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Nasal Morphology As A Predictor Of Craniofacial Growth Direction

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Abstract

It is important for an orthodontist to predict growth related changes and thereby appropriately time orthodontic treatment using the vertical indicators currently available. A potential predictor of craniofacial growth direction that has been discussed yet remains scientifically unexplored is nasal morphology. The objectives of this study are to determine if a difference in pre-adolescent nasal contour exists between post-adolescent normodivergent and hyperdivergent subjects, and if nasal contour morphology in pre-adolescent females is a reliable indicator of future craniofacial growth direction. A significant difference in pre-adolescent nasal contour morphology was found between normodivergent and hyperdivergent groups. A pre-adolescent nasal contour elevation >0.75mm may be indicative of future vertical craniofacial growth direction. However, preadolescent nasal contour morphology was judged to be a fair-to-poor diagnostic indicator of future craniofacial growth direction and should not be relied upon in craniofacial growth direction predictions.

Keywords: nasal morphology, nasal contour, craniofacial growth direction, vertical growth, nose, lower anterior face height, mandibular plane angle

Co-Authorship Statement

The completion of this thesis was possible due to the contribution of several individuals. It would not have been possible without their valued time and efforts, which was greatly appreciated.

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Introduction

Craniofacial Growth

The knowledge of craniofacial growth-related changes is essential in planning orthodontic treatment¹, and has been the fundamental basis of orthodontic practice.² For this reason, there has been a long-standing interest in maxillary and mandibular growth prediction.³ The relationship of nose, lips and chin are also important considerations⁴ and successful evaluation of facial balance must include a study of the facial profile. As the soft tissue profile can be altered by both growth and orthodontic treatment, it is imperative that the orthodontist have an understanding of not only the growth changes expected in the facial structures but also those occurring as a result of orthodontic treatment.

In addition to understanding growth-related changes, the timing of orthodontic treatment to achieve an optimal outcome is of paramount importance. 5 It must be remembered that orthodontic treatment is often commenced during early adolescence, before the peak growth spurt. As such, dentofacial growth after the completion of orthodontic treatment may influence the treatment outcome. ¹ Therefore, it is important for orthodontists to predict growth related changes to the best of their abilities and thereby appropriately time treatment given the knowledge and growth prediction variables that are available. As a result, many attempts have been made to describe the range of normal variation of the human face and design a system that identifies the various facial types. It is assumed that such a classification would be of value in the diagnosis and treatment planning of different craniofacial and dental discrepancies.⁶ With increased insight into proven indicators and

decision-making processes, the orthodontist should be better able to appropriately time treatment and deliver successful long-term results.⁵

The Significance of Growth in Orthodontics

It is difficult to predict how any one individual will respond to a particular plan of treatment. Expecting variability is the rule rather than the exception. In orthodontics, two interrelated factors contribute to most of the variability in response to treatment: the patient's growth pattern and the effect of treatment on the expression of growth. In the absence of growth, treatment responses are reasonably predictable while growth can be remarkably unpredictable.⁷

To achieve a successful orthodontic result, the orthodontist must have some understanding of the patient's future facial growth potential. The effects of growth in combination with orthodontic treatment in determining the ultimate post-treatment result have long been considered important in the growing patient.⁸ It would be ideal if orthodontists could identify where growth occurs, how much growth is remaining, in which direction and when growth will express itself, what roles genetics and environmental factors play in influencing facial growth and, in turn, how these factors can be influenced with treatment to achieve optimal results. ⁹ Previous longitudinal investigations have also indicated that the timing of orthodontic treatment to coincide with growth may be a considerable factor in the stability of the dentition.¹⁰ Since disproportionate growth of the jaws is a contributing factor in the manifestation of malocclusions, it is necessary to learn how facial growth is influenced and controlled.

Because predicting facial growth would be of great benefit in planning orthodontic treatment, repeated efforts have been made to develop methods to do this from cephalometric radiographs. Successful prediction requires specifying both the amount and direction of growth. Longitudinal cephalometric growth studies have been done to allow their use in growth prediction by providing means for normal growth changes. These studies include the Bolton, Burlington and Michigan craniofacial growth studies. Based on data from these studies, growth prediction for subjects under consideration for orthodontic therapy appear to be more accurate the closer the subjects relate to the mean, while the reverse is also true. 7

Having the ability to predict the magnitude and direction of craniofacial growth would provide a significant benefit in orthodontic diagnosis and facilitate better treatment designs. More specifically, predicting the development of extreme skeletal growth patterns would be of considerable value because of the difficulty in treating these patients and the sequelae of leaving them untreated.¹¹ However, the difficulty with growth prediction based on average changes is that any patient may have neither the average amount nor direction of growth, and thus there is the possibility of significant error.⁷ Our ability to predict facial growth, therefore, is poorest for the very patients in whom it would be most useful.

Although considerable data exist with regard to craniofacial growth, exactly what determines the growth of the jaws remains unclear and continues to be the subject of intensive research. ⁷ At present, accurate growth predictions are simply not possible for the children who need it most.⁷

Three major theories in recent years have attempted to explain the determinants of craniofacial growth:

1) bone, like other tissues, is the primary determinant of its own growth

- 2) cartilage is the primary determinant of skeletal growth, while bone responds secondarily and passively
- 3) the soft tissue matrix in which the skeletal elements are embedded is the primary determinant of growth, and both bone and cartilage are secondary followers⁷

The main difference in the theories is the location at which genetic control is expressed. The second theory ('cartilage theory'), suggests that genetic control is located in the cartilage, while bone responds passively to being displaced. Indirect genetic control, whatever its source, is called 'epigenetic'. In contemporary thought, the truth is to be found in some synthesis of the second and third theories, while the first, though it was the dominant view until the 1960s, has largely been discarded.⁷

Although there is no cartilage in the maxilla itself, there is cartilage in the nasal septum, and the nasomaxillary complex grows as a unit.⁷ Proponents of the cartilage theory of growth hypothesize that the cartilaginous nasal septum serves a pacemaker for other aspects of maxillary growth. The mechanism for maxillary growth would be at first a forward push from lengthening of the cranial base, then a forward pull from the nasal cartilage.⁷ Experiments have been carried out to test the idea that cartilage can serve as a true growth center. In early experiments by Copray et al.¹², transplanting cartilage from the nasal septum gave equivocal results: sometimes it grew, sometimes it did not. In more precise recent

experiments, however, nasal septal cartilage was found to grow nearly as well in culture as epiphyseal plate cartilage.⁷ In another study, Delatte et al.¹³ found that cartilage from the mandibular condyle showed significantly less growth in culture than the other cartilages. In rodent studies, removing a segment of the cartilaginous nasal septum caused a considerable deficit in growth of the midface. The loss of growth in experimental animals when nasal cartilage is removed is great enough to lead most observers to conclude that the septal cartilage does have some innate growth potential, and that its loss makes a difference in maxillary growth.⁷ From these experiments the other cartilages appear to be capable of acting as growth centers, but the mandibular condyle cartilage does not. The fact that, for many bones, cartilage does the growing while bone merely replaces it makes this theory attractive for the bones of the jaws. It appears that the nasal septum can and does act independently as a growing center. It is now understood throughout the orthodontic literature that the extent to which growth of cartilage of the nasal septum leads to translation of the maxilla remains unknown, but this cartilage probably does contribute to craniofacial growth.

The Challenge of Vertical Growth

In describing facial growth there are usually two important points to consider: (1) the increments or intensity of growth and (2) the direction of growth. ¹⁴ One of the first to appreciate the importance of the directions of facial growth was Hellman¹⁵ in the 1930s, but the first complete analysis to quantify variations in facial relationships was published by Downs in 1948.^{16, 17}

Three general categories of orthodontic problems exist in orthodontics. Horizontal problems may include large antero-posterior discrepancies between the maxilla and mandible, which can be assessed cephalometrically. Vertical problems may include a skeletal open bite or deepbite and or excessively large or small face heights, and transverse problems often include a discrepancy between the width of the upper and lower dentition and a narrow or wide mandible or maxilla. For the three planes of space in both the maxilla and mandible, there is a definite sequence in which growth is 'completed'. Growth in width is completed first, then growth in length (A-P), and finally growth in height (vertical).⁷

Two of the largest studies that investigated the prevalence of skeletal facial types were undertaken in the United States, and involved the evaluation of a large orthodontic based patient sample.^{18, 19} In both studies, the prevalence of the long face pattern was approximately 22%. ^{18, 19} This extreme form of vertical craniofacial growth was also reported to be the second most common cause for seeking and receiving orthodontic/surgical treatment. 18

In long face individuals who have excessive lower anterior face height, the mandible shows a backward rotation with an increase in the mandibular plane angle (MPA). Orthodontic cases which have a good morphological pattern with no substantial vertical or horizontal problems likely have the best prognosis if the growth directions and intensities are somewhere midway between the extreme growth variations.¹⁷ It thus follows that cases would probably have a higher degree of treatment success if the mandibular plane was relatively flat and the anterior face height relatively short.¹⁷ However, predicting the

likelihood of horizontal or vertical growth in pre-adolescent patients can sometimes be challenging.

Vertical malocclusions result from the interplay of many different etiological factors during the growth period. Vertical malocclusions can be divided into those that are dentoalveolar in origin and those that are predominantly skeletal due to the growth patterns of the jaws.²⁰ Vertical malocclusions that are skeletal in origin usually have little or no improvement in horizontal mandibular position over time.²⁰ Although the genetically determined mandibular growth pattern in general cannot be significantly altered by treatment, the orthodontist's goal should be to prevent further exacerbation of any deviation from normal by controlling the occlusal relationships of the dentition. Changes in the occlusion, particularly those produced by the eruption and exfoliation of teeth, produce vertical changes in the positioning of the mandible that are then translated into directional changes of growth. ¹⁷ For example, one particularly important factor in the development of a deep bite or open bite is the pattern of growth of the mandible. This is an important concept for the clinician to understand, as high angle patients are generally more prone to mechanical extrusion of posterior teeth during orthodontic treatment. The increased risk of extrusion in these patients is associated with their weaker masticatory musculature and bite force.^{20, 21}

In growing individuals, the long face growth pattern is difficult to modify and persists until the late teens.²² Therefore, persons with long faces may require therapeutic intervention at an earlier age than those with short facial vertical patterns.^{4, 23, 24} In addition, preventive or interceptive treatments to eliminate thumbsucking, prolonged infantile swallowing, tongue

thrust and other abnormal perioral muscle activities should be employed. ²⁵ It has also been documented that airway problems (such as large adenoids, tonsils or blocked airways due to septum deviations) are frequently observed in high angle cases and may affect mandibular posture.²¹ Interestingly, Linder-Aronson demonstrated the closing of the mandibular plane angle and reduction in lower face height following removal of adenoids and tonsillectomy 26, 27

Evidently, identifying the correct direction and pattern of craniofacial growth in a preadolescent patient can be invaluable to the clinician. Perhaps said best by Thomas Creekmore regarding vertical growth, "If it were possible to control the vertical growth of the face, it would be possible to solve almost all of our orthodontic problems". ²⁸ Therefore, it is useful to the profession to explore the possibility of discovering another measure that may serve as a reliable predictor for vertical craniofacial growth.

Current Knowledge on Growth Pattern Predictors

Severe skeletal pattern discrepancies represent at least one third of a typical orthodontic practice and are the major source of difficult cases.^{4, 29} These cases must be managed carefully and appropriately with full knowledge of what can happen in extreme variations in facial growth. Clearly, knowledge of dentoskeletal disharmonies is vital in planning orthodontic treatment and anticipating growth trends.²⁹

A large body of data exists with regard to the biology of growth and development in general, and craniofacial growth in particular, as it relates to orthodontic treatment and its

outcomes. ⁵Cephalometric methods have been widely used for estimating facial growth velocity to establish standards of growth to use in orthodontic diagnosis, treatment planning and evaluation of orthodontic treatment.³⁰ In studies of facial growth using the metallic implant technique Bjork $31-33$ and Bjork and Skieller $34-36$ demonstrated that the direction of growth of the lower jaw varies greatly in the normal population. According to earlier writers, most people have the same facial type from early childhood to adulthood.³¹⁻³³ Bishara and Jacobsen⁶ and Bishara et al.⁹ described the range of variation in the craniofacial relationships and also found that there was a strong tendency to maintain the original facial type with age. Bishara found that 77% of persons are categorized as having the same facial type at 5 years and at 25 years of age, equating to a strong tendency to maintain the overall facial type as facial growth progresses with age. Subsequently, Mitani et al.³⁷ found that the fundamental disharmony of Class III structure is established early in life, but that growth changes of the Class III mandible are fairly similar to those of the normal mandible *until* the pubertal growth peak. Thus, it seems that the outcome of facial growth is influenced at least in part by the original size and relationship of the jaws. However, there is a continuous demand for longitudinal growth data to better comprehend growth of the face, as well as identify variables that can be utilized in predicting craniofacial growth direction. As such, it would be advantageous if other variables in children and pre-adolescents could be identified that may aid in predicting future deviations from normal growth.

A number of craniofacial characteristics have been proposed as growth direction indicators. For example, mandibular plane angle, facial axis angle, and the antegonial notch have been found to be indicative of a vertically directed mandibular growth patter.^{38, 39} In 1988, a

study by Nanda evaluated the vertical growth in the face by examining patterns of facial growth in subjects with skeletal open bite and skeletal deep bite, with longitudinal data.²³

However, apart from a description of observed morphologic differences, there is a lack of understanding concerning the dynamics that typify the development of vertical dysplasia. Through his work, Nanda determined that the fundamental difference between the open-and deep-bite faces is found in the anterior region in the face, rather than in variations of ramal height or total posterior face height. His research led him to ask two important questions for future studies:

1) At what point in post-natal development is it possible to recognize the establishment of facial patterns in open-bite and deep-bite subjects, and

2) Do the facial patterns, once identified, tend to persist throughout development?

This led Nanda et al. to develop another study two years later, in 1990.⁴ The purpose of this study was to assess skeletal factors associated with the development of vertical facial disproportions. Previous research suggested that the mandibular plane angle is a prognostic criterion for predicting dimensions, proportions and direction of facial growth.⁴⁰⁻⁵⁰ From an analysis of the literature, Nanda ascertained six cephalometric angular measurements that were the best criteria for identifying subjects with vertical dysplasia: sella-nasion to palatal plane (SN-PP), sella-nasion to mandibular plane (SN-MP), gonial angle (Ar-Go-Me), palatalomandibular plane (MP-PP), cranial base (Ba-S-N), and sella-nasion to occlusal plane (SN-OP).^{23, 51} Another commonly used cephalometric indicator to distinguish between horizontal and vertical growth is the Y-axis (sella-gnathion to FH or SN), developed by

Downs. Deviations from the normal value were indications that one type of growth (horizontal or vertical) was prevailing over the other. The 'normal' Y-axis angle, was, therefore, intended to represent the direction of growth at gnathion in an ideal facial pattern. 17

Consequently, one is still unable to accurately forecast the amount and direction of mandibular growth.⁵¹ Some orthodontic estimations of growth can be complicated by uncertainty, and so any useful adjuncts that we can utilize in predicting craniofacial growth direction would be to both the clinician's and patient's advantage. As Weinstein once noted, the effects of any treatment are uncertain in any given patient. "Even in cases in which a diagnosis can be made with certainty and a preferred treatment is well established, the treatment will still fail in some patients who may be indistinguishable a priori from those in whom the treatment will be successful".⁵³

Mandibular Plane Angle as a Predictor for Growth Direction

As evident by previous research by many authors, multiple variables can describe craniofacial growth direction more complete than a single variable. However, vertical facial morphology has traditionally been studied by examining subjects chosen based on mandibular plane angle.⁴⁹ The larger the mandibular plane angle, the more the mandible tends to become steeper, and the more the chin moves down and backward, leading to a vertical deviation from normal. The smaller the angle, the greater the tendency of the mandible to become flatter and the chin to grow forward.⁵⁴ Schudy made a comprehensive study of four hundred malocclusions and found the mandibular plane angle to be an

excellent indicator of facial type.⁵⁵ Evidence suggests that the mandibular plane angle is an excellent indicator of vertical craniofacial growth.⁴⁹ The average mandibular plane angle (MPA) relative to the anterior cranial base (S-Na plane) is 28.9° and 21.9° if relative to Frankfurt horizontal.¹⁷ A mandibular plane angle > 32° relative to the anterior cranial base is considered a vertical growth tendency.⁵⁶ Schudy later introduced the term, facial divergence, the extremes being hypodivergent and hyperdivergent, as more descriptive terms for facial type.⁵⁶ Figure 1 depicts the mandibular plane angle formed by two planes (Sella-Nasion and Gonion-Menton).

Figure 1: The anterior cranial base (S-Na) and mandibular (Go-Me) planes. Their intersection forms the mandibular plane angle (MPA).

Some studies have hypothesized very little change in mandibular plane angle during growth. In a study by Love et al.⁵⁷ mandibular growth was found to be statistically significant for the age periods of 16-18 years and 18-20 years, but the mandibular plane angle closed an average of only 1.6 \degree over the study period.⁵⁷ The results of this study are in agreement with

others in concluding very little change in mandibular plane angle during growth for persons with a vertical craniofacial growth direction.^{34, 25} Bjork claimed that a child with vertical growth-movement of hard-tissue menton could not be expected to have their mandibular plane-cranial base angle altered appreciably with growth.¹⁷ In support of these claims, more recent studies have shown that the inclination of the mandibular plane in high angle cases remain fairly unchanged from 6 years to 15 years of age.²⁵

It is also important to note that many investigations have confirmed the strong association of the anterior face height on the mandibular plane angle and on the formation of different facial types at both younger and older ages.^{17, 58} The skeletal differences that lead to disproportionate lower face height in long-faced and short-faced children are related to mandibular morphology.⁴⁹ In a random sample of fifty malocclusions, Schudy⁵⁵ found the relationship of facial height to have a very high correlation with mandibular plane angle (SN-MP) and Y-Axis. He also correlated these measurements to lower face height and found highly significant readings for the mandibular plane angle. Schudy concluded that the Y-axis was not closely related with the morphology of the lower face but that the mandibular plane angle was.⁵⁵ In another study, Isaacson et al. also found that lower anterior face height was found to be significantly greater in a high angle group than in a normodivergent group.²¹ Recent studies even indicate that hyperdivergent patterns are predominantly due to increased lower face height.⁵⁹ Lower anterior face height in addition to mandibular plane angle has been shown to be an excellent predictor of vertical craniofacial growth direction. ⁴⁹ Figure 2 illustrates the method of determining the lower anterior face height as a percentage of total face height.

Figure 2: Lower anterior face height is the vertical distance from ANS to hard tissue menton (Me). It is often stated as a percentage of total face height. Total face height is the vertical distance from nasion (Na) to menton (Me).

Love et al.⁵⁷ and Foley and Mamandras⁵² studied growth of the facial skeleton during the teenage years in both sexes and reported that anterior facial height (AFH) increased over the observation time. In the females, the total change in AFH (N/Me) over the entire observation period was 4.3 mm, and about 40% of the growth in facial height occurred before age 15. For both sexes, about 60% to 70% of the increase in AFH occurred in the lower anterior face height (LAFH).

It has been discovered that for young patients with a long anterior face height and a steep mandibular plane angle, the chance of developing a skeletal open bite through vertical skeletal growth is increased.⁵⁸ A steep mandibular plane contributes to an anterior open bite by directing corpus growth in a more downward direction than normal, thus maintaining or

aggravating overdevelopment of lower anterior facial height.²⁵ In the absensce of dentoalveolar compensations, skeletal anterior openbite may occur at a juvenile age or later when a steep mandibular plane directs corpus growth more downward than normal, thereby maintaining or accentuating overdevelopment of LAFH.²⁵

It can be concluded that faces become disproportionately long as the mandibular plane and anterior face height increase. This finding is an excellent example of Solow's demonstration that many cephalometric variables are highly correlated and lack independence.⁴⁹ Because a steep MPA and a large LAFH are often inherent characteristic, the mandibular plane angle and lower anterior face height are useful to describe different facial types and must be taken into consideration when treatment planning and forecasting growth direction.

Previous Research on Nasal Morphology

As previously stated, many soft and hard tissue parameters cannot be predicted with sufficient accuracy and precision to be useful to the orthodontist in the planning of treatment and actual treatment.⁶⁰ In general, facial soft tissues are considered a dynamic structure that can develop along with or independent of their skeletal substructure. ⁶¹ However, the clinical impact on skeletal profile and influence in cephalometric soft tissue skeletal values cannot be denied.⁶²

In 1944, Tweed gave special attention to esthetics. He stated that "a thorough concept of the normal growth pattern of the child's face or any face is as important to orthodontists, if not more so, as complete mastery of the science of occlusion". ⁶³ Few soft tissue growth

studies^{64, 65} have centered on sagittal malrelationships, and at present very few longitudinal studies exist that assess the growth of the integument in extreme vertical patterns, i.e., patients with short- and long-face syndromes.⁶¹

One such characteristic that has been implicated in prediction of vertical growth is the morphology of the nose. Although craniofacial literature is replete with longitudinal and cross-sectional studies of skeletal growth and development, studies specifically devoted to nasal growth and development are infrequently found. ⁶⁶ Although limited studies have been conducted on nasal profile, there is a lack of quantitative data on the size, shape, and relative position of the nose.⁶² In addition, these studies that have assessed nasal characteristics did not examine whether the nose could be used as an indicator of facial growth direction.³⁹ Despite this, there does appear to be a relationship between nasal shape and malocclusion that has yet to be fully explored. 67

The form and profile of the nose depends upon both the bony and cartilaginous components and the overlying soft tissue integument.⁶⁸ Nasal growth is produced in part by an increase in size of the cartilaginous nasal septum, while growth of the nasal bone itself is complete at 10 years of age. ⁷ Growth thereafter is only of the nasal cartilage and soft tissues, both of which undergo a considerable adolescent spurt.⁷ A convex nasal contour develops when the growth of the septal cartilage at the bridge of the nose continues beyond the growth of the alar cartilage at the tip of the nose. The nose grows more rapidly than the rest of the face during the adolescent growth spurt, but growth of the nose is extremely variable, as a cursory examination of any group of people will confirm.³⁹

Shape changes of the nasal dorsum are particularly important. Generally, dorsum shape change is believed to occur after early childhood and is associated with positional changes of the nasal bone.⁷⁰ Elevation of the dorsum is due to the fact that during adolescence, the nose tip does not grow forward to the same extent as the nasal bone.⁷¹ Thus, a 'dorsal hump' develops as indicated by elevated nasal tissue along the bridge of the nose (Figures 3 and 4).

Figure 3: A 16-year old patient with a distinctive 'dorsal hump' ⁷²

Figure 4: The same patient's lateral cephalometric radiograph⁷²

In a study on the growth of the nose by $Posen⁷¹$, Posen's objectives were to evaluate the growth pattern of the nose in persons from infancy through adulthood. Posen found that one should expect the nose to become more prominent after the age of 13 years and should anticipate that the entire facial profile will become more convex. He did not conclude, but rather *suggested* that this may be the determining period for final nose contour. Posen also stated it is important to determine how much residual nasal growth expresses itself after the age of 13 years, as the form and shape of the nose and facial profile changed significantly from 13-17 years of age in his sample.⁷¹

There have been studies that have looked at the relationship between nasal contour and anterioposterior relationships of the jaws. In earlier years, a study by Chaconas et al.⁷³ found that the configuration of the dorsum of the nose in Class II subjects followed the general convexity of the Class II face, and those who exhibited an elevation of the nasal bridge were Class II subjects. Chaconas postulated that it is possible that the direction of growth of the nasal bones, and not the actual length, causes the elevation of the bridge of the nose, and questioned whether there was an association between elevation of nasal bridge and direction of growth of the mandible. However, the direction of growth of the mandible was not investigated by Chaconas; rather, he found that the correlation between the length of the nose and the linear measurement of the length of the mandible indicated that a long nose was associated with a large mandible.⁷³

In a study by Kothari designed to gain insight into the relationship of nasal size, Class II malocclusion, and maxillary skeletal dimensions, it was concluded that the size of the nose has an important influence on treatment objectives.⁷⁴ Kothari found that Class 1 groups tended to have straighter noses, and that skeletal Class II groups tended to have elevated nasal bridges. In agreement with Kothari was a study by Robison et al.⁷⁴ In 1986, Robison evaluated the relationship of skeletal facial pattern and soft tissue nasal form in 123 female subjects aged 11-20.6 years.⁷⁵ He reported significant correlations between anterioposerior (AP) skeletal patterns and certain features of soft-tissue nasal shape, such as height and width, measured angularly. However, whereas the AP profile skeletal pattern was significantly correlated with general nasal shape, the skeletal vertical dimension was not significantly related with nasal width and height.⁷⁵ Robison's study

did not attempt to quantify nasal contour nor clarify the threshold of clinical discernibility, and found that all nasal angular measurements remained stable during growth.

In a study by Ferrario et al. ⁶⁶, researchers found that the growth of the nose seems to be related to skeletal growth only to a certain extent. Ferrario also found that increments in nose height, depth and inclination are essentially complete in girls by 16 years of age, whereas they continue to increase in males up to and beyond 18 years.

In another study by Prasad et al., ⁶⁸ a statistically significant difference was seen regarding nasal length between males and females, with males having longer noses. Additionally, there was no statistically significant difference in nasal contour (measured angularly, not linearly) between males and females. Other studies have found the opposite, with a convex nasal contour being more prevalent in males than females.⁶⁹ Further, a prominent nasal dorsum has also been associated with long face syndrome.⁴⁰

Genecov et al.⁷⁶ found that nasal bone projection and dorsal hump to be most commonly found in Skeletal Class II groups. However, this was in sharp contrast with Prasad et al. who found that nasal contour represented an insignificant and weak correlation with all of the maxillary skeletal parameters in sagittal skeletal relationships.⁶⁸ Neither study assessed nasal contour quantitatively to craniofacial growth direction of the mandible.

It is quite clear that there has been minimal and inconclusive research that has investigated the relationship between nasal contour and craniofacial growth direction, specifically with respect to the vertical dimension. Additionally, information regarding a linear nasal contour measurement is sparse. An appropriate study investigating the relationship between nasal contour and craniofacial growth direction quantitatively in the vertical direction has yet to be done, as of this writing. As such, there is a need to investigate and quantitate this relationship further.

Growth During Adolescence in Males and Females

It is well documented that males lag behind females in reaching the adolescent growth spurt.²³ Females tend to have their adolescent growth spurt earlier than males, and long facial patterns tend to express themselves before those with short vertical patterns.^{23, 24, 51} Why this occurs is not known, but the phenomenon has an important impact on the timing of orthodontic treatment, which must be done earlier in girls than in boys to take advantage of the adolescent growth spurt⁷. Fortunately, growth of the jaws usually correlates with the physiologic events of puberty in about the same way as growth in height.⁷ There is an adolescent growth spurt in the length of the mandible, and a modest increase in growth at the sutures of the maxilla. More growth takes place in the mandible than the maxilla, and this results in differential jaw growth that can be unpredictable.⁷

Buschang et al. found that males have greater growth potential than females between age 10 and 15 years due to a more intense adolescent growth spurt and approximately 2 additional years of growth due to maturational differences.⁷⁷ This was confirmed by

Foley and Mamandras⁵² who reported that pubertal growth spurts in females occurred 2 years earlier than in males, and that it is generally accepted that the termination of active pubertal growth takes place in females at 14 years of age. In a longitudinal cephalometric study by Snodell and Nanda, the authors found the greatest rates of growth occurred at ages 13 and 14 years for females and at ages 15 through 17 years for males.¹⁰

It is also important to note that longitudinal data from studies of craniofacial growth indicate that a significant number of individuals, especially among girls, have a 'juvenile acceleration' in jaw growth that occurs 1-2 years before the adolescent growth spurt. This tendency for a clinically useful acceleration in jaw growth to precede the adolescent spurt is a major reason for careful assessment of physiologic age in planning orthodontic treatment.⁷⁸ Furthermore, Mellion et al. concluded that the common assumption that onset and peak adolescent growth in females occur at ages 10 and 12 is approximately 6 months to 1 year late.⁷⁹ This tendency for a clinically useful acceleration in jaw growth to precede the adolescent spurt is a major reason for careful assessment of physiologic age in planning orthodontic treatment.⁷⁸ If treatment is delayed too long, the opportunity to utilize the growth spurt is missed. In the timing of orthodontic treatment, clinicians have a tendency to treat girls too late and boys too soon, forgetting the considerable disparity in the rate of physiologic maturation.⁷

When examining the gender differences that may be present in soft tissue form, most studies agree that a trend for sexual dimorphism is evident.⁶¹ Genecov et al.⁷⁶ found that there is a considerable dichotomy in soft tissue growth between males and females

between 12 to 17 years of age. Enlow and Hans also reported that the male nose was proportionately larger, more protrusive and longer than the female nose.⁸⁰ Nanda found that the male nose had not attained adult size even at age 18, while the female nose had attained adult size by 16 years of age.⁴ Prahl-Andersen et al.⁸¹ found that the growth of the nose seems to be related to skeletal growth to a certain extent, and found that boys show an increase in growth velocity after the age of 12 years. In contrast, Meng et al.⁸² determined that increments in nose height, depth, and inclination are essentially complete in girls by 16 years of age.

Blanchette et al. found that boys showed continued growth of the soft tissue integument through age 16 in contrast to girls who attained the adult size of the soft tissue integument around 14 years of age.⁶¹ It was also found that subjects with long vertical facial patterns experienced their pubertal growth spurt earlier than the short-face subjects, and boys tended to grow for longer periods of time. ⁶¹ In general, the soft tissue integument of the face in girls attained its adult size at age 15 years. Males, however, have shown continued growth of the soft tissue integument past the age of 17 years.⁶¹ Evidently, these and other studies have shown that growth changes of the facial tissues occur predominantly before the age of 18 years in either gender.⁸

The Cervical Vertebral Maturation Method

For most developmental indicators, the correlation coefficient between developmental status and chronologic age is about 0.8, so the probability that one could predict the developmental stage from knowing the chronologic age or vice versa is $(0.8)^2 = 0.64$.⁷

However, since chronological age and the timing of maturation do not always coincide, the cervical vertebral maturation (CVM) method was also used to aid in confirming a preadolescent and post-adolescent lateral cephalogram was available for each potential subject.

Cervical vertebral stages were determined by using the method described by Baccetti et al.⁸³ The cervical vertebrae undergo a well-defined sequence of changes that are visible on routine lateral cephalometric radiographs.⁷⁹ Baccetti's method is based on changes in shape of the cervical vertebral bodies (2-4) and developing concavities on their lower borders (Figure 5).

Figure 5: The Cervical Vertebral Maturation Stage (CVMS) designations. Note the concavity that appears on the lower border of C4 during the third stage (CVMS III). The peak in mandibular growth has occurred within one or two years before this stage.

The CVM method has been shown to be a valid indicator of skeletal growth during the circumpubertal period, but is not significantly more reliable than chronological age.⁸⁴ However, it may be that the most reliable, valid and critical use of the CVM method is differentiating the pre-mandibular from post-mandibular growth peak phases. ⁷ Baccetti et al.⁸³ found that the peak mandibular growth occurs between cervical vertebral stages

CVM stage 3 and 4 and that the stages of vertebral maturation occur, on average, 1 year apart. Thus, CVM stage 2 would tend to precede the interval of maximum mandibular growth by about a year.

Nasal Contour as Predictor of Future Craniofacial Growth Direction:

Studies have shown that a convex nasal profile is indicative of retrusive mandibles and steep mandibular planes. Moreau looked for associations between dorsal nasal ridge contour and craniofacial growth direction. ³⁹ His study evaluated the cephalometric records of female patients treated orthodontically at Western's graduate orthodontic clinic, dividing his eventual sample of eighty-four (84) subjects into two groups based on nasal ridge contour. Forty-two subjects had a convex nasal contour while the other forty-two had a concave nasal contour (cut-off point arbitrarily defined as 1.5mm). The average age of each patient was 14.4 years of age. Cephalometric measures used to aid in predicting craniofacial growth direction were evaluated in each group to see if growth direction indicators were significantly different between the two groups. Moreau's most clinically significant finding was the vertical direction of growth found for the convex nasal profile group as compared to the concave nasal profile group. Moreau found that those with convex nasal profiles had steeper mandibular plane angles (by an average of 6.11°), larger lower anterior face heights and lower facial axis angles. These findings supported McNamara's belief that patients possessing a more convex nasal profile are characterized by steep mandibular planes.⁸⁵ Moreau also found that mandibles and maxillas were more retrusively positioned and gonial angles were larger in individuals with convex nasal profiles, and that lower face heights for the convex group increased
significantly during the treatment time interval. Moreau concluded that there is a definite relationship between females with a convex nasal profile and a vertically directed mandible, and affirmed that a clinician should be careful to control the vertical dimension in treating females with a convex nasal profile.

However, despite Moreau finding correlations between post-adolescent nasal morphology and cephalometric variables at a single point in time, it has yet to be determined if preadolescent nasal contour could serve as a predictor for *future* vertical growth. In other words, he found that convex nasal profile was associated with vertical growth parameters in females at a single point in time, but did not explore the potential predictive power of pre-adolescent nasal contour.³⁹

On the contrary, in the study by Nanda in 1990 it was believed that the sagittal growth of soft tissue nose was independent of the underlying skeleton. Rather, he found that the palatomandibular angle discriminated between open bites and deep bites throughout the developmental phase. ⁴ Nevertheless, proponents of the cartilage theory of growth hypothesize that the cartilaginous nasal septum serves as a pacemaker for other aspects of maxillary growth.⁷ It could be very beneficial to clinicians if nasal contour could serve as a reliable predictor suggesting vertical growth, as this is easily observable and requires no diagnostic records. Clearly, a better understanding of the normal growth trends of the nose would be advantageous to orthodontists who influence the facial profile.

Purpose

The possible association between facial morphology and craniofacial growth direction leads us to the following question: can we utilize a non-radiographic variable (facial characteristic) to predict future craniofacial growth direction in pre-adolescent patients? The aim of this study is to examine the relationship between pre-adolescent soft tissue nasal profile and cephalometric skeletal parameters indicative of vertical growth in females. The ability to have a soft tissue criterion that could be indicative of future vertical growth potential would be invaluable to the orthodontist. This study's objective is to quantify what may currently be understood as a merely general, un-quantified, unconfirmed observation.

This leads to the following two research questions:

1) "Is there a significant difference in the pre-adolescent nasal contour between subjects who grew vertically and those who did not?

2) "Is convex nasal contour in pre-adolescent females a reliable indicator of future vertical craniofacial growth direction?"

Assessing the Strength of a Diagnostic Test

When using a diagnostic test or criteria to determine the presence or lack thereof of a condition, a test's reliability and accuracy must be analyzed before it can be concluded that the test is useful. In other words, its capabilities of correctly predicting a future outcome (e.g., pre-adolescent nasal contour as a predictor of craniofacial growth direction) must be strong before it can reliably be put to use in a clinical setting. A simple

way of looking at the relationships between a test's results and the true diagnosis can be seen below in Figure 6.

Figure 6: Contingency table showing the relationship between a test's prediction and the observation (outcome)

There are four possible interpretations of the test results. There are two possibilities for the test result to be correct (true positive and true negative) and two possibilities for the result to be incorrect (false positive and false negative). The goal of all clinical studies describing the real value of a diagnostic test should be to obtain data for all four of the cells in Figure 6. Without information on each of these possibilities in the four cells, it is not possible to answer important questions about the performance of the test.⁸⁶

Sensitivity is defined as the ability of the test to correctly identify patients who have the condition. Specificity is defined as the ability of a test to correctly identify patients who do not have the condition. A highly sensitive test will rarely miss subjects with the condition, while a highly specific test will rarely misclassify people without the condition as erroneously having it. Thus, it is clear that we should ideally strive for tests high in both sensitivity and specificity. However, it is essential to understand that there is a trade-

off between sensitivity and specificity of a diagnostic test. One characteristic can only be increased at the expense of the other. In other words, at the expense of increased specificity is decreased sensitivity and vice versa. A trade-off between the two occurs when clinical data take on a range of values (e.g., nasal contour elevation in millimeters). In these situations, locating a cut-off point is an arbitrary decision with the investigator balancing specificity and sensitivity. Unfortunately, there is no perfect threshold score to utilize because the investigator is always balancing sensitivity and specificity. However, there are times in which specificity is favored over sensitivity and vice versa. It is recommended that a sensitive test (i.e. one that is usually positive in the presence of disease) should be chosen when there is an important penalty for missing the identification of a disease.⁸⁶ Sensitive tests are useful when the probability of a condition is relatively low and the purpose of the test is to discover it. High specific tests are particularly needed when false positive results can harm the patient. In sum, a specific test is most helpful when the rest result is positive.

Another way to express the relationship between sensitivity and specificity for a given diagnostic tool (in this case, pre-adolescent nasal contour) is to construct a curve, called a receiver operator characteristic (ROC) curve. The ROC curve plots the true positive rate (sensitivity) against the false positive rate (1-specificity), and is used to describe the accuracy of a test over a range of cut-off points. In other words, it indicates how severe the trade-off between sensitivity and specificity is and aids in deciding where the best cut-off point/threshold would be. Tests that discriminate well crowd toward the upper left corner of the ROC curve; tests that do not perform well have curves that fall closer to the

diagonal line (the diagonal line describes a test that contributes absolutely no useful information). This is important as it reflects the strength of the test. Ideally, the most reliable test would have an area under the curve >90% (exceptional test). Area under the curve that is >80% is considered a good test, while area under the curve that is 70-80% is considered a fair test.⁸⁶ See Figure 7.

Figure 7: An example of an ROC curve for a diagnostic test with excellent strength, as represented by the large area under the curve. The diagonal line is a theoretical line describing a test that contributes absolutely no useful information (image courtesy of MedCalc®)

Once the results of a test are available, whether positive or negative, the clinician's dilemma is to determine whether or not the patient actually has the condition based on the results of the test. In other words, the sensitivity and specificity are no longer important. Instead, the clinician would value two additional values: the positive predictive value and negative predictive value. The probability of a disease/condition is referred to as the predictive value of the test. Positive predictive value focuses on patients with a positive screening test in order to examine the probability of the condition in those patients. In other words, if a patient has a positive screening test, what is the probability that the

patient really has the condition? Negative predictive value focuses on patients with a negative screening test in order to examine the probability that patients with a negative test do not have the condition in question. The more sensitive a test (ability of the test to correctly identify patients who have the condition), the better will be its negative predictive value (probability that subjects with a negative test do not actually have the condition). The more specific a test is, the better will be its positive predictive value. It is also very important to note that the interpretation of a positive or negative diagnostic test result will vary according to estimated prevalence of disease in the particular setting.⁸⁶As the prevalence of a condition or disease in a population approaches 100%, the negative predictive value approaches zero (positive predictive value is high). Conversely, as the prevalence decreases, the positive predictive value decreases while the negative predictive value increases. Therefore, it is beneficial to know the prevalence of a condition in the general population so that the positive and negative predictive values can be adjusted to accurately characterize the diagnostic test being investigated.

Likelihood ratios are an alternative way of describing the performance of a diagnostic test. Likelihood ratios are the likelihood that a given test result would be expected in a patient with the target condition compared to the likelihood that same result would be expected in a patient without the target condition. They summarize the same kind of information as sensitivity/specificity and can be used to calculate the probability of disease after a positive or negative test. The main advantage of likelihood ratios is that they make it easier for us to go beyond the simple and perhaps clumsy classification of a test result as either positive or negative; they put more weight on extremely high or low

test results (e.g., large nasal convexity) than on the borderline ones, when estimating the odds that a particular condition (e.g., vertical growth) is/will be present. In other words, they tell us how much we should shift our suspicion (between having a condition or not) for a particular test result. The positive likelihood ratio tells us how much to increase the probability of disease if the test is positive, while the negative likelihood ratio tells us how much to decrease it if the test is negative. Likelihood ratios > 1 indicate an increased probability that the target condition is present, while likelihood ratios < 1 indicate a decreased probability that the target disorder is present. A likelihood ratio that >10 indicates a large and often conclusive increase in the likelihood of disease.

Hypotheses

The null hypotheses of this study are as follows:

1) There would be no statistically significant difference in pre-adolescent nasal contour between subjects who grew vertically (hyperdivergent) and those who grew normally. 2) Pre-adolescent nasal contour would not serve as a reliable indicator of future

craniofacial growth direction during adolescence

Materials and Methods

Sample Collection Information

The design of this pilot study was a retrospective case-control design. The cephalometric records utilized for this study were obtained from three longitudinal craniofacial growth studies of the American Association of Orthodontics Foundation (AAOF) Craniofacial Growth Legacy Collection: the Burlington, Bolton and Michigan growth studies. Each of the collections is independent from the other and has pursued its own sampling and data collection strategies. Taken together, these different and complementary strategies have produced a rich longitudinal record of craniofacial development among children who did not receive orthodontic treatment. Inclusion criteria for the sample included:

- 1) Female Caucasian subjects
- 2) No history of pathology or trauma
- 3) No craniofacial abnormalities or syndromes
- 3) No history of orthodontic, orthognathic or facial/nasal surgical treatment
- 4) Good quality radiographs allowing for landmark identification
- 5) Cephalometric records available at both age 10 and 16

Further control of ethnicity was done to the best of the examiner's ability by utilizing growth studies with a predominantly Caucasian and Angle-Saxon racial group.⁸⁷ Each subject (with both a pre- and post adolescent radiograph) was identified as belonging to the Burlington, Bolton or Michigan growth study. It is important to acknowledge that each growth study has its own independent cephalometric averages for various cephalometric measures.

Subject Collection

The available longitudinal records were accessed online via the AAOF and the available records of every subject within each growth study were screened and evaluated. Between the three growth study samples available from the AAOF Legacy Collection, the combined number of potential subjects was 304 (100 from Burlington, 102 from Michigan, 102 from Bolton); 137 females and 267 males. As this study analyzed only females, the records of 137 female patients were evaluated. During evaluation, it was ensured that each subject to be included in the study had a lateral cephalogram taken both pre-adolescently (approximately age 10; T0) and post-adolescently (approximately age 16; T1). Since it has been found that females with long vertical facial patterns can experience their pubertal growth spurts earlier than short-face patterns⁶¹, and the nasal bone is formed by 10 years of age^7 , pre-adolescent females were chosen at an average age of 10 for this study as to not exclude any potential early maturers. It was ensured that all pre-adolescent lateral cephalometric radiographs clearly showed the soft-tissue nasal profile before being included in the study. Subject radiographs were selected without regard to dental malocclusion and included Class 1, II and III dental malocclusions. After evaluating the records of the 137 female patients available for study, 40 subjects were eliminated from the study for either having inadequate or poor quality pre- or postadolescent lateral cephalometric radiographs. In total, 97 subjects (45 from Burlington, 17 from Michigan, and 35 from Bolton) met the inclusion criteria and were eligible for further screening.

In addition to using chronological age, lateral cephalograms were also staged according to the cervical vertebral maturation (CVM) method. The pre-adolescent lateral cephalograms had an approximate chronological age of 10, and a CVM stage 2 (indicative of peak mandibular growth occurring 1 year after this stage). The postadolescent lateral cephalograms had an approximate chronological age of 16, and a CVM stage 4 to ensure peak adolescent mandibular growth had already occurred within 1-2 years before this stage. Cervical vertebral maturation staging was assigned to the records of the 97 patients to ensure that the above criteria were met. The average age of the preadolescent lateral cephalograms was 10.3 years and the average age of the postadolescent cephalograms was 16 years. In order to ensure that a proper designation was made with respect to the cervical vertebrae maturation staging, an additional, blinded examiner quantified the CVM staging of each cephalogram independently of the primary examiner, with no knowledge of the primary examiner's CVM staging designation (to ensure inter-examiner blinding). Only those cephalograms that had consensus on CVM designation by the two examiners were included in the study. It was ensured that all lateral cephalograms included in the study were accurately categorized as CVM 2 (preadolescence) or CVM 4 (post-adolescence). Following this screening procedure, all 97 subjects were included in the study and represented the total sample size. There was no discrepancy between the primary and additional examiner regarding CVM staging.

Image Standardization

Measurements of all post-adolescent radiographs were made on standardized lateral cephalometric radiographs using *Dolphin Imaging Software*, *Version 12* (Dolphin

Imaging, Chatsworth, CA, USA) over a 2-day period for consistency in tracing methodology among films. All measures were traced using this program by the same investigator (CP). Because subjects from 3 growth studies were examined, linear measurements had to be adjusted because of different enlargement factors from each growth study. Images were calibrated based on dots per inch (DPI) and magnification factors were adjusted to ensure that the digital images were correctly scaled to the films from which they were scanned. The magnification factors used were 12.9% for images of the Michigan Growth study, 6% for images of the Bolton Growth study and 9.84% for the images of the Burlington Growth study. The AAOF Craniofacial Growth Legacy collection and Dolphin Imaging recommended this method of calibration.

Cephalometric Landmarks and Angles

Landmarks included in this study were contour of nasal profile (constructed point for this study), sella, hard tissue nasion, soft tissue nasion, gnathion, gonion, menton, pronasale, anterior nasal spine, posterior nasal spine, articulare, basion, and occlusal landmarks (cusps of molars and premolars and incisal edges to delineate the occlusal plane) were used. Overall, the custom analysis consisted of 15 hard tissue landmarks, 3 soft tissue landmarks, 7 angular measurements, and 3 linear measurements (two of which were used to determine lower anterior face height percentage).

The seven (7) angular measurements included the mandibular plane angle (SN-MP), sella-nasion to palatal plane (SN-PP), mandibular plane to palatal plane (MP-PP) sellanasion to occlusal plane (SN-OP), sella-gnathion to sella-nasion (SGn-SN; known as the

Y-axis), articulare-gonion-menton (Ar-Go-Me; known as the gonial angle), and basionsella-nasion (BaSN; known as the cranial base angle). The three (3) linear measurements included the upper anterior face height and lower anterior face height (utilized to determine lower anterior face height percentage), and convexity of nasal contour in profile. These are depicted in Figures 8 and 9.

Figure 8: Cephalometric landmarks and planes (1-7) used to measure the seven angular measures and 3 linear measures for this study.

The definitions of the landmarks used in this study correspond to those of Riolo et al.^{7,88} A full description of the landmarks, planes, angular measures, and linear measures are provided in Appendices I- III.

Radiographic Tracing Methodology

All cephalometric landmarks and variables previously discussed were traced on each post-adolescent radiograph. The first measure recorded on each post-adolescent radiograph was the convexity of nasal contour. This method attempted to reduce bias, as the other vertical measures were not yet recorded and therefore unknown to the tracer. Nasal contour morphology was evaluated by measuring the highest point (landmark denoted as the CNP point) of soft tissue on the bridge of the nose above a tangent line from soft tissue nasion (SNa) to the most anterior-inferior point at the tip of the nose, pronasale (Pn). The amount (distance in millimeters) of nasal soft tissue extending perpendicularly from this line to CNP point for each post-adolescence lateral cephalogram was recorded. This would serve as a direct measure of soft tissue nasal contour (Figure 9).

Figure 9: Nasal contour measurement methodology. The distance between the highest point of soft tissue elevation (CNP point) and a plane that connected soft tissue nasion (SNa) to the most anterior-inferior point at the tip of the nose (Pn).

The vertical growth direction indicators were then traced (MPA, LAFH, SN-PP, SN-OP, MP-PP, SGn-SN aka Y-axis, Ar-Go-Me, and BaSN).

After tracing each post-adolescent radiograph, the corresponding pre-adolescent lateral cephalograms were measured three weeks later. This three-week interval between preand post-adolescent tracings ensured that the examiner was blinded to each subject's post-adolescent measures, and reduced bias. The examiner was unbeknownst to the vertical measures that were measured previously for each subject's post-adolescent lateral cephalogram. Much like in post-adolescent tracings, nasal contour morphology was recorded first, followed by the tracing of the other cephalometric variables, one radiograph at a time. This method aided in reducing the likelihood of bias than if vertical cephalometric measures had been measured first. Aside from nasal contour, the preadolescent lateral cephalograms were also measured for the same growth direction indicators as the post-adolescent lateral cephalograms.

Error Study

An error study was performed to assess measurement errors in tracing and digitizing by assessing reproducibility of all cephalometric angles and measurements evaluated in the study. As stated previously, images were calibrated based on dots per inch (DPI) and magnification factors were adjusted appropriately for each radiograph depending on which study the radiograph belonged to (12.9% for Michigan subjects, 6% for Bolton subjects, and 9.84% for Burlington subjects). To rule out measurement error, 20 subjects (10 from each group, normodivergent or hyperdivergent) were randomly selected using a

complex computer algorithm (http://www.random.org) and were re-traced and remeasured on the *Dolphin Imaging Softwar*e by the principal investigator (CP) three weeks after the final pre-adolescent radiographs were traced. Each subject had the radiographs of both time points retraced and re-measured, resulting in 40 repeated tracings. All measurements were retraced in the same room on the same computer. Dahlberg's formula was then used to quantify the standard deviation of measurement error for each desired measurement, using the formula $\sqrt{\frac{\sum d^2}{2N}}$, where *d* is the difference between the first and second measure, and N is the sample size of the error study. The reproducibility of measurement (*R*) was calculated to assess the reliability of the measurement values with the formula: $R = [S^2x - (S^2e/2)]/S^2x$, where S^2x is the variance of the first set of tracings and S^2e is the variance of the difference between the initial and error study tracings. The closer the reliability coefficient is to 1.0, the more reliable the measurement. The purpose of the reproducibility of measurement (R) was to quantify the reliability of the cephalometric measures used in the study sample. Inter-class correlations were also determined. Reliability coefficients (intra-class correlations) were calculated for these measurements to estimate the size of the error that may have resulted from landmark selection, tracing and measurement. One-sample *t*-tests were carried out for all measurements to determine if they were within acceptable limits.

Distribution of Sample: Group Classification

The next step was to classify the subjects' post-adolescent lateral cephalograms based on their craniofacial growth direction (normal or vertical). In order to do this, certain criteria were used. From each growth study, the post-adolescent cephalometric averages for

mandibular plane angle and lower anterior face height were averaged among the three growth studies to give an overall average for each criterion. The mean mandibular plane angle and mean lower anterior face height percentages at 16 years old for each growth study were 32.27° and 55% , 31.2° and 55% , 28.9° and 55% for the Burlington, Michigan and Bolton studies respectively.⁸⁸⁻⁹⁰ Taken together, the average mandibular plane angle of the three growth studies was 30.8° (S.D. 2.9) and the average lower anterior face height was 55% (S.D. 4.0) These average values (30.8° and 55%) would now serve as a reference against individual measures amassed in this study to classify the 97 subjects based off of standard deviations from the mean. See Table 1.

Table 1: The average mandibular plane angle (°) and lower anterior face height (%) from each growth study, and the combined average of all three.

The combination of mandibular plane angle and lower face height to divide the subjects were used for this study because they are highly correlated and predictive of hyperdivergence.^{17, 55, 58} As the mandibular plane angle can be quantified differently based on the cephalometric points selected, the mandibular plane angle in this study was defined as the anterior angle formed by the intersection of the sella-nasion plane and the mandibular plane using the cephalometric points gonion and menton (Figure 1, page 13). Subjects with both their post-adolescent MPA and LAFH within one standard deviation of the average combined norms for MPA (30.8°) and LAFH (55%) from the 3 growth studies were allocated to a normodivergent group, and subjects having both their postadolescent MPA and LAFH greater than at least one standard deviation above the mean of the combined average were allocated to the hyperdivergent group. In order to be classified into one of the groups, the subject must have had both values either within a standard deviation or greater than at least one standard deviation. For example, if a patient had their MPA within one standard deviation of the mean but their lower anterior face height was not, the subject was excluded.

Following the division of the subjects based on LAFH and MPA, two groups were now created: a normodivergent group and hyperdivergent group. A total of 39 subjects were allocated to the hyperdivergent group and 34 to the normodivergent group. Twenty-four subjects (24) were eliminated from the study as they did not meet the inclusion criteria for either group. The hyperdivergent group included 7 subjects from Michigan, 17 from Burlington and 15 from the Bolton growth studies. The normodivergent group included 6 subjects from Michigan, 14 from Burlington and 14 from Bolton. Sample collection and distribution information can be seen in Table 2.

 ***** Included in study

Table 2: Sample collection and distribution information of the study subjects.

Pre-adolescent nasal contour in each group could now be statistically compared to determine a potential relationship with future craniofacial growth direction.

In addition to evaluating the association between nasal contour and craniofacial growth direction and if a significant difference existed in pre-adolescent nasal contour morphology between normal and vertical growers, the additional objective of this study was to determine if pre-adolescent nasal contour could be of any predictive power for future vertical growth. As such, based on the frequencies of nasal measurements found across groups in the sample, an attempt was made to determine what measurement of preadolescent nasal contour elevation could be indicative of future vertical growth.

Statistical Methods

Data was input into *SPSS Version 24* statistical software program (IBM Corporation, Armonk, NY, USA) to calculate and confirm descriptive statistics. Prior to analyzing the data with an independent-samples *t*-test, both normodivergent and hyperdivergent groups were checked for the presence of significant outliers by assessing boxplots of the data. Extreme outliers were defined as those lying more than three-box lengths from the edge of the box. There were no extreme outliers in the data.

Multiple *t*-tests were performed. Two independent-samples *t*-tests were done to ensure no statistical difference in chronological age existed between groups for both pre-adolescent and post-adolescent ages (p <0.05). An independent-samples *t*-test was run to identify any significant differences for mandibular plane angle and lower anterior face height between the two groups ($p < 0.05$).

Next, pre-adolescent nasal contour morphology was compared between the hyperdivergent and normodivergent groups using a *t*-test (*p* <0.05) to determine if any statistically significant difference could be found.

Lastly, pre-adolescent nasal contour measurements were divided into clusters based on ranges. The frequency of pre-adolescent nasal contour measurements found within these ranges was also noted for both the hyperdivergent and normodivergent groups. This was done to identify a potential pre-adolescent nasal contour measure that could serve as a clinically identifiable threshold for predicting future vertical craniofacial growth, if there was in fact a statistical significance between groups. Once this apparent pre-adolescent nasal contour elevation threshold was identified, a 2x2 contingency table was constructed to determine if there was an association with this threshold and future vertical growth. Since not all assumptions were met for a chi-square test value to hold significance (all

cells in the 2x2 table required an N=5), a Fisher's exact test was done on the data instead. Phi (φ) and Cramer's V test were assessed to determine the strength of the association. Sensitivity, specificity, and positive and negative predictive values were determined. Because the prevalence of hyperdivergent growth patterns in the general population was different than the proportion used in this study, sensitivity, specificity, and positive and negative predictive values were re-calculated to the appropriate prevalence. Accurate positive and negative predictive values more reflective of the general population were calculated using the formula based on Baye's theorem:

$$
P(A/B) = \frac{P(B/A) \cdot P(A)}{P(B)}
$$

where $P(A/B)$ is the probability of observing event A given that B is true, where $P(A)$ and *P(B)* are the probabilities of observing A and B without regard to each other, and where $P(B/A)$ is the probability of observing event B given that A is true. After using Baye's theorem to adjust the positive and negative predictive values that better represent the population.

The likelihood ratio was also calculated. In order to evaluate the robustness of using preadolescent nasal contour as a predictor for future craniofacial growth direction, a receiver operating characteristic curve (ROC curve) was computed to evaluate the area under the curve to see if pre-adolescent nasal contour morphology could serve as a reliable predictor for future vertical growth.

The effect size was calculated using Cohen's *d* to determine how large the effect was compared to the standard deviation of the samples. Cohen's *d* was calculated via the

following equation:

$$
d = \frac{M_1 - M_2}{SD_{pooled}}
$$

A *post-hoc* power study was then done following the t-test and calculation of effect size (d) to determine if the study had appropriate power (1-β error probability >0.8). Note that this was a pilot study with no previous information on the average difference in nasal contour morphology between hyperdivergent and normodivergent patients.

As stated previously, measures for each additional craniofacial growth direction indicator were also recorded for both pre-and post-adolescent radiographs in each group. These measures were simply adjunctive quantitative data for other vertical indicators examined in this study, but did not serve to answer either of the purposes of this study. These additional variables were the palatomandibular plane angle, gonial angle, sella-nasion to occlusal plane (SN-OP), sella-nasion to mandibular plane and Y-axis. In total, seven (7) angular measurements used to characterize vertical growth would be compared against nasal contour morphology. Average values were determined for each of the vertical measures in each group (at both T1 and T2) to note the differences in the vertical growth variables between the groups.

Results

An error study of the reproducibility of certain measures and intra-class correlations is shown in Table 3.

Table 3: Measurement Error and Reproducibility of Cephalometric Variables $(n = 40)$

The reproducibility (R) values were all 0.90 or larger, suggesting excellent reproducibility of the landmarks used for the cephalometric analyses. Reliability coefficients (intra-class correlations) were calculated for these measurements to estimate the size of the error that may have resulted from landmark selection, tracing and measurement. Results indicated that there was no statistically significant difference between initial and secondary measurements $(p > 0.05)$ for any of the measures. All measurements fell within acceptable limits.

Differences in mean ages (both pre- and post-adolescent) between the normodivergent and hyperdivergent groups are shown in Tables 4 and 5. For the hyperdivergent group, the mean pre-adolescent age was 10.4 years (9.1-11.1) and the mean post-adolescent age was 16 years (14-17.6). For the normodivergent group, the mean ages were 10.2 years (9- 11.4) at pre-adolescence and 15.9 years (14.1-17.9) at post-adolescence (Table 4 and 5).

Table 4: Comparing pre-adolescent records between normodivergent and hyperdivergent subjects

Table 5: Comparing post-adolescent records between normodivergent and hyperdivergent subjects

Examination of box plots revealed no outliers. Separate *t*-test results showed no significant differences in pre-adolescent or post-adolescent ages between groups (*p*= 0.220 and $p = 0.869$ respectively). Ages of the pre-adolescent subjects within each group were distributed normally ($p > 0.05$), and there was homogeneity of variances ($p > 0.05$). Ages of the post-adolescent subjects within each group were also distributed normally and also satisfied Levene's test for homogeneity of variances.

Differences between groups at each time point (T1 and T2) with respect to mandibular plane angle and lower anterior face height are shown in Table 6. The mean postadolescent mandibular plane angle in the hyperdivergent group was 38.12° compared to 31.61° for the normodivergent group. The mean post-adolescent lower anterior face height in the hyperdivergent group was 58.74% compared to 55.61% for the normodivergent group.

Table 6: Mandibular plane angle and lower anterior face height in normodivergent and hyperdivergent groups

Mandibular plane angle and lower anterior face height measures were distributed normally as determined by the Shapiro-Wilk test ($p > 0.05$), and there was homogeneity of variances as assessed by Levene's test for equality of variances. Examination of box plots revealed no outliers. Two independent-sample *t*-tests were done to ensure a significant difference existed in both MPA and LAFH between groups. This would ensure a difference existed between the normodivergent and hyperdivergent groups so pre-adolescent nasal contour could be contrasted between the groups. A significant difference in both mandibular plane angle (*p =*0.001) and lower anterior face height (*p =*0.001) was found between the normodivergent or hyperdivergent groups at postadolescence. Statistical tests were run for both equal variances assumed and equal variances not assumed, and the same result was found.

Group statistics on nasal contour are in Table 7. It was determined that the mean convexities of pre-adolescent nasal contour for the normodivergent and hyperdivergent groups were 0.00mm (S.D. 0.368mm; 95% CI -0.131 to 0.125) and 0.33mm (S.D. 0.68, 95% CI 0.105 to 0.546) respectively. It is important to note that the standard deviations for each measure were quite substantial.

Growth direction classification		Pre-adolescent nasal bridge contour elevation (mm)	Post-adolescent nasal bridge contour elevation (mm)
	N	34	34
	Mean	-0.0029	0.2676
	S.D	0.368	0.382
Normodivergent	Median	0	0.2
	Minimum	-0.8	-0.4
	Maximum	0.7	1.1
	Range	1.5	1.5
	N	39	39
	Mean	0.3256	0.7333
Hyperdivergent	S.D	0.680	0.485
	Minimum	-0.9	-0.4
	Maximum	1.5	1.5
	Median	0.5	0.7
	Range	2.4	1.9

Table 7: Descriptive Statistics for both pre- and post-adolescent nasal contours for each group

Following an independent-samples *t*-test, it was shown that a statistically significant difference in pre-adolescent nasal contour between hyperdivergent and normodivergent groups existed. The results of the t-test indicate that there was a statistically significant difference in mean pre-adolescent nasal contour measures between normodivergent and hyperdivergent subjects, -0.32 (95% CI, -0.58 to -0.076), *t*(60.09) = -2.6, *p* = 0.011. Since there was a statistically significant difference between means ($p < 0.05$) at the 5% level (α $= 0.05$), we can reject the null hypothesis and accept the alternative hypothesis (there is a difference in pre-adolescent nasal contour between normal and vertical growers).

The nasal profile was affected during adolescence, as the nasal contour in both groups became more convex, albeit by very small amounts. Subjects in the normodivergent group saw their nasal ridge contour elevate an average of 0.26mm from age 10 to age 16,

while those in the hyperdivergent group saw their nasal ridge contour elevate an average of 0.41 mm. Changes can be seen in Table 8.

Table 8: Average change in nasal contour during adolescence for each group

In addition to evaluating the association between nasal contour and craniofacial growth direction, the additional objective of this study was to determine if pre-adolescent nasal contour could be of any predictive value for future vertical growth. As such, based on the frequencies of nasal measurements found across groups in the sample, an attempt was made to determine what measurement of pre-adolescent nasal contour elevation could be indicative of future vertical growth. The frequency of pre-adolescent nasal contour measurements (mm) in both groups is depicted below in Table 9.

Pre-adolescent nasal bridge contour elevation (mm)					
Growth Direction	Measure			Cumulative	
Classification	(mm)	Frequency	Percent	Percent	
	-0.8	$\mathbf{1}$	2.9	2.9	
	-0.6	3	8.8	11.8	
	-0.4	1	2.9	14.7	
	-0.3	3	8.8	23.5	
	-0.1	3	8.8	32.4	
Normodivergent	$\mathbf 0$	15	44.1	76.5	
	0.2	1	2.9	79.4	
	0.3	$\mathbf{1}$	2.9	82.4	
	0.5	$\mathbf 1$	2.9	85.3	
	0.6	4	11.8	97.1	
	0.7	1	2.9	100	
	Total	34	100		
	-0.9	1	2.6	2.6	
	-0.8	1	2.6	5.1	
	-0.7	$\mathbf{1}$	2.6	7.7	
	-0.6	$\overline{\mathbf{c}}$	5.1	12.8	
	-0.5	$\overline{\mathbf{c}}$	5.1	17.9	
	-0.4	3	7.7	25.6	
	-0.2	$\mathbf{1}$	2.6	28.2	
Hyperdivergent	0	6	15.4	43.6	
	0.4	1	2.6	46.2	
	0.5	4	10.3	56.4	
	0.6	3	7.7	64.1	
	0.7	$\mathbf 1$	2.6	66.7	
	0.8	3	7.7	74.4	
	0.9	$\overline{\mathbf{c}}$	5.1	79.5	
	1	2	5.1	84.6	
	1.1	$\overline{\mathbf{c}}$	5.1	89.7 92.3	
	1.2 1.3	$\mathbf{1}$	2.6 2.6		
	1.4	$\mathbf{1}$ $\mathbf{1}$	2.6	94.9 97.4	
	1.5	$\mathbf{1}$	2.6	100	
	Total	39	100		

Table 9: Frequency distribution of pre-adolescent nasal bridge elevation measures (mm) for normodivergent and hyperdivergent subjects.

The range of these measurements ranged from -0.9 mm to $+1.5$ mm (values in both groups combined). Based on the distribution of these measurements in each group, a table was derived to classify the frequencies of pre-adolescent nasal contours within specified ranges, reflecting the distribution (Table 10). Interestingly, nasal contour elevation did not exceed 0.7mm in the normodivergent group, and almost half (44%) of preadolesecent subjects categorized with a normodivergent growth pattern had a straight preadolescent nasal profile (0mm).

Table 10: Frequency distribution of pre-adolescent nasal contour elevations in normodivergent and hyperdivergent groups

It is evident from Table 10 that a stark contrast exists between normodivergent and hyperdivergent groups when nasal contour elevation is > 0.7 mm. No pre-adolescent subjects in the normodivergent group had a nasal contour elevation >0.7mm, whereas 13 of the hyperdivergent subjects did have a nasal contour elevation ≥ 0.8 mm (33% of the group sample).

A contingency table (2x2) was conducted to determine whether there was an association between pre-adolescent nasal contour (threshold value of \leq 0.7mm) and future craniofacial growth direction (Table 11).

		Craniofacial Growth Direction Classification Group		
		Hyperdivergent	Normodivergent	Total
Nasal	Nasal contour > 0.7 mm	13	O	13
Contour Elevation	Nasal contour < 0.7mm	26	34	60
(mm)		39	34	73

Table 11: Contingency table (2x2) for association between pre-adolescent nasal contour elevation and future craniofacial growth direction.

The data in Table 11 indicates that there were 13 true positives, 0 false positives, 26 false negatives and 34 true negatives. The Fisher's exact test showed a statistically significant association between pre-adolescent nasal contour >0.7mm and future vertical craniofacial growth, $p = .001$.

Since the chi-square test for association was not plausible and the Fisher's exact test does not provide the strength/magnitude of the association, Phi (φ) and Cramer's V were calculated to determine the strength of association. There was a very strong association between pre-adolescent nasal contour > 0.7mm and future vertical craniofacial growth, φ $= 0.435$, Cramer's V value $= 0.435$, $p = .001$. The positive likelihood ratio value of 18.75 is > 10 which also suggests a large and conclusive increase in the likelihood of vertical growth when pre-adolescent nasal contour is > 0.7 mm. The negative likelihood ratio was 0.67 indicating a minimal decrease in the likelihood of the condition. Prevalence of vertical growth in the sample was calculated as 53.42% (39/73 = 0.5342), much higher than the true prevalence of vertical growers, 22% encountered in the general population.^{18, 19} Sensitivity (true positive rate) was calculated at 33% . The test's

specificity (true negative rate) was 100%. The positive predictive value was 100% and the negative predictive value is 56.67% $(34/60 = 0.5667$. See Table 12.

 Table 12: Various statistics calculated using the prevalence of the sample

Since the prevalence of hyperdivergent growth patterns in this study is not reflective of the prevalence of vertical growth in the general population (much lower at 22% than the 53.42% in this sample) $18, 19$, an adjustment of the positive and negative predictive values was required using Bayes' theorem. Adjusted for the correct prevalence, the negative predictive value increased to 83.8% (from 56.6%) and the positive predictive value remained unchanged at 100%.

A receiver operating characteristic curve (ROC curve) was then formed to evaluate the specificity and sensitivity of using the pre-adolescent nasal contour measure of 0.75mm as a threshold for forecasting hyperdivergent craniofacial growth (Figure 10). Coordinates of the curve are found in Table 13.

Diagonal segments are produced by ties.

Figure 10: ROC curve showing sensitivity and specificity. Area under the curve = 0.647.

The area under the curve is 0.647.

Coordinates of the Curve				
Pre-adolescent nasal bridge contour elevation (mm)				
Positive if Greater				
Than or Equal To \boldsymbol{a}	Sensitivity	1 - Specificity		
-1.9	1	1		
-0.85	0.974	$\overline{1}$		
-0.75	0.949	0.971		
-0.65	0.923	0.971		
-0.55	0.872	0.882		
-0.45	0.821	0.882		
-0.35	0.744	0.853		
-0.25	0.744	0.765		
-0.15	0.718	0.765		
-0.05	0.718	0.676		
0.1	0.564	0.235		
0.25	0.564	0.206		
0.35	0.564	0.176		
0.45	0.538	0.176		
0.55	0.436	0.147		
0.65	0.359	0.029		
0.75	0.333	0		
0.85	0.256	0		
0.95	0.205	$\overline{0}$		
1.05	0.154	$\overline{0}$		
1.15	0.103	$\overline{0}$		
1.25	0.077	$\overline{0}$		
1.35	0.051	$\overline{0}$		
1.45	0.026	0		
2.5	Ω	$\overline{0}$		

Table 13: Coordinates of the ROC curve for pre-adolescent nasal contour elevation a The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

The coordinates of the curve are shown in Table 13. A cut off score of 0.75mm (i.e. 0.8mm) was selected based on balancing the values of sensitivity and 1-specificty for a desired nasal contour measure of high sensitivity and high specificity. Based on the data, a soft-tissue elevation of \geq 0.75mm would be the pre-adolescent nasal contour measure

that would positively predict future vertical craniofacial growth 33.3% of the time (0.333 sensitivity), with a 0% chance of identifying a pre-adolescent subject incorrectly to be a normodivergent grower (0% false positive rate). The corresponding 1-specificty value is 0.000 (a false positive rate of 0%). This also translates to a specificity rate of 1.0 (100% true negative rate) implying that 100% of normodivergent growers would be correctly identified as such by having pre-adolescent nasal contour rates ≤ 0.7 mm.

Effect size and power were calculated for this study. Cohen's effect size value $(d =$ 0.631) suggested a moderate to high level of clinical significance. The *post-hoc* power of the study (given α = 0.05, d =0.631, N = 34 & 39) was calculated to 0.76, slightly less than ideal power of 0.80.

Descriptive statistics of each of the craniofacial growth indicators, both pre- and postadolescently for each group can be seen in Appendix IV. In general, all craniofacial growth direction indicators in the hyperdivergent group changed minimally through adolescence, whereas their changes were more variable in the normodivergent group.

Discussion

An understanding of craniofacial growth has been the fundamental basis of orthodontic practice². Treatment requirements will vary depending on the type of growth, and the success of many treatment methodologies requires proper timing relative to expected maxillary and mandibular skeletal growth rates. As a result, it is essential to have a basic understanding of the characteristics of growth on an individual basis through an analysis of longitudinal records. Although a relationship has been found between vertical growth and nasal profile in post-adolescent females, ³⁹ the predictive power of pre-adolescent nasal contour had yet to be evaluated. This study attempted to determine if a significant relationship existed between pre-adolescent nasal contour morphology and future craniofacial growth direction, and to determine if a specific pre-adolescent nasal contour measurement could serve as a threshold for accurately forecasting future craniofacial growth direction.

A significant difference was found in pre-adolescent nasal contour between the postadolescent normodivergent and hyperdivergent subjects (*p* = 0.011). Although the standard deviations for the mean of each group were high (0.368 and 0.68), this simply indicates the large variability in pre-adolescent nasal contours present in the samples. The effect size, measured by Cohen's *d* quantified the difference between the two groups and suggested a moderate to high level of practical (clinical) significance $(d = .62)$. Although the effect size in this study suggests a moderate to high level of clinical significance, its magnitude will serve a greater value for future studies involving pre-adolescent nasal morphology. Ultimately, it will allow future studies to take advantage of the information

in this study and determine the sample size needed to address a research question adequately.

Interestingly, it is also worth noting that those in the hyperdivergent group had a greater increase in nasal contour elevation from pre-adolescence to post-adolescence than those in the normodivergent group (0.41mm vs. 0.26mm).

To answer the second objective, the data was categorized into four groups and a Fisher's exact test was performed to test for an association. Through this, it was noted that no normodivergent grower had a pre-adolescent nasal contour measure of greater than 0.7mm. The Fisher's exact test produced a p value of $p = .001$, suggesting a statistically significant association between pre-adolescent nasal contour >0.7mm and craniofacial growth in the vertical direction.

The sensitivity and specificity of utilizing a cut-off value of 0.75mm for predicting future vertical growth was evaluated. The 1-specificity value was 0.000 (i.e. specificity value= 1.000) indicates that no subject with a pre-adolescent nasal contour <0.75mm would be incorrectly identified as a vertical grower (false positive rate of 0.000). This also means that there would be a specificity rate of 1.0 (100% true negative rate), signifying that 100% of normal growers would be correctly identified as such by having pre-adolescent nasal contour rates < 0.7mm. Sensitivity (true positive rate) was calculated at 0.33, indicating that a pre-adolescent nasal contour elevation threshold of 0.75mm is able to correctly forecast only 33% of the total number of subjects who grew vertically. If we were to accept a more liberal false positive rate (i.e. higher sensitivity), for example by

utilizing a pre-adolescent nasal contour of >0.10 mm as the cut-off value, the test would incorrectly identify a normal grower as a vertical grower 23.5% of the time (much higher than the 0% rate if the cut-off value of 0.75mm was used), while being correct 56.4% of the time (greater than the 33% value if 0.75mm were used as a cut-off). Utilizing a cutoff value of 0.75mm was determined to be the most appropriate threshold based on balancing sensitivity and specificity.

In general, clinicians are chiefly concerned with the predictive value of a test, rather than its sensitivity. The generalized clinical question is: how likely is a patient with a positive test result to actually have a condition? For this study, the positive predictive value represents the probability that subjects with a pre-adolescent nasal contour measure >0.7mm truly become vertical growers. The negative predictive value represents the probability that the subjects with a pre-adolescent nasal contour <0.7mm will not grow vertically. A crucial point is that prevalence affects the predictive value of any test. Using the same test (e.g., pre-adolescent nasal contour) in a population with higher prevalence increases positive predictive value. Conversely, decreased prevalence results in increased negative predictive value. This indicates that the same diagnostic test will have a different predictive accuracy according to the prevalence. When utilizing the 2x2 contingency table and Fisher's exact test to evaluate the strength of association, it was important that the prevalence of vertical growth in the sample was adjusted to reflect the true prevalence of vertical growth in the general population. Since the prevalence of hyperdivergent growth patterns in this study is not reflective of the prevalence of vertical growth in the general population, $(53.42\% \text{ vs. } 22\%)^{18, 19}$, an adjustment of the positive and negative predictive values was required following formula based on Bayes' theorem. Adjusted for
the correct prevalence, the negative predictive value was 83.3% meaning that among those who had a pre-adolescent nasal contour <0.75mm, the probability of having a normal growth pattern is 83.3%. Put another way, 16.7% of subjects who have a preadolescent nasal contour <0.75mm would nevertheless experience a hyperdivergent growth pattern. The positive predictive value was 100%, indicating that the test would accurately predict vertical growth 100% of the time if the pre-adolescent nasal contour threshold of 0.75mm was used.

In this case, because many orthodontists do not want to make the mistake of overlooking a true vertical grower, a cut-off value that is high in sensitivity is preferred. As such, a cut-off value of 0.1mm may be preferred over the cut-off value of 0.75mm that was initially selected (0.564 sensitivity and 0.765 specificity, Table 17). Additionally, the likelihood ratio value of 18.75 was > 10 which suggests a large and conclusive increase in the likelihood of vertical growth when pre-adolescent nasal contour is > 0.75 mm. Evidently, it is difficult to strike this very sensitive balance between specificity and sensitivity.

An ROC curve was used in this study to describe the accuracy of pre-adolescent nasal contour over a range of cut-off points. The overall accuracy of pre-adolescent nasal contour as a diagnostic predictor of future craniofacial growth is best defined as the area under the ROC curve; the larger the area, the better the test. This is important as it reflects the strength of using pre-adolescent nasal contour as a predictor for future vertical growth. Unfortunately, the area under the ROC curve for this data set was 64.7%,

indicating that using pre-adolescent nasal contour morphology is a fair to poor diagnostic test for reliably forecasting craniofacial growth direction.

A *post-hoc* (retrospective) power analysis uses the obtained sample size and effect size to determine what the power was in the study, assuming the effect size in the sample is equal to the effect size in the population. The *post-hoc* power analysis revealed a power of 0.76. Statistical significance was still achieved at $p = 0.011$. It is important to note that the effect size is required to calculate the power of a study *a priori* or calculate the power of a study *post-hoc* to determine sample size. Since effect size regarding differences in pre-adolescent nasal contour in hyperdivergent and normodivergent growers was not known prior to this study and this is the first study of its kind, power was calculated *posthoc.* Thus, the purpose of the *post-hoc* power value in this study is to estimate the sample size required for a future study given the current effect size revealed in this pilot study.

To evaluate the magnitude of the statistically significant result in this study, we can utilize the effect size (0.631) as an indicator of how large the difference between the groups was rather than strictly use the *post-hoc* power test. Effect sizes are essential as they assess the overall contribution of a study. In this study, an effect size of 0.631 suggests a moderate to high clinically significant difference (i.e., results of the study are meaningful beyond the likelihood of chance). Given the variability of the means in this study, a future study desiring equal participants in each group with the same criteria (effect size *d* of 0.631, power = 0.8 and α error probability = 0.05) would require 41 subjects in each group to support a statistically significant result between groups with

sufficient power. If it were desired that the sample sizes in each group accurately reflected the prevalence of vertical growers in the general population (22%), the allocation ratio could be adjusted so the required samples would require 90 subjects in the normodivergent group and 26 subjects in the hyperdivergent group (with effect size *d* of 0.631, power = 0.8 and α error probability = 0.05).

The design of this study was unique in that no prior study attempted to evaluate preadolescent nasal contour as a predictor of vertical growth during adolescence. As such, the way in which the study was carried out will be further explained. The mandibular plane angle and lower anterior face height were used to divide the subjects into normodivergent and hyperdivergent groups. In order for these variables to be used to predict craniofacial growth direction, evidence had to indicate that they did not change dramatically during growth and had a strong relationship to vertical growth. Providentially, an emphasis of early orthodontic research attempted to determine if the mandibular plane angle was stable over time.^{34, 91} Bjork found that the direction of mandibular growth does not alter appreciably with age³⁴ while Brodie⁹¹ found that once the growth pattern of the facial bones and mandibular plane is established, whether normal or abnormal, it is 'virtually constant and resists change'. Downs' research results were in agreement with this assessment, but with one small difference. He found that most patients with steeply-growing mandibles maintained their original steep morphological patterns, while the horizontal growing mandibles were associated with a greater decrease in the mandibular plane angle from pre- to post-adolescence.¹⁷ The result of this study confirm these findings, as the mandibular plane angle change from

pre- to post-adolescence in the normodivergent group was greater than the mandibular plane angle change in the normodivergent group (-2.15° vs. -0.5°).

Naturally, since the direction of mandibular growth does not alter appreciably with age and is proven to be an excellent indicator of facial type, $25, 49, 55$ using mandibular plane angle as a parameter to categorize craniofacial growth direction is rational and practical. It has also been well established that steeply growing mandibles are associated with greater anterior face heights at both younger and older ages.¹⁷ In addition, others have found that there is a strong tendency to maintain the original facial type with age, as skeletal open-bite types are associated with an excessive lower anterior face height relative to the upper face height.^{6, 9, 58} Since mandibular plane angle and lower anterior face height are highly correlated, and both have been indicative of describing facial pattern, they were used in this study to divide the overall sample into hyperdivergent and normodivergent groups.

Although the number of subjects in each group in the present study is relatively small, this was largely due to the limited release of records from the AAOF Legacy Collection of the three growth studies $(N=304)$. Other factors including inadequate or poor records lead to smaller sample size being used than anticipated. In addition, the criterion in the selection of the sample using two, not one, vertical measures had the disadvantage of limiting the number of persons to be included in the study. However, this was necessary to ensure a strong and fair comparison between groups, as using only one cephalometric variable to divide subjects across would limit the strength of the study. If more vertical

measures were utilized to more strongly distinguish the differences in facial types, the sample size in each group would have been dramatically smaller, yielding less predictive power of the results. Secondly, the size of the sample reported in this investigation compares favorably with other longitudinal studies.³⁹ As an example, the Bolton longitudinal cephalometric standards, derived from the Bolton study of 5,000 persons, were based on only sixteen individuals from each sex.⁹ On the contrary, this points to the difficulties encountered by most orthodontic researchers in obtaining and reporting on the cephalometric changes in dentofacial relationships in large numbers of persons between childhood and adulthood.⁹ Lastly, because this is a pilot study, a significantly large sample was not required. Results of this pilot study will aid in deducing the appropriate effect size (statistical variability) in an attempt to predict an appropriate sample size and improve upon the study design prior to performance of a full-scale study.

The rationale for using the chronological ages of 10 and 16 was for many reasons. First, evidence indicates that the growth of the nasal bone is complete at approximately 10 years of age.⁷ Growth thereafter is of the nasal cartilage and soft tissues (which is the focus of the current study). Secondly, age 10 was selected as a reliable point in time when the pubertal growth spurt has not yet occurred, as adolescence only begins at age 10 or 11 in females. Thirdly, longitudinal data from studies of craniofacial growth indicate that a significant number of females have a 'juvenile acceleration' in jaw growth that occurs 1- 2 years before the adolescent growth spurt. Fourthly, studies have found that long facial patterns are expressed earlier than those patients with short facial patterns^{23, 24, 51} and subjects with long vertical facial patterns experience their pubertal growth spurt earlier as

well.⁶¹ As such, in order to properly include those with potential juvenile vertical patterns, an age of 10 years was used. Establishing an average age of 10 years for the preadolescent sample ensured that the growth of the nasal bone was likely complete and the window of the 'juvenile acceleration' could be captured in the sample population. This tendency for a clinically useful acceleration in jaw growth to precede the adolescent spurt is a major reason for careful assessment of physiologic age in planning orthodontic treatment.⁷⁸ As such, the American Association of Orthodontists recommends that patients see an orthodontist at 7 years of age,⁹² and so the orthodontic community commonly evaluates children in this pre-adolescent stage of development. If treatment is delayed too long, the opportunity to utilize the growth spurt is missed. Generally, in the timing of orthodontic treatment, clinicians have a tendency to treat girls too late and boys too soon, forgetting the considerable disparity in the rate of physiologic maturation.⁷ Age 16 was chosen as it is generally accepted that the termination of active pubertal growth takes place in females at 14 years of age and increments in nose height, depth and inclination are essentially complete in girls by 16 years of age.^{10, 52, 66} In fact, research has shown that girls attain the adult size of the soft tissue integument as early as 14 years of age. 61

The other important aspects that must be considered are the average values to which study samples are compared against. The introduction of the lateral cephalogram in the 1930s allowed longitudinal studies to be performed, and encouraged references and coordinate systems to be established. ⁹³ These references have been proven to be instrumental when studying longitudinal changes in the face. ⁹⁴ It has been well

documented that different ages and different ethnicities exhibit facial characteristics and growth patterns unique to their race or age, and these differences can have quite an effect on what is perceived as 'normal' or 'abnormal'. The same can be said when undertaking cephalometric study. In order to establish proper conclusions, either unique cephalometric normals for the population should be utilized and/or there must be homogeneity within the sample (e.g., the same race and age). Farkas et al.⁹⁵ conducted the broadest study in attempting to establish the main facial characteristics of 25 national groups compared to norms established previously for North American whites (NAW).⁹⁵ Nose heights and widths contrasted sharply; in relation to North American Caucasians, the nose was significantly wider in both Asian and Black ethnic groups. As such, this stresses the importance of using the most homogeneous sample possible when comparing sample data to cephalometric standards, as racial variations do exist.⁹⁵ This was ensured in this study by utilizing growth study samples of three geographically and racially similar populations (Burlington, Cleveland and Michigan). It should be noted that American ethnic 'purity' is, at best, a largely cultural phenomenon. Other researchers have explored the possibility of developing a limited number of normative cephalometric standards for males and/or females between 5 years of age and adulthood. ⁹⁶ Bishara et al. developed normative cephalometric standards that are more closely related to the patient's age and sex than a single standard used for all ages and for both sexes.⁹⁶ Cephalometrically, the orthodontist is therefore faced with the dilemma of having to choose between practicality and accuracy; that is, either using one standard for all ages and sexes or using a large number of standards, each of which is specific for age and sex. This study utilized both age-specific and sex-specific means of all three growth studies

for the mandibular plane angle and lower anterior face height when classifying subjects; this was another method to establish homogeneity when classifying.

This study also determined that utilizing a pre-adolescent nasal contour threshold of 0.75mm was graded as a fair-to-poor test in identifying subjects who would grow vertically. It would be ideal to have a reliable value that could serve as a threshold indicating clinical significance for nasal contour elevation. However, no study exists in the literature that has determined the threshold amount of nasal bridge elevation that would be clinically observable and significant. Moreau arbitrarily defined convex nasal contour to be clinically discernible if the dorsum of the nose was > 1.5mm above the linear plane from soft tissue nasion to pronasale.³⁹ However, to arbitrarily use this value because Moreau did would be erroneous, given the data that has been collected in this study. A study investigating what this clinically observable threshold value is would be an interesting follow-up study and could then be compared to the results of the present study. This study identified a value of 0.75mm that could serve as a cut-off to forecast future vertical growth. Unfortunately, we do not know if this measure can accurately be identified clinically. Whether or not this measure is clinically discernible at such a young age remains unanswered.

Furthermore, measurements of six additional growth-direction planes and angles were recorded longitudinally on all 73 subjects evaluated. This data was collected to better understand the potential significance of these indicators in contributing to the morphological characteristics of the adult face. Because these were not used to classify

the overall study sample into normodivergent and hyperdivergent groups, comparisons between the two groups (which were based on differences between lower anterior face height and mandibular plane angle) would be inappropriate. However, each variable was recorded for each subject as this data could be utilized in future studies to investigate the relationship between nasal contour morphology and each of these vertical variables. Other than this purpose, the values did not serve to answer either of the objectives in this study.

The objective of this study aimed to utilize a clinically observable criterion that may serve as an indicator of future 'poor growth'. Because the pattern of facial growth is established early in life and rarely changes significantly, it would be ideal for orthodontists to accurately forecast the growth pattern in pre-adolescent patients.⁷ Unfortunately, our current predictions are largely based on the pre-treatment morphologic characteristics rather than on a reliable predictor of future change.^{96, 97} As practitioners of orthodontics, we find that of our estimates of future changes in facial dimensions are no better than simply comparing individual patients to average values for prediction of growth direction. Now that a nasal convexity measure of 0.75mm has been identified as a threshold in this study, this provides valuable insight into the relationship between preadolescent nasal contour and future craniofacial growth. In addition, this should encourage other orthodontic researchers to look further into this relationship. Optimistically, future research could establish a clinically detectable nasal contour measurement that would reliably serve the orthodontist well in the absence of a lateral cephalogram when forecasting future growth. Although the results of this present study

indicate a wide range of variability in pre-adolescent nasal contour morphology regardless of facial type, a statistically significant difference was found between normodivergent and hyperdivergent growers. Additionally, using a threshold elevation (0.75mm) to predict future vertical growth cannot be used to reliably anticipate future vertical growth in all patients.

Limitations

Although the goal of the study design was to be as efficient, practical and robust as possible, there are limitations to this study that will be addressed.

First, the sample size was not ideal. However, this could not be determined *a priori* as no effect size existed between pre-adolescent nasal contour morphology and future craniofacial growth direction. Still, this remains a limitation as slightly less than ideal power was found in the study.

A second limitation was that the normodivergent and hyperdivergent groups were split by one standard deviation away from the mean. Dividing the groups by a single standard deviation allowed for an increase in subjects per group (which turned out to be necessary to get as close to a power of 0.8). Despite the results of this study indicate a statistically significant difference in pre-adolescent nasal contour morphology, splitting the groups based on two standard deviations from the mean may have produced an even larger statistically significant difference in pre-adolescent nasal contour morphology and changed the cut-off value of 0.75mm as a diagnostic indicator of future vertical growth. Further, the results may have indicated that pre-adolescent nasal contour is a good diagnostic test and not a fair-to-poor test as the results of this study found. This change in methodology would have more strongly distinguished between the normodivergent and hyperdivergent groups, though a much smaller sample in each group would have resulted with less overall power to the study.

Another limitation is that it is unknown if the threshold value of 0.75mm is clinically discernible in profile to the orthodontist. Although this measure is unlikely to be obvious when a patient presents for a clinical exam, no study has been done to establish a level of nasal contour that is clinically noticeable. Ideally, a future study should be done to quantitate how much elevated nasal soft tissue is required to be clinically detectable by the naked eye. This could then serve as a baseline for future studies investigating the relationship between nasal contour and craniofacial growth direction.

The over-arching goal of this study was to determine if pre-adolescent nasal contour could serve as a reliable predictor of craniofacial growth direction. In order for this criterion to serve as a predictor, it would need to be evaluated prior to adolescence. As such, age 10 was selected as the pre-adolescent age. Despite the evidence indicating that the nasal bone was complete by age $10⁷$, the results of this study indicate that nasal contour morphology is not foretelling at this age. Unfortunately, the benefit of using a later age (e.g., 13 years of age) to evaluate differences in nasal contour morphology would be counterproductive in a practical sense since the orthodontist's role is to anticipate growth direction changes prior to adolescence. Utilizing a later age and then being able to potentially conclude a larger statistical difference between groups would not be as beneficial to the orthodontist. It is still quite possible that nasal contour morphology at age 10 is a poor predictor for future craniofacial growth direction because it is too early an age for enough nasal ridge shape to develop.

Another potential limitation, although unlikely, is that of bias. Though pre-adolescent and post-adolescent radiographic measurements were done three weeks apart with no knowledge of the vertical measurements taken for each post-adolescent radiograph, having a separate investigator trace all the pre-adolescent nasal contours would have eliminated any slight possibility of bias.

Lastly, it is possible for soft tissue compression to occur at soft tissue nasion from the cephalostat when the lateral cephalograms were taken. Unfortunately, this could not be verified, as this was a retrospective study. However, any radiographs that were of poor quality were discarded and not included in the study.

Conclusions

This retrospective case-control pilot study examined nasal contour morphology in preadolescent females and its value as an indicator of future craniofacial growth direction. The following conclusions can be derived from this investigation:

1) A statistically significant relationship was found between pre-adolescent nasal contour morphology and craniofacial growth direction. However, extreme variability existed in pre-adolescent nasal contour morphology.

2) Subjects who grew in a hyperdivergent pattern through adolescence had a larger increase in nasal contour elevation than those who grew in a normodivergent pattern.

3) Using data from this study, a nasal contour elevation threshold that could serve as a predictor of future vertical craniofacial growth was identified (>0.75mm).

4) Using pre-adolescent nasal contour morphology as a diagnostic predictor for future craniofacial growth direction is not reliable and was determined to be a fair-to-poor diagnostic criterion.

Potential Future Studies

In order to further examine the relationship between nasal contour and vertical craniofacial growth direction, further studies could involve the following:

- 1. Perform a study that aims to determine what threshold/level of nasal contour elevation is clinically detectable (judged by orthodontists). This information could be used in future studies as a reliable quantitative standard for future studies looking into clinical significance.
- 2. Conduct a study with the same design but ensuring the appropriate number of subjects is in each group to achieve optimal power. Additionally, ensure the study sample represents the correct prevalence of vertical growth in the population (22%).
- 3. Complete a study that is able to analyze two ROC curves of pre-adolescent nasal contour vs. mandibular plane angle and lower anterior face height individually. This may yield an ROC curve(s) with area under the curve >0.8 when preadolescent nasal contour is analyzed against each of these variables alone (rather than together as in this study; area under the curve $= 0.647$)
- 4. Perform a retrospective longitudinal study with two distinct pre-adolescent groups divided by convex nasal contour. Determine if their post-adolescent craniofacial growth direction indicators are significantly different between the groups.
- 5. Utilize the methods of this study to investigate males for the presence of convex nasal morphology in vertical and non-vertical growers
- 6. Perform a retrospective study using longitudinal cephalometric records to identify at what age and stage of maturation did the convex nasal morphology first develop (i.e. when did dorsal hump elevation begin and accelerate?)
- 7. Undertake a longitudinal, prospective study that aims to evaluate if pre-adolescent nasal contour is in fact a reliable indicator of future vertical growth

Based on the limited research concerning the relationship between nasal morphology and craniofacial growth direction, new studies can be attempted to confirm a true relationship. The knowledge of such data could be very useful to orthodontic treatment planning in attaining an excellent, more predictable, stable result. Knowledge of this relationship could serve the clinician to better understand the behavior of the mandible during growth and anticipate potential challenges during orthodontic treatment.

Appendix 1

Definitions of Cephalometric Landmarks

Appendix II

Definitions of Cephalometric Planes, Angles and Statistical Terms

Appendix III

Diagrammatic representation of the planes and angles used in this study

Appendix IV

Data for Additional Indicators of Craniofacial Growth Direction

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Curriculum Vitae

