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Development of a Three Dimensional Maxillary Superimposition
Plane Using Cone Beam Computed Tomography

by

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Introduction: Cone beam computed tomography (CBCT) is a new diagnostic and treatment planning tool in orthodontics. The purpose of this thesis is to determine precise landmarks that can be used for cephalometric superimposition of the maxilla and the mandible. A maxillary plane will then be determined for superimposition of CBCT and tested in a clinical context.

Methods: The CBCTs of ten skulls were used to test the precision and accuracy of the landmarks. Next, CBCTs and plaster models of thirty patients were used to test and validate the proposed 3D superimposition technique of the maxilla.

Results: Nasion, incisive foramen, bilateral infraorbital, mental foramina and anterior nasal spine were all precise and accurate landmarks to use in the formation of a maxillary superimposition plane. Comparison of the proposed superimposition technique with a gold standard demonstrated excellent agreement.

Conclusion: The proposed maxillary superimposition plane can be used as a regional superimposition technique.

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LIST OF ABREVIATIONS

A: *Subspinale*

ABO: American Board of Orthodontics

ANS: *Anterior Nasal Spine*

CBCT: cone beam computed tomography

CT: computed tomography

DICOM: Digital Imaging and Communications in Medicine

FOV: Field of View

ICC: Intraclass Correlation Coefficient

IF: *Incisal Foramen*

IOF: *Infraorbital Foramen*

L: *Lingula*

MF: *Mental Foramen*

mm: millimeter

MPR: Multiplanar Rendering

N: *Nasion*

RME: Rapid Maxillary Expander

SN line : *Sella-Nasion* line

2D: Two-dimensional

3D: Three-dimensional

DEFINITIONS

MPR, Multiplanar Rendering

Defined as visualization techniques developed and used on professional medical imaging workstations: three different views of the medical image in axial, frontal and sagittal views.

Precision

Defined as the degree to which repeated measurements under unchanged conditions show the same results

Synonyms: *reliability, repeatability*

Accuracy

Defined as the degree of closeness of measurements of a quantity to that quantity's actual (true) value.

Synonyms: *Validity*

X axis

Defined as the axial plane, running left to right

Y axis

Defined as the sagittal plane, running front to back or in and out

Z axis

Defined as the frontal plane, running up and down

Chapter 1- Introduction

Statement of the problem

The use of cone beam computed tomography (CBCT) is becoming evermore common in the fields of dentistry and orthodontics. In the transition from 2D to 3D, a new method of cephalometric superimposition should be developed and validated (i.e. tested clinically). To this day, cranial base 3D superimposition techniques for overall assessment of growth and treatment effect have been proposed in the literature and are being tested, but no well-known regional superimposition technique has been proposed for the maxillary complex. In order to develop such a technique, stable reference structures need to be identified in the nasomaxillary complex and mandible. First, the accuracy and precision of selected landmarks in the nasomaxillary complex and mandible must be examined. Secondly, the proposed landmark-derived plane of superimposition must be tested and compared against a gold standard reference before being accepted in the field of growth and development analysis.

Review of the literature: 2D versus 3D cephalometry

In 1893, Roentgen discovered the x-ray[1], forever changing the world of medicine and dentistry. It took approximately 40 years before Broadbent introduced this new technology to the field of orthodontics[2]. Prior to cephalometry, anthropology and craniometry were used to analyze facial anatomy and growth[3, 4]. Cephalometry came as an addition to the field of facial study. In 1932, the cephalostat was invented, allowing researchers to visualize skulls in 2D via plain films[3]. In its emerging phase, cephalometry was commonly used as a research tool to evaluate parameters such as facial skeleton growth[3]. Slowly but surely, cephalometry became an integral part of orthodontic diagnosis and treatment planning. Among others, Steiner[5] and Downs[6] pioneered 2D lateral cephalometry by establishing norms and standards to which 2D lateral cephalometric studies could be compared. At this point, the age of cephalometry was well underway, providing a powerful tool for orthodontists to quantify and qualify facial anatomic relationships.

2D superimposition cephalometry

Superimposition of cephalometric images followed after the introduction of cephalometry; providing a means to assess growth and treatment effect over time. Three main types of superimposition were proposed to evaluate treatment effects on bone and teeth and to assess normal growth changes: (1) the cranial base (2) the maxillary complex (3) the mandibular complex [3, 7]. Furthermore, for each superimposition type, multiple different landmarks can be employed depending on which study the method was derived from[7]. These methods are based on studies of growth looking at the most time-stable structures. Some of the most influential studies in the field of orthodontics and growth are the studies from Bjork and coworkers[8-10]. Bjork placed implants in strategic locations in the facial complex in 100 patients aged 4 to 24 years, followed them for several years and evaluated them with serial radiographs. The main goal of this longitudinal study was to understand the pattern of resorption and apposition and overall displacement and growth of the facial skeleton during childhood and adolescence. Aside from being unethical by today's research practices, Bjorks study has several limitations: implants were placed in unstable bone (remodelling) and 3D growth was analyzed using 2D cephalograms. The conclusions of their studies were divided into multiple papers in which they categorized vertical, anterior-posterior, width and rotational pattern of growth of the face, nasomaxillary complex and mandible. They were also able to determine which landmarks in the head are most stable over time (i.e. have minimal change during growth).

Proposed methods for 2D cephalometry superimposition

In terms of cranial base superimposition, the most widely accepted and used reference plane on which two or more serial cephalograms should be compared is the *Sella-Nasion* line (SN)[4]. The stability of the SN is questionable considering that nasion and sella points both change location in space with time due to bone remodelling. Bjork's experiment demonstrated that in 90% of cases, nasion remains clinically stable in the vertical position, therefore making the SN line an acceptably stable landmark for superimposition[4, 11]. Other less popular methods for superimposition on the cranial base are Weislander's grid method[12] and Johnston's pitchfolk analysis[13], both using the sella as a reference point and dropping perpendicular in order to evaluate the change in the position of the maxilla and mandible including their teeth.

With regard to the maxilla superimposition, the most popular method employs the palatal plane as a reference plane from the anterior nasal spine to the posterior nasal spine[4]. Downs recommended to superimpose serial cephalograms on the nasal floor and the anterior portion of the maxilla in order to limit the effect of the position change of the anterior nasal spine with time[14]. Bjork proposed a different method: to use the zygomatic arches as a superimposition reference[15]. He found out that the zygomatic arches did not undergo the same remodelling changes to the same extent as the nasal floor and orbital floor, therefore making the anterior surface of the zygomatic process of the maxilla an ideal surfaces on which to superimpose serial cephalograms[4]. In a study done by Gu and McNamara[7], the palatal plane best-fit superimposition method for the nasomaxillary complex was found to overestimate vertical displacement and overestimate forward movement of maxillary landmarks compared with Bjork's original superimposition technique. However, the Bjork method for superimposition also has its drawbacks; it requires high quality radiographs in order to minimize the double images generated by the bilateral zygomatic arches on a 2D radiograph[16]. Also, when the anterior portion of the zygomatic arch is small, chances of introducing a rotational component is increased in the Bjork superimposition method[16]. The current American Board of Orthodontics accepted technique is to superimpose using the vertical legs of the aligned key ridges (anterior and posterior contours of the zygomatic arches) and using the best fit of the internal structures of the maxillary bony complex[17]. This is considered to be the most accurate technique.

With respect to a mandibular superimposition technique, several methods have been described. In 1960, a workshop in cephalometry concluded that superimposing along the lower border of the mandible and inner aspect of the symphysis were reliable[4]. Bjork's study looked at the areas of resorption and apposition of bone throughout growth. He found that the lower border of the mandible remodelled extensively and that growth was primarily from the condyles (especially the anterior surface). It was therefore concluded that the tip of the chin, the inner aspect of the symphysis, border of the mandible canal, and lower contour of the wisdom tooth germ were the areas most appropriate for mandible superposition[18].

Main Drawbacks of Two-Dimensional Superimposition Cephalometry

Two-dimensional superimposition is a clinically accepted method for obtaining approximate estimates of the growth and treatment effect; however, the lack of precision and accuracy and time-related changes remain major limitations. In particular, the main drawback of 2D superimposition techniques is inerrant to the lack of precision of a 2D plain radiograph. Jacobson and Jacobson[4] stated that the lack of accuracy and stability of the superimposition techniques are due to the following:

1) Difference in the head position when head films are taken at different times by different operators

2) Double images of the bilateral structures often are not consistently equally spaced in serial head films because of minor head positioning problems resulting in distortion

3) Difference in film contrast and density at two time points

4) Anatomic or structural landmarks are inconsistently identifiable

5) The most important limitation of traditional cephalometric measurements is that three-dimensional changes are measured in only two-dimensions. Projection geometry errors are introduced by projecting a 3D image like a skull on to a 2D image[19], causing magnification and distortion of images.

6) Moreover, landmark identification errors must also be taken into account[19]. Since cephalometry is a two dimensional representation of a three dimensional structure, many bones are superimposed and identification errors are unavoidable. In this regard, midfacial single landmarks show better precision avoiding the superimposition and the magnification errors seen in bilateral landmarks.

The dilemma between Qualification Versus Quantification

In the field of orthodontics, precision is of paramount importance. A discrepancy of several millimeters can make all the difference in the success of a treatment. Also the inability to quantify the vectors of change is an inherent limitation of representing a 3D structure in a 2D plain film[19, 20]. Qualifying the types of movement is an important aspect, but quantifying precisely the direction of each movement and being able to describe this in 3 orthogonal planes should soon become the standard of care in orthodontics. Hence, the interesting switch from the mostly qualifying plain 2D radiographs to the more precise, quantifying 3D CBCT reconstruction.

Introduction of Cone Beam Computed Tomography

Following its development in Europe, the first CBCT machine was approved for usage in oral and maxillofacial imaging in the United States in 2001[21]. Since its introduction, it has opened up a world of possible opportunities in the field of dentistry and orthodontics. CBCT provides immediate and accurate radiographic images of the skull[21]. The relatively low radiation dose and low cost compared to standard computed tomography (CT) scans has made it extremely appealing to orthodontics[21]. Since its introduction, scanning time, voxels size, and field of view could be modified to maximize its adaptability depending of the clinical scenario. In orthodontics, CBCT has been used for many purposes and its use is increasing with time. The advent of 3D radiography has boosted the diagnostic capabilities of CBCT, aiding in treatment planning and virtual treatment planning. Impacted teeth localization, temporomandibular joint examination, upper airway and sinus assessment and cephalometric usage are only a few examples of its use[22-24].

In the past decade, numerous articles have been published regarding orthodontic cephalometric examination using 3D imaging[25-27]. For the purpose of this review, 3D cephalometry will be divided in the following sections: firstly, cephalometry comparing plain radiographs to CBCT will be done and secondly, an overview of the 3D cephalometry superimposition techniques and the recent studies using the different superimposition techniques will be provided.

Cephalometry Comparing CBCT Versus Plain Radiographs

Initially, with the advent of CBCT, there was an interest in demonstrating that cephalometric 2D derived from CBCT and plain radiograph cephalometry yielded similar results. Many papers focused on comparing the accuracy of CBCT generated cephalometric analysis with plain two-dimensional cephalometric analysis[20, 28, 29]. Measurements taken from a CBCT derived cephalograms have been proven to be on average similar to those on conventional plain cephalograms[20, 28, 30]. Catteneo *et al*[29] compared the cephalometric analysis measurements of 34 patient records obtained from both conventional and CBCT-derived cephalograms. The conclusion was that the new CBCT cephalograms could replace the traditional cephalogram while providing similar quality of reading. Chang *et al*[31] performed a similar study and came to similar conclusions.

Although knowing that CBCT-cephalogram could replace the conventional cephalogram without inducing clinically significant error in reading is useful, using the CBCT to create a 2D derived cephalogram seems to be excessive because it is exposing the patient to unnecessary additional radiation without using the CBCT to its full potential. Other studies decided to compare measurements derived directly from a 3D CBCT cephalograms with traditional 2D cephalograms. Zamora *et al*[26] found no statistical differences between the measurements of one versus the other. On the other hand, Van Vlijmen *et al*[32] did find different results following a study having a similar question and methodology as Zamora. One important difference between the two studies was the way the CBCT cephalometry was read. Zamora used multiplanar rendering MPR and 3D rendering CBCT views while Van Vlijmen used the 3D rendering CBCT view only. Grauer *et al*[30] explains this problem by saying that MPR view is more precise than a 3D CBCT view for reading of cephalometric measurements. He also explains that clear definitions of landmarks in three dimensions are required. Lagravere *et al*[33] agrees with de Oliveira *et al*[34] study with regards to the need for clear definitions but also affirms that landmarks need to be adjusted in 3D versus 2D cephalometry. If the 3D view is to be use to its full potential, new landmarks should be determined that can be easily and precisely identified in the 3D view or in the multiplanar rendering views. Therefore, craniofacial structures as foramina, bony projections or bony spine, rather than smooth bony surfaces like orbitale and subspinale should be sought. Once 3D cephalometry becomes well developed, orthodontists will have a precise tool for diagnosing and treatment planning as well as another means of communicating with patients and other health professionals.

Proposed Methods for CBCT Cephalometry Superimposition

To date, two superimposition methods are often quoted in the literature. Superimposition of CBCTs could be achieved manually by best fit of stable anatomical regions or by registering common stable landmarks.

A) Voxel Based Superimposition Technique – Best fit method

This method has been reported and used since 2005[22, 35, 36]. Voxel based image registration is a more or less newly developed semi-automated technique for superimposition and comparison of two CBCT scans[37]. The anterior cranial base has been traditionally considered a stable structure as most of its growth is completed early in childhood making it an ideal, easily identifiable and stable structure for superimposition[38, 39]. As explained by Cevidanes[22], the traditional 2D use of landmarks, planes and projection are no longer essential since the advent of software tools to optimally align 3D CBCT data at different time points with subvoxel accuracy after identification of the cranial base structures.

As a general overview of this cranial base superimposition method[30], here is how the process is done.

1- Both CBCTs taken at two different time points are uploaded in the software

2- The cranial base area is outlined automatically and then manually for refinement by the user on both images. This outline will be the registration references and must be anatomically stable between time points.

3- Once the landmarks are established, the program computes the best fit between the 2 CBCTs by matching the registration area. A transformation matrix is obtained (rotation and translation). The program then relocated 1 CBCT image relative to the other based on this transformation matrix, and the result is that both images share the same coordinate system.

4- Once both cranial bases are registered and superimposed on top of each other, the user can evaluate changes in the rendered volume with semi-transparencies or at the stack of slices and changes can be described relative to the registration landmarks.

As claimed by the authors[30], this method can be used for many purposes: upper airway analysis, surgical prediction, and soft tissue change prediction to name only a few. The authors claim that the quality of the registration and superimposition is done at the subvoxel level, making it extremely precise. The fact that segmentation and registration are used for the purpose of superimposition and that 2D traditional landmarks identification are not needed make this method superior to 2D cephalometry. Furthermore, they claim that the traditional landmarks used for cephalometry are not precise enough for 3D cephalometry; however, as mentioned earlier, this was disproven in the past[32].

Many articles were published on 3D superimposition using the voxel-based method. Both hard tissue and soft tissue changes have been investigated. De Paula *et al*[40] used voxel based registration superimposition to evaluate the short term surgical outcomes of orthognathic surgery for Class III patients. Regarding soft tissues changes, Kim *et al*[41] and Lee *et al*[42] did a similar study by comparing the soft tissue changes following a setback Le Fort I procedure. Heymann *et al*[43] used the voxel-based method to determine anatomic changes following maxillary protraction with intermaxillary elastics to miniplates. They concluded that 3D data from CBCT allowed a more thorough documentation of the treatment outcomes. Studies using this method encourage the use of this superimposition technique to formulate clinical guidelines based on the result of the superimposition.

Although promising, the voxel-based method of superimposition became popular without any rigorous clinical validation[37]. Finally, Nada *et al*[37] addressed this issue in a study looking at the accuracy and precision of the voxel based superimposition method. They outlined two principle shortcomings: first, the lack of proof of accuracy and precision of the cranial base superimposition method and secondly, the challenges of using this technique with a smaller field of view CBCT, which is common practice in a clinical setting. They looked at the mean distance difference between four superimposed areas of interest on the skull. Since all mean distances including their standard deviation were less than 1 mm, they concluded that all sites tested (i.e., cranial base, zygomatic arches and frontal bone) in non-growing individuals were appropriate for superimposition. When it comes to growing individuals, this voxel-based surface should not be applied, since superimposition cannot be based on a continuously changing anatomical area.

B) Landmarks based superimposition technique

Popularized by Lagravere *et al*[44], this technique is in a way quite similar to the traditional 2D superimposition technique. In this sense, reliable and accurate landmarks are located to form a common plane in two CBCTs at two points in time. Both planes are superimposed allowing for comparison between both images. A detailed description of the transformation process is given in Lagravere *et al*[45].

Description of the superimposition technique – simplified version[46]

1) Using a visualization software such as AVIZO (Visualization Sciences Group, Burlington, MA, USA) in which a Digital Imaging and Communications in Medicine DICOM file is uploaded, four landmarks located in a time-stable area are required to define a 3D anatomical reference coordinate system.

2) One landmark becomes the origin of the Cartesian coordinate system, hereinafter referred to as ELSA (i.e. the origin (0,0,0) in the (x,y,z) coordinate notation). In order to map all the points and landmarks of the CBCT to an ELSA coordinate system, the vector describing the position of ELSA in the software

coordinate system (ex: AVIZO software) was subtracted from all anatomical landmarks, thus zeroing the coordinate of ELSA.

3) **First transformation:** From the origin ELSA, 3D positional coordinates for the remaining three landmarks were determined. The coordinate system was constructed using two planes defined by the three other anatomical landmarks. The first plane was defined using two landmarks in the x,y directions and the second plane perpendicular to the first one was defined using the third landmark in the yz dimension, creating this new coordinate system. If and only if the landmarks chosen are stable in time will the coordinates system be the same and therefore be useful in the superimposition process.

4) **Second transformation:** If the created coordinate system is accurate, the relative distances and the angles between landmarks should remain the same at different time point. Using algorithms ensuring that the angles and linear distances that should be similar at both time point, the accuracy of the planes created are verified and adjusted if needed.

It was noted in previous articles that a small error in landmark identification produces a magnified error at the level of landmarks identification, therefore having the possibility of causing a significant clinical impact while generating the superimposition[45]. Among solutions offered to rectify that problem, the use of 6 landmarks instead of 4 to create the new Cartesian coordinates was proposed and tested[47]. When analyzing real patient data, it was found that the 6-point algorithm compared to the 4-point algorithm reduced errors between images and increases its precision[47].

Regional superimposition, for example using the maxilla, is a subject that has not been addressed extensively to date. There is a need for a 3D novel method of superimposition in the nasomaxillary complex. As discussed previously, the purpose of such method is to look at specific dentoalveolar changes in time compared to the overall cranial base superimposition. Moreover, the use of smaller field CBCT popularized by its lower radiation doses is another reason why regional superimposition planes should be proposed and tested.

Research Questions

Question #1

Within the nasomaxillary and mandibular complexes, which landmarks are precise and accurate?

Question #2

In a clinical setting, can the proposed CBCT-derived maxillary plane compare to the gold standard technique?

Paper #1 - Precision and Accuracy of Maxillary and Mandibular Landmarks Using Cone Beam Computed Tomography For Regional Superimposition

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Introduction

Since the 1930s, cephalometry has improved the field of orthodontics by augmenting anthropology and craniometry[2, 3]. Using a plain cephalogram, various anatomic landmarks were identified and a series of analysis were used to compliment diagnosis and enable the clinician to better monitor treatment. However, a main drawback of this technology is that it relies on a two dimensional (2D) projection of a three dimensional (3D) object, leading to projection and magnification errors[48, 49]. Furthermore, variability in head positioning on serial assessments further complicates the cephalometric superimposition[4]. The advent of cone beam computed tomography (CBCT) addresses these shortcomings by providing accurate cross sectional imaging[50]. While CBCT has become widespread in the field of orthodontics[21], its adoption for 3D cephalometry has not yet been widely accepted partly due to a lack of consistency and agreement between proposed methods[26, 32, 51].

CBCT has the potential of improving orthodontics by offering a precise quantitative analysis. Three-dimensional cephalometry may eventually become standard of care in our field[22, 52]. In order to create a precise 3D plane for regional superimposition similar to what has been done for the cranial base superimposition[46], the establishment of accurate and precise landmarks is required so that various measurement such as quantifying the size, position and shape of the cranium, maxilla and mandible can be performed consistently[34, 53].

A recurrent theme in the orthodontic literature is the need for precise landmark identification for cephalometric analysis[34, 52, 54]. Even minute errors in the landmark identification have the potential to incorporate substantial magnitude errors in the overall treatment process[45]. Due to problems with the consistent identification of landmark[30], few solutions have been proposed[25-55]. Multiplanar reconstruction of the CBCT seems to improve the precision of identification[25]. Similarly, anatomical landmarks, which are readily identified in 3D reconstructions such as foramina and spines have been already proposed[55] while benefiting of the 3D volumetric rendering view. Anatomical landmarks chosen for 3D cephalometry should be easily recognizable by clinicians as well as precisely and accurately identifiable on CBCT. Moreover, in the aim of using those landmarks for superimposition of CBCT images, the landmarks should be as stable as possible over time. For these reasons, the landmarks selected for this study were defined in both the 3D reconstruction and MPR views and were chosen to be bony projections, foramina, and spines located in the maxilla and the mandible[55].

The purpose of this study was to identify and validate bony landmarks in the maxilla and mandible that are reliably and accurately measured using CBCT. Such landmarks could ultimately be used to create a standardized coordinate system of the maxilla and mandible for 3D cephalometric superimposition.

Materials & Methods

Anatomic Landmarks

Six landmarks in the maxilla and four in the mandible were selected for this study and are described in Figure 1.1. Each landmark is based on easily identifiable anatomic entities such as a foramen or a sharp projection. In order to standardize the reading methodology for each observer, a complete description was provided in the multiplanar reference view (i.e. axial, coronal, and sagittal views) and the 3D volumetric rendering view.

Specimens and Experimental Setup

Ten well-preserved, dry skull specimens with a stable occlusion were used in this study. Ethics approval was obtained through the University of Alberta Research Ethics Board. A sample size of 10 was used based on the availability of specimens. The specimens were mounted in a double-layered

Plexiglas box with the outer compartment filled with water in order to simulate soft tissue attenuation[33]. The specimens were mounted onto a pedestal inside a CBCT scanner (ICAT, Imaging Science International, Hatfield, PA, USA) as shown in Figure 1.2. A standardized protocol of the ICAT was used (large field of view 9inx12in, voxel size 0.30mm, 120kVp, 23.87mAS). Raw images were exported into a DICOM file, which were subsequently loaded into Avizo version 6.0 software (Visualization Sciences Group, Burlington, MA, USA) for analysis. A Cartesian coordinate system was used throughout where the x-y, x-z, and y-z planes represent the axial, coronal, and sagittal planes respectively (Figure 1.3).

CBCT images were obtained for each skull with and without a radiopaque reference (Gutta Percha, Dentsply-Maillefer, Tulsa, OK) placed on the anatomic landmarks. These references identify the true location of each landmark and, when compared to the readings done without gutta percha, provide a measure of accuracy[33]. Inter-rater reliability was assessed by three observers: an experienced orthodontist, a senior orthodontic resident, and a dental student. For blinding, each CBCT image set was assigned a reference number and assigned in random order. Each observer was familiarized and trained with the software and asked to provide the coordinates of the ten landmarks for all ten specimens. The coordinates of each point were automatically provided in a standardized fashion by the software used. Intra-rater reliability was performed by the primary investigator of the study. Each CBCT with and without the radiopaque marker was read and additional two times at one-week intervals for a total of three readings.

In order to assess accuracy, two metallic reference markers that were already present on the skulls were employed. The most superior part of the metallic reference marker was located in the axial plane. The distance between the fixed markers and each anatomic landmark was calculated with and without the gutta percha using the following equation:

$$d = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$$

where d is the distance (mm), and x_2, y_2, z_2 are the coordinates of the fixed metallic marker and x_1, y_1, z_1 the landmark of interest as shown in Figure 1.4.

The accuracy error for each landmark will be calculated using this equation:

Accuracy error equation

Accuracy error for landmark 1 = mean of

$$\left(\text{Absolute value of } \sqrt{((x_2-x_1)^2+(y_2-y_1)^2+(z_2-z_1)^2)} - \sqrt{((x_2-x_{1*})^2+(y_2-y_{1*})^2+(z_2-z_{1*})^2)}\right) + \left(\text{Absolute value of } \sqrt{((x_{2*}-x_1)^2+(y_{2*}-y_1)^2+(z_{2*}-z_1)^2)} - \sqrt{((x_{2*}-x_{1*})^2+(y_{2*}-y_{1*})^2+(z_{2*}-z_{1*})^2)}\right)$$

Where

(x_1, y_1, z_1): the x,y,z values of the landmark without gutta percha (hypothesized location)

(x_{1*}, y_{1*}, z_{1*}): the x,y,z values of the landmark with gutta percha (true location)

(x_2, y_2, z_2): the x,y,z values of the right metallic landmark

(x_{2*}, y_{2*}, z_{2*}): the x,y,z values of the left metallic landmark

Statistical Analysis

Inter-rater and intra-rater reliability were assessed using intraclass correlation coefficients (ICC)[56] for each landmark in all three axis (x, y, z) using SPSS version 16.0 software (IBM, Armonk, NY, USA). Descriptive statistics were calculated for each landmark showing the mean error and standard deviation of the difference between observers. Accuracy was assessed graphically with the help of a boxplot showing the average error difference between the true and hypothetical location of the landmarks.

Results

Precision of Landmarks

The intra-rater reliabilities for each landmark are listed in Table 1.1. Overall, the ICCs of the landmarks were greater than 0.995, 0.93, and 0.877 in the x-, y-, and z-axes, respectively. The poorest ICC in x-, y- axes was for the A point; measuring 0.995, 0.93, and ANS in the z-axes measuring 0.877. The mean difference between measurements is listed in Table 1.2 where the largest difference was found in the location of subspinale point (A pt) and was 0.71 mm, 1.18 mm and 0.91 mm in the x-, y-, and z-axes respectively.

The inter-rater reliabilities for each landmark are listed in Table 1.3. Overall, the ICCs of the landmarks were greater than 0.924, 0.785, and 0.924 in the x-, y-, and z-axes, respectively. A pt, left and right lingula were the worst three landmarks. The poorest ICC was for the RL point, at 0.998, 0.785, and 0.924 in the x-, y-, and z-axes, respectively. The mean difference between measurements is listed in Table 1.4. The largest difference in the x-, y-, and z-axes varied for each point. All points were close or less than 1mm mean difference in the x-axis direction. Subspinale (A) and left and right lingula showed respectively a mean difference of 1.71mm, 2.33mm and 2.45mm in the y-axis. Again, in the z-axis, subspinale and left and right lingula showed the highest mean error, 1.89mm, 3.18mm and 3.27mm respectively.

Accuracy of Landmarks

The mean difference between the true and observed distance to each landmark (accuracy error) is shown in the boxplot of Figure. 1.5. Note that the accuracy errors from both markers were averaged. The mean error across all landmarks was 0.82 ± 0.28 mm. Point A had the largest accuracy error with a mean and standard deviation of 1.24 ± 1.22 mm.

Discussion

In the field of orthodontics and dentofacial orthopaedics, observation and analysis is commonly performed using a scale on the order of millimeters. For example, growth modification interventions typically employ an appliance to produce only a few degrees or millimeters of movement[57]. Until recently, the limited resolution of cephalometry did not allow the clinician to precisely quantify the magnitude of change due to either growth or treatment or both. With the advent of CBCT, the future of precise quantification of treatment may now be possible.

Damstra *et al*[54] concluded that most 3D cephalometric measurements using traditional landmarks are possibly but not sensitive enough for accurately detecting small differences in movement. Moreover, Grauer *et al*[30] pointed out that volumetric rendering of CBCT cephalometric could be use for a qualitative analysis of the overall pattern of growth. We hypothesized that, similarly to the common 2D cephalometric analysis, 3D volumetric and MPR CBCT could be use for precise three-dimensional cephalometric measurements if, and only if, precise and accurate landmarks are identified and validated.

Two factors need to be taken into consideration when looking at precision and accuracy of a landmark in 3D: voxel size and human error. Voxel size is variable and depends on the CBCT equipment and setting, which continues to improve as the technology evolves. The average voxel size used in CBCT varies from 0.08 mm to 0.4 mm[21]. Human error is defined as the error upon landmark identification. Three important factors are believed to be influencing this: 1) the ease of identification of the particular landmark 2) the level of experience of the observer and 3) the method of identification used. Both, an increased voxel size and the human error of identification together decrease the precision and the accuracy of the analysis. Since voxel size is inversely proportional to the amount of radiation, it is imperative to minimize the human error in order to take full advantage of 3D cephalometry and get the most accurate analysis without significantly increasing the ionizing radiation utilized.

Over the last century, reliable landmarks were established to be used in the plain cephalometric radiograph[19]. Bilateral and midline cranial landmarks have been accepted, with their limitations[19]. Projection error and magnification are two very important limitations to the accuracy of measurements from this technique[19, 49]. CBCT offers a radiographic method that avoids those limitations and offers the possibility of using other anatomic landmarks that were previously unidentifiable on plain x-ray[21]. Moreover, the landmarks used in traditional 2D cannot be blindly accepted in 3D cephalometry[25, 54]. The use of reliable and accurate landmarks on CBCT to establish a Cartesian coordinate system offers a promising way to implement 3D cephalometry and 3D superimposition[52, 55, 58].

An increasing number of studies on landmark identification have been published in recent years [59]. In this regard, the orthodontic community acknowledges the importance of determining accurate and precise landmarks in order to implement proper 3D analysis of CBCT cephalometry[58]. Schlicher[52] *et al* and Lagravere *et al*[55] claim that only precise landmarks will make it possible to clearly quantify the effect of treatment in the future. Many studies have now been published on the topics and their results and conclusion varied greatly. Contributing to the variation in results is the lack of consistency in the data collection and the different level of training of the examiners. Grauer *et al* reported that better reproducibility can be achieved when using a MPR images analysis instead of a 3D volumetric rendering approach[22, 30]. De Oliveira *et al* pointed out the importance of clearly defining, in all three planes of space, each landmark location[34]. This being said, familiarization of the examiners with the technique is also important. On the other hand, another well-controlled study[52] claimed that increase in experience did not improve the overall reproducibility of the landmarks. In conclusion, it seems that MPR and 3D volumetric should both be used and landmarks should also clearly be described in order to increase the accuracy of the landmarks.

The choice of landmarks is also important. Due to the familiarity of the traditional landmarks used in the 2D cephalometry, it seems logical that those same landmarks be used in 3D analysis. Unfortunately, these landmarks might not be the most reliable ones to choose. Schlicher *et al*[52] studied the reproducibility of the traditional landmarks and concluded due to inconsistent results that landmarks located on curves continue to have more errors than those with clear anatomic delineations. As described by Lagravere *et al*, new landmarks based on easily identified 3D structures, such as foramina and spines, are suitable choices[55].

Landmarks

This study focused on identifying precise and accurate landmarks that could be used in 3D cephalometry for orthodontics. Lagravere *et al* previously established that differences between landmark identification of less than 1 mm are clinically acceptable, that differences between 1-2mm are useful in most analyses and landmarks with mean differences greater than 2mm should be used with caution[55].

Intra-rater and Inter-rater reliability for the most precise and accurate landmarks

When located by the same experienced examiners, the foramina of the maxilla and mandible, the anterior nasal spine and the nasion showed the highest precision and accuracy among all the landmarks used in this study. The mean intra-rater error of the nasion, bilateral infraorbital foramina and bilateral mental foramen were all below 0.5 mm. The error in the z-axis is usually greatest. This may be related to the vertical orientation of the landmarks, size of the foramen, and view in which the point was located, hence reinforcing the importance of a uniform and clear definition for analysis. All accuracy errors of the foramina and nasion were below 1.5mm, with mean less than 1mm. The accuracy found in this study of the infraorbital foramina was proven to be better than that found in the study by Schlicher *et al*[52]. This can be explained by the fact that in our study, one examiner was tested for accuracy, while in Schlicher's study, the mean value of all 9 examiners was reported. While not being a foramen, the main examiner found nasion to be easily identified in a 3D reconstruction volumetric view, while validating its location with the MPR view afterward. Similar results for the inter examiner reliability are also showing that foramina and nasion are the most precise landmarks found in this study.

Intra-rater and Inter-rater reliability for the less precise and accurate landmarks

Subspinale (A point) and bilateral lingula were all landmarks with the lowest intraclass correlation values and higher mean errors in general. While reporting average to high ICC values (varying between 0.785-1), the mean errors in location of those landmarks were consistently higher than those for nasion and the foramina. It is to be noted that the highest variation in the mean error were mostly in the y and the z-axis. This can be explained by the different views used by the different observers. Measurements looking at anterior-posterior and vertical changes should be taken with cautious if the landmarks with higher y and z-axis errors are used. Ideally, for anterior-posterior and vertical assessments, landmarks with small and acceptable y and z-axis mean errors should be picked for measurement purposes.

Overall, intra-rater reliability shows excellent precision in landmark identification, whereas inter-rater reliability shows very high level of agreement in landmark identification [58]. In the clinical context, where serial cephalograms will be read by the same clinician, intra-rater reliability is of greater importance. The mild increased variability between different readers might be explained by different interpretation of the protocol; therefore emphasizing the importance of using clear definitions for each landmark. Furthermore, as Oliveira *et al*[34] pointed out, some landmarks may be easier to see in specific planes and more difficult in others. The plane used by the individual reader in this study was at their discretion and may vary between individuals. This could explain the overall higher mean errors in landmarks between examiners in our study. While the 3D reconstruction is more intuitive and easier to navigate for some, there appears to be more volume averaging error (loss of resolution due to oversized pixels relative to the scanned object[60]). It may therefore be advisable for clinicians using 3D cephalometry to familiarize themselves to the MPR views as well as the 3D reconstruction view. Furthermore, the most suitable plane to identify each landmark can perhaps be defined and standardized to further improve inter-rater reliability.

Limitations of our study

Accuracy testing

The assessment of accuracy in this study provides an approximation. An alternative approach would have been to use a radiopaque jig with four balls in the orientation of a standard Cartesian coordinate system so that the exact error vector (in x-y-z directions) could be calculated for each landmark.

Skulls without soft tissues versus fresh skulls

This study was conducted using dry skull specimens. The absence of soft tissue surrounding the dried skulls may introduce errors in landmark identification, altering its apparent location. In this study, soft tissue simulation was recreated during the design of the experience. Again, in order to determine not only repeatability but also accuracy of anatomical landmarks, the use of dry skulls are one way to assess accuracy. As pointed out by Periago *et al*[61], in a real life experiment, it is a possibility that nerves or other soft tissue structures exiting from the foramina affect the precision of landmark identification.

Observer experiment with software

Two out of the three examiners in this study had experience with the use of the software, while one observer had limited experience with it. This could affect the results in the inter-rater reliability testing. This being said, the purpose of this study is to determine easily located landmarks that can be identified by any doctor in a clinical setting. Various level of familiarization of the software is expected but it is unlikely to have a clinically significant effect on the agreement based on the results of this study.

Software limitation

The software used in this experiment did not give the option of viewing a skull in MPR and 3D views simultaneously (i.e. shared screens). This could be a limitation, since viewing in multiple views simultaneously could allow for potentially more precise landmark identification.

Conclusion

Based on the findings of this study:

1) The following landmarks showing adequate precision and accuracy and therefore may be used in 3D analysis of CBCT: infraorbital foramina, incisive foramen, nasion point, mental foramina, anterior nasal spine.

2) The following landmarks not showing consistent precision and accuracy and therefore shall not be used in 3D analysis of CBCT: lingula, subspinale point.

3) Standardization of 3D analysis is a must in order to provide a generally well-accepted and precise way of approaching 3D CBCT reading. The authors recommend clinicians to undertake a formation in the calibration with the software used favouring an approach viewing landmarks in MPR and 3D rendering view for identification.

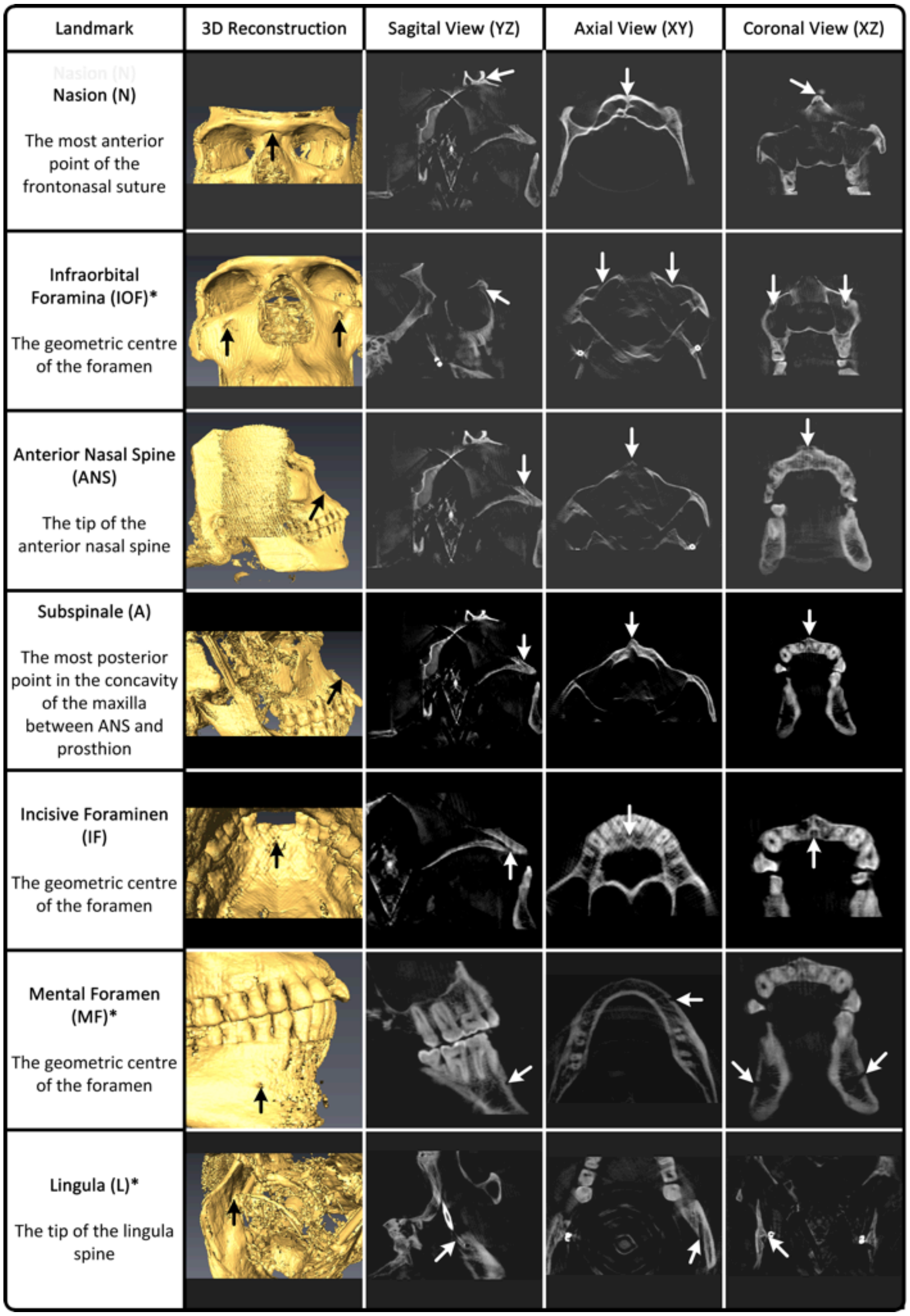

Figure 1.1 – Description of the anatomic landmarks in 3 planes (arrows denote the point of interest). *Represents bilateral landmarks (left and right).

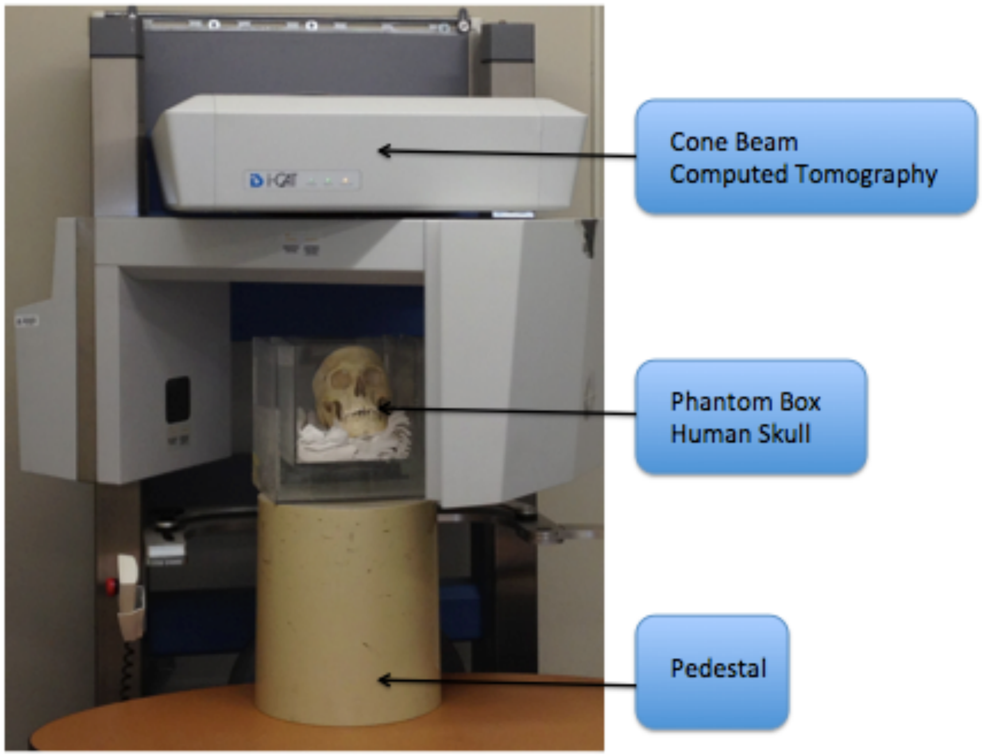

Figure 1.2 – Annotated photograph of the test setup.

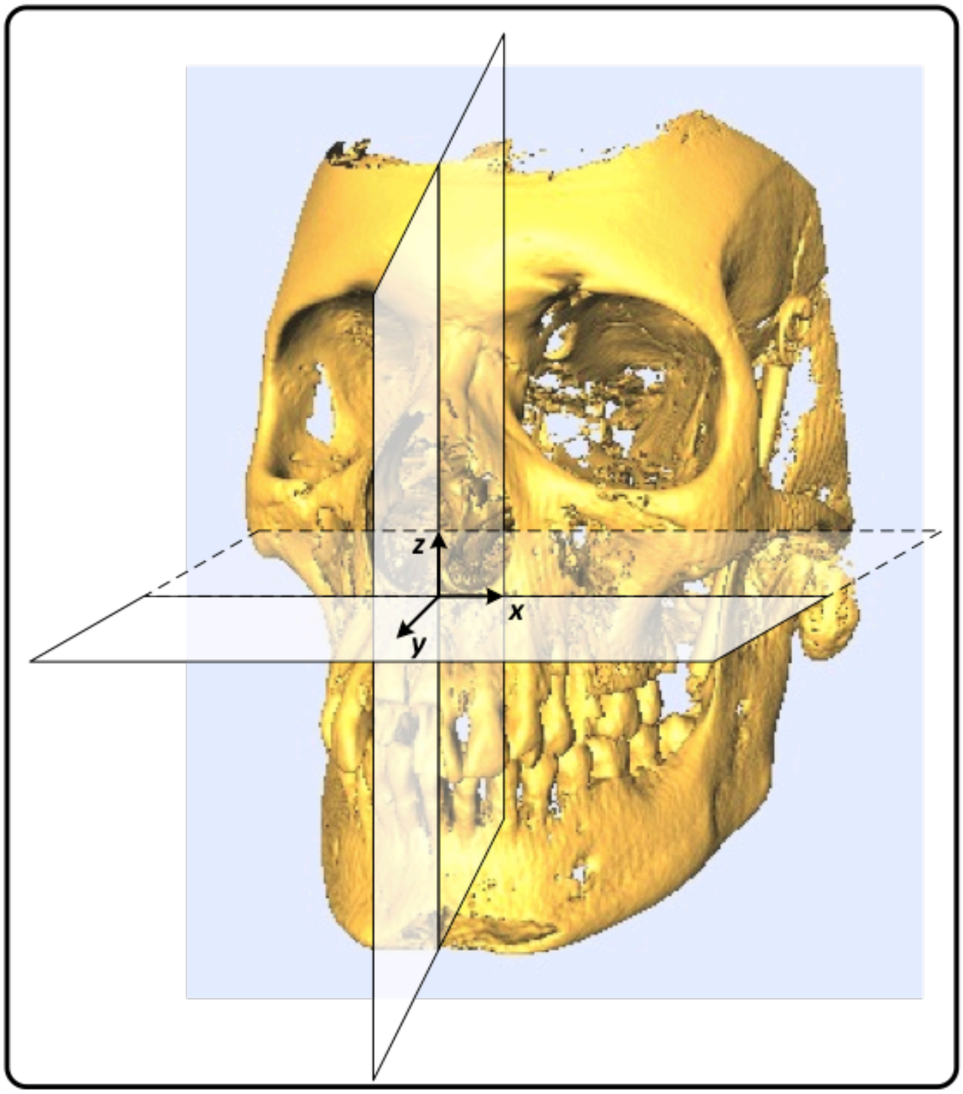

Figure 1.3 – Three-dimensional reconstruction of skull from CBCT showing Cartesian coordinate system.

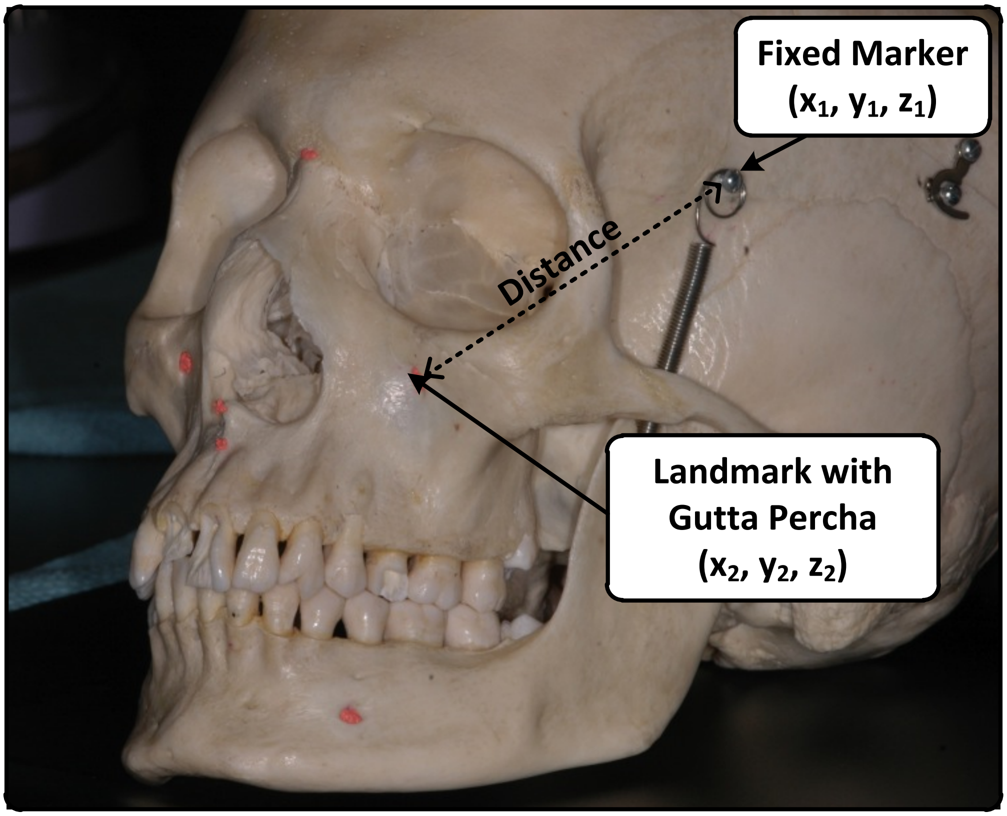

Figure 1.4 – Skull specimen with gutta percha filled landmarks and fixed marker used to assess accuracy of measurements.

Table 1.1 Intra-rater reliability. Using intraclass correlation coefficient, agreement testing was performed for the x,y,z values. Each of the 10 CBCT was read three times by the same reader.

	x			y			z		
	ICC	CI (lower bound)	CI (upper bound)	ICC	CI (lower bound)	CI (upper bound)	ICC	CI (lower bound)	CI (upper bound)
IC	0.999	0.998	1.000	1.000	0.999	1.000	0.984	0.952	0.996
ANS	0.998	0.994	0.999	0.970	0.909	0.992	0.877	0.673	0.968
A pt	0.995	0.985	0.999	0.930	0.802	0.982	0.880	0.848	0.987
RIF	1.000	0.999	1.000	0.993	0.978	0.998	0.997	0.989	0.999
LIF	1.000	0.998	1.000	0.996	0.988	0.999	0.996	0.988	0.999
Nasion	0.999	0.998	1.000	0.995	0.985	0.999	0.997	0.992	0.999
LMF	1.000	0.999	1.000	0.998	0.992	0.999	0.977	0.990	0.999
RMF	1.000	0.999	1.000	0.998	0.992	0.999	0.997	0.990	0.999
LL	0.999	0.998	1.000	0.992	0.975	0.998	0.995	0.983	0.999
RL	0.999	0.997	1.000	0.988	0.963	0.997	0.986	0.957	0.997

Table 1.2 Descriptive Statistics – intra-rater reliability. The mean error and standard deviation of the intra-rater reliability defined as the mean difference between readings for the x,y,z values respectively.

	x		y		z	
	mean error (mm)	standard deviation (mm)	mean error (mm)	standard deviation (mm)	mean error (mm)	standard deviation (mm)
IC	0.13	0.08	0.27	0.16	0.68	0.46
ANS	0.53	0.29	0.58	0.41	0.73	0.46
A pt	0.71	0.43	1.18	0.69	0.91	0.54
RIOF	0.24	0.16	0.27	0.18	0.32	0.2
LIOF	0.22	0.12	0.28	0.14	0.5	0.3
N	0.29	0.16	0.41	0.26	0.4	0.21
LMF	0.29	0.19	0.22	0.15	0.14	0.08
RMF	0.33	0.2	0.24	0.14	0.11	0.1
LL	0.52	0.38	0.59	0.45	0.54	0.41
LR	0.32	0.2	0.41	0.3	0.66	0.48

Table 1.3- Inter-rater reliability. Using intraclass correlation coefficient, agreement testing was performed for the x,y,z values. Each of the 10 CBCT was read once by three different readers.

	x			y			z		
	ICC	CI (lower bound)	CI (upper bound)	ICC	CI (lower bound)	CI (upper bound)	ICC	CI (lower bound)	CI (upper bound)
IC	1	0.999	1.000	0.995	0.985	0.999	0.998	0.994	0.999
ANS	0.996	0.988	0.999	0.975	0.923	0.994	0.977	0.930	0.994
A pt	0.998	0.994	0.999	0.911	0.767	0.975	0.937	0.829	0.982
RIF	0.999	0.996	1.000	0.994	0.983	0.998	0.980	0.995	1.000
LIF	0.996	0.988	0.999	0.992	0.977	0.998	0.995	0.987	0.999
Nasion	0.924	0.798	0.979	0.997	0.991	0.999	0.973	0.923	0.993
LMF	0.999	0.998	1.000	0.994	0.982	0.998	0.992	0.877	0.998
RMF	1.000	0.999	1.000	0.995	0.985	0.999	0.993	0.981	0.998
LL	0.998	0.995	1.000	0.941	0.818	0.987	0.948	0.838	0.988
RL	0.998	0.995	1.000	0.785	0.486	0.941	0.924	0.787	0.981

Table 1.4 Descriptive Statistics – inter-rater reliability. The mean error and standard deviation of the inter-rater reliability defined as the mean difference between readings for the x,y,z values respectively.

	x		y		z	
	mean error (mm)	standard deviation (mm)	mean error (mm)	standard deviation (mm)	mean error (mm)	standard deviation (mm)
IC	0.24	0.16	0.43	0.24	0.37	0.28
ANS	0.71	0.49	0.74	0.46	0.99	0.64
A pt	0.65	0.43	1.71	0.93	1.89	1.16
RIOF	0.48	0.31	0.45	0.25	0.36	0.23
LIOF	0.64	0.36	0.77	0.39	0.63	0.36
N	0.79	0.45	0.67	0.39	0.39	0.25
LMF	0.29	0.19	0.22	0.15	0.14	0.08
RMF	0.48	0.28	0.34	0.23	0.28	0.22
LL	0.58	0.42	2.33	1.51	3.18	2.12
LR	0.68	0.39	2.45	1.59	3.27	2.04

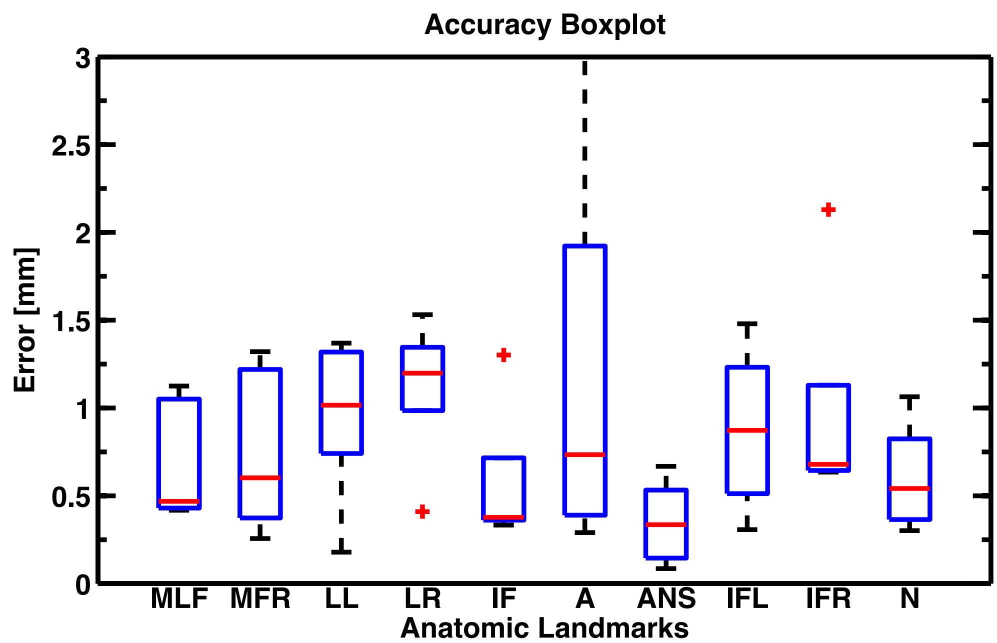

Figure 1.5 – Boxplot of accuracy errors (average distances in mm between the true and hypothesized location of each landmark to the metallic reference marker for all ten specimens). The true location is based on the gutta purcha tagged landmark whereas the hypothesized location is that obtained by the person reading the CBCT. Each boxplot represents the distribution of all 10 accuracy errors calculate for each landmark. The upper and lower lines extending from the boxplot represent the maximum and minimum values of the distribution, the upper and lower bars of the box represent the 3rd and the 1st quartile respectively and the midline bar inside the boxplot represents the median (the second quartile).

Paper #2 - Three-Dimensional Cephalometric Superimposition of the Nasomaxillary Complex

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Introduction

Over the past decade, cone beam computed tomography (CBCT) has improved the field of dentistry and orthodontics[21, 62]. The advanced imaging capabilities of CBCT have enabled: three dimensional (3D) cephalometric analysis, upper airway and temporomandibular joint assessment, and evaluation of dental anomalies to name only a few[21, 30]. Moreover, the superimposition of 3D cephalometric studies over time can be used to quantify growth and therefore evaluate treatment effects over time[30, 47].

Currently, there are two well-published methods for 3D cephalometric superimposition: the best-fit method and the landmarks-derived plane method[22, 47]. Both methods utilize the cranial base, a structure known to have completed growth before the adolescent growth spurt, therefore making it a stable reference structure to use for superimposition[38, 39]. The best-fit method popularized by Cevidanes and colleagues has been used over the past few years, which provides a color-coded 3D head reconstruction demonstrating the movement of bone over time[22]. The best-fit method attempts to match the cranial bases voxel-by-voxel between two CBCT taken at two different time points of the same individual and then computes the difference between all other points[30]. Although a preliminary study shows that this is a promising method[37], more research exploring the accuracy of this type of superimposition is needed. The second method comprises a landmark-derived plane and is similar to the traditional 2D cephalometric superimposition methods that are familiar to orthodontists[45, 46]. The landmark derived plane method makes use of several easily identifiable landmarks, such as foramina located in the cranial base, to align the two planes based on a 3D Cartesian coordinate system. The main drawbacks of this technique are operator dependent errors in identifying the landmarks[45] and the need of precise, time-stable landmarks[34, 52]. Three-dimensional regional superimposition techniques, including the maxillary and mandibular regions, have only sparsely been described in the literature[37]. Current superimposition techniques use the cranial base to describe the changes occurring in the maxilla and mandible hard and soft tissue with treatment[41-43]. In contrast, maxillary superimposition assesses the change in the dentition before and after treatment specifically and more precisely in that region.

Traditionally, in 2D cephalometry, the line of best fit on the palatal plane has been found to be a time-stable landmark for superimposition[7]. The main drawback of this 2D superimposition analysis is the inability to precisely quantify movement, which 3D superimposition analysis will be able to address. In 3D, the zygomatic arch superimposition has been suggested as a stable reference point on which the nasomaxillary complex could be superimposed[4, 15] ; however, this has not yet been extensively validated.

The maxilla are two fused bones that grow dynamically in all planes of space during different periods of adolescence[63]. Contrary to the cranial base, which is a more or less stable before the adolescent growth spurt, the maxilla grows throughout this period therefore complicating the 3D cephalometry (it is difficult to differentiate movement resulting from treatment versus movement from the patient's natural growth).

The purpose of the present study is to propose and test a maxillary superimposition plane using the transformation and optimization method described by Lagravere *et al*[45, 46]. Thirty patients undergoing maxillary expansion were evaluated using the proposed superposition technique and plaster models pre and post treatment in order to evaluate the new technique in a clinical setting.

Materials & Methods

Patient Selection

The records of 30 patients who were treated with rapid palatal expansion in a clinical research trial at the University of Alberta orthodontic clinic were analyzed. Ethics approval was obtained through the University of Alberta research ethics board. The inclusion criteria used for this research were: dental age, treatment received, complete and readable records. Only patients with a dental age of 12 (i.e. all permanent dentition present with the exception of the 2nd and 3rd molars) were included since it was assumed that most transverse growth was completed by this dental age[64]. The sex, the type of rapid maxillary expander (RME) and the chronological age of the patient were not considered since we are comparing methods rather than treatment effects.

Data collection

The methodology of this research is explained in Figure 2.1. The gold standard technique (plaster models measurements) of measuring the transverse dimension change from pre- and post-expansion was compared to the proposed 3D plane superimposition technique using pre- and post-treatment CBCTs looking at changes in the X axis (transverse direction) (Figure.2.2). Both data collection methods are explained below.

Plaster model technique

Plaster models were used as the gold standard for the measurement of the total expansion in the transverse dimension, referred here as the X-axis. (Figure. 2.2). Total *delta X* (i.e., the total change in the x dimension) between pre- and post-RME models at the level of the 1^{st} premolars (i.e., from tip to tip of the each buccal cusp) and 1^{st} molar (from tip to tip of each mesiobuccal cusp) (Figure 2.3) were measured. A digital calliper (Mitutoyo digital calliper, Aurora, IL, USA) with an accuracy of 0.01 mm was employed. Each measurement was repeated twice and checked for gross error (more than 0.2mm difference). Once both series of measurements were found to be exempt of gross measuring error, the average of both measures were taken as the final delta X of the plaster model.

CBCT technique

CBCTs from pre- and post-expansion treatments were used to test the maxillary plane superimposition technique. In order to reduce the scattering effect from the metal of the RME, we selected available CBCTs with imaging before and after the expander was installed and removed from each patient. The time between CBCTs was less than one year for each patient as to minimize any measurement error introduced by the patient's normal growth. In other words, a relatively short treatment time interval helps guarantee that the landmarks used in the superimposition were stable. Furthermore, the plaster models and CBCTs were taken on the same day for each patient pre- and post-expansion.

Three-dimensional superimposition

In order to create a plane for superimposition, 4 accurate and reliable landmarks were used. A detailed explanation on how this superimposition and Cartesian coordinate transformation technique is performed can be found in Lagravere *et al*[40, 41]. Briefly, the landmarks picked to create the maxillary superimposition plane were nasion, bilateral infraorbital foramina and the incisive foramen. All four landmarks were shown to be reliable and accurate (refer to Chapter 2). Nasion served as the origin of the new 3D coordinate system in which x,y,z values are (0,0,0). The remaining points are used to establish two planes through a series of transformations described in chapter 1.

As was done with the plaster models, the expansion of the first premolars and molars were examined using the superimposition plane as demonstrated in Figure 2.4. The difference in the x-axis pre and post expansion of the maxillary premolars and molars was computed. Note the expansion (delta X) is the overall expansion of both sides (right and left).

Statistics

The records of thirty patients were selected in this study without doing any power analysis due to the lack of preliminary studies in the field at the time of the data collection. Moreover, based on the article by Springate[65], 30 records seem to be an adequate number of specimens for determining significance in our research context. SPSS version 16.0 software (IBM, Armonk, NY, USA) was used for all statistics. Descriptive statistics were used to describe the error between the plaster and the CBCT superimposition expansion. Bland Altman plots[66, 67] and Intraclass Correlation Coefficients (ICC) were done to examine the level of agreement between the CBCT superimposition technique and the plaster model measurements. Finally, multivariate analysis was performed to evaluate a difference between the two techniques.

Results

Descriptive statistics are summarized in Table 2.1. The mean error between both methods was 0.59 mm +/- 0.67mm and 0.57mm +/- 0.42mm at the level of the premolar and molars respectively. Regarding the level of agreement, the ICC (Table 2.2) was higher than 0.9 at the level of each teeth, showing excellent level of agreement between both methods. Bland-Altman plots (Figure 2.5-2.6), which are another way to graphically demonstrate agreement between two measurement methods, also show strong agreement between the CBCT and the plaster models. It is to be noted that if the dotted lines of the Bland-Altman plot of the molars represented one standard deviation, about half of the dots would be located outside the dotted lines, reducing the level of agreement, from a excellent agreement level to a more averaged agreement level. After checking for normality, MANOVA testing was done using the Wilk's lamba and showed a p-value of 0.993, therefore we cannot reject the null hypothesis and deduce that both methods are not significantly different.

Discussion

In this experimental study assessing the maxillary expansion of 30 patients, the proposed superimposition technique using 3D CBCT was shown to be in excellent agreement with the gold standard plaster model technique. The mean error for both premolars and molars was less than 0.6 mm, which has been reported to be clinically acceptable[55]. Furthermore, the agreement assessed by ICC was also excellent. Finally, the Bland-Altman plots demonstrated that the error between the proposed technique and gold standard are evenly distributed across the magnitude of expansions; therefore demonstrating no bias. These promising results highlight the potential of CBCT in orthodontic treatment planning and evaluation of treatment through time.

The advent of CBCT in the field of orthodontics has brought an interesting tool adding to our diagnostic and treatment planning capabilities. One of those promising fields is the 3D superimposition cephalometry. Up until now, 2D cephalometry has been considered the gold standard in superimposition technique, even though very important deficiencies have been identified, including: projections errors, distortion, magnification and landmark identification errors[4, 19, 49]. While 2D superimposition cephalometry provides an overall estimate, the 3D superimposition cephalometry may be able to give the exact magnitude and direction of movement and growth in all planes of space, making the orthodontic analysis of each case more accurate and beneficial for the patient. In order to use the 3D superimposition to its full potential, we have proposed a new method to compare CBCTs over time so that the effects of treatment can be analyzed in all 3 plane of space (x, y, z) [53].

One 3D maxillary superimposition method proposed in the literature has been to superimpose the CBCT on the left and right zygomatic arches[37], similar to what Bjork proposed as a stable landmark for 2D cephalometry decades ago[4]. The rational for this landmark was that it permits for a narrower field of view (FOV) CBCT and commensurate reduction in radiation[68] since the cranial base does not need to be imaged. This landmark is part of the nasomaxillary complex and therefore could be used as a potential landmark for superimposition. Nada *et al*[37] therefore set out to test the accuracy of using the zygomatic arches and found that even if the zygoma superimposition gave less precise results when compared to the accuracy of the anterior cranial base superimposition, it was still a clinically acceptable stable reference landmark for superimposition. Notwithstanding Nada's results, the zygomas are areas of high bone turnover and might therefore be subject to significant growth over time.

Another promising method that could be developed in the future is the superimposition based on the palatal rugae of scanned models. Palatal rugae retain their shape and pattern throughout a person's lifetime[69, 70], which could be an ideal time-stable landmark for maxillary superimposition. Using palatal rugae on dental casts, Chen *et al* demonstrated that this superimposition technique is a stable method to register and analyse 3D orthodontic movement of the maxillary dentition[71]. Ashmore *et al*[72] and Miller *et al*[73] came to similar conclusions in clinical studies. Unfortunately, the rugae are ill-defined soft tissue structures, which are not clearly seen on CBCT. Further research is needed to test this landmark using CBCT.

Future refinement of the proposed superimposition technique might consider using more than four landmarks. De Cesare[47] describes a new 6 landmarks technique from which a plane can be derived more accurately. In the landmark derived plane technique, using more landmarks than the minimum four results in a more accurate superimposition (more angles and distances are available to check the position). Furthermore, employing more landmarks might help make the technique more robust since misplacement of one point will introduce less error. Future studies might establish a mandibular plane derived from landmarks that are stable and reliable in time. Park *et al*[69] demonstrated that the plane derived from the two mental foramina and the two lingual foramina was not the ideal way of doing mandibular superimposition. On the other hand, they suggested a surface best-fit method is more appropriate in non-growing individuals. It is the authors' opinion that the surface best-fit method will not work in growing individuals since the external surface of the mandible is constantly remodelling during puberty.

Limitations

Several important limitations exist in this study. First, the assumption that the landmarks are time-stable (do not change position over time and growth) must be verified. A common finding in the literature on superimposition is the fact that most studies used either the anterior cranial base superimposition technique with the assumption that it has completed growth in the pre-adolescent stage or that the population tested was not growing. This clearly demonstrated that the stability of landmarks in the other parts of the head, beside the cranial base has not been demonstrated. In order to limit the effect of growth on the location of our landmarks, CBCTs taken at short intervals were chosen for our research. Future research should look at the stability of the landmarks in the x,y,z coordinate over time in growing individuals in order to be able to apply our maxillary technique to this important population of patients.

A second important limitation of the present study pertains to the CBCT scanner. The quality of the images with regard to its voxel size can be a limitation in terms of precision of the landmark registration. The CBCT machine used in this study is relatively out-dated, but with concern about radiation to patients, it was justified to use these scans rather than repeating the CBCTs with a newer scanner in order to limit exposure to radiation.

Further research is needed to push this new technique into clinical practice by applying it in a prospective clinical study.

Conclusion

The present study assessed the accuracy of a novel landmark-derived maxillary plane for superimposition. Within a clinical setting, we demonstrated that maxillary dentoalveolar changes due to treatment with an expander are accurately characterized by the new technique. Furthermore, the proposed technique lends itself well to small field of view CBCTs as it does not rely on cranial base landmarks, therefore making it a promising tool for the future.

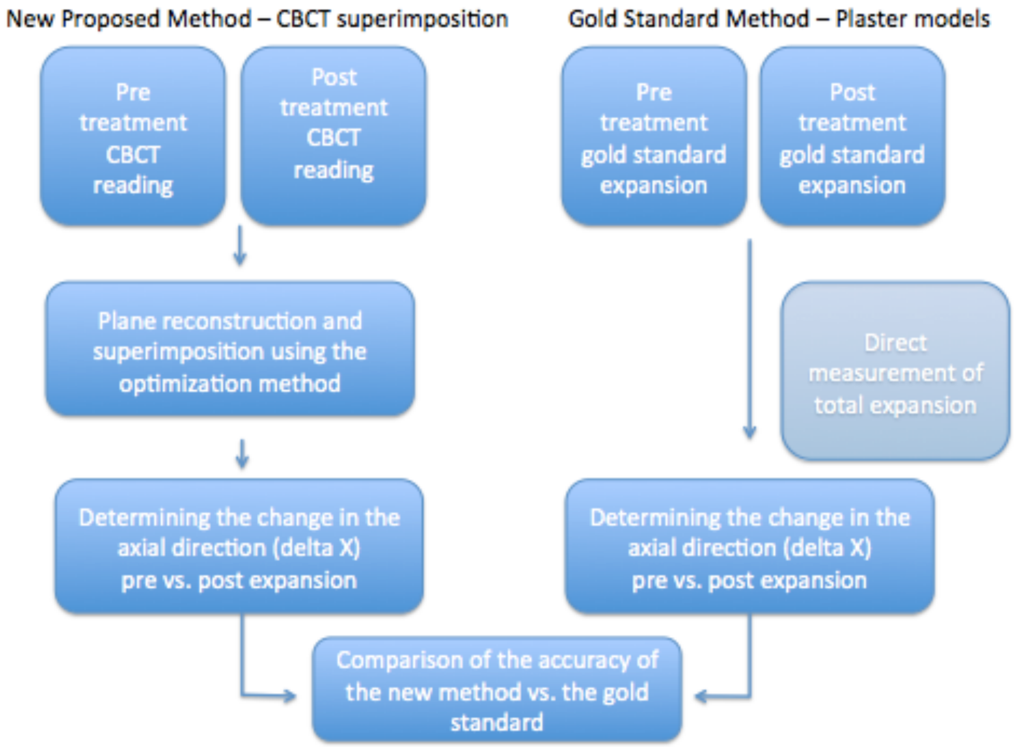

Figure 2.1 – Methodology

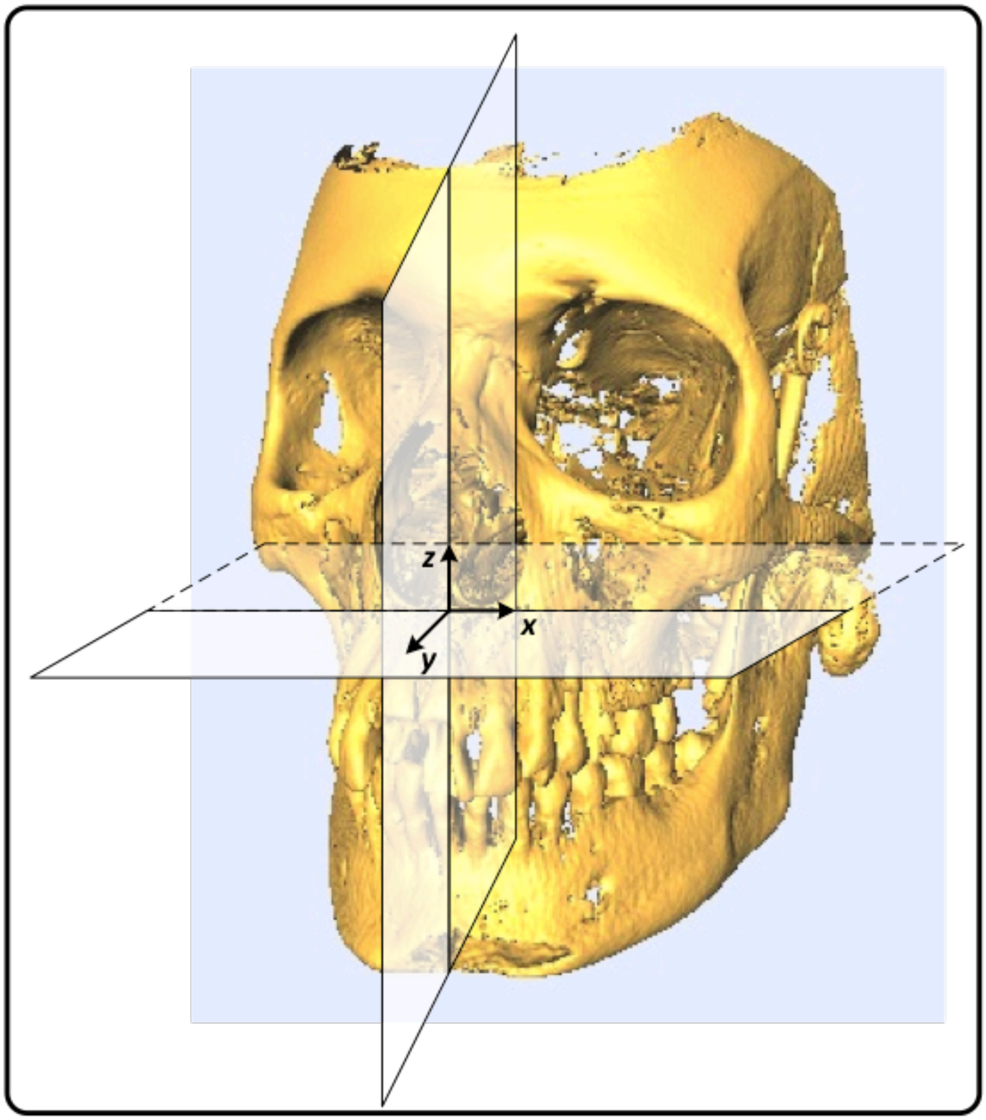

Figure 2.2 – Description of the anatomic landmarks in 3 planes

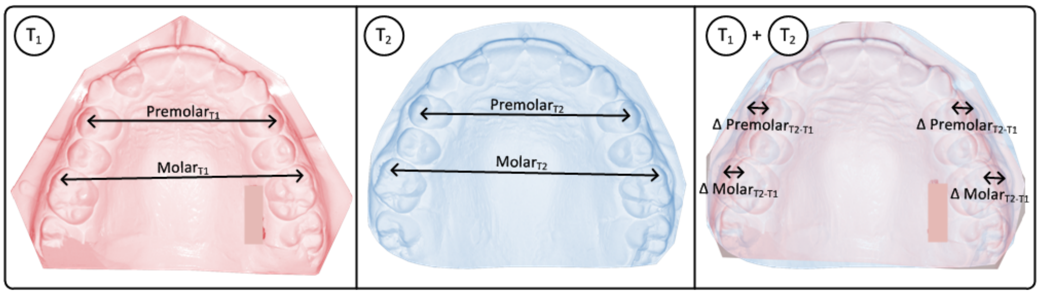

Figure 2.3 – Visual aid –plaster model measurement

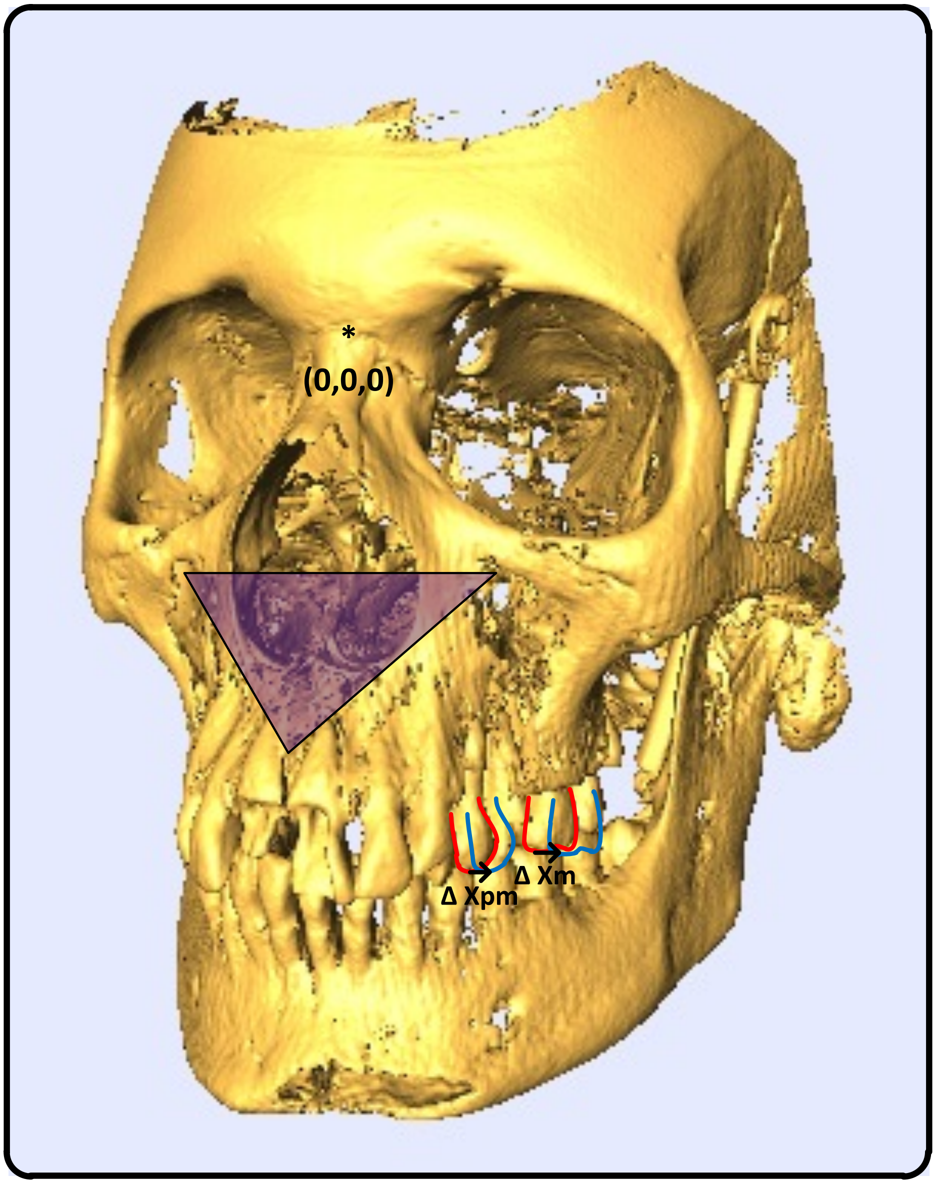

Figure 2.4- Visual aid- 3D plane superimposition

Table 2.1 – Mean and standard deviation of expansion measured on plaster models and 3D superimposistion technique. The difference between these two methods is the error (mean and standard deviation).

		Mean (mm)	Standard deviation	Mean error (mm)	Standard deviation of error
1^{st} Premolars	Plaster models	2.97	2.12	0.59	0.67
	3D plane superimposition	3.06	1.97		
1^{st} Molars	Plaster models	4.18	1.62	0.57	0.42
	3D plane superimposition	4.28	1.61		

Table 2.2- Results – Agreement assessment between methods using Intraclass Correlation Coefficient (ICC)

	ICC	95% Confidence Interval	
		Lower bound	Upper bound
Agreement level – 1^{st} premolars	0.951	0.900	0.976
Agreement level – 1^{st} molars	0.919	0.838	0.912

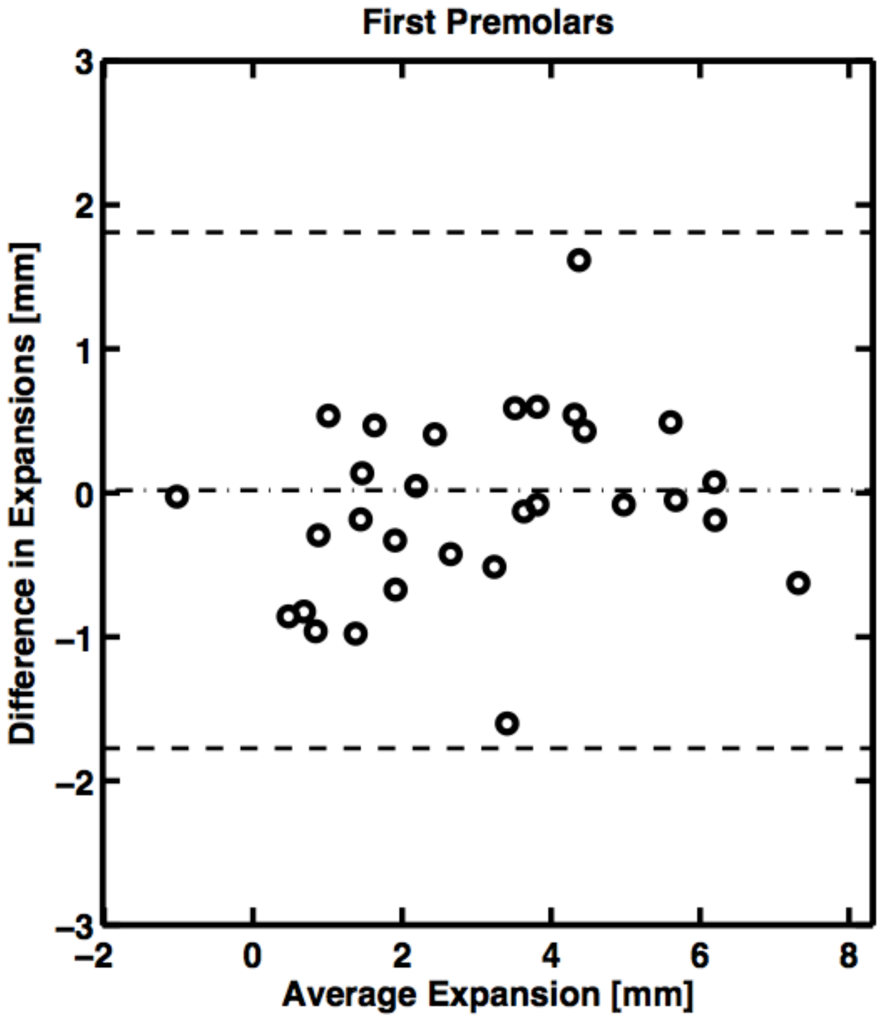

Figure 2.5- Bland Altman plot of premolar expansion. Each point in the plot represents the difference between the plaster and 3D superimposition measurements divided by their average. The upper and lower dotted lines represent the superior and inferior limits of two standard deviations.

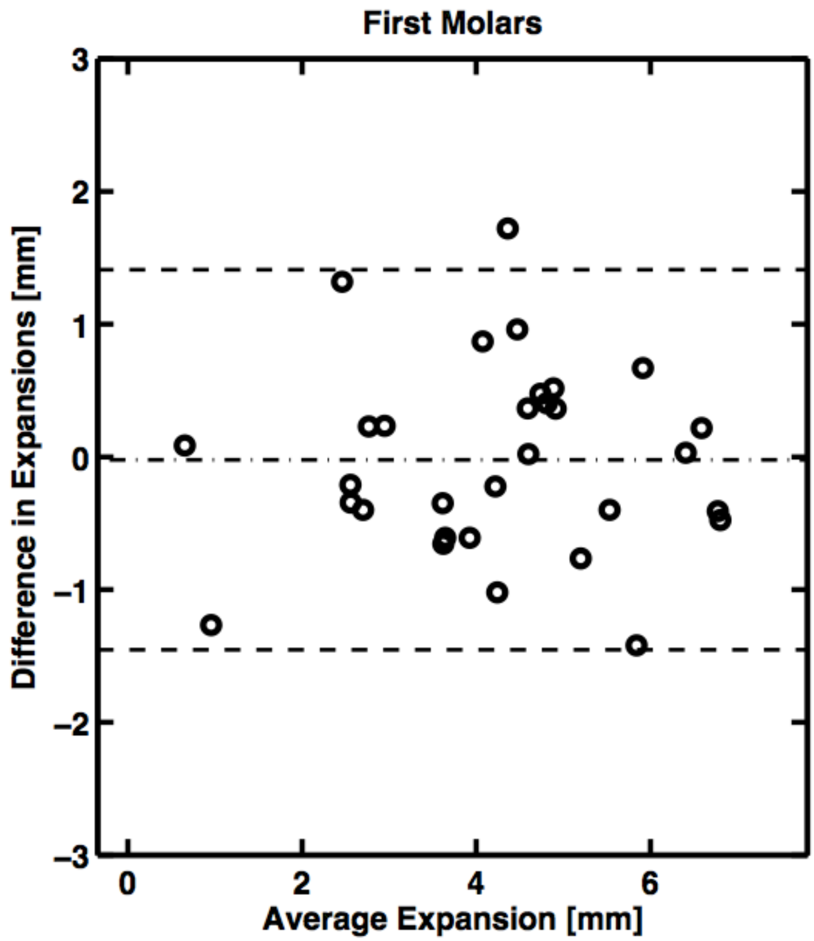

Figure 2.6 – Bland Altman plot of molar expansion. Each point in the plot represents the difference between the plaster and 3D superimposition measurements divided by their average. The upper and lower dotted lines represent the superior and inferior limits of two standard deviations. It is to be noted that if the dotted lines represented one standard deviation, about half of the dots would be located outside the dotted lines, reducing the level of agreement, from an excellent agreement level to a more average agreement level.

General Discussion

Discussion and Major Conclusions

The two research questions posed in this thesis were the following:

Question #1

Within the nasomaxillary and mandibular complexes, which landmarks are precise and accurate?

Ten landmarks in the nasomaxillary complex and mandible were analysed. The criteria for their evaluation were as follows:

1) The landmark needed to be visually observable on a CBCT. This excludes many alternative landmarks such as small foramina like the greater palatal foramina located in the palate and the zygomaticotemporal foramina with are both too small in dimensions to be easily located in a CBCT.

2) They needed to be easily identifiable, like the tip of spines or projections and the geometric center of foramina, rather then located on smooth surfaces, which makes it hard to delineate exactly the location of each landmark.

3) The landmark needed to be located in the nasomaxillary complex in order to proceed with the regional superimposition.

4) The landmark needed to be easily identifiable to clinicians. For this reasons, traditional cephalometric landmarks and major nerve foramina which are familiar to most clinicians were tested.

The mandibular landmarks were scrutinized by the same criteria. We ended up using the maxillary landmarks only for the elaboration of a plane, putting aside our initial idea of proposing a 3D superimposition for the mandible in addition to the maxilla. The main reason for that was that most of the growth of the mandible occurs in the adolescence age[18]. The patients' records available for this thesis were on average 14 years old. We could not assume that the landmarks of the mandible were not affected by growth since it continues until early childhood. Therefore, we decided to postpone the elaboration of a 3D mandible superimposition plane until the landmarks tested showed stability in the time. The assumption that the landmarks were stable for the maxilla was presumed since the study looked primarily on transverse expansion; growth in the transverse dimension is mostly completed at around age 12 years old, pre adolescence growth spurt[64]. Although we only tested our superimposition technique on the maxillary complex, future studies can use the mandibular landmarks identified here in a similar fashion to develop a superimposition plane for the mandible in 3D.

The major conclusions of the first paper are summarized here:

1) The following landmarks showed adequate precision and accuracy and therefore may be used in 3D analysis of CBCT: infraorbital foramina, incisive foramen, nasion point, mental foramina and anterior nasal spine. As predicted, foramina in both jaws turned out to be very easily visualized

in 3D view and MPR. Nasion was easy to identify due to its clear midline location on the frontonasal suture.

2) The following landmarks did not show consistent reproducibility and therefore are not recommended to be used in 3D analysis of CBCT: lingula and subspinale. Surprisingly, spines and projections like the lingula were not very precise landmarks. It can also be noted that the highest variation in the mean error were mostly in the y and the z-axis. This can be explained by the different views used by the different observers. Measurements looking at anterior-posterior and vertical changes should be taken with cautious if the landmarks with higher y and z-axis errors are used. Ideally, for anterior-posterior and vertical assessments, landmarks with small and acceptable y and z-axis mean errors should be picked for measurement purposes.

3) Standardization of 3D analysis is essential in order to provide a generally well-accepted and precise way of approaching 3D CBCT reading. We recommend that clinicians familiarize themselves with the software and develop a standardized approach to view landmarks in MPR and 3D rendering.

Question #2

In a clinical setting, can the proposed CBCT-derived maxillary plane compare to the gold standard technique?

Indeed, the present study demonstrated that maxillary dentoalveolar changes due to treatment with an expander are accurately characterized by the new superimposition technique. The mean error for both premolars and molars was less than 0.6 mm, which has been reported to be clinically acceptable. Furthermore, the agreement assessed by ICC was also excellent. Finally, the Bland-Altman plots demonstrated that the error between the proposed technique and gold standard are evenly distributed across the magnitude of expansions; therefore demonstrating no bias. These promising results highlight the exciting potential of CBCT in orthodontic treatment planning and evaluation of treatment through time.

In this research, transverse expansion was assessed by CBCT using nasion point as the origin of the new Cartesian system. Nasion point was proven to be unstable with time, moving forward and upward through growth in adolescence and to a lesser extent through adulthood[74]. Along these lines, it can be hypothesised that the landmark identification of the nasion in the y and z-axis values is not as steady and will keep on getting worst with time. Therefore, nasion point might not be a suitable point for the fabrication of a plane when looking at treatment effects in the anterior-posterior or vertical dimensions, like a distalization appliance or an extrusion appliance. In our research, nasion was acceptable since we were looking at the change in the x-values and that the value in the x-axis of the nasion has been proven to be clinically acceptable (paper #1).

Limitations

Accuracy testing

The assessment of accuracy in this study (paper #1) provides an approximation rather than a precise error. An alternative approach would have been to use a radiopaque jig with four balls in the orientation of a standard Cartesian coordinate system so that the exact error vector (in x-y-z directions) could be calculated for each landmark.

Skulls without soft tissues versus fresh skulls

This study was conducted using dry skull specimens (paper #1). The absence of soft tissue surrounding the dried skulls may introduce or alter the errors in identification of points. In this study, soft tissue simulation was recreated during the design of the experience. Again, in order to determine not only repeatability but also accuracy of anatomical landmarks, the use of dry skulls are one way to assess accuracy. As pointed out by Periago *et al*[61], in a real life experiment, it is a possibility that nerves or other soft tissue structures exiting from the foramina affect the precision of landmark identification.

Observer experiment with software

In paper #2, two out of the three examiners in this study had increase experience with the use of the software, while one observer had limited experience with it. This could affect the results in the inter-rater reliability testing. This being said, the purpose of this study is to determine easily located landmarks that can be identified by any doctor in a clinical setting. Various levels of familiarization of the software are expected but it is unlikely to have a clinically significant effect on the agreement based on the results of this study.

Stability of the landmarks in time

The assumption assumed in paper #2 that the landmarks are time-stable (do not change position over time and growth) is an important limitation in our study. A common finding in the literature on superimposition is the fact that most studies used either the anterior cranial base superimposition technique with the assumption that it has completed growth by the pre adolescent stage or that the population tested was not growing. This clearly demonstrated that the stability of landmarks in the other parts of the head, beside the cranial base has not been demonstrated. In order to limit the effect of growth on the location of our landmarks, CBCTs taken at short intervals were chosen for our research. Future research should look at the stability of the landmarks in the x,y,z coordinate over time in growing individuals in order to be able to apply our maxillary technique to this important population of patients.

Older generation CBCT scanner

The paper #2 used data collected from an early *NewTom* CBCT machine, one of the first CBCT released about a decade ago which by today's standards is relatively out-dated. The quality of the images with regard to its voxel size can be a limitation in terms of precision of the landmark registration. Using a newer scanner will likely provide the option of viewing more landmarks which previously were not visible with an older version of the CBCT machine (for example: the greater palatine foramina) and is also likely improve the accuracy of the proposed technique for superimposition.

Recommended future studies

- Using small FOV with smaller voxel size CBCTs, one can try to find more precise landmarks. This may facilitate incorporating additional landmarks (eg. 6 rather than 4 landmarks) in the future. Previously non-visible landmarks could be tested for accuracy and precision, for example the greater palatine foramina, the mental spines and the zygomaticotemporal foramina.
- The elaboration of the landmark derived mandibular plane should be proposed and tested in a similar way as paper 2.
- The stability of the landmarks in time should be assessed. In our paper, this was not checked due to a lack of CBCTs at different time period that did not receive treatment and therefore, it was assumed that the landmarks picked were stable. This is a crucial thing to do in order to be able to apply the superimposition technique to growing individuals who represent the majority

of our patients. Only time stable structures can be used for superimposition technique in growing individuals.

- Testing the proposed maxillary plane with different treatment effects, including anterior posterior, vertical and transverse analysis of the dentoalveolar movement should be done to complement.
- Finally, a study looking at how feasible the transformations and optimization method for superimposition is in a clinical setting should be undertaken. From the identification of the landmarks to the analysis of the results from the superimposition, an orthodontist should perform the exercise in order to see if it is feasible in a clinical setting.

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