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External Apical Root Resorption In Asian Orthodontic Patients In Alabama

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EXTERNAL APICAL ROOT RESORPTION IN ASIAN ORTHODONTIC PATIENTS IN ALABAMA

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ORTHODONTICS

ABSTRACT

The main goals of orthodontic treatment are to achieve a harmonious dental occlusion and enhance the patient's dentofacial appearance. External Apical Root Resorption (EARR) is a side effect of orthodontic treatment[1]. It results in the permanent loss of tooth structure from the root apex[2]. EARR is a multifactorial condition which includes patient related and treatment related risk factors. Patient-related factors include genetics, severity of malocclusion, tooth-root morphology, systemic factors, density of alveolar bone, root proximity to cortical bone, previous exposure to trauma, patient age and sex. Orthodontic treatment related risk factors include treatment duration, amount of force and mechanics used, direction of tooth and apex movement[3]. 1-2 mm of apical root resorption during orthodontic treatment is considered to be clinically important[5]. However, the factors contributing to EARR are not well documented.

Objective: To determine the prevalence of apical root resorption in the Asian population in Alabama and evaluate the effects of treatment on root integrity.

Methods: This study comprised 137 Asian patients treated at the orthodontic clinic of the University of Alabama at Birmingham School of Dentistry. The initial and final records of these patients were examined and the panoramic and cephalometric radiographs were used in the study. Exclusion criteria included unclear radiographic references, open root apices, history of dental trauma or history of craniofacial syndromes, and previous orthodontic treatment. Crown to root ratios were used to measure the root resorption using a technique developed by Lind[24] and then modified by Holtta et al.[18]. To examine whether root resorption on the maxillary incisors had occurred, we used Dolphin Imaging software (Chatsworth, CA) that enabled the pre and post treatment radiographs to be digitized.

Results: The prevalence of moderate root resorption with equal or greater than 20% loss of root structure in our sample was 22.6%. The lateral incisors showed a greater prevalence for EARR than central incisors. In our study, EARR was significantly associated with the Class III dental classification and an extraction treatment plan.

Conclusions: Our results suggested that care must be taken during orthodontic treatment of Asian patients with a Class III malocclusions that may require an extraction treatment plan.

Keywords: External apical root resorption, Asians, orthodontics, EARR

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INTRODUCTION

There are two types of root resorption that can occur: physiologic and pathologic resorption. Root resorption of the primary teeth is referred to as physiologic resorption; however, when the roots of permanent teeth resorb, we diagnose it as pathologic resorption[16,22]. Pathologic resorption can be divided into internal root resorption and external root resorption. Based on the manifestation of the resorption clinically and histologically, external root resorption is then classified into four different categories: ankylosis, replacement resorption, external surface resorption and external root resorption. External root resorption can be cervical resorption or external apical root resorption[12].

External Apical Root Resorption (EARR) is a complication that is commonly caused by orthodontic treatment[7,9,11]. Naturally, teeth that are subjected to force, such as in orthodontic patients, are more prone to apical root resorption[9]. Root resorption of 1-3 mm occurs in 7 to 13 percent of people that have not undergone orthodontic treatment[11,14]. However, due to the various methodologies used in different studies, the range of prevalence of external apical root resorption in non-treated individuals varies from 0 to 90.5%[12]. Furthermore, there is an increased prevalence of external apical root resorption in the group of individuals that have bruxism, anterior open bite with tongue thrust, chronic nail biting, or have undergone dental trauma[12].

Apical root resorption in orthodontic patients is categorized as minor, moderate and severe resorption. Severe root resorption is when more than 4mm or 1/3 of the root has resorbed and is seen in 1-5 percent of orthodontically treated patients[3,18,20]. In terms of dentition, the teeth most affected by root resorption are the maxillary incisors, the maxillary second premolars, and the maxillary first premolars in their respective order[25].

As teeth most susceptible to EARR, the maxillary incisors display an average of 1-2 mm of apical root resorption, with 1 out of 20 patients having up to 5mm of root resorption during orthodontic treatment[6,9,11]. When root resorption reaches the dentin it become irreversible and unpredictable and, as such, could affect and compromise orthodontic treatment outcome[7].

Histology

During initial orthodontic tooth movement, a pressure area on the periodontal ligament will cause hyalinization areas. This is an inevitable physiological response to orthodontic forces. When periodontal tissue is over compressed, it results in hyalinization tissue called sterile necrosis[8,11]. At the cellular level, resorption involves macrophages that are responsible for pre-cementum resorption. Macrophages are the first cells to appear[11]. They arise from the hemopoietic lineage and their function is to remove the necrotic tissue that develops from the compression during the initial hyalinization process[10]. Next, odontoclasts appear. These are multinucleated cells that are capable of resorbing and attacking cementum and dentin[11]. There is an association between root resorption and the removal of hyalinized tissues as resorption areas are seen close to hyalinization areas[8,11,17]. Tooth movement occurs when the hyalinized areas are removed. This is because hyalinization prevents the differentiation of osteoclasts that are responsible for bone resorption. For this reason, hyalinization areas could cause a delay in orthodontic treatment[8]. This biologic process that leads to tooth movement is the foundation of the root resorption process. In some studies this is also referred to as "orthodontically induced inflammatory root resorption" (OIIRR) [10,28].

Depending on severity, resorption can be divided into three classifications[28.] The first is cemental resorption which refers to the resorption of the cementum only, which can be repaired and regenerated, a process similar to the remodeling of trabecular bone. The second classification is dentinal resorption, which includes the resorption of both the cementum and dentin. The repair of the resorption is done with cementum only which leads to a final root shape that differs from the original. The final classification is known as circumferential apical root resorption and it is the resorption of all the layers of hard tissue of the root apex. This causes evident and easily identified root shortening[28].

Root resorption is repairable if the force magnitude and duration do not exceed the reparative speed of the cementum at tooth apex[11]. The root is separated into three vertical segments; coronal, middle and apical thirds. Once root resorption at the apical third is detected on radiographs, it is irreversible. Literature shows that root resorption mainly occurs in the apical third of the root. There are a few possible explanations for this. First, the angle of insertion of periodontal fibers and the center of tooth is above the apical half of the root which means there is an increased susceptibility to injury due to greater stresses being applied in this region[11,12]. Second, a different type of cementum known as cellular cementum covers the apical third that contains more blood supply than the coronal third which is covered by acellular cementum. This leads to a cellular reaction due to trauma being more likely in the apical third[11,12].

Diagnostic tools

External apical root resorption is asymptomatic and can be missed if radiographic imaging is not routinely and properly utilized[12]. Radiographic records and monitoring are essential tools used in the arsenal of every orthodontist for orthodontic diagnosis and treatment planning. Routinely taken radiographs are the panoramic x ray and the lateral cephalogram, but a survey among practitioners has found that there is an increasing number of dentists that request a full mouth radiograph on adult patients exclusively[6]. Despite panoramic films being more advantageous due to their reduced exposure to radiation, reduced operator time and ease, they still possess known limitations. These limitations include the quality of image that is dependent on the positioning of the patient and the proximity of the anatomical structures to the focal trough, and the magnification[6].

Orthodontic force can produce root resorption which may not be visible in radiographs. Though panoramic radiographs have been used to detect and measure root resorption, Sameshime et al. recommended periapical radiographs for patients that have an increased risk of root resorption. The image quality of the full mouth periapical radiographs allows them to be used for superior evaluation of finer details with less image distortion[6.] However, they are time consuming, harder to take, and increase the patients' exposure to radiation[6.]

CBCT scans are also invaluable when analyzing the root integrity as they provide a detailed and three-dimensional image of the roots. They may detect resorption whereas conventional x-rays such as periapical, lateral cephalometric radiographs and panoramic radiographs may miss.[28] However, their routine use during treatment still needs further discussion. It is recommended to take radiographs 6 months after starting treatment to evaluate root angulation and resorption[10,11]. If any resorption is detected, treatment should be paused two to three months with a passive arch wire[3,10,19,28]. It is advisable to take a new radiograph 6 months after continuing the treatment to reevaluate EARR[29].

Etiology

Mechanical factors. Multiple factors lead to root resorption including biological or patient related and mechanical or treatment related factors. Mechanical factors include treatment time, use of heavy forces, frequency of application of force, direction of movement, amount of apical movement and teeth extractions[3,7,9,11,19,20]. Extracting teeth results in moving the teeth greater distances during retraction. Another example of this can be seen in class II malocclusions with severe overjet where anterior teeth need to be moved significantly to reduce the overjet[12]. The increased movement is associated with increased external apical root resorption[12].

The type of forces used in orthodontics can also increase the risk of apical resorption. The forces applied are never pure translation. Tipping and torqueing, both common movements, create areas of compressed PDL in the apical region. Most of the time, the fulcrum of the forces used is incisal to the apical half of the root. This results in the concentration of forces at the apical region and increasing the risk and susceptibility to external apical root resorption[12].

Maxillary incisors show an increased susceptibility to apical root resorption more than other teeth because maxillary incisors move more than other teeth during orthodontic treatment. Clinically, it means that more attention should be directed towards the duration of force applied to a tooth rather than force magnitude, or put simply, more attention should be paid to the duration of active treatment time, which will be discussed later.

Biological factors. Biological factors include, age and gender, history of dental trauma, history of prior root resorption, systemic condition, type of supporting bone, tooth type and root morphology such as peg shaped maxillary lateral crowns or crown invaginations, initial malocclusion, missing teeth, taurodontism and genetics[22,28]. The ectopic eruption of a tooth can lead to root resorption in the adjacent teeth in its eruption path[26].

While there has been no association between gender and age and EARR, the root morphology has been suggested to play a role in the prevalence of resorption[12]. The evidence in literature shows that dilacerated, pointed, thin, eroded, and pipette shaped roots may lead to significantly greater root resorption than normal roots[6,15,20]. Blunt end roots have been associated with both an increase and decrease in EARR occurecne[12]. Root shape is best seen in periapical radiographs rather than panoramic radiogrphas[12].

Sameshima and Sinclair retrieved records of 868 patients treated in 6 offices and measured pretreatment and posttreatment crown and root length from the first molar to the contralateral first molar in both arches to see factors that associate with root resorption using periapical radiographs[6]. Maxillary lateral incisors were the most resorbed teeth followed by maxillary central incisors followed lastly by the maxillary canines[6,15,20,22]. Another study concluded that in a 5-10 year follow up of orthodontically treated patients, 28.8% of the incisors showed evidence of apical root resorption with 42.3% in the maxillary central incisors, and 38.5% in the maxillary lateral incisors[22].

Genetics also may contribute to the prevalence of EARR. An association between certain genetic markers and patient's display of root resorption during orthodontic treatment has been identified[11]. These genes encode proteins that may manage resorption and repair of the cementum during orthodontic forces[11]. Al-Qawasmi reported a strong association between *IL-1B* allele and apical root resorption. He also reported that homozygous individuals with the allele *IL-1B* showed 5.6-fold increase in risk for developing EARR greater than 2mm when compared to heterozygous individuals[12]. In contrast, Rossi et al.'s study found evidence to support that EARR is genetically heterozygous.

IL-1B cytokine is an inflammatory mediator, and in its absence, there is an increased likelihood of apical root resorption occurring with orthodontic treatment[9,12]. Interleukin 1 alpha (IL-1α) is a cytokine that has strong bone resorbing capabilities and has been seen in periapical legions alongside TNF-alpha[12]. Ketchman et al. reported that the decreased bone resorption that resulted from the absence of IL-1B cause prolonged stress on the root of the tooth. This prolonged stress then triggered fatigue failure in the bone leading to root resorption due to the dynamic functional loads[12]. Therefore, root resorption seems to be related to decreased bone resorption. EARR was concluded to be the result of varying mechanisms that operate in different individuals and in different sites in the same individual[12].

This association suggests that the genetic variable in respect to apical root resorption is out of the orthodontist's control[9]. Other associations to root resorptions have been studied. Shirazi et al, Loberg et al, and Poumpros et al found the hormone L-thyroxine to decrease root resorption and increase tooth movement. This remains a controversial and challenged theory[10]. On the other hand, dose dependent usage of corticosteroids showed a variety of effects on root resorption with a dose of 15 mg/kg resulted in an increase in EARR, while a decrease in root resorption was seen with a reduced dose of 1 mg/kg[10]. It was also found that alcohol consumption throughout orthodontic treatment increased root resorption due to increased vitamin D hydroxylation[10].

Tumors in the jaw can also result in root resorption. Malignant tumors that expand and metastasize rapidly do not produce significant amount of resorption. Resorption is more often seen in slow expanding tumors such as fibro-osseous lesions, cysts and ameloblastomas[22].

Systemic conditions should also be considered, such as hypothyroidism, hyperthyroidism and asthma[3]. It was reported that chronic asthma patients had apical root resorption in the maxillary molars. This could be due to the maxillary molar roots being close to the inflamed maxillary sinus[10,15]. Additionally, medications could have an effect on root resorption during orthodontic treatment. Bisphosphonates have been shown to reduce root resorption, but they will affect tooth movement as well[9,11,14].

Management

A study that was conducted on general dentists and dental specialties excluding orthodontics showed that several of the practitioners believe that external root resorption is avoidable and blame the orthodontist for its cause[9]. Furthermore, orthodontists are commonly sued due to the belief that their treatment had allegedly resulted in external root resorption[9]. Before starting orthodontic treatment, patients and/or parents should be made aware of the risk of root resorption that could occur during orthodontic treatment[10,14,28]. Naturally with a genetic association there is also an association between familial traits of inheritance and potential root resorption. As such, it is imperative to be vigilant of familial traits and genetic patterns of inheritance before the start of treatment[10,21].

There are differing views on how starting orthodontic treatment before completion of root formation affects the tooth's risk of developing EARR. Phillips et al and Oppenheimen et al. suggested that immature apices are at greater risk for EARR due to the deformation in Hertwig's sheath which modifies the calcification process and prevents the root from completing formation. On the other hand, Sameshima et al. found that roots with open apices had greater resistance to EARR[40].

During treatment, it is preferable to maintain light force levels, as heavy forces damage periodontal ligaments which in turn increase the risk of apical root resorption[10]. When compared to controls, heavy forces produced 9 times more root resorption, and light forces produced 5 times more root resorption[3]. Paetyangkul et al. stated that even if light forces were used, an increase in application time increases EARR[36]. With respect to forces, the use of continuous force shows more root resorption compared to the use of discontinuous or intermitted force[36]. The direction of force is also a factor to be considered with EARR. Harris et al. reported that intrusive forces created craters that were directly proportional to the to the magnitude of the intrusive force[3].

Furthermore, 2-phase treatments are reported to show less incidence of EARR than a one phase treatment where there is a significant reduction of overjet in one increased timepoint[3]. Caution must be taken when engaging intrusive forces and when treating Cl II in 1 phase[3,15]. Additionally, when using devices such as mini-implants or temporary anchorage devices to facilitate orthodontic movement, there should be a distance of more than 0.6 mm between the device and any adjacent root structure to prevent root resorption[15]

As previously mentioned, treatment duration and total apical displacement appear to be most often tied to apical root resorption. There is a difference between elongated treatment time and elongated active treatment. Patients that frequently miss appointments will have elongated treatment time but not necessarily elongated active treatment. Elongated active treatment time therefore is the main component in this context that correlates with total apical displacement[9]. Therefore, treatment time must be considered in treatment planning. With every additional month of treatment there is a risk of having 0.1 - 0.2 mm of additional root resorption[15].

After treatment, a full set of records with radiographs is recommended. Patients and/or parents must be informed if there is any root resorption present. Radiographic follow up for teeth with severe apical root resorption is suggested[10]. The reparative stage for cementum starts when the apical root resorption stops normally after active treatment is terminated and orthodontic appliances are removed[10,22]. If external apical root resorption is still active after the cessation of active orthodontic treatment, then endodontic treatment of the tooth with calcium hydroxide therapy may be considered[10]. The alkaline environment created by the calcium hydroxide will result in unsuitable conditions for the resorbing cells and promote alkaline phosphatase which is vital in the repair and formation of hard tissue[22]. Reports shows that teeth with severe root resorption are still stable[10]. Fixed retention should be used with caution in patients that demonstrated root resorption as they might lead to active external apical root resorption due to occlusal trauma[28]. Retainers should be passive and retainer check after treatment is advisable to make sure the retainer is still passive[29].

If severe root resorption develops, treatment objectives should be reevaluated and alternatives should be considered[3,10,19,28]. When re-evaluating, the clinician must assess the treatment progress and desired treatment outcomes. Then, with the patient, they must determine if treatment is to be continued with modification or concluded. Several considerations must be made to make this important decision: the current state of occlusion and aesthetics. If there are any occlusal interferences or a deep bite is present, then it is more beneficial for the patient's long-term oral health to continue treatment. Likewise, if the treatment is at a stage where the patient is unhappy with aesthetics, or further apical movement is needed for the affected teeth to be in the desired position, then alternatives can be put forth to aid the completion of treatment. These alternatives can include restorative work to close the extra spaces present instead of applying more force on the teeth to close them. Another option is to disengage the teeth that are suffering from root resorption from the archwires so that no active force will be directed to them. This option will allow the clinician to continue the treatment whilst no longer harming the resorbed roots, and if space is needed then we could create it by interproximal reduction rather than extraction, or fix the tooth in place[3,29]. Regardless of whether treatment modifications will be implemented or not, discontinued treatment is recommended for a period of at least 3 months to allow healing of the resorption lacunae at the apex of the roots[29].

Ethnicity

There is not enough evidence in literature about the prevalence and susceptibility of different ethnicities to EARR. Hispanic and Caucasians are reported to be more susceptible to apical root resorption during orthodontic treatment than Asian population, with Hispanics being the most susceptible[6]. The Hispanic population also has a higher prevalence of "short root anomaly"[27]. First discovered and diagnosed by Dr. Lind in Sweden, short root anomaly has been defined as "abnormally short blunt roots affecting maxillary central incisors and rarely any other teeth". Because of the lack of clinical signs and symptoms, it is hard to detect and can mistakenly be confused for external apical root resorption[27]. Due to its low prevalence amongst Caucasians, it is often attributed as apical external root resorption, but as a result of the rapidly increasing Latin population, it is now more often correctly diagnosed as short root anomaly[27].

According to the US census Bureau data, the Asian population currently makes up about 7% of the US population at more than 20 million individuals. Their data indicates a significant growth rate expected to be the fastest growing major ethnic group in the US. Asians make up 1.5% of Alabama's population of 5 million people. With their increased growth rate, it is important to see how EARR is affecting this population so that we are best able to diagnose and treat them. This study aims to evaluate the prevalence of EARR in the Asian population of Alabama.

HYPOTHESIS AND SPECIFIC AIMS

Our null hypothesis is that there are no significant associations between the risk to develop EARR and the patient- or treatment-related factors in the Asian population that have undergone orthodontic treatment in Alabama.

The goal of this study is to determine the prevalence of external apical root resorption in the Asian population in Alabama and evaluate the effects of treatment on root integrity.

For this hypothesis we will use the following specific aims:

Specific Aim 1: Determine the prevalence of external apical root resorption in the Asian population in Alabama.

Specific Aim 2: Evaluate the effect of patient- and treatment-related factors on external apical root resorption in the Asian population that have undergone orthodontic treatment in Alabama.

MATERIALS AND METHODS

This study was approved by the University of Alabama Institutional Review Board for Human Use (IRB: # 160428005).

Records of 137 Asian patients treated at the orthodontic department in University of Alabama at Birmingham, School of Dentistry were evaluated. Initial and final panoramic and cephalometric radiographs were included in this study. Patients were selected not only based on having been treated but also the availability of the complete records. Exclusion criteria included unclear radiographic references, open root apices, history of dental trauma, or history of craniofacial syndromes. Patients with a history of dental restorative work on the incisal edges of the crown were also excluded if the restorative work took place between the initial and final radiograph as the buildup of the incisal edges could potentially alter the length of the crown. Patients who had previously been treated orthodontically were also excluded. The study recorded treatment type (extraction vs non extraction), treatment time (months), sex, age, dental and skeletal classifications, ANB, IMPA, U1-SN and overjet (Figure1 and Table 1). These were recorded from pretreatment data.

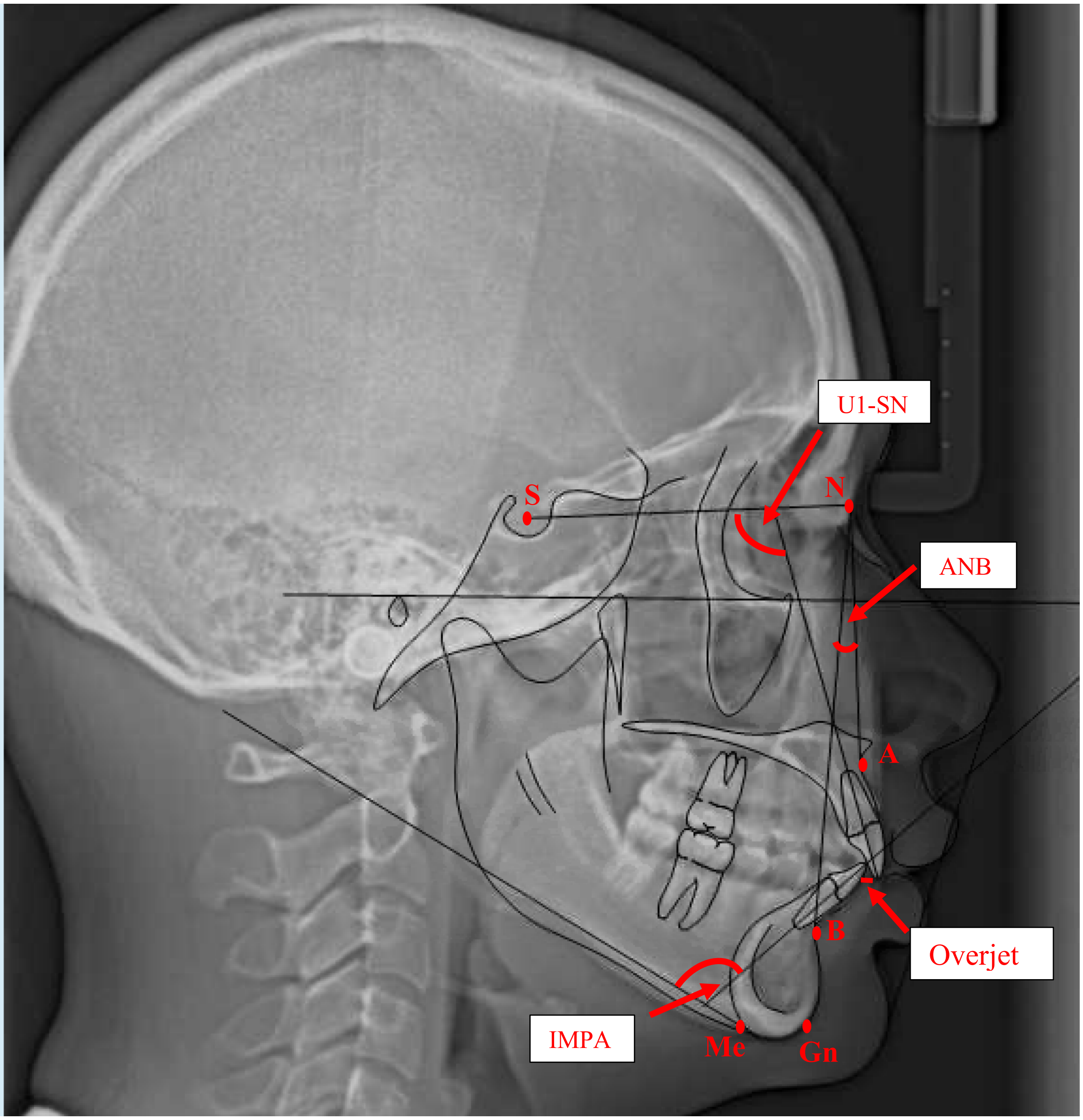

Figure 1. Cephalometric landmarks extracted from initial lateral cephalograms

Table 1. Cephalometric landmarks definitions

Sella (S)	The center of sella turcica
Nasion (N)	The most anterior point of the frontonasal suture
Point-A (A)	The innermost point on the contour of the maxilla between the anterior nasal spine and the incisor
Point-B (B)	The innermost point on the contour of the mandible between the incisor and the bony chin
Menton (Me)	The most inferior point on the mandibular symphysis in the midline
Gnathion (Gn)	The lowest, most anterior midline point on the symphysis of the mandible
ANB	Measures the relation of maxilla to mandible
U1-SN	Measures upper incisor angle in relation to the cranial base
IMPA	Lower incisor angle in relation to the mandibular plane (Menton to Gnathion)
Overjet	Distance measured from tip of upper incisor to labial surface of lower incisor

A crown to root ratio was used to measure the root resorption. This was done to reduce image distortion that is produced on panoramic radiographs. The technique devised for these measurements was developed by Lind[24] and then modified by Holtta et al.[18]. The radiographic references and the ratios were measured as follows; a midpoint line (M) was chosen on a line that bisects the distal and mesial points at the cementoenamel junction

(CEJ) (Figure 2). The length of the crown was then measured from the incisal edge to the midpoint mentioned above and roots were measured from the midpoint to the root apex. A formula was then used to calculate root resorption which was as follows: $((R_i \times C_f)/ C_i) - R_f$; where R_i is Root initial; C_f is Crown final; C_i is Crown initial; and R_f is Root final. The percentage of root resorption was then calculated by dividing the amount of root resorption by the initial root length and then multiplying by 100%.

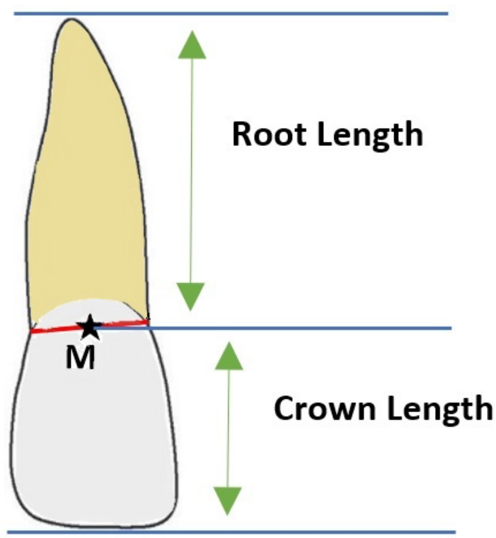

Figure 2. Crown root ratio measurement; M, midpoint along the line bisecting mesial and distal points of cementoenamel junction.

To examine whether root resorption on the maxillary incisors had occurred, we used Dolphin Imaging software (Chatsworth, CA). This enabled the pre- and post-treatment radiographs to be digitized and allowed EARR comparisons, evaluations and conclusion to be drawn. The initial and final digitized radiograph of each patient were examined to establish the presence of EARR on maxillary incisor roots. The standardized millimetric ruler present in the cephalometric radiographs was used to calibrate the software's measurements. The width of the molar crown on the cephalometric radiograph, measured from the height of contour and the mesial and distal aspects, was determined to aid in calibration of the measurements on the panoramic radiograph. Once the panoramic radiographs were calibrated, the crown and root ratios of the incisors were measured. This calibration method was repeated for both the initial and final panoramic radiographs.

A patient was determined to have mild EARR when less than 20% of the root structure of the four upper incisors (UR 2, UR 1, UL 1, or UL 2) was lost. A loss equal to or greater than 20% was categorized as moderate EARR, while 50% or more was categorized as severe EARR. The prevalence of EARR as a whole in the sample population was calculated by dividing the sample size with EARR by the whole sample size of 137. The average root and crown lengths were calculated for each of the four incisors followed by the calculation of the average root-to-crown ratios of each of the four upper incisors. Additionally, the prevalence of EARR was identified for each tooth type: the central incisors and the lateral incisors.

All patient- and treatment-related factors were calculated using descriptive statistics. These factors included: patient age (in years; <10, 11-20, 21-30, and >31), gender (male or female), treatment time (in months; >18, 19-30, and 31), dental classification (Class 1, 2 or 3), treatment type (non-extraction vs extraction treatment), treatment appliance (fixed conventional brackets vs removable appliances), skeletal classification (Class 1, 2, or 3), ANB (in degrees; <0, 0-5, >5), U1- SN (in degrees; <100, 100-115, and >115), IMPA (in degrees; <90, 90-100, and >100), and overjet (in mm; <0, 0-4, and >4). This data was obtained from the patient records and patient cephalometric radiographs.

Prevalence reports in existing literature were used to determine sample size. A 95% confidence interval with a +/- 5% margin of error was calculated for the sample size for the prevalence of EARR. Pearson chi-square test was used to calculate the effects of individual patient and treatment related factors on EARR. All statistical tests were two-sided and performed using a significance level of 5%. Statistical analysis was conducted sing SAS (version 9.4; SAS Institute, Cary, NC).

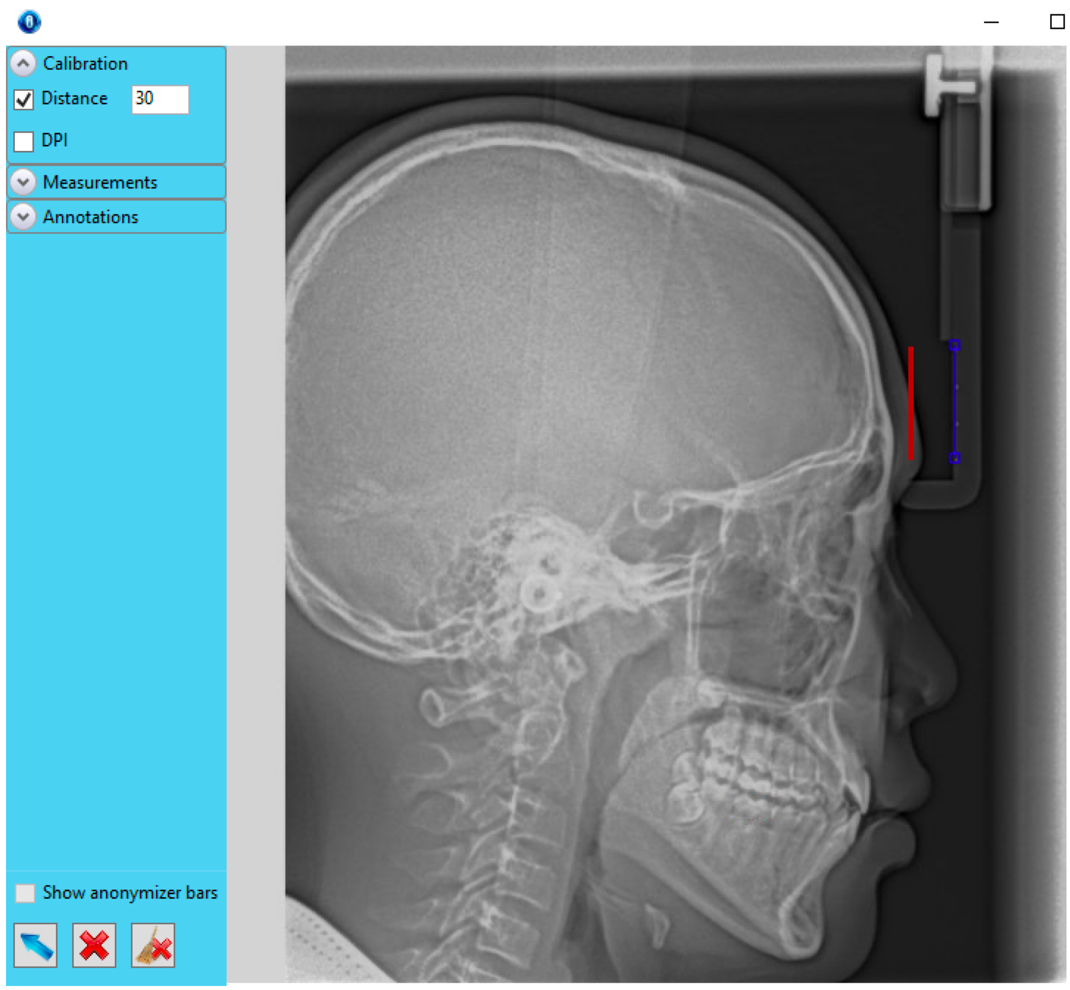

Fig 3. Cephalometric calibration from the 30 millimeter rule

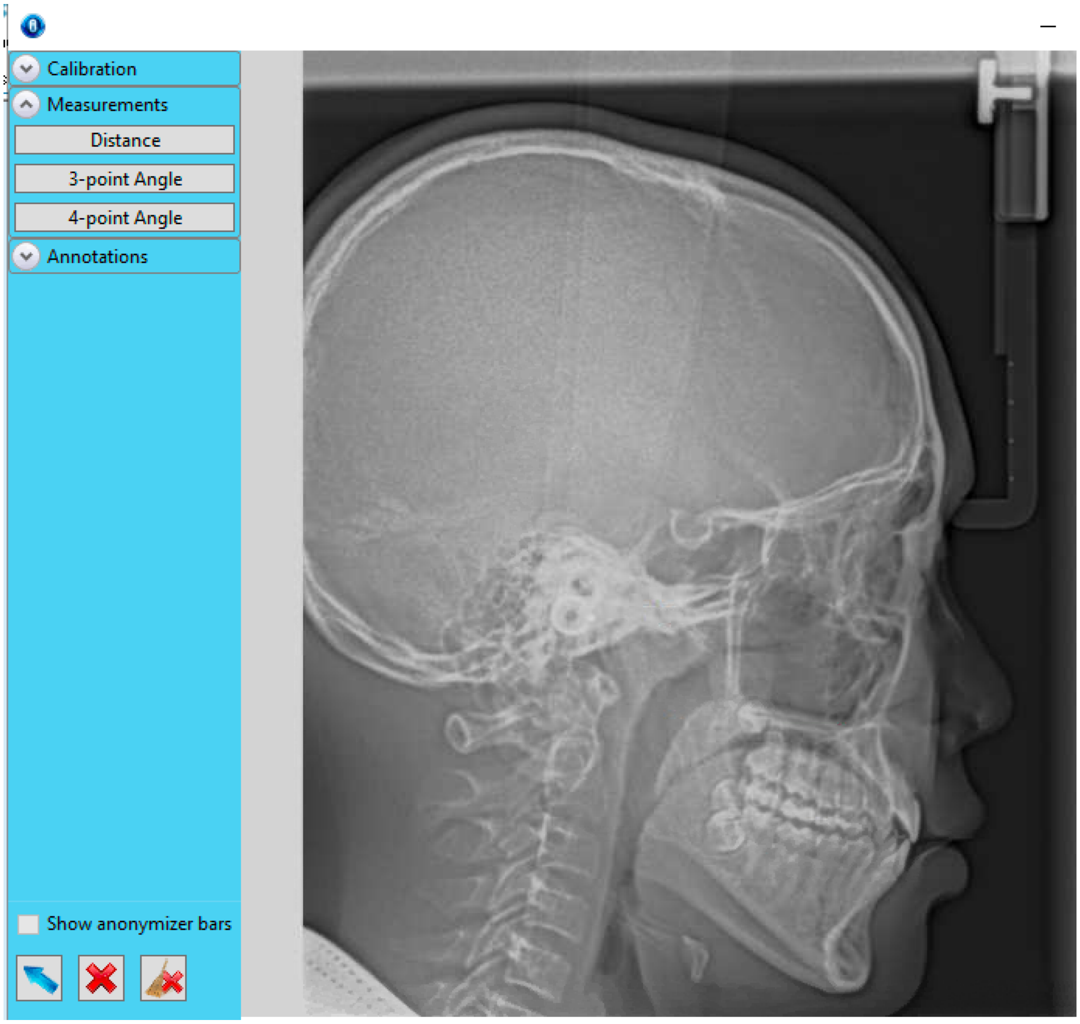

Fig 4. Cephalometric measurement of molar width

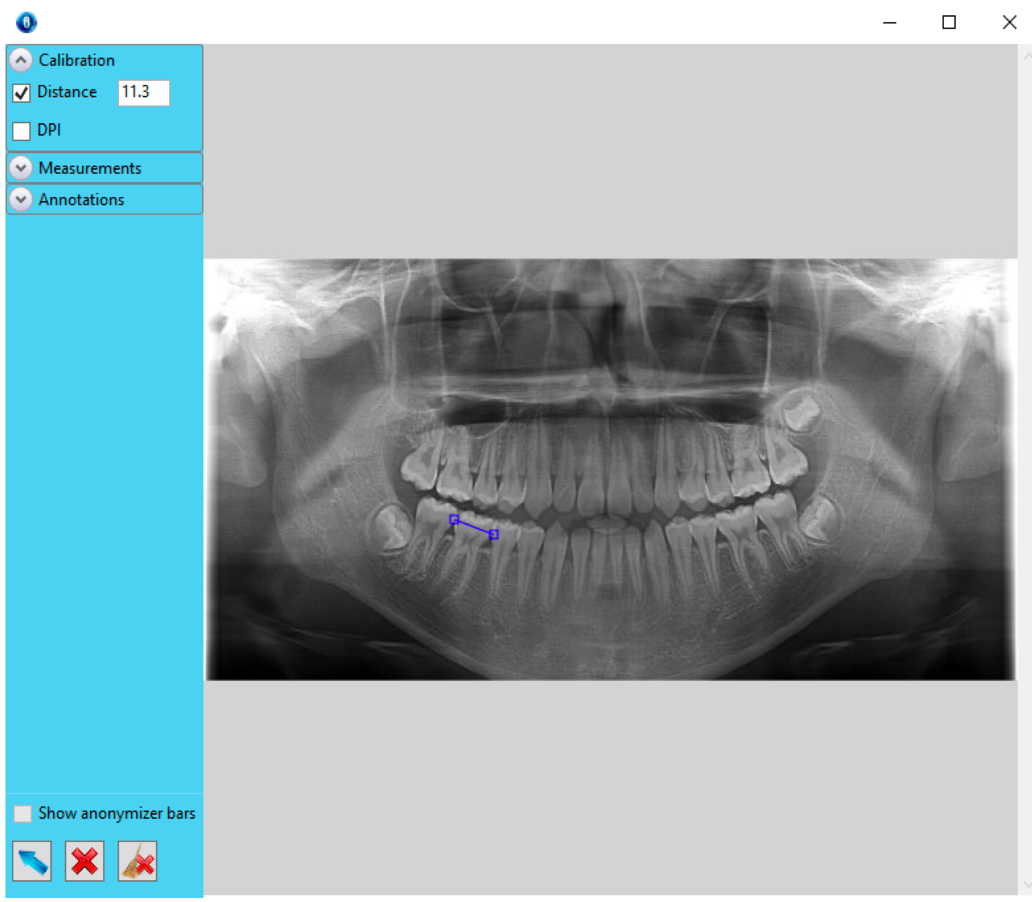

Figure 5. Panoramic calibration using known molar width

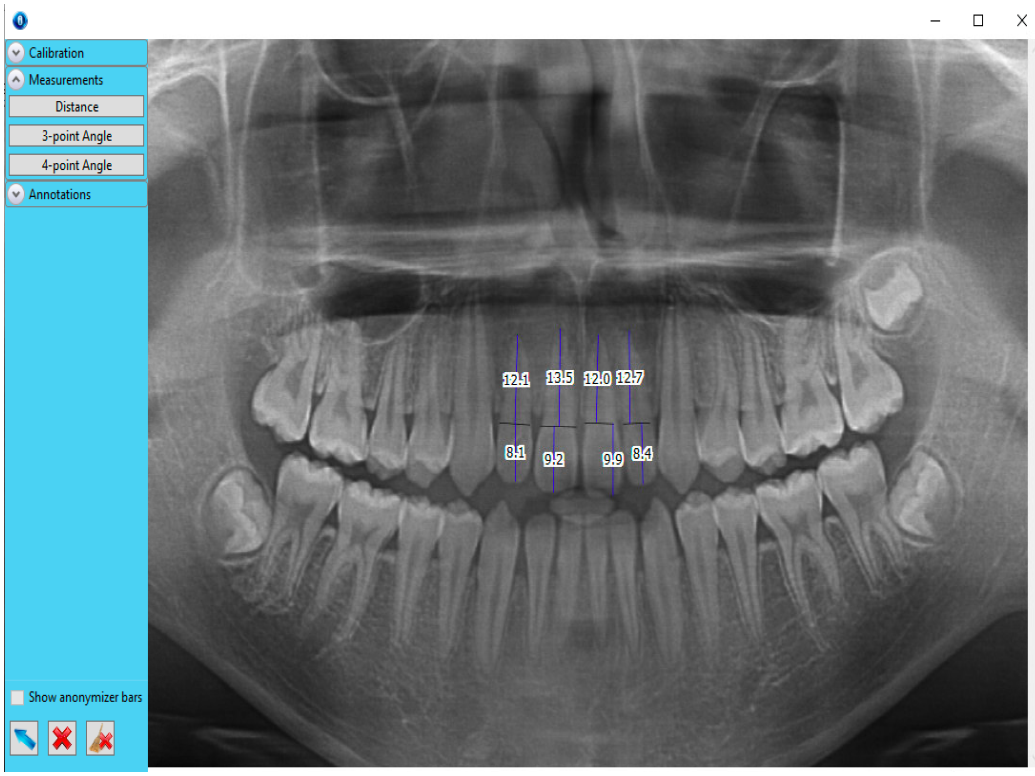

Figure 6. Initial panoramic radiograph measurements

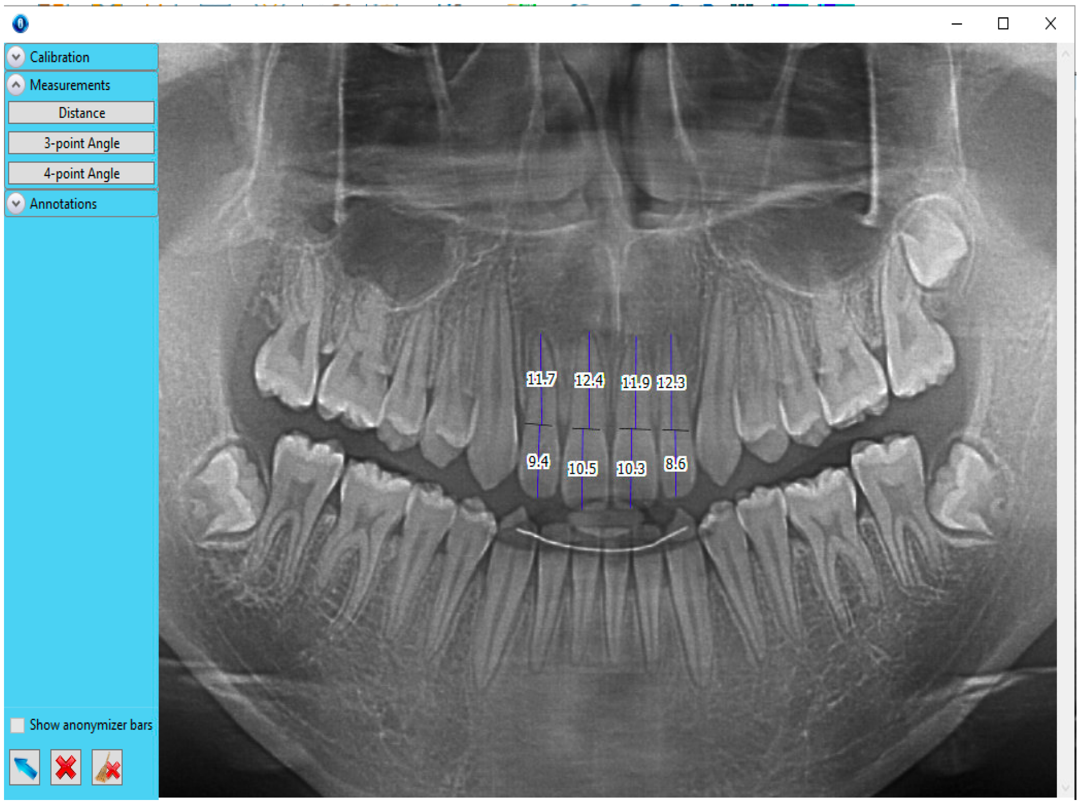

Figure 7. Final panoramic radiograph measurements

RESULTS

Sample Demographics

The sample of Asian patients included in this study consisted of 88 females and 49 males for a total of 137 (Table 2). The oldest patient was 59 years old and the youngest patient was 10 years old. The mean age of the sample was 18.1 years old (Table 2).

Table 2. Sample Demographics

Race	
Asian	137
Gender	
Male	49 (35.7%)
Female	88 (64.3%)
Age (Years)	
Mean	18.1
Std Dev	9.8
Median	13
Minimum	10
Maximum	59

Patient-Specific Factors

Skeletal and dental classifications are considered patient-related factors. The dental classification of the patients included 54 with Class 1, 69 with Class 2, and 14 with Class 3 (Figure 8). Skeletal classifications consisted of 52 Class 1 patients, 65 Class 2 patients, and 20 Class 3 patients (Figure 8).

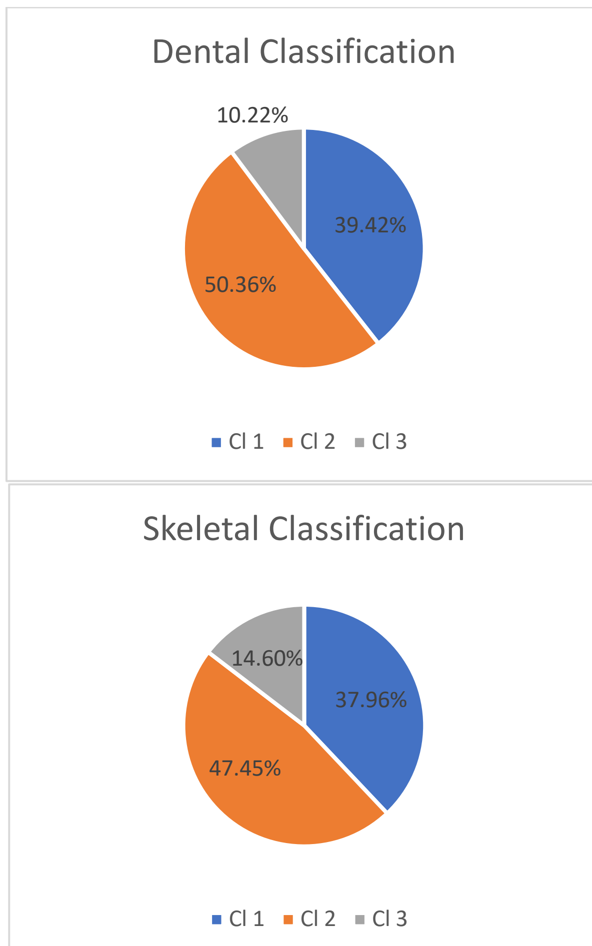

Figure 8. Dental and Skeletal Classifications of the patients included in the study

Other patient-specific factors include cephalometric measurements. Average cephalometric values for the sample included ANB of 2.9°, U1-SN of 109.9°, IMPA of 94.7°and an overjet of 3.7 mm (Table 3).

Table 3. Pretreatment cephalometric values

Cephalometric Value	Mean	Std Dev	Median	Minimum	Maximum
ANB (°)	2.9	2.6	2.9	- 4.2	10.4
OJ (mm)	3.7	2.3	3.7	- 2.9	10.4
IMPA (°)	94.7	7.3	94.5	71.2	113.6
U1-SN (°)	109.9	7.8	110.3	83.7	128.3

Treatment- Related Factors

Treatment type (extraction vs non-extraction) treatment, and appliance type (conventional fixed appliance vs removable appliances) used are orthodontic treatment-related factors. Our sample included 44 cases treated with extractions due to crowding and/or protrusion and 93 cases treated non-extraction. Treatment times averaged 24.9 months with a minimum treatment time of 7 months and a maximum treatment time of 55 months (Table 4).

Table 4. Treatment Related factors

Treatment Time (Months)	
Mean	24.9
Std Dev	8.7
Median	24
Minimum	7
Maximum	55
Treatment Type	
Extraction	44 (32.2%)
Non-Extraction	93 (67.8%)
Appliance Type	
Fixed	133 (97%)
Removable	4 (3%)

EARR Prevalence

Root resorption less than 20% was classified as mild EARR, while resorption of the root structure equal to or greater than 20% was classified as moderate EARR for any of the maxillary incisors measured on each patient. Resorption equal to or greater than 50% was classified as severe EARR.

The prevalence of mild root resorption in our sample was 77.4% (106/137). Root resorption with equal to or greater than 20% loss of root structure was 22.6% (31/137). Of these, only one patient displayed sever root resorption with greater than 50% of root structure loss (0.7%). In our sample, we had a total of 125 upper right central incisors, 117 upper left central incisors, 111 upper right lateral incisors and 109 of upper left lateral incisors measured, with a total of 242 central incisors and 220 lateral incisors.

Table 5. EARR Distribution

EARR (mm)	Mean (mm)	Std Dev	Median	Minimum	Maximum
U1 (n=130)	1.01	1.17	0.55	0.02	7.61
U2 (n=124)	1.01	0.99	0.69	0	4.70
U1 or U2 (n=137)	1.00	0.96	0.75	0.03	5.90

Table 6. Severity of EARR

EARR (%)	Overall EARR	≥ 20% EARR	≥ 50% EARR
U1 (n=130)	7.71%	13.1%	0.8%
U2 (n=124)	7.92%	16.1%	0%
U1 or U2 (n=137)	7.76%	22.6%	0.7%

Associations of EARR with particular patient-specific and treatment-specific factors were considered. We had 2 statistically significant ($P<.05$) associations between EARR and these factors. The first statistically significant association with EARR of the patient-specific factors was dental classification (Cl 1,2 or 3) with a P-value of 0.035, with the association seen in class 3 patients. Incisor inclination, when U1-SN is less than 100° or more than 115°, had a trend toward statistically significance with P-value of 0.059.

Related to treatment-specific factors, only treatment type (extraction or non-extraction) and specifically extraction treatment was found to be statistically significant associated with EARR with a P-value of 0.027. With regards to removable appliance, this study had an insufficient number of patients treated with removable appliances to be able to run a valid statistical comparison.

Table 7. Patient-Related Factors

Patient -Related Factors	**No EARR**	**EARR**	**P-Value**
Gender			0.97
Male	38 (77.5%)	11 (22.5%)	
Female	68 (77.3%)	20 (14.6%)	
Age			0.42
< 11	4 (57.2%)	3 (42.8%)	
11-20	74 (78.7%)	20 (21.3%)	
> 20	28 (77.7%)	8 (22.3%)	
Dental classification			0.035*
Class 1	44 (81.5%)	10 (18.5%)	
Class 2	55 (79.7%)	14 (20.3%)	
Class 3	7 (50%)	7 (50%)	
Skeletal classification			0.097
Class 1	40 (76.9%)	12 (23.1%)	
Class 2	54 (83%)	11 (16%)	
Class 3	12 (60%)	8 (40%)	
ANB			0.15
< 0	11 (61.1%)	7 (38.9%)	
0-5	71 (78%)	20 (22%)	
> 5	24 (85.7%)	4 (14.3%)	
U1-SN			0.059
< 100	10 (62.5%)	6 (37.5%)	
100-115	69 (84.1%)	13 (15.9%)	
> 115	27 (69.3%)	12 (30.7%)	
OJ			0.93
< 0	5 (71.4%)	2 (28.6%)	
0-4	53 (77.9%)	15 (22.1%)	
>4	47 (77%)	14 (23%)	
IMPA			0.40
< 90	22 (78.5%)	6 (21.4%)	
90-100	62 (80.5%)	15 (19.5%)	
>100	22 (68.7%)	10 (31.3%)	

* - denotes a significant association

Table 8. Treatment-Related Factors

Treatment Factors	**No EARR**	**EARR**	**P-Value**
Treatment time			0.70
< 20	32 (82%)	7 (18%)	
20-30	51 (76.1%)	16 (23.9%)	
> 30	23 (74.1%)	8 (25.9%)	
Treatment type			0.027*
Ext	29 (65.9%)	15 (34.1%)	
Non-Ext	77 (82.8%)	16 (17.2%)	

* - denotes a significant association

Inter-examiner reliability

A kappa test was used to evaluate the inter-examiner reliability. The kappa value of 0.656 and P-value of 0.001 indicates a moderate and strong agreement between the two examiners. This is statistically significant.

DISCUSSION

The complication of EARR, if severe, can result in a decreased crown to root ratio, and an increase in the rate of progressive periodontitis [3]. EARR can be diagnosed and monitored radiographically [7]. EARR has been seen to affect a variety of races of populations differently [6]. This study focuses on the rate of EARR in the Asian population of Alabama.

To evaluate the prevalence of EARR in the Asian population, we established the desired sample size based on previous literature. EARR of clinical relevance is primarily found in the anterior segment [6]. This segment consists of the upper central and lateral incisors and canines [6]. Different radiographic methods have been used to study the anterior segment. Wang et al., like our study, used panoramic radiographs for the measurements of the roots. Sameshima et al. and Nanekrungsan et al. used periapical radiographs, stating that periapical x-rays were more accurate than panoramic x-rays for measuring root resorption. However, Sameshima et al. have also reported that the difference in measurement in the maxillary anterior region between panoramic x-rays and periapical x-rays was less than 0.2 mm [31]. There is no consensus in literature on a protocol to identify and measure root resorption. The use of panoramic x-ray in our study may act as a limitation due to the presence of magnification and decreased resolution. Furthermore, patient positioning is vital when taking a panoramic x-ray. If the chin is titled too high, the hard palate will superimpose over the maxillary roots and obscure the image. If the chin is titled too low, the teeth will overlap, and measurements cannot be taken clearly.

The patients head must be aligned parallel to Frankfort plane. The CEJ may also be difficult to locate in panoramic images, and this has led to an overreporting of EARR[31]. Periapical x-rays increase chair time and operating time but have less magnification error (5% as opposed to the 20-35% in panoramic x-ray). CBCTs are costly, not routinely taken and expose the patient to higher doses of radiation and may violate the As Low As Reasonably Achievable principal.

Alternatively, CBCT imaging can be used for increased accuracy and repeatability as panoramic and radiographic x-rays are 2 dimensional and have varying degrees of magnification which may affect measurements [3]. A protocol should be developed to standardize the method of viewing, measuring and classifying external apical root resorption during orthodontic treatment so that future studies can compare more accurately.

Levander et al. highlighted the importance of radiographs taken 6-9 month after the beginning of the treatment; if the patient was found to have severe root resorption during this period then the patient is at a high risk for extreme root resorption. He categorized his index as minor resorption if the patient had less than 2 mm of EARR, and severe resorption if the loss was from 2 mm to one third of original root length, and if lost root structure exceeded one third of the original length, then it was classified as extreme root resorption[30]. Due to ethnic differences in root to crown ratio, percentage of root loss would be a preferred metric over the millimetric amount of root loss. In this study, the following classification was used: less than 20% was classified as mild EARR, equal to or greater than 20% root structure loss was classified as moderate EARR, and equal to or greater than 50% root loss structure was classified as severe EARR. Any result greater than 20% loss of root structure was classified as clinically significant.

The prevalence of moderate root resorption with equal to or greater than 20% loss of root structure in our sample was 22.6% (31/137). The majority, 77.4% of patients, had mild root resorption of less than 20%. Sever root resorption was recorded in 1 patient out of 137 patients (0.7%). This small percentage is coincident with another study, which found that only 2 % of its sample had EARR of 5 mm[33]. Similarly, a second study found 2.9% of its sample had severe EARR[34]. In contrast, Marques et al. found a high percentage of severe root resorption in his sample at 14.5%. He attributed this high percentage of severe EARR to the different classification method he used of the index that ranged from 0-4, where 0 means no resorption and 4 means root resorption exceeding a third of the original root length[19]. This high percentage in severe EARR can also be the result of a very large sample size (n=1049) that allowed the inclusion of more variables[34].

There is no conclusive evidence in the literature that determines which of the incisors exhibits more root resorption. The results of our study found that lateral incisors showed a greater prevalence for EARR (7.9%) than central incisors (7.71%). One of the factors affecting the prevalence of EARR that can account for the differences in results seen amongst different populations is race and ethnicity. Sameshima et al.'s sample consisted of Asian patients (N-198), Caucasian patients (N=516) and Hispanic patients (N=129). While Hispanic patients showed the highest rates of EARR, the Asian patients showed the lowest rates of EARR with 0.7-0.8 mm less resorption. These results along with Nanekrungsan's study and our study, also showed that the maxillary lateral incisor was the tooth that exhibited the most EARR in both children and adults. Other studies also have shown similar results [6, 7, 32, 35].

There are various reasons that have been attributed to the increased risk of EARR to the maxillary lateral incisors. Maxillary laterals have the highest percentage of root shape anomalies as seen in the high occurrences of barrel and pipette shaped roots[6]. Moreover, maxillary lateral roots have a higher percentage occurrence of dilaceration than central incisor roots. Since more force is needed to move dilacerated roots, there is a higher possibility of resorption in lateral than central incisors[7]. However, there is no consensus that abnormal root shape is associated with EARR. Brin et al. results showed that roots with abnormal morphology were not more likely develop EARR than normal roots[3]. Artun et al. also found that there were no indications that blunt ended roots had an increased risk of EARR after 12 months of treatment[35].

On the other hand, Maues et al. had results that contrasted our study with the central incisor showing more EARR than the lateral incisor. They stated that this could be due to the proximity of the central incisor roots to the cortical bone of the socket, the presence of the incisive canal, as well as the type of movement of the tooth during active treatment.

In this study we also evaluated the association of EARR to treatment-and patient-related factors. Patient-related factors analyzed were gender, age, dental and skeletal classification, as well as cephalometric measurements such as ANB, U1-SN, IMPA, and overjet. None of these factors, except for dental classification showed any statistically significant association to root resorption in our Asian patients. Gender has been previously attributed as a risk factor for EARR with males showing greater prevalence[3]; however, our study showed no statistical significance association.

To the best of our knowledge, there are no other studies that show a statistically significant association of EARR with dental classification (P-value: 0.035). Our results demonstrated an association and showed that 18.5% of Class I patients and 20.2% of Class II dental classification had EARR equal to or more than 20% resorption. However, it was the Class III patients that displayed the most (50%). In our sample, 64% of the patients who were only dentally classified as Class III were treated without extraction, and 80% of the patients in our sample who were dentally and skeletally classified as Class III were treated non-extraction. This high percentage of EARR that was present in Class III patients in our sample could be due to increased root torque since 80% of the patients with skeletal and dental Class III were treated by dental compensation which is achieved by flaring the upper anterior teeth and uprighting the lower anterior teeth.

Of the cephalometric measurements examined, only U1-SN showed a trend toward statistical significance (P value:0.059). This could be because 37% of the patients with an U1-SN of less than 100°, and 30% of patients that had an U1-SN greater than 115° displayed moderate EARR. This trend may support the association between torque and EARR that is mentioned in other studies[7, 30, 32, 34].

Previous studies have shown a significant correlation between EARR and overjet[6, 7, 32, 34]. However, in our study, the overjet variable was statistically insignificant. This may be justified by the use of different treatment methods to reduce overjet that do not displace the apex of the maxillary incisors. Nanekrungsan, whose study also only focused on Asian patients, classified mild EARR as less than 10% root loss structure, moderate EARR as 10-20% root loss structure, and severe EARR as 20% loss of root structure [7]. The classification we had used was more clinically relevant than the one in Nanekrungsan's study. We had broader classes, a mild category that started at less than 20% whereas his was equal to or less than 10 %, and our severe category was 50% and above whereas his started at above 20%. This difference in classification between our study and his study could describe the reason why he found an association between OJ and EARR and we did not. Additionally, he conducted his measurements using periapical x-rays whereas we used panoramic x-rays.

Treatment-related factors that we looked at were treatment time, treatment type (extraction or non-extraction) and appliance type (fixed or removable appliance). Regarding treatment duration, many studies [9,32,34,35] showed that there is a relation between treatment duration and the amount of external epical root resorption. In contrast, our study did not find this variable to be statistically significant. This can be the result of patients being in treatment for a long duration but the actual "active treatment time" is short. If appointments are made after long intervals or if patients regularly miss appointments, this decreases the time they are in "active treatment" as force levels decrease between appointments[9].

However, our results were in accordance with studies [7, 9, 19, 32, 34] that showed that there is more external apical root resorption in the maxillary anterior teeth when first or second premolars are extracted as part of orthodontic treatment. Extractions lead to increased tooth movement as the teeth are retracted into the extraction space. Extractions also increase treatment time, thus supporting the above evidence that longer treatment time and increased tooth movement increases the risk of external apical root resorption[34]. Sameshime et al. found that extraction of the upper and lower bicuspids led to greater EARR than non-extraction treatment plans. He also found that extraction of only upper premolars had the same EARR prevalence as patients that did not undergo extractions.

There is contrasting evidence that has stated there is no association between extraction and EARR due to the fact that in some cases, the extraction space is used to relieve crowding instead of retracting teeth therefore there is less root movement of the anterior teeth and therefore less resorption of the roots[7].

The patient-related (age, gender, dental classification, skeletal classification, ANB, U1-SN, overjet, IMPA) and treatment-related factors (treatment type and treatment time, and treatment appliance) discussed in this paper were measured in patients that were treated with fixed appliances. With regards to removable appliance, this study had an insufficient number of patients treated with removable appliances to be able to run a valid statistical comparison. Other studies such as Gay et al. and Wang et al. reported less incidence of EARR in removable appliances compared to fixed appliances[39]. One justification was the use of interrupted forces in removable appliances, as the patients remove the appliances during eating and brushing[39]. As previously discussed, interrupted forces seem to decrease the incidence of EARR. Gay et al. found the prevalence of root resorption of greater than 20% to be 3.69%, while our study found the prevalence of EARR equal to or greater than 20% to be 22.6% [40]. It is important to emphasize that EARR was still found in teeth treated with removable appliances and that removable appliances are not a preventable measure.

Although some of our results show evidence of an association between certain factors (dental classification and extraction treatment), there is no statistically significant association between EARR and the rest of the variables (age, gender, skeletal classification, ANB, U1-SN, overjet, IMPA, treatment time) in this study. This may be due to the multifactorial etiology of EARR. The variation in the prevalence of EARR has been mainly attributed to the patient's individual predisposition and susceptibility, with a very minor association of as little as 20% to the tooth root morphology [35]. Hartsfield et al. stated that 50-60% of the EARR found can be attributed to genetic heritability. Genetic factors in conjunction with orthodontic treatment account for up to two thirds of EARR variation[12]. Furthermore, some individuals show a significant clinical amount of root resorption. Sameshima's study is a primary literary source that exhibits the variation of EARR in different ethnic populations [6].

The Asian population has a Class III prevalence of 11-14%, compared to 1-3% in the Caucasian population[38]. The mechanics needed to treat Class III malocclusion include proclination of the upper incisors or extraction. Our study showed a significant association between Class III dental classification (P- value: 0.035) and extraction (P-value: 0.027) and EARR. We also showed an associative trend between the proclination of upper incisors and EARR (p value: 0.059). Precautions must be taken when planning treatment mechanics for these patients to decrease the risk of EARR such as patient awareness during informed consent and continuous monitoring with periodic x-rays, as well as careful mechanics during treatment and movement of teeth.

Limitation in our study include not evaluating the amount of crowding as another variable, as well as not identifying the specific extraction pattern, which would have shown how many premolars were extracted and whether the first or second premolar was extracted. This makes a difference in the amount of retraction the upper anterior segment undergoes. We also did not study the association between the method used to correct the malocclusion and EARR such as elastics, Forsus, Herbst, etc. Future studies to determine if there is an association between different anterior-posterior correction methods and EARR would be beneficial.

CONCLUSIONS

- EARR is a clinical risk of orthodontic treatment that the patient should be informed of prior to initiation of treatment.
- The overall maxillary incisor prevalence of moderate root resorption with equal to or greater than 20% loss of root structure in our sample was 22.6%.
- Our study found that lateral incisors showed a greater prevalence for EARR (7.9%) than central incisors (7.71%).
- We found that EARR was associated with dental classification with the greatest prevalence of EARR seen in Class III patients.
- The association between EARR and an orthodontic treatment plan involving extractions was found to be statistically significant.
- The association between EARR and U1-SN was trending towards a statistical significance. Further studies with a larger sample size could support this trend.
- The underlying genetic contribution could affect how the patient responds to treatment.
- A standardized method for radiographic diagnosis and measurement should be determined to allow for accurate comparison and increase of validity.
- Future studies with removable appliances, specified extraction patters, and different antero-posterior correction methods (Forsus, elastics, Herbst, etc) can be beneficial to determine their effect on EARR

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APPENDIX A

INSTITUTIONAL REVIEW BOARD APPROVAL

Subject: Approved IRB-160428005 Continuing Review
Date: Thursday, April 30, 2020 at 9:36:10 AM Central Daylight Time
From: Hill, Christopher Y
To: Lamani, Ejvis

Dr. Lamani,
IRB-160428005 has been approved but we have had issues sending approval memos from IRAP.
I am sending the approved consent to you now for your use and will send both the approval memo and consent from IRAP when available.

My apologies for the inconvenience.

Christopher Y. Hill | Protocol Analyst I
Office of the Institutional Review Board
UAB | The University of Alabama at Birmingham
AB 470 | 701 20th Street South | Birmingham, Al
205-934-3810 | cyh19697@uab.edu

Record Number
IRB-160428005
Done Save

Genetic Markers in Orthodontics
Ejvis Lamani - Orthodontics (AMERICAN ASSOCIATION OF ORTHODONTISTS FOUNDATION (AAO))

Human Subjects
View Mode - See Details
Change Project Info

Submissions (16) Linkages (2) Summaries ?

Home Summaries Personnel

Summary
Devices
Drugs
Personnel

Research Personnel

Add

All Certifications and Training ⚠

PI	Name	COI	Start Date		End Date
◉	Ejvis Lamani - Orthodontics Role: PI	✔	28-Apr-2016	Retire	Remove
	Certifications and Training	Responsible Person ☑		CV Email	
○	Najd Aswad - Graduate School Dean's Office Role: Other Personnel	✔	22-Nov-2019	Retire	Remove
	Certifications and Training	Responsible Person ☐		CV Email	
○	Nellie Baghaei - Biology Role: Other Personnel	?	25-Feb-2020	Retire	Remove
	Certifications and Training	Responsible Person ☐		CV Email	
○	Balraj Bains - Orthodontics Role: Other Personnel	✔	22-Nov-2019	Retire	Remove
	Certifications and Training	Responsible Person ☐		CV Email	
○	Kayla Holcomb - Students Role: Other Personnel	✔	21-Feb-2018	Retire	Remove
	Certifications and Training	Responsible Person ☐		CV Email	
○	Ahu Topkara - Graduate School Dean's Office Role: Other Personnel	?	26-Feb-2020	Retire	Remove
	Certifications and Training	Responsible Person ☐		CV Email	
○	Jue Wang - Orthodontics Role: Other Personnel	✔	22-Aug-2018	Retire	Remove
	Certifications and Training	Responsible Person ☐		CV Email	

Past Research Personnel

Name	Department	Start Date	End Date	
Clark Browne Email	Orthodontics Certifications and Training	22-May-2017	20-Feb-2018	Remove
Brenna Christensen Email	Graduate School Dean's Office Certifications and Training	20-Feb-2018	01-Jun-2019	Remove
Bhakti Desai Email	Graduate School Dean's Office Certifications and Training	20-Feb-2018	02-Feb-2020	Remove
Frank Litchfield Email	Graduate School Dean's Office Certifications and Training	08-Oct-2018	20-Feb-2020	Remove
Mary MacDougall Email	Oral & Maxillofacial Surgery Certifications and Training	22-May-2017	20-May-2019	Remove
Craig Rousso Email	Graduate School Dean's Office Certifications and Training	22-May-2017	06-Jul-2018	Remove