Mandibular Growth in Class II Patients with Severe Skeletal Dysplasia, After the Pubertal Growth Peak

by

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A thesis submitted in conformity with the requirements for the degree of Master of Science (Orthodontics)

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2015

Abstract

**Background.** Treatment of Class II malocclusion depends on the etiology and on skeletal maturation. **Objectives.** To evaluate the extent of mandibular growth in Class II patients with severe skeletal dysplasia, after the pubertal growth peak. **Materials and Methods.** 27 subjects with Class II malocclusion (13m, 14f; ANB ≥ 6° and unit length difference ≤ 19.5) and 27 Class I controls (matched for age, gender, and skeletal maturation) had lateral cephalograms studied at: (T1) after the pubertal growth spurt (CVM stages 4, 5, or 6) and (T2) minimum 2 years after T1. **Results.** No statistically significant difference (p=0.5) was seen between mandibular growth in the study group (2.7 ± 2.4 mm) and the control group (2.6 ± 3.2 mm). Age and gender were significant predictors of growth (p<0.05), while class of occlusion was not (p>0.05). **Conclusions.** Post-pubertal mandibular growth was not different between subjects with Class II skeletal dysplasia and Class I matched controls.
Acknowledgments

I would like to express my gratitude to the following people for their invaluable and continuous support throughout the course of this study:

Dr. Bryan Tompson, Thesis Supervisor, Discipline Head, Department of Graduate Orthodontics, University of Toronto, Faculty of Dentistry; for your excellent support and encouragement throughout this investigation and during the three years of this Orthodontics program.

Dr. Angelos Metaxas, Committee member, Associate Professor, University of Toronto, Faculty of Dentistry, Department of Graduate Orthodontics; for your especially warm spirit, encouragement and guidance during the three years of the program.

Dr. Siew-Ging Gong, Committee member, Associate Professor, University of Toronto, Faculty of Dentistry, Department of Graduate Orthodontics; for your excellent guidance during the three years of this graduate program, and especially for helping organize, plan and write this study.

Most importantly, I dedicate this thesis to my family. I am truly blessed with very special parents and a loving brother. Your constant support has strengthened me on this wonderful journey. To my wonderful classmates, Caroline and Fatima, our friendship experienced monumental life experiences and I thank-you.
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List of Abbreviations

AFH - anterior face height
ANS - anterior nasal spine
Gn - gnathion
Go - gonion
LFH - lower facial height
MP - mandibular plane
Me - menton
N - nasion
OP - occlusal plane
PFH - posterior facial height
S - sella
SN - sella to nasion plane
TFH - total facial height
UFH - upper facial height
CVM - cervical vertebral maturation
I. Introduction and Statement of the Problem

In individuals with Class I occlusion and normal skeletal relationships, maxillary and mandibular growth are well related, resulting in balanced and esthetic profiles.\textsuperscript{1,2} Skeletal disharmonies result when anteroposterior discrepancy exists between the position or size of the maxilla and/or mandible, which may or not be accompanied by dental malposition on the respective skeletal base.\textsuperscript{3-6} When the sagittal position of the mandibular first permanent molar is in a more distal position relative to the maxillary first permanent molar, the occlusion is classified as Class II.\textsuperscript{1} Class II malocclusion is a common clinical problem in North America because of the increased prevalence in the Caucasian population: multiple studies report Class II malocclusion prevalence of one-quarter to one-third in Caucasian children.\textsuperscript{7,8} A class II malocclusion is evaluated as having either dental, skeletal, and/or functional etiologies.\textsuperscript{2}

Mandibular growth plays a crucial role in forming the anteroposterior relationship with the maxilla. This affects the presence, the type (dentoalveolar or skeletal), and the severity of malocclusion. Individual variability exists between the velocity, direction and timing of mandibular growth. Clinicians evaluate growth to assess treatment timing. The growth potential of patients with Class II malocclusion is of particular concern for orthodontists because they represent a significant percentage of cases they treat.\textsuperscript{2,4} The mandible can grow favorably and may improve the deformity, or orthodontic treatment can improve the anteroposterior relationship, or a combined surgical-orthodontic correction of mandibular deficiency may be indicted to obtain esthetically pleasing and functional results.
Although post-pubertal mandibular growth exists, with gender differences, no study has evaluated post-pubertal mandibular growth in Class II subjects with severe dentoalveolar disharmony. This is especially important in deciding treatment timing in subjects planned for orthognathic surgery, where the aim is to correct sagittal maxillo-mandibular relationships. Surgical treatment of severe class II malocclusion due to an undersized mandible should be performed when minimal further growth is possible, to ensure clinical and functional stability. The present study aims to evaluate mandibular growth of untreated Class II subjects with underdeveloped, small-sized mandibles, after the pubertal growth peak.

The following sections will begin with a discussion of the types of malocclusion and the difference between dentoalveolar and skeletal etiologies, followed by discussion of craniofacial growth, of mandibular growth in patients with Class II malocclusion, and finally with discussion of the biologic indicators of skeletal maturity.
II. Review of Literature

A. Types of Malocclusion

Edward H. Angle’s classification of dental malocclusion allowed for the classification of malocclusion types and provided the first definition of normal occlusion in the natural dentition.\(^1\) The three classes of malocclusion were based on the position of the mesio-buccal cusp of the upper first permanent molar occluding with the buccal groove of the lower first molar; furthermore, when this finding was present, and teeth were arranged in a smooth curvi-linear line of occlusion, then normal occlusion was present.\(^1\) Based on occlusal relationships of the first molars, three classes of malocclusion developed\(^1\): 1) Class I malocclusion whereby molars were in a normal relationship, but malposed, rotated, or missing teeth caused an incorrect line of occlusion, 2) Class II malocclusion whereby lower first permanent molar was positioned in a more distal position compared to the upper first permanent molar, and 3) Class III malocclusion whereby lower molar was positioned in a more mesial position compared to the upper first permanent molar.

As the dentition develops, distal surfaces of the upper and lower second primary molars have either a mesial, flush, or distal relationship. Bishara et al.\(^9\) showed that all cases that began with a distal step of the lower second primary molar relative to the upper second primary molar, resulted in a Class II permanent molar and none of them self-corrected.\(^2\) The longitudinal growth study reported that once Class II malocclusion is established in either the primary, mixed, or permanent dentitions, it does not self-correct even though mandibular growth may occur faster and for a longer period of time than maxillary growth.\(^2,9\)
B. Class II Malocclusion: Dentoalveolar versus Skeletal Etiology

According to the Burlington Orthodontic Research Center, where longitudinal growth studies of 1194 Canadian children aged 3-12 were conducted, the prevalence of Class II malocclusion was 23%, with 60% of these patients having an underlying skeletal dysplasia. Therefore, approximately 40% of Class II malocclusions are due to dentoalveolar etiology and have well related skeletal bases. Such etiologies are attributed to tooth positional factors and predisposing factors such as maxillary incisor protrusion, excess overbite, excess spacing, dentoalveolar crowding, premature tooth loss, congenitally missing teeth, supernumerary teeth, tooth-size discrepancy, caries, ectopic eruption, and habits. The same longitudinal growth study reported the following: i) 14% of subjects had normal Class I occlusion and ii) the incidence of Class I occlusion with observable tooth positional defects was 45%.

Of the 60% of patients with Class II malocclusion due to an underlying skeletal dysplasia between maxilla and mandible, six possible morphological variations of skeletal dysplasia in the craniofacial complex have been described using cephalometric analysis. These groups are: (1) the maxilla and teeth are anteriorly situated in relation to the cranium; (2) the maxillary teeth are anteriorly placed in the maxilla; (3) the mandible is of normal size but posteriorly positioned; (4) the mandible is underdeveloped; (5) the mandibular teeth are posteriorly placed on an adequate base; (6) the final variation compromises various combinations of the aforementioned factors. The non-syndromic idiopathically deficient mandible with Class II malocclusion has been referred to as mandibular retrognathism, mandibular microgenia, mandibular retrusion, skeletal class II, and class II malocclusion. Multiple early reports found mandibular
deficiency due to smaller mandibular length in Class II subjects for both genders.\textsuperscript{16-18} Varrela\textsuperscript{19} showed that this skeletal finding is established early by comparing lateral cephalometric radiographs of Class II children in the primary dentition with children at the same developmental stage but with normal occlusal development. Children with Class II occlusion had shorter mandibular body length relative to those with normal occlusion.\textsuperscript{20} When McNamara performed a review of literature, he found that 12 studies reported that the main cause of Class II malocclusion was a retrognathic mandible.\textsuperscript{21} Subsequently, McNamara studied lateral cephalometric radiographs of 277 children with Class II malocclusion (153 males, 124 females) aged 8 years to 10 years 11 months and reported that the average position of the maxilla was found to be neutral relative to cranial base, but the most common significant finding was mandibular skeletal retrusion relative to cranial base.\textsuperscript{21} Pancherz et al.\textsuperscript{22} more recently evaluated dentoskeletal morphology using lateral cephalometric radiographs in 347 Class II division I subjects and reported that the majority (46-76\%) of subjects had posterior sagittal mandibular position indicating mandibular retrognathia. Therefore, Class II malocclusion is a common diagnosis in clinical orthodontics and most often attributed to skeletal etiology due to a small-sized or posteriorly positioned (retrognathic) mandible.

Previous craniofacial studies examining mandibular growth of subjects with Class II malocclusion did not account for the severity of skeletal dysplasia. In most of these studies, the severity of skeletal dysplasia causing the Class II malocclusion was determined by the degree of mandibular retrognathia and/or the decrease in total mandibular length. When Harvold\textsuperscript{23} performed a random sample of male and female children with serial cephalometric records from the Burlington Orthodontic Research
Centre, he reported that maxillary-mandibular unit length differential was a significant indicator of the degree of matching of maxillary and mandibular unit lengths, with differences indicating unfavorable dysplasia. Harvold\textsuperscript{23,24} reported mean unit length differential at 16 years of age of 27 mm in males and 26 mm in females. Greater than 4 mm anteroposterior discrepancy indicates a more severe underlying cause of moderate to severe malocclusion attributed to a problem with the size, form, or position of the skeletal base.\textsuperscript{25} In 1997, Ngan et al.\textsuperscript{26} performed a longitudinal evaluation of 20 Class II division I female subjects between ages 7 and 14 with moderate to severe skeletal dysplasia and compared them to 20 Class I female controls using defined inclusion criteria of sagittal maxillary-mandibular cranial base angular measurement (ANB) of $> 4^\circ$. The group reported: 1) normally related maxilla relative to cranial base in the study group, 2) significantly more retrusive mandibular position in the study group, and 3) significantly decreased mandibular length of 6 mm, between the study group and the control group, at age 12 which was maintained through puberty until age 14. More recently, in 2005, De Freitas et al.\textsuperscript{27} compared digitized lateral cephalograms of 55 subjects with Class II division I malocclusion to a group of subjects with normal occlusion using clear inclusion criteria of full-cusp malocclusion and ANB $> 4.5^\circ$. They reported that subjects with moderate to severe skeletal dysplasia had significantly reduced mandibular length and a posterior sagittal position of the mandible relative to cranial base. In summary, available literature confirms that the etiology of Class II malocclusion is most often skeletal dysplasia due to a retrognathic mandible and/or decreased mandibular sagittal length.\textsuperscript{21,26,28-30}
C. Craniofacial Growth

In order to understand skeletal dysplasia it is essential to understand craniofacial growth. Facial growth requires coordinated interrelationships between soft and hard tissue, which grow and remodel in function.\textsuperscript{31} Bones remodel during growth because as they increase in size, regional parts change shape.\textsuperscript{31-35}

i. Maxillary Growth

Primary craniofacial growth studies of the maxilla have shown that there is bone deposition on the posterior aspect of the maxillary tuberosity, adding length to the maxillary dental arch and to the sagittal dimension of the maxilla allowing for tooth eruption.\textsuperscript{2,14,33,36,37} According to Sicher, the overall dimensions of the maxilla are determined by the four sutures, or syndesmoses, that connect the maxilla to the frontal bone (fronto-maxillary suture), zygomatic bones (zygomatico-temporal and zygomatico-maxillary sutures), palatine bones and sphenoid bone (pterygo-palatine sutures), which are oriented in a downward and forward direction consistent with maxillary growth.\textsuperscript{38} Sicher reported that growth of the cranium and maxilla occurs primarily and initially at the connective tissue between the sutures in response to stimuli from enveloping soft tissues.\textsuperscript{38} As the maxilla is translated downward and forward, bony remodeling occurs: i) osseous deposition occurs at the zygomatic process, which grows laterally and posteriorly, at the palatal surface of the nasal floor, and at the sutures of the maxilla, while ii) resorption occurs at the anterior surface of the maxilla and at the superior surface of the nasal floor, allowing for definition of the nasal cavities and the superior border of the palatal vault.\textsuperscript{3,33,36,39,40}
Contrary to Sicher, Scott studied longitudinal growth with simultaneous anatomical studies of children’s skulls. He reported that cartilage, or synchondroses, has the ability to separate growing bones at sutures due to inherent properties: interstitial growth and resistance to deforming forces. According to Scott, growth of cartilage and the expansion of organs (eyes and brain) separate bones and thereby allow for osseous deposition at the circumaxillary sutural surfaces and passive displacement of the maxilla. Such passive displacement of the maxilla downward and forward results from growth of the four cartilaginous synchondroses of the cranial base: intra-sphenoidal, intra-occipital, spheno-ethmoidal, and spheno-occipital synchondroses. Soon after birth, the first center of ossification appears at the supero-posterior aspect of the cartilaginous nasal septum, which initiates ossification and union of all facial bones (except the mandible) with the nasal septum by age 7. Such passive displacement becomes less influential as growth at the synchondroses of the cranial base slows with completion of growth of the brain by age 7, after which, from ages 7-15, only 1/3 of the forward movement of the maxilla results from passive displacement. According to Scott’s nasal septum theory, cartilage of the nasal capsule is the primary growth center acting as the driving force for all facial bones (except the mandible) to propagate downward and forward. Moss later suggested that the nasal septum and the sutures are secondary (passive) growth sites that respond to primarily functional demands mediated by soft tissue of the respiratory, pharyngeal, and masticatory systems. According to Moss’ functional matrix theory, primary growth of the brain leads to growth of the cranium, and enlargement of the oral-pharyngeal airspaces cause passive displacement of the
craniofacial complex downward and forward.\textsuperscript{1,43} Similar to maxillary growth, theories of mandibular growth also vary.

\textbf{ii. Pre-Natal Mandibular Growth}

The mandible joins the temporal bone at the temporomandibular joint and serves very important functions such as mastication and speech.\textsuperscript{44} Embryologically, development of the mandible begins at week 5 of fertilization with the formation of Meckel’s cartilage and subsequent growth forming a mandibular arch protuberance.\textsuperscript{44} The mandible develops from the first pharyngeal arch as a condensation of mesenchyme lateral to Meckel’s cartilage, at the junction of the mental and incisive branches of the inferior alveolar nerve.\textsuperscript{1,45,46} Meckel’s cartilage is an essential element in normal intramembranous bone formation of the mandible.\textsuperscript{45-48} At the 15\textsuperscript{th} day post-insemination, the primary mandibular ossification center was the first membrane bone formed lateral to each Meckel’s cartilage and anterior to the deciduous first molar tooth buds.\textsuperscript{46} Lee et al.\textsuperscript{44} suggested that tongue movements directly induce early mandibular movement since Meckel’s cartilage was attached to genioglossus muscle at 5-7 weeks of gestation. By week 8 of fertilization, early muscles of mastication attach to the newly formed mandible and induce pulling forces which provoke appositional growth of the mandible independent of Meckel’s cartilage.\textsuperscript{44} The architecture of the mandibular body was complete by week 12 with the shapes of the body, coronoid process, mandibular angle, and symphysis formed.\textsuperscript{44} By 18 weeks, the pattern of contribution of Meckel’s cartilage to mandibular development was already established: anterior mandible involves ossification of the cartilage fusing to the medial aspect of the mandibular body, while the
sheath of Meckel’s cartilage persists as cartilage (sphenomandibuar and anterior ligament of malleus), and the posterior aspect contributes to middle ear ossicles malleus and incus.\cite{45,47,49} During weeks 20-25 of gestation, formation and growth of the mandible is most active as many linear bony trabeculations were radiating posteriorly from the primary ossification center apical to the primary first molar tooth germ extending to the coronoid process, mandibular angle, symphysis and to the alveolar ridge.\cite{44}

Adult shape of the temporomandibular joint is complete by week 14 of fetal life with the main muscular attachment being the lateral pterygoid muscle.\cite{50} Condylar cartilage forms firstly as an independent secondary cartilage separated from the mandibular body and fuses with the mandibular ramus early.\cite{1,51-53} The lateral pterygoid muscle is primarily attached to condylar tissue and elongates with rapid condylar growth by endochondral ossification during weeks 8-10 of fertilization.\cite{44} Early mandibular movements occur 2 weeks before temporomandibular joint movements and stimulate growth of the mandibular body and condyle, with condylar growth being independent and more accelerated than growth of the body.\cite{44,52,54,55} A mandibular growth spurt occurs during weeks 8-10 of fetal life, with the shape of the mandible changing from a wide V to a rounded U to a pointed V.\cite{51,53,56-59} Fetal ANB values range from of 4 to 28° and mean sagittal mandibular length (condyion to symphysis) increases from 21 to 54.83 mm between weeks 15 and 39.\cite{44,51,53,56} In summary, available literature on pre-natal mandibular growth demonstrates the following: 1) initial ossification from a primary center located apical to the deciduous first molar tooth germ and extending postero-superiorly to the condylar head, 2) maxillo-mandibular sagittal relationships in-utero range from normal to mandibular retrognathia to micrognathia, and 3) mean mandibular
length was 5.48 cm at 39 weeks of gestation. The following section will discuss mandibular growth after birth and through adolescence and show how directions of growth were established very early in fetal life.

iii. Post-Natal Mandibular Growth

At birth, the human mandible has an obtuse gonial angle (angle between mandibular body and ramus), a low inferior alveolar canal, and is composed of two symmetrical halves which fuse at the first year of life. Mandibular growth occurs through various types of bone formation: from connective tissue matrix (intramembranous) and from pre-existing cartilage at the condylar head (endochondral replacement of cartilage to bone and appositional growth of connective tissue layers). Mandibular cartilage differs from primary cartilage in the superficial layer of perichondrium whereby undifferentiated cells (and not chondrocytes) proliferate to effect growth. Such undifferentiated cells can become either cartilage or bone depending on the presence of mechanical forces, with thinning and degeneration of mandibular cartilage reported with immobilization of the temporomandibular joint. At the surface of the mandibular condyle lies cartilage that experiences hypertrophy, hyperplasia, and endochondral replacement. first reported that growth of condylar cartilage and appositional growth of bone determine the overall size of the mandible. Since the condylar cartilage is covered by a layer of connective tissue continuous with the periosteum of the condylar neck, proliferation of condylar cartilage elongates the mandibular neck both by interstitial (growth from within) and appositional
growth (addition of from the deeper layers of connective tissue). Growth of the condyle is directed upward and backward to maintain contact with the temporomandibular joint, thereby thrusting the mandible downward and forward.\(^{41,42}\)

Condylar growth was shown to be different from growth of the epiphyseal growth plate.\(^{67}\) Condylar cartilage (also called embryonic, or secondary, cartilage) is different from epiphyseal growth plate in the following ways: less well organized cellularly, little intercellular matrix in immature forms, different calcification patterns, and condylar cartilage are remodeling centers that grow by responsive adaptation, with far less response to hormones and dietary disturbances.\(^{67}\) In rat condylar transplantation experiments, it was shown that there was no inherent growth potential, thereby refuting the controversy over the condyle being a growth center able to determine the size and shape of the mandible.\(^{68-70}\) In contrast, epiphysis of long bones and cranial base synchondroses are known to be growth centers with independent growth potential, genetic control, and intrinsic separating abilities.\(^{68,69}\)

Molecular genetics research on condylar cartilage and condylar growth suggests that mandibular growth and condylar cartilage are under genetic control. The expression of Sox9 (chondrogenic) and Runx2 (osteogenic) genes determine the fate of condylar cartilage.\(^{65,68,71,72}\) Mice in which the Indian Hedgehog gene was inactivated during condylar growth resulted in inhibited expression of Sox9 with a severely shortened mandible.\(^{65,73}\) These mice also presented with condylar disorganization, growth retardation, and partial ankylosis of the disc to the condylar surface.\(^{74}\) In a 2014 review, Hinton\(^{65}\) suggested a hierarchy of gene interactions whereby multiple genes (Twist1, Notch, Dlx5, BMP, FGF, TGF-β) regulate morphology and growth of the
temporomandibular joint through expression of Runx2 or Sox9, with these two genes causing agenesis of condylar cartilage if inactivated. Single gene knockout experiments have demonstrated multiple genes that influence growth of condylar cartilage and mandibular growth, but future molecular genetic research is required to develop a coordinated model by which condylar growth interacts with the glenoid fossa to coordinate mandibular growth.

The finding of bone remodeling during growth is an old concept dating back to 1771: Hunter\textsuperscript{75} showed that as the mandible grows in a posterior direction toward the base of the skull, the ramus grows backward by bone deposition on the posterior border and resorption on the anterior border.\textsuperscript{76} In his classic growth study of bone remodeling, Enlow\textsuperscript{76} mapped the microscopic distribution of bone deposition and resorption in 25 sections of human mandibles from specimen of subjects aged 4 to 12 to study local growth directions and local remodeling in specific areas of the mandible. Three fundamental principles of remodeling were identified: area relocation, surface changes determined by growth directions, and the V-principle.\textsuperscript{32,76} Relocation refers to specific parts of the mandible being relocated with growth into other relative positions (for instance, as the mandible grows in a posterior direction, the anterior ramus becomes progressively relocated into the posterior ramus).\textsuperscript{76} As parts of the mandible relocate, structural changes occur with bone removal in the new area and addition of bone in old areas. Furthermore, Enlow\textsuperscript{76} reported that surfaces facing directions of growth are osseous depositing. He developed the V-principle of bone remodeling based on addition and removal of mandibular bone during growth on the periosteal (outer) and endosteal (inner) surfaces. While the V-shaped areas increase in size, movement and growth occurs
toward the wide end as the inner surface of the V faces the direction of growth (bone deposition) and the outer contralateral surface has bone resorption and removal.\textsuperscript{32,33} The V-principle of bone remodeling applies to specific areas of the mandible (Figure 1)\textsuperscript{32,76}: i) the condylar head has the V facing superiorly and grows with periosteal surface apposition and endosteal apposition ii) while the condylar neck grows to follow posterior ramal movement, the condyle neck relocates postero-superiorly. The condylar neck becomes narrower on the superior surface with periosteal resorption and simultaneous endosteal surface apposition, and also shifts medially with buccal resorption and lingual apposition, iii) ramus has buccal deposition (except for condylar neck and coronoid process), and lingual surface remodeling changes depending on relation to the mylohyoid line (deposition above the mylohyoid line, and resorption below the mylohyoid line). The posterior surface of the ramus had bone deposition and the anterior ramal surface had bone resorption. iv) the coronoid process remodels and relocates medially (lingual apposition and buccal resorption) and posteriorly (anterior resorption and posterior deposition), v) Inferior mandibular border is a depositing surface, with the antegonial notch being a reversal point with bone resorption, and vi) the chin has buccal resorption and lingual apposition on the anterior labial region between canines, with cephalometric B-point being a reversal point for inferior buccal apposition. Enlow’s classic study was a descriptive analysis with a small and potentially biased sample, which is difficult to replicate, and which only included specimens in the mixed dentition stage. Nonetheless, it remains the fundamental reference for bone remodeling during growth of the human mandible.
To summarize, while osseous deposition occurs, the contour of the mandible changes through resorption at the anterior surface of the coronoid processes, anterior ramus, and anterior symphysis above the chin. While the main site of most active bone deposition at the posterior ramus increases the width of the mandible, simultaneous resorption at the anterior ramus is what provides space for future eruption of permanent molars. Although the chin translates in a downward and forward vector, actual mandibular growth vectors are posterior and superior with appositional growth at the posterior ramus and vertical lengthening of the ramus by endochondral replacement and osseous surface remodeling of the condyle. More recent vital staining experiments demonstrated the main locations of mandibular growth are at the posterior surfaces of the ramus, at the condylar and coronoid processes, at the lower border of the mandibular body, on the lateral surfaces, and at the alveolar processes. Growth studies of Bjork
used metallic implants implanted in the mandible at the mid-line of the symphysis, on the mandibular body beneath the premolars, and on the external ramus at the level of the occlusal plane.\textsuperscript{36,77,78} Bjork showed that as the mandible grows, up and forward rotation (favorable in a Class II malocclusion) or down and backward rotation (unfavorable in a class II malocclusion) can occur.\textsuperscript{35,79}

In response to the previous emphasis on primary condylar growth by Sicher\textsuperscript{38,62} and Scott\textsuperscript{41} determining size and shape of the mandible and responsible for downward and movement growth, Moss\textsuperscript{80} suggested that mandibular growth was a secondarily passive displacement in response to the functional matrix of the vital organs in the respiratory system that expand in oral-pharyngeal air space. According to Moss\textsuperscript{43,80,81}, craniofacial growth happens according to the various functions (respiration, mastication), which are carried out by functional cranial components composed of two parts: 1) a functional matrix which carries out the function, and 2) a skeletal unit that supports a specific functional matrix. He reports two types of matrices exist: periosteal (muscles and teeth), and capsular (volumes enclosed by neuro-cranial and oral-facial capsules).\textsuperscript{43,80-82}

The mandible is composed of various micro-skeletal units that each carry out a function: 1) coronoid micro-skeletal unit supports the functional demands of the temporalis muscle, 2) angular micro-skeletal provides attachment for the masseter and medial pterygoid muscles, 3) alveolar micro-skeletal unit houses the dentition, and 4) basal micro-skeletal unit contains the inferior alveolar canal and associated artery, vein, and nerve.\textsuperscript{43,80,82}

Experiments performed by Schumacher and Dokladal\textsuperscript{83} demonstrated the dependence of the skeletal unit (coronoid process) upon the demands of the functional matrix (temporalis muscle) because resection of temporalis muscle leads to compensatory
reduction in size of the coronoid process by osseous resorption. Moss$^{43,80,84}$ reported that the condylar cartilages are not primary sites of mandibular growth, because complete bilateral condylectomy did not prevent mandibular translation in response to growth of the oral-pharyngeal air space. As the mandible passively translates downward and forward in response to expanding oral-pharyngeal capsular space, endochondral ossification occurs in condylar cartilage as a secondary compensatory growth in order to prevent disarticulation with the temporomandibular joint and thereby maintaining articulation with glenoid fossa.$^{43,80}$ Such classic reports by Moss were generalized concepts based on cross-sectional data with small sample sizes. Thirty years later, the functional matrix hypothesis was revisited and biological mechanisms were described by which information from a functional matrix stimulus translates into a skeletal unit signal that may regulate genomic activity and phenotypic expression.$^{85-88}$ Through osseous mechanotransduction, osteocyte cells in bone communicate through ionic transport or electrical signals and form an osseous connected cellular network (CCN) which regulates bone cell responses.$^{85}$ Furthermore, research on osteocytes reported stretch-activated channels for ionic channeling of $K^+$, $Ca^{2+}$, and $Na^+$, which can initiate intracellular electric potentials to regulate gene expression.$^{85}$ Development of molecular biology research has shown how environmental stimuli may regulate gene expression. In summary, craniofacial growth theories vary on the mechanisms by which growth occurs but the overall consensus of a downward and forward growth has been established. The following sections will begin by discussing mandibular growth before and after the pubertal growth peak and then discuss mandibular growth in patients where unfavorable mandibular growth resulted in class II malocclusion.
iv. Amount and Rate of Mandibular Growth

Longitudinal studies to measure the amount and rate of mandibular growth have shown the presence of a pubertal growth spurt, with gender difference. Harvold\textsuperscript{23} in a longitudinal growth study of 454 male and 340 female children aged 6 to 16 years (Table 1) obtained serial cephalometric records from the Burlington Research Center. Sagittal mandibular growth was studied measured from condylion point (posterior-superior point on the condylar head where the maximal mandibular length contacts the condylar head) to prognathion point (on the bony chin when maximum mandibular length can be measured, this point being very close to pogonion).\textsuperscript{23} For males, mandibular sagittal growth was 2.5 mm/year between the ages of 6 and 12 years, and 3-3.5 mm/year between the ages of 12 and 16 years.\textsuperscript{23} For females, mandibular sagittal growth was 2.7, 2 and 1 mm/year between the ages of 6 - 12, 12 - 14, and 14 – 16 years, respectively.\textsuperscript{23} Since females generally begin puberty and the growth spurt sooner than males, females experienced less increase in mandibular length after age 12.\textsuperscript{24} This gender difference in amount of mandibular growth and timing of growth spurt with females preceding males was consistent with other longitudinal growth studies.\textsuperscript{27,36,89-92}
Table I. Harvold’s standards of Mandibular Unit Length.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>99</td>
<td>97</td>
</tr>
<tr>
<td>9</td>
<td>107</td>
<td>105</td>
</tr>
<tr>
<td>12</td>
<td>114</td>
<td>113</td>
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<td>14</td>
<td>121</td>
<td>117</td>
</tr>
<tr>
<td>16</td>
<td>127</td>
<td>119</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Mandibular Growth in (mm/year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6-12</td>
</tr>
<tr>
<td>12-14</td>
</tr>
<tr>
<td>14-16</td>
</tr>
</tbody>
</table>

Growth rate of the mandible is not constant throughout development.\textsuperscript{1,6,39,78,90} Multiple longitudinal growth studies based on cephalometric analysis have shown a pubertal spurt in mandibular growth with individual variability in onset, duration, and rate.\textsuperscript{89-91,93} Lewis et al.\textsuperscript{89} assessed peak height velocity, in 33 females and 34 males, using bi-annual stature measurements and related to craniofacial changes on annual cephalometric radiographs. The group considered pubertal growth spurts as greatest successive annual increases occurring within two years of peak height velocity. At the pubertal growth spurt, greatest increase in statural height matched the greatest increase in mandibular length, occurring at mean age 13.1 in males (3.3 mm/year), and at mean age 11.6 in females (2.9 mm/year).\textsuperscript{89} Multiple studies have confirmed that acceleration in body growth at the pubertal growth spurt parallels the increase in development of the sexual organs; the mandible follows the general body growth at puberty.\textsuperscript{1,23,90} Considerable variation exists regarding the onset of puberty as chronological age is only a crude indicator of individual development; nonetheless, there is an adolescent growth spurt in mandibular length.\textsuperscript{89-91,93-95}
v. Post-pubertal Mandibular Growth

Multiple studies have shown that craniofacial growth may persist substantially beyond puberty.\textsuperscript{89-91,96-98} In 1966, Hunter\textsuperscript{98} performed a longitudinal growth study of 26 males and 34 females from age 7 to 17 and correlated changes in lateral cephalometric measurements with chronological age, skeletal age based on hand-wrist maturation indices, and changes in height. The author recognized continued anteroposterior growth after skeletal maturation in 88.3\% of male subjects, as measured from articolare-pogonion on each lateral cephalometric radiograph, and reported that from the end of the pubertal growth period in height to the completion of mandibular growth, males had greater increase in length of the mandible over a longer period of time (final mean length of the mandible was 122.3 mm in males and 106.6 mm in females).\textsuperscript{98} Furthermore, facial growth continued into the third decade in the majority of males and continued after growth of body height was complete, whereas in females facial growth stopped late in the second decade and was more likely to be completed when final body height was attained.\textsuperscript{98} Woodside\textsuperscript{99} studied relative growth rates and distance velocity of mandibular growth in subjects aged 3-20, using 45° lateral oblique radiographs for mandibular length measurements taken annually as part of the longitudinal records of the Burlington Growth Study.\textsuperscript{100} He reported that female mandibular growth ceases around 16 years, whereas males experience persistent mandibular growth after 20 years of age.\textsuperscript{100} Bjork studied mandibular condylar growth longitudinally using implants in 45 Danish male subjects, ranging from 5-22 years.\textsuperscript{77} The author reported that the earliest age at which mandibular growth was complete was 17 years, 5 months, whereas others grew beyond 20 years.\textsuperscript{77} In their cephalometric growth study of 20 adults from ages 17 to 50, Lewis and Roche\textsuperscript{101} reported that maximum mandibular length was obtained in the age range of 29 to 39
years. Behrents\textsuperscript{102} evaluated craniofacial growth with aging and reported continued mandibular growth into the fifth decade. Neither of these longitudinal growth studies discussed evaluated growth based on dentoskeletal relationships. Nonetheless, such longitudinal growth studies identified gender differences in facial growth and found that mandibular growth persists beyond the pubertal period.

D. Mandibular Growth in Patients with Class II Malocclusion

Multiple reports exist in the literature that Class II patients with altered maxillo-mandibular skeletal relationships grow differently from people with normal dentoskeletal relationships in both the amount and the direction of craniofacial growth.\textsuperscript{103}

i. Pre-pubertal mandibular growth with Class II Malocclusion

A number of studies have been conducted that analyzed pre-pubertal and circumpubertal mandibular growth in patients with Class II malocclusion. Significant differences in growth changes in the mandible between Class II and Class I subjects have been reported in four studies. The majority of these studies evaluated the change in mandibular length from the deciduous to the mixed to the permanent dentitions and compared to the growth of a Class I control group. These studies, discussed below, showed decreased mandibular length and less mandibular growth in Class II subjects.\textsuperscript{20,26,104,105} Furthermore, the common significant finding in these studies was that Class II craniofacial and occlusal patterns were established early and most cases did not self-correct with growth.\textsuperscript{20,26,104,105}
Baccetti et al.\textsuperscript{20} studied 25 untreated children (ages 5 to 8 years) in the deciduous dentition with distal-step relationship of second primary molars, increased overjet and Class II deciduous canines, and compared to a control group (with flush terminal plane, and minimal overjet). Results suggest that mandibular length increases at a lesser rate in children with Class II malocclusion than with Class I occlusion.\textsuperscript{20} The major negative aspects of the study are the small sample size (25), the short observation period of 2 years 6 months ± 9 months, and the fact that all subjects were significantly pre-pubertal and in complete primary dentition. Kerr\textsuperscript{104} evaluated 85 lateral skull radiographs of children at 5, 10, and 15 years of age with Class I and Class II occlusion, and reported that subjects with Class II malocclusion had 2.5 mm less mandibular growth than subjects with Class I according to skeletal cephalometric measurements. Ngan et al.\textsuperscript{26} studied serial radiographs of 20 female Class II subjects from ages 7 to 14 from the Ohio State University Growth Study and reported skeletal differences that remained through puberty\textsuperscript{35}: more retrognathic mandible in Class II subjects, shorter mandibular length in Class II subjects, and greater maxillo-mandibular cranial base difference (ANB) in class II subjects. The significant common factor in these three studies was the use of chronological age or dental eruption times.

Chronological age or dental ages have been reported to be unreliable growth analyses for skeletal maturation.\textsuperscript{90,93,105,106} Stahl et al.\textsuperscript{105} studied longitudinal growth in 17 Class II subjects and compared to 17 Class I controls using the cervical vertebral maturation analysis in order to evaluate growth before and after the pubertal growth peak, but not prematurely. This study had clear inclusion criteria for severity of Class II malocclusion: full-cusp or half-cusp Class II molar relationship, increased overjet, and sagittal maxillo-
mandibular cranial base angular measurement (ANB) > 3°. By measuring mandibular length on lateral cephalograms from condyion point on the condylar head to gnathion point on the chin, Stahl et al.\textsuperscript{105} showed that the peak of mandibular growth was significantly smaller in Class II subjects than in Class I subjects. Subjects with Class II malocclusion grew 2 mm less at the growth spurt, and 2.9 mm less in the overall circumpubertal period, thereby reporting that deficiency of growth in Class II subjects was maintained in the post-pubertal period, with no “catch-up” growth.\textsuperscript{105}

One study, however, showed different results compared to previous studies discussed in that mandibular growth was similar between Class II subjects and Class I controls. Bishara et al.\textsuperscript{9} evaluated growth in 41 subjects with Class II malocclusion and 35 Class I control subjects from the deciduous through the permanent dentitions with average ages of 5 years at the start and 12.2 years after treatment. The group reported that differences in mandibular length and position were more evident in the early stages of development than in later stages.\textsuperscript{4} Cases of severe Class II malocclusion or skeletal dysplasia were excluded from the study and growth was only analyzed until 12.2 years of age, making the study inadequate for long-term mandibular growth evaluation. Since no consistent differences were seen between the study group and the control group, the author suggested that “catch-up” growth was possible, but such conclusions are biased and false for the following reasons: 1) there is no mention of severity of Class II malocclusion; the study sample may be a mild dentoalveolar Class II malocclusion with normal skeletal relationships, 2) cross-sectional comparisons at these time points are weak due to evaluation of skeletal growth based on chronological age stopping at 12 years of age. Many subjects may not have begun their pubertal growth spurt and evaluating mandibular
length before the termination of active growth may provide false representation of skeletal relationships and invalid results, and 3) subsequent studies, as discussed above, did not reproduce such findings.

Individual growth trends in patients with Class II malocclusion may be favorable or unfavorable and each individual has unique patterns of growth that affect response to treatment. While one patient may experience favorable growth, assisting the anteroposterior correction, other patients experience unfavorable growth which may require orthognathic surgery to treat. When Moore evaluated changes in 46 treated patients with retrognathic facial profiles and Class II malocclusion, only 50% of the cases ended with more prognathic chin points, whereas 25% had no change in the chin point, and 25% ended with more retrognathic chin points. Above all, an untreated Class II patient with severe retrognathia may have improved facial convexity but is likely to remain retrognathic with increasing age.

In summary, Class II malocclusion of skeletal etiology is not likely to self-correct with growth. Studies that evaluated mandibular growth have shown that subjects with Class II malocclusion have less magnitude of mandibular growth than subjects with Class I occlusion.
ii. Post-pubertal Mandibular Growth with Class II Malocclusion

Few studies provide information on the dentoskeletal growth of Class II patients specifically after the peak in pubertal growth. Two studies have addressed the question of whether mandibular growth persists beyond puberty in the Class II population. Pollard and Mamandras\textsuperscript{100} studied postpubertal facial growth, using lateral cephalograms, in 39 untreated males with Class II malocclusions as defined by ANB > 4°. Growth changes were assessed by measuring the increase in mandibular length (condylion-gnathion) in each subject at 2 time-points: ages 16 and 20. This group reported mandibular growth from ages 16-20 of 4.26 mm.\textsuperscript{100} Similar increases in mandibular length of 4.29 mm and 4.36 mm from ages 16 to 20 years were reported in two post-pubertal longitudinal growth studies of subjects with Class I malocclusion.\textsuperscript{99,109} Therefore, by comparing growth studies, increases in mandibular length were similar between male skeletal Class I and Class II subjects.\textsuperscript{100} Limitations of the Pollard and Mamandras\textsuperscript{100} study included: 1) Use of chronological age to determine the post-pubertal period, a method that has been shown to be a poor predictor of skeletal age and growth\textsuperscript{89,90,105,106,110} 2) Lack of an age-matched control group with Class I occlusion, and 3) Inclusion of only males in the sample. Results are therefore not generalizable for mandibular growth of females as males generally begin the pubertal growth spurt later than females, and grow for longer periods of time, which further decreases the validity of the study’s use of chronological age as the biologic indicator of skeletal maturity.\textsuperscript{89-91,111}

In the second study, Baccetti et al.\textsuperscript{112} studied lateral cephalograms of 23 subjects with Class II division I malocclusion as measured by full-cusp Class II molar relationship, increased overjet > 5 mm, and ANB > 4°. Thirty subjects with Class I occlusion formed
the control group. Increase in mandibular length (condyion-gnathion) was measured between two consecutive time-points: (1) post-pubertal, according to CVM\(^{113}\) stage 6 and (2) young adulthood (roughly 3.5 years after T1). An analysis of the sample of patients in the study showed that chronological ages were 15.7 (T1) and 19.1 (T2), and therefore quite similar to the sample from the Pollard and Mamandras\(^{100}\) post-pubertal growth study. Baccetti et al.\(^{112}\) found minimal growth changes after puberty in the Class II subjects and in the Class I controls. The group reported 1.1 mm of mandibular growth in the Class II subjects and 1.2 mm of growth in the Class I control group, and differences were not statistically significant (p>0.05).

Interestingly, although they differed in terms of one study showing minimal growth\(^{112}\) in both Class I and Class II subjects versus the other study showing the presence of post-pubertal mandibular growth\(^{100}\), both studies showed no difference in mandibular growth between subjects with Class II malocclusion and Class I occlusion in the post-pubertal period.\(^{100,112}\) Two major contributors to the differing results between these two post-pubertal longitudinal growth studies arise from the inclusion criteria of the patient sample. Firstly, in the Pollard and Mamandras\(^{100}\) study, only males were included in the sample and multiple studies report that males begin facial growth later than females and grow for a more prolonged duration.\(^{23,90,91,98}\) Secondly, even though the chronological ages were very similar, the skeletal maturation may differ. The Baccetti\(^{112}\) study used the CVM analysis\(^{113}\) as a biologic indicator of skeletal maturity, a method that more accurately represents skeletal maturation and the mandibular pubertal growth spurt. Therefore, subjects were more skeletally mature in this post-pubertal growth study and the amount of mandibular growth was less than previous studies that used chronological
age to identify the post-pubertal period. Multiple studies confirm reduced growth with increased skeletal maturation.\textsuperscript{92,93,114,115} Therefore, in the study by Pollard and Mamandras\textsuperscript{100} the males could have been in active growth at the two observation time-points based on chronological ages (16 and 20).\textsuperscript{91,113,115-119}

In both these studies, the inclusion of subjects with Class II malocclusion was based on maxillo-mandibular cranial base difference (ANB) > 4°, indicating these subjects had dentoalveolar malocclusions, and not skeletal discrepancies, since normal values for ANB are 2.7 ± 2°.\textsuperscript{1} The sample selection from the two studies discussed above did not consist of skeletal Class II malocclusions as the craniofacial measurements were within normal range. Since the majority of patients that present with Class II malocclusion have underlying skeletal dysplasia, such growth studies are not true representations of the Class II population.

E. Orthognathic Surgery to Treat Skeletal Discrepancy

Orthodontic treatment maximizes anatomic compensations to obtain an esthetically harmonious masticatory system.\textsuperscript{120} The age of the patient influences orthodontists’ treatment recommendations for orthodontic treatment and orthognathic surgery.\textsuperscript{120} A survey of 512 orthodontists showed that the earliest recommended age for orthognathic surgery was when skeletal growth, as measured by chronological age, is 99% complete: males 16.5 years, females 14.9 years.\textsuperscript{15,120} No scientific evidence supported deferring the surgical correction of mandibular deficiency until adulthood.\textsuperscript{1,15,121} According to Proffit, mandibular advancement can be a viable treatment option when the pubertal growth spurt completes, which can be as early as 14 or 15.\textsuperscript{1} The author's reporting that the pubertal
growth spurt can be complete by 14 or 15 has been confirmed by previous longitudinal growth studies but this treatment timing does not account for potential post-pubertal growth.\textsuperscript{89,90} Furthermore, subjects that have delayed maturity, especially males, may still be in active growth based on such chronological ages.\textsuperscript{90,93,101,106,117,122,123} Interpretation of these findings demonstrates that generally the earliest orthognathic surgery is not postponed until after post-pubertal growth is complete. This post-pubertal mandibular growth occurs between the ages of 14 to 20 years for female patients, and 16 to early twenties for male patients (as discussed in previous section).\textsuperscript{77,98,122} Such results reveal that surgery at the end of the pubertal growth spurt places the skeletal bases in ideal positions for each respective patient, but ignores any late pubertal growth spurt that might be present. In summary, since some authors are advocating earlier mandibular advancement surgery based on chronological ages, after the growth spurt, information is required regarding the magnitude of facial growth in patients with severe deficiency during late adolescence.

According to longitudinal growth studies from the Burlington Orthodontic Research Center, Class III malocclusion represents 2-3\% of the Caucasian population.\textsuperscript{10} Such cases can be due tooth positional factors (tooth size discrepancy, missing teeth, crowding or spacing), or due to skeletal dysplasia (retrognathic maxilla of small size, and/or prognathic mandible of large size).\textsuperscript{10,124-127} Staudt et al.\textsuperscript{128} randomly selected 3358 Swiss Army recruits and reported that 75.4\% of the subjects with Class III malocclusion had underlying skeletal dysplasia: 47.4\% of the class III population had mandibular prognathism, 19.3\% had maxillary retrognathism, and 8.7\% had a combination of mandibular prognathism and maxillary retrognathism. Multiple reports confirm that the
majority of subjects with Class III malocclusion have mandibular prognathism as the etiology of the skeletal dysplasia. Surgical treatment of class III malocclusion is generally performed at the cessation of growth, in young adulthood, because mandibular growth is unpredictable and sagittal grow can continue until young adulthood, especially in males. Since the present study is an evaluation of mandibular growth in subjects with Class II malocclusion due to an under-sized mandible, this study will not address mandibular prognathism or mandibular growth in the class III population.

F. Biologic Indicators of Skeletal Maturity

Since chronological age, historically, is not considered a reliable indicator of skeletal maturity, multiple analysis have been used: body height increases, hand-wrist radiograph assessment, dental development and eruption, and cervical vertebral maturation. Baccetti et al. recognized five aspects of a model biologic indicator of mandibular skeletal maturity: efficacy in mandibular growth peak detection, minimal radiographic exposure, and ease, consistency, and usefulness in prediction of when the peak will occur. In a comparative analysis of the biologic indicators of skeletal maturity, Mellion et al. studied serial records of 100 subjects (50 boys, 50 girls) from 6 to 11 years and found that hand-wrist analyses correlated best, and better than the CVM analysis, with the maximum increase in mandibular length during the growth spurt (4.79 mm for boys and 3.88 mm for girls). Such findings have not been reproduced in other studies. Multiple reports with larger sample sizes have shown the validity and reliability of the cervical vertebral maturation analysis in predicting the timing of pubertal growth
and mandibular growth peaks by comparing to hand-wrist radiographic evaluation.\textsuperscript{92,94,95,113} Such reports evaluated lateral cephalometric radiographs and hand-wrist analyses in order to show that morphological changes in cervical vertebrae are reliable indicators of skeletal maturation.\textsuperscript{92,94,95,136} In summary, although chronological age has been suggested as being the most reliable indicator of skeletal maturity, multiple other comparative studies with larger sample sizes have reproduced the reliability of hand-wrist analyses and CVM analysis for identifying skeletal maturation and the pubertal growth peak.

Mandibular size, body height and cervical vertebrae correlated strongly with one another and body height increase was correlated strongly with hand bones and cervical vertebral changes, but the timing of peak mandibular growth varies between individuals.\textsuperscript{111} The importance of having clearly defined vertebral maturation indices defined by Lamparski et al.\textsuperscript{137} and by Baccetti et al.\textsuperscript{113,138} are therefore apparent. The CVM method appraises 3 cervical vertebrae (C2, C3, C4) from a single lateral cephalogram in order to assess the individual’s skeletal maturity:\textsuperscript{113}

(i) Cervical Stage 1: Flat lower borders and trapezoidal shapes to C3 and C4. The peak in mandibular growth will occur on average 2 years after this stage.

(ii) Cervical Stage 2: Concavity on the lower border of C2, and the bodies of C3 and C4 are trapezoid in shape. The peak in mandibular growth will occur 1 year after this stage.

(iii) Cervical Stage 3: Concavities are present at the lower borders of both C2 and C3. The bodies of C3 and C4 can be trapezoidal or rectangular horizontal in shape. This stage represents the peak in mandibular growth will occur in the following year after this stage.
(iv) Cervical Stage 4: Concavities are present at the lower borders of all 3 cervical vertebrae. The bodies are rectangular horizontal in shape. This stage represents the point where mandibular growth peak occurred within the past 1 or 2 years.

(v) Cervical Stage 5: Concavities are present at the lower borders of all 3 cervical vertebrae. At least one of the bodies of C3 and C4 is square in shape. At this stage, the peak in mandibular growth has ended 1 year before this stage.

(vi) Cervical Stage 6: All three lower borders have concavities, and at least one of the bodies of C3 and C4 is rectangular vertical in shape. The peak in mandibular growth has ended at least 2 years before this stage.

According to the six maturational stages of the Cervical Vertebral Maturation (CVM) analysis, the peak in mandibular growth occurs between CS3 and CS4, and active growth is completed when CS6 is attained. Franchi et al. evaluated the validity of CVM analysis as a biologic indicator of skeletal maturity by comparing changes in statural height to developmental stages of maturity of the cervical vertebrae. The group reported that 93.5% of individuals had the greatest increase in height between cervical vertebral stages 3 and 4 and confirmed the reliability of CVM to predict skeletal maturity. Subsequently, Baccetti et al. related increases in mandibular length to cervical vertebral morphological changes using lateral cephalograms and reported that the CVM analysis is reproducible and evaluates the individual’s skeletal maturity with high validity for identifying the peak in mandibular growth at puberty. In the present study, the CVM analysis will be used to identify the timing of the pubertal growth spurt, in order to select subjects after the growth spurt.
III. Purpose of the Study

The current literature requires clarification on whether there is mandibular growth, in late adolescence, in patients with severe skeletal dysplasia. The purpose of this study is to clarify the magnitude of mandibular growth in Class II subjects with severe mandibular retrognathia, after the pubertal growth spurt. Skeletal maturation will be evaluated using the CVM analysis\textsuperscript{138} to identify the pubertal growth peak.

Growth studies are important to assist the clinician in planning the timing and modality of treatment. Information is needed about the growth characteristics of Class II division I subjects with small-sized mandibles observed longitudinally in the post-pubertal period, because severe skeletal disharmonies are sometimes treated surgically in adolescence. Currently, minimal literature is available regarding post-pubertal mandibular growth in patients with a severely undersized mandible.
IV. Research Aims

1. To quantify mandibular growth, after the pubertal growth peak, in Class II patients with severe skeletal dysplasia.

2. To compare post-pubertal mandibular growth between Class II subjects and Class I controls.
V. Hypothesis

Statistically significant differences are seen between mandibular growth, after the pubertal growth spurt, in class II patients with severe skeletal dysplasia compared to Class I controls.
VI. Materials & Methods

A. Sample Selection

Longitudinal records of subjects with Class II division I malocclusion were requested and accessed from the AAOF Craniofacial Growth Legacy Collection, an online database supported by the American Association of Orthodontists Foundation (AAOF). The online database contains independent longitudinal growth collections from different growth centers in North America of children and adolescents who did not receive orthodontic treatment. Records from untreated subjects were obtained from the following six longitudinal growth centers: (i) Burlington Growth Center, (ii) Case Western Bolton Brush Growth Study, (iii) Iowa Facial Growth Study, (iv) Michigan Growth Study, (v) Oregon Growth Study, and (vi) Matthews Implant Growth Study.

Cephalometric radiographs of diagnostic quality were selected from the Craniofacial Growth Legacy Collection to obtain a sample of Class II division I subjects with severe skeletal dysplasia. The following inclusion criteria were used:

1. ANB \( \geq 6^\circ \)

2. Full-cusp Class II molar relationship on each lateral cephalometric radiograph

3. Maxillo-mandibular unit difference \( \leq 19.5 \)

Exclusion criteria included all of the following:

1. ANB \( < 6^\circ \)

2. Maxillo-mandibular unit length difference \( > 19.5 \)
Radiographs were obtained at 2 time points: T1 (after the pubertal growth spurt, corresponding to CS4, CS5, or CS6) and T2 (minimum 2 years after T1).

A control group with Class I occlusion matched for age, gender, and CVM stage was also obtained from the AAOF Craniofacial Growth Legacy collection. The matched control group was selected based on the lateral cephalometric radiographs at T1 and T2 demonstrating Class I molar relationship, ANB angle between $2.7 \pm 1.4^\circ$, and maxillo-mandibular unit length difference $\geq 22$.23

In total, the study group of subjects with Class II division I malocclusion consisted of 27 subjects (13 males, 14 females) and the control group consisted of 27 subjects (matched for age, gender and CVM stage113). All cephalograms were traced by a single investigator (G.S.).

**B. Lateral Cephalometric Analysis**

All lateral cephalometric images were recorded in centric occlusion with an enlargement factor of approximately 9% (the anode-center of subject distance was 152.4 cm, and the distance from the center of subject-film was 15.0 cm). All film images had been digitally converted (Epson Perfection V700 Photo scanner) and stored as a TIFF (Tagged Image File Format) for long-term storage. Using Adobe Photoshop 6 (San Jose, CA, USA), each radiograph was converted to JPEG (Joint Photographic Experts Group) format and resampled at a resolution of 300 pixels per inch, as performed previously.140,141 Each lateral cephalometric radiograph was imported as a JPEG format into version 11.7 of the Dolphin Imaging software (Dolphin Imaging and Management Systems, Chatsworth, CA, USA) program for tracing.
Using Dolphin Imaging program, a custom cephalometric analysis (Figure 1) was formed using the following craniofacial and dental reference points in order to subsequently analyze linear, angular, and proportional measurements\textsuperscript{140,141}:

- A point – the deepest (most posterior) midline point on the curvature between ANS and prosthion
- Anterior nasal spine (ANS) – the tip of the bony anterior nasal spine at the inferior margin of the piriform aperture in the mid-sagittal plane.
- B point – the deepest (most posterior) midline point on the bony curvature of the anterior mandible, between infradentale and pogonion, in the mid-sagittal plane.
- Condylion (Co) – the most superior posterior point on the head of the mandibular condyle (bilateral)
- Gnathion (Gn) – the most anterior inferior point on the bony chin in the mid-sagittal plane
- Gonion (Go) – the most posterior inferior point on the outline of the angle of the mandible
- Menton (Me) – the most inferior point of the mandibular symphysis (mid-sagittal)
- Nasion (N) – the intersection of the internasal and frontonasal suture (mid-sagittal)
- Pogonion (Pg) – the most anterior point on the contour of the bony chin (mid-sagittal)
o Posterior nasal spine (PNS) – the most posterior point on the bony hard palate (mid-sagittal)

o Sella (S) – the geometric center of the pituitary fossa (sella turcica) constructed in the mid-sagittal plane

**Figure 2.** Lateral cephalometric radiograph of a female study subject at T1 (age 16).

The following linear, angular and proportional measurements were analyzed\(^{23,140,142}\):

**Lengths of maxilla and mandible:**

- Maxillary length – the linear millimetric distance from condylion to ANS
- Mandibular length – the linear millimetric measurement from condylion to gnathion.
Sagittal (Anterior-posterior) measurements:

- ANB angle: the difference between SNA angle and SNB angle to determine the anteroposterior relationship between the maxilla and mandible relative to cranial base.\(^1\,^{142}\)

- Unit length difference (Co-Gn minus Co-ANS) – the maxillomandibular differential as determined by the mandibular length minus the maxillary length.\(^23\)

Vertical measurements:

- Upper facial height (UFH) – the linear millimetric measurement between nasion and ANS.

- Lower facial height (LFH) – the linear millimetric measurement between ANS and menton.

- UFH to LFH ratio (UFH:LFH)

**C. Reliability Analysis**

Images were measured and re-measured several days later by the same clinician, a test-retest approach to estimate reliability. Assessment of the stages in cervical vertebral maturation on the lateral cephalometric radiograph for each subject was confirmed by a second investigator (F.E.).

**D. Statistical Analysis**

Means of all measures were compared between Class I and Class II patients at baseline using independent t-tests. General linear models were constructed to compare mean mandibular growth differences at T2 while controlling for other variables in the model.
T-tests and general linear models assume that the model residuals are roughly normally distributed with equal variances. The general linear model evaluated differences in mandibular growth between subjects with Class II division I and Class I occlusions. The model also included the following variables: gender, age and CVM Stage\textsuperscript{113} at T1. Including CVM stage and gender in the model allows the assessment of the effects of these variables independent of all other variables on the outcome (change in mandibular dimension condyion-gnathion). This allows the assessment of the independent effect of class of occlusion on growth.
VII. Results

A. Sample Analysis

The sample consisted of 27 subjects with Class II division I malocclusion and a control group of 27 subjects with Class I occlusion, each group consisting of 13 males and 14 females (Table 1). At T1, the mean age of the Class II group was 14.9 years ± 1.3 and 14.9 ± 0.2 for the Class I control group. At T2, mean age was 19 years ± 1.9 for both the study group and control group. The mean observation period of both groups (T2-T1) was 4.1 years ± 1.8.

Table II. Study Sample Descriptive Statistics for Age, Sex and Observation Interval.

<table>
<thead>
<tr>
<th></th>
<th>Class II</th>
<th>Class I</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 27</td>
<td>n = 27</td>
</tr>
<tr>
<td></td>
<td>(13 m, 14 f)</td>
<td>(13 m, 14 f)</td>
</tr>
<tr>
<td>Mean Age at T1 (y)</td>
<td>14.9</td>
<td>14.9</td>
</tr>
<tr>
<td>SD</td>
<td>1.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Mean Age at T2 (y)</td>
<td>19</td>
<td>19</td>
</tr>
<tr>
<td>SD</td>
<td>1.9</td>
<td>1.9</td>
</tr>
<tr>
<td>T2-T1 interval (y)</td>
<td>4.1</td>
<td>4.1</td>
</tr>
<tr>
<td>SD</td>
<td>1.8</td>
<td>1.8</td>
</tr>
</tbody>
</table>

m, male; f, female

A comparison of the mean mandibular and maxillary lengths between the two groups revealed statistically significant differences in maxillary length, mandibular length, and maxillo-mandibular unit length differential (Table II). At T1, the mean mandibular length as measured by the distance between condylion-gnathion was 24.3 mm less in the Class II subjects than in the control group (95.9 ± 12.9 mm, compared to 120.2 mm ± 5.2 mm). Mean maxillo-mandibular unit length differential was 16.8 ± 2.2 mm in the study group, and 26.6 ± 3.6 mm in the control group. The sagittal relationship between the maxilla and mandible relative to cranial base (ANB°) had a mean of 6.7° ± 0.7° in the study group,
compared to a mean of $2.7^\circ \pm 1.4^\circ$ for the control group. The face: height ratio (UFH: LFH) was 79.8 in the study group, and 78.7 in the control group.

**Table III.** Descriptive statistics and statistical comparisons for cephalometric measurements in Class II subjects and Class I controls at T1 (CVM Stages 4 - 6).

<table>
<thead>
<tr>
<th></th>
<th><strong>Class II</strong></th>
<th><strong>Class I</strong></th>
<th><strong>Difference</strong></th>
<th><strong>P</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>n = 27</em></td>
<td><em>n = 27</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Maxillary skeletal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxillary length (Co-ANS, mm)</td>
<td>79.1 11.9</td>
<td>93.6 4.5</td>
<td>-14.5</td>
<td>0.000</td>
</tr>
<tr>
<td>SNA (°)</td>
<td>82.7 3.3</td>
<td>81.2 3.2</td>
<td>1.5</td>
<td>0.200</td>
</tr>
<tr>
<td><strong>Mandibular skeletal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandibular length (Co-Gn, mm)</td>
<td>95.9 12.9</td>
<td>120.2 5.2</td>
<td>-24.3</td>
<td>0.000</td>
</tr>
<tr>
<td>SNB (°)</td>
<td>76 3.2</td>
<td>78.5 2.8</td>
<td>-2.5</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Maxillary/mandibular</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max/mand diff (mm)</td>
<td>16.7 2.13</td>
<td>26.6 3.75</td>
<td>-9.8</td>
<td>0.001</td>
</tr>
<tr>
<td>ANB (°)</td>
<td>6.7 0.7</td>
<td>2.7 1.4</td>
<td>4.0</td>
<td>0.002</td>
</tr>
<tr>
<td>UFH (mm)</td>
<td>45.3 6.3</td>
<td>54.6 2.3</td>
<td>-9.3</td>
<td>0.010</td>
</tr>
<tr>
<td>LFH (mm)</td>
<td>57.2 8</td>
<td>69.5 4.5</td>
<td>-12.3</td>
<td>0.022</td>
</tr>
<tr>
<td>Face: Height Ratio</td>
<td>0.79 0.51</td>
<td>0.78 0.39</td>
<td>0.1</td>
<td>0.341</td>
</tr>
</tbody>
</table>

At T2, the mean mandibular length (condylion-gnathion) was 25.1 mm less (p<0.05) in the Class II subjects than in the control group (98.5 ± 14.3 mm, compared to 123.6 ± 4.6 mm) (Table III). Mean maxillo-mandibular unit length differential was $18.4 \pm 2.2$ mm for the study group, and $28.2 \pm 4$ mm in the control group (p<0.05). The sagittal relationship between the maxilla and mandible relative to cranial base (ANB°) had a mean of $5.87^\circ \pm 1.2^\circ$ for the study group, compared to a mean of $1.7^\circ \pm 2.9^\circ$ for the control group (p<0.05). The face: height ratio (UFH: LFH) was 79.8 in the study group, and 79.1 in the control group.
Table IV. Descriptive statistics and statistical comparisons for cephalometric measurements in Class II subjects and Class I controls at T2 (minimum 2 years after T1).

<table>
<thead>
<tr>
<th></th>
<th>Class II</th>
<th></th>
<th>Class I</th>
<th></th>
<th>Difference</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 27</td>
<td></td>
<td>n = 27</td>
<td></td>
<td></td>
<td>value</td>
</tr>
<tr>
<td><strong>Maxillary skeletal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maxillary length (Co-ANS, mm)</td>
<td>80.1</td>
<td>12.7</td>
<td>95.4</td>
<td>4.6</td>
<td>-15.3</td>
<td>0.000</td>
</tr>
<tr>
<td>SNA (°)</td>
<td>82.2</td>
<td>3.6</td>
<td>82</td>
<td>3.2</td>
<td>0.2</td>
<td>0.870</td>
</tr>
<tr>
<td><strong>Mandibular skeletal</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mandibular length (Co-Gn, mm)</td>
<td>98.5</td>
<td>14.3</td>
<td>123.6</td>
<td>4.6</td>
<td>-25.1</td>
<td>0.001</td>
</tr>
<tr>
<td>SNB (°)</td>
<td>76.2</td>
<td>3.5</td>
<td>79.1</td>
<td>3.5</td>
<td>-2.9</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>Maxillary/mandibular</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Max/mand diff (mm)</td>
<td>18.34</td>
<td>2.25</td>
<td>28.2</td>
<td>4</td>
<td>-9.8</td>
<td>0.021</td>
</tr>
<tr>
<td>ANB (°)</td>
<td>5.87</td>
<td>1.2</td>
<td>3</td>
<td>1.7</td>
<td>2.9</td>
<td>0.034</td>
</tr>
<tr>
<td>UFH (mm)</td>
<td>47.3</td>
<td>7.3</td>
<td>56</td>
<td>2.3</td>
<td>-8.7</td>
<td>0.041</td>
</tr>
<tr>
<td>LFH (mm)</td>
<td>58.5</td>
<td>9</td>
<td>71</td>
<td>4.1</td>
<td>-12.5</td>
<td>0.000</td>
</tr>
<tr>
<td>Face: Height Ratio</td>
<td>0.81</td>
<td>0.58</td>
<td>0.79</td>
<td>0.42</td>
<td>0.19</td>
<td>0.370</td>
</tr>
</tbody>
</table>

In the Class II subjects, the mandible was significantly retruded and undersized, represented by the large ANB angle (mean 6.7° ± 0.7°) and small maxillomandibular unit length difference (mean 16.8 ± 2.2 mm) with both measurements being statistically significant. Vertical relationships were also decreased in the Class II subjects for upper face height and lower face height; however, the ratios were within normal limits.

**B. Mandibular Growth Analysis**

In order to determine mandibular growth, the change in mandibular dimension (condylium-gnathion) from T1 to T2 was examined and stratified according to occlusal class and gender (Table IV). Mean mandibular growth for the study group was 2.7 mm, males (2.8 mm) and females (2.6 mm). Mean mandibular growth for the control group was 2.6 mm, males (4.4 mm) and females (1.1 mm).
Table V. Mean Mandibular Growth (T2-T1 mm) by Class of Occlusion and Patient Gender.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Class I</th>
<th></th>
<th>Class II</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (+/-SD)</td>
<td>N</td>
<td>Mean (+/-SD)</td>
<td>N</td>
</tr>
<tr>
<td>Females</td>
<td>1.1 (1.1)</td>
<td>14</td>
<td>2.6 (2.8)</td>
<td>14</td>
</tr>
<tr>
<td>Males</td>
<td>4.4 (3.8)</td>
<td>13</td>
<td>2.8 (1.9)</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>2.6 (3.2)</td>
<td>27</td>
<td>2.7 (2.4)</td>
<td>27</td>
</tr>
</tbody>
</table>

A plot comparing mandibular growth to occlusal class shows very similar relationships between mandibular growth in the study group and the control group (Figure 2).

Figure 3. Plot comparing Class of Occlusion to Mandibular Growth (condyion-gnathion) T2-T1.

The general linear statistical model was used to compare differences in mandibular growth T2-T1 between subjects with Class II occlusion and Class I controls. The statistical model also included each subject’s gender, age, and CVM stage at T1. The model results (Table V) demonstrate that age at T1 and gender are significant predictors of growth.
Table VI. Reduced Statistical Model Assessing the Effect of Occlusion, Gender, Age and CVM on Mandibular Growth (mm).

<table>
<thead>
<tr>
<th>Source</th>
<th>$MS$</th>
<th>$F$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class</td>
<td>2.3</td>
<td>0.5</td>
<td>0.500</td>
</tr>
<tr>
<td>Age</td>
<td>72.8</td>
<td>14.8</td>
<td>0.000</td>
</tr>
<tr>
<td>Gender</td>
<td>22.1</td>
<td>4.5</td>
<td>0.020</td>
</tr>
<tr>
<td>CVM</td>
<td>1.6</td>
<td>0.3</td>
<td>0.700</td>
</tr>
<tr>
<td>Error</td>
<td>4.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Model adj. R squared =0.66; Parameter estimates (SE): 
Age(slope)$=-1.17$ (0.3); Female mean $=2.1$ (0.68), Male mean $=4.0$ (0.5)

After controlling for these factors, differences in growth between Class I and Class II and between the three CVM groups, was not statistically significant. The parameter estimates reported in Table V show that on average, mandibular growth between T1 and T2 decreased by approximately 1.1 mm for every increase of one year of age at T1, and males grow about twice as much as females between T1 and T2 (4.0 mm versus 2.1 mm).

A pattern was observed showing that as the age at T1 increases, the amount of mandibular growth decreases (Figure 4).

Figure 4. The relationship between age at T1 and mandibular growth among male and female subjects.
Differences in growth between class I occlusion and class II occlusion were very small (2.6 versus 2.7 respectively) and differences were not statistically significant (P=0.50). Data suggests that although severe Class II subjects may grow to the same amount as Class I subjects during the observation period, the greatest increase in mandibular length was seen in males of the Class I control group (mean 4.4 ± 3.8 mm).

C. Reliability Analysis

Images were measured and re-measured several days later by the same clinician (G.S.). Figure 4 shows that the two sets of measures were highly correlated (r=0.99). Subsequently, to measure the closeness of the measurements, the difference was calculated between each pair of measures made on the same images. The average difference was 0.1 mm and the results of a one-sample t-test showed that this mean was not significantly different from zero.

Figure 5. Reliability analysis measurement of mandibular length (Condylion-Gnathion) made on 24 images from 12 patients (each patient measured at T1 and T2) on 2 different non-consecutive days.
In summary, our findings are:

- Lateral cephalometric radiographs of 27 subjects (13 males, 14 females) with Class II skeletal dysplasia (mean ANB of 6.7°; mean maxillo-mandibular unit length difference of 16.8 mm) and 27 matched controls (mean ANB of 2.7°; mean maxillo-mandibular unit length difference of 26.6 mm) were selected at 2 time-points (T1 and T2) after the pubertal growth peak.

- The average age of patients at T1 was 14.9 years and at T2 was 19 years. The average length of time between T1 and T2 was 4.1 years in both groups.

- No statistical difference was found in the change of mandibular length (condylion-gnathion) from T1-T2 between control and study groups (p=0.50). The mandibular length increased by 2.7 mm in the study group and by 2.6 mm in the control group between T1 and T2.

- Class II skeletal dysplasia was present at T2 (mean ANB of 5.87°; mean maxillo-mandibular unit length difference of 18.4 mm)

- Gender (p<0.05) was a statistically significant predictor of mandibular growth. Males in both groups had the greatest magnitude of mandibular growth - 4.4 mm in the control group and 2.8 mm in the study group.

- Age (p<0.05) was a statistically significant predictor of mandibular growth. As the yearly age at T1 increased, the amount of mandibular growth decreased by 1.1 mm in both groups.
VIII. Discussion

The present study was different from other published work so far in that this is the first post-pubertal longitudinal growth study to select subjects with Class II malocclusion based on maxillo-mandibular cranial angular measurements (ANB), maxillo-mandibular unit length differential, and vertical facial proportions. Previous studies on post-pubertal growth in Class II subjects used ANB measurement without accounting for mandibular length or maxillo-mandibular unit length difference. An increased ANB may be due to a normally sized mandible with downward-backward rotation, with an increased lower face height. In the current study, maxillo-mandibular unit length differential and vertical facial proportions were used to maximize the chance of selection of subjects with a true mandibular skeletal dysplasia. Also, measurement of maxillary unit length in some other studies was performed by measuring condylion to A-point. The position of A-point, however, changes with alveolar remodeling and position of the maxillary incisors. The present study used ANS (maxillo-mandibular unit length differential), which is more reliable for studying skeletal growth. Furthermore, the maxillo-mandibular unit differential in the sample in our study was 18.3 mm compared to 26.5 mm in the Baccetti et al. study and 25.63 mm in the Pollard et al. study. Therefore, it can be argued that, in contrast to other previous similar studies, the sample in the current study represented patients with true skeletal dysplasia.

The 27 matched subjects in the control and study groups in the current study showed statistically significant gender differences in mandibular growth at the two time points (Table VII). Gender was found to be a statistically significant predictor of
mandibular growth after the pubertal growth peak. Males had the greatest magnitude of mandibular growth in both groups. Other studies showed that the pubertal growth spurt occurs later in males than females and that the mandible grows for a longer period of time.\textsuperscript{1,36,39,89,90,101} In terms of the study group, i.e. Class II patients with skeletal dysplasia, our findings of 2.7 mm of mandibular growth were in contrast to that of 1.1 mm in the Baccetti et al.\textsuperscript{112} study. Gender differences may be responsible for the differences in findings between the current study and that of Baccetti et al.\textsuperscript{112} where data analysis was performed without separation of males and females.

Males in the control group of the present study experienced 4.4 mm of mandibular growth after the pubertal growth peak, a figure very similar in magnitude to other studies by Woodside\textsuperscript{99} and Love et al.\textsuperscript{109} that evaluated increases in mandibular length in Class I male subjects between ages 16 and 20 (4.36 mm and 4.26 mm, respectively). Interestingly, the magnitude of post-pubertal mandibular growth in the Class I male sample was similar to the amount reported by Pollard and Mamandas\textsuperscript{100} in their sample of males with Class II malocclusion (4.26 mm). Two possibilities exist as to why the Class II sample in the Pollard\textsuperscript{100} study had a similar amount of post-pubertal mandibular growth as the amount reported in Class I subjects.\textsuperscript{99,109} The first possibility is that their study sample of subjects with Class II malocclusion was truly a skeletal Class I sample, whereby the increased ANB was a normally sized mandible with downward-backward rotation. This highlights the importance of evaluating the maxillo-mandibular unit length differential in order to select subjects with true skeletal dysplasia. The second possibility, as the authors report\textsuperscript{100}, is that skeletal Class II subjects grow the same amount as skeletal Class I subjects, which is a finding confirmed by the results obtained in the current study.
Table VII. Comparative Analysis of Studies of Post-pubertal Growth in Subjects with Class II malocclusion.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Sample Size</th>
<th>Mean Age (T1, T2)</th>
<th>Gender</th>
<th>ANB</th>
<th>Unit Diff.</th>
<th>Skeletal Maturation</th>
<th>Md Growth (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baccetti et al. (2009)</td>
<td>Control</td>
<td>30</td>
<td>15.8, 19 T2-T1: 3.8y</td>
<td>13m, 17f</td>
<td>1.3 ± 2.9</td>
<td>T1: CVM 6 T2: CVM 6</td>
<td>1.1</td>
</tr>
<tr>
<td></td>
<td>Study</td>
<td>23</td>
<td>15.7, 19 T2-T1: 3.7y</td>
<td>10m, 13f</td>
<td>5.3 ± 1.1</td>
<td>T1: CVM 6 T2: CVM 6</td>
<td>0.7</td>
</tr>
<tr>
<td>Pollard et Mamandras (1995)</td>
<td>Control</td>
<td>0</td>
<td>16, 20 T2-T1: 4y</td>
<td>only males</td>
<td>5.55 ± 1.21</td>
<td>T1: age 16 T2: age 20</td>
<td>4.26</td>
</tr>
<tr>
<td></td>
<td>Study</td>
<td>39</td>
<td>14.9 (M:15.3, F:14.3), T2: 19 (M:19.2, F:18.9)</td>
<td>13m, 14f</td>
<td>2.7 ± 1.4</td>
<td>T1: CVM ≥ 4 T2: CVM &gt; 6</td>
<td>M: 4.4 F: 1.1</td>
</tr>
<tr>
<td>Scalia et al. (2015)</td>
<td>Control</td>
<td>27</td>
<td>14.9 (M:15.3, F:14.4), T2: 19 (M:19.3, F:18.7)</td>
<td>13m, 14f</td>
<td>6.7 ± 0.7</td>
<td>T1: CVM &gt; 4 T2: CVM &gt; 6</td>
<td>M: 2.8 F: 2.6</td>
</tr>
<tr>
<td></td>
<td>Study</td>
<td>27</td>
<td>14.9 (M:15.3, F:14.4), T2: 19 (M:19.3, F:18.7)</td>
<td>13m, 14f</td>
<td>6.7 ± 0.7</td>
<td>T1: CVM &gt; 4 T2: CVM &gt; 6</td>
<td>2.7</td>
</tr>
</tbody>
</table>

Mandibular growth was measured as change in mandibular length (condylion-gnathion) between T1 and T2 (Md – Mandible).

In our study, Class II subjects with severe skeletal dysplasia had 2.7 mm increase in mandibular length, on average, after the peak in pubertal growth, an amount greater than the one reported by Baccetti et al.\textsuperscript{112} of 1.1 mm, where all subjects were at CVM\textsuperscript{113} Stage 6 at T1. In the current study, skeletal maturation at T1 was after the pubertal growth peak, but subjects at CVM\textsuperscript{113} stages 4, 5, and 6 were included in the study sample. This allows for speculation that mandibular growth is present after the peak in pubertal growth, but decreases in magnitude as the patient becomes more skeletally mature because after CVM\textsuperscript{113} stage 6, minimal growth\textsuperscript{112} (1.1 mm) was reported.

The increase in mandibular length, after the pubertal growth peak, was not different in subjects with Class II skeletal dysplasia compared to Class I subjects. These
findings contradict previous reports that evaluated pre-pubertal and circumpubertal mandibular growth and suggested decreased inherent growth potential and deficient mandibular growth in patients with Class II malocclusion.\textsuperscript{20,26,104,105} The current study has found that Class II skeletal relationships were still present at T2, suggesting that even though post-pubertal mandibular growth exists, Class II skeletal relationships do not self-correct. This supports the findings of previous studies\textsuperscript{20,26,104,105} that opposed possible “catch-up” growth suggested by Bishara et al.\textsuperscript{9}

Data analysis demonstrated that the relationship between the magnitude of mandibular growth and the individual CVM\textsuperscript{113} stage at T1 (4, 5, or 6) was not statistically significant. Mandibular growth was present after the peak in pubertal growth regardless of the individual stage of morphologic changes of cervical vertebrae through maturation. The insignificant relationship between the maturation of cervical vertebrae and mandibular growth was also reported in a comparative study of the biological indicators of skeletal maturity by Mellion et al.\textsuperscript{117} Difficulty in differentiating individual morphological stages of the CVM analysis and subjective nature of the CVM analysis have been suggested as attributing factors.\textsuperscript{117} Multiple comparative studies with larger sample sizes have shown a strong correlation between mandibular growth and the CVM analysis.\textsuperscript{92,95,103,113} It is important to recognize that although an insignificant relationship was found between CVM stage and amount of mandibular growth, the primary use of the CVM analysis, in the current study, was to identify the pubertal growth peak.

Age appeared to be a statistically significant predictor of mandibular growth after the pubertal growth peak. The mean ages of the sample in the current study (14.9 ± 1.3 years at T1 and 19 ± 1.9 years at T2) did not appear to differ greatly from those of
Pollard and Mamandras\textsuperscript{112} where the chronological ages ranged from 16 (T1) to 20 (T2) years and $15.7 \pm 1.3$ (T1) to $19.1 \pm 1.4$ years (T2) in the study by Baccetti et al.\textsuperscript{112} Mellion et al.\textsuperscript{117} reported that chronological age may be a successful predictor of the mandibular growth peak, which confirms the high correlation and statistical significance between chronological age and post-pubertal mandibular growth found in the present study. In the current study, for every year increase in age at T1, the subject experienced 1.1 mm less mandibular growth. Multiple studies have reported that CVM analysis reliably identifies the post-pubertal period.\textsuperscript{103,105,112,113} The present study suggests that chronological age may be successful at identifying the post-pubertal period of skeletal maturation since the older a subject is, the more likely that they passed the pubertal growth spurt.

The mean ages of the sample in the present study, 14.9 to 19 years, parallels the period of time whereby orthodontists initiate post-pubertal treatment of Class II malocclusion in mild-to-moderate dysplasia or evaluate timing for combined orthognathic surgery in patients with severe skeletal dysplasia.\textsuperscript{112} When evaluating a patient with Class II malocclusion due to skeletal etiology, reliable evaluation of skeletal maturity is essential because mandibular growth after the pubertal growth peak can be clinically significant. During this observation period, the older a subject was the less mandibular growth they experienced. Nonetheless, clinicians may consider utilizing remaining mandibular growth but with limited expectations.
IX. Study Limitations

Mean mandibular growth between the two time-points (Table V) was not reported as annualized changed, but as a total growth in millimeters from T1 to T2. Annualized changes would provide information and identification of growth patterns regarding chronological age and yearly increases in mandibular size. However, growth was not related to the interval of time between two measures of mandibular length. As such, expressing growth as a yearly growth rate (mm/year) would be misleading because patients with a long interval would have smaller rates than patients seen over a shorter interval. For this reason, it was decided not to express growth as a per year rate.

This study is limited by the available lateral cephalometric radiographs on the online database of the American Association of Orthodontic Foundation’s (AAOF) Craniofacial Growth Legacy Collection. Lateral cephalometric radiographs of diagnostic quality had to be available at the two time-points after the pubertal growth peak. The sample size of 27 subjects is due to the difficulty in obtaining longitudinal growth records with such specific inclusion criteria based on specific cephalometric measurements (see Materials and Methods).
X. Future Directions

Future studies should include clinical photographs as part of the records used to study longitudinal growth. When evaluating post-pubertal mandibular growth, clinical photographs will aid in deciding whether the amount of growth is clinically acceptable. Especially in patients with psychosocial, esthetic, or functional limitations due to severe skeletal dysplasia, the timing of orthognathic surgery is of concern. Our study has shown that post-pubertal mandibular growth exists, but the clinical relevance of this degree of growth has yet to be investigated.
XI. Conclusions

1. The amount of mandibular growth in the post-pubertal period was not different between pooled Class II subjects (males and females) with severe skeletal dysplasia and Class I controls.

2. Post-pubertal mandibular growth in Class II subjects with severe skeletal dysplasia was 2.8 mm (males), 2.6 mm (females) with a mean growth of $2.7 \pm 2.4$ mm.
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XIII. Copyright Acknowledgment

August 5, 2015

Dear Mr. Scalia,

You have my permission to use the copyrighted FIGURE 1.4 from Essentials of Facial Growth, Second Addition. This is a one-time use, for your thesis, “Mandibular Growth in Subjects with Severe Skeletal Dysplasia, After the Pubertal Growth Spurt.”

Please contact me should you have any questions.

Sincerely,

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Mark G. Hans, DDS, MSO
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