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Cervical Vertebral Maturation Stage as a Growth Predictor

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Cervical Vertebral Maturation Stage as a Growth Predictor

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Abstract

The purposes of this study were to establish the reproducibility of skeletal age assessment as determined by the stage of cervical vertebral maturation (CVM) and to assess the ability of the CVM method to predict timing of peak mandibular growth velocity (PMdGV). The longitudinal records of 104 females (age 8 to 14 inclusive) were used to determine skeletal age (as assessed by the CVM) and mandibular length.

Reproducibility of skeletal age estimates was tested by comparing five sets of first and second determinations done 2 months apart for 20 subjects chosen from the total sample before and after the principal operator calibration. The reproducibility of skeletal age assessments done prior to calibration was unacceptable. The reproducibility improved to acceptable limits following calibration. Improved definitions, the addition of an extra stage and the development of a Sequential Conditional Flow Chart rendered the modified CVM method, introduced in this study, even more reproducible.

The kappa for 20 double assessments of the timing of PMdGV was 59% (not acceptable) but of the 55 subjects for whom two determinations of timing of PMdGV coincided, only 61% were at cervical vertebral stage 3 thus lending some measure of uncertainty to the use of the cervical vertebral maturation method for predicting timing of PMdGV.

Key Words: CVM, cervical vertebrae maturation, mandible, growth, reproducibility, peak mandibular growth velocity, ideal treatment timing

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INTRODUCTION

Forecasting the timing of peak mandibular growth velocity is of particular interest to orthodontists since it is believed that better results are obtained for severe retrognathic cases if treatment is delivered during the period of accelerated mandibular growth[1]. Many studies using longitudinal cephalometric data have identified a pubertal spurt in mandibular growth characterized by wide variation in amount and timing[2-7]. Although the direction of growth is often maintained at puberty, the amount and timing of the mandibular growth spurt is frequently a mystery.

There is general agreement[8,9] that neither chronological age nor dental development are good predictor of timing of peak facial growth. Various biologic indicators such as: standing height, sexual maturity as determined by menarche onset in girls, voice changes in males, and skeletal age assessed by hand wrist ossification stages or by cervical vertebral maturation stage have been suggested[8,10-14].

There is abundant support[2,4,15-23] for the belief that statural growth peak velocity generally coincides[24,25] or precedes facial growth peak velocity by 6 to 12 months[2,15]. That must be taken in the light of an observation by Houston et al[26] which may be too restricting but certainly merits serious consideration: "If advantage is to be taken of the growth spurt, it is necessary to predict its timing at least 1 or 2 years in advance of peak height velocity."

Several investigators[24,27,28] have shown that menarche almost always occurs after peak height velocity and Hägg and Taranger[28] found that the pubertal voice change may be regarded as an indicator of the male pubertal growth spurt. Possibly one can identify the peak and the end, but not the beginning of the pubertal growth spurt by menarche and voice change but not with sufficient advanced notice to ensure treatment may coincide with pubertal growth.

The hand wrist method is considered the most reliable procedure to date for the assessment of skeletal age[14,18,26,29] and many methods are available for its determination including those developed by Todd[30], Greulich and Pyle[31], Tanner and Whitehouse[32], Grave and Brown[18] and Fishman[33].

In 1937, Todd[30] suggested that in healthy individuals, roentgenograms of any area of the body would yield the same skeletal age rating. Greulich and Pyle[31] wrote: "the skeleton of the healthy, adequately nourished child develops as a unit, and its various parts tend to keep pace with one another". Thus, the assessment of skeletal maturation using cervical vertebrae should be equivalent to that determined from hand wrist radiographs.

Lamparski[34] introduced the cervical vertebral method in 1972 and maintained that it is as reliable and as valid as the hand wrist method for the assessment of skeletal age. Based on a sample of 69 males and 72 females, he suggested a series of standards comprising 6 maturational stages for both males and females. This method is known as the **Lamparski** method (see Appendix I and Table 1)[34].

In 1988, O'Reilly and Yanniello[35] used a sample of 13 Caucasian females with ages ranging from 9 to 15 years from the files of the Bolton-Broadbent growth study in Cleveland. Using Lamparski's method, they concluded that the cervical vertebral stages of maturation are related to mandibular growth changes during puberty. On average, stages 1 through 3 occurred prior to peak mandibular growth velocity, with stages 2 and 3 in the year immediately preceding peak mandibular growth velocity.

In 1995, after evaluating 220 subjects from 8 to 18 years of age from the Bolton-Brush growth centre at Case Western Reserve University and using the hand wrist method developed by Fishman[33], Hassel and Farman[36] developed a six stage index using cervical vertebrae 2, 3 and 4 only. They noted that in general, cervical vertebrae 3 and 4 changed from wedge shaped to rectangular horizontal to square to rectangular vertical. The curvatures of the lower borders were seen to appear sequentially from C2 to C3 to C4 as the skeleton matured. Based on their findings, a new index that evaluated the 2nd, 3rd and 4th cervical vertebrae only called the **CVMI method** was suggested (Appendix II, Table1). Kucukkeles et al[37] reported that three investigators found 13 of 20, 18 of 20 and 9 of 20 double determinations were the same when evaluating the intra-operator reproducibility.

In 2000 Franchi, Baccetti and McNamara[38] published the first of three papers on the topic of cervical vertebral determination of skeletal age using 6 stages and 5 vertebrae which they called the **Cvs method**. (Appendix III, Table 1). By 2002, in their 2nd publication[39], they had reduced the number of stages to 5 and the number of vertebrae rated to 3 which they called the **CVMS method** (Appendix IV, Table 1). With their third publication in 2005[40], they reverted to 6 stages but stayed with 3 vertebrae. This last method was called the **CS method** (Appendix V, Table 1). In all cases, the development of inferior surface concavity and the sequence of change for C3 and C4 through the 5 or 6 stages is the same. The six stages are not meant to be age specific although they may appear to be so because the serial data upon which their findings are based were obtained annually. They reported that the inter examiner agreement was 96.7% which presumably means that two examiners rated subjects the same 96.7% of the time.

Other authors have suggested different formulas for assessment of the cervical vertebral stage and for the prediction of mandibular growth in millimeters as it relates to the cervical stage. In 2002, Mito et al[41] proposed a regression formula to assess the cervical vertebral bone age based on the length and width ratios of the 3rd and 4th cervical vertebrae. Using this formula, the same group studied a sample of 40 Japanese girls in 2003 and developed a second formula for prediction of mandibular growth potential in Class I skeletal cases (in millimeters) = -2.76 x cervical vertebral bone age + 38.68 (r=0.857)[42]. Chen at al[43] developed a similar formula: MLI (mandibular length increment) = 36.20 - 0.71 x AH3 - 0.97 x PH3 - 0.90 x AH4. AH3, PH3, and AH4 stand for: anterior vertebral body height of the third vertebra, posterior vertebral body height of the third vertebra, and anterior vertebral body height of the fourth vertebra respectively.

Since the hand-wrist method has been considered as the ultimate reference for the assessment of skeletal maturation, many authors have tried to evaluate the effectiveness of the cervical vertebrae as a maturational indicator by measuring the correlation between these two methods.

Lamparski 1972[34] reported a high correlation between the cervical vertebrae assessment and the hand-wrist method and concluded that since the validity of the wrist assessments has been proven many times and since it is shown that there are no significant differences between vertebral and wrist assessments , the vertebrae can be validly used to assess skeletal age. His thesis was never published and is no longer available on inter library loan so we are not able to confirm these conclusions. Hassel and Farman 1995[36] agreed with Lamparski's conclusion but condensed eleven SMI groupings into six CVMI stages. Thus the six CVMI stages of Hassel and Farman are based upon Fishman's[33] stages for the hand wrist whilst Lamparski's 6 stages are based upon the hand wrist stages of Greulich and Pyle[31].

Garcia-Fernandez et al[44], Kucukkeles et al[37] and Uysal et al[45] supported the validity of Hassel and Farman's method (CVMI) of evaluating skeletal maturity and suggested that there is no significant difference between hand-wrist and cervical vertebrae for the assessment of the skeletal age. Kucukkeles et al[37] reported that agreement between investigators was only 66% for stage 3 (peak growth) as oppose to 78 and 74% agreement for pre and post peak respectively.

In 2002, San Roman et al[46], based on a cross sectional sample of 958 Spanish children (5-18 years of age), studied the correlation between skeletal age as determined by the hand-wrist method of Grave and Brown[18] and the cervical vertebrae maturation stage as determined by Lamparski's method[34] (0.79 for females and 0.69 for males) and by Hassel and Farman method[36] (0.84 for females and 0.77 for males) (Appendix VI). They also proposed an equation to estimate the maturation stage of the hand and wrist. In the same year, Mito et al[41] developed a regression formula to obtain cervical vertebral bone age based on the length and width ratios of the 3rd and 4th cervical vertebrae. Using this formula, they found a high correlation between cervical vertebral bone age and finger bone age as assessed by the Tanner and Whitehouse (TW2) method[47].

More recently, Carlos Flores Mir et al[48] studied the correlation between the Fishman maturation prediction method (FMP) of the hand-wrist and the cervical vertebral maturation (CVM) method for skeletal maturation stage determination. They concluded that correlation values between FMP and CVM were moderately high and that this may be high enough to use either of the methods for research purposes but not for the assessment of individual patients. They suggested skeletal level (advanced, average, or delayed) influenced the correlation values and should be considered whenever possible.

In their publication of 2000, Franchi et al[38] reported on a subsample of 15 females and found that on average, 87% (i.e.13 subjects) of the females had the greatest increment in statural height occurring between Cvs3 and Cvs4. The remaining 13% (i.e. 2 subjects) of the sample had their peak between Cvs4 and Cvs5.

The most recent method of cervical vertebral maturation presented by Baccetti, Franchi and McNamara in 2005[40], the CS method (Appendix V), is presently the most popular method referred to in many presentations but as yet not tested for reproducibility or ability to predict timing of Peak Mandibular Growth Velocity. Therefore the aim of this study was to assess the reproducibility of the CS method, assess the ability of this method to predict timing of peak mandibular growth velocity (PMdGV) and to test the hypothesis that peak mandibular growth velocity (PMdGV) falls between CS3 and CS4.

The Vertebral Column

The vertebral column extends in the midline from the base of the skull above to the pelvis below and then beyond as a rudimentary tail. It is made up of a number of individual components (vertebrae) that articulate above and below with each other, thus forming a segmented structure[49].

Although somewhat variable, there are normally said to be 33 vertebrae in the adult column (figure 1): 7 cervical vertebrae in the neck region, 12 thoracic vertebrae in the chest region, 5 lumbar vertebrae in the small of the back region, 5 fused vertebrae forming the sacrum, and the remaining 4 fusing to form the diminutive coccyx[49].

Although the morphology of each vertebra is a product of both localized factors and general requirements that are placed on the column as a whole, there is a basic pattern that can be identified in all adult vertebrae throughout the length of the column (Figure 2). When viewed from above, the typical vertebra has an anterior body and a posterior vertebral arch, which forms the boundaries of the vertebral (spinal) canal. The vertebral arch is formed from paired anterior pedicles and posterior laminae and seven processes that extend outwards from this arch: A single spinous process, paired lateral transverse processes and paired superior and inferior articular processes[49].

The cervical Column

The cervical column extends from the base of the skull above to the articulations with the first thoracic vertebra below at the root of the neck. This is the most mobile region of the column and is the site of attachment for the strong vertebral muscles of the neck, which contributes to the maintenance of the erect position of the head[49].

A typical cervical vertebra is to be found in the middle of the segment, for example, C3-C6 (Figure 3 and Figure 4)[49]. C1 the atlas, C2 the axis (figure 5)[49] and C7 are atypical. C1 and C2 vertebrae have changed extensively permitting the movements of nodding and rotation of the head on the neck. They are strikingly different in appearance from the remainder of the presacral vertebrae and, as such, are perhaps the easiest to identify.

Growth of cervical vertebrae at puberty

Around puberty, the typical cervical vertebrae grow via six secondary centers of ossification or epiphysis for each vertebrae: one for the tip of each transverse process, an annular ring that covers the superior and inferior surfaces of the vertebral body and one for each terminal ending of the bifid spinous process. The literature seems to agree on the fact that the secondary centers appear at the beginning of puberty (12-16) and finally fuse at the end of puberty (18+ years), and certainly by 24 years of age.

In orthodontics, when using the cervical vertebrae maturation method to assess skeletal maturation, the clinician is mainly looking at the growth of the superior and inferior annular epiphyses of the 2nd, 3rd, and 4th cervical vertebrae.

Before the appearance of the secondary ossification centers (especially the superior and inferior annular ring) the body of the cervical vertebrae has a flat horizontal inferior surface and a superior surface that is flat posteriorly but slopes anteriorly so that it is wedge-shaped. With the appearance of the secondary ossification centers and their growth, the body of the cervical vertebrae changes form and dimensions. It progresses from a trapezoid wedge shape, to horizontal rectangle, to square, to vertical rectangle as skeletal maturity is reached.

MATERIALS AND METHODS

Pilot Study

A pilot study was conducted in order to determine the landmarks that were to be used to measure mandibular length; to train the principle operator to trace and measure mandibular length; to trace the 2nd, 3rd and 4th cervical vertebrae; and to determine the cervical stage.

Forty six lateral headfilms were traced and mandibular length was measured on two different occasions, 2 weeks apart. Two different measures were used to determine mandibular length: Ar-Gn and Co-Gn (Ar: Articulare is the point of intersection of the inferior cranial surface and the averaged posterior surfaces of the mandibular condyles; Gn : Gnathion is the most anterior inferior point on the contour of the bony chin symphysis determined by bisecting the angle formed by the mandibular plane and a line through Pogonion and Nasion; Co: Condylion is the most posterior superior point on the curvature of the average of the right and left outlines of the condylar head).

Co-Gn is sometimes used for mandibular length determination because it includes the entire mandibular length whereas Ar-Gn leaves out the condyle. Several authors have shown that Co cannot be located accurately and consistently on a lateral cephalogram in maximum intercuspation position[50,51]. Haas[52] demonstrated that Ar is a good substitute for condylion when measuring total mandibular length. This was confirmed in the present pilot study in which the Intra Class Correlation Coefficient (ICC) for Ar-Gn was 99.4% and for Co-Gn was 96% (Table #2). Consequently Ar was used for the measurement of mandibular length

Materials and methods

The sample used in this study (Appendix VII) was derived from the records of the Burlington Orthodontic Research Centre (BORC), which is located in the Department of Orthodontics, Faculty of Dentistry, University of Toronto[53]. This same sample was used in a previous publication by Hunter et al[54].

The entire longitudinal group of 110 females for whom annual lateral headfilms were available from 8 to 14 years of age, inclusive, was used. The records for six subjects could not be used because of severe underexposure or inadequate coverage, reducing the sample to 104. The *same definitions used by* Hunter et al[54] in 2002, for the following terms were used.

Chronological age

Chronologic age was the age at the subject's nearest birthday as determined from the demographic records of the BORC. With very few exceptions, the records were obtained within one month of the subject's actual birthday.

Mandibular length increments (see Appendix VIII)

The entire female sample that had 7 consecutives cephalograms from the BORC (Appendix VII) were utilized for this study, excluding the exceptions previously mentioned.

Seven lateral cephalograms taken in CO were traced for each one of the 104 subjects including ages 8 through 14 **(First tracing)**. The mandible, upper and lower incisors, cranial base, and all cervical vertebrae appearing on the x-ray were traced on 0.003-inch matte acetate with a 0.5mm diameter mechanical lead pencil as shown in Figure 6. Tracings and assessments were performed by the principal operator (BJ) in a darkened room with a radiographic illuminator to ensure contrast enhancement of the bone images. All tracings were photocopied with no magnification. The distance between Articulare and Gnathion on each lateral headfilm was measured using a sharpened calibrated digital caliper (**Md1**). Annual increments of mandibular growth for each subject were then derived by subtracting each annual value for ArGn from that of the next year.

The tracings were measured randomly and the operator was blinded to patient names and ages. All measurements were entered into the JMP statistical program for analysis. Data were checked for entry error and when an age related increment differed from the average by more than 7mm, the measurement was retrieved and corrected if necessary. Because the enlargement factor of 9.8% was constant, it was not necessary to correct for it.

Since none of the x-rays were obtained on the subject's exact birthday, linear regression was used to adjust all mandibular length increments to coincide with a full year. For example, subject #2093 had her 9 year record taken 8 days after her birthday and the 10 year record taken 3 months and 20 days after her birthday. The increment from 9 to 10 years was 2 mm. This value became 1.58 mm when adjusted from 9 to 10 years to her exact birthdate. It was assumed that mandibular length increments between two consecutive ages are linear. In this manner, prediction of the exact amount of mandibular length increment at exact ages was possible. Annual increments were positioned at the midpoints between birthdays. The Mandibular Length increments were connected and plotted as shown in Figure 7.

Pre-Pubertal Mandibular Growth Minimum (PPM)

PPM was defined by Hunter et al[53,55] as the age-year during which minimal annual mandibular growth occurred between the ages of 8 and 14. PPM was used to identify the age of Peak Mandibular Growth Velocity (PMdGV) as explained next. Because that range included 11 subjects whose PPM was at 13 or 14 years of age with no significant growth after, it was decided to define PPM as the age of minimal annual mandibular growth between the ages of 8 and 12. Subject #2050 is one of those 11 subjects (see Figure 8).

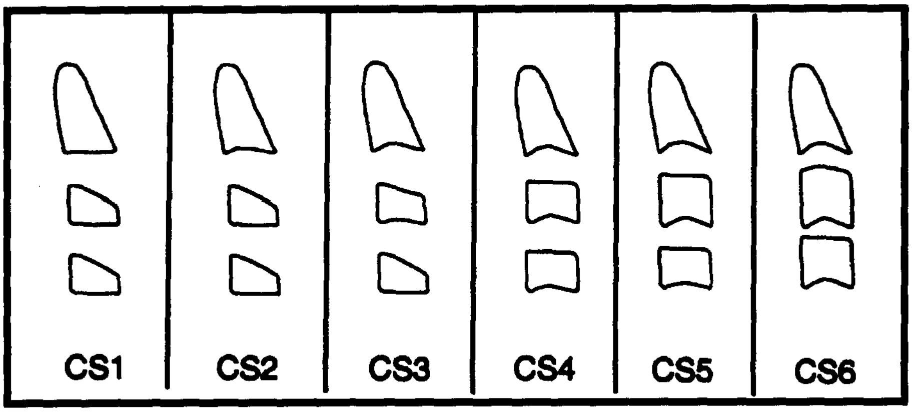
Peak Mandibular Growth Velocity (PMdGV) (Appendix VIII)

PMdGV was defined as the age-year during which maximum annual mandibular growth occurred after the PPM, determined by inspection of the plotted increments for ArGn as described above. It should be noted here that 2 subjects did not have a lateral cephalogram at age 14. The 14 year value was determined simply as the increment from 13 to 15 divided by two. Peak Mandibular Growth Velocity was identified for the 104 subjects **(PMdGV1).**

For three subjects PPM occurred between 11 years and 12 years and no further significant growth was present. PPM was preceded by significant growth. Rather than modify the definitions again to accommodate these 3 subjects, PMdGV was selected at the time when it made most sense. For example subject #2062 (Figure 9): Following the definition PPM is at 12 years but if we look at the mandibular increment graph, there is no significant growth happening after age 12. Rather PMdGV seems to be occurring at age 10. So PMdGV was recorded as occurring at age 10.

Skeletal maturation as determined by the Cervical Vertebral Stage (Appendix VIII)

Method used for the assessment of the Cervical Vertebral stages (adapted from: Baccetti T; Franchi L; McNamara Jr JA. The Cervical Vertebral Maturation (CVM) Method for the Assessment of Optimal Treatment Timing in Dentofacial Orthopedics. Semin Orthod 2005; 11: 119-129)[40].



Cervical stage 1 (CS1): the lower borders of all the three vertebrae (C2-C4) are flat. The bodies of both C3 and C4 are trapezoid in shape (the superior border of the vertebral body is tapered from posterior to anterior). The peak in mandibular growth will occur on average 2 years after this stage.

Cervical stage 2 (CS2): A concavity is present at the lower border of C2 (in four of five cases, with the remaining subjects still showing a cervical stage 1). The bodies of both C3 and C4 are still trapezoid in shape. The peak in mandibular growth will occur on average 1 year after this stage.

Cervical stage 3 (CS3): Concavities at the lower border of both C2 and C3 are present. The bodies of C3 and C4 may be either trapezoid or rectangular horizontal in shape. The peak in mandibular growth will occur during the year after this stage.

Cervical stage 4 (CS4): Concavities at the lower border of C2, C3, and C4 now are present. The bodies of both C3 and C4 are rectangular horizontal in shape. The peak in mandibular growth has occurred within 1 or 2 years before this stage.

Cervical stage 5 (CS5): The concavities at the lower borders of C2, C3, and C4 still are present. At least one of the bodies of C3 and C4 is squared in shape. If not squared, the body of the other cervical vertebra still is rectangular horizontal. The peak in mandibular growth has ended at least 1 year before this stage.

Cervical stage 6 (CS6): The concavities at the lower borders of C2, C3, and C4 still are evident. At least one of the bodies of C3 and C4 is rectangular vertical in shape. *If not rectangular vertical, the body of the other cervical vertebra* still is squared. The peak in mandibular growth has ended at least 2 years before this stage.

Following the initial sets of double determinations (intra-operator agreement prior to calibration) the results of which were unacceptable it was felt that the results might be improved by instruction in the method with Drs Baccetti, Franchi and McNamara. Therefore, those investigators provided a calibration session at the school of Dentistry, University of Michigan, Ann Arbor Michigan for the principal investigators using the latest cervical vertebral procedure at this time.

Following calibration of the principal operator, the morphology of the 2nd, 3rd, and 4th cervical vertebrae on the seven consecutive lateral cephalograms of each of the 104 subjects of the entire sample (same as the one used for determining mandibular length) was assessed by visual inspection to determine CS. This assessment was called the **calibrated visual assessment**. Cervical vertebral stages were determined using the latest method of Baccetti et al[40]: the CS method (Appendix 5), which assesses maturational changes of the second, third and fourth cervical vertebrae.

All assessments of the CS were done by visual reading of the lateral headfilms under the same conditions: darkened room with a radiographic illuminator to ensure contrast enhancement of the bone images. All assessments were done randomly and the operator was blinded to subject names and ages.

Cervical vertebral stages were entered in the JMP program. Data were checked for entry error and corrected if necessary.

ERROR STUDIES (Appendix 8)

Mandibular length as determined by ArGn and Identification of Peak Mandibular Growth Velocity

The headfilms of 20 subjects selected randomly were retraced two months after the first tracing **(Second tracing)** for each age from 8 years up to and including 14 years of age. Ar and Gn were identified and mandibular length was measured again **(Md 2)**. The increments were calculated in the same way as described previously, adjusted, plotted and graphed. Peak Mandibular Growth Velocity **(PMdGV2)** was identified a second time for those 20 subjects. The intra Class Correlation Coefficient was used to calculate the intra-operator error of measurement for ArGn (Table 3) and a kappa statistical test was used to determine the exact agreement beyond chance between double assessments of timing of PMdGV (Table 4).

Reproducibility of the Cervical Stage assessment

Intra-operator agreement done <u>prior to calibration</u> (see Appendix 8)

Examiner agreement was determined for four different methods of CS assessment. The exact agreement beyond chance between double assessments was determined using the Kappa[56,57] statistical test. Kappa values higher than 0.75 will be considered marginally acceptable since in this study values less than 0.75 represent more than 3 differences in assessments out of a total of 20 assessments.

1. 1st visual assessment vs 2nd visual assessment (Table 5): The principal operator (BJ) on two occasions two months apart carried out visual readings of the cervical veterbrae according to the CS method. These were named **1st visual assessment** and **2nd visual assessment** (see Appendix 8).The lateral head films of the same random subsample of 20 subjects (7 cephalograms each) used to assess the error of measurement of mandibular length were reused.

2. CS assessment of tracing #1 vs 1st visual assessment (Table 6): The principal operator used **tracing #1** previously produced from the radiographs of the same subsample to assess CS. These were called **1st CS assessment of tracing #1** vs **1st visual assessment.**

3. CS assessment of tracing #1 vs 2nd CS assessment of tracing #1 (Table 7): The First Tracing was assessed for the CS a second time also two month later. This CS assessment was called **2nd CS assessment of tracing #1.**

4. CS assessment of tracing #1 vs CS assessment of tracing #2 (Table 8) The principal operator used the tracings (**tracing #1** and **tracing #2**) previously produced from the radiographs of the same subsample to assess CS (Appendix 8). These were called **CS assessment of tracing #1** and **CS assessment of tracing #2**. These 2 different assessments were done also 2 months apart.

Intra-operator agreement following calibration (see Appendix 8)

The intra-operator agreement calculated following the principal operator calibration was performed on the lateral headfilms of the same 20 randomly selected subjects for ages 8 through and including age 14 two months after the

Calibrated visual assessment of the whole sample. This assessment was called **3rd visual assessment** (Table 9).

The cervical vertebral maturation method and timing of PMdGV

Simple linear regression was used to determine to what extent cervical stage as determined by visual assessment as used in this study can predict the time at which Peak Mandibular Growth Velocity will occur.

RESULTS

The study sample consisted of 104 females from the Burlington Growth Centre. The chronological age at PMdGV was normally distributed with a mean of 11.74 years and a standard deviation of 1.12 years (Table 10).

Table 11 demonstrate that the majority of girls at age 8 were in CS1, at age 9 were in CS3, at age 10 were in CS3, at age 11 were in CS3, at age 12 were in CS3, at age 13 were in CS4, and at age 14 were in CS4. Note that for 2 subjects lateral headfilms were not available at age 14 so that there was also no CS for 2 subjects at age 14. A correlation of chronological age with cervical stage revealed the variables to be moderately correlated ($r = 0.73$). Chronologic age accounted for about half of the variability of CS ($R^2 = 0.53$).

Measurement error of mandibular length as determined by ArGn

The ICC for the measurement error between the first and second measurement of mandibular length (Md1 and Md2) was 96.3 % for age 8 and higher than 98% for all other ages which is within acceptable limits (Table 3).

Examiner Agreement for the identification of Peak Mandibular Growth Velocity

For 6 (30%) of the 20 double determinations of the age of PMdGV, the second determination was not the same as the first. Of those, 4 were one year younger, 1 was 2 years younger, and 1 was 1 year older. The kappa statistic for intra examiner agreement for PMdGV was 58.8% (Table 4).

Examiner Agreement for the assessment of the cervical stage (reproducibility of the CS procedure)

Prior to calibration

The exact agreement beyond chance between the **1st** and **2nd visual assessments** (Table 5) varied from a low 35 % at 12 years of age to a high 78% at age 8. For age 9, 10, 11 and 12 the exact intra-operator agreement beyond chance was less than 50%. This level of agreement is below that commonly accepted as excellent to substantial (above 75%)[56,57].

The highest exact agreement beyond chance between **CS assessment of tracing #1** and **1st visual assessment** (Table 6) was at age 12 (44.1%),and between **CS assessment of tracing #1** and **CS assessment of tracing #2** (Table 8) was at age 13 and was only 48.9%. Again the level of examiner agreement is low.

The exact agreement between **CS assessment of tracing #1** and **Second CS assessment of tracing #1** (Table 7) ranged from 58% to 92%. Acceptable examiner agreement was achieved for 3 age groups (11, 12 and 14).

Following calibration

Table 9 contains the Kappa values for 20 double determinations done after calibration. The exact agreement between the calibrated visual assessment and the 3rd visual assessment ranged from 77.8% and 91.4%. Kappa values for all ages were within acceptable limits.

The cervical vertebral maturation method and timing of PMdGV

Table 12 summarizes the distribution of Cervical stages (CS) at the time of Peak Mandibular Growth Velocity (PMdGV) for the whole sample (104 subjects) and for the subsample of 55 subjects for whom two independent determinations of the timing of PMdGV were the same.

At the time of peak mandibular Velocity, of the 104 subjects, 15 females were at cervical stage 1 (14.4%), 11 were at cervical stage 2 (10.6%), 61 females were at cervical stage 3 (58.7%), and 17 were at cervical stage 4 (16.3%). None were at stage 5 or stage 6 (Table 12). The subsample of 55 subjects had substantially the same data. Simple linear regression was used to determine to what extent cervical stage can predict the time at which Peak mandibular growth will occur. The cervical stage was able to account only for 20 % of the variability in the age at which peak mandibular growth velocity occurs.

Table 13 presents the mean number of years that a patient remained in a certain cervical stage. On average, subjects remained in CS1 for 1.14 year (SD: ±1.55year), in CS2 for 0.95 year (SD: ±1.26year), in CS3 for 2.86 years (SD: ±1.79 year), in CS4 for 1.41 year (SD: 1.15 year), in CS5 for 0.46 year (SD: ±0.67 year) and finally in CS6 for 0.20 year (SD: ±0.51 year) in this sample.

Discussion

Testing the hypothesis that PMdGV occurs between CS3 and CS4 involves estimates of the reproducibility of PMdGV timing and estimates of reproducibility of the cervical vertebral stage assessments.

Errors in location of PMdGV

For 20 double determinations of PMdGV, 6 were not the same which is neither reliable nor acceptable. The problem is that a trivial error of 0.5 mm in the length of a mandible of 110 mm from Ar to Gn becomes substantial when the 0.5 mm error is carried over to an incremental value of 3 or 4 mm. Very small differences in mandibular length can change the location of PMdGV and of PPM. For example, the first and second determination of PMdGV differed by 12 months for subject #2041 (Figure 10). Had the mandibular length at age 12 been 0.2 mm larger, the increment at age 11.5 would have been 3.26 mm and the increment at 12.5 would have been 3.40 mm so that PMdGV2 would have coincided with PMdGV1 (age 12.5).

The Kappa, for the 20 double determinations of timing of PMdGV was 0.58 (not acceptable). However, for a previous study using the same subjects and finger bone age[54], the age at PMdGV had been determined independently. There are 55 subjects for whom the location of PMdGV was the same as for the present iteration. These "same" age determinations were added to Table 12 wherein it is seen that the two sets of data are substantially the same. The subset of 55 "same" age determinations may be seen as twice as likely to be correct as the first set of 104.

Reproducibility of the Cervical Vertebral Maturation method

None of the reports relating to the use of cervical vertebrae for determining skeletal age which include double determinations to assess the reproducibility of the estimates, explain how their statistical manipulations show whether the procedures in question are reproducible and if so to what extent. Table 14 summarizes the procedures reported in recently published documents with an attempt to illustrate how each would evaluate the reproducibility of different procedures.

If the intra-operator agreement (reproducibility) is not acceptable, it can be assumed that inter-operator reproducibility would be even less reproducible. Therefore we calculated only various intra-operator agreements in this study. The principal operator was a 3rd year graduate student who had been using the CS method for two years. Prior to calibration, the principal operator would have been considered representative of any orthodontist who had used the CS method since 2005.

The Kappa statistic which is used to evaluate the intra-operator agreement for the cervical vertebral maturation stages assessments in this study is a numerical value which ranges from 0 (no agreement between 1st and 2nd determinations beyond chance) and 1(perfect agreement between 1st and 2nd determinations beyond chance). Negative values of Kappa can occur if agreement is weaker than expected by chance, but this is rare. It is recognized as suitable for categorical data.

Table 4, 5, 6, 7, 8, 9 and 15 report Kappa statistics. The number in the Kappa column may be read as a % of theoretically exact agreement beyond what is expected to occur by chance between repeat assessments of the same condition on two separate occasions by the same examiner. A kappa of 0.5 means that an examiner, when looking at the same thing a second time, or two examiners looking at the same thing at the same time agree 50% of the time in their calls beyond the theoretically expected % of agreement that is determined by the marginal totals of the fourfold table. There is a confidence interval (CI) associated with every Kappa value under the CI column. The 95% confidence interval indicates the range within which the true kappa value lies with 95% confidence. In other words, there is a 5% chance that the true value of kappa could lie outside of the CI range.

In general, the reproducibility of the cervical stage assessment calculated **prior to calibration** was not within acceptable limits.

Often when reading CS from tracings, to the error of CS assessment, we are adding a tracing error.

Table #6 (1^{st} visual assessment vs CS assessment of tracing #1) demonstrated that assessing the CS from a tracing was not satisfactory. This may be explained by the fact that to the error of CS assessment, we are adding a tracing error. Table #8 (CS assessment of tracing #1 vs CS assessment of tracing #2) confirmed this finding with the greatest exact agreement beyond chance being of 48.9%.

The CS assessment error of 2 visual assessment of the same lateral headfilm (Table 5) was higher than the CS assessment error of 2 visual assessment of the same tracing (Table 7). Often on lateral cephalograms, the external contour of the cervical vertebrae is not sharply delineated, but is fuzzy. Once the shadow of the cervical vertebrae is converted to a well delineated contour, as in a tracing, assessment of the cervical stage is much easier and is more likely to be duplicated. .

This is confirmed by Table #7 (CS assessment of tracing #1 vs 2^{nd} assessment of the same tracing #1), where the unweighted kappa was generally better. But even when the CS was read twice from the same tracing the reproducibility of the CS method was still not always acceptable. This may be due to 4 factors:

a. The CS method includes only 6 stages of development. In many cases the morphology of the 2^{nd}, 3^{rd}, and 4^{th} cervical vertebrae does not correspond to any of the definitions suggested.

b. Several initial definitions given by the authors of the new CS method are not clear. For example when discussing concavity, how much concavity was considered concave? At calibration, the authors of the new CS method defined that a concavity must be at least 0.8 mm in order to be able to classify a cervical vertebra as concave.

c. When a patient has passed one CS stage but has not reached the next, how do we classify the CS? During calibration, the CS authors clarified this issue by suggesting that one should always nominate the lowest cervical stage.

d. Often on the lateral cephalogram of the immature cervical vertebrae we see bone condensations that look like spikes on the superior and inferior corners of the cervical vertebrae (Figure 11). Should these bone condensations be included in the overall shape of the vertebrae? Once again, at calibration the authors of the CS method ruled that only the upper condensations should be included in the overall shape of the vertebrae. This is logical because if the lower bone condensations were considered, every cervical vertebra would appear to be concave.

The Kappa values for the double determinations done **after calibration** shows that all ages have been moved into the acceptable category. The same conclusions may be drawn from the other statistical methods included in Table 9 for comparison. The double determinations of stages of cervical vertebral maturation did not achieve acceptable levels of reliability until a training (calibration) session was incorporated. Even so, there remained some uncertainty as shown by the number of disagreement between first and second cervical vertebral stages assessments.

Since the calibration procedure ameliorated the major problems with the CS method, it was felt desirable to incorporate those improvements in a modified method (the JaHM method) for general use and for future research (see Appendix IX).

The advantages of this improved method when compared to the previously published methods are the following.

1. Many variations of the form and shape of the 2^{nd}, 3^{rd} and 4^{th} cervical vertebrae are included in the JaHM template (Appendix IX)). The operator has only to match the x-ray of the patient to one of the sub-categories of the cervical vertebrae maturation stages. Hopefully this new template will increase the reproducibility of the CVM method.

2. Also, in order to improve the reproducibility of the CVM method, a **Sequential Conditional Flow Chart** (see Appendix X) is presented in order to help the operator in the determination of the cervical stage of maturation.

3. An extra stage has been added between CS3 and CS4 in order to reduce the time that a patient remains in CS3 which has been renamed CS-3^1. This new cervical stage will help to predict more closely the timing of peak mandibular growth and is called CS-3^2.

4. Finally, every term used in the JaHm method is clearly defined.

The addition of the **Sequential Conditional Flow Chart** clearly moves the reproducibility of the method into the acceptable category as seen in Table

15.The same subsample of 20 subjects and the same methodology previously used for calculating the intra-operator agreement for the CS assessments was reused.

However, it must be kept in mind that despite the best intentions to improve the method a major problem remains: when does one shape becomes the next? For example, how flat does the superior surface of a vertebra have to be in order to be classified as rectangular horizontal? How parallel does the superior surface have to be to the inferior surface to classify the vertebra as rectangular horizontal?

Reproducibility of the Cervical Vertebral Maturation method as reported in previous studies

Only few authors have reported on the intra-operator reproducibility of any of the cervical vertebral methods (Table 14). In the majority of these studies the results of intra-operator reproducibility are better than the ones found in this study. This may be due to several factors:

- **a.** Different studies use different methods for assessing the cervical vertebral stage.
- **b.** As seen in Table 14, different authors use different statistical tests.

In this study, unweighted (simple) Kappa statistical tests were used to determine intra-operator reliability. This statistical test measures the amount of intra-operator agreement that occurs beyond what would be expected by chance[56,57,58]. It is the ratio of the number of observed concordant items divided by the chance expected number of concordant numbers as determined by the marginal totals. The Kappa statistic (1) measures only exact agreement, (2) treats all disagreements as identical and (3) assumes independence of ratings and (4) it is recognized as suitable for categorical data.

The use of a correlation coefficient (r)[36,37] to assess reproducibility of the CVM method, can give spurious results. The correlation coefficient overestimates agreement and is unaffected by the presence of systematic error (bias). Also it is used to measure association rather than agreement and therefore it should not be used as a measure of reproducibility.

Flores Mir et al[48] used an intra class correlation coefficient (ICC). An ICC is usually indicated with numerical data whereas when assessing a cervical stage, we are dealing with categorical data. Finally, Percent agreement between examiners as used by Franchi et al[38] does not take into account agreement due to chance.

c. When evaluating different intra and inter-operator error of reproducibility, some authors[36,37] assessed their error of measurement from a tracing of the cervical vertebrae which automatically transforms a shadow into a well delineated form and this increases reproducibility but not accuracy.

d. Some studies[36] are based on a sample that includes only clear and easily readable lateral headfilms. This introduces bias in the evaluation of the reproducibility of the method because often the 2nd, 3rd and 4th cervical vertebrae are not very clear on lateral headfilms and one can assume that the results of these studies have a poor generalizability.

e. Different studies are based on different samples: different sample size, different chronological ages and different sex (males and/or females).

The cervical vertebral maturation method and timing of PMdGV

The fact that the average length of stay in CS3 is 2.85 years (Table 13)means that a patient can be in CS3 and have been there for more than 3 years or less than 1year, with no way of knowing which it is. For example, subject #2022 was in CS1 at 8 years, CS2 at 9 years, CS2 at 10 years, CS3 at 11 years, CS3 at 12 years, CS3 at 13 years, and finally at CS3 at 14 years. If this patient wanted treatment at age 11 and a cephalogram was taken to assess that she was at CS3, according to Baccetti et al, her peak mandibular growth should occur during the year after this stage. When looking at her graph of mandibular length increments (Figure 12) we see that if we treated her during the year after this stage, we would miss her PMdGV.

Respecting the test of the hypothesis that PMdGV occurs between CS3 and CS4; in this sample only 61 subjects or 59% had their PMdGV in CS3 (Table 12). The distribution of the 55 subjects for whom PMdGV had been located twice at the same age was closely similar confirming the accuracy of the determinations of PMdGV. 26 subjects appeared to have PMdGV at CS1 or CS2. Since in this study we did not look at serial cephalogram beyond age 14 for any of the subjects, there is a slight possibility that few of these 26 subjects may have had PMdGV after age 14. After reviewing the cervical vertebral stages of these 26 subjects at age 14, it was found that only 4 of the 26 subjects were at CS1, CS2 or CS3 with all the other subjects being at CS4 or more. After reviewing the annual cephalometric records for these 4 subjects up to 19 years of age, it was found that none of them experienced significant amount of growth subsequently. Fifty nine % does not constitute support for the hypothesis thus lending some uncertainty to the use of the cervical vertebral maturation method for locating PMdGV.

CONCLUSIONS

- The reproducibility of the CS method was acceptable only after calibration of the operator
- An even more reproducible method for assessment of the cervical vertebral maturation stage is needed.
- The average tenure in CS3 was 2.85 years in our sample with no way of knowing when PMdGV will occur.
- PMdGV occurred between CS3 and CS4 only in 58.7% of the sample in this study.
- None of the subjects in this study had their PMdGV in CS5 or in CS6.
- The maturation stage of the 2^{nd}, 3^{rd} and 4^{th} cervical vertebrae as assessed by the CS method is poorly reproducible (if the operator is not calibrated) and is a poor predictor for determining timing of PMdGV.

TABLES

Table 1: Summary of different methods suggested for assessment of the cervical vertebrae maturation stage

Publication	Method developed	# of subjects included in the study	Age of subjects included in the study	Longitudinal or cross sectional study
Lamparski D.G., 1972 (AA)	Lamparski's original CVM method	69 males 72 females to come up with the new index 15 males and 25 females to test the new method	10-15years	Cross sectional
Hassel and Farman, 1995 (CC)	CVMI	110 males 110 females	8-18 years	Cross sectional
Franchi et al., 2000 (DD)	Cvs	9males 15 females	3-18 years	Longitudinal
Baccetti et al., 2002 (EE)	CVMS	18 males 12 females	N/A	Longitudinal
Baccetti et al., 2005 (FF)	CS	18 males 12 females	N/A	Longitudinal

Table 2: Error variance and intra-class correlation coefficient for two methods used for measuring mandibular length

	Error variance	ICC
Measurement		
Ar-Gn	0.289	99.41%
Co-Gn	2.404	96.01%

Table 3: Error variance and intra-class correlation coefficient for mandibular length as determined by ArGn

	Error variance	ICC
Age (years)		
8	0.3001	96.34%
9	0.2108	98.10%
10	0.1894	98.40%
11	0.2285	98.58%
12	0.1603	99.17%
13	0.0884	99.56%
14	0.2929	98.43%

Table 4: Intra-operator agreement between <u>timing of 1st PMdGV and timing of 2nd PMdGV</u> as determined by an unweighted Kappa statistical test

Number of subjects	Unweighted Kappa	# of double assessment in disagreement (n=20)
20	0.5876	6

Table 5: Intra-operator agreement between <u>1st visual assessment and 2nd visual assessment</u> of the cervical stage as determined by an unweighted Kappa statistical test (*assessments done <u>prior to calibration</u>*) and other statistical tests reported in the literature

	Unweighted Kappa	95% CI	# of double assessment in disagreement (n=20)	ICC	% agreement	r^2	% of standard deviation
Age (years)							
8	0.776	0.502-1.05	3	0.850	85%	77.2%	15.3%
9	0.476	0.209-0.743	7	0.478	65%	42%	48.2%
10	0.42	0.146-0.694	8	0.501	60%	27.5%	50.0%
11	0.358	0.048-0.667	7	0.615	65%	31.9%	32.9%
12	0.346	0.055-0.638	5	0.214	75%	40.6%	117.4%
13	0.747	0.377-1.117	2	0.780	90%	56.9%	10.2%
14	0.668	0.333-1.003	4	0.791	80%	57.7%	14.9%

Table 6: Intra-operator agreement between CS assessment of tracing #1 and 1st visual assessment of the cervical stage as determined by an unweighted Kappa statistical test (*assessments done prior to calibration*)

	Unweighted Kappa	95% CI	# of double assessments in disagreement (n=20)
Age (years)			
8	0.394	0.107-0.681	8
9	0.441	0.185-0.696	8
10	0.275	0.002-0.549	10
11	0.304	0.014-0.595	8
12	0.365	0.134-0.597	6
13	0	(-)0.304-0.304	10
14	0.271	(-)0.045-0.593	9

Table 7: Intra-operator agreement between CS assessment of tracing #1 and Second CS assessment of tracing #1 as determined by an unweighted Kappa statistical test (*assessments done prior to calibration*)

	Unweighted Kappa	95% CI	# of double assessments in disagreement (n=20)
Age (years)			
8	0.612	0.320-0.905	5
9	0.724	0.472-0.976	4
10	0.58	0.325-0.836	6
11	0.92	0.625-1.214	1
12	0.904	0.656-1.153	1
13	0.689	0.402-0.975	4
14	0.846	0.538-1.154	2

Table 8: Intra-operator agreement between CS assessment of tracing #1 and CS assessment of tracing #2 of cervical stage as determined by an unweighted Kappa statistical test (*assessments done prior to calibration*)

	Unweighted Kappa	95% CI	# of double assessments in disagreement (n=20)
Age (years)			
8	0.252	0.005-0.499	11
9	0.167	(-)0.080-0.423	12
10	0.435	0.190-0.679	8
11	0.391	0.138-0.645	7
12	0.485	0.248-0.721	6
13	0.489	0.227-0.751	7
14	0.457	0.154-0.760	7

Table 9: Intra-operator agreement between Calibrated visual assessment and 3rd visual assessment of cervical stage as determined by an unweighted Kappa statistical test (assessments done after calibration) and other statistical tests reported in the literature

	Unweighted Kappa	95% CI	# of double assessments in disagreement (n=20)	ICC	% agreement	r^2	% of standard deviation
Age (years)							
8	0.778	0.493-1.062	3	0.803	85%	67.4%	20.8%
9	0.867	0.617-1.116	2	0.956	90%	85.9%	4.8%
10	0.848	0.557-1.140	2	0.950	90%	80.6%	4.8%
11	0.825	0.523-1.126	2	0.946	90%	73.9%	5.1%
12	0.914	0.671-1.157	1	0.982	95%	94.2%	2.5%
13	0.913	0.614-1.211	1	0.958	95%	90.8%	4.0%
14	0.840	0.525-1.155	2	0.900	90%	72.1%	7.0%

Table 10: The mean & standard deviation (SD) for age of occurrence of Peak Mandibular Growth Velocity (PMdGV) in years

	N	mean	SD
PMdGV	104	11.74	±1.12

Table 11: Distribution of Cervical Stages (CS) at different chronological ages

	CS1	CS2	CS3	CS4	CS5	CS6	Missing
Age (years)							
8	50	25	28	1	0	0	0
9	32	26	45	1	0	0	0
10	20	23	56	5	0	0	0
11	8	15	68	13	0	0	0
12	6	5	57	29	7	0	0
13	2	2	31	49	15	5	0
14	1	0	11	48	26	16	2

Table 12: Distribution of Cervical stages (CS) at the time of Peak Mandibular Growth Velocity (PMdGV) for the whole sample (104 subjects) and for a subsample of 55 subjects with 2 concordant double determination of the timing of PMdGV

	N	CS 1	CS 2	CS 3	CS 4	CS 5	CS 6
PMdGV	104	15 (14.4%)	11 (10.6%)	61 (58.7%)	17 (16.3%)	0	0
	55	11 (20%)	6 (10.9%)	31 (56.4%)	7 (12.7%)	0	0

Table 13: Mean & standard deviation (SD) for number of years that a subject remained in different cervical stages in this study

	Mean # of years in the same CS	SD
CS1	1.14	±1.55
CS2	0.95	±1.26
CS3	2.85	±1.8
CS4	1.41	±1.15
CS5	0.46	±0.67
CS6	0.20	±0.51

Table 14: Reproducibility of the cervical vertebral method as reported by previous authors

Studies	Cervical vertebral method used	Statistical test used	Intra-operator agreement	Inter-operator agreement
Hassel and Farman,1995[36]	Hassel and Farman	r^2	0.85-0.90	1.00
Kucukkeles et al, 1999[37]	Hassel and Farman	r^2	0.74-0.96	0.88
Franchi et al, 2000[38]	Cvs	% agreement	100%	98.6%
Flores-Mir et al, 2006[48]	CVMS	ICC	0.889 (0.723-0.968)	N/A
Uysal et al, 2006[45]	Hassel and Farman	Spearman Brown Formula	0.955-0.987	0.955-0.987

Table 15: Intra-operator agreement between 1st visual assessment and 2nd visual assessment using the JaHM template of cervical stage as determined by an unweighted Kappa statistical test (assessments done after calibration)

	Unweighted Kappa	95% CI	# of double assessments in disagreement (n=20)
Age			
8	0.913	0.564-1.262	1
9	0.845	0.531-1.159	2
10	0.923	0.651-1.195	1
11	0.902	0.619-1.184	1
12	1	0.739-1.261	0
13	0.846	0.555-1.137	1
14	0.843	0.523-1.162	2

FIGURES

Figure 1: Lateral view of the adult vertebral column
(Adapted from: L. Scheuer, S. Balck, A. Christie. Developmental juvenile osteology. ISBN 0-12-624000-0, 2000, p172)

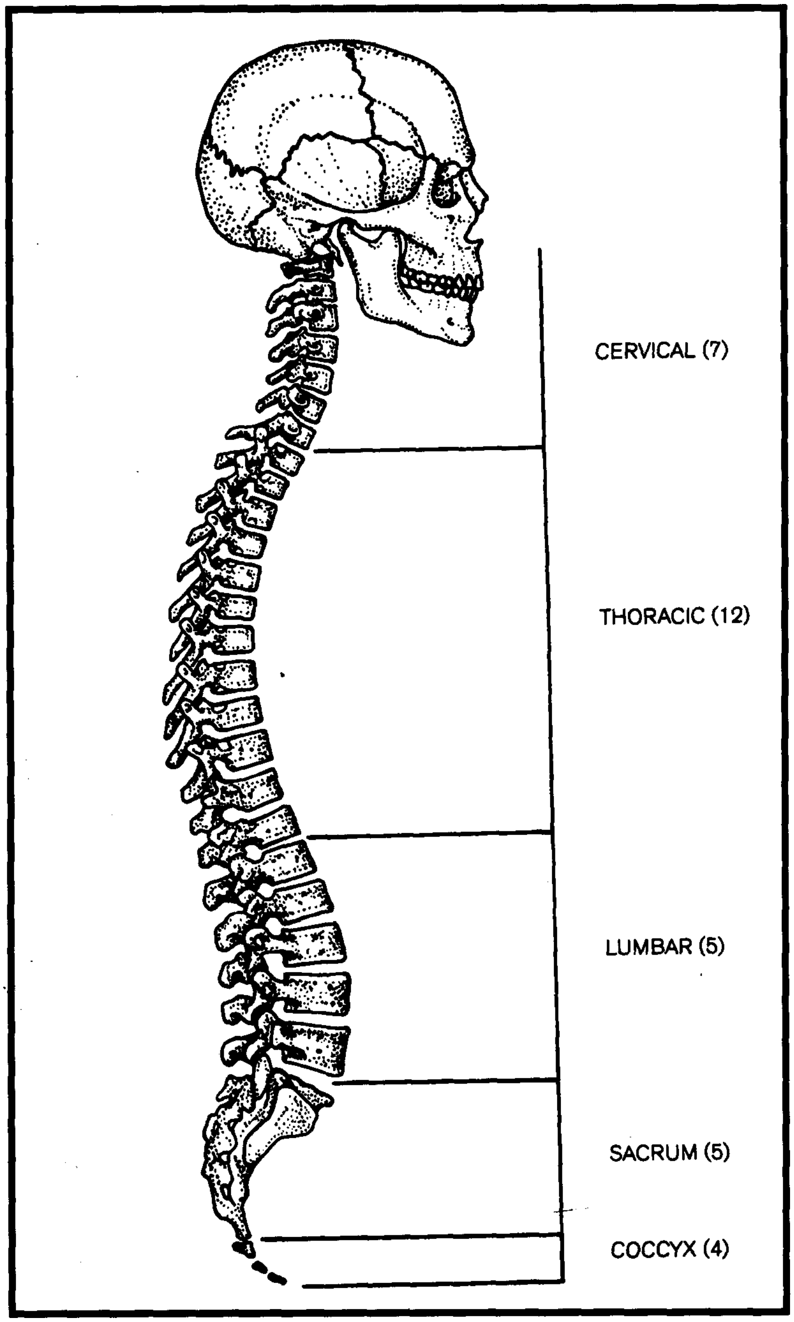


Figure 2: A typical adult vertebrae
(Adapted from: L. Scheuer, S. Balck, A. Christie. Developmental juvenile osteology. ISBN 0-12-624000-0, 2000, p175)

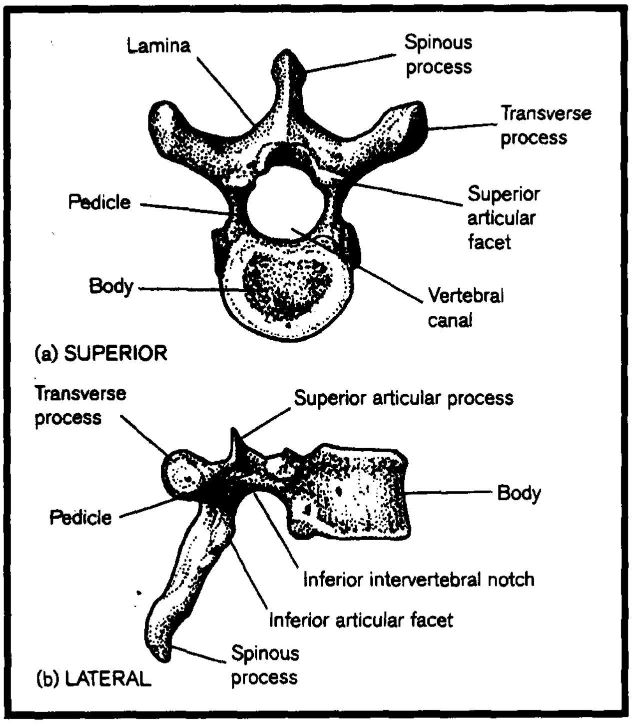


Figure 3: A typical adult cervical vertebrae
(Adapted from: L. Scheuer, S. Balck, A. Christie. Developmental juvenile osteology. ISBN 0-12-624000-0, 2000, p177)

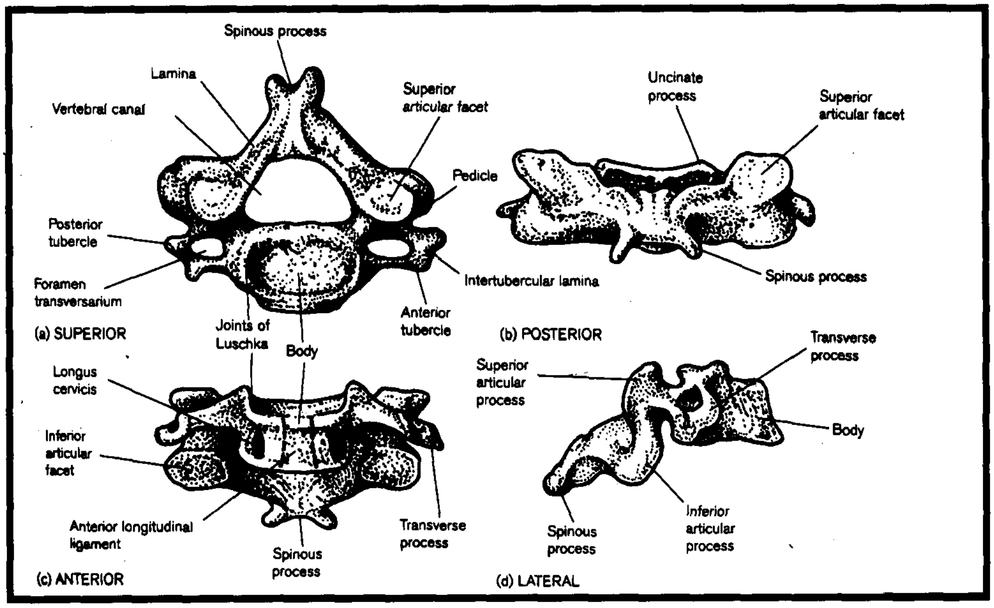
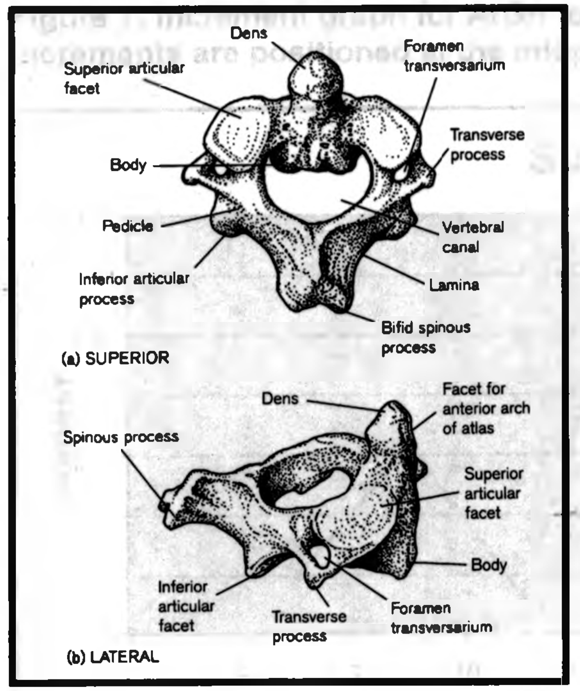


Figure 4: radiograph of a typical adult cervical vertebrae

Figure 5: A typical adult axis
(Adapted from: L. Scheuer, S. Balck, A. Christie. Developmental juvenile osteology. ISBN 0-12-624000-0, 2000, p177)



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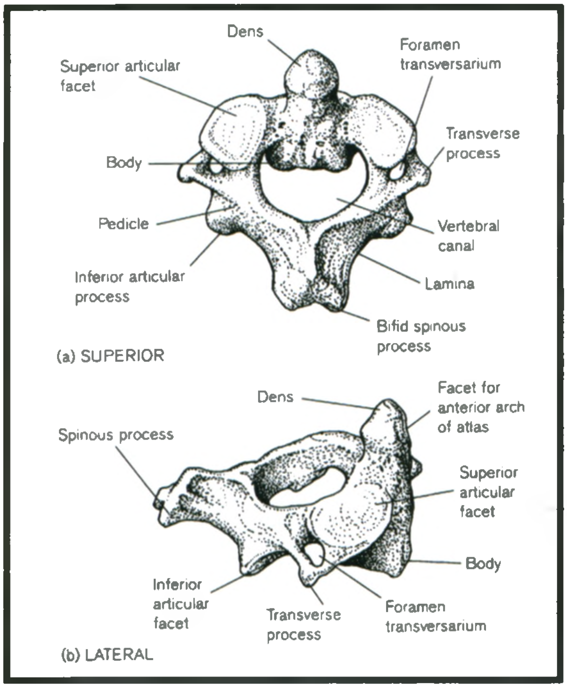


Figure 6: Example of tracing of a lateral headfilm for subject 2092 at age 10 and measurement of Ar-Gn

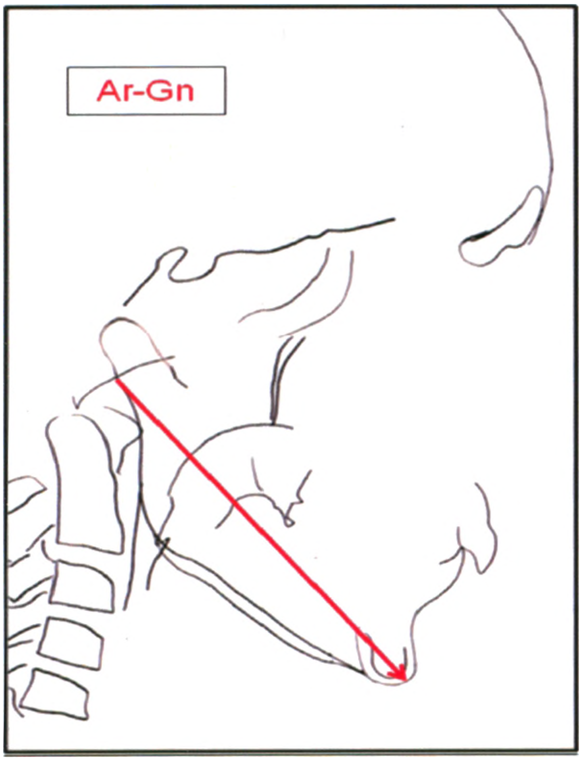


Figure 7: Increment graph for ArGn for subject 2089. Note that annual increments are positioned at the midpoints between birthdays

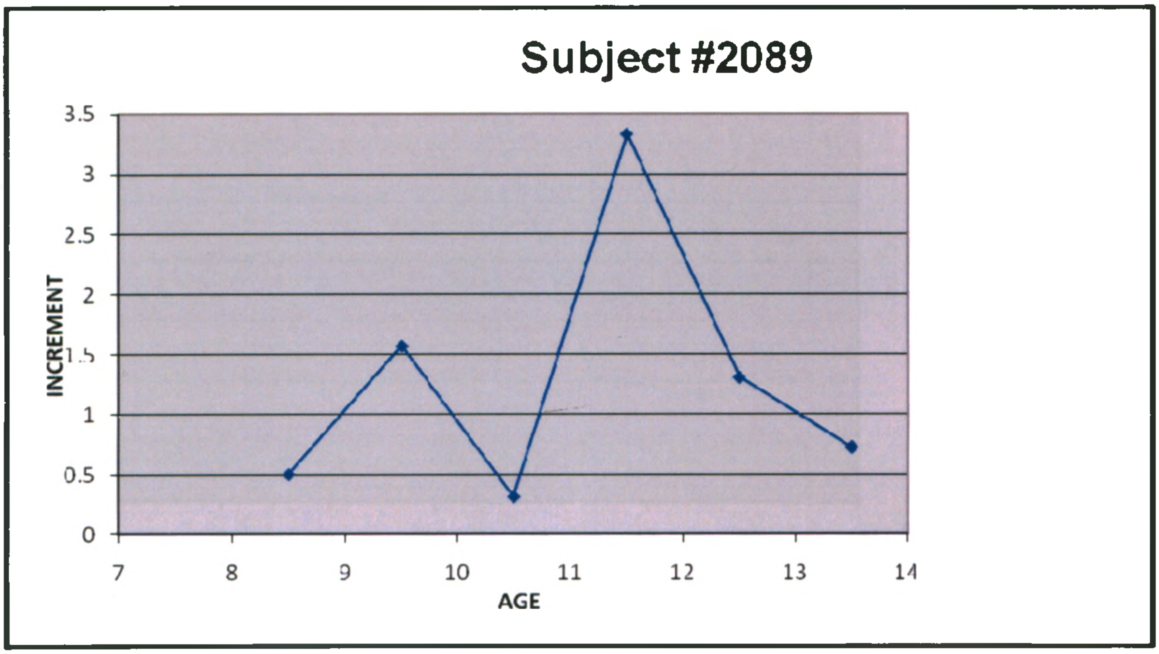


Figure 8: Increment graph for ArGn for subject #2050

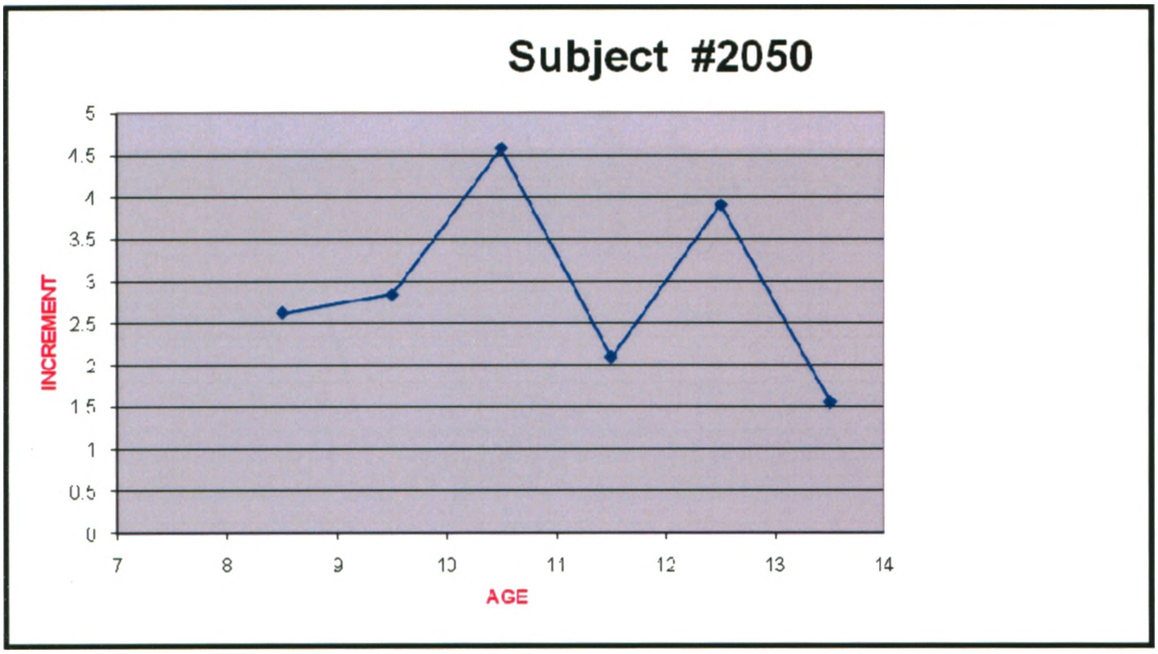


Figure 9: Increment graph for ArGn for subject #2062

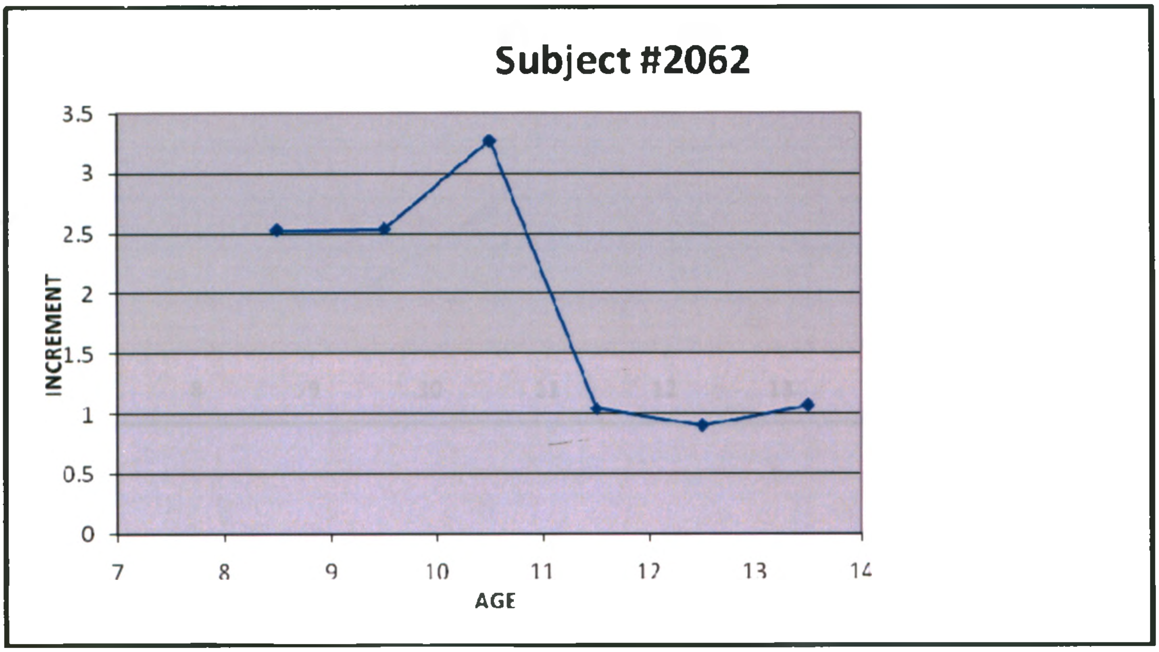
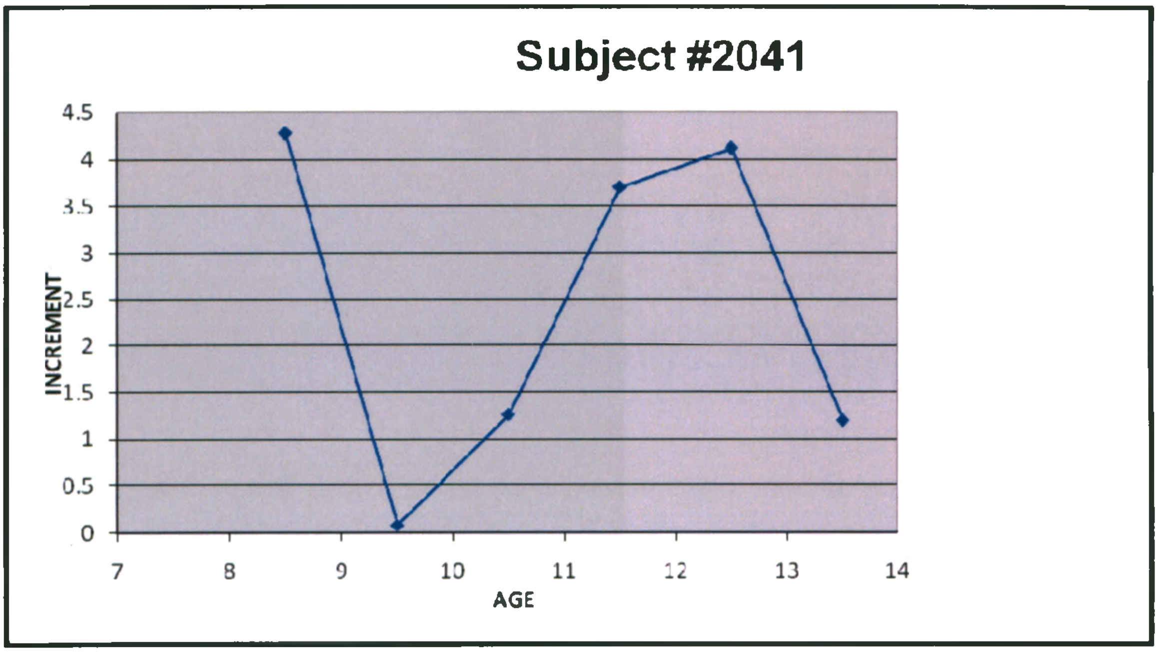


Figure 10: mandibular length increment graphs using Md1 and Md2 for subject #2041. Note that PMdGV1 and PMdGV2 are not coincident



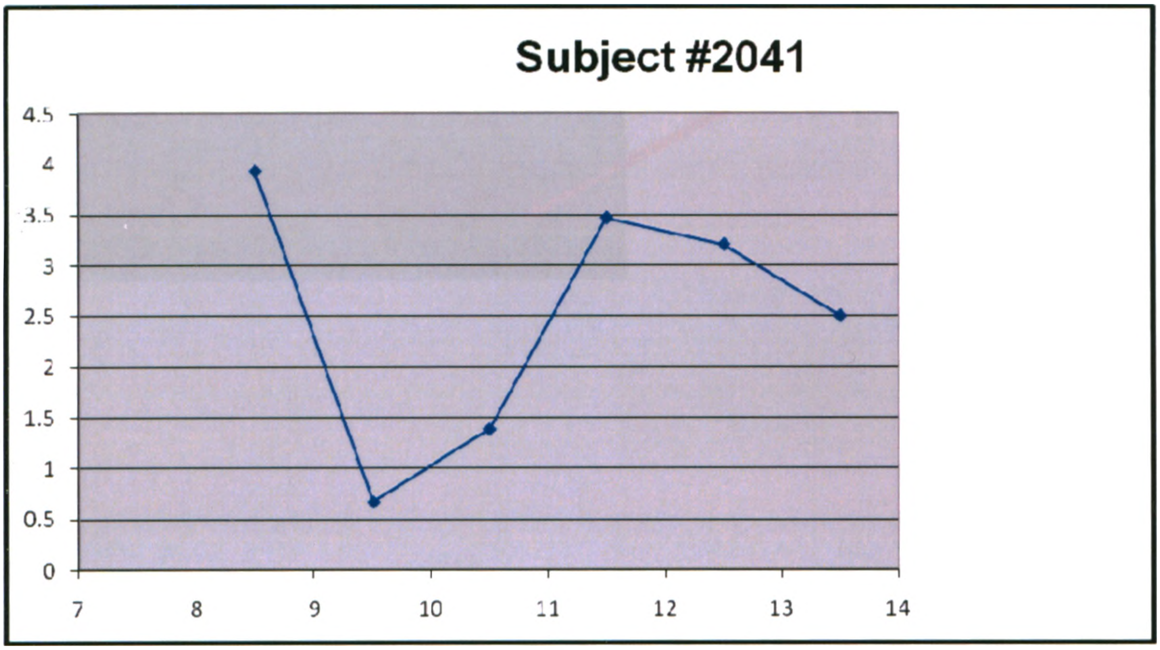


Figure 11: Bone spikes of the cervical vertebrae

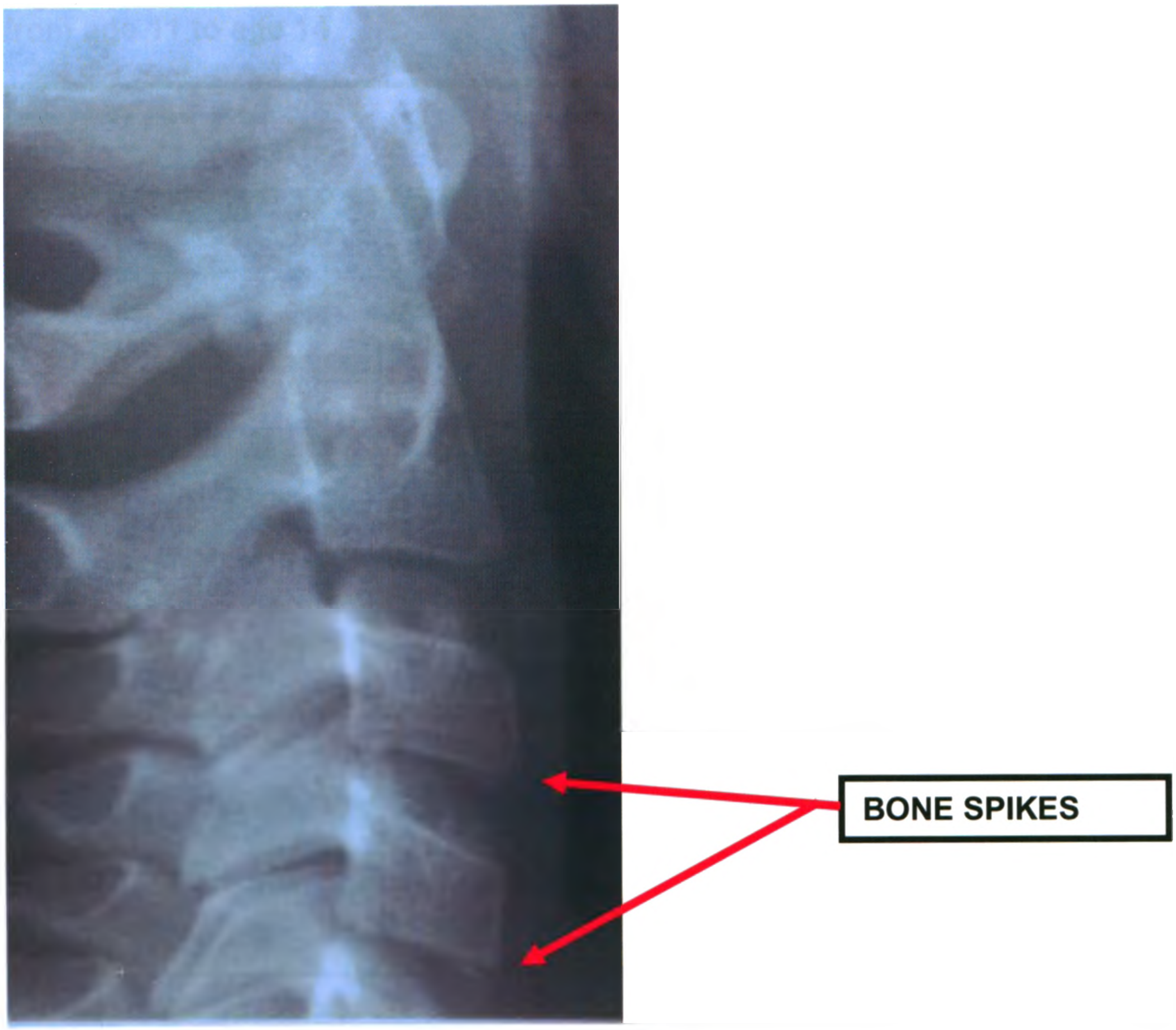


Figure 12: Increment graph for ArGn for subject 2022. Pt stayed in CS3 from age 11 to age 14

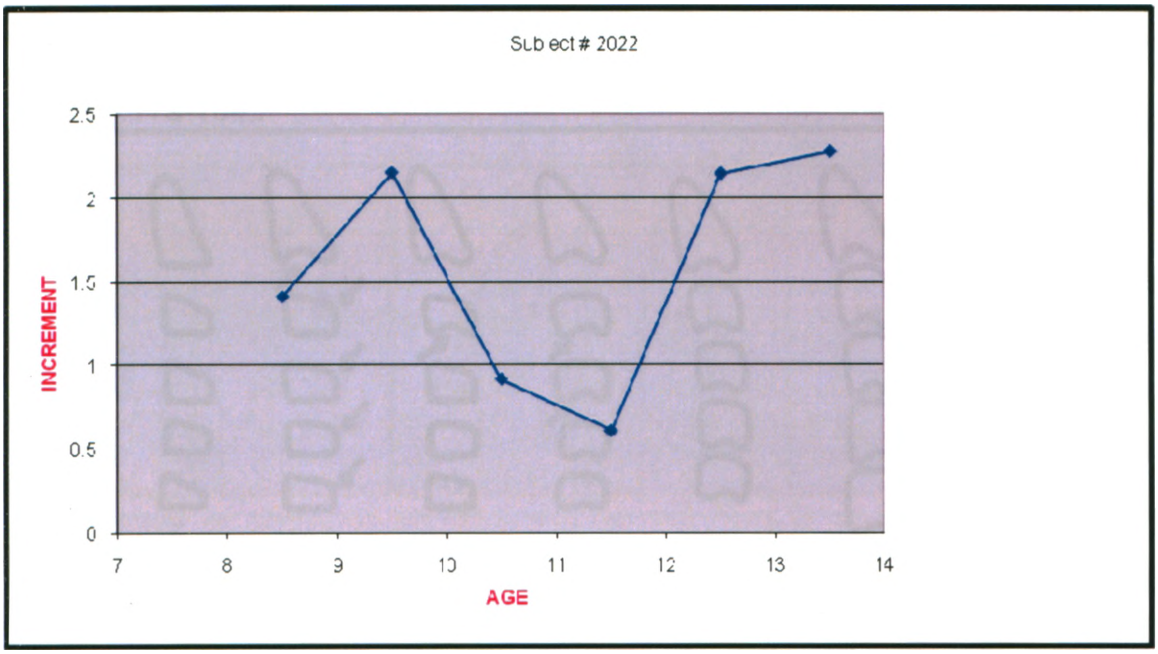
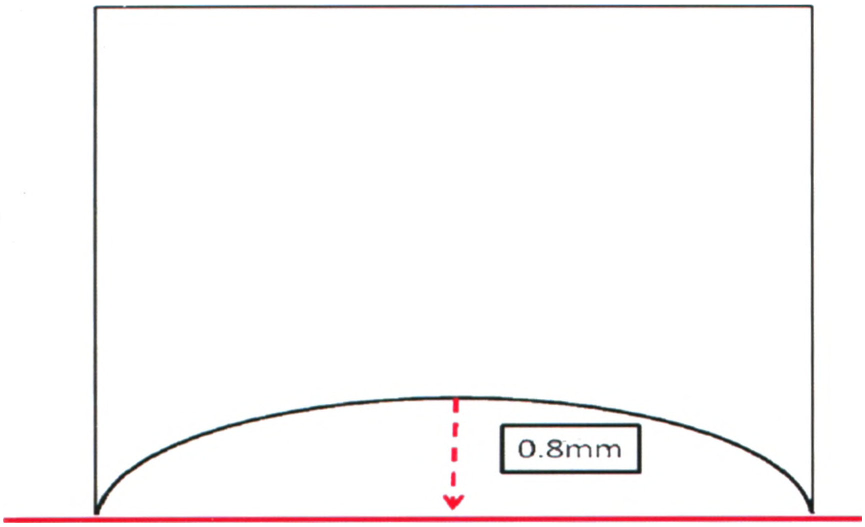


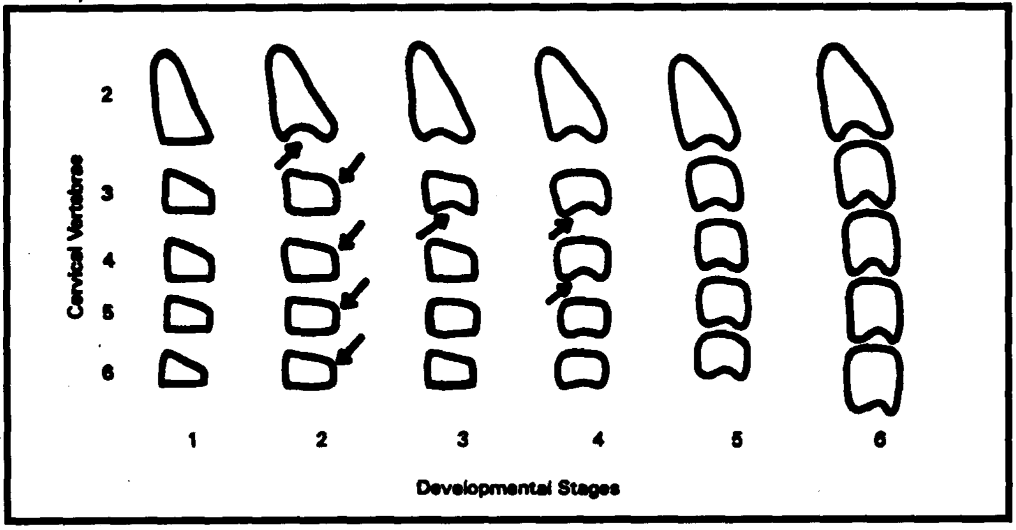
Figure 13: Concave: concavity of 0.8mm



APPENDIX I

Lamparski's method for the assessment of the cervical vertebral maturation stages for females

Adapted from: O'reilly MT, Yaniello GJ. Mandibular growth changes and maturation of the cervical vertebrae: A longitudinal study. Angle Orthod 1988;58:179-184..



Stage 1: All inferior borders of the bodies are flat. The superior borders are strongly tapered from posterior to anterior

Stage 2: A concavity has developed in the inferior border of the 2nd vertebra. The anterior vertical heights of the bodies have increased.

Stage 3: A concavity has developed in the inferior border of the 3rd vertebra. The other inferior borders are still flat.

Stage 4: all bodies are now rectangular in shape. The concavity of the 3rd vertebra has increased, and a distinct concavity has developed on the 4th vertebra. Concavities on 5 and 6 are just beginning to form.

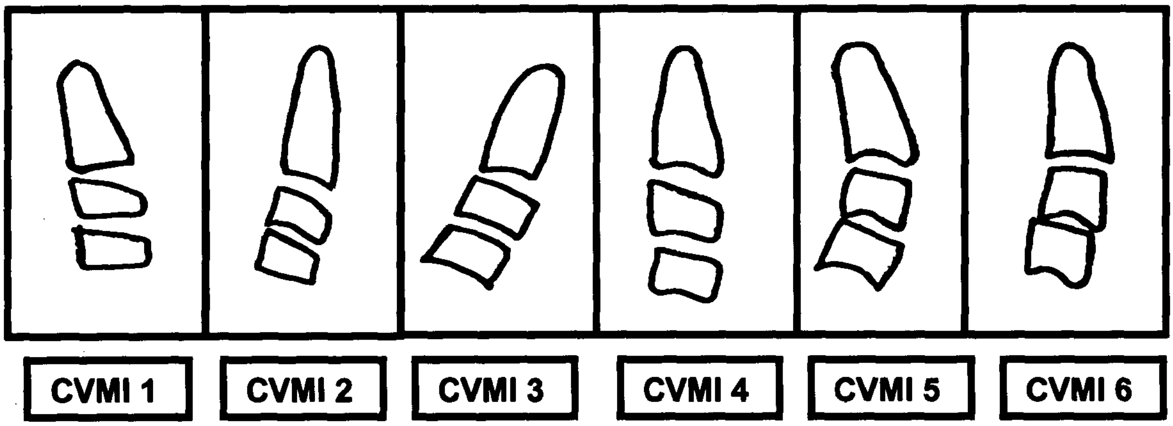
Stage 5: the bodies have become nearly square in shape, and the spaces between the bodies are visibly smaller. Concavities are well defined on all 6 bodies.

Stage 6: All bodies have increased in vertical height and are higher than they are wide. All concavities have deepened.

APPENDIX II

CVMI method for assessment of cervical vertebral maturation stages

Adapted and modified from: Hassel B, Farman AG. Skeletal maturation evaluation using cervical vertebrae. Am J Orthod Dentofacial Orthop 1995;107:58-66



Category 1 was called INITIATION. This corresponded to a combination of SMI 1 and 2. At this stage,adolescent growth spurt was just beginning and 80% to 100% of adolescent growth was expected. Inferior borders of C2, C3, C4 were flat at this stage. The vertebrae were wedge shaped, and the superior vertebral borders were tapered from posterior to anterior (CVMI 1).

Category 2 was called ACCELERATION. This corresponded to a combination of SMI 3 and 4. Growth acceleration was beginning at this stage, with 65% to 85% of adolescent growth expected. Concavities were developing in the inferior borders of C2 and C3. The inferior border of C4 was flat. The bodies of C3 and C4 were nearly rectangular in shape (CVMI 2).

Category 3 was called TRANSITION. This corresponded to a combination of SMI 5 and 6. Adolescent growth was still accelerating at this stage toward peak height velocity, with 25% to 65% growth expected. Distinct concavities were seen in the inferior borders of C2 and C3. A concavity was beginning to develop in the inferior border of C4. The bodies of C3 and C4 were rectangular in shape (CVMI 3).

Category 4 was called DECELERATION. This corresponded to a combination of SMI 7 and 8. Adolescent growth began to decelerate dramatically at this stage, with 10% to 25% of adolescent growth expected. Distinct concavities were seen in the inferior borders of C2, C3, and C4. The vertebral bodies of C3 and C4 were becoming more square in shape (CVMI 4).

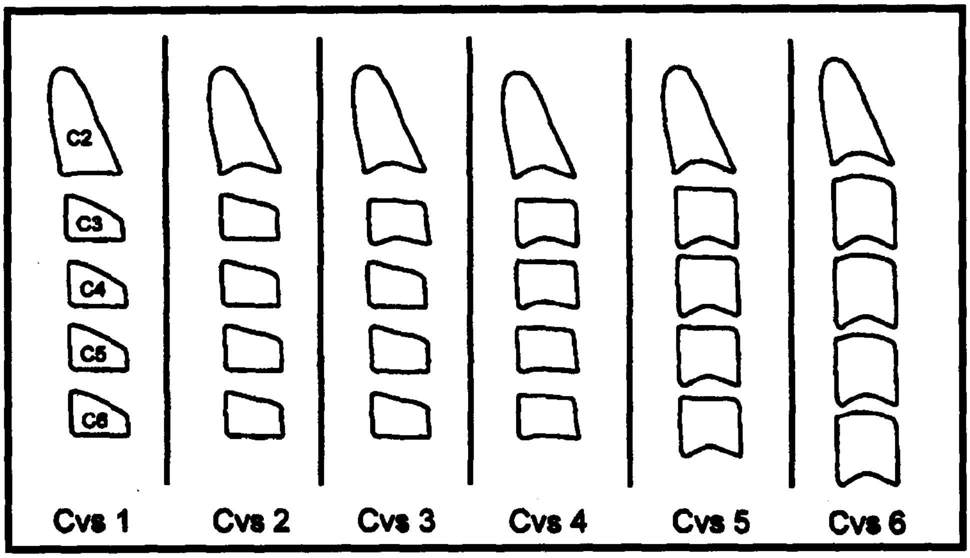
Category 5 was called MATURATION. This corresponded to a combination of SMI 9 and 10. Final maturation of the vertebrae took place during this stage, with 5% to 10% of adolescent growth expected. More accentuated concavities were seen in the inferior borders of C2, C3, and C4. The bodies of C3 and C4 were nearly square to square in shape (CVMI 5).

Category 6 was called COMPLETION. This corresponded to a combination of SMI 11. Growth was considered to be completed at this stage. Little or no adolescent growth was expected. Deep concavities were seen in the inferior borders of C2, C3, and C4. The bodies of C3 and C4 were square or greater in the vertical dimension than in the horizontal dimension (CVMI 6).

APPENDIX III

Cvs method for assessment of cervical vertebral maturation stages

Adapted from: Franchi L, Baccetti T, McNamara Jr JA. Mandibular growth as related to cervical vertebral maturation and body height. Am J Orthod Dentofacial Orthop 2000;118:335-340.



Stage 1 (Cvs 1): the inferior borders of the bodies of all cervical vertebrae are flat. The superior borders are tapered from posterior to anterior.

Stage 2 (Cvs 2): a concavity develops in the inferior border of the second vertebra. The anterior vertical height of the bodies increases.

Stage 3 (Cvs 3): a concavity develops in the inferior border of the third vertebra.

Stage 4 (Cvs 4): a concavity develops in the inferior border of the fourth vertebra. Concavities in the lower borders of the fifth and of the sixth vertebrae are beginning to form. The bodies of all cervical vertebrae are rectangular in shape.

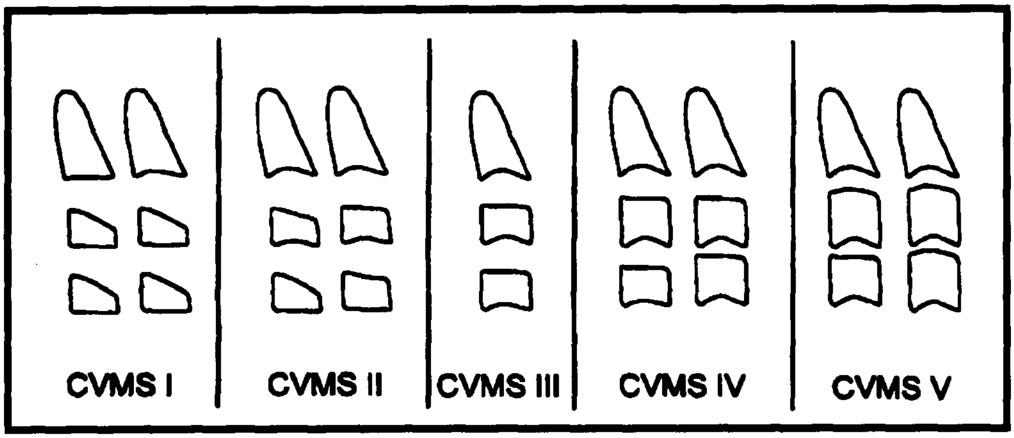
Stage 5 (Cvs 5): concavities are well defined in the lower borders of the bodies of all 6 cervical vertebrae. The bodies are nearly square in shape and spaces between the bodies are reduced.

Stage 6 (Cvs 6): all concavities have deepened. The bodies are now higher than they are wide.

APPENDIX IV

CVMS method for assessment of cervical vertebral maturation stages

Adapted from: Baccetti T, Franchi L, McNamara Jr AJ. An improved Version of the Cervical Vertebral Maturation (CVM) Method for the Assessment of Mandibular Growth. Angle Orthod 2002:72:316-323.



CVMS I: The lower borders of all the three vertebrae are flat, with the possible exception of a concavity at the lower border of C2 in almost half of the cases. The bodies of both C3 and C4 are trapezoid in shape (the superior border of the vertebral body is tapered form posterior to interior). The peak in mandibular growth will occur not earlier that one year after this stage.

CVMS II: concavities at the lower border of both C2 and C3 are present. The bodies of C3 and C4 maybe either trapezoid or rectangular horizontal in shape. The peak in mandibular growth will occur within one year after this stage.

CVMS III: concavities at the lower borders of C2, C3, and C4 are now present. The bodies of both C3 and C4 are rectangular horizontal in shape. The peak in mandibular growth has occurred within one or two years before this stage.

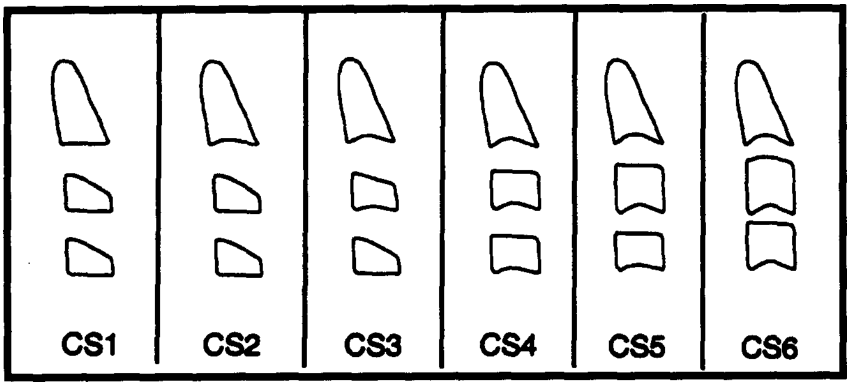
CVMS IV: The concavities at the lower borders of C2, C3, and C4 still are present. At least one of the bodies of C3 and C4 is squared in shape. If not squared, the body of the other cervical vertebra still is rectangular horizontal. The peak in mandibular growth has occurred not later than one year before this stage.

CVMSV: The concavities at the lower borders of C2, C3, and C4 still are evident. At least one of the bodies of C3 and C4 is rectangular vertical in shape. If not rectangular vertical, the body of the other cervical vertebra is squared. The peak in mandibular growth has occurred not later than two years before this stage.

APPENDIX V

CS method for assessment of cervical vertebral maturation stages

Adapted from: Baccetti T, Franchi L, McNamara Jr AJ. The Cervical Vertebral Maturation (CVM) Method for the Assessment of Optimal Treatment Timing in Dentofacial Orthopedics. Semin Orthod 2005;11:119-129.



Cervical stage 1 (CS1): the lower borders of all the three vertebrae (C2-C4) are flat. The bodies of both C3 and C4 are trapezoid in shape (the superior border of the vertebral body is tapered from posterior to anterior). The peak in mandibular growth will occur on average 2 years after this stage.

Cervical stage 2 (CS2): A concavity is present at the lower border of C2 (in four of five cases, with the remaining subjects still showing a cervical stage 1). The bodies of both C3 and C4 are still trapezoid in shape. The peak in mandibular growth will occur on average 1 year after this stage.

Cervical stage 3 (CS3): Concavities at the lower border of both C2 and C3 are present. The bodies of C3 and C4 may be either trapezoid or rectangular horizontal in shape. The peak in mandibular growth will occur during the year after this stage.

Cervical stage 4 (CS4): Concavities at the lower border of C2, C3, and C4 now are present. The bodies of both C3 and C4 are rectangular horizontal in shape. The peak in mandibular growth has occurred within 1 or 2 years before this stage.

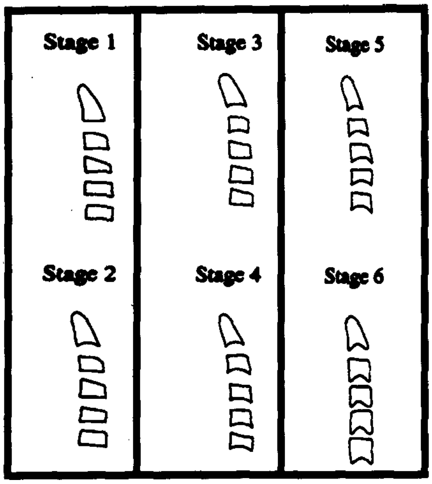
Cervical stage 5 (CS5): The concavities at the lower borders of C2, C3, and C4 still are present. At least one of the bodies of C3 and C4 is squared in shape. If not squared, the body of the other cervical vertebra still is rectangular horizontal. The peak in mandibular growth has ended at least 1 year before this stage.

Cervical stage 6 (CS6): The concavities at the lower borders of C2, C3, and C4 still are evident. At least one of the bodies of C3 and C4 is rectangular vertical in shape. If not rectangular vertical, the body of the other cervical vertebra still is squared. The peak in mandibular growth has ended at least 2 years before this stage.

APPENDIX VI

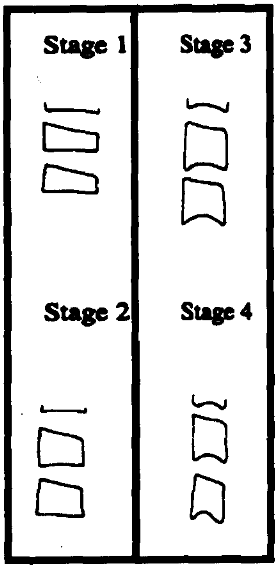
San Roman et al stages of cervical vertebral maturation used to assess stages of Hand-wrist development

Adapted and modified from: San Roman P, Palma JC, Oteo D, Nevado E. Skeletal maturation determined by cervical vertebrae development. European Journal of Orthodontics 2002;24:303-311.

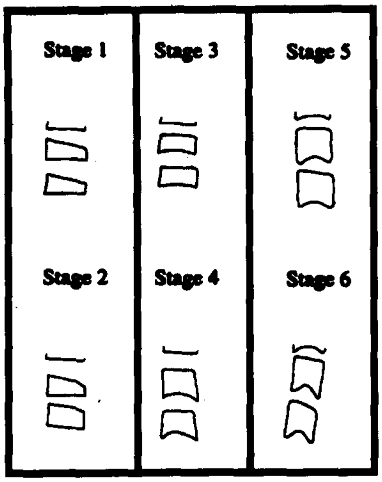


APPENDIX VI (Figure A): cervical vertebrae maturation according to the concavity of the lower border of the vertebral body. (1) All vertebrae have a flat lower border; (2) a concavity is present in the C2 lower border; (3) a concavity is present in the C3 lower border; (4) C2 and C3 concavity increases and a concavity is present in C4, C5, and C6; (5) concavity increases in all vertebrae; (6) a deep concavity is present in all vertebrae and the inferior borders are rounded.

APPENDIX VI (continued)



APPENDIX VI (Figure B): Cervical vertebrae maturation stages according to the vertebral body height. (1) Height is less than 80% of width; (2) height is between 80 and 90% of width; (3) height and width are equal; (4) height is greater than width.



APPENDIX VI (Figure C): Cervical vertebrae maturation stages according to the shape of the vertebral body. (1) upper border is tapered from the posterior to the anterior and wedge shaped; (2) wedge shaped C3 and nearly rectangular shaped C4 with absence of supero-anterior angles; (3) rectangular shaped bodies; (4) nearly squared bodies; (6) rectangular bodies with height greater than width.

Appendix VII

The Burlington Growth Study

Adapted from: Hunter, Baumrind, Moyers. An inventory of United States and Canadian growth records sets: preliminary report. AJODO 1993;103:545-55.

Appendix VII Table A: The various samples of the Burlington Ontario Research centre, by sex and number treated (The numbers shown are for the initial age. There are fewer than 100 sets for each sex at ages 16 and 20 years for any of the controls)

	Males	*Females*	*Total*	*Number treated*
Serial Experimental 4-20	167	136	303	208
Control 6, 9, 12, 14, 16, 20	168	129	297	59
Control 8, 16, 20	96	123	219	40
Control 10, 16, 20	111	106	217	29
Control 12, 20	113	99	212	45
Sibs	29	43	72	
Parents	151	161	312	
TOTAL	835	797	1632	

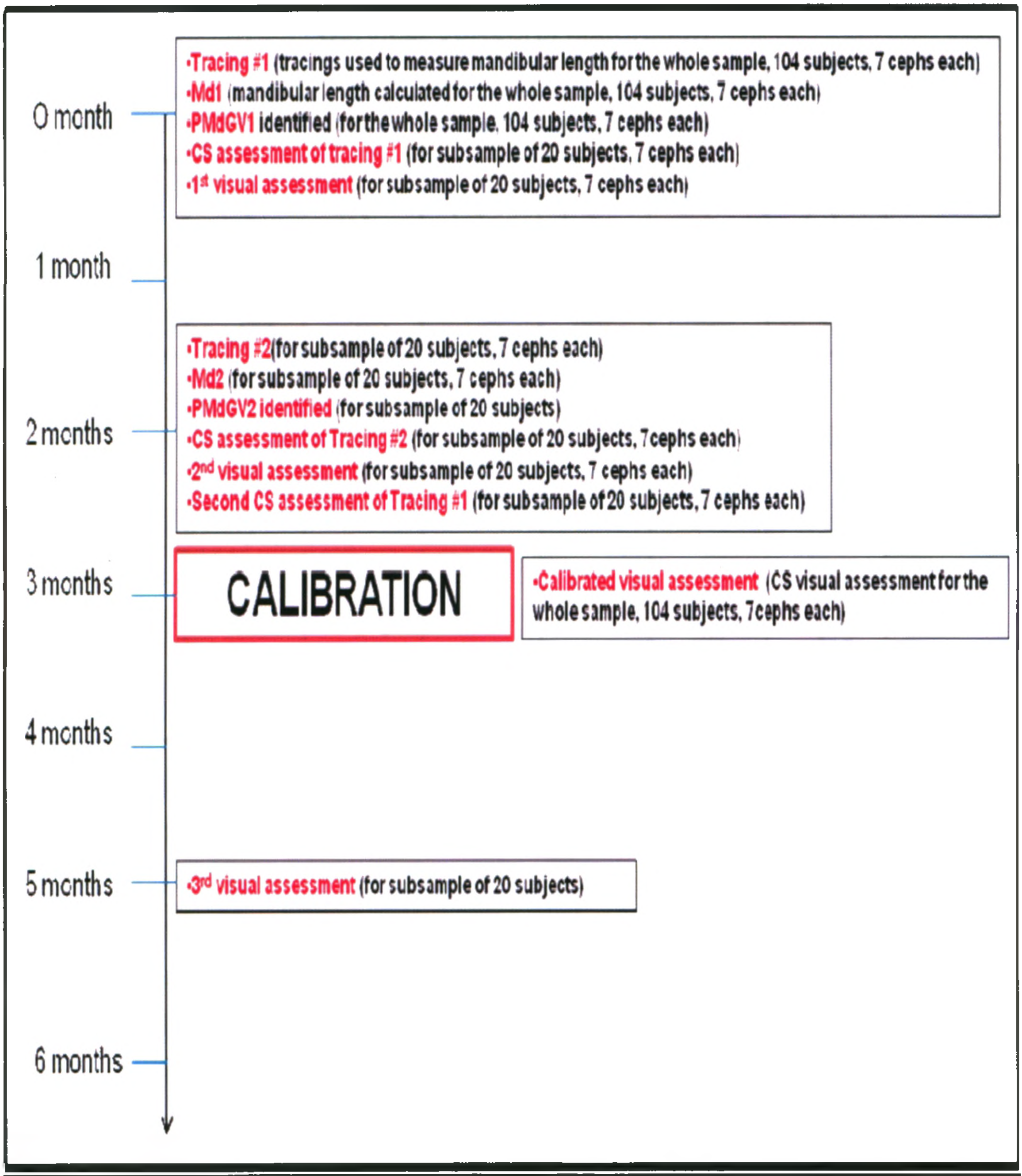
The Burlington Growth Study is located at the Burlington, Ontario Orthodontic Research Center at the University of Toronto. Its various longitudinal samples contain 1632 subjects in all (see table A). All samples are of the "diminishing" longitudinal type, so that the largest number of subject is, for example, at age 4 years (for the annual series) and includes 167 male and 136 female subjects. These numbers diminish to 68 male and 57 female subjects at age 20 years, although there are over 100 subjects for each sex at age 16 years of age. Details, including the number who had orthodontic treatment, are shown in table A.

There are four control samples that have longitudinal records at the ages shown in table A. The control "longitudinal" data sets include lateral headfilms (taken at rest, in occlusion, and with mouth open), PA, 45° oblique, and hand-wrist films, photographs, study casts (with wax bites), height, weight, written treatment records (for the annual series only), and some medical histories. The enlargement factor is 9.8% at the midsagittal plane for all lateral films. Records of the same types are available for many siblings and for about half the parents. All subjects are of Northern European white ancestry.

All films and casts have been duplicated. Work space is available adjacent to the files. All duplicate materials are accessible on approval of a detailed proposal by the director and payment of a user's fee (about 5$ per case record). However, all of the lateral and PA head films have been digitized so that many investigations can be done directly from the computers files.

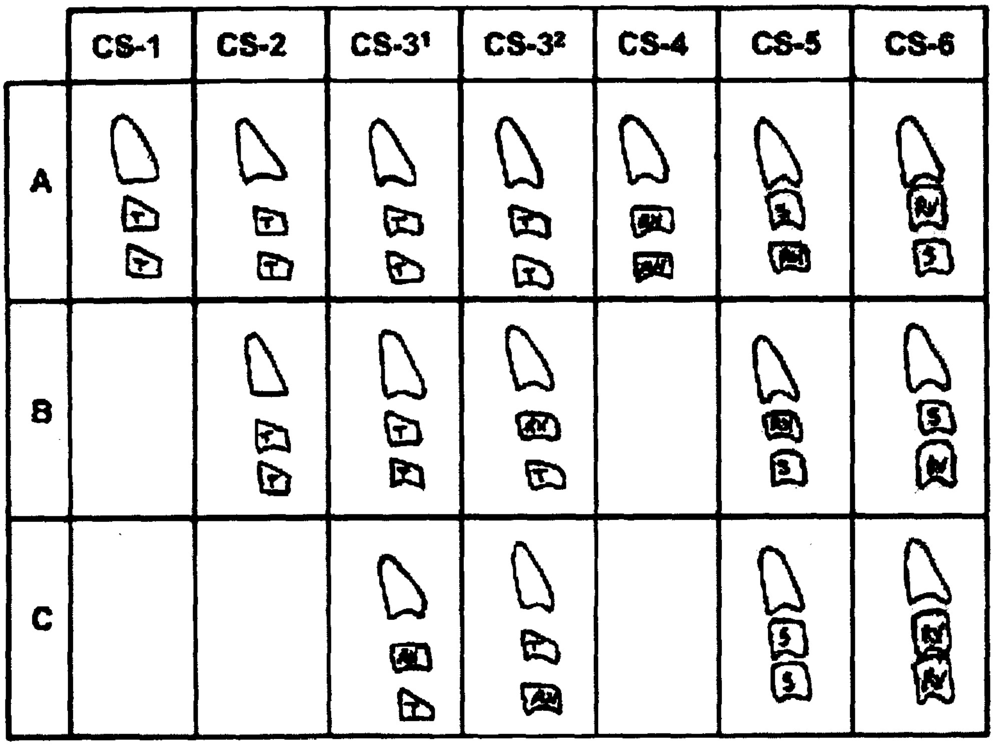
APPENDIX VIII

Time table of the study



APPENDIX IX

The JaHM method (Jamal, Hunter, Mamandras) for assessing Stages of Cervical Vertebral Maturation



DEFINITIONS

Flat: no concavity on the lower border of the cervical vertebra or a concavity of less than 0.8mm.

Concave: concavity of more than 0.8mm of the lower border of the cervical vertebra (Figure 13).

Trapezoid (T): the superior border of the vertebral body is tapered from posterior to anterior. The posterior border of the vertebra is longer than the anterior border of the vertebra.

Rectangular Horizontal (RH): the superior and inferior borders of the cervical vertebrae are longer than the anterior and posterior borders of the cervical vertebrae. The anterior and posterior borders are of the same length (superior border is not sloping at all).

Square (S): all 4 borders of the cervical vertebra are the same length.

APPENDIX IX (continued)

Rectangular Vertical (RV): the superior and inferior borders of the cervical vertebra are shorter than the anterior and posterior borders of the cervical vertebrae.

Other specifications:

- When hesitating between 2 cervical vertebral stages, always use the lesser stage.
- When the operator is not sure about the presence or absence of a concavity, we suggest to the operator to measure the lower concavity as shown in Figure 13.
- Bone condensations present above the superior border of the cervical vertebrae should be included in the overall shape of the cervical vertebrae while bone condensations below the lower border of the cervical vertebrae should not be included (see figure 11).

The seven stages of the <u>JaHM method</u> with all variations (found in this sample) are defined as follow (see page 57 for radiographic representation)

Cervical Stage 1 (CS-1)

C2 ***lower border***: flat
C3 ***lower border***: flat ***Form:*** trapezoid in shape
C4 ***lower border:*** flat ***Form:*** trapezoid in shape

Cervical stage 2 (CS-2A, CS-2B)

A-C2 ***lower border:*** concave
C3 ***lower border:*** Flat ***Form:*** Trapezoid
C4 ***lower border:*** Flat ***Form:*** Trapezoid

B-C2 ***lower border:*** Flat
C3 ***lower border:*** Concave ***Form:*** Trapezoid
C4 ***lower border:*** Flat ***Form:*** Trapezoid

Cervical stage 3^1 ($CS3^1(A)$, $CS3^1(B)$, $CS3^1(C)$)

A-C2 ***lower border:*** concave
C3 ***lower border:*** concave ***Form:*** trapezoid
C4 ***lower border:*** flat ***Form:*** trapezoid

APPENDIX IX (continued)

B-**C2** ***lower border:*** Concave
C3 ***lower border:*** Flat ***Form:*** Trapezoid
C4 ***lower border:*** Concave ***Form:*** Trapezoid

C-C2 ***lower border:*** Concave
C3 ***lower border:*** Concave ***Form:*** Rectangular Horizontal
C4 ***lower border:*** Flat ***Form:*** Trapezoid

Cervical stage 3^2 (CS-3^2(A), CS-3^2(B), CS-3^2(C))

A- C2 ***lower border:*** Concave
C3 ***lower border:*** Concave ***Form:*** Trapezoid
C4 ***lower border:*** Concave ***Form:*** Trapezoid

B- C2 ***lower border:*** Concave
C3 ***lower border:*** Concave ***Form:*** Rectangular Horizontal
C4 ***lower border:*** Concave ***Form:*** Trapezoid

C-C2 ***lower border:*** Concave
C3 ***lower border:*** Concave ***Form:*** Trapezoid
C4 ***lower border:*** Concave ***Form:*** Rectangular Horizontal

Cervical stage 4 (CS-4)

C2 ***lower border:*** Concave
C3 ***lower border:*** Concave ***Form:*** Rectangular Horizontal
C4 ***lower border:*** Concave ***Form:*** Rectangular Horizontal

Cervical stage 5 (CS-5(A), CS-5(B), CS-5(C))

A- C2 ***lower border:*** Concave
C3 ***lower border:*** Concave ***Form:*** Square
C4 ***lower border:*** Concave ***Form:*** Rectangular Horizontal

B- C2 ***lower border:*** Concave
C3 ***lower border:*** Concave ***Form:*** Rectangular Horizontal
C4 ***lower border:*** Concave ***Form:*** Square

C- C2 ***lower border:*** Concave
C3 ***lower border:*** Concave ***Form:*** Square
C4 lower border: Concave, form: Square

Cervical stage 6 (CS-6(A), CS-6(B), CS-6(C))

A- C2 ***lower border:*** Concave
C3 ***lower border:*** Concave ***Form:*** Rectangular Vertical
C4 ***lower border:*** Concave ***Form:*** Rectangular Vertical

B- C2 ***lower border:*** Concave
C3 ***lower border:*** Concave ***Form:*** Rectangular Vertical
C4 ***lower border:*** Concave ***Form:*** Square

APPENDIX IX (continued)

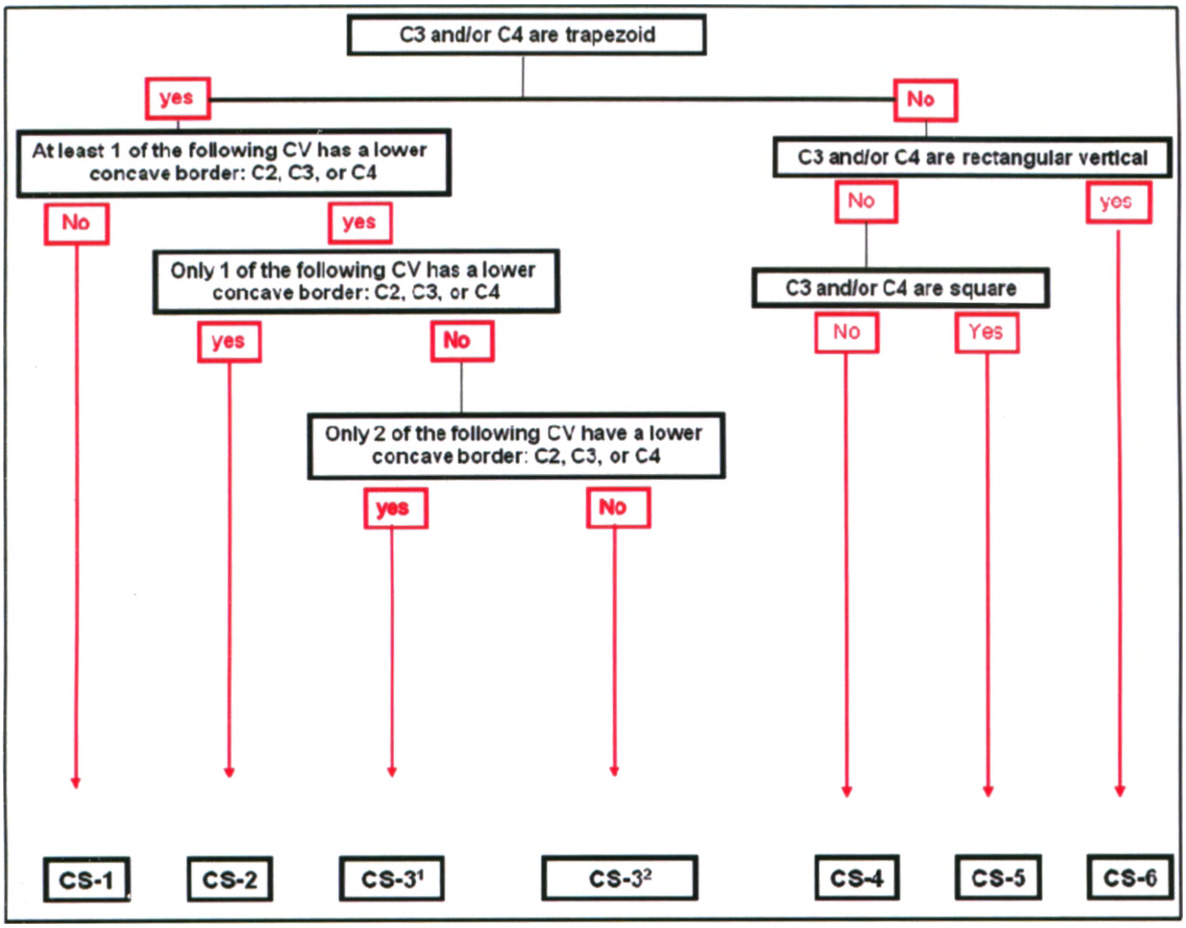
C-C2 ***lower border:*** Concave
C3 ***lower border:*** Concave ***Form:*** Square
C4 ***lower border:*** Concave **Form:** Rectangular Vertical

RADIOGRAPHIC REPRESENTATION OF EVERY CERVICAL STAGE

CS-1	CS-2	CS-3[1]	CS-3[2]	CS-4	CS-5	CS-6
						
						
						

APPENDIX X

Conditional Sequential Flow Chart for the JaHM method



C2: second cervical vertebra
C3: Third cervical vertebra
C4: fourth cervical vertebra
CS-1: cervical stage 1
CS-2: cervical stage 2
CS-3^1: cervical stage 3^1
CS-3^2: cervical stage 3^2
CS-4: cervical stage 4
CS-5: cervical stage 5
CS-6: cervical stage 6

REFERENCES

1. Pancherz H, Hägg U. Dentofacial Orthopedics in relation to somatic maturation. Am J Orthod 1985;88:273-286.

2. Nanda RS. The rates of growth of several facial components measured from serial cephalometric roentgenograms. Am J Orthod 1955;41:658-673.

3. Bjork A. Variations in the growth pattern of the human mandible: longitudinal radiographic study by the implant method. J Dent Res 1963;42:400-411.

4. Hunter CJ. The correlation of facial growth with body height and skeletal maturation at adolescence. Angle Orthod 1966;36:44-54.

5. Ekström C. Facial growth rate and its relation to somatic maturation in healthy children. Swed Dent J (Suppl) 1982;11:1-99.

6. Lewis A, Roche AF, Wagner B: Pubertal spurts in cranial base and mandible: comparisons within individuals. Angle 1985;55:17-30.

7. Hägg U, Pancherz H, Taranger J. Pubertal growth and orthodontic treatment in Carlson DS, Ribbens KA (eds): Craniofacial Growth Series, Vol 20. Ann Arbor, MI, Center for Human Growth and Development, University of Michigan 1987:87-115.

8. Fishman LS. Chronological versus skeletal age, an evaluation of craniofacial growth. Angle Orthod 1979;49:181-187.

9. Rotch TM. Chronological and anatomic age in early life. J Am Med Assoc 1908;51:1197-1203.

10. Tofani M. Mandibulaar growth at puberty. Am J Orthod 1972;62:176-195.

11. Bowden BD. Epiphyseal changes in the hand/wrist area as indicators of adolescent stage. Aust Orthod 1976;4:87-104.

12. Hägg U, Taranger J. Skeletal stages of the hand and wrist as indicators of the pubertal growth spurt. Acta Odontol Scand 1980;38:187-200.

13. Grave KC. Physiological indicators in orthodontic diagnosis and treatment planning. Aust Orthod 1978;5:114-122.

14. Chapman SM. Ossification of the adductor sesamoid and the adolescent growth spurt. Angle Orthod 1972;42:136-244.

15. Bambha J. Longitudinal cephalometric roentgenograhic study of face and cranium in relation to body height. J Am Dent Assoc 1971;63:776-99.

16. Bergersen EO. The Male Adolescent Facial Growth Spurt: Its Prediction and Relation to Skeletal Maturation. Angle Orthod 1972;42:319-336.

17. Grave KC. Timing of facial growth: a study of relations with stature and ossification in the hand of puberty. Ans Orthod J 1973;3:117-22.

18. Grave KC, Brown T. Skeletal ossification and the adolescent growth spurt. Am J Orthod 1976;69:611-619.

19. Johnston F, Hufham H. Skeletal maturation and cephalofacial development. Angle Orthod 1965;35:1-11.

20. Krogman W. The meaningful interpretation of growth and growth data by the clinician. Am J Orthod 1958;44:411-32.

21. Pike J. A serial investigation of facial and statural growth in 7 to 12 year old children. [Thesis.] Minneapolis: University of Minnesota, 1961.

22. Pileski R. Relationship of the ulnar sessamoid and maximum mandibular growth velocity. Angle Orthod 1973;43:162-170.

23. Rose J. A cross-sectional study of the relationship of facial areas with several body dimensions. Angle Orthod 1960;30:6-1.

24. Bjork A, Helm S. Prediction of the age of maximum pubertal growth in body height. Angle Orthod 1967;37:134-43.

25. Björk A, Skieller V. Facial development and tooth eruption: an implant study at the age of puberty. Am J Orthod 1972;62:339-383.

26. Houston WJB, Miller JC, Tanner JM. Prediction of the timing of the adolescent growth spurt from ossification events in hand-wrist films. Br J Orthod 1979;6:145-152.

27. Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls, Arch Dis Child 1969;44:291-303.

28. Hägg U, Taranger J. Maturation indicators and the pubertal growth spurt. Am J Orthod 1982;82(4):299-309.

29. Tanner JM, Landt KW, Cameron N, Carter BS, Patel J. Prediction of adult height from height and bone age in childhood. A new system of equations (TW Mark II) based on a sample including very tall and very short children. Arch Dis Child 1983;58(10):767-776

30. Todd TW. Atlas of skeletal maturation, Part I, hand. London; Kimpton, 1937.

31. Greulich W, Pyle SI. Radiographic atlas of skeletal development of the hand and wrist. 2nd ed. Stanford, Calif: Stanford University Press; 1959.

32. Tanner JM, Whitehouse RW. Atlas of children's growth; normal variation and growth disorders. 1st ed. London: Academic Press, 1982.

33. Fishman L.S. Radiographic evaluation of skeletal maturation; a clinically oriented method based on hand wrist films. Angle Orthod 1982;52:88-112.

34. Lamparski DG. Skeletal age assessment utilizing cervical vertebrae. Unpublished master's thesis. Pittsburgh, PA, Department of Orthodontics, University of Pittsburgh, 1972.

35. O'reilly MT, Yaniello GJ. Mandibular growth changes and maturation of the cervical vertebrae: A longitudinal study. Angle Orthod 1988;58:179-184.

36. Hassel B, Farman AG. Skeletal maturation evaluation using cervical vertebrae. Am J Orthod Dentofacial Orthop 1995;107:58-66.

37. Kucukkeles N, Acar A , Biren S, Arun T. Comparisons between cervical vertebrae and hand-wrist maturation for the assessment of skeletal maturity. J Clin Pediatr Dent 1999;24(1):47-52.

38. Franchi L, Baccetti T, McNamara Jr JA. Mandibular growth as related to cervical vertebral maturation and body height. Am J Orthod Dentofacial Orthop 2000;118:335-340.

39. Baccetti T, Franchi L, McNamara Jr AJ. An improved Version of the Cervical Vertebral Maturation (CVM) Method for the Assessment of Mandibular Growth. Angle Orthod 2002:72:316-323.

40. Baccetti T, Franchi L, McNamara Jr AJ. The Cervical Vertebral Maturation (CVM) Method for the Assessment of Optimal Treatment Timing in Dentofacial Orthopedics. Semin Orthod 2005;11:119-129.

41. Mito T, Sato K, Mitani H. Cervical vertebral bone age in girls. Am J Orthod Dentofacial Orthop 2002; 122:380-385.

42. Mito T, Sato K, Mitani H. Predicting mandibular growth potential with cervical vertebral bone age. Am J Orthod Dentofacial Orthop 2003;124:173-177.

43. Chen F, Terada K, Hanada K. A New Method of Predicting Mandibular Length Increment on the Basis of Cervical Vertebrae. Angle Orthod 2004;74:630-634.

44. Garcia-Fernandez P, Torre H, Flores L, Rea J. The Cervical Vertebrae as Maturational Indicators. J Clin Orthod. 1998;32(4):221-225.

45. Uysal T, Ramoglu SI, Basciftci FA, Sari Z. Chronologic age and skeletal maturation of the cervical vertebrae and hand-wrist: Is there a relationship. Am J Orthod Dentofacial Orthop 2006;130:622-628.

46. San Roman P, Palma JC, Oteo D, Nevado E. Skeletal maturation determined by cervical vertebrae development. European Journal of Orthodontics 2002;24:303-311.

47. Tanner JM, Whitehouse RH, Cameron N, Marshall WA, Healy MJR, Goldstein H. Assessment of skeletal maturity and prediction of adult height (TW2 method). 2nd ed. London: Academic Press 1983: 22-37, 50-85.

48. Flores-Mir C, Burgess CA, Champney M, Jensen RJ, Pitcher MR, Major PW. Correlation of Skeletal Maturation Stages Determined by Cervical Vertebrae and Hand-wrist Evaluations. Angle Orthod 2006;76:1-5.

49. Scheuer L, Balck S, Christie A. Developmental juvenile osteology. ISBN 0-12-624000-0, 2000, p172.

50. Moore RN, Du Bois LM, Boice PA, Igel KA. The accuracy of measuring condylion location. AJODO 1989;95:344-347.

51. Adenwalla ST, Kronman HJ, Attarzdeh F. Porion and condyle as Cephalometric landmarks-an error study. AJODO 1988; 94: 411-415.

52. Haas DW, Martinez F, Eckert GJ, Diers NR. Measurements of mandibular length: a comparison of articulare Vs condylion. Angle Orthod 2001;71: 210-215.

53. Hunter, Baumrind, Moyers. An inventory of United States and Canadian growth records sets: preliminary report. AJODO 1993;103(6):545-55.

54. Hunter, Baumrind, Popovich and Jorgensen. Skeletal age and Peak mandibular growth velocity at puberty. In: McNamara JA Jr, editor. Treatment timing: orthodontics in 4 dimensions, Craniofacial Growth Series. Ann Arbor: Center for Human Growth and Development: University of Michigan; 2002. P.185-98.

55. Hunter, Baumrind, Popovich and Jorgensen. Forecasting the timing of peak mandibular growth in males by using skeletal age. AJODO 2007;131:327-33.

56. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-174.

57. Shrout PE. Measurement reliability and agreement in psychiatry. Stat Methods in Medical Research 1998;7:301-317.

58. Cohen J. A coefficient of agreement for nominal scales. Psychol Bull 1960;20:37-46.