

6-30-2014

# Three-Dimensional Evaluation of Root and Alveolar Ridge Width of Maxillary Lateral Incisors in Patients with Unilateral Agenesis

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## Recommended Citation

AlRushaid, Sharifah, "Three-Dimensional Evaluation of Root and Alveolar Ridge Width of Maxillary Lateral Incisors in Patients with Unilateral Agenesis" (2014). *Master's Theses*. 624.  
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# **Three-Dimensional Evaluation of Root and Alveolar Ridge Width of Maxillary Lateral Incisors in Patients with Unilateral Agenesis**

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B Dent. Sc., Trinity College Dublin, 2008

A Thesis

Submitted in Partial Fulfillment of the

Requirements for the Degree of

Master of Dental Science

At the

University of Connecticut

2014

# APPROVAL PAGE

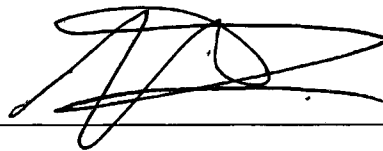
Masters of Dental Science Thesis

## **Three-Dimensional Evaluation of Root and Alveolar Ridge Width of Maxillary Lateral Incisors in Patients with Unilateral Agenesis**

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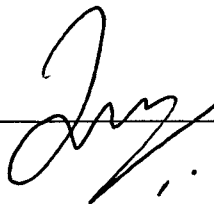
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2014

## Acknowledgements

I would like to thank my committee members who assisted and supported me during my project. I like to express special appreciation to Dr. Uribe for introducing me to this research and for being a great mentor providing me with encouragement and guidance throughout the entire process. He was readily available for any assistance offering advice, directing me to the right path and providing me with resources. I am thankful to Dr. Nanda for allowing me to be part of this orthodontic program and for helping progress with this research. I thank Dr. Tadinada for sharing his knowledge and experience with CBCT.

I would also like to thank Dr. Sheeba Zaidi for allowing me to visit her private orthodontic practice and providing me with patient records and CBCTs. I am grateful to Dr. Carl Roy for his permission to access and use CBCT images from his private offices. I am also grateful to Dr. Derek Sanders for his cooperation and for sharing CBCTs from his private office. I thank my co-resident Dr. Greg Ross and his father Dr. Scott Ross for offering me CBCT's from Dr. Ross's private periodontal office to further develop this research. I thank my co-resident, Dr. Achint Utreja for processing my data and helping with statistics.

I would like to thank my co-residents, especially the Class of 2014, for their support and encouragement throughout my residency. I would like to express my gratitude to the government of the State of Kuwait for sponsoring and funding my residency and research. I am deeply grateful to my friends for their motivation and assistance. Special thanks to my husband for his patience and tolerance and my loving family for their support during my entire life.

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## Abstract

**Introduction:** The objective of this study was to measure the maxillary lateral incisor root dimensions and quantify the labial and palatal bone in patients with unilateral maxillary lateral incisor agenesis (MLIA) and compare them to non-agenesis controls using cone beam computed tomography.

**Methods:** The labiopalatal and mesiodistal root dimension and labiopalatal bone width of maxillary lateral incisors were assessed on pre-treatment and post-treatment cone beam computed tomography scans of 23 subjects (mean age 14.5 years, 17 females and 6 males) with maxillary lateral incisor agenesis and 23 gender-matched subjects (mean age 13.5 years, 17 females and 6 males) with no dental agenesis or anterior Bolton discrepancy. The Mann-Whitney Test was used to distinguish any differences in root width, crown width or changes in labial or palatal bone between the two groups. The Wilcoxon Signed Rank Test was used to compare the pre-treatment and post-treatment findings within each group.

**Results:** The mean labiopalatal root width was narrower in the maxillary lateral incisor agenesis group than controls by 1.25mm ( $P \leq 0.000$ ) at the level of the CEJ. The mesiodistal root width did not differ significantly between the groups. Both groups had thin labial bone with a mean post-treatment labial bone of 0.4mm and 0.8 mm at 4mm apical to CEJ for the maxillary lateral agenesis group and the control group, respectively. At the end of orthodontic treatment the MLIA group lost about 60% of labiopalatal bone width. The mesiodistal crown width was significantly smaller in the maxillary lateral agenesis group at both the incisal edge and at crown midpoint by an average of 1.5mm and 1.4mm, respectively.

**Conclusion:** The buccolingual root, the mesiodistal crown widths, and the labial bone width at 10mm apical to the CEJ of the maxillary lateral incisor in patients with unilateral agenesis were significantly smaller than normal controls.

## Introduction

### Agenesis of the Maxillary Lateral Incisor

Teeth *agenesis*, defined as the congenital absences of one or more teeth, is the most common developmental anomaly in man<sup>1,2</sup>. The term *anodontia* is referred to the complete absences of teeth in the arches, while *oligodontia* is defined as absence of six or more teeth excluding the third molars<sup>3</sup>. *Hypodontia* is a complex term used to describe the absence of teeth, but usually pertains to subjects with less than six missing teeth, and often associated to abnormalities in size and shape of the remaining teeth, as well as abnormalities in the rate and timing of the dental development<sup>4</sup>. The prevalence of anodontia is relatively rare<sup>2</sup> and oligodontia is uncommon with a prevalence of 0.14%<sup>3</sup>. However, the agenesis of one or more teeth is more common and ranges between 1.6% and 9.6%<sup>2</sup> depending on demographic and geographic distribution. The permanent dentition is generally more affected than the primary dentition<sup>1</sup> and dental agenesis is 1.37% more common in females than males<sup>3</sup>.

Maxillary lateral incisor agenesis (MLIA), denoted by the absence of formation of either deciduous or permanent upper lateral incisors, is one of the most common forms of dental agenesis. The maxillary lateral incisor is the second most affected permanent tooth in the dental arch following mandibular second premolar, when third molars are excluded<sup>1,3,5</sup>. The prevalence of MLIA in the permanent dentition ranges from 1% to 4%<sup>5</sup> depending on gender, race and continent. The frequency of MLIA in primary dentition is less common and estimated to be between 0.1% and 0.7%<sup>6</sup>; though, it is considered the most frequent form of hypodontia in the primary dentition<sup>1</sup>. In the Portuguese population, it is estimated that 1.3% are affected by MLIA<sup>6</sup>; however, MLIA has been reported to be more common in Israeli Jews and the United Kingdom with a prevalence of 2.1%<sup>7</sup> and 2% respectively<sup>8</sup>. Bilateral agenesis of maxillary lateral incisor is the most frequent form; although, unilateral agenesis can occur and it is often associated with malformation of the contralateral incisor<sup>6</sup>. In unilateral MLIA cases, the right side is usually more affected than the left side<sup>2,6</sup>.

## **Esthetic consideration with MLIA**

MLIA greatly affects smile esthetics because of its position in the esthetic zone featuring midline diastemas, midline deviations, tipping of teeth and retention of primary dentition<sup>9</sup>. Asymmetries associated with MLIA are present both in the dentition and gingival margins, influencing the harmony of dentofacial complex and negatively impacting patient's self-esteem<sup>10, 11</sup>. An esthetic smile is defined as having teeth size, color, shape and position in harmony, proportion and relative symmetry in relation to each other and to other structures around them<sup>12</sup>. Producing an esthetic smile in cases with MLIA is challenging since these individuals present altered mesiodistal and vertical tooth proportions and asymmetric gingival characteristics which are considered major contributors to an esthetic smile.<sup>12, 13</sup> These alterations may be bilateral or unilateral leading to significant asymmetries and different treatment approaches.

Smile perception of dental professionals and laypeople in cases with MLIA was investigated by Rosa et al.<sup>9</sup> Both laypeople and dental professionals ranked dental tipping, spacing and midline diastemas associated with either unilateral or bilateral MLIA as unattractive. In addition, asymmetric alterations associated with the treatment of MLIA were also considered unattractive by both dental professionals and laypeople. Interestingly, the presence of a deciduous canine was well tolerated by dental professionals and laypeople. Orthodontic treatment to close spaces with the canine cusp alteration in unilateral or bilateral MLIA was considered more attractive than the placement of anterior restorations to close the spaces.

In summary, MLIA has a major impact on smile esthetics and patient's psychological status and poses unique treatment challenges related to teeth proportions and gingival characteristics. Therefore, such cases will require an interdisciplinary treatment approach involving an orthodontist, restorative dentist and periodontist. However, it is important to consider patient's objectives at the initial stages of treatment to avoid overtreatment.



## **Treatment Options:**

Treatment options for management of MLIA can be broadly categorized into orthodontic space closing or space recreation. Orthodontic space closure involves mesial movement of the maxillary canine into the lateral incisor site with significant crown remodeling and possible crown restoration to mimic the lateral incisor with or without gingival recontouring. On the other hand, space recreation involves distal movement of the maxillary canine into its original position and opening space for the missing lateral incisor. The lateral incisor space can be restored by a fixed or removal partial denture, a single tooth implant, or less commonly by autotransplantation of a premolar<sup>14, 15</sup>. It is often challenging to achieve esthetic results because agenesis of a maxillary lateral incisor is generally associated with deficiencies in the alveolar ridge, space problems, uneven gingival margins and short papillae<sup>16</sup>.

The decision in selecting the most appropriate treatment option depends on a number of factors such as: the type of malocclusion, the position of the anterior teeth and their relationship to the cranial base and mandibular dentition, the condition of the adjacent teeth, the amount of space available in the maxillary arch, and the lip level. The treatment of choice should always be the most conservative option that fulfills individual's esthetic and functional expectations<sup>17</sup>. The selection of treatment protocol in cases with MLIA is more likely dependent on the orthodontist's experience and working environment rather than treatment effectiveness. In fact, Louw et al.<sup>8</sup> investigated treatment preferences among orthodontists in the United Kingdom on patients with MLIA. The results showed that orthodontists who worked in practices limited to orthodontics were more likely to perform space closure with canine reshaping. However, orthodontists who worked in practices with available restorative dentists preferred restorative treatment with minimal preparation bridges. The above results indicate that treatment of MLIA generally requires an interdisciplinary treatment approach to achieve the best esthetic and functional outcome.

The best treatment option for MLIA is still very controversial in the orthodontic literature. Recently, a systematic review was conducted to review the evidence regarding the efficacy and safety of

the three MLIA treatment options: orthodontic space closure, space opening with fixed partial denture or a single tooth implant. Unfortunately, there were no randomized clinical trials on this topic, highlighting the fact that there is no scientific evidence on any of the treatment options of MLIA and most of the literature in this area is based on case reports, expert's opinion, and post-intervention evaluation<sup>18</sup>.

### **Etiology of MLIA:**

The etiology of dental agenesis is still not completely understood; though, there is strong support for a genetic hypothesis. Tooth agenesis can be manifested as an isolated trait, part of a syndrome, or a systemic disorder. Non-syndromic tooth agenesis can either be sporadic or familial, and familial agenesis can be a single dominant, a recessive or X-linked gene defect<sup>4</sup>. Odontogenesis, the process of tooth development, is a complex mechanism that involves a series of well-ordered interactions between epithelial and mesenchymal cells that are controlled by genetic factors. This complex genetic system is responsible for the position, number, dimension, and shape of the teeth and any alteration can result in dental anomalies. Different anomalies can result depending on the developmental stage when the alteration takes place. These anomalies include: number anomalies (extra teeth or missing teeth), structural abnormalities and shape abnormalities<sup>2,5</sup>.

There are several hypotheses that were developed before the era of genetic mapping to describe the etiology of tooth agenesis, which can be broadly classified into evolutionary and anatomical theories. Evolutionary theories explain tooth agenesis as related to reduced functional chewing as a result of soft, convenient diet which in turn causes shrinking of the maxilla-mandibular complex and therefore reduction in the number of teeth<sup>2</sup>. Clayton<sup>19</sup> observed that the most commonly missing tooth was the last tooth of each class (lateral incisors, second premolars and third molars). He referred to them as “*vestigial organs*”, meaning these teeth will eventually be lost as part the evolutionary process. On the other hand, one anatomical theory hypothesizes that agenesis mostly occurs in fragile lamina sites, which are more susceptible to epigenetic factors and hence resulting in agenesis. The MLIA occurs at the site of fusion of lateral maxillary process and medial nasal process, while the lower central incisor occurs in the area of

fusion of the mandibular processes. A neural hypothesis was also described stating that areas where innervation develops last embryologically are the most sensitive areas for tooth agenesis<sup>2, 4</sup>. However, recent studies have shown that odontogenesis is under genetic control and the most accepted statement is that tooth agenesis is an autosomal dominant hereditary anomaly with incomplete penetrance and variable expressivity<sup>2</sup>. Penetrance as defined by Galluccio et al.<sup>2</sup>, is “ the percentage of individuals with a particular gene combination showing the respective characteristic at a particular degree”, while expressivity refers to “the degree of phenotype expression”<sup>2</sup>. Hence, variation in tooth size or shape such as peg lateral incisor may reflect variable expression while unilateral agenesis may have resulted from incomplete penetrance<sup>4</sup>. On the other hand, dental agenesis can less frequently be caused by environmental or acquired factors such as infection, trauma to the dentoalveolar process, drugs or other chemicals, or radiation therapy, which can disturb or arrest the process of odontogenesis<sup>1</sup>.

Although, there are more than 200 genes expressed during odontogenesis, only a few are frequently associated with non-syndromic tooth agenesis. These genes are: paired box gene 9 (PAX9) and muscle segment homebox 1 (MSX1), both are transcription factors expressed in mesenchymal cells; ectodysplasin A (EDA), which is a membrane protein expressed by external epithelial cell; and axis inhibition protein 2 (AXIN2), which is a gene that suppresses the Wingless (WNT) pathway during odontogenesis<sup>2, 20</sup>. Mutations in PAX9 sequence are generally linked to the agenesis of molars, while alterations in MSX1 are associated with missing premolars, and incisor agenesis is primarily associated with mutations in EDA. Alterations in AXIN2 are associated with severe molar and premolar agenesis. The agenesis pattern associated with mutations of the above genes varies considerably between individuals and some mutations may be associated with not only dental agenesis but other anomalies or increased cancer risk. Mutations of MSX1 have been linked to cleft lip and palate and increased risk of breast cancer. In addition, EDA mutations are also associated with ectodermal dysplasia and more importantly, AXIN2 gene defects are related to predisposition for both colorectal and breast cancer<sup>20</sup>.

MLIA, like other forms of agenesis, seems to have a strong genetic component with variable expressivity. Data from families of the Mormon Church in Salt Lake City, established that the frequency of individuals with missing maxillary lateral incisor was significantly higher in parents and siblings of families with missing lateral incisor compared to parents and siblings of a control group. These findings lead to the conclusion that mutations of several genes and genotypes may affect the permanent dentition. Furthermore, some of those genotypes may be specific to maxillary lateral incisor agenesis, some may cause multiple agenesis, and some may cause maxillary lateral incisor agenesis and other dental anomalies such as peg laterals<sup>21</sup>.

More recently, Pinho et al. looked at familial aggregation of maxillary lateral incisor agenesis and the occurrence of other types of agenesis or microdontia in a Portuguese population. The relative risk ratio was then calculated and compared to earlier familial studies. The relative risk ratio for a first degree relative of a proband was 15 times greater than the general population for the Portuguese sample, 12 in the Utah population and 5 in the Israeli population. These findings indicate a significant familial aggregation for maxillary lateral incisor agenesis and that microdontia of maxillary lateral incisor is part of the same phenotype, which is considered a milder form of maxillary lateral incisor agenesis phenotype. Bilateral maxillary lateral incisor agenesis or unilateral maxillary lateral agenesis with microdontia was more common than unilateral microdontia alone<sup>7</sup>.

The genetic risk factors of MLIA have been identified by Alves-Ferreira et al. in a large case control study. The following genes PAX9, EDA, SPRY2 (Sprouty), SPRY4 and Wingless 10A (WNT10A) were identified as risk factors for the development of MLIA in the Portuguese sample. Moreover, three pairs of gene-gene interactions have been discovered to be strongly related to MLIA, these are TGF $\alpha$  (transforming growth factor alpha)- AXIN2, MSX1-TGF $\alpha$ , and SPRY2-SPRY4<sup>5</sup>.

In conclusion maxillary lateral incisor agenesis is transmitted as an autosomal dominant trait with incomplete penetrance and variable expressivity.<sup>4, 7, 21</sup> Peg-lateral incisor may reflect incomplete

expression of the maxillary lateral incisor gene and unilateral incisor agenesis can be manifested as reduced penetrance<sup>4</sup>.

### **Agenesis and Associated Anomalies:**

The variable expressivity of tooth agenesis frequently leads to other associated dental anomalies such as: reduction in tooth size, certain types of ectopic eruption, impactions, or delayed dental development<sup>22-25</sup>. Peck et al.<sup>26</sup> evaluated the association between dental agenesis and palatally displaced canines, transposition of mandibular canines with mandibular lateral incisors, and transposition of maxillary canines with premolars. Their results showed that patients with maxillary first premolar and canine transposition were 13 times more likely to have MLIA, and 5 times more likely to have mandibular second premolar agenesis. Also, patients with palatally displaced canines had higher frequency of third molar and mandibular second premolar agenesis<sup>26</sup>. Shapira et al.<sup>24</sup> studied the characteristic features of maxillary canine transposition and associated anomalies in orthodontic patients. Higher incidence of dental anomalies which frequently occurred on the same side as the transposition was seen in their sample. These include MLIA, small maxillary lateral incisor, premolar agenesis, retained primary teeth, impacted canines and central incisors, and severe rotations of adjacent premolars. These results further emphasize that dental anomalies may share a common genetic origin with varying expressivity.

More specifically, the agenesis of maxillary lateral incisor is related to certain transpositions<sup>26</sup>, palatally displaced canines, and premolar rotations<sup>27, 28</sup>. Garib et al.<sup>29</sup> investigated the prevalence of dental anomalies in patients with maxillary lateral incisor agenesis. They reviewed panoramic radiographs and dental casts of 126 patients with agenesis of at least one maxillary lateral incisor and compared them to reference data from a control population group. Subjects with MLIA had 18.2% increased prevalence of permanent tooth agenesis (excluding third molars) than the general population. The frequency of maxillary second premolar agenesis was found to be 10.3%, mandibular second premolar agenesis 7.9% and microdontia of maxillary lateral incisor was seen in nearly 40% of the sample. Moreover, the

frequency of distoangulation of mandibular second premolar was significantly increased compared to general population. Finally, the prevalence of palatally displaced canines was also elevated by 5.2%. The authors stated that mutation of one gene may interfere in morphogenesis of more than one tooth and certain genetic mutations may cause different phenotype expression<sup>29</sup>.

Celikoglu et al.<sup>30</sup>, investigated the prevalence of MLIA and associated dental anomalies in Turkish orthodontic patients. It was estimated that 2.4% of the orthodontic patients had MLIA and females were affected more than males. The prevalence of ectopic eruption of maxillary canines was the most common finding with a prevalence of 21.3%, followed by the reduction in maxillary lateral incisor size or the presence of peg-lateral incisor with a prevalence of 20.2%, which both were significantly greater than the published data for the general population. Other less common anomalies were also observed such as hypodontia of other teeth, impacted canines, and transposition. Interestingly, patients with MLIA had greater prevalence of skeletal Class III malocclusion<sup>30</sup>.

These findings are of clinical relevance especially in cases with unilateral maxillary lateral incisor agenesis where the reduction in size of the contralateral incisor should be taken into consideration when planning to replace the missing incisor. Furthermore, agenesis of a maxillary lateral incisor might be an early risk factor for palatally displaced canines<sup>29</sup>.

### **Agenesis and Microdontia:**

*Microdontia*, is referred to a dental anomaly of having one or more small teeth, and its association with dental agenesis is well documented in the literature<sup>31-33</sup>. The reduction in tooth size usually occurs in both buccolingual and mesiodistal dimensions, but it is more prominent in the buccolingual dimension<sup>32</sup>. There is a great variation in teeth dimensions among agenesis cases, the greater the number of missing teeth, the smaller the tooth size<sup>32, 33</sup>. Yaqoob et al.<sup>34</sup> studied the relationship between bilateral MLIA and anterior tooth width. The authors measured the mesiodistal width of maxillary and mandibular anterior teeth on study models using a digital caliper on 52 subjects with bilateral MLIA and compared them with

54 fully dentate subjects. The maxillary anterior teeth were 0.33mm smaller in the MILA group compared to controls and mandibular anterior teeth were 0.42mm smaller in the mesiodistal dimension.

Mirabella et al<sup>35</sup>, investigated the association between maxillary lateral incisor agenesis and coronal size of the dentition. The authors used a digital caliper to evaluate the mesiodistal dimension of crowns of teeth on plaster casts on 81 patients with maxillary lateral incisor agenesis and 90 controls. Results revealed that patients with maxillary lateral incisor agenesis had smaller teeth compared to controls except for maxillary right and left first molars. This finding was true for both unilateral and bilateral maxillary lateral incisor agenesis. Among the patients with unilateral maxillary lateral incisor agenesis, 44.8% had a microdontic contralateral maxillary incisor that was narrower than 5 mm in width. The average difference in the mesiodistal width of the maxillary and mandibular central incisors in the patients with MLIA was 0.47mm and 0.43mm respectively<sup>35</sup>. These findings can be explained by the fact that dental anomalies are caused by complex interactions of genetic, environmental, and epigenetic factors occurring during the dental development with different phenotype expressions<sup>36</sup>. Therefore, those factors that resulted in maxillary lateral incisor agenesis may have affected tooth width for all teeth except the maxillary first molars. The authors recommend restoring the maxillary anterior teeth to achieve the best esthetic outcome in either treatment alternative: space recreating or canine substitution<sup>35</sup>.

## **The Use of Cone Beam Computed Tomography**

The use of cone-beam computed tomography (CBCT) is becoming popular in dentistry, particularly in orthodontics as a three-dimensional method for diagnosis and treatment planning. CBCT imaging provides several advantages over the conventional two dimensional (2D) radiographs because of its unique features, namely: image reconstruction and the ability to produce linear and curved planar projections from a single CBCT that can be used for diagnosis and treatment planning<sup>37</sup>. Images produced by CBCT are highly accurate because voxel resolution is isotopic, equal in all 3 dimensions, producing sub-millimeter resolution ranging from 0.09mm to 0.4mm<sup>38</sup>. Furthermore, CBCT images are produced with short scanning time (10-70 seconds) and hence, inaccuracies related to patient movement and

positioning are minimized as these scans are not affected by skull orientation<sup>38, 39</sup>. In addition, CBCT is considered not only a diagnostic tool but also a measuring instrument in which accuracy is related to smaller voxel size<sup>40</sup>.

The use of CBCT in measuring buccal and palatal bone has been documented<sup>41-43</sup>. Moreover, the validity of CBCT in measuring the mesiodistal tooth dimension was investigated by Celikoglu et al<sup>44</sup>. The authors compared the mesiodistal diameter of maxillary and mandibular teeth on plaster models and on CBCTs using the records of 26 patients. The results revealed that the mesiodistal width of the teeth were similar in both methods and concluded that CBCT measurements can be used instead of those obtained on plaster models.

More specifically, the use of CBCT to assess the maxillary lateral incisor morphology has been evaluated by Liuk et al.<sup>45</sup> The authors compared maxillary lateral incisors in cases with palatally impacted canines and to controls. The sample consisted of 40 patients with palatally displaced canines with a control group that consisted of 30 normal subjects matched for age and sex. The measurements of the mesiodistal and buccolingual root width of the maxillary lateral incisor root were done on axial sections of the CBCT images at three levels: at the cementoenamel junction (CEJ), 4mm apical to CEJ level, and 8mm apical to CEJ level, and the root length was measured on the sagittal section. The results demonstrated that in the group with palatally displaced canines, the mean root width was smaller especially in the buccolingual dimension by 0.7mm, and mean root length was 1.2mm shorter.

Several studies reported on the association of MLIA with other anomalies such as: reduction of crown width, other agenesis, palatally displaced canines, and distoangulation of mandibular second premolar<sup>25, 29, 34, 46</sup>. However, none of these studies measured root or bone dimension. The use of three dimensional imaging such as CBCT made it possible to measure the labiopalatal root and bone width clinically with high accuracy<sup>40, 45</sup>. Nevertheless, no study evaluated the maxillary lateral incisor root and bone morphology using CBCT imaging in subjects with unilateral maxillary lateral incisor agenesis.



## **Rationale**

Clinicians often face a dilemma when treating patients with maxillary lateral agenesis as it usually requires a complex multidisciplinary approach because of its position in the esthetic zone. The management of MLIA poses unique challenges since smile symmetry and harmony are affected, thus impacting the individual's self-esteem. Treatment options include orthodontic space closure with canine substitution with subsequent recontouring or space recreation for prosthetic replacement by means of an endosseous dental implant or a tooth-supported restoration.

The generalized reduction in tooth size associated with maxillary lateral agenesis complicates both orthodontic and restorative treatment plans in achieving ideal buccal interdigitation, overjet, overbite and esthetics. Previous studies reported the lack of crowding in maxillary lateral incisor agenesis cases because of microdontia and hence, recommended space recreation with prosthetic replacement preferably with a single tooth implant. The contralateral lateral incisor is often used as a guide for restorative space in unilateral agenesis cases. However, studies have demonstrated that the mesiodistal width of the contralateral tooth in unilateral MLIA is often reduced and therefore should not be used as a guide. A recent CBCT study illustrated that the maxillary lateral incisor crown as well as root width was significantly reduced in cases with palatally impacted canines<sup>45</sup>. To our knowledge no study has looked at the dimensions of lateral incisor root, crown and bone in unilateral maxillary lateral incisor agenesis.

This study will measure the labiopalatal root width, the mesiodistal crown and root width as well as the surrounding bone in patients with unilateral maxillary lateral incisor agenesis and compare them to controls.

## **Null hypothesis:**

There is no difference in the morphology of maxillary lateral incisors roots and surrounding bone width between subjects with unilateral maxillary lateral agenesis and controls.

## **Goal**

This study will measure the dimensions of the maxillary lateral incisor crown and root, and quantify the amount of labial and palatal bone in relation to the present lateral incisor in subjects with unilateral maxillary lateral incisor agenesis and non-agenesis controls.

## **Specific Objectives**

- To measure the labiopalatal and mesiodistal root dimensions and labiopalatal alveolar bone widths of maxillary lateral incisors in unilateral maxillary lateral incisor agenesis.
- To measure mesiodistal crown width of maxillary lateral incisors in unilateral maxillary lateral incisor agenesis.
- To compare root and bone dimensions of maxillary lateral incisors between subjects with unilateral maxillary lateral agenesis and non-agenesis controls.

## **Materials and Methods**

In accordance with the institutional review board protocol approved by the University of Connecticut (IRB 14-015-2), this pilot study was comprised of 46 patients treated in four private orthodontic offices (Dr. Sheeba Zaidi in Wallingford, CT, Dr. Derek Sanders in Miami, FL, and Dr. Carl Roy's offices in Virginia Beach and Chesapeake, VA) and one periodontic office (Dr. Scott Ross in Miami, FL) that routinely use cone beam imaging for diagnostic purposes. Approximately 7,000 patient records (clinical examination notes, dental radiographs, photographs, and CBCT scans) were searched to select patients that would fit into the following study criteria:

Inclusion criteria for the study group: (1) healthy patients with no history of systemic conditions or serious illnesses; (2) unilateral missing lateral incisor; (3) at least 10 years old at the time when initial records were taken with completed maxillary lateral incisor root formation; (4) availability of previously acquired pre-, post-treatment or both pre-and post CBCT scans of good quality.

Exclusion criteria for study group: (1) bilateral congenitally missing maxillary lateral incisor; (2) history of trauma, root canal therapy, restorations, or incisal edge abrasion of the maxillary lateral incisor; (3) more than 90 degrees rotation or blocked out maxillary lateral incisor; (4) previous root resorption; (5) transposed canines and lateral incisors; (6) patients with cleft palate or any other dentofacial deformities.

Inclusion criteria for the control group: (1) healthy patients with no history of systemic conditions or serious illnesses; (2) at least 10 years old at the time of initial records with completed maxillary lateral incisor root formation; (2) complete eruption of maxillary incisors; (3) availability of previously acquired pre- and post-treatment CBCT scans of good quality; (4) absence of abnormal morphology or reduced size of lateral incisors or other teeth.

Exclusion criteria for the control group: (1) history of trauma, root canal therapy, restorations, or incisal edge abrasion of the maxillary incisors; (2) severe rotation ( $>90^\circ$ ) or blocked out maxillary lateral incisor; (3) dental agenesis or Bolton Index  $> 1$  SD; (4) previous root resorption.

Fifty-six subjects were identified with unilateral MLIA and 30 subjects were excluded because of unavailable CBCT, two subjects were excluded due to severe root resorption on the maxillary lateral incisor, and one subject had congenitally missing lower incisors. The study group therefore was compromised of 23 subjects (17 females and 6 males), with an average age of  $14.5 \pm 4.5$  years at the beginning of active treatment, when fixed appliances were bonded (T1). These subjects were gender matched with 23 subjects (17 females and 6 males) with no MLIA or Bolton discrepancy that served as controls, with an average of  $13.51 \pm 2.98$  years at T1. A summary of patients' descriptive characteristics can be found in **Table 1**.

CBCT images were obtained of all subjects using either the Classic i-CAT (14-bit gray-scale resolution, 0.3mm voxel size), or Next Generation i-CAT (14-bit gray-scale resolution, 0.3mm voxel size) cone beam 3-D dental imaging system and reconstructed through i-CAT Vision software (Imaging Sciences International, Hartfield, Pa). One CBCT was produced with Picasso-Trio (14-bit gray scale

resolution, 0.2mm voxel size) cone beam 3-D dental imaging system and reconstructed through Ez3D Plus software (VATECH Global, Korea). All images were transported as digital imaging and communications in medicine (DICOM) files and were imported into Dolphin Imaging software 3D (version 11.0; Dolphin Imaging & Management Solutions, Chatsworth, CA) for secondary reconstruction.

CBCT images for each patient in the control group were taken at two time points: 1) Pre-treatment scans taken before active orthodontic treatment was initiated (T1), and 2) Post-treatment scans taken after orthodontic treatment was completed (T2). However, only 12 patients in the study group had both T1 and T2 CBCT images with a total of 20 pre-treatment and 15 post-treatment CBCT images. Both the volumetric rendering and multiple planar views (sagittal, axial and coronal) features of the software were used to orient and determine the reference planes.

All measurements were made on the maxillary lateral incisor on the non-agenesis side for all subjects in the MLIA group. For the control group the measurements were done on both right and left maxillary lateral incisors and the mean value was recorded. Measurements were made on the multiplanar view rather than the three-dimensional (3-D) reconstructed image as the virtual renderings are projected images and not actual surfaces<sup>47</sup>. In addition, reliability was found to be higher when landmarks were identified on the multiplanar views compared to the 3-D reconstructed images<sup>48</sup>. All sagittal, axial and coronal CBCT sections were analyzed with slice thickness of 1 voxel and measured to the nearest 0.1 mm.

The multiplanar view and the volumetric rendering were used to identify the long axis and the center of the incisor root. Images were reoriented so that the lateral incisor was standing vertically with root canals parallel to the software's vertical line in both sagittal and coronal slices (**Figure 1**).

Two methods were used to assess the labiopalatal and mesiodistal root width. In the first method, lateral incisor root width was measured using the method described by Liuk et al<sup>45</sup>. Measurements were made on three axial sections taken perpendicular to long axis of the tooth as determined by the sagittal

section: at the cementoenamel junction (CEJ), 4mm apical to CEJ and 8mm apical to CEJ of the maxillary lateral incisor. The labiopalatal root thickness was measured on axial slices across the root from the labial-most surface of the incisor root to the palatal-most surface of the incisor root. The mesiodistal root width was measured from the widest point on the mesial surface to the widest point on the distal surface (**Figure 2**).

In the second method the labiopalatal root width was measured on the sagittal section parallel to the long axis of the lateral incisor through the center of the root. These measurements were again at the CEJ, 4 mm apical to CEJ, and 8 mm apical to CEJ of the lateral incisor. Root width was measured from the labial to the palatal root surface of the lateral incisor (**Figure 3**).

For the mesiodistal root width, a second method utilized the coronal section which was made parallel to the long axis of the lateral incisor, through the center of the root. Measurements were done at the same three levels: at CEJ, 4 mm, and 8 mm apical to CEJ. Root width was measured from distal most to mesial most incisor root surface (**Figure 4**).

The labiopalatal thickness of the maxillary lateral incisor alveolar bone was measured on four axial sections made perpendicular to the long axis of the lateral incisor (**Figure 5. Labial and palatal bone width on axial slice 6mm apical to CEJ**). In a study measuring alveolar bone thickness on CBCT after space-opening for implants in cases with MLIA by Uribe et al<sup>49</sup>, the buccolingual alveolar bone width was measured on 5 slices: 2mm, 4mm, 6mm, 8mm and 10mm apical to alveolar bone crest. The CEJ is an easily identifiable landmark on the CBCT that can be located with accuracy that is limited to the voxel size and a margin of error of about 0.4mm. The location of the alveolar bone margin is affected by both the voxel size and the spatial resolution of the CBCT machine, and hence can be located with an accuracy of 0.86mm<sup>42, 50</sup>. Therefore, a modification was made to the Uribe et al<sup>49</sup> method for buccolingual bone width measurements. Four measurements were done on the labial surface and four on the palatal surface of the lateral incisor. The first axial section was done 2mm apical to the CEJ as determined by the

sagittal section of the lateral incisor. The second axial section was taken 4mm apical to the CEJ; the third axial section was taken 6mm apical to the CEJ of the tooth; and the fourth axial section at 10mm apical to the CEJ of the tooth. The labial bone thickness was determined by a line from the labial most limit of the buccal bone to outermost labial surface of the incisor. The palatal bone thickness was measured by a line from the palatal most limit of the bone to the outermost palatal surface the incisor.

The total labiopalatal bone width was determined mathematically by adding labial bone width to the palatal bone width as determined by the axial slices, at pre-treatment and post-treatment scans.

The mesiodistal crown width was measured on two axial section made perpendicular to the long axis of the lateral incisor. The first axial section was made at the level of incisal edge as determined by the sagittal section (**Figure 6**). The second axial section was made at the crown's midpoint between the incisal edge and the CEJ. The mesiodistal crown width was measured by a method similar to that described by Benninger et al., from the widest identifiable point on the mesial surface to the widest identifiable point on the distal surface of the incisor crown.<sup>51</sup>

All measurements of the lateral incisor root width, labiopalatal bone thickness, and mesiodistal crown width were done on available T1 and T2 scans on both study and control groups and values were compared.

## **Statistical Analysis**

All measurements were performed by one investigator (S.S. A). To assess intra-examiner reliability, 14 subjects of each group were randomly selected and measurements were repeated again for both time points. The second measurement was done at least two weeks later. The two sets of measurements were then compared and reliability was investigated with the Cronbach alpha coefficient.

Statistical analysis was performed with SPSS Statistics (Version 20; IBM, Chicago, Ill). The data were first assessed for normality using both Kolmogorov-Smirnov and Shapiro-Wilks test. The data did

not show normal distribution for all the variables and therefore non-parametric tests were used. The parent sample consisted of a total of 23 subjects and different analyses were used for specific measurements. The Wilcoxon Signed Rank Test was used to compare paired samples of 12 pre- and post-treatment measurements in the MLIA group and 15 in the control group. The Mann-Whitney *U* Test was used to compare the data of 20 subjects from the MLIA with 20 controls at T1, and 15 subjects from MLIA group to 15 controls at T2. A significance level was set at  $p < 0.05$ .

## **Results**

### **Reliability Analysis**

The intra-examiner reliability was established using the Cronbach alpha coefficient. The reliability of the same rater was repeated on 14 randomly selected subjects from the study group and 14 randomly selected subjects from the control group, measured at two different time points at least two weeks apart. The Cronbach's alpha for selected measurements ranged from 0.75 (Labial bone width at T2 4mm apical to CEJ on study group) to 0.99 (**Table 2**).

### **Descriptive Analysis**

A total of 23 lateral incisors with MLIA and 46 control lateral incisors were analyzed; the mean value for right and left lateral incisor in controls was recorded for each variable. Seventy three percent of the subjects with MLIA were females and 60% of the agenesis of the maxillary lateral incisor occurred on the left side. About half of the subjects were between 12 years and 14 years at the start of the treatment. At the end of orthodontic treatment the majority of the subjects in the MLIA group were above 16 years of age while, 60% of the control group were 16 years or younger at the end of orthodontic treatment (**Table 1**).

The data for some variables were not normally distributed and therefore non-parametric tests were used. The lateral incisor means for each variable were compared between subjects with MLIA and

the control group using the Mann-Whitney *U* Test. **Table 3** compares means for lateral incisor variables between the two groups at pre-treatment (T1), and Table 4 at post-treatment (T2).

The pre-treatment and post-treatment measurements of 12 lateral incisors with MLIA and 15 controls were analyzed. Again, the data of some variables were not normally distributed. Therefore, the Wilcoxon Signed Rank Test was used to compare the lateral incisor variables of the same patients between T1 and T2. Error! Reference source not found. Compares the lateral incisor variables between T1 and T2 for 12 subjects with MLIA and **Table 6**, shows the same variables in 15 controls.

### **Labiopalatal (LP) Root Width**

Both methods of measuring LP root width showed similar values. In the MLIA group the mean LP width at the CEJ was 6.0mm for both methods (axial and sagittal). The mean LP root width at 4mm and 8mm from the CEJ in the MLIA group was 5.0mm and 4.1mm respectively with both methods. On the other hand, the control group had a wider LP root with an average value of 7.1mm, 5.9mm, and 4.8mm at the level of the CEJ, 4mm apical to CEJ, and 8mm apical to the CEJ, respectively. The MLIA group had significantly narrower LP root width at all levels. The mean difference at the CEJ was 1.15mm ( $P \leq 0.000$ ), 0.9mm at 4mm ( $P < 0.000$ ) and 0.75mm at 8mm ( $P \leq 0.01$ ). The difference between the LP root width at T1 and T2 was negligible for both groups.

### **Mesiodistal (MD) Root Width**

The mean MD root width at the CEJ was 4.9mm for subjects in the MLIA group and 5.4mm for the control group. The MLIA group had slightly narrower roots at both the CEJ and at 4mm apical to CEJ than the control group, with mean differences of 0.3mm and 0.4mm, respectively; these were significant at T2 only. Interestingly, the mean difference between the two groups at 8mm apical to the CEJ was less than 0.1mm. The difference between the mean MD root width at T1 and T2 ranged from 0.0 to 0.4mm. The MD root width measurements made on the axial slices and coronal slices were of similar values.



## **Labial Bone (LB) Width**

The labial bone width was very thin for both groups when registered at all levels; the mean LB width at 2mm apical to the CEJ ranged from 0 to 0.1mm for both groups. The labial bone approached 1mm at 4mm and 6mm apical to the CEJ for both groups at T1. However, at 10mm apical to the CEJ the labial bone in the control group was 0.4mm thicker than the MLIA group and this was statistically significant ( $P<0.02$ ) at T1.

From pre-treatment to post-treatment both groups experienced labial bone loss of 0.1mm at 2mm apical to the CEJ and 0.4mm at 4mm apical to the CEJ. Conversely, both groups showed bone gain of 0.4mm at T2 when measured 10mm apical to the CEJ which was significant for the MLIA group ( $P\leq 0.004$ ).

## **Palatal Bone (PB) Width**

The PB width was generally greater than the LB width for all four levels in both groups, especially at T1. The mean pre-treatment PB width at 2mm apical to the CEJ was 0.4mm for the MLIA group and 0.2mm for the control group. The palatal bone increased in width in the apical direction; this trend was noted for both controls and MLIA group but was more pronounced in MLIA group. The PB width in the MLIA group was thicker when compared to controls with an average difference of 0.6mm, 0.5mm, and 0.8mm at 4mm, 6mm and 10mm apical to the CEJ, respectively. Yet, these differences were not statistically significant.

Subjects in the MLIA group experienced a significant amount of palatal bone loss after orthodontic treatment. This was evident at 4mm, 6mm, and 10mm apical to the CEJ with an average PB loss of 1.2mm ( $P\leq 0.003$ ), 1.3mm ( $P\leq 0.002$ ) and 2.1mm ( $P\leq 0.003$ ), respectively. The subjects in the control group also experienced PB loss post-treatment but less severely than the MLIA group. The average PB loss at 10mm apical to the CEJ was 1.4mm ( $P\leq 0.001$ ) and 0.7mm ( $P\leq 0.002$ ) at 6mm apical to the CEJ.

## **Total Labiopalatal (LP) Bone Width**

The total labiopalatal bone width was determined by adding the palatal bone width to the labial bone width at 4 different heights from the CEJ: at 2mm, 4mm, 6mm and 10mm apical to the CEJ. Subjects in the MLIA group had slightly more LP bone compared to controls, but differences were not significant. The mean LP bone width ranged from 0.25mm at 2mm apical to the CEJ to 5.0mm at 10mm apical to the CEJ for the MLIA group, and from 0.2mm at 2mm apical to the CEJ to 4.45mm at 10mm apical to the CEJ for the control group.

The mean bone loss from pre-treatment to post treatment was significant for levels 4mm, 6mm, and 10mm apical to the CEJ for both groups. The average bone loss was 1.4mm ( $P \leq 0.008$ ) at 4mm apical to the CEJ and 1.7mm ( $P \leq 0.004$ ) at 10mm apical to the CEJ for the MLIA group. The control group experienced a mean bone loss of 1mm ( $P \leq 0.001$ ) at 4mm apical to CEJ and 1mm ( $P \leq 0.007$ ) at 10mm apical to the CEJ.

## **Crown Morphology**

The MD crown width was measured at the incisal edge (IE) and at the midpoint between the incisal edge and the CEJ to determine the crown morphology. The mesiodistal crown width was significantly smaller in subjects with MLIA. The mean MD width measured at the IE was 4.3mm for the MLIA group and 5.9mm for control group. The average difference in the MD crown width measured at midpoint was 1.4mm ( $P \leq 0.000$ ) and 1.6mm at the incisal edge ( $P \leq 0.000$ ). The difference from T1 to T2 was 0.4mm at midpoint for the MLIA group and 0.2mm for the control group.

## **Discussion**

The agenesis of the maxillary lateral incisor is one of the most common forms of dental agenesis<sup>1,3,5</sup> and its management poses unique challenges because of its location in the esthetic region. In this pilot retrospective CBCT study, the agenesis of the maxillary lateral incisor was more frequently

found in females (73 % of the subjects in the MLIA group). This increased prevalence is in agreement with others<sup>3, 6, 30</sup> such as Pinho et al.<sup>6</sup>, who investigated the prevalence of MLIA in a Portuguese sample and reported out of the 219 subjects with MLIA, 131 (60%) were females. Among the unilateral MLIA, the authors showed that 60% of the agenesis occurred on the right side in the Portuguese sample<sup>6</sup> and Galluccio et al. stated that the right side was the most common agenetic site<sup>2</sup>. This is countered by our findings as agenesis was more likely to occur on the left side (60%) rather than right side, which is supported by Behr et al.<sup>52</sup>. The authors investigated the prevalence of dental agenesis in orthodontic patients in Eastern Bavaria, and the maxillary left lateral incisor was the third most common missing tooth followed by the maxillary right lateral incisor.

Unilateral MLIA leads to dental asymmetry and disproportion greatly affecting esthetics and treatment outcome<sup>9</sup>. However, management of MLIA is based on the clinician's experience and work environment as there is no scientific evidence to support the best treatment approach<sup>8, 18</sup>. It is well documented that the MLIA has a strong genetic background, transmitted as an autosomal dominant trait with incomplete penetrance and variable expressivity<sup>4, 7, 21</sup>, and it is usually associated with other anomalies such palatally displaced canines, agenesis of other teeth, and microdontia. Yet, very little is known about bone thickness and root morphology of lateral incisor in cases of unilateral MLIA which can greatly affect treatment decision and outcome.

The mean labiopalatal root width of the maxillary lateral incisor in the maxillary lateral incisor agenesis group was significantly reduced in this study, especially at the CEJ level by 1.2mm on average ( $P \leq 0.000$ ). This finding is supported by Liuk et al.<sup>45</sup> who reported that on average maxillary lateral incisor buccolingual width was 0.7mm smaller in subjects with palatally displaced canines compared to controls. Their measurements were also based on CBCT. Similarly, the MD tooth width was smaller in the MLIA group by an average of 0.5mm at the CEJ, but it was only significant in the post-treatment measurements ( $P \leq 0.000$ ). This can be explained by the inconsistent reliability of the MD tooth width at the CEJ in the control group especially at T2 that was low relative to the other variables (Cronbach alpha 0.76).

Likewise, Liuk et al.<sup>45</sup> reported a smaller reduction of the mesiodistal root width of the maxillary lateral incisor in the palatally displaced canine group.

The CEJ of the lateral incisor in this study was identified by the change of tooth outline from crown to root and change in density and opacity from enamel to less dense and less opaque cementum<sup>45</sup>. The CEJ on CBCT is considered an accurate and a reliable landmark<sup>42</sup>. The validity of the use of CBCT to measure tooth height and width was investigated by Benninger et al.<sup>51</sup>, who compared mesiodistal, buccolingual and tooth length measurements on CBCT and on extracted teeth. The authors found no significant difference between the two methods. Moreover, Celikoglu et al.<sup>44</sup> demonstrated that the mesiodistal dimensions of anterior teeth and Bolton ratios showed acceptable Pearson's Correlation Coefficient when they compared measurements on CBCT and plaster models. The authors concluded that CBCT can replace conventional plaster models for dental measurements and analysis.

Several studies reported the presence of a microdont or a peg shaped lateral incisor in cases with unilateral MLIA<sup>30, 35, 53</sup>. McKeown et al.<sup>31</sup> found a reduction in crown width in both buccolingual and mesiodistal dimensions in cases with oligodontia. Gungor and Turkkahraman<sup>33</sup> evaluated tooth dimensions in mild and severe hypodontia cases and found that the mesiodistal and buccolingual dimensions of the teeth in both mild and severe hypodontia were smaller. In addition, the maxillary lateral incisor showed the greatest reduction in the mesiodistal dimension. However, all reported studies measured the crown dimension on dental casts using digital calipers and none of the previous studies looked at the root dimension.

The use of CBCT in dentistry had gained popularity and is considered a useful tool in diagnosis and treatment planning as it produces three-dimensional images with high accuracy<sup>37</sup>. One study investigated the morphology of maxillary lateral incisors on CBCT in cases with palatally displaced maxillary canines<sup>45</sup>. The mean buccolingual width was 5.9mm at the CEJ, 4.8mm at 4mm apical to the CEJ and 3.6mm at 8mm apical to the CEJ. Moreover, the mean MD width was 4.3mm at the CEJ, 3.4mm

at 4mm apical to the CEJ and 2.5mm at 8mm apical to the CEJ. The labiopalatal dimension was similar to our findings as the mean labiopalatal root width was 6mm at the CEJ, 5mm at 4mm apical to the CEJ and 4.1mm at 8mm apical to the CEJ. However, in the mesiodistal dimension our findings were slightly greater than their sample, 4.9mm at the CEJ, 3.9mm at 4mm apical to the CEJ and 3.25mm at 8mm apical to the CEJ. Though, the MD width of the control group in our study was also greater than controls in that sample<sup>45</sup>. On the other hand, the mean MD width at the CEJ in our sample was 4.9mm for MLIA group and 5.4mm for control group, which were similar to the anatomic dimensions of extracted teeth.<sup>54</sup>

The slight differences between pre-treatment and post-treatment LP and MD width measurements can be related to voxel size. Since all the measurements were based on the location of the CEJ, Leung<sup>42</sup> et al. reported that the CEJ can be identified accurately with a margin of error of at least one voxel size (0.3mm in our study).

The thickness of labial bone in the esthetic zone is considered the most important factor in determining the best treatment option for MLIA. Adequate facial bone in the anterior maxilla is crucial to create soft tissue profile and prevent future bone resorption when an implant is placed<sup>55, 56</sup>. In our study, the labiopalatal bone thickness was evaluated at 4 levels: 2mm apical to the CEJ, 4mm apical to the CEJ, 6mm apical to the CEJ and 10mm apical to the CEJ. The reason behind taking these measurements were to investigate labial and palatal bone width at different heights which can affect the treatment decision for the contralateral edentulous ridge. Both control and MLIA groups had thin LB width at all heights. The mean labial bone width ranged between 0.0mm to 1.6mm. These findings are in accordance with reported labial bone thickness around healthy maxillary lateral incisors which averaged from 0.5mm at the level of alveolar crest, to 0.84mm at 4mm apical to alveolar crest<sup>56</sup>. Therefore, the mean post-treatment labial bone width is considered less than the recommended 2mm of labial bone thickness for esthetic anterior implants even at 10mm apical to the CEJ. Uribe et al.<sup>49</sup>, evaluated alveolar ridge width using CBCT in cases with MLIA after ridge development and the mean bone width at 2mm apical to the alveolar crest was 4.58mm and most of the bone was located palatally. The total labiopalatal bone thickness was

similar in both groups at 2mm and 4mm apical to the CEJ, but the MLIA group had slightly more bone at 10mm apical to the CEJ though the difference was not statistically significant. The total labiopalatal ridge width at 4mm apical to the CEJ was 8mm for the MLIA group and 8.4mm for the control group at pre-treatment and 6.2mm compared to 7.6mm for MLIA and controls, respectively, at post-treatment scans. Both groups experienced significant amounts of bone loss from pre-treatment to post-treatment especially at levels of 4mm, 6mm and 10mm apical to the CEJ ( $P \leq 0.008$ ) but bone loss was more severe in the MLIA group with mean loss of 1.6mm at 4mm and 1.7mm at 10mm apical to the CEJ. This finding is important when deciding the best treatment option for patients with MLIA as almost 60% of the total labiopalatal bone is lost at the end of orthodontic treatment in the MLIA group compared to less than 40% in the control group at 4mm apical to the CEJ. This reduction in the labiopalatal bone is also reflected in the edentulous site following the distalization of the maxillary canine during ridge development and space opening for prosthetic replacement of the maxillary lateral incisor<sup>49</sup>. Out of 15 final CBCT scans investigated in this study 12 patients had a space opening procedure and three had unilateral canine substitution. Therefore, the significant amount of bone loss in the MLIA group may be related to incisor proclination to create space for the missing incisor.

The accuracy of alveolar bone thickness measurements on CBCT have been evaluated by several authors<sup>42, 57-59</sup>. Nevertheless, bone and cementum have similar densities and the accuracy of determining the alveolar bone margin is affected by the physical spatial resolution, which is the minimum distance needed to distinguish two objects. The physical spatial resolution is affected by 3 major factors: firstly, partial volume averaging which in turn is dependent on the voxel size; secondly, noise which is related to field of view and scan time; and thirdly metallic artifacts. The spatial resolution for the i-CAT machine was found to be 0.86mm, meaning the CBCT machine will only be able to detect the difference between two objects if they were 0.86mm apart<sup>50</sup>. Therefore the labial bone width in this study may not be accurate especially at 2mm and 4mm apical to the CEJ.

The crown morphology in the MLIA group varied significantly, where the MD incisal edge width varied from 2.3mm to 5.8mm with a mean of 4.3mm. This was significantly lower than the mean MD width at the incisal edge of 5.85mm in the control group with a mean difference of 1.5mm ( $P \leq 0.000$ ). The mean MD width at crown midpoint was 5.5mm in the MLIA group and was 1.4mm ( $P \leq 0.000$ ) less than controls. These findings are in support of other studies where microdontia of the maxillary lateral incisor was seen in 40% of cases with unilateral MLIA<sup>29</sup> and a peg lateral incisor was seen in 20% of the subjects in a Turkish sample with unilateral MLIA<sup>30</sup>. This is of clinical relevance as the reduction in clinical crown width should be taken into consideration when planning the best restorative option for the contralateral missing incisor. In most cases the lateral incisor should be restored to achieve a balanced proportionate smile, especially when an endosseous implant is planned as it is generally recommend to have 6-6.5mm of space for an implant in the lateral incisor area<sup>60</sup>.

It was suggested that the mesiodistal crown width of the maxillary lateral incisor is a reflection of incomplete expression of the lateral incisor gene and unilateral agenesis is the result of incomplete penetrance. In our study, there was a large variation in the buccolingual dimension of the maxillary lateral incisor root from (4.5mm to 7.5mm) at the CEJ and in the crown morphology, reflecting the complexity of the genetic control of odontogenesis, suggesting great variation in expressivity of the affected gene.

The inclusion of a control group in our study with a similar age and gender distribution is an important factor when drawing conclusions from results, and thus removing confounding factors that may affect labial and palatal bone width. Nevertheless, sample size and voxel size were the two major shortcomings of this study. To better decide best treatment option for patients with MLIA studies utilizing higher resolution CBCT with larger sample size and long-term follow up are needed.

The treatment challenges that accompany MLIA warranted an accurate examination of root morphology and alveolar bone thickness because of its position in the esthetic zone. This study was one of the first studies to evaluate lateral incisor root morphology and surrounding bone using CBCT.

## **Conclusions**

1. The labiopalatal root width in the MLIA group was smaller than the control group.
2. The mesiodistal dimension of the root of the maxillary lateral incisor was similar in both groups.
3. Both groups had thin labial bone around the maxillary lateral incisor that was less than 1mm at 2mm apical to the CEJ.
4. The MLIA group experienced significant labiopalatal bone loss at the end of orthodontic treatment.
5. The mesiodistal width of the lateral incisor crown was significantly reduced in the MLIA group when compared to controls.



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## Figures

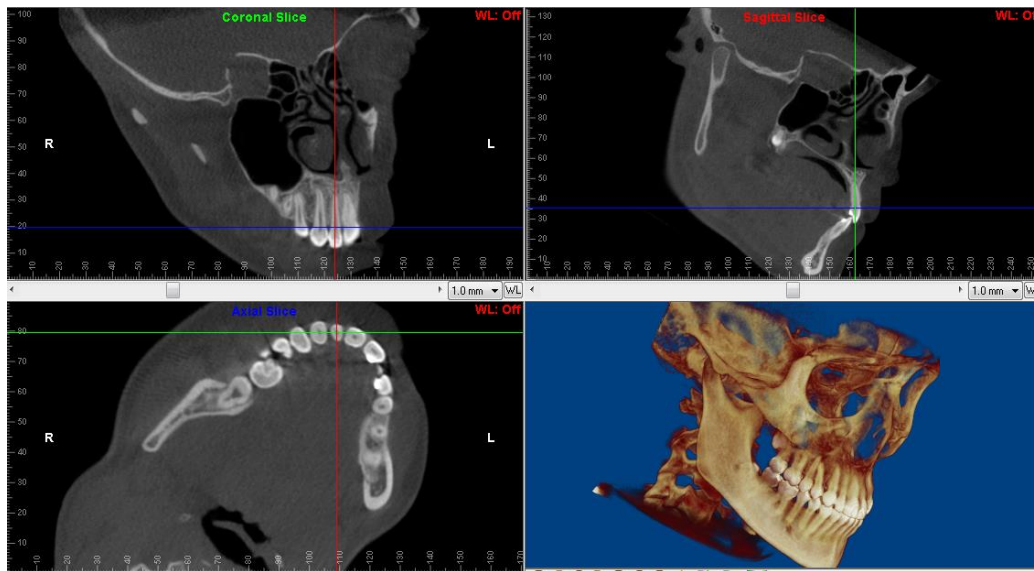


Figure 1. Volumetric rendering, sagittal, coronal, and axial views parallel to the long axis of maxillary central incisor, through the center of the incisor

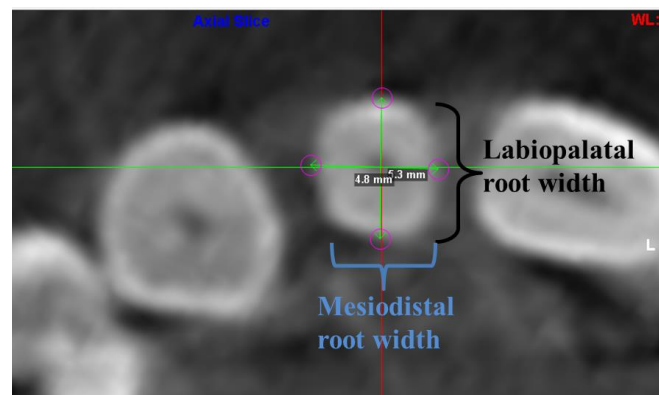


Figure 2. Labiopalatal (LP) and mesiodistal (MD) root widths of the lateral incisor at level of cemento-enamel junction (CEJ)

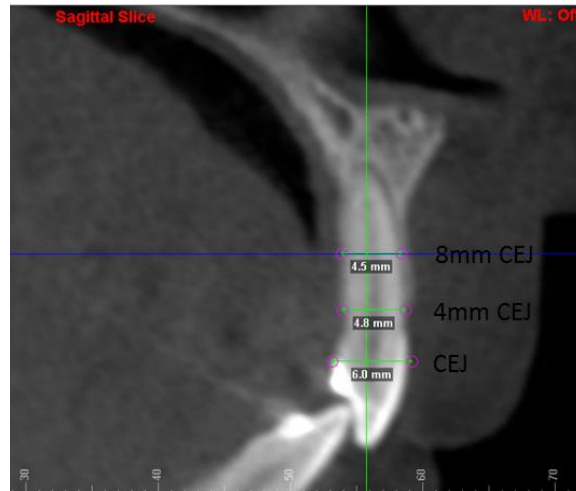


Figure 3. Labiopalatal root width on sagittal section at the CEJ, 4mm apical to CEJ and 8mm apical to CEJ

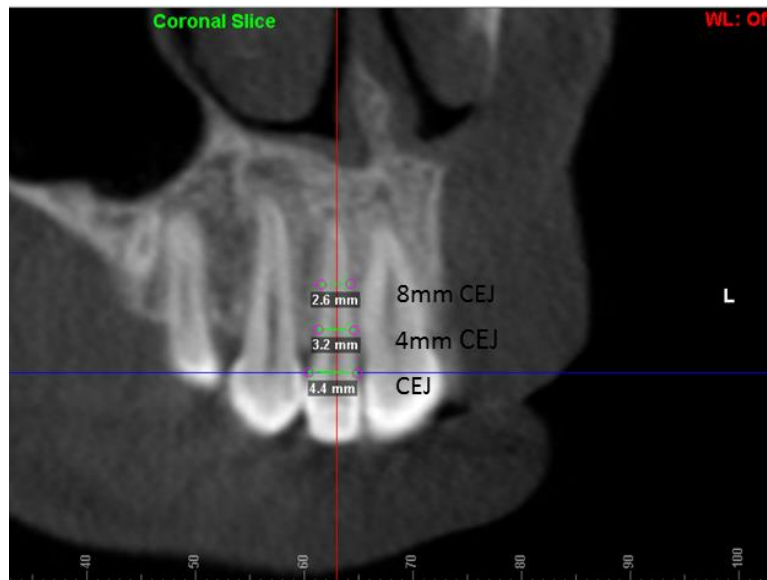


Figure 4. Mesiodistal root width on coronal section at the CEJ, 4mm apical to CEJ and 8mm apical to CEJ





Figure 5. Labial and palatal bone width on axial slice 6mm apical to CEJ

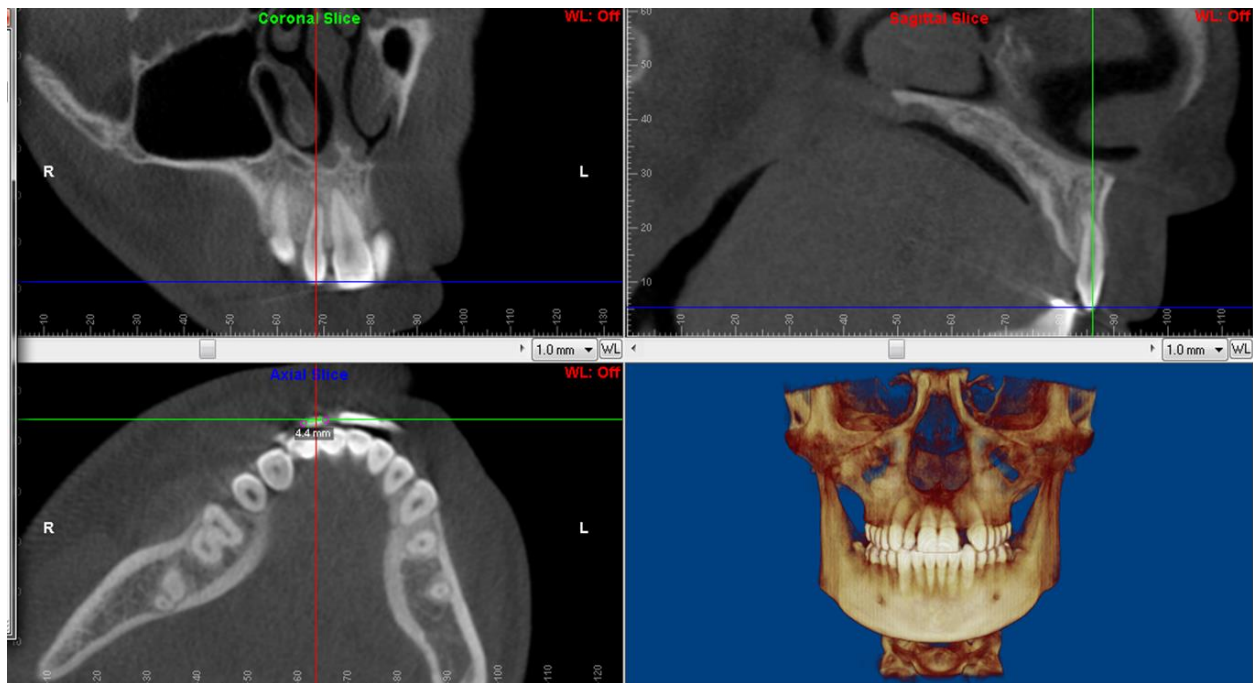


Figure 6. The multiplanar, sagittal, coronal and axial views parallel to long axis of the tooth used to measure the incisal edge on axial view

## Tables

**Table 1. Descriptive patient characteristics for study and control group (pre-treatment and post-treatment)**

		Study Group		Control Group	
		Frequency	%	Frequency	%
Pre-treatment (T1)		20		20	
Sex	Female	15	75	15	75
	Male	5	25	5	25
Age	10-12yr	4	20	5	25
	12.1-14yr	9	45	10	50
	14.1-16yr	5	25	4	20
	16.1-30yr	2	10	1	5
Side of Agenesis	R	9	45	0	0
	L	11	55	0	0
Post-treatment (T2)		15		15	
Sex	Female	9	60	9	60
	Male	6	40	6	40
Age	10-12yr	1	6.67	0	0
	12.1-14yr	0	0	2	13.3
	14.1-16yr	5	33.3	7	46.6
	16.1-30yr	9	60	6	40
Side of Agenesis	R	7	46.6	0	0
	L	8	53.3	0	0
Treatment of Agenesis	Space opening	12	80	0	0
	Space closure	3	20	0	0

**Table 2. Reliability analysis for pre-treatment (T1) and post-treatment (T2) measures: Cronbach alpha values** LP= Labiopalatal, MD= mesiodistal, CEJ= cementoenamel junction. \* The scale had zero variance and therefore was unable to determine ICC as all values were zero

Variable		Cronbach alpha value			
		Study Group		Control Group	
		T1	T2	T1	T2
LP root width Method 1, on axial section	At CEJ	0.968	0.973	0.95	0.945
	4mm apical to CEJ	0.959	0.99	0.967	0.913
	8mm apical to CEJ	0.982	0.98	0.962	0.955
MD root width Method 1, on axial section	At CEJ	0.925	0.809	0.941	0.904
	4mm apical to CEJ	0.893	0.974	0.964	0.921
	8mm	0.77	0.978	0.967	0.879
LP root width Method 2, sagittal section	At CEJ	0.962	0.972	0.964	0.925
	4mm apical to CEJ	0.953	0.99	0.94	0.936
	8mm apical to CEJ	0.983	0.964	0.967	0.937
MD root width Method 2, Coronal section	At CEJ	0.877	0.764	0.937	0.845
	4mm apical to CEJ	0.933	0.831	0.976	0.9
	8mm apical to CEJ	0.825	0.974	0.965	0.957
Labial bone thickness	2mm apical to CEJ	0.839	0*	0.9	0.774
	4mm apical to CEJ	0.752	0.852	0.929	0.934
	6mm apical to CEJ	0.881	0.772	0.929	0.876
	10mm apical to CEJ	0.767	0.921	0.972	0.963
Palatal bone thickness	2mm apical to CEJ	0.852	0.995	0.846	0.802
	4mm apical to CEJ	0.976	0.841	0.91	0.894
	6mm apical to CEJ	0.991	0.945	0.95	0.99
	10mm apical to CEJ	0.99	0.985	0.972	0.989
MD crown width	at IE	0.988	0.943	0.889	0.808
	Crown midpoint	0.972	0.896	0.968	0.901

**Table 3. Means, standard deviations, and differences (mm) for 20 subjects with MLIA and 20 controls at pre-treatment (T1).** LP= Labiopalatal, MD= mesiodistal, CEJ= cementoenamel junction. \*indicates significance at  $P \leq 0.05$ , \*\*indicates significance  $P \leq 0.005$

Outcome	MLIA Group		Control Group		MLIA - Control	
	Mean	SD	Mean	SD	Mean difference	P value
At CEJ	6.0	0.68	7.1	0.46	-1.1	0.000**
LP root width method 1, Axial						
4mm apical to CEJ	5.0	0.62	5.8	0.51	-0.8	0.000**
8mm apical to CEJ	4.1	0.74	4.8	0.63	-0.7	0.005**
At CEJ	5.0	0.52	5.3	0.44	-0.3	0.056
MD root width method 1, Axial						
4mm apical to CEJ	4.1	0.53	4.3	0.57	-0.2	0.231
8mm apical to CEJ	3.4	0.39	3.4	0.54	0.0	0.968
At CEJ	6.1	0.67	7.2	0.47	-1.1	0.000**
LP root width method 2, Sagittal						
4mm apical to CEJ	5.0	0.64	5.8	0.52	-0.8	0.000**
8mm apical to CEJ	4.1	0.75	4.8	0.62	-0.7	0.002**
At CEJ	5.0	0.50	5.3	0.40	-0.3	0.068
MD root width method 2, Coronal						
4mm apical to CEJ	4.1	0.52	4.3	0.53	-0.2	0.165
8 mm apical to CEJ	3.4	0.45	3.4	0.57	0.0	0.968
2mm apical to CEJ	0.1	0.25	0.1	0.32	-0.1	0.602
Labial bone width						
4mm apical to CEJ	0.9	0.49	1.1	0.30	-0.2	0.114
6mm apical to CEJ	1.0	0.31	1.0	0.34	0.0	0.429
10mm apical to CEJ	0.8	0.41	1.2	0.60	-0.4	0.011*
2mm apical to CEJ	0.4	0.61	0.2	0.37	0.2	0.478
Palatal bone width						
4mm apical to CEJ	2.1	1.40	1.5	0.38	0.6	0.341
6mm apical to CEJ	3.0	1.99	2.3	0.77	0.7	0.398
10mm apical to CEJ	4.8	2.93	3.9	1.29	0.9	0.529
2mm apical to CEJ	0.4	0.71	0.3	0.63	0.2	0.862
Total labiopalatal bone width						
4mm apical to CEJ	3.0	1.67	2.6	0.43	0.6	0.925
6mm apical to CEJ	3.97	2.10	3.3	0.82	0.7	0.62
10mm apical to CEJ	5.6	3.02	5.1	1.47	0.9	0.968
At IE	4.2	0.90	5.6	0.68	0.1	0.000**
MD crown width						
At Midpoint	5.6	0.99	7.0	0.49	0.4	0.000**

**Table 4. Means, standard deviations, and differences (mm) for 15 subjects with MLIA and 15 controls at post-treatment (T2)** LP= Labiopalatal, MD= mesiodistal, CEJ= cementoenamel junction. \*indicates significance at  $P \leq 0.05$ , \*\*indicates significance  $P \leq 0.005$

Outcome		MLIA Group		Control Group		MLIA - Control	
		Mean	SD	Mean	SD	Mean difference	P value
LP root width method 1, Axial	At CEJ	5.9	0.7	7.2	0.47	-1.3	0.000**
	4mm apical to CEJ	5.0	0.6	6.0	0.40	-1.0	0.000**
	8mm apical to CEJ	4.1	0.7	4.9	0.59	-0.8	0.007*
MD root width method 1, Axial	At CEJ	4.9	0.3	5.5	0.53	-0.6	0.000**
	4mm apical to CEJ	3.9	0.4	4.5	0.59	-0.6	0.002**
	8mm apical to CEJ	3.1	0.4	3.5	0.60	-0.4	0.067
LP root width method 2, Sagittal	At CEJ	5.9	0.7	7.2	0.42	-1.2	0.000**
	4mm apical to CEJ	5.0	0.6	6.0	0.39	-1.0	0.000**
	8mm apical to CEJ	4.1	0.7	4.9	0.61	-0.8	0.013*
MD root width method 2, Coronal	At CEJ	4.8	0.3	5.6	0.53	-0.7	0.000**
	4mm apical to CEJ	3.8	0.4	4.5	0.58	-0.6	0.002**
	8 mm apical to CEJ	3.1	0.4	3.5	0.58	-0.4	0.045*
Labial bone width	2mm apical to CEJ	0.0	0.0	0.1	0.32	-0.1	0.539
	4mm apical to CEJ	0.4	0.6	0.8	0.62	-0.4	0.098
	6mm apical to CEJ	1.1	0.5	1.2	0.59	0.0	0.539
	10mm apical to CEJ	1.5	0.6	1.6	0.63	0.0	0.285
Palatal bone width	2mm apical to CEJ	0.1	0.4	0.1	0.22	-1.3	0.967
	4mm apical to CEJ	0.8	0.8	0.8	0.71	-1.0	0.389
	6mm apical to CEJ	1.6	1.1	1.4	0.79	-0.8	0.744
	10mm apical to CEJ	2.8	1.7	2.3	1.42	-0.6	0.653
Total labiopalatal bone width	2mm apical to CEJ	0.1	0.4	0.2	0.41	-0.6	0.775
	4mm apical to CEJ	1.2	1.3	1.6	0.86	-0.4	0.202
	6mm apical to CEJ	2.8	1.2	2.6	0.89	-1.2	0.775
	10mm apical to CEJ	4.4	1.8	3.8	1.32	-1.0	0.744
MD crown width	At IE	4.4	0.8	6.1	0.48	-0.8	0.000**
	At Midpoint	5.5	0.9	6.9	0.29	-0.7	0.000**

**Table 5. Means, standard deviations, and differences (mm) for 12 subjects with MLIA at T1 and T2.** LP= Labiopalatal, MD= mesiodistal, CEJ= cementoenamel junction. \*indicates significance at  $P \leq 0.05$ , \*\*indicates significance  $P \leq 0.005$

Outcome		T1		T2		T1-T2	
		Mean	SD	Mean	SD	Mean difference	P value
LP root width method 1, Axial	At CEJ	6.0	0.7	5.9	0.8	0.1	0.256
	4mm apical to CEJ	5.0	0.5	5.0	0.6	0.0	0.475
	8mm apical to CEJ	4.1	0.6	4.1	0.6	0.0	0.677
MD root width method 1, Axial	At CEJ	4.9	0.5	4.9	0.3	0.0	0.752
	4mm apical to CEJ	4.0	0.5	3.8	0.4	0.1	0.452
	8mm apical to CEJ	3.3	0.4	3.0	0.3	0.3	0.007*
LP root width method 2, Sagittal	At CEJ	6.0	0.7	6.0	0.8	0.0	0.685
	4mm apical to CEJ	5.0	0.5	5.0	0.5	0.0	0.608
	8mm apical to CEJ	4.1	0.6	4.2	0.7	-0.1	0.215
MD root width method 2, Coronal	At CEJ	4.9	0.5	4.9	0.3	0.1	0.798
	4mm apical to CEJ	3.9	0.5	3.7	0.4	0.2	0.225
	8 mm apical to CEJ	3.3	0.4	2.9	0.3	0.4	0.003*
Labial bone width	2mm apical to CEJ	0.1	0.3	0.0	0.0	0.1	0.18
	4mm apical to CEJ	0.8	0.5	0.4	0.6	0.4	0.061
	6mm apical to CEJ	1.0	0.3	1.2	0.4	-0.2	0.153
	10mm apical to CEJ	0.8	0.3	1.3	0.3	-0.4	0.004**
Palatal bone width	2mm apical to CEJ	0.2	0.5	0.1	0.3	0.2	0.109
	4mm apical to CEJ	2.0	1.6	0.8	0.8	1.2	0.003**
	6mm apical to CEJ	3.0	2.3	1.7	1.2	1.3	0.002**
	10mm apical to CEJ	4.9	3.4	2.8	1.9	2.1	0.003**
Total labiopalatal bone width	2mm apical to CEJ	0.4	0.7	0.1	0.3	0.3	0.109
	4mm apical to CEJ	2.8	1.8	1.2	1.2	1.6	0.008*
	6mm apical to CEJ	4.0	2.4	2.8	1.2	1.2	0.004**
	10mm apical to CEJ	5.7	3.4	4.1	2.0	1.7	0.004**
MD crown width	At IE	4.3	0.8	4.3	0.8	0.0	0.928
	At Midpoint	5.7	1.0	5.3	1.0	0.4	0.042*

**Table 6 Means, standard deviations, and differences (mm) for 15 controls at T1 and T2.** LP= Labiopalatal, MD= mesiodistal, CEJ= cemento enamel junction. \*indicates significance at  $P \leq 0.05$ , \*\*indicates significance  $P \leq 0.005$

Outcome		T1		T2		T1-T2	
		Mean	SD	Mean	SD	Mean difference	P value
LP root width method 1, Axial	At CEJ	7.2	0.49	7.2	0.43	-0.1	0.527
	4mm apical to CEJ	5.8	0.55	6.0	0.43	-0.2	0.128
	8mm apical to CEJ	4.9	0.69	4.9	0.65	0.0	0.932
MD root width method 1, Axial	At CEJ	5.4	0.43	5.7	0.54	-0.3	0.063
	4mm apical to CEJ	4.4	0.64	4.6	0.69	-0.2	0.132
	8mm apical to CEJ	3.5	0.58	3.6	0.68	-0.1	0.309
LP root width method 2, Sagittal	At CEJ	7.2	0.51	7.2	0.40	0.0	0.886
	4mm apical to CEJ	5.8	0.55	5.9	0.42	-0.1	0.096
	8mm apical to CEJ	4.9	0.68	4.9	0.67	0.0	0.752
MD root width method 2, Coronal	At CEJ	5.4	0.37	5.7	0.52	-0.4	0.011*
	4mm apical to CEJ	4.4	0.59	4.5	0.67	-0.2	0.141
	8 mm apical to CEJ	3.4	0.61	3.5	0.67	-0.1	0.395
Labial bone width	2mm apical to CEJ	0.2	0.36	0.1	0.34	0.1	0.416
	4mm apical to CEJ	1.2	0.32	0.7	0.61	0.4	0.021*
	6mm apical to CEJ	1.1	0.36	1.2	0.62	-0.1	0.426
	10mm apical to CEJ	1.3	0.66	1.6	0.73	-0.4	0.079
Palatal bone width	2mm apical to CEJ	0.2	0.41	0.1	0.26	0.1	0.197
	4mm apical to CEJ	1.5	0.40	1.0	0.74	0.5	0.011*
	6mm apical to CEJ	2.3	0.74	1.5	0.85	0.7	0.002**
	10mm apical to CEJ	3.8	1.19	2.4	1.59	1.4	0.001**
Total labiopalatal bone width	2mm apical to CEJ	0.4	0.70	0.2	0.46	0.2	0.4
	4mm apical to CEJ	2.7	0.46	1.7	0.75	1.0	0.001**
	6mm apical to CEJ	3.3	0.81	2.7	0.91	0.7	0.003**
	10mm apical to CEJ	5.0	1.49	4.0	1.47	1.0	0.007*
MD crown width	At IE	5.8	0.69	6.2	0.51	-0.3	0.040*
	At Midpoint	7.2	0.42	7.0	0.23	0.2	0.025*