Newly defined landmarks for a three dimensionally based cephalometric analysis: A retrospective cone beam CT scan review

Introduction

One of the most important aspects of orthodontic diagnosis and treatment planning is an accurate analysis of the patient's anteroposterior (AP) skeletal relationship. Among many other factors, the skeletal age of the patient and the severity of the maxillomandibular discrepancy play a significant role in determining the ideal method of treatment. The use of lateral cephalometric radiographs and various linear or angular analyses is a commonly used method for clinicians to diagnose the patient's AP skeletal pattern.

Steiner's ANB angle has traditionally been a popular and relatively straightforward method for diagnosing the patient's skeletal relationship. The angular measurement relies on four cephalometric landmarks (sella, nasion, A-point and B-point) and is calculated by taking the difference between the SNA and SNB angles (ANB angle), which both depend on the sella-nasion (SN) reference plane[1]. Although this plane reliably represents the patient's anterior cranial base, it has high interindividual variability when compared to a true horizontal, which makes it a poor reference for cephalometric measurements[2,3,4].

With the exception of A-point, all of the other landmarks are relatively easy to identify on a traditional lateral cephalogram and the angular measurement itself provides a convenient way to classify the patient's AP skeletal relationship; traditionally, a patient with an ANB measurement of 0-4 degrees is considered to be Class I skeletal, while a measurement greater than 4 degrees is considered Class II skeletal. A measurement less than 0 degrees is considered Class III skeletal. The literature has shown that the ANB measurement itself can be influenced by a variety of different factors such as maxillary incisor inclination, maxillary prognathism and the anteroposterior position of nasion[5,6,7]. These factors can result in altered ANB angular measurements, thus potentially leading to an incorrect diagnosis and treatment plan.

The Wits appraisal is often used as an adjunct to Steiner's ANB angle to diagnose the patient's AP skeletal relationship and utilizes a linear, as opposed to an angular measurement. The patient's A and B points are projected as perpendiculars to the functional occlusal plane and the distance is measured in millimeters[5,8]. A positive Wits measurement results when the projected A point is more anterior with respect to the projected B point. Traditionally, a patient with a Class I skeletal pattern will have a Wits value ranging from 0 to -1. A Class II skeletal patient will have a higher positive Wits value, while a Class III skeletal patient will have a higher negative Wits value.

The Wits analysis, unlike Steiner's ANB angle does not rely on the anterior cranial base as a reference plane and has proven to be more useful and reliable in diagnosing the patient's AP skeletal relationship[9]. The analysis, however, does have some disadvantages, which need to be considered. First, the measurement relies on A point, which can be influenced by maxillary incisor inclination and maxillary prognathism[6], thus subjecting this analysis to the same shortcomings associated with the ANB angle. Second, the Wits analysis relies on the patient's functional occlusal plane, which is also difficult to determine on a conventional lateral cephalogram, because it relies on the accurate identification of and the presence of the patient's premolar occlusion. And finally, the measurement itself utilizes a dental parameter (the functional occlusal plane) which can be influenced independent of skeletal change, thus making it potentially unreliable for diagnosing a skeletal relationship[5].

The anteroposterior dysplasia indicator (APDI) is another cephalometric analysis that can be used to diagnose the patient's AP skeletal relationship. The measurement is obtained from the facial angle, plus or minus the A-B plane angle, plus or minus the palatal plane angle[10]. Unlike the previous cephalometric studies, Kim and Han utilized various measurements and correlated them against the patient's actual molar occlusion, which could easily be measured from diagnostic models. Receiver operating characteristic (ROC) analysis on the popular AP cephalometric measurements, with the molar relationship as a reference showed that APDI was statistically more effective in diagnosing Class II and Class III malocclusions compared to ANB and Wits[10]. In order to perform this analysis, it is important to note that the authors assumed Class II and III skeletal patterns yield Class II and III malocclusions, respectively; thus the patient's molar occlusion was used as a "gold standard" from which to measure cephalometric AP skeletal discrepancy. This assumption is necessary because currently there is no agreement on an ideal cephalometric analysis to define AP skeletal patterns.

Although the literature suggests that APDI is a more predictable method for diagnosing AP skeletal patterns, the analysis itself is subject to a variety of limitations. The measurements depend on the patient's palatal plane, which has been shown to be more stable when compared to SN[2], but is still subject to the limitations of an intracranial reference plane; the angulation of the palatal plane will change with respect to the patient's head position. Furthermore, like ANB and Wits, the APDI analysis relies on accurately identifying A-point, thus exposing it to the weaknesses found in the other measurements.

The Steiner analysis, the Wits appraisal and the APDI can all be used to assist the clinician in diagnosing the patient's AP skeletal relationship. All three of these analyses, however, have critical disadvantages. First, they all utilize an intracranial reference plane (SN line, functional occlusal plane, palatal plane) from which the measurements are analyzed. Second, they all rely on A-point, which is difficult to locate and can be influenced by other variables. In order to predictably and accurately diagnose the patient's AP skeletal relationship, the flaws of traditional two dimensional analysis need to be addressed.

The concept of natural head position (NHP) was introduced in the 1950's. It is defined as the natural, reproducible position of the head when a relaxed subject looks at an external eye reference. Traditionally, NHP has been determined by asking the patient to look into the reflection of his/her own eyes in a mirror; in this position, a photograph or radiograph would be taken with a true vertical plumb line as a reference. An analysis that utilizes NHP and a true vertical or a true horizontal reference plane has many advantages. First, the reference plane itself is extracranial and is thus not subject to high interindividual variability[12] compared to SN and the functional occlusal plane. Furthermore, true horizontal is incredibly reproducible and on average, it can be determined to within 2-4 degrees of error. By comparison, the more traditional reference planes when compared to the true horizontal exhibit 25-36 degree variation. Third, NHP represents the patient's "true life appearance," which is an ideal position to determine the patient's skeletal diagnosis and treatment planning options[3,13].

Although NHP is a more accurate and reproducible reference plane, the traditional method of transferring a true vertical reference line from a profile photograph to the lateral cephalometric radiograph requires time consuming superimpositions. Natural head orientation (NHO) was proposed as a better alternative and is defined as the head position that the orthodontist believes that the patient will hold when looking at a distant point at eye level[14,15].

The clinician's experience can also compensate for certain individuals who have a habitual tendency to hold their head in a flexed or extended posture. The main disadvantage of NHO is that it can be influenced by the patient's facial form, specifically the chin prominence; a four degree change in chin prominence produced an average of two degree change in NHO[15]; the error of repeatability for NHO was less than 1.5 degrees. Although statistically significant, a two degree change in orientation with respect to chin prominence falls within the 2-4 degrees of accepted reproducible error when orienting true natural head position.

The use of natural head orientation and a true horizontal extracranial reference line resolves one of the major disadvantages encountered with the traditional cephalometric analyses. The second concern, which involves the use of A-point is slightly more difficult to address. Specific landmarks that approximate the alveolar bone are influenced by the position and location of the dentition and therefore should not be used to determine true maxillary and mandibular skeletal relationships. Basal bone, however, which is the part of the mandible and maxilla from which the alveolar process develops is considered to be more stable. An evaluation of the height of mandibular basal bone, as measured from the inferior border of the mental foramen to the lower border of the mandible, showed no significant difference in young or old dentate and edentulous patients[16].

The apical base therefore, which was previously defined by Lundstrom as the junction of the alveolar and basal bones[19], can be used as a stable landmark for skeletal cephalometric analysis. Clinically, the apical base was defined as the band of keratinized tissue adjacent to the mucogingival junction; this was defined by Andrews as the "WALA ridge[18]." Investigators have utilized WALA points and the facial axis (FA points) of corresponding teeth to investigate the relationship between dental and basal arch forms in specific types of malocclusions[19,20]. To date there have been no studies that utilize WALA points or the apical base as a reference to analyze maxillomandibular skeletal relationships.

Unfortunately, there are currently no methods to accurately locate the apical base on a traditional lateral cephalogram and WALA points are by definition clinical intraoral landmarks that cannot be translated to radiographs. The advent of cone beam CT (CBCT) scans, however, has allowed orthodontists to visualize the maxilla and mandible in three dimensions. Recently there has been a large push towards CBCT imaging, but many clinicians are still using the standard two dimensional landmarks and measurements, such as ANB and Wits to analyze their three dimensional patient records.

Although the current trend in orthodontics is shifting from the analysis of lines and distances to areas an volumes[23], a true three dimensionally based cephalometric analysis has yet to be proposed. Most models either average left and right two dimensional landmarks or utilize the midsagittal plane to perform the traditional analyses, but the reliability of these measurements is in question. Damstra et al performed a study to determine the reliability and measurement error of common cephalometric measurements that are made on CBCT scans. The results showed that most measurement errors (with the exception of ANB angle) were clinically relevant, thus questioning the use of these 3D measurements to detect treatment effects[22]. A study by Berco et al, however compared linear measurements on a CBCT scan, to the same measurements on a dry skull and found that they were accurate to within 0.3 mm with clinically insignificant measurement errors[25].

Although the literature shows conflicting results with regards to CBCT measurement errors, the main concern that needs to be addressed is landmark identification. The landmarks on a traditional lateral cephalogram were only defined in two dimensions and therefore should not be translated to a three dimensional model; new landmarks that are specific in all three planes of space are needed. The ability to sagittally, coronally and axially slice a CBCT image provides an excellent tool to define new landmarks that can serve as the basis for a three dimensional analysis.

Objectives

1. Utilize CBCT scans to locate new cephalometric landmarks that are based in three dimensions. (anterior maxillary and mandibular centroids).
2. Establish a new method of analyzing AP skeletal relationship with the molar relationship as a reference. The new analysis will: a) be based in three dimensions, and b) utilize the newly defined landmarks and a true horizontal extracranial reference plane with the patient positioned in natural head orientation.
3. Determine whether this new AP measurement can statistically differentiate Class I, II and III patients.
4. Determine whether the new AP skeletal analysis is statistically more accurate at predicting the patient's molar relationship compared to the traditional two dimensional lateral cephalometric analyses.

Study Hypothesis

The new three dimensionally based AP skeletal analysis can statistically differentiate between Class I, II and III skeletal patterns.

The new three dimensionally based AP skeletal analysis is statistically more accurate or reliable at predicting the patient's molar relationship compared to the traditional two dimensional lateral cephalometric analyses.

Materials and Methods

Subjects

This study is a retrospective record review. The subjects were divided into three groups based on first molar occlusion:

a) Class I - The primary second molars exhibit a flush terminal plane occlusion. The permanent first molars are in an end-on relationship.

b) Class II - The primary second molars exhibit a distal step occlusion. The permanent first molars are in a Class II relationship (greater than end-on relationship).

c) Class III - The primary second molars exhibit a mesial step occlusion. The permanent first molars are in a Class I relationship.

The patient's pretreatment first molar occlusion was used as a reference because it can be accurately viewed and measured on the CBCT scans. For the purpose of this study, we assumed that the patient's molar occlusion was directly correlated to his/her AP skeletal relationship. For example, if a patient has a Class II molar relationship, we assumed that he/she had a Class II skeletal relationship as well. The molar relationship, therefore served as the reference for the patient's skeletal relationship. This assumption was made to prevent controversy over defining the patient's actual AP skeletal pattern, which can vary depending on the type of analysis used.

Inclusion Criteria

a) Male and female patients who have pretreatment full head CBCT scans as part of their initial diagnostic records.

b) Subjects have all permanent first molars erupted and in occlusion.

c) Subjects have all primary second molars present.

It was imperative to select patients in the mixed dentition, who still had all primary second molars present. This would ensure that premature loss of leeway space has not occurred and that the existing first molar occlusion was not influenced by any other dental factors. The eruption of the first molars into occlusion without being influenced by external factors was the basis for the assumption that the molar relationship was equivalent to the patient's skeletal pattern.

Exclusion Criteria

a) Patients who have experienced premature loss of leeway space (severely decayed, missing or heavily restored primary second molars).

b) Patients who have missing permanent teeth (except 3rd molars).

c) Patients with craniofacial deformities.

d) Patients with subdivision malocclusions.

e) Patients with previous orthodontic treatment.

f) CBCT scans with distortion or artifacts that directly influenced landmark identification.

Methodology

The CBCT scans for each subject were provided by a private orthodontic office in Cranston, RI where initial scans are taken for every new patient on an Iluma cone beam CT scanner with a 40 second scan time, allowing a 0.3 mm slice thickness. Each scan was taken with the patient in maximum intercuspation. Subject names, birth dates or other identification criteria were not be included. All subjects were assigned a reference number as the only identification criteria. A de-identifier list was created and the identity of subjects was known only by the practicing orthodontist in Cranston, RI. All de-identified information and measurements were stored on an iWork Numbers ('09 version 2.1) spreadsheet on a password protected lap top computer.

Locating Maxillary and Mandibular Centroids

Invivodental (Anatomage) software network version 5.1 was used for CBCT analysis. The alignment tool was first used to orient the initial image in all three planes of space (Figure 1). The sagittal slice of the scan was adjusted to natural head orientation, followed by reorientation of the coronal slice so that a line drawn from both zygomaticofrontal sutures was approximately parallel to true horizontal. Finally, the axial slice was adjusted so that the midpalatal suture was approximately perpendicular to the true horizontal reference plane (Figure 2).

Following proper orientation of each plane, the midsagittal view, which was used for measurements, was determined by accurately sectioning the coronal slice between the two central incisors. The Anatomage software tools were used to outline the premaxillary bone anterior to the premaxillary suture in the form of a closed polygon (Figure 3). The y and z coordinates of each vertex were recorded on a Microsoft Office Excel spreadsheet and used to calculate the centroid of the premaxilla in the sagittal plane. The x-coordinate of the centroid was fixed according to the specific midsagittal slice.

An axial slice through the z-coordinate of the centroid that was calculated in the sagittal plane was then viewed (Figure 4). The maxillary bone in the axial slice was used to define a second closed polygon. The anterior and posterior boundaries were defined by the alveolar bone, while lines tangent to the distal root surface of each maxillary lateral incisor served as the lateral borders. If the maxillary lateral root was not visible on the specific axial slice, a tangent to the mesial surface of each canine was used as lateral borders (Figure 5). The x and y coordinates of each vertex was recorded as described above to calculate the axial centroid.

The x,y and z-coordinates of each centroid were averaged into one point that was projected onto the midsagittal plane. This point served as the maxillary centroid, which will be referenced later for the linear measurement.

The mandibular centroids were determined in a similar fashion as described above. The midsagittal view was used to outline the visible mandibular symphysis to form a closed polygon (Figure 6). In patients with a pronounced pogonion, a true vertical from point B to the inferior border of the mandibular symphysis served as the anterior border (Figure 7). A prominent pogonion projection would ultimately cause the mandibular sagittal centroid to be displaced anteriorly and inferiorly, thus influencing the final measurement. This extra step was only performed in a small percentage of patients in an attempt to control for small skeletal variations that may have a small influence on the final AP skeletal measurement. The y and z-coordinates of each vertex were recorded and the centroid was calculated. Similar to the maxillary centroid, the z-coordinate was used to view the axial slice (Figure 8). A second centroid was calculated based on the mandibular bone in the axial view. Lines tangent to the distal surface of the lateral incisor root served as the lateral boundaries (Figure 9). The mesial surface of the canine was used if the lateral incisor was not visible on the given axial slice. The x, y and z-coordinates of each centroid were averaged into one point and projected onto the midsagittal plane.

The averaged maxillary and mandibular centroids were used as new landmarks for a linear measurement (μ). True vertical lines were drawn from each centroid and the linear distance between the two lines was measured along the true horizontal (Figure 10). If the maxillary centroid was anterior to the mandibular centroid, the measurement was positive, and if the maxillary centroid was posterior to the mandibular centroid, the measurement was negative. All of the outlines and linear measurements were performed twice (at least two weeks apart) and values were averaged. A second examiner was trained in the methodology and made the same measurements in ten randomly selected CBCT scans to determine inter-rater reliability.

Finally, the angle between SN and the true horizontal ($SN\text{-}T_H$) was measured and utilized to determine the inter and intra rater reliability of natural head orientation (Figure 11).

Two dimensional cephalometric analysis

Digital tracing and two-dimensional cephalometric analysis for the initial CBCT scans were also performed with the Anatomage Invivo5.1 tracing software (Figure 11). The ANB, Wits appraisal and APDI were measured and recorded on the Numbers spreadsheet. All tracings and measurements were performed twice and the values were averaged.

Confidentiality

All measures were taken to ensure subject confidentiality. Subject names, birth dates or other identification criteria were not included. All subjects were assigned a reference number as the only identification criteria. A de-identifier list was created and the identity of subjects was known only by the practicing orthodontist in Cranston, RI. All de-identified information and measurements were stored on an iWork Numbers ('09 version 2.1) spreadsheet on a computer that was password protected.

Data Analysis

The primary objective of the study was to determine if the newly determined AP skeletal analysis could statistically differentiate between the three molar classification groups. The average measurements between each group was statistically analyzed with a one-way ANOVA (Tukey HSD). A power analysis was performed using nQuery Advisor (Version 7.0) with unequal sample groups (approximately 600 CBCT scans will be reviewed until a sample size of at least 55 Class I's, at least 20 Class II's and at least 20 Class III's are obtained); assuming an average difference between groups of 2 millimeters (4 millimeters between Class II and III groups) and a standard deviation of 1.8 millimeters, the given sample size would provide over 99% power for the study.

The secondary objective of the study was to compare whether the new three dimensionally based analysis is statistically better at predicting the subject's molar relationship compared to the traditional two dimensional analyses. Volume under curve (VUC) as described by Nakas & Yiannoutsos[24] was used to determine which measurement was statistically better at predicting the patient's molar relationship, which ultimately would allow us to draw conclusions regarding the patient's skeletal relationship; 95% confidence intervals were calculated using 1000 bootstrap samples.

ROC analysis is used for two class testing and the area under the curve determines the accuracy of a diagnostic test. The VUC analysis is used for multi group classification problems and is an extension of the area under the curve; it was the appropriate statistical test for this study because we wanted to compare the accuracy of different diagnostic tests (AP skeletal cephalometric measurements) at predicting three different skeletal patterns (Class I, II and III). The analysis itself measures the probability that three measurements, one from each class, will be in the correct order. For the μ measurement, ANB and Wits the correct order was the following: Class II would have the highest value, Class I would have the middle value, and Class III would have the lowest value. For the APDI measurement, the correct order was: Class III would have the highest value, Class I would have the middle value, and Class II would have the lowest value. The confidence intervals were calculated by repeating the statistical test with the given data 1000 times and obtaining the lowest and highest probability values for each measurement.

Results

Kolmogorov-Smirnov test for each molar group and each measurement was greater than 0.05, indicating normally distributed data. Descriptive data for linear and angular measurements of each group are given in Table I and the one-way ANOVA (Tukey HSD) statistical comparisons between each of the three molar groups are given in Table II. The mean measurements for the fifty seven Class I patients were 3.64 mm (μ measurement), 5.04 degrees (ANB), 2.01 mm (Wits) and 79.6 degrees (APDI). The mean measurements of the twenty six Class II patients were 4.48 mm (μ measurement), 5.84 degrees (ANB), 2.71 mm (Wits) and 76.7 degrees (APDI). Finally, the mean measurements of the twenty two Class III patients were 0.51 mm (μ measurement), 2.93 degrees (ANB), -0.79 mm (Wits) and 84.0 degrees (APDI).

The p-value of the one-way ANOVA analysis for each of the four different measurements was less than 0.001, indicating statistical significance. Tukey HSD test for the μ measurement, ANB angle and Wits revealed statistically significant differences between the means of Class I and III patients ($p < 0.001$, $p < 0.01$ and $p < 0.001$, respectively), as well as Class II and III patients ($p < 0.001$ for each group), but no significant difference between Class I and II patients. The Tukey HSD test for APDI revealed statistically significant differences between the means of Class I and III patients ($p < 0.001$), Class II and III patients ($p < 0.001$) and Class I and II patients ($p=0.043$). The Tukey HSD results are summarized in Table II.

Volume under curve (VUC) was used to determine whether the new measurement (μ) was statistically better at predicting the patient's molar relationship compared to the traditional two dimensional measurements. The VUC value for the μ measurement, ANB, Wits and APDI were 0.421, 0.385, 0.368 and 0.385 with 95% confidence intervals of (0.301, 0.551), (0.276, 0.503), (0.242, 0.520) and (0.266, 0.507), respectively. The data results and 95% confidence intervals based on 1000 bootstrap samples are given in Table III.

Each of the measurements for the various analyses were performed twice (T_1 and T_2), at least one week apart. Intra-rater reliability for the μ measurement, ANB, Wits, APDI and SN-T_H were calculated using two different methods. The first is expressed as the mean and standard deviation of $|T_1-T_2|$ of the above analyses; the μ measurement showed a mean of 0.92 mm with a SD of 0.74, the ANB showed a mean of 0.65 degrees with a SD of 0.52, the Wits showed a mean of 1.21 mm with a SD of 1.03, the APDI showed a mean of 1.60 degrees with a SD of 1.32 and the SN-T_H showed a mean of 0.65 degrees with a SD of 0.52. The results are summarized in Table IV.

As the second method to demonstrate intra-rater reliability, we created a scatterplot as described by Bland and Altman[27]. For each of the above analyses (μ measurement, ANB, Wits, APDI and SN-T_H), the average value of the measurements taken at the two separate time points was plotted against the difference of values to create a scatterplot. The results are shown in Figures 13-17. With the exception of a few outliers, the difference of values between T_1 and T_2 was relatively low, which resulted in points that were near the center of the chart's y-axis; the figures indicate that the various measurements have high intra-rater reliability.

The second examiner, who was trained in the methodology performed all of the analyses on ten randomly selected CBCT scans. The T_1 values performed by the author for the μ measurement, ANB, Wits, APDI and SN-T_H were compared to the second examiner's measurements (SS_1) to determine inter-rater reliability by using the same methods as described above. The μ measurement showed a mean of 2.14 mm with a SD of 1.23, the ANB showed a mean of 1.22 degrees with a SD of 1.03, the Wits showed a mean of 1.13 mm with a SD of 0.96, the APDI showed a mean of 2.43 degrees with a SD of 2.23 and the SN-T_H showed a mean of 2.93 degrees with a SD of 1.31. The results are summarized in Table V. Scatterplots of the average values between the two examiners against the difference of values for each of the analyses are shown in Figures 18-22.

Discussion

CBCT technology within general dentistry has greatly increased in popularity over the past ten years, and more recently it has begun to influence the field of orthodontics. Although new technology can be a valuable tool for diagnosis and treatment planning, it is ultimately limited by the way clinicians can analyze this new data. Most orthodontists still use traditional two dimensional cephalometric measurements to analyze three dimensional images, which is an inefficient use of CBCT imaging. A true three dimensional analysis is needed to optimize the benefits of CBCT scans for diagnosis; this requires not only newly defined landmarks, angular and linear measurements, but also longitudinal and cross sectional data to redefine norms and growth patterns.

In this retrospective CBCT record review, we attempted to generate new cephalometric landmarks that were based on average centroid calculations in the sagittal and axial planes. The projections of the new points onto a midsagittal plane between the patient's maxillary incisors were used to generate a linear measurement (μ) that can be used as a novel AP skeletal analysis and compared to the standard two dimensional analyses used in orthodontic diagnosis (ANB, Wits, APDI). Although the new landmarks themselves are based in three dimensions, the linear measurement is recorded in two dimensions. Thus, the proposed measurement combines methods of two dimensional and three dimensional analysis that will hopefully serve as a bridge to future studies and analyses that are truly based in three dimensions.

The results from the study showed that the μ measurement, ANB and Wits values could statistically differentiate between Class I and III patients, and Class II and III patients, but could not statistically differentiate between Class I and II patients. The APDI value, however, could statistically differentiate between all classes. This could potentially be explained by our use of molar relationship as a reference for classifying patients. Molar classification itself does not necessarily correlate with skeletal relationship, but we did not want to utilize conventional skeletal measurements to classify patients as they all have inherent flaws and can give inconsistent results. Utilizing molar relationship to classify patients, however, does have several advantages. First, it completely eliminates any controversy involved with classifying the patient because the molar relationship can be easily classified based on the CBCT scan, diagnostic models or upon clinical examination. Second, as orthodontists, we inherently focus on treatment of the patient's dentition, while our influence on the patient's skeletal pattern is debatable; it makes sense, therefore to classify patients in this manner. Another method that could potentially be used in future studies for classifying patients would be soft tissue profile, which is another factor that orthodontists inherently base their treatment.

In our sample, the Class I patients were defined as having an end-on first molar occlusion, which we assumed would become a normal Class I molar occlusion following the exfoliation of the primary second molars, although clinically this does not always happen. This may have influenced how Class I and II patients were classified, thus making it more difficult to find statistical significance between the two groups. Furthermore, the age/development of the sample population may have also contributed to the inability to distinguish between Class I and II patients. Because the sample population included patients with all four primary second molars present, most if not all of the Class I and II patients would not have completed mandibular growth. Although cervical vertebrae maturation could not be used to confirm growth stage, the population as a whole tended to look slightly Class II, which was evidenced by the larger ANB angles and Wits appraisal values. Future studies could potentially use similar methodology in a non-growing/un-treated patient population with fully erupted maxillary and mandibular permanent dentition. This would not only eliminate any complexities involved with patient classification, but would also control for growth as a potential confounding variable.

Although the μ measurement was unable to statistically differentiate between all three molar classifications, we still wanted to determine if the measurement itself was a better predictor of the patient's molar relationship/skeletal pattern compared to the traditional two dimensional analyses. The VUC calculations for each analysis were greater than 0.167, indicating that the four measurements are better than chance at predicting molar relationship, but the overlapping confidence intervals show that no one particular measurement exhibited a statistically significant improvement over any other method. It is important to note, however, that the VUC analysis for the μ measurement (0.421) was greater than those of the three 2D measurements (0.385 and 0.368). Although statistically not significant, these results show that there is potential to use three dimensional imaging for skeletal diagnosis and a 3D analysis may provide the practitioner with valuable diagnostic information that standard imaging cannot.

The fact that one analysis is not statistically better than another may be due to the inherent flaws with each particular measurement or flaws in the actual 3D tracing process. Baumrind and Frantz[26] concluded that even when one person replicates a tracing of the same head film, there are significant errors in landmark identification and the probability of successfully identifying sixteen landmarks on a conventional analysis was 44%. This percentage may decrease further if we were to consider the identification of constructed three dimensional landmarks. Flaws in landmark identification will ultimately translate to the analyses from which these landmarks are based, thus making angular and linear measurements less reliable[17].

The ANB angle, Wits appraisal and APDI rely on the accurate identification of A-point, which can be challenging to locate on a traditional lateral cephalogram and can be influenced by maxillary incisor position[5,6,7]. Furthermore, ANB relies on the point nasion which is highly variable, and the Wits appraisal and APDI rely on intracranial reference planes for measurements (functional occlusal plane and palatal plane, respectively), which have been shown to have high interindividual variability[2,3,4]. The new measurement (μ) attempted to address the weaknesses associated with the existing analyses by using an extracranial reference plane (NHO) and a constructed point based on average centroids in two planes. While certain concerns were addressed with this new measurement, other complications became evident. Accurately and consistently outlining the anterior maxilla for centroid calculation was difficult, especially in the axial plane. The axial slice through the centroid of the sagittal slice often included large sections of the palate and alveolar bone, making the posterior boundary of the polygon difficult to determine and consistently locate. The mandibular polygon in the axial and sagittal planes were easier to visualize, but variations in the vertical position of the sagittal centroid influenced our ability to visualize the lateral incisor or canine root in the axial view, thus at times, making the lateral boundaries of the axial polygon difficult to determine. Furthermore, the details of the CBCT scans were often not clear or accurate enough to make ideal measurements. This is likely due to the age of the sample population and the challenge of requiring young children to remain absolutely still for forty seconds. Unfortunately, patient movement during the scan can result in blurry images that lose diagnostic value.

Future research studies should focus on identifying boundaries and landmarks on three dimensional images that can be more consistently located and identified with less chance of distortion. The main concern from this project was locating the polygon's posterior boundary on the maxillary axial slice. It may be beneficial to repeat a similar study design utilizing the entire area of the maxilla and mandible in the sagittal and axial slices to calculate the centroids; the boundaries of the maxilla and mandible are much easier to visualize on the CBCT scan and complex identification of polygon borders would be unnecessary.

The intra-rater reliability between T_1 and T_2 was high for each of the measurements performed. The greatest average difference in angular measurements was 1.60 degrees (APDI), while the linear measurement was 1.21 mm (Wits); both measurements fall within standard tracing error, which has been reported to be as high as 1.72 mm and 6.6 degrees for certain linear and angular measurements[29]. The SN-T_H angle showed an average difference of 0.65 degrees between the two time points, confirming the reproducibility of the measurement, which had previously been established as 2-4 degrees of error for orienting true natural head position[3].

Inter-rater reliability between T_1 and SS_1 was also relatively high for each of the measurements performed. The greatest average difference in angular measurement was 2.93

degrees (SN-T_H), which further confirms the reproducibility of orienting natural head position between examiners. The greatest average difference in linear measurement was 2.14 mm (μ measurement), which falls within previously reported standard tracing error. As expected, the inter-rater reliability was not as consistent as the intra-rater reliability, which is likely a result of operator experience. The methodology as defined by the author was determined after numerous pilot studies and repeated tracings. The second examiner was trained in a much shorter time period and it is likely that inter-rater reliability would increase as the examiner becomes more familiar with the methodology.

Although there were certain challenges associated with calculating the μ measurement, and identifying the polygon borders, this study is the first to show that novel three dimensional landmarks can be created and reproduced with high inter and intra rater reliability. The results from the study showed that this method of three dimensional AP skeletal analysis was not statistically better at predicting skeletal pattern compared to the standard 2D analyses, but the study itself can be used as a stepping stone for future CBCT research. The current technology provides a vast amount of potential information and it is necessary for future studies in 3D imaging to move away from the familiarity of angular and linear measurements. A realistic goal should be the creation of additional stable and reproducible three dimensional landmarks and the development of analyses based on volumetric data, rather than areas.

<u>*Limitations*</u>

The main limitations of this study were patient selection and patient classification. In order to categorize the patients according to unaltered first molar occlusion, only patients with all four primary second molars were included. At this age, most of the patients (especially males) would not have gone through their pubertal growth spurt and appear to have a slightly more Class II skeletal pattern. Classification of the patients into molar occlusion also has limitations. We assumed that patients with an end-on first molar occlusion were Class I skeletal, patients with a Class II molar occlusion were Class II skeletal and patients with a Class I molar occlusion were Class III skeletal. We made this assumption based on the idea that natural exfoliation of the primary molars would result in mesial drift of the lower molars, thus equating the final molar occlusion to the patient's skeletal pattern. The problem, however, is that the amount of mesial drift that occurs between patients is unpredictable and the developing first molar occlusion in the permanent dentition does not always correlate to the patient's skeletal pattern. Misclassification of the patients as a result, would influence the final results. Fortunately, future studies can easily overcome both of these limitations by changing the population sample to an older group of untreated patients with fully erupted maxillary and mandibular dentition.

Another limitation of this study was landmark identification. Defining the boundaries of the polygons in the axial slice was often challenging and inexact, especially if the slice included parts of the patient's palate. These discrepancies influence the location of the centroids and ultimately effect the final measurements. Patient movement during the scan resulted in blurry images and also created some concerns with landmark identification. These limitations can also be easily addressed by utilizing the entire maxilla and mandible in the sagittal and axial slices as the area for centroid calculation. These landmarks are more consistent and easier to identify on the CBCT scans.

Clinical Considerations and Recommendations

Full head CBCT scans provide an extraordinary amount of information to the practicing orthodontist. The full potential of these scans however, is currently limited by how the data is analyzed and used to make clinical decisions. The results from this study suggest that a limited three dimensional AP analysis with new landmarks has the potential to provide valuable diagnostic information to the practitioner, but currently cannot statistically distinguish between the three molar classifications. When compared to traditional two dimensional measurements, the μ measurement does not add significant value to diagnosing the patient's skeletal pattern.

A review of the current literature shows that CBCT scans offer minimal additional information with regard to diagnosis or treatment decisions, and are only recommended for specific cases/situations: cleft palate patients, assessing unerupted tooth position, supernumerary teeth or root resorption, and planning for orthognathic surgery[28]. Future research need to focus on the development of a true three dimensional analysis with newly defined landmarks that move away from linear and angular measurements. This study has demonstrated that three dimensional landmarks can be created and reproduced based on area measurements in two different planes; calculating the center of volume (of the maxilla or mandible) would be an ideal method for defining additional landmarks in space. Providing practitioners with the ability to consistently and reliably analyze CBCT images in three dimensions will ultimately justify the replacement of standard diagnostic imaging.

Conclusion

The μ measurement was created as a new method for analyzing a patient's AP skeletal relationship; it was measured from newly defined landmarks that were based in three dimensions and projected onto the patient's midsagittal plane between the maxillary central incisors. Further research is needed to create additional three dimensional landmarks and a true 3D CBCT analysis. Based on the results and analyses from this study, the following conclusions were made:

- The μ measurement, ANB, Wits, APDI and SN-T_H angle can be analyzed on a CBCT scan and show high inter and intra-rater reliability.
- The μ measurement could not statistically differentiate between the three molar classifications and was not a better predictor of molar relationship compared to the standard two dimensional analyses (ANB, Wits and APDI).
- There is insufficient evidence to suggest that the new linear measurement is an accurate method to analyze AP skeletal relationship.

List of Figures

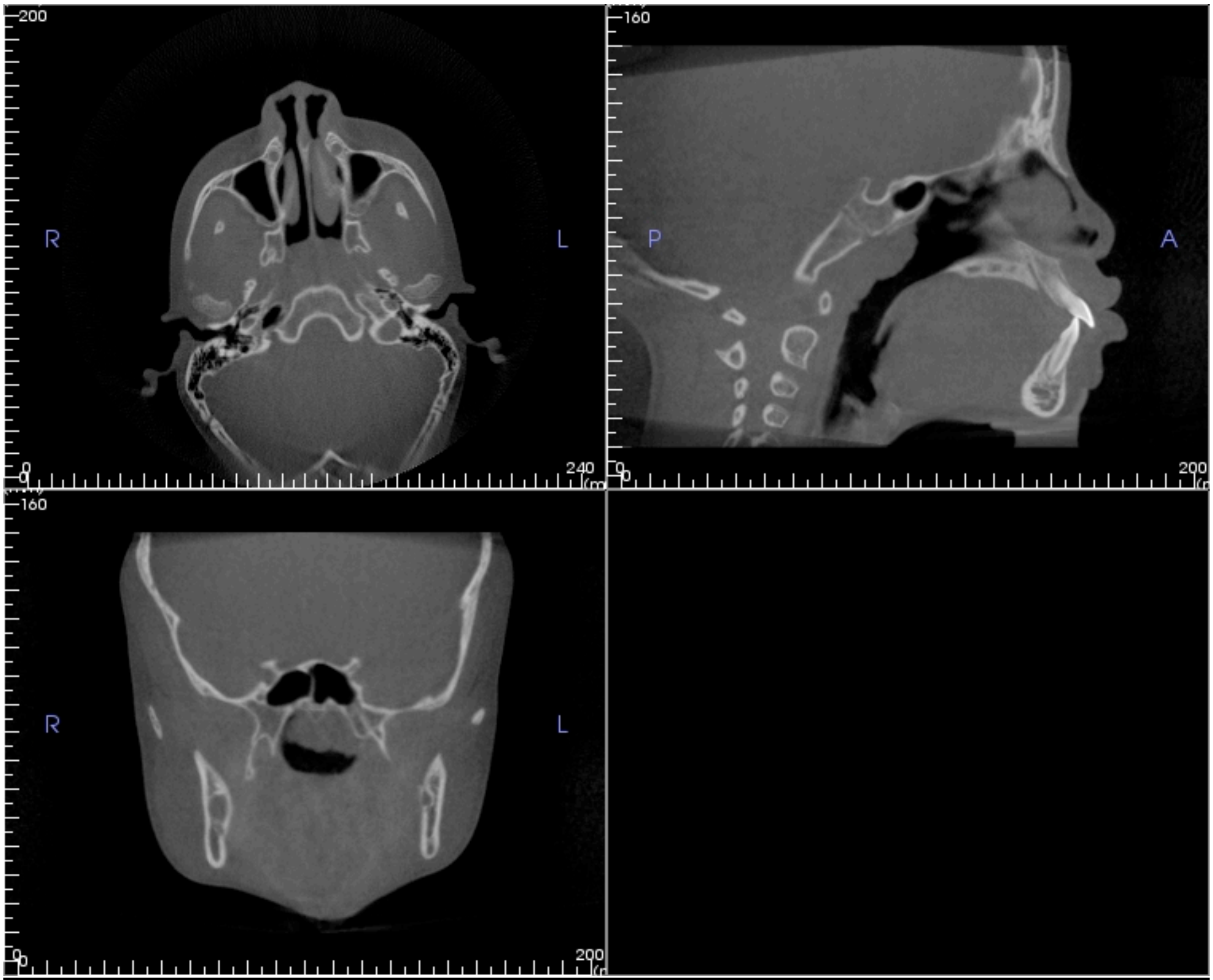

Figure 1. Axial, sagittal and coronal slices of the initial CBCT image prior to reorientation.

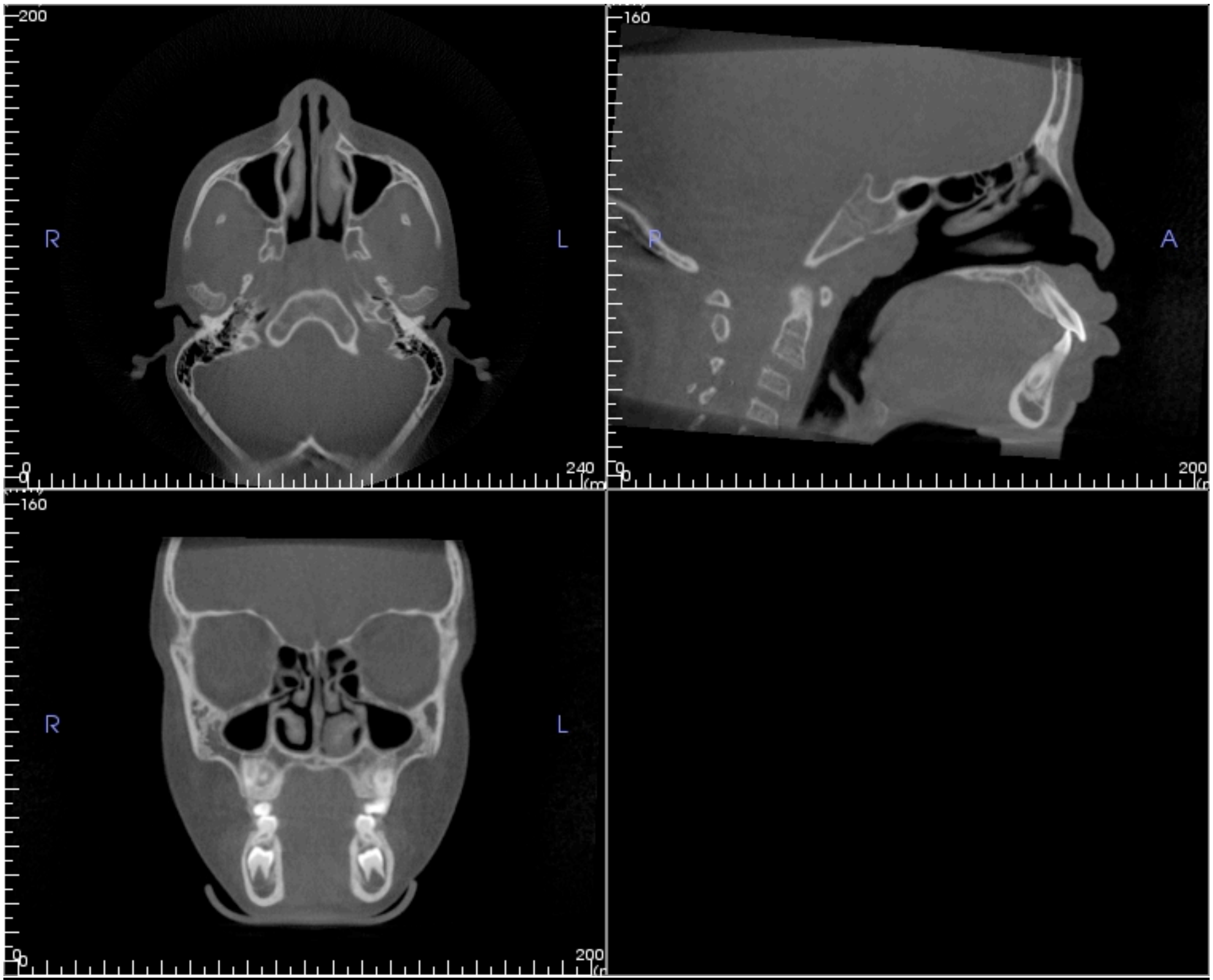

Figure 2. Reoriented CBCT image. The sagittal slice is oriented according to natural head orientation (NHO). The axial slice is oriented so the midpalatal suture is approximately perpendicular to the true horizontal. The coronal slice is oriented so a plane connecting the zygomaticofrontal sutures is approximately parallel to the true horizontal.

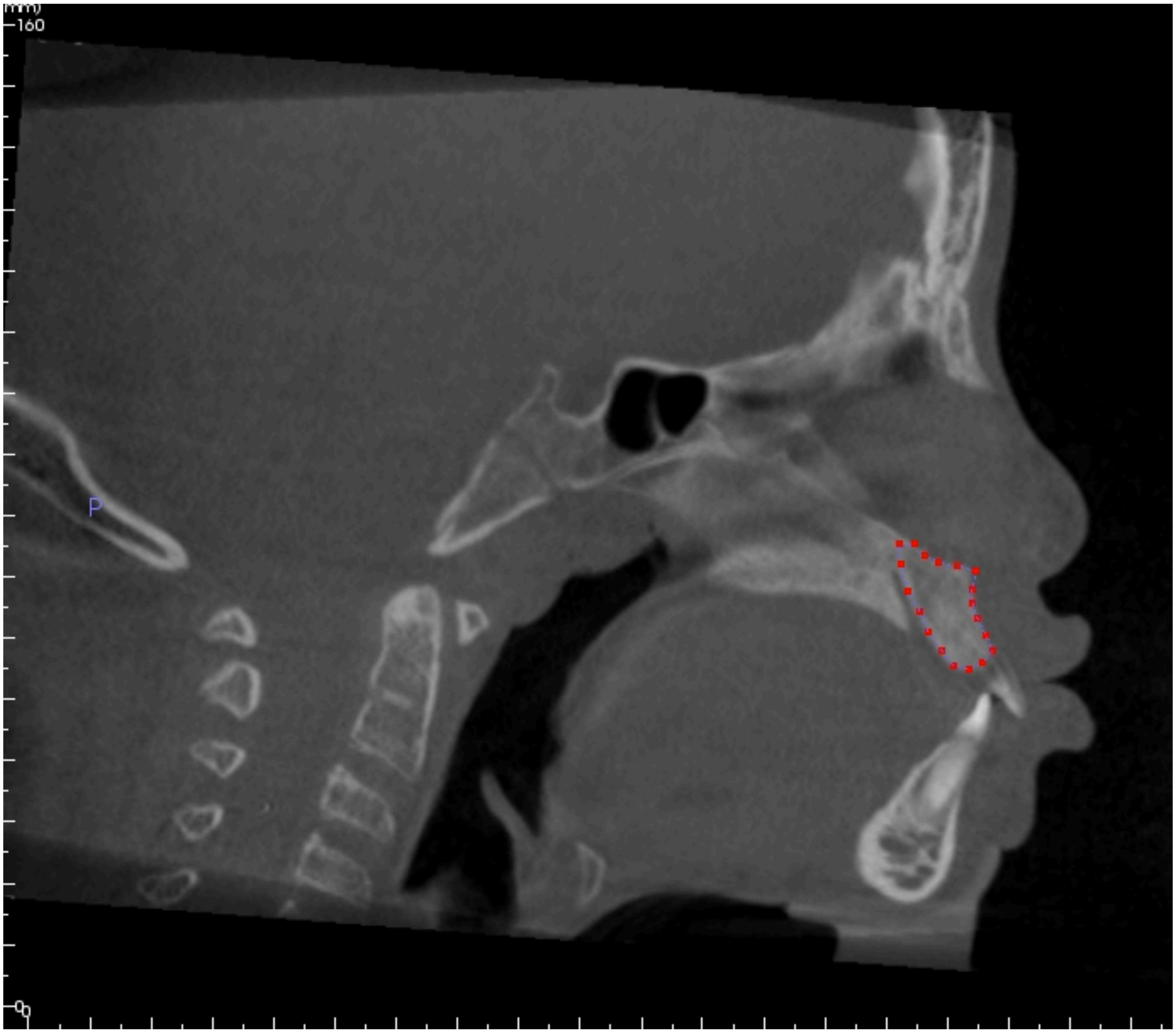

Figure 3. The midsagittal slice of the CT scan is located between the two maxillary central incisors. Anatomage software is used to outline the premaxilla, anterior to the premaxillary suture.

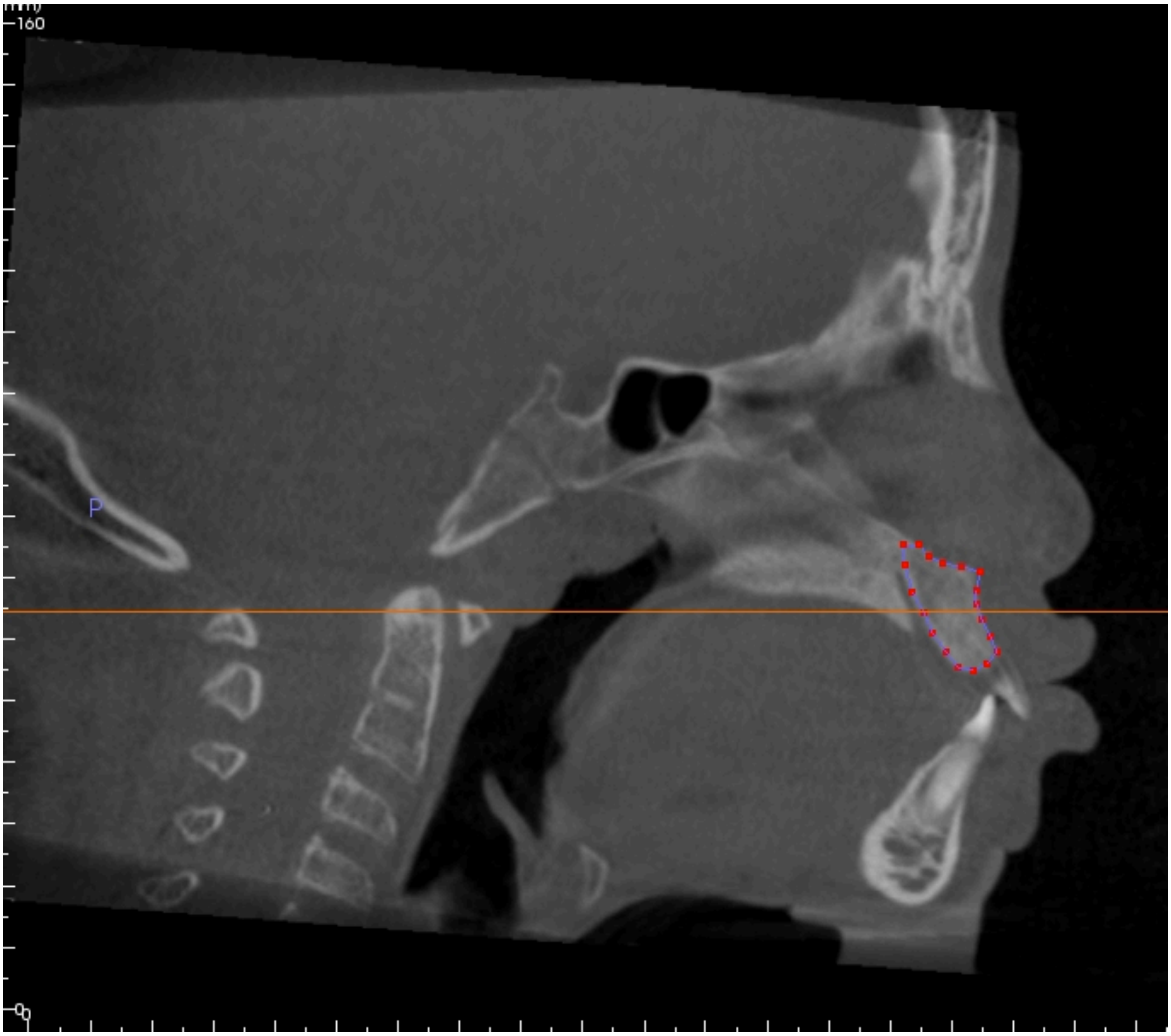

Figure 4. The orange line represents a true horizontal through the centroid of the outlined premaxilla. This horizontal will serve as the location for the axial slice.

Figure 5. Axial slice of the premaxilla through the centroid that was calculated on the midsagittal slice. The alveolar bone is outlined with the lateral borders tangent to the mesial surfaces of the maxillary canines.

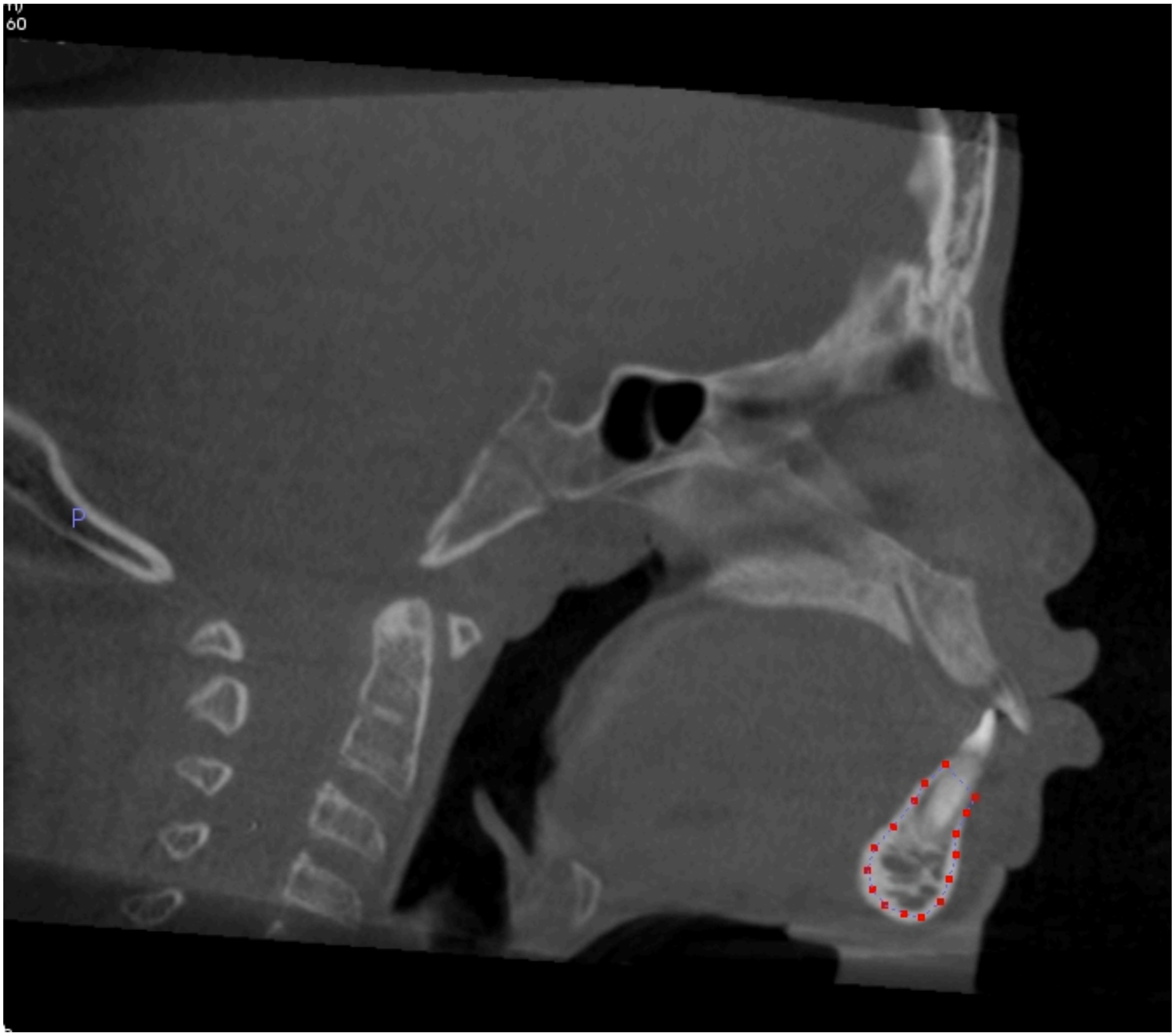

Figure 6. The midsagittal slice of the CT scan is located between the two maxillary central incisors. Anatomage software is used to outline the visible mandibular symphysis.

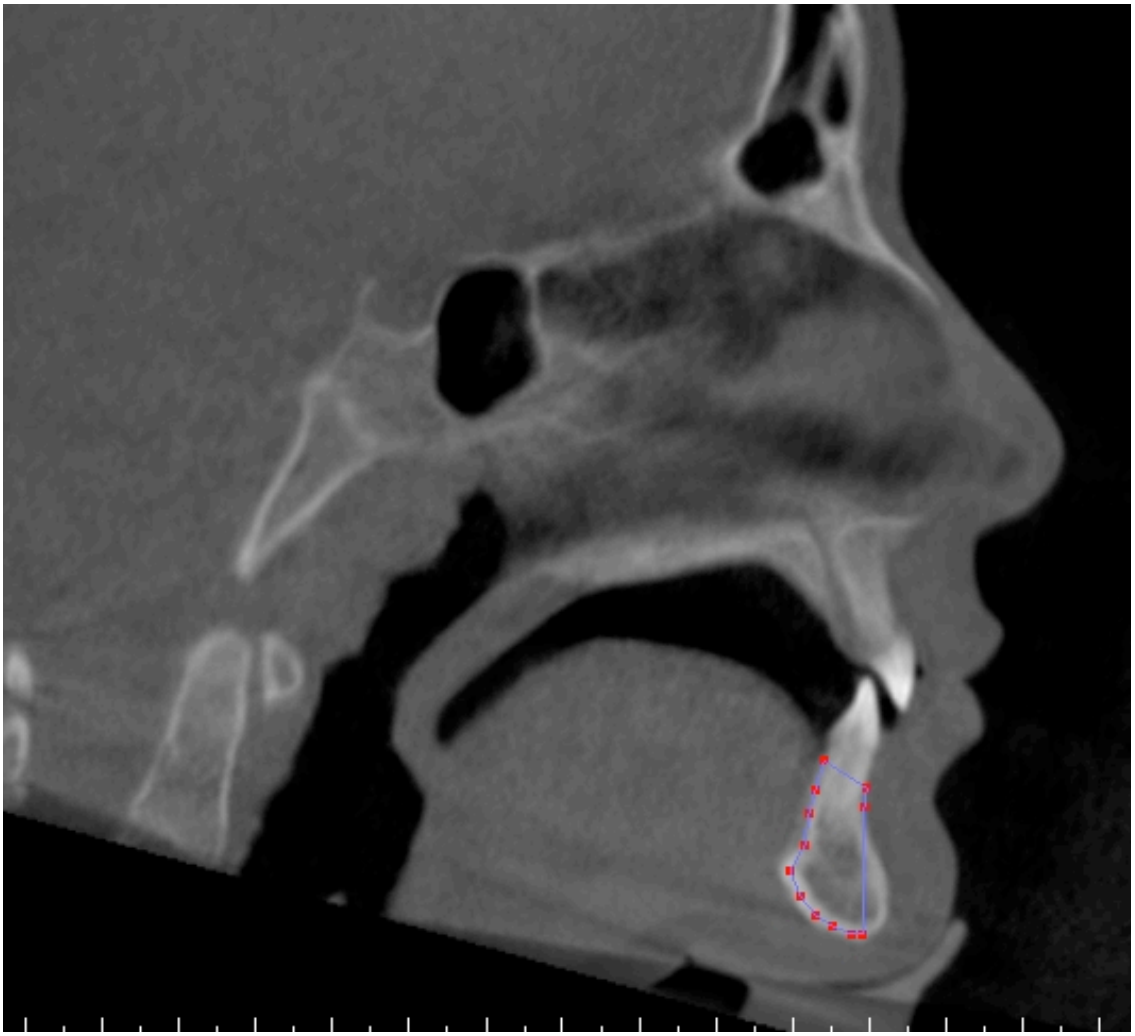

Figure 7. If the patient has a prominent pogonion, a true vertical from point B to the inferior border of the mandibular symphysis will be used as the anterior border for the mandibular centroid calculation.

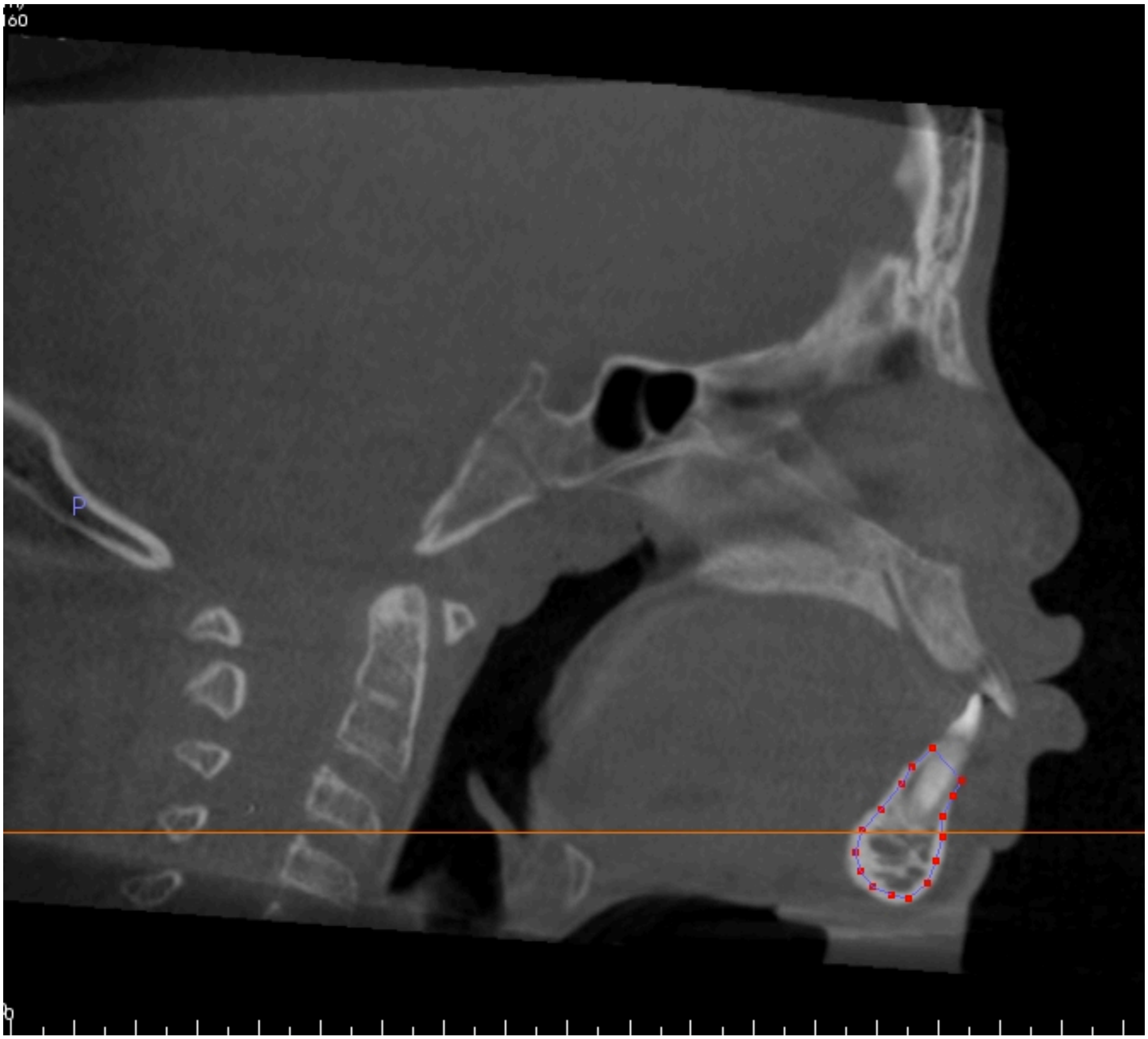

Figure 8. The orange line represents a true horizontal through the centroid of the outlined mandibular symphysis. This horizontal will serve as the location for the axial slice.

Figure 9. Axial slice of the mandibular symphysis through the centroid that was calculated on the midsagittal slice. The alveolar bone is outlined with the lateral borders tangent to the mesial surfaces of the maxillary canines.

Figure 10. The axillary and sagittal centroids are averaged to create the new landmarks and projected onto the midsagittal plane. True vertical lines are drawn through the points. The linear distance between the two lines is measured along the true horizontal and recorded in millimeters. If the mandibular centroid is anterior to the maxillary centroid, the millimeter value is negative.

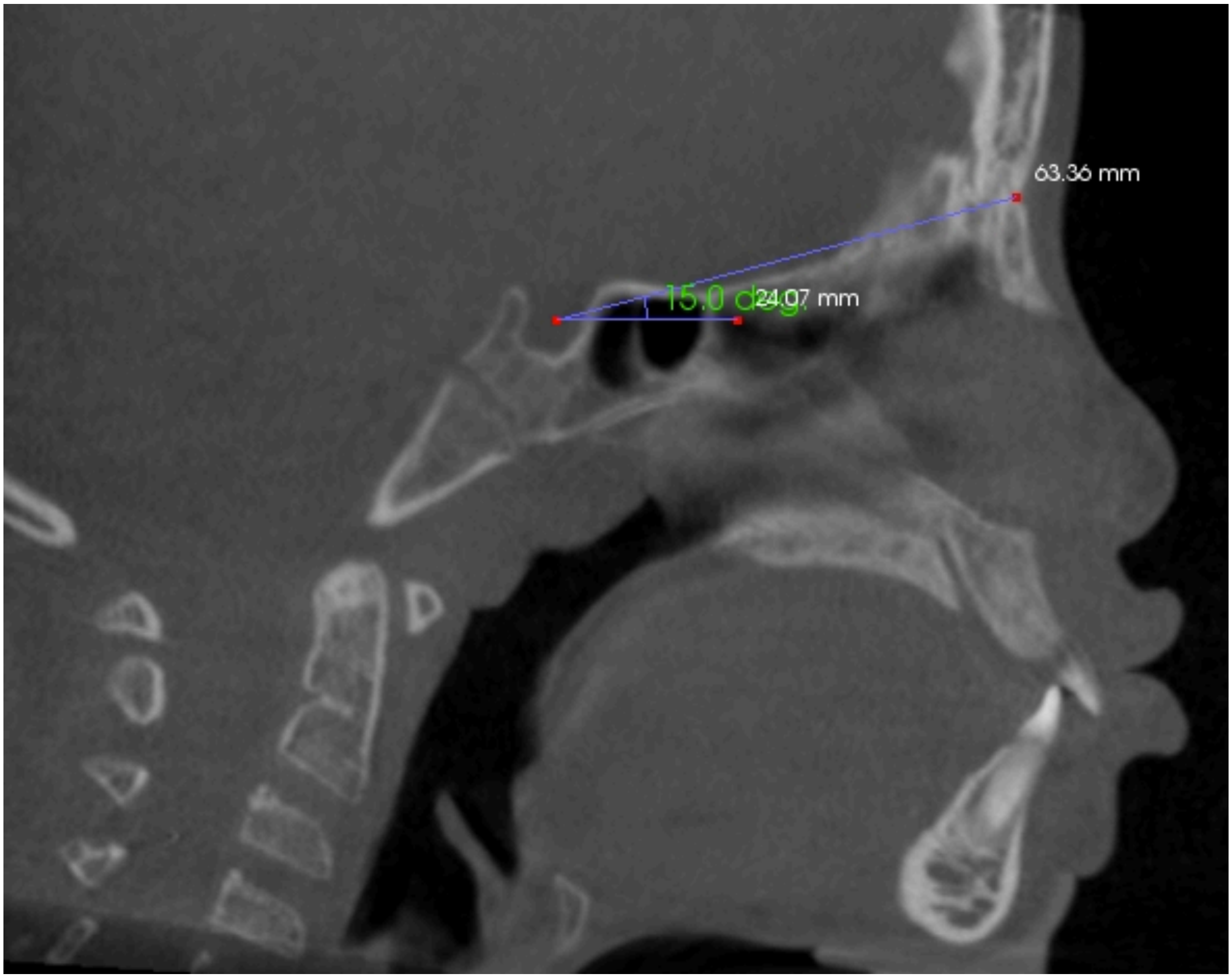

Figure 11. The angle between SN and true horizontal is measured and recorded. This angle will be used to determine inter and intra rater reliability for natural head orientation.

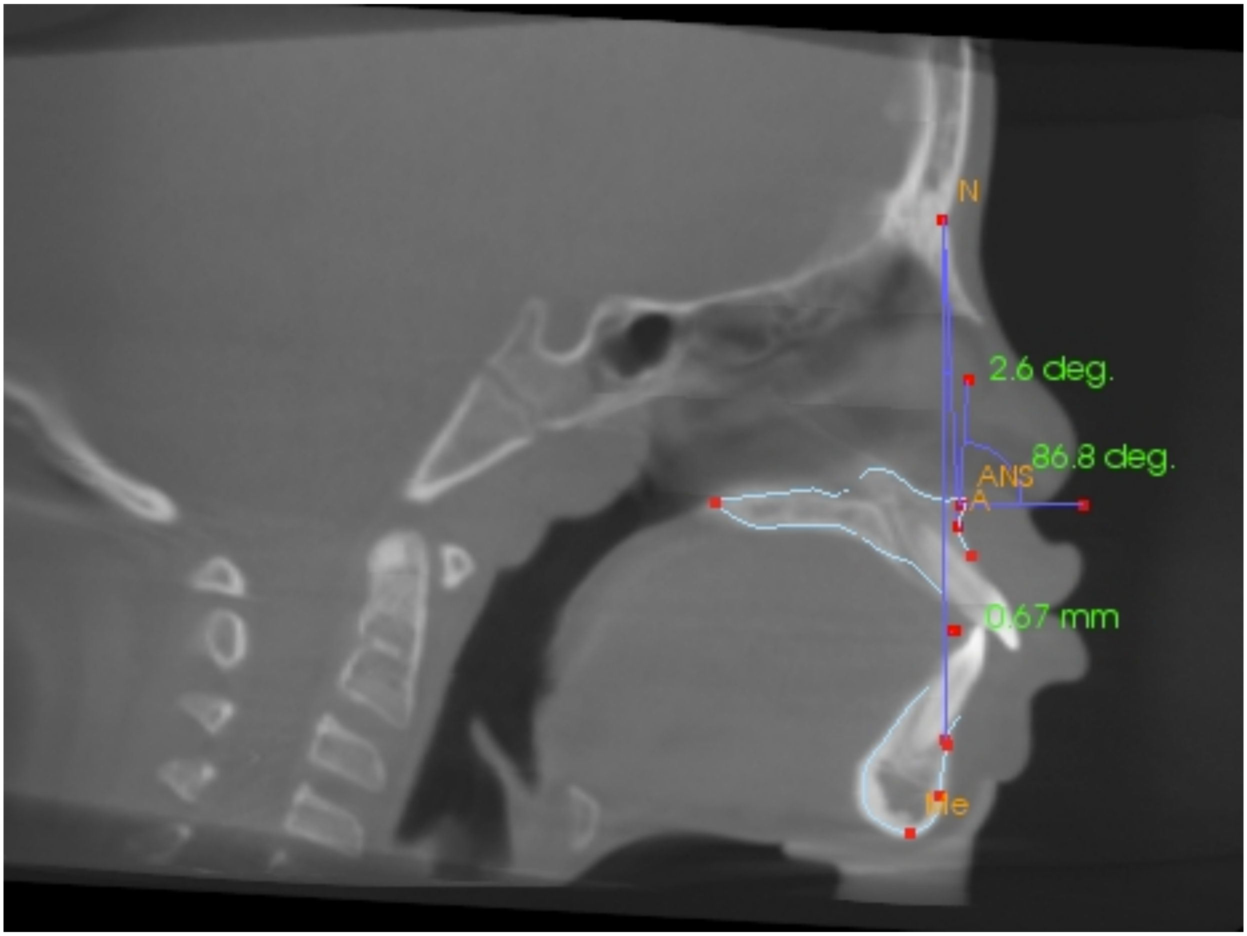

Figure 12. Anatomage software is used to perform two dimensional cephalometric analysis. The ANB angle, Wits appraisal and APDI are measured and recorded.

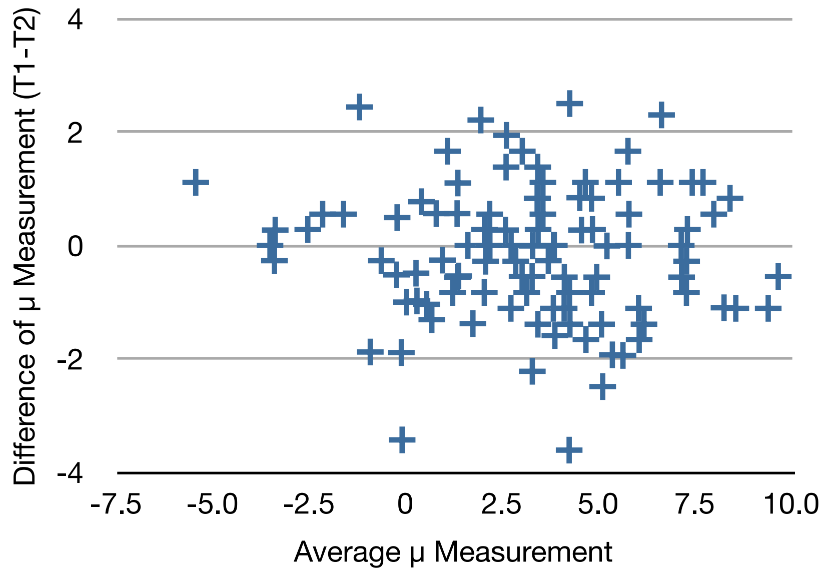

Figure 13. The average µ measurement (mm) was plotted against the difference (T_1-T_2) to demonstrate intra-rater reliability.

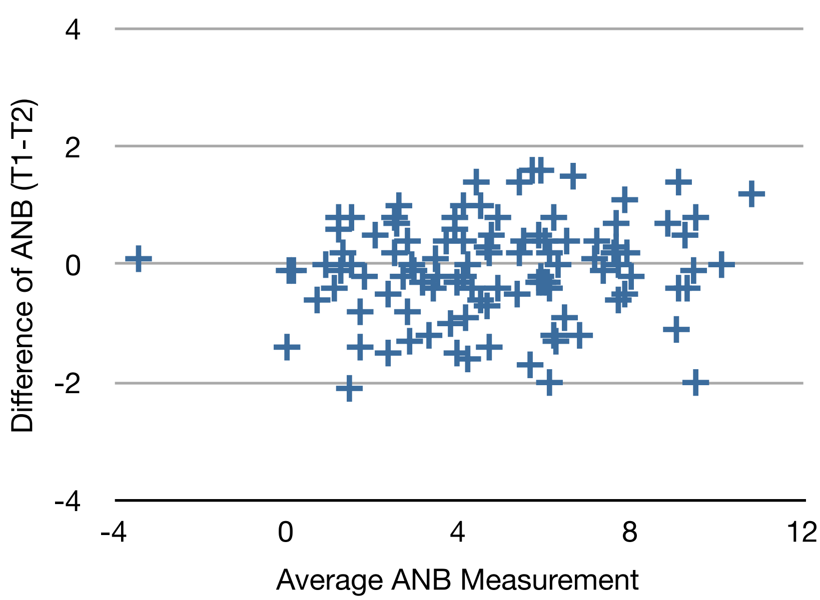

Figure 14. The average ANB angle was plotted against the difference (T_1-T_2) to demonstrate intra-rater reliability.

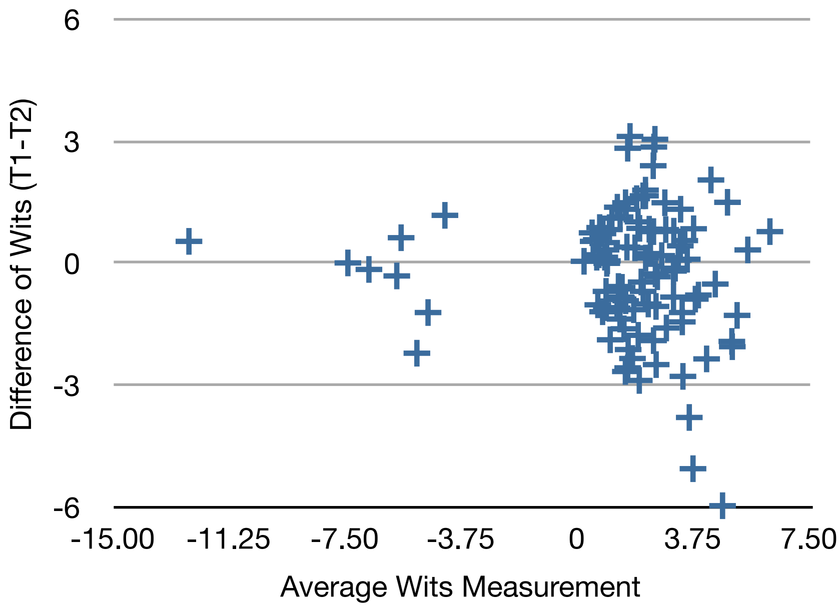

Figure 15. The average Wits measurement (mm) was plotted against the difference (T_1-T_2) to demonstrate intra-rater reliability.

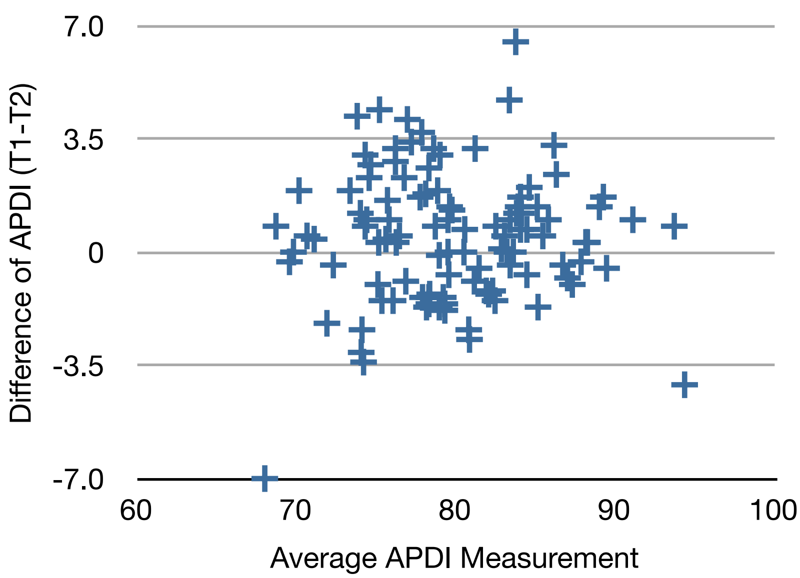

Figure 16. The average APDI angle was plotted against the difference (T_1-T_2) to demonstrate intra-rater reliability.

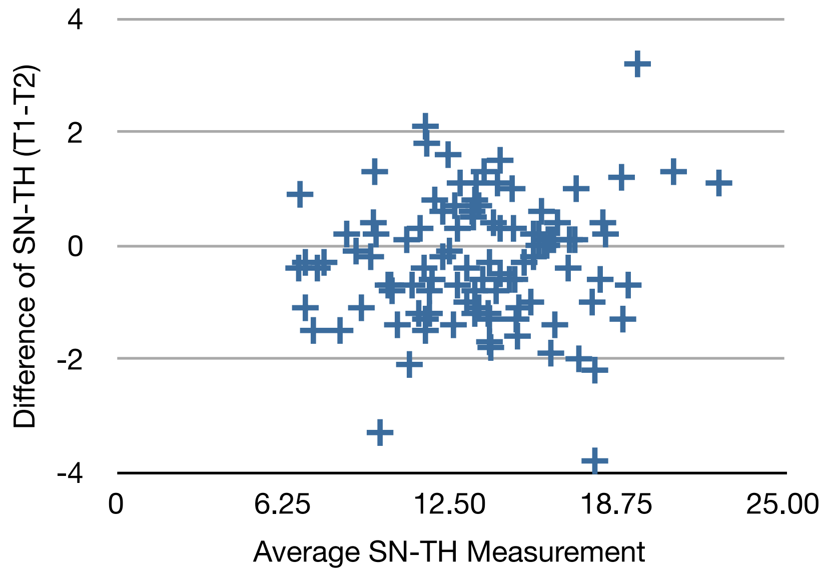

Figure 17. The average SN-T_H angle was plotted against the difference (T_1-T_2) to demonstrate intra-rater reliability.

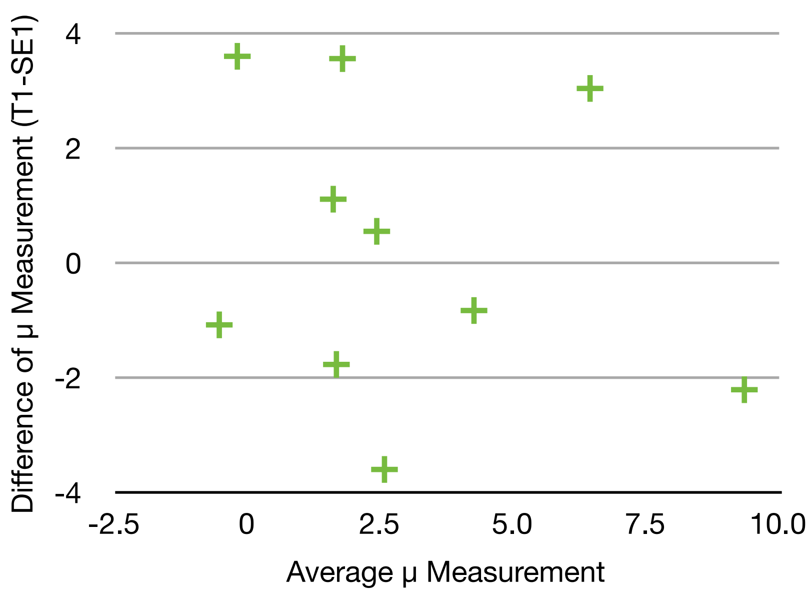

Figure 18. The average µ measurement (mm) was plotted against the difference (T_1-SS_1) to demonstrate inter-rater reliability.

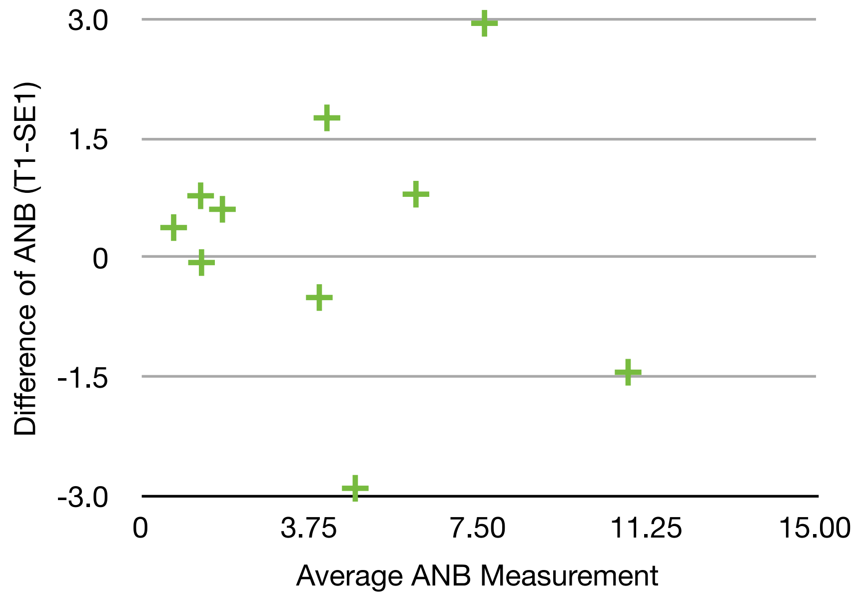

Figure 19. The average ANB angle was plotted against the difference (T_1-SS_1) to demonstrate intra-rater reliability.

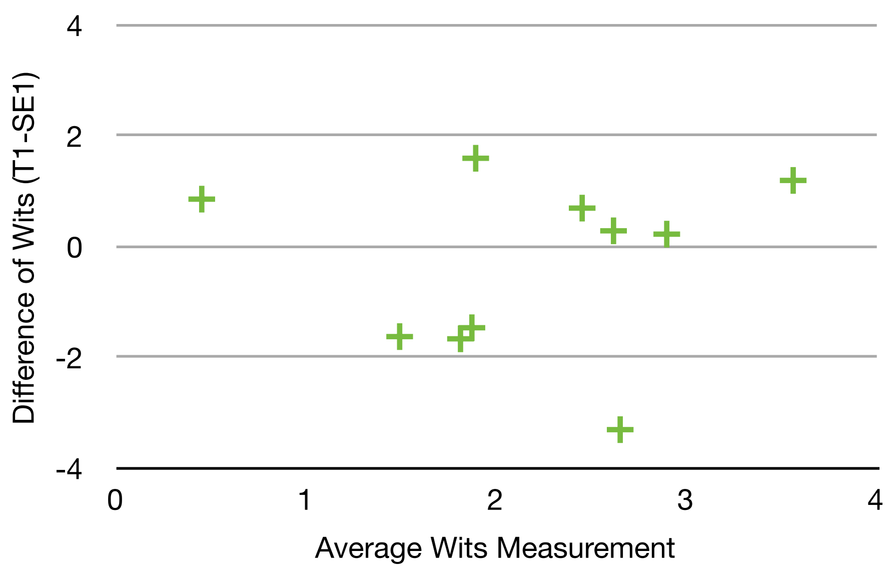

Figure 20. The average Wits measurement (mm) was plotted against the difference (T_1-SS_1) to demonstrate intra-rater reliability.

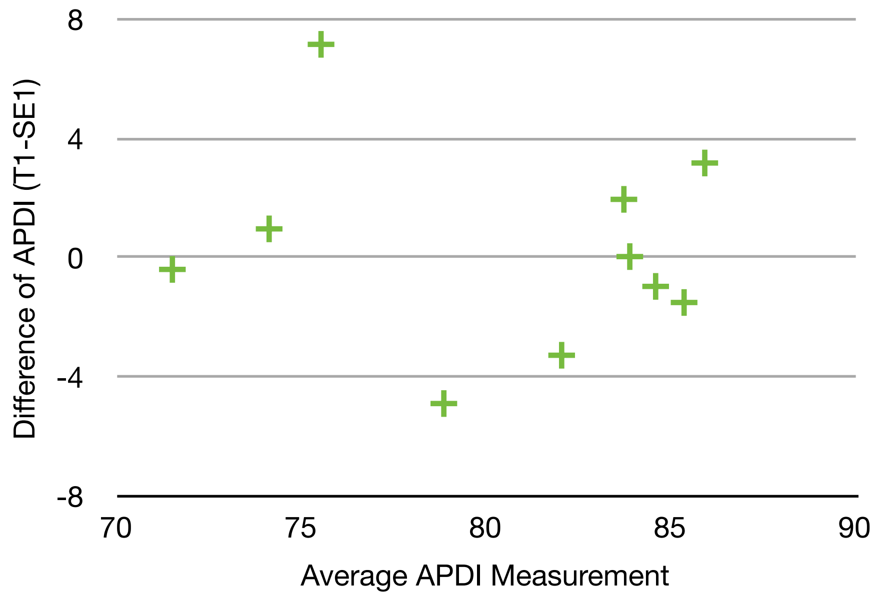

Figure 21. The average APDI angle was plotted against the difference (T_1-SS_1) to demonstrate intra-rater reliability.

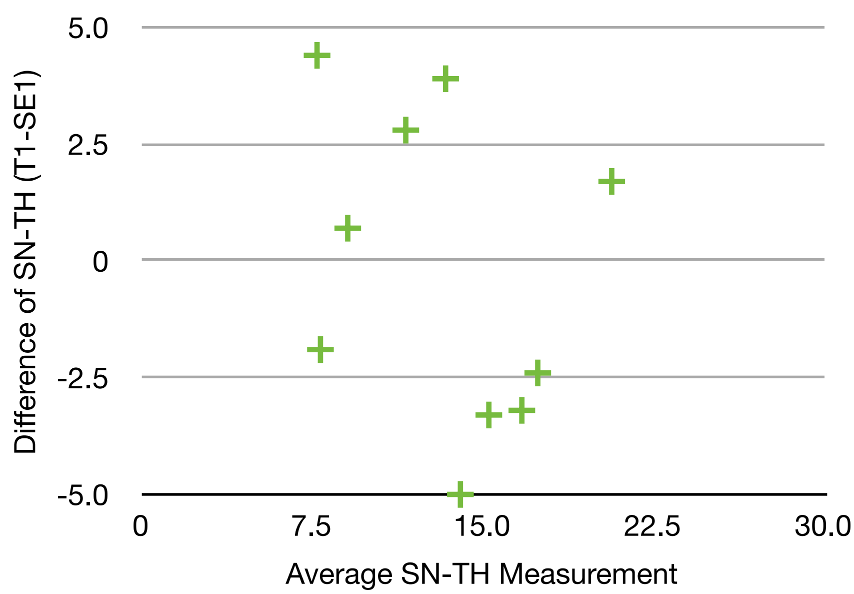

Figure 22. The average SN-T_H angle was plotted against the difference (T_1-SS_1) to demonstrate inter-rater reliability.

List of Tables

Table I. Mean linear and angular measurements for Class I, II and III patients.

Molar Relationship	n	μ Measurement		ANB		Wits		APDI	
		Mean	*SD*	*Mean*	*SD*	*Mean*	*SD*	*Mean*	*SD*
Class I	57	3.64	2.66	5.04	2.64	2.01	1.08	79.6	5.32
Class II	26	4.48	1.85	5.84	1.71	2.71	1.36	76.7	3.22
Class III	22	0.51	3.27	2.93	2.92	-0.79	4.91	84.0	5.48

Table II. The p-value for the one-way ANOVA statistical analysis was less than 0.001 for each measurement. Tukey HSD tests were performed for each measurement to determine statistical significance between the three molar groups.

μ Measurement	ANB	Wits	APDI
I/II	I/II	I/II	I/II*
I/III††	I/III†	I/III††	I/III††
II/III††	II/III††	II/III††	II/III††

$^{*}p < 0.05$; $^{†}p < 0.01$; $^{††}p < 0.001$

Table III. Volume under curve (VUC) calculations and 95% confidence intervals based on 1000 bootstrap samples.

μ Measurement		ANB		Wits		APDI	
VUC	95% CI	*VUC*	95% CI	*VUC*	95% CI	*VUC*	95% CI
0.421	(0.301, 0.551)	0.385	(0.276, 0.503)	0.368	(0.242, 0.520)	0.385	(0.266, 0.507)

Table IV. The mean and standard deviation of $|T_1\text{-}T_2|$ were used to calculate intra-rater reliability for the μ measurement, ANB, Wits, APDI and SN-T_H.

		μ Measurement	**ANB**	**Wits**	**APDI**	**SN-T_H**
$\lvert T_1\text{-}T_2\rvert$	Mean	0.92	0.65	1.21	1.60	0.89
	SD	0.74	0.52	1.03	1.32	0.70

Table V. The mean and standard deviation of $|T_1$-SS (second examiner)$_1|$ were used to calculate inter-rater reliability for the μ measurement, ANB, Wits, APDI and SN-T_H.

		μ Measurement	**ANB**	**Wits**	**APDI**	**SN-T_H**
$\lvert T_1\text{-}SE_1\rvert$	Mean	2.14	1.22	1.13	2.43	2.93
	SD	1.23	1.03	0.96	2.23	1.31

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