

Differences between Posteroanterior Cephalometric Analysis By 2D Conventional Posteroanterior Cephalograms and 3D Models Generated from Cone Beam Computed Tomography

Natthiya Rueangnithithanakit* Kulthida Parakonthun **

Abstract

Background: This study compared the differences in posteroanterior (PA) cephalometric analysis on a two-dimensional (2D)-PA cephalogram with cone beam computed tomography (CBCT) via Dolphin imaging software[®]. **Materials and methods:** Retrospective data from 35 patients who required orthodontic treatment (35 2D-PA cephalograms and 35 CBCT images) were obtained. All radiographs were imported into the Dolphin imaging program[®], aligned, and calibrated for magnification using patients' tooth sizes derived from dental models. Landmarks were identified, and linear measurements modified from Grummons analysis were evaluated. 2D-PA cephalograms and CBCT measurements were compared via paired *t* tests ($P < 0.05$). **Results:** According to Grummon PA cephalometric analysis, significant differences ($P < 0.05$) were observed in 10 horizontal, 2 vertical, and 2 mandibular length variables between 2D-PA cephalograms and CBCT. **Conclusion:** Compared with CBCT, 2D-PA cephalography could acceptably indicate the degree of menton deviation. However, the measurements above the maxillary area from 2D-PA cephalograms are significantly different from those from CBCT. PA cephalograms could be used as an initial tool to evaluate lower facial asymmetry. However, for cases requiring detailed analysis and comprehensive planning, CBCT might be necessary.

Keywords: CBCT, Dolphin imaging software[®], Grummons analysis, PA cephalometric analysis, 2D PA cephalogram

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Corresponding author: Kulthida Parakonthun

E-mail: kulthidap@g.swu.ac.th

* Dentist, Professional Level, Nakhonphanom Hospital, Mueang Nakhon Phanom, Nakhon Phanom, Thailand

** Assistant Professor, Faculty of Dentistry, Srinakharinwirot University, Bangkok, Thailand

Introduction

During clinical examination for orthodontic treatment, various tools, such as the study model, intra- and extraoral photographs, and associated radiographs, are necessary for making an accurate diagnosis and proper treatment planning. Typically, the most common radiographs used for orthodontic evaluation are lateral cephalometric radiographs, which are used to examine the relationships among the cranial base, maxilla, and mandible in the anteroposterior and vertical dimensions,¹ and panoramic radiographs, which provide an overview of the teeth, basal bones, and peripheral structures, such as the temporomandibular joint (TMJ), and various parts of the mandible.^{2,3}

Additional radiographs, such as posteroanterior cephalometric radiographs (PA cephalograms) and periapical films, which are frequently taken in conjunction with previous radiographs for evaluating abnormalities in all three dimensions (transverse, anteroposterior, and vertical), may be considered in cases of facial or dental asymmetry. If a patient has severe malocclusion or facial deformity or has undergone orthognathic surgery, cone beam computed tomography (CBCT) should be used.^{2,3} There are several benefits of CBCT in orthodontics, including the assessment of anomalies in the dental position, impacted teeth, and the detection of any supernumerary teeth. CBCT can be utilized in craniofacial orthodontics to assess the effects of maxillary expansion and evaluate clefts; it also provides a three-dimensional (3D) assessment for alveolar boundary conditions, assesses the relationship between dentition and jaw bones, and detects root resorption in the labial and palatal surfaces of the teeth that are not visible in two-dimensional (2D) radiographs. Additionally, CBCT can provide information regarding the bony structure of the TMJs and help in deciding on mini-implant placement.^{2,4-7} However, there are still some drawbacks to using CBCT in orthodontics, such as higher radiation doses than conventional techniques do, difficulty in distinguishing soft tissue types, greater

time consumption for landmark identification, lower accuracy for caries detection, the presence of inherent artifacts from metal orthodontic brackets and bands, and greater time and greater cost than conventional radiography does.^{3,4,7}

The analysis of 2D cephalometric radiographs, both lateral and posteroanterior, frequently reveals problems with magnification, distortion, and superimposition of the surrounding structures. These are significant issues that could result in landmark identification errors in cephalometric analysis,⁸ leading to incorrect diagnoses and treatment plans, particularly in posteroanterior cephalometric radiographs. Therefore, CBCT images have been widely used in orthodontics^{3,4,9} due to the lack of magnification, overlap, and distortion of structures, and CBCT can generate real-size 3D images of patients, allowing for precise and accurate analysis and measurements.^{7,10}

Several previous studies have examined the validity and accuracy of landmark identification via PA cephalograms and reported that midline landmarks are more reproducible than bilateral skeletal landmarks.¹¹ Most landmarks showed good reproducibility, except for some landmarks located in the zygomatic arch, mandible, and dentition. This factor could cause inaccurate PA cephalometric analysis when evaluating dental discrepancies or maxillary–mandibular relationships.¹² Bajaj K. et al., compared the reliability of landmark identification between PA cephalograms and CBCT images. They reported that CBCTs were more accurate and reliable than were PA cephalograms.⁸ Damstra J. et al., reported that, compared with PA cephalograms, CBCT images were more reliable and accurate in detecting mandibular asymmetry.¹³ In contrast, some studies reported that there was no difference between the PA cephalogram and CBCT in measuring and diagnosing landmarks and evaluating asymmetry. However, CBCT provides more comprehensive and detailed information about craniofacial anatomy.^{14,15}

Many previous studies^{8,11-15} focused on the accuracy and reliability of landmark identification, including the comparison of linear or angular measurements in PA cephalometric analysis on 2D PA cephalograms and on CBCT-generated PA cephalograms. Reports on differences in posteroanterior cephalometric analysis between 2D PA cephalograms and 3D skull models generated from CBCT images directly are still limited. Therefore, the aim of this study was to compare the differences in linear measurements in PA cephalometric analysis between 2D PA cephalograms and 3D skull models generated from CBCT images.

Materials and methods

Sample size

This retrospective study used original radiographic data from 35 patients who underwent orthodontic treatment at the Faculty of Dentistry, Srinakharinwirot University, from 2018-2023. All 35 patients had received initial records and examinations with additional tools, such as dental models and cephalometric radiographs. Ethical approval for this study was obtained from the Human Research Ethics Committee of Srinakharinwirot University (Certificate Number SWUEC/E-213/2565). The inclusion and exclusion criteria were as follows:

Inclusion criteria

- 1) Patients aged 20 years and over.
- 2) The patients had previously undergone 2D PA cephalometric radiography (Soredex Cranex D Panoramic & Ceph X-ray) and CBCT imaging (Acteon Whitefox) before the beginning of orthodontic treatment.
- 3) The quality of the 2D PA cephalograms was good (proper density, blackness, contrast, and proper head position).
- 4) All patients had dental models that were in perfect condition, especially upper or lower central incisors.

Exclusion criteria

- 1) Patients with congenital genetic abnormalities

such as cleft lip and palate or craniofacial anomalies, including a history of facial and jaw injuries.

2) The radiographs revealed signs of head tilting or rotation or where the occlusion was not positioned in centric occlusion.

3) Radiographs with full crown restorations on the upper or lower central incisors.

Patients with any skeletal classification (Classes I, II, or III) were eligible for inclusion in this study if they satisfied the specified criteria.

A sample size calculation was performed with G*power software version 3.1.9.6 (Heinrich Heine, Universitat Dusseldorf, Germany), assuming that the effect size was 0.5 ($d = 0.5$), $\alpha = 0.05$ with 80 % statistical power. The total sample size was 34 patients per study group.

Methods for importing 2D PA cephalograms and 3D reconstructions from CBCT images via Dolphin Imaging Software®

For 2D PA cephalography

1) The file of the PA cephalogram was imported into Dolphin Imaging Software®.

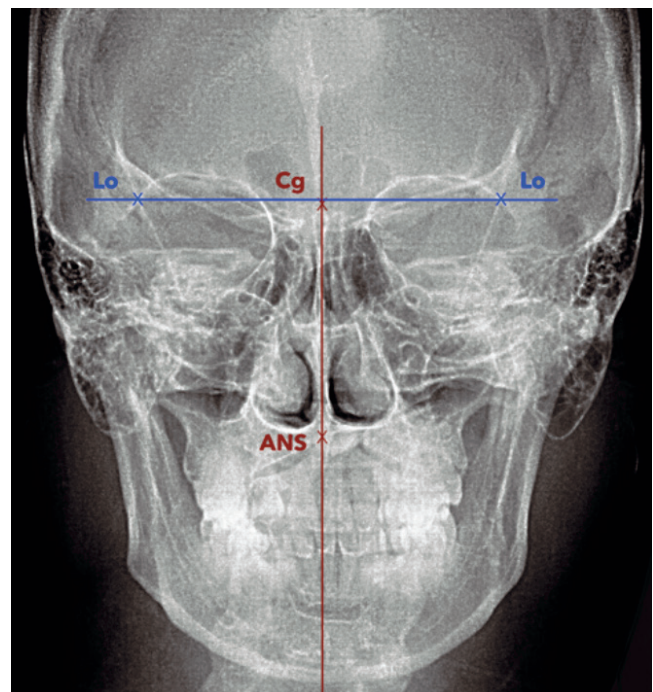


Figure 1 Orientation of a 2D PA cephalogram, with the midsagittal reference plane aligned perpendicular to the Latero-Orbital Line.

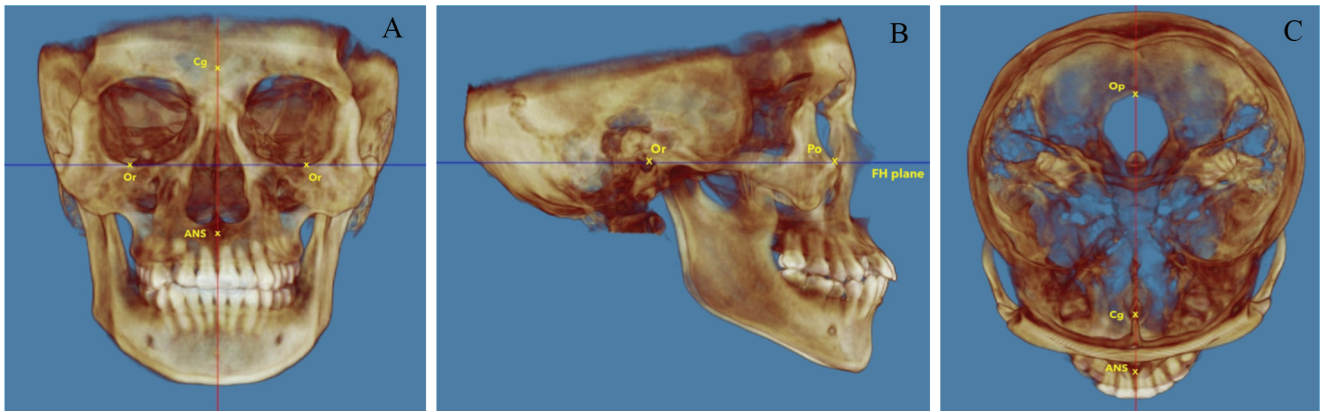


Figure 2 Orientation of 3D CBCT: (A, C) The midsagittal plane passing through Cg (Crista galli), ANS (anterior nasal spine), and Op (opisthion) was aligned perpendicular to the Frankfort Horizontal Plane. (B) The Frankfort Horizontal Plane was defined by Po(R) (Porion Right), Or (Orbitale), and Po(L) (Porion Left).

2) The radiographs were adjusted to the proper position, ensuring that the midsagittal plane (a line passing through the Crista galli and anterior nasal spine) was perpendicular to the horizontal reference plane (latero-orbital line: Lo-Lo),^{16,17} as shown in Figure 1.

CBCT data

1) The DICOM data of the CBCT image were copied to the computer.

2) By using Dolphin Imaging Software®, the patient's DICOM data were downloaded with 30 % downsizing (recommended by the company).

3) The program processed and rendered the data into a 3D skull model.

4) The head position was reoriented by aligning the midsagittal reference plane (Cg-ANS-Op)¹⁸ perpendicular to the horizontal reference plane (Po(R)-Or-Po(L)). Unrelated parts, such as the cervical vertebrae, were trimmed off for clarity, as shown in Figure 2.

The landmark measurements on the 2D PA cephalogram and 3D skull model generated from CBCT according to the Grummons PA cephalometric analysis

The measurement in this study was performed by one examiner (NR) who has had orthodontic treatment experience for 4 years. The data from 35 patients were divided into 2 groups.

Group 1–2D PA cephalometric radiographs

Group 2–3D skull model generated from CBCT images

1) The landmark points were determined in both groups (Figure 3). The definitions of each landmark on the 2D PA cephalogram and 3D skull image are shown in Table 1.

2) The midsagittal reference plane (MSR), which was the line from the Crista galli (Cg) to the anterior nasal spine (ANS), was set in Group 1, and the MSR from the Cg to the ANS and opening (Op) were set in Group 2.

3) Linear horizontal distances were measured from landmark points on each side to the midsagittal reference plane (MSR), linear vertical distances were measured from the Cg (Crista galli) point to the given landmarks, and the mandibular length was measured according to the Grummons PA cephalometric analysis on both 2D PA cephalogram and 3D skull image to compare the differences between the two groups. In 3D imaging, linear horizontal and vertical distances are measured by projecting the landmark points onto the anterior facial plane, resulting in 2D distances, whereas the mandibular length is measured directly in 3D distances, as shown in Figures 4-6.

4) Owing to the different magnifications of different radiographs, the size of the upper or lower

Table 1 Abbreviations and definition of reference points and midsagittal plane used in this study.¹

The reference points and midsagittal plane in the Grummons PA cephalometric analysis		
AG(R)/AG(L)	: Antegonial notch	The deepest point of the antegonial depression
ANS	: Anterior nasal spine	The most anterior point above the hard palate and below the nasal cavity
Cg	: Crista galli	The highest point of the triangular protrusion of the ethmoid bone that protrudes from the cribriform plate
Co(R)/Co(L)	: Condylion	The highest point on the mandibular condyle
J(R)/J(L)	: Jugal process	The highest point on the maxillary alveolar process
Me	: Menton	The lowest point of the mandibular symphysis
NC(R)/NC(L)	: Nasal cavity	The outermost point of the nasal cavity
ZA(R)/ZA(L)	: Zygomatic arch	The outermost (lateral) point of the zygomatic arch
MSR	: Mid-Sagittal reference plane	The mid-facial line through the Cg and ANS points

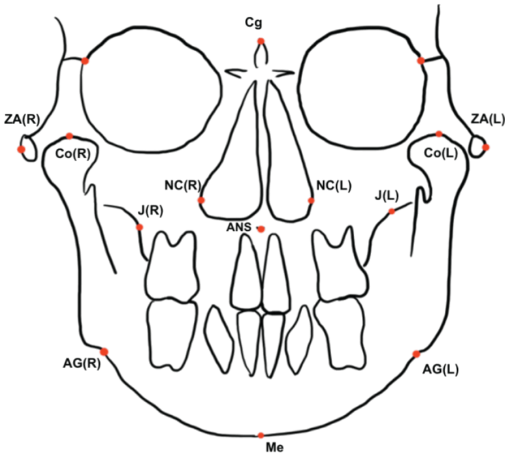


Figure 3 Reference points on PA cephalogram according to the Grummons analysis.¹⁹

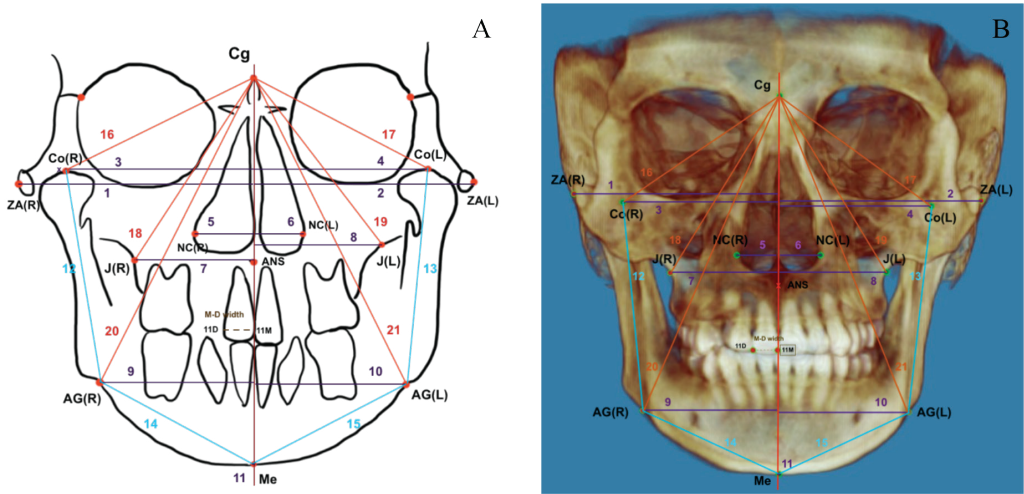


Figure 4 (A) The horizontal-vertical linear measurements and mandibular length used in this study.¹⁹ Purple lines were linear horizontal measurements that represented the distances between the bilaterally skeletal landmarks and MSR. Orange lines were linear vertical measurements that represented the distances between the given landmarks and Cg. Blue lines were mandibular length measurements that represented the distances of Co-AG and AG-Me. (B) 3D skull generated by the Dolphin imaging software.

incisors was used to calibrate scales (depending on the skeletal relationship type I, II, or III). The tooth size was measured directly from the patient's dental model. All the measurements were repeated twice at least one week apart, and the average of the measurements was used for further analysis and interpretation. All measurements were recorded in millimeters (mm).

5) All samples in each group were identified at landmark positions and measured twice within 1-week intervals to assess intraexaminer reliability.



Figure 5 An example of a 2D PA cephalogram with all variables measured.

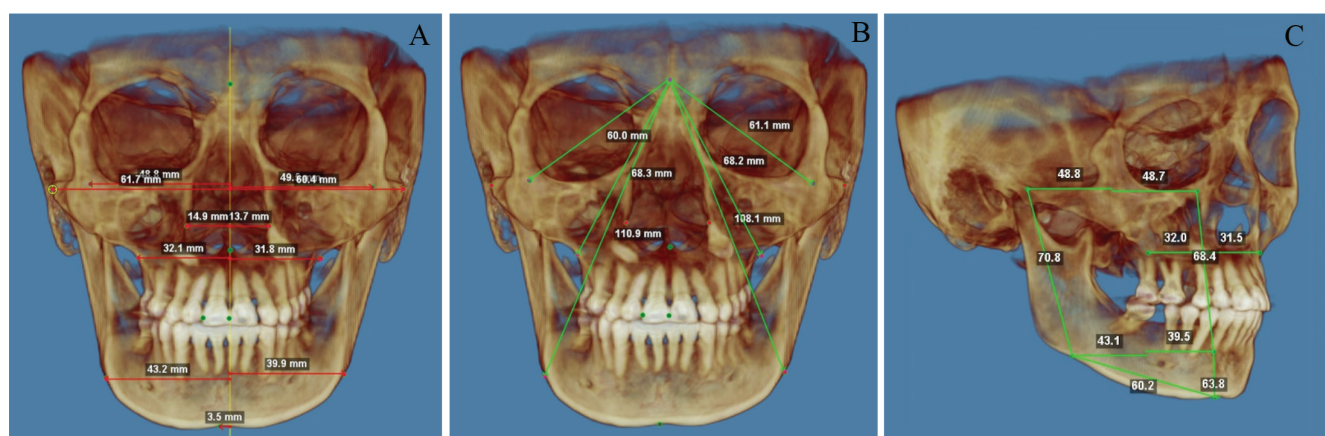


Figure 6 An example of CBCT in Dolphin Software with all variables measured. (A) Linear horizontal distances, (B) linear vertical distances, and (C) mandibular length measurements.

Statistical analysis

1) Intraexaminer reliability was analyzed via the intraclass correlation coefficient (ICC).

2) All the data were tested for normality via the Shapiro–Wilk test, and the mean difference between the two groups was compared via paired *t* tests or Wilcoxon tests (IBM SPSS Statistics, Version 28.0.1.0 (IBM, Armonk, NY)). A *P* value < 0.05 was considered statistically significant.

Results

All variables were normally distributed. The intraclass correlation coefficient was high (the average

ICC value of the 2D group was 0.925 [0.833–0.974], and the ICC value of the 3D group was 0.963 [0.895–0.998]), indicating good to excellent intraexaminer reliability.

In this study, 21 variables were measured from thirty-five 2D PA cephalometric radiographs and a 3D skull model generated from CBCT images. The results from the measurements are summarized in Table 2. The results of the Grummons PA cephalometric analysis revealed significant differences (*P* < 0.05) in 10 horizontal variables (ZA(R)-MSR, ZA(L)-MSR, Co(R)-MSR, Co(L)-MSR, NC(R)-MSR, NC(L)-MSR, J(R)-MSR, J(L)-MSR, AG(R)-MSR, AG(L)-MSR), 2 vertical variables (Cg-Co(R), Cg-Co(L)), and 2 mandibular length variables (AG(R)-Me, AG(L)-Me) when the PA cephalometric

analysis of the 2D-PA cephalogram and CBCT data was compared. All the significant variables are shown in the figure below (Figure 7). However, other areas were not significantly different.

Table 2 The results of the 21 variables measured in this study were presented, with those showing significant differences highlighted.

Variables		n	Paired differences (mm)					t	df	P value
			Mean	Std. Deviation	Std. Error Mean	95 % Confidence Interval of the Difference				
						Lower	Upper			
Horizontal measurements	(2D) ZA(R)-MSR - (3D-P) ZA(R)-MSR	35	4.92	4.60	0.77	3.34	6.50	6.32	34	< 0.001*
	(2D) ZA(L)-MSR - (3D-P) ZA(L)-MSR	35	4.84	5.53	0.93	2.94	6.74	5.17	34	< 0.001*
	(2D) Co(R)-MSR - (3D-P) Co(R)-MSR	35	6.40	4.21	0.71	4.95	7.85	8.99	34	< 0.001*
	(2D) Co(L)-MSR - (3D-P) Co(L)-MSR	35	5.20	4.78	0.80	3.55	6.84	6.43	34	< 0.001*
	(2D) NC(R)-MSR - (3D-P) NC(R)-MSR	35	4.85	1.74	0.29	4.25	5.45	16.44	34	< 0.001*
	(2D) NC(L)-MSR - (3D-P) NC(L)-MSR	35	4.15	2.13	0.36	3.41	4.88	11.49	34	< 0.001*
	(2D) J(R)-MSR - (3D-P) J(R)-MSR	35	0.94	2.47	0.41	0.09	1.79	2.25	34	0.031*
	(2D) J(L)-MSR - (3D-P) J(L)-MSR	35	1.50	3.02	0.51	0.46	2.54	2.94	34	0.006*
	(2D) AG(R)-MSR - (3D-P) AG(L)-MSR	35	2.45	3.47	0.58	1.26	3.64	4.17	34	< 0.001*
	(2D) AG(L)-MSR - (3D-P) AG(L)-MSR	35	3.73	4.34	0.73	2.24	5.22	5.08	34	< 0.001*
	(2D) Me-MSR - (3D-P) Me-MSR	35	-0.75	2.68	0.45	-1.67	0.17	-1.65	34	0.108
Vertical measurements	(2D) Cg-Co(R) - (3D-P) Cg-Co(R)	35	4.08	5.21	0.88	2.29	5.87	4.63	34	< 0.001*
	(2D) Cg-Co(L) - (3D-P) Cg-Co(L)	35	2.29	6.22	1.05	0.15	4.42	2.17	34	0.037*
	(2D) Cg-J(R) - (3D-P) Cg-J(R)	35	1.23	5.73	0.96	-0.73	3.20	1.27	34	0.213
	(2D) Cg-J(L) - (3D-P) Cg-J(L)	35	1.62	5.99	1.01	-0.43	3.68	1.60	34	0.117
	(2D) Cg-AG(R) - (3D-P) Cg-AG(R)	35	2.09	8.86	1.49	-0.94	5.14	1.40	34	0.171
	(2D) Cg-AG(L) - (3D-P) Cg-AG(L)	35	2.24	9.27	1.56	-0.94	5.42	1.43	34	0.161
Mandibular length	(2D) Co(R)-AG(R) - (3D) Co(R)-AG(R)	35	0.83	6.33	1.07	-1.34	3.00	0.77	34	0.442
	(2D) Co(L)-AG(L) - (3D) Co(L)-AG(L)	35	1.34	6.15	1.04	-0.76	3.46	1.29	34	0.204
	(2D) AG(R)-Me - (3D) AG(R)-Me	35	-16.20	5.34	0.90	-18.03	-14.36	-17.94	34	< 0.001*
	(2D) AG(L)-Me - (3D) AG(L)-Me	35	-17.58	5.53	0.93	-19.48	-15.67	-18.79	34	<.001*

Abbreviations: 2D, two-dimensional distances; 3D-P, 3D-projected distances; 3D, three-dimensional distances.

* Statistically significant at P value < 0.05

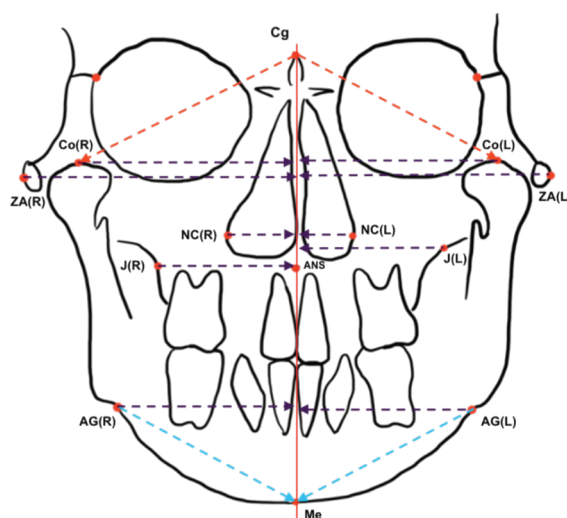


Figure 7 The diagram indicated significant differences in 10-horizontal (purple dashed line), 2-vertical (orange dashed line), and 2-mandibular body length (blue dashed line) measurements when comparing the PA cephalometric on 2D-PA cephalogram and CBCT.

Discussion

Posteroanterior (PA) cephalograms are additional radiographs that are frequently taken in conjunction with lateral cephalograms and panoramic radiographs to assess abnormalities, especially in cases of facial or dental asymmetry.^{2,19,20} PA cephalometric analysis is usually performed on conventional 2D PA skull images, which frequently reveals problems with magnification, distortion, and superimposition of the surrounding structures. Although the PA cephalogram has several limitations, it is nevertheless widely used because of its simplicity, rapidity, cost-effectiveness, and minimal radiation exposure.^{4,8,21} When the advantages and disadvantages of this image are compared with the benefits that the patient receives, the 2D PA cephalogram is generally considered sufficient for initial diagnosis, treatment planning, monitoring, and posttreatment evaluation in uncomplicated cases.⁴ CBCT, on the other hand, is increasingly regarded as the gold standard for oral and maxillofacial imaging, particularly in orthodontics, including the assessment of dental position anomalies, as well as in patients undergoing orthognathic surgery. Unlike conventional radiographs, CBCT provides volumetric data, enabling the generation of real-size 3D images without distortion

or overlapping structures, thus offering more precise and reliable landmark identification and measurement.⁶ Our study corroborates these benefits, with high intrarater reliability observed in both imaging modalities (ICC for 2D = 0.925; ICC for 3D = 0.963). This is consistent with findings by Bajaj et al., who reported higher accuracy and reliability in CBCT imaging than in PA cephalograms.⁸

Dolphin imaging software[®] was used in this study, and we found that the results from this study were similar to those of the studies by Damstra et al., and Tai et al. The right and left mandibular body lengths (AG(R)-Me and AG(L)-Me), including the mandibular width (AG(R)-MSR and AG(L)-MSR), which were measured in the 2D group, were significantly different from those in the 3D CBCT group.^{13,22} Furthermore, our study revealed contrasting results with prior studies, particularly in the PA cephalometric analysis of the upper face, where significant differences were observed for ZA(R)-MSR, ZA(L)-MSR, Co(R)-MSR, Co(L)-MSR, NC(R)-MSR, NC(L)-MSR, J(R)-MSR, J(L)-MSR, Cg-Co(R), and Cg-Co(L). No significant differences were found for mandibular ramus length (Co(R)-AG(R), Co(L)-AG(L)), lower facial height (Cg-J(R), Cg-J(L), Cg-AG(R), Cg-AG(L)), or menton deviation from the midline (Me-MSR)). These findings highlight the differential reliability of 2D imaging across craniofacial regions

and align with previous studies emphasizing the challenges posed by magnification and beam divergence in conventional radiographs. However, the results of this study differed from those of prior studies using Ricketts analysis and software such as Viewbox (for conventional PA cephalograms) and Simplant Ortho Pro 2.00 (for CBCT).^{13,22} By employing Grummons PA cephalometric analysis, a comparative and quantitative approach, we focused on differences in landmark-based measurements rather than normative data.^{1,15,20}

Clinical Significance of Findings

While statistically significant differences were observed in several variables, their clinical relevance varies. For example, a difference of approximately 0.94 mm in (2D) J(R)-MSR - (3D-P) J(R)-MSR may fall within clinically acceptable limits for routine orthodontic evaluations. However, larger differences, such as mandibular body lengths (AG(R)-Me, AG(L)-Me) exceeding 16 mm, are likely to have significant clinical implications, particularly in cases involving facial asymmetry or surgical planning. Furthermore, a consistent trend of overestimation in horizontal and vertical distances was identified in 2D imaging compared with 3D projections, with statistically significant differences across multiple variables (e.g., ZA(R)-MSR, ZA(L)-MSR, Co(R)-MSR, Co(L)-MSR, NC(R)-MSR, NC(L)-MSR; all P values < 0.001). This overestimation is attributed primarily to the inherent limitations of traditional 2D cephalometric radiography, particularly magnification and distortion effects. Conversely, mandibular length measurements (e.g., AG(R)-Me and AG(L)-Me) were significantly underestimated in 2D imaging relative to 3D imaging (- 16.20 mm and - 17.58 mm, respectively; P values < 0.001). This discrepancy can be explained by the fundamental differences in landmark positioning in 3D space. While 2D imaging captures linear distances along a perpendicular axis, which results in a lack of depth perception, 3D imaging accounts for complex spatial trajectories, leading to increased measured

distances. This limitation is particularly relevant in mandibular assessments, where anatomical curvatures and spatial positioning necessitate precise measurement techniques. The observed discrepancies emphasize the need for caution when relying solely on 2D imaging for transverse discrepancy or asymmetry evaluations. While 2D imaging may suffice for uncomplicated cases, CBCT is advantageous in scenarios requiring high precision, such as craniofacial surgery, severe malocclusions, or detailed assessments of anatomical structures.

Utility of Dolphin Imaging Software

This study utilized Dolphin Imaging Software® to perform measurements based on the Grummons method for both 2D and 3D images. The software facilitated the projection and identification of landmarks within 3D images; however, measurements were conducted in 2D due to the positioning of landmarks and reference planes in different planes within the 3D dataset. Notably, the software's ability to measure true 3D distances, such as mandibular ramus and body lengths, highlights the advantages of CBCT imaging over conventional 2D techniques by providing more accurate and clinically relevant measurements.^{23,24}

While CBCT is currently recommended as the gold standard method and has many advantages in orthodontics, it is not universally indicative or a standard diagnostic radiograph for all orthodontic patients. Clinicians must carefully weigh the potential risks, such as increased radiation exposure and additional costs, against the benefits of enhanced diagnosis and treatment planning before recommending CBCT for their patients.^{2,4,25}

Limitations of research

Several limitations of this study should be acknowledged. First, the retrospective design of this study inherently limits control over the consistency of data collection, particularly with respect to radiograph quality and initial positioning. Additionally, the calibration method used to adjust for magnification in the 2D X-ray images was a modification of the

standard approach due to the absence of a ruler on the radiographic images. Second, the sample size ($n = 35$) was relatively small, which limits the generalizability of the findings. A larger sample population could have provided greater statistical power and enabled subgroup analyses based on factors such as skeletal classification or age group to explore the potential influence of demographic or clinical variations. Finally, differences between imaging modalities present inherent limitations. While CBCT provides volumetric data, enabling more precise localization of landmarks, conventional 2D radiographs are subject to magnification and superimposition of anatomical structures. Despite efforts to calibrate for magnification differences, eliminating this bias has proven challenging.

For further research, a prospective design with standardized imaging protocols and larger, more diverse sample populations should be included to validate these findings. Additionally, comparisons between conventional 2D PA cephalograms and CBCT-reconstructed 2D images could provide further insight into the clinical value of CBCT in orthodontics.

Conclusions

This study led to several important conclusions regarding imaging techniques used to assess facial asymmetry. 2D PA cephalograms were found to be useful for evaluating menton deviation. However, significant differences were observed in measurements of the upper facial region when compared to CBCT, indicating limitations of 2D imaging in this area. Additionally, caution is recommended when using 2D PA cephalograms to assess lower facial asymmetry, particularly in the mandibular angle and body regions, due to notable discrepancies in measurements compared with CBCT. Overall, CBCT provided more accurate and reliable landmark identification and cephalometric measurements, highlighting its importance in cases that require precise anatomical assessment.

Author contributions

NR: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Resources, Data curation, Writing-Original draft, Writing-Review & Editing, Visualization; KP: Conceptualization, Writing-Review & Editing, Supervision, Project administration.

Ethical statement

The study protocol was approved by the Human Research Ethics Committee of Srinakharinwirot University (Certificate Number: SWUEC/E-213/2565).

Disclosure statement

The authors have no conflicts of interest.

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