Growth Prediction Using the Morphologic Characteristics of the Third and Fourth Cervical Vertebrae on Lateral Head Films

by

Jason M. Cohen DDS

Thesis

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Abstract

Orthodontic treatment in the mixed and early permanent dentition involves children at varying stages of pubertal development. During this treatment period there may be opportunity to take advantage of skeletal growth to improve skeletal, dental and soft tissue relationships. Utilizing knowledge of the potential for growth can improve the efficiency with which orthopedic changes can be accomplished. Although many growth studies aim to determine the peak height velocity or time of maximum velocity of growth, understanding the stage of pubertal development may be more valuable since an optimum range of time can be identified for orthodontic treatment. This study aims to develop a new, objective method to assess cervical vertebral morphologic characteristics at various stages of pubertal development.

Annual cephalograms from thirty-one patients, 15 male and 16 female, were used in this study. A custom computer program, written in Borland C++, was developed to analyze the morphologic features of the vertebrae using a new, objective method of vertebral analysis. Linear and ratio measurements of the third and fourth vertebrae were used in this analysis. Tangential lines approximating the borders of the vertebrae were used to improve the ease of landmark identification and to exaggerate the morphologic changes of the vertebrae throughout maturation. A growth velocity curve was developed for each patient. The age of each patient at three distinct stages of growth were defined based on each individual curve; the onset of puberty, the peak height velocity and the end of the pubertal spurt.

The results indicate a highly significant association between pubertal stage and the posterior border, anterior border and curvature depth of the third and fourth cervical vertebrae. The morphologic characteristics of cervical vertebrae three and four can be used to accurately predict the pubertal stage of 13% more subjects versus the use of age and sex alone. This new method of cervical vertebral analysis can be used to determine clinically relevant stages of pubertal development for treatment planning using a single cephalogram.

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Introduction

Orthodontic treatment in the mixed and early permanent dentition involves children at varying stages of pubertal development. During this treatment period there may be opportunity to take advantage of skeletal growth to improve skeletal, dental, and soft tissue relationships. Knowing the pubertal stage of an individual is essential in order to efficiently accomplish orthopedic changes. Although many growth studies aim to determine the peak height velocity or time of maximum velocity of growth, understanding the stage of pubertal development may be more valuable since an optimum range of time can be identified for orthodontic treatment. This study aims to develop a new, objective method to assess cervical vertebral morphologic characteristics at various stages of pubertal development.

Puberty and its significance for orthodontic treatment

Puberty is defined as the period of life during which sexual maturation occurs. The onset of puberty is a physiologic event in human growth that begins with the activation of the hypothalamic-pituitary-gonadal system and ends with the attainment of reproductive capability and the acquisition of adult body composition.[1] Typically, pubertal growth consists of a phase of acceleration, followed by a phase of deceleration and the eventual cessation of growth with the closure of the epiphyses.[1] The beginning of the pubertal growth spurt has been noted to occur 16 to 24 months earlier in girls than in boys,[2-5] although the length of the spurt is roughly the same.[4] The size of the spurt has no correlation to the age when puberty begins or the final height of an individual.[5]

The importance of predicting growth has been understood for some time, and orthodontists have tried to develop techniques to determine the onset of the growth spurt and peak height velocity. Hand-wrist radiographs are widely accepted as the most accurate method. For example, it has been shown that the formation of the sesamoid bone of the thumb precedes the pubertal growth spurt in males by 12 months and in females by 9 months.[3] However, this technique requires additional radiographic exposure for the individual. Other factors used to predict growth include the development of secondary sex characteristics, increases in the growth velocity as measured by height changes, dental development, tooth eruption, and initiation of menarche.[3,4,6-10]

In more recent years, the radiographic representation of the cervical vertebrae has been used to predict stages of growth.[11-19] This study aims to develop an objective method to assess cervical vertebrae morphologic characteristics at various stages of growth. To better understand how the vertebrae can be used to predict growth, one must understand the maturation process of the cervical vertebrae and how each individual characteristic of the cervical vertebrae projects itself on a lateral cephalogram.

Anatomy of the cervical vertebrae and vertebral maturation

In order to properly evaluate the cervical spine, a clear understanding of the anatomy is essential. The cervical spine is comprised of seven sequentially numbered cervical vertebrae, C1-C7. At maturation the first two, the atlas and axis, are unique, while the remaining 5 cervical vertebrae, C3-C5, are very similar. From birth to maturity, C-3 through C-7 undergo similar physical changes but in descending order in relation to time.[11] The cervical vertebrae are articulated by means of fibrocartilaginous inter-vertebral disks and are connected with ligaments. The vertebral column encloses the spinal cord through vertebral canals.

Growth and development of the cervical vertebrae have been studied longitudinally.[20,21] The cervical canal increases rapidly during the first three years of life. The increase in height of the third, fourth and fifth vertebral bodies is linear from the age of 6 months to maturity, and the majority of growth of the cervical vertebrae occurs before the age of 3 years.[21]

Vertebral growth takes place from the cartilaginous layer on the superior and inferior surfaces of each vertebrae. Secondary ossification nuclei on the tips of the bifid spinous processes and transverse processes appear during puberty. Secondary ossification nuclei unite with the spinous processes when vertebral growth is complete.

Following endochondral ossification, growth of the vertebral body takes place by periosteal apposition on the front and sides.[22] Radiological analysis of postnatal vertebral development in ambulatory and nonambulatory children support the concept that the vertebral body height in the sagittal plane is unaffected by mechanical factors and is most likely genetically determined.[21]

Radiographic interpretation of vertebral parts

Due to the complexity of the cervical vertebral column, radiographic projections of this anatomy are often difficult to interpret. This can be further complicated by disease or poor positioning of a patient. Deluca and Rhea, in 1980, defined the contributions of each anatomic component of the cervical vertebrae to a radiographic projection.[23] This was done by dissecting the main anatomic parts of all seven cervical vertebrae from an adult human cadaver. Radiographs were made in the A-P, lateral and oblique projections of all seven vertebrae, and then C-3 through C-5 were used for the remainder of the study. The spinous process and the left and right pedicle, lateral masses (articular pillars), transverse processes, and laminae were then dissected from each of the C-3 through C-5 vertebrae. The anterior bodies of C-3 through C-5 were then radiated, each subsequent posterior piece was added, and the image was interpreted to determine the radiographic contribution of each anatomic feature. After radiating the anterior body, the left pedicle was added. The lateral view will only be discussed due to its specific correlation to our study.

In the lateral view, the pedicle, which is poorly seen, appears as a very short, stubby density projected posterior to the superior portion of the vertebral body. The left lateral mass, or articular pillar, is superimposed on the posterior position of the vertebral body. The left transverse process is superimposed on the vertebral body, and the posterior or anterior tubercles of the transverse process may or may not be visualized. The left lamina extends beyond the lateral mass posteriorly and is shaped like a rectangle. The right pedicle superimposes on its left counterpart and is not distinguishable. The right lateral mass adds an area of increased density posterior to the vertebral body, and the lateral mass adds another cortical rectangular segment. The right transverse process adds an ill-defined curvilinear area of density over the posterior portion of the vertebral body. The right lamina is superimposed on the left lamina and projects posteriorly and superiorly. Lastly, the spinous process is seen in the profile posterior to the lamina.[23]

Recent studies determined that C-2 increased in height from 26.5mm to 34.2mm for boys and from 27.4mm to 33.5mm for girls. The mean posterior height of C-3 through C-6 increased from 6mm to 12mm from 8 to 15 years of age in boys and girls. The mean anterior height increased from 5mm to 13mm. Neither the anterior or posterior heights differed statistically between boys and girls. The mean length of C-3 through C-6 increased from 11mm to 14mm with the highest values for 15 year old boys.[20] These values for cervical dimensions have been supported by more recent studies.[21] However, most studies use variations in measurement technique, which makes comparisons difficult.

Previous studies on cervical vertebrae as predictors of growth

Several investigators have attempted to correlate the radiographic maturation of the cervical spine with mandibular and statural growth, but only recently have these studies aimed to objectively quantify the association. Lamparski, in 1972, introduced the method of utilizing cervical vertebrae as an indicator of skeletal age, and demonstrated its efficacy in relation to the hand-wrist method.[24] He was the first to develop a set of standards for the assessment of the cervical vertebrae to be used as indicators of growth for both males and females.

Oreilly and Yanniello, in 1988, were the first to use Lamparski's standards in a longitudinal study for the purpose of determining the relationship of the stages of cervical vertebral maturation to growth changes in the mandible.[17] A sample was obtained from the Bolton study in Cleveland, consisting of yearly lateral cephalometric radiographs of 13 caucasian females, in age from 9 to 15 years. They found statistically significant associations between mandibular length, corpus length, and ramus height with specific maturational stages in the cervical vertebrae.

Mitani and Sato, in 1992, aimed to examine the timing of mandibular growth during puberty and to relate it to the growth of several other facial components. This study was unique because it aimed to compare the timing of mandibular growth with several facial components, unlike previous studies that used only one parameter. The sample consisted of 33 Japanese girls, with yearly lateral cephalograms from 9 to 14 years of age. This study included individuals with normal occlusion or minor Class I malocclusions. Orthodontic treatment was not done on any of the subjects. Mandibular growth was then compared with growth rates, cervical vertebrae, hyoid bones, hand bones, and body height. The vertebral measurement, however, included only the overall length measurement of the vertebrae from C2-C5. The timing of maximum growth velocity for each parameter was examined and similarities were sought. They were able to show that within 1 year, the mandible showed a correlation in peak height velocity with body height in approximately 73% of the sample, and with hand bone or cervical vertebrae, in 82% of the sample.

Hassel and Farman, in 1995, took cervical vertebrae data and correlated it with skeletal maturation as measured from hand-wrist data[22]. Based on the presence of characteristic features of the vertebrae at different time points, the vertebrae were categorized and analyzed. Six categories of cervical vertebrae maturation were defined.[22] This independent study confirmed Lamparski's data and supported the conclusion that a subjective analysis of the vertebrae could be used to approximate skeletal age. Hassel et al.,[22] recommended this technique as a supplement to the usual orthodontic records examination. Garcia et al., in 1998, later used Hassel and Farman's modification of Lamparski's criteria to test the validity of this technique on a Mexican population, as did McNamara, in 2000, on a sample from the Michigan growth study.[12,13]

Roman, in 2002, introduced a new modification to the Lamparski and Hassel and Farman classification method.[18] Using 958 subjects, a new technique emphasizing the curvature of the lower border and the height to width ratio of the vertebrae was developed.[18] Later, in 2002, Baccetti and McNamara became the first to use objective measurements to optimize their subjective analysis tool which was modified to simply emphasize the curvature of C-3 in relation to C-4[11].

Most recently, Mito and Mitani, in 2002, moved the analysis of the cervical vertebrae from a subjective measure to an objective analysis, resulting in an equation that approximates vertebral bone age based on specified measurements of the cervical vertebrae.[16] Mohr et al., questioned the validity of an equation that approximates the bone age using vertebral analysis due to its lack of prediction capability in comparison to chronologic age.[25]

The pubertal growth spurt

Many longitudinal studies on growth during puberty have been published. In a sample of normal boys, studied longitudinally in Geneva, the peak height velocity, which occurred at 13.9 years of chronological age and 13.7 years of bone age, was 10 cm/year. Boys who began their growth spurt early, had peak height velocities of 11 cm, while those who hit their growth spurt later had peak height velocities of 9.5 cm. Similar findings were found in girls with an average peak height velocity of 8.5 cm. Girls reaching puberty early had peak height velocities of 8.8 cm versus 7.9 cm for adolescents with delayed puberty. From 3 yrs to puberty, the increase in growth percentage stays relatively constant and rarely drops below 5 cm/year in healthy individuals. There is no correlation between pre-pubertal height and final height, therefore, "late bloomers" have a higher growth percentage during puberty then "early bloomers." On average, growth is normally 18 cm from pre-pubertal to adult height with the approximate end of most of the major facial growth at 2 years from the beginning of puberty and the approximate end of facial growth at 3 years from the beginning of puberty.[26]

Maturational stage must also be distinguished from maturational level. Whereas maturational stage correlates to bone age, maturational level is defined by the difference between bone age and chronological age. A person with a low maturational level, or delayed puberty, normally has a higher percentage of growth left in both height and facial structures (87.75% mandibular growth complete versus 91.5% mandibular growth complete) than for early maturers.[9]

Pubertal growth and the growth of the craniofacial structures

The relationship between the pubertal growth spurt and mandibular and maxillary growth has been studied by several investigators. Although there is general agreement that a correlation exists between mandibular and maxillary growth and the timing of peak height velocity, the data are mixed on the difference between males and females, and the time between maximum pubertal growth and mandibular and maxillary growth. Hunter, in 1966, identified mandibular length to have the most consistent relationship with growth in statural height throughout adolescence.[4] Bjork supported these findings with implant studies showing that the cranial sutures and the mandibular condyles had similar velocity curves which were closely associated in time to that of height measurements.[2,3] This is similar to findings of Bhamba who concluded, that although there is a correlation between mandibular growth and peak height velocity, mandibular growth follows peak height velocity by 3 to 6 months.[27] Hassel, in 1995, added that statural growth acceleration could precede facial growth acceleration by as much as 12 months in some individuals.[22] In 1983, Buschang et al., analyzed 663 lateral cephalograms from a mixed longitudinal sample of 26 males and 25 females between 4 and 16 years of age. They concluded that both the ramus height and corpus length of the mandible correlated with statural growth through adolescence, with the ramus height maturing at 7% per year versus a statural growth acceleration of 5% per year.[28] These data were not supported by Mitani and Sato in 1992, when they determined that although body growth correlated well with the cervical vertebrae development, mandibular growth tended to show more variation with regard to the timing of the pubertal growth period. However, with a time lag of ± 1 year, there was a correlation between body height and mandibular growth in 73% of the sample based on crude measurements of the cervical vertebrae.[29] Some investigators also noted that females were less predictive than males in the correlation between the growth spurt and mandibular growth.[4,26] The data support the concept that mandibular growth follows or slightly trails peak height velocity, although mandibular growth can be variable and may potentially be more predictive in males than females.

In order to properly evaluate the morphologic features of the cervical vertebrae, an analysis technique must reliably and consistently model the morphologic characteristics of the cervical vertebrae. This new analysis aims to increase the consistency and reliability of vertebral analysis by objectifying the analysis process using a unique landmark identification method that both exaggerate the morphologic changes of the vertebrae while decreasing the potential for operator error. The specific aims of this study are: 1) to determine which linear or ratio measurements of the morphologic characteristics, of cervical vertebrae 3 and 4, change during puberty; 2) to determine if these morphologic characteristics of the 3rd and 4th cervical vertebrae can be used to predict stages of pubertal development better than chronologic age; and 3) to evaluate the reproducibility of the landmark identification method using this new technique.

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Jason Michael Cohen DDS
Division of Orthodontics, Department of Growth and Development, School of Dentistry,
University of California, San Francisco
50 Palm Avenue Apt#1
San Francisco, CA 94118
Phone: 415-971-6101
E-mail: Jasonc45@aol.com

Karin Vargervik DDS
Chair, Department of Growth and Development, Larry L. Hillblom Professor in
Craniofacial Anomalies, School of Dentistry University of California, San Francisco

John Huang, DDS
Professor, Division of Orthodontics
University of California, San Francisco

Division of Orthodontics, Department of Growth and Development, University of
California at San Francisco, San Francisco, USA, 94143

Corresponding author: Dr. Karin Vargervik, Division of Orthodontics, Department of Growth and Development, School of Dentistry, University of California at San Francisco, 707 Parnassus St., San Francisco, California, 94143-0438

Introduction

Orthodontic treatment in the mixed and early permanent dentition involves children at varying stages of pubertal development. During this treatment period there may be opportunity to take advantage of skeletal growth to improve skeletal, dental, and soft tissue relationships. Knowing the potential for growth can improve the efficiency with which orthopedic changes can be accomplished. Although many growth studies aim to determine the peak height velocity or time of maximum velocity of growth, understanding the stage of pubertal development may be more valuable since an optimum range of time can be identified for orthodontic treatment. This study aims to develop a new, objective method to assess cervical vertebral morphologic characteristics at various stages of pubertal development.

Puberty is defined as the period of life during which sexual maturation occurs. During this period, it has been shown that individuals experience an acceleration of growth, known as the "growth spurt." Typically, pubertal growth consists of a phase of acceleration, followed by a phase of deceleration and the eventual cessation of growth with the closure of the epiphyses.[1] To better predict when the growth spurt will occur, several studies have attempted to identify maturational indicators for pubertal development.[11-13,16-19,22,30] These studies have evaluated chronologic age, skeletal age, dental maturation, height, weight, and secondary sexual characteristics. From these studies it has been widely accepted that chronologic age is a poor indicator of maturational development while skeletal age, secondary sexual characteristics, and the onset of menarche are useful predictors.

In recent years, the radiographic representation of the cervical vertebrae has been used to predict stages of growth.[11-19] Several investigators have attempted to correlate the radiographic maturation of the cervical spine with mandibular and statural growth. Lamparski, in 1972, introduced the technique of utilizing the vertebrae as an indicator of skeletal age and was the first to demonstrate its efficacy in relation to the hand-wrist method.[24] Lamparski's standards used changes in the morphologic characteristics of the body of cervical vertebrae 2 through 6. Using Lamparski's standards, Oreilly and

Yanniello[17] found a statistically significant association between mandibular length, corpus length, and ramus height with specific maturational stages in the cervical vertebrae. In an attempt to limit the number of vertebrae in the analysis to vertebrae 2, 3 and 4, Bachetti et al., introduced a simplified analysis method using 5 stages of vertebral development. Hassel and Farman [22] later developed the cervical maturation index (CVMI) as a comparison to the skeletal maturation index (SMI) developed by Fishman for hand-wrist analysis. Garcia-Hernandez later used the CVMI criteria to prove the validity of this technique on a Mexican population, while Bachetti et al., proved the validity on a sample from the Michigan growth study.[12,13]

Most recently, investigators have aimed to objectify the cervical analysis process to identify the time of peak height velocity. San Roman, in 2002, introduced a new modification to the Lamparski and Hassel and Farman classification method. Using 958 subjects, a new technique, emphasizing the curvature of the lower border and the height to width ratio of the vertebrae, was developed.[18] Later, in 2002, Baccetti and McNamara created objective measurements to optimize their subjective analysis tool which was modified to emphasize the curvature of C-3 in relation to C-4.[11]

Mito and Mitani became the first to introduce an equation that approximates vertebral bone age based on specific measurements of the cervical vertebrae.[16] Mohr et al.,[25] questioned the validity of an equation that approximates the bone age using vertebral analysis due to its lack of prediction capability in comparison to chronologic age.

In order to properly evaluate the morphologic features of the cervical vertebrae, an analysis technique must accurately and consistently model the morphologic characteristics of the cervical vertebrae. The new analysis described in this paper aims to improve the reproducibility and accuracy of vertebral analysis by objectifying the analysis process using a unique landmark identification method that both exaggerates the morphologic changes of the vertebrae while decreasing the potential for operator error. The specific aims of this study are: 1) to evaluate the reproducibility of the landmark identification method using this new technique; 2) to determine which linear measurements or ratio of morphologic characteristics of cervical vertebrae 3 and 4 change during puberty; 3) to determine if the morphologic characteristics of the 3rd and 4th cervical vertebrae are more predictive of stages of pubertal development than chronologic age.

Hypothesis: This objective method to assess cervical vertebral morphologic characteristics can be used to determine the stage of pubertal development using a single cephalogram.

Method and Materials

Subjects

Thirty-one subjects were used in this study, 15 males and 16 females, selected from a clinical study of activator treatment in Class II malocclusions by Vargervik and Harvold at the University of California, San Francisco.[31] The original study extended over a 7 year period, from 1962 to 1969, and originally included 120 children, 56 girls and 64 boys. The subjects were recruited into the study by answering an ad placed in a local San Francisco newspaper. The archives included annual cephalograms and height measurements for each patient.[31] Records were selected randomly. Patients with too few time-points, missing radiographs, radiographs of poor contrast, and vertebrae with double borders, were eliminated from the study. Radiographs were taken at the University of California, San Francisco Craniofacial Department by two technicians. All radiographs had a magnification of 9.8% and were digitized at 300 dpi, 8-bit grayscale[32] using an Epson Expression 1600 scanner (Epson America Inc, Long Beach, Ca).

Method of Vertebral Analysis

A custom computer program, developed by the first author and written in Borland C++, was used to analyze the morphologic features of the vertebrae using a new, objective method of vertebral analysis. A tangent to the border of the posterior, anterior, top and bottom of the 3rd and 4th vertebrae were identified by selecting two points on each border (Figure 1a). The intersection of each tangent was then automatically identified by the software and was used to define the shape of each vertebrae (Figure 1b). Although defining the shape of the vertebrae could be done by hand, the process was automated to improve the efficiency of this method of analysis. A point was also recorded at the most superior point of the curvature of the lower border of vertebrae 3 and 4. All radiographs were analyzed on a 17" Gateway Vivitron computer monitor (Gateway Inc, San Diego, CA) set to a resolution of 1024 x 768 dpi.

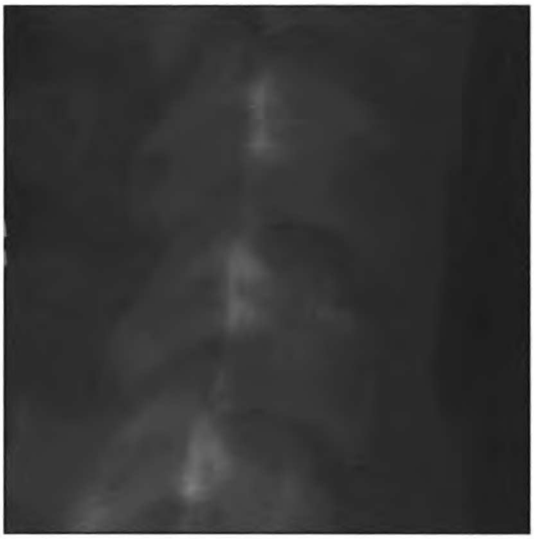


Figure 1a

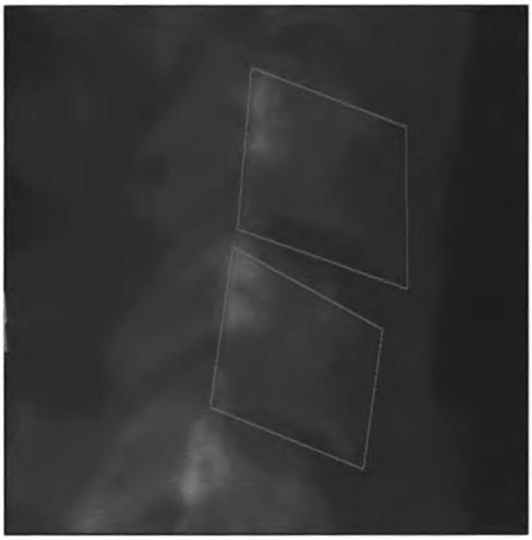


Figure 1b

Figure 1. Cervical vertebrae 3 and 4 from a conventional lateral cephalometric radiograph. (a) An example of the landmark points (green) selected by the examiner, and (b) a recreation of the vertebral shape completed by the computer once the landmarks are identified.

Radiographic Measurements

Following the creation of the vertebral shapes of the 3rd and 4th vertebrae, 7 linear measurements were measured for each vertebra (Figure 2). The linear measurements included a measure of the lengths of the posterior, anterior, top and bottom borders of vertebrae 3 and 4, as well as the height of the lower curvature of each vertebrae measured by a perpendicular to the lower border. Ratios of all linear measurements was also analyzed within and between each vertebra. The ratios included combinations of the anterior, posterior, top, and bottom borders of the 3rd and 4th vertebrae.

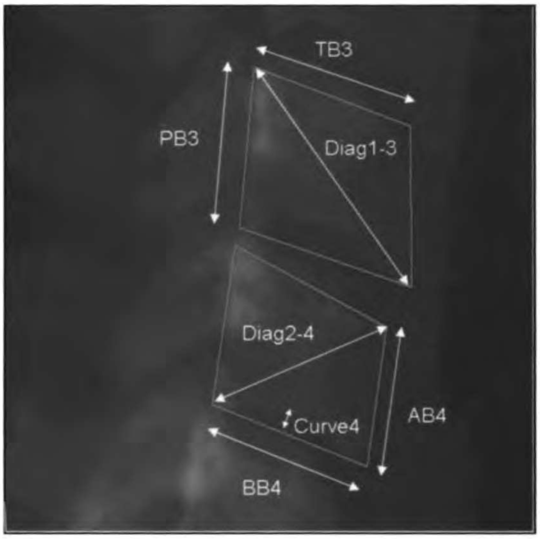


Figure 2. An example of the linear measurements recorded for each vertebra on each subject.

Determination of Stages of growth

A growth velocity curve was developed for each subject (Figure 3). A locally weighted smoothing curve was used on each individual graph. The age of each patient at three distinct stages of growth was defined based on each individual curve. The stages of growth were the onset of puberty, the peak height velocity, and the end of the pubertal spurt. The onset of puberty was defined as the age when the velocity curve changed direction originating from the peak height velocity towards the beginning of the growth spurt. The peak height velocity was recorded as the peak of the smoothed curve. The completion of puberty was defined as the age when the velocity of growth dropped below that recorded during the onset of puberty.

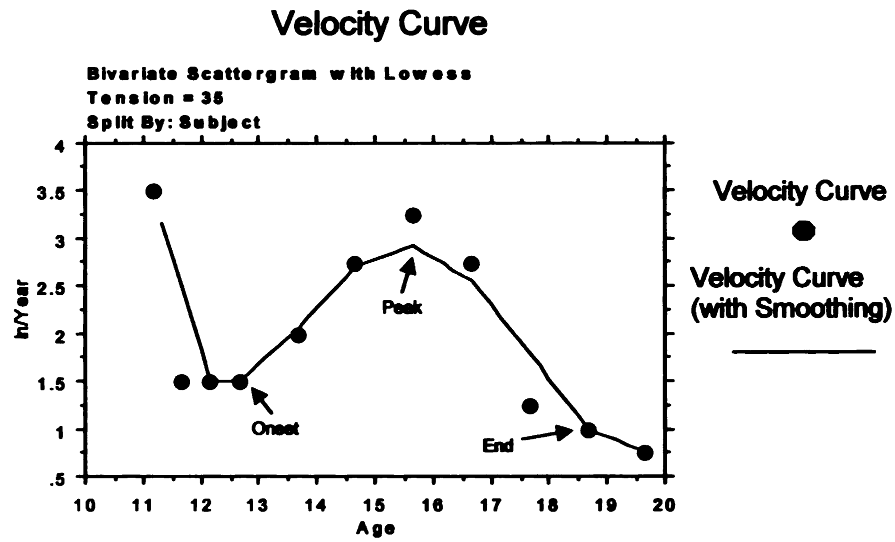


Figure 3. An example of a growth velocity curve and its corresponding smoothing curve

Error Measurement

All radiographs were analyzed in random order over a month period. Ten radiographs, chosen at random, were analyzed a second time in order to assess the intra-operator reliability. Each of the ten radiographs was analyzed at least two weeks following the original measurement. Correlation coefficients were used to evaluate the reproducibility of the landmark identification method.

Statistical Evaluation

A multivariate ANOVA analysis was done on each set of variables. The first compared the vertebral variables by stage, the second compared the variables across the stages after adjustment for age, and the third was adjusted for both age and sex. Model equations were determined by backward elimination, starting with a model including all of the predictors and eliminating non-statistically significant variables one at a time until the most predictive equation remained with the least variability.

Results

Error of the Method

Correlations between repeated measurements									
Vertebrae 3					**Vertebrae 4**				
Posterior	**Top**	**Anterior**	**Bottom**	**Curve**	**Posterior**	**Top**	**Anterior**	**Bottom**	**Curve**
r = .9594	r = .9388	r = .9914	r = .9605	r = .9854	r = .9632	r = .9001	r = .9919	r = .9632	r = .9768

Table 1. Correlations between repeated measurements of cervical vertebrae 3 and 4

The average error for all linear measurements was 0.3 mm ± 0.3 mm (r=.961). The absolute error was greatest for the posterior border (0.52 mm ± 0.4 mm) while the error for the curvature depth was least (0.15 mm ± 0.1 mm). The anterior borders showed the lowest error of the method (r=.99) while the top measurements showed the highest error of the method (r=.90); (Table 1). No bias was noted for any of the variables.

Growth characteristics

On average, boys began their growth spurt at 11.51 years (SD 0.902) and reached their peak at 13.77 years (SD 0.597). Data were not available for the completion of the growth spurt in boys. Girls began their growth spurt at 10.38 years (SD 0.88), reached their peak at 12.38 years (SD 1.139) and ended their spurt at 14.50 years (SD 1.10). The length of the growth spurt was 4.12 years on average for girls (SD 0.56 years) with a range of 3 to 5 years in length. Both girls and boys had 2.2 years (SD 0.57 years) from the onset of puberty to the peak and in females there was an average of 2 years (SD 0.45 years) between the peak of puberty and the completion of the spurt. The data showed a significant difference between onset of puberty ($p < .002$) and peak height velocity ($p < .0002$) for boys compared with girls (Figure 4).

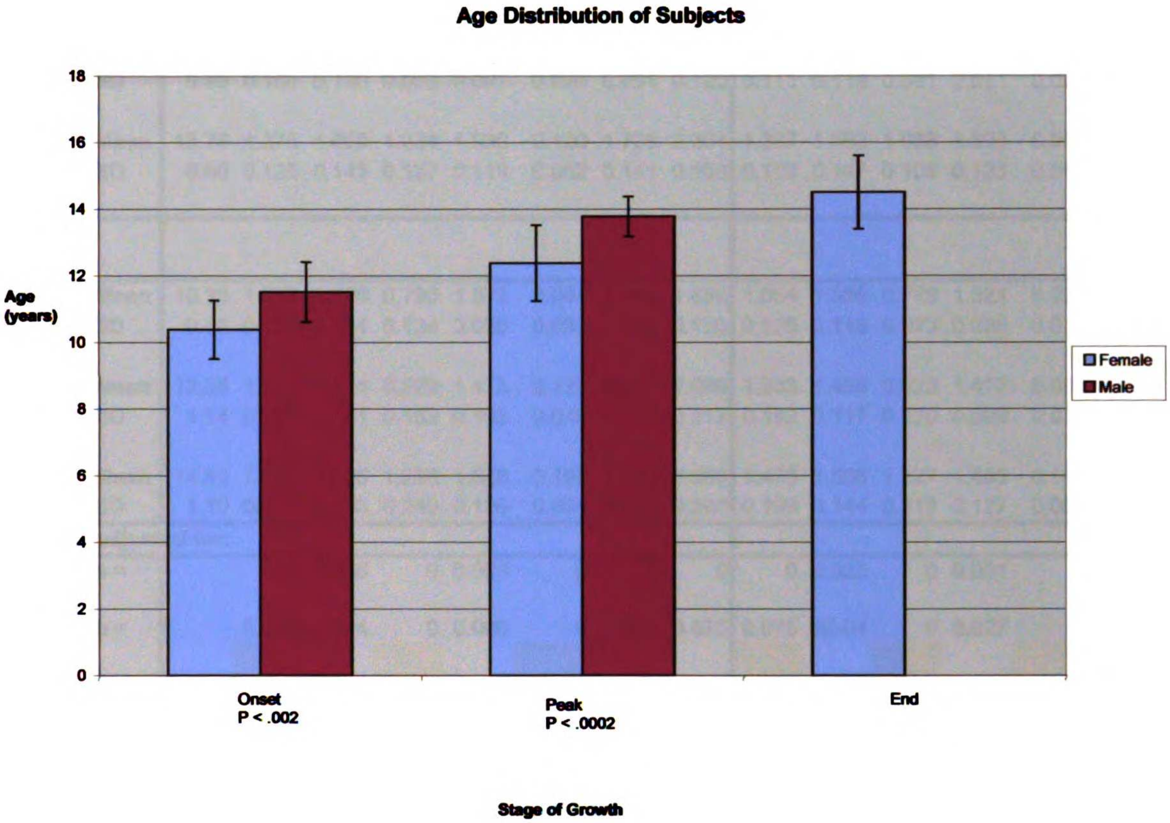


Figure 4. Age distribution at onset, peak, and end of the pubertal growth spurt (15 boys, 16 girls)

Analysis

A summary of the data is shown in Table 2 and Figure 5. The top and bottom borders of both the 3rd and 4th vertebrae were significantly different ($p < .01$) in boys versus girls. However, the anterior and posterior borders showed no statistical difference. No statistically significant difference was seen between the 3rd and 4th vertebrae in boys or girls. Using ratios to account for variability in the sizes of the vertebrae did not lead to more statistically significant data then looking at linear measurements alone.

Male		Age (yr)	Vertebrae 3 Post (mm)	Top (mm)	Ant (mm)	Bot (mm)	Curve Depth (mm)	UR to LL (mm)	UL to LR (mm)	Vertebrae 4 Post (mm)	Top (mm)	Ant (mm)	Bot (mm)	Curve Depth (mm)	UR to LL (mm)	UL to LR (mm)
Onset	Mean	11.51	1.130	1.537	0.819	1.514	0.048	1.528	2.043	1.172	1.534	0.806	1.454	0.038	1.538	1.996
	SD	0.90	0.106	0.130	0.088	0.097	0.026	0.091	0.120	0.111	0.118	0.081	0.071	0.029	0.080	0.127
Peak	Mean	13.78	1.375	1.660	1.034	1.636	0.120	1.726	2.304	1.397	1.663	1.038	1.603	0.091	1.739	2.281
	SD	0.60	0.120	0.143	0.127	0.119	0.052	0.141	0.168	0.153	0.147	0.108	0.123	0.047	0.161	0.177
Female																
Onset	Mean	10.38	1.090	1.389	0.790	1.373	0.044	1.410	1.886	1.054	1.366	0.749	1.321	0.028	1.414	1.785
	SD	0.88	0.128	0.151	0.124	0.095	0.031	0.113	0.155	0.126	0.118	0.073	0.095	0.019	0.113	0.133
Peak	Mean	12.38	1.258	1.474	0.990	1.475	0.112	1.580	2.086	1.233	1.458	0.923	1.412	0.081	1.595	1.962
	SD	1.14	0.197	0.141	0.159	0.103	0.045	0.147	0.217	0.152	0.117	0.120	0.099	0.039	0.139	0.152
End	Mean	14.50	1.509	1.536	1.296	1.526	0.199	1.760	2.350	1.468	1.506	1.227	1.485	0.169	1.789	2.212
	SD	1.10	0.217	0.193	0.240	0.126	0.064	0.199	0.280	0.199	0.144	0.213	0.127	0.064	0.195	0.258
ANOVA adjusted for:																
stage	p =		0	0.056	0	0.003	0	0	0	0	0.023	0	0.001	0	0	0
stage, age	p =		0.005	0.034	0	0.006	0	0.418	0.573	0.075	5E-04	0	0.027	0	0.292	0.716
stage, sex, age	p =		0.008	0.739	0	0.45	0	0.096	0.117	0.006	0.324	0	0.36	0	0.053	0.127

Table 2. Raw measurements of each variable at each stage of pubertal development with correlating p values adjusted for stage, stage and age, and stage, age and sex.

A summary of the statistical analysis of each of the variables is included at the bottom of Table 2. In each case there were three ANOVAs. The first compared the vertebral variables by stage of pubertal development, the second compared the variables across the stages after adjustment for age, and the third was adjusted for both age and sex. In all cases, with the exception of the top border of the third vertebrae, there are statistically significant differences for the variables between the stages of pubertal development. In the cases highlighted above, the variables are statistically significant even after adjustment for age and sex. Therefore, there is statistically significant information in these vertebral variables above and beyond sex and age.

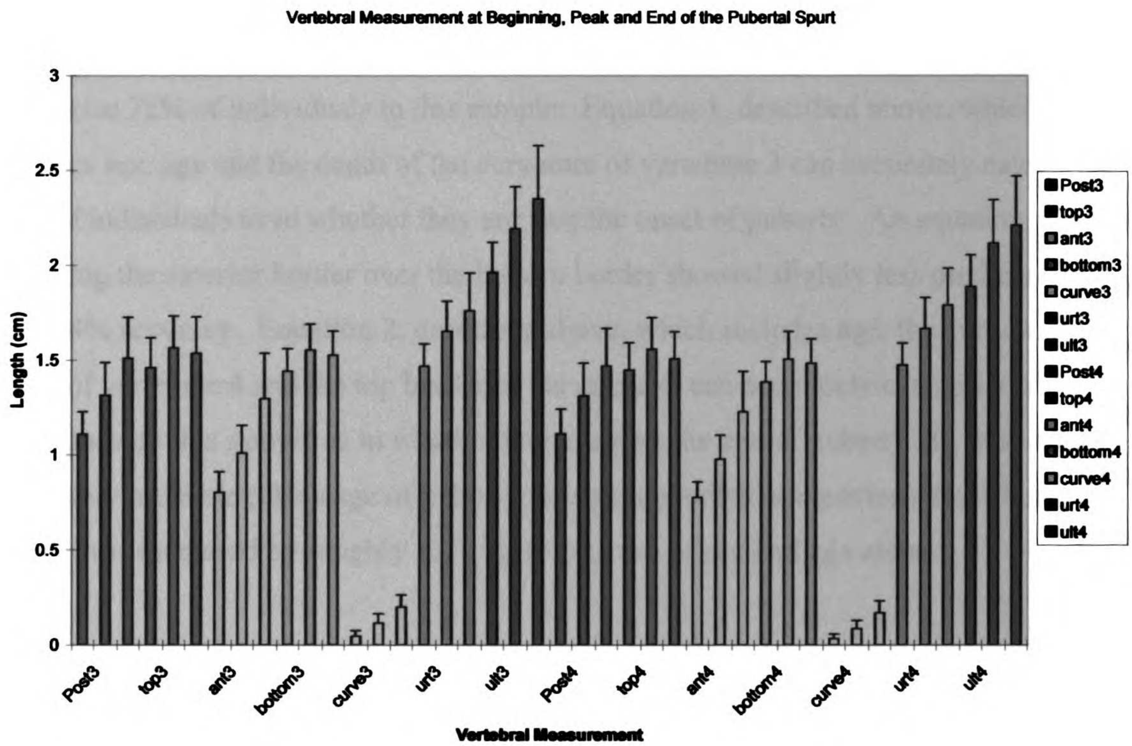


Figure 5. Graph of the mean and standard deviation, of each variable, at the onset, peak and end of pubertal development for boys and girls combined

Prediction Models

In order to develop a clinically relevant application from the data, two predictive model equations were developed to determine whether the subject was past the beginning of the pubertal spurt and a separate equation to determine if the subject was at or past the end of the pubertal spurt. These equations can be used in conjunction to determine the stage of puberty of an individual.

Equation 1 - Onset vs Peak and End

(4.223 * Age) + (69.275 * Curve3) + (5.0413 * Sex) – 64.3035

Equation 2 - Onset and Peak vs End

(2.672 * Age) + (86.438 * Curve4) – (28.3917 * Top4) – 3.43112

Sex: Male = 1, Female = 2

Using age alone as a predictor, the stage of puberty of 54% of individuals from our sample could accurately be categorized at the onset of puberty and 41% at the end of puberty. Adding the sex of an individual to the age in a model equation can accurately categorize 72% of individuals in this sample. Equation 1, described above, which includes sex, age and the depth of the curvature of vertebrae 3 can accurately categorize 86% of individuals as to whether they are past the onset of puberty. An equation including the anterior border over the bottom border showed slightly less predictability with 84% accuracy. Equation 2, described above, which includes age, the curvature depth of vertebrae 4 and the top border of curvature 4, can accurately categorize 85% of individuals in this sample as to whether they are past the end of puberty. In this sample, accurately predicting the stage of puberty, using the predictive equations described above, was increased by roughly 13% versus the use of sex and age alone.

Discussion

The time of onset, peak height, and completion of the growth spurt, in this sample, was in agreement with other studies for boys and girls over similar time periods.[9,27,33-38] Previous studies on growth have used varying methods of analysis to identify stages of the growth spurt.[4,27,33,34,36,37] Although average curves are easily characterized, individual curves can vary significantly, and any one method for characterizing a curve cannot be used for every growth curve. Factors which contribute to the variability of growth include nutrition, environment, genetics, and socioeconomic status.[39-41] In this study, subjects with growth spurts that could not be identified, were excluded. These included individuals with no growth spurts or significantly variable growth patterns. All curves were analyzed twice to compare the consistency with which these curves could be identified using the defined method. In this sample, boys began their spurt 1½ years later then girls which is in agreement with previous studies.[41] Although the length of the growth spurt is not different between males and females, the extra 1½ years of growth before the spurt accounts for the difference in height between boys and girls at the completion of the growth spurt.[41]

Stages of growth were correlated in this study to changing morphologic characteristics of the growing cervical vertebrae. Accurately determining whether an individual is before, beginning, in the middle, soon to complete or complete with their growth spurt, gives the clinician a simple reference to aid in the treatment planning process. In order to stage growth, previous studies have aimed to define the peak height velocity (PHV), and then correlate morphologic characteristics of the cervical vertebrae with years from PHV. This is inaccurate for staging growth due to the inherent difference in the stage of growth seen in individuals a specified year from PHV. While one individual may be complete with growth one year after their PHV, another may still be experiencing significant growth. This is also seen one year or more prior to PHV. In this study, the age from onset to peak in girls and boys ranged from 1 to 3 years. Therefore, correlating morphologic variations in the cervical vertebrae with stages of growth is more clinically useful then looking at years from PHV.

A unique landmark identification method was used in this study to improve on the reproducibility of the landmark identification methods used in previous studies.[11,12,17,18,22] The anterior superior landmark on the cervical vertebrae used in previous studies[11,12,42] changes dramatically as the vertebra matures. At the beginning of puberty, this point is broad and rounded, making it a challenge to define a single point. As the vertebra mature, however, this point becomes more easily defined.

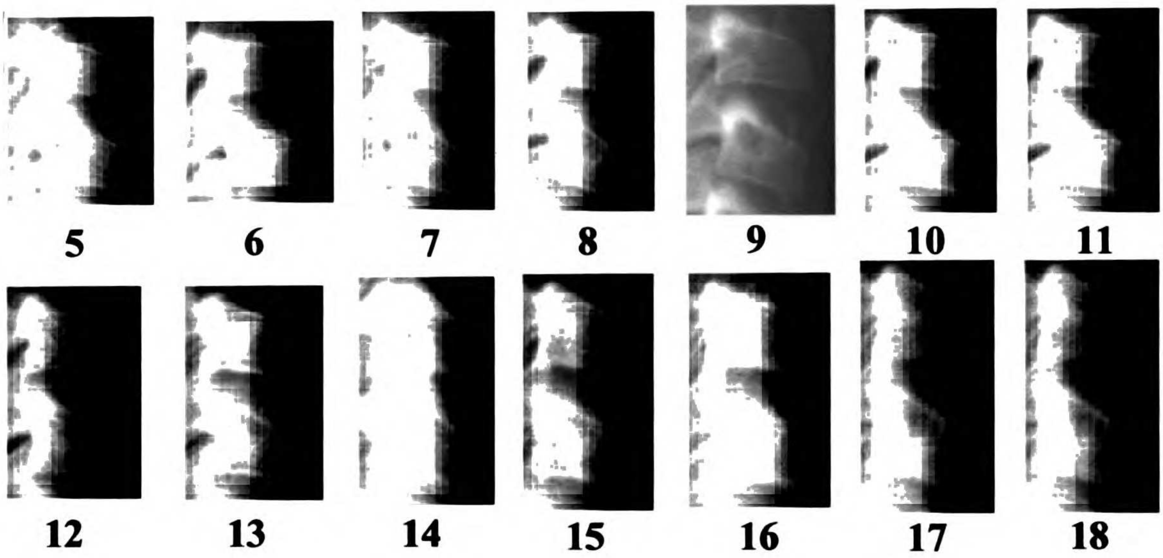


Figure 6. Example of lateral cephalometric radiographs of a female subject (subject 504) from age 5 to 18.

A progression of growth of the third and fourth vertebrae can be seen in Figure 6. The inferior border appears longer earlier in puberty, exaggerating a wedge shaped appearance of the vertebrae. As puberty progresses, the anterior border begins to lengthen, and the top border increases in length at a greater rate than the lower border until the vertebrae begin to take on a rectangular appearance as the growth spurt wanes.[22] Measuring the anterior border over time using the method described was 99% reproducible with the lowest reproducibility measurement being the top border at 90%. The results of the correlation measurements show that this new method of analysis is highly reproducible.

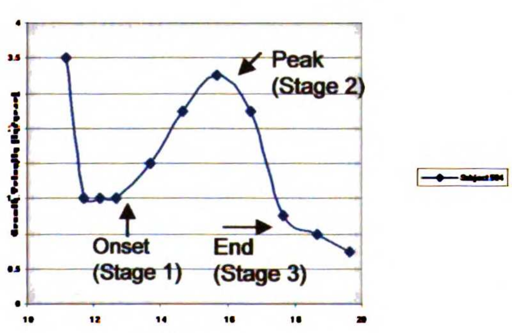
This study showed that boys have larger vertebrae then girls in the horizontal dimension but did not support previous findings that the 3rd vertebrae matures before the 4th vertebrae.[11] The variables that had the most significant growth changes during puberty were the anterior border and the curvature depth with the posterior border showing significance, as well. This is in agreement with previous studies that the anterior border and the curvature depth show the most discernable growth during maturation,[14,16] however this study also demonstrated their significance in relation to sex and age. Using sex, age, and these significant variables, two predictive equations were developed to help determine the stage of puberty.

		Probability of Peak or End versus Onset	Probability of End versus Onset or Peak	Example for Interpreting Probability Results		
	Subject values	Age, sex, vert model	Age, top4, curv4 model	Probability of Peak or End versus Onset	Probability of End versus Onset or Peak	Interpretation of Prediction
Constant	1	-64.30349	-3.93112	0	0	Before Onset
Age	12.66667	4.223	2.671838	0.75	0	Onset
Sex	2	5.047337		1	0.25	Between Onset and Peak
Curve3	0.059868	69.27484		1	0.5	At Peak
Top4	1.565947			1	0.75	Between Peak and End
Curv4	0.011853			1	1	At or Past End

Probability of peak or end versus onset
0.846
Probability of end versus onset or peak
0.000

Figure 7. Example of an excel spreadsheet incorporating the predictive equations described above and an example of how to interpret the results.

Figure 7 shows an example of how the predictive equations can be used to help determine the stage of pubertal development once entered into a spreadsheet. The areas in yellow are determined from measurements of the vertebrae with the age and sex of the individual. The red numbers are probabilities returned from the predictive equations once the yellow data is entered. The right side of Figure 7 gives an example of how to interpret the probability results for an individual.



Subject 504			
Age	Stage 2 or 3 versus 1	Stage 3 versus 1 or 2	Interpretation of Prediction
11.16667	0.009	0	Before Onset
12.66667	0.846	0	Onset
14.16667	1	0.014	Between Onset and Peak
15.66667	1	0.889	Between Peak and End
17.16667	1	1	At or Past End

Figure 8. Growth curve for female (subject 504) including predictions at 1 1/2 year intervals from before the onset of puberty and the appropriate interpretations for the predictive results.

The cervical vertebrae in Figure 6 shows the progression of the cervical vertebral development for a specific individual (subject 504). Using averages, it would be reasonable to assume that this female would begin puberty at 10, reach her pubertal peak at 12, and be completed with her growth spurt at 14½. In actuality, this patient began puberty at 12.67, reached her peak at 15.67, and completed her spurt at 17.67. Figure 8 shows the results of the predictive equations for this subject using 5 time-points, in 1½ year intervals from before the onset of puberty. The stage of puberty, for this individual, could have been predicted accurately before, during and after puberty.

Conclusions

Growth changes during puberty of the posterior border, anterior border, and curvature depth of the 3rd and 4th vertebrae can be used to predict stages of pubertal development better then age and sex alone. The findings from this study showed that the vertebral analysis method described is both reproducible and effective at measuring morphologic characteristics of the cervical vertebrae during puberty. This study also demonstrated that boys have larger vertebrae than girls, but did not show that the 3rd vertebra matures before the 4th vertebrae. As well, it was shown that the morphologic characteristics of cervical vertebrae three and four can be used to accurately predict the pubertal stage of 13% more subjects versus the use of age and sex alone. Based on these findings, the hypothesis that this objective method to assess cervical vertebral morphologic characteristics can be used to determine the stage of pubertal development using a single cephalogram cannot be rejected.

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