Development of a Three Dimensional Analysis of Buccolingual Inclinations in Maxillary Transverse Deficiencies

by

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Abstract

Introduction: The purpose of this thesis was to develop a new 3D transverse analysis that utilizes a 3D Cartesian coordinate system to assess buccolingual inclinations of first molars and canines using a previously described 3D maxillary reference plane. Landmarks used to create this analysis were assed for reliability and compared to the reliability of the previously described CWRU transverse analysis. Resulting buccolingual inclinations from this new analysis and CWRU transverse analysis were compared.

Methods: CBCTs of 10 skulls were used to test reliability of the landmarks chosen to develop a novel analysis and reliability of the angular measurements produced by the CWRU transverse analysis. CBCTs of 60 patients were then used to compare resulting angular measurements, molar and canine buccolingual inclinations, between the two methods.

Results: All 20 Avizo landmarks for the novel 3D analysis were reliable. The 8 angular CWRU measurements demonstrated good intra-examiner reliability but reduced inter-examiner reliability. There was a statistically significant difference for all measured teeth when techniques were compared but only maxillary canines showed a clinical difference between both methods.

Conclusion: The developed Alberta DS transverse analysis was demonstrated to be very reliable and produced results clinically similar to the CWRU transverse analysis except for maxillary canines. This novel analysis can provide a new, reliable tool to aid in diagnosing maxillary transverse deficiencies by identifying dental compensations.

Preface

This thesis is an original work by Dena Sawchuk. Ethics approval was received for this research project from the University of Alberta Ethics Board, Project name "Comparison of two methods of establishing a reference plane for three dimension superimposition to diagnose and evaluate maxillary transverse deficiencies", No. Pro00057195, May 13 2015. All data analysis as well as the literature review are the original work of Dena Sawchuk.

Chapter 1, systematic review of this thesis has been published as Sawchuk D, Currie K, Lagravere-Vich M, Palomo JM, Flores-Mir C. Diagnostic methods of assessing maxillary skeletal and dental transverse deficiencies: A systematic review. Korean J Orthod. 2016 Sep 19.

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Chapter 1: Introduction and systematic review

Statement of Problem

Maxillary transverse deficiencies are a key component of many malocclusions and addressing this deficiency aims at reducing periodontal problems, improving dental and skeletal stability, and esthetics[1]. It is vital to be able to assess the craniofacial skeleton in the transverse dimension, identify dental compensations and accurately diagnose the need for expansion, either only dentally or also skeletally, to improve treatment efficiency and effectiveness. Diagnosis of maxillary transverse deficiencies can be difficult often involving more then one of the following methods: clinical evaluation, analysis of dental casts, occlusograms and dental radiography[2]. None of these employed diagnostic methods have been established as a universal reference standard for diagnosing transverse deficiencies. With three-dimensional imaging emerging in the dental field as a diagnostic modality, it would be beneficial to determine if 3D analyses have the potential to improve the diagnosis of maxillary transverse deficiencies specifically by identifying the presence of dental compensations over true skeletal deficiencies. Currently, no 3D transverse analysis has been reported that fully utilizes the 3D data in CBCT images, rather several exist that make 2D linear and angular dental and skeletal measurements on coronal slices to quantify dental buccolingual inclinations. Also, a stable reference plane for 3D buccolingual inclination measurements has not yet been identified.

It remains necessary to develop a 3D transverse analysis with a stable 3D reference plane that fully utilizes 3D data to assess buccolingual inclination of upper and lower teeth and assess the intra-rater and inter-rater reliability of identified skeletal and dental landmarks. Secondly, these 3D buccolingual inclinations can be compared to an existing CBCT transverse analysis, specifically the CWRU transverse analysis that uses a different measurement reference plane. The next step after development of a novel 3D analysis will be to assess for accuracy and clinical validity.

Research Objectives

Three research objectives were identified:

Objective #1:

a.) To identify and assess the repeatability and reproducibility of dental and skeletal landmarks on three-dimensional images that will be used to establish 3D reference and measurement planes in developing a novel transverse analysis.

b.) Reliability of the dental and skeletal landmarks used for the novel analysis will be compared to the reliability of angular measurements obtained using the existing CWRU transverse analysis.

Objective #2: To develop a novel 3D transverse analysis that identifies the buccolingual inclinations of maxillary and mandibular first molars and canines using a previously described 3D maxillary reference plane for angular measurements.

Objective #3: To compare the newly developed Alberta DS transverse analysis angular measurements to the previously described CWRU transverse analysis for maxillary and mandibular canine and molar buccolingual inclinations.

References

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Diagnostic methods for assessing maxillary skeletal and dental transverse deficiencies:

A Systematic Review

Sawchuk, D., Currie, K., Lagravere-Vich, M., Palomo, JM. & Flores-Mir, C. (2016). Diagnostic methods for assessing maxillar skeletal and dental transverse deficiencies: A systematic review. The Korean Journal of Orthodontics, 46(5), 331-342.

Introduction

Assessment of facial growth as well as development of the dental occlusion is part of the process of diagnosing orthodontic abnormalities that if prevented or treated would provide measurable benefit to patients [1]. Orthodontists have acknowledged that maxillary transverse deficiencies are a significant component of many malocclusions [2].

Treatment of transverse deficiencies is aimed at reducing potential periodontal problems, improving dental and skeletal stability as well as improving smile esthetics [2]. Lateral expansion of the boney halves of the maxilla at the mid-palatal suture was reported as early as the mid 19th century as a method to overcome transverse maxillary deficiencies [3]. Current treatment methods to address skeletal maxillary constriction include application of orthopedic forces with slow or rapid maxillary expansion protocols in children and adolescents and surgical mid-palatal splitting in adult patients [4-6]. After the completion of the adolescent growth spurt, as the mid-palatal suture progressively becomes more fused, heavier forces across the suture are required to produce meaningful maxillary skeletal expansion [6]. Therefore it becomes vital to be able to assess as early as possible the craniofacial skeleton in the transverse dimension and accurately diagnose the need for transverse maxillary expansion to improve its treatment efficiency and effectiveness. This drives the continued evolution and development of diagnostic tools that evaluate the maxillary transverse dimension.

Diagnosis of maxillary transverse deficiencies can be difficult and often includes the use of more than one of the following methods: clinical evaluation, dental casts analysis, occlusograms and/or craniofacial radiography [7]. Postero-anterior cephalograms (PAC) have previously been considered the most readily available and reliable way to evaluate transverse skeletal discrepancies [8]. Nevertheless, it is known that conventional 2D imaging of skeletal structures has technical limitations that affect the accuracy of landmark placement and along with practitioner inexperience in identifying PAC landmarks has resulted in a significant amount of landmark identification errors [9-11].

To further complicate the scenario an universal gold standard has not been identified in the literature for diagnosing maxillary transverse deficiencies; however, it has been suggested that a clinically accurate enough diagnosis involves both clinical and radiographic evaluation, with PAC considered the current standard for evaluating transverse skeletal dimensions [8]. Most commonly, clinicians use a method that relies on a combination of clinical and dental cast assessment that evaluates presence of crossbites, degree of crowding, arch width measurements, perceived buccolingual inclination of teeth and the shape and height of the palatal vault [6,8].

With three-dimensional imaging emerging in the orthodontic field as a feasible diagnostic modality for clinical use, the development of improved diagnostic utilization of CBCT images to diagnose maxillary transverse deficiencies could be useful. As 3D images are not affected by the technical limitations associated with 2D PAC the use of this technology has demonstrated so far significantly less variability and more reproducibility of transverse measurements on CBCT-constructed PAC images compared to conventional 2D PA cephalograms [12,13]. The ability to make localized and specific transversal radiographic cuts of CBCT images to assess areas of clinical interest is also of significant potential in diagnosis of the craniofacial transverse dimension.

As the availability of CBCT imaging in clinical practice increases, it would be beneficial to determine if CBCT imaging improves the diagnosis of transverse maxillary deficiencies or it just improves landmark location precision. Clinically meaningful accuracy and reliability should be secured before a more widespread use of CBCT and its associated ionizing radiation is suggested. The objective of this review is therefore to evaluate the accuracy and reliability of the available diagnostic tools used to assess maxillary transverse deficiencies.

Methods

Reporting of this review was based on The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) as a template [14].

Protocol and registration

Protocol registration was not available.

Eligibility criteria

The clinical question was generated using the PICOS format:

Population: Orthodontic patients with mixed or permanent dentitions with all permanent first molars present.

Intervention: 3D diagnostic analysis.

Comparison: Combination of clinical, plaster models, and/or PAC as a proxy for a gold standard as there is no known and universally accepted gold standard.

Outcomes: Accuracy and reliability of the 3D diagnostic analysis.

Study Design: Diagnostic, observational or interventional studies. From the latter only data pertinent to the SR question would be collected.

Inclusion criteria included studies that reported accuracy, validity and/or reliability of a diagnostic method or evaluation technique for maxillary transverse dimensions in humans with mixed or permanent dentitions and all first permanent molars present. Exclusion criteria includes primary dentition, studies that only evaluate vertical and/or anteroposterior maxillary deficiencies, syndromic patients and cleft lip and/or palate patients.

<u>Information sources</u>

A systematic search of three electronic databases was completed to identify relevant studies with the aid of a health sciences librarian using MEDLINE (OvidSP), PubMed and EMBASE (OvidSP) from the date of establishment of the databases to the second week of April 2015.

<u>Search Strategy</u>

The search was conducted irrespective of language using key words, combinations of key words with truncations and Medical Subject Headings (MeSH). The search strategy was designed for MEDLINE as shown in Appendix 1.1 and was adapted to facilitate searching in the other databases. Reference lists of retrieved articles were hand searched to identify additional relevant articles. Limited search of grey-literature was completed using Google search (analyzing first 100 hits) and relevant textbooks by searching key words.

Study Selection

In the initial stage of article selection, titles and abstracts were reviewed by two reviewers (DS and KC) from each electronic database's results to remove all articles that appear to be unrelated to the topic or that fit the exclusion criteria. At this stage, any articles that evaluated maxillary transverse dimensions were included. Results between reviewers were compared to identify discrepancies. If they existed they were resolved by a third party (ML). For any abstract that did not contain sufficient information or was unavailable, the full article text was also obtained for review. For those abstracts that were deemed potentially useful full text articles were then reviewed in the final selection stage. Inclusion and exclusion criteria were applied again in duplicate (DS and KC) as some of the information provided by the abstracts may have been misleading. References lists of full text articles that were included in the review were also hand searched to identify any additional articles.

Data collection process

Two independent reviewers (DS and KC) assessed and obtained data from each of the selected articles. Data collected was compared and a third party (ML) resolved identified discrepancies.

Data items

Data that was obtained from the final selected studies included sample size, mean age, type of diagnostic tool including machine used, degree of maxillary transverse dimensional deficiency, diagnostic accuracy, accuracy and reliability of each tool, analysis or assessment method used. (Table 1.1)

Table 1.1: Summary of study characteristics of included articles

Authors/Year	**Sample size & sex**	**Mean Ages**	**Description of maxillary dimensions or degree of malocclusion**	**Diagnostic tool/analysis used (including machine)**	**Results**	**Accuracy/validity or reliability of diagnostic tool/method**
Cheung et al (2013) [15]	- 28 undocumented human skulls - not identified by sex	- skulls not identified by age - all have permanent dentitions	- lack of gross asymmetry - reproducible and stable occlusions	- Measurement of bilateral jugale and antegonion landmarks for transverse intermaxillary analysis - Comparison made between direct craniometric skull (BS) measurements, CBCT direct volumetric measurements (Sirona Galileos Cone Beam Imaging System) and PA Cephalometric images	- with 95% confidence interval, no statistically significant difference between measurement types - CBCT values compared to skulls had smallest mean difference and highest ICC (0.964) without overestimation - PA Cephs had larger mean differences and tended to overestimate results - Ratio of J-J/Ag-Ag correlation coefficients were 0.87 for CBCT-BS, 0.81 for PAC-BS, 0.80 for PA-CBCT	- all three methods shown to be reliable with mean error less than 0.5mm between repeated measurements - J-J/Ag-Ag ratio used as indicator of transverse discrepancy to assess diagnostic validity of CBCT & PA - Compared to BS ratios, PAC measurements incorrectly valued 5 skulls (18%), CBCT incorrectly valued 2 skulls (8.3%) - CBCT more accurately identified intermaxillary discrepancies

Dalidjan et al (1995) [16]	- 40M, 40F Australian Aborigines - 30M, 30F Indonesians - 30M, 30F white Australians Total = 200	- 14.2M, 14.7F - 23.9M, 22.0F -17.9M, 18.0F	- normal occlusions and minimal dental irregularity selected for - Angle Class I molar, overbite <4mm, overjet <3mm, full permanent dentition from second molar to second molar, no missing teeth, no supernumeraries, no crossbite, minimal rotations, no orthodontic treatment, minimal attrition - Subjects selected that do not have transverse discrepancies	- Pont's index using digital caliper measurements of dental cast mesiodistal crown widths of maxillary permanent incisors and arch widths to an accuracy of 0.1mm Pont's Formulas: P width = SI x 100/80 M width = SI x 100/64 P = premolar transverse distance M – molar transverse distance SI = sum of mesiodistal widths of four maxillary incisors	Correlation coefficients between observed arch widths and those predicts by Pont's index ranged from 0.12-0.56, the highest for male Indonesians - Only 1%-32% of variation in observed arch widths could be explained by variation in predicted arch widths - Australian Aboriginals: 20.6% of arch widths were within +/- 1mm of Pont's prediction - White subjects: 30.8% of arch widths within +/- 1mm of Pont's prediction - Indonesians: 17.5% of arch widths within +/- 1mm of Pont's Prediction	- Pont's prediction generally underestimated actual arch widths in various populations, only 17.5%-30.8% of arch widths were within +/- 1mm of Pont's prediction, this demonstrates Pont's index did not accurately predict dental arch widths and is unreliable for use in diagnosis & treatment planning .
Lee et al (2014) [17]	- 20M, 20F - Total 40	- 27.2M - 26.4F	- Normal occlusions with Angle's Class I canine and molars - Excluded skeletal dysplasia, asymmetric arches, moderate-severe crowding, missing teeth, previous prosthodontic or orthodontic treatment	- Mx and Md basal bone width differences compared between CBCT images and PA cephalograms with measurements at 3 sites (1st premolar, 2nd premolar and 1st molar) at 5 different bone levels - CBCT (CB MercuRay): Axial and coronal slices standardized prior to measurements - PA cephalograms (OrthoCeph OC100): - The differences between maxillary and mandibular bone widths were calculated and compared between CBCT and PA Ceph	- Maxillomandibular width of molar area at three levels on CBCT showed statistically significant correlation with PA cephalograms (0.4-0.49 correlation coefficient $P < 0.05$) - Maxillomandibular widths at 1st and 2nd premolars did not show any significant correlation between CBCT and PA cephalograms (0.03-0.34 $P < 0.05$)	- intraexaminer error $P<0.5$ and ICC mean of 0.88 indicated good reliability of measurements - study suggests assessment of skeletal transverse discrepancies using PA cephalograms with jugale and antegonial points has limitations and may be less accurate than CBCT images

Miner et al (2012) [18]	- 241 total, no sex differentiation	- 13 for M & F	- mixed and permanent dentitions with first permanent molars. Angle class I molars and canines - crowding, overbite and overjet <4mm - 21 unilateral posterior crossbite - 33 bilateral posterior crossbite - 79 control, normal transverse dimension - 61 superior convergent - 47 inferior convergent	- CBCT scans from i-CAT scanner - images oriented using specified reference planes for 2D consistency - CBCT transverse analysis was developed in the coronal plane using 2 linear measurements (maxillary and mandibular skeletal arch width) & 4 angular dental measurements (maxillary and mandibular molar angulations) - Mean values derived from the non-crossbite group	- linear skeletal measurements significantly different between control and bilateral crossbite groups, molar angulations not significantly different - bilateral and unilateral crossbite groups have significantly narrower maxillary widths than controls, but wider mandibles - Unilateral crossbite group have more upright teeth on non-crossbite side - non-crossbite groups with dental compensations (superior convergent, inferior convergent) had significantly different skeletal and dental measurements from controls	- high intraexaminer and interexaminer reliability (mean 0.95)
Nimkarn et al (1995) [19]	20M, 20F - Total 40	- not specified	- all permanent teeth present first molar-first molar - degree of malocclusion not specified	- measurements taken with digital calipers from study models to use with Pont's Index, Schwarz's Analysis and McNamara rule of thumb - A more objective crowding index was proposed and validity was evaluated	- Crowding index correlated highly with objective measures of crowding (correlation of 0.88-0.96) - Pont's index overestimated intermolar with and interpremolar width by 2.5mm to 4.7mm - Schwarz's analysis overestimated interpremolar width by 2.5mm-4.3mm - McNamara's rule of thumb overestimated intermolar widths by 2.7mm-3.7m	- Crowding index is a valid and more reproducible measure of dental crowding/need for expansion than objective assessments - The indices advocate an overexpanded arch, therefore treatment plans should not be based on such simplistic mathematical concepts that are not clinically valid

Podesser et al (2004) [20]	- 3M, 7F - Total 10	- 26 years	- subjects chosen irrespective of occlusion and facial morphology	- CT scans obtained with high-resolution bone algorithm (Tomoscan 7000R) with standardized frontal plane orientation - Quantitative evaluation of linear and angular parameters based on two slices, molar slice and canine slices, digitized points used for Cephalometric analysis - method evaluated nose, maxillary bones and dental arches including molar & canine inclinations	- Correlation between first and second digitized readings very high r = 0.96-0.99, no significant difference - Intra-observer error had no statistically significant differences r = 0.89-0.99 - inter-observer error with the exception of one measurement had no significant statistical differences but had more variation than intra-observer error, r = 0.43-0.98 - Variation between observers was small compared with biologic variation subject to subject	- Study suggested measurements were reproducible and reliable when performed by the same person
Rastegar-Lari et al (2012) [21]	- 69M, 74F - Total 143	- 13.3M, 13.2F	- Ideal class I occlusion, class I posterior intercuspation, no transverse discrepancy, no lateral shift, no midline deviation, overjet less than 3.5mm	- dental model measurements made with digital caliper for archwidth predictions according to the indexes of Pont, Schwarz, Gratzinger,& Howe - Lateral and PA cephalograms taken and reference points identified including interzygomatic width, interjugular width, Maxillomandibular discrepancy (intergonion width minus interjugular width) - Multivariate regression including vertical & transverse Cephalometric parameters along with dental measurements to predict arch width	- Correlation of Pont's index with measured distances R = 0.37-0.42, were generally larger than measured distances, only 27-37% of predictions were within 1.0mm of actual distances - Correlation of Schwarz and Gratzinger index with measured distances R=0.35-0.44, only 26.5-42.1% of predictions were within 1.0mm of actual measurements - Howe's stated averages of maxillary widths were within 1.0mm of only 28% of subjects actual measurements - Linear regression showed R^2 0.32-0.44	- Pont's index , Schwarz and Gratzinger index and rule of thumb of Howe provided poor estimates of maxillary arch width and were inaccurate at width predictions - Most accurate prediction was combination of summed width of maxillary incisors and maxillary/interjugular width with the multivariate linear regression

Tai et al (2014) [22]	- 12M, 19F - Total 31	-12-18 years	- full complement of permanent teeth - Patients randomly selected from private orthodontic practice, individual malocclusions not described	- CBCT (Sirona Galileos) and PAC images gathere - Images processed and landmarks identified on CBCT and PAC to measure transverse widths of maxilla, mandible and dentition - Skeletal transverse dimensions investigated with the following points: zygomaxillary, jugale and antegonial landmarks - Dental dimensions recorded at the position of canines and molars	- CBCT ICC = 0.90-1.00 - PAC ICC = 0.90-0.98 - CBCT and PAC measurements showed a statistically significant difference for majority of measurements - Multiple linear regression of Maxillary width, U6 to predict J-J: PAC R^2 = 47%, CBCT R^2 = 73%, -CBCT using additional predictors for maxillary width unique to CBCT R^2 = 80% - CC of intermaxillary width ratios of PAC and CBCT was 0.7 - CBCT identified 5/31 subject with intermaxillary width ratios below 77% - PAC identified 11/31 subject with intermaxillary width ratios below 77% (4/11 of these were identified below 77% with CBCT)	- High intraexaminer reliability reported for both CBCT and PAC measurements - CBCT measurements had more explanatory power for J-J and Ag-Ag ratios when compared to the same predictors used for PAC AND additional variables measured only by CBCT provided more information to predict J-J - enhanced accuracy of CBCT for diagnosis of maxillary deficiencies demonstrated - PAC had 5/31 false positives in identifying intermaxillary transverse discrepancy, questioning accuracy of PAC in intermaxillary transverse diagnosis
Thu et al (2005) [23]	- 28M, 57F - Total 85	- 23.9M, 23.2F	-"Subjects with maxillary dental arch irregularities and missing teeth were excluded." - Did not specify inclusion criteria for the malocclusions beyond the above statement	- Head measurements taken - maxillary dental cast measurements taken (mesiodistal distance of four maxillary incisors and premolar & molar arch widths for Pont's and Korkhaus Index's	- predicted dental arch measurements from Pont's index's were significantly greater than dental cast measurements, and for Korkhaus significantly lower than cast measurements (P<0.01) - Weak correlation coefficients (0.26-0.48) - Observed arch measurements on dental casts were not in proportion with measured incisor widths from the indices	- Does not support the accuracy of Pont's index and Korkhaus index

Risk of bias in individual studies

Two reviewers (DS and KC) used the Quality Assessment Tool for Diagnostic Accuracy Studies (QUADAS) to evaluate risk of bias [24]. The reviewers assessed the risk of bias of each study independently and discrepancies were resolved by a third reviewer (ML).

Summary measures

Accuracy and reliability of each method was considered as well as sensitivity and specificity of each diagnostic technique used to assess maxillary transverse dimensions. In addition, PPV, NPV, LR+, LR-, ROC curves were considered if available.

Results

Study Selection

A flow chart of the article selection process at each stage of the systematic review is presented in Figure 1.1. A total of twenty-one full text articles were retrieved and reviewed, of those twelve were later excluded due to reasons outlined in Appendix 1.2. Only nine articles were found to meet the selection criteria and were included for qualitative synthesis.

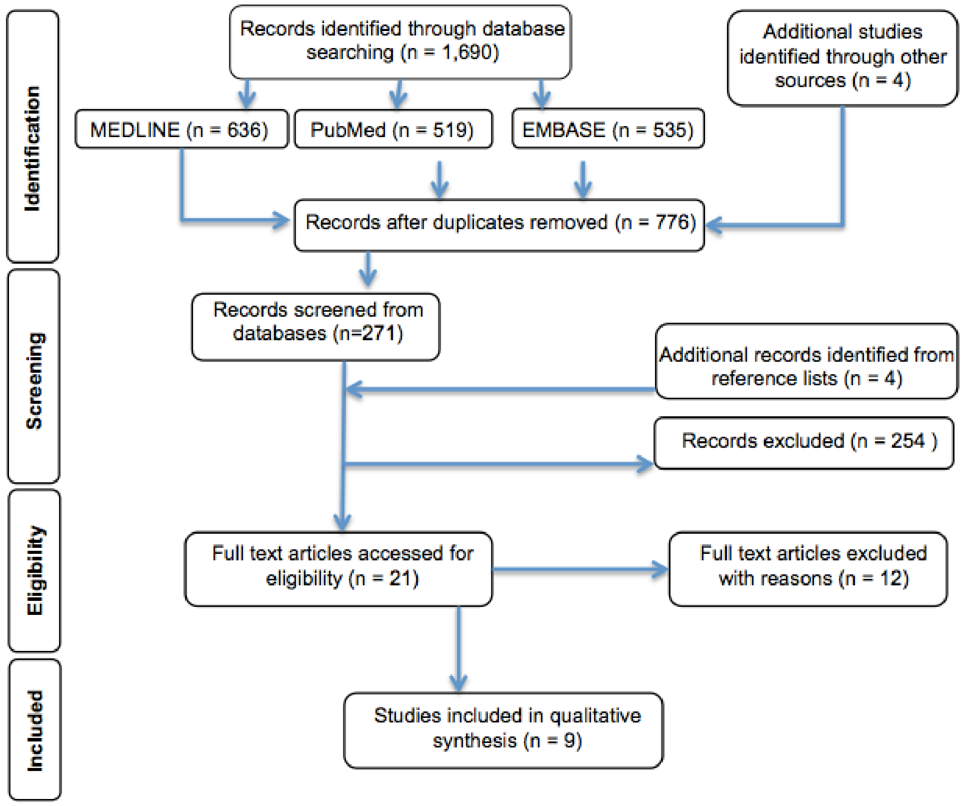

Figure 1.1: Flow Diagram of Article Selection Process

Study Characteristics

A summary of key study characteristics and results of the selected articles is presented in Table 1.1. Articles were all in English and were published between 1995-2014, with sample sizes ranging from 10-241. Only two studies [15,22] assessed the validity of the use of the investigated tool to diagnose maxillary transverse discrepancies. Five articles assessed the accuracy of each tool or analysis to measure or predict arch widths, [16,17,19,21,23] while two articles [18,20] only evaluated the reliability of a proposed transverse analysis or assessment technique. No studies reported sensitivity or specificity, PPV, NPV, LR+, LR-, ROC curves of the method in diagnosis of transverse deficiencies.

Risk of Bias within Studies

The risk of bias assessment of the articles was completed with use of the QUADAS tool (Table 1.2). The studies were heterogeneous with moderate to low methodological quality, all found to have a high risk of bias potential. Six articles were of moderate quality fulfilling 50-64% of the QUADAS criteria and 3 articles were of low quality fulfilling 29-32% of the QUADAS criteria. Common weaknesses included inconsistent reference standard attributed to a lack of a true gold standard (all studies), inadequate sample sizes, [15,20,22] no blinding (all studies), spectrum of patients not representative of the population that would receive the assessment in practice, [15-17,20,21] failure to validate the accuracy of the diagnostic method in identifying maxillary transverse deficiencies. [16-21,23]

Table 1.2: QUADAS Methodological scores of selected articles

Article	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total	% of Total
Cheung et al (2013)	✗	✓	✓	✓	✓	✓	✓	✓	✓	✗	✗	✗	?	✗	8.5	61%
Dalidjan et al (1995)	✗	✓	✗	?	✓	✓	✓	✓	✓	✗	✗	✓	✗	✗	7.5	53%
Lee et al (2014)	✗	✓	✗	✓	✓	✓	✓	✓	✗	✗	✗	✓	✗	✗	7	50%
Miner et al (2012)	✓	✓	✗	✗	✗	✗	✗	✓	✗	✗	✗	✓	?	✗	4.5	32%
Nimkarn et al (1995)	✓	✗	✓	?	✓	✓	✗	✓	✓	✗	✗	✓	✗	✗	7.5	53%
Podesser et al (2004)	✗	✓	✗	✗	✗	✗	✓	✓	✗	✓	✗	✗	✗	✗	4	29%
Rastegar-Lari et al (2012)	✗	✓	✗	✗	✗	✗	✗	✓	✗	✓	✗	✓	✗	✗	4	29%
Tai et al (2014)	✓	✓	✗	✓	✓	✓	✓	✓	✓	✗	✗	✓	✗	✗	9	64%
Thu et al (2005)	✓	✗	✓	✓	✓	✓	✗	✓	✓	✗	✗	✗	✗	✗	7	50%

1-14, Methodologic criteria in Table 2.

✓ Yes, fulfilled QUADAS methodologic criteria (1 point)
✗ No, did not fulfill QUADAS methdlologic criteria (0 point)
? Unclear, did not provide sufficient information to evaluate (0.5 point)

Results of Individual Studies

Table 1.1 provides a summary of the included individual articles.

The studies that evaluated stone dental casts with calipers to apply various indices to predict arch width demonstrated that Pont's Index, Schwarz's analysis, McNamara rule of thumb, Korkhaus index, Gratzinger Index and Howe were inaccurate at predicting arch widths and unreliable for use in diagnosis when compared to the actual arch width measurements. [16,19,21,23] The crowding index [19] and multivariate linear regression[20], which combined dental cast measurements and posteroanterior cephalogram landmarks, [21] were shown to be more accurate tools to use for predicting arch width dimensions compared with the other dental cast indices.

The studies [17,22] that compared transverse landmark identification and analysis of CBCT images to PAC, including one [15] that compared both imaging techniques to dry skull measurements, concluded CBCT images more accurately and reliably assessed intermaxillary transverse discrepancies.

Two studies [18,20] proposed new 3D transverse analyses with CBCT images using skeletal and dental linear and angular measurements. These demonstrated the methods were reliable and reproducible, but did not compare them to other existing diagnostic tools to assess their accuracy in identifying transverse discrepancies.

Synthesis of Results

A meta-analysis was not possible due to the heterogeneity of the diagnostic tools assessed and the variability seen in study designs.

Discussion

Summary of Evidence

Accurate diagnosis of maxillary transverse deficiencies is critical for long term periodontal stability as an undiagnosed discrepancy may result in adverse periodontal effects and gingival recession [25]. In this systematic review the literature was analyzed to evaluate the accuracy and reliability of the available diagnostic tools used to assess maxillary transverse deficiencies in mixed and permanent dentitions. Our results demonstrated there is a lack of strong evidence and high quality diagnostic studies available that evaluate the actual sensitivity and specificity of such diagnostic methods. This may partially be attributed to the absence of scientific literature providing evidence that supports the identification of a true gold standard diagnostic tool for evaluating skeletal transverse deficiencies. The nine selected studies in this review were of low to moderate evidence levels, but were of the best level available to address the research question; although none of them reported their actual sensitivity and specificity.

Clinical evaluation of skeletal transverse discrepancies was not addressed in any of the included studies although it is one of the most widely used evaluation methods of transverse deficiencies [26]. As mentioned in the introduction, chair side assessment evaluates the presence of crossbites, degree of crowding, arch widths measured at the muccogingival junction and dental crowns, perceived buccolingual inclination of posterior teeth and the shape and height of the palatal vault. [6,8] The difficulty of clinical assessment is that it is based on dental crowns without considering the buccolingual inclination roots which may camouflage a true skeletal transverse deficiency [26]. There may be minimal soft tissues changes associated with a maxillary transverse deficiency including paranasal hollowing, a narrow nasal base, deepened nasolabial folds and zygomatic hypoplasia, as a result anteroposterior and vertical maxillary hypoplasias are much easier to clinically diagnose due to observable soft tissue changes [8]. When AP and vertical maxillary dysplasias exist, they can clinically mask a transverse deficiency making clinical evaluation alone inadequate in the diagnosis of transverse skeletal discrepancies [27,28].

Historically, orthodontics has attempted to develop arch width predictions and average measurements using dental casts to assess the transverse dimension but few of these proposed associations are clinically useful and accurate for individualized arch width predictions [29]. Pont's index [30] was proposed in 1909 to predict maxillary arch widths from the sum of the mesiodistal widths of the four maxillary incisors. Four articles in this review demonstrated Pont's Index poorly estimates maxillary arch widths, explaining less than 32% of arch width variations and consistently over or under estimating actual widths with low correlations between observed and predicted maxillary measurements [16,19,21,23]. Schwarz & Gratzinger's analysis [31] modified Pont's index by presenting ideal maxillary interpremolar and intermolar widths corrected for facial type, but was shown to generally overestimate interpremolar width by two included studies [19,21]. Rastegar et al. [21] also found Korkhaus index to under estimate arch widths in their study population. McNamara & Howe proposed a simple rule of thumb

[32] for arch width predictions by determining an average maxillary intermolar width of 37.4mm for males and 36.2mm for females. Two articles [19,21] included in the review found McNamara's simple rule of thumb to overestimate intermolar distances and inaccurately predict maxillary arch widths.

In summary, these indices were developed to help determine how much expansion is needed to resolve crowding, but even with the limited evidence available in this review, it is strongly suggested that such methods are inaccurate, biased and not clinically valid for diagnosis and treatment planning in the transverse dimension [21,29]. Dental cast measurements that are compared with averages or used with mathematical indices lead to errors simply due to individual variation and possible selection bias of the patient population used to initially develop such tools. It is also pertinent to note none of these methods considered the skeletal component of maxillary constrictions, questioning the usefulness of such indices and suggesting study models are not the basis for skeletal diagnosis in the transverse dimension [25]. An objective Crowding Index was developed by Nimkarn and was found to be a more valid and reproducible tool, but this method was not evaluated in the included articles.

Multivariate linear regressions have been proposed by Alvaran et al. [29] & Rastegar et al. [21] that included cephalometric parameters, facial height, and width measurements to enhance the reliability of index predictions, providing better estimates. However, Alvaran et al. [29] did not meet the inclusion criteria for this review because primary dentitions were also included in their sample and their removal from the provided data was not possible. Rastegar et al. [21] had poor quality diagnostic evidence with neither study validating or reporting the accuracy of the method.

Accurate diagnosis and treatment objectives should be based on both clinical and radiographic evaluation of transverse deficiencies, especially when surgical expansion may be required [8]. In the 1990s, PACs were considered the most readily available and reliable radiograph for evaluating transverse skeletal dysplasias [8,25]. Using Ricketts Rocky Mountain Analysis [33] norms and landmarks, Betts et al. [8] developed a PA cephalometric analysis that calculates the Maxillomandibular width differential. This differential indicates that a transverse discrepancy greater than Ricketts norm of 19.6mm requires skeletal expansion and a surgical approach may need to be considered in adults [8,25]. However, clinicians do not routinely use PA cephalograms because they have limitations related to landmark identification errors, superimposition, magnification distortion and head rotation affecting horizontal relationships [11,34,35],resulting in possible miscalculation of the maxillomandibular width and an inaccurate diagnosis [26]. As a result, CBCT images are being nowadays investigated for possible diagnostic superiority over 2D imaging because they have shown to have high accuracy for quantitative and qualitative analyses as they are able to better represent the 3D nature of the craniofacial skeleton [36].

Three of the included articles in this review compared transverse landmark identification and analysis of CBCT images to conventional PA cephalograms [17,22] with one article using direct dry bone skull measurements as a reference standard to compare both imaging modalities to [15]. Cheung et al. [15] assessed the validity of the transverse intermaxillary analysis, ratio of J-J/Ag-Ag, on dry skulls to identify potential errors with using PAC compared to CBCT. It was demonstrated that CBCT landmark identification was better correlated with bone skulls and more reliable than PAC in assessing the intermaxillary transverse discrepancy with CBCT incorrectly diagnosing fewer skulls (8%) than PAC (18%). Another article demonstrated there was no significant correlation of Maxillomandibular width between CBCT images and PA cephalograms except in the first molar area suggesting the assessment of transverse discrepancies using PA cephalograms may result in misunderstanding due to its 2D spatial limitations [17]. Tai et al. [22] also demonstrated a significant difference between specific landmarks on CBCT images compared to PAC, with CBCT better identifying patients with an intermaxillary width discrepancy. Interestingly this article did not provide a gold standard to be compared to. Therefore the CBCT superiority was a false premise in that article[17]. At best they were able to demonstrate that both methods do provide different results. Which one was actually more precise cannot be demonstrated without a gold standard. Cheung et al. [15] used a dry skull as gold standard, therefore, they were able to reasonably claim superiority. Their problem lied in the questionable clinically representation of real life conditions when soft tissues were not depicted.

These articles had moderate methodological quality scores that although suggest there was less potential risk of bias compared to other included studies, the evidence is not strong enough to make reliable conclusions and further validation is required to determine the diagnostic superiority of CBCT imaging.

The clinical use of CBCT has grown from 0-50% recently in orthodontics [37] which is not surprising as numerous studies support the accuracy of CBCT scans, showing that 3D measurements closely approximate anatomic measurements [36,38]. CBCT demonstrates superior results over conventional 2D imaging, but its role in diagnosing intermaxillary transverse discrepancies is inconclusive [15]. Additional standardization of structure identification, measurement process and image orientation is needed to enhance the quality of CBCT data [22]. The article by Miner et al. [18] included in this review aimed to develop a transverse CBCT analysis with valid skeletal and dental landmarks to analyze the width of the jaws and inclination of first molars. The reliability of this newly proposed method was confirmed, but the sample size needed to be larger to investigate the clinical validity of the results and to examine sensitivity and specificity [18]. Podesser et al. [20] suggested another method to quantify the transverse dimension with CT scans by assessing nasal and maxillary bones, dental arches and molar and canine inclinations, demonstrating a reasonably reliable 3D method to evaluate the transverse maxillary dimension, but again did not report on its diagnostic accuracy. Both 3D transverse analysis methods were found to be reliable and reproducible, but diagnostic validity, sensitivity and specificity are still required to support clinical superiority to current diagnostic techniques. This is a clear important limitation in our current understanding of this area. It is also critical to note both 3D analyses used 3D scans, but confined the analysis to specific 2D slices for evaluation, underutilizing the full 3D potential of the data and introducing error due to potential inconsistencies in 3D image orientation.

Limitations

At the systematic review methodological level no reportable limitations exist as the commonly accepted PRISMA guidelines were followed to conduct this review and two reviewers independently selected articles and collected data to reduce selection bias. The fact that a meta-analysis was not possible is not a SR limitation but a reflection of the limited available identified evidence.

At the study level, the most notable limitation to this review was the lack of quality diagnostic studies available for orthodontic craniofacial assessment. Of the articles retrieved, they all demonstrated limited to poor evidence with a high risk of bias for the reporting of diagnostic tools. None of the included articles addressed the sensitivity or specificity of the diagnostic methods to assess clinical applicability, and seven articles failed to validate the accuracy of the diagnostic method in identifying transverse discrepancies [16-21,23]. Blinding did not occur in any of the included studies and 5 articles evaluated a spectrum of patients with normal ideal class I malocclusions, not representative of the population that would receive the assessment in practice [15-17,20,21]. One of the most notable weaknesses that impacted methodological QUADAS scores for the majority of included studies is the use of an inconsistent reference standard. This is likely due to a lack of scientific evidence indicating a true gold standard that correctly identifies maxillary transverse deficiencies.

The establishment of a gold standard requires identifying the most accurate available method that hypothetically always positively identifies the presence of a disease or in this case, a malocclusion.[39] The difficulty in evaluating the sensitivity and specificity of a diagnostic method to identify maxillary deficiencies is the continuous nature of dental and skeletal measurements without a clearly defined or agreed upon threshold to identify patients as being normal or abnormal.[40] With extensive variation in the normal population, it is difficult to clearly differentiate most patients with a high degree of certainty into normal versus abnormal groups for diagnostic comparison to develop a gold standard method. In orthodontics, defining dental and skeletal proportions that produce a functionally stable and esthetic result can be quite subjective and lead to a lack of consensus among clinicians. Shown by Streit *et al.*[41] when provided with intraoral and extraoral photographs, study models, frontal radiographs and CBCT images for evaluation, there was only a 55.6% agreement among experienced orthodontic clinicians in placing patients into “transverse deficient” or “not transverse deficient” categories. With expert clinicians unable to come to a consensus in identifying an ideal population, this questions the applicability of determining normative data for radiographic measurement. The subjective nature of orthodontic diagnosis in evaluating malocclusions that exist on a continuum is an inherent limitation to developing a gold standard diagnostic method. This is not a problem unique to the transverse dimension but pertains to anteroposterior and vertical orthodontic diagnosis as well.

Conclusions

- Current evidence does not allow for definitive conclusions to be drawn from this evidence synthesis due to a lack of diagnostic studies with low risk of bias that evaluate maxillary transverse deficiencies. Nevertheless some clinical pertinent conclusions follow.

- Clinical evaluation alone seems likely inadequate for diagnosing transverse skeletal discrepancies. An objective assessment would be more useful to the clinician.
- Arch width prediction indices and average measurements on dental casts are not clinically valid for the general population and do not consider the skeletal component of transverse deficiencies.
- CBCT images appear to be more reliable, and offer an unobstructed view in assessing transversal intermaxillary discrepancies compared to PAC's; although further validation is required to confirm CBCT diagnostic superiority. The CBCT accuracy has not been evaluated enough.

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Appendices

Appendix 1.1

Search Strategy for MEDLINE via OVID (1946 to Present)

Steps	Combination words
1	(maxill* OR palat*).mp
2	(transverse OR arch width*).mp
3	(deficien* OR dimension* discrepanc* OR constrict* OR crossbite*).mp
4	occlusogram*.mp
5	pont's index*.mp
6	(dental model* OR dental cast*).mp
7	(CBCT* OR computed tomography).mp
8	((posteroanterior OR posterior anterior OR frontal) AND (cephalo* OR radiog*)).mp
9	(diagnos* OR quantif* OR evaluat* OR analys*).mp
10	1 and 2 and 3
11	4 or 5 or 6 or 7 or 8 or 9
12	10 and 11

Appendix 1.2 with references

Articles Excluded in Phase 2

Author	*Reason*
Alvaran et al. [1]	• Primary dentitions included in study sample
Bayome et al. [2]	• Did not evaluate the transverse dimension to identify deficiencies • Only evaluated transverse measurements between sexes and to identify correlations between vertical and transverse measurements
Belluzo et al. [3]	• Did not address accuracy, validity or reliability of PA radiographic analysis in evaluating transverse deficiencies
de Oliveira et al. [4]	• Proposed a method to assess and predict the transverse dimension but did not report accuracy, validity or reliability of the method
El-Zanaty et al. [5]	• Did not apply a method or tool to assess the transverse dimension, only compared

	measurements between plaster and 3D casts
Goldenburg et al. [6]	• Only evaluated the reliability of CT in assessing post-SARPE changes, did not evaluate the use of CT as a diagnostic tool
Ghislanzoni et al. [7]	• Did not evaluate the use of tip & torque in identifying transverse deficiencies • Did not assess accuracy, validity or reliability of the presented method for use in diagnosis of transverse deficiencies
Lemieux et al. [8]	• Did not evaluate the 3D superimposition method to be used in identifying maxillary transverse deficiencies • Only evaluated changes that occurred with expansion treatment
Ovsenik et al. [9]	• Article evaluated degree of malocclusion in a general sense • Did not evaluate the accuracy, reliability or validity of assessing the maxillary transverse dimension with the method presented
Sygouros et al. [10]	• Only assessed transverse changes after SARME • No evaluation of accuracy, reliability or validity of the method for use in diagnosing the transverse dimension
Talaat et al. [11]	• Did not specifically assess maxillary arch dimensions for diagnostic purposes
Varghese et al. [12]	• Did not specifically assess maxillary arch dimensions for diagnostic purposes

Appendix 1.2 References

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Chapter 2: Reliability of dental and skeletal landmarks and buccolingual angular measurements in a three-dimensional transverse analysis

Introduction

Orthodontists recognize that maxillary transverse deficiencies are a significant component of many malocclusions and if such discrepancies go undiagnosed it can result in periodontal problems, unstable dental camouflage and reduced esthetics[1]. It becomes therefore essential to be able to accurately diagnosis in all three planes of space the dental and skeletal components of maxillary deficiencies to improve treatment outcomes and long-term stability[2].

Diagnosing maxillary transverse deficiencies requires a clinical examination; however, clinical evaluation alone has been found to be inadequate[3,4]. Clinical assessment is based on dental crown's spatial positions without considering the buccolingual inclinations of roots which may camouflage a clinically unnoticed true skeletal transverse deficiency[5]. Therefore accurate diagnosis and treatment planning should rely on both clinical and radiographic assessment[6]. However, the use of conventional two-dimensional (2D) posteroanterior cephalograms for transverse assessments have fallen out of favor due to limitations related to landmark identification errors, superimposition, magnification distortion and head rotation[7-9].

Three-dimensional (3D) imaging has the potential to enhance diagnosis and treatment planning because it is an accurate representation of the 3D anatomical nature of the craniofacial skeletal[10]. However, due to a lack of existing appropriate 3D analyses for diagnosis and increased risk of additional ionizing radiation, routine use is not recommended. Instead, three-dimensional imaging should be selected for use on an individual basis when it will provide improved diagnostic and treatment planning information[11] [12]. Only a few studies to date have focused on use of cone-beam computed tomography (CBCT) in diagnosis and treatment planning of transverse deficiencies. Cheung *et al.* [11] and Tai *et el.* [13] both separately assessed the accuracy and reliability of identifying intermaxillary width discrepancies from coronal slices of CBCT images. Miner *et el.* [14] and Podesser *et al.* [15] proposed 3D transverse analyses that quantified buccolingual inclinations of maxillary and mandibular molars from standardized frontal slices of CBCT and CT scans. These authors recognized the limitations of the analyses proposed in that they underutilized the volumetric 3D data by confining the analysis to linear and angular measurements on 2D sections that had to be consistently oriented for reliable measurements[14,15]. Most recently, the Case Western Reserve University (CWRU) transverse analysis was developed to assess buccolingual inclinations of maxillary and mandibular first molars and canines from CBCT scans to help diagnose the dental and skeletal components of transverse discrepancies[16-18].

Therefore there is a need for the development of appropriate 3D analyses that fully utilize the volumetric data provided from CBCT imaging as this has the potential to improve orthodontic diagnosis. The currently published transverse analyses, including the CWRU transverse analysis, were developed for 3D imaging, but only utilized 2D linear and angular measurements from cross sectional slices. Studies have shown that 3D landmark identification from CBCT volumetric data are closer to anatomical measurement than conventional 2D measurements, and offer consistent and reliable data in the X, Y & Z planes when multiplanar (MPR) views and 3D renderings are used[19,20]. It is therefore necessary to begin developing and confirming the reliability of analyses that fully utilize the accurate 3D nature of CBCT images to benefit from the improved accuracy of this diagnostic modality.

The purpose of this study was to evaluate the reliability of landmark identification and buccolingual angulation measurements using two different methods of analyzing 3D images to assess the transverse dimension. The first method assessed for reliability of dental and skeletal landmark placement utilizing 3D volumetric data, using both 3D reconstructions and MPR views. The second method assessed reliability of angular measurements on 2D coronal views using the CWRU transverse analysis.

Methods

The study population consisted of adolescents with permanent dentition 6-6 who received pre-treatment CBCT scans as part of Dr. Carlos Flores-Mir's randomized clinical trial at the University of Alberta. Ten CBCT scans (iCAT, Imaging Science International, Hatfield, PA, USA) were randomly selected from this pool of patients, ages 12-15, for this reliability study. Ethics approval was obtained through the University of Alberta Research Ethics Board. A standardized protocol of the iCAT was used (large field of view 16cm x 13.3, voxel size 0.30mm, 120kVp, 18.54mAS, 8.9 seconds). Raw images were exported as DICOM files and subsequently loaded into Avizo version 8.1 software

(Visualization Sciences Group, Burlington, MA, USA) and Dolphin Imaging 11.7 Premium (Dolphin Imaging & Management Solutions, Chatsworth, CA, USA) for analysis. The primary investigator (DS) assessed intra-examiner reliability by marking 3D landmarks in Avizo and identifying the CWRU transverse analysis angular measurements in Dolphin for each CBCT scan in random order three times with 1-week separation between measurements. Inter-examiner reliability for both methods was assessed by three examiners, an experienced orthodontist (ML), an orthodontic resident (KC) and the principal investigator (DS). Each examiner was trained visually and verbally as well as provided with detailed written instructions to identify 20 landmarks in Avizo and 8 angular measurements in Dolphin on each CBCT image. The CBCT images were codified for investigator blinding.

Avizo Volumetric Landmark Identification

Twenty anatomical landmarks were selected, four skeletal and sixteen dental as shown in Table 2.1. The dental landmarks selected were as described in the CWRU analysis as the cusp tips and apices of mandibular and maxillary molars and canines[17,18]. Lemieux *et al* [21] previously identified four skeletal landmarks which were chosen as being accurate and reliable skeletal landmarks to define a 3D anatomical reference Cartesian coordinate system from which a stable and reproducible maxillary plane could be established[22]. With establishment of a virtual reference plane, coordinate transformation can be performed with MATLAB software for future studies in which all other dental landmarks can be compared to [23].

In Avizo, a Cartesian coordinate system was used for analysis where the X-Y, X-Z and Y-Z planes represented axial, coronal and sagittal planes respectively. Landmarks were marked using 0.25mm diameter virtual spherical markers on the X, Y and Z-axes with the center of the spherical marker considered the landmark position (Figure 2.1). In a standardized automatic fashion, the software generated landmark coordinates of each point.

CWRU Transverse Analysis in Dolphin

The method to measure buccolingual inclinations of maxillary and mandibular canines and first molars was previously described and demonstrated to be reliable by Karamitsou[17] and Shewinvanakitkul[18] at Case Western Reserve University. In Dolphin Imaging, measurements were obtained by first orienting the CBCT dicom files in the sagittal, axial and finally coronal views to consistently identify the required 2D coronal slice for measurements. For maxillary molars, the angle measured was that formed by a line at the inferior border of the nasal cavity with a line passing through the apex of the maxillary first molar palatal root to mesial palatal cusp tip. Maxillary canine inclinations were measured by the angle formed between the line tangent to the inferior border of the nasal cavity and the line down the long axis of the tooth. For mandibular molars, inclinations were obtained by measuring the angle between a line tangent to the inferior border of the mandible and a line passing through the central groove and root apex. Mandibular canine inclinations are measured at the angle between a line tangent to the inferior border of the mandible and the line through the long axis of the tooth (Table 2.2 & Figure 2.2)

Statistical Analysis

Intra-examiner and inter-examiner reliability were assessed with the Intraclass Correlation Coefficient (ICC) using standard statistical software package (SPSS Statistics version 23 for Mac, IBM). ICC was chosen to assess the consistency and reproducibility of quantitative measurements taken at different time points by the principal investigator and between different investigators on 10 randomly chosen pre-treatment CBCT images. The repeatability of all three coordinates (X, Y, Z) for the 20 landmarks in Avizo was analyzed as well as 8 angular measurements in Dolphin as described by the CWRU analysis. For statistical analysis, a single measure with absolute agreement under a two-way mixed model was chosen in SPSS to ensure all raters and time points are in absolute agreement on the individual measurements rather than simply being correlated with each other on average. The general guidelines for ICC interpretation were used to evaluate the resulting values[24].

Mean error was also assessed for each landmark and angular measurement. Landmark interexaminer variations greater than 1.5mm were considered clinically significant and intraexaminer variations greater than 1mm were considered clinically significant based on Lagravere *et al.* [25]. As for angular measurements, a clinical significance level for reliability testing of 5 degrees was considered based on one standard deviation of the CWRU normative values determined by Streit *et al.*[26].

Results

Avizo Volumetric Landmarks

The intra-examiner reliability of X, Y & Z coordinates of all 20 landmarks were excellent as shown in Table 2.3. The ICCs were greater than 0.937, 0.987 and 0.997 for the X, Y and Z coordinates respectively for all landmarks. Mean errors were less than 0.516mm, 0.601mm and 0.391mm for the X, Y and Z coordinates respectively for all landmarks (Table 2.4). An example of a scatter plot and profile plot with excellent reliability is presented in Figure 2.3a & 2.3b.

The inter-examiner reliability of X, Y & Z coordinates of all 20 landmarks were good to excellent as shown in Table 2.5. The ICCs were greater than 0.838, 0.963 and 0.980 for the X, Y and Z coordinates respectively for all landmarks. Mean errors were less than 1.012mm, 1.069 and 0.841mm for the X, Y and Z coordinates respectively for all landmarks (Table 2.6).

CWRU Transverse Analysis

The intra-examiner reliability of the 8 CWRU angulations demonstrated excellent agreement, all greater than 0.913 as shown in Table 2.7. Mean errors were less than 2° as shown in Table 2.8.

The inter-examiner reliability of the CWRU angulations demonstrated a range of ICC values from poor to good agreement as shown in Table 2.7. Four measurements, UR3, LL6, LR3 and LL3 showed poor agreement with ICC values less than 0.50. Three measurements demonstrated moderate agreement, UL6, UL3 and LR6, with ICC values from 0.564-0.710. Finally, one measurement showed good agreement with an ICC value of 0.760 for UR6. Mean errors ranged from 3.153° to 5.874° as shown in Table 2.8. An example of a scatter plot and profile plot with poor reliability is presented in Figure 2.4a & 2.4b.

Discussion

Reliability assessment in orthodontic digital analyses is vital to confirm reproducibility and repeatability of landmark placement and measurements and ensure effective clinical use of new diagnostic modalities. This study assessed the reliability of landmark placement and angle measurement of two 3D methods that can be utilized in future studies to diagnose transverse deficiencies. The landmarks selected for measurement in the 3D volumetric Avizo software were based on those used to develop angular measurements on the 2D coronal slices utilized in the CWRU transverse analysis. The decision was made to assess only landmark placement in Avizo instead of angular buccolingual measurements as seen in the CWRU analysis to reduce the inherent increased error associated with angular measurements. More intra-observer and inter-observer variation is expected to be seen with angular measurements than individual landmarks, as each examiner must reliably identify three separate points or two separate lines, each which have their own degree of identification error, to construct the angle required for analysis. Our goal is to develop a more accurate version of the CWRU analysis that fully utilizes 3D images rather than 2D coronal slices preceded by the confirmation that the 3D landmarks chosen to represent the transverse analysis in Avizo software are reliable.

Conventional cephalometric landmarks on 2D images have errors that result in an inaccurate representation of true craniofacial structures, but 3D analyses could offer advantages in identification and anatomic visualization [27]. There is a need for 3D based measurement analyses that use a 3D Cartesian coordinate system because current validated 3D analyses are lacking [28]. The results of this study suggested that 3D volumetric landmark placement in Avizo had good to excellent intra-examiner and inter-examiner reliability with mean errors that were not clinically significant. This is in agreement with a previous study that supports the use of a voxel-based 3D cephalometric anatomic Cartesian reference system is both accurate and reliable[28]. Both 3D volume reconstructions and multiplanar views were utilized in Avizo to identify the dental and skeletal landmarks because it has been previously shown that the use of 3D surfaces alone for landmark identification are less reliable than multiplanar views for both intra-examiner and inter-examiner reliability[29]. The four skeletal landmarks chosen were shown to be highly reliable in this study, which confirms the findings of Lemieux *et al.*[21]. This supports the use of these skeletal landmarks for the formation of X-Y & Z-Y planes to adequately and reliably standardize reference plane orientation of 3D images[30] and apply this reference plane to a 3D transverse analysis.

The ICC values from this study suggested that the buccolingual inclination measurements in the CWRU transverse analysis have good intra-examiner reliability, but compared to landmark placement, the angular measurements were not as reliable between different examiners. However, when considering the largest mean error for the angular inter-examiner reliability testing was 5.874°, for maxillary left first molars (UL6), this does not suggest that the reduced reliability seen with the angular measurements is necessarily clinically significant. Previous studies carried out by Case Western Reserve

University orthodontic faculty and graduate students support that the CWRU transverse analysis is a reliable method [16-18]. Therefore we could also hypothesize that the reduced inter-examiner reliability seen may in part be due to a lack of thorough training and clinician calibration with the CWRU analysis. Without a standard calibration between all clinicians involved in reliability testing, it can be expected there will be greater inter-examiner variation as the two other clinicians, excluding the primary investigator, are using the analysis for the first time. Even with improved training and calibration it may also be argued that the fact the CWRU method itself has more steps involved compared to simple landmark identification would lead to increased variation between examiners. With this method, CBCT images must be manually oriented in Dolphin on multiple planes prior to identifying a coronal 2D section in which the angular measurements are taken for each tooth. It can be expected there is subjective observer variation with each step of plane orientation as well as error in identifying the nasal cavity and mandibular border reference planes. As mentioned previously, the nature of creating an angular measurement from three separate points will automatically increase the amount of error as compared to one precisely identified landmark.

Our reliability testing of Avizo landmark identification is the first step in applying the basic buccolingual angulation measurement concepts of the CWRU analysis to diagnose transverse deficiencies, but by using a 3D Cartesian coordinate system in Avizo. A common factor seen in other existing 3D transverse analysis studies is the use of linear and angular measurements on 2D sections instead of a using a 3D coordinate system to assess all three planes[25]. Our goal is to establish a 3D transverse analysis reflective of the CWRU transverse analysis that utilizes the full 3D potential of CBCT images using a reliable 3D virtual reference plane constructed mathematically on a coordinate system with reliably identifiable landmarks. From this, software algorithms would be used to transform the Avizo landmark data to establish a 3D maxillary reference plane and produce buccolingual inclinations with improved reliability and potentially improved accuracy. Following the reliability testing of this new approach, subsequent studies will be able to directly compare these two methods to identify if discrepancies exist between them in analyzing buccolingual inclinations.

Limitations

It is pertinent to note some of these mean error values should be interpreted with caution for both analyses, but particularly the CWRU inter-examiner mean errors, as they show relatively large standard deviations. This demonstrates large variation that may be considered clinically significant when the mean error plus the standard deviation is taken into account. This may be due to the small sample size used and use of a larger sample size could have potentially reduced some of this variability.

Both software's and measurement techniques require a significant learning curve and operator familiarization before landmarks and angulations can be consistently identified. This limitation may be reflected in the decreased inter-examiner reliability.

The impact of using other imaging software in the landmark identification and angle measurement generations has not been assessed.

Conclusion

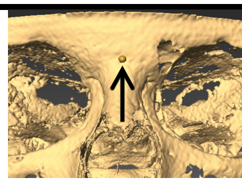
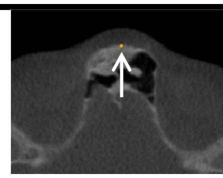
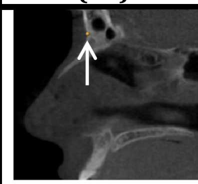
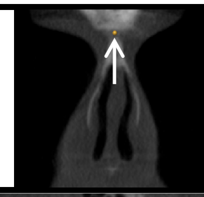
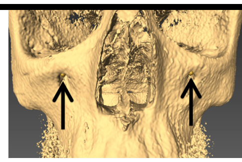
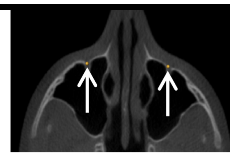
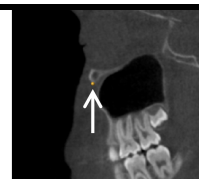
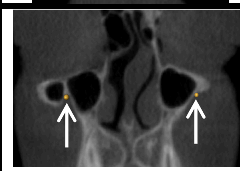
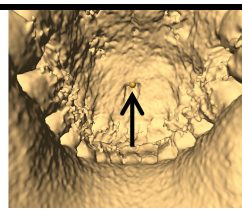
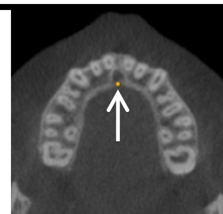
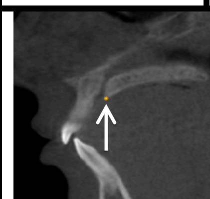
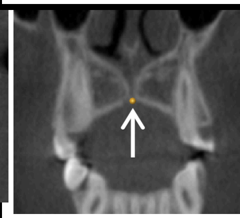
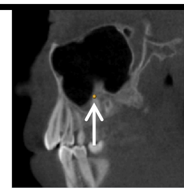
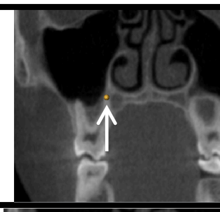
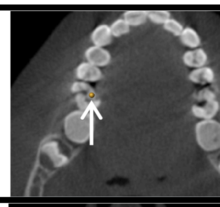
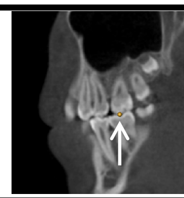
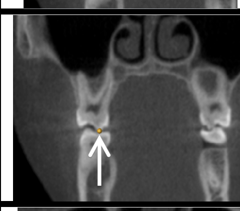
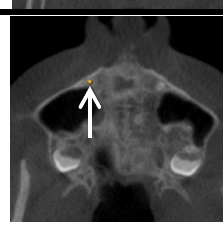
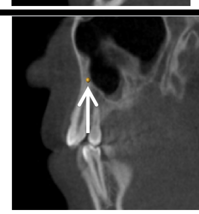
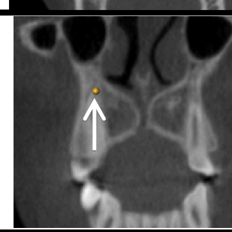
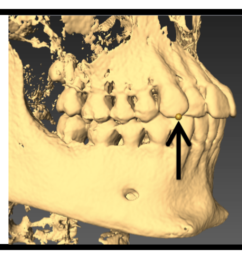
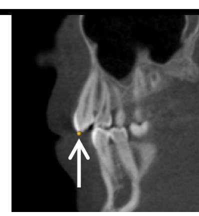
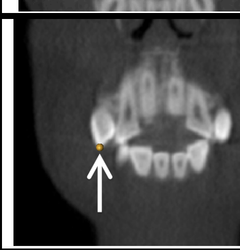
3D volume reconstructions and multiplanar utilization of CBCT images for 3D landmark placement is highly reliable for both intra-observer and inter-observer identification and analysis.

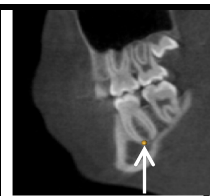
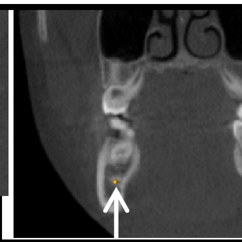
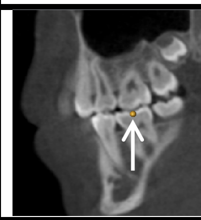
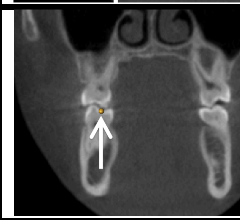
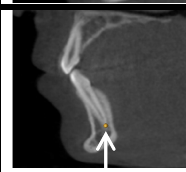
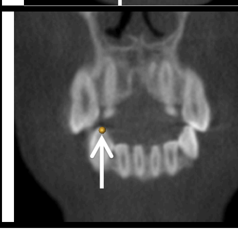
For the 3D CWRU transverse analysis, although it demonstrated good intra-observer reliability, the reduced inter-observer reliability may be attributed to lack of clinician calibration and lack of clarification of the steps needed to successfully utilize this method. Also pertinent to note is the variability and large standard deviations seen with the CWRU inter-observer reliability which may be the result of the use of a small sample size.

With the demonstration of both methods being reliable, further research will be able to directly compare measurement techniques to determine if utilization of 3D volumetric data leads to improved accuracy of buccolingual measurements and hence improved diagnosis of maxillary transverse deficiencies.

Appendix

Table 2.1: Description of the skeletal and dental anatomic landmarks used for angular measurements in all 3 planes.

Landmark	3D Reconstruction	Axial View (XY)	Sagittal View (ZY)	Coronal View (XZ)
Nasion Most Anterior point of the frontonasal suture				
Infraorbital Foramina (Bilateral) Center of the most superior border of the foramen				
Incisive Foramen Center of the most posterior border of the foramen				
Maxillary 1st molar palatal root apex (Bilateral)				
Maxillary 1st molar mesiolingual cusp tip (Bilateral)				
Maxillary canine root apex (Bilateral)				
Maxillary canine cusp tip (Bilateral)				

Mandibular 1st molar mesial root apex (Bilateral)				
Mandibular 1st molar central groove (Bilateral)				
Mandibular canine root apex (Bilateral)				
Mandibular canine cusp tip (Bilateral)				

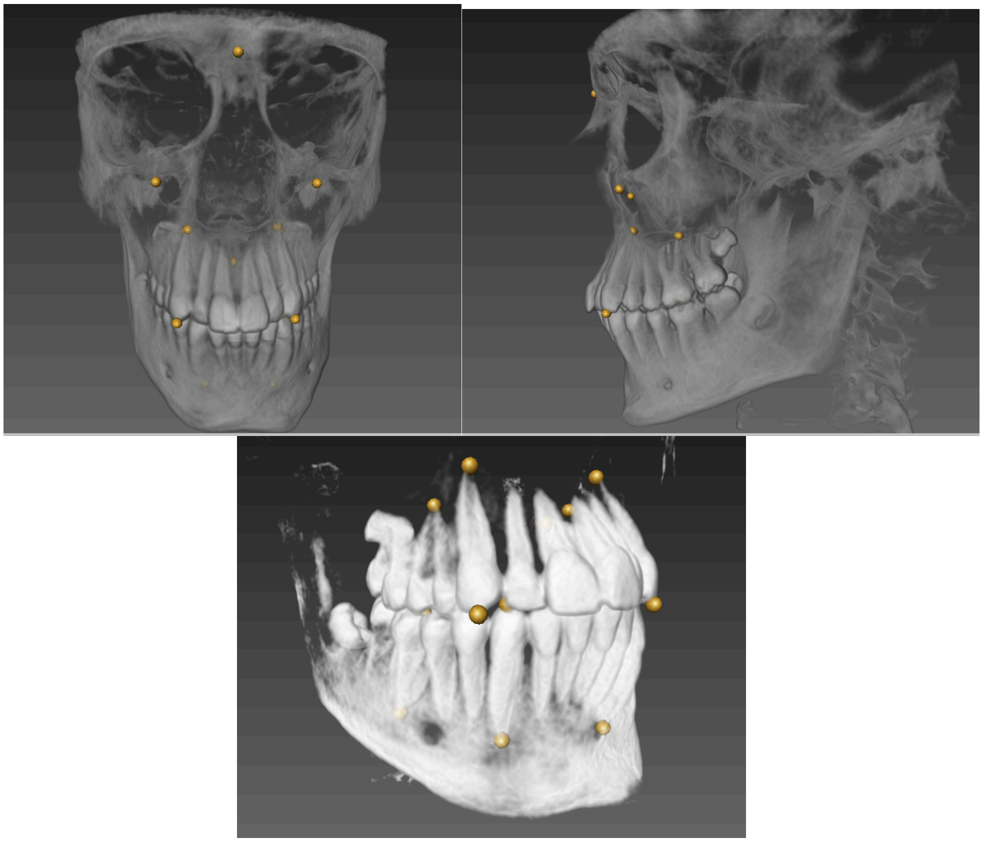


Figure 2.1 – Landmarks as visualized in Avizo software version 8.1

Table 2.2 – Description of teeth measured in CWRU Transverse analysis.

UL3	Upper (maxillary) left canine
UR3	Upper (maxillary) right canine
UL6	Upper (maxillary) left first molar
UR6	Upper (maxillary) right first molar
LL3	Lower (mandibular) left canine
LR3	Lower (mandibular) right canine
LL6	Lower (mandibular) left first molar
LR6	Lower (mandibular) right first molar

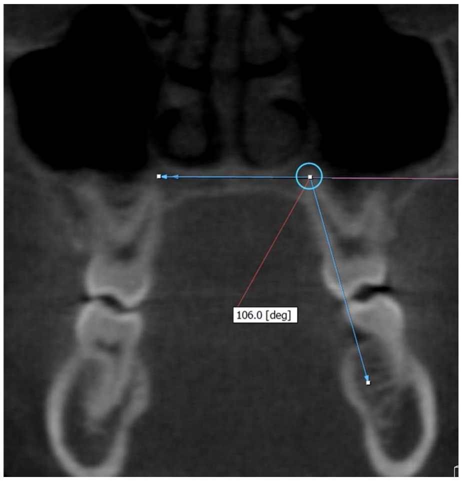


Figure 2.2a: Maxillary first molar buccolingual inclination (UL6, UR6).

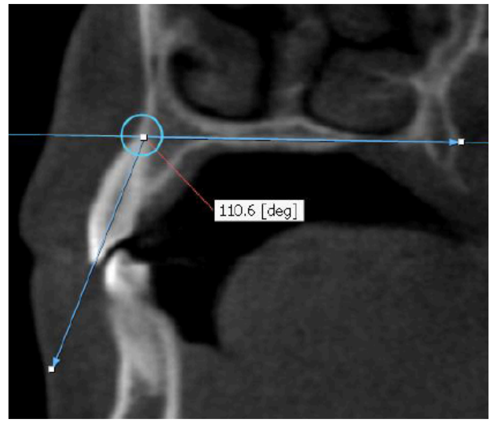


Figure 2.2b: Maxillary canine buccolingual inclination (UL3, UR3)

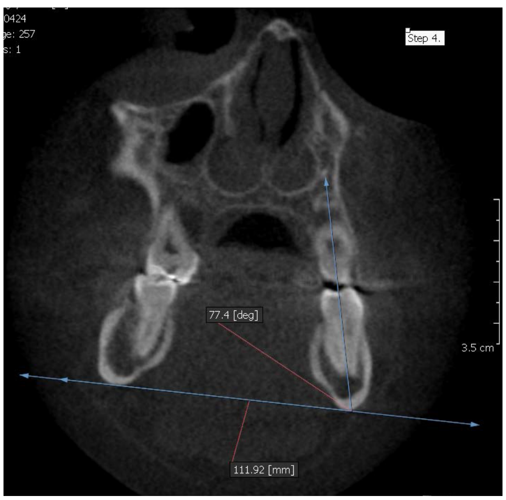


Figure 2.2c: Mandibular first molar buccolingual inclination (LL6, LR6)

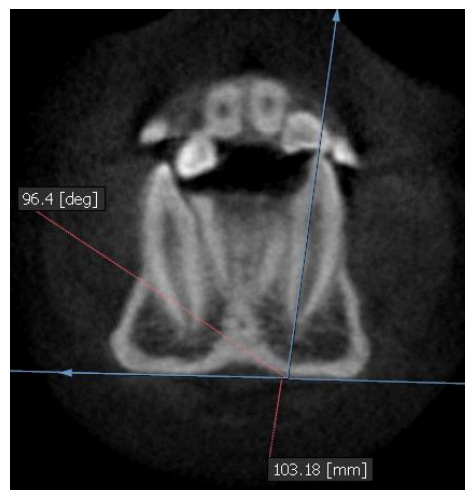


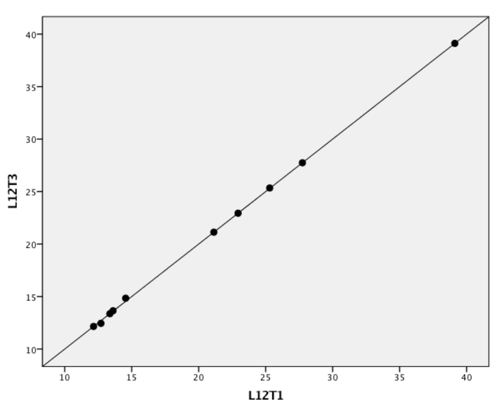
Figure 2.2d: Mandibular canine buccolingual inclination (LL3, LR3)

Table 2.3: Intraclass correlation coefficients for Avizo software 3D landmark intra-examiner reliability testing.

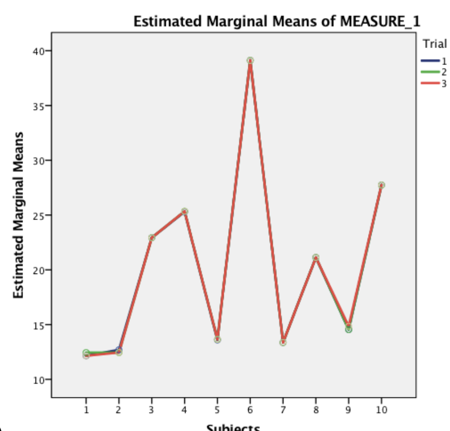
	X			Y			Z		
	ICC	lower bound	upper bound	ICC	lower bound	upper bound	ICC	lower bound	upper bound
1	0.937	0.833	0.982	0.996	0.989	0.999	0.997	0.992	0.999
2	0.976	0.935	0.994	0.998	0.994	0.999	1.000	0.999	1.000
3	0.990	0.971	0.997	0.998	0.995	1.000	1.000	0.999	1.000
4	0.945	0.855	0.985	0.999	0.997	1.000	0.998	0.994	1.000
5	0.991	0.974	0.998	0.998	0.994	1.000	0.998	0.995	1.000
6	0.986	0.962	0.996	0.987	0.964	0.997	1.000	0.999	1.000
7	0.986	0.961	0.996	0.997	0.992	0.999	0.999	0.997	1.000
8	0.986	0.960	0.996	0.988	0.950	0.997	0.999	0.998	1.000
9	0.990	0.973	0.997	0.998	0.994	1.000	0.997	0.99	0.999
10	0.982	0.937	0.995	0.999	0.996	1.000	1.000	0.999	1.000
11	0.990	0.971	0.997	0.999	0.997	1.000	0.998	0.995	1.000
12	0.996	0.989	0.999	0.999	0.997	1.000	1.000	1.000	1.000
13	0.987	0.964	0.997	0.997	0.992	0.999	0.997	0.992	0.999
14	0.994	0.982	0.998	0.996	0.988	0.999	0.999	0.997	1.000
15	0.970	0.916	0.992	0.997	0.991	0.999	0.998	0.991	0.999
16	0.966	0.907	0.991	0.993	0.981	0.998	0.999	0.997	1.000
17	0.995	0.985	0.999	0.999	0.997	1.000	0.999	0.997	1.000
18	0.976	0.93	0.993	0.999	0.996	1.000	1.000	0.999	1.000
19	0.996	0.989	0.999	0.999	0.998	1.000	0.999	0.998	1.000
20	0.974	0.929	0.993	0.997	0.990	0.999	1.000	0.999	1.000

Table 2.4: Mean errors and standard deviations for Avizo software 3D landmark intra-examiner reliability testing (mm).

		X		Y		Z	
		Mean error	**Standard Deviation**	**Mean Error**	**Standard Deviation**	**Mean Error**	**Standard Deviation**
1	**Nasion**	0.283	0.253	0.385	0.215	0.203	0.145
2	**R. Infraorbital foramen**	0.516	0.409	0.336	0.269	0.337	0.224
3	**L. Infraorbital foramen**	0.335	0.353	0.535	0.421	0.280	0.288
4	**Incisive Foramen**	0.134	0.283	0.134	0.283	0.274	0.074
5	**U6 R. palatal root apex**	0.300	0.123	0.556	0.329	0.235	0.117
6	**U6 R. palatal cusp tip**	0.302	0.124	0.518	0.351	0.243	0.147
7	**U6 L. palatal root apex**	0.335	0.353	0.601	0.798	0.327	0.305
8	**U6 L. palatal cusp tip**	0.335	0.353	0.468	0.450	0.355	0.251
9	**U3 R. root apex**	0.067	0.212	0.401	0.466	0.233	0.232
10	**U3 R. cusp tip**	0.067	0.212	0.536	0.283	0.286	0.193
11	**U3 L. root apex**	0.335	0.353	0.469	0.324	0.253	0.209
12	**U3 L. cusp tip**	0.200	0.450	0.334	0.471	0.193	0.105
13	**L6 R. mesial root apex**	0.402	0.346	0.335	0.353	0.333	0.206
14	**L6 R. central groove**	0.536	0.283	0.402	0.346	0.260	0.316
15	**L6 L. mesial root apex**	0.201	0.324	0.335	0.353	0.260	0.240
16	**L6 L. central groove**	0.134	0.283	0.402	0.346	0.277	0.216
17	**L3 R. root apex**	0.402	0.346	0.401	0.467	0.240	0.188
18	**L3 R. cusp tip**	0.335	0.353	0.268	0.346	0.288	0.185
19	**L3 L. root apex**	0.296	0.268	0.411	0.278	0.262	0.217
20	**L3 L. cusp tip**	0.267	0.249	0.260	0.248	0.391	0.298



a.)



b.)

Figures 2.3ab: Example scatter plot and profile plot of a landmark coordinate with excellent intra-examiner reliability demonstrated strong positive correlation, z-axis for point 12.

Table 2.5: Intraclass correlation coefficients for Avizo software 3D volumetric landmark inter-examiner reliability testing.

	X			Y			Z		
	ICC	**lower bound**	**upper bound**	**ICC**	**lower bound**	**upper bound**	**ICC**	**lower bound**	**upper bound**
1	0.929	0.788	0.981	0.963	0.898	0.990	0.980	0.943	0.994
2	0.960	0.876	0.989	0.990	0.933	0.998	0.999	0.997	1.000
3	0.958	0.885	0.989	0.991	0.915	0.998	1.000	0.999	1.000
4	0.939	0.838	0.983	0.991	0.963	0.998	0.997	0.990	0.999
5	0.989	0.968	0.997	0.998	0.995	1.000	0.998	0.989	0.999
6	0.918	0.758	0.978	0.979	0.942	0.994	0.992	0.946	0.998
7	0.978	0.938	0.994	0.997	0.991	0.999	0.999	0.997	1.000
8	0.943	0.848	0.984	0.981	0.946	0.995	0.995	0.985	0.999
9	0.968	0.882	0.992	0.997	0.989	0.999	0.991	0.940	0.998
10	0.970	0.907	0.992	0.999	0.996	1.000	1.000	0.999	1.000
11	0.986	0.958	0.996	0.998	0.994	0.999	0.995	0.971	0.999
12	0.988	0.965	0.997	0.996	0.988	0.999	1.000	0.999	1.000
13	0.847	0.534	0.959	0.990	0.948	0.998	0.993	0.961	0.998
14	0.977	0.936	0.994	0.993	0.945	0.999	0.998	0.990	1.000
15	0.838	0.568	0.954	0.983	0.864	0.996	0.996	0.961	0.999
16	0.949	0.864	0.986	0.988	0.948	0.997	0.998	0.991	1.000
17	0.974	0.928	0.993	0.998	0.993	0.999	0.996	0.973	0.999
18	0.962	0.880	0.990	0.995	0.985	0.999	0.999	0.997	1.000
19	0.975	0.932	0.993	0.998	0.995	1.000	0.997	0.989	0.999
20	0.960	0.891	0.989	0.996	0.988	0.999	0.999	0.995	1.000

Table 2.6: Mean errors and standard deviations for Avizo software 3D landmark inter-examiner reliability testing (degrees).

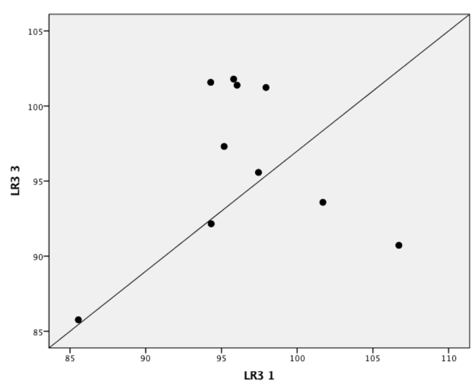
		X		Y		Z	
		Mean error	**Standard Deviation**	**Mean Error**	**Standard Deviation**	**Mean Error**	**Standard Deviation**
1	**Nasion**	0.596	0.243	0.959	1.055	0.841	0.802
2	**R. Infraorbital foramen**	0.527	0.222	0.735	0.332	0.265	0.202
3	**L. Infraorbital foramen**	0.428	0.196	0.704	0.335	0.207	0.137
4	**Incisive Foramen**	0.419	0.301	0.585	0.462	0.578	0.265
5	**U6 R. palatal root apex**	0.291	0.131	0.351	0.156	0.393	0.210
6	**U6 R. palatal cusp tip**	0.840	0.502	0.956	0.859	0.719	0.530
7	**U6 L. palatal root apex**	0.425	0.222	0.456	0.230	0.272	0.229
8	**U6 L. palatal cusp tip**	0.679	0.365	1.040	0.612	0.604	0.413
9	**U3 R. root apex**	0.416	0.102	0.442	0.187	0.830	0.437
10	**U3 R. cusp tip**	0.365	0.133	0.367	0.155	0.198	0.124
11	**U3 L. root apex**	0.343	0.216	0.348	0.169	0.600	0.353
12	**U3 L. cusp tip**	0.281	0.193	0.460	0.354	0.124	0.132
13	**L6 R. mesial root apex**	1.004	0.596	0.848	0.456	0.820	0.439
14	**L6 R. central groove**	0.395	0.226	0.643	0.235	0.378	0.194
15	**L6 L. mesial root apex**	1.012	0.644	1.069	0.385	0.662	0.320
16	**L6 L. central groove**	0.442	0.199	0.864	0.375	0.425	0.221
17	**L3 R. root apex**	0.424	0.265	0.321	0.297	0.741	0.189
18	**L3 R. cusp tip**	0.482	0.225	0.498	0.486	0.257	0.141
19	**L3 L. root apex**	0.354	0.184	0.402	0.122	0.638	0.338
20	**L3 L. cusp tip**	0.452	0.410	0.560	0.329	0.288	0.190

Table 2.7: Intraclass correlation coefficients for CWRU transverse analysis intra-examiner and inter-examiner reliability in Dolphin.

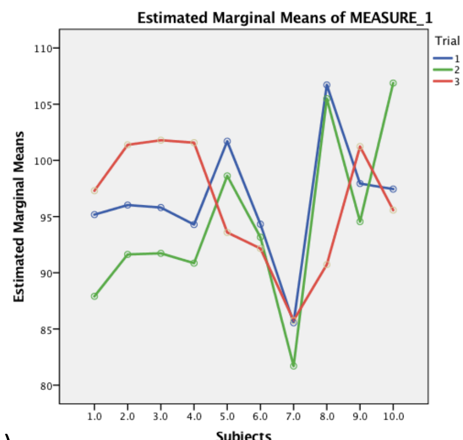
	Intraexaminer			**Interexaminer**		
Tooth	**ICC**	**Lower bound**	**Upper bound**	**ICC**	**Lower bound**	**Upper bound**
UR6	0.960	0.887	0.989	0.760	0.424	0.928
UL6	0.969	0.912	0.991	0.710	0.383	0.909
UR3	0.927	0.805	0.98	0.401	0.050	0.760
UL3	0.931	0.815	0.981	0.564	0.049	0.868
LR6	0.967	0.908	0.991	0.576	0.184	0.856
LL6	0.959	0.886	0.989	0.385	0.041	0.750
LR3	0.946	0.852	0.985	0.348	0.003	0.731
LL3	0.913	0.772	0.976	0.232	0.133	0.662

Table 2.8: Mean errors and standard deviations of CWRU angular measurements for intra-examiner and inter-examiner reliability testing (degrees).

	Intraexaminer		Interexaminer	
Tooth	**Mean Error**	**Standard Deviation**	**Mean Error**	**Standard Deviation**
UR6	1.053	0.505	3.800	2.084
UL6	1.268	0.552	5.874	5.075
UR3	2.001	0.897	3.860	2.405
UL3	1.591	0.944	5.041	4.119
LR6	0.846	0.639	3.980	3.814
LL6	1.187	0.519	3.887	2.591
LR3	1.146	0.428	4.980	2.429
LL3	1.281	0.512	3.153	1.938



a.)



b.)

Figures 2.4ab: Example scatter plot and profile plot of angular CWRU measurement with poor inter-examiner reliability, tooth LL3.

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Chapter 3: Comparison of two techniques for three-dimension measurement of buccolingual inclinations in maxillary transverse deficiencies

Introduction

Maxillary transverse deficiencies are one of the most prevalent skeletal craniofacial problems encountered by orthodontics, but typically this dimension is not necessarily fully considered during diagnosis[1]. Although no universal reference standard transverse diagnosis has been consistently supported based on the literature, most clinicians tend to make this diagnosis based on a combination of clinical signs and radiographic evaluation. Unfortunately the validity of a clinical diagnosis is hard to assess because maxillary deficiencies exist on a continuum and the threshold to identify patients as normal versus abnormal is not clearly defined. Therefore, it is difficult to clearly identify abnormal maxillary dimensions with a high degree of accuracy, which explains the lack of a universal reference standard for diagnosis in this dimension. Some clinical signs that are easily recognizable include the presence of anterior or posterior crossbites, degree of crowding, shape of the maxillary dental arch, height and width of the palatal vault and size of buccal corridors on smiling[1,2]. However, dental compensations in the form of bucally flared maxillary posterior teeth that camouflage a skeletal transverse deficiency may be difficult to detect clinically without considering radiographically the buccolingual inclination of roots[2,3].

Buccolingual tooth inclination is one of six characteristics of normal occlusion identified by Andrews that has been suggested contributes to successful and stable orthodontic treatment[4]. The ABO Objective Grading System states that to establish proper occlusion and avoid balancing interferences, there should not be an appreciable difference in the heights of buccal and lingual cusps of maxillary and mandibular molars[5]. This is typically assessed on dental models to identify the presence of an increased curve of Wilson with the lingual cusps of the maxillary posterior teeth extending below the occlusal plane[1]. The shortcoming of this measurement approach is that due to variation in dental crown anatomy, the occlusal surface inclination does not necessarily correspond to the actual long axis of the teeth[6]. Therefore, adequate assessment of buccolingual inclination requires radiographic evaluation to visualize root position within the alveolar bone and identify the long axis of the teeth. Although conventional postero-anterior cephalograms were previously considered an adequate method to identify transverse skeletal discrepancies[7] the use of 2D imaging for transverse diagnosis has fallen out of favor due to documented limitations that affect accuracy of landmark placement[8-10].

Three-dimensional assessment of buccolingual inclination of teeth has the potential to improve diagnosis in the transverse dimension and better supplement clinical information[11]. Although CBCT imaging is becoming more frequently utilized in clinical orthodontics, due to the improved imaging accuracy of 3D anatomy and unobstructed anatomical views, it's use must be justified by demonstrating a proven advantage in diagnosis and treatment planning[12]. Currently, the use of 3D imaging as a diagnostic tool is constrained to specific clinical scenarios by a lack of reproducible, quantifiable 3D analyses that demonstrate superior accuracy over traditional diagnostic methods[13].

There have already been attempts to develop 3D transverse analyses to identify and diagnose the dental and skeletal components of maxillary transverse deficiencies. Miner *et al.* [14] and Podesser *et al.* [15] developed transverse analyses for CBCT and CT scans respectively that evaluated dental and skeletal landmarks as well as buccolingual molar inclinations on standardized 2D coronal slices. Case Western Reserve University (CWRU) also developed a transverse analysis to assess buccolingual inclinations of maxillary and mandibular molars and canines using coronal slices of CBCT images[2]. The CWRU analysis evaluates angular dental measurements to identify the presence of dental compensations and aid clinicians in making decisions about the need for dental versus skeletal expansion with quantifiable numbers[2]. The main limitation of the above previously developed 3D transverse analyses is the underutilization of the 3D volumetric data by confining linear and angular measurements to 2D coronal slices that had to be consistently oriented. There is also a lack of confirmation as to the stability during craniofacial growth of the chosen measurement reference planes and the approach to the teeth by viewing the coronal slices that were not exactly perpendicular to the buccolingual plane[2,14-17].

Due to the limitations of these previously proposed 3D transverse analyses, there remains a need for the development of an analysis that fully utilizes 3D data. Maybe such approach would have more valid clinical implications. Studies have shown that 3D landmark identification from CBCT volumetric data is closer to anatomical measurements than conventional 2D measurements, and offers consistent and reliable data in the x, y & z planes when multiplanar (MPR) views and 3D renderings are used[18,19]. Swennen *et al*[20] recognized a need for voxel based 3D measurement analyses using a 3D Cartesian coordinate system. With a 3D Cartesian coordinate system, landmark derived x-y, x-z, y-z planes can be aligned using several identifiable landmarks, providing a way to standardize 3D image orientation[21,22]. A 3D volumetric landmark-derived maxillary reference plane has already been confirmed reliable and reproducible for CBCT superimposition using four accurate and reliable skeletal landmarks[23]. Using this previously establish 3D maxillary reference plane for image orientation and angular measurements, a 3D transverse analysis can be developed with potentially improved measurement accuracy of anatomical structures.

The purpose of this present study is therefore to develop a 3D transverse analysis that fully utilizes 3D data on a Cartesian coordinate system using the transformation method described by Lagravere *et al*[21,22] and the 3D maxillary reference plane described by Lemieux *et al*[23]. The second objective is to compare the buccolingual inclinations of maxillary and mandibular molars and canines between this novel 3D buccolingual analysis and the CWRU transverse analysis, which is a previously described 3D transverse analysis.

Materials & Methods

<u>Patient Selection</u>

The pre-treatment CBCT scans of 60 patients were randomly selected from a pool of patients that had clinically determined unilateral or bilateral crossbites involving more than a two teeth and had been identified as requiring maxillary expansion by two orthodontists as part of Lagravere *et al.* [24] randomized clinical trial at the University of Alberta. Ethics approval was obtained from the University of Alberta Research Ethics Board. The study population consisted of adolescents aged 11-17 years old with permanent dentition from first molar to first molar in both dental arches. Patients with partially erupted, unerupted or vertically impacted maxillary canines were included as this appeared quite prevalent in the patient pool of maxillary transverse deficiencies. Sex, type of maxillary expansion and chronological age were not considered because treatment effects or change over time are not being assessed in this study. A standardized protocol for the CBCT scans was used with the iCAT (iCAT, Imaging Science International, Hatfield, PA, USA. Large field of view 16cm x 13.3, voxel size 0.30mm, 120kVp, 18.54mAS, 8.9 seconds).

Avizo 3D Landmark Identification Technique: Alberta DS Transverse Analysis

Raw CBCT images were exported as DICOM files and loaded into Avizo version 8.1 software (Visualization Sciences Group, Burlington, MA, USA) for analysis. Using isosurface rendering and sagittal, axial and coronal multiplanar slices, 4 skeletal and 16 dental landmarks were reliably identified for measurement (Table 3.1, Refer to reliability chapter). All landmarks were placed using 0.25mm diameter virtual spherical markers with Avizo software using the center of the spherical markers to generate 3D coordinates in a standardized order. The 4 skeletal landmarks chosen (nasion, bilateral infraorbital foramina and the incisive canal) were previously identified by Lemieux[23] as being both accurate and reliable in creating a 3D anatomical Cartesian coordinate system from which a reproducible maxillary reference plane could be established.

In this current study, the same 3D maxillary reference plane that represents the xz-plane was used to obtain buccolingual angular measurements from. The reference plane was created by transforming the landmark points with MATLAB software as described in detail by Lagravere *et al.* [22] and was then represented on a global coordinate system for the CBCT scan. Four points were necessary to determine the orientation of the orthogonal Cartesian coordinate system on 3D craniofacial images. Nasion became the origin (0,0,0) of a new 3D coordinate system and the remaining 3 skeletal landmarks established the x, y and z planes (Figure 3.1). The yz-plane (y-axis) passes through the incisive foramen and nasion points, this makes the yz-plane split the skull down the center. The xy-plane (x-axis) is set using the infraorbital and nasion points. Finally, the xz plane (z-axis) is set by knowing that it must be orthogonal to the other two axes, needing only one point to define it, nasion. The xz-plane used for measurement reference is shown in Figure 3.2. The dental landmarks selected were as described in the CWRU analysis as the cusp tips and root apices of the maxillary and mandibular molars and canines to define the long axis of each tooth for buccolingual measurement[2,16,17]. As described in this study, this is how the long axis of the teeth was defined for only the related CWRU studies however, there is no literature defining exactly what ideal buccolingual root position should be or defines the true long axis of the teeth.

Three points are required to establish the buccolingual tooth plane for using Avizo software so additional points were placed at the most buccal contour of the middle third of each tooth, or the buccal cortex immediately adjacent to the tooth (Table 3.2). These points were meant to form a measurement plane so that the approach to each tooth for angular measurement was perpendicular to a buccolingual plane that ran directly through the long axis of each tooth (Figures 3.3 & 3.4). If only two points per tooth were used to construct a line instead of a measurement plane to intersect with the reference plane, cusp tip and root apex, the resulting measurement would be affected by mesiodistal tip and rotation, providing angles that do not reflect the buccolingual position of the measured tooth. Also, in 3D coordinate analysis use of only a line intersecting a 3D plane does not clearly define the measurement angle as there would be many angles that exist 360° around a single line. Instead, there needs to be two distinct 3D intersecting planes to identify one angle for measurement in 3D.

Coordinates were run through a MATLAB algorithm that was developed by ND and DS and modified from that previously described by Lagravere *et al.* [22] that both transformed the data to establish the 3D coordinate reference system and calculated the buccolingual angle formed by the intersection of the long axis of each tooth and the xz reference plane. This can be repeated for all teeth and the reference plane is constant for all angles measured off of the same patient scan. When viewing the established buccolingual plane for each tooth, the reference line and tooth line are shown in Figure 3. Eight buccolingual angular measurements were taken along the buccolingual plane that was created by placement of a third point on the buccal of each tooth (Figures 3.5a-d). The angles calculated from the developed algorithm, named as the Alberta DS transverse analysis, were confirmed by hand with a protractor on a select few cases prior to running all 60 case coordinates with the MATLAB software.

CWRU Transverse Analysis

Using Dolphin Imaging 11.7 Premium (Dolphin Imaging & Management Solutions, Chatsworth, CA, USA) CBCT dicom files were uploaded and oriented in the sagittal, axial and coronal views following a standardized approach (Figure 3.6) The developed technique to consistently orient CBCT images and measure buccolingual inclinations of maxillary and mandibular molars and canines from a 2D coronal slice was shown to be reliable and is described in Figures 3.7-3.10[2,16,17,25]. For maxillary molars, the angle measured was that formed by the inferior border of the nasal cavity with a line passing through the apex of the maxillary first molar palatal root to mesial palatal cusp tip. Maxillary canine inclinations were measured by the angle formed between the line tangent to the inferior border of the nasal cavity and the long axis of the tooth. For mandibular molars, inclinations were obtained by measuring the angle between the inferior border of the mandible and a line passing through the central groove and root apex. Mandibular canine inclinations are measured at the angle between a line tangent to the inferior border of the mandible and the line through the long axis of the tooth. All angles were shown to have high intraexaminer reliability (refer to reliability chapter) [16,17,25].

Statistical Analysis

A sample size calculation was not completed for this study as 60 records of pre-treatment CBCT scans were deemed adequate in determining the significance of the results. All statistics were analyzed using standard statistical software package (SPSS Statistics version 23 for Mac, IBM). Descriptive statistics were generated for each of the 8 continuous dependent variables, including the mean absolute and mean relative difference of angular measurements between the two methods. A paired-observations multivariate analysis of variance (MANOVA) of the absolute difference between the two methods was used to determine significance and test the null hypothesis that there is no difference between the two methods of buccolingual measurement. A p value of less than 0.05 was considered significant. Of note, for radiographic angular measurements an absolute difference ≥ 10° was considered clinically significant. This clinical significance level was based on twice the mean standard deviation of the normative data collected by Streit *et al.* [25] A clinical significance of two standard deviations was chosen to encompass 95% of the data distribution such that anything outside of this range would be considered abnormal. At this level, differences or changes in measurements could demonstrate a practical difference that has a noticeable, meaningful treatment effect. Frequency of the angular measurements between the two methods having a difference of more then 10° was reported to aid in understanding the variability of the two methods.

Prior to statistical analysis, model assumptions were assessed. The MANOVA is robust to violations of normality and homogeneity of variance if groups are of equal size, as is the case for this data set. The data was checked for multivariate normality and presence of outliers prior to hypothesis testing with the MANOVA. This was completed visually via a box plot and normal Q-Q plot of the Mahalanobis distance of the difference between the CWRU and Alberta DS transverse analysis values..

Results

Descriptive statistics of the absolute mean difference between methods is summarized in Table 3.3, relative mean differences were noted as well. Multivariate normality and outliers was assessed using a box plot and a Q-Q plot of the Mahalanobis distance (Figure 3.11a & 3.11b), before MANOVA testing was completed. Three multivariate outliers were identified in the slightly right-skewed data set. Hypothesis testing using MANOVA was run both with and without the identified outliers and no difference in the resulting *p*-values was noted therefore, all further statistics were completed with outliers included. The paired-observations MANOVA revealed strong evidence of a statistically significant difference between the CWRU and Alberta DS transverse analysis, $F(8, 52) = 132.345$, $p < 0.001$, Wilks' Lambda = 0.047 (Table 3.4). Follow-up univariate ANOVAs indicated that the CWRU transverse analysis and the Alberta DS transverse analysis measurements were significantly different for all 8 measured teeth (Table 3.5).

- Maxillary right first molar (UR6) differed by 7.97degrees (95% CI: 7.00 - 8.93, $p < 0.001$)
- Maxillary left first molar (UL6) differed by 7.78 degrees (95% CI: 6.59 – 8.96, $p < 0.001$)
- Maxillary right canine (UR3) differed by 13.93 degrees (95% CI: 12.34-15.51, $p < 0.001$)
- Maxillary left canine (UL3) differed by 15.96 degrees (95% CI: 14.21-17.72, $p < 0.001$)

- Mandibular right first molar (LR6) differed by 2.74 degrees (95% CI: 2.22-3.26, $p < 0.001$)
- Mandibular left first molar (LL6) differed by 3.08 degrees (95% CI: 2.50-3.66, $p < 0.001$)
- Mandibular right canine (LR3) differed by 5.30 degrees (95% CI: 4.30-6.29, $p < 0.001$)
- Mandibular left canine (LL3) differed by 5.74 degrees (95%CI: 4.59-6.90, $p < 0.001$)

The frequency with which the difference between the two measurement methods was below a clinically significant value of 10 degrees is reported in Table 3.6. Of the teeth measured, mandibular first molars showed no clinically significant difference between methods demonstrating a less than 10-degree difference at 100% and 98.3% of the time for right and left molars respectively. Maxillary canines most frequently demonstrate a clinically significant difference between measurement techniques having a less than 10-degree difference only 18.3% and 15% of the time for right and left canines respectively.

Clinical Applications

The following is a presentation of clinical cases identified as having maxillary transverse deficiencies through conventional clinical methods. The buccolingual inclinations of molars and canines of each case were assessed before starting treatment and 6 months after rapid maxillary expansion using both CBCT buccolingual measurement methods. The intention is to demonstrate how these analyses aid in identifying the skeletal and dental components of maxillary constrictions prior to treatment and if they demonstrate similar changes in buccolingual inclinations following maxillary expansion treatment. The norms presented by Streit *et al.* [25] (Figure 3.12) for the CWRU transverse analysis will be referred to as currently normative data has not been developed for the Alberta DS transverse analysis presented in this paper. The change in buccolingual inclinations seen from pre-expansion to post-expansion was compared between methods. The cases shown were treated with simultaneous anterior maxillary bonding, full mandibular arch bonding and insertion of a hyrax for semi-rapid expansion. Hyrax appliances were removed after 6 months from insertion at which point progress CBCT images were taken. Buccolingual inclinations of first maxillary molars will only be discussed for the following cases as the post-expansion records taken at 6 months of treatment do not represent completion of other treatment goals, but best reflect the changes seen in first maxillary molars immediately following hyrax expansion.

Pre-treatment maxillary first molar inclinations for case #1 (Figure 3.13) are shown in Table 3.7, the right first maxillary molar was 88.5° and the left first maxillary molar was 108°. Comparing these to CWRU normative values (Figure 3.12) reveals the right maxillary molar was lingually inclined pre-treatment. However, the left maxillary molar was flared bucally beyond normative values and was still in crossbite supporting the need for skeletal expansion with use of a hyrax. Post-treatment buccolingual inclinations of 89.1 and 106.8 for right and left first maxillary molars respectively demonstrate a non-clinically significant buccolingual change with hyrax treatment suggesting the majority of the short-term expansion achieved was skeletal with bodily movement of the maxillary molars rather than buccal flaring (Figure 3.14). The buccolingual inclination change seen with hyrax treatment measured by the Alberta DS transverse analysis is similar to the change shown with the CWRU measurements with only a 1-2° change that is not clinically significant and could simply be attributed to measurement error.

The pre-treatment CWRU buccolingual inclinations for case 2 (Figure 3.15) show the right first maxillary molar was outside the normative range, bucally compensated for a skeletal deficiency with an inclination of 107.4° whereas the left first maxillary molar was within the normative range at 99.0°. Following hyrax expansion (Figure 3.16), both molars ended up within a normative range at 99.7° and 98.6° for right and left molars respectively. This demonstrated not only successful skeletal expansion but an actual improvement in the originally compensated, bucally flared right maxillary molar which may be explained by variability in appliance manufacturing, fitting and cementation. The Alberta DS transverse analysis buccolingual measurements also reflected this reduction seen in the buccolingual inclination of the right first maxillary molar following hyrax treatment although the magnitude of change was different between the two methods. The differences seen between the right and left molars in response to expansion could be due to variability and asymmetry in the vertical position of molar bands at cementation or simply due to measurement error.

The final case presented (Figure 3.17) began with pre-treatment buccolingual inclinations that indicated the right first maxillary molar was lingually inclined prior to treatment at 93.5° and the left maxillary molar was within the normative range at 99.7°. Following treatment buccolingual inclinations increased to 99.4° for the right molar into a normative range and 106.6° for the left indicating buccal flaring that was potentially the result of overexpansion as seen in Figure 3.18. Both molars tipped bucally about 5°

and a similar magnitude increase in buccolingual inclination was also shown with the Alberta DS transverse technique.

Discussion

Orthodontic assessment and treatment of maxillary transverse deficiencies focuses on centering teeth above their basal bone upright within the alveolus while establishing proper intercuspation and coordination between the dental arches. Therefore, proper diagnosis of the transverse dimension involves identifying the presence of dental compensations resulting from jaws that do not relate well to each other[26]. When maxillary molars are excessively bucally flared to compensate for maxillary constrictions, the lingual cusps hang below the occlusal plane exaggerating the curve of Wilson[27]. This can lead to CR-CO discrepancies that vertically distract the condyles[28], cause periodontal stress and recession[29] and result in working and non-working side interferences that may lead to increased masticatory muscle activity[30]. Since transverse maxillary skeletal and dental widths and mandibular dental widths can be orthodontically modified, it is important to be able to identify dental compensations to improve diagnostic accuracy and effectiveness of maxillary expansion treatment[2].

With the increased clinical utilization of 3D imaging and a general awareness of the higher radiation associated with its use, it becomes necessary to develop and validate 3D analyses that aid in quantifying malocclusions and improve orthodontic diagnosis to justify CBCT use. There is speculation that CBCT imaging may provide information that results in enhanced diagnosis and improved ability to define transverse deficiencies but a lack of clinically validated 3D analyses that demonstrate superior accuracy constrains the use of CBCT as a routine diagnostic tool[13].

This present study aimed at developing and testing the reliability of a novel 3D analysis for assessing dental compensations by measuring molar and canine buccolingual angulations by fully utilizing the 3D nature of CBCT dicom images. Our findings were compared to an existing transverse analysis that used 3D images for 2D buccolingual measurements on true coronal sections, the CWRU transverse analysis[2,16,17,25]. The Alberta DS transverse analysis presented demonstrated excellent reliability (refer to reliability chapter), but was statistically significantly different from the CWRU buccolingual angular measurements for all assessed teeth. The real direction of those changes is impossible to figure out without a reference standard to demonstrate ideal position. This statistical difference can mainly be attributed to the different reference planes utilized by the two methods. Considering a clinically significant difference of only 10 degrees, all measured teeth except maxillary canines, did not demonstrate clinically significant differences between methods. Mandibular molar buccolingual angular measurements differed between the two methods by only 2-3 degrees. These findings are consistent with those of Shewinvanakitkul *et al.* [16], where the approach to mandibular molars was not exactly perpendicular to the buccolingual plane. Shewinvanakitkul[16] completed a pilot study to compare the perpendicular buccolingual approach and a parallel to the midline approach, or a true coronal section, acknowledging that mesio-distal inclination and rotation will influence buccolingual angulation when it is not assessed exactly perpendicular to the buccolingual plane. Their pilot study identified a difference of only 2 degrees, similar to the difference seen between the two compared methods in this study, which is not clinically significant.

The largest difference between compared methods was noted for both maxillary canines at 13-15 degrees. Maxillary canines were the only teeth assessed with the CWRU transverse analysis in which the tooth was approached perpendicular to the buccolingual plane, same as the approach to all teeth with the newly proposed 3D volumetric method. Although approach to the tooth was similar, we see the largest difference, which can be attributed to the different reference planes utilized between methods. The 3D Cartesian coordinate xz-plane was different from the CWRU inferior border of the nasal cavity reference plane by about 15 degrees when the canine is viewed perpendicular to the buccolingual plane. Maxillary molars demonstrated a difference of about 7-8 degrees between the two methods, which was deemed not clinically significant and can be explained by both the different approaches to these teeth and the different reference planes used between the two methods. It is pertinent to note that with no studies to support the clinical validity and accuracy of either method, the true position of the teeth is unknown and hence it is unknown which measurement method is closer to the anatomical truth.

The three clinical cases presented demonstrated variable responses although treatment approaches were similar. This can be due to variability in ages, variability of relative vertical position of the cemented bands and sutural maturation at the time of hyrax expansion such that different skeletal expansion responses occurred. It is pertinent to recognize that these two buccolingual analyses only determine dental angulations, they do not directly measure skeletal response or quantify the extent of a skeletal deficiency.

The Alberta DS transverse analysis presented in this study was unique in that previously described CBCT transverse analyses for assessing buccolingual dental compensations associated with maxillary transverse deficiencies have been limited to 2D measurements of true coronal sections[14-17,25] There are no previous studies that propose a 3D transverse analysis that fully utilizes 3D data and approaches the teeth perpendicular to the buccolingual plane. The University of Pennsylvania has developed a CBCT transverse analysis that assessed maxillary and mandibular skeletal basal widths but this analysis as well only utilized 2D coronal slices, recognizing the limitations of not evaluating slices that are perpendicular to the alveolus being identified for landmark placement[26]. Initial landmark identification with the Alberta DS transverse analysis is easier than drawing the CWRU angles in Dolphin. However, the requirement of running CBCT landmarks through a software algorithm separate from the program in which landmarks are actually identified in does make the Alberta DS transverse analysis more time consuming and cumbersome than the CWRU transverse analysis. Integration of the developed analysis algorithm into a 3D program used for landmark identification would make use of the newly proposed technique more practical and friendly for clinicians.

Various other studies have proposed 3D tools for buccolingual measurements and have used several different horizontal references planes including palatal, mandibular and occlusal reference planes[31]. With growth and treatment, changes to these reference planes can compromise the validity of tooth inclination measurements[31]. As a result, an accurate and error free technique for 3D buccolingual measurements has yet to be proposed. The 3D skeletal reference plane used in the development of the Alberta DS transverse analysis although has been shown to be accurate and reproducible[23], its stability over time in response to growth has yet to be examined. The superior location of the 4 skeletal landmarks that established our 3D maxillary reference plane can potentially imply this 3D maxillary reference plane is more stable over the course of treatment than other horizontal reference planes that are closer to the skeletal and dental units that are being altered with orthodontic treatment but the stability of these skeletal landmarks has yet to be verified.

Although this novel transverse analysis fully utilizes the 3D potential of CBCT images and approaches teeth perpendicular to their buccolingual plane, it cannot be concluded that it this analysis improves quantification of buccolingual inclinations. It has been shown to be reliable but future studies are required to assess the accuracy and clinical validity of its use as well as the stability of the 3D maxillary reference plane over time. The accuracy of the Alberta DS transverse analysis could be confirmed by developing a method to compare to dry skull craniometric measurements similar to that described by Tong *et al.* [32]. Their study involved use of transparent plastic anatomic typodont maxilla and mandible with synthetic teeth and stainless steel balls placed a cusp tips and apices, mounted on a dry human skull. The ability to compare to craniometric measurements would allow confirmation of the accuracy of this newly proposed method. Along with confirming accuracy and validity, further research is needed to develop and test normative data and assess clinical outcomes with the diagnostic utilization of this analysis for quantifying dental compensations and maxillary transverse deficiencies.

Conclusion

In this study we developed a novel 3D method for assessing buccolingual inclinations of mandibular and maxillary molars and canines on a 3D Cartesian coordinate system, utilizing a 3D maxillary reference plane. Excellent reliability of the method was confirmed, but there were significant differences between this newly proposed method and the already described CWRU transverse analysis, attributed to the use of different reference planes. Although accuracy and diagnostic clinical applicability is yet to be studied, this method offers a promising step forward in justifying the use 3D imaging by fully utilizing the 3D potential of CBCT images which may potentially lead to improved diagnosis and more effective treatment outcomes.

Appendix

Table 3.1 – Avizo Landmark Descriptions (Refer to Chapter 2 appendix for detailed images)

1	Nasion
2	Right infraorbital foramen
3	Left infraorbital foramen
4	Incisive foramen
5	Maxillary right 1st molar palatal root apex
6	Maxillary right 1st molar palatal cusp tip
7	Maxillary left 1st molar palatal root apex
8	Maxillary left 1st molar palatal cusp tip
9	Maxillary right canine apex
10	Maxillary right canine cusp tip
11	Maxillary Left canine apex
12	Maxillary Left canine cusp tip
13	Mandibular right 1st molar mesial root apex
14	Mandibular right 1st molar central groove
15	Mandibular left 1st molar mesial root apex
16	Mandibular left 1st molar central groove
17	Mandibular right canine apex
18	Mandibular right canine cusp tip
19	Mandibular left canine apex
20	Mandibular left canine cusp tip

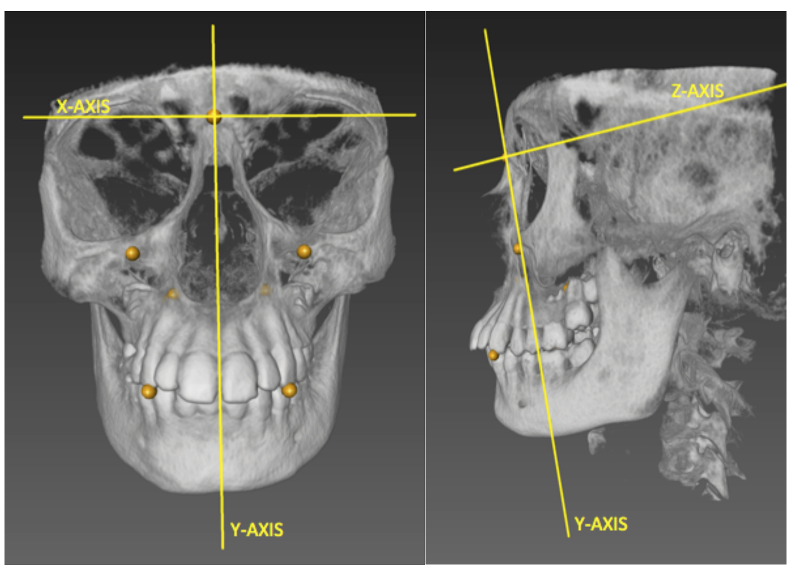


Figure 3.1: 3D Cartesian coordinate system established using 4 skeletal landmarks, nasion, bilateral infraorbital foramen and incisive foramen.

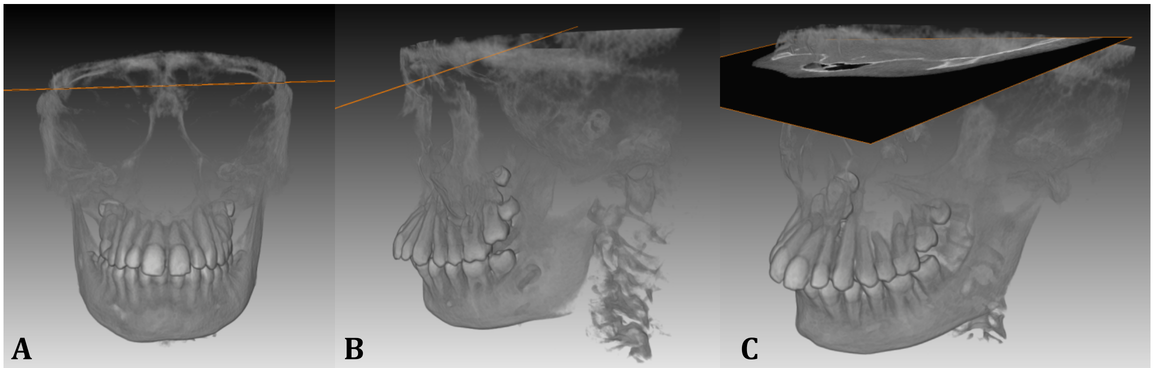
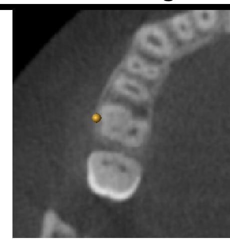
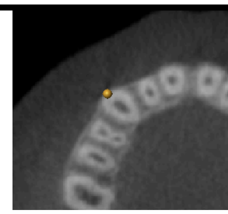
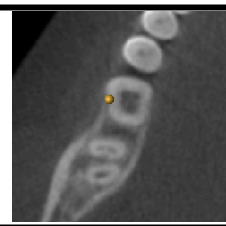
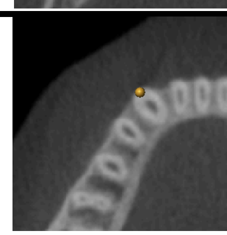


Figure 3.2. Frontal (A), Lateral (B), and isometric (C) views of the reference plane.

Table 3.2: Axial views and descriptions of the additional landmarks required to orient a buccolingual measurement plane for each tooth.

Tooth	Description	Axial Image
Maxillary first molar (Bilateral)	Adjacent buccal cortex, between cusp tip and apex, centered relative to the center of the tooth from the axial view.	
Maxillary canine (Bilateral)	Adjacent buccal cortex, between cusp tip and apex, centered relative to the center of the tooth from the axial view.	
Mandibular first molar (Bilateral)	Most buccal portion of the tooth at the root trunk.	
Mandibular canine (Bilateral)	Adjacent buccal cortex, between cusp tip and apex, centered relative to the center of the tooth from the axial view.	

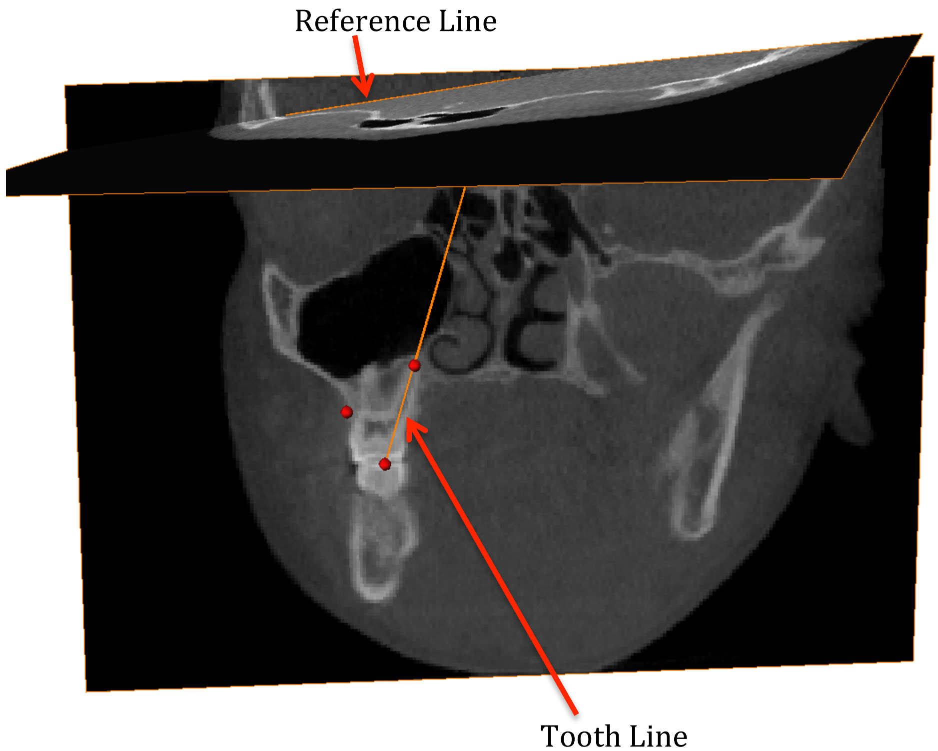


Figure 3.3. The reference line and tooth line are shown for the maxillary right first molar along the buccolingual plane. The reference line is taken as the intersection of the reference plane and tooth plane. The tooth line is created by extending a line between the palatal root apex and palatal cusp tip of the tooth.

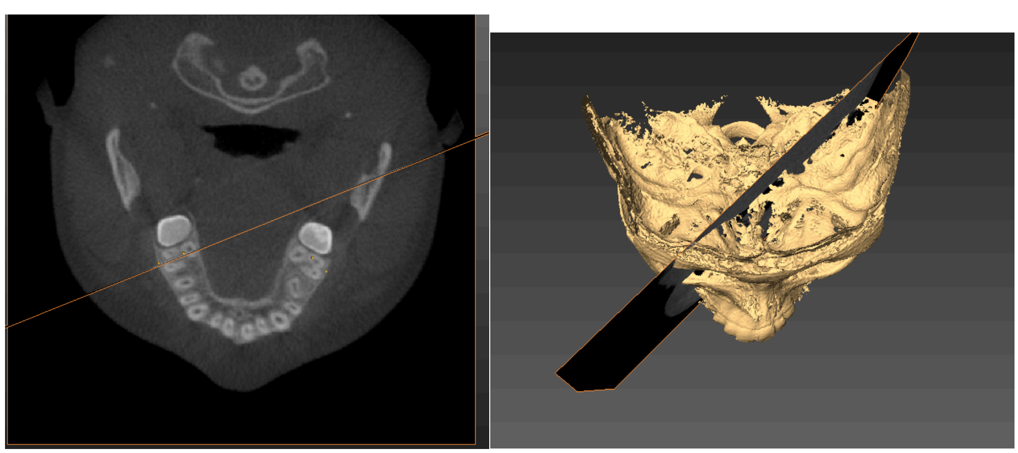


Figure 3.4. The buccolingual tooth plane from which angular measurements were taken.

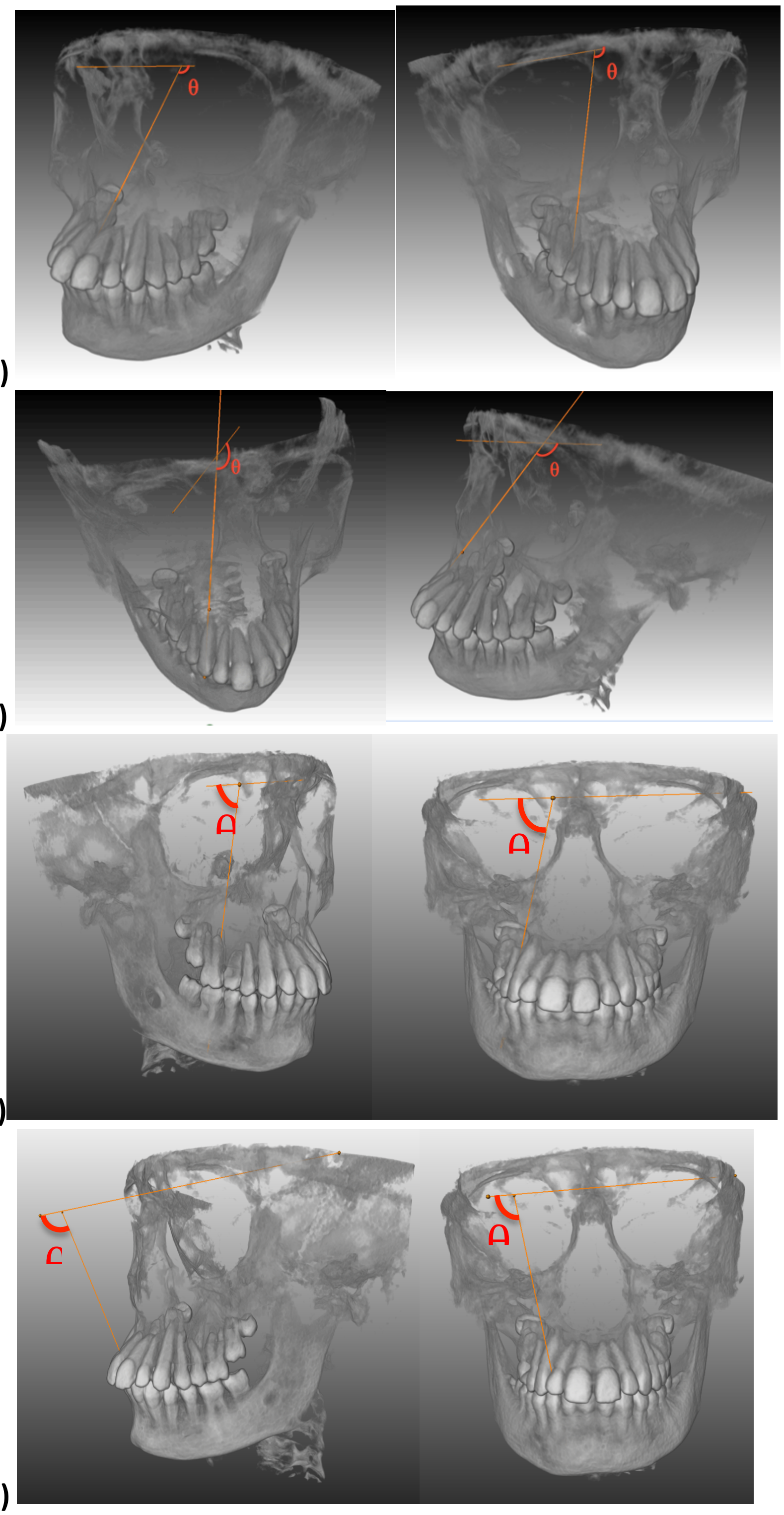

A.) B.) C.) D.)

Figure 3.5: Measured buccolingual angle between the long axis of each tooth and the reference plane along the established buccolingual plane for each tooth **A.)** Maxillary right first molar **B.)** Maxillary right canine **C.)** Mandibular right first molar **D.)** Mandibular right canine.

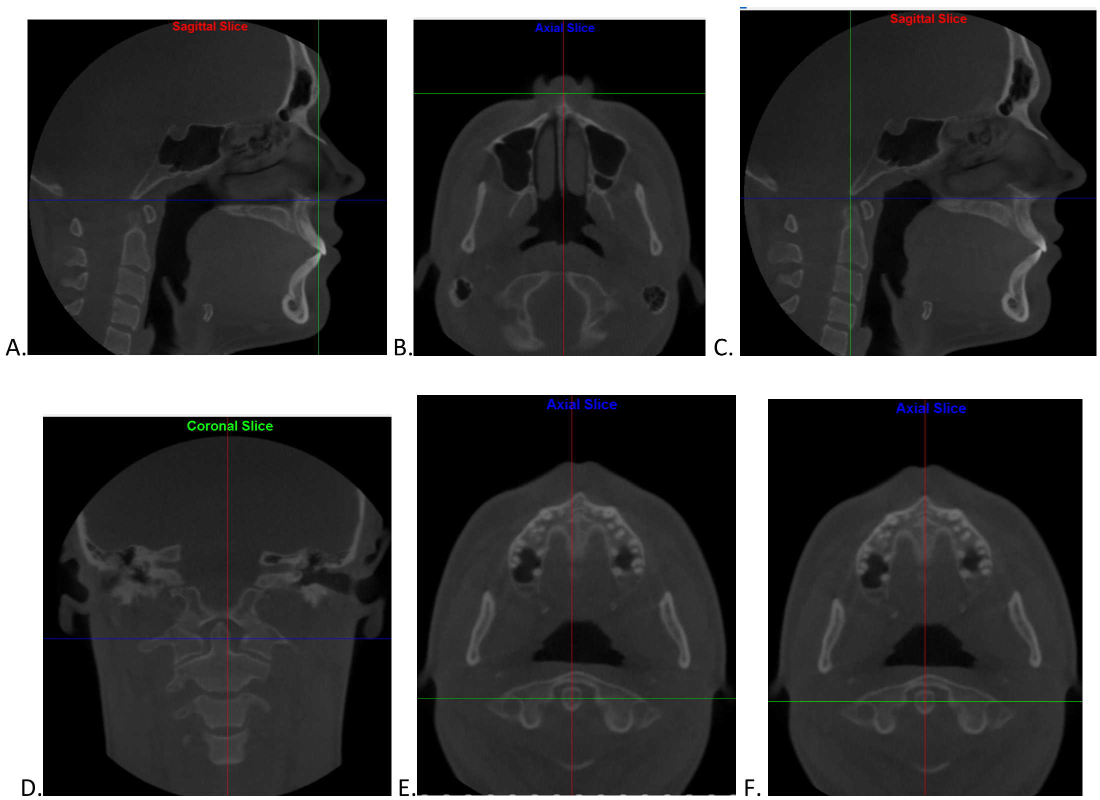


Figure 3.6: CWRU standardized CBCT image orientation procedure. A.) In the sagittal view, move the cross to ANS B.) In the axial view, move the red vertical line to bisect ANS C.) In the sagittal view, move the green vertical line to bisect the vertebrae D.) In the coronal view, move the blue horizontal line down to bisect atlas E.) In the axial view, move the red vertical line to bisect odontoid process F.) Rotate the slice around odontoid process so the red line bisects ANS as well

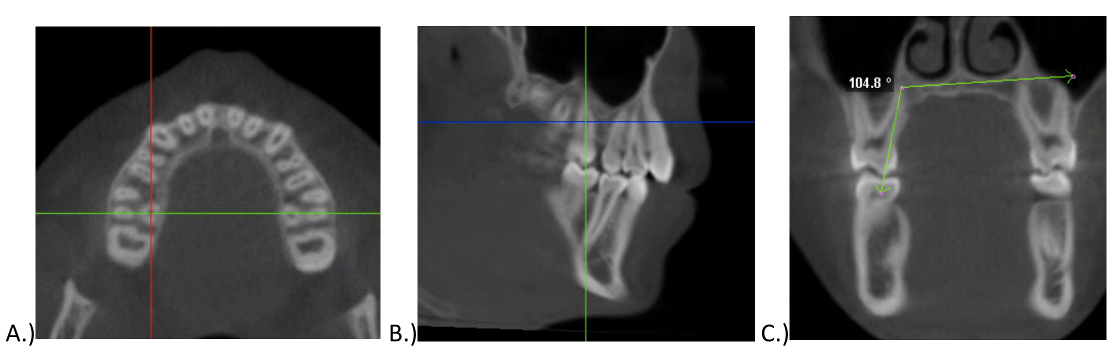


Figure 3.7: CWRU maxillary 1st molar inclination measurement A.) Locate the palatal root in axial view B.) In sagittal view, position the coronal slice line along the long axis (mesiopalatal cusp tip to palatal root apex) C.) In coronal view, draw the reference line tangent to inferior border of the nasal cavity then measure the inclination through the long axis of the molar.

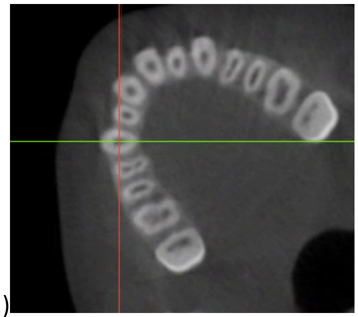
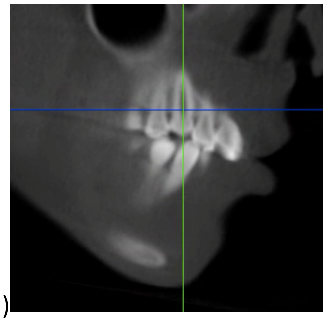
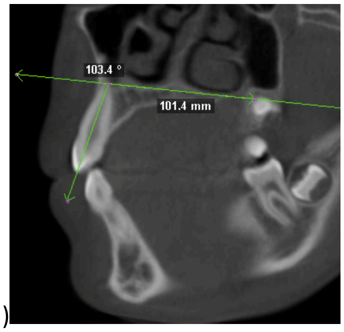
A.)  B.)  C.) 

Figure 3.8: CWRU maxillary canine inclination measurement A.) Locate the canine in axial view and rotate the image so the vertical line representing the sagittal plane is tangent to the buccal cortical plate B.) In sagittal view, position the coronal slice line along the long axis of the tooth C.) In coronal view, draw the reference line tangent to the inferior border of the nasal cavity then measure the inclination through the long axis of the canine.

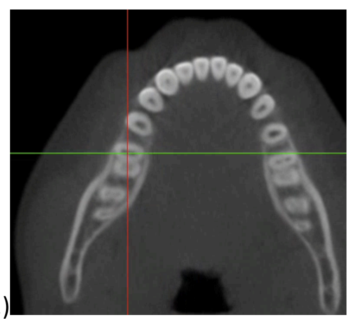
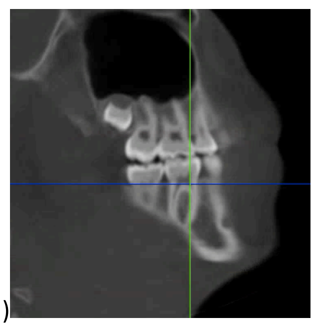
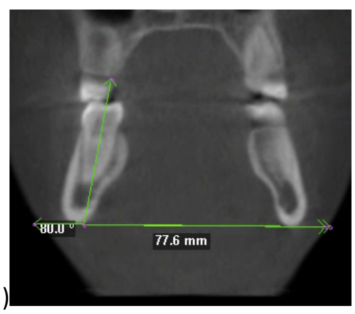
A.)  B.)  C.) 

Figure 3.9: CWRU mandibular 1st molar inclination measurement A.) Locate the molar in the axial view B.) In the sagittal view, position the coronal slice line along the long axis of the tooth (mesial cusp tip to mesial root apex) C.) In the coronal view, draw a reference line tangent to the inferior border of the mandible then measure the inclination through the long axis of the tooth.

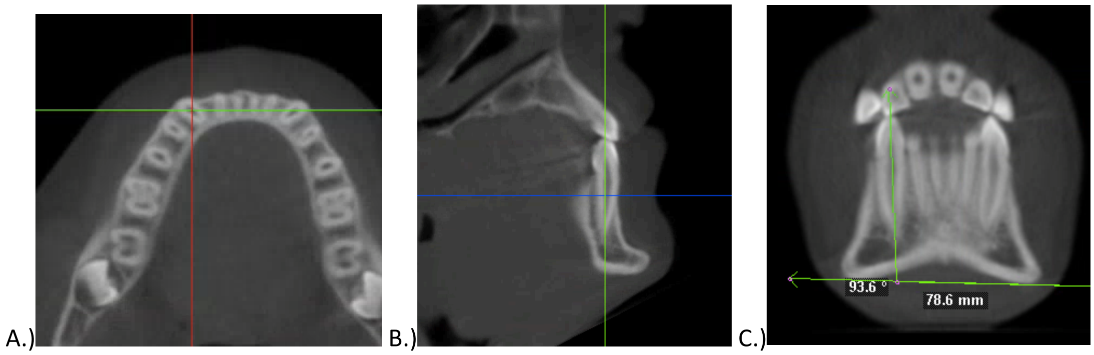
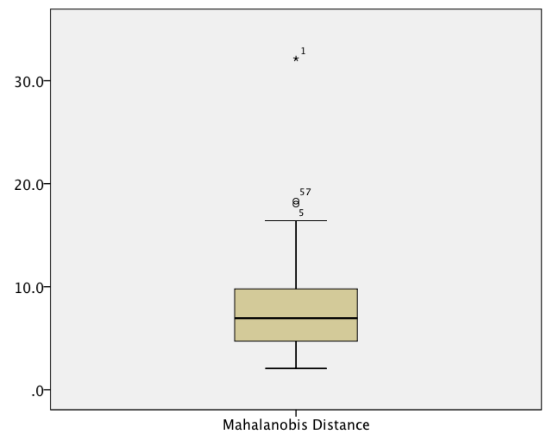


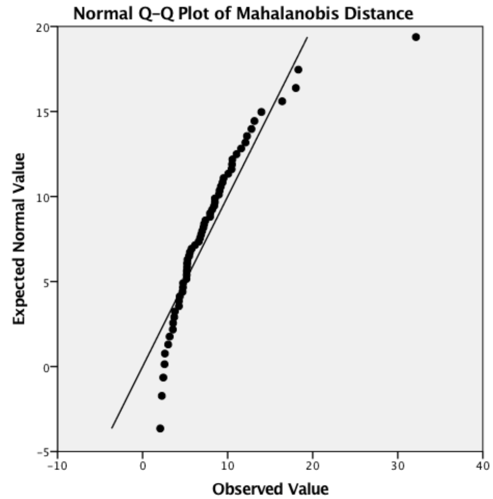
Figure 3.10: CWRU mandibular canine inclination measurement A.) Locate the canine in the axial view B.) In the sagittal view, position the coronal slice line along the long axis of the tooth (cusp tip to root apex) C.) In the coronal view, draw a reference line tangent to the inferior border of the mandible then measure the inclination through the long axis of the tooth.

Table 3.3: Descriptive statistics measured in degrees. Mean, standard deviation, mean error and 95% confidence intervals of absolute differences. Relative difference is 3D volumetric – CWRU transverse analysis.

	Absolute Mean Difference	Standard Deviation	Standard Error	95% CI Lower Bound	95% CI Upper Bound	Relative Mean Difference
UR6	7.98	3.75	0.48	7.00	8.93	7.91
UL6	7.78	4.58	0.59	6.59	8.96	7.29
UR3	13.93	6.12	0.79	12.34	15.51	13.93
UL3	15.96	6.80	0.88	14.21	17.72	15.90
LR6	2.74	2.00	0.26	2.22	3.26	-1.09
LL6	3.08	2.24	0.29	2.50	3.66	-0.42
LR3	5.30	3.86	0.50	4.30	6.29	0.78
LL3	5.74	4.46	0.58	4.59	6.90	-0.91



A.



B.

Figure 3.11: Box plot (A) and Q-Q plot (B) of the Mahalanobis distance of the absolute difference between methods.

Table 3.4: Paired –observations multivariate test results.

Effect Intercept	Value	F	Hypothesis df	Error df	Sig.
Pillai's Trace	.953	132.345	8.000	52.000	.000
Wilks' Lambda	.047	132.345	8.000	52.000	.000
Hotelling's Trace	20.361	132.345	8.000	52.000	.000
Roy's Largest Root	20.361	132.345	8.000	52.000	.000

Table 3.5: Tests of between subject effects, univariate ANOVAs.

Dependent Variable	Type III Sum of Squares	df	Mean Square	F	Sig.
UR6diff	3806.539	1	3806.539	270.640	.000
UL6diff	3629.934	1	3629.934	172.756	.000
UR3diff	11635.268	1	11635.268	210.593	.000
UL3diff	15289.114	1	15289.114	331.056	.000
LR6diff	450.211	1	450.211	112.211	.000
LL6diff	569.551	1	569.551	113.461	.000
LR3diff	1682.290	1	1682.290	113.140	.000
LL3diff	1979.412	1	1979.412	99.543	.000

Table 3.6: Frequency with which the two measurement methods differed less than 10 degrees.

Tooth	No. of cases where both methods differed less than 10 degrees	Frequency
Maxillary right first molar (UR6)	43/60	71.7%
Maxillary left first molar (UL6)	38/60	63.3%
Maxillary right canine (UR3)	11/60	18.3%
Maxillary left canine (UL3)	9/60	15.0%
Mandibular right first molar (LR6)	60/60	100%
Mandibular left first molar (LL6)	59/60	98.3%
Mandibular right canine (LR3)	52/60	86.7%
Mandibular left canine (LL3)	51/60	85.0%

Figure 3.12: CWRU Transverse analysis normative values

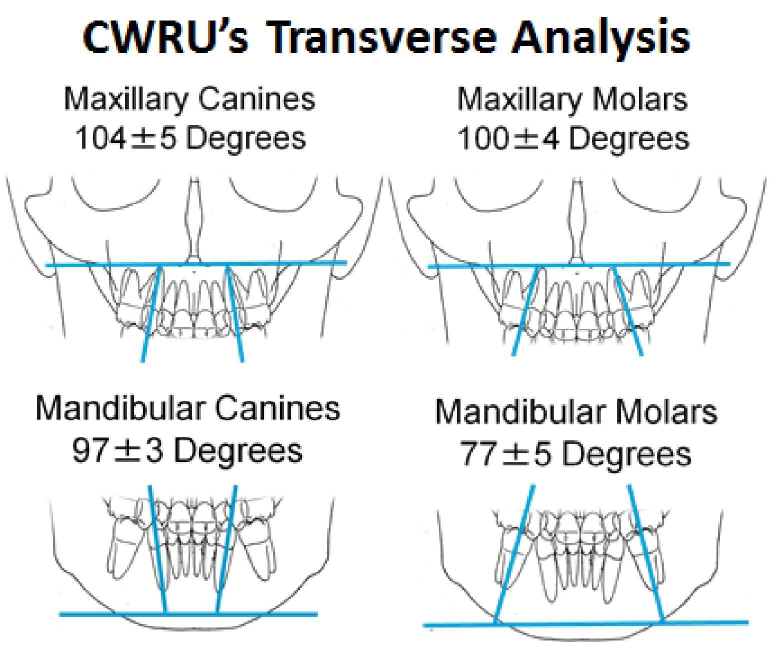


Figure 3.13: Case 1 initial composite exhibiting bilateral posterior crossbite

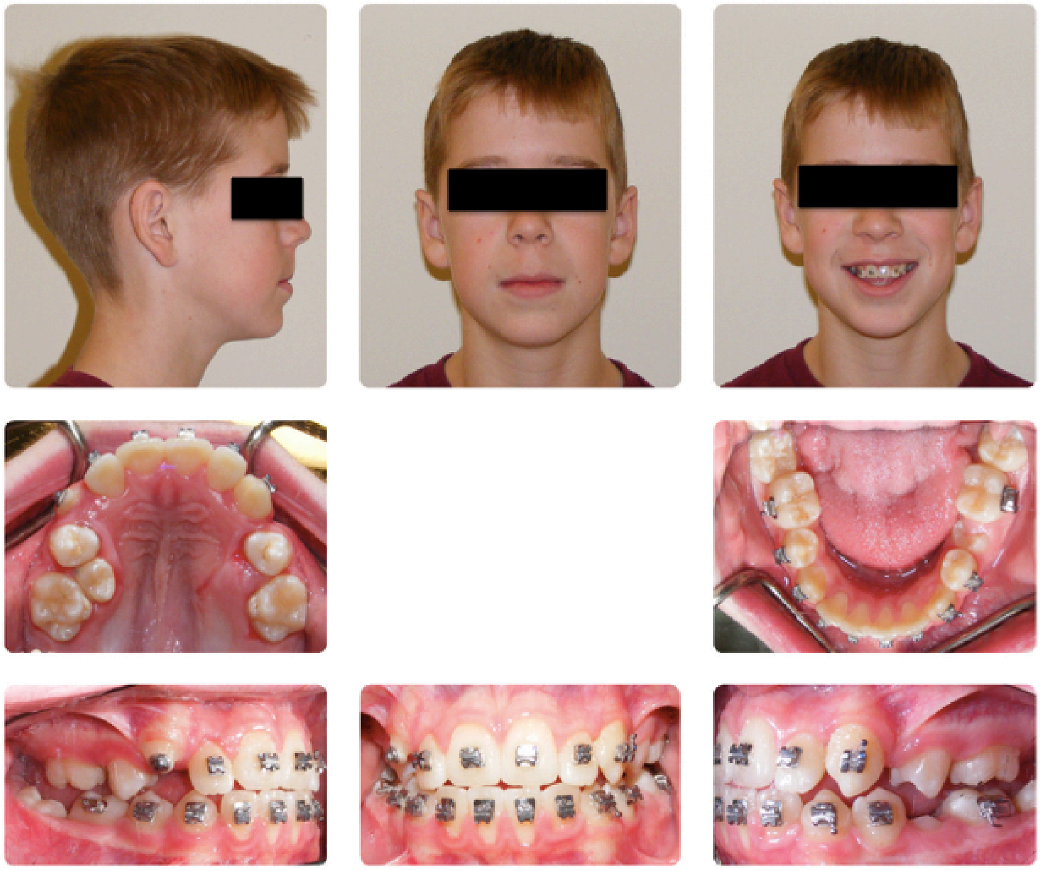


Figure 3.14: Case 1 6 month progress after hyrax removal.

Figure 3.15. Case 2 initial composite exhibiting bilateral posterior crossbite.

Figure 3.16. Case 2 6 months progress after hyrax removal, maxillary posterior brackets were placed at time of hyrax removal.

Figure 3.17: Case 3 initial composite exhibiting bilateral posterior crossbite

Figure 3.18: Case 3 6 months progress after hyrax removal

Table 3.7: Pre and post hyrax expansion buccolingual inclinations with both measurement techniques.

Case	Landmark Name	CWRU	Avizo	6mo CWRU	6mo Avizo	Δ CWRU	Δ Avizo
1	Max right first molar (UR6)	88.50	96.76	89.1	95.32	0.60	-1.44
1	Max left first molar (UL6)	108.00	105.23	106.8	107.34	-1.20	2.11
1	Max right canine (UR3)	107.90	119.58	111.5	118.40	3.60	-1.18
1	Max left canine (UL3)	124.10	121.98	111.1	120.78	-13.00	-1.21
1	Mand right first molar (LR6)	68.70	74.96	69	69.81	0.30	-5.15
1	Mand left first molar (LL6)	61.30	71.91	67.3	67.85	6.00	-4.06
1	Mand right canine (LR3)	96.00	94.28	99.6	100.00	3.60	5.72
1	Mand left canine (LL3)	96.10	101.39	88.9	94.21	-7.20	-7.18
2	Max right first molar (UR6)	107.40	111.96	99.7	107.72	-7.70	-4.23
2	Max left first molar (UL6)	99.00	106.90	98.6	104.55	-0.40	-2.36
2	Max right canine (UR3)	98.00	115.22	110.6	122.93	12.60	7.71
2	Max left canine (UL3)	86.70	115.62	98.2	121.00	11.50	5.38
2	Mand right first molar (LR6)	78.50	78.71	78	74.75	-0.50	-3.96
2	Mand left first molar (LL6)	86.30	83.26	79.1	76.19	-7.20	-7.07
2	Mand right canine (LR3)	99.80	96.64	97.6	95.30	-2.20	-1.34
2	Mand left canine (LL3)	92.60	91.89	92.6	93.76	0.00	1.88
3	Max right first molar (UR6)	93.50	100.39	99.4	107.21	5.90	6.82
3	Max left first molar (UL6)	99.70	105.21	106.6	109.91	6.90	4.70
3	Max right canine (UR3)	113.40	126.42	104	118.96	-9.40	-7.46
3	Max left canine (UL3)	108.50	126.43	104.7	123.15	-3.80	-3.28
3	Mand right first molar (LR6)	73.40	74.22	68	67.17	-5.40	-7.05
3	Mand left first molar (LL6)	69.40	74.70	72.1	74.64	2.70	-0.06
3	Mand right canine (LR3)	95.00	93.79	89.1	90.14	-5.90	-3.65
3	Mand left canine (LL3)	95.30	96.41	88	92.02	-7.30	-4.39

General Discussion & Major Conclusions

Discussion

This research project began with a plan to develop a novel 3D analysis similar to the previously described CWRU transverse analysis that measures buccolingual dental inclinations, but with the intention of overcoming the limitations of this existing transverse analysis. The main limitations identified in the CWRU transverse analysis are the concern for identifying a stable and reliable source of reference to determine buccolingual inclinations. Also, measurements were conducted from 2D coronal slices rather than approaching teeth exactly perpendicular to the buccolingual plane of the long axis of each tooth. Therefore there is not complete use of the available 3D information.

Three research objectives were proposed for this thesis as follows:

Objective #1: Reliability Assessment

a.) To identify and assess the repeatability and reproducibility of dental and skeletal landmarks on three-dimensional images that will be used to establish 3D reference and measurement planes in developing a novel transverse analysis.

Of the 16 dental and 4 skeletal landmarks assessed using MPR views and 3D reconstructions, all demonstrated good to excellent intra- examiner and inter-examiner reliability. The mean errors did not exceed 1mm, suggesting that the variability that was present between time points for a single observer and between three different observers were not clinically relevant. These results support that the landmarks identified to develop our novel 3D analysis can be adequately visualized on CBCT images. With relatively easily identifiable landmarks the Alberta DS Transverse Analysis can be reliably standardized among clinicians after appropriate training and familiarization of the use of MPR views and 3D surface renderings to identify landmarks. Since clinicians are only required to identify the point landmarks with this analysis with the reference plane construction along with buccolingual angulation measurements being completely carried out with a computer algorithm, it can be deduced that the Alberta DS Transverse Analysis should be a more reliable and reproducible method to identify buccolingual inclinations of teeth compared to methods where reference plane identification and buccolingual measurements are generated by the operator. Training time to familiarize each clinician to use the software and properly identify the landmarks was relatively minimal as landmark descriptions were easy to follow and the image manipulation techniques within the 3D imaging software made it relatively easy to precisely identify the landmarks being described. However, the algorithm would need to be incorporated into commercial software's to improve ease and friendliness of use for clinicians.

b.) Reliability of the dental and skeletal landmarks will be compared to the reliability of angular measurements obtained using the existing CWRU transverse analysis.

Of the 8 CWRU angular measurements assessed from 2D slices of 3D images, all demonstrated excellent intra-examiner reliability with mean errors less than 2°. Although inter-examiner reliability for the CWRU angular measurements ranged from poor-good, mean errors did not exceed 5.9° which suggests this inter-observer variation may not be clinically significant.

It was predicted that the CWRU reliability values may not be as high as the Alberta DS Transverse Analysis as naturally angular measurements have inherent increased error because 3 different points or two separate lines, all with their own variability, must be identified to create a single angle. Also identification of the reference plane, particularly the inferior border of the nasal cavity, becomes fairly subjective due to anatomical variations in the shape of the inferior border and different observer interpretations as to where the tangent reference line should fall.

Objective #2: To develop a novel 3D transverse analysis that identifies the buccolingual inclinations of maxillary and mandibular first molars and canines using a previously described 3D maxillary reference plane for angular measurements.

The basis of developing this new transverse analysis was to utilize a 3D Cartesian reference system to develop a truly 3D based measurement analysis of buccolingual inclinations. The limitations of making 2D measurements on coronal slices or approaching teeth parallel to the midline for identifying transverse or buccolingual dimensions has been discussed throughout this thesis as mesio-distal tip and rotation does affect the buccolingual angle. Therefore, a 3D transverse analysis has the potential to offer visualization and identification advantages while potentially improving accuracy. In order to establish a reproducible reference system for 3D images, an anatomic voxel based Cartesian coordinate system was used so that buccolingual inclinations of maxillary and mandibular molars and canines could be identified. Lemiuex *et al.*[23] previously described the 3D maxillary reference plane utilized as being accurate and reproducible, established by identifying 4 reliable and reproducible skeletal landmarks that can be consistently identified.

In order to measure the buccolingual angles effectively an algorithm was produced in MatLab (Mathworks, Inc., Nantick, MA, USA). The algorithm required the input of the four skeletal landmarks used to define the coordinate system, and the three points defining the location of the tooth (the cusp tip, root tip, and most buccal point). The algorithm then constructs the anatomically based planes (xy-plane, xz-plane and yz-plane). A tooth-based plane is then constructed using the three points placed on the tooth. A line (referred to as the “tooth line”) is drawn within that plane, passing through the root tip and the cusp tip. The angle the tooth line makes with its projection onto the anatomical XZ plane is then measured as the buccolingual angle. This is kept consistent between all the teeth measured in this analysis.

Clinical validity and accuracy of this novel analysis was not the intended objective of this study, instead future research will be required to assess this so that the analysis can be practically implemented for clinical use.

Objective #3: To compare the newly developed Alberta DS transverse analysis angular measurements to the previously described CWRU transverse analysis for maxillary and mandibular canine and molar buccolingual inclinations.

When compared, there was a statistically significant difference between the CWRU and Alberta DS transverse analysis measurements for all teeth. However, since a true reference standard for ideal buccolingual position radiographically determined has not been identified in the literature, the real direction of any difference is impossible to determine. The statistical difference can be attributed to the different reference planes utilized by both methods and the different approaches to the teeth when buccolingual measurements were obtained. However, only maxillary canines demonstrated a clinically significant difference (set as a 10° difference as described previously as being two standard deviations of the normative data). Interestingly, for mandibular teeth buccolingual inclinations, the Alberta DS Transverse analysis compared all teeth to a nasomaxillary reference plane whereas the CWRU compared mandibular inclinations to a mandibular reference plane, but mandibular molars and canine measurements differed the least between measurement methods. This can potentially suggest mandibular dental buccolingual measurements can be obtained using a maxillary skeletal reference plane in patients that are not overtly mandibular asymmetric.

Without a reference standard, it cannot be concluded which method is more accurate at this time. Initial landmark identification with the Alberta DS transverse analysis was found to be easier, requiring less time than image orientation and manually drawing angles for the CWRU analysis in Dolphin on 2D slices. However, the Alberta DS Transverse analysis requires a specific MATLAB software algorithm to determine buccolingual inclinations from the identified landmarks, which generally makes the Alberta DS Transverse analysis more time consuming and cumbersome to use. Ideally, future integration of this developed analysis into a 3D imaging program used for landmark identification such that the reference plane and angulations can be instantly calculated after landmark placement would make use of this newly proposed technique more clinically applicable.

Limitations

Reliability Testing

The principle investigator in this study had significantly more experience with use of the CWRU software, whereas the other two observers received limited hands on training, mostly learning to navigate with previously written descriptions from the creators of the CWRU transverse analysis. All observers had previous experience with navigating Avizo imaging software, but also did not receive hands on training or calibration, rather point identification was carried out by landmark descriptions provided by the principle investigator. Different levels of experience, comfort and calibration with the software's used could have affected the results of inter-examiner reliability testing. Potentially, the Alberta DS Transverse Analysis initial landmark identification may be easier to use in a doctor clinical setting instead of the need to orient images in a standardized approach and drawing subjective lines to identify reference planes and the long axis of teeth with the CWRU analysis. However, until the

Alberta Transverse analysis can be integrated into a 3D commercial imaging program, the CWRU is more clinically practical.

Stability of Reference Planes

For both analyses, we cannot confirm the references planes used are a stable source of reference over time which can significantly effect measurements compared over the course of treatment due to growth. Potentially, use of a 3D nasomaxillary reference plane established from skeletal landmarks that lie superior to the skeletal and dental units that would be most affected by treatment and growth may be more stable over time. Stability of these reference planes and landmarks has yet to be confirmed.

Future Recommendations

- Evaluate the stability of the skeletal landmarks used to derive the 3D nasomaxillary reference plane over time. Stability would ideally need to be confirmed to be able to precisely evaluate buccolingual changes over the course of treatment. However, the effect of growth on this reference plane would be difficult to study in untreated controls without being able to justify the use of CBCT imaging in patients not receiving treatment.
- Creation of a 3D mandibular reference plan could be proposed, tested and compared to mandibular buccolingual measurements obtained using a 3D nasomaxillary reference plane
- To confirm the accuracy of the Alberta DS Transverse analysis, there would need to be a study to compare this 3D volumetric method directly to skull craniometric measurements to validate its use.

- Further research is needed to develop and test normative data to allow this analysis to be used at initial diagnosis to better enable clinicians to confidently identify which cases require skeletal expansion instead of just dental to achieve successful results.
- After development of normative data for the diagnostic application of this analysis, further research would allow the assessment of clinical outcomes after utilization of the Alberta DS Transverse analysis for diagnosis of maxillary transverse deficiencies.

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