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Dental Dimensions In Non-Syndromic Patients With Unilateral Cleft Palate

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DENTAL DIMENSIONS IN NON-SYNDROMIC PATIENTS WITH UNILATERAL CLEFT PALATE

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ABSTRACT

Objective: The main objective of this study is to determine if any difference in tooth size exists between the maxillary quadrants in non-syndromic patients with unilateral cleft palate using cone beam computed tomography. By understanding the effects of cleft palate on tooth morphology, the multidisciplinary team of specialists involved with the care and treatment of a patient with cleft lip/palate can better understand the intricacies of necessary therapy. This understanding can, in turn, be used for proper planning of desired treatments which can increase the chance of successful achievement of desired outcomes.

Materials and Methods: CBCT volumes for 18 patients between ages 9 years, 10 months and 19 years, 4 months meeting inclusion/exclusion criteria were identified. CBCTs were selected from patients receiving orthodontic treatment at the University of Alabama at Birmingham and from a group of patients receiving surgical therapy in the private practice of oral and maxillofacial surgeon, Dr. Peter Waite. CBCTs were viewed and oriented for measurement purposes on the Carestream Dental viewing software. A total of 34 measurements were obtained on each subject by one of two examiners.

Results: After strict comparison of all measures from the cleft vs. non-cleft side of included individuals, only central incisor (CI) root length and CI – dilaceration angle were found to be significantly different.

Conclusions: After comparison of 34 total measures, CI – root length and CI – dilaceration angle were found to be significantly different between the affected and non-affected sides. For the selected sample, the average CI-dilaceration angle was 175.83 (SD=2.358, min, max=171, 180, median=176 (IQR=174-177)) for the cleft side of the dental arch. These findings can be significant in cases where incisor root resorption occurs with shorter than average initial root length. In addition, teeth with noteworthy root dilaceration can inhibit proper orthodontic alignment.

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TABLE OF CONTENTS

Page

ABSTRACT ii

ACKNOWLEGEMENTS iv

TABLE OF CONTENTS v

LIST OF TABLES vii

LIST OF FIGURES viii

LIST OF ABBREVIATIONS 10

INTRODUCTION 1
- Prevalence 2
- Etiology 4
- Classification 7
- Multidisciplinary Approach 9
- Dental Dimensions 10
- Aim 12

MATERIALS AND METHODS 15
- Sample Acquisition 15
- Positioning of anterior teeth for coronal measurements: 17
- Positioning of 1st molar for coronal measurements: 18
- Positioning of 1st molar for the axial view measurement (mid-mesiodistal diameter): 18
- Definition of central incisor and canine measures (coronal view): 19
- Definition of maxillary first molar measures (coronal view): 19
- Definition of maxillary first molar measurement (axial view): 23

RESULTS 26
- Statistical Analysis 26

Reliability 27
Comparison of Dental Dimensions 31

DISCUSSION 33

CONCLUSIONS 40

REFERENCES 42

LIST OF TABLES

Table		*Page*
1	Interrater and intra-rater reliability, results of two-way mixed effects ANOVA for consistency, and interrater Pearson correlation coefficients……..	39-41
2	Comparison of cleft and non-cleft measures……...	42

LIST OF FIGURES

Figure *Page*

1 Example of Carestream Dental Viewing Software……..26

2 Example of central incisor orientation for measures in the coronal view……...27

3 Example of coronal view measurements taken on a central incisor……..30-31

4 Example of coronal view measurements taken on a 1st molar……..32-33

5 Example of the midmesio-distal measure taken from the axial view on a 1st molar……...34

6 Example of the dilacerations angle being measured on a central incisor……...35

LIST OF ABBREVIATIONS

CBCT(s)	Cone-beam computed tomograph
CEJ	Cementoenamel junction
CI	Central Incisor
DNA	Deoxyribonucleic acid
EUROCAT	European Surveillance Systems of Congenital Anomalies
ICC	Intraclass correlation coefficient
ICBDSR	International Clearinghouse for Birth Defects Surveillance and Research
IPDTOC	International Perinatal Database of Typical Orofacial Clefts
NBDPN	National Birth Defects Prevention Network
OIIRR	Orthodontically induced inflammatory root resorption
RNA	Ribonucleic acid
UAB	University of Alabama at Birmingham

CHAPTER 1

INTRODUCTION

Orofacial clefts, which include cleft lip and cleft palate, are among the most common birth defects worldwide (Panamonta, Pradubwong, Panamonta, & Chowchuen, 2015). Individuals with cleft lip are described as having a developmental fissure in the upper section of the lip. Defect severity can vary significantly from a slight notch to a complete cleft involving the nostrils. Individuals with cleft palate have a fissure in either the soft palate or often both the soft and hard palate. The severity of a cleft palate can range from a complete cleft involving both the hard and soft palates communicating with the nasal cavity to a less severe form known as a submucosal cleft. Also, the mildest expression of a soft palatal cleft, known as a bifid uvula, is sometimes observed (Merritt, 2005).

Cleft lip and cleft palate can occur separately, however, they often occur together. Roughly 70% of individuals with unilateral cleft lip and 85% of newborns with bilateral cleft lip will also have a palatal cleft (Merritt, 2005). When a patient is born with a cleft, management of the defect requires multidisciplinary care from the time of birth through adulthood (Panamonta et al., 2015). Panamonta et al. discusses the importance of acquiring precise data about worldwide orofacial clefts. Despite the care provided by multidisciplinary care teams, orofacial clefts present a variety of significant global health problems each year, particularly in low socio-economic populations. By obtaining data indicative of worldwide orofacial cleft birth prevalence, a better understanding of cleft

etiology as well as management of public health resources can be gained. (Panamonta et al., 2015).

Prevalence

While there is some variation in the reported prevalence, an occurrence rate of 1 in 700 live births is generally accepted (Panamonta et al., 2015). Cleft lip with or without cleft palate has been reported as the most common craniofacial abnormality and the fourth most common congenital birth defect overall with males being most commonly affected. However, cases of isolated cleft palate are most often seen in females (Merritt, 2005). Despite data on the occurrence of cleft lip and palate not being known in some regions of the world, extensive research has been performed on certain population samples (Mossey, 2009). In a systematic review by Panamonta et al., forty-four articles resulted in a study population of 30, 665, 615 live births. Of these live births, 45, 193 patients were identified as having an orofacial cleft (Panamonta et al., 2015). When the results were further described by continent, orofacial cleft birth prevalence was identified as 1.57, 1.56, 1.55, 1.33, 0.99, and 0.57 per 1,000 live births for Asia, North America, Europe, Oceania, South America and Africa respectively (Panamonta et al., 2015). This same study also showed ethnic variation in birth prevalence rates as well. North American Indians, followed by the Japanese and Chinese have been shown to have the highest prevalence; while African populations have produced the lowest. This leaves the Caucasian group as the median population in terms of prevalence (Panamonta et al., 2015). One must keep in mind, however, that variations in acquisition of data, sources of the reported sample, and criteria for inclusion/exclusion may have notable differences (Mossey, 2009).

In an update presented by the National Birth Defects Prevention Network (NBDPN), based on adjusted national estimates of selected defects from fourteen population-based birth defect registries in the United States, 4, 038, 506 births occurred exhibiting 21 defects from 2004 through 2006. These defects included: central nervous system defects (ex: anencephaly), eye defects (anophthalmia/microphthalmia), cardiovascular defects (transposition of great arteries), orofacial defects (cleft palate, cleft lip with or without cleft palate), gastrointestinal defects (esophageal atresia/tracheoesophageal fistula), musculoskeletal defects (reduction defects of the upper limbs), and chromosomal anomalies (trisomy 13, trisomy 18 and trisomy 21) (Parker et al., 2010). In this study by Parker et al., Down syndrome was confirmed the most common birth defect of conditions examined. After accommodation for maternal race and ethnicity, national prevalence of Down syndrome was reported as 13.56 per 10,000 live births or 1 in 737 live births. The second most common condition observed was cleft lip with or without cleft palate. Adjusted prevalence was found to be 10.63 per 10,000 live births or 1 in 940 (Parker et al., 2010). It should also be noted that it is not uncommon for cleft palate alone or cleft lip with or without cleft palate to be identified along with other significant congenital abnormities recorded in these population studies. When these anomalies are more physically apparent, more thorough clinical examinations are routinely completed. This, without doubt, results in discovery of mild expressions of cleft palate that otherwise could have gone unnoticed and unreported (Mossey, 2009).

In 2003, the International Perinatal Database of Typical Orofacial Clefts (IPDTOC) was created. This group worked as part of a larger collaboration which was

funded by the National Institutes for Dental and Craniofacial Research through the Human Genetics Programme of the World Health Organization. Individual case information on cleft lip with and without cleft palate, as well as cleft palate alone, was collected from one of three major collaborative organizations: the European Surveillance Systems of Congenital Anomalies (EUROCAT), the National Birth Defects Prevention Network (NBDPN), and the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR) (Mastroiacovo, 2009). The results of the data gathered included 54 registries from 30 countries encompassing a time span of one full year between 2000 and 2005. A total of 7,704 cases of cleft lip with or without cleft palate were reported from >7.5 million births. Of these cases, 7,141 were livebirths, 237 were still births, 301 pregnancies were terminated prior to birth, and 25 pregnancy outcomes were not available. This represented an overall prevalence of 9.92 per 10,000 which could be further subdivided into 3.28 per 10,000 for cleft lip alone and 6.64 per 10,000 for cleft lip and palate (Mastroiacovo, 2009). With expression this frequent, cleft lip and palate is a condition orthodontists, along with the other health care professionals involved in an effected patient's care, should be more than familiar with.

Etiology

The etiology behind the cleft is often complex and may include environmental and/or genetic factors (Panamonta et al., 2015). Merritt et al. lists disruptions of normal developmental processes due to exposure to teratogens, genetic disorders leading to malformations, and physical forces interfering with normal tissue formation as potential influences. While no single gene has been identified as a definitive explanation for all

clefts, mutations on 1q24, 2p, 3p20, 3q, 4q32, 10p15, 17q, 18q and 21q have been shown to result in cleft lip and/or cleft palate (Merritt, 2005). In addition, genes such as transforming growth factor alpha, β3, AP2, and MSX1, which are responsible for altering signaling molecules, transcription factors, or growth hormone related to the developing prominences of the lip or palate, can affect the normal joining of these prominences (Merritt, 2005). In a book review of Cleft Lip and Palate: From Origin to Treatment by Diego F. Wyszynski, Prescott states most conclusions about the genetics and the recurrence of cleft lip/palate in families are unclear; however, it does seem that cleft lip/palate is not monogenetic. In fact, it is extremely likely that an estimated 2-8 genes are involved (Wyszynski, 2002).

Teratogens are agents that have been associated with birth defects by disrupting a normal process of development during a critical stage. Examples include medications, maternal cigarette smoking, maternal alcohol use, and proper nutrition or the lack thereof during pregnancy. Many medications, when taken during the first trimester, have been linked to the development of cleft lip and palate. In addition to well-known associations with groups of drugs such as anticonvulsants, studies performed on mice have shown cortisone to affect the developing palatal shelves in a number of ways including number of cells present, appropriate shelf elevation, and disruption of proper shelf positioning (Merritt, 2005).

During the first trimester, maternal cigarette smoking has been linked to an increased risk of cleft lip with or without cleft palate. While the precise mechanism for smoking's association is unknown, nicotine induced intermittent hypoxia has been suggested to have an effect on facial development (Merritt, 2005). In a study by Lieff et

al., a positive dose-response in individuals with cleft lip and palate based on the number cigarettes per day was found with increasing odds ratios of 1.09, 1.84, and 1.85 for light, moderate, and heavy smokers respectively (Lieff et al., 1999). Frequently associated with smoking, maternal alcohol use, has been shown to increase the risk of cleft palate. When an embryo is exposed to alcohol, an interruption in the differentiation and migration of neural crest cells can occur (Merritt, 2005).

Nutrition has also been shown to play a very important role in prevention of cleft lip and palate. Starting prior to conception, it is recommended that women of childbearing age take 400 μg of folic acid per day and to continue this level of intake through an entire pregnancy (Merritt, 2005). Folate is essential for synthesis of DNA and RNA. When a folic acid deficiency is present, DNA damage occurs. Damage can occur in the form of single or double strand DNA breaks, alkali labile sites, DNA cross links, and base/base pair damages. Since DNA and RNA are the building blocks of the cell, issues in their synthesis can also cause neural tube and abdominal wall defects in addition to orofacial clefts (Brooklyin, Jana, Aravinthan, Adhisivam, & Chand, 2014). In a study by De Wals et al., the prevalence of neural-tube defects was decreased significantly after the implementation of folic acid enriched food. From 1993-2002, defects decreased from 1.58 per 1000 births to 0.86 per 1000 births, a reduction of 46% (De Wals et al., 2007).

Finally, the influence of mechanical forces has been reported as a potential mechanism of cleft lip and cleft palate. Mainly, the tongue's position in the developing oral cavity has been theorized as a potential cause due to physical obstruction of palate formation. It has been suggested that a higher than normal tongue position could prevent fusion of the palatal shelves. When this happens, the defect can be expressed as a cleft of

the uvula, soft palate, or both the soft and hard palates. The extent of the defect depends on the point in development when the interference occurred (Merritt, 2005).

Classification

Many classification systems describing the morphological characteristics of the cleft exist including: the Davis and Ritchie Classification, the Veau Classification, the Arturo Santiago Classification, the LAHSAL Classification of Cleft Lip and Palate, and the Elnassry Classification (Shah, Khalid, & Khan, 2011). Two of the oldest morphological classification systems used to describe clefts are the Davis and Ritchie Classification and the Veau Classification. The Davis and Ritchie Classification was proposed in 1922 and categorizes clefts into three main groups based on the cleft's position to the alveolar process. Group I includes pre-alveolar clefts: unilateral cleft lip, bilateral cleft lip and median cleft lip. Group II includes post-alveolar clefts: cleft hard palate alone, cleft soft palate alone, cleft soft and hard palate, and sub-mucous clefts. Group III alveolar clefts: unilateral alveolar cleft, bilateral alveolar cleft, and median alveolar cleft (Shah et al., 2011).

Later, in 1931, Victor Veau proposed his classification for cleft description which included four distinct groups: Group I (A) – defects of the soft palate only, Group II (B) – defects involving the hard palate and soft palate but the secondary palate alone, Group III (C) – complete unilateral cleft, extending from the soft palate to the alveolus, usually involving the lip, and Group IV (D) – complete bilateral clefts (Shah et al., 2011). More recently, in 2007, the Elnassry classification was proposed which divided patients with cleft lip and palate into seven classes. These classes are described as follows: Class I –

unilateral cleft lip, Class II - unilateral cleft lip and alveolus, Class III – bilateral cleft lip and alveolus, Class IV – unilateral complete cleft lip and palate, Class V – bilateral complete cleft lip and palate, Class VI – cleft hard palate, and Class VII – bifed uvula (Shah et al., 2011).

Clefts can also be further described as syndromic or non-syndromic. Clefts considered non-syndromic occur in individuals with no other physical or developmental anomalies in addition to the cleft and no known exposure to a teratogen. Merritt et al. reports 10% of all individuals with cleft lip and cleft palate will also have an associated syndrome. However, if the cleft lip occurs without cleft palate, affected individuals will have an identifiable syndrome in 30% of cases. In addition, 50% of individuals with cleft palate alone will have an identifiable syndrome (Merritt, 2005). In a study by Calzolari et al., specific types of defects associated with clefts were examined. Of the 5,449 cases of cleft lip with or without cleft palate, 3,860 were identified as isolated anomalies while 1,589 were expressed along with other defects. Among these were 970 anomalies appearing congenitally of unknown origin, 455 chromosomal abnormalities, and 164 recognizable syndromes or conditions. Of these, musculoskeletal, cardiovascular, and central nervous system defects were reaffirmed as those most often associated with cleft lip and palate (Calzolari et al., 2007). With this in mind, clinicians should be aware of cognitive or functional issues related to these associated defects as they could influence clinical management of the patient and treatment outcomes.

Considering these reported rates of expression, birth defects, especially major defects including structural malformations leading to a significant impact on the overall health and development of the child, are an important public health concern. Defects

such as these are considered a leading cause of infant mortality, and in many other cases, have a lasting impact in the form of lifelong disability. In 2005, birth defects were documented to contribute to more than 5500 infant deaths, which accounted for 20% of the overall infant mortality in the United States (Parker et al., 2010). Consequently, birth defects have a substantial impact on health care cost. In the United States, hospital costs for patients admitted solely for treatments of birth defects totaled $2.6 billion in 2004 (Parker et al., 2010).

Multidisciplinary Approach

Children born with cleft lip and/or cleft palate require the collaboration of a specialized group of health care professionals to ensure the treatment the child receives is well organized and comprehensive in nature. Complications related to feeding, hearing loss, and speech are common. Often, these conditions are monitored and treated by various specialists of a cleft lip and palate team (Robin et al., 2006). In order to establish guidelines designated to address the complex treatment cleft individuals are in need of, the American Cleft Palate-Craniofacial Association developed a document entitled "*Parameters for Evaluation and Treatment of Patients with Cleft Lip/Palate or Other Craniofacial Anomalies*." Cleft and craniofacial care teams in the United States and Canada use this document as an outline for the implementation of an organized multidisciplinary approach. Individuals comprising these teams often include: (1) dental specialties (orthodontics, oral surgery, pediatric dentistry, and prosthodontics), (2) medical specialties (genetics, otolaryngology, pediatrics, plastic surgery and psychiatry), and (3) allied health care fields (audiology, nursing, psychology, social work, and speech pathology) (Vinson, Huebener, Jones, Flores, & Dean, 2016).

As part of a cleft or craniofacial team, the orthodontist plays an essential role in the diagnosis and treatment planning of an affected individual. Obtaining and analyzing records including panoramic and cephalometric radiographs, intraoral and extra-oral photographs, and study casts enables the orthodontist to describe the effects of the cleft on a patient's facial skeleton and soft-tissue. In addition to providing comprehensive orthodontic treatment, the orthodontist's knowledge of growth and development can assist other team members in planning procedures such as orthognathic surgery. In many cases, in conjunction with comprehensive orthodontics, surgical repositioning of the facial skeleton provided by oral and maxillofacial surgeons is often required to achieve adequate function, esthetics, and stability of treatment (Vinson et al., 2016).

Dental Dimensions

When compared to the general population, individuals with cleft lip and palate often present with a higher frequency of dental anomalies such as missing teeth and alterations in size, shape, and timing of tooth formation. Of these, changes in morphology and tooth size are considered two of the most common variations observed (Antonarakis, Tsiouli, & Christou, 2013). Many potential factors have been reported to attribute to this variation in tooth size, primarily genetic and environmental influences are to blame. Of these, race, sex, hereditability and the presence of an associated syndrome have been identified as major contributors. (Lewis, Stern, & Willmot, 2008). With that being said, Antonakaris et al. states that genetics are believed, by many, to play an important part in the dictation of tooth size. This suggests the genetic make-up of every patient plays a role in their individual tooth dimensions. Furthermore, etiological factors

in the prenatal and postnatal time frames have also been reported to cause anomalies in the morphology and overall dimensions of teeth (Antonarakis et al., 2013).

A review of the literature on tooth morphology in patients with cleft lip and palate reveals significant variation in published results. In 1971, Foster and Lavelle reported significantly smaller crowns of permanent teeth in both the upper and lower arches of cleft patients when compared to a non-cleft control group (Foster & Lavelle, 1971). More specifically, in later studies by Markovic and Djordjevic, their results showed significantly smaller central and lateral incisors in the permanent dentition. Also, the canines, first/second premolars and molars were smaller on the cleft side but not to a significant statistical level (Markovic, 1981). In contrast, in 1983, Peterka and Mullerova's results showed no significant differences between the mesiodistal tooth dimensions of individuals with clefts and those without (Peterka & Müllerová, 1983). These studies, however, could be viewed with caution because in some instances the right quadrant only or the non-cleft side was measured.

Even though deviations from the norm are more frequently associated with tooth morphology and size, changes in formation and eruption should not be ignored. It has been reported that both primary and permanent dentitions are affected in children with cleft lip, cleft palate, or both. Studies have indicated that the formation of the permanent dentition has been found to be delayed an average of 6 months. Interestingly, this delay occurred throughout the entire dentition, not just the maxillary teeth alone. A study on a group of 251 Finnish children showed a delay of 8.4 months in tooth formation compared with data collected from a non-cleft control group (Ranta, 1986). Not surprisingly, when there is a delay in tooth formation, there is a corresponding delay in the eruption of teeth.

While no statistical differences have been found between sexes, the premolars and canines on the side of the arch effected by the cleft have displayed later eruption than their counterparts on the contralateral side of the arch (Ranta, 1986).

In addition to these findings, a link between the number of missing teeth and the extent of the delay was also revealed. As the number of missing teeth increased, the delay in tooth formation also increased (Ranta, 1986). In a study by Tortora et al., congenital absence of the permanent maxillary lateral incisor was identified as the most common dental anomaly in the cleft area (Tortora, Meazzini, Garattini, & Brusati, 2008). Absence of the lateral incisor on the cleft side was observed in 48.8% of unilateral cleft lip and palate patients included in their study, an occurrence rate similar to previous reports. Somewhat unexpected, the second most commonly reported missing tooth was the second maxillary premolar in the cleft area (Tortora et al., 2008). Consequently, teeth selected for comparison in this study were chosen taking into account these findings.

Aim

In order to accomplish a treatment goal such as proper inter-arch relationships and occlusion, alignment of the teeth in both arches with adequate overjet and overbite must be achieved. Considering this, tooth size must often be taken into account to obtain an occlusion considered esthetic, functional and stable over time. Antonarakis et al. suggests that during treatment planning, clinicians must not forget to thoroughly consider tooth size. When discrepancies in tooth size are present between arches, proper alignment of teeth may be prevented. Thus, in order to obtain ideal occlusion after

treatment is complete, accounting for these discrepancies prior to treatment is certainly necessary (Antonarakis et al., 2013).

The main objective of this study is to determine if any difference in tooth size exists between the maxillary quadrants in non-syndromic patients with unilateral cleft palate using cone beam computed tomography. Previous studies on tooth size in patients with cleft lip and palate have been centered on obtaining measurements on dental casts through standardized photography or computerized scans. Also, these studies have focused on crown dimensions, neglecting root size and morphology (Lewis et al., 2008). By understanding the effects of cleft palate on tooth morphology, the multidisciplinary team of specialists involved with the care and treatment of a patient with cleft lip/palate can better understand the intricacies of necessary therapy. This understanding can, in turn, be used for proper planning of desired treatments which can increase the chance of successful achievement of desired outcomes.

The null hypothesis suggests that differences in size or morphology of selected teeth would not be present between the cleft and non-cleft quadrant in the maxillary dentition of non-syndromic patients with unilateral cleft palate.

Specific aims include:

Aim 1 is to compare measurements of the central incisors, canines, and 1st maxillary molars on the cleft side of the arch versus the non-cleft side of the arch in non-syndromic patients with unilateral cleft palate.

Aim 2 is to identify an average dilaceration angle between the crown and root of the central incisor on the cleft side of the patient's arch and to determine if there is a significant difference in this angle compared to that of the contralateral central incisor.

CHAPTER 2

MATERIALS AND METHODS

Sample Acquisition

The study group was comprised of 18 non-syndromic individuals between the ages of 9 years, 10 months and 19 years, 4 months with unilateral cleft lip and palate. Subjects were selected from a list of 80 patients who previously received or are receiving orthodontic treatment at the University of Alabama at Birmingham and from a group of 225 patients who have received or are planning to receive surgical treatment in the private practice of oral and maxillofacial surgeon, Dr. Peter Waite. Patients were not included if they were currently in orthodontic treatment, had large restorations or decay present on target teeth, or lacked full root development on selected teeth. Patients at UAB were identified through keyword search of the computer record system (Dolphin) and evaluation of the initial orthodontic records. Patients receiving surgical therapy in the oral surgeon's office were identified from a list constructed for previous research on patients with cleft lip and palate. CBCTs from UAB and the office of the oral and maxillofacial surgeon were obtained on the Carestream CS 9300 or Kodak 9500 series

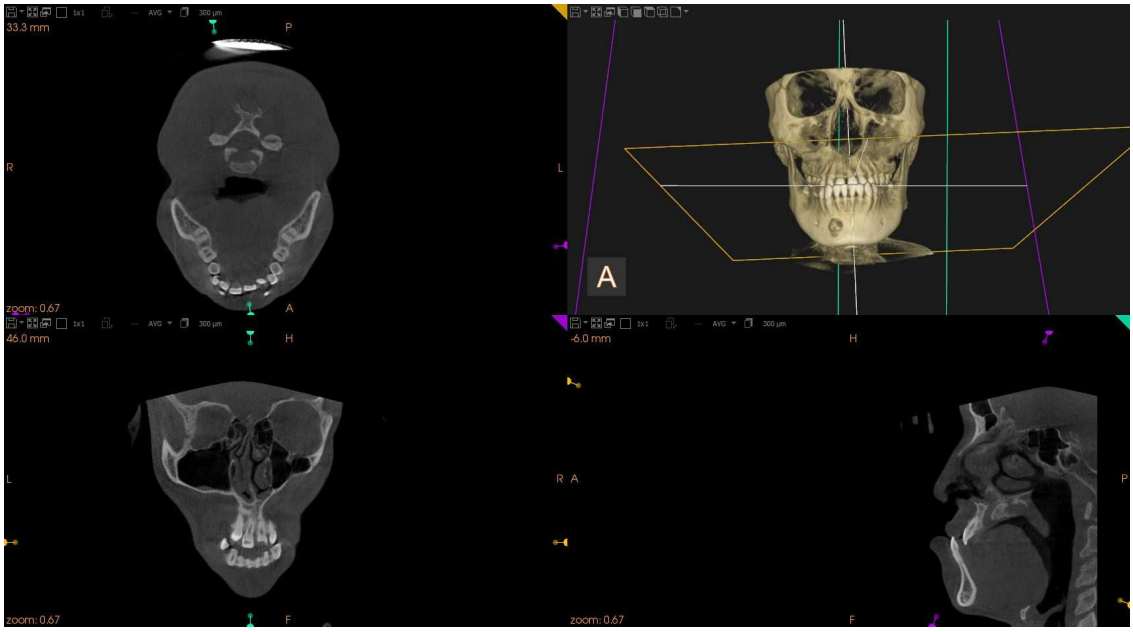

Figure 1: Example of Carestream Dental viewing software.

cone beam 3D system machine. CBCTs were oriented based on a modified version of the process outlined in the article "*Accuracy and reliability of tooth and root lengths measured on cone-beam computed tomographs*" by Sherrard et al using the Carestream Dental viewing software (Sherrard, Rossouw, Benson, Carrillo, & Buschang, 2010). Each tooth was positioned using the multi-step process outlined below:

For coronal view measurements (tooth length, root length, crown height, crown to root ratio, mesio-distal diameter of anterior teeth, dilaceration angle of central incisor, and buccal-palatal dimension of 1st molar teeth):

Positioning of anterior teeth for coronal measurements:

1. Using the axial, sagittal and coronal views, each plane was adjusted to intersect on the pulp chamber of the selected tooth.
2. Using the sagittal view, the axial and coronal planes were adjusted/rotated until the coronal plane was parallel to the long axis of the tooth and the axial plane passed through the facial and lingual CEJ.
3. Using the coronal view, the 'scroll' feature was then used on the computer's mouse to move through the coronal slices until the entire tooth was clearly visible (root apex to incisal edge).

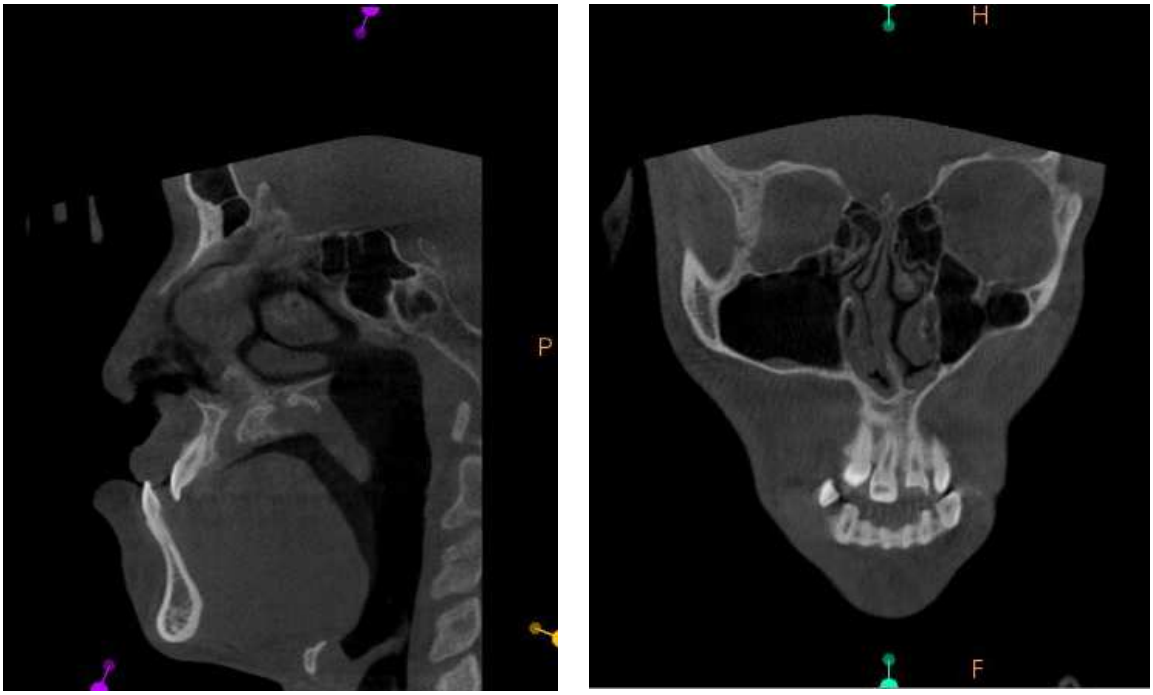

Figure 2: Depicts examples of central incisor orientation for measurements in the coronal view.

Positioning of 1st molar for coronal measurements:

1. Using the axial, sagittal and coronal views, each plane was adjusted to intersect on the pulp chamber of the selected tooth.
2. Using the sagittal view, the 'scroll' feature was then used on the computer's mouse to move through the sagittal slices until the entire palatal root of the 1st molar was visible. Then, the coronal plane was rotated until the coronal plane passed through the long axis of the palatal root.
3. Using the coronal view, the 'scroll' feature was then used on the computer's mouse to move through the coronal slices until the entire crown and palatal root was visible (root apex to cusp tip).

Positioning of 1st molar for the axial view measurement (mid-mesiodistal diameter):

1. Using the axial, sagittal and coronal views, each plane was adjusted to intersect on the pulp chamber of the selected tooth.
2. Using the axial view, the 'scroll' feature was then used on the computer's mouse to move through the axial slices until the mesial and distal contact points were visible.

After CBCT selection and the proper orientation of each tooth was determined, the following measurements were evaluated in the coronal plane: tooth length, root length, crown height, crown-to-root ratio, and mesio-distal diameter of anterior teeth, as well as the buccal-palatal dimension of the 1st molar. All measurements used are defined

as described in "*Dimensions of central incisors, canines, and first molars in subjects with Down syndrome measured on cone-beam computed tomographs*" by Maria T. Abeleira et al.

Definition of central incisor and canine measures (coronal view):

- Tooth length – distance from the incisal edge to the apex of the tooth
- Root length – distance from a perpendicular line between the mesial and distal CEJ to the apex of the tooth
- Crown height – distance from a perpendicular line at the CEJ as described above to the incisal edge
- Crown-to-root ratio – the ratio of crown height to root length as defined above
- Mesio-distal diameter – maximum mesio-distal crown diameter

Definition of maxillary first molar measures (coronal view):

- Tooth length – distance from the tip of the mesio-lingual cusp to the apex of the palatal root
- Root length - distance from a perpendicular line between the buccal and palatal CEJ to the apex of the palatal root
- Crown height - distance from a perpendicular line at the CEJ as described above to the tip of the mesio-lingual cusp
- Crown-to-root ratio – same as described above using the palatal root
- Buccal-palatal dimension – distance determined by a line drawn perpendicular to the long axis of the tooth through the buccal and palatal height of contour

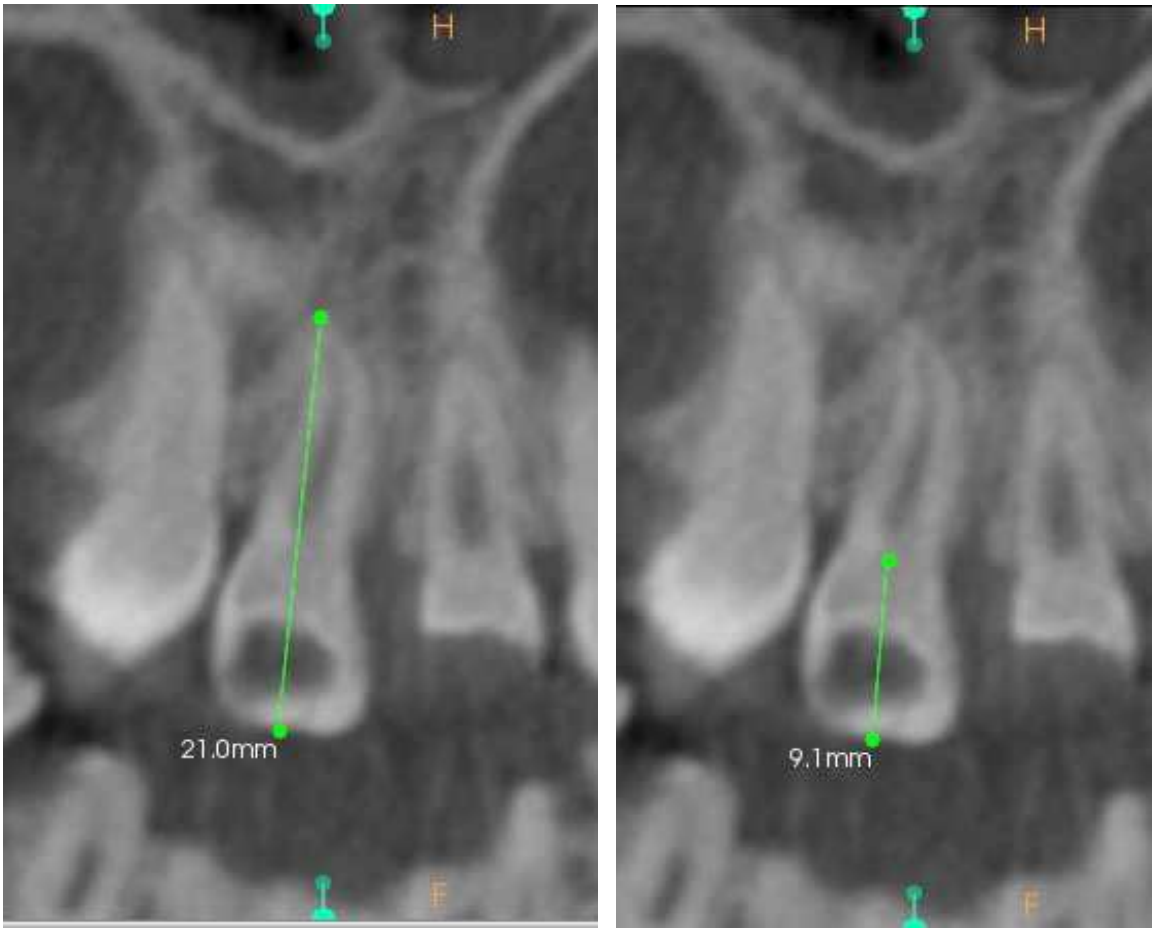

Figure 3: Examples of coronal view measurements taken on a central incisor.

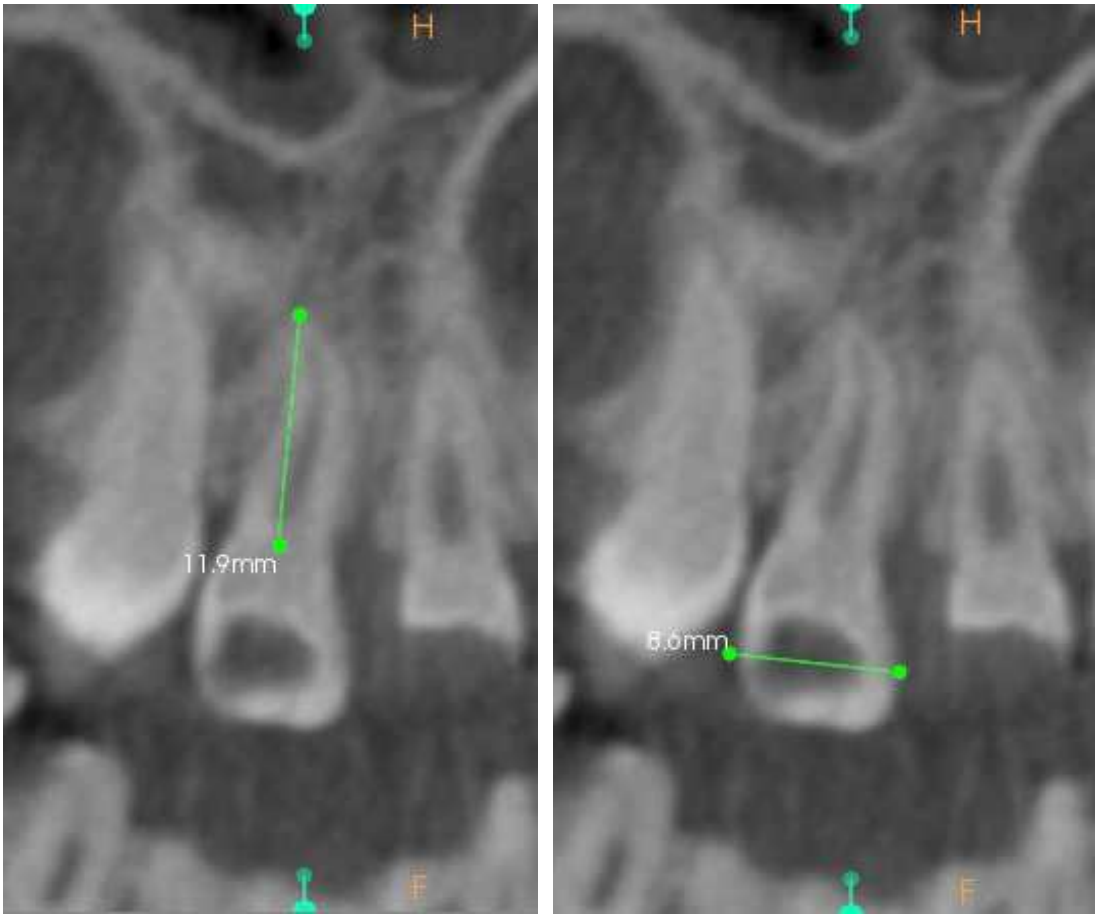

Figure 3 continued: Examples of coronal view measurements taken on a central incisor.

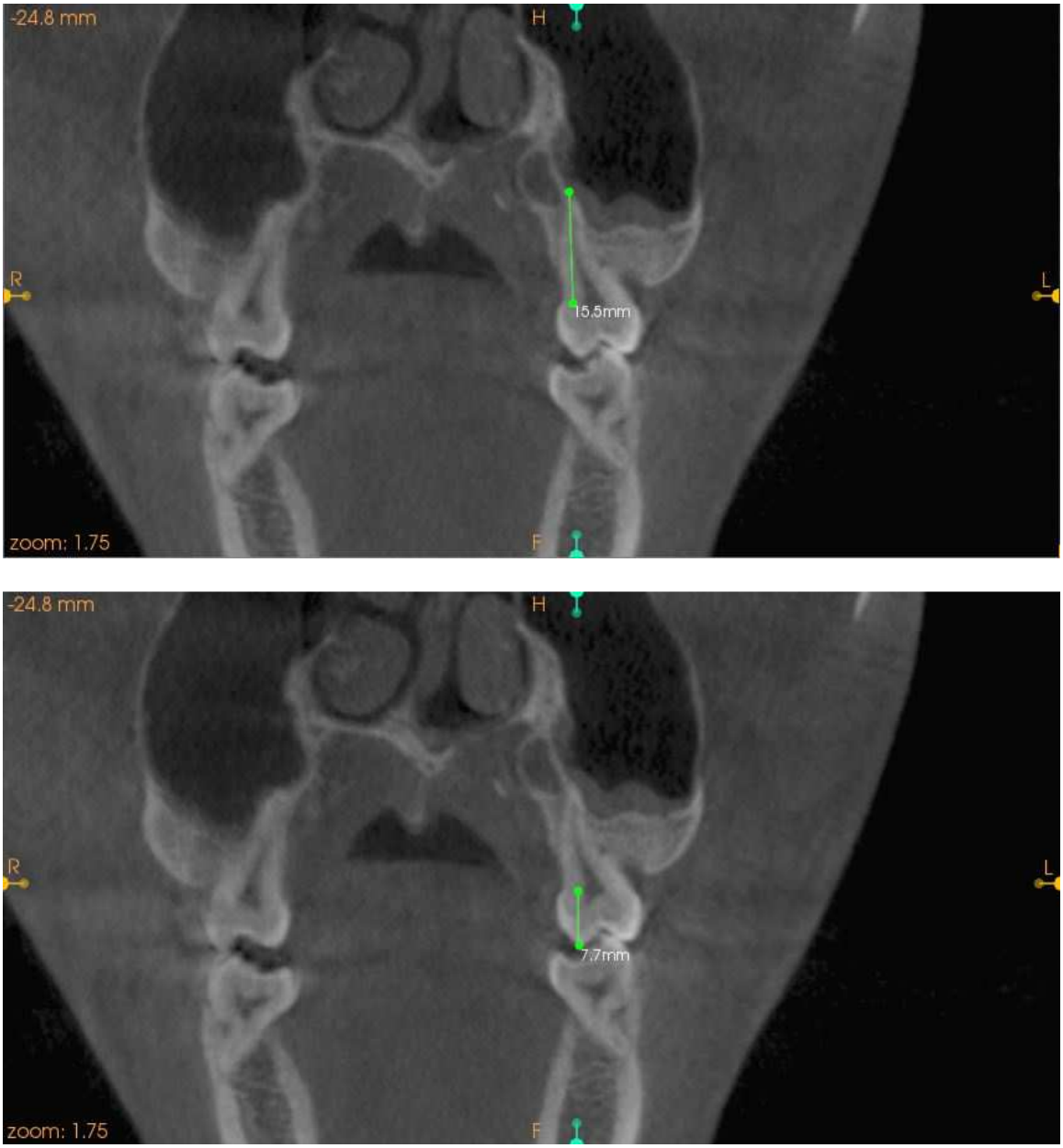

Figure 4: Examples of coronal view measurements taken on a 1st molar.

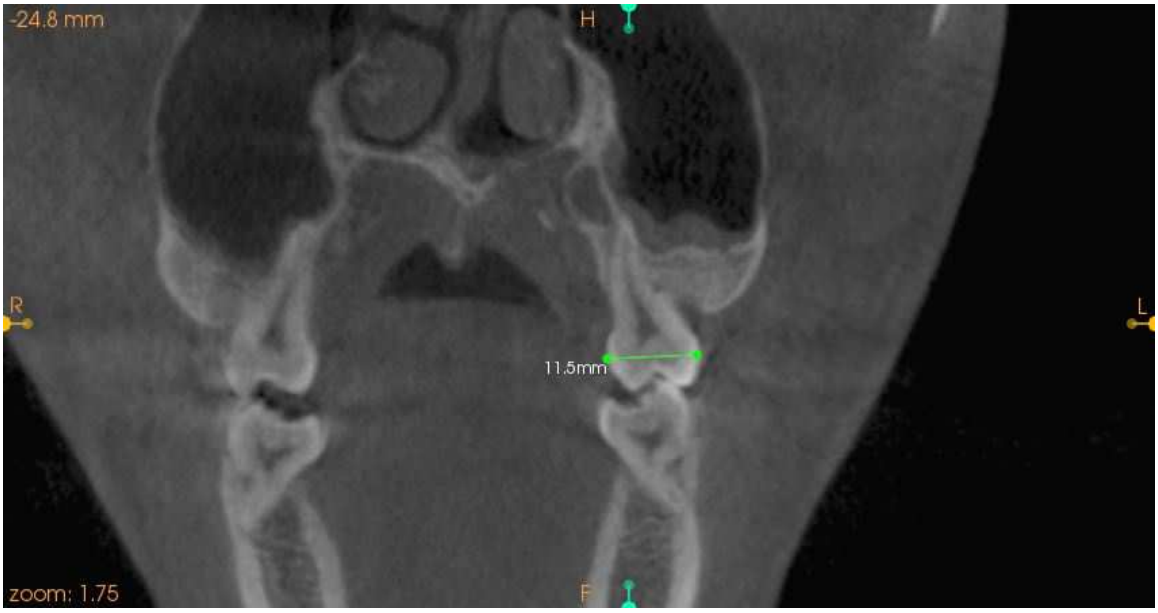

Figure 4 continued: Examples of coronal view measurements taken on a 1st molar.

In the axial plane, the following measurement was obtained: midmesio-distal diameter (1st molar).

Definition of maxillary first molar measurement (axial view):

- Midmesio-distal diameter – the distance between interproximal contact points (Abeleira et al., 2014).

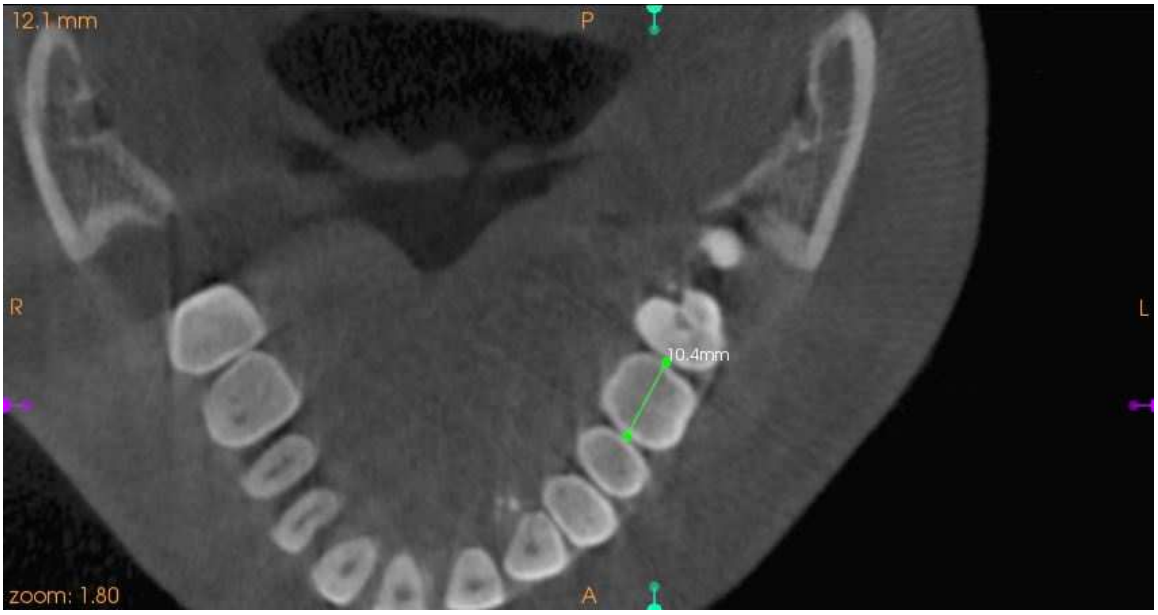

Figure 5: Example of the midmesio-distal measurement taken from the axial view on a 1st molar.

The final measurement, the dilaceration angle was measured using the angle created by the intersection of a line through the long axis of the tooth root and a line through the long axis of the tooth crown intersecting at the CEJ. This angle was measured on the central incisor on the side of the patient's cleft and non-cleft side of the arch.

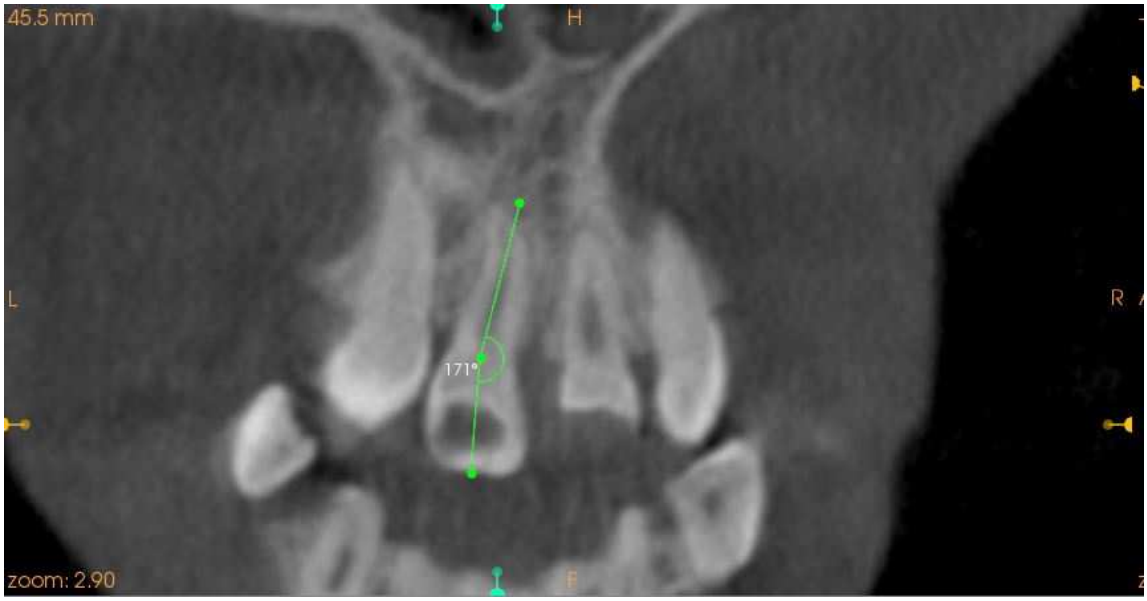

Figure 6: Example of the dilaceration angle being measured on a central incisor.

CHAPTER 3

RESULTS

Statistical Analysis

To evaluate interobserver and intraobserver reliability, five subjects were selected from the individuals meeting the inclusion criteria. After appropriate training, the two examiners completed the required measurements for the selected subjects. Two complete sets of measurements were obtained by each examiner on separate days following the orientation process outline earlier in this section. Using this data, intraclass correlation coefficient (ICCs) were calculated using a two-way mixed effects ANOVA model where the selected raters were the only raters of interest, i.e., the results cannot be generalized to other raters. Both inter- and intra-rater ICCs are based on the "Shrout-Fleiss reliability: fixed set" for consistency, i.e., ICC (3:1) (Shrout & Fleiss, 1979). For additional information about intra-rater reliability, Pearson correlation coefficients are presented and are based on comparisons of the respective grader's (Examiner 1, or Examiner 2) 1st and 2nd measurement. The inclusions of these measurements are intended to show the pattern of measurements and is not a measure of reliability (Shrout & Fleiss, 1979). ICCs < 0 were deemed to be an "unreliable scale**.**" The ICC is the ratio of the sums of various variance component estimates and defined to be between 0 and 1. Negative ICC values occur when the between-subject variation is smaller than the within-subject variation, e.g. due to different raters (Shrout & Fleiss, 1979). The results of these analyses are outlined below in Table 1.

Paired differences between cleft and non-cleft measures were examined using a Wilcoxon signed rank test, which is a nonparametric test, and p-values < 0.05 were noted as statistically different. A parametric test, e.g., the paired t-test, was not used because, in general, differences were not normally distributed. When there are multiple comparisons, methodologist frequently suggest an alpha correction so that spurious results can be avoided. Known as a Bonferroni correction, a stricter cut point for statistical significance is used based on the formula 0.05 / 16 (# of comparisons), and in this instance, is 0.003125. Note than even with the correction, the indicated results for "CI – root length" and "CI - dilaceration angle" would still be significantly different. Results of this comparison are seen below in Table 2.

Reliability

Overall the interrater and intra-rater reliability was very good. The average ICC (intraclass correlation coefficient) for interrater reliability was 0.857 suggesting near excellent reliability. In fact, out of 34 total measurements, only the measure of CI – crown height was considered an unreliable scale. Reliability frequently increases over time between raters as experience improves. Considering only 5 subjects were selected for the reliability measures, improvement would be likely as the number of subjects increased. With this in mind, the presented interrater reliability could imply significant accuracy pertaining to the process of CBCT orientation and measurement acquisition.

Intra-rater reliabilities were also very high. Intra-rater reliability for Examiner 1, 0.92529, displays excellent reliability. Only two measures were found to be unreliable: 1st molar mesiodistal diameter and CI – crown height. Examiner 2's intra-rater reliability

was less than Examiner one, at 0.85351, indicating slightly less reliability. However, this is still considered good reliability overall. Again, out of 34 total measures, only three measurements were considered unreliable from Examiner 2's data: 1st molar – crown height, 1st molar – crown/root ratio, and CI mesiodistal diameter.

Interpretation of ICC estimates:

- <0.5 => poor reliability
- 0.5-0.75 => moderate reliability
- 0.75-0.9 => good reliability
- >0.9 => excellent reliability

The Pearson correlation, also known as the product-moment correlation coefficient, is a statistic intended to represent the extent of linear relation between two separate variables. Its reported interval is from 1.00, through 0, to -1.00. For perfect positive correlation, a Pearson correlation value would equal 1.00. A value of zero would represent uncorrelated variables, and -1.00 would indicate perfect negative correlation (Colman, 2015). For both examiners, the majority of the results of the Pearson correlations were positive. Many were approaching 1.00, suggesting a strong positive relationship between the 1st measurement and the 2nd measurement.

Table 1. Interrater and intra-rater reliability, results of two-way mixed effects ANOVA for consistency, and interrater Pearson correlation coefficients						
Tooth	**Cleft**	**Interrater Reliability (ICC)**	**Examiner 1 Intra-rater Reliably (ICC)**	**Examiner 1 Pearson Correlation***	**Examiner 2 Intra-rater Reliably (ICC)**	**Examiner 2 Pearson Correlation***
1st molar - buccal-palatal dimension	No	0.88548	0.92593	0.87520	0.89794	0.79861
1st molar - buccal-palatal dimension	Yes	0.91613	0.95419	0.94356	0.95241	0.88961
1st molar - crown height	No	0.67666	0.98097	0.97702	**Unreliable scale**	-0.06206
1st molar - crown height	Yes	0.88931	0.94254	0.92091	0.87910	0.74602
1st molar - mesiodistal diameter	No	0.42244	**Unreliable scale**	-0.25672	0.89502	0.84443
1st molar - mesiodistal diameter	Yes	0.81176	0.95288	0.95022	0.89882	0.98519
1st molar - root length	No	0.88505	0.98719	0.97264	0.81128	0.62292
1st molar - root length	Yes	0.93257	0.96784	0.96258	0.86158	0.80882
1st molar - tooth length	No	0.90182	0.99085	0.98539	0.84428	0.74353
1st molar - tooth length	Yes	0.95611	0.98467	0.99214	0.93954	0.95191
1st molar-crown/root ratio	No	0.46058	0.96649	0.92687	**Unreliable scale**	-0.64480
1st molar-crown/root ratio	Yes	0.87511	0.91412	0.88490	0.83560	0.68736
CI - crown height	No	**Unreliable scale**	**Unreliable scale**	0.03955	0.38109	0.25735
CI - crown height	Yes	0.90041	0.97688	0.94998	0.76952	0.56290

Table 1. Interrater and intra-rater reliability, results of two-way mixed effects ANOVA for consistency, and interrater Pearson correlation coefficients						
Tooth	**Cleft**	**Interrater Reliability (ICC)**	**Examiner 1 Intra-rater Reliably (ICC)**	**Examiner 1 Pearson Correlation***	**Examiner 2 Intra-rater Reliably (ICC)**	**Examiner 2 Pearson Correlation***
CI - crown/root ratio	No	0.79313	0.96422	0.96141	0.50814	0.51365
CI - crown/root ratio	Yes	0.82477	0.97672	0.95505	0.63070	0.66259
CI - mesiodistal diameter	No	0.47461	0.60622	0.82404	**Unreliable scale**	0.09074
CI - mesiodistal diameter	Yes	0.91264	0.95936	0.97341	0.89185	0.91636
CI - root length	No	0.97478	0.99597	0.99033	0.94312	0.96042
CI - root length	Yes	0.97387	0.99867	0.99775	0.92650	0.96104
CI - tooth length	No	0.96908	0.97690	0.96182	0.98236	0.97770
CI - tooth length	Yes	0.98541	0.99763	0.99537	0.96615	0.98528
CI- dilaceration angle	Yes	0.92467	0.95699	0.90267	0.86207	0.77522
Canine - crown height	No	0.86581	0.82620	0.93014	0.85106	0.80220
Canine - crown height	Yes	0.91758	0.91951	0.94054	0.94919	0.95268
Canine - crown/root ratio	No	0.79469	0.22864	0.22496	0.87474	0.80209
Canine - crown/root ratio	Yes	0.78432	0.91002	0.88325	0.63488	0.48650
Canine - mesiodistal diameter	No	0.90260	0.96031	0.95743	0.98338	0.96199

Table 1. Interrater and intra-rater reliability, results of two-way mixed effects ANOVA for consistency, and interrater Pearson correlation coefficients						
Tooth	**Cleft**	**Interrater Reliability (ICC)**	**Examiner 1 Intra-rater Reliably (ICC)**	**Examiner 1 Pearson Correlation***	**Examiner 2 Intra-rater Reliably (ICC)**	**Examiner 2 Pearson Correlation***
Canine - mesiodistal diameter	Yes	0.90875	0.95674	0.97496	0.90894	0.85527
Canine - root length	No	0.98744	0.99807	0.99580	0.97733	0.99191
Canine - root length	Yes	0.97905	0.99571	0.99254	0.95715	0.98048
Canine - tooth length	No	0.98554	0.98944	0.99909	0.97484	0.97928
Canine - tooth length	Yes	0.98508	0.99568	0.99029	0.97014	0.99203
AVERAGE ICC		0.85704	0.92529		0.85351	

Comparison of Dental Dimensions

As seen below in Table 2, after comparison of the 34 afore mentioned measurements was completed, the majority of measures were not found to be significantly different. Only the p-values for CI - root length and CI – dilaceration angle were determined to be significantly different on the cleft side vs. the non-cleft side of the dental arch. Considering the inclusion of the Bonferroni correction in the comparison, the p-values for these measures of 0.0022 and 0.0013 are highly significant for this sample of individuals. With a p-value of <0.05 considered statistically different, the only measures approaching significance, besides the two previously mentioned, were CI – crown/root ratio and CI – tooth length with p-values of 0.0870 and 0.0872 respectively.

Table 2. Comparison of cleft and non-cleft measures.					
	Cleft		**No Cleft**		
Measure	**Mean**	**Std Dev**	**Mean**	**Std Dev**	**p-value***
1st molar - buccal-palatal dimension	11.78	0.6717	11.54	0.816	0.2469
1st molar - crown height	7.16	0.593	7.13	0.687	0.5033
1st molar - mesiodistal diameter	10.07	0.4615	10.16	0.504	0.2354
1st molar - root length	14.37	0.876	14.32	1.043	0.6858
1st molar - tooth length	21.53	0.969	21.45	1.357	0.9079
1st molar- crown/root ratio	0.50	0.054	0.50	0.053	0.8111
CI - crown height	8.22	0.941	8.19	0.407	0.6624
CI - crown/root ratio	0.59	0.063	0.56	0.064	0.0870
CI - mesiodistal diameter	8.25	0.638	8.28	0.412	0.8446
CI - root length	14.13	1.805	14.89	1.515	**0.0022**
CI - tooth length	22.35	2.512	23.07	1.455	0.0872
Canine - crown height	8.11	1.019	8.33	0.910	0.2326
Canine - crown/root ratio	0.51	0.053	0.51	0.073	0.9173
Canine - mesiodistal diameter	7.77	0.819	7.81	0.493	0.5159
Canine - root length	16.11	2.202	16.56	2.160	0.4712
Canine - tooth length	24.21	2.990	24.88	2.575	0.1682
CI – dilaceration angle	175.83	2.358	178.11	1.451	**0.0013**

*Wilcoxon signed rank test

CHAPTER 4

DISCUSSION

Many studies have been completed revealing evidence of the differences in jaw size and tooth dimensions in patients with cleft lip and palate. Defects in tooth size, number, and shape are often observed (Dixon, 1966). Abnormalities of the dentition are most commonly expressed in the formation of the lateral incisor. Following this, hypoplasia of the central incisor in the cleft region has also been reported (Foster & Lavelle, 1971). Without question, agenesis of one lateral incisor or both can present complex challenges during treatment, however, even when a full complement of teeth is present, more subtle expression of differences in tooth size can exist.

Often times, as it should in cases of cleft lip and palate, the focus of a patient's care can be centered on addressing 'bigger issues' such as those pertaining to surgical repair of the defect to achieve appropriate form and function. When this occurs, it is easy to overlook the finer details needed to make comprehensive treatment complete. With the help of oral and maxillofacial surgeons, patients with cleft lip and palate can have the proper skeletal foundation for achievement of treatment goals. As orthodontists, a thorough assessment of the patient's dentition must also be completed in these cases in order to aid in the attainment of not only proper form and function but esthetics as well.

In the past, this aspect of treatment in cleft lip and palate has not been blatantly overlooked. In fact, a plethora of research exists on the evaluation of tooth size and shape in individuals with cleft lip and palate. Most of these studies, however, were performed on study models or two-dimensional radiographs. In these studies, certain

dimensions of the teeth cannot be evaluated or cannot be viewed accurately. Hence, the motivation for the design of this study. Cone beam computed tomography combats these issues.

In addition, many study designs have included a control group of non-cleft subjects. This potentially introduces a conglomerate of variables that cannot entirely be accounted for due to the complexity of tooth as well as cleft development (Jordan, 1966). In this study, an internal control group was utilized for several reasons. The use of an internal control could eliminate some of the potential variables unaccounted for by using an external control. However, by doing so, the inclusion and exclusion criteria became more complex. Patients included in this study were required to be non-syndromic, present with unilateral cleft lip and palate, and have complete formation of the maxillary central incisors, canines, and first molars. Also, fixed orthodontic appliances were required to be absent from CBCT scans, as well as restorations or damage to the anatomy of selected teeth caused by trauma or decay. Once these criteria were applied to the original sample of 305 subjects, many were quickly eliminated from participation in this study. Patients receiving multidisciplinary treatment often spend years in active orthodontic treatment, especially once the dentition has matured enough to include fully formed maxillary central incisors and canines. Hence, the difficulty in identifying individuals presenting with the appropriate dental age without orthodontic appliances in place.

In this study, the null hypothesis was rejected. Despite the majority of measures resulting in no significant difference, the CI – root length and CI – dilaceration angle were shown to be significantly different when comparing the cleft side to the non-cleft

side of the dental arch. Specific aims 1 and 2 were both accomplished. This demonstrates the importance of initial evaluation of tooth size and form in these cases. Root length of the maxillary incisors and dilaceration of roots can both have an impact on orthodontic treatment and successful achievement of treatment goals. Teeth that present with anatomically short roots can and should be of particular concern.

When a patient presents with shorter than average initial root length, this finding should be noted in the initial exam and monitored carefully throughout the duration of treatment. Initial tooth position, which can be heavily dependent on the extent of the cleft, could be off substantially from the desired final position. This brings the amount of planned apical displacement and duration of treatment immediately into play in the patient's initial treatment plan. Practitioners should devise a treatment plan with those factors in mind. A well thought-out initial plan, including precise movements and methods of force application, can potentially limit treatment duration and hopefully mitigate risk of root resorption.

Risk factors relating orthodontic treatment and root resorption have been the focus of many studies. Weltman et al. reported OIIRR (orthodontically induced inflammatory root resorption) in greater than 90% of treated cases (Weltman, Vig, Fields, Shanker, & Kaizar, 2010). That said, in several studies performed on panoramic or periapical radiographs, 6-13% of root resorption was likely to be less than 2.5mm (Blake, 1995). However, more extreme expressions of root resorption can occur. Root resorption surpassing one third of the original root length or more than 4 mm is considered severe. Unfortunately, this is seen in 1-5% of treated teeth (Levander & Malmgren, 1988).

Factors reported to have an effect on OIIRR include: treatment duration, amount of apical displacement caused by orthodontic tooth movement, method of force application, tooth/root length, tooth morphology, roots with development abnormalities, and others (Brezniak & Wasserstein, 1993; B. O. Linge & Linge, 1983; L. Linge & Linge, 1991; Segal, Schiffman, & Tuncay, 2004). Perhaps more concerning is the fact that followed by mandibular incisors and first molars, the maxillary incisors were found to experience more average root resorption during orthodontic treatment (Kaley & Phillips, 1991; L. Linge & Linge, 1991). The findings of this study indicate that CI-root length is decreased on the cleft side. It is advisable for practitioners to educate their patients on their initial presentation and take time to explain the mechanism of external root resorption, in case resorption was to occur on a previously noted shorter root during treatment.

During treatment planning, morphology of the teeth, including dilaceration between the tooth root and crown, is another key factor to consider. According to the glossary of dental terms by the British Standards Institute, dilaceration is defined as the deformity of a tooth caused by a disruption between the mineralized and non-mineralized portions of a developing tooth bud ("British Standards Institute. Glossary of Dental Terms," 1983). Andreasen et al., further described dilaceration as apparent deviation between the long axis of the crown and root portion of a tooth due to displacement of previously formed hard tissue in relation to the soft tissue in a non-axial direction during development (Andreasen, 2007). Furthermore, it has been said that the etiology behind dilaceration is not completely understood. While general agreement amongst most researchers cannot be reached, two explanations seem to prevail. First, a mechanical

displacement injury to the preceding primary tooth causing damage to the developing permanent tooth bud appears to be the most commonly accepted. However, considering the prevalence of primary tooth trauma and the reported prevalence of permanent tooth dilaceration, this is not fully supported, meaning trauma in the primary dentition occurs significantly more frequently than permanent tooth dilaceration. Therefore, primary trauma cannot be credited with every expression of dilaceration or the incidence of permanent tooth dilaceration would be substantially higher. In contrast, the second explanation is the possibility of an idiopathic developmental disturbance (Walia, 2016). This claim is supported by discrediting the mechanical displacement theory based on the premise that most primary tooth trauma occurs before age four, at which time, root formation on the apical permanent tooth has not formed. In addition, dilaceration is said to occur more often in the posterior dentition, which is much less likely to receive a traumatic injury (Hamasha, 2002).

If the displacement of the calcified portion of a developing tooth in relation to the non-calcified portion is indeed the cause of a dilaceration, it is possible that a patient with cleft lip and palate receiving orthodontic and/or surgical treatment could sustain such an insult. Dental arch development through orthodontic expansion and alignment, primary alveolar bone grafting, and other interventions occurring prior to complete permanent tooth root formation could contribute. The results of this study did indicate a significant difference in the maxillary CI – dilaceration angle when comparing the cleft side to the non-cleft side of the dental arch. However, although statistically significant, the average CI – dilaceration angle on the cleft side being approximately 175 degrees does not seem to be clinically significant in most cases. In-depth evaluation of the dilaceration can be

performed readily utilizing CBCT imaging. With this in mind, appropriate treatment of a dilacerated tooth is at the discretion of the treating clinician.

Dilacerated teeth can frequently present partially or fully impacted. It must be determined if the dilacerated tooth can be brought into the dental arch with proper alignment. If possible, the dilacerated tooth can be exposed and brought into the mouth with orthodontic traction. However, in more extreme presentations, the dilacerated tooth may have to be extracted and surgically repositioned or extracted and replaced through prosthetic means (Walia, 2016). If the impacted dilacerated tooth can be brought into the arch with reasonable root alignment with the rest of the dentition, it still may require restorative dentistry in the form of a veneer or full coverage crown to achieve ideal esthetics.

All things considered, the results shown here should be viewed as preliminary due to a small sample size. In order to improve the power of this study, access to a larger number of potential subjects or adjustment of the inclusion/exclusion criteria would be necessary. Allowing CBCTs of patients in active orthodontic treatment would increase the sample size without question, however, acquiring measurements with fixed appliances in place would surely affect their accuracy.

Reliability between examiners was shown to be close to excellent overall, although, several measures were considered 'unreliable' upon conclusion of the comparison. This could have been due in part to the difficulty of consistently identifying landmarks, such as the cemento-enamel junction (CEJ), on selected teeth. Inconsistent identification of the CEJ would undoubtedly affect measurements such as crown height, root length, and crown/root ratio. Again, with a larger sample size, the effect of this

would likely be minimized. In addition, as examiners completed measurements on additional subjects, it would be expected for landmark identification to improve which would therefore improve accuracy of measures.

If future studies replicating this design, aimed at evaluation of tooth dimensions in patients with cleft lip and palate, are to be completed with more powerful results, the initial focus should be on sample acquisition. This would likely necessitate the inclusion of multiple practitioner patient groups and/or patients from additional orthodontic programs. Pooling data from a larger sample size across these sources would improve the odds of reaching a more significant sample size, and, therefore, more significant results.

CHAPTER 5

CONCLUSIONS

1) After comparison of 34 total measures, CI – root length was found to be significantly different on the cleft side versus the non-cleft side of the dental arch. The average root length of the central incisor on the cleft side was 14.13mm and the average root length of the central incisor on the non-cleft side was 14.89mm. Shorter initial root lengths should be noted at the start of treatment, and patients/guardians should be informed. If root resorption is noted during treatment, a pause in treatment or alteration of the orthodontic treatment plan should be considered.

2) For the selected sample, the average CI-dilaceration angle on the cleft side of the dental arch was 175.83 (SD=2.358, min, max=171, 180, median=176 (IQR=174-177)).

3) The CI – dilaceration angle was also found to be significantly different on the cleft side versus the non-cleft side of the dental arch. The average dilaceration angle on the cleft side was 175.83 degrees and the average dilaceration angle on the non-cleft side was 178.11. In cases of more significant dilaceration, ideal alignment of teeth through orthodontic therapy may be inhibited. In these cases,

it should be decided as part of the initial treatment plan whether or not dilacerated teeth can be moved safely and effectively. Teeth with extreme dilacerations may have to be extracted. In less severe cases, restorative dentistry may be necessary to achieve proper esthetics.

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APPENDIX A

IRB APPROVAL FORM

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
Office of the Institutional Review Board for Human Use

470 Administration Building
701 20th Street South
Birmingham, AL 35294-0104
205.934.3789 | Fax 205.934.1301 | irb@uab.edu

APPROVAL LETTER

TO: Souccar, Nada M

FROM: University of Alabama at Birmingham Institutional Review Board
Federalwide Assurance # FWA00005960
IORG Registration # IRB00000196 (IRB 01)
IORG Registration # IRB00000726 (IRB 02)

DATE: 20-May-2019

RE: IRB-300003423
Dental dimensions in patients with Cleft Lip and Palate

Determination: Not Research
Approval Date: 20-May-2019

The Office of the IRB has reviewed your Application for Not Human Subjects Research Designation for the above referenced project. The reviewer has determined this project is not subject to FDA regulations and is not Human Subjects Research. Note that any changes to the project should be resubmitted to the Office of the IRB for determination. If you have questions or concerns, please contact the Office of the IRB at 205-934-3789.

Not Research - Quality Improvement program

Documents Included in Review:

- nhsr.190502.doc

APPENDIX B

APPLICATION FOR DESIGNATION OF NOT HUMAN SUBJECTS RESEARCH (NHSR)

Application for Designation of Not Human Subjects Research (NHSR)

- This form is to be used to request a determination by the IRB (or designated reviewer) of whether an activity is research involving human subjects.
- Complete every numbered item, using a font different from the items for your **responses**.
- Retain the order, numbering, and general layout of this form.
- Please direct questions or comments to the Office of the IRB at 205-934-3789 or irb@uab.edu.

GENERAL INFORMATION

1. Title of Project	**Dental dimensions in patients with Cleft Lip and Palate**

2. Principal Investigator	Name	**Nada Souccar**			
	Department/Division	**Orthodontics**			
	Mailing Address	**302A- 1919 7th Ave S**			
	Telephone	**205-934-3737**		BlazerID	**nsouccar**
3. Contact Person	Name	**Same**			
	Telephone	**[telephone]**	Fax **[fax]**	BlazerID	**[blazer ID]**

4. Is this activity funded in any way?			☐ Yes ☒ No
If yes, *attach* 1 copy of completed funding application and complete (a)-(d):			
a. Grant or Contract Title		**[title]**	
b. PI of Grant or Contract		**[PI]**	
c. OSP Proposal Number		**[OSP]**	
d. Funding Source	Gov't Agency or Agencies	**[name]**	
	UAB Departmental Funds	**[dept/div]**	
	Other	**[other]**	

OTHER INVESTIGATORS, SUPERVISORS

5. Is anyone listed as a Co- or Other investigator on this project?		☒ Yes ☐ No
If yes, indicate Co- or Other and complete (a)-(c) for each investigator. Copy/paste the three rows below as necessary for additional investigators.		
a. Name	**Co-** ☒ **Other** ☐	**Chung How Kau**
b. Job Title		**Professor and Chair**
c. Primary UAB Dept., or non-UAB Employer		**Orthodontics**
a. Name	**Co-** ☒ **Other** ☐	**Peter Waite**
b. Job Title		**Professor and Chair**
c. Primary UAB Dept., or non-UAB Employer		**Oral and Maxillofacial Surgery**
a. Name	**Co-** ☐ **Other** ☒	**Blake Boleware**
b. Job Title		**Resident**
c. Primary UAB Dept., or non-UAB Employer		**Orthodontics**
a. Name	**Co-** ☐ **Other** ☒	**Paul Lewis**
b. Job Title		**Resident**
c. Primary UAB Dept., or non-UAB Employer		**Oral and Maxillofacial Surgery**

a. Name Co- ☐ Other ☒	**Bhumika Patel**
b. Job Title	**Student**
c. Primary UAB Dept., or non-UAB Employer	**Predoctoral Dental Program**

6. Is the principal investigator (named in Item 2) a UAB student? Yes ☐ No ☒

If yes, provide name, phone, and BlazerID of student's supervisor, and ***obtain signature*** of supervisor.

Name **[name]** Telephone **[telephone]** BlazerID **[blazer ID]**

Signature of Student's Supervisor:

CRITERIA FOR DETERMINATION

7. Is the activity a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge? ☐ Yes ☒ No

8. Does the activity involve obtaining information about living individuals? ☐ Yes ☒ No

9. Does the activity involve intervention or interaction with any living individuals? ☐ Yes ☒ No

10. Does the activity involve information that is *individually identifiable*, that is, "the identity of the subject is or may readily be ascertained by the investigator or associated with the information"? ☐ Yes ☒ No

If yes, is the information private, that is, "about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public"? ☐ Yes ☐ No

11. Does the activity involve one or more human subjects and any use of a drug other than the use of a marketed drug in the course of medical practice; that is, is it subject to FDA IND regulations? ☐ Yes ☒ No

12. Does the activity involve one or more human subjects and any evaluation of the safety or efficacy of a medical device; that is, is it subject to FDA IDE regulations? ☐ Yes ☒ No

13. Are the results of the project to be submitted later to, or held for inspection by, the FDA as part of an application for a research or marketing permit? ☐ Yes ☒ No

ACTIVITIES INVOLVING HUMAN MATERIALS

To help the IRB determine that your project does not need further review, complete the following items.

14. Does the activity involve *only* cadaveric materials? ☐ Yes ☒ No

If yes, *attach* documentation from source.

15. Does the activity involve *only* blood products from the Red Cross or other blood banks? ☐ Yes ☒ No

If yes, *attach* documentation from source.

16. Does the activity involve potentially identifiable human materials, such as those from an autopsy? ☐ Yes ☒ No

If yes, describe the materials, their origin, the coding system, and plans for use: **[description]**

17. Briefly describe the proposed research, including what materials you are obtaining and the source of those materials:

The purpose of this retrospective study is to evaluate the dimensions of the teeth using Cone Beam Computed Tomography (CBCT) volumes of individuals with cleft lip and palate, as they often have a retrusive maxilla and smaller teeth on the affected side of the jaw. The CBCT images will be de-

identified and provided by the Oral and Maxillofacial department. This is a retrospective study. Tooth size need to be carefully considered during any dental treatment to achieve harmonious function and esthetics. This is particularly true in individuals with Cleft Lip and palate, as they are often missing bone and/or teeth. All studies that have been conducted have measured the size of the dental crowns, but the length of the roots as well as the bony housing of the tooth have not been evaluated. Thus using three dimensional radiographic images would allow a better understanding of the dental environment and prepare providers to better plan treatment.

Mail or deliver all IRB materials and correspondence to
Room 470, Administration Building (AB)
701 20th Street South, Birmingham, AL 35294-0104
Phone 205-934-3789 — Fax 205-934-1301

ORIGINAL, DATED SIGNATURE OF PRINCIPAL INVESTIGATOR			
Signature:	N. Saucedo	**Date:**	5/2/2019

For IRB Use Only

Notes