

AIRWAY VOLUME AND SHAPE FROM CONE-BEAM CT:
RELATIONSHIP TO FACIAL MORPHOLOGY

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ABSTRACT

Dan Grauer: AIRWAY VOLUME AND SHAPE FROM CONE-BEAM CT:
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James L. Ackerman)

Cone beam computed tomography (CBCT) records of 62 non-growing patients were used to evaluate the pharyngeal airway volume (upper and lower components), and the shape of the airway, using semi-automatic segmentations to calculate real volumes instead of estimates based on linear measurements. The sample was divided according to antero-posterior jaw relationships and vertical proportions. There was a statistically significant relationship between the volume of the lower component and a-p jaw relationship, and between airway volume and both the size of the face and gender. No differences in airway volumes related to vertical facial proportions were observed. Skeletal Class II patients tended to display forward inclination of the airway, greater projection of the tongue into the airway, and narrower airways. Skeletal Class III patients usually had a vertically-oriented airway. This study is a pioneer in measuring real 3-D models and controlling for face size.

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CHAPTER I

LITERATURE REVIEW

After a century of controversies, we are still not certain on the relationship between airway volume and facial morphology. Different orthodontists have different approaches, and there is a lack of consensus among different medical specialties. Most studies of airway shape are based in two dimensional representation of the airway on lateral cephalograms. With the advent of cone beam computed tomography (CBCT), it is possible now to evaluate the airway volume and the airway shape in three dimensions with a low cost in terms of radiation to the patient.

Relationship of Nasal Obstruction to the Pattern of Craniofacial Growth

Facial morphology is defined during growth and development. Today we are certain that there are a number of genetically encoded regulatory factors influencing growth and development, and that these factors operate in an epigenetic environment. We also know that morphogenesis, prenatal and postnatal development can be modified, but that does not imply in a predictable controlled way.¹

Several cross-sectional studies evaluated the association between breathing obstruction and craniofacial morphology. Linder-Aronson² has found that on average, patients scheduled for adenoidectomy who were presumed to have obstructed nasal breathing showed: increased lower and total facial height, more retrognathic maxilla and mandible,

smaller sagittal depth of bony nasopharynx, and lower position of the tongue. In a second Swedish study,³ compared to the normal population at age four, the adenoidectomy patients showed smaller a cranial base angle and a lower ratio of posterior/anterior face height. Small differences were also seen for the inclination of the mandible and maxilla relative to the cranial base. At seven years of age children with enlarged adenoids displayed more protrusive incisors and a dorsal rotation of the ramus in relation to the palate.⁴

At age ten Behlfelt et al⁵ reported that children with enlarged tonsils, and consequently different contours of the airway passages, displayed different cranio-facial morphology. The sample consisted of 73 children with enlarged tonsils and a matched control group. Compared to the control children, on average the children with enlarged tonsils had more retrognathic and posteriorly inclined mandibles ($p < 0.001$), larger anterior total and lower facial heights ($p < 0.001$), and larger mandibular plane angles ($p < 0.001$). In 49 mouth breathers from 10 to 16 years of age Ung et al⁶ found a weak but significant tendency towards a Class II skeletal pattern and retroinclined maxillary and mandibular incisors.

In an adult sample of patients with obstructive sleep apnea (25 subjects 48 +/-11 years of age) Lowe et al found a posteriorly positioned maxilla and mandible, steep occlusal plane, proinclined incisors, large gonial angle, higher upper and lower facial heights, overerupted maxillary and mandibular teeth and steep mandibular plane.⁷ Martin et al studied nasopharyngeal soft-tissues in patients with normal occlusion and reported a marked sexual dimorphism, and suggested possible specific respiratory adaptations for each type of malocclusion.⁸

All these studies were based on two dimensional representations of the airway on cephalograms. The use of lateral cephalometric radiographs to evaluate the upper airway is somewhat limited because the nasopharynx consists of complex 3-dimensional anatomical

structures.⁹ It is not possible to presume significant nasal obstruction from the apparent degree of adenoid encroachment on the airway in a cephalometric radiograph.

Growth of the pharynx

Transverse growth of the pharynx seems to level off at the end of the second year of life. Antero-posterior growth is small relative to the vertical component of growth and it is thought to stabilize during early infancy.¹⁰ Many authors have reported that the distance between the hyoid bone and the cervical vertebrae remains constant.¹¹⁻¹³ The main component of growth of the pharynx is vertical, and it continues until adulthood.¹⁴ The lymphoid tissue at the pharynx is believed to follow distinct growth patterns to the ones reported by Scammon, whose sample was based on structures other than the tonsils and adenoids.¹⁵

Linder-Aronson and Leighton¹⁶ characterized the growth of the posterior nasopharyngeal wall. They found that at age 5 the posterior wall of the pharynx displayed its greater thickness, and from age 5 to 10 underwent a decrease in thickness. Growth of the pharynx is influenced by the posterior cranial base growth, given that this bony structure represents its upper limit. The position and orientation of the maxilla and mandible are different in extreme vertical growth variations. In the long face pattern both the maxilla and the mandible are usually located in a more retrusive position. This has been interpreted as a mechanism to restore the pharyngeal space at the level of the tongue.¹⁷ An increase of space in both the oral cavity and pharynx occurs with growth. The hyoid bone descends providing more space for the tongue, the oral cavity increases its size, and the lymphoid tissues undergo regression towards puberty.

Growth in patients undergoing changes in patency of airway passages. Some interaction between the volume and shape of the airway and craniofacial growth can be detected when adenoids are removed. In a study^{1, 18} with a five-year follow-up of 41 children who had undergone adenoidectomy and 54 matched controls, Linder-Aronson et al have shown that among the sample, those children who changed from mouth- to nasal breathing, had changes in incisor inclinations that resulted in similar inclinations to the matched controls. Changes also took place in the angle between the palatal and mandibular planes. On a later 5-year longitudinal study of 17 children suffering from OSA who underwent adenoidectomy with matched control,¹⁹ Zettergren-Wijk et al showed differences between the groups in inclination of the mandible ($p < 0.05$) and maxilla ($p < 0.001$) relative to the cranial base, anterior face height ($p < 0.01$), length of cranial base ($p < 0.01$), inclination of upper and lower incisor ($p < 0.05$ and $p < 0.01$), airway space ($p < 0.05$ and $p < 0.001$) and nose size ($p < 0.05$). Five years after treatment both cases and controls exhibited no differences except for the length of the anterior cranial base and nose size ($p < 0.05$).

Conversely Guray and Karaman who attempted to replicate the former study concluded that adenoidectomy alone may change only the breathing pattern, without having a significant effect on malocclusion and facial type.²⁰ They reported that during the six years following adenoidectomy, the differences in incisor inclinations and mandible length between the two groups remained statistically significant ($p < 0.05$). Changes in vertical tongue position were also reported ($p < 0.05$). Patients in the Guray and Karaman (20) sample were older (9.1 ± 2 years of age), than the patients in the Lindon-Aronson (1) sample (7.9 years of age) and Zettergren-Wijk (19) sample (5.6 ± 1.34).

Freng and Kvam studied a group of patients affected with choanal atresia. Treatment for this inborn obstruction of the posterior nares involves eliminating the occluding

membrane. Patients were divided into five groups according to their age at the surgical procedure, and compared to matched unaffected individuals. These authors have found that the resection had no significant influence on sagittal facial growth. However when the nasal obstruction was allowed to persist during growth it appeared to result in a shorter maxilla and a tendency towards a retrognathic face.²¹

In a case series McNamara reported changes in growth pattern in four patients.²² The sample is small to establish any causal relationship but the morphology and changes during the observation time were described. In case number one: the patient with an untreated airway obstruction presented vertical pattern of facial growth, and retrognathic face. Case number two was a patient which underwent adenoidectomy, and showed an improvement in skeletal and dental relationships; the changes experienced by the patient were greater than the ones expected with normal growth. Case number three was similar to case number two; following adenoidectomy and tonsillectomy, the patient showed lessening of the severe vertical growth pattern. The last case presented a late obstruction of the nasopharynx due to pharyngeal flap. Four and a half years later the patient developed a vertical pattern of growth, presumably due to the adaptations necessary to maintain oral breathing. Linder-Aronson reported a case of a patient with a cleft lip and palate who, as a result of a surgery of the palate and nose, developed an almost total nasal obstruction during growth. When specific growth increments of this patient were plotted over growth curves, these did not channelize, meaning that the patient experienced a change in growth pattern, and developed a long face pattern.²³

Induced oral breathing in animals: Harvold et al performed experiments on induced nasal airway restriction. The animal model used was the *Macaca mulatta*. The experimental animals were matched with controls and observed longitudinally. The ones selected as

experimental group underwent total nasal obstruction by means of silicon nose plugs. In the experimentally-induced oral respiration group, animals developed different types of adaptations. Certain functional and morphologic traits which developed in the rhesus monkey resemble familial clinical conditions in humans: anterior open bite, skeletal Class III, lower position of the tongue, dental malocclusion and open gonial angles.²⁴

In a more recent animal study of induced nasal respiratory obstruction, growth was studied by the implant method. The animal model used in this study was young *Macaca fuscata*. The experimental group underwent an injection of dental impression material into the nasopharyngeal region that induced nasal obstruction. Compared to the control monkeys the experimental showed: anterior open bite, spacing among the lower incisors, less increase in posterior facial height, increased mandibular plane and a downward direction of growth. Differences between groups were considered significant at 5% level of confidence. The authors suggests an association between nasopharyngeal obstruction and downward and backward rotation of the mandible, upward and backward growth of the condyle and divergent gonial angle, which resulted in anterior open bite and spaced dental arch at the lower anterior segment. The degree of adaptation was related to the degree of nasal obstruction.²⁵

Three-Dimensional studies of the Airway Passages: Most three-dimensional studies of the airway to this time evaluated changes before and after orthognatic surgery. Findings were usually based in linear measurements within the three dimensional airway space, making comparisons difficult. Aboudara et al²⁶ reported one of the first studies that tried to measure the volume of the nasopharynx in CBCT. The authors compared the volume of the nasopharynx to its area measured on cephalograms. They concluded that the variability of the airway volume was greater than that of the airway area. Rachmiel et al²⁷ reported that in 12

young children presenting obstructive sleep apnea (OSA), bilateral mandibular distraction on average rendered a 72% increase of the volume of the upper airway passage. They used a method developed by Posnick et al²⁸ which was originally designed to measure intracranial volume based on hard, not soft tissue. These authors used CT scanners and the segmentation method is not mentioned. Kawamata et al²⁹ reported changes of airway dimensions in patients who had undergone mandibular setback. Even though the figures depicted volumetric changes, measurements were done in a linear manner and were not segmented volumes. Doruk et al³⁰ evaluated changes in nasal volume during rapid maxillary expansion (RPE). They compared two methods: acoustic rhinometry and conventional computed tomography. The authors concluded that nasal volume increases during RPE and that there were no differences between the two measuring methods.

In a more recent article Fairburn et al³¹ reported three-dimensional changes in upper airways of patients with OSA following maxillo-mandibular advancement. Again linear measurements and not volumetric measurements were reported. They did not indicate how the authors standardized the position of the head during the CT acquisition, and how registrations were made. In a study evaluating the effect on pharyngeal volume of continuous positive airway pressure (CPAP) that was based on magnetic resonance imaging; Abbey et al³² reported an increase in volume of 27.7%.

Strateman et al³³ have studied the relationship between airway and malocclusion and concluded that specific sites of upper airway constriction are associated with specific patterns of skeletal adaptations of the craniofacial complex. This was based on CBCT data from patients with non-extreme facial types and real volumes were used; the precise sites and adaptations were not yet characterized.

Hypothesis on etiological mechanisms

According to Woodside, humans in response to breathing obstruction adopt one or all of three neuromuscular responses: an altered position of the mandible with downward and backward rotation; an altered tongue posture moving superiorly and anteriorly, and an extended head posture.³⁴ There is no conclusive evidence regarding the association between skeletal facial development and the posture of the head and the cervical column. Solow et al³⁵ found low but statistically significant correlations between cranio-cervical postural measurements and craniofacial morphology (See Figure 2 in reference 35); in a longitudinal study of the relationship between growth rotation of the mandible and cranio-cervical posture. A reduction of cranio-cervical angles have been reported following corticoid administration as a nasal decongestant,³⁶ in children whose airway resistance was reduced following adenoidectomy,³⁷ and post orthognatic surgery.³⁸ Patients with OSA also tend to display increased cranio-cervical angles.³⁹

A theoretical hypothesis to relate the obstruction of the airway and the changes of the craniofacial development is that the obstruction of the airway starts a neuromuscular adaptation which triggers a postural change involving soft-tissue stretching.⁴⁰ These changes alter the equilibrium of forces around the skeleton and against the dentition, which produces hence producing a morphological change. Because the upper structures, those above the palate, are fixed and motionless during function, the compensations must occur at a lower level (see Reference 11).

The adaptable portion of the nasopharynx is encompassed between the caudal limit of the palate and the cartilages of the larynx and trachea. Durzo and Brodie (see Reference 12) have shown that even in persons with severe pathologic conditions the anteroposterior dimension of the oropharynx is maintained. The adaptation involved a downward movement

of the hyoid bone and can involve a change of extension of the head. This phenomenon is also seen after surgical setback of the mandible.^{30, 41}

Hellsing and L'Estrange⁴² have found that changes in head extension correlates with an increase of the pressure of the lips on the incisors. These researchers used pressure transducers placed on the central incisors and instructed the patients to change their head extension. In their study patients were also asked to breathe through their mouth and then a decrease of lip pressure was noted.

Both teeth and bone are subjected to an equilibrium of environmental forces that determines their position.⁴³ Hellsing have reported that in a sample of 20 adults, a change from natural head posture to 20 degrees of head extension resulted in an increment in cervical lordosis and craniocervical inclination, a change in position of the hyoid bone and an increase in cross-sectional dimensions of the pharyngeal airway.⁴⁴ Tourne and Schweiger⁴⁵ induced total nasal obstruction in 25 adults and compared cephalometric measurements in natural head position before and 1 hour after the total nasal obstruction. Significant changes were: parting of the lips ($p<.05$), a drop of mandibular position ($p<.001$), and a downward movement of the hyoid bone ($p<.05$). Cranial extension did not reach statistical significance ($p=.06$). If a compromise in patency of airway leads to a change in head extension and hence to a change in the equilibrium forces around the teeth and bones, a change in growth may occur.

Functional considerations

According to Bosma⁴⁶, respiratory needs are the primary determinant of the posture of the jaws and tongue. Humans are partially mouth breathers depending on airflow needs.

When the ventilatory exchange rates become higher than 40-45L/min, the average individual undergoes a transition to partial oral breathing.⁴⁷ Even though a greater effort is required to breathe through the nose than through the mouth, nasal breathing is physiologically accepted in order to perform the function of warming and humidifying the inspired air. The nasal mucosa immune system also plays its role during inspiration.

It is important to note the difference between airway obstruction, mouth breathing and enlarged adenoids and tonsils. While these conditions can coincide within the same patient, this is not always the case. Trotman et al⁴⁸ studied a group of 207 children who were seeking evaluation of tonsil and/or adenoid problems. These authors assessed the separate associations of lip posture, sagittal airway size and tonsil size based on cephalometric measurements. They concluded that lip posture, sagittal airway size and tonsil size represent three different and unrelated phenomena with respect to their effect on craniofacial growth.

A study by Fields et al,⁴⁹ using special instrumentation to totally account for the amount of oral versus nasal airflow in normal and long-face children, has shown that the relationship between oral versus nasal breathing and growth in the long face pattern is not clear-cut. Long-face children were over-represented in the group of these subjects, who had a high percentage of oral breathing, but predominately oral breathing was found in some children with normal facial morphology and some long face children had a low percentage of oral breathing. The normal and long-face subjects displayed similar tidal volumes and minimum nasal cross-sectional areas.

Warren et al⁵⁰ using instrumentation to measure the airway resistance, showed that in humans, normal speech and normal respiration require a controlled level of airway resistance. Because of this, there is a limit to how big an airway could be, as well as a limit for how small that is based on air flow needs.

Many studies are performed in the obstructive sleep apnea field. Their main goal is to find out why the airway collapses in many of the OSA patients. Airway patency is considered to be strongly related to the equilibrium between the extraluminal tissue pressure and the intraluminal pressure. Transmural pressure is defined as the difference between the intraluminal and the extraluminal pressures. When the transmural pressure is positive the airway remains patent, and it occludes when transmural pressure is negative.⁵¹ It is logical to think that this equilibrium of pressures depends on the airflow through the airway. For instance, the continuous positive airway pressure machines (CPAP) preserves the patency through the airway by maintaining a greater intraluminal pressure than the extraluminal pressure. A second factor influencing the airway patency is the mucosal tension; when airways are subjected to tension their collapsibility decreases.⁵² It could be interesting to know the relationship between the tension of the external soft-tissues to the tension of the internal soft-tissues in order to establish a physiologic connection between these equilibrium mechanisms.

In order to better evaluate the pharyngeal airway in relationship to facial proportions, a cross-sectional study on CBCT records of 62 patients that involved creation of real 3-D models of the pharynx was undertaken at the Department of Orthodontics at the University of North Carolina. This study is presented in detail in part 2 of the thesis below.

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CHAPTER II

MANUSCRIPT

AIRWAY VOLUME AND SHAPE FROM CONE-BEAM CT: RELATIONSHIP TO FACIAL MORPHOLOGY

INTRODUCTION

Several lines of evidence from cephalometric studies support a link between presumed respiratory mode and facial morphology. These include the classic studies of mandibular orientation and growth in patients before and after adenoidectomy by Linden-Aronson et al,^{1,2} and case reports that document downward-backward rotation in patients with total nasal obstruction.³ More recently Zettergren-Wijk et al⁴ showed a certain degree of normalization of growth after adenoidectomy in a group of obstructive sleep apnea patients. Guray et al,⁵ studying a similar population, were not able to replicate the Linden-Aronson results and concluded that adenoidectomy alone may change only the breathing mode, without having a significant effect on malocclusion and facial type. A study by Fields et al,⁶ using special instrumentation to totally account for the amount of oral versus nasal airflow in normal and long-face children, has shown that the relationship between oral versus nasal breathing and growth in the long face pattern is not clear-cut. Long-face children were over-represented in the group of these subjects who had a high percentage of oral breathing, but predominately oral breathing was found in

some children with normal facial morphology and some long face children had a low percentage of oral breathing. The normal and long-face subjects displayed similar tidal volumes and minimum nasal cross-sectional areas.

Postural relationship of the head, jaws and tongue are established in the first moments after birth as the airway is opened up and stabilized, and are altered as necessary thereafter to maintain the airway.⁷ It seems reasonable that the link between respiratory mode and the development of malocclusion could be soft tissue pressures against the dentition, which might affect the amount of tooth eruption, dental arch form and possibly the direction of mandibular and maxillary growth. Solow et al^{8,9} formally expressed this view in their “soft-tissue stretching hypothesis”. A change in jaw posture that led to downward-backward rotation of the mandible, or a change in head posture like head extension, could lead to stretching of the lips, cheeks and musculature. The result would be upright incisors and narrower dental arches, which often (but not always) are observed in patients with a long-face open bite growth pattern.

The Solow hypothesis implies that oral and pharyngeal soft tissues also would be affected by a change in head / jaw / tongue posture. The value of lateral cephalometric radiographs to evaluate the upper airway is limited because they provide 2-dimensional images of complex 3-dimensional anatomical structures.¹⁰ Three-dimensional analysis of the airway volumes and shape is required in order to understand oral and pharyngeal adaptation to varying respiratory conditions and proprioceptive stimuli. Records from cone-beam computed tomography (CBCT) of the head that were obtained for clinical problems like impacted teeth or TMD problems now offer an acceptable way to evaluate pharyngeal soft tissue relationships and airway volume in patients with and without

malocclusion that affects antero-posterior and vertical facial dimensions.¹¹ The goal of this study was to examine the hypothesis that pharynx volumes and shape would differ among various facial morphologies, especially those involving altered face height.

METHODS

Subjects

Records of 1200 consecutive patients seeking radiographic examination at a radiology clinic between January 2005 and August 2006 were screened. Those for whom facial photographs and an iCAT (Imaging Sciences International, Hatfield, Pa) CBCT of the head was obtained were pre-selected, approximately 450 patients. Initial inclusion criteria for this study were a medium or full field of view which allowed visualization of both the cranial base and the face, and age between 17 and 46 years. Exclusion criteria were previous orthognatic surgery, apparent syndromic condition, and presence of pathology detectable along the upper airway.

These criteria identified 126 patients, and the first consecutive 62 patients stratified by a-p skeletal type were used for this study. Before they were entered into the data base for this study, the CBCT images were anonymized by an algorithm included in the iCAT CBCT software that removes any patient identifiers from the files.

Establishment of Antero-Posterior and Vertical Skeletal Types

Antero-posterior skeletal type (Class I, II or III) was established initially from visual inspection of the facial photographs and the lateral cephalometric radiograph (which was not included in the data base for this study) (Figure 1). The CBCT data was loaded into Dolphin 3D version 2.3 beta (Dolphin Imaging Chatsworth, CA), and

synthetic lateral and P-A cephalograms were created. These were used for confirmation of the antero-posterior groups. Two patients had been erroneously assigned initially to the wrong A-P group, and were re-classified to the correct group. The discrimination process for the vertical groups was based on a bony facial index, calculated as the ratio between the bony bizygomatic width (from the synthetic P-A cephalogram) divided by the Na-Me distance projected onto an orthogonal coordinate system (from the synthetic lateral cephalogram). The facial index values were split into tertiles to establish the vertical groups. Demographic and skeletal-type data for the sample are shown in Table I.

For both the lateral and P-A synthetic cephalograms, the head was oriented with a line six degrees down from Sella-Nasion as the horizontal axis (which approximates the true horizontal in most individuals). Whenever this orientation method created a non-realistic head posture, which occurred in some individuals with extreme jaw disproportion or long faces, the synthetic cephalogram was redone according to the soft tissue appearance on the CBCT data.

The size of the face was established from the P-A and lateral synthetic cephalograms, as a rectangular prism encompassing the facial bones. This prism was constructed as shown in Figure 2.

3-D Models of Airway

In order to build 3-D models of the airways for the 62 subjects, the anonymized CBCT data were loaded into InsightSNAP 1.4.0 software (Congitica, Philadelphia, PA & Neuro Image Analysis Laboratories, University of North Carolina, NC) for semi-automatic segmentation of the upper airway. The process of 3-D segmentation is defined as the construction of 3-D models (called segmentations) by examining cross-sections of

a volumetric data set to outline the shape of structures. Segmentations were performed by means of a user-initialized 3-D surface evolution method¹² (Figure 3, c). The limits for segmentation are shown in Figure 3 a, b, d. Once segmented, airways were refined to obtain the true shape of the airway by eliminating the projections that did not belong to the airway. The segmented airways then were subdivided into an upper and lower portion of the airway by a plane perpendicular to the sagittal plane which included the posterior nasal spine and the lower medial border of the first cervical vertebra. The anatomical relationships of the airway to the facial bones can be observed in Figure 4. Airway volumes were measured in mm³ with the InsightSNAP 1.4.0 measuring tool. The reliability of the volumetric measurements was assessed on five randomly selected individuals stratified on antero-posterior grouping criteria. Segmentations were created three times for each case, and their volume was measured. The mean coefficient of variation (COV=SD/ mean volume) was measured at 1.9% by averaging the coefficient of variation for each of the five individuals. This rather low COV value is likely due to the semi-automatic nature of the segmentation procedure, as comparable purely manual segmentations have normally larger COV's (see Ref.11). This COV is further more than an order of magnitude smaller than the volumetric variability within the groups, and thus the segmentation can be judged as reliable and unlikely introduces any noticeable errors into our analysis.

Statistical Analysis

Bivariate relationships between variables were assessed by Spearman correlation. Type III sums of squares from linear regression models were used to assess the

relationship between face morphology and airway volume, controlling for age, gender, size of face, and the interaction between size of face and gender. The variable age was centered at its average. The reference group for the antero-posterior pattern was the Class I group, and the middle group of the vertical pattern variable was used as the vertical reference group. A partial F-test showed that among all possible interactions of explanatory variables, only the interaction between size of face and gender was potentially related to airway volume. The interaction between size of face and gender was included in the regression model along with the covariate and primary main effects.

RESULTS

Airway Volumes

Descriptive Statistics (Table I). Descriptive statistics of the 62 subjects are displayed according to vertical and antero-posterior proportions in Table I. The average age for females and males did not differ statistically ($p=.12$). The average size of the face was statistically significantly different for males and females ($p<.01$). The average volume of the airway was 20.3cm^3 , with a mean volume for the upper portion of 8.8cm^3 and mean volume for the lower portion of 11.5cm^3 .

Bivariate Analysis of Correlations (Table II). There was no statistically significant relationship between volume of the airway and age or gender. The size of the face was significantly associated with the total, lower and upper airway volumes, with Spearman correlations of 0.399 ($p<.01$), 0.368 ($p<.01$), and 0.303 ($p=.02$) respectively. Among the covariate variables, size of the face was significantly correlated to gender (Spearman correlation of -0.668 , $p<.01$).

Regression Models (Table III). For both grouping criteria, size of face was a statistically significant explanatory variable for the upper and lower portions of the airway volume (referred as upper and lower airway volumes). Upper airway volume differed significantly for male and female for both vertical and antero-posterior groups, being the female volume smaller.

A-P groups (Table IV). There was a statistically significant difference ($p=.02$) in lower airway volume between the A-P groups, after controlling for the effects of age, gender, size of face and interaction between size of face and gender. From the contrast tests, the mean value for the Class II subjects was significantly different from Class I ($F = 7.97, p<.01$) and Class III ($F= 4.12, p=.05$), but there was no difference between Class I and Class III ($F= 0.50, p=.48$). (Table IV).

There was no significant difference ($p=.26$) in upper airway volume among the A-P groups, after controlling for the effects of age, gender, size of face, and interaction between size of face and gender. There was a significant relationship ($p<.01$) between upper airway volume and gender.

Vertical groups. There were no significant differences in the lower, upper or total airway volumes among the long/normal/short vertical groups, after controlling for the effects of age, gender, size of face and interaction between size of face and gender. There was a statistically significant relationship ($p=.01$) between gender and upper airway volume.

Airway Shape

A-P groups. Quantitative analysis of airway shapes is not available yet. This type of shape description is an ongoing research project at our lab at the University of North

Carolina Department of Orthodontics, Department of Computer Sciences and Department of Oral Biology. From visual inspection the following qualitative observations were noted:

- The segmentation contours were highly variable in all 3 groups;
- subjects with a Class III skeletal pattern displayed a more vertical orientation of the airway compared with the other groups, while a Class II skeletal pattern was associated with a more forward orientation of the airway (Figure 5 a, c);
- the postero-superior area of the tongue dorsum was visualized at the anterior wall of the airway segmentation in the form of a blunt indentation (Figure 5, b, c). The apparent projections of the tongue into the airway at various points along the anterior wall of the pharynx show how a 2-D view of the tongue-pharynx relationship could be misleading;
- the plane used to bisect the segmentations from PNS to the lower medial anterior border C1 had a more horizontal orientation in the skeletal Class III group and was more oblique, down towards the posterior in the skeletal class II group (Figure 6); and
- the airway passages of the skeletal Class II group were narrower when viewed from the coronal plane than the other two groups (see Figure 5, c).

Vertical groups. Variability was greater among the vertical groups and differences in shape were more difficult to characterize. An extremely narrow airway, both antero-posteriorly and coronally, was observed more often in patients from the long face group when compared to normal face patients. Most long face patients were

also classified as skeletal antero-posterior malocclusions, and often a strong tongue indentation was noted at the anterior wall of the airway (see Figure 5 b, c).

DISCUSSION

The advent of new technology allows us to establish a volumetric characterization of the pharynx. No linear or angular measurements were used. Whenever comparison was made, the size of the face was taken into account. The segmentations of the airway were real 3-D models, as opposed to projections of the 3-D data based in thresholding filters and isometric visualization.

Influences on Airway Dimensions and Shape

In this study a significant difference in the lower portion of the airway volume was found between skeletal Class II and Class I / III patients, (being skeletal Class II lower airway volume smaller), but there were no differences in airway volume among the long, normal and short face height groups. Airway orientation and shape differed between Class II and Class III groups, with much less difference between the long- and short-face groups. We had expected the reverse, more differences between the vertical than the a-p groups. Several factors may have contributed to this outcome:

Assignment of patients to a-p and vertical groups It is possible that the process we used to select the patients from the data base, which focused initially on a-p characteristics, was a factor in this outcome. Each individual was in both an a-p and a vertical group, with the vertical grouping created by simply dividing the sample into 3 equally-sized groups by face height. There was a definite relationship between vertical and a-p characteristics of the patients. Most of the patients with a longer face height also

were classified as skeletal Class II or III, while the shorter face height patients tended to be classified as skeletal Class I.

Patient positioning and respiration phase during data acquisition

Cephalometric studies in Lowe's laboratory have shown that with a change in body position from upright to supine, changes in volume and contours occur in the upper airway in both patients with obstructive sleep apnea (OSA) and control subjects.¹³ For our study, the iCAT scanner was chosen because the patient is sitting upright during CBCT acquisition. In the other most widely used CBCT scanner, NewTom 3G (Aperio Services, Sarasota, Fla), patients are scanned while in a supine position. The supine position is appropriate for study of airway contours in OSA patients, given that OSA episodes happen when patients are in supine position and sleeping. In our view, the upright sitting position is closer to the normal position outside sleeping hours, and a better starting point for a study of this type. It will be interesting, however, to see if the differences in airway shape between the two positions lead to different upper and lower airway volumes, and also to determine whether the differences in airway shape that we observed in Class I, II and III subjects would be seen in supine CBCT scans.

One other aspect of positioning inside the iCAT machine, which might lead to differences in supine versus upright scans, is the influence that the patient's chin position exerts on head orientation during CBCT acquisition. With iCAT, the radiology technician positions the subject with a strap around the forehead and a platform for the chin. A more prominent chin could lead to changes in the extension of the head, and a less prominent chin could have the opposite effect. During NewTom 3G scan acquisition patients are in supine position with their heads lying on a non-customized pillow for head support. This

type of positioning is not reproducible for studies where head orientation has to be controlled for.

No attempt was made during CBCT acquisition for our subjects to control for the respiratory movements (inspiration, resting, exhalation). Lowe et al¹⁴ reported changes in airway dimensions related to the respiration phase. The acquisition time for the iCAT scanner we used is between 20 and 38 seconds, which is too long to ask the patient not to breathe during the scan. Newer scanners have reduced the acquisition time to around 10 seconds, and that will allow control of the respiration phase. For this study, we have considered the changes in volume during respiration as part of the systematic error, and have no reason to think that the respiratory rate was systematically different between our various groups.

In contrast, several other factors that could have affected our results almost surely did not influence the differences that we observed. These include:

Patient age The age of the sample ranged from 17 to 46 years with an average of 24.7 years, so these individuals had already undergone their adolescent growth spurt; hence it is no surprise that the volume of the airway did not correlate with age. To date there are no three-dimensional longitudinal data on airway changes during growth. From 2-D cephalometric data, Bench et al¹⁵ and later Tourne et al¹⁶ described the growth of the bony nasopharynx as having mainly a vertical direction, with minimal change after the growth spurt.

Face Size In this study, the size of the face was established as a rectangular prism encompassing the facial bones. Given that the lines used to determine the lengths of the edges of the prism were not perpendicular, their projection was transposed into an

orthogonal system that created the edges of the prism (see Figure 2). That way the size of the face was independent of the head orientation and the face morphology, and by simple trigonometry the 2D planes could be projected onto an orthogonal coordinate system.

Airway volumes (total, lower and upper) were significantly if weakly correlated with face size ($r = 0.40$ ($p < .01$), 0.37 ($p < .01$), and 0.30 ($p = .02$) respectively. Individuals with larger faces would be expected to have larger airway volumes. There is no reason to think, however, that larger or smaller individuals were non-randomly distributed in our groups.

Gender Face size was significantly larger in males than females, and as the airway volume is correlated to size of the face, it would be expected to be different between genders. Martin et al¹⁷ reported that two-dimensional nasopharyngeal soft-tissue patterns were different in men and women. In an earlier longitudinal study Linden-Aronson et al also found sexual dimorphism during growth of the posterior wall of the pharynx.¹⁸ Sexual dimorphism between airways was not addressed in our study, but our data confirm that airway volumes are significantly larger in males. Because the male/female composition of our groups was quite similar, these expected differences in airway volumes should not have affected the differences by facial morphology groups that we found.

Airway resistance A potentially quite important factor in airway volumes and shape is the need for a given level of airway resistance in order to maintain normal respiration and allow normal speech. Warren et al¹⁹ have utilized sophisticated instrumentation to measure the airway resistance and have shown that in humans, normal speech and normal respiration require a controlled level of airway resistance. Because of this, there is a limit to how big an airway could be, as well as a limit for how small that is

based on air flow needs. In our subjects, the need for an appropriate level of airway resistance undoubtedly affected the total airway volume, but did not necessarily contribute to the differences in upper and lower airway volumes.

Clinical Implications of Airway Dimensions and Shape

Maintenance of an appropriate airway, neither too small nor too large, has a high physiologic priority. Airflow demands trigger reflex changes in the posture of the head, mandible and tongue. Compared with control children, children with enlarged tonsils have an extended posture of the head and an antero-inferior posture of the tongue²⁰ (shown in cephalometric radiographs by the position of the hyoid bone), and patients who underwent a mandibular setback display a more inferior position of the hyoid bone afterward.²¹ The antero-posterior position of the tongue seen in 2-D images is closely related to the oro-pharyngeal depth. Many authors have reported an association between extended head posture and facial retrognathism.²² Straterman recently reported that specific sites of upper airway constriction are associated with specific patterns of skeletal adaptations of the craniofacial complex. This was based on CBCT data from patients with non-extreme facial types, and the precise sites and adaptations are still to be characterized.²³

Physiological considerations

Airway patency is considered to be strongly related to the equilibrium between the extraluminal tissue pressure and the intraluminal pressure. Transmural pressure is defined as the difference between the intraluminal and the extraluminal pressures. When

the transmural pressure is positive the airway remains patent and it occludes when transmural pressure is negative.²⁴ It is logical to think that this equilibrium of pressures depends on the airflow through the airway, for instance the Continuous Positive Airway Pressure machines (CPAP), preserves the patency through the airway by maintaining a greater intraluminal pressure than the extraluminal pressure. A second factor influencing the airway patency is the mucosal tension; when airways are subjected to tension their collapsibility decreases.²⁵ It could be interesting to know the relationship between the tension of the external soft-tissues to the tension of the internal soft-tissues in order to establish a physiologic connection between these equilibrium mechanisms.

It is quite likely that 3-D images of the airway will allow an improved evaluation of sites of airway obstruction and an improved understanding of the physiologic response to pharyngeal stenosis. It already is possible to use the cranial base surface to superimpose 3-D models for different time points within the same patient,²⁶ so that changes in airway volume and orientation relative to this stable reference can be studied before and after surgery (Figure 7, a). New registration methods for growing patients and inter-patient comparison are being created (Figure 7, b); in the future we can expect a much better understanding of adaptive changes in the airway shape and volume. Head posture, mandibular rotation, hyoid position and patency of the airway are interrelated, and further 3-D studies of the airway should clarify the relationships.

TABLE I

	Descriptive Statistic by Vertical Proportions			Descriptive Statistic by Antero-posterior Groups		
	Short (n= 21)	Average (n= 20)	Long (n=21)	I (n= 21)	II (n= 22)	III (n=19)
Age						
Mean (SD)	24.54 (7.36)	26.00 (7.88)	23.55 (7.42)	25.16 (7.63)	24.83 (7.61)	23.97 (7.57)
Gender						
Female	12 (32%)	13 (35%)	12 (32%)	14 (38%)	14 (38%)	9 (24%)
Male	9 (33%)	7 (28%)	9 (36%)	7 (28%)	8 (32%)	10 (40%)
Size of Face						
Mean (SD)	0.99 (0.12)	0.98 (0.11)	1.03 (0.13)	1.01 (0.13)	0.98 (0.11)	1.03 (0.12)

Table I: Sample distribution in terms of age, gender and size of face according to the two grouping criteria: vertical and antero-posterior

TABLE II

Spearman Correlation (N = 62)						
	Total Airway	Lower Airway	Upper Airway	Age	Gender	Size of Face
Total Airway	1.000	0.930 (p < .01)	0.855 (p < .01)	-0.161 (p = .21)	-0.238 (p = .06)	0.399 (p < .01)
Lower Airway	0.930 (p < .01)	1.000	0.634 (p < .01)	-0.164 (p = .20)	-0.238 (p = .06)	0.368 (p < .01)
Upper Airway	0.855 (p < .01)	0.634 (p < .01)	1.000	-0.072 (p = .58)	-0.128 (p = .32)	0.303 (p = .02)
Age	-0.161 (p = .21)	-0.164 (p = .20)	-0.072 (p = .58)	1.000	0.210 (p = .10)	-0.028 (p = .83)
Gender	-0.238 (p = .06)	-0.238 (p = .06)	-0.128 (p = .32)	0.210 (p = .10)	1.000	-0.668 (p < .01)
Size of Face	0.399 (p < .01)	0.368 (p < .01)	0.303 (p = .02)	-0.028 (p = .83)	-0.668 (p < .01)	1.000

Table II. Bivariate analysis (Spearman correlation) including upper, lower and total airway and the covariate. Lower, upper and total airway volume correlates with size of the face. Gender and size of the face are also correlated.

TABLE III**Analysis Airway Volume for vertical groups**

Source	Lower Portion Airway		Upper Portion Airway	
	F Value	Pr > F	F Value	Pr > F
Age	2.96	0.09	0.26	0.62
Gender	1.52	0.22	5.1	.01*
Size of Face	4.72	.01*	7.39	<.01*
Vertical proportion	2.08	0.13	2.35	0.11

Analysis Airway Volume for Antero-posterior groups

Source	Lower Portion Airway		Upper Portion Airway	
	F Value	Pr > F	F Value	Pr > F
Age	2.55	0.12	0.17	0.68
Gender	2.73	0.07	5.07	.01*
Size of Face	4.57	.02*	7.16	<.01*
Antero-posterior groups	4.27	.02*	1.25	0.29

* significant at the level .05

Table III. Regression models controlling for age, gender, size of face and the interaction between gender and size of face for upper and lower airway volumes by antero-posterior and vertical groups.

TABLE IV

Contrast Analysis for Lower Airway Volume with Antero-posterior groups

Antero-posterior groups (AP)	DF	F Value	Pr > F
I vs. II	(1, 55)	7.97	<.01*
I vs. III	(1, 55)	0.5	0.48
II vs. III	(1, 55)	4.12	.05*

* significant at the level .05

Table IV. Contrast analysis between antero-posterior groups: the volume of the lower portion of the airway in skeletal Class II individuals is statistically different than those of skeletal Class I and skeletal Class III individuals.

Figure 1. Facial morphology reflects the underlying skeletal configuration and internal soft tissues. Sample was divided into three groups according to each of the two criteria. (a) The antero-posterior relationship of the jaws; and (b) the vertical pattern of the face.

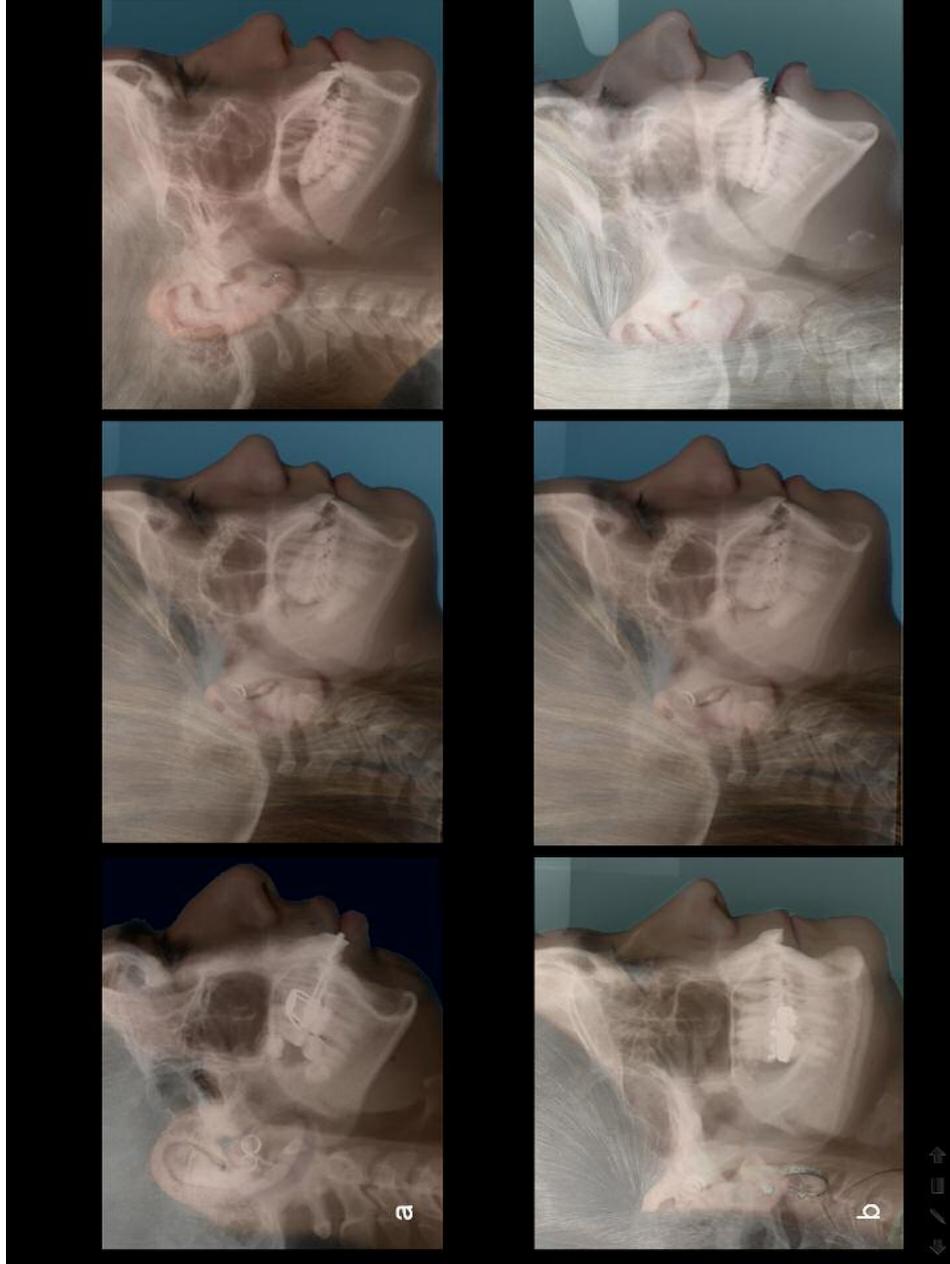


Figure 2. Size of face was established by creating a prism (c) with edges as (a) the bizygomatic width, which is parallel to the true horizontal and does not need to be projected, (b) the Na-Me distance projected on the Y-axis and (d) the Ba-ANS distance projected on the Z-axis.

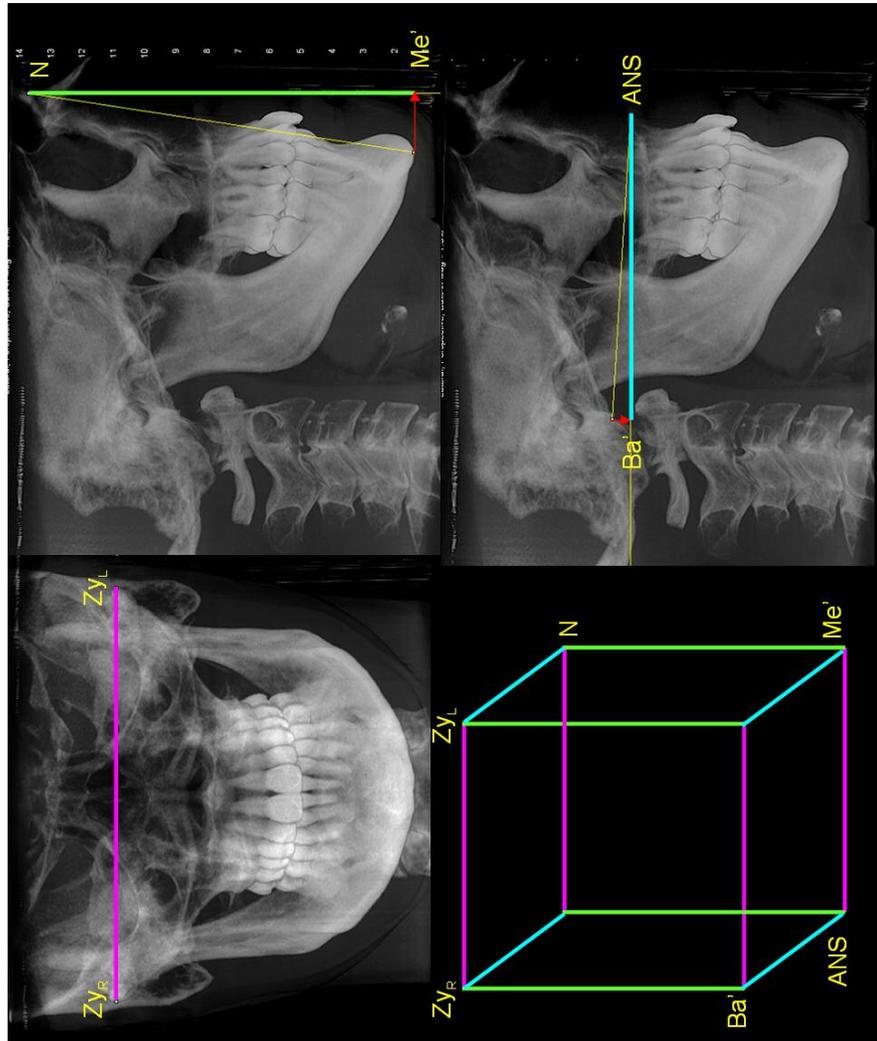


Figure 3. Segmentation by user-initialized 3-D surface evolution (c). Limits for airway analysis are: (a, b) anterior, a vertical plane through posterior nasal spine perpendicular to the sagittal plane at the lowest border of the vomer; posterior, the posterior wall of the pharynx; lateral, the lateral walls of the pharynx, including the full extensions of the lateral projections; lower, a plane tangent to the most caudal medial projection of C3 vertebra perpendicular to the sagittal plane; (b, d) upper, the highest point of the nasopharynx, coinciding with the posterior choanae and consistent with the anterior limit.

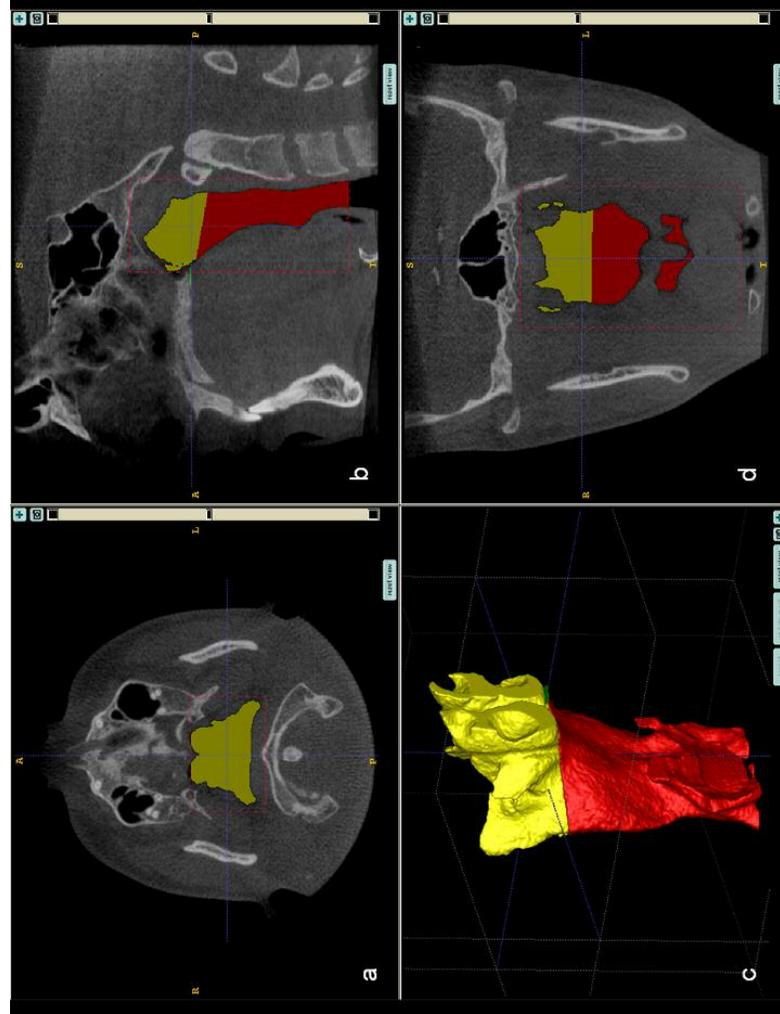


Figure 4. (a) 3-D model of airway. (b) Bony anatomic relationship of the airway to the frontal bones, cranial base and mandible. (c) Relationship with naso-maxillary complex. (d) Posterior view facial bones and cranial base.

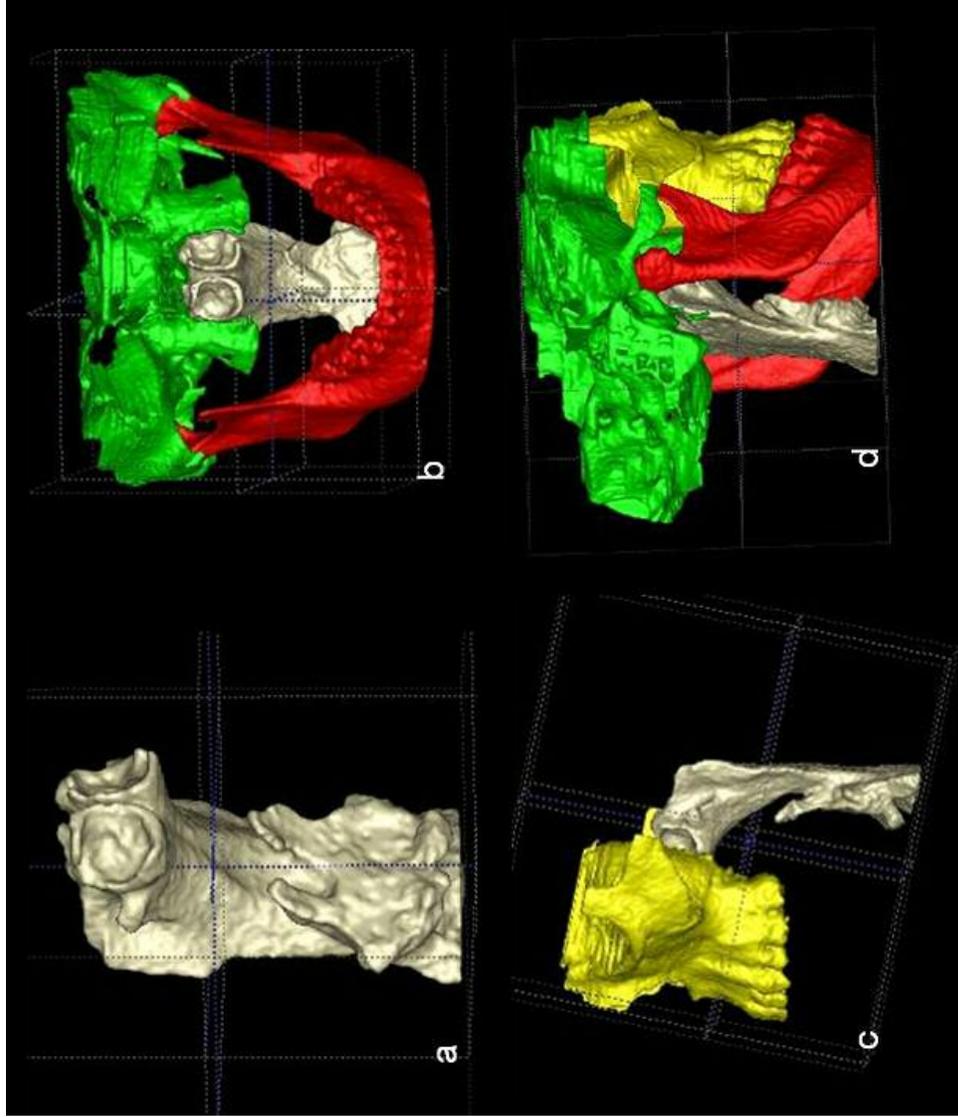


Figure 5. Different shape between airway of skeletal Class II individuals and skeletal Class III depicting a more vertical orientation of airway in Class III subjects (a, c). The differences between subjects in the vertical groups are less apparent (b, d).

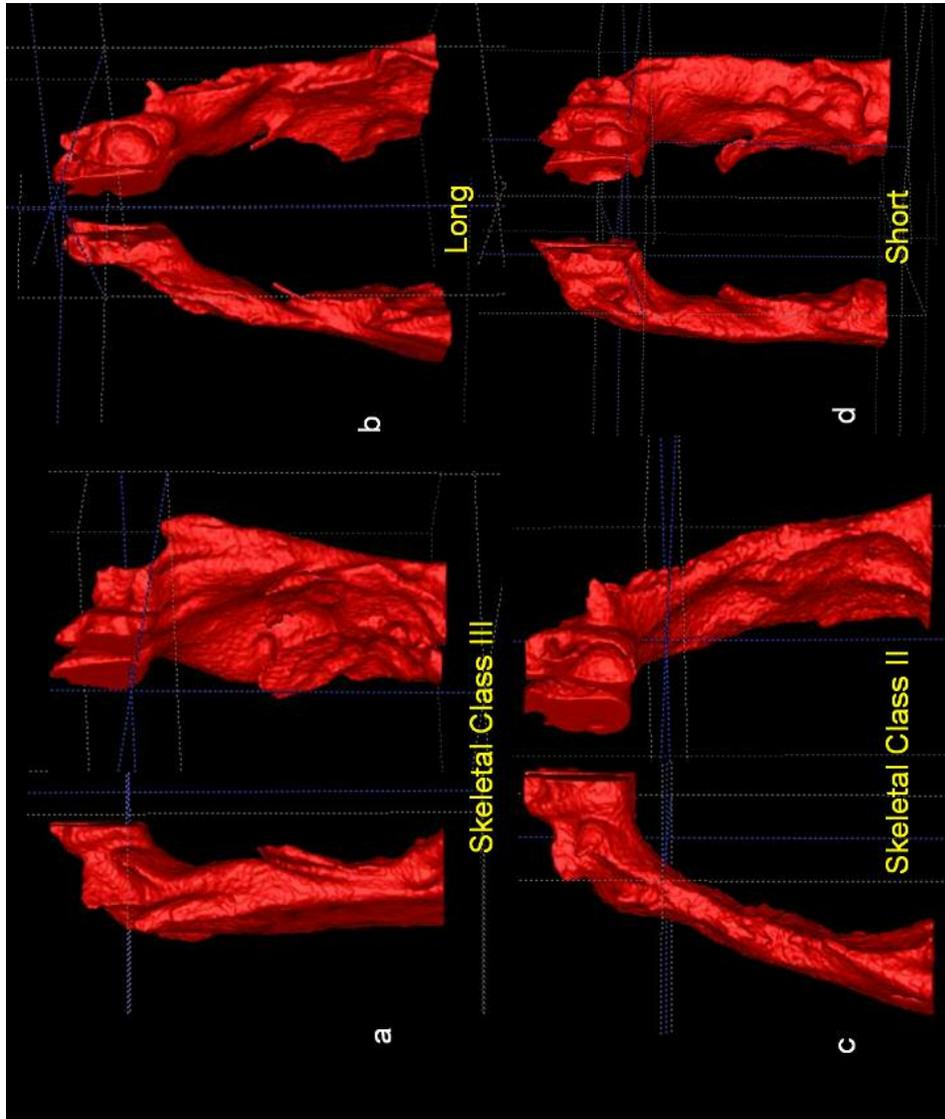


Figure 6. The orientation of bisecting plane for upper/lower airway portions was different between skeletal Class II (a, b) and skeletal class III (c, d), the latter being more horizontal and the former more oblique.

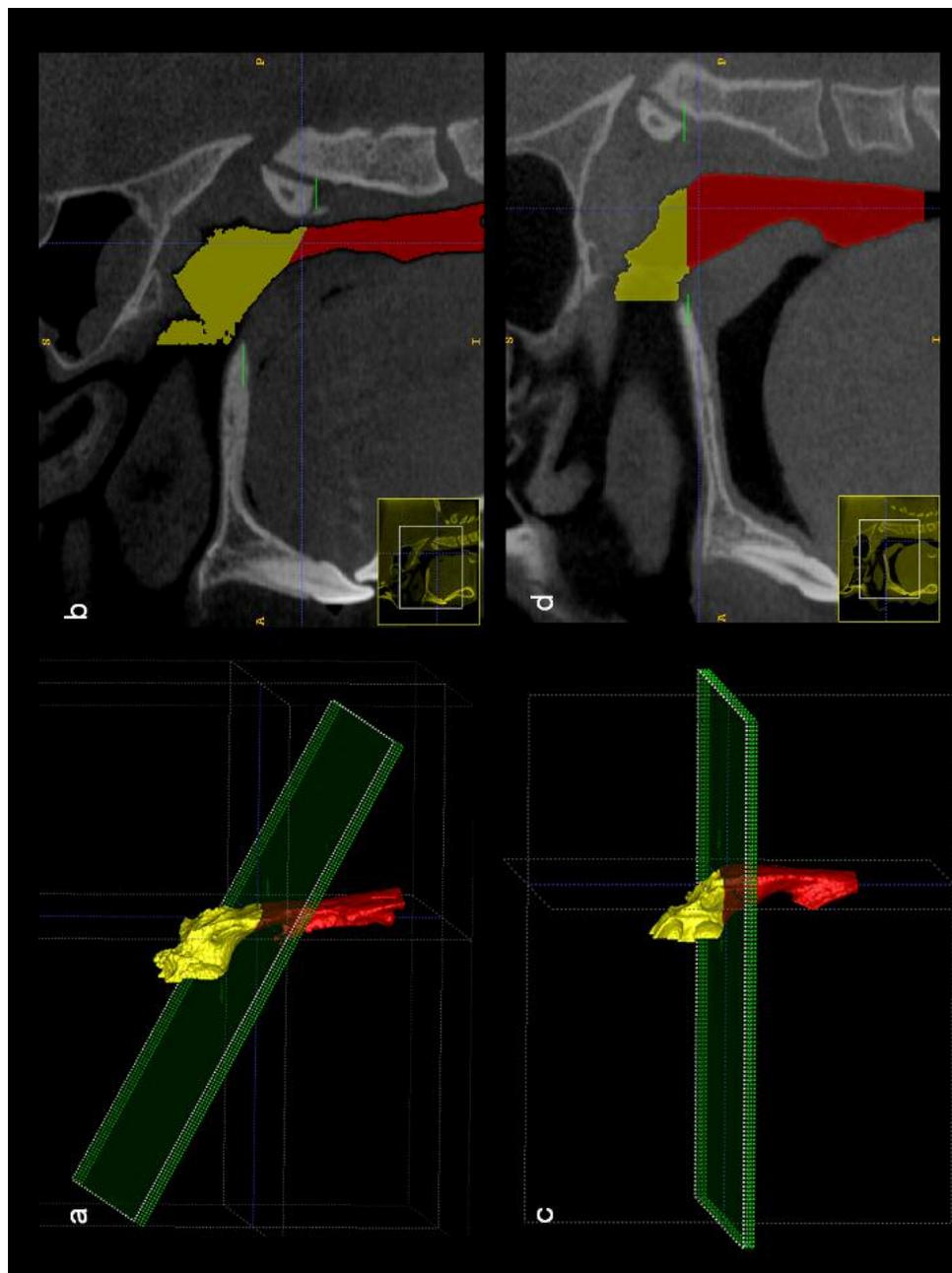
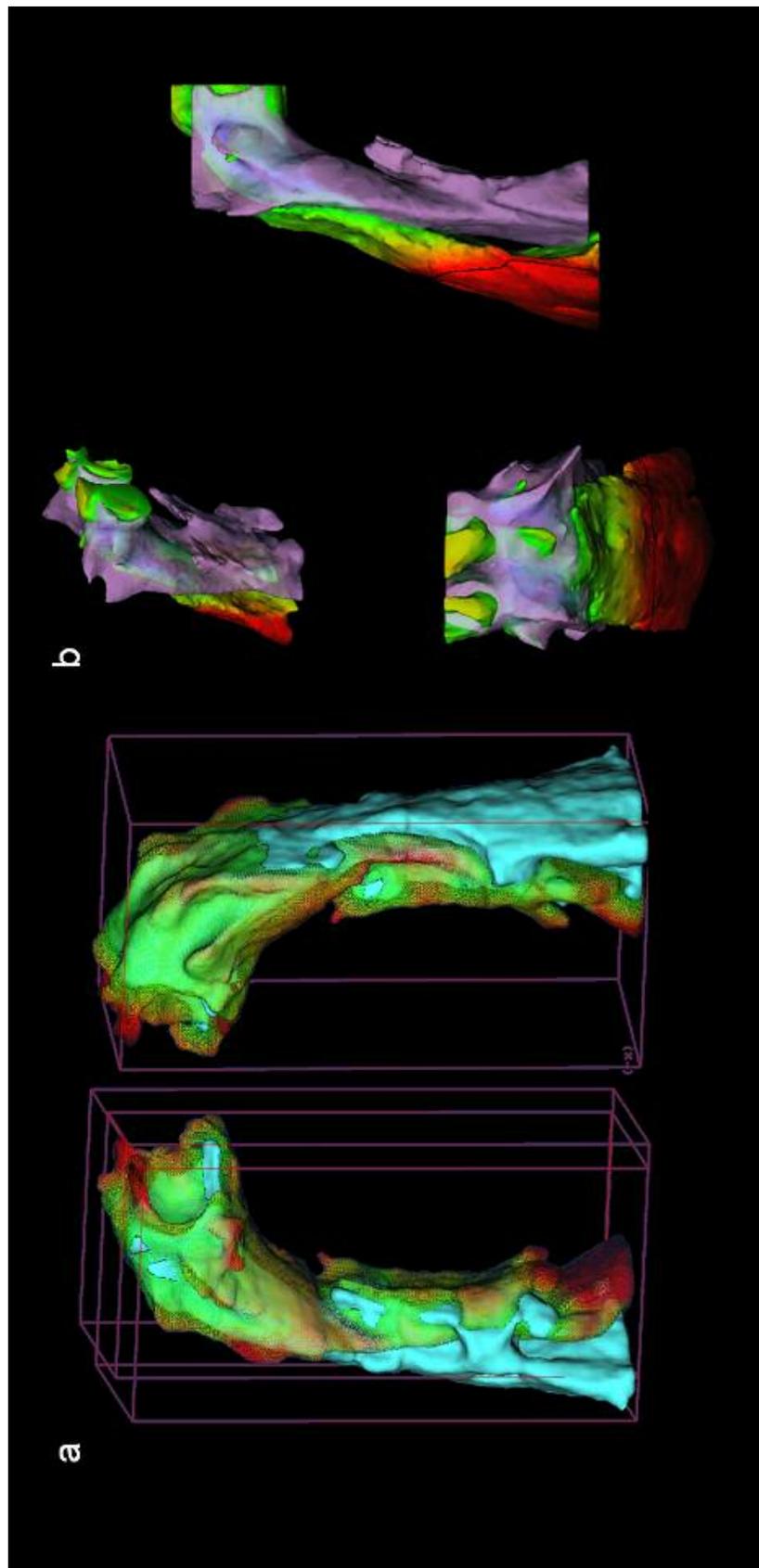


Figure 7. Registration techniques for three dimensional data are being adapted for airway study use. (a) Pre- and post-mandibular advancement 3-D models of the airway registered on the cranial base (semi-automatic registration); (b) Inter-patient manual airway registration displaying a skeletal Class II individual and a skeletal Class I individual.



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