Original Article

Reproducibility of three-dimensional coordinate systems based on craniofacial landmarks

A tentative evaluation of four systems created on images obtained by cone-beam computed tomography with a large field of view

Momoko Shibata^a; Hiroyuki Nawa^b; Yoshitaka Kise^c; Mariko Fuyamada^d; Kazuhito Yoshida^e; Akitoshi Katsumata^f; Eiichiro Ariji⁹; Shigemi Goto^h

ABSTRACT

Objectives: To propose a method for evaluating the reproducibility of anatomical coordinate systems based on craniofacial skeletal landmarks and to tentatively evaluate four systems created on preoperative cone-beam computed tomography (CBCT) data obtained from mandibular prognathism patients in order to confirm the utility for actual patients' data.

Materials and Methods: In three-dimensional images of 10 patients obtained by a CBCT with a large field of view, six dentists set four coordinate systems that were created in different ways, twice by plotting some landmarks situated in the superior portion of the maxillofacial skeletons. The 95% confidence ellipse of six objective landmarks related to the jaw and teeth (upper incisor, left upper first molar, lower incisor, left lower first molar, menton, and left gonion) were three-dimensionally drawn for each coordinate system. The ellipsoid volume was calculated to evaluate the reproducibility of the coordinate systems.

Results: The reproducibility could be evaluated for each coordinate system using the method proposed. The coordinate systems that were created by landmarks situated at greater distances from each other showed relatively small ellipsoid volume in comparison to those with shorter distances between landmarks.

Conclusion: Anatomical coordinate systems with larger distances between the landmarks used were stable when landmarks related to the jaw and teeth were assigned as objective landmarks. The method proposed here was effective in terms of the reproducibility evaluation of a coordinate system. (*Angle Orthod.* 2012;82:776–784.)

KEY WORDS: Cone-beam computed tomography; Reproducibility of results; Imaging; Threedimensional; Facial bones

^a Instructor, Department of Orthodontics, Aichi-Gakuin University School of Dentistry, Nagoya, Japan.

^b Assistant Professor, Department of Pediatric Dentistry, Aichi-Gakuin University School of Dentistry, Nagoya, Japan.

° Instructor, Department of Oral and Maxillofacial Radiology, Aichi-Gakuin University School of Dentistry, Nagoya, Japan.

^d Postgraduate student, Department of Orthodontics, Aichi-Gakuin University School of Dentistry, Nagoya, Japan.

° Part-time instructor, Department of Oral and Maxillofacial Radiology, Aichi-Gakuin University School of Dentistry, Nagoya, Japan.

^t Professor, Department of Oral Radiology, Asahi University School of Dentistry, Mizuho, Japan.

^g Professor, Department of Oral and Maxillofacial Radiology, Aichi-Gakuin University School of Dentistry, Nagoya, Japan.

^h Professor, Department of Orthodontics, Aichi-Gakuin University School of Dentistry, Nagoya, Japan.

INTRODUCTION

Computed tomography (CT) and cone-beam computed tomography (CBCT) for dental use are playing a role in the diagnosis and treatment of various diseases in the maxillofacial region,^{1–11} including the fields of orthodontic treatment and orthognathic surgery.^{9–11} Several methods have been reported^{4,12–18} for threedimensional (3D) measurements using volumetric data obtained by CT or CBCT. In addition to a high-level accuracy, effective reproducibility is essential for 3D measurements of CT images. The accuracy of 3D measurement is regarded to be strong enough for use

Corresponding author: Dr Momoko Shibata, Department of Orthodontics, Aichi-Gakuin University School of Dentistry, 2–11 Suemori-dori, Chikusa-ku, Nagoya, Aichi 464-8651, Japan (e-mail: peach316@dpc.agu.ac.jp)

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as a clinical application to measure the distance between two landmarks or the angle made by three landmarks.¹⁵ However, it cannot be specified which landmark is problematic when the distance or angles show poor reliability (reproducibility). To solve this problem, an alternative is to express a target landmark as a coordinate (x, y, and z components) and to evaluate the reproducibility of the landmark itself.^{19,20} In such a system, a new coordinate system (usually termed an anatomical coordinate system) is created based on some craniofacial skeletal landmarks to investigate the difference in characteristics between subjects. Although the reproducibility of a certain landmark could be evaluated, 19,20 there have been no reports addressing the reproducibility of the anatomical coordinate system itself. In this regard, we have developed an evaluation method to test the reproducibility of coordinate systems and have verified the utility of this method based on phantom study.²¹ However, it has not been verified using actual patient data.

Of course, it is also important to remember that radiation exposure to patients should also be taken into account. If highly reproducible coordinate systems can be established based on the landmarks situated relatively inferiorly in the craniofacial skeleton, the exposure could be reduced because the area scanned for evaluating the landmarks related to jaw and teeth could also be reduced.

The purposes of the present study were to propose a method for evaluating the reproducibility of anatomical coordinate systems and to tentatively evaluate four coordinate systems created based on preoperative CBCT data obtained from mandibular prognathism patients.

MATERIALS AND METHODS

Subjects

Subjects were selected from an image database of patients who were diagnosed with mandibular prognathism and who were preoperatively examined by CBCT in 2008 at our hospital, according to the following criteria:

- Skeletal deformities other than mandibular prognathism were not found in the craniofacial region.
- Craniofacial growth was completed, and the incisors and molars in both the maxillary and mandibular arches were present and unrestored.
- Apparent asymmetry and maxillary hypoplasia were not identified on cephalometric analysis.

As a result, 10 patients (mean age: 23.0 ± 4.8 years; three males and seven females) were selected for this study. All patients were positioned with the occlusal plane horizontally and scanned in an intercuspal

position of occlusion. This study was approved by the ethics committee of our university (approval No. 132).

Acquisition and Manipulation of Image Data

A CBCT machine (Alphard VEGA 3030, Asahi Roentgen Ind Co, Kyoto, Japan) was used. A cylindrical volume (20 cm in diameter and 18 cm in height) was scanned for each patient with exposure conditions of 80 kV and 5 mA and a 17-second exposure time. The voxel size was 0.39 mm \times 0.39 mm \times 0.39 mm.

The CBCT data were saved in DICOM format and transferred to a personal computer using a portable hard disk. Thereafter, 3D images were created employing the volume-rendering method using image analysis software (VG Studio MAX 1.1, Volume Graphics, Heidelberg, Germany). On this initial 3D image, the origin was automatically set outside the skull (a corner of the volume data) (Figure 1A). The coordinate axes (Xi, Yi, and Zi axes) were defined as the initial coordinate system. The 3D coordinates (x, y, and z components) were determined on each voxel and represented as actual size. This software allowed us to simultaneously observe three sectional images in X, Y, and Z directions and to freely select the most appropriate slice for plotting landmarks. A landmark plotted in a slice image was automatically presented in the other two slice images. The landmarks used in the present study and their image-based definitions are presented in Table 1.

Anatomical Coordinate Systems Evaluated

Anatomical coordinate system 1 (Figure 2A). The YZ plane was first determined based on the sella (S), nasion (N), and basion (Ba). Next, the XY plane was determined as the plane including the Ba as the origin, parallel to the axial plane perpendicular to the YZ plane, and including the S and N. Finally, the coronal plane perpendicular to both YZ and XY planes and including the Ba (the origin) was defined as the ZX plane.

Anatomical coordinate system 2 (Figure 2B). First, the XY plane was determined as the axial plane including the Ba (the origin) and parallel to the plane created by the left orbitale (Or-L), left porion (Po-L), and right porion (Po-R). Second, the plane including the Ba perpendicular to the XY plane and parallel to the coronal plane including the Po-L and Po-R was defined as the ZX plane. Finally, the sagittal plane including the Ba perpendicular to the XY and ZX planes was defined as the YZ plane.

Anatomical coordinate system 3 (Figure 2C). First, the XY plane was determined as the axial plane



Figure 1. The initial coordinate system (Xi, Yi, and Zi axes) is automatically determined by image analysis software (A). The origin is set at a corner of the volumetric data transferred from those obtained by cone-beam computed tomography (CBCT). The coordinate of the menton (Me) in the initial coordinate system is defined as the Mei (A). If examiner 1 sets a new anatomical coordinate system 1 based on the sella (S), nasion (N), and basion (Ba), the Mei can be converted to a new coordinate (defined as the Mec1) (B, top). In a similar manner, if examiner 2 sets anatomical coordinate system 1, the Mei can be converted to another coordinate, defined as the Mec2 (B, bottom). When coordinate systems are created with perfect reproducibility between two examiners, the Mec1 and Mec2 will be completely consistent (C). Therefore, the difference between the Mec1 and Mec2 indicates the reproducibility of the coordinate system being evaluated.

Table 1. Definitions of Landmarks

Landmark	Definition				
Landmark used for creating anatomical	l coordinate system				
Sella (S)	Center of the pituitary fossa				
Nasion (N)	Nasofrontal suture at the midline				
Basion (Ba)	Anterior-inferior margin of the foramen magnum				
Left orbitale (Or-L)	Center of the left infraorbital margin				
Left porion (Po-L)	Most superior and lateral point of the bony structure of the external auditory meatus on the left side				
Right porion (Po-R)	Most superior and lateral point of the bony structure of the external auditory meatus on the right side				
Left foramen spinosum (FS-L)	Center of the left foramen spinosum				
Anterior nasal spine (ANS)	Most anterior point of the anterior nasal spine				
Objective landmark					
Upper incisor (U1)	Midpoint between the medial angles of the maxillary central incisors				
Upper left first molar (U6-L)	Most superior point of the medial buccal cusp of the maxillary left first molar				
Lower incisor (L1)	Midpoint between the medial angles of the mandibular central incisors				
Lower left first molar (L6-L)	Most superior point of the medial buccal cusp of the mandibular left first molar				
Menton (Me)	Most inferior point on symphysis of the mandible				
Left gonion (Go-L)	Most inferior and posterior point of the left mandibular angle				



Figure 2. The four anatomical coordinate systems evaluated. Anatomical coordinate system 1 (A) is set based on the sella (S), nasion (N), and basion (Ba). Anatomical coordinate system 2 (B) is set based on the left orbitale (Or-L), left and right porions (Po-L and Po-R), and Ba. Anatomical coordinate system 3 (C) is set based on the left foramen spinosum (FS-L), Po-L, Po-R, and Ba. Anatomical coordinate system 4 (D) is set based on the anterior nasal spine (ANS), Po-L, Po-R, and Ba.



Figure 3. The confidence ellipses of objective landmarks in a patient are presented for anatomical coordinate systems 1 (A), 2 (B), 3 (C), and 4 (D). The scale is 2 mm.

including the Ba (the origin) and parallel to the plane created by the left foramen spinosum (FS-L), Po-L, and Po-R. The coronal and sagittal planes were determined by the same procedure used for determination of anatomical coordinate 2.

Anatomical coordinate system 4 (Figure 2D). First, the XY plane was determined as the axial plane including the Ba (the origin) and parallel to the plane created by the anterior nasal spine (ANS), Po-L, and Po-R. The coronal and sagittal planes were determined by the same procedure used for determination of anatomical coordinate 2.

Theoretical Consideration and Method for Evaluating Reproducibility

According to our previous report,²¹ the underlying theory and method concerning anatomical coordinate system 1 were explained, with the Me being assigned as an objective landmark. In this study, the landmarks to be actually measured for evaluating the patient's status were defined as objective landmarks to differentiate them from those used for setting coordinate systems. The initial coordinate of the Me on the initial coordinate system (Xi, Yi, and Zi axes) was defined as the Mei (Figure 1A). If a new anatomical coordinate system 1 was created by examiner 1, the Mei could be converted to a new coordinate and it would be defined as the Mec1 (Figure 1B, top). Similarly, if examiner 2 set anatomical coordinate 1, the Mei could be converted to another coordinate, defined as the Mec2 (Figure 1B, bottom). With perfect reproducibility between two examiners, the Mec1 and Mec2 should be completely consistent. Therefore, the difference between the Mec1 and Mec2 could reflect the variation (reproducibility) of coordinate systems set by two examiners (Figure 1C). In the present study, six dentists (four orthodontists and two radiologists) set

Table 2. The Mean Ellipsoid Volumes of Objective Landmarks (mm³)

	Anatomical Coordinate System			
Objective Landmark	1	2	3	4
Upper incisor (U1)	99.8	9.6	67.6	7.6
Upper left first molar (U6)	75.8	5.7	40.2	5.6
Lower incisor (L1)	115.4	9.7	73.4	7.6
Lower left first molar (L6)	87.4	6.4	55.5	6.3
Menton (Me)	216.9	14.2	195.9	10.2
Left gonion (Go-L)	91.4	4.3	28.8	5.2



Figure 4. Volumes of confidence ellipsoids.

a coordinate system twice with more than a week interval. A total of 12 converted Me's (Mec1, Mec2, ..., Mec12) were created for each coordinate system. Variation in the 12 coordinates was evaluated threedimensionally with the use of the 95% confidence ellipse method.

In addition to the Me, five landmarks (the upper incisor [U1], upper left first molar [U6-L], lower incisor [L1], lower left first molar [L6-L], and left gonion [Go-L]) were assessed as objective landmarks. The initial coordinates of six objective landmarks were determined on the initial coordinate systems. An author (MS) plotted each landmark three times and averaged the coordinates (x, y, and z components) as the initial coordinates. Coordinate conversion was performed using an in-house–developed macro program on Microsoft Excel 2003 (Microsoft Japan, Tokyo, Japan). The 95% confidence ellipses were created with statistical software (JMP, SAS Institute Japan, Tokyo, Japan). The volume of ellipsoids was calculated and their differences were evaluated using a Tukey-Kramer

test for the four anatomical coordinate systems with a significance level of less than .05.

RESULTS

A patient's 95% confidence ellipses are presented as an example (Figure 3). The 95% confidence ellipse represents the 95% range of data distributed, and it shows a characteristic future of reproducibility in each landmark. The reproducibility is high when the 95% confidence ellipse is small. The ellipses of objective landmarks showed different patterns among the four coordinate systems. The ellipses spread along the Xand Z-axes in anatomical coordinate systems 1 and 3, respectively. In contrast, they were markedly convergent in all directions in systems 2 and 4. All other patients showed similar patterns.

The volumes of ellipsoids in systems 2 and 4 were significantly smaller than those in systems 1 and 3 for almost all objective landmarks (Table 2; Figure 4). There were no significant differences in volumes between anatomical coordinate systems 2 and 4 for

Table 3. Difference in Ellipsoid Volumes of Objective Landmarks Between Anatomical Coordinate Systems

Objective Landmark	System 1 vs System 2	System 1 vs System 3	System 1 vs System 4	System 2 vs System 3	System 2 vs System 4	System 3 vs System 4
Upper incisor (U1)	*		*	*		*
Upper left first molar (U6)	*	*	*	*		*
Lower incisor (L1)	*		*	*		*
Lower left first molar (L6)	*		*	*		*
Menton (Me)	*		*	*		*
Left gonion (Go-L)	*	*	*			

* Significant difference, with P < .05 (Tukey-Kramer test).



Figure 5. An example of the mean distances (mm) between the landmarks used for the initially created planes in anatomical coordinate systems 1 (A), 2 (B), 3 (C), and 4 (D) in a patient.

all objective landmarks (Table 3). Consequently, anatomical coordinate systems 2 and 4 showed higherlevel reproducibility. Objective landmarks far from the origin (Ba) showed relatively large ellipsoid volumes. The largest volume was seen for the Me situated most distant from the Ba among the objective landmarks evaluated.

DISCUSSION

Recently, de Oliveira et al.²² reported landmark reliabilities through the use of an interclass correlation coefficient. We also evaluated the reproducibility of landmarks with use of the 95% ellipse method¹⁹ and reported characteristic features of some landmarks. The Ba was revealed to be a key landmark because it was stable in all directions. Lagravère and Major²³ and Lagravère et al.^{24,25} also proposed the foramen spinosum as a new stable landmark. Comprehension of each landmark characteristic in reproducibility enables proposing various coordinate systems with high-level reproducibility. The four coordinate systems tested here were proposed taking such characteristics of reproducibility into consideration.

Based on a systematic review regarding the reliability and accuracy of landmarks on craniofacial CT images, Lou et al.²⁶ argued that future research should focus on identifying and testing landmarks that would be different from those used for traditional cephalometric analysis. We agree with them because

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two-dimensional landmark definitions could not be completely applied to 3D images. However, we believe it reasonable to define 3D landmarks by modifying those used for cephalography.

In the case of new coordinate systems created employing some skeletal landmarks, the method for evaluating reproducibility would be more complicated. The reproducibility of objective landmarks, which are expressed as coordinate values (x, y, and z components), depends on the reproducibility of newly created anatomical coordinate systems as well as the plotting reproducibility of the objective landmarks themselves. The method proposed here enables one to exclude the plotting variability of the objective landmarks themselves.

Anatomical coordinate systems 2 and 4 showed higher-level reproducibility than systems 1 and 3. A possible cause for this result would be the difference in the distance between the landmarks used for setting coordinate systems. The mean distances are shown in a patient between landmarks on the initially created plane for each coordinate system (Figure 5). The distances in anatomical coordinate systems 2 and 4 were greater than those in systems 1 and 3. In spite of the fact that anatomical coordinate systems 3 and 4 were created with a similar procedure, and despite the fact that the FS and ANS showed a similar level of high reproducibility, ^{19,24} coordinate system 4 showed higher reproducibility, probably because the distances

between the three landmarks determining the first plane were large. Comparing the reliabilities between six objective landmarks, the Me, which was located most inferiorly among the six objective landmarks evaluated and was situated far from the origin (Ba), showed a relatively large ellipsoid volume.

In comparison with anatomical coordinate system 1, systems 2 or 4 can contribute to reducing radiation exposure to patients. The scan for coordinate systems 2 and 4 does not need to include the S and N, which are located in the upper part of the maxillofacial skeleton, thus reducing the scanning area and the patient's dose. Future research should be required focusing on other coordinate systems created by other stable landmarks.

CONCLUSIONS

- Although coordinate systems 2 and 4 showed high reproducibility, the results do not imply that they were most appropriate for clinical use.
- Appropriate coordinate systems should be determined taking system purpose and radiation exposure into account.

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REFERENCES

- Kwon TG, Park HS, Ryoo HM, Lee SH. A comparison of craniofacial morphology in patients with and without facial asymmetry—a three-dimensional analysis with computed tomography. *Int J Oral Maxillofac Surg.* 2006;35:43–48.
- Kawamata A, Ariji Y, Langlais RP. Three-dimensional computed tomography imaging in dentistry. *Dent Clin North Am.* 2000;44:395–410.
- 3. Kawamata A, Ariji Y, Langlais RP. Three-dimensional imaging for orthognathic surgery and orthodontic treatment. *Oral Maxillofac Surg Clin North Am.* 2001;13:713–725.
- 4. Park SH, Yu HS, Kim KD, Lee KJ, Baik HS. A proposal for a new analysis of craniofacial morphology by 3-dimensional computed tomography. *Am J Orthod Dentofacial Orthop.* 2006;129:600.e23–600.e34.
- Kawamata A, Fujishita M, Nagahara K, Kanematu N, Niwa K, Langlais RP. Three-dimensional computed tomography evaluation of postsurgical condylar displacement after mandibular osteotomy. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1998;85:371–376.
- Ariji Y, Kawamata A, Yoshida K, Sakuma S, Nawa H, Fujishita M, Ariji E. Three-dimensional morphology of the masseter muscle in patients with mandibular prognathism. *Dentomaxillofac Radiol.* 2000;29:113–118.
- 7. Ono I, Ohura T, Narumi E, et al. Three-dimensional analysis of craniofacial bones using three-dimensional computer tomography. *J Craniomaxillofac Surg.* 1992;20:49–60.
- 8. Yeshwant K, Seldin EB, Gateno J, Everett P, White CL, Kikinis R, Kaban LB, Troulis MJ. Analysis of skeletal

movements in mandibular distraction osteogenesis. *J Oral Maxillofac Surg.* 2005;63:335–340.

- Maki K, Inou N, Takanishi A, Miller AJ. Computer-assisted simulations in orthodontic diagnosis and the application of a new cone beam X-ray computed tomography. *Orthod Craniofac Res.* 2003;6(suppl 1):95–101.
- Scarfe WC, Farman AG, Sukovic P. Clinical applications of cone-beam computed tomography in dental practice. *J Can Dent Assoc.* 2006;72:75–80.
- 11. Dudic A, Giannopoulou C, Leuzinger M, Kiliaridis S. Detection of apical root resorption after orthodontic treatment by using panoramic radiography and cone-beam computed tomography of super-high resolution. *Am J Orthod Dentofacial Orthop.* 2009;135:434–437.
- Hwang HS, Hwang CH, Lee KH, Kang BC. Maxillofacial 3dimensional image analysis for the diagnosis facial asymmetry. *Am J Orthod Dentofacial Orthop*. 2006;130:779–785.
- Baek SH, Cho IS, Chang YI, Kim MJ. Skeletodental factors affecting chin point deviation in female patients with class II malocclusion and facial asymmetry: a three-dimensional analysis using computed tomography. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;104:628–639.
- Cavalcanti MGP, Rocha SS, Vannier MW. Craniofacial measurements based on 3D-CT volume rendering: implications for clinical applications. *Dentomaxillofac Radiol*. 2004; 33:170–176.
- 15. Waitzman AA, Posnick JC, Armstrong DC, Pron GE. Craniofacial skeletal measurements based on computed tomography: Part I. Accuracy and reproducibility. *Cleft Palate Craniofac J.* 1992;29:112–117.
- 16. Lascala CA, Panella J, Marques MM. Analysis of the accuracy of linear measurements obtained by cone beam computed tomography (CBCT-NewTOM). *Dentomaxillofac Radiol.* 2004;33:291–294.
- Periago DR, Scarfe WC, Moshiri M, Scheetz JP, Silveria AM, Farman AG. Linear accuracy and reliability of cone beam CT derived 3-dimensional images constructed using an orthodontic volumetric program. *Angle Orthod.* 2008;78: 387–395.
- Lopes PML, Moreira CR, Perrella A, Antunes JL, Cavalcanti MGP. 3-D volume rendering maxillofacial analysis of angular measurements by multislice CT. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2008;105:224–230.
- Muramatsu A, Nawa H, Kimura M, Yoshida K, Maeda M, Katsumata A, Ariji E, Goto S. Reproducibility of maxillofacial anatomic landmarks on 3-dimensional computed tomographic images determined with the 95% confidence ellipse method. *Angle Orthod.* 2008;78:396–402.
- Fuyamada M, Nawa H, Shibata M, Yoshida K, Kise Y, Katsumata A, Ariji E, Goto S. Reproducibility of landmark identification in the jaw and teeth on 3-dimensional conebeam CT images. A comparison of tentative methods to those based on cephalometric definitions. *Angle Orthod.* 2011;81:843–849.
- 21. Kimura M, Tokumori K, Nawa H, et al. Reliability of a coordinate system based on anatomical landmarks of the maxillofacial skeleton: an evaluation method for threedimensional images obtained by cone-beam computed tomography. *Oral Radiol.* 2009;25:37–42.
- de Oliveira AE, Cevidanes LH, Phillips C, Motta A, Burke B, Tyndall D. Observer reliability of three-dimensional cephalometric landmark identification on cone-beam computerized tomography. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2009;107:256–265.
- 23. Lagravère MO, Major PW. Proposed reference point for 3dimensional cephalometric analysis with cone-beam com-

puterized tomography. *Am J Orthod Dentofacial Orthop.* 2005;128:657–660.

- 24. Lagravère MO, Hansen L, Harzer W, Major PW. Plane orientation for standardization in 3-dimensional cephalometric analysis with computerized tomography imaging. *Am J Orthod Dentofacial Orthop.* 2006;129:601–604.
- 25. Lagravère MO, Major PW, Carey J. Sensitivity analysis for plane orientation in three-dimensional cephalometric

analysis based on superimposition of serial cone beam computed tomography images. *Dentomaxillofac Radiol.* 2010;39:400–408.

 Lou L, Lagravère MO, Compton S, Major PW, Flores-Mir C. Accuracy of measurements and reliability of landmark identification with computed tomography (CT) techniques in the maxillofacial area: a systematic review. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;104:402–411.