Original Article

Stability of fiducial cephalometric landmarks of growing Class II malocclusion patients: a three-dimensional retrospective study

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ABSTRACT

Objectives: To evaluate three-dimensionally (3D) the stability of Nasion (Na), Sella (S), Basion (Ba), Porion (Po), and Orbitale (Or) in different age groups of growing Class II malocclusion patients and, additionally, to assess rotational changes of the S-Na and Ba-Na lines and the Frankfurt Horizontal Plane (FHP).

Materials and Methods: Cone-beam computed tomography studies of 67 Class II division 1 malocclusion patients, acquired at baseline (T0) and 1 year later (T1), were retrospectively assessed. Anterior cranial fossa was used for volumetric superimposition. Subjects were grouped according to their age at T0: group 1 (G1) (8–10 years), G2 (11–13 years), and G3 (14–17 years). Quantitative assessments of the 3D linear displacements (Euclidean distance) in the position of Na, S, Ba, Po, and Or were performed. Displacement in the X, Y, and Z projections and the rotation of S-Na, Na-Ba, and FHP were also quantified.

Results: All cephalometric landmarks showed 3D displacement ($P = .001$) in the three age groups. Orbitale remained stable in the vertical and sagittal dimension from 8 to 17 years ($P > .05$). S-Na, Na-Ba, and the FHP showed statistically significant angular rotation ($P < .05$) in younger patients (G1), while in older individuals (G2 and G3) they were stable ($P > .05$).

Conclusions: Na, S, Ba, and Po showed vertical and sagittal positional changes relative to the anterior cranial fossa during the growth of Class II individuals. After age 11, S-Na, Na-Ba, and FHP did not show rotation and, thus, are valid parameters for angular cephalometric analysis in Class II growing patients. (*Angle Orthod.* 2022;92:619–627.)

KEY WORDS: Growth and development; Cephalometry; Cone-beam computed tomography; Imaging; Three-dimensional

INTRODUCTION

The dentoskeletal assessment of orthodontic/orthopedic treatment of growing patients with Class II malocclusion is based on several factors, including cephalometric measurements. Therefore, a stable region for the superimposition of different time point records is required. Classically, cephalometric landmarks and constructed lines located at the cranial base (CB) or the Frankfort horizontal plane (FHP) have been used as fiducial references.[1,2] But are these landmarks and lines stable during the growth phase?

Although the CB shows early ossification, some structures remain actively growing until later stages of development.[3] The most frequently used fiduciary landmarks in cephalometrics are Sella (S), Nasion (Na), and Basion (Ba),[1,4] but all of these might theoretically undergo spatial changes during normal growth. Point S is displaced downward and backward because of bone resorption at the posterior wall of the

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sella turcica. In the same way, increases in the thickness of the frontal bone contribute to increased length of the outer surface of the anterior cranial base.[4–6] Therefore, point Na displaces as the outer layer of the frontal bone is significantly remodeled with aging.[4] The role of the spheno-occipital synchondrosis during growth may also influence the position of point Ba.[2,7] The FHP has been used as an alternative in several cephalometric analyses, but its role in cephalometric analysis depends on the stability of the spatial changes of Porion (Po) and Orbitale (Or).

Up to this point, the evaluation of the spatial changes of the anatomic structures used as references for cephalometric analysis was challenging because of the two-dimensional (2D) limitations within the region of interest for superimposition. The introduction of cone-beam computed tomography (CBCT) brought about the ability to evaluate the real changes that occur in the craniofacial complex in three planes of space, overcoming limitations of 2D evaluation, such as the overlap of multiple structures, distortion of images, and difficulty in identifying anatomical landmarks accurately.[8,9] CBCT scans enable a fully automated volumetric superposition based on the voxels in the anterior cranial fossa.

Three-dimensional (3D) studies quantifying the stability of structures used as references for craniofacial analysis are scarce,[10] and studies with different populations are needed to increase the effectiveness of evaluations of skeletal changes in orthodontic/orthopedic treatments. The objective of this study was to test, using 3D assessment, whether traditional cephalometric landmarks and lines used as references are spatially stable in different age groups of growing Class II, division 1 individuals.

MATERIALS AND METHODS

Study Design and Sample

The STROBE statement[10] was followed for transparent reporting of this retrospective cohort study. This investigation was approved by the Review Board of Pontifical Catholic University of Minas Gerais (approval no. 21534013.8.0000.5137).

This investigation was based on a review of a sample of 1328 consecutive orthodontic patient records from the databases of two graduate programs for patients treated between February 2009 and December 2015 (Pontifical Catholic University of Minas Gerais: n = 578; Positivo University: n = 750). The following inclusion criteria were used: (1) skeletal Class II malocclusion, characterized by an ANB angle greater than 4° before treatment (T0); (2) dental Class II canine relationship of 4 mm or more at T0; (3) no previous orthopedic/orthodontic treatment; (4) no reported signs or symptoms of temporomandibular joint disorder; (5) availability of CBCT scans at two time points; (6) age ranging from 8 years to 17 years at T0; and (7) no craniofacial syndrome or deformity.

During the pilot study, measurements of 30 randomly selected patients were carried out. Sample size calculation was then performed, with a level of significance of 5%, power of 80%, and effect size of 1, considering the measured standard deviations relative to the primary outcome of the current investigation (3D displacement of cephalometric landmarks), as follows: 0.68 mm (Na), 0.29 mm (S point), 0.77 mm (Po), and 0.28 mm and 0.35 mm (Or). Thus, the minimum sample required for each group was 16 individuals. The final sample comprised 134 CBCT scans from 67 patients who completely fulfilled the inclusion criteria. The sample included 43 boys and 24 girls. The mean time between T0 and final T1 was 10.9 months (range 8.2 to 12.4 months). For the assessment of the association between the aging of growing patients and the changes in the position of the cephalometric landmarks, the patients were allocated into three observational groups according to their age at T0. Group 1 (G1) included individuals aged 8 to 10 years (n = 21); group 2 (G2), 11 to 13 years (n = 30); and group 3 (G3), 14 to 17 years (n = 16).

Orthodontic and dental treatments were performed between T0 and T1 scans. Patients received full fixed orthodontic appliances or mandibular advancement therapy. Other dental treatments included management of impacted teeth, deviations in tooth eruption, and marsupialization of cysts. It was assumed that the orthodontic or dental treatment provided did not influence cranial base growth.

Image Acquisition

CBCT scans were acquired using i-CAT (Imaging Sciences International, Hatfield, Pa), with a field of view of 16 cm × 22 cm, voxel of 0.3 × 0.3 × 0.3 mm, 36.90 mA, 120 kV, and 40 seconds of exposure. All patients were instructed to maintain maximum bite pressure during acquisition of the CBCT.

Image Analyses

The image analysis procedures were performed using ITK-SNAP (open-source software, www.itksnap.org) and 3D SLICER software (open-source software, www.slicer.org). The sequence included (1) virtual 3D surface model construction; (2) head orientation of the T0 scans in the same Cartesian coordinate system[11]; (3) manual approximation to achieve the best fit of T1 scans in T0 pre-oriented scans, using the anterior cranial fossa[12]; (4) automated voxel-based registration of the T1 scan to improve the

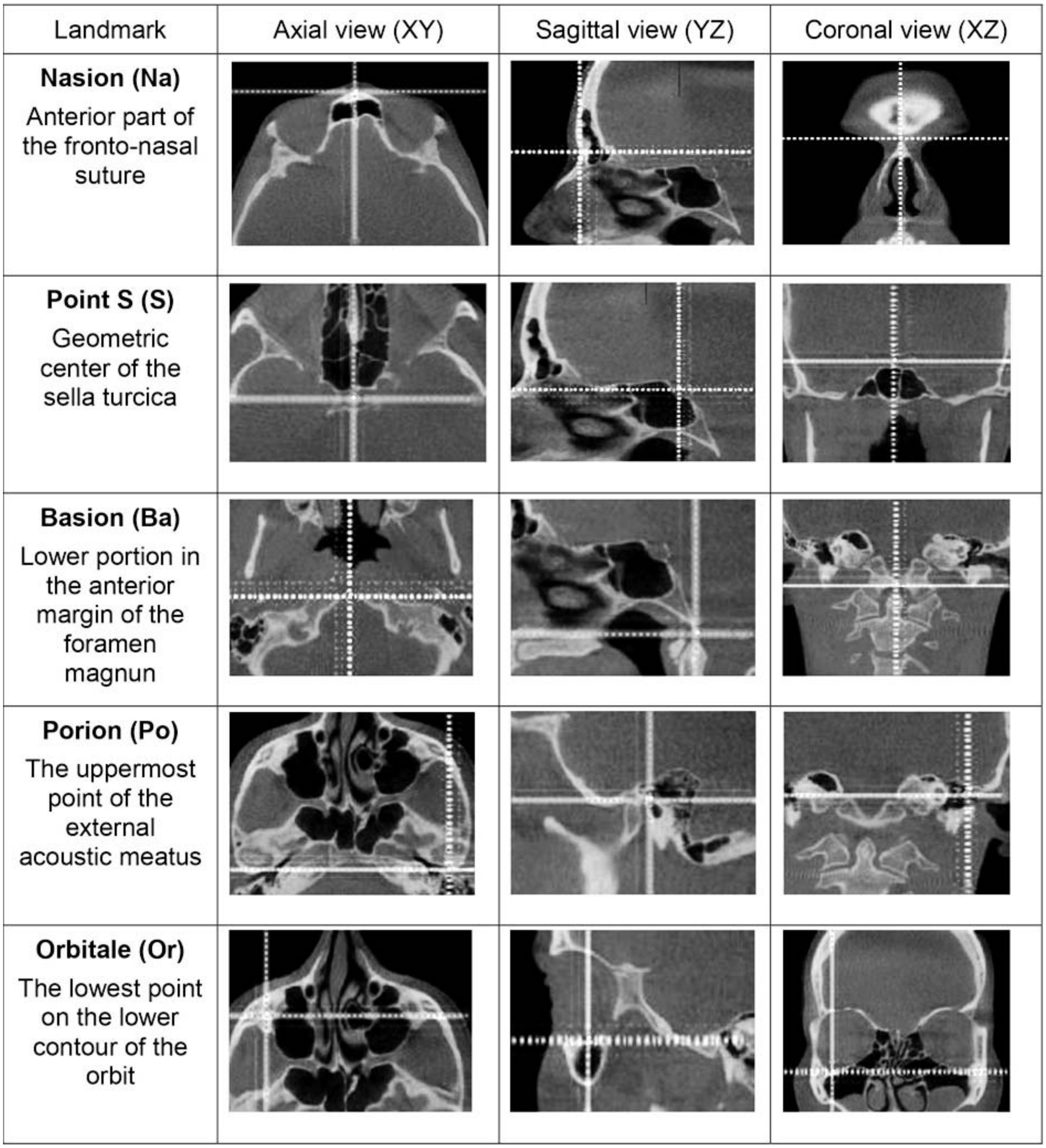

Figure 1. Three-dimensional identification of the landmarks on CBCT images.

manual approximation with the T0-oriented scan; (5) identification of landmarks (Figure 1); and (6) quantitative measurements (Figure 2).

Identification of the Anatomic Landmarks

To avoid problems in the identification of the cephalometric landmarks, the identification of points Na, S, Ba, Po, and Or in the T0-oriented scan and T1 registered scan were performed simultaneously in multiplanar views (axial, sagittal, coronal; Figure 1). Landmarks identified and plotted in planar views became a 3D sphere after their volumetric reconstruction. The position of each landmark was verified further on the 3D models for accuracy. To standardize the identification of bilateral landmarks, the left-side point Po (in sagittal view) and the right-side point Or (in coronal view) were arbitrarily chosen.

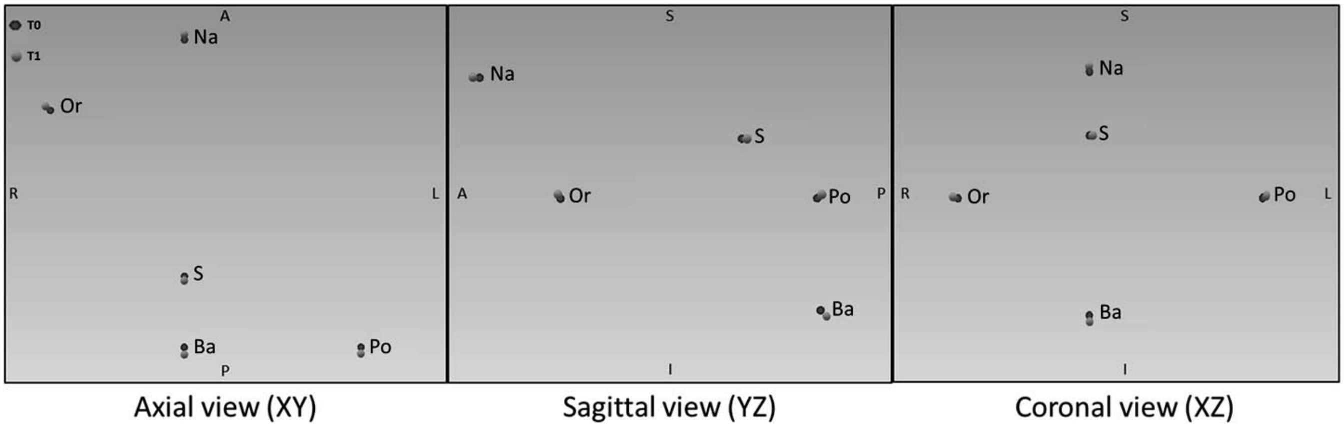

Figure 2. Three-dimensional virtual model with 0.3-mm spherical landmarks.

Quantitative Evaluation

The 3D spatial changes of the cephalometric landmarks between T0 and T1 were quantitatively evaluated by measuring the point-to-point displacement using the Q3DC tool of 3D Slicer software. Displacements were also evaluated as linear projections in the multiplanar 2D Cartesian coordinates (X, Y, and Z), as illustrated in Figure 2. The 2D linear projections of the anterior-posterior displacement (ΔY) and the inferior-superior displacement (ΔZ) were measured in the sagittal plane (YZ), and the right-left 2D linear displacement (ΔX) was measured in the axial plane (XY). Negative values indicated backward, downward, and away from the midline displacements, while positive values indicated forward, upward, and toward the midline of the cranial displacements. Pitch rotation (ie, rotation on the X-axis) was measured as the angular change of the S-Na line, Na-Ba line, and FHP between T0 and T1 in the sagittal view.

Statistical Analysis

Data analysis was performed using SPSS (version 20.0; SPSS, Chicago, Ill). Twenty days after the completion of the first analysis of all cases, the same investigator (LGS) repeated identification of the landmarks in 20 randomly selected patients to calculate the repeatability of the method using intraclass correlation coefficient (ICC) with a confidence level of 95%. Paired *t*-test was used to test systematic errors, while the method of moments (MME) was used to test the random error. The MME variance estimator has the advantage of not being affected by any unknown bias or systematic error between pairs of measurements.[13] The Kolmogorov-Smirnov test and Levene's test confirmed the normal distribution and homoscedasticity of the variables, respectively. Paired *t*-test was used to evaluate the changes in variables over time between T0 and T1. The significance level was set at 5% ($P <$ .05).

RESULTS

A total of 67 Class II individuals were eligible for inclusion in the current sample. Six female and 15 male patients, with a mean age of 9.1 ($\pm$0.70) years, were in G1; 14 female and 16 male patients, with a mean age of 12.3 ($\pm$0.74) years, comprised G2; G3 consisted of four female and 12 male patients, with a mean age of 14.5 ($\pm$1.03) years. As the study participants possessed similar demographic and clinical conditions, the presence of potential confounders was minimized.

The ICC showed agreement between readings (greater than 0.80) in the X, Y, and Z axes. Random errors ranged between 0.02 mm (point Or in the Z-axis) and 0.14 mm (point Po in the Y-axis). There were no statistically significant systematic errors between the two measurements performed by the same operator ($P >$ .05).

All landmarks showed positional changes relative to the anterior cranial fossa from T0 to T1 in each of the three age groups. Statistically significant differences ($P =$ .001) in the 3D Euclidean distance were observed. Additionally, there were significant differences in the pattern of the changes among the different age groups in the 3D components (X, Y, and Z) (Table 1). Statically significant ($P <$ .05) displacements of the landmarks within the three age groups are summarized in the scheme presented in Figure 3 as follows:

1. G1: Nasion moved 0.87 mm forward, while point S moved 0.38 mm backward. Basion moved 0.70 mm backward and 0.56 downward. Porion moved backward 0.39 mm and upward 0.24 mm. Orbitale moved 0.71 mm in the X-axis away from the median line (Table 2).
2. G2: Nasion moved 0.61 mm forward, while point S moved 0.27 mm backward. Basion moved 0.62 mm

Table 1. Changes in Euclidean Distance (3-D) Between T0 and T1 of the Landmarks in G1, G2, and G3[a]

Landmark	Group	Mean 3-D[b]	SD, mm	*P*-Value	95% CI for Difference	
					Minimum	Maximum
Na	G1	0.956	0.438	.001*	0.757	1.156
	G2	0.804	0.440	.001*	0.645	0.962
	G3	1.189	1.890	.024*	0.181	2.196
S	G1	0.576	0.269	.001*	0.453	0.699
	G2	0.480	0.296	.001*	0.373	0.587
	G3	0.462	0.248	.001*	0.329	0.594
Ba	G1	1.118	0.617	.001*	0.837	1.399
	G2	1.026	0.712	.001*	0.769	1.283
	G3	1.014	0.757	.001*	0.610	1.417
Po	G1	0.702	0.448	.001*	0.497	0.906
	G2	0.693	0.574	.001*	0.486	0.900
	G3	0.609	0.350	.001*	0.422	0.796
Or	G1	0.863	0.525	.001*	0.623	1.102
	G2	0.877	0.566	.001*	0.673	1.082
	G3	0.981	0.600	.001*	0.661	1.301

[a] T0 indicates baseline; T1, 1 year after baseline; G1, group 1; G2, group 2; G3, group 3; SD, standard deviation; CI, confidence interval; Na, Nasion; S, Sella; Ba, Basion; Po, Porion; Or, Orbitale.
[b] Euclidian distance in millimeters.
* Statistically significant difference between T0 and T1.

backward and 0.57 mm downward. Porion moved 0.42 mm backward and 0.12 mm upward. Orbitale moved 0.43 mm in the X-axis away from the median line (Table 3).

3. G3: Point S moved 0.17 mm backward and Basion moved 0.50 mm backward (Table 4).

Table 5 shows the pitch rotation for G1, G2, and G3. In G1, the S-Na line had a rotation of 0.35° ($P = .004$), the Na-Ba line had a rotation of 0.20° ($P = .011$), and FHP rotated 0.34° ($P = .002$) between T0 and T1. All rotations were clockwise (Figure 4). In groups G2 and G3, the pitch of the S-Na, Na-Ba, and FHP lines were not statistically significant.

DISCUSSION

This sample of Class II growing individuals showed that the cephalometric landmarks used as fiducial references for growth analysis were not three-dimensionally stable relative to the anterior cranial fossa, with statistically significant displacements in the years of growth (8 to 17 years). Therefore, the use of lines, planes, and landmarks in cephalometric total superimpositions for the evaluation of maxillary-mandibular skeletal changes during the growth phase has some limitations. Clinicians should be aware of those to correctly interpret ordinary findings. Nevertheless, the findings suggested that, in individuals after the age of

Table 2. Displacement (mm) Between T0 and T1 of the Points in the X, Y, and Z Coordinates of G1[a]

Landmark	Coordinates	Mean	SD	*P*-Value	95% CI for Difference	
					Minimum	Maximum
Na	x	−0.005	0.040	.532	−0.023	0.012
	y	0.871	0.435	.001*	0.673	1.069
	z	−0.134	0.381	.123	−0.307	0.039
S	x	−0.008	0.028	.196	−0.021	0.004
	y	−0.383	0.296	.001*	−0.518	−0.248
	z	0.077	0.414	.403	−0.111	0.266
Ba	x	−0.016	0.043	.093	−0.036	0.003
	y	−0.708	0.622	.001*	−0.991	−0.425
	z	−0.568	0.662	.001*	−0.870	−0.266
Po	x	−0.008	0.057	.518	−0.034	0.018
	y	−0.394	0.634	.010*	−0.683	−0.105
	z	0.247	0.291	.001*	0.115	0.380
Or	x	0.712	0.556	.001*	0.459	0.965
	y	−0.008	0.078	.643	−0.043	0.027
	z	−0.150	0.432	.127	−0.346	0.046

[a] T0 indicates baseline; T1, 1 year after baseline; X, right-left; Y, anterior-posterior; Z, superior-inferior; G1, group 1; SD, standard deviation; CI, confidence interval; Na, Nasion; S, Sella; Ba, Basion; Po, Porion; Or, Orbitale.
* Statistically significant difference between T0 and T1.

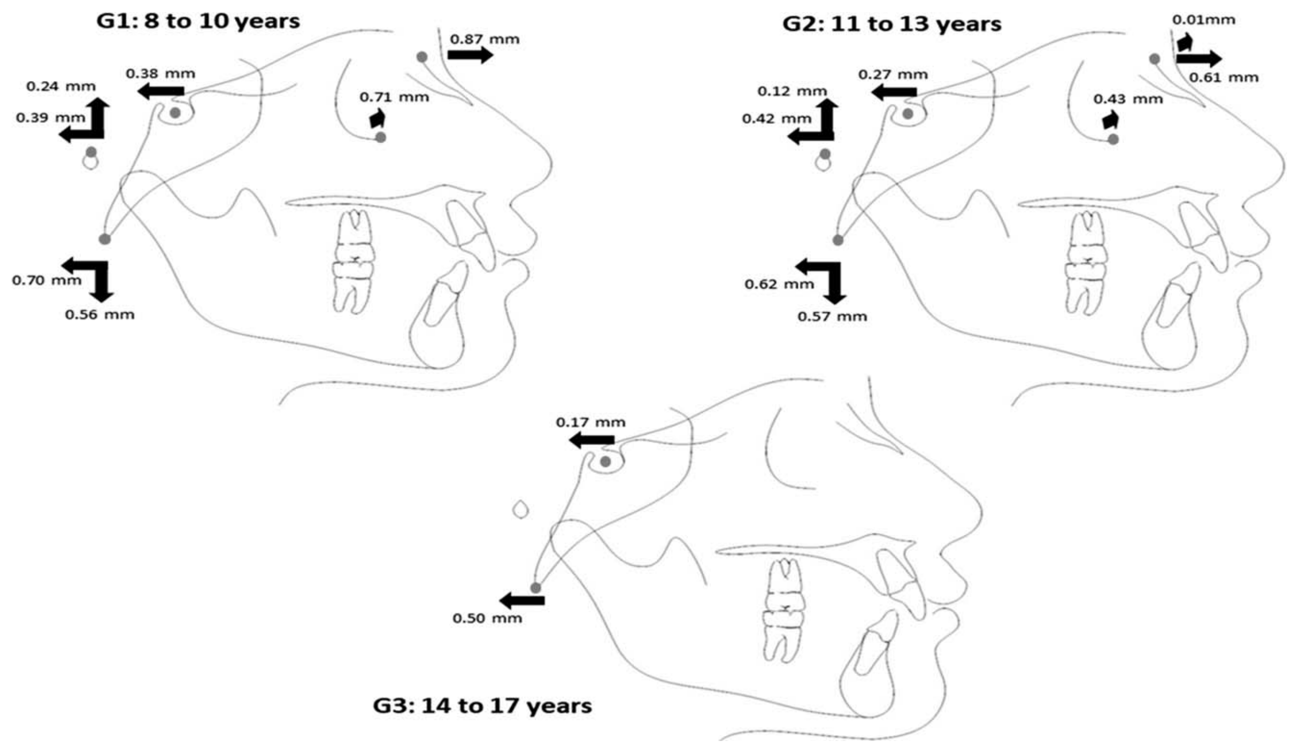

Figure 3. Direction of the statistically significant displacements of the landmarks represented in a classic cephalogram.

11 years, the FHP, S-Na, and Na-Ba lines are reliable as references for the total superposition cephalograms taken at different time points.

Previous 2D studies[4,6] reported forward displacement of Na in young adulthood because of a late increase in frontal bone thickness by apposition at glabella and frontal sinus enlargement. During facial development, even in the late stages of growth, there is remodeling of the frontal bone by apposition in the glabellar region and enlargement of the frontal sinus.[14] Nevertheless, in the present investigation it was observed that Na point was stable sagittally after 13 years of age. There was no specific forward (Y projection) displacement of Na point, in contradiction to what was shown by 2D image analysis in previous studies.[4,6]

A previous systematic review evaluating growth of the posterior CB showed that the displacement of

Table 3. Displacement (mm) Between T0 and T1 of the Points in the X, Y, and Z Coordinates of G2[a]

Landmark	Coordinates	Mean	SD	*P*-Value	95% CI for Difference Minimum	95% CI for Difference Maximum
Na	x	−0.015	0.037	.030*	−0.028	−0.001
	y	0.616	0.456	.001*	0.451	0.781
	z	0.127	0.491	.152	−0.049	0.304
S	x	−0.008	0.040	.248	−0.022	0.006
	y	−0.272	0.370	.001*	−0.406	−0.139
	z	0.096	0.317	.094	−0.017	0.211
Ba	x	−0.012	0.050	.188	−0.030	0.006
	y	−0.625	0.650	.001*	−0.860	−0.391
	z	−0.574	0.652	.001*	−0.810	−0.339
Po	x	−0.086	0.387	.219	−0.225	0.053
	y	−0.426	0.583	.001*	−0.636	−0.216
	z	0.129	0.351	.045*	0.003	0.256
Or	x	0.437	0.838	.006*	0.135	0.739
	y	0.012	0.089	.440	−0.019	0.044
	z	−0.013	0.455	.868	−0.177	0.150

[a] T0 indicates baseline; T1, 1 year after baseline; X, right-left; Y, anterior-posterior; Z, superior-inferior; G2, group 2; SD, standard deviation; CI, confidence interval; Na, Nasion; S, Sella; Ba, Basion; Po, Porion; Or, Orbitale.

* Statistically significant difference between T0 and T1.

Table 4. Displacement (mm) Between T0 and T1 of the Points in the X, Y, and Z Coordinates of G3[a]

Landmark	Coordinates	Mean	SD	*P*-Value	95% CI for Difference	
					Minimum	Maximum
Na	x	0.074	0.244	.244	−0.056	0.204
	y	0.849	2.018	.113	−0.226	1.924
	z	0.079	0.406	.445	−0.136	0.296
S	x	−0.010	0.089	.647	−0.057	0.037
	y	−0.174	0.270	.021*	−0.319	−0.030
	z	0.112	0.403	.281	−0.102	0.327
Ba	x	0.021	0.040	.056	−0.000	0.043
	y	−0.507	0.706	.012*	−0.883	−0.130
	z	−0.307	0.890	.187	−0.782	0.166
Po	x	−0.014	0.069	.431	−0.051	0.023
	y	−0.252	0.519	.071	−0.529	0.024
	z	0.085	0.410	.417	−0.132	0.304
Or	x	0.476	1.000	.076	−0.056	1.010
	y	−0.027	0.085	.218	−0.072	0.017
	z	0.044	0.366	.633	−0.150	0.239

[a] T0 indicates baseline; T1, 1 year after baseline; X, right-left; Y, anterior-posterior; Z, superior-inferior; G3, group 3; SD, standard deviation; CI, confidence interval; Na, Nasion; S, Sella; Ba, Basion; Po, Porion; Or, Orbitale.

* Statistically significant difference between T0 and T1.

points Ba and S occurred in the backward direction.[15] However, no 3D studies previously reported on the growth of these landmarks, which has been a weakness in the literature. In the present 3D analysis, it was confirmed that Ba and S points moved backward for patients up to the age of 17 years. The potential growth at the spheno-occipital synchondrosis until adulthood[3,7] may explain the backward displacement of Ba point. Regarding point S, development of the pituitary gland may affect the position of the sella turcica as well as its geometric center. This may be related to the backward displacement observed by point S. The downward and backward displacement of point S was also described by Melsen, who showed bone resorption at the posterior wall of the sella turcica.

Concerning vertical displacements, Afrand et al.[5] observed three-dimensionally that there were no vertically stable structures in the anterior CB region in adolescents. In the current study, however, all age groups showed vertical stability of point Na. Notwithstanding this finding, it is important to mention that there were methodological differences between the studies, including skeletal characteristics of the samples and mean observation times (10.9 months vs 1.6 years). Some evidence suggested that the posterior CB and points Ba and S moved downward during growth periods and on follow-up.[4,15,16] The current data found that point Ba drifted down at younger ages (G1 and G2), in agreement with the findings of previous studies.[4,15,16] However, point S remained stable vertically at all ages evaluated.

The position of Or moved only in the transverse perspective in the two younger age groups, and there were no spatial changes in the three planes of space in the older group. This was an important finding, since transverse changes are not identified with 2D cepha-

Table 5. Pitch Rotation of the Cephalometric Lines Between T0 and T1

Line[a]	Group	Mean, °[b]	SD	*P*-Value	95% CI for Difference	
					Minimum	Maximum
S-Na	G1	0.357	0.507	.004*	0.126	0.588
	G2	0.146	0.450	.076	−0.016	0.308
	G3	0.124	0.591	.414	−0.190	0.439
Na-Ba	G1	0.205	0.336	.011*	0.052	0.359
	G2	0.019	0.323	.734	−0.096	0.136
	G3	0.084	0.523	.528	−0.194	0.363
FHP	G1	0.341	0.443	.002*	0.139	0.543
	G2	0.148	0.504	.105	−0.032	0.330
	G3	0.035	0.452	.756	−0.205	0.277

[a] T0 indicates baseline; T1, 1 year after baseline; SD, standard deviation; CI, confidence interval; Na, Nasion; S, Sella; Ba, Basion; Po, Porion; Or, Orbitale; G1, group 1; G2, group 2; G3, group 3; S-Na, line between the points Nasion and Sella; Na-Ba, line between Nasion and Basion points; FHP, Frankfort Horizontal Plane.

[b] Angle measurement in degrees.

* Statistically significant difference between T0 and T1.

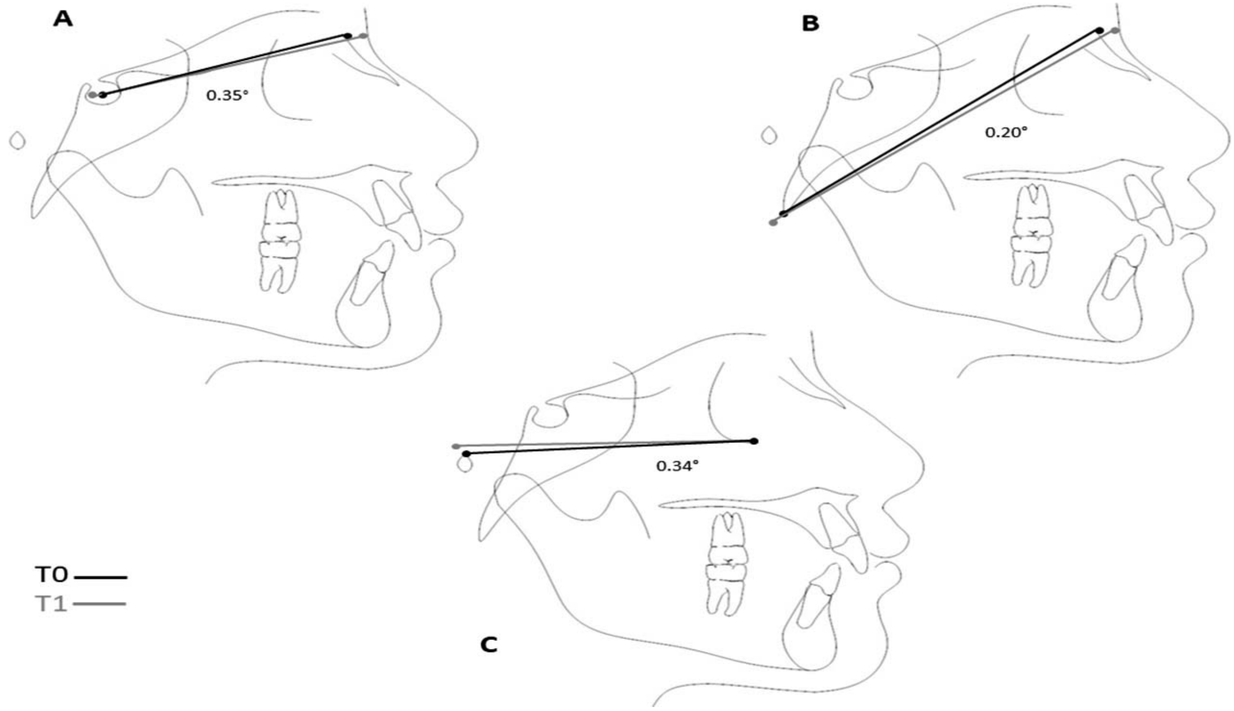

Figure 4. Pitch of cephalometric lines in group 1 (only group that displayed a statistically significant difference). (A) S-Na: line between points Nasion and Sella; (B) Na-Ba: line between Nasion and Basion; (C) FHP: Frankfort horizontal plane.

lometric superposition. Thus, point Or seems to be a valid and reliable landmark for 2D cephalometric assessment of growing Class II individuals.

It was suggested that the FHP plane is more reliable for angular measurements because it does not connect structures of the CB.[2] In this sense, because of the positional changes found in CB landmarks in the X, Y, and Z coordinates, it would be expected that the cephalometric lines reflect their respective landmark displacements and would not be a reliable method for dentoskeletal comparisons. Nevertheless, vertically balanced compensations prevented the rotation (pitch) of the lines in patients older than 11 years, and, thus, S-Na and Na-Ba were reliable for volumetric superposition. Recently, automatic superposition methods based on multiple landmarks have been proposed[17,18] to mitigate spatial changes and overcome the accuracy errors of traditional 2D reference assessment, showing promising improvements in the control of some of the sources of error in cephalometry.

Although a recent publication[19] suggested that the spheno-occipital synchondrosis might undergo minor volumetric changes following rapid maxillary expansion, another 3D study[12] did not find significant changes after Herbst appliance treatment. The development of 3D imaging methods should enhance further studies designed to assess whether volumetric changes in the spheno-occipital synchondrosis are associated with dentofacial orthopedics and if they can influence growth of the maxillary-mandibular complex.

The use of multiplanar views to identify and generate the landmarks was a strength of the current study. This methodology reduced the error of measurements compared to previous methods that had used surface models for the identification of landmarks. Also, the voxel-based automated registration method is the gold standard tool for the volumetric superimposition of hard tissue regions.[9]

A limitation of this study was that the CBCTs were acquired using a voxel size of 0.3 mm. As the size of the landmarks corresponded to 3 voxels, the smallest spatial differences that could be detected were 0.9 mm, as a result of the intrinsic error of the method and not because of growth over the observation time. The sample for this study involved growing skeletal Class II individuals, and the results should be interpreted with caution in populations with other skeletal patterns. Finally, the ratio of boys to girls could be considered a source of bias.

CONCLUSIONS

- Cephalometric landmarks Na, S, Ba, and Po underwent positional changes during facial growth.
- Orbitale did not display vertical and sagittal changes from 8 to 17 years of age and, thus, is a stable reference for 2D cephalometric superposition.

- The S-Na, Na-Ba, and FHP lines underwent statistically significant angular changes from 8 to 10 years. However, from 11 to 17 years these lines were stable and reliable for facial growth analysis of Class II individuals.

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