Results Discussed (√)** | √ | √ | √ | √ | √ |
| **TOTAL (PERCENTAGE)** | **9 (60)** | **12 (80)** | **14 (93)** | **12 (80)** | **11 (73)** |

* Adapted from von Elm and colleagues[15]
† Maximum number of (√) possible is 15. X indicates that the criterion was not met

## Synthesis of Results

Owing to the heterogeneity in study design of the included articles (in aspects such as imaging parameters, scanner type, indication for scanning and base-line population characteristics), grouping of all the data was not reasonable, and taking a meta- analytical approach was impossible. Therefore, determination of risk of bias across the studies was not feasible, and the reported results of this review are descriptive. In articles in which investigators described IFs by using the absolute number of IFs detected (18-20), the frequency ranged from 1.3 to 2.9 IFs per CBCT scan. Conversely, in articles in which investigators reported IFs as the number of scans containing IFs (16-20), the frequency ranged from 24.6 to 93.4 percent of CBCT scans. In three articles, the authors described results by using both methods of reporting (18-20). Comprehensive detailed reporting regarding specific locations and descriptions of all IFs in the complete study population was not provided in one article (17) but was provided in the other four articles (16,18-20). From among these, the most common IFs identified were vertebral degenerative changes (0.5-45.6 percent), sinusitis or mucosal thickening (7.7-41.7 percent), pineal gland calcification (0.5-19.2 percent), impacted third molars (18.8 percent), mucous retention cysts (2.9-17.0 per- cent), TMJ condylar degenerative changes (3.9-21.7 percent) and concha bullosa (3.1-21.7 per- cent). Table 2-5 shows common findings identified in at least two of the included studies (16,18-20). Extragnathic findings, those outside the region of the dentition and alveolus, constituted from 65.8 to 97.4 percent of all identified findings. Clinical significance was mentioned in two studies (19,20), in which the authors suggested that 16.1 to 37.0 percent of IFs were clinically significant (that is, required further follow-up or intervention).

Table 2-5: Common incidental findings reported in at least two cone-beam computed tomography studies in which authors provided comprehensive detailed reports.

| IMAGING FINDING | NO. (PERCENTAGE), ACCORDING TO STUDY | | | |
|---|---|---|---|---|
| | **Caglayan and Tozoglu[16] (2012)** | **Pette and Colleagues[18] (2012)** | **Pliska and Colleagues[19] (2011)** | **Price and Colleagues[20] (2011)** |
| **Airway** | | | | |
| Mucous retention cyst | 6 (2.9) | 52 (16.4) | 24 (12.4) | 51 (17.0) |
| Concha bullosa | 8 (3.9) | 24 (7.6) | 6 (3.1) | 65 (21.7) |
| Sinusitis/Mucosal thickening | 65 (31.3) | 81 (25.5) | 15 (7.7) | 125 (41.7) |
| Deviated septum | 26 (12.6) | 30 (9.4) | 10 (5.2) | - |
| Nasal/Antral polyp | - | 6 (1.9) | 10 (5.2) | 46 (15.3) |
| **Temporomandibular Joint** | | | | |
| Flat condylar margin | - | - | 25 (12.9) | 50 (16.7) |
| Condylar degenerative change | - | 69 (21.7) | 14 (7.2) | 34 (3.9) |
| Subcondylar cyst | - | 17 (5.4) | 3 (1.5) | 24 (8.0) |
| Osteophyte | 7 (3.4) | - | 14 (7.2) | 17 (5.7) |
| Bifid condyle | 6 (2.9) | - | 2 (1.0) | 1 (0.3) |
| **Vertebral** | | | | |
| Degenerative changes | - | 145 (45.6) | 1 (0.5) | - |
| **Vascular** | | | | |
| Carotid artery calcifications | - | 37 (11.6) | - | 17 (5.7) |
| **Soft-Tissue Calcifications** | | | | |
| Tonsillolith | - | 32 (10.1) | - | 43 (14.3) |
| Sialolith | - | 3 (1.0) | 1 (0.5) | 2 (0.7) |
| Calcified stylohyoid ligament | - | 10 (3.1) | - | 80 (26.7) |
| Calcified pineal gland | - | 61 (19.2) | 1 (0.5) | - |
| **Dentoalveolar** | | | | |
| Supernumary teeth | - | - | 2 (1.0) | 6 (2.0) |
| Periapical rarefying osteitis | - | - | 18 (9.3) | 50 (16.7) |
| * A dash indicates data not specified in the study | | | | |

## 2.4 Discussion

The results of our review of CBCT studies regarding the frequency of IFs in the head-neck region show that the frequency of IFs ranges from 1.3 to 2.9 IFs per CBCT scan or from 24.6 to 93.4 percent of CBCT scans, depending on the reporting method.

Regarding the selected studies, the populations were not standardized. It is likely that this variability in population characteristics explains the inconsistency in the study results.

We observed a wide range in participants' mean age (13.0-64.7 years) when we compared the included studies. Authors of other studies have demonstrated that IFs are detected more frequently in populations of advanced age (8,24). This same trend was evident in our review; we found that IFs characteristic of advanced age, such as carotid artery calcifications or degenerative vertebral changes, were rare in studies involving young populations (19) but were reported frequently in studies involving older populations (18,20). Pette and colleagues (18) demonstrated that condylar pathologic changes and incidental vascular pathologies were, respectively, 3.6 and 13.4 times more likely to be detected on CBCT scans in patients 65 years and older than on those in patients aged from 16 to 40 years (18). Because the patient's age factors into the indication for CBCT imaging, the incidence of certain IFs will differ in varying study populations. For example, a population undergoing imaging for orthodontic care typically will demonstrate IFs at a frequency and of a nature different from those of a population undergoing imaging for evaluation of dental implant placement. Therefore, these differences help explain the variability among the selected studies.

The method of reporting IFs also may be responsible for the variability in the results. As mentioned previously, the frequency of IFs can be described either as the absolute number of IFs detected or as the number of scans containing IFs. It is probable that multiple IFs may be detected in a single CBCT scan and, if the latter method of reporting is used, that the actual frequency of IFs will be underreported. Pette and colleagues (18) clearly stipulated that in their study, even if multiple IFs were observed within the same category, the occurrence of an IF was to be recorded only once. However, this stipulation was not mentioned in any of the other included studies (16,17,19,20). In addition, differences in authors' definitions of what was significant enough to report also may contribute to the inconsistency in IF rates we observed among the studies. For example, the study with the highest frequency of IFs (20) included findings of little clinical significance (such as idiopathic sclerosis and tori), whereas these to-be-considered variants of normal anatomy were not mentioned in other studies with lower IF rates (17-19).

All of the included studies were of retrospective cross-sectional based design and, as such, they do have an inherent risk of potential bias; however, this may be the best evidence available for this type of data. All the included studies involved review of consecutive images; however, the methodology used for CBCT review was not standardized. In four of the five studies (16-19), CBCT images were reviewed by at least one board-certified oral and maxillofacial radiologist (OMFR). In the other study (20), all scans were analyzed by a third-year radiology resident, who consulted a board-certified OMFR regarding questionable cases. The potential for reporter bias exists when a CBCT image is evaluated by only a single reviewer (17-19). A more acceptable method is independent review by more than one radiologist, using consensus to resolve conflicts (16). Reported data depend on detailed and consistent reporting of IFs by the radiologist; however, inconsistencies may exist among radiologists in identification of and decisions to report IFs. These inconsistencies may be due in part to the radiologist's educational background, level of experience, work setting (office, hospital, academia) or simply personal style of reporting. The masking of the radiologist as to study scope was mentioned only by Pette and colleagues (18). Without proper masking as to the study's scope, indication for imaging and population characteristics, radiologists may be prone to reporting IFs at increased rates. It also is impossible to ascertain from these studies whether the IFs represent false-positive findings or were already known to the patient or whether subsequent reviewers would have labeled them as artifacts.

Although it is difficult to know with certainty, which IFs are truly of clinical significance, clinical significance was mentioned in two of the five studies (19,20). From these two articles, common IFs labeled as clinically significant were endodontic lesions (10.8-32.7 percent), carotid artery calcifications (4.3 percent) and dentigerous cysts (2.6 percent). We expect that clinically significant findings were identified in all of the selected studies but simply were not labeled in this manner. The effect of clinically significant IFs on patient care is difficult to assess, although at minimum it may be important to record them. However, standardized systems of managing IFs in a clinical setting have not yet been established, and the benefit of detection must be balanced with the burdens of possible increased cost and anxiety placed on the patient and, potentially, the health care system. The investigators in several studies who used medical-grade CT examined the costs of additional diagnostic workup for these unexpected findings (25,26), but the influence of CBCT imaging on the cost of subsequent patient care requires further investigation.

Investigators in similar studies have examined the frequency of IFs in the head-neck region by using traditional CT. Thompson and colleagues (27) and Munk and colleagues (28) demonstrated IF rates of 23.7 percent (96 IFs in 405 scans) and 8.8 percent (36 of 407 scans), respectively, in patients undergoing CT scanning of the head for trauma investigation. In patients undergoing CT examination for various reasons, Lumbreras and colleagues (24) demonstrated an IF rate of 5.9 percent (10 of 170 scans). These rates are lower than the majority of those in the CBCT studies included in this review. A possible explanation is that inconsistency exists between the medical and dental fields regarding the definition of the term "incidental finding," because there is an absence of dental findings (that is, TMJ, endodontic and so forth) in the medical CT reports. Possibly, emergency department physicians or radiologists do not consider the relevance of dental findings to warrant reporting.

In comparing CBCT with 2-D dental imaging, Granlund and colleagues (13) found that 43 percent of orthodontic patients who underwent panoramic imaging had IFs, the most common of which were hypodontia (40.7 percent) and external root resorption (9.2 percent). In contrast with the majority of IFs identified via CBCT imaging, they found that only 13 percent of IFs reported were outside of tooth-bearing regions. In other studies, investigators found IF rates from 6 to 9 percent on interpretation of 2-D dental images (11,12). With the exception of the rates reported by Granlund and colleagues (13), these IF rates are considerably lower than those reported in the CBCT studies in our review.

Recent guidelines have outlined CBCT protocols regarding indications for use, radiation dose optimization and documentation (4,6). However, the establishment of protocols to ensure adequate CBCT interpretation has been problematic. Most guidelines stipulate that the entire image must be reviewed by a dentist who has appropriate training and education in CBCT imaging, but difficultly exists in establishing exactly what constitutes proper training. Formal training in CBCT interpretation within dental education programs is not well established. In a 2011 article, Smith and colleagues (29) wrote that CBCT imaging was being used in 83 percent of North American postgraduate orthodontic programs but that only 59.1 percent of residents received didactic CBCT training. In addition, image interpretation was the direct responsibility of a radiologist in 59.1 percent of the programs, whereas reading and referring abnormal findings were the responsibility of the residents in 31.8 percent of the programs. Ahmed and colleagues (30) demonstrated a mean improvement in the CBCT lesion detection rate from 41.1 to 56.7 percent among orthodontists and orthodontic residents after a single three-hour training session. Specifically, the mean percentage of correctly identified extragnathic and TMJ lesions improved from 22 to 48 percent and from 20 to 55 percent, respectively. Before training, false-positive identifications were made on average in 5.4 per 10 scans by orthodontists and 4.5 per 10 scans by orthodontic residents, with the majority of errors being incorrect assessment of normal anatomical structures. After training, reviewers demonstrated significant decreases in false-positive findings. Given these findings, even after training, the orthodontists and residents failed to detect a large number of lesions. Depending on the significance of these lesions, failure to identify IFs could have medico-legal ramifications.

From this review, we conclude that further investigation must occur regarding the establishment of a standardized method of reporting and definition of the term “incidental finding” to be used both clinically and in research. It is recommended that formal CBCT interpretation training be established in the dental curriculum and that, at present, CBCT review by a radiologist should be common clinical practice unless the clinician has undergone specific training in this regard. Future research should include exploration of the sensitivity and specificity of the CBCT findings relative to medical pathological diagnoses, as well as determination of the intra-rater and inter-rater reliability of clinicians who interpret CBCT images and of oral radiologists providing the reports.

### 2.5 Conclusions

IFs are relatively frequent in CBCT imaging, and they vary considerably in respect to their frequency and nature. The majority are extragnathic findings, thus emphasizing the need for complete and proper review of the entire image, regardless of FOV or region of interest. The most commonly identified IFs were vertebral degenerative changes (0.5-45.6 percent), sinusitis or mucosal thickening (7.7-41.7 per- cent), pineal gland calcification (0.5-19.2 per- cent), impacted third molars (18.8 percent), mucous retention cysts (2.9-17.0 percent), TMJ condylar degenerative changes (3.9-21.7 per- cent) and concha bullosa (3.1-21.7 percent). However, the effect of these IFs in terms of requirement for follow-up care, need for intervention and potential expense of subsequent treatment requires further investigation.

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# Chapter 3: The Frequency and Nature of Incidental Findings in Large Field of View Cone-Beam Computed Tomography Scans of an Orthodontic Sample

(This chapter has been adapted for this thesis as it was previously published in: Edwards R, Alsufyani N, Heo G, Flores-Mir C, "The frequency and nature of incidental findings in large field of view cone-beam computed tomography scans of an orthodontic sample," *Progress in Orthodontics*. 2014;15:37. doi: 10.1186/s40510-014-0037-x)

## 3.1 Introduction

Cone-beam computed tomography (CBCT) has been rapidly integrating into the field of dentistry to produce 3-dimensional (3-D) imaging of the craniofacial complex. Current applications include, but are not limited to, specific orthodontic diagnosis, evaluation of the temporomandibular joint (TMJ), visualization of impacted teeth, evaluation of root resorption, pre-operative implant planning, upper airway analysis and pre-surgical treatment planning for both orthognathic surgery and craniofacial/cleft lip and palate cases. (1-10)

When compared with conventional 2-D imaging, CBCT captures a much larger field of view. As such, there is an increased potential to identify incidental findings (IFs). IFs are defined as any and all discovered findings, detected by CT, MRI, CBCT or any other imaging modality that are unrelated to the clinical indication for the imaging being performed (11). Arguably, as important as the detection, is the action that each unexpected finding invokes, in terms of deciding the necessity for further evaluation and/or management (12). As a large majority of IFs detected in CBCT imaging are extragnathic (13), the dental clinician may be unfamiliar with interpretation of anatomical structures outside the primary region of interest

(14). As such, the European Academy of Dento-Maxillofacial Radiology (EADMFR) and the American Academy of Oral and Maxillofacial Radiology (AAOMR) outline that if the interpreting clinician is not highly experienced in CBCT interpretation, appropriate referral is required to an oral and maxillofacial radiologist (OMFR) for review and that the entire volume must be interpreted regardless of the region of interest. (15,16)

A number of studies in the literature have investigated the frequency of IFs in CBCT imaging in various patient samples (14,17-23). Of these, only two have investigated an orthodontic sample exclusively (17,20). Thus, additional studies are required to further define the nature of IFs in CBCT imaging in order to provide an accurate estimation of potential findings and pathologies, specifically in orthodontic patients. This descriptive study aims to assess the type, frequency and location of incidental findings in large field maxillofacial CBCT imaging, collected retrospectively via radiologic reports from an orthodontic sample.

**3.2 Methods**

From a private diagnostic imaging center, 427 consecutive patients were retrospectively evaluated via chart review. No sample size calculations were performed. Instead, the chosen sample was deemed appropriate in size by comparison with similar studies in the literature. All patients received a single large field of view CBCT scan between the dates of April 21, 2011, and May 21, 2013, for the purpose of comprehensive diagnostic orthodontic records. All scans were acquired using an i-CAT Next Generation machine (Imaging Sciences International, Hatfield, PA, USA). Ethics approval for the retrospective chart review was obtained from the University of Alberta Health Research Ethics Board - Health Panel.

The kilovoltage (kV) and milliamperage (mA) were fixed (120kV, 5 mA), but volume height, imaging time and reconstruction voxel size varied slightly. All scans were acquired using a large field of view, which extended from the roof of the orbits inferiorly to at least the second cervical vertebrae. The voxel size ranged from 0.2-0.3 mm, with the vast majority (97.2% of scans) using a voxel size of 0.3 mm. The time of exposure for the scans was 4.8 seconds for 195 subjects, 8.9 seconds for 215 subjects and 26.9 seconds for 17 subjects, after acquiring the scout image.

Following comprehensive interpretation of each scan by a single, board-certified oral maxillofacial radiologist, the same OMFR generated written radiologic reports for each image. All scans were reviewed by the OMFR using the imaging software InVivoDental 5.0 (Anatomage, San Jose, CA, USA). If the OMFR had any uncertainties or doubts regarding any of the findings, other OMFRs were contacted to seek a consensus-based opinion. The radiology reports followed a consistent format, and contained a listing of all radiographic findings, which were used to tabulate the data in this study. If an additional reason for imaging was indicated (ie. investigation of a clinically detected impacted cuspid), the specific finding(s) was/were not considered as incidental. The subject's charts were not reviewed for any coincidence between systemic conditions and the findings. The radiologist was considered blinded to the objective of the present study, as at the time the radiologic reports were generated, it was not apparent that this data would be collected retrospectively for analysis.

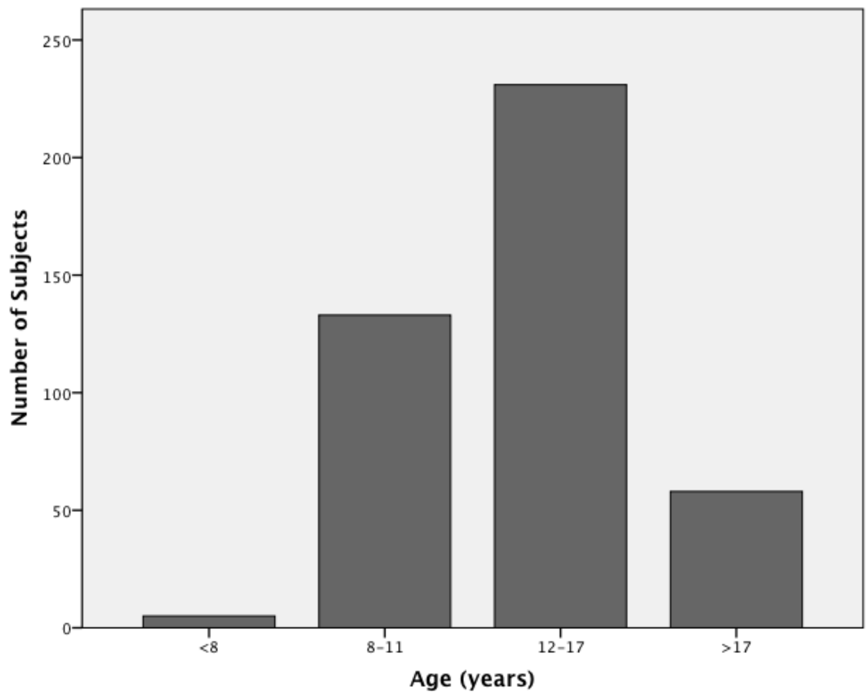
A single researcher (R.E.), not associated with the imaging center, retrospectively reviewed the radiologic reports and tabulated all findings for descriptive analysis by entering data into formulated tables using Microsoft Excel. Decisions regarding the placement of the individual findings into the specific anatomic categories were performed via consensus of three researchers. If a subject had more than one finding for any given anatomic region, the total number of findings was recorded. For example, if a subject had both adenoid hyperplasia and concha bullosa, both were recorded as airway findings. The absence of 3rd molars was not included as an incidental finding, as these teeth are commonly missing (24) or may have been previously extracted.

The complete data collection process was repeated by the single researcher, separated by a 60-day period. Intra-examiner agreement was assessed using the Kappa statistic. Both age and sex of the patients were collected. Using a Bonferroni corrected $\alpha$ of 0.008 (0.05/6), a series of logistic regression analyses were performed to investigate if for any given age, the odds of identifying an incidental finding was different between sexes, for any of the six individual anatomic regions.

### 3.3 Results

Of the 427 subjects, 180 (42.2%) were male and 247 (57.8%) were female. The age of the patients who received scans ranged from 5 to 46 years; the mean age was 14.2 (± 6.3) years and the median age was 12.0 years. The sample was divided into 4 age categories, aimed at representing subjects in the primary to early mixed dentition (<7 years), mid-mixed to early permanent dentition (8-11 years), adolescents in the permanent dentition (12-17 years) and adults (>17 years). The distribution of the total sample by age can be viewed in Figure 3-1.

Figure 3-1: Age distribution of orthodontic sample.




All findings were categorized and placed into 1 of 6 common subgroups based on anatomic region. The groupings created for analysis were: dentoalveolar, nasal-oral-pharyngeal airway, paranasal sinuses, temporomandibular joint, cervical vertebrae and surrounding hard/soft tissue. The groupings and frequency of individual findings can be viewed in Table 3-1 and Figure 3-2. With the exception of twenty-three patients in whom further investigation of suspected impacted canines was indicated in the clinical referral, no other additional clinical, radiographic or histological information was used. For these twenty-three patients, the impacted canines were not included as incidental findings.

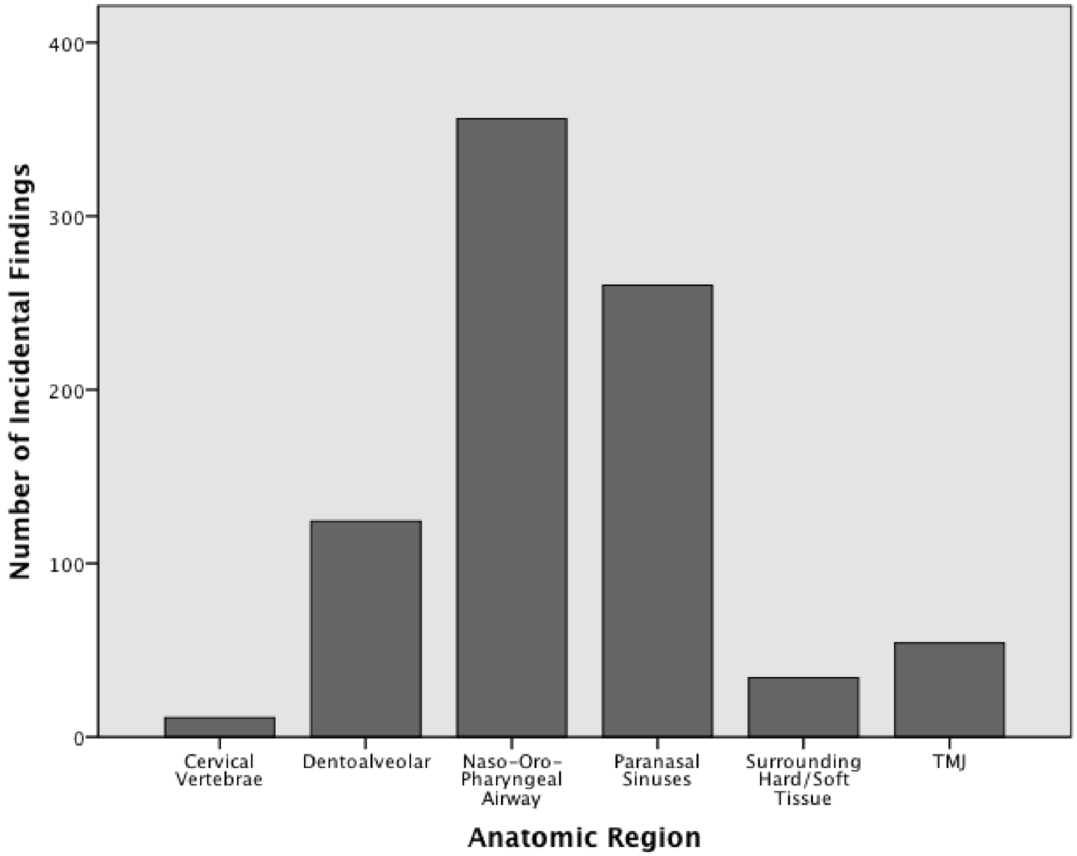
A total of 842 incidental findings were identified in 356 of the 427 scans (83.4%), representing an overall rate of 1.97 Incidental findings per scan. The most common number of incidental findings per scan was two, which occurred in 117 of 427 scans (Table 3-2). Non-odontogenic findings, defined as those located outside the dentition and associated alveolus, represented 718 of the 842 (85.3%) findings.

Table 3-1: Frequency of incidental findings among the 6 designated anatomic regions.

| Incidental Finding Category | Frequency (n) | Percentage of IFs |
|---|---|---|
| **Cervical Vertebrae** | **11** | **1.3%** |
| Cervical vertebrae fusion | 5 | 0.59% |
| Cervical vertebral flattening | 1 | 0.12% |
| Cervical osteoarthritis | 1 | 0.12% |
| Mediolateral rotation (to L) of C2-C3 in relation to C1 | 1 | 0.12% |
| Bony ossicle in C1-C2 region | 1 | 0.12% |
| Posterior ponticle of C1 | 2 | 0.24% |
| **Dentoalveolar** | **124** | **14.7%** |
| Supernumerary | 6 | 0.71% |
| Hypodontia (excluding third molars) | 37 | 4.39% |
| Microdontia | 4 | 0.48% |
| Impactions | 28 | 3.33% |
| Enamel pearl | 1 | 0.12% |
| Gemination | 1 | 0.12% |
| Retained primary tooth/fragment | 6 | 0.71% |
| Dilaceration | 1 | 0.12% |
| Microrhizy | 1 | 0.12% |
| Ectopic position | 2 | 0.24% |
| Idiopathic osteosclerosis (DBI) | 16 | 1.90% |
| Odontogenic cyst | 1 | 0.12% |
| Simple bone cyst | 2 | 0.24% |
| Buccal bifurcation cyst | 1 | 0.12% |
| Torus mandibularis | 1 | 0.12% |
| Periapical cemento-ossesous dysplasia | 2 | 0.24% |
| External root resorption | 5 | 0.59% |
| Periapical rarefying osteitis | 8 | 0.95% |
| Periapical sclerosing osteitis | 1 | 0.12% |
| **Nasal-Oral-Pharyngeal Airway** | **356** | **42.3%** |
| Choanal-retrochoanal polyp | 1 | 0.12% |
| Meatal obliteration | 1 | 0.12% |
| Adenoid hypertrophy | 154 | 18.3% |
| Lingual tonsil hypertrophy | 55 | 6.53% |
| Palatine tonsil hypertrophy | 8 | 0.95% |
| Concha bullosa | 30 | 3.56% |
| Nasal mucosal thickening; rhinitis | 25 | 2.97% |

| | | |
|---|---|---|
| Nasal septal deviation | 45 | 5.34% |
| Nasal septal deviation (with bone spur) | 22 | 2.61% |
| Turbinate hypertrophy | 5 | 0.59% |
| Nasal polyps | 1 | 0.12% |
| Irregular soft tissue border of naso-oropharynx | 2 | 0.24% |
| Dystrophic calcification of tonsils | 5 | 0.59% |
| Concha enlargement | 1 | 0.12% |
| Opacification of the middle and superior nasal meatuses | 1 | 0.12% |
| **Paranasal Sinuses** | **260** | **30.9%** |
| Localized inflammatory conditions (mucositis- sinusitis) | 152 | 18.1% |
| Pansinusitis | 11 | 1.31% |
| Ostia blockage | 11 | 1.31% |
| Retention pseudocyst | 58 | 6.89% |
| Sinus hypoplasia | 14 | 1.66% |
| Sinus pnuematization | 11 | 1.31% |
| Sinus aplasia | 1 | 0.12% |
| Accessory ostia | 1 | 0.12% |
| Antrolith | 1 | 0.12% |
| **Surrounding Soft/Hard Tissues** | **34** | **4.0%** |
| Osteoma | 1 | 0.12% |
| Fibrous dysplasia | 5 | 0.59% |
| Jugular bulb pseudolesion | 4 | 0.48% |
| Pnuematization of mastoid air cells | 12 | 1.43% |
| Enlarged sella turcica | 3 | 0.36% |
| Soft tissue polyp | 1 | 0.12% |
| Ventriculoperitoneal shunt | 1 | 0.12% |
| Pineal gland calcification | 1 | 0.12% |
| Osteoma cutis | 1 | 0.12% |
| Calcified stylohyoid ligament | 2 | 0.24% |
| Dystrophic calcification of lymph node | 1 | 0.12% |
| Depression/notch along the anterior surface of clivus | 1 | 0.12% |
| **Temporomandibular Joint** | **54** | **6.4%** |
| Condylar hypoplasia | 16 | 1.90% |
| Physiologic remodeling (flat margins, subchondral | 19 | 2.26% |
| Degenerative changes (osteophytes, erosions) | 18 | 2.14% |
| Bifid condyle | 1 | 0.12% |
| Enlarged incisive (naso-palatine) canal | 1 | 0.12% |

Figure 3-2: Distribution of incidental findings among the 6 designated anatomic regions.




The most frequently identified incidental findings were those located in the nasal oral-pharyngeal airway, representing 42.3% of all findings. The second most common form of incidental findings were those identified in the paranasal air sinuses, representing 30.9% of all findings. Dentoalveolar findings represented 14.7%, while TMJ findings represented 6.4% of all incidental findings. Findings in the surrounding hard/soft tissues and cervical vertebrae represented 4.0% and 1.3% respectively.

The kappa score measuring the level of inter-examiner agreement in the data collection was 1.0, indicating perfect agreement. The results of the logistic regression analysis suggest that, when controlling for age, only one anatomic category demonstrated statistically significant differences between males and females (Table 3-3), where females were 2.55 times ($P=<0.001$, 95% CI [1.29,5.03]) more likely to have a TMJ finding than men.

Table 3-2: Incidental finding frequency categorized by number.

| Number of Incidental | Frequency | Percentage of |
|---|---|---|
| **0** | 71 | 16.6% |
| **1** | 109 | 25.5% |
| **2** | 117 | 27.4% |
| **3** | 65 | 15.2% |
| **4** | 34 | 8.0% |
| **5** | 21 | 4.9% |
| **6** | 8 | 1.9% |
| **7** | 1 | 0.2% |
| **8** | 1 | 0.2% |

Table 3-3: P-values obtained from a series of logistic regression analyses for each of the six anatomic regions.

| Anatomic Region | Sex (p-value) |
|---|---|
| Dentoalveolar | 0.447 |
| Naso-oropharyngeal | 0.556 |
| Paranasal Sinus | 0.416 |
| Temporomandibular | <0.001 |
| Surrounding Hard/Soft | 0.144 |
| Cervical Vertebrae | 0.808 |

* $\alpha = 0.05/6 = 0.008$

Further follow-up was specifically suggested by the interpreting OMFR for the following 7 findings:

1) Polypoidal soft-tissue mass on the superior surface of soft palate (Figure 3-3).

2) An irregular thickening of the nasal cavity; nasal polyps cannot be ruled out (Figure 3-4).

3) Severe adenoid hypertrophy affecting patency of nasopharyngeal airway (Figure 3-5).

4) Complete obliteration of maxillary, sphenoid, frontal and ethmoid sinuses with soft tissue/mucosal like density (Figure 3-6).

5) Enlarged sella turcica (Figure 3-7).

6) Odontogenic cyst pericoronal to tooth 48 (Figure 3-8).

7) Soft tissue asymmetry with enlargement of the left side pharynx and larynx (Figure 3-9).

Figure 3-3: A polyploidal soft-tissue mass on the superior surface of the soft palate as viewed on sagittal slice.

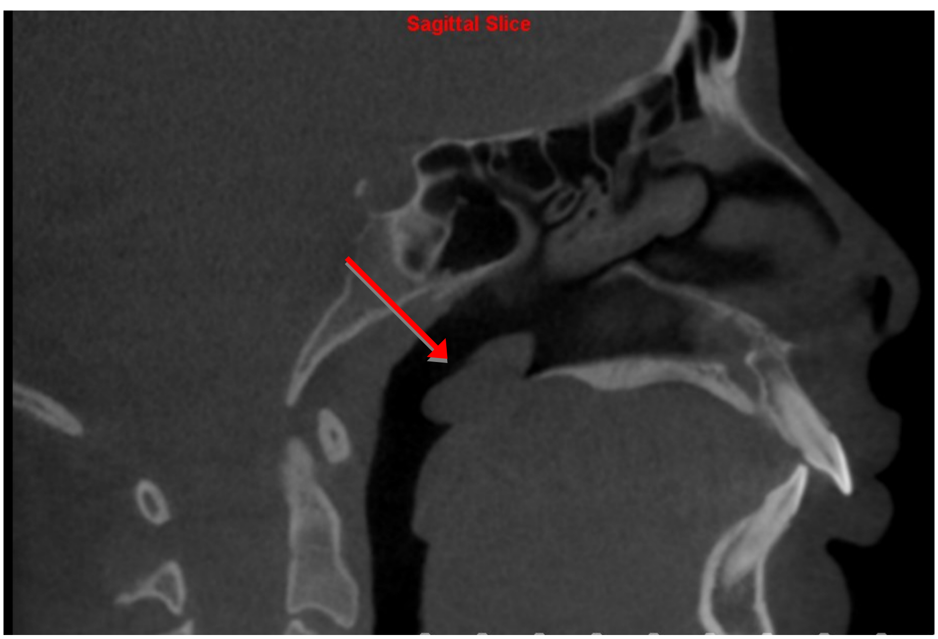


Figure 3-4: An irregular thickening of the nasal cavity as viewed on coronal slice.

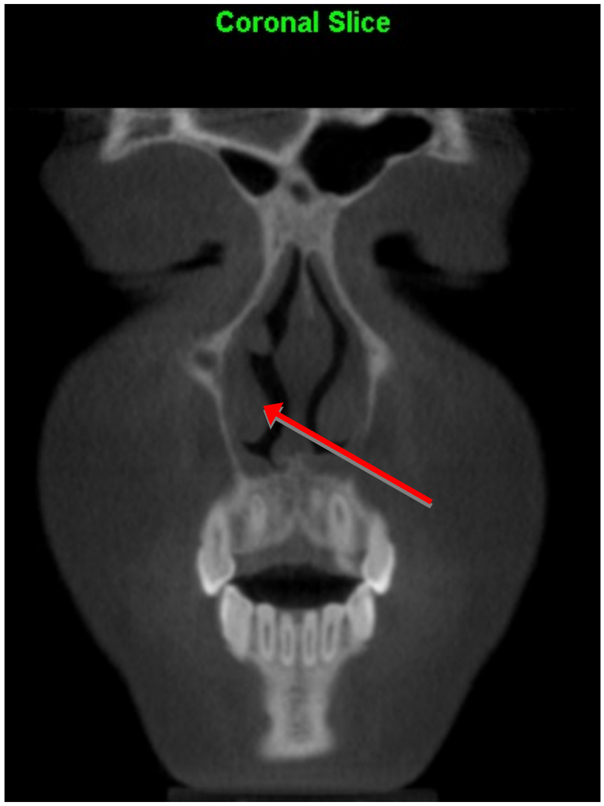



Figure 3-5: Severe adenoid hypertrophy affecting patency of the nasopharyngeal airway as viewed on sagittal slice.

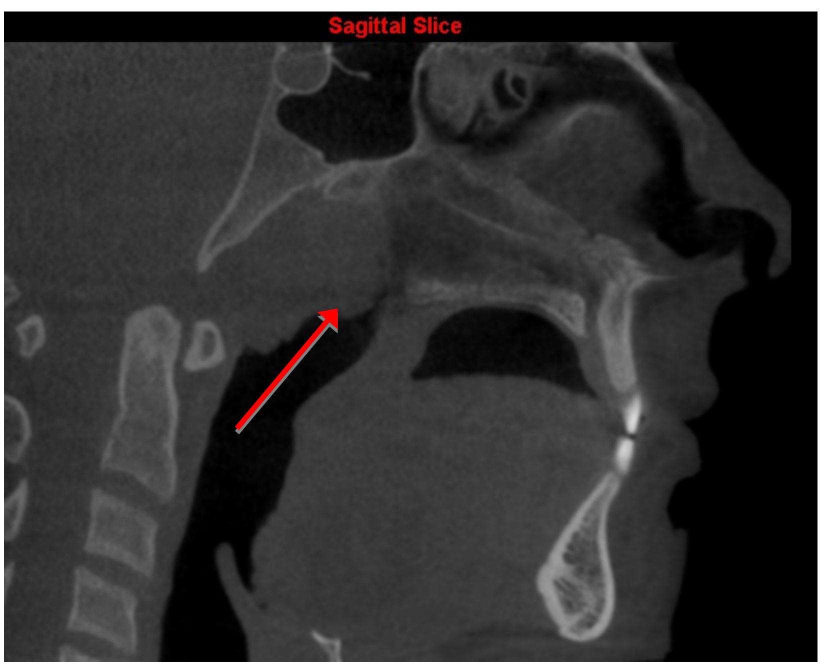
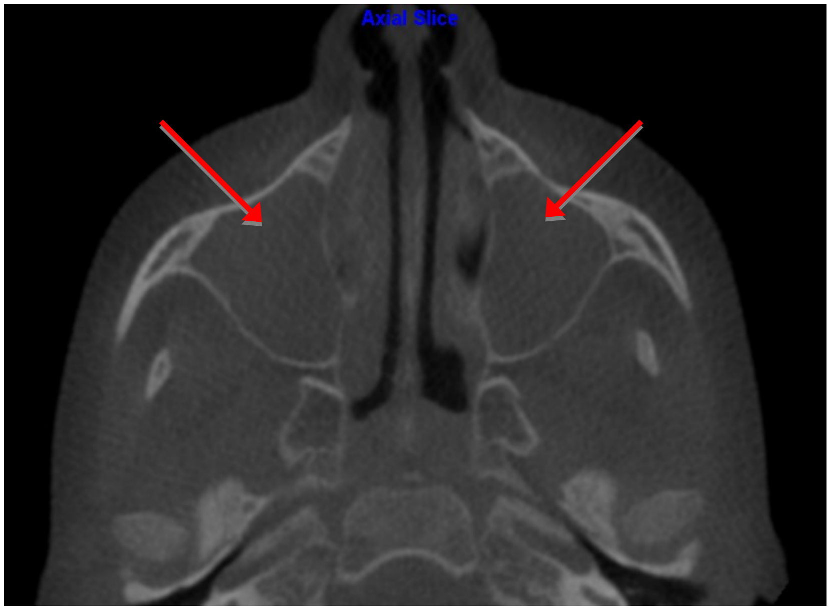


Figure 3-6: Complete obliteration of maxillary, sphenoid, frontal and ethmoid sinuses with soft tissue/mucosal like density as viewed on a) axial and b) sagittal slices.

a)




b)

Figure 3-7: Enlarged sella turcica as viewed on sagittal slice.

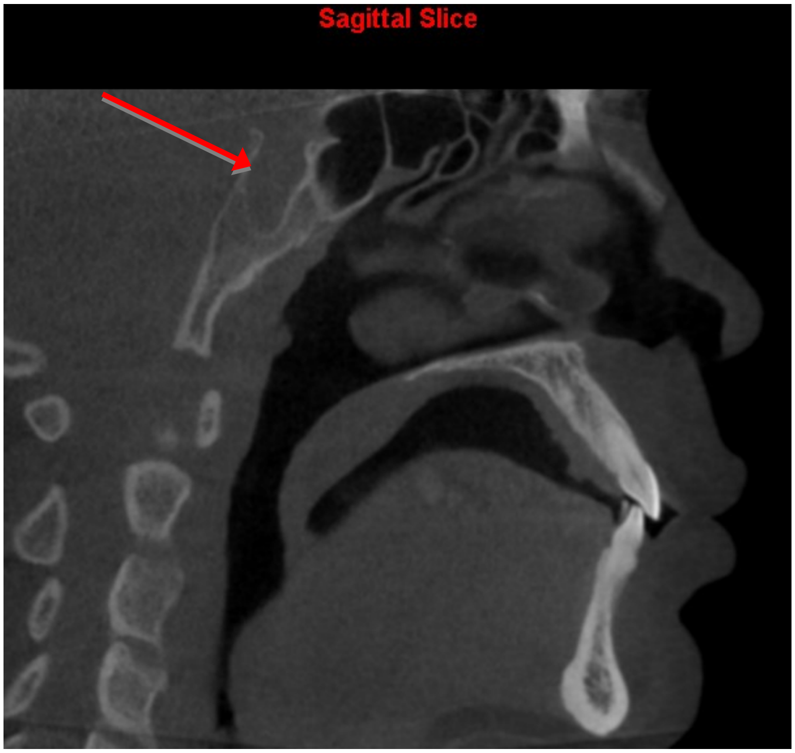



Figure 3-8: Odontogenic cyst pericoronal to tooth 48 as viewed on axial slice.

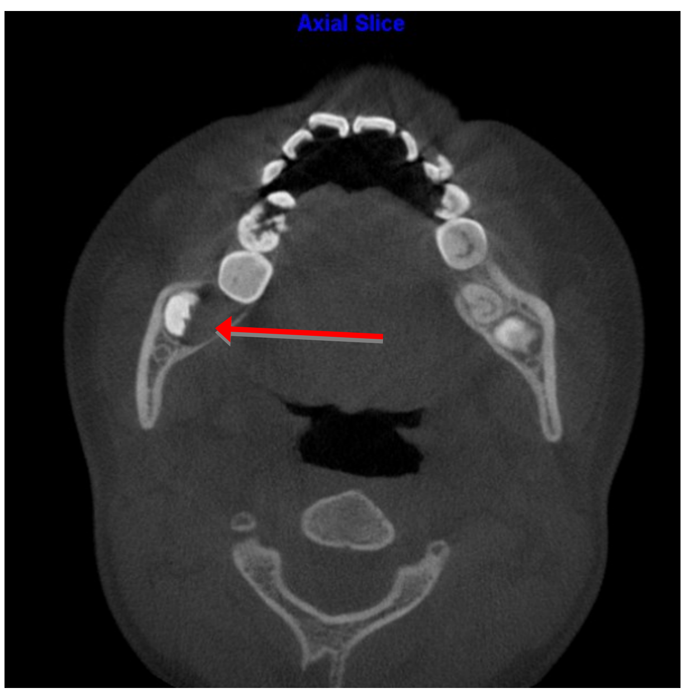
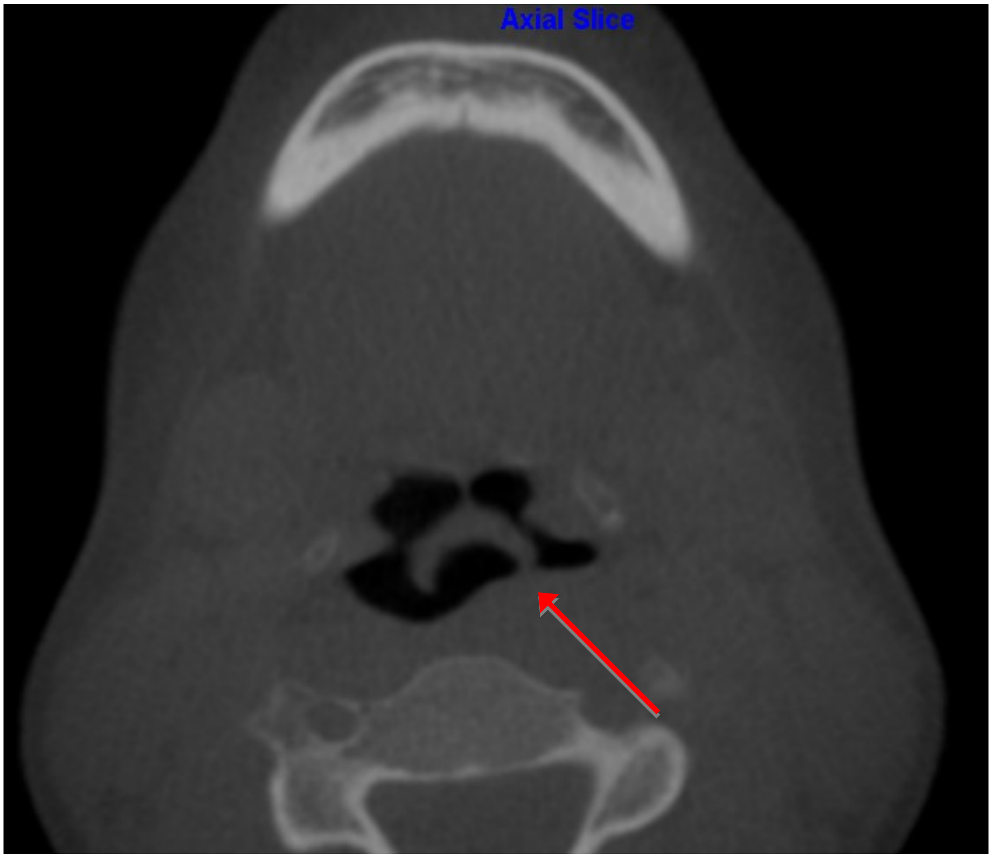


Figure 3-9: Soft tissue asymmetry with thickening and enlargement of the left side pharynx and larynx as viewed on axial slice.




### 3.4 Discussion

CBCT imaging is increasingly being utilized in diagnosis and treatment planning in orthodontics. In this study, 427 consecutive CBCT radiologic reports of orthodontic patients were retrospectively reviewed from a private diagnostic imaging center. Reported findings include developmental findings, normal anatomic variants, age-related findings and pathological findings. As mentioned in a previous systematic review (13), at least two methods for reporting the incidence of incidental findings are described in the literature; i) by describing the absolute number of IFs detected or ii) describing the number of CBCT scans that contain IFs.

The former method, using the absolute number of IFs, is favored because it is highly likely for multiple IFs to be detected in a single CBCT scan; our results confirm this.

From our sample of orthodontic patients, a total of 842 IFs were identified in the 427 scans, representing an overall rate of 1.97 IFs per scan. It is known that the frequency of IFs in CBCT imaging varies among studies in the literature, ranging from 1.1 to 2.9 IFs per CBCT scan (14,17-21). The IF rate reported from our sample is thus similar to that of other studies. At least one IF was identified in 356 of 427 scans (83.4%), which is also similar to that of other studies in the literature, which report the number of CBCT scans containing at least one IF to be between 90.7-94.3% (14,18,21,23). However, in studies by Rheem et al (22) Pliska et al (17), Rheem et al (22) and Cha et al (19), it was respectively reported that IFs were identified in only 66%, 65.5%, 40.1% and 24.5% of CBCT scans, which is significantly less than in our sample. These observed variations in the literature can likely be attributed to differences in the samples, such as age groups, differences in radiologist's reporting styles and in the definition of the term incidental finding.

*<u>Naso-oropharyngeal Airway</u>*

The most common location for identified IFs were those located in the nasal-oro-pharyngeal airway, representing 42.3% of all findings, with adenoid hyperplasia (18.3%), nasal septal deviations (8.0%) and lingual tonsil hyperplasia (6.5%) identified most frequently. This high rate of airway findings is consistent with the literature, as various other CBCT studies have demonstrated that airway findings represent 8.4-35.0% of total CBCT findings (14,17-19,21,23).

Septal deviations represented 8.0% of findings in our sample, which is less than the 19.4% reported by Smith et al (25). Concha bullosa, a common anatomical variation of the sinonasal anatomy characterized by pneumatization of the nasal turbinates, represented 3.6% of findings. This is much less than other reports in the literature, in which the prevalence of concha bullosa varied from 35% to 68% (25-28). The joint incidence of septal deviation and concha bullosa has been previously reported to be high (19.5-44.6%) (25,29). In our sample, of the 30 findings of concha bullosa, septal deviations were also identified in 9 of these subjects (30%).

The majority (25.8%) of upper airway findings in our sample were due to varying forms of adeno-tonsillar hypertrophy; specifically, adenoid/pharyngeal (18.3%), lingual (6.5%) and palatal tonsil (0.1%) hypertrophy. Upper airway obstruction has been described as a possible environmental cause of malocclusion and disharmonious dento-facial development observed in growing subjects (30-32). Various studies have discussed the contributing role of not only adeno-tonsillar hypertrophy (33-35), but also of nasal septum deviation (35,36), allergic rhinitis (37) and inferior turbinate hypertrophy (38,39) in partial upper airway obstruction.

The high frequency of airway findings in our sample demonstrates that CBCT can be an important tool in screening for airway abnormalities. However, the current reference standard for assessing the nasal cavity and nasopharynx remains nasoendoscopy (NE) (40). An important distinction must be made between identifying potential upper airway constriction in CBCT imaging and relating it to the actual presence and/or severity of clinical obstruction. Specifically regarding adenoid size, it has been demonstrated in a recent study that CBCT imaging demonstrated excellent sensitivity (88%) and specificity (93%) when compared with NE (41). In addition, the assessment of adenoid size using CBCT had strong accuracy (Intraclass coefficient

(ICC)=0.80, 95% CI ± 0.15), and very good inter- (ICC=0.85, 95% CI ± 0.08) and intra-rater reliability (ICC=0.84, 95% CI ± 0.08) amongst subjects. This suggests that CBCT can be a reliable and accurate tool for identifying adenoid enlargement. Similar studies should be conducted to investigate the sensitivity and specificity of CBCT compared to NE in regard to other airway findings, such as septal deviation and turbinate hypertrophy.

Despite the validation of CBCT for adenoid assessment, management decisions should be made on the basis of clinical history and NE, rather than entirely on radiologic findings(42). Furthermore, CBCT imaging should never be considered a replacement to NE. However, when available because it was indicated for other reasons, this imaging technology does provide orthodontic clinicians with an accurate and reliable tool for the assessment of adenoid size, facilitating screening for and early detection of adenoid enlargement and other potential airway problems (41).

*Paranasal Air Sinus Region*

Paranasal sinus changes represented 30.9% of all findings in our sample, which is similar to other CBCT studies, in which sinus changes have been commonly demonstrated ranging from 23.9-62.6% of findings (14,18,20,21,43). Many studies using MRI and medical CT imaging also confirm a high prevalence of incidental sinus findings. Havas et al (44), using CT, reported changes in one or more paranasal sinuses in up to 42.5% of asymptomatic patients. Diament et al (45) identified maxillary and ethmoid sinus opacifications in 50% of a pediatric sample referred for cranial CT. Lim et al (46) and Gordts et al (47) respectively reported that 32.3% and 45% of pediatric subjects have sinus abnormalities in non-ENT MRI imaging.

Localized inflammatory conditions consisting of mucositis-sinusitis (18.1%) and retention psuedocysts (6.89%) were the most frequently identified sinus findings. Concerning sinus mucosal inflammation in CBCT imaging, it is known from the literature that it is a common finding identified in 15.0-55.1% of patients (14,18,20-23,48). For the purposes of this study, sinusitis was defined as the radiographically detectable thickening of the sinus mucosa. Findings were based entirely on radiographic appearance, as no clinical information was assessed. Pansinusitis, an inflammation of all the paranasal sinuses, was present in 11 subjects, representing 1.31% of findings. In 10 of 11 pansinusitis patients, other concomitant airway findings were also reported, including adenoid hypertrophy (6 subjects), blocked ostia (2 subjects), and maxillary sinus hypoplasia (2 subjects). Maxillary mucous retention pseudocysts are identified as incidental findings in 2.9-16.4% of CBCT scans (14,17,20,23). They usually spontaneously regress or show no significant change in size over the long term and rarely lead to symptoms (49). It is suggested that, in the absence of associated complications, conservative monitoring is the appropriate management strategy.

In evaluating maxillary sinus abnormalities using 2-D panoramic imaging, Vallo et al. (50) identified mucosal thickening in 12% and mucous retention cysts in 7% of radiographs. Bondemark et al (51) identified sinus mucosal thickening in 26.8% of panoramic radiographs. Thus, panoramic radiography does allow for the identification of sinus abnormalities. However, it may not be as reliable a method as CBCT based on the limitations of 2-D imaging: magnification, distortion, superimposition (52). It must be mentioned that the frequency of sinus mucosal thickening and retention cysts can vary due to odontogenic factors, age, gender, season and presence of allergies (53,54). As with airway findings, the importance of careful clinical correlation must be stressed when interpreting 3-D images of the paranasal sinuses, since minor opacification is a common finding, even in asymptomatic subjects (55,56). 3-D imaging may provide information regarding the extent of the mucosal disease, but findings correlate poorly with clinical signs and symptoms (55-57). Therefore, 3-D imaging may help to support a clinical diagnosis, but it should not be interpreted out of context.

*Dentoalveolar Region*

There were 118 incidental findings (14.7%) located in the dentoalveolar region, most commonly hypodontia (4.4%). As mentioned, missing or non-developing third molars were not included as hypodontia in this study because it would inflate the number of findings, as it has been shown that the 3rd molars are the most common congenitally missing tooth, with 1 or more missing in 9-20% of individuals (24). In addition, due to the large range in age of our sample, in some subjects the third molar tooth germs would not yet be visible, while in others they may have been previously extracted. In the literature, opinions vary on the second most commonly missing tooth (58). Some investigators (59-62) believe that it is the maxillary lateral incisor, whereas others (63,64) believe that mandibular second premolar agenesis has a higher incidence. In our sample, of the total 37 congenitally missing teeth, 24 were second premolars (4.39%), 11 were maxillary laterals (1.31%), and 2 were mandibular central incisors (0.24%). These rates are comparable, but slightly less than rates described in the literature (65). Other common dentoalveolar findings were dental impactions (3.33%), idiopathic osteosclerosis (1.90%) and supernumerary teeth (0.71%). All of these findings can be readily identified in traditional 2-D imaging (66). However, CBCT offers the advantage of more accurate localization (67) and assessment of adjacent structures, (68) both of which have the potential to impact management decisions (69).

*Temporomandibular Joint Region*

There were 54 findings in the temporomandibular joint (TMJ) region, representing 6.4% of all findings. The main findings were physiologic remodeling (2.3%), degenerative changes (2.1%) and condylar hypoplasia (1.9%). According to logistic regression analysis, when controlling for age, females were 2.55 times more likely to exhibit TMJ IFs than men (P=<0.001, 95% CI, [1.29,5.03]). This finding is commonly supported in the literature (14,22,70).

The decision was made to place condylar changes into 2 main categories, either physiologic remodeling or actual degenerative changes, even though the radiographic signs of mild degenerative joint disease (DJD) can be similar to those associated with joint remodeling. Isolated TMJ flattening and/or subcondral sclerosis were interpreted as physiologic remodeling, while condylar erosions and/or osteophyte formation were interpreted as active condylar degeneration (DJD). Pette et al (14) and Allareddy et al (21) reported higher rates of degenerative TMJ changes in patients receiving CBCT imaging primarily for dental implant assessment, identifying degenerative changes in 39.0% and 6.2% of patients respectively; while other studies investigating orthodontic populations report degenerative TMJ changes in only 0.5-3.6% of subjects (19,20). It has been demonstrated that the progression and severity of TMJ osseous changes are increased with advancing age (70,71). This lower incidence of degenerative changes in our sample, and other orthodontic cohorts in the literature, is likely due to the nature of an orthodontic population; that is, consisting primarily of adolescents.

*Cervical Vertebrae Region*

Cervical vertebral findings represented only 1.3% of all CBCT findings, a similar prevalence to other CBCT studies examining orthodontic populations (17,20). This low rate of vertebral findings may be expected, given the low mean age of our orthodontic sample and variation in the number of vertebrae included in each of the scans. This is in contrast to CBCT studies by Pette et al (14) and Allareddy et al (21) which examined samples with much higher mean ages. In these studies, cervical vertebral findings were respectively identified in 47.8% and 9.7% of subjects, with the degenerative changes representing the main finding. Vertebral fusion was the most predominant finding in this region in our sample (0.6%). The prevalence as demonstrated in other studies is 0.4-0.7% with no sex predilection, with C2–C3 being the most common location (72). Generally, patients are asymptomatic, but increasing age or injury may precipitate symptoms as discal tear, rupture of the transverse ligament and odontoid process fracture are common consequences. In addition to vertebral fusion, other findings have been identified in CBCT studies, including osteoarthritis, clefts, subchondral cysts and osteophyte formation (14,20,21). Many abnormalities of the cervical spine do not manifest themselves symptomatically until young adulthood, and if progressive degenerative defects are identified early, this may aid in the mitigation of the severity of their consequences (73). With CBCT, the orthodontist and/or OMFR may be the first person to detect them, and thus serve to screen and to refer for further assessment.

In our orthodontic sample, of the 842 reported findings, 718 (85.3%) were located in extragnathic locations (i.e. outside the dentition and alveolus). This is comparable to similar

CBCT studies in the literature. Price et al (18), in a sample of 300 consecutive patients, reported a total of 881 incidental findings, with 775 (88.0%) of these being extragnathic. In a sample of 318 dental implant patients, Pette et al (14) reported that 93.7% of subjects had incidental extragnathic findings. They also identified both vascular and intracranial findings that were not reported in our sample. Internal carotid artery (ICA) calcifications were reported in 23.6% of their subjects and pineal gland calcification in 19.2% (14). ICA calcifications were also identified in 5.7% of CBCT subjects by Allareddy et al (21). Similarly, ICA calcifications in CBCT were identified in 4.8% of subjects by Price et al(18). These findings were likely not identified in our sample due to major differences in mean age, as advanced age has been demonstrated to be a major risk factor for ICA calcification (74). In panoramic imaging of large samples, Bayram et al (75) and Kumagai et al (76) respectively reported that ICA calcifications were identified in 2.1% and 4.0% of subjects. However, the presence of ICA calcifications doesn't always imply stenosis. The gold standard for the diagnosis of carotid artery stenosis (CAS) is duplex ultrasound, and is utilized in cases of suspected CAS (77). A number of studies have compared the incidence of ICA calcifications identified on panoramic radiography to CAS (77-80). These studies, investigating populations over the age of 55, have observed positive ICA calcification in 2-5% of images (78-81). Therefore panoramic radiographs appear to be a valuable screening tool for CAS. However, due to the advantages of CBCT imaging (i.e. lack of overlapping structures, sub-millimeter voxel resolution, etc.), it may result in superior and more accurate screening for CAS. The relationship between ICA calcifications identified in CBCT imaging and CSA identified in duplex ultrasound must be further evaluated.

The frequency of IFs in CBCT imaging is much larger in number and in scope when compared to traditional 2-D imaging. Bondemark et al (51) and Asaumi et al (82) reported that incidental findings were respectively identified in only 8.7% and 6.1% of patients when panoramic radiographs were reviewed. Granlund et al (66) reported an IF frequency of 2.2 IFs per panoramic image, a rate that is consistent with CBCT studies. However, in these three studies, there is no mention of airway, vascular or cervical vertebral findings, presumably because these anatomic structures are poorly visible in panoramic imaging. Consequently, between 75.0-100% of the reported findings were confined within the dento-alveolus (51,66,82); a region that dental clinicians should be competent in interpreting. This is in sharp contrast to CBCT studies.

*Clinical Significance*

Two fundamental matters are apparent upon review of the results, both relating to the clinical implications of the findings. Firstly, of clinical relevance is the percentage of IFs that require further follow-up and/or management from other medical/dental professionals and secondly is how many IFs alter the orthodontic management of the patient. It must be stated, that our study was based solely on radiographic interpretation, as no clinical information or other records were collected and/or considered. Therefore, inference into clinical significance is limited, specifically when relating to airway, sinus and TMJ findings, as clinical signs/symptoms play an integral role in determining the presence and severity of disease. Thus, the researchers elected to categorize findings as significant, only if they required immediate follow-up. The authors determined by consensus that 11.2% (94/842) of findings required immediate follow-up based on radiographic appearance. The number of findings determined to require immediate follow-up based on anatomic category are listed in table 4. Only adeno-tonsillar hypertrophy and sinus inflammation reported as severe by the OMFR were included as clinically significant. Examples of the most common significant findings include periapical rarefying osteitis, external root resorption, severe adeno-tonsillar hypertrophy, degenerative TMJ changes and enlargement of sella turcica. Regarding our sample, it can be argued that the identification of four of the seven findings (Figures 3,4,6 & 9) recommended for follow-up by our OMFR may have been difficult using only 2-D imaging traditionally utilized in orthodontics.

It is difficult to discern the impact of these IFs on future orthodontic management in our sample. Several other studies have investigated the impact of CBCT findings on subsequent treatment planning decisions. Based on these, it is suggested that CBCT may provide more reliable information than 2-D images, and that the interpretation of CBCT volumes may result in a different diagnosis and/or an alternative treatment plan for specific conditions such as root angulation, root resorption, third molar impaction and canine impaction (69,83-87).

Only one study has investigated the impact of CBCT IFs on treatment decisions regarding subsequent orthodontic treatment planning. Drage et al (20) determined that 45% of IFs required further follow-up, but less than 1% of IFs were likely to influence orthodontic management. However, further investigations are needed to assess the impact of IFs on the management decisions made by clinicians and their impact on subsequent orthodontic treatment.

*<u>Limitations</u>*

There are several limitations with this descriptive cross-sectional study. Only a single board-certified OMFR interpreted all CBCT scans. Thus, the interpretation reports are subject to reporter bias, with an unknown possibility of inconsistent diagnoses and errors. The subjective process of placing findings into anatomic categories can lead to differences when comparing studies in the literature. This is common when examining airway versus sinus findings, as some studies combined them into a single group, while they were separated in other studies, leading to either an under- or over-estimation of findings for certain anatomic regions. Another inadequacy is that limited clinical and no prior radiographic or histological information was obtained to determine if the identified CBCT findings had been previously detected; this analysis was outside the scope of this study. Also, no clinical correlations of the findings were obtained as this study exclusively evaluated only the image data. Ideally, forthcoming research will investigate the impact of these findings on subsequent orthodontic management in terms of potential alteration of the treatment plan or the need for further multi-disciplinary care.

### 3.5 Conclusions

This study confirms the high occurrence of incidental findings in large field of view maxillofacial CBCT scans in an orthodontic population. These findings suggest that the large majority are extragnathic findings, which can be normally considered outside the regions of interest and expertise of many dental clinicians. Specifically, incidental findings in the nasal-oro-pharyngeal and paranasal air sinuses are the most frequent. This underscores the need for comprehensive review of the entire data volume and the requisite to properly document all findings, regardless of the region of interest.

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# Chapter 4: The impact of maxillofacial findings using multi-planar and 3-D reconstructed views assessed by cone beam computed tomography

## 4.1 Introduction

Cone-beam computerized tomography (CBCT) provides 3D evaluation of craniofacial structures, and its use is becoming more widespread in the diagnosis and treatment planning in the field of orthodontics. The traditional approach to orthodontic imaging involves a panoramic radiograph and a lateral cephalogram for initial treatment planning. More recently, some orthodontic clinicians are implementing CBCT imaging to either supplement for the limitations of 2-D imaging or as a substitute for conventional 2-D imaging. Proper justification of CBCT imaging in orthodontics has been demonstrated in cases where suspicion of root resorption, supernumerary teeth, canine impaction, surgical planning and/or assessment of upper-airway obstruction (1).

Several studies (2-7) have contrasted the reliability of panoramic imaging with that of CBCT in orthodontic related-issues. Based on the literature, there is some evidence indicating that CBCT may offer improved diagnostic potential, which may lead to alternative orthodontic treatment plans. This literature also suggests that panoramic imaging may be unreliable when compared with CBCT imaging in specific circumstances, such as in the assessment of root angulation, root resorption, third molar impaction and canine impaction. In those cases, CBCT interpretation may result in a different diagnosis and/or an alternative treatment plan for these specific conditions.

When compared with conventional 2-D imaging, CBCT captures a much larger field of view. As such, there is an increased potential to identify incidental findings (IFs). IFs are defined as any discovered findings detected by any diagnostic imaging modality that are unrelated to the clinical indication for the imaging being performed (8). Arguably, as important as the detection, is the action that each unexpected finding invokes, in terms of deciding the necessity for further evaluation and/or management (9). As a large majority of IFs detected in CBCT imaging are extragnathic (10), the dental clinician may be unfamiliar with interpretation of anatomical structures outside the primary region of interest (11). The European Academy of Dento-maxillofacial Radiology (EADMFR) and the American Academy of Oral and Maxillofacial Radiology (AAOMR) outline that the entire volume must be interpreted regardless of region of interest, and, if the interpreting clinician is not highly experience in CBCT interpretation, a referral is required to an oral and maxillofacial radiologist (OMFR) or medical radiologist for review (12,13).

A number of studies in the literature have demonstrated the high frequency of IFs in large field CBCT imaging in various patient samples (11,14-21). Of these, only a few have investigated an orthodontic sample exclusively (14,17,21), in which reported rates of IFs range from 1.1-2.0 IFs per CBCT scan. Given the expected high rate of IFs, in combination with the relative novelty of CBCT imaging in clinical practice and lack of formal training requirements in CBCT interpretation in some regions and dental curriculums, it may be difficult to ensure that orthodontic clinicians who utilize CBCT are meeting interpretation standards. Specifically, the reliability or agreement among orthodontic clinicians in their assessment of the impact of maxillofacial incidental findings identified in CBCT imaging has not been evaluated.

### 4.2 Study Aim

This study aims to assess the agreement between orthodontic clinicians regarding the impact of maxillofacial incidental findings using multi-planar, TMJ, and 3-D reconstructed views in large field CBCT imaging. Specifically, it will evaluate the inter- and intra-rater agreement of orthodontic clinicians in their assessment of reported incidental findings in regard to both the need for additional follow-up and impact on future orthodontic treatment in large field maxillofacial CBCT imaging.

### 4.3 Methods and Materials

Approval to conduct this prospective, cross-sectional study was obtained from the University of Alberta Health Research Ethics Board panel. (Appendix 4)

The study sample consisted of 18 non-randomly selected large field maxillofacial CBCT volumes containing a reported total of 88 radiographic findings. All scans were associated with formal radiologic reports. The CBCT volumes were hand-selected from a larger sample of 427 consecutively obtained CBCT images acquired for orthodontic purposes at a private diagnostic imaging center (Edmonton Diagnostic Imaging- EDI - Edmonton, Alberta). The selected volumes were chosen to best represent the approximate distribution of expected findings based on anatomic region, as previously demonstrated in the literature (10,17,19,21). When appropriate, CBCT volumes containing findings that were specifically recommended for follow-up by the interpreting oral and maxillofacial radiologist (OMFR) were chosen with priority. However, the suggestion of further follow-up was removed from the radiologic reports, so as to not bias the subjects in subsequent decision making.

All selected CBCT images were acquired using an i-CAT Next Generation machine (Imaging Sciences International, Hatfield, PA, USA) with the patient in the upright position using similar imaging parameters (kilovoltage (kV): 120kV; millamperage (mA): 5mA, 0.3mm voxel size, exposure time 4.8-8.9 seconds, field of view of at least 17 cm (h) x 23 cm (d)). Each CBCT scan was associated with a formal radiologic interpretation provided by a single board-certified OMFR. All image volumes were reviewed by the OMFR using the imaging software InVivoDental 5.0 (Anatomage, San Jose, CA, USA). The radiologist was blinded to the objective of the present study, as they were not aware that their data would be retrospectively collected for analysis. All CBCT images were coded for blinding and randomized for prospective evaluation by an independent consultant who held the code hidden until all evaluations were completed.

Subject CBCT evaluation

Evaluation of the CBCT findings was completed independently by three evaluators; consisting of licensed orthodontic clinicians recruited via email solicitation on the basis of holding a high level of experience in CBCT interpretation. The evaluators had on average 7.6 years of CBCT usage and self-interpretation experience (Evaluator A-5 years; Evaluator B-10 years; Evaluator C-8 years). Consent for participation was obtained from all subjects using a prepared and approved standardized consent form. (Appendix 5)

The evaluators were initially introduced to an instruction and calibration session, where they completed a mock evaluation consisting of 3 sample CBCT volumes. They were directed in how to access and manipulate the CBCT volumes using the imaging software (Dolphin Imaging

11.5- Dolphin 3-D- Chatsworth, California, USA) and were able to ask any questions throughout the instruction session.

Upon completion of the calibration session, evaluators were instructed to review each CBCT volume; assessing both the CBCT volume using slices in all three planes of space (multi-planar, TMJ slices and 3-D volume rendering) and the modified associated radiologic report. Again, any suggestion of further follow-up by the OMFR was removed from the radiologic reports. For convenience, a data collection instrument was provided (Appendix 6), which listed all specific reported radiographic findings in each volume. For each finding, the evaluator was asked to locate the finding in the volume, and to answer yes or no to the following statements:

- This finding requires follow-up with dental or medical professional (yes/no);
- This finding may alter the orthodontic treatment plan (yes/no)

Evaluators were instructed to complete this for all findings in the radiologic report, and then proceed to the next CBCT volume. Sequential progression of CBCT volumes 1-18 occurred in this manner. All evaluators were blinded to the subject's identity and detailed clinical history, evaluated the images in a unique random order, and evaluated each image set on 2 separate occasions, separated by a minimum 30 day wash-out period. All evaluators reviewed the CBCT images using the same computer hardware (Lenovo-Intel HD graphics 2000, 1920x1080 resolution) and viewing monitor (Sharp Aquos 70 inch LCD television).

Statistical analysis

Reliability was determined by quantifying the level of agreement between the 3 evaluator's assessments for both research questions for all 88 findings using the binary response (yes/no) as the outcome measure. Cohen's kappa statistic (κ) was calculated to quantify intra-rater and inter-rater agreement globally for both statements. Kappa statistics were computed using SPSS Statistics software package (version 20.0, Chicago, USA). All 95% confidence intervals were obtained using bootstrap method, which utilizes the concept that inference about a population from sample data can be modeled by resampling the sample data and then performing inference. Raw agreement measures (proportion of overall agreement ($P_{Overall}$)) and proportions of specific agreement ($P_{Yes}$, $P_{No}$) were also calculated in cases of unbalanced marginal total distribution to overcome the possible paradox of the kappa statistic (22,23), using the value of 0.75 to represent the defining value, above which represents acceptable agreement. In addition, proportion of overall agreement was assessed separately for findings in each individual anatomic category for descriptive purposes.

Guidelines on what value of kappa reflects adequate agreement do exist in the literature (24) (Table 4-1) and are useful in interpretation; however, these guidelines are not universally accepted.

Table 4-1: Fleiss's interpretation of Cohen's Kappa values (24)

| Kappa score | Interpretation |
|---|---|
| <0.40 | Poor agreement |
| 0.4-0.75 | Fair-to-good agreement |
| >0.75 | Excellent agreement |

Sample size was determined using suggestions provided by Donner and Rotondi (25), in which they defined the following variables for inter-observer agreement studies with a binary outcome using multiple raters: $K_L$= minimal acceptable of kappa, $K_0$= the anticipated value of kappa, π= the probability that the rating is a success. To determine $K_0$, a small pilot study was performed utilizing the same research methodology outlined above, but assessed 3 orthodontic residents analyzing only 15 CBCT findings. From this, it was suggested that the value of $K_0$ should be K=0.8, while $K_L$ was set at 0.6. As a conservative strategy, π was set at 0.1. Using these values for 3 raters, Donner and Rotondi (21) suggest a minimal sample size of 78 radiographic findings, if the lower bound value of a 95% confidence interval is to be at least K=0.6.

**4.4 Results**

In total, 18 CBCT volumes were hand selected containing a total of 88 radiologic findings, and these findings were subdivided into the following previously determined anatomic categories (Table 4-2): 37 upper airway findings, 17 paranasal sinus findings, 12 dento-alveolar findings, 10 findings in the surrounding hard/soft tissues, 9 temporomandibular joint (TMJ) findings and 3 cervical vertebrae findings. The age of selected imaged subjects ranged from 6 to 33 years; the mean age was 14.6 years and the median age was 14.0 years.

All values of kappa are reported using the minimum and maximum obtained values of kappa ($K_{min,max}$). Using Fleiss's interpretation of kappa values (24), inter-examiner agreement in

Table 4-2: Number of findings included in the sample based on anatomic category.

| Incidental Finding Category | Frequency (n) |
|---|---|
| **Cervical Vertebrae** | **3 (3.4%)** |
| Cervical vertebrae fusion | 3 |
| **Dentoalveolar** | **12 (13.6%)** |
| Supernumerary | 3 |
| Hypodontia (excluding third molars) | 1 |
| Periapical osteitis | 2 |
| Impactions | 3 |
| Root resorption | 1 |
| Enlarged follicular space/ possible odontogenic cyst | 2 |
| **Nasal-Oral-Pharyngeal Airway** | **37 (42.1%)** |
| Enlarged inferior nasal turbinate | 5 |
| Irregular mucosal thickening of nasal cavity; possible polyps | 1 |
| Adenoid hypertrophy | 9 |
| Lingual tonsil hypertrophy | 1 |
| Palatine tonsil hypertrophy | 3 |
| Concha bullosa | 4 |
| Nasal mucosal thickening; rhinitis | 2 |
| Dystrophic calcification in tonsils | 3 |
| Nasal septal deviation | 6 |
| Polypoidal soft-tissue mass on soft palate | 1 |
| Soft tissue mass of L side pharynx and larynx | 1 |
| Complete opacification of the middle and superior meatuses | 1 |
| **Paranasal Sinuses** | **17 (19.3%)** |
| Localized inflammatory conditions (mucositis- sinusitis) | 9 |
| Pansinusitis | 2 |
| Ostia blockage | 1 |
| Retention pseudocyst | 3 |
| Paranasal sinus hypoplasia | 1 |
| Obliteration of maxillary, sphenoid, frontal, ethmoid sinuses with soft tissue/mucosal | 1 |
| **Surrounding Soft/Hard Tissues** | **10 (11.4%)** |
| Calcification of stylohyoid ligament | 1 |
| Fibrous dysplasia | 2 |
| Idiopathic osteosclerosis (dense bone island) | 4 |
| Mandibular tori | 1 |
| Enlarged sella turcica | 1 |
| Notch along the nasopharyngeal surface of the clivus suggestive of ectopic blood vessel | 1 |
| **Temporomandibular Joint** | **9 (10.2%)** |
| Condylar hypoplasia | 2 |
| Physiologic remodeling (flat margins, subchondral sclerosis) | 5 |
| Degenerative changes (osteophytes, erosions) | 2 |

the assessment of need for further follow-up of the reviewed findings was “fair-to-good” ($K_{min,max}$=0.606,0.710), and proportions of overall agreement ranged from 0.807-0.855 (Table 4-3). Inter-examiner agreement in the assessment of potential impact on future orthodontic treatment was also “fair-to-good” ($K_{min,max}$=0.643,0.684), with overall agreement ranging from 0.898-0.921 (Table 4-4).

Again, using Fleiss’s interpretation of kappa values (24), intra-examiner agreement regarding the need for further follow-up of the reviewed findings was “excellent” ($K_{min,max}$=0.846,0.909) (Table 4-5). Intra-examiner agreement regarding the impact of the reviewed findings on future orthodontic treatment was also “excellent” ($K_{min,max}$=0.860,0.910) (Table 4-6).

The proportion of overall inter-observer agreement in the assessment of need for further follow-up was assessed separately for findings in each individual anatomic category (Table 4-7). Only $P_{Overall}$ was assessed for descriptive purposes, because the sub-sample size for a few of the anatomic categories was very small. Proportion of overall agreement at $T_1$ was highest for dentoalveolar findings for all subjects ($P_{Overall}$ = 1.000), and lowest for cervical vertebrae findings for all subjects ($P_{Overall}$=0.666). The results were similar at $T_2$ (Table 4-7).

The proportion of overall intra-observer agreement in the assessment of need for further follow-up was also assessed separately for findings in each individual anatomic category (Table 4-8). Proportion of overall inter-observer agreement was fair-to-excellent, ranging from 0.700-1.000 between the 3 subjects. The lowest $P_{Overall}$ values occurred in the assessment of findings in the surrounding hard/soft tissues, ranging from $P_{Overall}$=0.700-0.800.

Table 4-3: Inter-examiner agreement regarding the need for further follow-up of the reviewed findings at time-point 1.

| **Ortho A vs. Ortho B** | | **Ortho B** | | | **K (95% CI)** | **$P_{Yes}$** | **$P_{No}$** | **$P_{Overall}$** |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Ortho A** | **No** | 46 | 17 | 63 | 0.606 (0.447, 0.758) | 0.755 | 0.844 | 0.807 |
| | **Yes** | 0 | 25 | 25 | | | | |
| | **Total** | 46 | 42 | 88 | | | | |

| **Ortho A vs. Ortho C** | | **Ortho C** | | | **K (95% CI)** | **$P_{Yes}$** | **$P_{No}$** | **$P_{Overall}$** |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Ortho A** | **No** | 55 | 8 | 63 | 0.710 (0.531, 0.855) | 0.800 | 0.909 | 0.885 |
| | **Yes** | 3 | 22 | 25 | | | | |
| | **Total** | 58 | 30 | 88 | | | | |

| **Ortho B vs. Ortho C** | | **Ortho C** | | | **K (95% CI)** | **$P_{Yes}$** | **$P_{No}$** | **$P_{Overall}$** |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Ortho A** | **No** | 45 | 1 | 46 | 0.677 (0.525, 0.815) | 0.806 | 0.865 | 0.841 |
| | **Yes** | 13 | 29 | 42 | | | | |
| | **Total** | 58 | 30 | 88 | | | | |

K= kappa statistic
CI= confidence Interval
$P_{yes}$= proportion of specific agreement for yes ratings
$P_{No}$= proportion of specific agreement for no ratings
$P_{Overall}$= proportion of overall agreement

Table 4-4: Inter-examiner agreement regarding the potential impact of the reviewed findings on future orthodontic treatment at time-point 1.

| **Ortho A vs. Ortho B** | | **Ortho B** | | | **K (95% CI)** | $P_{Yes}$ | $P_{No}$ | $P_{Overall}$ |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Ortho A** | **No** | 66 | 8 | 74 | 0.684 (0.466, 0.861) | 0.778 | 0.943 | 0.909 |
| | **Yes** | 0 | 14 | 14 | | | | |
| | **Total** | 66 | 22 | 88 | | | | |

| **Ortho A vs. Ortho C** | | **Ortho C** | | | **K (95% CI)** | $P_{Yes}$ | $P_{No}$ | $P_{Overall}$ |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Ortho A** | **No** | 71 | 5 | 76 | 0.674 (0.412, 0.876) | 0.741 | 0.953 | 0.921 |
| | **Yes** | 2 | 10 | 12 | | | | |
| | **Total** | 73 | 15 | 88 | | | | |

| **Ortho B vs. Ortho C** | | **Ortho C** | | | **κ K (95% CI)** | $P_{Yes}$ | $P_{No}$ | $P_{Overall}$ |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Ortho A** | **No** | 66 | 2 | 68 | 0.643 (0.441, 0.831) | 0.769 | 0.936 | 0.898 |
| | **Yes** | 7 | 13 | 20 | | | | |
| | **Total** | 73 | 15 | 88 | | | | |

K= kappa statistic
CI= confidence Interval
$P_{yes}$= proportion of specific agreement for yes ratings
$P_{No}$= proportion of specific agreement for no ratings
$P_{Overall}$= proportion of overall agreement

Table 4-5: Intra-examiner agreement regarding the need for further follow-up of the reviewed findings.

| **Orthodontist A** | | **Time 2** | | | **K (95% CI)** | **$P_{Yes}$** | **$P_{No}$** | **$P_{Overall}$** |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Time 1** | **No** | 60 | 3 | 63 | 0.891 (0.774, 0.976) | 0.923 | 0.968 | 0.955 |
| | **Yes** | 1 | 24 | 25 | | | | |
| | **Total** | 61 | 27 | 88 | | | | |

| **Orthodontist B** | | **Time 2** | | | **K (95% CI)** | **$P_{Yes}$** | **$P_{No}$** | **$P_{Overall}$** |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Time 1** | **No** | 46 | 0 | 46 | 0.909 (0.803, 0.977) | 0.949 | 0.958 | 0.955 |
| | **Yes** | 4 | 38 | 42 | | | | |
| | **Total** | 50 | 38 | 88 | | | | |

| **Orthodontist C** | | **Time 2** | | | **K (95% CI)** | **$P_{Yes}$** | **$P_{No}$** | **$P_{Overall}$** |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Time 1** | **No** | 56 | 2 | 58 | 0.846 (0.716, 0.952) | 0.897 | 0.949 | 0.932 |
| | **Yes** | 4 | 26 | 30 | | | | |
| | **Total** | 60 | 28 | 88 | | | | |

K= kappa statistic
CI= confidence Interval
$P_{yes}$= proportion of specific agreement for yes ratings
$P_{No}$= proportion of specific agreement for no ratings
$P_{Overall}$= proportion of overall agreement

Table 4-6: Intra-examiner agreement regarding the impact of the reviewed findings on future orthodontic treatment.

| Orthodontist A | | Time 2 | | | K (95% CI) | $P_{Yes}$ | $P_{No}$ | $P_{Overall}$ |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Time 1** | **No** | 73 | 1 | 74 | 0.860 (0.653, 0.1.000) | 0.846 | 0.973 | 0.955 |
| | **Yes** | 3 | 11 | 14 | | | | |
| | **Total** | 76 | 12 | 88 | | | | |

| Orthodontist B | | Time 2 | | | K (95% CI) | $P_{Yes}$ | $P_{No}$ | $P_{Overall}$ |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Time 1** | **No** | 66 | 0 | 66 | 0.875 (0.730, 0.974) | 0.952 | 0.985 | 0.977 |
| | **Yes** | 2 | 20 | 22 | | | | |
| | **Total** | 68 | 20 | 88 | | | | |

| Orthodontist C | | Time 2 | | | K (95% CI) | $P_{Yes}$ | $P_{No}$ | $P_{Overall}$ |
|---|---|---|---|---|---|---|---|---|
| | | **No (n)** | **Yes (n)** | **Total** | | | | |
| **Time 1** | **No** | 73 | 0 | 73 | 0.910 (0.752, 1.000) | 0.931 | 0.993 | 0.989 |
| | **Yes** | 1 | 14 | 15 | | | | |
| | **Total** | 74 | 14 | 88 | | | | |

K= kappa statistic
CI= confidence Interval
$P_{yes}$= proportion of specific agreement for yes ratings
$P_{No}$= proportion of specific agreement for no ratings
$P_{Overall}$= proportion of overall agreement

Table 4-7: Inter-examiner agreement in the assessment of the need for further follow-up based on anatomic category at time 1 and time 2.

| **Ortho A vs. Ortho B** | **Anatomic Category** | **N** | **$P_{Overall}$ at $T_1$** | **$P_{Overall}$ at $T_2$** |
|---|---|---|---|---|
| | Cervical Vertebrae | 3 | 0.666 | 0.666 |
| | Dentoalveolar | 12 | 1.000 | 1.000 |
| | Nasopharyngeal Airway | 37 | 0.778 | 0.861 |
| | Paranasal Sinuses | 17 | 0.778 | 0.778 |
| | Surrounding Hard/Soft | 10 | 0.800 | 0.600 |
| | Temporomandibular Joint | 9 | 0.667 | 0.778 |
| **Ortho A vs. Ortho C** | **Anatomic Category** | **N** | **$P_{Overall}$** | **$P_{Overall}$** |
| | Cervical Vertebrae | 3 | 0.666 | 0.666 |
| | Dentoalveolar | 12 | 1.000 | 1.000 |
| | Nasopharyngeal Airway | 37 | 0.889 | 0.861 |
| | Paranasal Sinuses | 17 | 0.833 | 0.889 |
| | Surrounding Hard/Soft | 10 | 0.800 | 0.900 |
| | Temporomandibular Joint | 9 | 0.889 | 0.889 |
| **Ortho B vs. Ortho C** | **Anatomic Category** | **N** | **$P_{Overall}$** | **$P_{Overall}$** |
| | Cervical Vertebrae | 3 | 0.666 | 0.666 |
| | Dentoalveolar | 12 | 1.000 | 1.000 |
| | Nasopharyngeal Airway | 37 | 0.778 | 0.889 |
| | Paranasal Sinuses | 17 | 0.944 | 0.889 |
| | Surrounding Hard/Soft | 10 | 0.700 | 0.700 |
| | Temporomandibular Joint | 9 | 0.778 | 0.778 |

N= number of findings in the specific anatomic category
$P_{Overall}$= proportion of overall agreement
$T_1$= timepoint 1
$T_2$= timepoint 2

Table 4-8: Intra-examiner agreement in the assessment of the need for further follow-up based on anatomic category.

| Orthodontist A | Anatomic Category | N | $P_{Overall}$ |
|---|---|---|---|
| | Cervical Vertebrae | 3 | 1.000 |
| | Dentoalveolar | 12 | 1.000 |
| | Nasopharyngeal Airway | 37 | 0.972 |
| | Paranasal Sinuses | 17 | 0.944 |
| | Surrounding Hard/Soft | 10 | 0.800 |
| | Temporomandibular Joint | 9 | 1.000 |
| **Orthodontist B** | **Anatomic Category** | **(n)** | $P_{Overall}$ |
| | Cervical Vertebrae | 3 | 1.000 |
| | Dentoalveolar | 12 | 1.000 |
| | Nasopharyngeal Airway | 37 | 0.944 |
| | Paranasal Sinuses | 17 | 1.000 |
| | Surrounding Hard/Soft | 10 | 0.800 |
| | Temporomandibular Joint | 9 | 0.889 |
| **Orthodontist C** | **Anatomic Category** | **(n)** | $P_{Overall}$ |
| | Cervical Vertebrae | 3 | 1.000 |
| | Dentoalveolar | 12 | 1.000 |
| | Nasopharyngeal Airway | 37 | 1.000 |
| | Paranasal Sinuses | 17 | 0.944 |
| | Surrounding Hard/Soft | 10 | 0.800 |
| | Temporomandibular Joint | 9 | 0.889 |

N= number of findings in the specific anatomic category
$P_{Overall}$= proportion of overall agreement

### 4.5 Discussion

This study was designed to assess the inter- and intra-rater agreement of orthodontic clinicians in their assessment of reported findings in regard to both the need for additional follow-up and impact on future orthodontic treatment in large field maxillofacial CBCT imaging. Given that orthodontic clinicians predominantly treat healthy young patients, the array of incidental findings was chosen to be representative of findings that could typically present in an orthodontic patient pool. Thus, the chosen findings were designed to test the ability of orthodontists in their assessment of the clinical significance of reasonably common findings that could occur in practice. It could be argued that the impact of findings such as dystrophic calcification of tonsils is insignificant, however, it is valuable to the orthodontic community to assess if clinicians can and do agree regarding the significance of all finding types.

When using only radiographic images, without supplementation from either clinical history or examination, the assessment of clinical significance is challenging, and has limitations. However, this study was designed to simulate one component of clinical practice in which the orthodontic clinician, who should be following the EADMFR recommended guidelines (26), receives a radiographic report from the OMFR, and is faced with clinical decisions on need of further management. The decision was made to evaluate using the yes/no binary response to the two research questions to assess the clinical significance of CBCT findings, accepting the limitation that the clinical information was provided by radiographic images only.

Inter-examiner Agreement

All values of Kappa are reported using the minimum and maximum obtained values ($K_{min,max}$). The subjects exhibited “fair-to-good” inter-examiner agreement in the assessment of the need for further follow-up of the included findings ($K_{min,max}$=0.606,0.710; $P_{overall}$=0.807-0.885) (Table 4-3). It must be taken into account that the lower bound value of the 95% confidence intervals are below the anticipated $K_L$= 0.6, and thus, these results must be interpreted with caution. Estimates of the conditional probabilities supported the acceptable level total proportional agreement. Evaluators A and C had the highest agreement scores in terms of kappa (0.710) and overall agreement (0.885).

An important observation can be made when examining agreement scores ($P_{overall}$) based on individual anatomic categories. For both $T_1$ and $T_2$, it can be suggested that the inter-examiner agreement between the subjects based on $P_{overall}$ was “perfect” for findings in the dentoalveolar category. This is in contrast with $P_{overall}$ scores for extragnathic findings (i.e. outside the dentition and alveolus), which ranged from $P_{overall}$=0.666 for findings in the cervical vertebrae to $P_{overall}$=0.944 for paranasal sinus findings. That is, no other anatomic category demonstrated perfect agreement between examiners. Perhaps this can be explained based on the basic dental training received and comfort level of dental professionals in evaluating radiographic findings in the dentoalveolar region; whilst it may be outside the usual comfort zone to interpret or evaluate findings in extragnathic regions. The decision to refer or follow-up with certain radiographic findings that the clinician may be unfamiliar with can be difficult. This is compared to common findings in which clinicians should be well adept, and thus it would be anticipated that agreement should be higher for these common dental findings in the dentoalveolar region. However, these results are merely descriptive in nature and must be interpreted with caution, as the sub-sample size of some anatomic categories was very small.

The evaluators also exhibited “fair-to-good” inter-examiner agreement in the assessment of potential impact on subsequent orthodontic treatment ($K_{min,max}$=0.643,0.684; $P_{overall}$=0.898-0.921) (Table 4-4). Subjects A and B had the highest agreement scores in terms of kappa (0.724).

This modest level of inter-rater agreement may have potential consequences. Possibly, the differences in clinician decision making in how each radiologic finding is managed may result in additional medical or dental costs associated with further imaging or examinations. If follow-up were warranted, this would be prudent. However, if unnecessary, this could lead to increased patient burden. Additionally, if certain findings do indeed require follow-up, it would be paramount if agreement between clinicians were high, thus reducing the risk of failed follow-up when necessary. In a study by Ahmed et al (27), it was demonstrated that CBCT interpretation skills can be improved through training. However, they only assessed the ability of clinicians to directly identify findings in CBCT imaging, and did not assess their ability to determine their clinical significance. Arguably, it is equally important for clinicians to discern clinical significance in terms of patient management, but it is also likely that this skill can be acquired with standardized training.

It must be mentioned that Cohen's kappa statistic is a statistical measure of two-rater agreement for qualitative variables (28), applied to determine both inter- and intra-rater agreement. Specifically, it is a ratio of the proportion of observed non-chance agreements to the proportion of possible non-chance agreements. Thus, kappa statistic is designed to be a chance-corrected measure of agreement and is considered to be a more robust measure than total proportional agreement, since the agreement occurring by chance is taken into account. However, there are limitations to kappa, which can lead to interpretation paradox. This can occur when unbalanced marginal totals produce misleading values of the kappa statistic (22). Since the marginal totals are symmetrically unbalanced in our study, the kappa values could be inflated.

The proportions of specific agreement estimate the conditional probability given that one of the raters, randomly selected, makes a "yes" or "no" rating, that the other rater will also do so. A high value for both $P_{Yes}$ and $P_{No}$ would imply that the observed level of agreement is higher than would occur by chance, and is required to consider agreement satisfactory (22,23). It has been suggested by Cicchetti et al (21) that for better understanding of individual results, the value of kappa should always be accompanied by separate individual values of $P_{Yes}$ and $P_{No}$ to help overcome the possible interpretation paradox. In our study, all proportions of specific agreement support the agreement levels suggested by the kappa values.

Intra-examiner Agreement

The evaluators exhibited "excellent" intra-examiner agreement in the assessment of CBCT findings regarding both need for follow-up ($K_{min,max}$=0.846,0.909; $P_{overall}$=0.932-0.955) and potential impact on future orthodontic treatment ($K_{min,max}$=0.860,0.910; $P_{overall}$=0.955-0.989) (Table 4-5 and Table 4-6). In the assessment of need for further follow-up, evaluators A and B had the highest level of intra-examiner agreement with K=0.891 and K=0.909 respectively. This is in contrast with the between-subject agreement, in that the with-in subject agreement is higher. Essentially, the clinicians demonstrated a moderate level of agreement between one another, but demonstrated excellent agreement within themselves between the two time-points. This implies that there is potential for inadvertent differences in management due to dissimilarities in how clinicians view clinical significance. Findings that particular clinicians consider significant, may be viewed as insignificant by others. This could cause unnecessary anxiety to the patient and family, and/or could add unnecessary costs to health care.

When dividing the findings into anatomic categories, intra-examiner agreement, using proportion of overall agreement, was also “excellent” ranging from 0.800-1.000 (Table 4-8). For each subject, $P_{overall}$=1.000 for both dentoalveolar findings and cervical vertebrae findings. While, findings of surrounding soft/hard tissues had the lowest $P_{overall}$=0.800 for all 3 evaluators. Therefore, the pattern of agreement observed was similar to between-subject agreement. Specifically, with the evaluators demonstrating higher levels of intra-examiner consistency for findings in the dentoalveolar category.

Although this study does demonstrate acceptable levels of agreement, of concern is the FOV size, or specifically which anatomic region(s) of the head the neck should be included in the image based on the information required by the clinician. The basic principles outlined by the EADMFR indicate that CBCT equipment should offer choices in the FOV, and that the volume size should be reduced to the smallest possible field while still ensuring compatibility with the clinical indication, to protect the patient from unnecessary radiation (26). Given that tested evaluators demonstrated highest levels of agreement for dentoalveolar findings, it is suggested that the FOV be reduced to minimize the extent of extragnathic structures in the captured area. In other words, to use the smallest FOV that captures only the localized anatomic region of interest. This would limit the need for interpretation of extragnathic regions in which the clinician may lack experience.

CBCT interpretation training, including knowledge of clinical significance of all possible findings, should become fundamental in orthodontic residency programs. The improved abilities of the orthodontist in interpreting CBCT volumes could be beneficial in enhancing and directing further patient care as warranted, and additionally in orthodontic diagnosis and treatment planning on the basis of the CBCT-derived information. Establishing a baseline of CBCT competence would aid the clinician in review of findings presented by the radiologist, while the OMFR should remain the primary diagnostician.

Limitations

The limitations of this study must be recognized. Notably, this study was intended to assess agreement, but this is not equivalent to accuracy. Therefore, despite the moderate-to-high levels of agreement demonstrated by the evaluators on the two research questions, it does not imply that their decisions are indeed correct. To make such claims, a gold standard would have to be established such that comparisons could be made. This is not feasible as interpretation of the two research questions may have a degree of subjectivity, making the establishment of a gold standard difficult. The OMFR report does indeed serve as the gold standard for radiologic finding identification, but not for determining clinical significance in terms of further patient management.

There is the potential that voxel size may impact some clinical decisions regarding certain radiographic findings, and that specific findings may be more impacted than others.

Image parameters were largely held constant in this study. In particular, 0.3mm voxel size was utilized for all included CBCT scans. In our study, there was a diverse range of radiographic findings, making a clear standard imaging protocol difficult to determine (29). However, we believe that changing the voxel size would have minimal impact on the findings of this study, as it has been demonstrated that 0.3mm voxel size is appropriate for accurate diagnosis of certain radiographic findings, including root resorption (30).

Clinical significance of findings was assessed using only the CBCT volumes and the associated radiologic reports. No medical history or clinical information was provided. Therefore, this likely limits the level of evaluation capable by the subjects. Thus, we may be misrepresenting (over- or underestimating) the level of agreement between clinicians by not providing the comprehensive clinical information.

A fundamental aspect of our study was the rationale. Current regulations in many regions do not require the clinician to demonstrate any specific level of training or competence in CBCT interpretation. Therefore, there may be no standard of agreement in terms of level of interpretation and/or management of identified findings. To investigate above the baseline level of "minimal knowledge", we selected evaluators experienced in CBCT use. Perhaps it would be more prudent to also include subjects that do represent the baseline knowledge, so that the results could be more broadly applied to the population of orthodontic clinicians. It can be hypothesized that less experienced clinicians regarding CBCT usage may have lower agreement values. This investigation was limited to only 3 evaluators. Reasons for this include more efficient interpretation of agreement assessed by kappa statistic and simpler logistics in recruitment of evaluators. The use of 3 evaluators was deemed satisfactory when comparing other agreement studies in the literature. There would likely be minimal impact of having more than three evaluators, given that the binary yes/no response focused on the representative number of IFs, rather than the representativeness of evaluators.

Random selection was not utilized for either the selection of the CBCT volumes or subject selection. Instead, hand-selection was utilized to meet two objectives. Firstly, CBCT volumes were hand-selected from a large sample to obtain a collection of findings that accurately represented the anatomical distribution reported in the literature, to avoid over- or under-representation of a specific category. Secondly, orthodontic clinicians were hand-selected based on a high level of CBCT experience. This selection bias likely limits the extent to which the conclusions can be applied to the population of currently practicing orthodontic clinicians.

**4.6 Conclusions**

The following conclusions can be made concerning the tested evaluators who were considered experienced in CBCT use:

- Evaluators demonstrated “fair-to-good” inter-rater agreement in the assessment of CBCT findings in terms of the need for further follow-up
- Evaluators demonstrated “fair-to-good” inter-rater agreement in the assessment of CBCT findings regarding their potential impact on future orthodontic treatment
- Evaluators demonstrated “excellent” intra-rater agreement in the assessment of CBCT findings regarding need for follow-up
- Evaluators demonstrated “excellent” intra-rater agreement in the assessment of CBCT findings regarding the potential impact on future orthodontic treatment

- Evaluators demonstrated higher levels of agreement for dentoalveolar findings compared with all other extragnathic regions when assessing clinical significance

**4.7 References**


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# Chapter 5: Conclusions

## 5.1 Research Questions

The primary research questions of this study were:

1. What are the frequency, location and characteristics of incidental findings in CBCT imaging in an orthodontic population imaged for preliminary orthodontic records?
2. For any given age, are the odds of identifying an incidental finding in CBCT imaging greater for either gender, for any of individual anatomic regions?
3. What is the intra-rater and inter-rater reliability of orthodontic clinicians in the determination of the need for further follow-up and potential impact on future orthodontic management of findings in CBCT imaging?

## 5.2 Conclusions

From Chapter 2 of the study, the following can be suggested:

- IFs are relatively frequent in CBCT imaging, and they vary considerably in respect to their frequency and nature
- The most commonly identified individual IFs in CBCT imaging were sinusitis/mucosal thickening (7.7-41.7%), pineal gland calcification (0.5-19.2%), impacted third molars (18.8%), mucous retention cysts (2.9-17.0%), TMJ condylar degenerative changes (3.9-21.7%) and concha bullosa (3.1-21.7%)

From Chapter 3 of the study, the following can be suggested:

- A total of 842 incidental findings were reported in 427 CBCT scans for a rate of 1.97 findings/scan
- The most prevalent findings were those located in the airway (42.3%), followed by the paranasal sinuses (30.9%), dentoalveolar (14.7%), surrounding hard/soft tissues (4.0%), TMJ (6.4%) and cervical vertebrae (1.3%) regions
- Non-odontogenic findings represented 718 of the 842 (85.3%) findings, and thus represented the majority of the findings
- When controlling for age, only one anatomic category demonstrated statistically significant differences between males and females. Specifically, when controlling for age, females were 2.55 times (P=<0.001, 95% CI [1.29,5.03]) more likely to have a TMJ finding than men.

From Chapter 4 of the study, the following can be suggested:

- Subjects demonstrated “fair-to-good” inter-rater agreement in the assessment of CBCT findings in terms of the need for further follow-up
- Subjects demonstrated “fair-to-good” inter-rater agreement in the assessment of CBCT findings regarding their potential impact on future orthodontic treatment
- Subjects demonstrated “excellent” intra-rater agreement in the assessment of CBCT findings regarding both need for follow-up and potential impact on future orthodontic treatment

- Subjects demonstrated higher levels of agreement for dentoalveolar findings compared with all other extragnathic regions when assessing clinical significance

**5.3 Directions for Future Research**

Firstly, an assessment to analyze the accuracy of orthodontic clinicians in the identification of findings in CBCT imaging compared to the gold standard of an OMFR report must occur. If clinicians are to self-interpret CBCT volumes, levels of competency must be established, along with investigation of anatomic regions that clinicians may be deficient in interpreting. This could help influence both future CBCT continuing education programs for practicing clinicians and in the establishment of formal CBCT curriculums for dental education programs.

Secondly, further investigation must occur regarding the establishment of a standardized method of reporting and defining the term “incidental finding” to be used both clinically and in research. Currently, there is some discrepancy between the medical and dental professions, in that, it appears that medical professionals do not often report dentally relevant findings in medical CT reports. This makes cross-comparison between medical and dental literature difficult. Even within the dental literature, discrepancies occasionally exist regarding the placement of certain incidental findings into specific categories. At least two methods for reporting the incidence of incidental findings are described in the literature; i) by describing the absolute number of IFs detected or ii) describing the number of CBCT scans that contain IFs. The former method, using the absolute number of IFs, is favored because it is highly likely for multiple IFs to be detected in a single CBCT scan.

Finally, to test the educational implications of this project, a group of orthodontists with limited baseline CBCT knowledge could be examined twice using a similar CBCT series. However, in between the two time points, the subjects could receive standardized CBCT interpretation training. Then, comparisons in agreement levels could be investigated between pre- and post-training. Analysis of the subject's performance may reveal an improvement in the final agreement of clinical significance.

# Appendix

## Appendix 1: Search strategies for various databases

| Database | Key Words & Mesh Terms Used | Number of Results |
|---|---|---|
| **MEDLINE via OvidSP** (1948 to July 14th, 2012)<br><br>Limits: none | 1) cone-beam computed tomography [MeSH] OR cone beam computed tomography OR CBCT OR cone beam OR 3D cone beam OR cone-beam OR digital volumetric tomography OR volumetric computed tomography OR digital volumetric reconstruction OR cone beam computer assisted tomography OR cone beam computerized tomography OR spiral cone-beam computed tomography<br>2) incidental findings [MeSH] OR incidental finding* OR occult finding OR abnormal finding OR unexpected finding<br>3) skull base [MeSH] OR skull [MeSH] OR cervical vertebrae [MeSH] OR head [MeSH] OR neck [MeSH] OR brain [MeSH] OR skull base OR skull OR cervical vertebrae OR cervical spine OR (maxillofacial region) OR (head and neck) OR (paranasal sinus*) OR dental OR orthodontic* OR face OR brain OR intracranial OR trauma OR mandible OR maxilla<br>4) #1 AND #2 AND #3 | 17 |
| **EMBASE Via OvidSP** (1980 to July 14th, 2012)<br><br>Limits*:* none | Same search strategy at MEDLINE via OvidSP | 15 |
| **PubMed** (1950 to July 14th, 2012)<br><br>Limits: none | 1) cone-beam computed tomography [MeSH] OR spiral cone-beam computed tomography [MeSH] OR cone beam computed tomography OR CBCT OR cone beam OR cone-beam OR digital volumetric tomography OR volumetric computed tomography OR digital volumetric reconstruction OR cone beam computer assisted tomography OR cone beam computerized tomography OR spiral cone-beam computed tomography<br>2) incidental findings [MeSH] OR incidental OR incidental finding* OR occult finding OR abnormal finding OR unexpected finding<br>3) #1 AND # 2 | 43 |
| **Scopus (Elsevier)** (1960 to July 14th, 2012)<br><br>Limits: none | 1) "cone beam computed tomography" OR "CBCT" OR "cone beam" OR "digital volumetric tomography" OR "volumetric computed tomography" OR "digital volumetric reconstruction" OR "cone beam computer assisted tomography" OR "cone beam computerized tomography"<br>2) “incidental finding*” OR “occult finding” OR “abnormal finding” OR “unexpected finding”<br>3) #1 AND #2 | 24 |
| **Web of Science** (1898 to July 14th, 2012)<br><br>**Limits: none** | 1) "cone beam computed tomography" OR "CBCT" OR "cone beam" OR “cone-beam” OR "digital volumetric tomography" OR "volumetric computed tomography" OR "digital volumetric reconstruction" OR "cone beam computer assisted tomography" OR "cone beam computerized tomography"<br>2) “incidental finding*” OR “occult finding” OR “abnormal finding” OR “unexpected finding”<br>3) #1 AND #2 | 11 |
| **Cochrane Library** (1991 to the 2nd quarter of 2012) | 1) cone-beam computed tomography [MeSH] OR cone beam computed tomography OR CBCT OR cone beam OR 3D cone beam OR cone-beam OR digital volumetric tomography OR volumetric computed tomography OR digital volumetric reconstruction OR cone beam computer assisted tomography OR cone beam computerized tomography OR spiral cone-beam computed tomography<br>2) incidental findings [MeSH] OR incidental finding* OR occult finding OR abnormal finding OR unexpected finding<br>3) #1 AND #2 | 14 |

## Appendix 2: STROBE Statement checklist of items for assessment of cross-sectional studies

| | Item No | Recommendation |
|---|---|---|
| **Title and abstract** | 1 | (*a*) Indicate the study's design with a commonly used term in the title or the abstract |
| | | (*b*) Provide in the abstract an informative and balanced summary of what was done and what was found |
| **Introduction** | | |
| Background/rationale | 2 | Explain the scientific background and rationale for the investigation being reported |
| Objectives | 3 | State specific objectives, including any pre-specified hypotheses |
| **Methods** | | |
| Study design | 4 | Present key elements of study design early in the paper |
| Setting | 5 | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| Participants | 6 | (*a*) Give the eligibility criteria, and the sources and methods of selection of participants |
| Variables | 7 | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| Data sources/ measurement | 8* | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| Bias | 9 | Describe any efforts to address potential sources of bias |
| Study size | 10 | Explain how the study size was arrived at |
| Quantitative variables | 11 | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| Statistical methods | 12 | (*a*) Describe all statistical methods, including those used to control for confounding |
| | | (*b*) Describe any methods used to examine subgroups and interactions |
| | | (*c*) Explain how missing data were addressed |
| | | (*d*) If applicable, describe analytical methods taking account of sampling strategy |
| | | (*e*) Describe any sensitivity analyses |
| **Results** | | |
| Participants | 13* | (a) Report numbers of individuals at each stage of study—e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed |
| | | (b) Give reasons for non-participation at each stage |
| | | (c) Consider use of a flow diagram |
| Descriptive data | 14* | (a) Give characteristics of study participants (e.g. demographic, clinical, social) and information on exposures and potential confounders |
| | | (b) Indicate number of participants with missing data for each variable of interest |
| Outcome data | 15* | Report numbers of outcome events or summary measures |
| Main results | 16 | (*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included |
| | | (*b*) Report category boundaries when continuous variables were categorized |

| | | |
|---|---|---|
| | | (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period |
| Other analyses | 17 | Report other analyses done—e.g. analyses of subgroups and interactions, and sensitivity analyses |
| **Discussion** | | |
| Key results | 18 | Summarize key results with reference to study objectives |
| Limitations | 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias |
| Interpretation | 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence |
| Generalizability | 21 | Discuss the generalizability (external validity) of the study results |
| **Other information** | | |
| Funding | 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based |

**Appendix 3.: Ethics approval for retrospective chart review.**

# Approval Form

Date: December 12th, 2012
Principal Investigator: Dr. Carlos Flores Mir
Study ID: Pro00032248

Study Title: Frequency and characteristics of incidental findings using CBCT in an orthodontic population upon imaging for preliminary orthodontic records

Approval Expiry Date: December 11th, 2013

Thank you for submitting the above study to the Health Research Ethics Board -Health Panel. Your application, including revisions received December 8, 2012, has been reviewed and approved on behalf of the committee.

The Health Research Ethics Board assessed all matters required by section 50(1)(a) of the Health Information Act. It has been determined that the research described in the ethics application is a retrospective chart review for which subject consent for access to personally identifiable health information would not be reasonable, feasible or practical. Subject consent therefore is not required for access to personally identifiable health information described in the ethics application.

In order to comply with the Health Information Act, a copy of the approval form is being sent to the Office of the Information and Privacy Commissioner.

A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew on or before the renewal expiry date (December 11, 2013), you will have to re-submit an ethics application.

Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries regarding Alberta Health approvals should be directed to (780) 407-604. Enquiries regarding Covenant Health approvals should be directed to (780) 735-2274.

Sincerely,

Dr. Jana Rieger

Chair, Health Research Ethics Board - Health Panel

*Note: This correspondence includes an electronic signature (validation and approval via an online system).*

**Appendix 4: Ethics approval for prospective reliability study.**

# Approval Form

Date: July 10, 2013
Principal Investigator: Dr. Carlos Flores Mir
Study ID: Pro00039467

Study Title: The impact of maxillofacial findings using multi-planar and 3-D reconstructed views in cone beam computed tomography

Approval Expiry Date: July 9, 2014

Thank you for submitting the above study to the Health Research Ethics Board -Health Panel. Your application has been reviewed and approved on behalf of the committee.

A renewal report must be submitted next year prior to the expiry of this approval if your study still requires ethics approval. If you do not renew on or before the renewal expiry date, you will have to re-submit an ethics application.

Approval by the Health Research Ethics Board does not encompass authorization to access the patients, staff or resources of Alberta Health Services or other local health care institutions for the purposes of the research. Enquiries regarding Alberta Health Services approvals should be directed to (780) 407-6041. Enquiries regarding Covenant Health should be directed to (780) 735-2274.

Sincerely,

Dr. Glen J. Pearson, BSc, BScPhm, PharmD, FCSHP
Associate Chair, Health Research Ethics Board - Health Panel

*Note: This correspondence includes an electronic signature (validation and approval via an online system).*

**Appendix 5: Consent form for Orthodontic clinicians**

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# CONSENT TO PARTICIPATE IN RESEARCH

**Reliability of orthodontists in determination of clinical significance of maxillofacial findings using multi-planar and 3-D reconstructed views in CBCT**

You are asked to participate in a research study by the department of Dentistry at the University of Alberta. You have been asked to participate in this study because you are a certified orthodontic clinician. Your participation in this study is entirely voluntary. You should read the information below, and ask questions about anything you do not understand, before deciding whether or not to participate.

## Identification of the Investigators

If you have any questions about the research, please contact any of the investigators listed below:

**Supervisor**: Dr. Carlos Flores-Mir……………………………………………carlosflores@ualberta.ca
**Orthodontic Graduate Masters Student**: Ryan Edwards…………... rje@ualberta.ca

## Purpose of Study & Research Question

**Research Question:** What is the reliability of orthodontists in the determination of clinical significance of findings using multi-planar and 3-D reconstructed views in CBCT imaging? (i.e. do clinicians agree on the clinical significance of findings in CBCT?)

Specifically, we hope to accomplish the following:

- To better understand differences between the types and locations of findings that lead clinicians to assign clinical significance.
- To investigate the level of inter- and intra-rater agreement between clinicians on what findings require follow-up.

## Procedures

If you volunteer to participate in this study, it is expected to take <u>60-90 minutes</u> of your time, as you will be asked to do the following:

- Review multi-planar and 3-D reconstructed views using Dolphin 3-D imaging for a series of CBCT images, as well as the associated radiologic reports generated from a single oral and maxillofacial radiologist

- For each reported finding, use the radiographic report and its radiographic appearance in the 3-D and multi-planar views, to answer **<u>Yes or No</u>** to the following statements:

  - This finding requires follow-up with dental or medical professional **(yes/no)?**
  - This finding may alter the orthodontic treatment plan **(yes/no)?**

## Privacy and Confidentiality

No personal information about you, or provided by you during this research, will be disclosed to others. When/if the results of the research are published or discussed in conferences, no information will be included that would reveal your identity. Collected information will be stored in an encrypted and password protected computer inside the Department of Dentistry (ECHA - 5th Floor). Data will be stored for a time period of 5 years.

## Direct Benefit or Risk of Participation

Involvement will benefit participants by gaining insight into what findings are considered to warrant further investigation, what findings impact orthodontic diagnosis/treatment planning and allow for comparisons of consistency in the assessment of clinical significance. However, you may not get any benefit from being in this research study. No risks of participation are expected.

## Participation and Withdrawal

Your participation in this research is entirely <u>VOLUNTARY</u>. If you choose not to participate, that will not affect your relationship with the University of Alberta. If you decide to participate, you are free to withdraw your consent and discontinue participation at any time without prejudice. If you have any questions regarding your rights as a research subject, you may contact the University of Alberta's Research ethics office at (780) 492-2615.

**Title: The reliability of oral and maxillofacial radiologists in the reporting of maxillofacial findings using multi-planar and 3-D reconstructed views in CBCT**

Principal Investigator(s): Ryan Edwards (Orthodontic Graduate Masters Student)
Dr. Carlos Flores-Mir (Supervisor)
Phone Number(s): 780-952-4876 or 780-492-7409

---

| | **Yes** | **No** |
|---|---|---|
| Do you understand that you have been asked to be in a research study? | ☐ | ☐ |
| Have you read and received a copy of the attached Information Sheet? | ☐ | ☐ |
| Do you understand the benefits and risks involved in taking part in this research study? | ☐ | ☐ |
| Have you had an opportunity to ask questions and discuss this study? | ☐ | ☐ |
| Do you understand that you are free to withdraw from the study at any time without prejudice and without affecting your relationship with the University of Alberta? | ☐ | ☐ |
| Has the issue of confidentiality been explained to you? | ☐ | ☐ |

Who explained this study to you?

________________________________________

**I agree to take part in this study: YES ☐ NO ☐**

Signature of Research Subject ____________________________________

(Printed Name) ____________________________________________

Date: ________________________

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

Signature of Investigator or Designee: ______________________Date: ________

**THE INFORMATION SHEET MUST BE ATTACHED TO THIS CONSENT FORM AND A COPY GIVEN TO THE RESEARCH SUBJECT**

**Appendix 6: Chapter 4 data collection instrument sample**

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# The impact of maxillofacial findings using multi-planar and 3-D reconstructed views in cone beam computed tomography (CBCT)

## Instructions for Participants

You have been provided with the following items:

i) A computer connected to Dolphin 3D Imaging software.

ii) A package containing:

- a collection of associated radiologic reports for a group of 18 patients (1-18), in the appropriate order.
- a collection of the data instrument pages that you are to complete, in the appropriate order.

Instructions:

1) You have been logged into Dolphin 3D Imaging software
2) A demonstration of how to use Dolphin 3D for viewing CBCT scans will be provided.
3) Please click on the "Patient 1" tab on the top of the screen
4) Review the CBCT 3-D reconstructed and multi-planar views for "Patient 1".
5) Then, review findings in the provided radiographic report entitled "Patient 1".
6) For each reported finding, use the radiographic report and its radiographic appearance in the 3-D and multi-planar views, to answer **Yes or No** to the following statements:
   i) This finding requires follow-up with dental or medical professional **(yes/no)?**
   ii) This finding may alter the orthodontic treatment plan **(yes/no)?**
7) Circle your selection in the appropriate box (Yes or No; but not both) to indicate the chosen selection for each statement.
8) Repeat for all findings reported in the radiographic report.
9) Progress through patients 1-18 in the same manner.
10) At any point, you are able to search unknown terms via the Internet.

Once you have finished, close Dolphin 3-D imaging by clicking on the "X" in the top right corner.

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**Radiographic Report #1**

**Patient: 1 Age: 12 Sex: Male**

This report is based on an iCAT cone beam CT of the maxilla and mandible. Field of view extends from roof of orbits superiorly to the inferior border of the mandible/level of C4 inferiorly.
The purpose of this study was to assess impaction of teeth #13 and #23. Reformatted images in the sagittal, coronal and axial planes were viewed.

**Radiographic findings:**

Teeth #13 and #23 are mesio-angularly and partially impacted.

The apex of tooth #13 is subjacent to the floor of the nasal cavity at the level of tooth #14. It extends mesially and partially erupts labial and superior to the cemento-enamel junction of tooth #12.

Similarly, the apex of tooth #23 is subjacent to the floor of the nasal cavity at the level of tooth #25. It extends mesially and partially erupts labial and superior to the cemento-enamel junction of tooth #22.
Both canines, #13 and #23, are in contact with their respective lateral incisors with no radiographic evidence of tooth resorption.

There is an impacted supernumerary tooth (S) in the left maxilla. It is a fully developed (crown and root) and inverted mesio-dens. Its apex extends to the apex of tooth #22 and the crown of tooth #23. The supernumerary extends palatally to the palatal midline and superiorly to the mid-floor of nasal cavity.

The follicular spaces and cortices of teeth #13, #23, and S are within the range of normal. Other findings:

- Mucosal thickening and partial opacification of all paranasal sinuses: pansinusitis.
- Mucosal thickening of the nasal cavity: rhinitis.
- Bilateral mild hypoplasia of the maxillary sinuses.
- Congenital fusion of cervical vertebrae C2 and C3 (full fusion at spinous and transverse process. Partially at the body).
- Hypertrophy of the tonsils: Cross-sectional dimensions of the upper airway at the level of the palatine tonsils are extremely narrow.

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**Patient: 1**   **Age: 12**   **Sex: Male**

| | **Requires follow-up with dental or medical professional:** | | | **Orthodontic treatment plan may be altered:** | |
|---|---|---|---|---|---|
| **1. Impacted 13** | YES | NO | | YES | NO |
| **2. Impacted 23** | YES | NO | | YES | NO |
| **3. Impacted supernumerary in Left maxilla** | YES | NO | | YES | NO |
| **4. Hypertrophy of palatine tonsils** | YES | NO | | YES | NO |
| **5. Pansinusitis** | YES | NO | | YES | NO |
| **6. Mucosal thickening nasal cavity; rhinitis** | YES | NO | | YES | NO |
| **7. Bilateral mild hypoplasia of maxillary sinuses** | YES | NO | | YES | NO |
| **8. Congenital fusion of C2-C3** | YES | NO | | YES | NO |

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