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USE OF CVM STAGES IN ASSESSMENT OF YOUNG ORTHODONTIC PATIENTS TO ESTIMATE GROWTH POTENTIAL

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ABSTRACT

Harnessing a patient's growth to correct parasagittal discrepancies is an important part of Class II correction in orthodontic treatment; however, orthodontists rarely have the opportunity to choose when a patient is referred to them. Diagnostic records can assist the orthodontist in determining how much growth a patient has remaining. The purpose of this retrospective cephalometric study was to determine whether the amounts of in-treatment facial growth differ significantly by sex and by cervical vertebral maturation (CVM) stage. The sample consisted of 133 Class II division 1 patients from a single private practice office treated with a combination of a functional appliance (Bionator, Frankel or MARA) and full Edgewise appliances. This sample was compared to a conventionally treated edgewise sample of 183 Class II division 1 patients from the University of Tennessee Department of Orthodontics. The cervical vertebral maturation (CVM) stage was determined for the lateral cephalometric radiographs available for each patient using Lamparski's original 6 stages. Amounts of facial bony growth were evaluated for 5 linear dimensions (Se-Na, Se-A, Se-B, Se-Gn, Se-Go) that occurred over the course of treatment (*i.e.*, pre- to posttreatment changes). There was no association between CVM stage and duration of treatment. CVM stages were analyzed statistically to determine if craniofacial growth was linked to CVM grade assessed. The results showed that as individuals develop, less growth occurs with treatment. Maximum growth occurred for cases starting at CVM 1, and the average amounts of growth diminish monotonically across the 6 stages. Using a two-way ANOVA, growth for CVM stages 1-4 was highly significant for each stage as well as between sexes ($P < 0.0001$). Girls achieved CVM stages more than one year ahead of boys on the average, while boys have larger amounts of growth than girls at each CVM grade. Interestingly, little facial growth occurred after the age of 15 in either sex in the sample, and orthodontists need to keep this in mind if their goals are to modulate jaw growth and not rely solely on orthodontic tooth movement for correcting skeletal discrepancies.

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CHAPTER I
INTRODUCTION

When formulating a treatment plan, the orthodontist not only assesses the malocclusion but also the patient's growth potential that can be harnessed to correct any parasagittal discrepancy (*e.g.*, Bergensen 1972; Fishman 1987). Growth in the maxillary-mandibular facial complexes can be modulated orthodontically to improve results, but only if the patient is indeed growing (Baccetti *et al.* 2002; McNamara and Burdon 2001). However, the orthodontist rarely can choose when a patient presents for treatment. Start of treatment usually is decided by a parent or the referring dentist. Fortunately, the orthodontist can use some measure of the patient's physiological age to estimate the amount of facial growth anticipated during treatment, and the treatment plan can be adjusted accordingly to take advantage of the growth anticipated in that patient (Baccetti *et al.* 2002).

Treatment planning options can be adjusted according to the patient's growth potential. It is well established, however, that individuals vary greatly in their growth rates (van der Linden 1986). Chronological age has been used to gauge a person's degree of biological maturity, but it is a weak predictor due to the large variation in growth tempos among children (*e.g.*, Fishman 1979). Skeletal maturity has been shown to be more closely tied to facial growth rates than chronological age (Bergersen 1972; Björk and Helm 1967; Flores-Mir *et al.* 2004).

Conveniently, the orthodontist has a valuable indicator of skeletal maturity located in the lateral cephalograph that is routinely taken as part of the diagnostic record. The morphology of the cervical vertebrae is a useful indicator of skeletal age (Lamparski 1972; O'Reilly and Yanniello 1988). The maturation of the cervical vertebrae has been statistically linked to the tempo of mandibular growth (O'Reilly and Yanniello 1988; Mito *et al.* 2003; Baccetti *et al.* 2005; Chance 2006).

One of the most common orthodontic problems in the United States is Class II malocclusion (McNamara and Brudon 2001). Conventional orthodontic appliances (*e.g.*, Sandusky 1964) modify the jaw relationships primarily by restraining maxillary growth. Functional appliances can be used to correct Class II malocclusion in a growing patient with the aim of enhancing mandibular growth (Voudouris *et al.* 2003a, b). When a functional appliance is used in orthodontic treatment, it alters the patient's mandibular position in the sagittal and vertical dimensions, and it is anticipated that these positional changes will result in orthopedic changes. The main goal of functional appliance therapy

commonly is to induce supplementary mandibular growth at the condylar process (Franchi *et al.* 2000). Clinicians who advocate the use of functional appliances claim that the forward positioning of the mandible (hyperpropulsion) stimulates mandibular growth. Research has shown that the length of the mandible can be increased modestly compared to untreated Class II controls, at least over the short term (McNamara and Brudon 2001). The long term effects of functional appliances continue to be a topic of debate in the literature (Pangrazio-Kulbersh *et al.* 2003).

An optimal treatment plan in orthodontics usually calls for some facial growth modification to aid in the correction. Since orthodontic treatment modifies growth, the best time to treat is before growth is at its peak rate (Pancherz and Hägg 1985). Research suggests that when treatment overlaps the circumpubertal interval of rapid growth it has the potential to reduce treatment time (Pancherz and Hägg 1985).

The purpose of the present study was to determine whether the amounts of in-treatment facial growth differ significantly by sex and by Cervical Vertebral Maturation (CVM) stage. The assessment will help define differences in the expected amounts of growth using CVM stages as a clinical predictor of the degree of biological maturity. The study used cases treated with functional appliances to explore whether the variability of outcomes with these appliances is based on when they are employed during a period of growth.

The intent of the present study was two-fold: One, it focused on cases treated with functional appliances because these cases often are started at a younger age to allow for greater growth modification. Therefore the sample of patients treated has a larger age span than conventionally treated orthodontic cases. A previous study has shown that cases started at an earlier age have better outcomes (Pancherz and Hägg 1985). The second emphasis was to determine if cases started earlier have a better outcome. To determine outcome (skeletal correction), the study looked at skeletal profile, CVM stage and related these to growth.

CHAPTER II
REVIEW OF THE LITERATURE

Parapubertal Growth Spurt

The human somatic growth curve can be divided into four intervals stemming from birth to about age 20: infancy, from birth to 3 years of age; childhood, from about 3 to 12 years of age; adolescence, from 12 to 18 years of age, and adulthood, from 18 years onward (Tanner 1978). All of these intervals occur in all developing individuals, but the adolescent growth spurt seems to have the greatest variability as regards duration, amount, and timing of growth (Moore *et al*. 1990). Despite the variation in timing, the parapubertal growth spurt follows a similar pattern in most adolescents, which is an interval of accelerated growth followed by decelerating growth as biological maturity is attained. The intensity of the growth spurt tends to be greater in children with early growth acceleration (van der Linden 1986). While late growers have a less intense growth spurt but, these also are the children who tend to have a longer duration of preadolescent growth, which contributes substantially to adult size (Figure 1).

Methods for predicting the parapubertal growth spurt, like chronological age, dental development, menarche, and body weight have been shown to be impractical and unreliable due to the great variation in the parapubertal growth spurt among individuals (Özer *et al*. 2006; Hunter 1966; Hägg and Taranger 1982).

Sex Differences in Parapubertal Growth

An individual's sex has a major influence on both the timing and rate at peak velocity of the parapubertal growth spurt (Fishman 1979; van der Linden 1986). Björk and Helm (1967) studied 32 boys and 20 girls, finding that girls, on the average, have their maximum pubertal growth in height (stature) at age 12.6 and boys were later at age 14.0. Lewis *et al*. (1985) studied the parabubertal growth spurt in cephalometric data from 34 boys and 33 girls. The pubertal growth spurt occurred an average of 1.6 years earlier in girls than boys. The mean size or intensity of the parapubertal growth spurt was from 25 to 33% greater in boys than girls. However, the rate of growth the year before the spurt tended to be greater in girls. Boys tended to have greater growth the year after the parapubertal growth spurt (Lewis *et al*. 1985). Guo *et al*. (1992) found that girls have their parapubertal growth spurt approximately two years before boys.
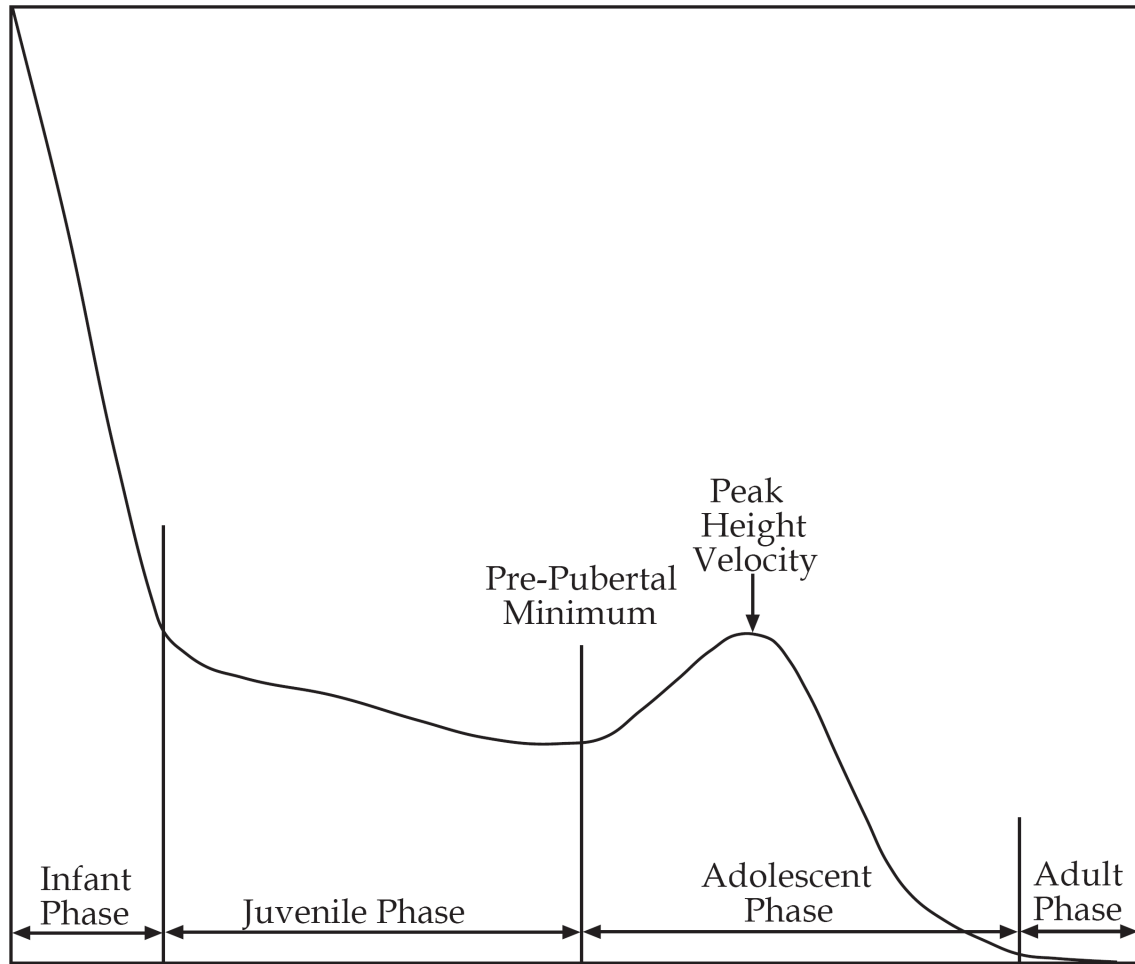
Figure 1. Human growth velocity chart for somatic tissues partitioned into the four major intervals of postnatal growth. (Diagram provided by E.F. Harris, The University of Tennessee Health Science Center).

Since boys have a growth spurt that occurs later than girls, boys benefit from two or more years of preadolescent growth, which accounts for part of the approximately 10 cm difference in stature between adult males and females (Largo *et al*. 1978).

Sexual Dimorphism in Mandibular Growth

Growth of the face parallels the general growth velocity curve (Fishman 1982), meaning that the growth of the mandible also differs significantly between boys and girls at the parapubertal growth spurt. Bushang *et al*. (1999) studied the cephalometric radiographs of 113 males and 108 females from 6 to 16 years of age. Condylion was identified on each radiograph and tracings were superimposed on: (1) the anterior contour of the chin, (2) inner contour of the cortical plate at the lower border of the symphysis, (3) trabecular structures that were radiographically distinct in the symphysis, and (4) the contour of the mandibular canal. A two-level polynomial model was used to create an average growth curve for males and females. Percentiles were used to describe individual variation. Males exhibited a mean maximum condylar growth rate of 3.1 mm/year at 14.3 years, while females exhibited a mean maximum condylar growth rate of 2.3 mm/year at 12.2 years. These results suggest the rate of condylar growth is less intense in females and occurs approximately 2 years earlier than in boys, coinciding with previous literature on craniofacial growth and the parapubertal growth spurt (Hunter 1966; Björk and Helm 1967; Bergersen 1972; Lewis *et al*. 1985). When using functional appliances as a treatment modality, the sexual dimorphism of orthodontic patients must be considered in order to use them at a time to take advantage of maximum growth potential in those individuals. Orthodontists may need to consider treating patients earlier to harness childhood growth instead of relying on an inconsistent parapubertal growth.

Largo *et al*. (1978) documented the inconsistency of the parapubertal growth spurt. They examined height velocity curves in 112 boys and 110 girls from the Zurich Longitudinal Study. A peak height of 4 cm/year is found in only 70% of boys and 11% of girls. While the average age at peak for boys and girls is 13.9 and 12.2 years, respectively, there is a wide range for both sexes (5 to 7 years for girls and 3 to 8 years for boys). Many orthodontists wait until these average ages to begin orthodontic treatment on patients, meaning that the patient may have reached their peak height or it may have past. The opportunity to use growth to help correct the malocclusion may be lost or not as effective when treating at a later age. Treating at an earlier age allows the orthodontist to take advantage of peak adolescent growth and, more importantly, capture some

childhood growth, which averages approximately 4 cm/year and is fairly consistent in both sexes (Largo *et al*. 1978).

<u>Stature and Facial Dimensions</u>

Both stature and facial dimensions undergo proportional changes that occur from birth to adulthood. In a study by Hunter (1966), 25 boys and 34 girls were assessed for chronological age, skeletal age, stature, and facial growth. Data for chronological age, hand-wrist skeletal age, and stature were recorded every six months over the course of seven years. Skeletal age was determined using the Greulich and Pyle standards (1959). Annual cephalometric radiographs were taken on the ninth month of the chronological year from age 7 to approximately age 13. After 13 years of age, the radiographs were taken the month of the subject's birthday. To assess facial growth, Hunter made the following seven cephalometric measurements: (1) Articulare-Gonion, (2) Gonion-Pogonion, (3) Articulare-Pogonion, (4) Articulare-A Point, (5) Sella-Nasion, (6) Sella-Gonion, and (7) Nasion-Menton. The results indicated that girls entered their parapubertal growth spurt approximately 2.4 years earlier (average 10.4 years of age), than males (average 12.8 years of age).

When maximum increments of facial growth and maximum statural velocity were compared, they occurred simultaneously in 57% of the cases, before in 14% of the cases, and the remaining 29% of cases occurred after maximum statural velocity. According to Hunter, the peak in the anteroposterior length of the mandible was the most consistent with peak statural velocity of the seven facial growth measurements tested. However, these findings must be considered with the examination interval (ninth month of the chronological year), meaning that consistent maxima occurred within the same nine months. In some of the subjects (13/59) peak mandibular growth occurred after peak statural velocity. Hunter did not elaborate on how inconsistent the other facial dimensions are from the statural velocity.

Hunter concluded that facial growth in girls ceases sometime during the second decade, usually finishing about the same time as final stature was attained. For boys, Hunter found five boys to have continued facial growth after peak statural growth, two to have facial growth cease before statural growth completion, and 10 had not completed statural growth during the age interval of the study. Throughout the adolescent growth period, Hunter found that boys had greater absolute facial growth, as well as greater rate of facial growth than girls.

Serial cephalometric radiographs and statural height were studied for 23 American white males by Bergersen (1972). The following seven measurements

were collected: (1) Articulare-Gnathion, (2) Nasion-Menton, (3) Sella-Gnathion, (4) Anterior Nasal Spine-Menton, (5) Sella-Nasion, (6) Sella-Anterior Nasal Spine, and (7) Nasion-Anterior Nasal Spine. Skeletal age was determined from hand-wrist radiographs using the Greulich-Pyle atlas (1959). The results of the study showed significant associations among the parapubertal growth spurt in stature and all facial dimensions (Bergersen 1972).

Bishara *et al.* (1981) specifically studied mandibular growth in relation to statural height. The subjects were from the Facial Growth Study at the University of Iowa and consisted of 20 boys and 15 girls with a range of 5 to 17 years of age. Statural height and lateral cephalometric radiographs were taken biannually from ages 5 to 12, and then annually through age 17. Cephalometric analysis was used with Articulare-Pogonion as the linear measurement and Sella-Nasion-Pogonion and Sella-Nasion-B Point were the angular measurements. The following three time periods were compared: (1) premaximum growth period, (2) maximum growth period, and (3) post-maximum growth period. After statistical testing with analysis of variance, Bishara found that both Articulare-Pogonion and statural height significantly differed between the three periods of growth for both boys and girls. Boys exhibited greater amounts of growth in statural height than girls, and these changes occurred later than in girls. The findings were similar for Articulare-Pogonion. In contrast, no angular measurement was significantly different between the sexes. Bishara concluded that except for mandibular length, mandibular growth patterns do not follow the growth pattern of standing height. Bishara claimed due to this result, that mandibular growth spurts do not occur in all children, and if these spurts do happen, they are highly variable among individuals. However, the flaw of this study is that the conclusions are based on angular rather than linear measurements. Mandibular length (Articulare-Pogonion) did show a high correlation, r = 0.83, with statural height. Craniofacial growth can be evident in linear measurements, but hidden in angular measurements due their slow change during growth. Ricketts described this gnomic growth, when he noted that craniofacial structures tended to follow grid lines as they "grew" from a central point in the skull, around the foramen rotundum, during development (Ricketts 1979). Ochoa and Nanda (2004) found evidence to support this claim through comparing maxillary and mandibular growth in 15 girls and 13 boys. These authors found no significant difference in Sella-Nasion-A Point between ages 6 to 20 years of age. However, a statistically significant difference was found in Sella-Nasion-B Point for ages 12 to 14 and 14 to 16, but it was only a 1.2° and 1.1° difference, respectively. These changes are similar to what Bishara *et al.* (1981) found for SNB, which only shifted 1.0° between the ages. While angular measurements remained almost constant, as in Bishara *et al*. (1981), the linear measurement analyzed (Articulare-Pogonion) by Ochoa and Nanda (2004) were drastically different. Mandibular length increased

16.5 mm on the average from ages 6 to 14, with the peak increase for girls between ages 10 and 12. For boys, mandibular length increased an average of 18.7 mm, with a peak increase between ages 14 and 16. This example demonstrates a flaw in the conclusions of Bishara *et al*. (1981) because the growth spurts of the mandible could have occurred and not have been detected when using angular measurements due to their consistency throughout growth.

In a study by Pancherz and Hägg (1985), dentofacial orthopedic effects were related to somatic maturation. Consecutive cases (n = 70) of children with Class II malocclusions (52 boys and 18 girls) were treated with the Herbst appliance and compared to 23 untreated Class II controls. The purpose of the investigation was to relate dental and skeletal mandibular changes in each sex to the level of somatic maturation. In all subjects, the mandibles were advanced by the Herbst appliance to achieve an end-to-end incisal relationship at the start of treatment. Cephalograms were taken at the start of treatment and after treatment, specifically the day the appliance was removed. The untreated controls had cephalograms taken before and after the examination period. Mandibular cephalometric tracings were done on the pre- and posttreatment cephalograms. Longitudinal growth records of stature were available for each subject over a 5 to 10 year period. Individual distance and velocity curves for stature were constructed. Then the peak height velocity was identified by visual inspection and the examination period for each subject was assigned to one of three growth intervals: (1) prepeak, (2) peak, or (3) postpeak. Paired t-tests were calculated to determine how the changes in the mandible related to the growth period and the differences in the changes between the treated and untreated controls. Parasagittal condylar growth changes occurred most frequently when the child was treated during the peak treatment period, while dental changes occurred most frequently in the postpeak treatment period. The authors found that the level of somatic maturation influenced the results of functional appliance therapy. Treating patients near their peak rate of growth, resulted in the best orthopedic outcome (Pancherz and Hägg 1985).

However, a more recent study by Ruf and Pancherz (2006) has shown that Herbst appliances can be successfully used on adult Class II division 1 patients. They looked at 23 consecutively treated patients with a mean pretreatment age of 21.9 years (range 15.7 to 44.4 years of age) using normal growth standards as control parameters.   They looked at three time periods: pretreatment (T1), after the Herbst phase (T2), and after fixed appliances (T3). Cephalometric analysis revealed that Class II correction was achieved in all patients with an average of 22% skeletal correction and 78% dental correction. This result differed from younger patients who experienced more orthopedic correction, *i.e.* skeletal correction, during functional appliance treatment. Adolescents experience a greater mandibular advancement than adults due to condylar growth being

greater in patients treated closer to the parapubertal growth spurt (Ruf and Pancherz 2006). While this study may show that functional appliances work on adult patients, it also reinforces the view that these appliances achieve better orthopedic results if they are used in a growing patient.

Physiological Age

Chronological age is used by laypersons to determine maturity; however, many studies have shown that chronological is not a good indicator of maturity (Fishman 1979; Kopecky and Fishman 1993; Franchi 2000). In orthodontics, this is especially true because most orthodontic patients are adolescents and their developmental status or biological age may be very important to achieving treatment goals in order to harness that child's growth for treatment. A majority of children can be viewed as "average maturers," or those who have concordance between chronological and biological age. However, some children develop more slowly than implied by their chronologically and are termed "late maturers," while others develop faster than gauged by their chronological age and are termed "early maturers"(Tanner *et al.* 1975).

The connective tissue framework of the body serves as a standard for general body development. Biological or skeletal age, also termed bone, developmental or physiological age, as discussed previously, echo the level of maturity an individual has attained. Skeletal age can be determined in a variety of ways including: stature, hand-wrist measurements, menarche, voice change, and dental development (Mito *et al.* 2002). The most common skeletal technique is to use hand-wrist radiographs. As with other organs in the body, bones of the skeleton progress through various morphological stages at different times. New (secondary) ossification centers appear in a child over a period of time, and existing centers are remodeled. When bones of the hand and wrist begin ossification processes with the subsequent morphological changes, these changes provide a way to relate skeletal age to chronological age (Greulich and Pyle 1959).

Fishman developed a simplified scheme for evaluating hand-wrist radiographs based on the Greulich and Pyle's 1959 standards (1982). Based on his analysis, he proposed four phases of bone maturation, which he localized to six sites on the thumb, third finger, fifth finger and radius. More specifically, the sites are the adductor sesamoid of the thumb, the distal, middle, and proximal phalanges of the third finger, the middle phalanx of the fifth finger, and the epiphysis on the distal end of the radius. Fishman divided his assessment into 11 grades of maturity and depicted in Figure 2 as a flow chart. His work stressed

importance of measuring skeletal age and applying it to clinical orthodontic diagnosis and therapy.

Skeletal Age versus Chronological Age

Skeletal age has been shown to more accurately predict the parapubertal growth spurt than chronological age. Björk and Helm (1967) showed a relationship between the ages of maximum growth in statural height and ossification of the ulnar metacarpophalangeal sesamoid of the thumb. The ossification either preceded or coincided with the growth spurt, but never mineralized afterwards. These findings have been supported by Chapman (1972). Chronological age has been shown to be less reliable in predicting the maximum growth in statural height and the parapubertal growth spurt (Björk and Helm 1967; Fishman 1979).

Bergersen (1972) found a significant difference in the variances between skeletal and chronological ages when he analyzed growth of facial areas and their relationship to skeletal maturity. Skeletal age mean range was 1.5 years, while chronological age was 4.2 years. That is, if chronological age was used to estimate the parapubertal growth spurt, it would involve greater inaccuracy than when using skeletal age. However, Bergersen found no significant difference between the chronological and skeletal age in onset of the growth spurt in normal maturing individuals, which concurs with the findings of Hunter (1966). A significant difference was found in chronological and skeletal age, when early or late maturers were compared. Again, these findings show that chronological age is not as accurate in predicting facial growth in early or late maturing individuals. If skeletal age is used to predict rates of growth, all estimations, even early and late maturers, would fall within one year of the mean.

Early, Average and Late Maturers

Fishman compared the use of chronological age and skeletal age to see which method provided the more accurate estimate of craniofacial growth (1979). A longitudinal series of cephalometric and hand-wrist films was studied from 60 boys and 68 girls randomly selected. Stature was also recorded. Subjects had an age range of 7 to 15 years, and records were taken at 6 month intervals. Seven cephalometric measurements were made to assess craniofacial growth, namely: (1) Articulare-Gonion, (2) Gonion-Pogonion, (3) Gonion-Gnathion, (4) Articulare Gnathion, (5) Sella-Gnathion, (6) Articulare-A Point, and (7) Sella-A Point. Skeletal age was assessed on the basis of the hand-wrist radiograph using the

4
Ossification
Adductor Sesamoid

no ⟍ *yes*

1
Width
Proximal Phalanx III

8
Fusion
Distal Phalanx III

2
Width
Middle Phalanx III

no ⟍ *yes*

5
Capping
Distal Phalanx III

9
Fusion
Proximal Phalanx III

3
Width
Middle Phalanx V

6
Capping
Middle Phalanx III

10
Fusion
Middle Phalanx III

7
Capping
Middle Phalanx V

11
Fusion
Radius
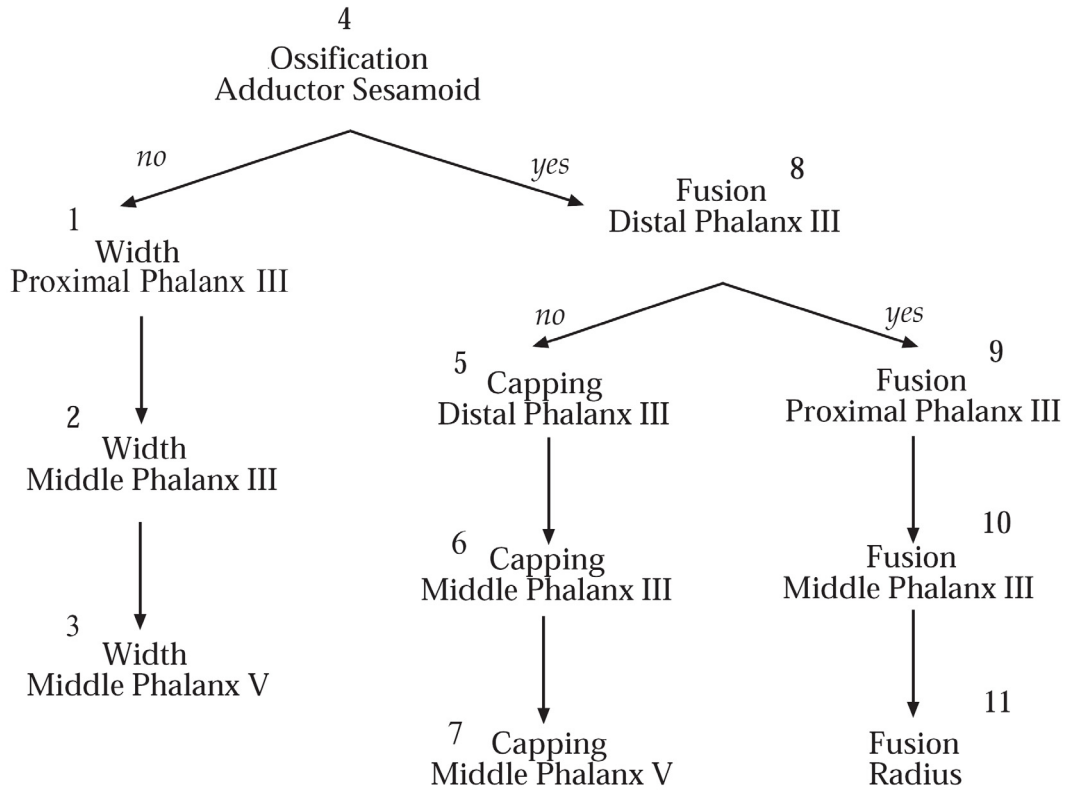
Figure 2. Fishman's 11-grade scheme used to assess skeletal maturity from a hand-wrist radiograph. (Diagram provided by E. F. Harris, The University of Tennessee Health Science Center.)

Greulich and Pyle hand-wrist radiographic atlas (1959). Fishman found that only a small percentage of the total sample exhibited a coincident skeletal and chronological age. When the sexes were separated, Fishman found that girls with advanced skeletal age exhibited less growth than their later maturing counterparts. Males with delayed skeletal age exhibited less growth velocity than those with a skeletal age that more closely follows their chronological age. Fishman reiterated the importance of skeletal assessment of individuals due to its close relationship with craniofacial growth, while chronological age does not exhibit as tight a relationship. This assessment is especially important in orthodontics where the use of growth modification appliances, like headgear and chincup therapy, may not yield as successful results as anticipated if the individual's chronological age is used and the individual is an early or late maturer.

Silveria *et al*. quantified the differences in craniofacial growth between early, average and late maturers by measuring the rates of maxillary and mandibular growth using Fishman's SMI method of assessment (1992). Hand-wrist radiographs of 70 adolescents were evaluated and divided into three maturation groups that represented progressively later stages of maturation (SMI 8-9, SMI 9-10, and SMI 10-11), and further divided into three sub-groups: early, average and late maturers. Lateral cephalographs were traced and the following six linear measurements were recorded: (1) Sella-A point (S-A), (2) Articulare-A point (Ar-A), (3) Sella-Gnathion (S-Gn), (4) Articulare-Gonion (Ar-Go), (5) Articulare-Gnathion (Ar-Gn), and (6) Gonion-Pogonion (Go-Po). Growth increments were represented in percentage change values and analyzed using ANOVA at P = 0.05. The results showed that overall facial growth (S-Gn, S-A), horizontal maxillary growth increments (Ar-A), overall mandibular growth increments (Ar-Gn), and mandibular body length (Go-Po) were significantly larger statistically in late maturers in the different SMI stages when compared with average and early maturers. During the late stages of maturation, average and late maturers mandibular growth increments were significantly larger than maxillary growth increments. Meaning that the maxilla showed a greater percentage of growth completion until these late stages when the growth of the mandible tended to catch up. This study supports the findings of Fishman (1979) and the importance of skeletal age in timing and efficacy of orthodontic treatment regimens.

For example, in the study by Kopecky and Fishman (1993) 41 patients with Class II, division 1 malocclusions were treated with a cervical pull headgear. All cases had cephalometric and hand-wrist radiographs taken before, during and after headgear treatment. Maturational age was determined for each patient record according to the 11-grade Skeletal Maturity Indicators (SMI). The SMIs are grouped as follows (Figure 3):

(1) SMIs 1 to 3 indicate a period of accelerating growth velocity,
(2) SMIs 4 to 7 represent a period of very rapid growing velocity and includes the peak velocity of growth,
(3) SMIs 8 to 11 represent a period of decelerating growth rate.

Cephalometric analysis including SNA and Lande's angle (Frankfort Horizontal to Nasion–Point A) was conducted via computer. Data were compared between patients receiving headgear treatment at different SMI stages using a regression analysis and analysis of variance. When comparing chronological and skeletal age, the reduction in SNA and Lande's angle was more than four times as predictable with skeletal rather than chronological age. The results showed that the greatest reduction of SNA and of Lande's angle occurred during the very rapid growing period, while the decelerating growth period showed the least amount of reduction. Also, the mean reduction in SNA was two times as great during the very rapid growth period as during the accelerating growth period. The results of this study show that the timing of orthodontic treatment can have a significant effect on the results of treatment and that skeletal age is a more reliable indicator of when best to start orthodontic treatment than chronological age.

Remodeling of the Temporomandibular Joint in Animal Models

When dentofacial orthopedics is employed in orthodontics, one of the major aims is to enhance the growth at the condyle by displacing the mandible anteriorly (ventrally). However, the extent to which the temporomandibular joint (TMJ) can be remodeled and whether this remodeling is clinically significant is controversial in the literature (McNamara and Brudon, 2001; Pangrazio-Kulbersh *et al*. 2003). Both rat and nonhuman primate models have been used to study the responsiveness of the TMJ to dentofacial orthopedics.

Using a rat model, Rabie *et al*. (2002) identified a number of factors important in normal condylar growth. These factors include Sox-9, a transcription factor that regulates the synthesis of type II collagen in cells of the proliferative layer of the condylar cartilage. Sox-9 is essential in regulating the differentiation of mesenchymal cells into chrondrocytes (Rabie *et al.* 2002). In later experiments, rats were fitted with a bite-jumping appliance and compared to matched controls, which were followed for an experimental period of 17 days. Both the mandibular condyles and the glenoid fossae showed increased levels of Sox-9 and of type II collagen in the experimental groups when compared to controls. Rabie argues that the increase in Sox-9 and thus type II collagen are

SMI
1-3

SMI
4

SMI
5-7

SMI
8-11

Epiphyseal
Widening

Sesamoid
Ossification

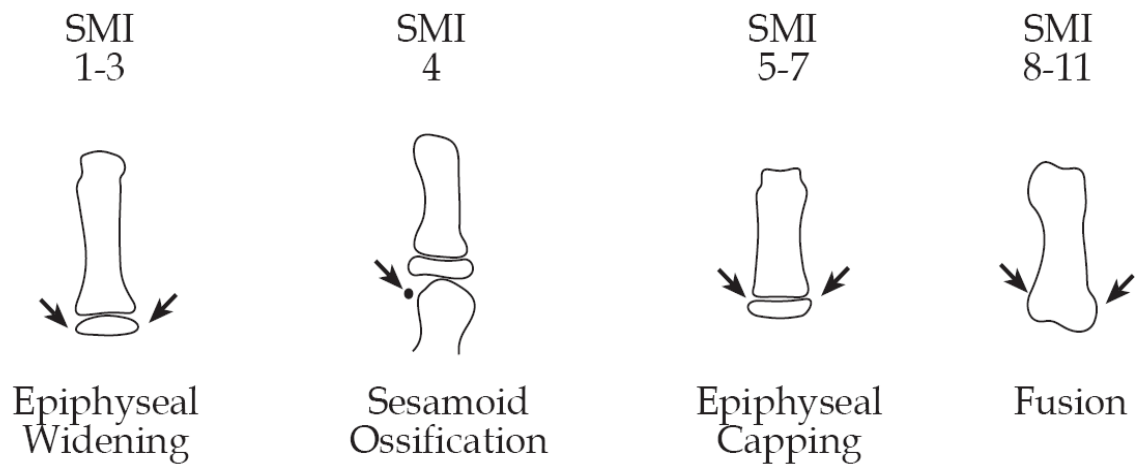Epiphyseal
Capping

Fusion

Figure 3. Skeletal maturity indicators as grouped by Kopecky and Fishman (1993).

Modified with permission. Kopecky GR, Fishman LS. Timing of cervical headgear treatment based on skeletal maturation. Am J Orthod Dentofacial Orthop. 1993;104:162-9.

evidence that the condylar and articular cartilages are stimulated to grow in response to mandibular hyperpropulsion (Rabie *et al.* 2003a,b). The authors' concept is that the increase in Sox-9 leads to increased chrondrocyte differentiation, which leads to more bone matrix formation because the chrondrocytes become capable of producing bone matrix (Rabie *et al.* 2003b). However, these increases appear to be transient because Sox-9 reached a peak on day 7 and then returned to near control levels. Also, it is established that tissues and individual cells exposed to mechanically induced strain show changes in metabolic activity and proliferation (Sandy *et al.* 1993). Therefore, it is not surprising that chondrocytes act similarly.

While rat models have produced controversial evidence of TMJ remodeling, functional appliances used in monkeys have consistently shown change in TMJ morphology (Brietner 1940; McNamara and Bryan 1987; Woodside *et al.* 1987). Brietner (1940) was the first to study the effects of orthodontics on the craniofacial structures; his histological study showed that other parts of the craniofacial complex were remodeled by orthodontic forces, including the condyle and the glenoid fossa. Criticism of Brietner's work has been that his experimental groups consisted of only one animal and very little control material (Meikle 2007). However, Brietner's theory that forward displacement of the mandible could remodel the TMJ and enhance condylar growth has been supported by more recent research (McNamara and Bryan 1987; Woodside *et al.* 1987).

A sample of 7 experimental monkeys and 4 controls was used in a histological study by Woodside *et al.* (1987) to evaluate the effects of a Herbst appliance on the glenoid fossa. The experimental animals were followed between 45 and 61 weeks. At the end of the experimental period, the condyle and glenoid fossa were prepared for histological examination. Control and experimental groups contrasted in morphology. Extensive bone apposition on the anterior border of the postglenoid spine was observed in the experimental group along with bone resorption on the posterior border of the spine. Control sections showed the opposite. The authors claim that this shows that the glenoid fossa is remodeling anteriorly, contributing to the anterior repositioning of the mandible and altered jaw relationships in monkeys due to the Herbst appliance (Woodside *et al.* 1987).

McNamara and Bryan (1987) studied 23 male juvenile rhesus monkeys (12 control and 11 experimental) to measure cephalometric changes in mandibular growth when using a functional appliance was used. Initial radiographs were compared with radiographs taken at 48 weeks, 96 weeks, and 144 weeks. At both 48 and 96 weeks, the experimental group had statistically significant increases in overall length of the mandible (Condylion to Infradentale and

Condylion to symphyseal point), which resulted in an approximately 4 mm and 2 mm increase, respectively, in length over the control group. When overall mandibular length was measured at 144 weeks, the mandibles of the animals with functional appliances showed between 5 and 6 mm of increased length compared to the controls. To study the change between the body and ramus of the mandible, the condylar-ramus-occlusal (CRO) angle was measured. Normal growth (control) resulted in a mean closure of 8.8 degrees in the CRO angle, while the experimental group experienced an opening that averaged 2.8 degrees, thereby reversing the normal growth pattern (McNamara and Byran 1987). Anterior displacement of the mandible in this study demonstrated condylar remodeling posteriorly, which would offset the forward growth rotation observed in the control group and account for the increased length in the mandible. These findings may explain what may be happening clinically in growing children when functional appliances are used as the treatment modality (Meikle 2007).

<u>Condylar Cartilage</u>

Condylar cartilage is essential for growth of the condyle and its uniqueness is a source of debate in the literature (Meikle 2007). Prenatally, most synovial joints have formed well before the TMJ develops. This statement is supported in a fetal rat model using immunohistochemistry (Shibata *et al*. 1997). Since the condylar cartilage forms later, along with the rest of the TMJ, it is classified as a secondary cartilage. Shibata *et al*. (1997) asserts that their study supports previous research that condylar cartilage is derived from periosteum and has the potential to become either osteoblasts or chrondroblasts based on functional demands (Miekle 1973). Once the condylar cartilage is formed, it is still surrounded by these multipotent mesenchymal cells on the articular surfaces. Functional demands placed on the TMJ, both mechanical and positional, maintain the cartilage throughout life by causing the condylar cartilage to exhibit this multipotency (Rabie *et al*. 2003a; Shen and Darendeliler 2005). However, Miekle (2007) states that in the absence of functional activity, epiphyseal cartilage is also surrounded by multipotent cells.

Studies have shown that mandibular advancement by functional appliances causes remodeling of the condylar complex in humans (McNamara *et al*. 1985; Ruf and Pancherz 1998). McNamara *et al*. (1985) studied the cephalometric differences in 100 patients with a Class II malocclusion treated with the Fränkel (FR-2) functional regulator compared to a matched group of 41 untreated Class II controls from the University of Michigan Elementary and Secondary Growth Study. All groups were divided by age into two groups to see the effects that age itself had on Fränkel treatment. Fifty-one patients were

treated before 10.5 years of age and 49 patients were treated at or after 10.5 years of age. Two cephalometric analyses were performed on the lateral cephalgrams, a conventional (McNamara analysis) and a tensor analysis (McNamara *et al.* 1985). The tensor analysis uses cephalometric landmarks to construct triangles, for example, Sella, Nasion and Anterior Nasal Spine (ANS) form a triangle. The first triangle at one time point is compared to that triangle at a different time point by constructing a circle in the first triangle that touches the three sides of the triangle. The shape change from a circle to an ellipse needed to fit into the second triangle is statistically analyzed to search for differences in the two cephalograms of a growing individual. In the traditional analysis, both age ranges had statistically significant increases in mandibular length (Condylion to Gnathion), 8.0 mm for the older group and 6.4 mm for the younger group compared with 4.4 mm and 4.0 mm, respectively, for the control groups. In tensor analysis, Condylion can be visualized as growing an additional amount upward and backward in the treated groups, which is the conventional report of the effect of the FR-2 appliance (McNamara *et al.* 1985). That is, in order for the condyle to "grow" upward and backward, the whole TMJ complex must be remodeled to accommodate this treatment effect.

In order to further understand the changes at the TMJ complex during functional appliance therapy, Ruf and Pancherz (1998) conducted a Magnetic Resonance Imaging (MRI) study of the remodeling of the TMJ using the Herbst appliance. The first 15 subjects applying for treatment at the Department of Orthodontics at the University of Giessen in 1995 with a Class II malocclusion in the permanent dentition (4 girls and 15 boys) were selected for the study. All subjects were treated with a Herbst appliance. The mean age of the group was 13.5 years and average treatment time was 7 months. MRIs of the TMJs were taken at the following four stages: (T0) before Herbst treatment, (T1) when the appliance was placed, (T2) during Herbst treatment (6 to 12 weeks after appliance placement), and (T3) when the appliance was removed. Signs of condylar remodeling were seen at the posterior superior border in 29 of 30 condyles, while signs of glenoid fossa remodeling at the anterior surface of the postglenoid spine were seen in 22 joints. During remodeling of the TMJ, the condyle seems to remodel before the fossa. However, only visual inspection was used on the MRIs because a quantitative analysis was attempted but superimpositions of the MRI were deemed impossible due to changes in patient positioning at different treatment stages. Despite this technical problem, Ruf and Pancherz offer evidence that the condylar remodeling aids in the correction obtained by the Herbst appliance.

<u>Comparison of One- and Two-Phase Treatment</u>

For children with a Class II malocclusion, the optimal time for treatment is a topic of controversy in the literature (*e.g.*, Tulloch *et al.* 1997). The goals of "early" treatment are to correct existing or developing skeletal, dentoalveolar, and muscular imbalances before the eruption of permanent teeth is complete (McNamara and Brudon 1993). Presumably, this early intervention will reduce or eliminate future fixed appliance therapy, potentially reduce the incidence of premolar extraction, and reduce the need for surgical orthodontics along with correcting other dental problems, for example, reducing incisor protrusion (Dugoni 1998). Logically, it seems reasonable to correct an abnormality early rather than waiting until it is fully developed.

The Department of Orthodontics at the University of Pacific conducted a randomized retrospective study to evaluate changes in the early mixed dentition (Dugoni 2006). Subjects were chosen from patients who came for evaluation during the early to mid mixed dentition stage, which yielded the following three groups: (1) delayed full orthodontic treatment (*i.e.,* no early treatment), (2) phase 1 treatment only, and (3) full 2 phase treatment. All the patients are being treated by the same orthodontist and have complete records (lateral cephalogram, full mouth radiographs, study casts, intraoral and extraoral photographs). Preliminary analysis of 61 patients indicates that 42% of patients who had phase 1 treatment did not require a second phase of full banded appliances. Furthermore, patients who were treated with only one phase had fewer visits, shorter treatment times and lower orthodontic fees. Also, 82% of the early treatment patients did not require premolar extractions in the permanent dentition (Dugoni 2006).

Opponents to early or 2 phase treatment state there are few, if any, unique benefits to treatment at an earlier stage. Gianelly (1995) stated that when treatment is begun in the late mixed dentition, all treatment goals can be met in one phase of orthodontic treatment for at least 90% of patients. The remaining patients may benefit from "immediate resolution" of their problem, which includes those with crossbite and Class III malocclusion. Tulloch *et al.* (2004) performed a randomized clinical trial (RCT) of early (preadolescent) treatment with a functional appliance or headgear followed by full appliances versus treatment in one phase during the adolescent growth spurt with children who presented with a severe Class II malocclusion. A severe malocclusion was defined as an overjet of 7 mm or more. A total of 166 subjects with Class II division 1 malocclusions completed the phase I treatment and were randomly assigned to one of the following groups: (1) observation, (2) functional appliance, or (3) headgear. After 15 months of treatment, 145 of the subjects continued into phase 2 treatment, which consisted of being randomly assigned to

one of four orthodontists for full appliance therapy. Cephalometric radiographs were used to assess skeletal changes, while the peer assessment rating (PAR) was used to rate alignment and occlusion. Statistically significant changes were seen in the phase I treatment group compared to the observation group, but there was a wide variation in response. For example, the change in jaw relationship measured by the annual reduction in the ANB angle was favorable in 31% of the observation group, 83% of the functional appliance group, and 76% in the headgear group. After phase 2, treatment was evaluated to see if these initial changes were maintained long term. It appears that the initial corrections achieved during phase 1 disappeared almost completely by phase 2. With respect to skeletal relationship and PAR score at the end of phase 2, the results did not differ significantly between any of the groups. Also, early treatment seemed to be inefficient because it did not reduce the time in treatment in full appliances during the phase 2 interval and it did not reduce the complexity of the treatment (*i.e.,* need for extractions or orthognathic surgery).

<div align="center">Development of the Cervical Vertebrae</div>

O'Reilly and Yanniello (1988) studied the relationship of mandibular growth and the stages of the cervical vertebral maturation. The study was conducted using 13 Caucasian females from the Bolton-Brush Growth Center previously described by Tofani (1972). For each subject, annual lateral cephalometric radiographs had been taken between ages 9 and 15 years. Mandibular length (Articulare-Pogonion), corpus length (Gonion-Pogonion), and ramus height (Articulare-Gonion) were measured on each cephalometric radiograph to assess the changes in facial dimensions. The cervical vertebral stage was assigned based on Lamparski's (1972) standard for females and compared with the cephalometric measurements. The authors found significant increases in growth in all three measurements of mandibular growth at vertebral stages 1 and 2. Mandibular length had a maximum rate of growth during stages 3 and 4, while ramus height had the greatest rate in stage 3. Stages 2 and 3 occurred the year prior to peak velocity in for all three mandibular dimensions. Peak growth velocity occurred between stages 3 and 4 (O'Reilly and Yanniello 1988).

Hassel and Farman (1995) studied the relationship between the hand-wrist skeletal maturation index (SMI) developed by Fishman (1982) and the cervical vertebrae to develop a cervical vertebral maturation index, CVMI, from lateral cephalographs and hand-wrist radiographs from the Bolton-Brush Growth Center at Case Western Reserve University. The sample of 220 subjects was divided into groups of 10 males and 10 females based on their SMI. The morphological changes in the third cervical vertebrae (C3) were chosen as a

guide and compared across these 11 groups and they found six recognizable indicators (Figure 4). The six categories were defined as follows:

(1) Initiation: beginning of the adolescent growth spurt,
(2) Acceleration: growth acceleration beginning with between 65% and 85% of adolescent growth expected,
(3) Transition: adolescent growth continuing toward peak height velocity,
(4) Deceleration: growth past peak with 10 to 25% of adolescent growth remaining,
(5) Maturation: only 5 to 10% of adolescent growth remaining, and
(6) Completion: growth is considered complete.

The authors conclude by stating their study confirms what Lamparski (1972) found, namely that the cervical vertebrae are a dependable method of skeletal assessment to estimate maturational age in orthodontic patients.

Kucukkeles *et al.* (1999) conducted a study also testing whether the morphological changes in the cervical vertebrae can be used as a worthwhile skeletal maturity index. Lateral cephalograms and hand-wrist films of 180 untreated subjects, 99 girls and 81 boys, ages 8 to 18 years, were collected from Marmara University's department of orthodontics (Turkey). Skeletal maturity was assessed using the SMI developed by Fishman (1982) for hand-wrist radiographs. Cervical vertebrae, specifically the third (C3) and fourth (C4), were assessed using the six CVMI stages described by Hassel and Farman (1995). Both the SMI and CVMI groups were then divided into three growth groups: (1) pre-peak height velocity (SMI 1-4 and CVMI 1-2), (2) peak height velocity (SMI 5-8 and CVMI 3-4), and (3) post-peak height velocity (SMI 9-11 and CVMI 5-6). The authors found the reproducibility of SMI stages was greater than CVMI stages. They concluded that the cervical vertebrae provide a dependable method for growth assessment, and use of CVMI has the benefit of reducing radiation exposure to patients.

Franchi *et al.* (2000) looked at mandibular growth as a function of cervical vertebral maturation and also compared it to stature. Subjects (15 females and 9 males) from the University of Michigan Growth Study were evaluated using annual cephalograms and records of stature. These subjects had cephalograms available at all six stages of cervical vertebral maturation. To quantify mandibular growth, the following cephalometric measurements were used (1) mandibular size (Condylion-Gnathion, Condylion-Gonion, and Gonion-Gnathion) and (2) mandibular position (Sella-Gnathion, Sella-Gonion, Nasion-Menton, and ANS-Menton). Only 2 of the 24 subjects (2 females) showed a peak in statural height between stages 4 and 5. For all other subjects (93.5%), stature
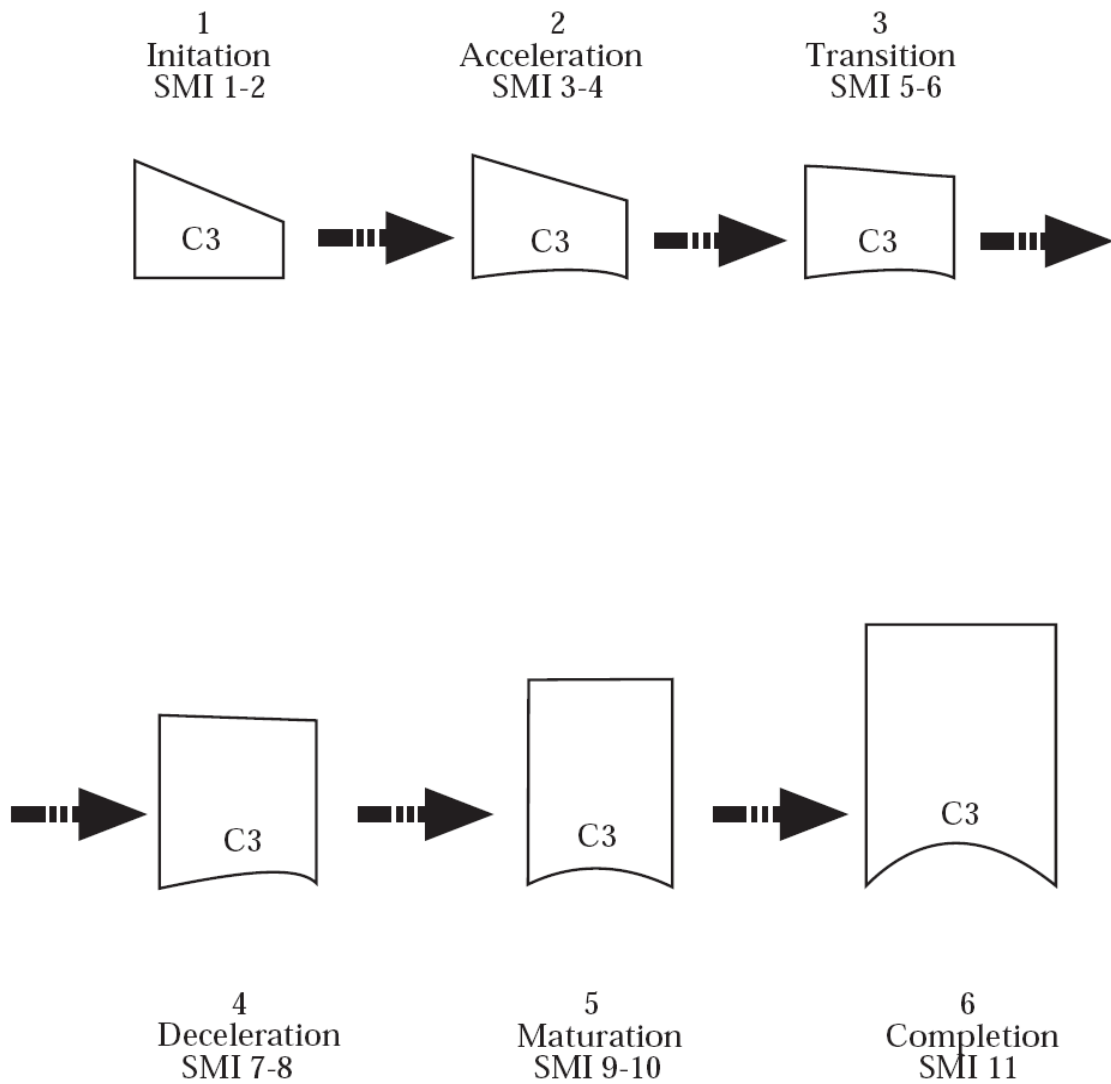
Figure 4. Six categories of morphological changes in cervical vertebrae 3.

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

and mandibular growth exhibited peak growth between stages 3 and 4. However, a wide chronological age range was found for the subjects when stage 3 in CVM was observed, with girls having an age range of 8 to 11 years and boys ranging from 10 to 14 years. The study supports the use of CVM as an accurate indicator of the peak in mandibular growth.

Baccetti *et al.* (2002) studied peak mandibular growth as a function of CVM stage based on analysis of the second through fourth cervical vertebrae. Subjects were chosen from the University of Michigan Elementary and Secondary School Growth Study who had two consecutive cephalograms before the peak of mandibular growth, two during the peak of mandibular growth, and two after the peak of mandibular growth. In other words, there were six consecutive cephalograms available for the subject and they encompassed peak mandibular growth. Using these criteria the study was limited to 30 subjects (18 boys and 12 girls). The morphology of the second through fourth cervical vertebrae (C2-C4) was visually identified and also measured on the six consecutive cephalograms (T1-T6). Specifically, the authors analyzed vertebral bodies for the presence of a cavity on the inferior border. The purpose of the study was to provide a version of the CVM method for the detection of the peak in mandibular growth based on C2-C4. Cephalometric measurements of the cervical vertebral bodies at each interval between the consecutive cephalograms were analyzed to identify morphological variables accounting for the differences between consecutive observations. Analysis of variance was performed to see whether the morphological changes were significantly associated with the rates of mandibular growth. The statistical analysis found no significant difference between the first two cephalometric radiographic observations (T1 and T2), which led the authors to state that the first two stages of Lamparski's six stages could not be discriminated, and they therefore combined the two. Now with a "new" method, Baccetti *et al.* (2002) found that concavities on the inferior borders of C2 and C3, coded as CVMS II, indicate the stage prior to the peak in mandibular growth, which is stage 3 in Lamparski's original scheme.

<u>Predicting Mandibular Growth Based on Skeletal Age</u>

Sato *et al.* studied 44 Japanese girls, with longitudinal cephalograms and hand-wrist radiographs, divided into two groups to determine a formula to predict final mandibular total length and clarify which skeletal maturation indicators is most accurate in predicting this length (2001). The first group of 22 was used to determine the formula and the second group was used to compare the predictive values with the actual values. Mandibular total length was measured from Condylion to Gnathion (Cd-Gn) and hand-wrist radiographs

were evaluated based on the Tanner-Whitehouse 2 (TW2) system of hand-wrist evaluation of bone ages. The mandibular total length was then predicted based on following five methods:

(1) The ossification events method, which determines mandibular growth potential by progression of ossification events of hand-wrist radiographs,
(2) The growth potential method, where growth potential of the mandible is determined by analysis of bone age based on hand-wrist radiographs using a linear equation,
(3) The growth percentage method, which determines relative mandibular total length as a percentage of final length based on bone age from hand-wrist radiographs,
(4) The multiple regression method, which predicts final mandibular total length by a multiple regression formula,
(5) The growth chart method, which the SD score ([value-mean]/SD) of present mandibular length at that skeletal age is consistent with the final mandibular length when growth has ceased.

The average error was calculated for each method between the predicted mandibular total length and the actual mandibular total length. The growth potential and the growth percentage method were the most accurate predictors of mandibular growth, with errors of 2.1 mm and 2.3 mm respectively.

In a similar study, Chen *et al.* (2004) attempted to establish a method to use the cervical vertebrae to predict mandibular length with a regression equation and then compare the accuracy of their equation with other available methods. The study consisted of 46 girls from Niigata University in Niigata, Japan. The girls met the following criteria: Class I or III molar, no systematic disease; hand-wrist and cephalometric radiographs that were taken between CVMS I and CVMS V based on Baccetti *et al.* (2002); and no orthodontic treatment that could affect mandibular growth. They were divided into two groups, one to construct the predictive equation and the other to compare to other methods. The cervical vertebrae were traced on the lateral cephalographs and measured with micrometer calipers. Articulare to Pogonion (Ar-Pg) was measured for mandibular length and mandibular length increment (MLI) was the differences in mandibular lengths between CVMS I through CVMS V. They selected six factors as independent variables and MLI as the dependent variable. The equation explained 61.3% of the variability (R^2) of the dependent variable. When the authors compared their equation to the growth potential and growth percentage method, which used the hand-wrist radiographs, the average error was higher in both methods than their equation (0.34 to 1.48 mm for the growth potential, and 0.34 to 1.50 mm for the growth percentage). The authors conclude

that this equation might be a useful method for predicting mandibular growth potential on the basis of one lateral cephalograph.

CHAPTER III
MATERIALS AND METHODS

Sample Description

Subjects in the present study were collected from a single private orthodontic practice office. The criteria for subject selection were (1) Angle's Class II buccal segment dental relationship at the start of treatment, (2) American Caucasian, with no selection for chronological age, (3) a functional appliance as part of treatment, either a MARA, a Fränkel, or a Bionator, and (4) availability of diagnostic pretreatment and posttreatment cephalometric radiographs. The Angle's Class II molar relationship was determined from analysis of the pretreatment cephalometric radiograph.

Cervical Vertebrae Maturation

The assessment of the CVM bone age were determined using Lamparski's six stage scheme as described in O'Reilly and Yanniello (1988). Cervical vertebral bodies are scored according to visually-assessed morphological criteria. The first cervical vertebra is not used in the scheme because it does not have a body. Lamparski's skeletal assessment system consists of six stages that can be applied to the second (C2) through the sixth (C6) vertebra:

Stage 1: All of the cervical vertebral bodies are flat and the superior borders taper from posterior (dorsally) to anterior (ventrally).
Stage 2: A concavity has developed on the inferior border of C2. C3 and C4 are trapezoid in shape, but the anterior height of the bodies has begun to increase.
Stage 3: A concavity is present on the inferior border of C3, but the inferior borders of the remaining vertebrae (C4-C6) are still flat.
Stage 4: Concavities are now present on C2 through C4. Concavities on C5 and C6 are beginning to form. All the bodies now have a rectangular shape.
Stage 5: Concavities are well defined on all the bodies and they are all nearly square in shape.
Stage 6: All bodies are now rectangular in a vertical direction and the concavities on the inferior borders have deepened (Figures 5-10).

The CVM stage was scored twice by the same examiner, with the second scoring session at least three weeks after the first and the examiner being blind to the first scores. Any differences between scoring were resolved with a third examination of the cervical vertebrae.

Figure 5. Sketches of morphological grade 1 of the cervical vertebrae. All inferior borders are flat. The superior borders all taper from dorsal (left) to ventral (right).
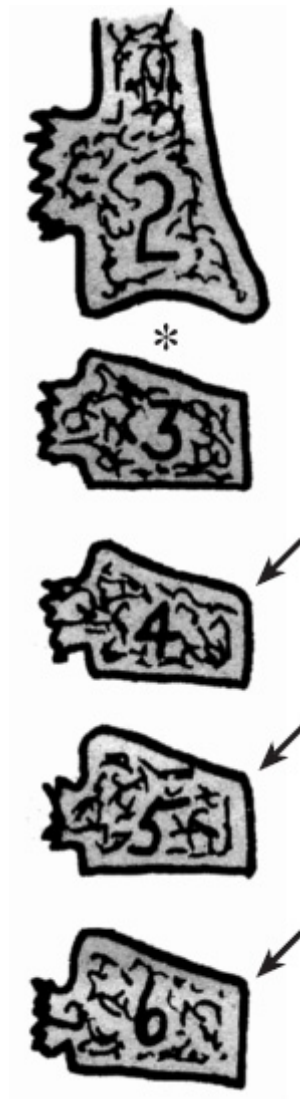
Figure 6. Sketches of morphological grade 2 of the cervical vertebrae. The concavity has developed in the inferior border of the second vertebra (*). The anterior vertical heights of the bodies have increased (arrows).

Figure 7. Sketches of morphological grade 3 of the cervical vertebrae. A concavity has developed in the inferior border of the third vertebra. The remaining borders are still flat.
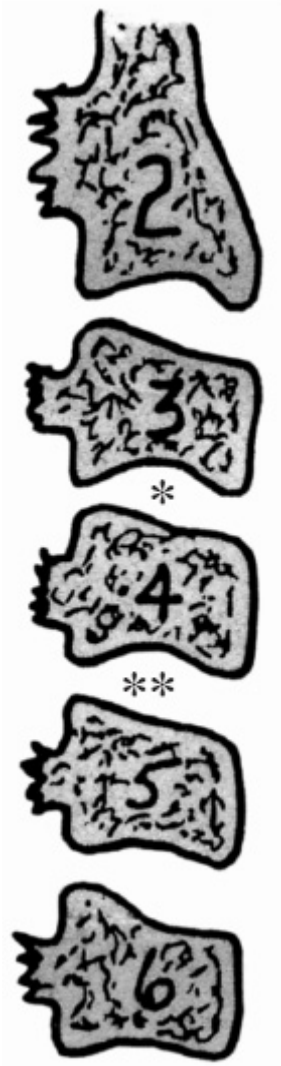
Figure 8. Sketches of morphological grade 4 of the cervical vertebrae. The concavity of the third vertebra has increased (*) and a definite concavity has formed on vertebra 4 (**). Concavities on 5 and 6 are just beginning to form. All bodies are now rectangular.

Figure 9. Sketches of morphological grade 5 of the cervical vertebrae. The spaces between bodies are visibly smaller. Concavities are now well defined on all six bodies. The bodies are now nearly square in shape.

Figure 10. Sketches of morphological grade 6 of the cervical vertebrae. All bodies have increased in vertical height and are higher than they are wide. All concavities have deepened.

Previous research by Chance (2006), showed a strong intercorrelation between cervical vertebrae, specifically C2, C3 and C4, even though there is a cranial-to-caudal gradient. This gradient results in cranial elements reaching maturity at an earlier chronological age. Chance (2006) showed correlation between C2 and C3 was 0.976, and between C3 and C4 was 0.982; therefore due to the considerable redundancy of information in the vertebrae, C3 was used as the maturity indicator in this study due to obstruction of more caudal vertebrae by a thyroid collar on many of the radiographs.

The amount of in-treatment craniofacial growth was determined for each pretreatment cervical vertebral assessment. Amounts of craniofacial growth were compared among cervical vertebral stage within each sex, as well as comparing differences in growth at each stage between sexes.

Facial Bony Growth

The pretreatment, progress, and posttreatment radiographs were scanned into a computer via a UMAX Powerlook III flatbed scanner at 300 dpi and 265 gray scale and were saved as TIFF files. Patients treated with the MARA appliance had two radiographs (pretreatment and posttreatment). A file for each subject was created in a commercial orthodontic imaging program, Dolphin Imaging® (version 10, Dolphin Imaging & Management Solutions, Chatsworth, CA). The radiographs in TIFF format were imported into the appropriate patient file and traced using the Dolphin® digital cephalometric tracing. Relevant landmarks were identified on the digitized radiographs, as well as additional hard and soft tissue landmarks to allow for traditional cephalometric analysis. The cephalometric landmarks used in the study are defined as follows:

A   Point A (Subspinale): the most posterior point on the exterior ventral curve of the maxilla between the anterior nasal spine and supradentale

B   Supramentale: the most posterior point on the bony curvature of the mandible between Infradentale and Pogonion.

Gn   Gnathion (anatomic): the most anterior-inferior point of the mandibular symphysis.

Go   Gonion (anatomic): the most posterior-inferior point on the gonial angle of the mandible.

Na   Nasion: the anterior point of the intersection between the nasal and frontal bones.

Se   Sella turcica: the center of the hypophyseal fossa, determined by inspection.

A custom analysis was created using the "custom analysis builder" function of Dolphin® Imaging 10.0 with the following cephalometric distances (1) Sella-Nasion, (2) Sella-A Point, (3) Sella-B Point, (4) Sella-Gnathion, (5) Sella-Gonion, and (6) AOBO. These dimensions can be related as follows:

(1) Se-Na is the growth of the anterior cranial base length,
(2) Se-A Point is maxillary growth,
(3) Se-B Point is mandibular growth,
(4) Se-Gn is a comprehensive measure of facial growth,
(5) Se-Go is the growth of posterior facial height (Figure 11),
(6) AOBO (Jacobson 2003) is a measure of treatment outcome (Figure 12).

Measurements were exported from Dolphin® into a spreadsheet in Microsoft® Excel 2003. The spreadsheet combined all necessary patient information including demographic information (patient's birth date, sex, treatment start date, progress date, treatment end date, and treatment time) and their cervical vertebral stage from each radiograph.

Statistical Analysis

The measurements were collated in the Microsoft® Excel spreadsheet then, transferred to the statistical package JMP® 5.0.2 (SAS Institute Inc., Cary, NC). Sample size (n), arithmetic mean ($\bar{x}$), standard deviation (sd) and standard error of the mean (sem) are the conventional descriptive statistics that are used in this study (Sokal and Rohlf, 1995). A factorial analysis of variance (ANOVA) was used for the inferential statistics (Ott and Longnecker 2000).

The prime analytical questions explored in this study were (1) whether the amounts of facial growth differed significantly by the cervical vertebral maturation stage within each sex, (2) if the CVM stage when functional appliance therapy is initiated significantly affects outcome of treatment, and (3) did the CVM stage predict how well posttreatment profile met desired cephalometric values? These questions were tested in the ANOVA model using the CVM stages as "treatments" and amounts of facial growth for one of the 6 dimensions as the dependent variable. The ANOVA model was used to explore how facial growth was affected by the following factors: subject's skeletal age at start of treatment, duration of treatment, and subject's sex.

Several of the data in this study are graphed because it is so helpful to visualize the distributions. A word, then, is helpful in interpreting the boxplots that are commonly encountered. A box plot (also known as a stem-and-whisker plot) is a graphic device to help show the distribution of cases. Typically, more
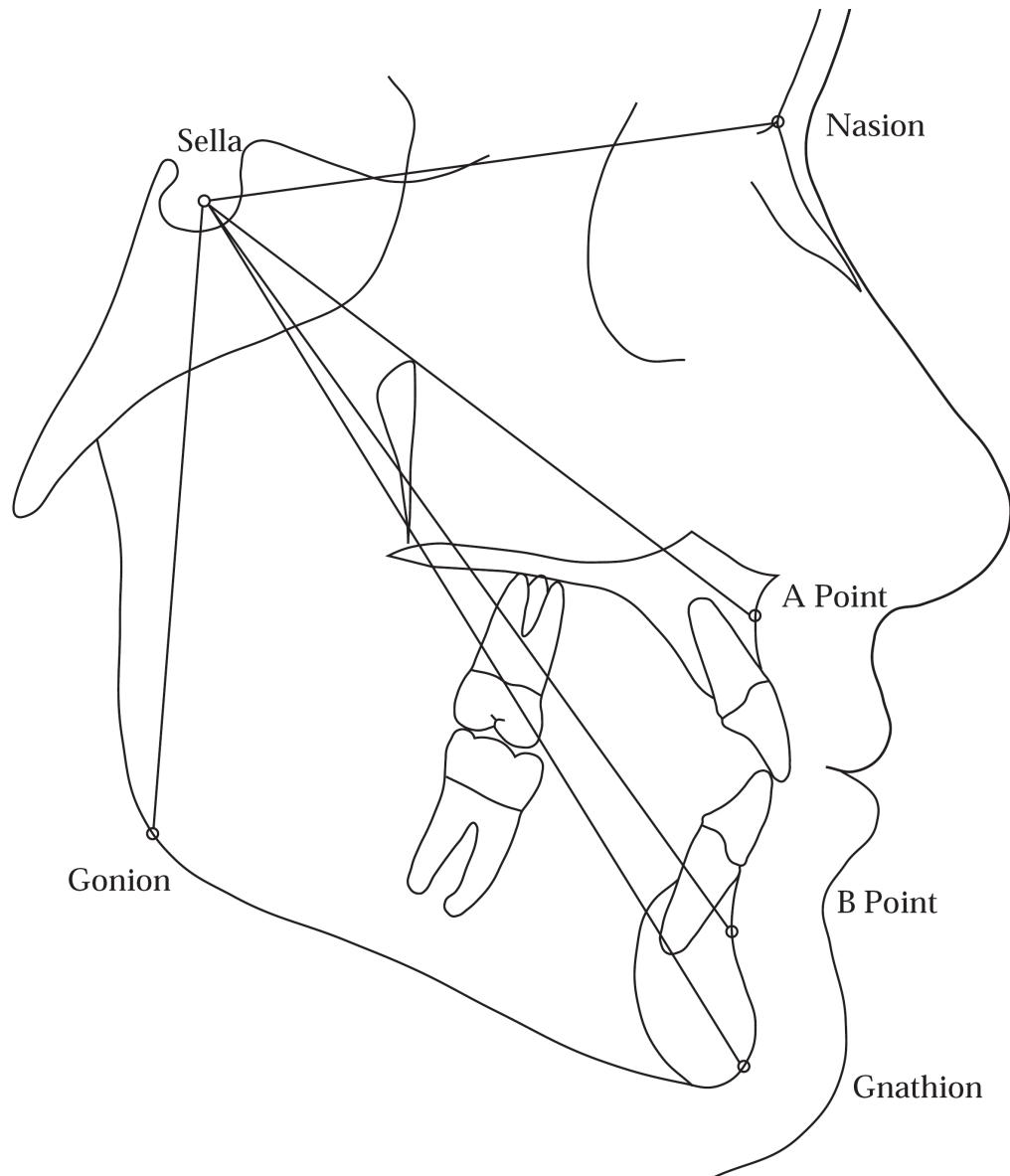
Figure 11. Illustration of the six cephalometric landmarks and five of the six cephalometric measurements used in the study.
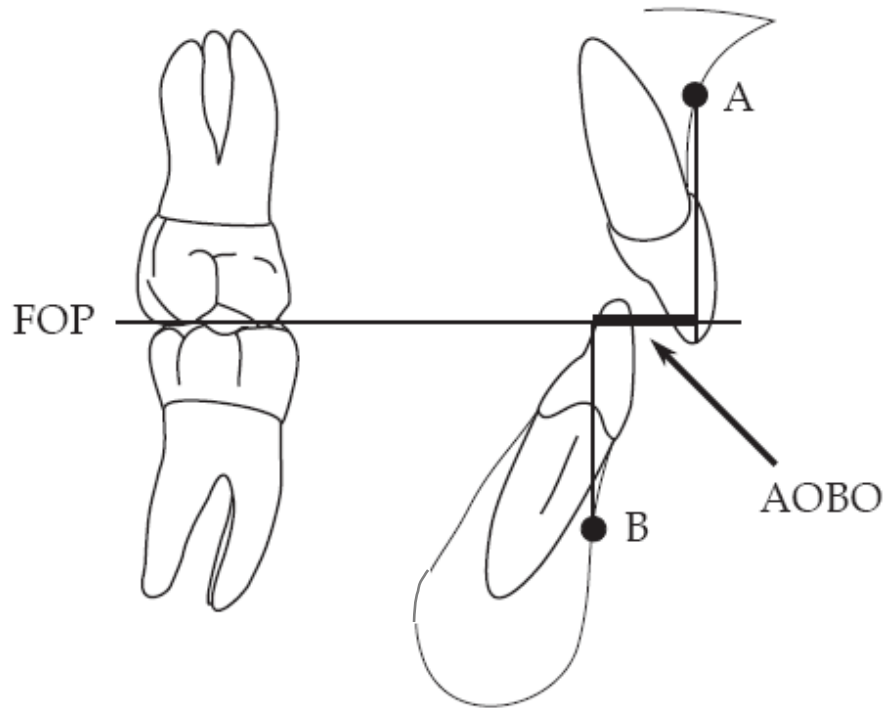
Figure 12. Schematic of the method of measuring the AOBO discrepancy.

than one box plot is shown in a plot to emphasize the relationships between groups. A simple example is shown in Figure 13, where the distribution of the amounts of growth (Sella-Gnathion distance) are plotted separately for boys and girls. Each symbol (dot) is the value for one case, though identical cases may be superimposed. To guard against cases being plotted atop one another, the software offers an option for the symbols to be "jittered," which offsets them a bit to the left and right.

There is a rectangular box laid over the distribution of cases, where the top of the box is the 75th percentile and the bottom in the 25th percentile. In other words, the box vertically spans the interquartile distance of the distribution of cases (i.e., 50% of the cases in that group). The horizontal line near the middle of the box is the median (50th percentile), which is the midpoint of the series when they are arranged from smallest to largest. The upper and lower "whiskers" of the plot are vertical line segments that terminate in horizontal lines. These horizontal markers denote the 10th and 90th percentiles of the distribution, and they will only be equidistant from the median of the distribution is perfectly symmetrical. Some symbols (cases) may occur beyond the ends of the whiskers. These may be statistical outliers if they are far enough from the rest of the sample. On the other hand, one should expect that approximately 10% of the sample will be above the top whisker and another below the bottom marker, depending on the nature of the dispersion.

Notice the differences between the box plots for males and females in Figure 13. The distribution (and the median) is higher for boys in this chart because boys experienced more growth (as measured here). Notice too that boys exhibited greater variability here than girls; both the minimum and maximum cases observed were in the male plot. Box plots, by themselves, do not determine whether there is a statistically significant difference between the groups, though, of course, the greater the chance that an inferential test will discover a significant difference.
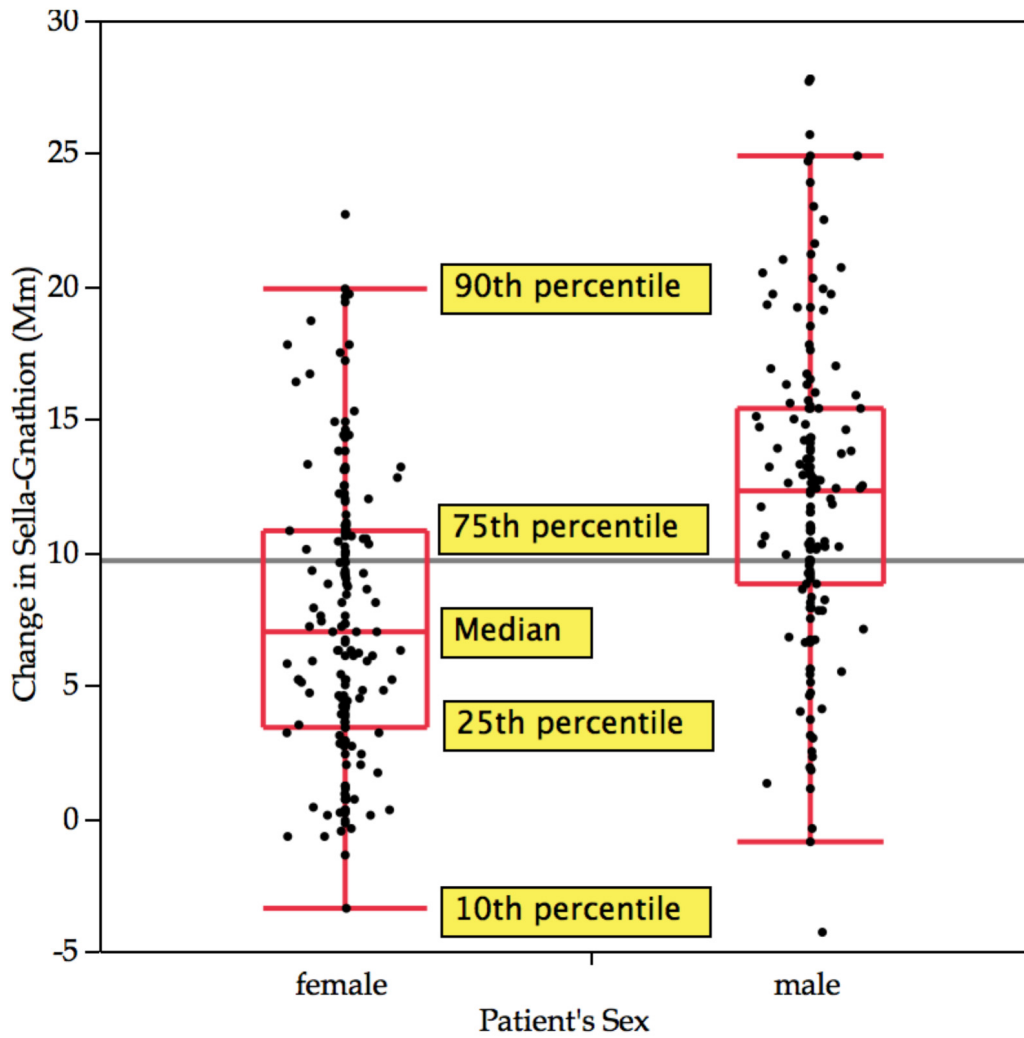
Figure 13. Box plots of the change in Sella-Gnathion (mm) for females and males to illustrate the features of this graphical device for displaying distributions.

CHAPTER IV
RESULTS

CVM Stages

The CVM stages are a means of estimating a person's physiological age. As discussed in prior chapters, the CVM stages estimate where a subject is along his or her somatic growth curve. In turn, then, the CVM stage should be usable as an estimate of a person's developmental status, as a measure of his growth rate and his growth potential. As such, CVM stages should aggregate cases by their stage of biological maturity. One measure of this is shown in Figure 14, where the age at the start of treatment is aggregated by CVM stage (sexes pooled). It is evident that the median ages (the horizontal midpoint of the boxplots) increase across the 6 CVM stages. This trend is confirmed statistically in Table 1, which shows the results of a one-way ANOVA testing for the differences in average chronological age among the six CVM stages. Results are highly significant statistically, and inspection of Figure 14 shows that (A) there is a monotonic increase in mean ages from CVM 1 through 6 and (B) the large jump from stages 5 to 6 is due to CVM stage 6 being the terminal stage, so all subjects who have matured beyond stage 5 are in this category of biological "adulthood."

The mean age at each CVM stage is listed at the bottom of Table 1. Differences among stages are somewhat less than a year starting around 10 years of age and progressing to about 13 years of age for CVM 5. Again, CVM 6 is a "catch-all" category that encompasses everyone over the age of roughly 14, the median age at each CVM stage might better be estimated using survival analysis (*e.g.*, Faulkner and Harris, 2004), but these averages are close enough for present purposes. One can see, in passing, that the ages at CVM 1 and 6 are easily distorted depending on the ages sampled: All cases developmentally younger than CVM 2 are scored as CVM 1, and comparably, all cases developmentally beyond CVM 5 are lumped in stage 6 where vertebral morphology is mature.

Sexual Dimorphism

It is well-known that girls develop faster than boys and tend to reach markers of biological maturity sooner than their male counterparts (Tanner 1962; Greulich and Pyle 1959). This is shown for the six CVM stages in Figures 15 through 20. These six graphs display box plots for median age of attainment, by sex, for the six CVM stages. Table 2 supports these visual impressions with an ANOVA test for mean differences in chronological age between boys and girls for each stage.
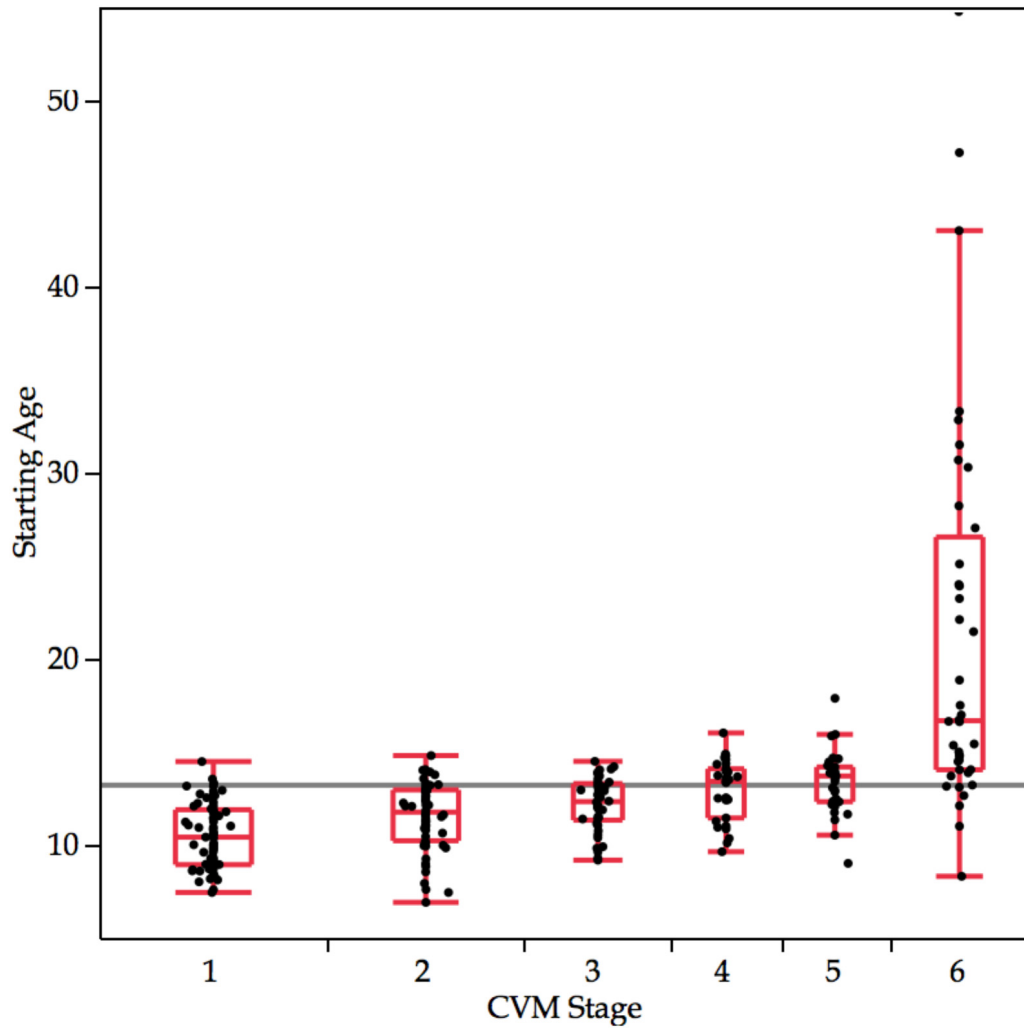
Figure 14. Box plots of CVM stages 1-6.

Table 1. Results of ANOVA testing for a difference between mean chronological ages sorted by CVM stage (sexes pooled).

Source	df	Mean Square	F Ratio	P Value
CVM Stage	4	17.8045	6.3134[1]	0.0002
Error	77	2.8201		
Total	81			

Level	Number	Mean	Sem	L_1	L_2
1	42	9.9466	0.25912	9.431	10.463
2	16	9.9091	0.41983	9.073	10.745
3	13	11.1841	0.46576	10.257	12.112
4	7	12.2042	0.63472	10.940	13.468
5	4	13.0684	0.83966	11.396	14.740
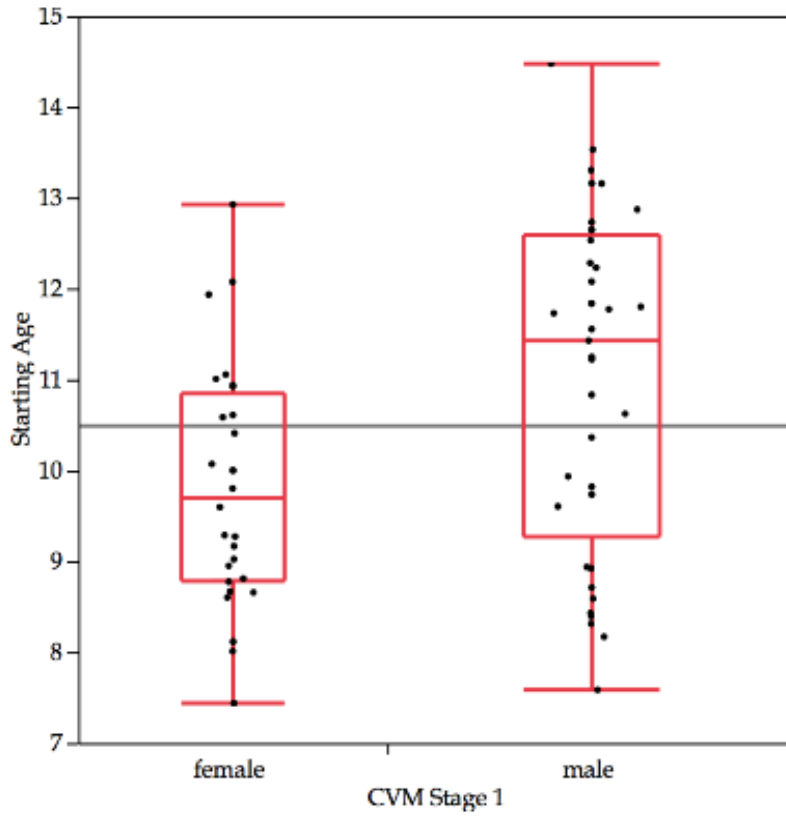
Figure 15. Box plot for CVM Stage 1.
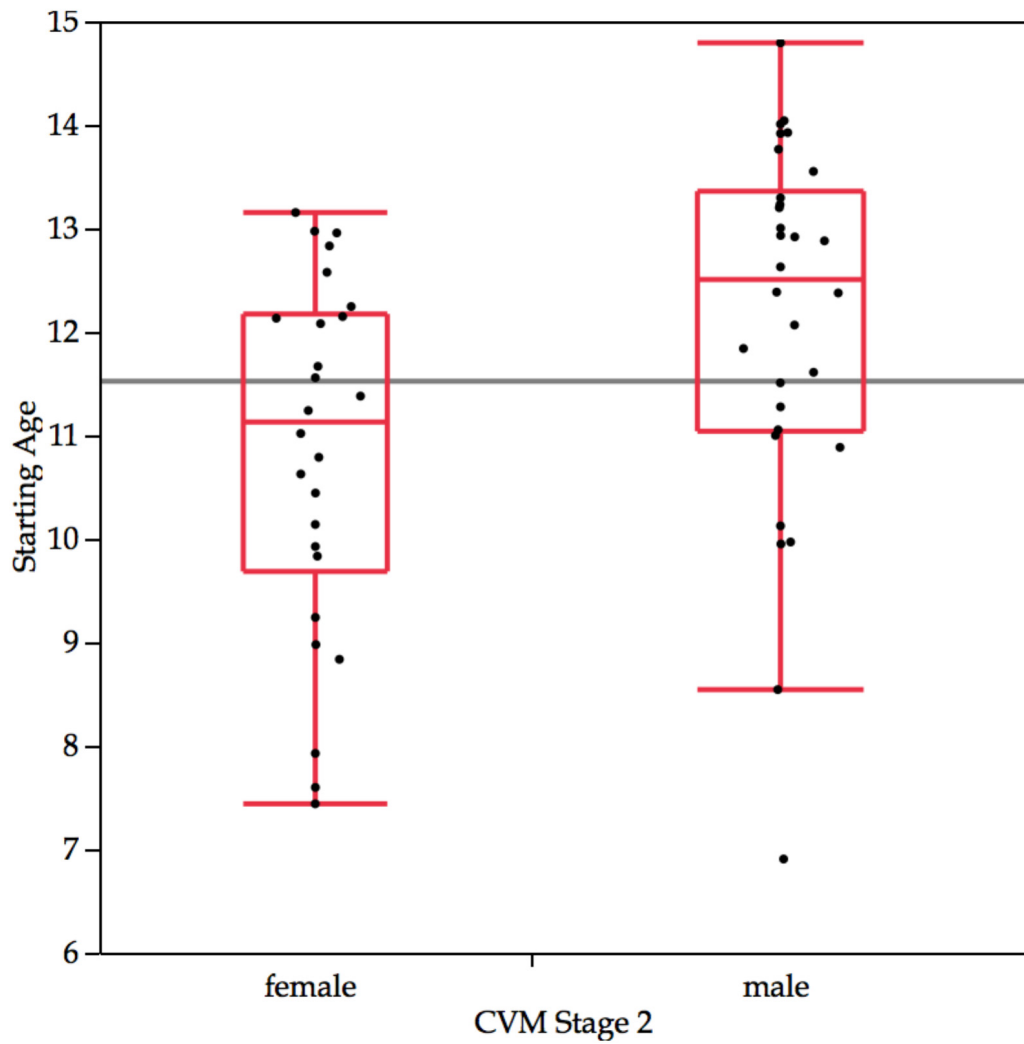
Figure 16. Box plots of pretreatment age for females and males at CVM stage 2.
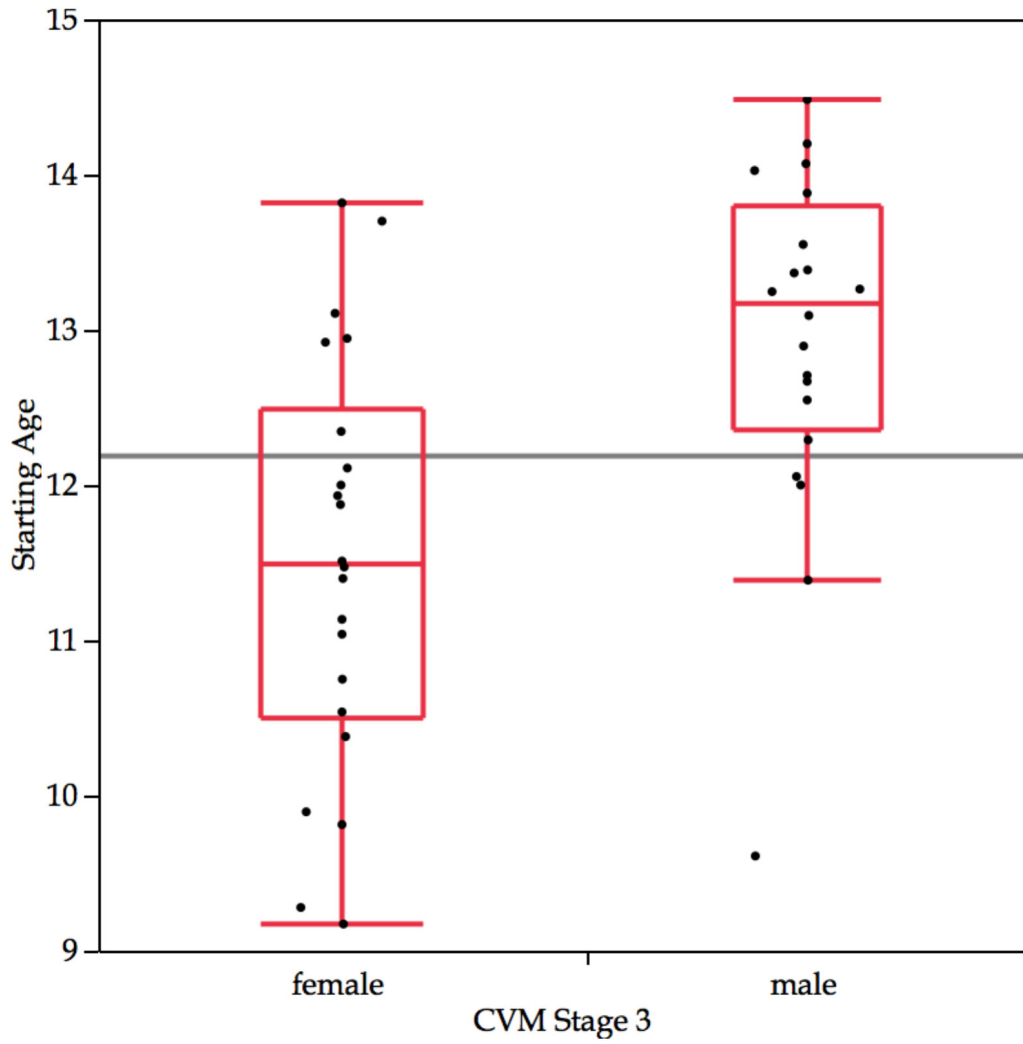
Figure 17. Box plots of pretreatment age for females and males at CVM stage 3.
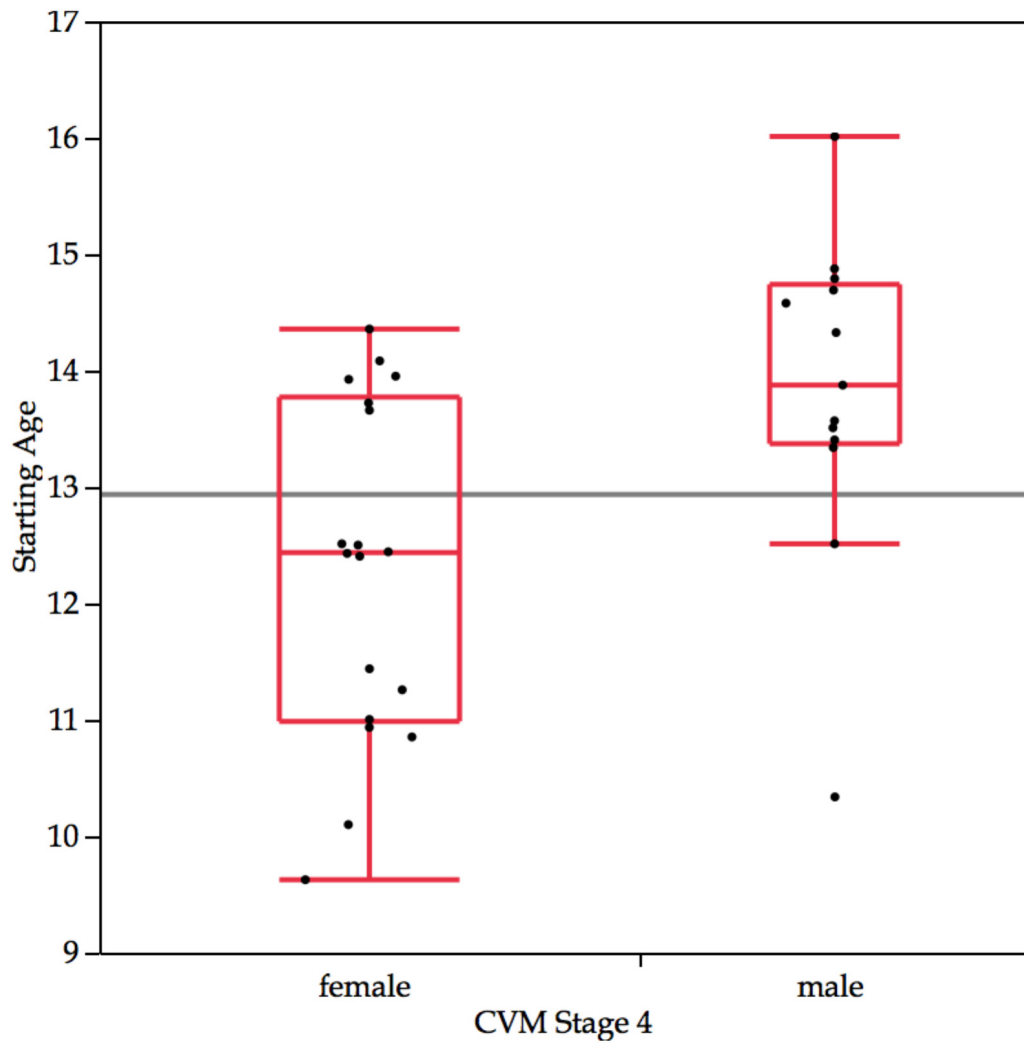
Figure 18. Box plots of pretreatment age for females and males at CVM stage 4.
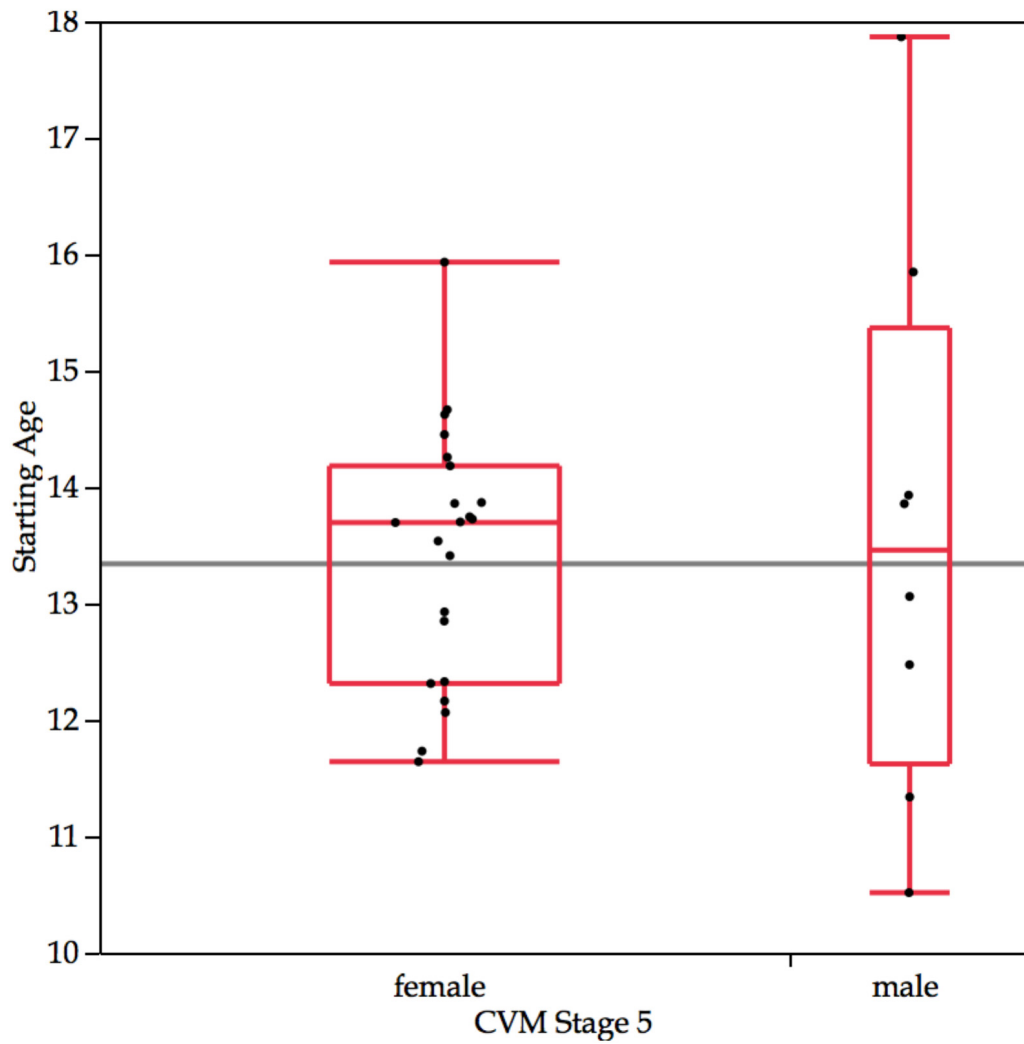
Figure 19. Box plots of pretreatment age for females and males at CVM stage 5.
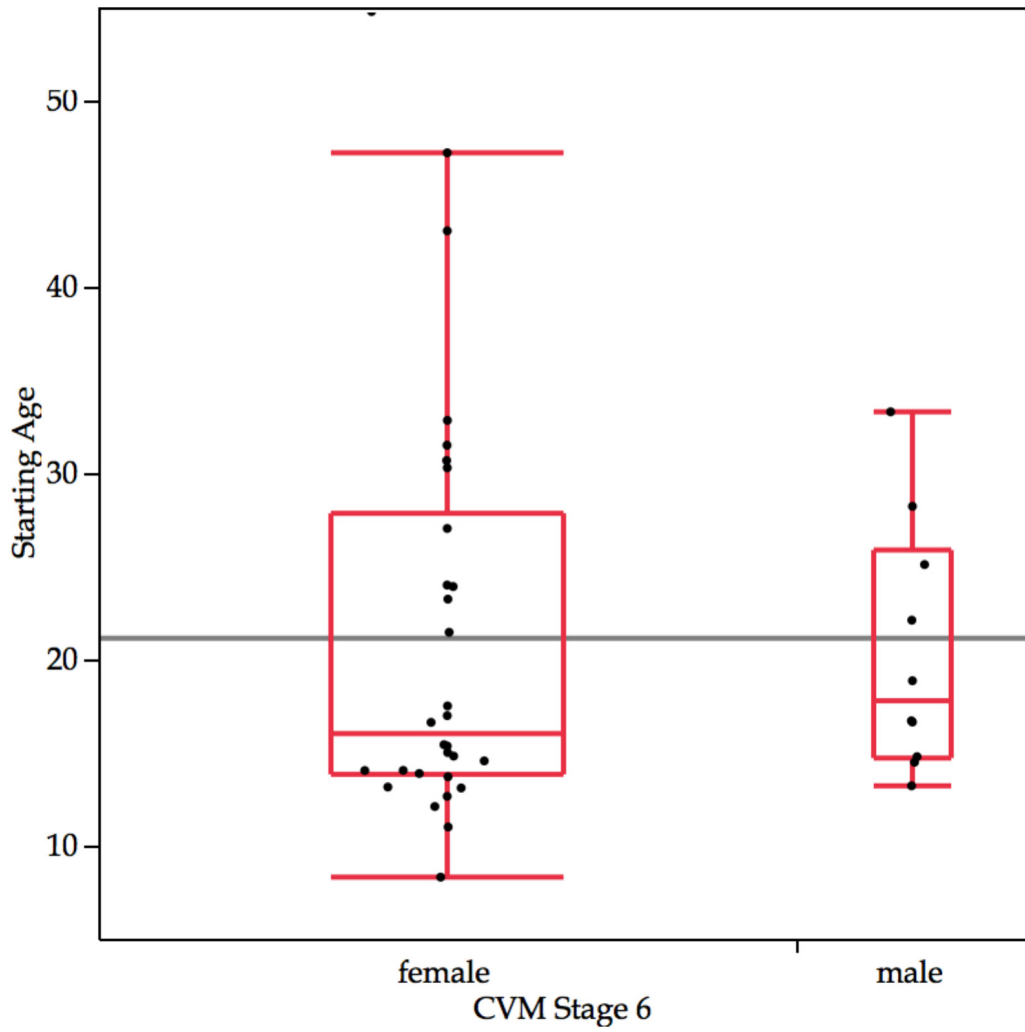
Figure 20. Box plots of pretreatment age for females and males at CVM stage 6.

Table 2. Descriptive Statistics by sex and CVM stage and tests for sexual dimorphism.

Stage	Median Age	L_1	L_2
	Girls		
1	9.80	9.17	10.56
2	11.38	10.64	12.00
3	12.49	12.00	12.93
4	14.13	13.66	14.37
5	14.73	14.26	15.33
	Boys		
1	11.22	9.93	11.77
2	12.76	12.35	13.20
3	13.44	13.16	13.83
4	14.76	14.56	15.31
5	15.65	15.43	16.41

CVM is achieved in girls more than a year ahead of boys (Table 2), but, as noted, these averages are easily manipulated by sample selection. On the other hand, these ages actually are the chronological ages at the start of orthodontic treatment, which probably reflects the earlier eruption of the permanent dentition in girls compared to boys (*e.g.*, Hurme 1949). The mean difference for CVM 2 is 1.3 years, meaning that the average girl achieves CVM 2 well over a year ahead of the typical boy (Table 2), and this difference is highly significant statistically. Comparably, CVM stage 3 is attained an average of 1.4 years earlier in girls than boys (P < 0.001). The difference between means is likewise highly significant at CVM 4, where the average girl is 1.5 years ahead of the average boy.

The average age at CVM 4 is 12.3 years of age for girls and 13.8 years for boys, which is appreciably into the adolescent growth spurt for both sexes (*e.g.*, Marshall and Tanner 1969, 1970). Interestingly, this seems to be the end of the precedence in CVM stages because CVM 5 exhibits no difference by sex. While males are roughly one-half year behind females, the difference is nonsignificant (P = 0.60). Inspection shows that this overlapping of the two sexes is due to enhanced variability in each sex (as indicated, *e.g.*, by the larger standard errors for CVM stages 5 and 6). The results to here show that the morphological CVM stages are ordered and are achieved at progressively older ages, though generally earlier in girls than boys. What is not tested here is whether the tempo (rate) of growth differs by CVM stage.

Cephalometric Changes

Of course, the impetus for inspecting CVM stages is the expectation that they will help us anticipate the extents of facial growth during treatment (*e.g.*, O'Reilly and Yaniello 1988). At the least, knowing a patient's CVM at the start of treatment should provide a better (read "more narrow, more specific") estimate of the amounts of in-treatment change compared to not knowing the CVM stage.

One simple test of this is that the extents of facial growth need to differ by CVM stage, and this should be true for sexes pooled, but the more so when boys' and girls' growth patterns are distinguished. Figures 21 through 25 provide coarse measures of this expectation: In each instance, the greatest treatment changes occur for the earliest CVM stages, and the average amounts decrement systematically to CVM 6, where growth is the least. These trends are, however, confounded by pooling the sexes.

Tables 3 through 7 provide the statistical results of testing each of the five cephalometric dimensions for a difference among CVM stages while controlling for patient's sex (*i.e.*, a series of two-way factorial ANOVA). To complement
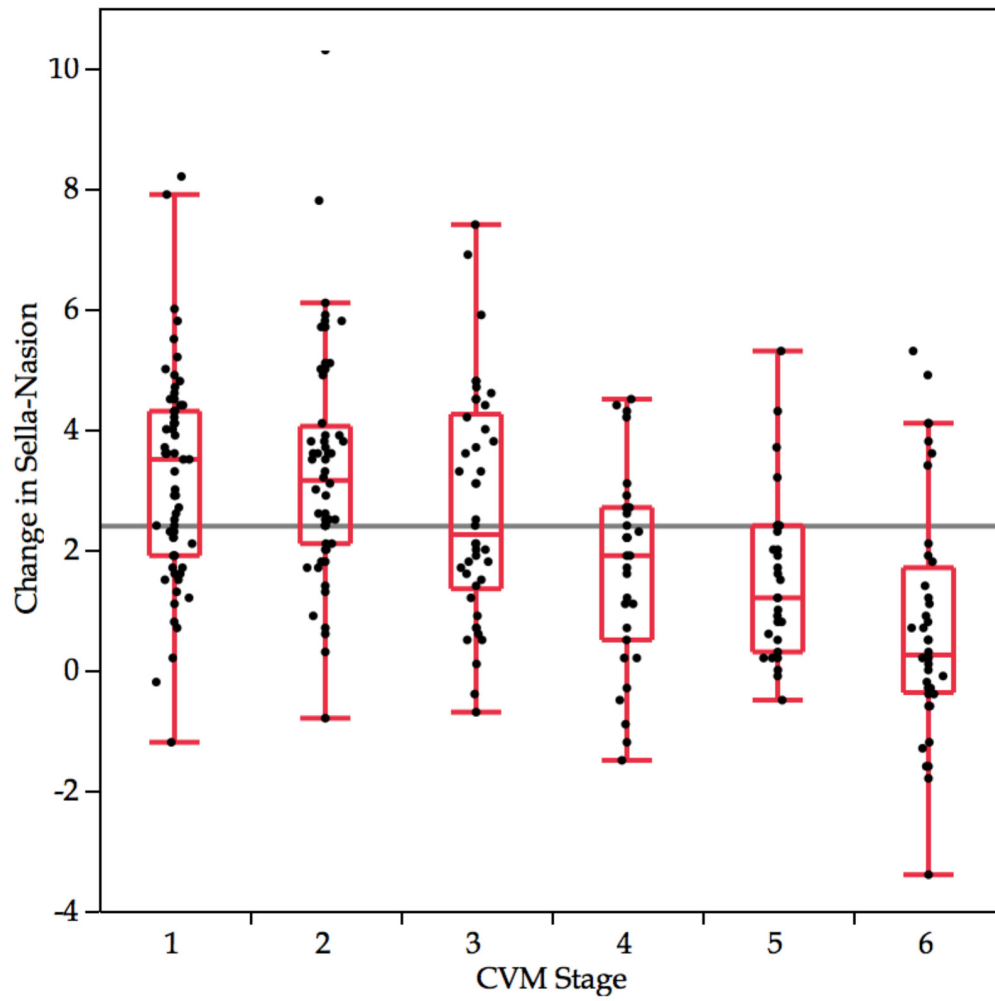
Figure 21. Box plots of change in Sella-Nasion for CVM stages 1 through 6.
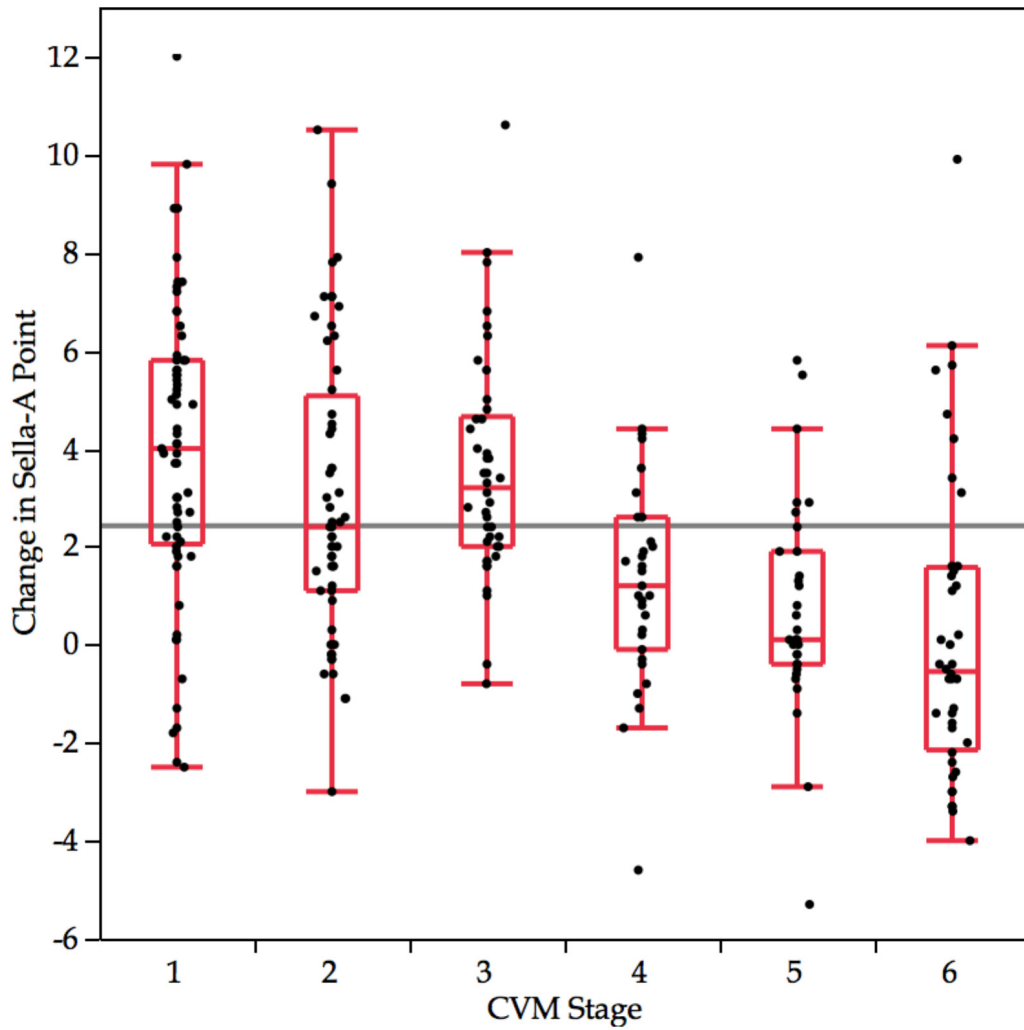
Figure 22. Box plots of the change in Sella-A Point for CVM stages 1 through 6.
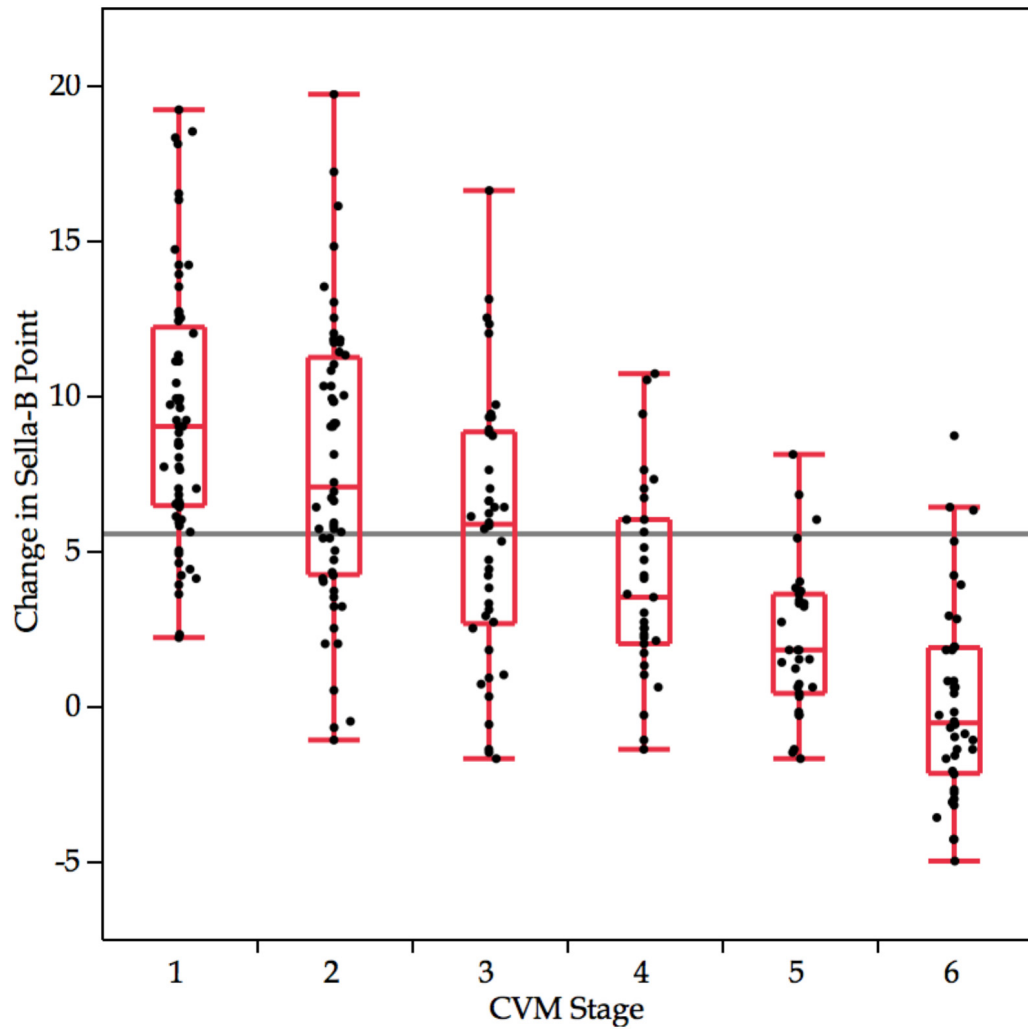
Figure 23. Box plots of the change in Sella-B Point for CVM stages 1 through 6.
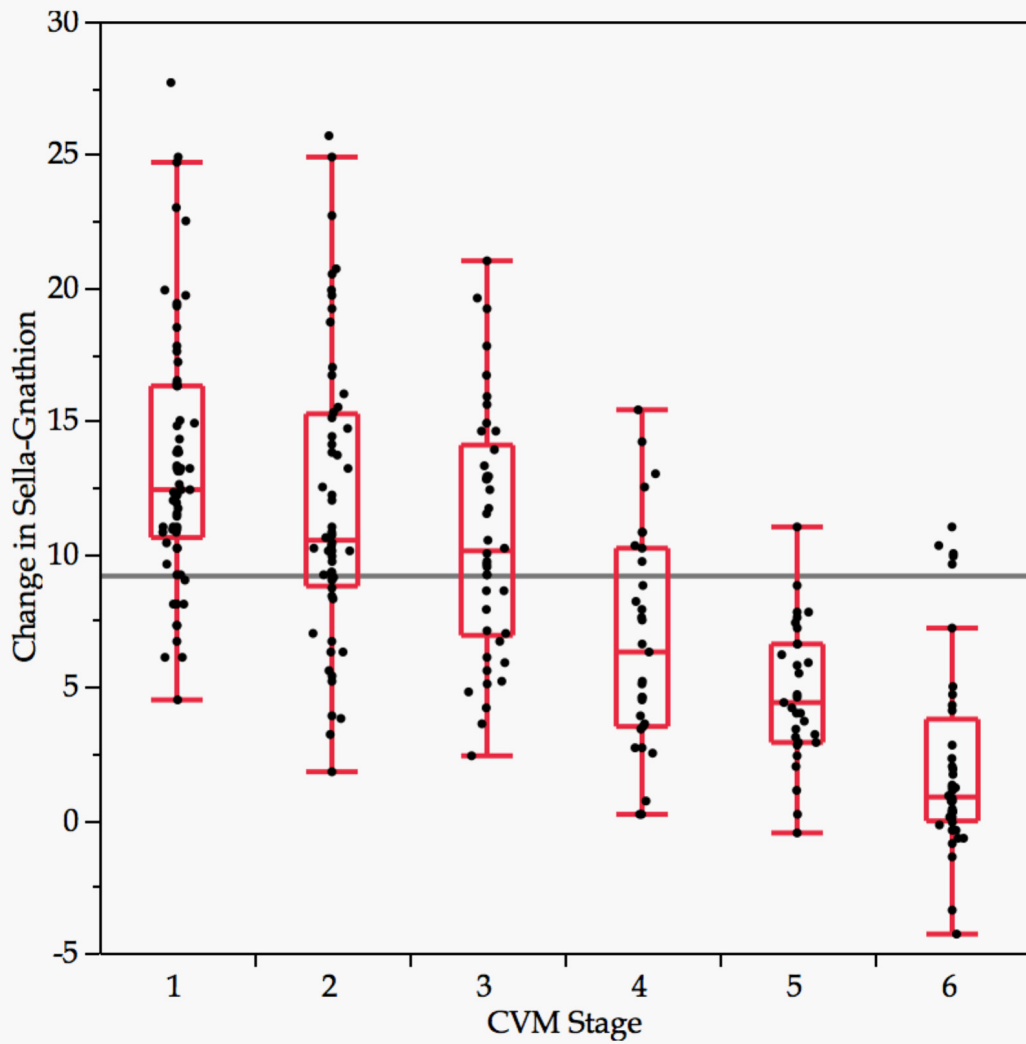
Figure 24. Box plots of the change in Sella-Gnathion for CVM stages 1 through 6.
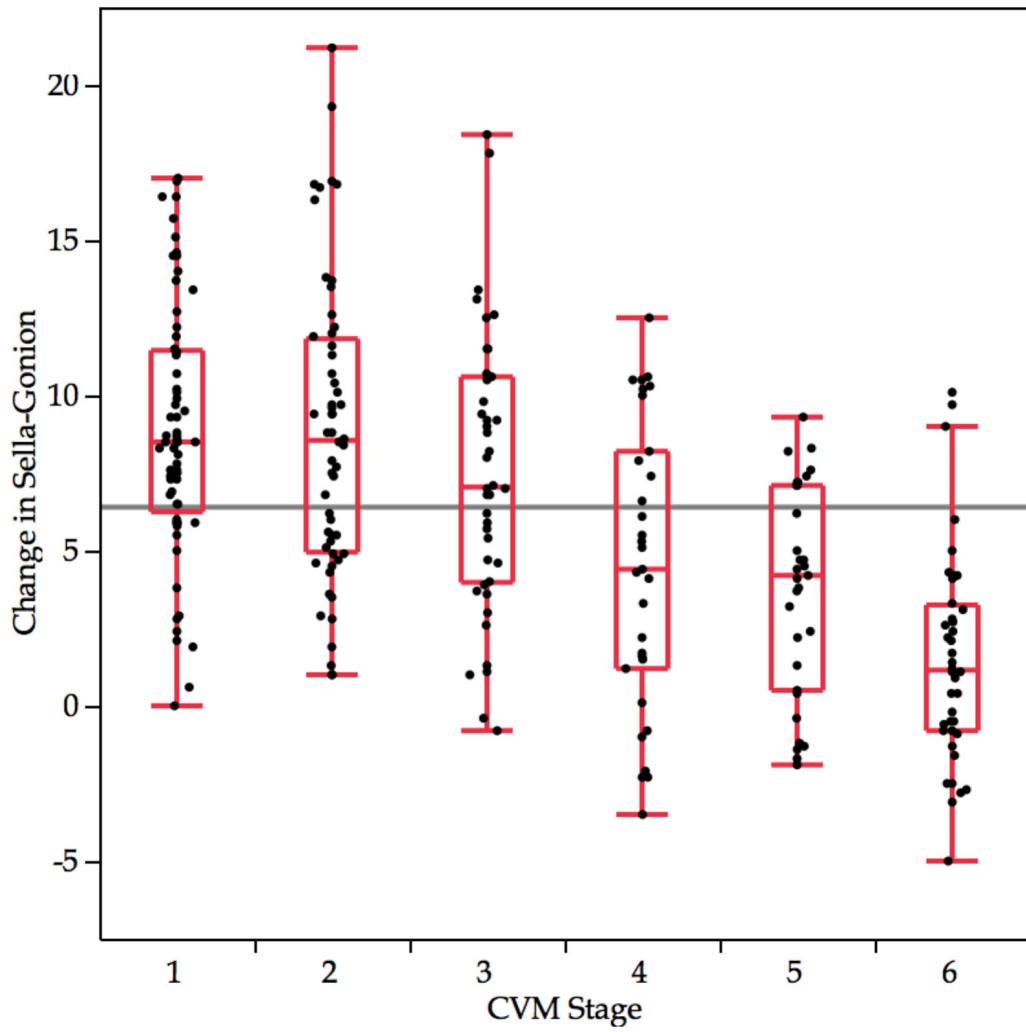
Figure 25. Box plots of the change in Sella-Gonion for CVM stages 1 through 6.

Table 3. Two-way ANOVA results for the change in Sella-Nasion.[1]

Source	df	Sum of SSQ	F Ratio	P Value
CVM Stage	5	168.55	11.21	< 0.0001
Sex	1	73.50	24.44	< 0.0001
CVM-x-Sex	5	6.92	0.46	0.8058

[1]Associated table of least squares means:

	Males			Females	
Stage	LS Mean	St Error	Stage	LS Mean	St Error
1	3.751	0.285	1	2.500	0.328
2	3.750	0.317	2	2.846	0.340
3	3.420	0.388	3	2.050	0.370
4	2.777	0.481	4	0.917	0.409
5	1.913	0.613	5	1.174	0.362
6	1.390	0.548	6	0.527	0.317

Table 4. Two-way ANOVA results for the change in Sella-A Point.[1]

Source	df	Sum of SSQ	F Ratio	P Value
CVM Stage	5	396.61	10.85	< 0.0001
Sex	1	62.80	8.59	0.0037
CVM-x-Sex	5	15.61	0.43	0.8297

[1]Associated table of least squares means:

	Males			Females		
Stage	LS Mean	St Error		Stage	LS Mean	St Error
1	4.616	0.445		1	2.964	0.511
2	3.293	0.494		2	2.650	0.530
3	4.080	0.605		3	3.050	0.576
4	2.415	0.750		4	0.539	0.637
5	1.275	0.956		5	0.548	0.564
6	0.600	0.855		6	0.070	0.494

Table 5. Two-way ANOVA results for the change in Sella-B Point.[1]

Source	df	Sum of SSQ	F Ratio	P Value
CVM Stage	5	2027.43	28.78	< 0.0001
Sex	1	176.09	12.50	0.0005
CVM-x-Sex	5	58.13	0.83	0.5328

[1]Associated table of least squares means:

	Males			Females		
Stage	LS Mean	St Error	Stage	LS Mean	St Error
1	10.395	0.617	1	7.896	0.709
2	7.973	0.685	2	7.438	0.736
3	6.520	0.839	3	4.859	0.800
4	5.462	1.041	4	2.894	0.885
5	2.450	1.327	5	1.996	0.783
6	2.410	1.187	6	-0.690	0.685

Table 6. Two-way ANOVA results for the change in Sella-Gnathion.[1]

Source	df	Sum of SSQ	F Ratio	P Value
CVM Stage	5	3390.06	36.50	< 0.0001
Sex	1	362.10	19.49	< 0.0001
CVM-x-Sex	5	70.54	0.76	0.5797

[1]Associated table of least squares means:

	Males			Females		
Stage	LS Mean	St Error	Stage	LS Mean	St Error
1	14.857	0.709	1	11.382	0.814
2	13.093	0.787	2	10.573	0.845
3	12.335	0.964	3	9.277	0.919
4	9.246	1.195	4	4.833	1.016
5	5.388	1.524	5	4.530	0.899
6	3.000	1.363	6	1.813	0.787

Table 7. Two-way ANOVA results for the change in Sella-Gonion.[1]

Source	df	Sum of SSQ	F Ratio	P Value
CVM Stage	5	1406.25	18.19	< 0.0001
Sex	1	425.82	27.55	< 0.0001
CVM-x-Sex	5	123.76	1.60	0.1602

[1]Associated table of least squares means:

	Males			Females	
Stage	LS Mean	St Error	Stage	LS Mean	St Error
1	10.278	0.646	1	6.936	0.743
2	9.857	0.718	2	7.492	0.771
3	9.095	0.879	3	6.050	0.838
4	7.792	1.090	4	2.100	0.927
5	3.625	1.390	5	3.817	0.820
6	3.430	1.243	6	0.863	0.718

these, Figures 26 through 30 graph these results. What is obvious is that each of the five tests shows both a highly significant inter-stage difference and a highly significant between-sex difference.

One should not, however, be uncritically accepting of these results because they do not control for the duration of treatment. That is, one simple way of "gaining" more growth is to treat for a longer interval of time; with longer treatment, the child has more time to grow.

Orthodontic Treatments

The present research evaluated CVM stages in four groups of patients, distinguished by their treatment modalities. There were a total of 316 cases: (1) 50 were treated with a combination of Bionator appliance and Edgewise mechanics; (2) 34 were treated with a Fränkel appliance and then finshed with Edgewise mechanics; (3) 49 were treated with a MARA and Edgewise appliances; and (4) 183 were treated with standard Edgewise appliances alone. The intent of including all four groups was to span the preadolescent and adolescent ages when the cervical vertebrae are growing and changing their morphologies and, thus, are practical for estimating a person's physiological age. On the other hand, these four treatment modalities are not used for patients of the same ages. The Bionator and Fränkel are most appropriate for cases in the mixed dentition, while the MARA and the Edgewise appliance alone are better suited for the (early) permanent dentition. Consequently, each of the four treatments does not involve all CVM stages.

The differences in the chronological ages among the treatments are shown in Figure 31, where ages at the start of treatment are graphed. Mean ages are 10.0 years for the Bionator sample, 9.0 years for the Fränkel sample, 12.6 years for the MARA sample, and 14.4 years for this Edgewise sample. Not surprisingly, these differences among groups are highly significant statistically. A two-way ANOVA was used to test for group and sex differences at the start of treatment, and the inter-group difference was $F = 18.8$ ($P < 0.0001$), whereas the difference between sexes was trivial ($F = 0.0$; $P = 0.9406$).

In prior work (Chance 2006), a sample of cases treated with Edgewise mechanics was studied, and there was no association between the patient's chronological age or their CVM stage and the duration of treatment. On the other hand, this was a homogeneous treatment, where all cases were started after attainment of the full permanent dentition (discounting third molars). The situation is different here, primarily because regardless of how early a case might be started, it is required for that patient to remain in treatment until the full

Figure 26. Plot of the mean changes in Sella-Nasion, by sex, across the six CVM stages. Error bars are ± one standard error of the mean.

Figure 27. Plot of the mean changes in Sella-A Point, by sex, across the six CVM stages. Error bars are ± one standard error of the mean.

Figure 28. Plot of the mean changes in Sella-B Point, by sex, across the six CVM stages. Error bars are ± one standard error of the mean.
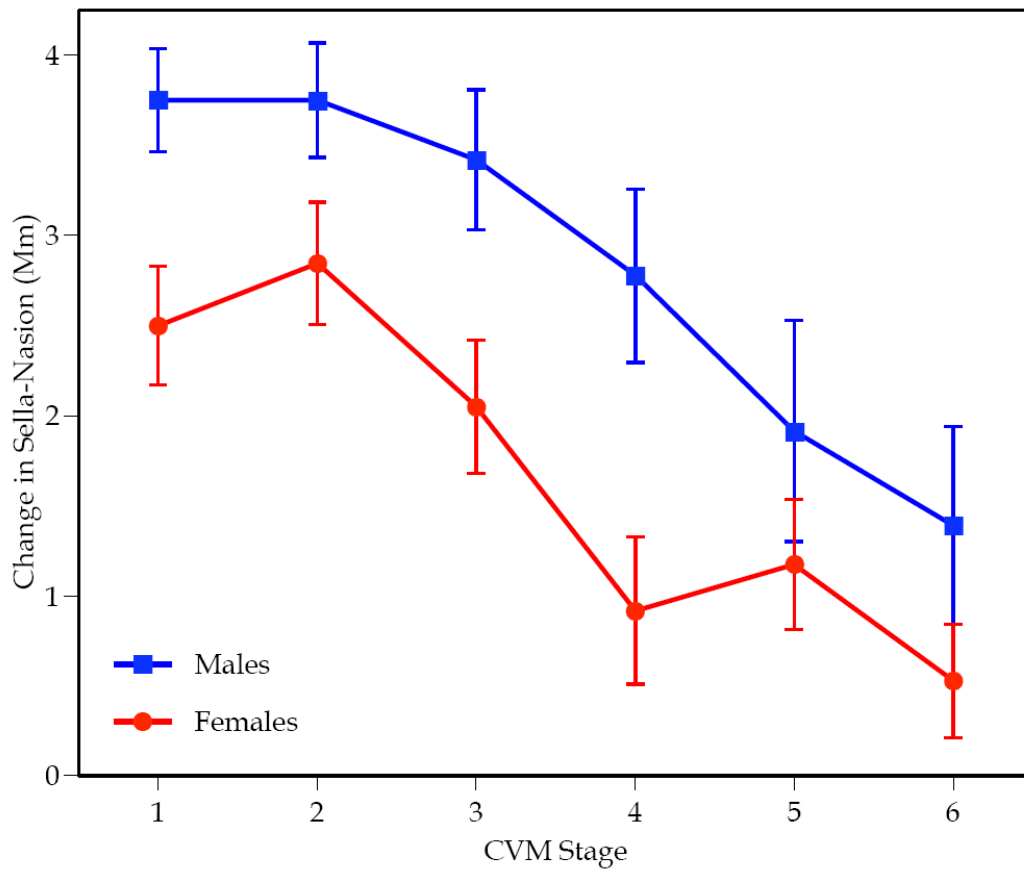
Figure 29. Plot of the mean changes in Sella-Gnathion, by sex, across the six CVM stages. Error bars are ± one standard error of the mean.
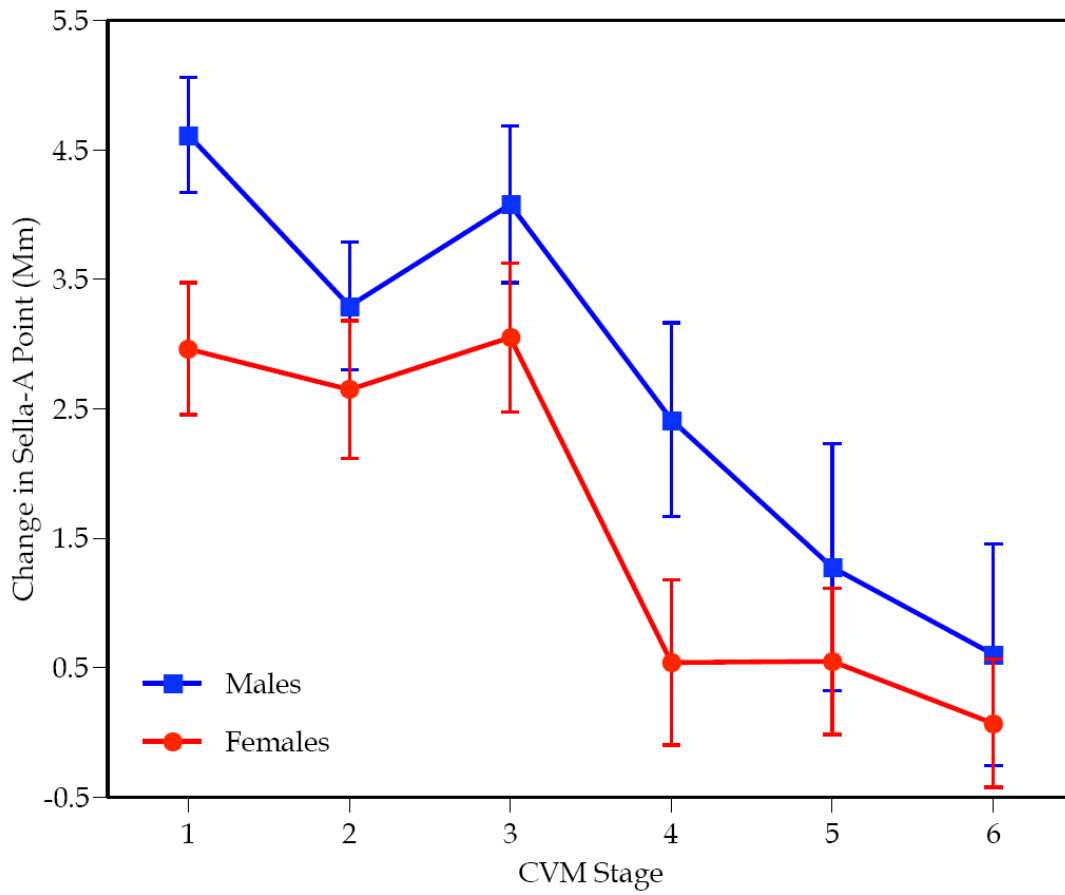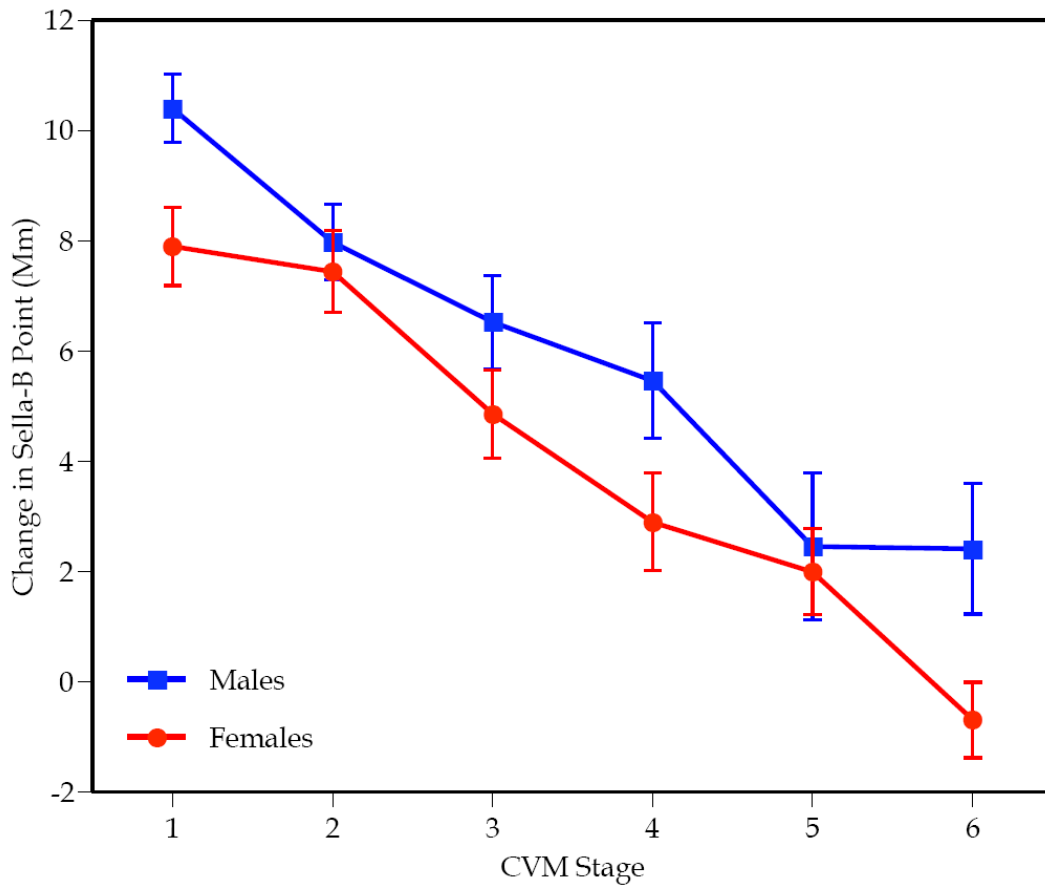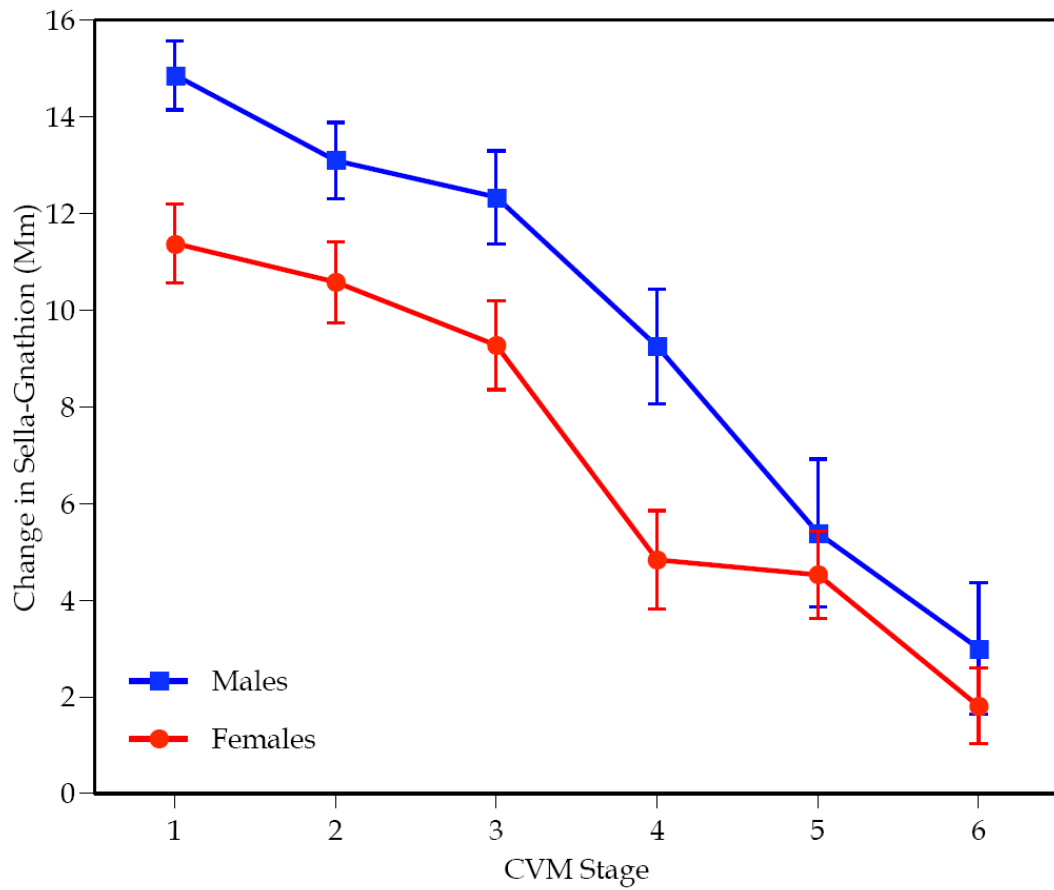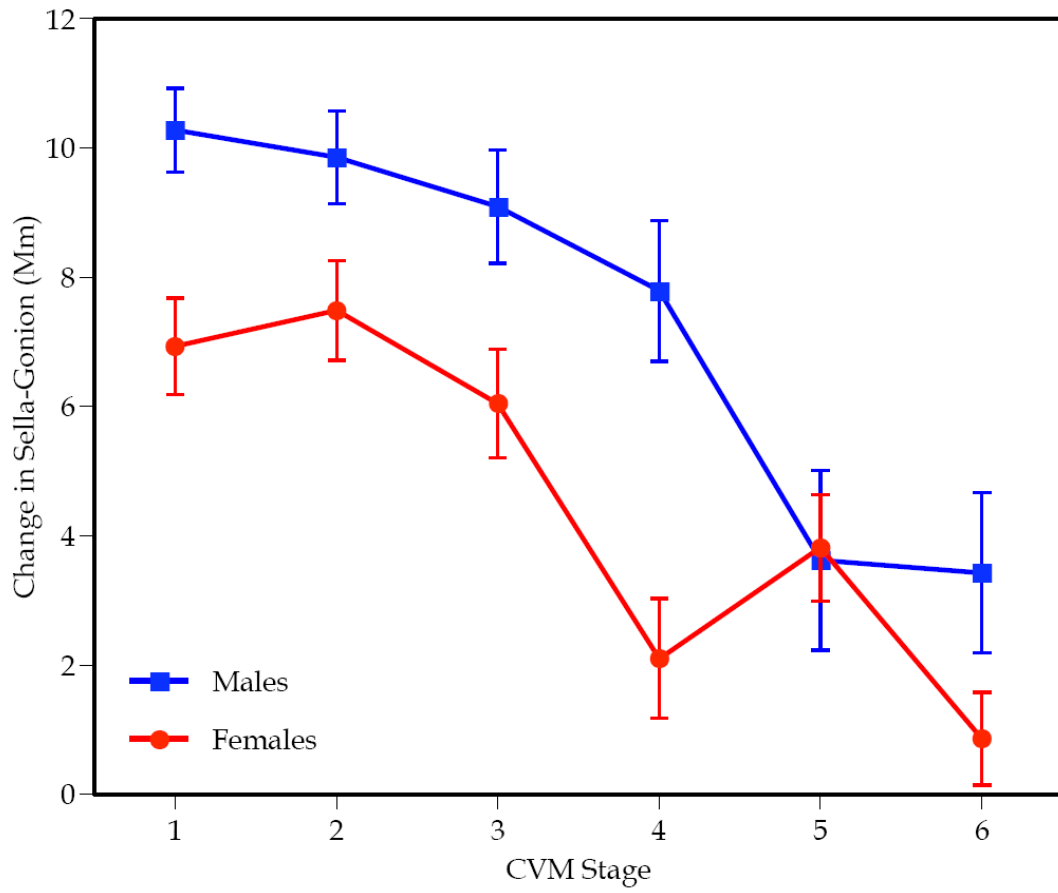
Figure 30. Plot of the mean changes in Sella-Gonion, by sex, across the six CVM stages. Error bars are ± one standard error of the mean.
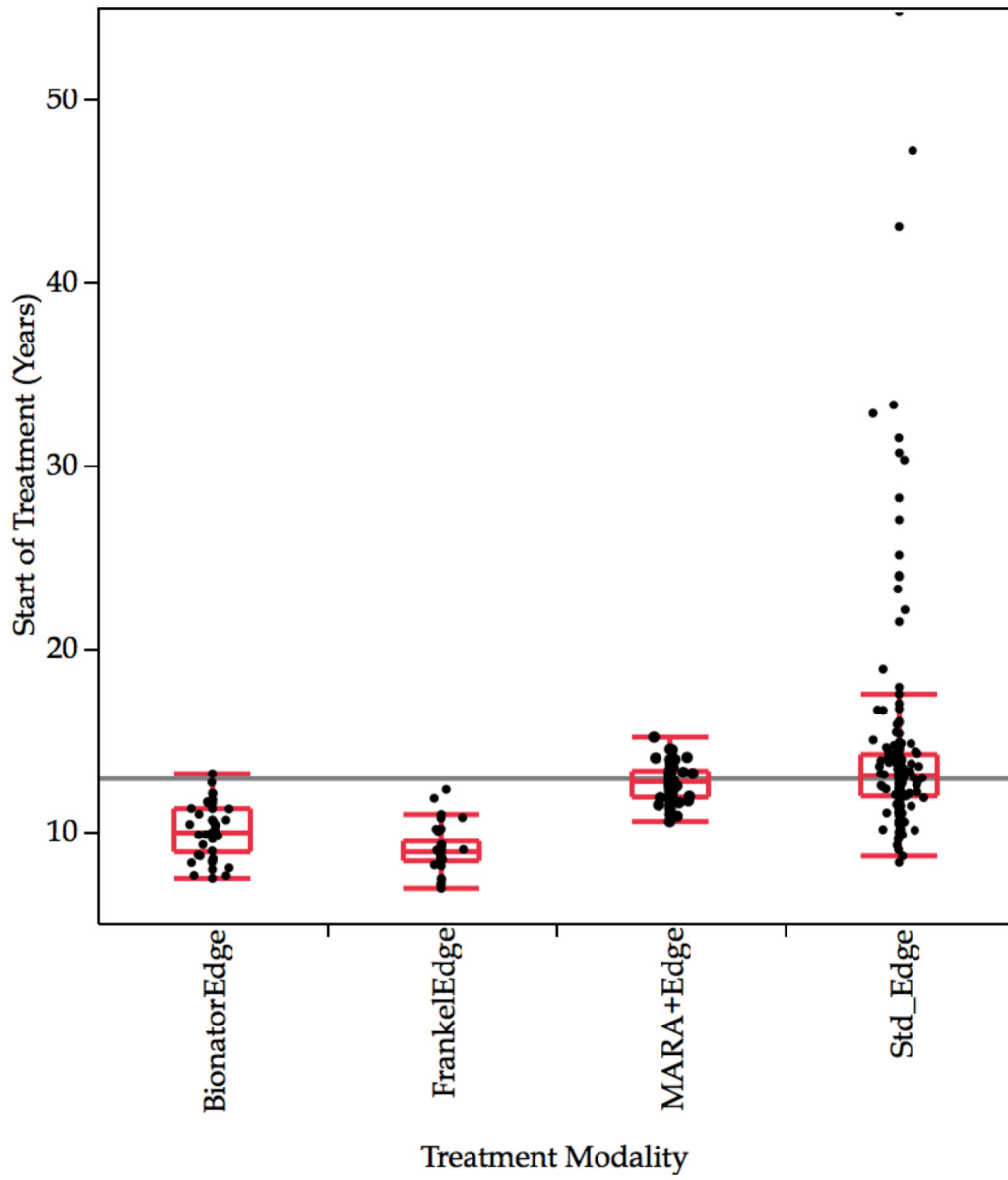
Figure 31. Box plots of the four treatment modalities at pretreatment age.

permanent dentition is in place so that all teeth can be properly positioned. There is, then, the likelihood that time-in-treatment is tied to the patient's age at the start of treatment. Indeed, we show that this is quite clearly the case. Figure 32 shows that time in treatment decreases significantly the older the patient is at the start. A straight line fits the data well ($r^2 = 7\%$), but a curvilinear (reciprocal) equation fits better ($r^2 = 21\%$) because older patients already have all of their teeth fully erupted, so there is no "waiting." Conversely, the youngest patients have disproportionately longer treatment duration (shown by the very steep portion of the curve). This is in no way an indictment of early intervention, but it does confound the study of whether the rate of growth of craniofacial dimensions varies by CVM stage because most of our study data are the changes from start to end of treatment, and this duration is itself dependent on CVM stage.

Figure 32. Graph of time in treatment versus starting age.

CHAPTER V
DISCUSSION

When determining an orthodontic treatment plan for a patient, the orthodontist has little control over the age at which the patient presents for treatment. However, the patient's growth potential, great or small, has a substantial effect on the approach the orthodontist can take in treatment.
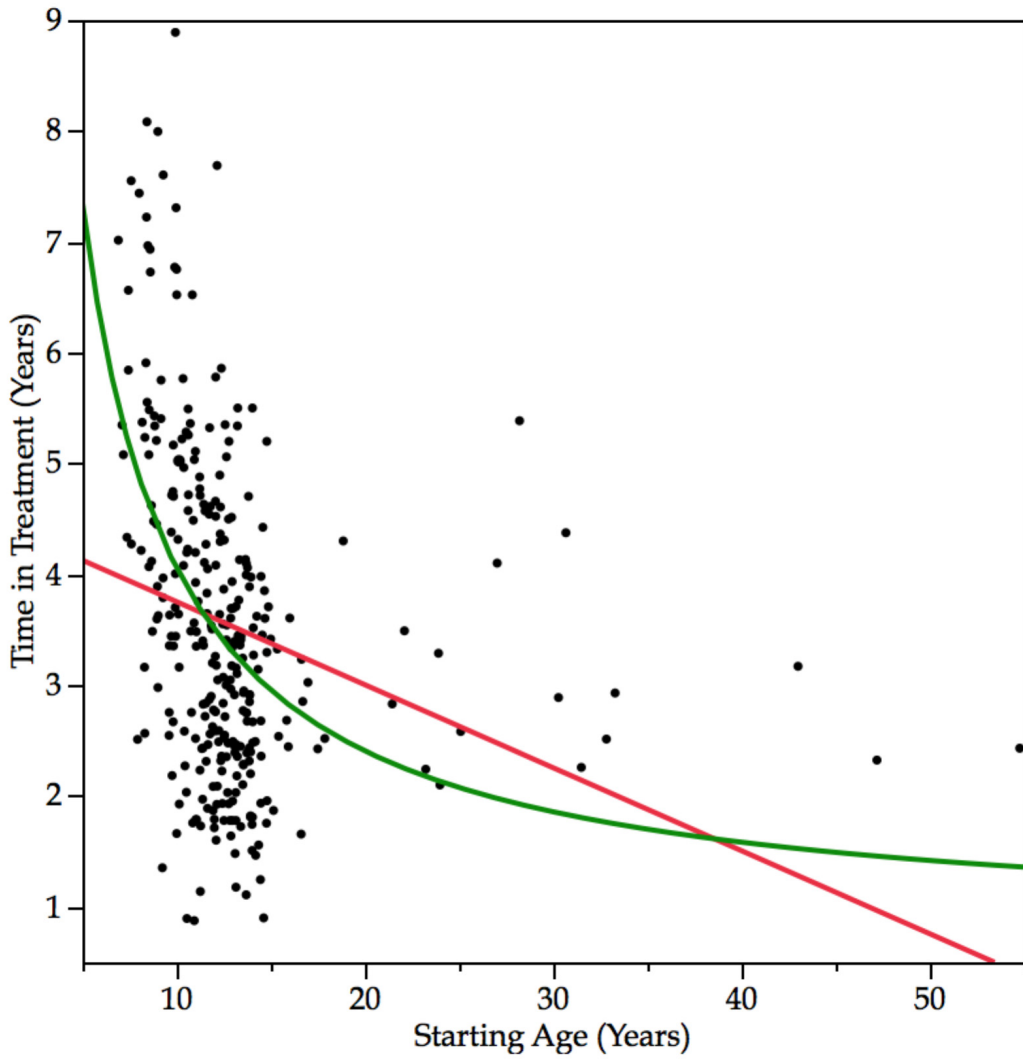
The orthodontist not only has to treat the dental malocclusion, but also diagnose skeletal deformities, and determine, if there is skeletal growth remaining to correct these disharmonies (Harris 2001). Fortunately, there are methods available to assess the "biological maturity" of the patient so that treatment can be adjusted as appropriate. Most orthodontists use chronological age to assess whether there is remaining growth, holding to the perception that older patients have less growth than younger patients. While this is true in a grand sense of distinguishing between children, adolescents, and adults, but it does not take into account the individual being treated. Chronological age has not been shown to be well tied to an individual's tempo of growth (Fishman 1979; Kopecky and Fishman 1993; Franchi 2000). Physiological age has been more closely associated with an individual's tempo of growth (Hunter 1966; Bergersen 1972).

Chronological versus Physiological Age

Physiological or skeletal age can be determined in a variety of ways including: stature, menarche in girls, voice change, and dental development (Mito *et al*. 2002; Steel 1965). The most common way to assess skeletal age in an orthodontic office is with hand-wrist radiographs. More recently, the application of Lamparski's (1972) method of scoring the cervical vertebrae has been shown to be just as reliable as hand-wrist evaluations (Hassel and Farman 1995; Kucukkeles *et al*. 1999), and it has two distinct advantages: (1) the cervical vertebrae are readily visible on the standard lateral cephalogram and (2) due to the proximity of the cervical vertebrae to the craniofacial complex there is an increased potential for accurate assessment of facial skeletal maturity.

The present study supports the previous literature that CVM stages provide a dependable method for the determining skeletal age. Also, it confirms that CVM stages are an effective method of evaluating a patient's maturity status—which indicates where the patient is physiologically along his or her progress towards skeletal maturity. The reason for this is that chronological age does not account for the tempo of growth in individuals, so there is wide

variability in children of the same age. When physiological age, like CVM stage, is used, each stage narrows the variability in the amount of growth, leading to a more individualized assessment.

Sexual Dimorphism

Sex differences in timing, duration, and magnitude of the pubertal growth spurt have been well documented. Numerous studies show that girls begin their growth spurt approximately 2 years earlier than boys, and have a growth spurt that is smaller in velocity (*e.g.,* Björk and Helm 1967; Fishman 1979; Lewis *et al.* 1985). The present study shows that girls achieve CVM stages 2, 3, and 4 more than a year ahead of their male counterparts. However, at CVM stages 5 and 6, magnitude of the sexual dimorphism was smaller, even though boys were half a year behind the girls. One possible reason for the enhanced variability at these stages may be the effect of early and late maturers on later CVM stages. For example, a patient in either sex is an early maturer, he or she would reach maturity at an earlier chronological age therefore affecting the age at later stages of CVM. This variability may also be more pronounced at later stages due to change in velocity that occurs in early and late maturers as growth slows down or ceases.

The current study also examined whether amounts of facial growth during treatment differed significantly by stage and sex. Figures 26 through 30 illustrate these differences graphically and show clearly that boys experience more facial growth than girls at each CVM stage.

The Physiological-Age Model

The benefit of knowing a child's physiologic age (whether estimated from a HW film, from the cervical vertebrae, from the status of tooth mineralization, or the like) is that it estimates where along the trajectory of growth a given child is located. The model is that all children experience much the same trajectory of growth—for example the tissue-specific patterns described by Scammon (1930)—but the tempo (or "speed") of growth varies appreciably among children (*e.g.,* Acheson 1954 ; Greulich and Pyle 1959). Facial dimensions are known to follow the somatic ("general") pattern of growth, meaning that there is a perceptible growth spurt during adolescence following the protracted phase of near-constant growth in childhood (Figure 33).
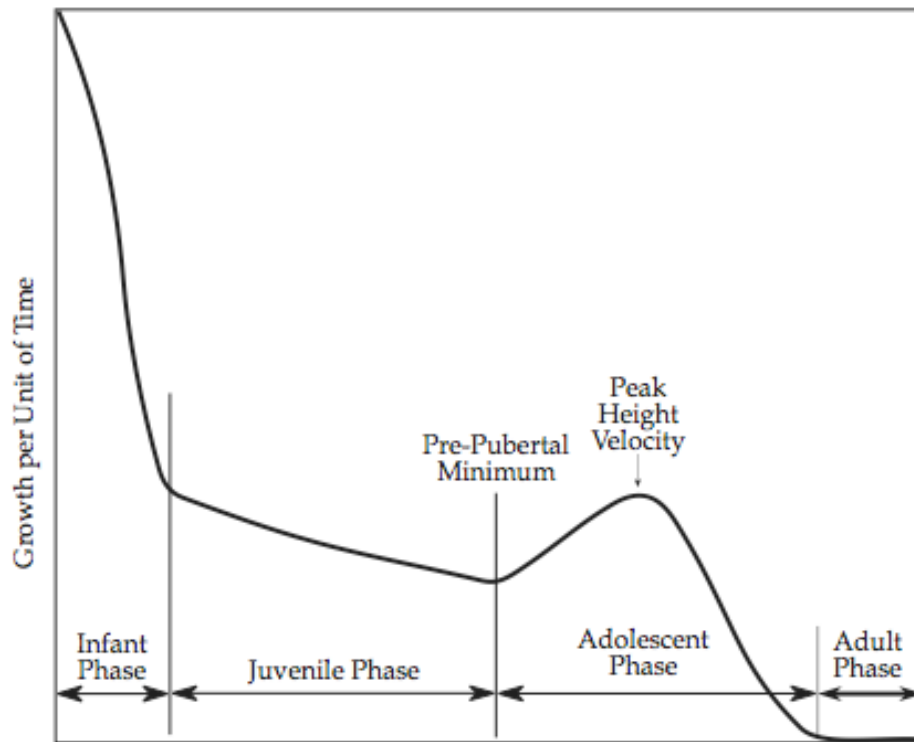
Figure 33. Illustration of the general (somatic) growth curve. The horizontal axis is age. (Diagram provided by E. F. Harris, The University of Tennessee Health Science Center.)

Chronological age provides a reasonable gauge of where a given child is relative to his growth trajectory and, thus, his growth potential during the 2-to-3 years of orthodontic treatment. Expectation is that a measure of physiological age is a more accurate estimate of the child's position along the X axis (Figure 34) because it accounts for the child's biological tempo of development.

Another way of viewing the association is that the hormonal influences that modify the morphology of the cervical vertebra are presumed to be related (if not the same) as the endocrine influences that modulate the rates of bony growth, both as expressed in the appendicular skeleton and in the facial dimensions. Consequently, the visible changes in the vertebral morphology ought to be predictive of the rates of skeletal growth—more so than chronological age that is less strongly tied to a child's tempo of growth. Indeed, there are numerous sorts of "physiological age" assessments, ranging through "height age" (Hamill *et al.* 1970) the onset of secondary sexual characteristics (Marshall and Tanner 1969, 1970), tooth mineralization (Moorrees *et al.* 1963; Demirjian *et al.* 1973), various measures of bone age (Greulich and Pyle 1959; Hoerr *et al.* 1962; Pyle and Hoerr 1969), and so forth. All of these diverse measures are claimed to "work" (to varying degrees) probably (A) because of the systemic effects of governing endocrine regulators and (B) because of eons of selection favoring harmonious, integrated patterns of growth (Bogin 1988).

Again, expectation is that a measure of physiological age is a more accurate estimate of a child's maturational status because it accounts for the child's biological tempo of development. This is exactly what was tested by Bergersen (1972) who calculated the annualized rates of cephalometric growth for each individual in a sample of 23 boys (Articulare-Gnathion, Nasion-Menton, and Sella-Gnathion). He then used the velocity curves for each variable of each individual to identify the onset of the adolescent growth spurt. The two sorts of age were chronological age and skeletal age (derived from HW films). The key issue (Figure 35) is that the variability of the initiation of the adolescent growth spurt is substantially larger when using chronological age compared to HW skeletal age. In other words, aggregating the data on skeletal age provided a significantly more precise measure of where a child is relative to the onset of adolescence compared to aggregation on chronological age. A child's bone age is a more precise measure of identifying when the onset of the spurt is going to occur than when using chronological age. The benefit is that skeletal age more accurately estimates where each child is along his track towards biological maturity.

This "model" of why biological age is more precise than chronological age has not gone unchallenged. One of the best-supported reviews is by Smith (1980). Smith's consensus of the literature was that (1) biological issue does not
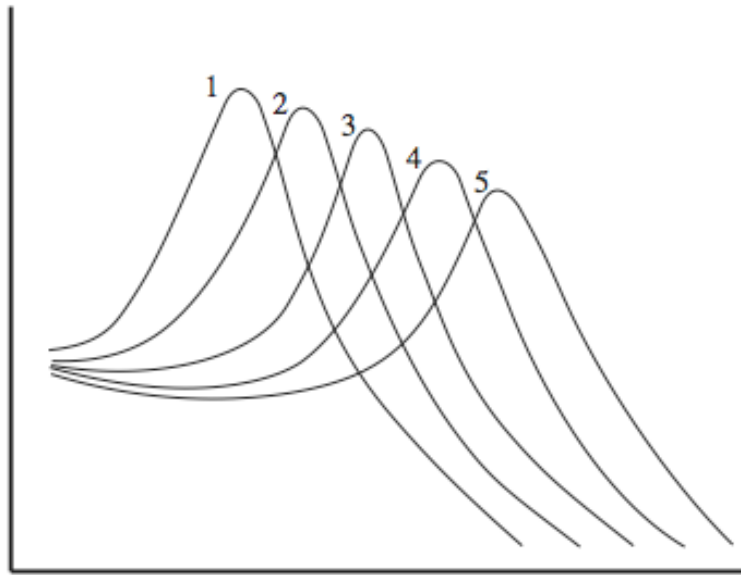
Figure 34. Illustration of a hypothetical range of adolescent growth spurts. The shapes of the velocity curves are essentially the same, but the timing of the onset of puberty varies depending on the child's tempo of growth. (Figure supplied by E. F. Harris, The University of Tennessee.)
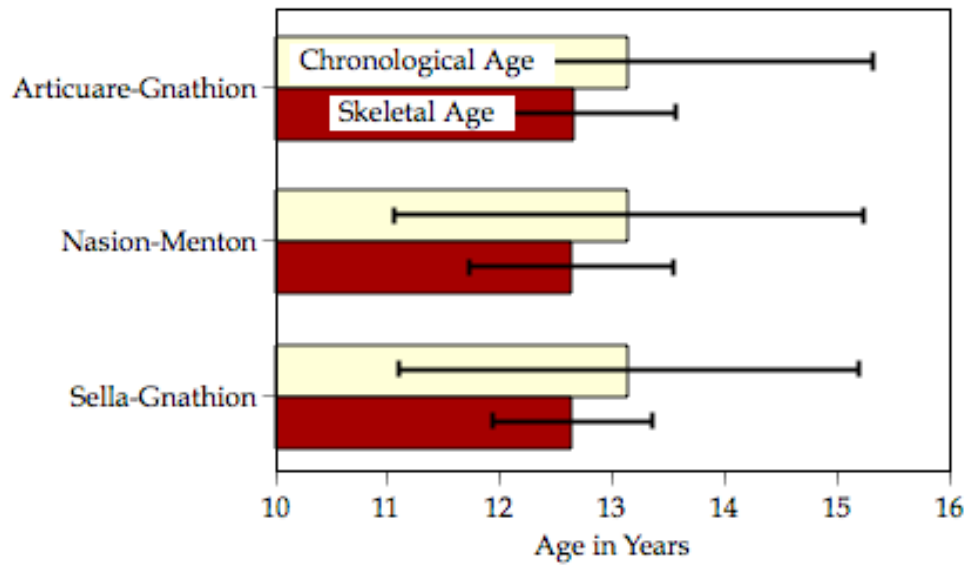
Figure 35. Plot of the average onset of the adolescent growth spurt in a series of American white boys (data from Bergersen 1972). Error bars are 2 standard deviations around the mean, and the pertinent issue is that the error bars are significantly smaller for the skeletal age assessments.

measurably improve growth prediction in girls and (2) it is only somewhat helpful in boys. The issue with girls is that their adolescent intervals of steroid-mediated rapid growth (*i.e.*, the adolescent growth spurt) is much less on the average than in boys (where testosterone seems to have a major impact), and some girls fail to exhibit a discernible adolescent growth spurt at all (*e.g.*, Roche *et al*. 1975; Largo *et al*. 1978;). This latter feature may be due to the fact that estrogen—which increases in titer at the onset of female adolescence—promotes obliteration of the metaphyses, so there is an acceleration of maturation with little actual growth (Chagin and Sävendahl 2007; Simm *et al*. 2008).

Some of the striking features of Smith's review is (A) the paucity of studies of this topic and (B) the broad differences in strategies used by researchers to address this question. In our opinion, this latter issue substantively limits the reliability of any "consensus." Rather few cephalometric (or anthropometric) studies have provided adequate longitudinal data to permit studies of the adolescent growth spurt, though its presence in bony facial dimensions is apparent (*e.g.*, Bjork 1963; Broadbent *et al*. 1975). More extensive data are available for stature (standing height), and this dimension has been studied in greater detail (Largo *et al*. 1978; Gasser *et al*. 2001).

Part of the ambiguity among studies is how to effectively test whether the variance of growth is usefully reduced when data are aggregated by some measure of biological age. Operationally, (A) the onset of the adolescent spurt and (B) peak height velocity have been the two commonly identified events. These inflection points are used because they are identifiable; there is no evidence that they are biologically the most informative.

Even when serial cephalometric data are available (*e.g.*, Bambha 1961; Thompson *et al*. 1976), films are rarely taken at less than a one-year interval, which makes capturing the initiation, the peak, or the end of a two-year adolescent growth spurt imprecise. When the interval between X-rays is one year, the precision of an estimate is only one-half the interval (namely ½ year). That is, if the rate of growth between X-rays taken at 13 and 14 is appreciably larger than the change during the prior year (12 and 13), the researcher necessarily assumes that the true inflection point occurred somewhere between 13 and 14, but he cannot estimate the time more precisely than by choosing the midpoint of the age interval. In actuality, the onset of steroid-mediated growth may have been initiated anywhere during the one-year interval. This imprecision hampers analysis.

Another issue that is poorly addressed in the literature is that (A) most studies with appropriate longitudinal data are based on children where chronological age is equivalent to biological age, yet (B) when CA = BA, there is

too little variation to be informative. Bergersen (1972) touches on this issue, namely that the value of biological age is small in children who are progressing normally; it is the aberrant growth pattern (where CA > BA or CA < BA) that are informative. In other words, the inter-individual variation in normal growth patterns swamps out any informative association. Samples of children in whom CA and BA noticeably depart are much more informative, yet these have never been studied in this context.

Testing the Physiolgical-Age Model

The important missing piece of data in a cross-sectional study such as the present research is identifying the statistical association between CVM stages and the adolescent growth spurt. That is, it is evident from Figure 26 that the rate of growth depends on the CVM stage, with maximum velocity for facial dimensions occurring during CVM stages 3 and 4 (O'Reilly and Yanniello 1988). On the other hand, chronological age also is predictive of the rate of growth simply because most children are, by definition, average maturers. Mostly as a thought experiment (as opposed to a critical statistical test), consider the following graph (Figure 36) where the age at the start of treatment was simply structured into 2-year intervals using chronological age. In the present study, children beginning treatment between 8 and 10 years of age exhibited the greatest growth during treatment. Older children (10 to 12 years) exhibited less growth, and the oldest group (12 to 14) exhibited the least. This is consistent across boys and girls, with greater growth in boys than girls at each age interval.

These results are not particularly different from the ordered results obtained by grouping the data by CVM stage (see Figure 26-30). In other words, while no statistical test is possible here, it is suggestive that both methods of aggregating the patients' growth potential may work—either (A) using biological markers like CVM stages or (B) something as approximate as chronological age. Sorting children by chronological age "works" because the majority of children are average maturers; CA and BA are positively intercorrelated so sorting on one is about the same as sorting on the other. An important caveat here is that the patients in this study are phenotypically normal "average growers" where CA and BA are not particularly disparate.

We are unaware of how to create a directly comparable test using CVM stages and chronological ages with cross-sectional data, but this rough comparison is suggestive (Figure 36). What is needed are longitudinal data where some common measure of maturity can be identified on both biological and chronological scales, such as (A) the onset of the adolescent spurt, (B) peak
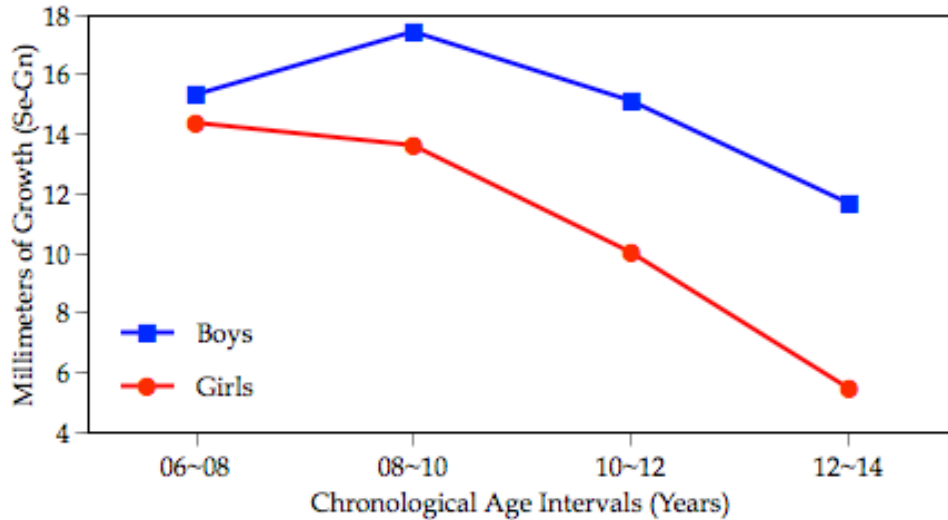
Figure 36. Graph of the amounts of Sella-Gnathion growth observed during the course of treatment. The data are partitioned into two-year intervals at the start of treatment.

velocity, (C) the end of the spurt, or (D) the duration of the spurt (*e.g.*, Bambha 1961; Bergersen 1972).

CVM Stages

Lamparski defined six stages of cervical vertebral morphology (1972). The stages are visually distinguishable, but he made no effort in his study to characterize the modal chronological ages at which each stage occurred. Our group evaluated this issue some years ago (Faulkner and Harris 2003) and found that the median ages between CVM stages are roughly one year apart, starting at approximately 10 years of age and progressively to the mid-teens.

We have added the data from the present study to the earlier data base (whites only) in order to estimate the mean ages at attainment of each stage. (Even with almost 200 cases in the present study, there are too few when divided by sex and stage to reliably estimate median ages using the present data alone.) Since the data are cross-sectional, with each person examined just once (at the start of treatment), we used survival analysis (*e.g.*, Cox and Oakes 1994) to estimate the median age of attainment of each CVM stage by sex. The terminal stage 6 (mature morphology) was ignored since it persists from sometime in adolescence throughout the rest of life. For boys, the following graph plots the cumulative curves for each of stages 1 through 5 (Figure 37). The key parameter here is the median, which is the age at which half of the sample has achieved the stage. Each cumulative curve has the "S" shape that is characteristic of ogives

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(Croxton and Cowden 1939). Notice that Lamparski's scheme is nicely ordered and the stages are well separated. On the other hand, notice too the horizontal overlap of each stage. For example, stage 2 is achieved at just over 7 years of age in the earliest maturers, but it is not achieved until about 12 years of age in late maturers. Inspection of the figure shows that there is considerable overlap of each stage when the abscissa (the X axis) is chronological age. It is this inter-individual variation that seems, in our opinion, to warrant the use of biological age in place of chronological age. Insofar as the onset of the adolescent growth spurt is tied developmentally to the stages of bony maturation, knowing a child's CVM stage is a more precise measure of his progress towards biological maturation than chronological age.

Table 8 lists the results of the survival analysis, and several features are disclosed. These results show that the stages—between about 9 and 15 years of age--overlap the modal age of orthodontic treatment, so they are generally applicable for gauging the end of childhood and the onset of the adolescent growth spurt. It is evident too that girls achieve each maturation stage significantly ahead of boys, which stresses the importance of sex-specific standards (O'Reilly and Yanniello 1988). The data also show the ordinal nature of the stages. That is, Lamparski chose the stages because they are visually (anthroposcopically) distinguishable one from the other. This means that the stages are invariantly ordered (so, for example, stage 3 never occurs in an individual's vertebra before stage 2), but it does not mean that the stages are equidistant. It is evident that the intervals between the stages are unequal. An obvious example is that the age interval between stages 1 and 2 is larger in both sexes than between stages 4 and 5. For completeness, the ogives for the subset of males are plotted in Figure 38. Inspection shows that, as discussed above, the median of each stage occurs at an appreciably earlier chronological age in girls than boys, which is characteristic of the earlier (faster) skeletodental maturation of girls compared to boys (*e.g.*, Tanner 1962).

Class II Correction

Traditional correction of a Class II malocclusion involves the extraction of permanent teeth to reduce overjet and achieve a Class I molar and canine relationship via restraint of maxillary growth. In contrast, functional appliances can be used in growing patients to enhance mandibular growth and position to help correct a Class II malocclusion. Evaluating a patient's remaining growth potential is important to the orthodontist when correcting a Class II malocclusion. If a patient has remaining growth, it can be utilized by the orthodontist to correct skeletal relationships. In many Class II malocclusions, the patient is diagnosed with a retrognathic mandible, meaning the mandible is a
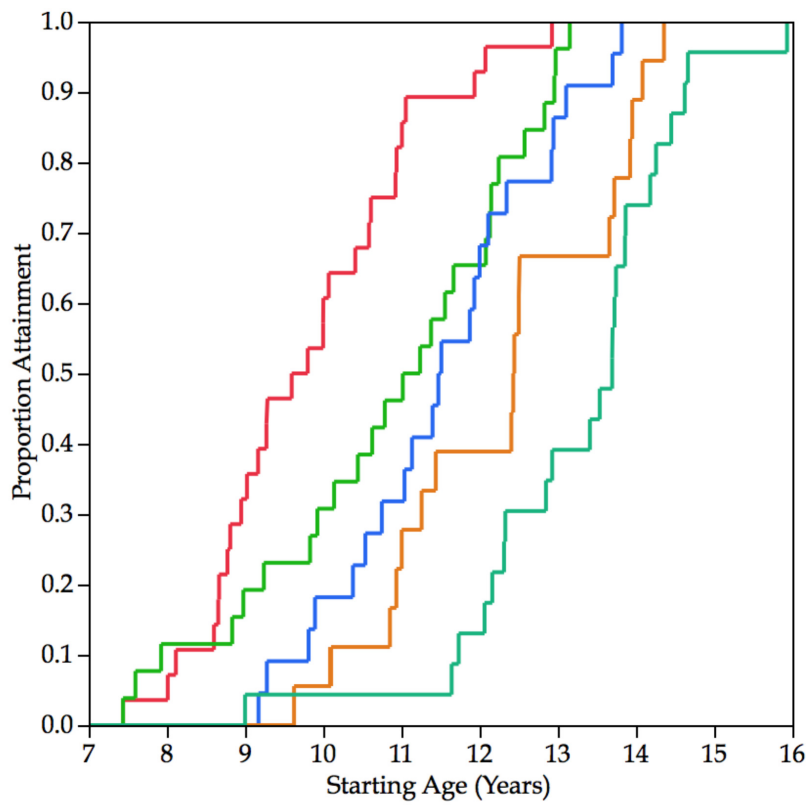
Figure 37. Graph of the cumulative percentage curves for the five CVM stages in the subsample of girls. The curves are, from left to right, CVM 1, 2, 3, 4, and 5.

Table 8. Results of survival analysis of chronological age partitioned by CVM stage (and sex of the patient).*

Stage	Median Age	L_1	L_2
	Girls		
1	9.80	9.17	10.56
2	11.38	10.64	12.00
3	12.49	12.00	12.93
4	14.13	13.66	14.37
5	14.73	14.26	15.33
	Boys		
1	11.22	9.93	11.77
2	12.76	12.35	13.20
3	13.44	13.16	13.83
4	14.76	14.56	15.31
5	15.65	15.43	16.41

*L_1 and L_2 are the lower and upper 95% confidence limits of the median, respectively.
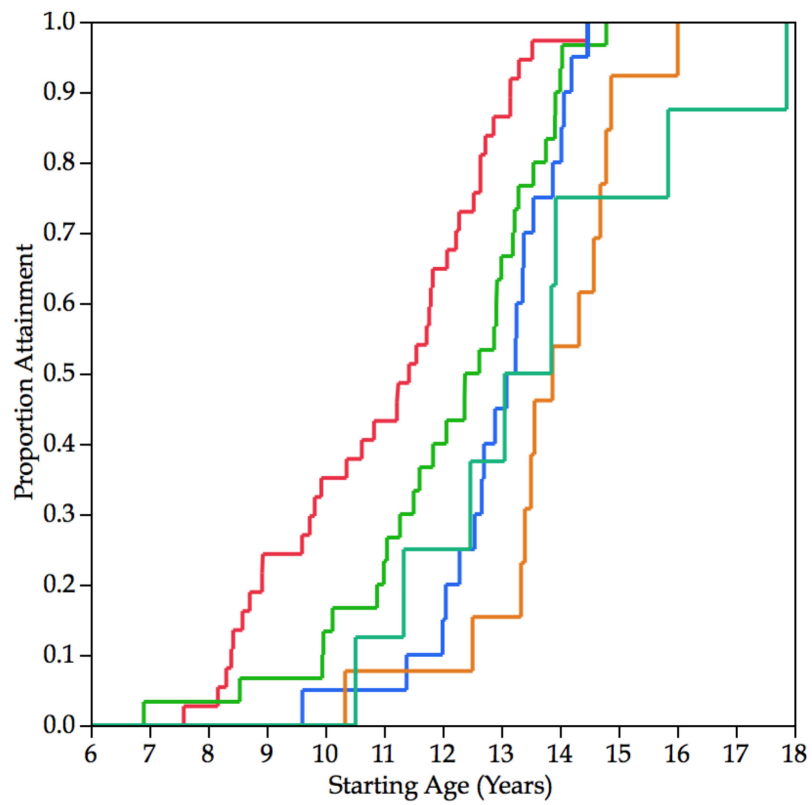
Figure 38. Graph of the cumulative percentage curves by CVM stage in the subsample of boys. The curves are, from left to right, CVM 1, 2, 3, 4, and 5.

position that is posterior to the ideal (orthognathic) relationship. It would seem reasonable to correct the skeletal relationship by advancement of B Point (mandible) instead of restriction of A Point (maxilla). Maxillary restriction would essentially be treating the "good" jaw to the "bad" or retrognathic jaw.

When treating Class II malocclusions, the orthodontist should recall that boys grow more and faster than girls. Our results not only show that boys grow more, but they also grow for a longer interval of time than girls, meaning more potential (anticipated) growth exists at later stages of CVM for Class II correction. In treating growing girls, it is important to evaluate how much growth is remaining, so that this potential growth can be used to correct skeletal discrepancies since girls have a substantially shorter time than boys during which growth occurs. Using functional appliances, like the Fränkel and Bionator, that are based in "harnessing" available jaw growth often benefits from early treatment that captures both late childhood and early adolescent growth. This issue is shown graphically in Figures 39 and 40 for girls and boys, respectively. Here the amount of growth during treatment is plotted against the patient's chronological age at the start of treatment.

A simple straight line (least-squares best fit) is shown for each of the plots, but an important facet is that the amount of growth goes down with age. That is, even with cases starting at 8 or 9 years of age, they do not discernibly precede the adolescent growth spurt; there is no segment of early treatment where the amount of growth ascends with age. Orthodontists commonly hold off treatment until all of the permanent teeth are emerged to start treatment. This is convenient for the practitioner because it reduces time in treatment, but it also causes a good deal of the higher rates of facial growth to be missed. These two graphs also show that, after roughly 15 years of age, little facial growth is present, so most of the orthodontic correction needs to be achieved by tooth movement, not modulating bone growth (*e.g.*, McKinney and Harris 2001; Harris 2001). Another obvious feature of these graphs is that they are drawn to the same scale, but males have higher rates of growth; for example, there are several males with growth in excess of 2 cm, while very few girls achieve this.

Overall, there is more growth available at earlier CVM stages than at later stages for Class II correction and this should be taken into account when treatment planning. Our sample consists of patients that span the six CVM stages, and this is due to the different treatment modalities that were employed, hence more growth is seen in subjects who were treated with the Fränkel and Bionator than with the MARA and fixed appliances only group.
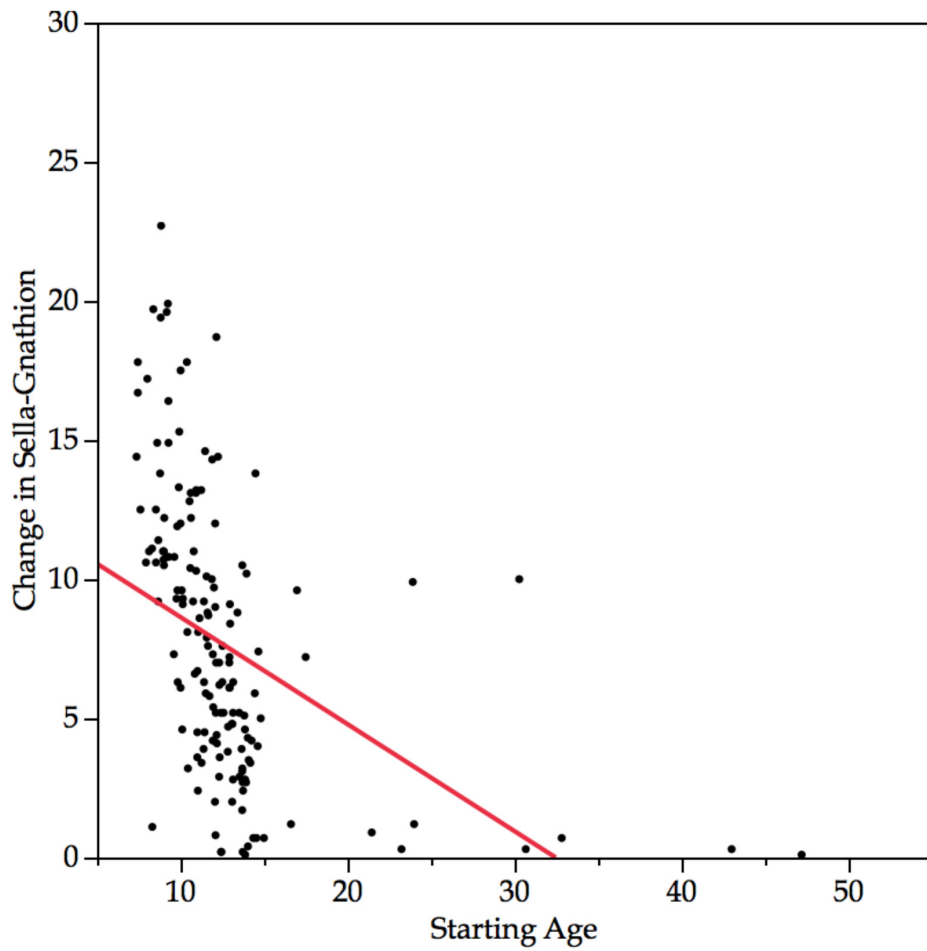
Figure 39. Plot of the amount of facial growth (Sella-Gnathion) during treatment against the patient's starting age (females only).
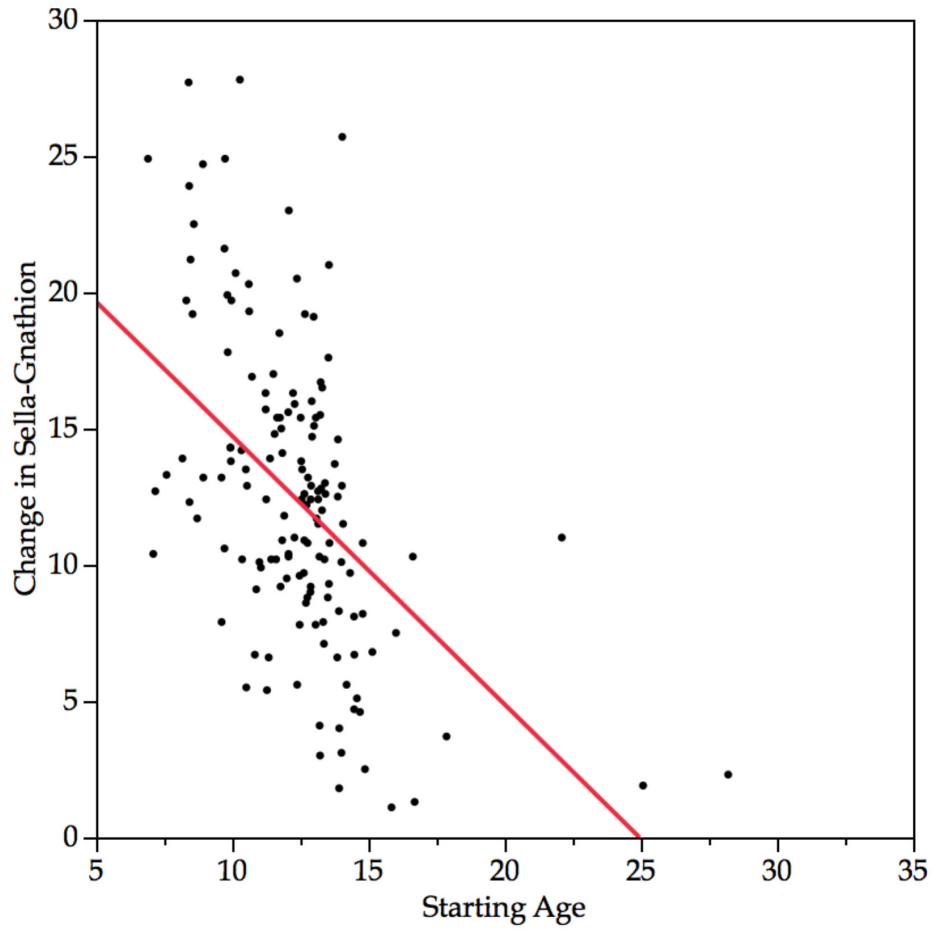
Figure 40. Plot of the amount of facial growth (Sella-Gnathion) during treatment against the patient's starting age (males only).

It is worth appreciating some of the modal conditions seen in these treated cases (Figure 41). Perhaps foremost, mandibular growth (Sella-B Point) is appreciably greater than maxillary growth (Sella-A Point) in both sexes and at all CVM stages. This is a desirable situation since most cases exhibit Class II malocclusions, and it is normally desirable to promote mandibular growth rather than restraining maxillary growth. These data show the anticipated sex differences, with more growth in boys than girls at each age, and, as discussed earlier, there is no detectable slower pre-adolescent rate even in the youngest patients (CVM 1). Instead, there is a progressive slowing of growth with increasing CVM stage, which reemphasizes the contention that the most skeletal correction can be achieved in the youngest patient as a statistical average.

It also is obvious in this figure that the decelerating curves for Sella-A and Sella-B converge with advancing age, primarily because the downward slope of Sella-B growth is greater. This means that, on the average, the ability to modulate growth differences between the arches is greater at the earlier CVM stages (notably CVM 1 and 2), and that there is less opportunity for differential jaw growth at the older stages.

It should be noted that these treated cases all experienced fixed, Edgewise treatment, and the use of Class II elastics and other inter-arch mechanics probably reduced the forward growth of the maxilla compared to untreated cases. On the other hand, untreated norms are of little interest because by definition they are outside the realm of orthodontic treatment.

Time in Treatment

The results from this study show that patients treated with a functional appliance followed by Edgewise appliances had a treatment time that was significantly longer than patients treated with Edgewise appliances. This is due to the younger age of these patients at the start of treatment. These "two-phase" or, more correctly, "compound treatments" were started earlier and, intuitively, it would seem that these patients would take longer to complete treatment. However, much of this "treatment time" is spent waiting for the emergence of the late-erupting permanent teeth to allow full fixed appliances to be placed and treatment completed. Once the jaw correction is achieved with the functional appliance, one could consider time between this correction and fixed appliances to be a form of retention. In fact, this is how it is viewed by the practitioner whose cases were used in this study. On the other hand, the patient is still wearing the functional appliance, in the case of the Bionator and Fränkel, at night, so it could be argued that the patient is still in active treatment.
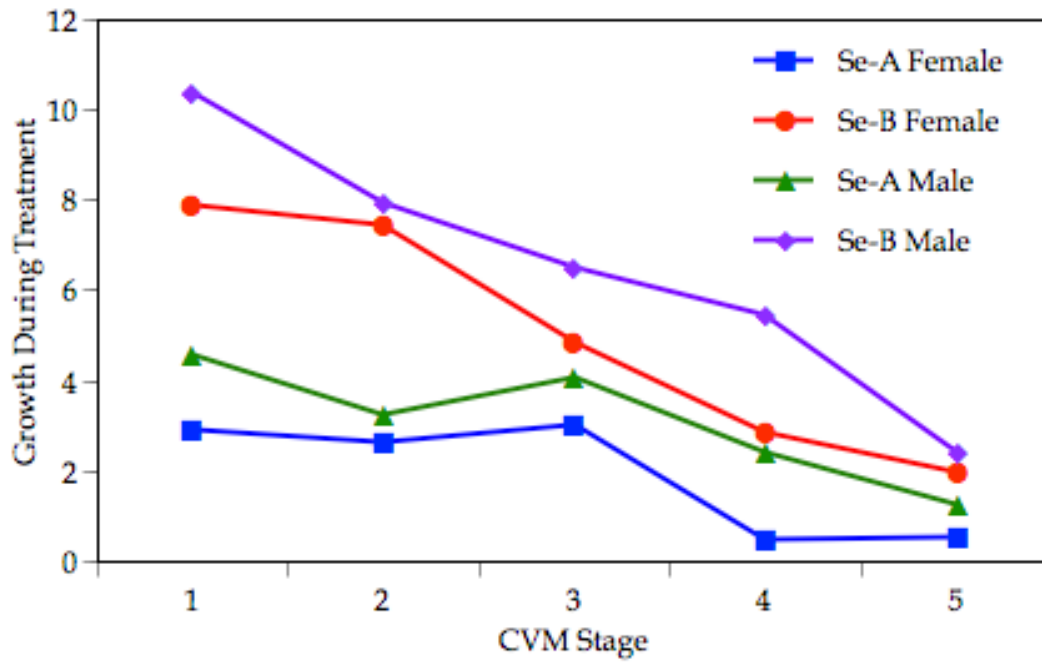
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Figure 41. Plot of sex-specific mean changes in Sella-A and Sella-B arranged by CVM stage.

In the present collection of four treatments (Figure 42), average duration of treatment was 4.4 years for the Bionator-Edgewise series, 5.1 years for the Frankel-Edgewise sample, 2.8 years for the MARA-Edgewise sample, and 3.2 years for Edgewise treatment alone. Differences between these times are highly significant (F = 33.9 with 3 and 311 df; P < 0.0001). Use of the Tukey-Kramer HSD post-hoc test showed that the source of the significance was between the Bionator and Frankel groups (with longer treatment times) compared to the MARA and Edgewise-alone. These differences are expected since the Bionator and the Frankel typically are used in preparation for Edgewise treatment, which necessarily increases time in treatment. The MARA is used in conjunction with Edgewise treatment, and these two treatment times are indistinguishable statistically.

It recently has been popular to discuss "treatment efficiency" which in effect is how quickly a case can be completed, but this simple statistic does not account for differences in actual chair-side time and difficulty of the mechanics. For example, appointment times are shorter, fewer, and farther apart with some of these treatments, so the net burden on the orthodontist can easily be less than with conventional treatment alone.
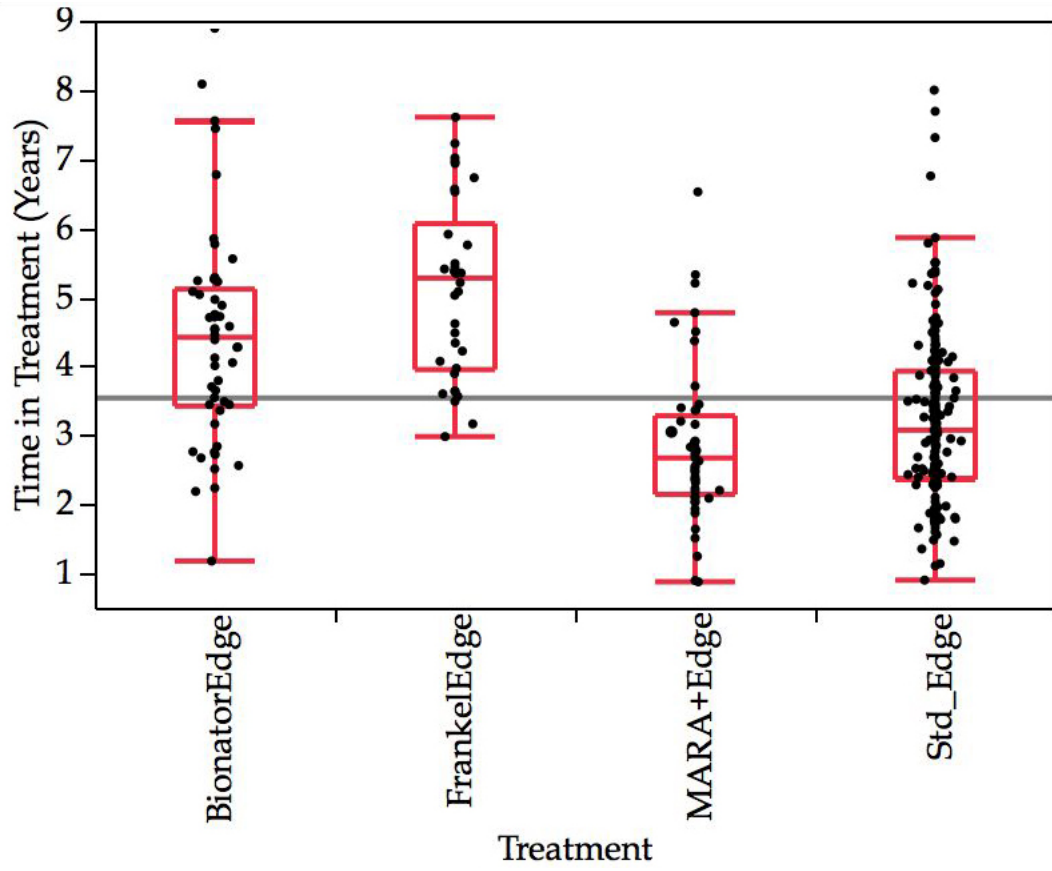
Figure 42. Treatment ages (years) sorted by type of treatment.

CHAPTER VI
SUMMARY AND CONCLUSIONS

The amount of anticipated growth is an important part of treatment planning in orthodontic patients. For Class II division 1 patients, it is particularly important because if a patient grows more during treatment, generally, the more favorable the treatment outcome due to compensatory mandibular growth aiding in skeletal Class II correction. Considerable discussion in the orthodontic literature involves the efficacy and timing of functional appliances in Class II malocclusions. The present study compared four groups, three treated with a functional appliance, either a Bionator, a Fränkel, or a MARA, followed by edgewise appliances, and a group treated only with edgewise mechanics. The purpose of this retrospective cephalometric study was to determine whether the amounts of in-treatment facial growth differ significantly by sex and by Cervical Vertebral Maturation (CVM) stage.

All three groups treated with functional appliances were treated by a single practitioner, and consisted of 50 Bionator , 32 Fränkel, and 50 MARA patients. The standard edgewise group consisted of 183 patients. The CVM stage was assessed for each patients pretreatment, progress (if available), and post-treatment lateral cephalometric radiograph. Cephalometric measures were used to evaluate the amount of craniofacial growth during treatment. The major findings of the study are as follows:

(1) CVM stage is more closely associated with all dimensions of craniofacial growth than chronological age.
(2) Boys' growth is greater and more accelerated than girls, while girls begin their parapubertal growth spurt approximately 2 years before boys.
(3) Maximum growth of the facial bones occurs in CVM stages 3 and 4, which corresponds to roughly 12 years of age in girls and 13 in boys.
(4) Little facial growth occurs after about 15 years of age in either sex, so most of the orthodontic correction needs to be accomplished by tooth movements alone rather than modulating jaw growth.

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VITA

David Justin Sander, the son of Dr. Paul and Sylvia Sander, was born in Columbia, Missouri, on January 12, 1980. David graduated from Belleville Township High School West in 1998 and attended Illinois Wesleyan University in Bloomington, where he received a Bachelor of Science degree in Biology, graduating Magna Cum Laude. He received his dental training and a Doctor of Dental Medicine degree from Southern Illinois University, Alton, in June of 2006, graduating Cum Laude. In August of 2006, he entered The University of Tennessee Health Science Center as a graduate student in the Department of Orthodontics and is expected to receive his Master of Dental Science in May 2009. David, his wife, Dawn, and their son, Jack, plan to live in West Plains, Missouri upon graduation.