Nasal Septal Deviation and Nasofacial Skeletal Form: A Cross-Sectional CBCT Study of a 7-18 Year-Old Cohort

A thesis submitted to the faculty of the Graduate School
of the University of Minnesota

By

Matthew Joseph Goergen

In partial fulfillment of the requirements
for the degree of Master of Science

Adviser: Thorsten Grünheid, DDS, Dr med dent, PhD

August 2016

Acknowledgements

I would like to thank all those who helped me in completing this project. Specifically, I would like to thank Nathan Holton for his expertise on the subject and guidance throughout the project. Also, thank you to Thorsten Grünheid for serving as my thesis adviser and for the invaluable insights and advice while reviewing the manuscript. Thank you to Gary Anderson and Kim Mansky for serving on my thesis committee and offering support and useful feedback. Thank you also to Angela Bukstein for help with data collection and being available to assist when needed. I would finally like to thank the entire University of Minnesota Department of Orthodontics for allowing me to pursue a career in orthodontics and for fostering such a strong research program.

Abstract

Objective: The objective of this study was to examine the relationship between nasal septal deviation and the shape of the nasofacial skeleton during ontogeny.

Materials and Methods: Nasal septal size was retrospectively measured on existing cone-beam computed tomograms (CBCT) in 66 mixed-sex orthodontic patients of European ancestry aged 7-18 years. First, the septum was manually segmented using CBCT reconstructions and the volume of the structure calculated. Next, a midsagittal volume that followed the borders of the septum was constructed as a model for a non-deviated septum. Nasal septal deviation was then calculated for each individual. Nasofacial skeletal form was quantified using a series of coordinate landmarks of the facial skeleton in the nasal region and the cranial base. Using geometric morphometric techniques, size and shape information was distilled from the landmark data. Multivariate regression analyses were used to assess the interactions between the septum and the nasofacial skeleton.

Results: There was no significant correlation between nasal septal deviation and age or nasofacial size. Nasofacial shape changes correlated with septal deviation followed a different pattern than allometric shape changes. In individuals with a deviated septum, the sphenoid body was anteriorly positioned, reducing the size of the nasofacial skeleton. This pattern of morphological variation was independent of the stage of development.

Conclusion: Normal developmental changes in nasal cavity and cranial base form are not related to an increase in nasal septum deviation. Rather, a nasofacial skeletal configuration with anterior displacement of the sphenoid may place spatial constraints on the growth of the septum, resulting in deviation.

Table of Contents

List of Tables

List of Figures

Introduction

The nasal septum is a midline structure that divides the nasal cavity into bilateral nasal passages. It is composed of the septal cartilage, the perpendicular plate of the ethmoid, the vomer, and the crests of the maxillary and palatine bones (Kim *et al.*, 2010). The nasal septum has been described as a key facial growth center that has a morphogenetic influence on facial skeletal development (Scott, 1953). During development, the nasal septum often becomes deviated indicating a complex interaction between the septum and surrounding skeleton. Nasal septal deviation is defined as the displacement of the bony or cartilaginous septum to one or both sides. Numerous etiological factors for nasal septal deviation have been described. For instance, septal deviation can occur due to a failure of development at any embryological stage, from either genetic or environmental causes (Pirsig, 1992). During normal development, septal deviation can result at an early stage from prolonged intrauterine pressures and transnatal pressures on the fetus (Gray, 1978). Septal deviations can also be caused by genetic influences, mechanical injuries, and, rarely, by congenital malformations, infections, or neoplasia. Therefore, septal deviation can occur *in utero*, during delivery, and throughout the entire life (Pirsig, 1992).

It has been suggested that humans, when compared to other mammals, may be predisposed to nasal septal deviation (Gray, 1978; Takahashi, 1987). Across mammals, there is an inverse relationship between the size of the facial skeleton and nasal septal deviation (Gray, 1978; Takahashi, 1987). Humans, having comparatively short faces to other mammals, have a high incidence of nasal septal deviation, whereas this condition is virtually non-existent in long-snouted animals. This pattern may suggest that nasal septal deviation results from discordant growth between the septum and surrounding facial skeleton. Indeed, studies indicate smaller facial dimensions in individuals with deviated septa (Freng *et al*., 1988). Smaller nasal cavities were present in adults with deviated nasal septal cartilage in comparison to individuals without septal deviation, suggesting that an undersized skeletal frame in the sagittal plane may have led to the buckled non-fitting septal cartilage (Freng *et al*., 1988). This notion is supported by animal studies in which anteroposterior facial growth was experimentally reduced via fixation of the circummaxillary sutures. The spatial constraint altered nasal septal and facial skeletal relationships resulting in an increase nasal septal deviation (Rönning and Kantomaa, 1985; Holton *et al.,* 2011). Collectively, these studies suggest that the surrounding skeletal architecture of the nasal cavity may impose constraints on nasal septal growth resulting in deviation.

In contrast to the above, there is also evidence that nasal septal deviation may be the result of increased septal growth, rather than resulting from an undersized surrounding facial skeleton (Vetter *et al*., 1984; Van Loosen *et al*., 1996; Holton *et al*., 2012). Looking at population variation in septal size and magnitude of septal deviation, individuals of European descent have both increased prevalence of septal deviation and larger nasal septa when compared to individuals of African descent (Holton *et al*., 2012). Studies on the postnatal growth of the nasal septum also show that the nasal septal cartilage and perpendicular plate of the ethmoid continue to grow into adulthood following the cessation of skeletal growth (Vetter *et al.*, 1984; Van Loosen *et al.*, 1996). Therefore, it is possible that the continued growth of the nasal septum into adulthood is at least partly responsible for septal deviation in humans.

Although discordance between the nasal septum and facial skeleton has been shown, the ontogeny of septal deviation and the interaction between the nasal septum and surrounding nasofacial skeleton during ontogeny is not well understood. “Ontogeny” refers to growth and development. Part of the difficulty in determining the influence of the nasal septum on nasofacial form in human samples is the paucity of data regarding the interaction between the nasal septum and facial form during human ontogeny. This data has been difficult to obtain historically due to the lack of practical, low-cost, non-invasive methods for analyzing the human nasal septum *in vivo*. Cone-beam computed tomography (CBCT) imaging offers a non-invasive, three-dimensional (3-D), high-resolution method of analyzing the nasal septum and facial form in growing individuals from a normal population. A thorough understanding of this relationship is particularly important given that nasal septal deviation, especially in more severe cases, can result in a higher incidence of mouth breathing, which may be associated with aberrant patterns of facial growth and the development of certain types of malocclusion (Freng *et al*., 1988). Therefore, the goal of the present study was to assess the developmental patterns of nasal septal deviation and the morphological relationship between the nasal septum and surrounding nasofacial skeleton in a cross-sectional human sample using data derived from CBCT scans.

Literature Review

The Nasal Septum as a Facial Growth Center

The nasal septum has been suggested to be a key growth center of the facial skeleton (Scott, 1953). However, the precise role of the nasal septum on facial growth is not well understood and various models have been proposed. The nasal septal traction model describes the nasal septum as having a morphogenetic influence on surrounding skeletal structures (Scott, 1953). This growth model maintains that the nasal septum has intrinsic growth potential and therefore serves as an endochondral growth plate that drives anteroposterior and vertical craniofacial growth (Scott, 1953; Copray, 1986; Wealthall and Herring, 2006). As the cartilaginous component of the nasal septum expands, it exerts a force on the surrounding skeletal tissues inducing growth at key facial growth sites, the craniofacial sutures (Latham, 1970; Siegel *et al*., 1990; Wealthall and Herring, 2006; Al Dayeh and Herring, 2014).

The nasal septal traction model is supported by a number of experimental studies using animal models. For instance, Copray (1986) investigated the intrinsic capacity for growth of the nasal septum using a rat model *ex vivo*. The nasal septal cartilage was excised and cultured for 10 days and the growth of the septum was analyzed. Overall, the nasal septal cartilage increased considerably in size while the shape was preserved. The center of the septum and the area adjacent to the septo-ethmoidal junction were the areas of greatest cellular proliferation and the greatest increase in size was found in the anterior posterior direction. These results suggest a prominent role for the nasal septum on midfacial growth of the rat (Copray, 1986).

Following from the work of Copray (1986), Wealthall and Herring (2006) investigated whether growth of the nasal septum in mice elongates the facial skeleton in the same way that the epiphyseal growth plates of the long bones and synchondroses of the cranial base elongate the long bones and neurocranium of mammals. The authors examined endochondral ossification at the caudal end of the cartilaginous nasal septum in mice from postnatal days 0-15 compared to known cranial growth sites, the synchondroses. It was found that the septum contributes to enlarging the facial skeleton by displacing facial bones, primarily by septal interstitial growth and also, to a lesser degree, endochondral ossification along the perpendicular plate of the ethmoid (Wealthall and Herring, 2006). The same group also measured the mechanical properties of the nasal septum to determine if the septum is mechanically able to play an active role in midfacial growth (Al Dayeh and Herring, 2014). It was hypothesized that if the nasal septum is a growth center, then its growth pressure should be enough to separate the facial sutures and stiff enough to withstand recoil pressure of the sutures (Al Dayeh and Herring, 2014). Experiments in pigs showed that the force produced by septal expansion corresponded to latent mechanical separation of the facial sutures, which suggests that the growth of the nasal septum is capable of placing pressure on surrounding structures in order to drive sutural opening and facial growth.

In contrast to the nasal septal traction model, which emphasizes the morphogenetic influence of cranial cartilages on skeletal growth, others have suggested that the nasal cartilage plays a minimal role in facial growth (Moss *et al.*, 1968; Moss and Salentijn, 1969, Stenström and Thilander, 1970). The functional matrix hypothesis, for example, describes the nasal septum not as driving facial growth itself, but rather skeletal and cartilage growth occurring in response to the functional need for respiration and secondary to growth of the soft tissues (Moss *et al.*, 1968; Moss and Salentijn, 1969). Essentially, the functional matrix model argues that the septum does little more than contribute to projection of the external nose and elevation of the nasal bridge and does not play an important role in the anterior growth of the facial skeleton (Moss *et al.*, 1968; Moss and Salentijn, 1969, Stenström and Thilander, 1970). Additional evidence for this model is seen in patients with congenital craniofacial anomalies that affect the nasal septum. For instance, patients with holoprosencephaly and cyclopia with arrhinencephaly, conditions where the nasal septum is absent, have normal midfacial growth except for a lack of external nose projection and nasal bridge elevation during craniofacial development (Moss *et al*., 1968; Moss and Salentijn, 1969).

Evidence from Animal Experiments

Septal excision experiments have demonstrated that the nasal septal cartilage is an intrinsic growth center for facial growth in several animal species. Experimental studies in rabbits, for example, have shown that surgical extirpation of all or part of the nasal septum decreases the anteroposterior growth pattern of the midface (Wexler and Sarnat, 1961; Sarnat and Wexler, 1966, 1967; Rhys-Evans and Brain, 1981). Wexler and Sarnat (1961) and Sarnat and Wexler (1966) showed this by resecting the cartilaginous nasal septum in young growing rabbits and comparing them to rabbits that were used as unoperated and sham-operated controls. Postmortem analysis of the experimental animals revealed that the snout was shorter and smaller with a severe relative mandibular prognathism, the nasal and premaxillary bones were smaller, and the nasal cavity and piriform aperture were smaller than in the control animals. In addition, the incisors were in malocclusion, malshaped, and overerupted (Wexler and Sarnat, 1961; Sarnat and Wexler, 1966). When these experiments were repeated on adult rabbits, however, there was very little difference in facial form between experimental animals and controls (Sarnat and Wexler, 1967). These results support the nasal septum's importance during growth in rabbits.

Holton *et al*. (2011) used a novel approach of experimentally induced synostosis in the craniofacial skeleton rather than altering the nasal septum itself. Using a pig model, the length of the facial skeleton was experimentally reduced via rigid plate fixation of the frontonaso-maxillary and zygomaticomaxillary sutures (Holton *et al.,* 2011). Despite sutural restriction, the nasal septum grew to normal length as measured by vomer length, and the reduction in facial length led to compensatory lengthening of the premaxilla (Holton *et al*., 2011). This experiment supports the nasal septal traction model and is indicative of integration between nasal septal and premaxillary growth.

Some nasal septal extirpation experiments, however, did not find significant changes in facial growth following extirpation. Surgical resections of the nasal septum on guinea pigs, for example, showed minimal effect on anterior growth of the facial skeleton (Stenström and Thilander, 1970). Experiments focusing on shorter-face mammals, such as the work done on chimpanzees by Siegel and Sadler (1981), also showed that septal resection had minimal effect on facial growth when compared to controls. In addition, experiments using short-snouted animals, such as domestic cats by Freng (1981) and ferrets by Cupero *et al*. (2001), contradict the findings from experiments on long-snouted animals. For instance, surgical extirpation of the entire cartilaginous nasal septum and vomer of growing domestic cats showed no difference in sagittal mid-facial development among the three groups when compared to sham-operated and unoperated control cats (Freng, 1981). Similarly, following partial resection of the vomer or nasal septal cartilage in ferrets, there was no change in anteroposterior facial length compared to controls (Cupero *et al*., 2001). These findings suggest taxonomic variation in the role of nasal septal traction in facial growth and that the nasal septum may play less of a role in the anterior growth of the face in shorter-face taxa.

Role of the Nasal Septum in Human Facial Growth

While there is considerable experimental evidence indicating that the nasal septum can have a significant morphogenetic influence on the growth of the facial skeleton, much of this work is derived from long-snouted animal models. As such, it is unclear to what degree the findings are applicable to growth dynamics in shorter-faced humans. One method previously used to analyze the contribution of the nasal septum to anterior facial growth in the human skeleton was to evaluate individuals with congential labiomaxillary clefts or facial injury (e.g. Delaire and Precious, 1986; Mooney *et al*., 1989; Siegel *et al*., 1991; Hall and Precious, 2013). Based on experiments using path analysis to examine the anatomical relationships between the cleft premaxilla and several other midfacial structures in both cleft and normal fetal samples, it has been concluded that the septopremaxillary segment is important in anterior facial growth and the nasal septal traction model is more explanatory than the functional matrix model in both normal and cleft samples (Mooney *et al*., 1989; Siegel *et al*., 1991).

Surgical repair of unilateral or bilateral facial clefts also provides insight into the role of the nasal septum as pacemaker for midfacial growth and shows that the maxillary labial frenum is an important constituent of the septopremaxillary traction system. The frenum houses the septopremaxillary ligament, which extends from the nasal septum to the mucosal part of the lip (Hall and Precious, 2013). Forces generated by the nasolabial muscles are transmitted to this structure, and in turn to the anterior surfaces of the maxilla during facial growth. In individuals with complete unilateral cleft lip, the perioral and nasolabial muscles on the side of the cleft are underdeveloped, retracted, and laterally displaced, while the nasolabial muscles on the non-cleft side insert into the cartilaginous septum and anterior nasal spine. This results in displacement and abnormal development of the premaxillary region (Hall and Precious, 2013).

There are only few reports in the literature about when the nasal septal cartilage stops growing. For instance, Van Loosen *et al.* (1996) quantified growth rates by creating growth curves using a specially designed algorithm for surface area measurements from a sample of *post-mortem* human specimens from birth to 62 years of age. These measurements showed that the growth rate of the nasal septum is highest in the newborn until two years of life, and then slows down continuously until a plateau is reached at an age of approximately 36 years. The size of the cartilaginous septum was found to increase in the sagittal dimension during the first two years of life. After that, the total area of the cartilaginous part of the septum remains constant due to a balance between new formation of cartilage and an equal amount of cartilage transformed into bone by endochondral ossification. Based on these findings, it has been concluded that the cartilaginous septum reaches adult size at the age of two years, and any subsequent growth is caused by expansion of the perpendicular plate (Van Loosen *et al*., 1996).

Nasal Septal Deviation

The study of the role of the nasal septum on the growth of the facial skeleton in humans is complicated by the presence of septal deviation, a condition that is virtually non-existent in long-snouted animals. This may suggest that the role of the nasal septum in human facial growth may differ from the patterns identified in most animal models. While the nasal septum may be a key growth center in long-snouted animals, its influence may be limited in humans.

Nasal septum deviation occurs when the septum is displaced away from the midline, for which numerous etiological factors have been described. Some of these factors are related to intrauterine pressures. For instance, Gray (1978) examined 2,380 infants at birth and found that 4% had anterior cartilage deformity, giving credence to his theory of transmitted pressures during pregnancy or childbirth. Podoshin *et al*. (1991) investigated 4,090 neonates with no evidence of birth trauma as the cause of congenital nasal deformities for nasal septal deviations and proposed that the majority of dislocations originated during intrauterine life. Other etiological factors include discordant growth between the septum and surrounding facial skeleton. For instance, Freng *et al*. (1988), in a study examining cephalometric morphology in adults with deviated septal cartilage, found that smaller nasal cavities were present in adults with deviated nasal septal cartilage. This suggests that an undersized skeletal frame in the anteroposterior dimension may have led to the deviated septal cartilage and that nasal septal deviation may result from growth restriction of the nasal septum due to space constraints from the surrounding facial skeleton.

On the other hand, there is also evidence that nasal septal deviation may be the result of increased septal growth. Kim *et al.* (2012) found that reduced ossification of the sphenoidal process of the septal cartilage led to greater overall septal length and increased nasal septal deviation. Similarly, individuals with larger nasal septa were found to have increased deviation (Holton *et al*., 2012). The notion of increased septal growth is further supported by the finding that the nasal septum continues to grow into adulthood following the cessation of skeletal growth (Vetter *et al*., 1984; Van Loosen *et al*., 1996).

Accurately determining the prevalence of nasal septal deviation is complicated by differences regarding the definition of nasal septal deviation and measuring techniques used (Vig, 1998). This leads to a significant variation of the reported range of nasal septal deviation in newborns across studies. For instance, Gray (1978) found that 42% of septa of Caucasian infants were straight, 27% deviated, and 31% kinked, whereas Kent *et al*. (1988) reported an incidence of nasal septum deformity in only 2.9% of 1000 consecutive neonates. Similarly, Podoshin *et al.* (1991) found an incidence of 0.93% of anterior nasal septal cartilaginous dislocation in newborns investigated for nasal septal deviations while Šubarić and Mladina (2002) reported a prevalence of 28% children aged 2-6 to 41.8% in young adults aged 19-22. It appears that there is a gradually increasing prevalence of deformities involving the posterior (bony) parts of the septum with age. This age-related increase in septal deformity is consistent with studies on the prevalence of septal deformity worldwide (Šubarić and Mladina, 2002).

More recently and using newer technology, such as computed tomography (CT) and magnetic resonance imaging (MRI), Reitzen *et al.* (2011) measured the tortuosity of the septum at four points along the septum in order to overcome the shortcomings of previous studies in which deviation was evaluated only at one specific point along the septum. Tortuosity was measured in 81 patients from age 2 months to 80 years by dividing “actual” length of the septum by the “ideal” length that was represented by a straight line from the superior to the inferior aspect of the septum. The results show that nasal septum deviation is more common in older children and adults when using tortuosity as a measure of deviation (Reitzen *et al.*, 2011). Similarly, Mladina *et al.* (2008) found the incidence of septal deviation to be as high as 89.2% using anterior rhinoscopy in adult patients seeking medical care for nasal complaints.

Clinical Significance of Nasal Septal Deviation

There are several clinical implications to nasal septal deviation. The space between the septum and lateral walls of the nasal cavity regulates nasal airflow and respiration. In infants, open nasal passages are required to feed properly. Severe and bilateral deviation in infants can result in poor feeding and/or choking from food in the respiratory tract and sudden infant death syndrome (Kawalski and Spiewak, 1998). In adults, deviation can lead to mouth breathing, nasal crusting, epistaxis, and sinusitis depending on the severity and location of the deviation (Aziz *et al*., 2014). Dental findings in patients with nasal obstruction as a consequence of septal deviation have been reported as Class II malocclusion with increased anterior facial height, retrognathic mandible with increased overjet and constricted maxilla (D’Ascanio *et al*., 2010).

Aims and Hypotheses

The present work aimed at examining the magnitude of nasal septal deviation and patterns of covariation between the nasal septum and nasofacial skeleton during ontogeny in a cross-sectional human sample using data derived from CBCT scans. First, the magnitude of ontogenetic variation in nasal septal deviation was assessed using a measured midsagittal nasal septum volume and a model for a non-deviated septum in each subject. The modeled non-deviated volume served as a measure of the minimum amount of space available in the midline nasal. It was hypothesized that, if the magnitude of nasal septal deviation increases with age, the discrepancy between measured septal volume and modeled non-deviated volume will increase with age. Next, the allometric relationship between measured nasal septal volume and modeled non-deviated volume was examined. "Allometry" refers to changes in shape with development. If the magnitude of nasal septal deviation increases during growth and development, then measured nasal septal volume should scale with greater positive allometry compared to modeled non-deviated septal volume. Finally, the interaction between the septum and surrounding nasofacial skeleton during ontogeny was assessed. If the pattern of covariation between nasal septal deviation and the shape of the nasofacial skeleton corresponds to changes reflective of normal growth and development in the nasofacial region, this would indicate that the magnitude of septal deviation is associated with ontogenetic changes in the shape of the nasofacial skeleton. Alternatively, if septal deviation is not associated with shape changes in nasofacial region that occur during normal growth and development, this would suggest that the magnitude of septal deviation varies independent of ontogeny.

Subjects and Methods

Subject selection

The research protocol including the use of existing CBCT scans was approved by the Institutional Review Board at University of Minnesota (Study Number 1410M54305). A total of 66 patients (34 male, 32 female) who presented for orthodontic treatment at the University of Minnesota were included in this retrospective cohort study. The patients ranged from 7-18 years in age and were selected using the following inclusion criteria: 1) CBCT scan prior to the start of orthodontic treatment, and 2) being seen only for the treatment of skeletal or dental malocclusion. Patients were excluded if they had craniofacial anomalies (e.g., cleft lip/palate), syndromes, or were undergoing surgical or simultaneous craniofacial treatments. All patients were grouped by age in two-year intervals (e.g., 7-8, 9-10, etc.) to achieve a minimum of n=10 individuals within each age group, while maintaining approximately equal numbers of males and females. Study sample demographics are shown in Table 1.

All CBCT scans were full field-of-view (17x23 cm) and were taken using an iCAT Next Generation (Imaging Sciences International, Hatfield, PA, USA) at 120 kV and 18.54 mAs with a pulsed scan time of 8.9 s. The scan data were reconstructed with a voxel size of 0.3 mm^3.

Table 1. Study sample demographics.

Age Group	Age Range (years)	Males (n)	Females (n)	**Total**
7	7-8	5	6	**11**
9	9-10	6	5	**11**
11	11-12	6	6	**12**
13	13-14	6	6	**12**
15	15-16	6	4	**10**
17	17-18	5	5	**10**
Total		**34**	**32**	**66**

Quantification of Nasal Septal Deviation

Data collection was performed using digital imaging and communications in medicine (DICOM) volumes. DICOM imaging software (OsiriX Version 5.6, Pixmeo, Geneva, Switzerland) was used for all segmentations. The magnitude of nasal septal deviation was calculated by first manually segmenting the nasal septum from the anterior-most extent of the nasal septal cartilage to the posterior aspect of the vomer using coronal CBCT images (Fig. 1). Next, a non-deviated midline volume (mm^3) following the space directly between the superior and inferior attachment sites of the nasal septum was segmented. Both the measured nasal septum volume and the modeled non-deviated volume were segmented using a constant thickness of 1.0 mm in order to account for potential within- and between-individual variation in the thickness of the cartilaginous and osseous elements of the septum and the overlying mucosa. Examples of *in situ* reconstructed volumes are shown in Fig. 2. Nasal septal deviation was then calculated for each individual as a percentage of the measured nasal septal volume relative to the modeled non-deviated septal volume. This way, a non-deviated septum is indicated by a value of 100% (i.e., measured septal volume and modeled non-deviated volume are equal), while values greater than 100% indicate septal deviation. An example of the discrepancy between a deviated nasal septum and corresponding non-deviated model is illustrated in Fig. 2.

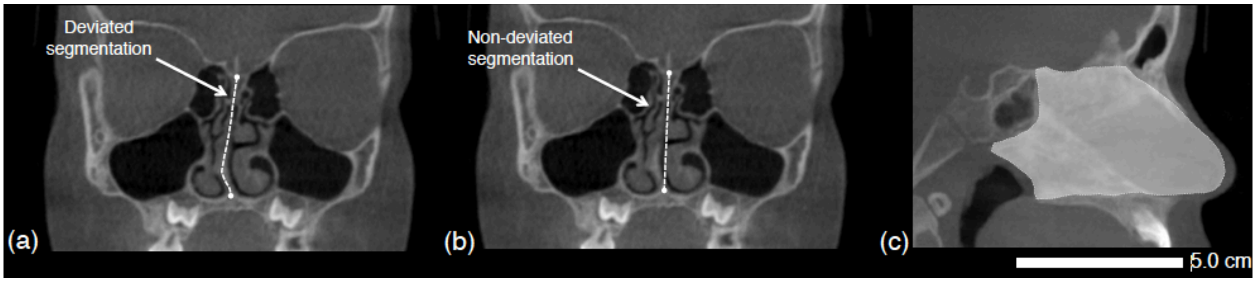

Fig. 1. Nasal septum image segmentation. Segmentation of the nasal septum (a) along the length of the entire nasal septum and (b) following the borders of the nasal septum outlined in (c).

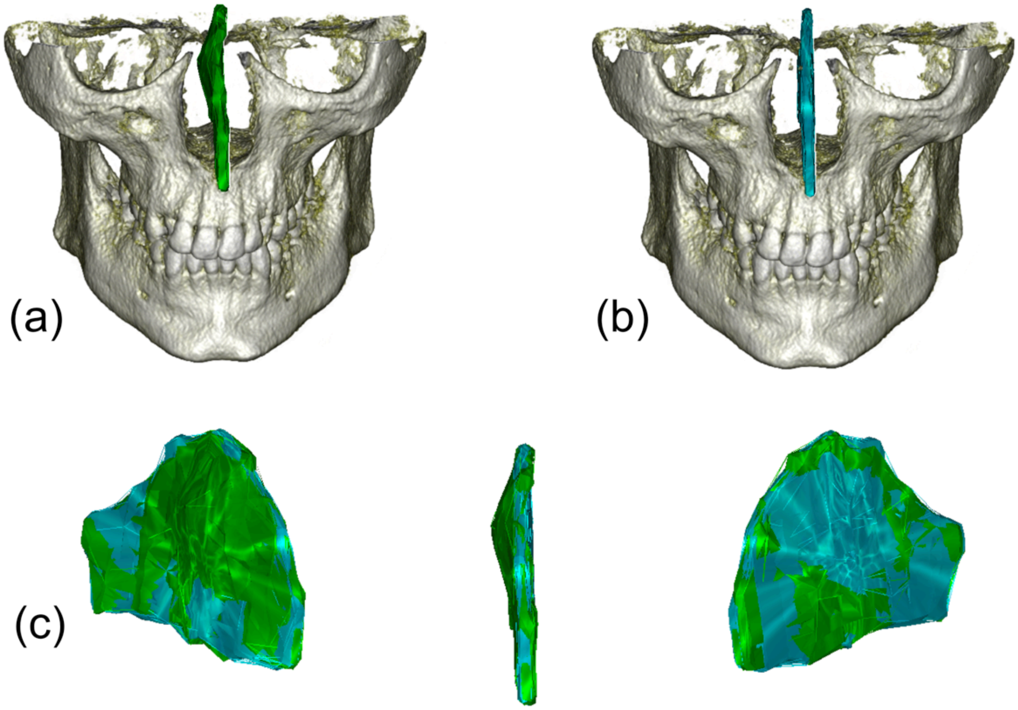

Fig. 2. Examples of 3-D reconstructions of a nasal septum (green) and a non-deviated septal model (blue) *in situ*. The top one-third of the skull has been cropped to aid in the visualization of the septal reconstructions. Deviation is visible in the reconstructed nasal septum (a), while the reconstruction in (b) follows the borders of the nasal septum but is non-deviated. The difference between the deviated and non-deviated models is illustrated in (c). Note that for illustrative purposes reconstructions are thicker than 1.0 mm.

Coordinate Landmark Data Collection

A series of midsagittal coordinate landmarks was collected using Dolphin Imaging software (Version 11.8, Patterson Dental, St. Paul, MN, USA) to represent the external nose and nasal cavity. The external nose was represented by: nasion (the articulation between the frontal and nasal bones in the midsagittal plane); rhinion (the anterior tip of the nasal bones); pronasale (a soft-tissue landmark located on the anterior-most point on the external nose); and ANS (the tip of the anterior nasal spine). The nasal cavity was represented by: PNS (posterior-most landmark on the hard palate/nasal floor); hormion (posterior-most aspect of the vomer in the midline); the anterior-inferior articulation between the sphenoid body and the nasal septum (i.e., inferior aspect of the sphenoethmoidal synchondrosis); the anterior-superior articulation between the sphenoid body and the nasal septum (i.e., the superior aspect of the sphenoethmoidal synchondrosis); and the anterior-most aspect of the anterior cranial base. The landmarks are shown in Fig. 3.

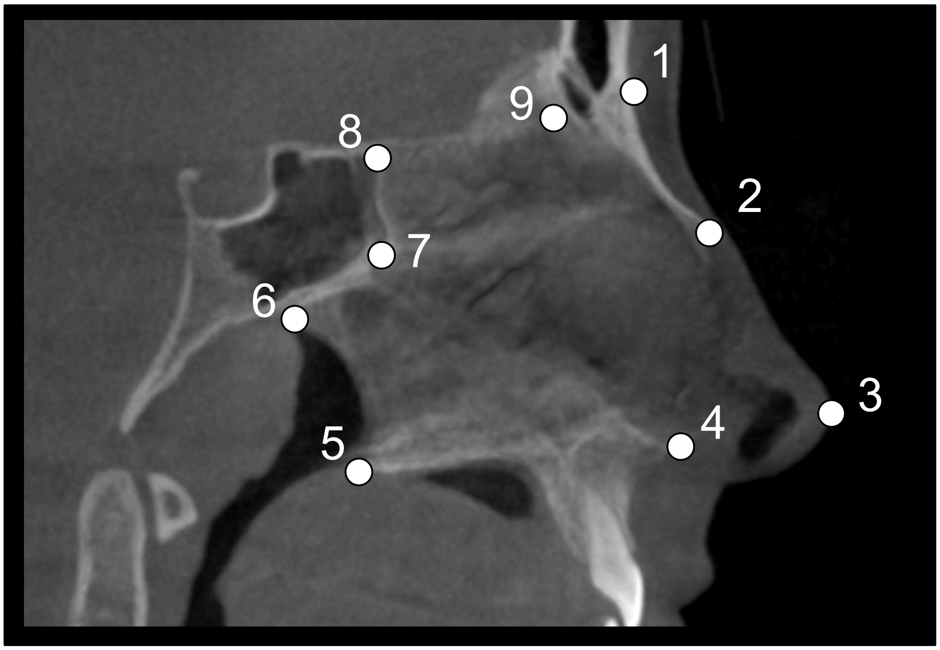

Fig. 3. Landmarks used to quantify the size and shape of the nasofacial region in a midsagittal section of a cone beam computed tomography image. 1=nasion; 2=rhinion; 3=pronasale; 4=anterior nasal spine; 5=posterior nasal spine; 6=hormion; 7=anterior-inferior sphenoid body; 8=anterior-superior sphenoid body; 9=anterior cranial base.

Quantitative Methods

The magnitude of septal deviation was assessed across all age groups to examine ontogenetic variation in nasal septal deviation. This included examining within-age group distributions to determine whether there was an ontogenetic trend for the magnitude of septal deviation (e.g., increase in magnitude with age). Next, the ontogenetic relationship between measured nasal septal volume and modeled non-deviated volume used to calculate the magnitude of deviation was assessed to determine whether measured nasal septal volume was consistently larger than modeled non-deviated volume across age groups.

Given that chronological age is only a general proxy measure for growth and development, it was also examined whether there was a correlation between septal deviation and nasofacial size. To test this, the nasofacial size was measured as the centroid size of the coordinate landmarks used to represent the nasal region as detailed above (Fig. 3). Centroid size is a composite size measure that is calculated as the sum of the squared distances between each landmark in a configuration and a centroid landmark (i.e., the mean x and y coordinates for all landmarks in the configuration). For this comparison, pronasale, an external landmark located at the anterior aspect of the nasal septal cartilage, was excluded from the nasal cavity centroid size measure.

All measurements were made by a single operator and repeated after a washout period of 5 weeks for 13 randomly chosen subjects to assess intra-examiner reliability.

Statistical Analyses

Intra-examiner reliability was tested by calculating the percentage difference between the two observations and intra-class correlations coefficients. With regard to coordinate landmark data, the Euclidean distance between homologous landmarks (i.e., the milimetric distance between a landmark in the first observation and second observations) was calculated to assess the absolute landmark distance between the two observations.

Differences between measured septal volume and modeled non-deviated volume were tested for statistical significance using Wilcoxon signed-rank tests. The relationship between septal deviation and nasofacial size was examined using reduced major axis (RMA) regression. The cube root of measured nasal septal and modeled non-deviated values were log-transformed and regressed against log-transformed nasofacial centroid size. The variation in the regression slopes was determined to assess whether measured septal volume and the modeled non-deviated volume exhibited differences in slope values relative to nasofacial centroid size. Analysis of covariance (ANCOVA) was used to compare least-squares (LS) regression slopes. Additionally, the allometric relationship between measured nasal septal volume and modeled non-deviated volume was assessed using RMA regression of log-transformed variables. Specifically, it was tested whether measured septal volume scaled with positive allometry relative to modeled non-deviated volume (indicating an ontogenetic increase in septal deviation), or whether the two variables scaled isometrically (indicating that the magnitude of septal deviation is maintained through ontogeny).

Finally, an assessment was made whether there was a morphological relationship between nasal septal deviation and the shape of the nasofacial region (i.e., external nose and internal nasal cavity) during growth and development. For this, the individual nasofacial region landmark configurations were superimposed using Procrustes analysis. This superimposition method rotates, translates, and scales all landmark configurations, leaving only residual shape information. Shape variation was visualized using wireframe models and thin plate splines. All geometric morphometric analyses were conducted using MorphoJ (Klingenberg, The University of Manchester, Manchester, UK). Multivariate regression was used to examine the correlation between the Procrustes scaled landmark configurations (dependent variables) and nasofacial centroid size calculated for all landmarks (independent variable) in order to examine the allometric component of shape variation in the sample (i.e., the component of shape that varies with ontogeny). Thereafter, a multivariate regression analysis was performed to assess the relationship between the Procrustes scaled landmark configurations (dependent variables) and the magnitude of nasal septal deviation (independent variable) to determine whether there was a significant correlation between septal deviation and the shape of the nasofacial region, and if the pattern of correlated shape variation mirrored ontogenetic changes in the nasal region. All statistical analyses were performed using SPSS (IBM Corporation, Armonk, NY, USA) with P-values of less than 0.05 considered statistically significant.

Results

Intra-examiner Reliability

With regard to measured septal volume and modeled non-deviated volume values, there was, on average, a 2.2% and 3.1% difference between the first and second observation, with intra-class correlation coefficients of r=0.99 ($P<0.001$) indicating a high degree of intra-examiner reliability. With regard to coordinate landmark acquisition, the Euclidean distance values between landmarks at the two observations ranged from 0.91 mm to 1.96 mm, indicating a similarly high degree of intra-examiner reliability.

Ontogenetic Variation in Nasal Septal Deviation

Septal deviation values are shown in Fig. 4. There was no discernable pattern with regard to nasal septal deviation across age groups. Examples of deviation across the different age groups are depicted in Fig. 5.

Both measured septal volume and modeled non-deviated volume increase in size from the 7 to 17 year age groups (Fig. 6). In all age groups, measured septal volume was significantly larger than the corresponding modeled non-deviated volume ($P<0.01$).

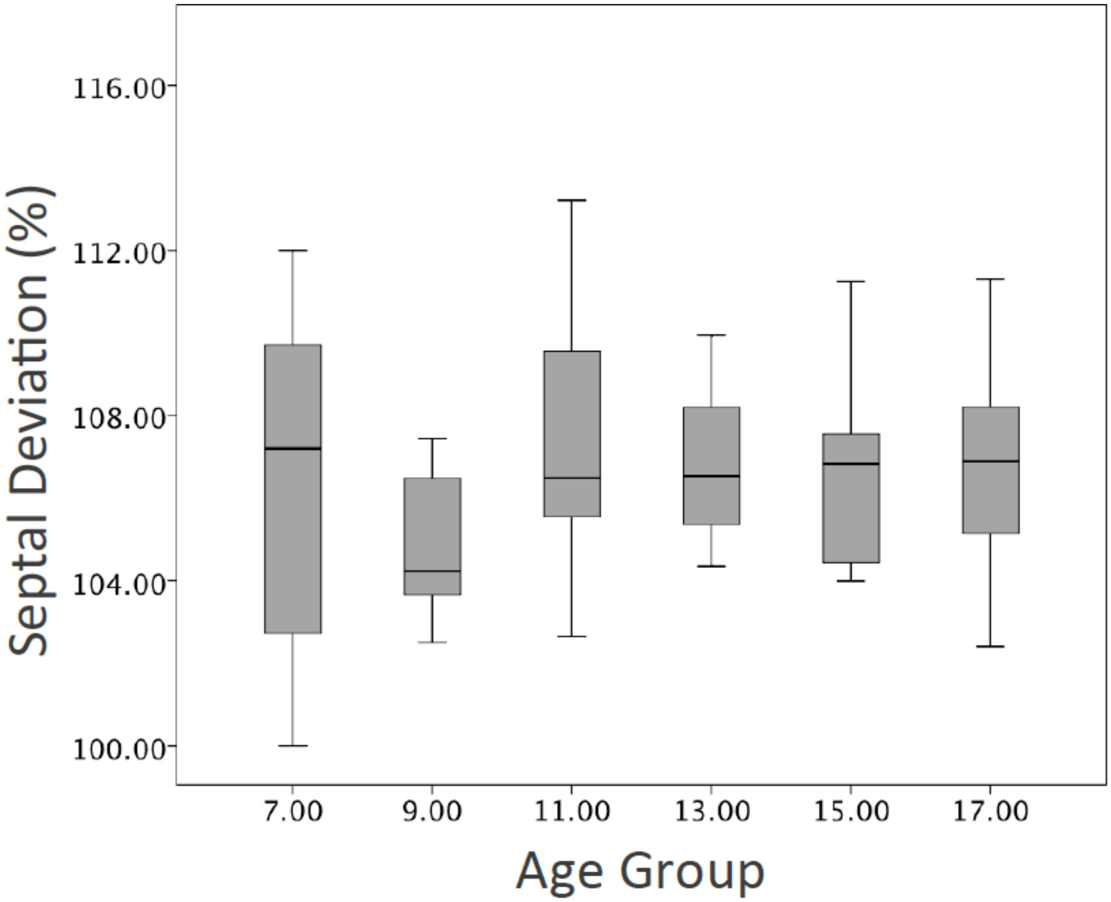

Fig. 4. Box plot of septal deviation values for each age group.

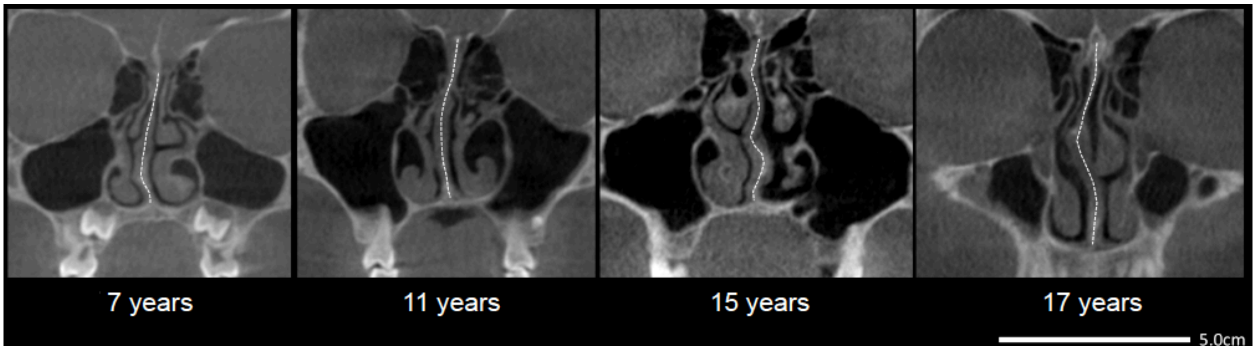

Fig. 5. Examples of coronal cone beam computed tomography images of subjects with nasal septal deviation. Nasal septal deviation (white dashed line) is present throughout all ages in the sample.

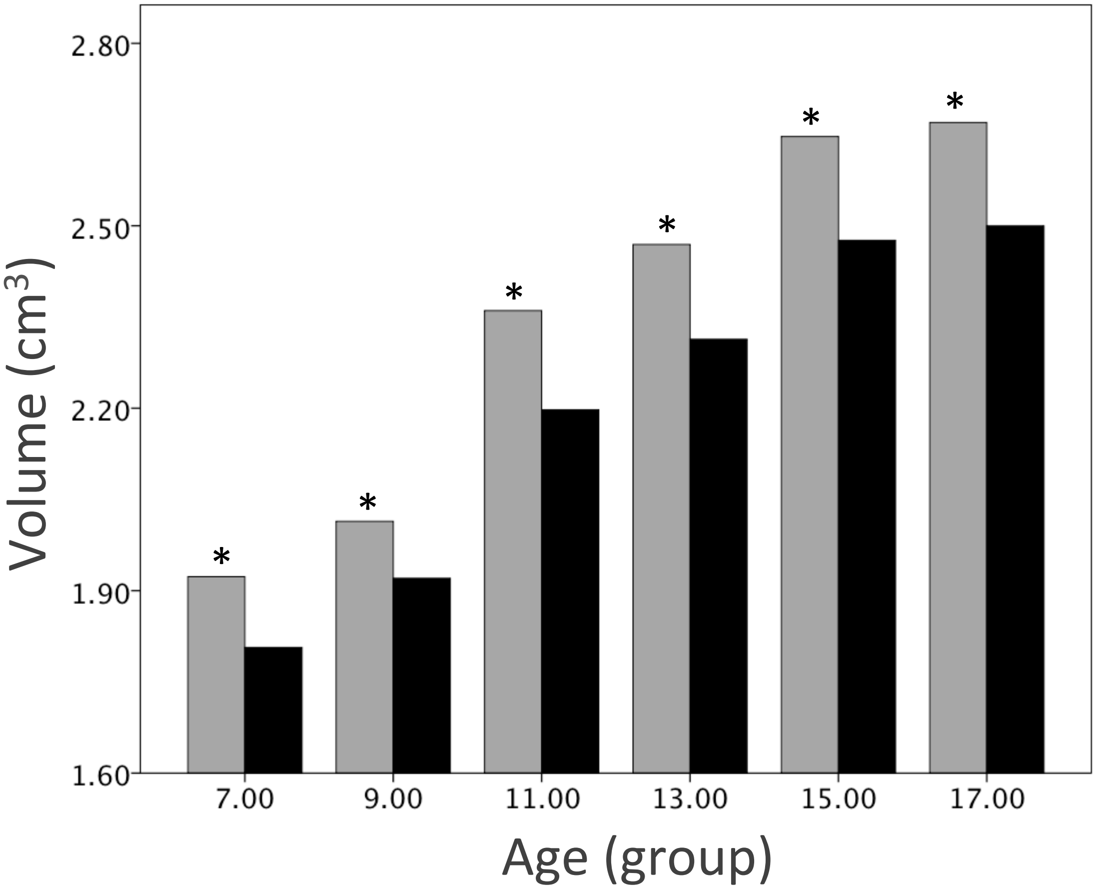

Fig. 6. Mean values for measured nasal septal volume (gray bars) and modeled non-deviated volume (black bars). Measured nasal septal volume was significantly larger than modeled non-deviated volume in all age groups* (*P*<0.01).

While nasofacial centroid size increased during ontogeny, there was no significant correlation between the size of the nasofacial region and nasal septal deviation (r=0.06; P=0.627; Fig. 7). Measured nasal septal volume was consistently larger than modeled non-deviated volume across the entire range of nasofacial centroid size values.

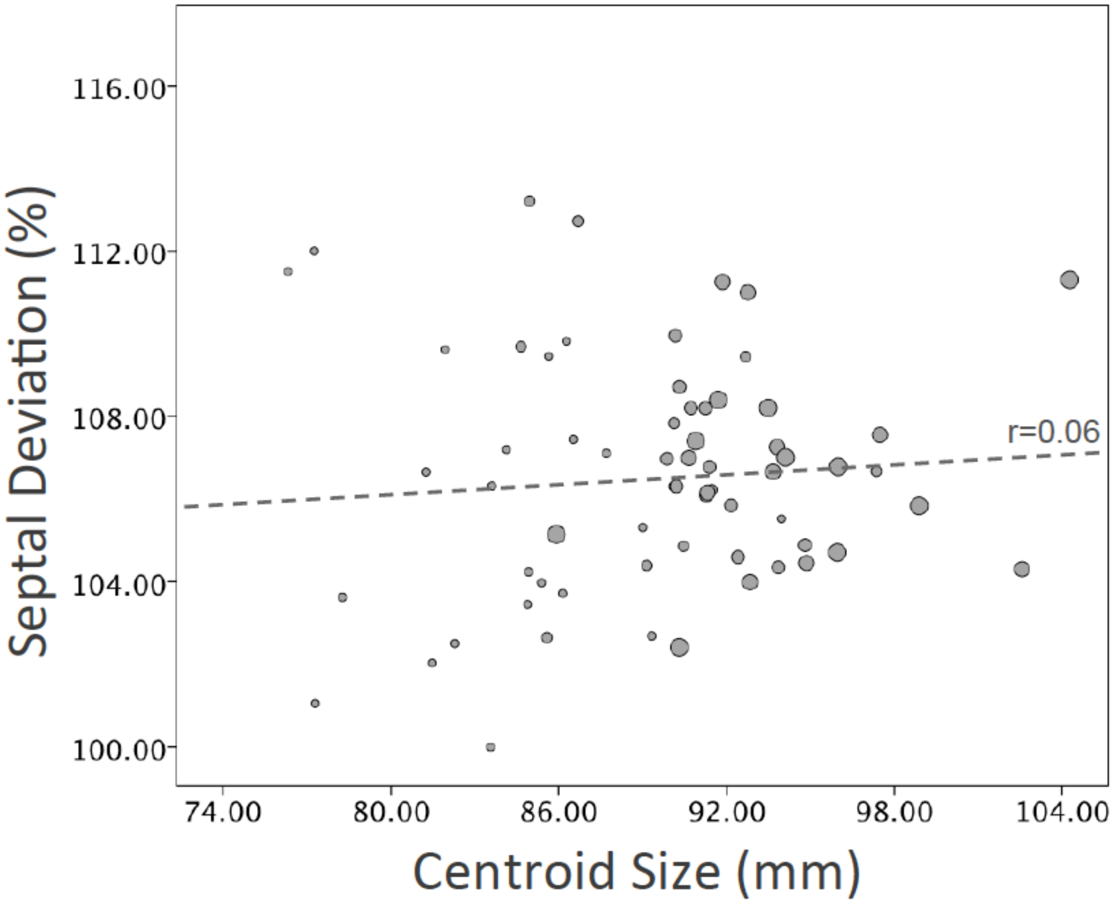

Fig. 7. Scatter plot of septal deviation on centroid size. Variation in symbol size represents age group (smaller symbols=younger age groups; larger symbols=older age groups).

Measured nasal septal volume and modeled non-deviated volume exhibited the same allometric relationship with regard to nasofacial size. RMA regression analysis indicates that the slopes for both variables were nearly identical (slope=0.89 and 0.87 respectively; Table 2). Moreover, there was no significant difference in LS regression slopes for measured nasal septal volume and modeled non-deviated volume relative to nasofacial size (P=0.892). The RMA regression line for measured nasal septal volume was transposed above the modeled non-deviated volume regression line (Fig. 8), and the ANCOVA results revealed a significant difference in Y-intercept values for the LS regression lines (P<0.001). For a given nasofacial size, measured nasal septal volume was consistently larger than modeled non-deviated volume.

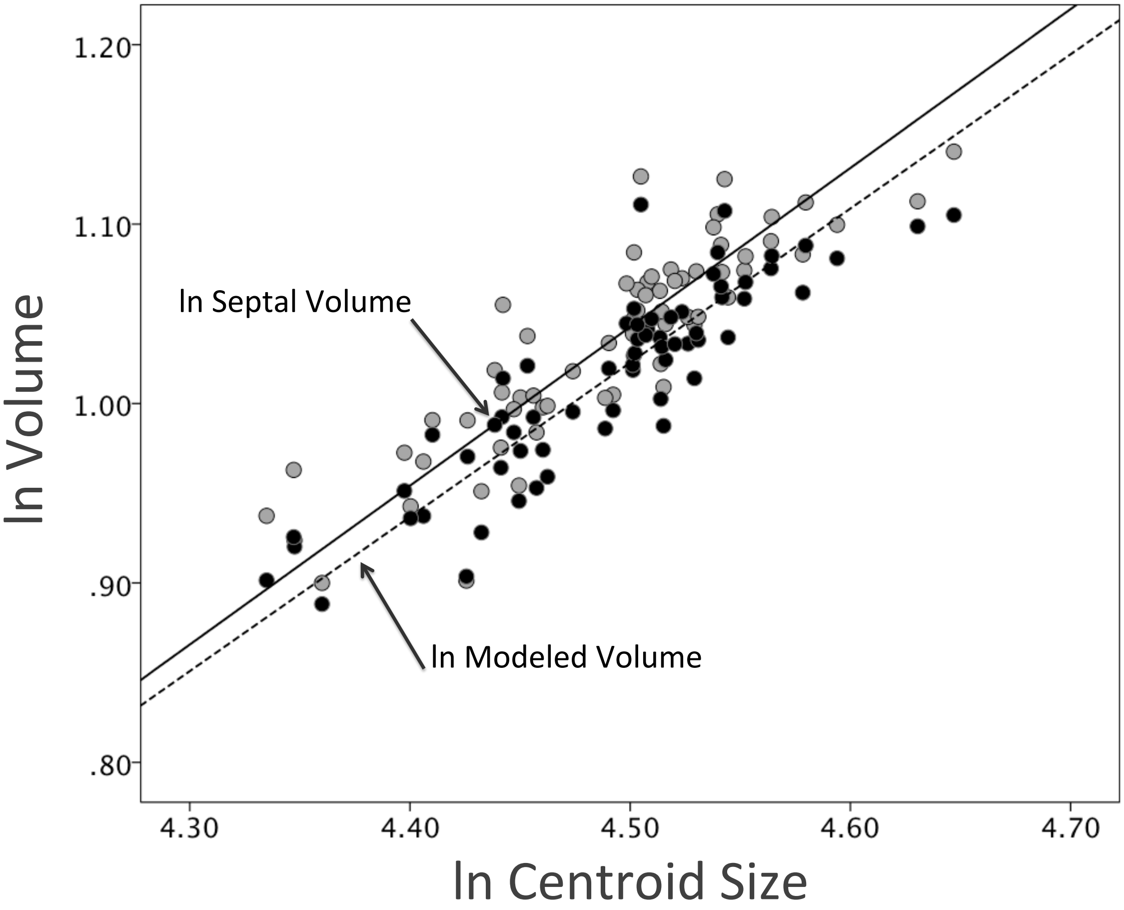

Fig. 8. Scatter plot of log transformed measured nasal septal and modeled non-deviated volumes on log transformed centroid size (excluding pronasale). Parallel RMA regression lines are shown.

Table 2. Reduced major axis (RMA) regression parameters.

	ln Measured Volume	ln Modeled Volume
RMA Slope	0.89	0.87
RMS 95% CI	0.77-1.00	0.77-0.97
RMA *Y*-intercept	-2.96	-2.84
RMA R^2	0.75	0.79

Septal Deviation and Nasal Shape

There was a significant correlation between nasofacial centroid size values and Procrustes scaled landmarks (*P*=0.004), and as illustrated in Fig. 9, shape changes were largely confined to the external nasal region. In particular, an ontogenetic increase in size was associated with an increase in nasal projection as evidenced by an anterior displacement in pronasale, and increased nasal bridge elevation evidenced by an anterior displacement of rhinion and slight posterior displacement of nasion. Allometric changes in the nasofacial region were also evident in the anterior cranial base, which exhibited a relative reduction in anterior-posterior dimensions due to a posterior displacement of the anterior cranial base landmark.

There was a significant correlation between the magnitude of deviation and the shape of the nasofacial region (*P*=0.037). The correlated pattern of shape variation differed from the allometric pattern of shape variation. As illustrated in Fig. 10, nasal septal deviation was correlated with variation restricted to the anterior sphenoid body.

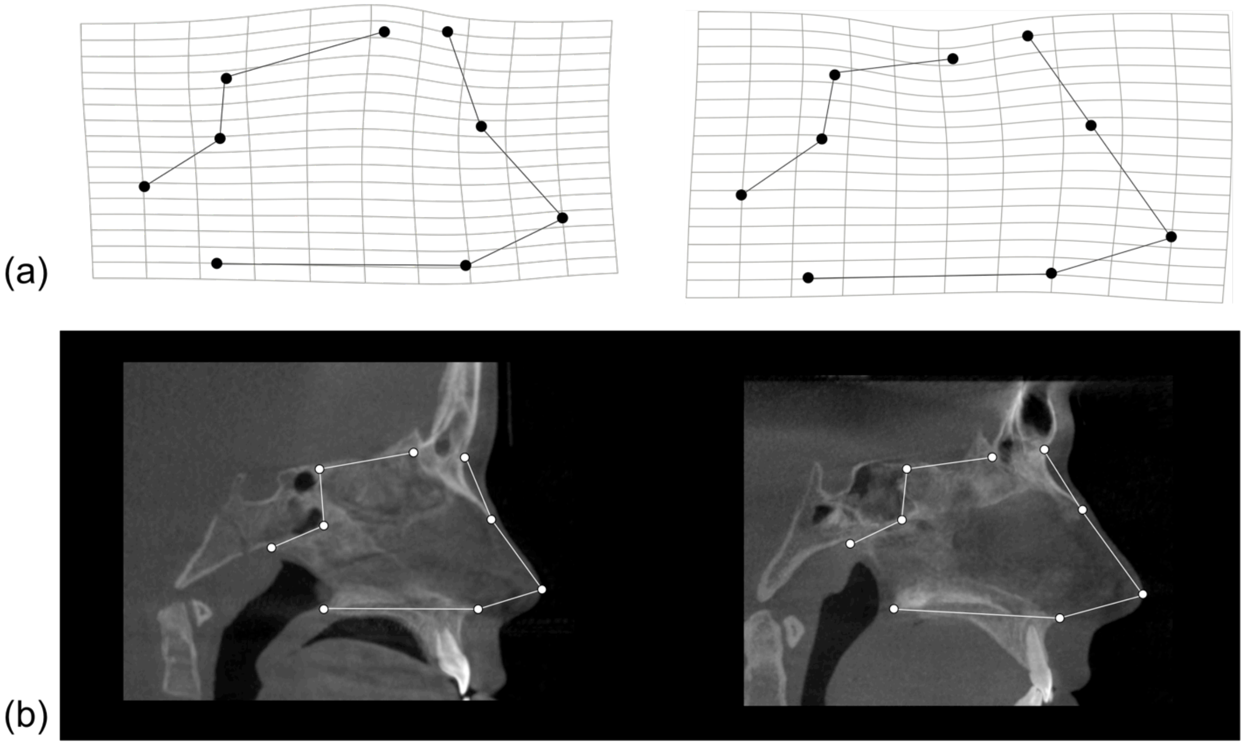

Fig. 9. Allometric shape variation. (a) Thin plate spines and wireframe models representing the range of shape variation correlated with centroid size. The spline and wireframe model on the left represents shape associated with smaller centroid values (i.e., younger individuals), while the spline and wireframe model on the right represents shape associated with larger centroid values (i.e., older individuals). (b) Midsagittal cone beam computed tomography images of individuals spanning the range of centroid size values from small (left) to larger (right).

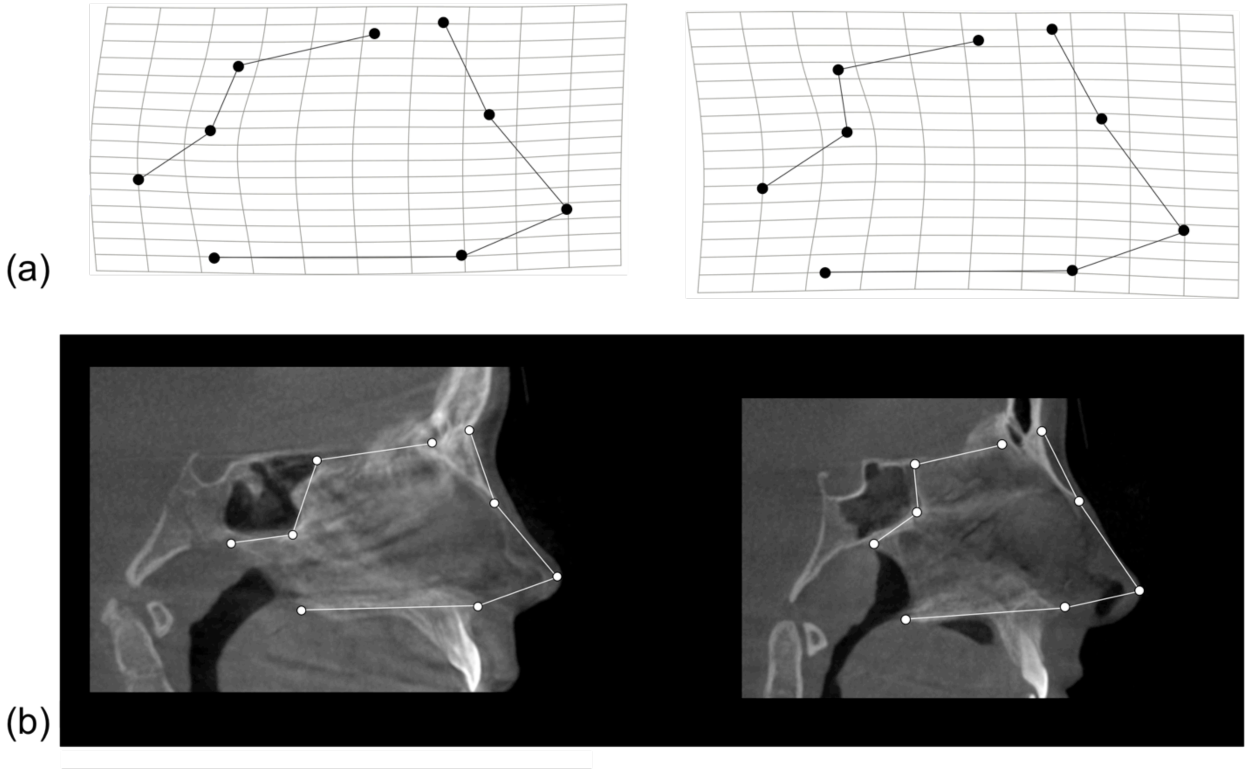

Fig. 10. Shape variation correlated with nasal septal deviation. (a) Thin plate spines and wireframe models representing the range of shape variation correlated with nasal septal deviation. The spline and wireframe on the left represents shape variation associated with no septal deviation, while the spine and wireframe on the right represents variation associated with greater levels of septal deviation. (b) Midsagittal cone beam computed tomography images of individuals spanning the range of septal deviation values from small (left) to larger (right).

Discussion

The nasal septum has been described as a key growth center in the facial skeleton and discordance in growth between the septum and the surrounding facial skeleton is thought to result in septal deviation (e.g., Scott, 1953; Gray, 1978; Takahashi, 1987). Currently, we lack a good understanding about the ontogeny of septal deviation, both with regard to changes in deviation and developmental interaction between the septum and surrounding nasofacial region. In an attempt to add to the current body of knowledge on the ontogeny of septal deviation, we used CBCT data of individuals ranging from 7 to 18 years to study ontogenetic variation in the magnitude of nasal septal deviation, and its correlation to nasofacial size and shape during development. In the sample studied, there was no evidence of an ontogenetic increase in nasal septal deviation with regard to age (as an approximation of growth) or nasofacial centroid size (as a more direct measure of growth). As the nasofacial region increased in size, the magnitude of nasal septal deviation was maintained across the entire size range, indicating a relatively isometric relationship during ontogeny.

In addition, the findings suggest that the magnitude of nasal septal deviation is established early in ontogeny by 7-8 years, and is maintained through 17-18 years of age. This resembles the findings of Yildirim and Okur (2003), who found that 16.5% of subjects aged 4-6 years presented with septal deviation. This frequency increased to 38.7% in their 7-12 year age group and was maintained through later ages. In contrast, other studies report ontogenetic increases in deviation later in development. For instance, Šubarić and Mladina (2002) found an increase in deviation from their 7-14 to their 15-18 year age groups. These findings suggest that there is variation in the frequency of septal deviation across studies. The most likely explanation for this observed variation is variation in the study population. For instance, most study samples consist of patients who were receiving medical intervention for nasal obstruction problems or other head and neck conditions (e.g., Mladina *et al.,* 2008; Reitzen *et al*., 2011). In contrast, the present study sample consisted of orthodontic patients without obvious airway restrictions. Patients with nasal obstruction may have greater magnitudes of deviation than the orthodontic patients who were not undergoing surgical or simultaneous craniofacial treatments and were being seen only for the treatment of skeletal or dental malocclusion. Therefore, the present sample is potentially more representative of the population as a whole rather than a pathological subset.

Another possible explanation for the variation in septal deviation reported across studies is the lack of consistency in how deviation is measured. Nasal septal deviation has been measured in several different ways in previous studies, such as acoustic rhinometry, rhinomanometry, and nasal spectral sound analysis (Aziz *et al.*, 2014). Moreover, deviation has often been measured at only one specific point along the septum or qualitatively using a yes/no categorical scale from photographs or two-dimensional (2-D) radiographs (e.g., Gray, 1978; Hafezi *et al*., 2010; Kim *et al*., 2011; Akbay *et al.*, 2013). This inconsistency in measurement methods across studies likely contributes to the variation in results.

The present study utilized a quantitative 3-D approach that characterized the morphology of the entire nasal septum. Using this approach, rather than relying on qualitative or 2-D approaches to measuring septal deviation as in previous studies, allowed us to more accurately characterize the magnitude of deviation and gave us finer resolution for assessing morphological variation in the nasal septum, and the relationship between the nasal septum and the surrounding skeletal anatomy. The method has been shown to be accurate at measuring septal deviation in previous studies that have assessed the relationships between septal deviation, facial skeletal form, and facial asymmetries (Holton *et al*., 2012; Hartman *et al*., 2016).

The use of CBCT data allowed quantification of the magnitude of deviation along the entire septum rather than evaluation of the frequency of nasal septal deviation using a yes/no scale. Thus, deviation was measured as a continuous rather than a categorical variable. If the septum exhibited deviation in one region, that individual would be considered deviated when using a categorical scale, as done in previous studies. However, quantifying deviation across the entire septum may help explain why we do not see ontogenetic changes in septal deviation in this study. As a result, we cannot assess ontogenetic changes in the frequency of deviation, but we can conclude that the magnitude of deviation is maintained in our sample.

The developmental interaction between the nasal septum and the surrounding nasofacial skeleton was studied using multivariate regression analyses. These analyses were performed to examine correlations between nasofacial region shape variation and normal growth and development, and correlations between nasofacial region shape variation and nasal septal deviation. The results indicate that nasofacial region shape changes correlated with septal deviation are different than shape changes correlated with normal growth. As the magnitude of nasal septal deviation increased, the inferior aspect of the sphenoid body tended to be positioned more anteriorly. A relatively more anterior position of the sphenoid body may restrict space in the nasal cavity leading to septal deviation. This assumption is corroborated by a number of studies that have shown that reduced midfacial dimensions are associated with deviation (Gray, 1978; Takahashi, 1987; Freng *et al*., 1988; Rönning and Kantomaa, 1985; Holton *et al.,* 2011). Given the developmental relationship between the nasal septum and sphenoid that begins during early chondrocranial development through fusion of the spheno-ethmoid synchondrosis around age 6 (Scott, 1958), these results suggest that the differences in the position of the sphenoid body are established early in development. Thus, while patterns of covariation between nasal septal deviation and nasofacial form are non-allometric and are established by at least 7 years of age, they are potentially established much earlier in ontogeny.

The finding that the magnitude of nasal septal deviation is established by at least 7 years of age and maintained throughout ontogeny contradicts the findings of previous studies in which deviation was found to increase during ontogeny (e.g., Šubarić and Mladina, 2002). Moreover, nasal septal deviation was not associated with normal shape changes in the nasofacial region during growth and development, suggesting that normal developmental changes in nasal cavity and cranial base form are not related to an increase in nasal septum deviation. Finally, this study supports previous research that has found septal deviation to be the result of an undersized facial skeletal frame (e.g., Freng *et al*., 1988). Specifically, a nasofacial skeletal configuration with a relatively anterior position of the sphenoid may place spatial constraints on the growth of the septum, resulting in deviation. While these findings cannot establish a causal relationship between nasal septal deviation and nasofacial size and shape, they do support the nasal traction model of midfacial growth, which emphasizes the morphogenetic influence of the nasal septum on growth of the facial skeleton (Scott, 1953; Latham, 1970; Copray, 1986; Siegel *et al*., 1990; Wealthall and Herring, 2006; Al Dayeh and Herring, 2014). These findings are in contrast to the functional matrix theory, which suggests that the nasal cartilage plays a minimal role in facial growth (Moss *et al.*, 1968; Moss and Saletijn, 1969, Stenström and Thilander, 1970). Future works should assess the longitudinal interaction between nasal septal deviation and other components of the facial skeleton to help gain a better understanding of the role of the nasal septum on facial growth.

Conclusions

1. The magnitude of nasal septal deviation and the position of the sphenoid are established by approximately 7 years of age and then maintained throughout ontogeny.
2. Normal developmental changes in nasal cavity and cranial base form do not result in an increase in nasal septum deviation.
3. A facial skeletal configuration with an anteriorly positioned sphenoid may place spatial constraints on the growth of the septum, resulting in deviation.

References

1. Akbay E, Cokkeser Y, Yilmaz O, Cevik C (2013). The relationship between posterior septum deviation and depth of maxillopalatal arch. *Auris Nasus Larynx* 40:286–290.

2. Al Dayeh AA, Herring SW (2014). Compressive and tensile mechanical properties of the porcine nasal septum. *J Biomech* 47:154–161.

3. Aziz T, Biron VL, Ansari K, Flores-Mir C (2014). Measurement tools for the diagnosis of nasal septal deviation: a systematic review. *J Otolaryngol Head Neck Surg* 43:11.

4. Copray JC (1986). Growth of the nasal septal cartilage of the rat in vitro. *J Anat* 144:99–111.

5. Cupero TM, Middleton CE, Silva AB (2001). Effects of functional septoplasty on the facial growth of ferrets. *Arch Otolaryngol Head Neck Surg* 127:1367–1369.

6. D'Ascanio L, Lancione C, Pompa G, Rebuffini E, Mansi N, Manzini M (2010). Craniofacial growth in children with nasal septum deviation: a cephalometric comparative study. *Int J Pediatr Otorhinolaryngol* 74: 1180–1183.

7. Delaire J, Precious, D (1986). Influence of the nasal septum on maxillonasal growth in patients with congenital labiomaxillary cleft. *Cleft Palate J* 23:270–277.

8. Freng A (1981). Mid-facial sagittal growth following resection of the nasal septum-vomer: a roentgencephalometric study in the domestic cat. *Acta Otolaryngol* 92:363–370.

9. Freng A, Kvam E, Kramer J (1988). Facial skeletal dimensions in patients with nasal septal deviation. *Scand J Plast Reconstr Surg Hand Surg* 22:77–81.

10. Gray LP (1978). Deviated nasal septum. Incidence and etiology. *Ann Otol Rhinol Laryngol Suppl* 87:3–20.

11. Hafezi F, Naghibzadeh B, Nouhi A, Yavari P (2010). Asymmetric facial growth and deviated nose: a new concept. *Ann Plast Surg* 64:47–51.

12. Hall BK, Precious DS (2013). Cleft lip, nose, and palate: the nasal septum as the pacemaker for midfacial growth. *Oral Surg Oral Med Oral Pathol Oral Radiol* 115:442–447.

13. Hartman C, Holton N, Miller S, Yokley T, Marshall S, Srinivasan S, Southard T (2016). Nasal septal deviation and facial skeletal asymmetries. *Anat Rec (Hoboken)* 299:295–306.

14. Holton NE, Franciscus RG, Marshall SD, Southard TE, Nieves MA (2011). Nasal septal and premaxillary developmental integration: implications for facial reduction in *Homo*. *Anat Rec (Hoboken)* 294:68–78.

15. Holton NE, Yokley TR, Figueroa A (2012). Nasal septal and craniofacial form in European- and African-derived populations. *J Anat* 221:263–274.

16. Kawalski H, Spiewak P (1998). How septum deformations in newborns occur. *Int J Pediatr Otorhinolaryngol* 44:23–30.

17. Kent SE, Reid AP, Nairn ER, Brain DJ (1988). Neonatal septal deviations. *J R Soc Med* 81:132–135.

18. Kim J, Cho JH, Kim SW, Kim BV, Lee DC, Kim SW (2010). Anatomical variation of the nasal septum: Correlation among septal components. *Clin Anat* 23:945–949.

19. Kim J, Kim SW, Kim SW, Cho JH, Park YL (2012). Role of the sphenoidal process of the septal cartilage in the development of septal deviation. *Otolaryngol Head Neck Surg* 146:151–155.

20. Kim YM, Rha KS, Weissman JD, Hwang PH, Most SP (2011). Correlation of asymmetric facial growth with deviated nasal septum. *Laryngoscope* 121:1144–1148.

21. Latham, RA (1970). Maxillary development and growth: the septo-premaxillary ligament *J Anat* 107 (Pt 3):471–478

22. Mladina R, Čujić E, Šubarić M, Vuković K. Nasal septal deformities in ear, nose and throat patients: an international study. *Am J Otolaryngol* 29:75–82.

23. Mooney MP, Siegel MI, Kimes KR, Todhunter J (1989). A test of two midfacial growth models using path analysis of normal human fetal material. *Cleft Palate J* 26:93–99.

24. Moss ML, Bromberg BE, Song IC, Eisenman G (1968). The passive role of nasal septal cartilage in mid-facial growth. *Plast Reconstr Surg* 41:536–542.

25. Moss ML, Salentijn L (1969). The primary role of functional matrices in facial growth. *Am J Orthod* 55:566–577.

26. Pirsig W (1992). Growth of the deviated septum and its influence on midfacial development. *Facial Plast Surg* 8:224–232.

27. Podoshin L, Gertner R, Fradis M, Berger A (1991). Incidence and treatment of deviation of nasal septum in newborns. *Ear Nose Throat J* 70:485–487.

28. Reitzen SD, Chung W, Shah AR (2011). Nasal septal deviation in the pediatric and adult populations. *Ear Nose Throat J* 90:112–115.

29. Rhys Evans PF, Brain DJ (1981). The effects of nasal surgery on the growth of the rabbit snout. *Rhinology* 19:101–105

30. Rönning O, Kantomaa T (1985). Experimental septal deviation in the rat. *Eur J Orthod* 7:248–254.

31. Sarnat BG, Wexler MR (1966). Growth of the face and jaws after resection of the septal cartilage in the rabbit. *Am J Anat* 118:755–767.

32. Sarnat BG, Wexler MR (1967). The snout after resection of nasal septum in adult rabbits. *Arch Otolaryngol* 86:463–466.

33. Scott JH (1953). The cartilage of the nasal septum. *Brit Dent J* 95:37–44.

34. Scott JH (1958). The cranial base. *Am J Phys Antropol* 16:319–48.

35. Siegel MI, Sadler D (1981). Nasal septum resection and craniofacial growth in a chimpanzee animal model: implications for cleft palate surgery. *Plast Reconstr Surg* 68:849–853.

36. Siegel MI, Mooney MP, Eichberg JW, Gest J, Lee RD (1990). Septomaxillary ligament resection and midfacial growth in a chimpanzee model. *J Craniofac Surg* 1:182–186.

37. Siegel MI, Mooney MP, Kimes KR, Todhunter J (1991). Developmental correlates of midfacial components in a normal and cleft lip and palate human fetal sample. *Cleft Palate Craniofac J* 28:408–412.

38. Stenström SJ, Thilander BL (1970). Effects of nasal septal cartilage resections on young guinea pigs. *Plast Reconstr Surg* 45:160–170.

39. Šubarić M, Mladina R (2002). Nasal setum deformities in children and adolescents: a cross sectional study of children from Zagreb, Croatia. *Int J Pediatr Otorhinolaryngol* 63: 41–48.

40. Takahashi R (1987). The formation of the nasal septum and the etiology of septal deformity. The concept of evolutionary paradox. *Acta Otolaryngol Suppl* 443:1–160.

41. Van Loosen J, Van Zanten GA, Howard CV, Verwoerd-Verhoef HL, Van Velzen D, Verwoerd CD (1996). Growth characteristics of the human nasal septum. *Rhinology* 34:78–82.

42. Vetter U, Pirsig W, Heinze E (1984). Postnatal growth of the human septal cartilage. Preliminary report. *Acta Otolaryngol* 97:131–136.

43. Vig KW (1998). Nasal obstruction and facial growth: the strength of evidence for clinical assumptions. *Am J Orthod Dentofacial Orthop* 113:603–611.

44. Wealthhall RJ, Herring SW (2006). Endochondral ossification of the mouse nasal septum. *Anat Rec A Discov Mol Cell Evol Biol* 288:1163–1172.

45. Wexler MR, Sarnat BG (1961). Rabbit snout growth. Effect of injury to septovomeral region. *Arch Otolaryngol* 74:305–313.

46. Yildirim I, Okur E (2003). The prevalence of nasal septal deviation in children from Kahramanmaras, Turkey. *Int J Pediatr Otorhinolaryngol* 67:1203–1206.