European Journal of Orthodontics, 2016, 563–568
doi:10.1093/ejo/cjv088
Advance Access publication 17 December 2015

OXFORD

Original article

A new mandible-specific landmark reference system for three-dimensional cephalometry using cone-beam computed tomography

Pisha Pittayapat*,, Reinhilde Jacobs*, Michael M. Bornstein*,***, Guillaume A. Odri****, Min Sung Kwon*, Ivo Lambrichts*****, Guy Willems******, Constantinus Politis* and Raphaël Olszewski*********

*OIC, OMFS-IMPATH Research Group, Department of Imaging & Pathology, Faculty of Medicine, University of Leuven and Oral & Maxillofacial Surgery, University Hospitals Leuven, Belgium, **Department of Radiology, Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand, ***Department of Oral Surgery and Stomatology, School of Dental Medicine, University of Bern, Switzerland, ****Service de chirurgie orthopédique et traumatologique, Centre Hospitalier Régional d'Orléans, Orléans cedex 2, France, *****Biomedical Research Institute, Laboratory of Morphology, Hasselt University, Campus Diepenbeek, Diepenbeek, Belgium, ******Orthodontics, Department of Oral Health Sciences, KU Leuven & Dentistry, University Hospitals Leuven, University of Leuven, Belgium, and *******Department of Oral and Maxillofacial Surgery, Cliniques Universitaires Saint Luc, Université Catholique de Louvain, Brussels, Belgium

Correspondence to: Pisha Pittayapat, OIC, OMFS IMPATH Research Group, Department of Imaging & Pathology, Faculty of Medicine, University of Leuven and Oral & Maxillofacial Surgery, University Hospitals Leuven, Kapucijnenvoer 33, Leuven 3000, Belgium. E-mail: p.pittayapat@gmail.com

Summary

Objectives: To develop a novel 3D landmark reference system that is specific for mandibular midline cephalometric landmarks and to assess its repeatability and reproducibility.

Methods: Cone-beam computed tomography (CBCT) scans (3D Accuitomo® 170) were performed on 26 dry human skulls. The CBCT data were exported into DICOM files and imported to Maxilim® software to create 3D surface models. Two observers identified five landmarks to create a specific mid-sagittal mandibular plane: two mandibular foramina, two molar landmarks and one interincisive landmark. On this mid-sagittal mandibular plane, four mandibular cephalometric landmarks were marked: Point B, Pogonion, Gnathion and Menton. All observations were repeated by the two observers after an interval of 4 weeks. The coordinates (x, y, z) of each landmark were exported, and statistical analyses were performed to evaluate inter- and intra-rater precision.

Results: The intra-observer median precision in locating all landmarks ranged between 0.17 and 0.61 mm. The intra-observer repeatability was generally good with a precision under 1 mm in more than 50 per cent. The overall median inter-observer precision was 0.26–2.30 mm. The mandibular foramina showed the best inter-observer reproducibility. The general inter-observer reproducibility was moderate to good, except for Pogonion and Point B.

Limitations: Dry human skulls may not represent anatomical conditions found in living patients, thus the system should be validated using patients' data.

Conclusion: The novel reference system offered good precision and generally good to moderate repeatability and reproducibility for mandibular midline cephalometric landmark identification in three dimensions. These findings will be useful for further improvement of 3D cephalometric systems.

Introduction

Cephalometric analysis is an essential part of orthodontic treatment planning. This technique was first introduced by Hofrath (1) in Germany and Broadbent (2) in the USA. It is traditionally performed on a lateral and a frontal cephalogram. Although this widely accepted technique has been used as a standard tool for orthodontic treatment planning for several decades, known disadvantages of the technique are geometric distortion and the superimposition of structures on two-dimensional radiographs (3, 4).

A cephalometric analysis comprises several cephalometric landmarks. Mandibular midline landmarks are important elements in many cephalometric analyses. The landmarks in this region are Point B (B), Pogonion (Pog), Gnathion (Gn) and Menton (Me). These important landmarks are used to define mandibular planes and to investigate the relationship of the mandible in relation to the maxilla. These landmarks are part of angular measurements such as Sella-Nasion-Point B and Nasion-Pogonion to the Frankfort horizontal plane. They are also used to analyse the vertical relationship of the jaws (Sella-Nasion to Gonion-Gnathion) and to analyse the inclination of the lower incisors to the mandibular plane (incisor mandibular plane angle) (5).

Three-dimensional imaging modalities, especially cone-beam computed tomography (CBCT), have become important diagnostic tools in dentistry. CBCT generates a lower radiation dose than multi-slice CT (MSCT) sans (6) and produces detailed images of the dentition and maxillofacial region. Therefore, the use of CBCT has become very popular for maxillofacial diagnosis and treatment planning. Three-dimensional images allow orthodontists to accurately visualise craniofacial structures in all dimensions, without superimposition of anatomic structures as seen on two-dimensional radiographs. This modality is useful in orthodontic indications such as canine impaction, root resorption, sleep disorders, orthognathic surgery, and also in three-dimensional cephalometry (6–11). Three-dimensional cephalometry allows clinicians to identify cephalometric landmarks in three dimensions with the aid of 3D image viewing software (12, 13). Several studies have shown the advantages of this technique over traditional 2D cephalometric analysis (14–17).

When using 3D maxillofacial imaging software, the mandibular midline landmarks are usually identified based on 2D cephalometric images generated from a 3D dataset (12). Studies have demonstrated the reliability and accuracy of 3D cephalometric landmark identification, including B, Pog, Gn and Me (18–20). However, it is not clear if these landmarks, identified on the generated 2D image, actually refer to the appropriate mid-sagittal plane of the mandible. In a recent systematic review, the main reason for this was because the reference system provided by several studies used landmarks that are not related to the mandible (21). No accurate method or system that allows the operator to identify mandibular midline landmarks on 3D models without generating 2D lateral cephalometric views has been described to date (21).

Therefore, the aims of this study were to develop a 3D reference system that is specific for mandibular midline cephalometric landmarks and to assess its repeatability and reproducibility.

Materials and methods

Samples

Twenty-six dry human skulls with present upper and lower first incisors and first molars were collected from the Department of Anatomy.

The study protocol (reference number: BE322201010078) was approved by the Medical Ethics Committee. All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

The mandibles were attached to the skulls by taping from the temporal area of both sides. The occlusion was fixed at the maximum intercuspation.

Imaging modalities

CBCT scans of the samples were taken using 3D Accuitomo® 170 (J. Morita, Kyoto, Japan) with the largest field of view (FOV): 170 mm diameter × 120 mm height (High-Fidelity mode: 90 kVp, 154 mAs, voxel size 0.25 mm). A 1.7-mm-thick copper filter was attached to the machine during image acquisition to simulate soft tissue attenuation (22). CBCT data were exported to Digital Imaging and Communications in Medicine (DICOM) files and imported to Maxilim® software version 2.3.0.3 (Medicim NV, Sint-Niklaas, Belgium). A 3D surface model was created for each sample using the full CBCT volume with 0.5 mm sub-sampling of voxels. The recommended voxel size by the software company is 0.4 mm, but this size was not available for this CBCT device. Furthermore, a finer sub-sampling would create more noise and put a heavy load to the computer. Therefore, a 0.5 mm sub-sampling of voxels was selected. The threshold was set at 276 to segment the hard tissues for the 3D models, as the skulls were similar in size, had a similar amount of soft tissue attenuation, the same FOV and position. This threshold value was also recommended by the manufacturer of the software.

3D reference system and observers

A reference system was created in the Maxilim® software to identify the mandibular midline cephalometric landmarks. The reference frame was composed of five mandibular landmarks to create the individual mid-sagittal mandibular plane. Subsequently, four mandibular midline cephalometric landmarks were located on this mid-sagittal mandibular plane (Table 1 and Figure 1).

Two observers, one dentomaxillofacial radiologist with 8 years of experience and one oral and maxillofacial surgeon with 20 years of experience, identified the mandibular landmarks, and were initially calibrated. Detailed instructions about landmark definition and software manipulation were given. The observers completed each set of observations twice with an interval of 4 weeks.

Identification of landmarks and statistical analysis

The coordinates (x, y, z) of the identified landmarks were exported into Excel files. For each pair of landmarks identified by the observers, the Euclidean distance (d) between the two points in a 3D space was calculated by the formula:***

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

Point 1 coordinate (x_1, y_1, z_1) = coordinate at time point 1 or coordinate from observer 1.
Point 2 coordinate (x_2, y_2, z_2) = coordinate at time point 2 or coordinate from observer 2.

Non-parametrical tests were used because the distribution of the data was not normal.

The distance between point 1 (1st observation) and point 2 (2nd observation) was used to determine the intra-observer precision. The

Table 1. Definitions of the landmarks and planes used in the reference system.

Name	Definition
Landmarks	
Mandibular foramen right and left (MF-R, MF-L)	The point at the superior margin of the mandibular foramen
Molar right and left (M-R, M-L)	The point located on the alveolar crest at the area perpendicular to the lingual fissure of the mandibular first molar
Interincisive (II)	The point located at the alveolar crest in the middle between two mandibular central incisors
Point B (B)	The intersection between the mid-sagittal plane and the most posterior point of the anterior surface of the mandibular symphysis
Pogonion (Pog)	The intersection between the mid-sagittal plane and the most anterior point of the mandibular symphysis
Gnathion (Gn)	The intersection between the mid-sagittal plane and the the most anteroinferior point of the mandibular symphysis, bisecting the angle between Pog and Me
Menton (Me)	The intersection between the mid-sagittal plane and the lowest point of the mandibular symphysis
Planes	
Horizontal plane	The plane formed by MF-R, MF-L and II landmarks
Vertical plane	The plane passing through M-R, M-L and perpendicular to the horizontal plane
Mandibular mid-sagittal plane	The plane passing through II and perpendicular to the horizontal and vertical planes

intra-observer precision of each landmark was defined as 'the median distance of all samples.'. The intra-observer precision between observers and the intra-observer precision between landmarks was compared using the multiple Wilcoxon's test with Bonferroni's correction.

To determine the inter-observer precision, four possible distances between the two points of each observer were calculated for each landmark. The inter-observer precision for each landmark was defined as 'the median distance of all samples of these four measures'. The inter-observer precision between landmarks was compared by a multiple Wilcoxon's test with Bonferroni's correction.

Repeatability (intra-observer) and reproducibility (inter-observer) was presented as a percentage and categorised into three levels defined as the percentage of the precision in locating the landmark by less than 0.5 mm, less than 1 mm, or ≥1 mm. Good, moderate and poor reproducibility were defined as when more than 50 per cent of the precision in locating the landmark were less than 1 mm, 51–75 per cent were more than 1 mm and when more than 75 per cent were more than 1 mm, respectively.

Results

Intra-observer precision and repeatability

The median intra-observer precision was more than 1 mm for all landmarks (Table 2). The landmarks that were located the most precisely were the mandibular foramina. Point B (B) showed the highest maximum value at 3.47 mm (median 0.48 mm).

No statistically significant difference was found when comparing the precision between the two observers. When examining the intra-observer precision in locating the landmarks, the right and left mandibular foramina (MF-R, MF-L) were located with significantly better precision than all other landmarks *($P < 0.0001$)*.

The intra-observer repeatability is shown in Table 3. All the landmarks were located with more than 50 per cent of the precision in locating the landmarks 1 mm. The right and left mandibular foramina (MF-R, MF-L) were located with more than 90 per cent precision in locating the landmarks less than 0.5 mm.

Inter-observer precision and reproducibility

The median inter-observer precisions in locating the landmarks are presented in Table 4. Comparison of the inter-observer precision between landmarks showed that MF-R (0.28 mm) and MF-L (0.26 mm) were significantly better than other landmarks *($P < 0.001$)*. The median precision in locating Pog was significantly lower than those of the landmarks *($P < 0.001$)*.

The inter-observer reproducibility is shown in Table 5. All landmarks resulted in more than 50 per cent of the precision in locating the landmark below 1 mm except for Pog, Gn, Me and B. MF-R and MF-L showed the best inter-observer reproducibility with more than 70 per cent of the precision in locating the landmark below 0.5 mm. The distribution of the inter-observer precision of Pog, Gn, Me and B (two observers, two times) are shown in Figure 2. The distribution of the precision of landmark identification mostly ranged between 1 and 3.5 mm. However, a few measurements had a precision of 5 mm (Figure 2).

Discussion

The present study investigated the precision, repeatability and reproducibility of locating landmarks used in a new reference system developed to indicate important mandibular cephalometric landmarks in three dimensions using CBCT scans. The results showed good intra-observer precision and repeatability and moderate to good inter-observer precision and reproducibility in locating the landmarks, except for Pog and B.

In the present 3D cephalometric study, dry human skulls were used to represent human subjects. An *in vitro* design was chosen, as the large field of view for CBCT scans applied (17 cm × 12 cm) is only used on rare occasions for orthodontic patients. Furthermore, the novel 3D reference system is ideally tested regarding repeatability and reproducibility without further bias and limiting factors such as motion artefacts (23). A limitation in using dry human skulls is the lack of soft tissue. Therefore, they may not represent anatomical conditions found in a patient. Due to ethical concerns about exposing healthy human subjects to ionising radiation, it is generally accepted to use dry skulls in cephalometric studies (24). A copper filter was used during image acquisition to simulate soft tissue attenuation and to prevent overexposure (22).

On a 2D lateral cephalogram, the midline landmarks are located using the image-indicated midline. In 3D analysis, one dimension is added, thus to use the same midline landmarks as in 2D, a mid-sagittal plane must be created (21). In the present study, Maxilim®

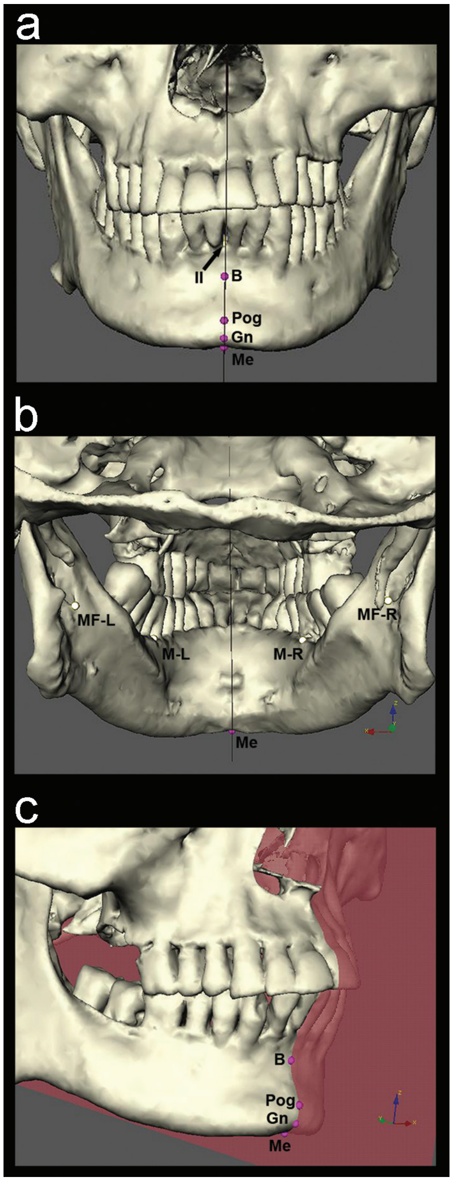

Figure 1. The mandibular landmark reference system. (a) Anterior view of the 3D model of a sample skull showing identified landmarks: II, B, Pog, Gn and Me located on a mid-sagittal plane created based on the reference system. (b) Posterior view of the sample skull with landmarks: MF-R, MF-L, M-R, M-L and Me. (c) Oblique view with 25 per cent transparent of the mid-sagittal plane showing B, Pog, Gn and Me.

software was used to develop the 3D landmark reference system. The reference system developed in our study comprised five operator-indicated mandibular landmarks (MF-R, MF-L, M-R, M-L and II), and four mandibular midline cephalometric landmarks (Pog, Gn, Me and B), which were located on the mandibular mid-sagittal plane created by the reference system. The selection of the landmarks used in the reference frame was based on a previous pilot experiment (data not published) that indicated that these are easily identifiable mandibular landmarks.

A potential limitation of the present study was that the definitions of some landmarks in this new reference system are related to the dentition rather than the skeleton. The locations of the M-R, M-L and II landmark are based on tooth position in the dental arch. Skeletal landmarks are suggested in future studies to avoid the

Table 2. Intra-observer precision (mm).

Landmarks	Median	Min	Max
MF-R	0.23	0.03	1.25
MF-L	0.17	0.03	0.75
II	0.33	0.06	2.31
M-R	0.47	0.07	2.18
M-L	0.61	0.06	2.59
Me	0.40	0.09	2.19
Pog	0.41	0.11	1.95
Gn	0.41	0.07	1.67
B	0.48	0.03	3.47

Table 3. Intra-observer repeatability exhibiting percentages (%) of the precision in locating the landmarks (<0.5 mm, 0.5–1 mm and >1 mm).

	% precision		
Landmarks	<0.5	0.5–1	>1
MF-R	92.3	5.8	1.9
MF-L	92.3	7.7	0.0
II	61.5	30.8	7.7
M-R	55.8	26.9	17.3
M-L	40.4	40.4	19.2
Me	69.2	21.2	9.6
Pog	57.7	23.1	19.2
Gn	59.6	32.7	7.7
B	50.0	21.2	28.9

Table 4. Inter-observer precision (mm).

Landmarks	Median	Minimum	Maximum
MF-R	0.28	0.01	1.30
MF-L	0.26	0.02	1.08
II	0.71	0.03	2.80
M-R	0.80	0.12	2.85
M-L	0.60	0.02	1.98
Me	1.41	0.11	3.05*
Pog	2.30	0.22	5.01*
Gn	1.61	0.12	3.74*
B	1.16	0.06	5.00*

*The maximum inter-observer precision value more than 3 mm.

relation with the tooth position. Potential skeletal landmarks are the mandibular genial tubercle and the mental foramina.

The mandibular specific mid-sagittal plane may deviate from the upper and mid-face mid-sagittal plane where the sella turcica (S) is usually used as one of the elements in connecting this plane (12). However, the mandibular specific mid-sagittal plane represents the mandibular specific midline. Using this mandibular mid-sagittal plane, the mandible can be analysed in three dimensions instead of using a lateral virtual view created from the CBCT image dataset for 3D cephalometry. This plane will be different based on each individual. A review of the literature did not reveal any studies on a 3D reference system that is specific for the mandibular region (21).

The intra-observer precision results indicated that the mandibular foramina were the most precisely located landmarks. Locating Point B had the poorest intra-observer precision and reproducibility among all landmarks. This can be explained by a previous study that found that when a landmark is situated on a curved surface the

Table 5. Inter-observer reproducibility exhibiting percentages (%) of the precision in locating the landmarks (<0.5 mm, 0.5–1 mm and >1 mm).

Landmarks	% precision <0.5	0.5–1	>1
MF-R	74.0	24.0	1.9
MF-L	80.8	17.3	1.9
II	34.6	31.7	33.7
M-R	21.2	49.0	29.8
M-L	39.4	34.6	26.0
Me	15.4	21.2	63.5
Pog	4.8	8.7	86.5*
Gn	4.8	11.5	83.7*
B	25.0	21.2	53.9

*More than 75 per cent.

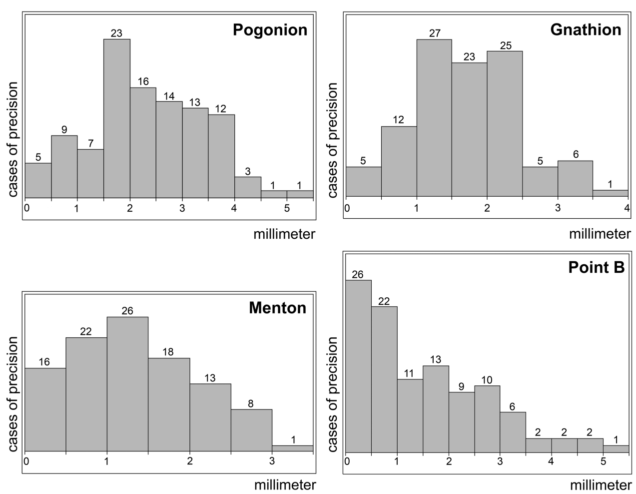

Figure 2. The distribution of the inter-observer precision in locating Pogonion (Pog), Gnathion (Gn), Menton (Me) and Point B (B). The precision distribution of Pog ranged mostly between 1.5 and 4 mm. For Gnathion, the precision ranged between 1 and 2.5 mm. For Me, the precision ranged from 0 to 3 mm and lastly for B, the precision ranged mostly between 0 and 3.5 mm.

accuracy of its identification could be affected (25). Thus, Point B, which is normally defined as the point of maximum concavity in the midline of the alveolar process of the mandible, may be located less accurately compared to a landmark situated on a small specific area, for example MF-R and MF-L. In this study, Point B was less reliable and more difficult to define or prone to subjectivity even though the mid-sagittal mandibular plane could help limit the error. Our results are also supported by other studies that demonstrated that landmarks on a curved surface were usually less reliably located (16, 20). Differences between x-, y- and z-coordinates of the landmarks exhibited that the deviations were randomly distributed among the x-, y- and z-axes.

The difficulty in locating landmarks on a curved surface can also account for the inter-observer precision and reproducibility results. The mandibular cephalometric landmarks Me, Pog, Gn and B were located with a median precision more than 1 mm and the reproducibility in locating these landmarks ranged from poor to moderate. These results might be influenced by several factors. One factor is that these landmarks are located on a curved surface (25). Another factor is the observer itself (subjectivity). Observer performance can be affected by background experience, the familiarity of the observers with the software, and their ability to identify landmarks according to the definitions (19). Therefore, inter-observer performance can be expected to be poorer than intra-observer performance. In addition, landmark definition can also affect precision and reproducibility. A previous study indicated that good landmark definitions improved observer performance (19). A calibration session was conducted prior to the first observation to minimise the effect of these factors as much as possible. Lastly, the measurements can also be influenced by the subjects or samples, that is anatomical variation at the chin area, and the quality of the CBCT scan (artifacts and noise).

A number of studies have investigated general cephalometric landmark identification precision and reproducibility (16, 20, 26, 27). Ludlow *et al.* (26) compared the precision of landmark identification using displays of multiplanar CBCT volumes and conventional lateral cephalograms. The multiplanar reconstructed images (MPR) resulted in generally more precise landmark identification than on lateral cephalograms. The authors found that 3D Pogonion received higher observer variation, similar to the results of the present study. Schlicher *et al.* (20) showed the same trend as in the present study, where landmarks situated on broad curved surfaces without clear anatomical boundaries had a tendency to have errors in identification. The authors determined that Gn was the most consistent landmark among landmarks at the chin area (Pog, Gn and Me) (20). In contrast, in the present study, Me was the most precisely located landmark among the three. Due to differences between the methods of Ludlow *et al.* (26), Schlicher *et al.* (20), and the present study, the results may not be directly compared. In their studies, 3D landmarks were identified on MPR images. In contrast, in present study the landmarks were solely identified on 3D surface models. These differences might affect how the observers viewed the landmarks and where the cursor was placed to identify the respective landmarks.

In 2010, Olszewski *et al.* (16) compared the reproducibility of osseous landmark identification from two 3D cephalometric analyses: 3D-ACRO and 3D-Swennen analyses. Their results were in agreement with the present study, finding that intra-observer repeatability was better than inter-observer reproducibility and that Pogonion was located with poor inter-observer reproducibility. A more recent study by Hassan *et al.* (27) evaluated the precision of landmark identification on MPR, 3D models and MPR with 3D models. Their study found that the precision of measurements ranged between 0.29 ± 0.17 mm for the upper incisor right and 2.82 ± 7.53 mm for the Porion right landmark. The authors suggested that utilising both 3D models and MPR images could improve the precision of landmark identification.

The reference system presented in this study allows clinicians to generate a patient specific mandibular mid-sagittal plane without the need to generate 2D images from 3D data. This system can be used with a limited FOV 3D dataset, which is a significant advantage for 3D cephalometry. It requires only that the mandible is included in the image to create the mandibular specific mid-sagittal plane. It can be utilised when other reference areas, such as the base of skull (14), are not available or in a situation where only a limited size of FOV can be obtained.

Although in this study, the reference system was not tested and validated in asymmetric mandibles, based on its principle, this reference system could be used in asymmetric faces. This system is constructed by using only landmarks in the mandible. Therefore, it is in fact a 3D representation of the mandible both for symmetric and asymmetric ones. The locations of the mandibular midline cephalometric landmarks (Pog, Point B, Gn and Me) are dependent only on the shape and morphology of the mandible and are independent of the overall skull mid-sagittal plane.

In this study, a specific reference system for locating mandibular cephalometric midline landmarks was developed. This system can aid clinicians by generating a patient specific mandibular mid-sagittal plane without the need to generate 2D images from 3D data. To avoid errors from the segmentation, in 3D cephalometric analysis, the clinicians should be aware of this potential issue. Taking into account published data from the literature (27), we recommend to use MPR images together with 3D models in order to confirm the location of 3D landmarks and to reduce landmark identification error as much as possible. Further studies should be performed to improve the definitions of landmarks to be more specific and to test whether the reference system may be improved by using both MPR images and 3D models and to integrate the system into 3D cephalometric analyses.

Funding

The Interfaculty Council for Development Co-operation (IRO, doctoral scholarship).

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