RESEARCH ARTICLE

Cervical vertebrae maturation index estimates on cone beam CT: 3D reconstructions vs sagittal sections

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Objectives: The aim of this study was to evaluate the performance of CBCT three-dimensional (3D) reconstructions and sagittal sections for estimates of cervical vertebrae maturation index (CVMI).

Methods: The sample consisted of 72 CBCT examinations from patients aged 8–16 years (45 females and 27 males) selected from the archives of two private clinics. Two calibrated observers (kappa scores: ≥ 0.901) interpreted the CBCT settings twice. Intra- and interobserver agreement for both imaging exhibition modes was analyzed by kappa statistics, which was also used to analyze the agreement between 3D reconstructions and sagittal sections. Correlations between cervical vertebrae maturation estimates and chronological age, as well as between the assessments by 3D reconstructions and sagittal sections, were analyzed using gamma Goodman–Kruskal coefficients ($\alpha = 0.05$).

Results: The kappa scores evidenced almost perfect agreement between the first and second assessments of the cervical vertebrae by 3D reconstructions (0.933–0.983) and sagittal sections (0.983–1.000). Similarly, the agreement between 3D reconstructions and sagittal sections was almost perfect (kappa index: 0.983). In most divergent cases, the difference between 3D reconstructions and sagittal sections was one stage of CVMI. Strongly positive correlations (>0.8 , $p < 0.001$) were found not only between chronological age and CVMI but also between the estimates by 3D reconstructions and sagittal sections ($p < 0.001$).

Conclusions: Although CBCT imaging must not be used exclusively for this purpose, it may be suitable for skeletal maturity assessments.

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Introduction

The interpretation of radiographic images of the cervical vertebrae may provide clinically useful information on the degree of skeletal maturation for patients in need of dentofacial orthopaedics.^{1–12} Evaluation of morphological characteristics of the cervical vertebrae has been the

object of investigations, including CBCT studies.^{12–15} More recently, the maturation stages of the cervical vertebrae on lateral cephalograms and sagittal sections of CBCT were compared with ossification events on hand and wrist radiographs.¹² That study analyzed only radiographs and CBCT sagittal sections of 100 patients aged 3–35 years, being that 15 patients were aged 3–5 years and 22 had chronological ages from 16 to 35 years. There

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was high correlation between estimates of skeletal maturation obtained on CBCT sagittal sections and lateral cephalograms (Spearman coefficient correlation: 0.975; $p < 0.001$).¹²

The application of CBCT in orthodontics is relevant because it allows more complete and detailed evaluation of craniofacial anatomy in some cases.¹⁶ The request of a CBCT examination may provide an assembly of data that allows exhibition of images in sections (axial, coronal and sagittal) and by three-dimensional (3D) reconstructions,¹⁷ which are very didactic and may even be morphologically more expressive than images of isolated sections. Professionals in charge of a CBCT machine or requesting the CBCT examination must provide information on the possible findings based on complete interpretation of images achieved.¹⁷ The potential utilization of CBCT for evaluation of skeletal maturation has been suggested by 3D analysis of the cervical vertebrae.¹³ However, no studies were found in the PubMed database comparing the interpretations of CBCT 3D reconstructions and sagittal sections. Therefore, this study analyzed the performance of images obtained by CBCT 3D reconstruction and sagittal sections of the full head to estimate the cervical vertebrae maturation index (CVMI). The hypothesis encouraging this study considered the possibility of an innovative application of images of 3D image reconstruction obtained from CBCT examinations requested as part of the records for some orthodontic patients, additionally to any clinical indication that may lead to request of this examination.

Methods and materials

This study followed the universally accepted standards for research in human beings and was approved by the Institutional Review Board of the University of São Paulo City (protocol number 13656689).

Sample selection

CBCT images of 72 patients (45 females and 27 males) aged 8–16 years were selected (Table 1). This convenience sample was collected to investigate the period of

occurrence of greatest changes in the skeletal maturation stages of the cervical vertebrae. CBCT examinations of the full head were obtained from a selection of image files of two private clinics at the city of São Paulo, Brazil, where all patients live. The files had CBCT images with different fields of view (FOVs). Image selection was based on the following inclusion criteria: CBCT images (obtained for orthodontic or surgical indication) of good quality concerning the detail and distinctness; presumably healthy individuals, without skeletal changes or developmental anomalies (congenital or acquired); and the absence of syndromes or cleft lip and palate.¹³ The study excluded CBCT images with impairment of full visualization of the cervical vertebrae, the presence of pathological changes in cervical vertebrae images, and the presence of foreign bodies in the images of the cervical vertebrae.

The method for evaluation of morphological changes of the cervical vertebrae provides the CVMI based on the interpretation of lateral cephalograms,² which should constitute a control group when testing an innovative methodology. However, there are two important reasons for the non-utilization of lateral cephalograms in this study. First, if the CBCT images may be processed and provide multiplanar reconstructions with visualization of similar sagittal sections as the lateral cephalograms,^{12–14,17,18} these radiographs are not substantial. In addition, the As Low As Reasonably Achievable principle should be considered. Therefore, aiming to reduce the radiation dose to the patient, only the CBCT documentation was requested, eliminating the need of several other radiographs included in the orthodontic records (orthopantomogram, lateral cephalogram, and even transcranial and hand and wrist radiographs). Consequently, the surveyed files did not have a sample of CBCT records of the full head and their two-dimensional counterparts, *i.e.* lateral cephalograms and hand and wrist radiographs, but cervical vertebrae were visible.

Protocol of image acquisition by CBCT

The CBCT images had been previously acquired on a tomograph i-CAT[®] Next Generation (Imaging Sciences, Hatfield, Philadelphia, PA), which presents a flat-panel image receptor, set to operate at 120 kVp, 8 mA, exposure time of 26.9 s and isotropic voxel with resolution of 0.4 mm. Patients were placed in a seated position in this equipment. The head position was maintained by devices in the equipment, such that the mid-sagittal plane is perpendicular to the ground and the Frankfort plane (that connects the acoustic meatus to the infraorbital rim) is parallel to the ground. During examination, the patient remained in maximum intercuspation. The selected FOV had 23 cm diameter and 17 cm height.

Interpretation of CBCT images

The CBCT images were interpreted by two trained and calibrated examiners with 10 years' experience. The examiners received verbal and written instructions on

Table 1 Sample distribution according to chronological age by sex

Age (years)	Sex				Total	
	Female		Male			
	n	%	n	%	n	%
8	6	13.3	0	0.0	6	8.3
9	4	8.9	2	7.4	6	8.3
10	4	8.9	2	7.4	6	8.3
11	3	6.7	5	18.5	8	11.1
12	4	8.9	5	18.5	9	12.5
13	7	15.6	6	22.2	13	18.1
14	3	6.7	5	18.5	8	11.1
15	6	13.3	1	3.7	7	9.7
16	8	17.8	1	3.7	9	12.5
Total	45	100.0	27	100.0	72	100.0

the method for evaluation of skeletal maturity proposed by Hassel and Farman.² Subsequently, they participated in a training that consisted of interpretation of 10

conventional lateral cephalograms of patients aged 8–16 years. The films used for achievement of lateral cephalograms presented dimensions of 18×24 cm.

INITIATION

ACCELERATION

TRANSITION

Figure 1 Cervical vertebrae maturation stages on CBCT sagittal slices (left) and three-dimensional reconstructions (right); Part 1.

Only radiographs with good image quality for the diagnosis, *i.e.* with satisfactory distinctness, density and contrast, as well as absence of distortions, were evaluated during training.

The identification of lateral cephalograms used for training was covered by a black mask to hide the chronological age and gender, avoiding any type of

influence on the examiners. After training, the examiners selected another set of 35 conventional lateral cephalograms of patients of both genders, aged 8–16 years, for calibration.

Calibration was performed in two stages, aiming to analyse the intra- and interexaminer agreement. In the first stage, the examiners identified and recorded the

Figure 2 Cervical vertebrae maturation stages on CBCT sagittal slices (left) and three-dimensional reconstructions (right); Part 2.

skeletal maturation stages of 35 patients on a film viewer with constant light intensity, in a darkened room. The identification on these cephalograms was also covered by a black mask to hide any information on the patient. Also, they were stored in individual envelopes containing a number. The sequence of cephalograms was randomly assorted. After 21 days, the second stage comprised repetition of the procedures performed in the first stage, maintaining the random assortment. Data recorded in the two stages were submitted to analysis of agreement to check the calibration. The kappa coefficients were ≥ 0.901 , indicating optimal agreement between evaluations.¹⁹

The examiners were given a training session with CBCT images after initial instruction, demonstrating the functions of the software and evaluating the images.

The CBCT 3D reconstructions and sagittal sections were randomly assorted and evaluated twice using the software OsiriX[®] (The Osirix Foundation, Geneva, Switzerland).²⁰ The images were exhibited on the screen of a 13" MacBook Pro (Apple Computer Inc., Cupertino, CA). Using the software OsiriX, the 3D image reconstructions were obtained from digital imaging and communications in medicine files by direct volume rendering technique using the 3D tool. The sagittal sections obtained by multiplanar reformatting were selected by positioning the cursor on a line along the midpalatal suture and at the centre of the anterior nasal spine.¹² To avoid visual fatigue, only 20 images were evaluated per day. The evaluations occurred in stages, selecting one exhibit mode each time, on the first and second occasions. The CBCT images were interpreted in a darkened room, on a screen with constant characteristics of brightness and contrast, allowing utilization of zoom, brightness and contrast tools of the software to enhance the diagnosis. The minimum period for image interpretation for each exhibition mode was 15 days. At 1 month after the first evaluation, the examiners interpreted the 72 records again, considering the 3D reconstructions and sagittal sections (Figures 1 and 2).

The classification method of vertebrae C2, C3 and C4 presents six stages, which may be described as follows:^{2,12}

Initiation (cervical vertebrae maturation index—1): This corresponds to the initial stage of the pubertal growth spurt (PGS), in which 80–100% of growth is expected.

The inferior borders of the vertebrae are plain. There is a slope from posterior to anterior direction on the upper borders of C3 and C4.

Acceleration (cervical vertebrae maturation index—2):

This stage is close to the peak PGS, in which 65–85% of growth is expected. The inferior border of vertebrae C2 and C3 present a small concavity, which is still plain on C4. The bodies of C3 and C4 assume a rectangular shape.

Transition (cervical vertebrae maturation index—3):

This corresponds to the peak growth of an individual, in which 25–65% of growth is expected. The inferior borders of C2 and C3 present different concavities, and this is subtle on C4. The bodies of vertebrae C3 and C4 are rectangular.

Deceleration (cervical vertebrae maturation index—4):

The expected growth is 10–25%. The inferior borders of vertebrae C2, C3 and C4 present distinct concavities, and the bodies of vertebrae C3 and C4 assume a nearly square shape.

Maturation (cervical vertebrae maturation index—5):

This corresponds to the final stage of maturation of the vertebrae, and 5–10% of growth is expected. More distinct concavities are observed on vertebrae C2, C3 and C4. The two latter have square-shaped bodies.

Finalization (cervical vertebrae maturation index—6):

Growth is complete at this stage. The bodies of vertebrae C3 and C4 have greater vertical than horizontal dimensions and the inferior borders keep well-defined concavities.

Statistical analyses

The reproducibility of estimates of skeletal maturation stages on images of 3D reconstruction and sagittal sections was analyzed by the kappa statistics, which was also used to evaluate the agreement between the two modes of CBCT image exhibition. The association between the maturation stages of the cervical vertebrae and chronological age, as well as between estimates based on images of 3D reconstruction and sagittal sections, was evaluated by the Goodman–Kruskal gamma correlation coefficient²¹ ($\alpha = 0.05$). The analyses were performed on the

Table 2 Intraobserver agreement (Observer 1) for the cervical vertebrae maturation stages using the CBCT three-dimensional (3D) reconstructions

		<i>Second assessment</i>					
<i>3D reconstructions</i>	<i>Observer 1</i>	<i>Initiation</i>	<i>Acceleration</i>	<i>Transition</i>	<i>Deceleration</i>	<i>Maturation</i>	<i>Finalization</i>
First assessment	Initiation	15					
	Acceleration	1	13				
	Transition		1	12	1		
	Deceleration				9	1	
	Maturation					9	
	Finalization						10

The kappa coefficient = 0.933 ($p < 0.001$).

Table 3 Intraobserver agreement (Observer 2) for the cervical vertebrae maturation stages using the CBCT three-dimensional (3D) reconstructions

3D reconstructions Observer 2		Second assessment					
		Initiation	Acceleration	Transition	Deceleration	Maturation	Finalization
First assessment	Initiation	15	1				
	Acceleration		13				
	Transition			13			
	Deceleration				10		
	Maturation					10	
	Finalization						10

The kappa coefficient = 0.983 ($p < 0.001$).

software R version 2.15.1 (the R Foundation for Statistical Computing, Vienna, Austria).

Results

Intraobserver reliability

Despite the divergence between the first and second evaluations of maturation stages of the cervical vertebrae on 3D reconstruction examination of four patients evaluated by Examiner 1, the kappa test evidenced almost perfect agreement for both examiners (Tables 2 and 3). Data of the diagonal lines immediately superior and inferior to the central diagonal line in Tables 2 and 3 evidence that, in most divergent cases, the difference was limited to one maturation stage of the cervical vertebrae. Similarly, the intraexaminer agreement was almost perfect for the evaluations of sagittal sections by CBCT (Tables 4 and 5).

Correlation between cervical vertebrae maturation stages and chronological age

After a third evaluation of discordant cases estimated by CBCT 3D reconstructions and sagittal sections, the association between chronological age and maturation stages of cervical vertebrae was analyzed. The Goodman–Kruskal gamma correlation coefficients (non-parametric test) were calculated based on estimates obtained on CBCT 3D reconstructions and sagittal sections. As presented by bubble graphs on Figure 3, there were strongly positive correlations (0.813, $p < 0.001$) between chronological age and the maturation stages of the cervical vertebrae. Strongly positive correlations between chronological age and

maturation of the cervical vertebrae were also observed for both genders (Figures 4 and 5).

Comparison between cervical vertebrae maturation stages on CBCT three-dimensional reconstructions and sagittal sections

The agreement between the two modalities of CBCT image exhibition was almost perfect (Figure 6). There was discordance between the modalities of CBCT image exhibition that comprised the maturation stages by 3D reconstruction and image finalization by sagittal section (Figure 4). However, despite this disagreement, there was high (strongly positive) correlation between the modalities of CBCT image exhibition.

Discussion

Interpretation of hand and wrist radiographs is considered the most standardized method for evaluation of skeletal maturation because of the large number of bones present in this region and some ossification events.^{12,22–24} However, there are also limitations in the estimates provided by this method. The sequence of ossification at the hand and wrist region may present polymorphism.^{24,25} Also, there are considerations on an additional exposure to X-ray related to this method, and its utilization should be questioned if a comparable method is clinically available.^{3,6,9,10,26}

The estimate of maturation stages of the cervical vertebrae on CBCT sagittal sections provided a reliable evaluation of PGS, presenting strongly positive correlations with lateral cephalograms and hand and wrist radiographs.¹² Additionally, this study demonstrated that

Table 4 Intraobserver agreement (Observer 1) for the cervical vertebrae maturation stages using the CBCT sagittal sections

Sagittal sections (2D) Observer 1		Second assessment					
		Initiation	Acceleration	Transition	Deceleration	Maturation	Finalization
First assessment	Initiation	15					
	Acceleration		14				
	Transition			14			
	Deceleration				10		
	Maturation					8	
	Finalization						11

2D, two dimensions.

The kappa coefficient = 1.000 ($p < 0.001$).

Table 5 Intraobserver agreement (Observer 2) for the cervical vertebrae maturation stages using the CBCT sagittal sections

Sagittal sections (2D) Observer 2		Second assessment					
		Initiation	Acceleration	Transition	Deceleration	Maturation	Finalization
First assessment	Initiation	15					
	Acceleration		14				
	Transition			13			
	Deceleration				9		1
	Maturation					8	
	Finalization						12

2D, two dimensions.

The kappa coefficient = 0.983 ($p < 0.001$).

when examining CBCT images of 3D reconstruction or sagittal sections, the trained examiner is able to record the maturation stages of the cervical vertebrae (Figure 5). The examiners were trained for visualization of the six stages of CVMI and performed a calibration analysis on lateral cephalograms, following the conventional method.² The kappa scores indicated almost perfect agreement between evaluations by the two modalities of CBCT image exhibition (Tables 2–5), which indicates high reproducibility for the interpretation of 3D reconstructions and sagittal sections. Also, both modalities of CBCT image exhibition demonstrated progression of the maturation stages of the cervical vertebrae in relation to chronological age, as expected in healthy individuals (Figure 1) and in agreement with previous authors.⁸ Conversely, there was wide variation between chronological aged and skeletal maturation stages in the total sample (Figure 1) and in female and male genders (Figures 2 and 3). These data corroborate other studies that evidenced chronological age as a weak biological indicator of skeletal maturity.^{8,11,12,23} However, it is interesting to notice that the bubble graphs of 3D reconstructions are very similar to the bubble graphs of sagittal section images, for both genders (Figures 3 and 4), which confirms the correspondence between the two modalities of CBCT image exhibition.

A higher number of female patients were observed in the maturation and finalization stages (Figures 3 and 4), based on both modalities of CBCT image exhibition, confirming that the skeletal maturity is reached earlier in females than in males.^{8,12,23} Concerning the classification of CVMI on images of 3D reconstruction and sagittal sections, the correlation coefficient was slightly higher for the females (Figures 3 and 4). Some authors mention that the method for the estimate of CVMI would be more reliable for the female gender.^{6,8} However, the reduced number of male individuals may have influenced the analysis of correlation, and thus this finding should be carefully interpreted.

Most studies investigating the utilization of radiographic analyses of maturation of the cervical vertebrae have been cross-sectional and did not report any type of sample randomization, blinding of examiners as to the sample characteristics and sample size calculation.^{10,24} A systematic literature review evidenced six studies with moderate to high scores.²⁴ However, the only study that reached a high score, similar to this study, was cross-sectional and did not present the sample size calculation;⁸ presumably, the cause of methodological limitations of studies on the evaluation of skeletal maturation is related to the need of examinations using

Figure 3 Correlation between cervical vertebrae maturation stages [as seen on CBCT three-dimensional (3D) reconstructions and sagittal sections] and chronological age for the total sample ($n = 72$). 2D, two dimensions.

Figure 4 Correlation between cervical vertebrae maturation stages as seen on CBCT three-dimensional (3D) reconstructions and chronological age for female ($n = 45$) and male ($n = 27$) groups.

X-rays. This study selected a convenience sample aiming to primarily analyze the agreement between the two modalities of CBCT image exhibition, rather than determining the progression of skeletal maturation in a population of adolescents. If this was the main goal, it would be necessary to collect data from a large number of individuals uniformly distributed by gender and age ranges, besides considering the ethnicity.^{3,6,8} However, following the current guidelines on the more complete application of CBCT,¹⁷ i.e. not only for visualization of pathologies or dentoskeletal anomalies, which may have led to indicate the examination, but also aiming to explore several modalities of image exhibition (3D and sagittal sections), the examiners achieved a relatively small sample, yet with standardized examinations and from patients in an age range with diverse stages of skeletal maturation. This sample is very scarce by the

need to analyze the risk/benefit relationship before the indication of CBCT, to avoid unnecessary exposure to X-rays. The same difficulty is observed in the single study using CBCT with two different FOVs to evaluate the maturation of the cervical vertebrae in a sample of orthodontic patients.¹²

Considering the chief goal of this study, the agreement between CVMI classifications by 3D reconstructions and sagittal sections was almost perfect (Figure 5). The difference between the CBCT image exhibition modalities was one stage in an advanced stage of the PGS (maturation vs finalization), and the correlation between 3D reconstructions and sagittal sections was strongly positive (1.000, $p < 0.001$). It may be assumed that a greater sample size would further increase the power of the agreement test. Concerning the very high positive correlation between modalities,

Figure 5 Correlation between cervical vertebrae maturation stages as seen on CBCT sagittal sections and chronological age for female ($n = 45$) and male ($n = 27$) groups. 2D, two dimensions.

Figure 6 Correlation between cervical vertebrae maturation stages as seen on CBCT three-dimensional (3D) reconstructions and sagittal sections for the total sample ($N = 72$). 2D, two dimensions.

since 3D reconstructions and sagittal sections were used for evaluation of growing patients, the correlation tends to be high, even because of the progression of CVMI events. Both images of 3D reconstruction and sagittal sections may be used for the evaluation of CVMI. Possibly, the sagittal sections are easier to evaluate, because the method of Hassel and Farman² was initially suggested for application on lateral cephalograms. However, professionals interpreting the CBCT images should consider the great quantity of information that may be offered by this examination, using the different exhibition modes.¹⁷

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The present results agree that the estimates of skeletal maturation may be performed by morphological evaluation of the cervical vertebrae on CBCT images of the full head.¹² However, this examination should not be requested only for that purpose, even because not all orthodontic patients need CBCT with such wide FOV. Moreover, the orthodontists should not use the evaluation of the cervical vertebrae as an entirely accurate method to estimate skeletal maturation.^{24,27} The clinical experience during orthopaedic treatment, aiming to maximize the mandibular growth in patients with Class II pattern, also indicates the observation of stages of tooth development.²⁷

The skeletal maturation is a continuous process and several attempts have been made to categorize different events in this progressive process. However, the stages are interrelated and the identification of borderline cases may be difficult.^{2,12} Figure 4 presents a discordant pair (3D reconstruction and sagittal section) that involved two later stages of CVMI. In summary, the evaluation of images of the cervical vertebrae on lateral cephalograms or CBCT examinations may be used to widen the clinical analysis of the orthodontist²⁸, yet a single auxiliary diagnostic examination should not have a high influence on the decision on therapeutic measures.^{2,12,24,27}

Conclusion

The results of the present study suggested that the CBCT images may be useful for estimates of skeletal maturation, although they should not be used solely for that purpose.

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