A 3-D AIRWAY COMPARISON BETWEEN HIGH AND LOW RISK PEDIATRIC SLEEP DISORDERED BREATHING PATIENTS

By

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Dedication

I would first like thank my parents for all the love and support throughout my life. They have taught me to always pursue my dreams and the value of hard work. I want to thank my incredible wife for being an amazing person. She has provided me with love and support during my residency and makes me smile each day. She fills my life with joy and I am incredibly thankful to have her in my life.

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Abstract

Introduction: Our objective is to determine if there is an anatomical difference in the upper airway of adolescents who were deemed to be high risk on the Pediatric Sleep Questionnaire (PSQ) compared to their low risk counterparts. **Methods:** Using the PSQ, Cone Beam Computed Tomography (CBCT) data was retrospectively analyzed for 20 high risk and 20 low risk patients. The high risk patients were matched for sex, BMI and age. Airway volumes were calculated for the nasal passage, nasopharyngeal airway and oropharyngeal airway. Maximum constriction was also measured for the nasopharyngeal airway and the upper airway, which was measured from Posterior Nasal Spine (PNS) to the inferior boarder of CV4. Linear measurements were also gathered for the nasopharynx length, retropalatal length, oropharynx length and the sagittal and vertical position of the hyoid bone. **Results:** A statistically significant difference was found for the nasal cavity volume, nasopharyngeal volume, oropharyngeal volume, constriction of the nasopharyngeal airway and the linear nasopharynx measurement. No differences were found with the constriction of the upper airway, retropalatal linear, retrolingual linear, hyoid to mandibular plane or hyoid horizontal. **Conclusions:** Sleep disordered breathing is a complex and multi-factorial disease in which there is a documented relationship between OSA and constriction of the upper airway. High risk patients for SDB exhibit a reduced upper airway volume and a constricted nasopharyngeal airway and nasal

passage. Orthodontic records taken with CBCT can aid in identification of an airway obstruction and help inform patients of a possible problem. SDB can not only affect the facial growth and development of the patient, but also impact the patients' overall health.

Keywords: Pediatric Sleep Questionnaire, Sleep disordered breathing, Cone Beam Computed Tomography

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REVIEW OF THE LITERATURE

Sleep is a major element in the early development of a child; as such, children spend almost one-half of their life asleep.[1] Sleep disordered breathing (SDB), a term which includes obstructive sleep apnea (OSA) and upper airway resistance syndrome, affects between one and four percent of young children.[2] SDB disrupts normal ventilation during sleep which can lead to neurocognitive and cardiovascular complications as well as disturbances in growth and mood.[2, 3]

The upper airway consists of the nasal cavity, oral cavity, nasopharynx, oropharynx, hypopharynx and larynx.[4] These sections allow for movement of air to the lungs and also participate in phonation and deglutition. [5] The upper airway requires proper function of musculature to create patency for air travel. Dilation of the airway lumen and active constriction of the airway during swallowing create an environment for proper function.[6] There are more than twenty upper airway muscles responsible for management of the airway lumen, which maintain its patency.[5]

Most children affected by OSA breathe normally while awake, but sleep induces changes in the respiratory system. These changes may result in clinically significant abnormalities in the upper airway function and gas exchange. OSA is a disorder of breathing during sleep that is characterized by episodic upper airway obstruction that interferes with normal respiratory

gas exchange.[7] Clinical manifestations of OSA in children includes continuous heavy snoring, excessive daytime somnolence, hyperactivity, failure to thrive, frequent upper airway infections and restlessness during sleep.[8]

Sleep disordered breathing (SDB) interrupts normal breathing due to collapse of the airway by the pharyngeal and tongue muscles as they relax during sleep.[9] In children, OSA is thought to be secondary to a combination of enlargement of the lymphoid tissues (tonsils and adenoids) and sometimes, obesity, as well as the reductions in neuromuscular tone.[10] Decreased mandibular and maxillary lengths, skeletal retrusion, increased lower facial height, small posterior airway space and inferiorly positioned hyoid bone are all predisposing factors for OSA.[11] The leading anatomic factor associated with childhood OSA is adenotonsillar hypertrophy. [1, 12, 13] Consequently, adenotonsillectomy is the first-line surgical treatment for pediatric OSA patients.[14] Chervin et al. demonstrated significant improvement in neurobehvorial issues following adenotonsillectomy. [15] Marus et al. suggested children with SDB had a structurally narrow airway which predisposed them to airway obstruction, typically from adenotonisllar hypertrophy. [16]

Soft tissue and boney structures also help form the upper airway. The walls of the upper airway are formed by the tonsils, soft palate, uvula, tongue and lateral pharyngeal walls.[17] In addition to creating the walls of the upper

airway, these soft tissues can also influence the air flow. Adeno-tonsillar hypertrophy and soft palate enlargement have been linked to impeding air flow through the upper airway and manifesting as symptoms associated with sleep disordered breathing.[18, 19] The size and shape of the upper airway has also been linked to influencing air flow. Soft palate enlargement and upper airway length have been shown to be more prevalent in patients with sleep disordered breathing.[18, 20] Overall, individuals with decreased upper airway diameter have increased resistance to flow and are linked to sleep disordered breathing. [20, 21]

Boney structures may also help determine airway size. Studies have shown that the posterior displacement and decreased size of the mandible has been linked to obstructive sleep apnea.[18, 22] However, Schiffman et al. showed a smaller mandible was not a feature in children with sleep disordered breathing, which is often linked to a decrease in airway volume.[23] Controversy surrounds another boney structure associated with the upper airway, the hyoid bone. The vertical position of hyoid bone has been shown to be related to airway volume and thus, often described as being a risk factor for obstructive sleep apnea. [18, 19, 21, 24-26] However, using lateral cephlograms, Graf et al. found no correlation between hyoid bone position and risk of sleep disordered breathing or posterior airway space. [27]

Throughout the course of a given day, our airway must adapt for postural changes. We move our heads, swallow, walk and talk. Despite these

changes, our airway maintains patency by managing the interactions between cervical postural and pharyngeal muscles.[28] During sleep, muscular control is decreased, transient decreases occur in ventilation and upper airway resistance is increased.[5] Obstructive sleep apnea is characterized by repetitive collapse of the upper airway, commonly defined as the soft tissue region bounded by the nasopharynx superiorly, the epiglottis inferiorly, the maxillomandibular complex anteriorly and the spinal column posteriorly. Collapse of the upper airway decreases its intra-luminal diameter and increases airway resistance further, in accordance with Pouiselle's Law.[29] This increased resistance to flow results in reductions in ventilation (hypopneas) or complete cessation of ventilation (apneas). These events lead to metabolic disturbances seen as respiratory acidosis due to hypoventilation and sleep disturbances.[29]

Collapse of the upper airway can be defined as those forces acting within the airway (intra-luminal) and those acting on the airway wall itself (extra-luminal). Whichever collapsing force is applied, the outcome is the same, decreased intra-luminal diameter and obstruction of airflow due to increased resistance to flow. The force needed to collapse the airway is determined using pressure-flow curves.[30, 31] Nasal airway pressure required to maintain airway patency is defined as the critical closing pressure (P_{crit}). Studies have shown that P_{crit} can be related to anatomical structures. Studies have shown

a correlation between the soft palate length in obese patients and airway length and hyoid-mandibular distances in non-obese patients.[32, 33]

During wakefulness, individuals are able to maintain airway patency. However, with sleep onset, this compensation is lost and the airway collapses.[34] The repetitive collapse of the upper airway during sleep is a characteristic of obstructive sleep apnea. In 2001, Malhotra et al. evaluated the collapsibility of the upper airway in both normal and apneic subjects during both sleep and wakefulness. [32] Using negative pressure pulses (NPP's), they concluded that collapsibility during wakefulness correlated significantly with collapsibility during sleep. Pharyngeal collapsibility during sleep was significantly greater during sleep as compared to wakefulness and they found apnea patients had a significantly greater pharyngeal collapsibility than control subjects during wakefulness as well. Generally, subjects with higher upper airway collapsibility during wakefulness had higher collapsibility during sleep. They noted that apneic patients had greater collapsibility than normal subjects.

Craniofacial anatomy plays a role in OSA, and screening for anatomical abnormalities is an important tool in its diagnosis.[11] Over the years, studies have been done to evaluate risk factors for OSA using radiographs. Radiographic evaluations have shown the presence of airway narrowing to increase the probability of predicting OSA on PSG.[35] Pracharktam et al. evaluated 2D lateral cephlograms to determine the feasibility of using a

specific set of cephalometric and anthropometric variables to classify people into a snoring and an OSA group. Using 28 patients diagnosed with OSA and 30 patients labeled as habitual snores, they measured thirteen cephalometric and four anthropometric data points. Of the measured data, they found hyoid bone to mandibular plane, body mass index and soft palate length had the highest predictive value in determining OSA and snoring.[19]

Graf et al. evaluated the prevalence of snoring and its correlation with cranial and upper airway morphology in young individuals with orthodontic treatment needs. [27] Using 2D lateral cephalograms obtained from 53 patients with parent reported snoring and 47 non snorers, they found posterior airway dimensions were significantly reduced in orthodontic adolescent patients that snored compared to the non-snoring controls. The sagittal position of the maxilla was also found to be significantly correlated to the posterior airway space, indicating a more forward maxilla was associated with larger sagittal posterior airway space dimensions at the maxillary level. While they found differences in posterior airway space and maxillary position, no difference was found in the hyoid position.

A cross sectional study by Banhiran et al. was aimed at comparing lateral cephalometric measurements of varying degrees of obstructive sleep disordered breathing and determine if there were radiographic variables that increased the risk of obstructive sleep apnea.[26] Using ten linear and five angular parameters from cephalograms collected from 188 adjust subjects,

47 controls and 141 patients with OSA, they found patients who had long mandibular plane to hyoid bone lengths, narrower posterior airway space and skull base angle increased the risks of moderate to severe OSA. Other imaging studies have shown obstructive sleep apnea patients to have a smaller pharyngeal airway and increased upper-airway soft tissues than normal subjects when assessed during wakefulness.[17, 36-38]

The airway is a three dimensional image. Traditional cephlograms which have been used measure airway depth cannot be accurately evaluated without a 3-D image.[39] Lateral cephalograms have many limitations. There are inherent errors in a 3D structure being distorted, magnified or superimposed on a 2D image. There is also a lack of cross-sectional area and volume information on a 2D image.[39] Tsolakis et al. studied the accuracy of CBCT volumetric measurement compared to acoustic rhinometry. Using 59 patients, they compared volumes and minimal cross-sectional areas from CBCT and rhinometry and found that CBCT airway volumetric measurement was as accurate as the gold standard- acoustic rhinometry. They concluded that CBCT is an accurate method for measuring anterior nasal volume, nasal minimal cross-sectional area, phyarngeal volume and phyarngeal minimal cross sectional area. [40, 41]

Knowing that upper airway morphology plays a role in the development of obstructive sleep apnea, studies have been performed to evaluate upper airway dimensions of sleep apnea patients compared to control subjects.

Buchanan et al. evaluated upper airway dimensions of obstructive sleep apnea and control subjects using cone beam computed tomography.[20] This retrospective study reviewed sixteen OSA patients and sixteen control subjects. The average area, average volume, total volume, and total length of the upper airway were computed. Width and anterior-posterior measurements were obtained on the smallest axial slice. The found that OSA subjects had a significantly smaller average airway area, average airway volume, total airway volume and mean airway width. OSA subjects had a significantly larger airway length measurement. They did find that the mean A-P distance was not significantly different between the two groups. They concluded that OSA patients have a smaller upper airway compared to controls with the exception of airway length.

Further three dimensional airway analysis were done by Abramson et al. where they evaluated forty four patients with OSA and compared them to fourteen control subjects.[42] Using CBCT scans, airway size and shape were analyzed using twelve parameters for airway size and four for shape. Their findings indicate the presence of OSA is associated with an increase in airway length. They also noted that airways that were more elliptical in shape and mediolaterally oriented (greater lateral/retroglossal anterioposterior dimension ratio) had a decrease tendency toward obstruction. El et al. presented a case report of a 32 year-old female showing significant changes in both the apnea-hypopnea index (AHI) and oropharyngeal volume following

maxillomandibular advancement.[43] Post-surgical AHI fell from 33.7 to 6.7 while also seeing a significant increase in airway volume. Suleiman et al. evaluated the validity of CBCT as one of the many predictive tools to help identify high risk cases of OSA in adults.[44] They found that while patients with OSA had larger body mass index and neck circumferences, they also showed significantly smaller airway narrowest cross-sectional areas and larger posterior nasal spine and second cervical vertebrae distances compared to non-OSA controls. They concluded that CBCT can provide findings that entail earlier referral of suspected adult patients with OSA for further assessment from a sleep physician.

While AT is the first-line surgical treatment for pediatric OSAS, the gold standard for diagnosing OSA is the nocturnal polysomnography (PSG).[11, 45] However, PSG can be expensive, time consuming and intrusive for some children. [13, 46] Knowing sleep disordered breathing is a multi-factorial disease, attempts have been made to develop questionnaires to aid in the screening of OSA and SDB.[1] The Berlin questionnaire and STOP questionnaire have both demonstrate moderately high levels of sensitivity for OSA screening.[47] Chervin et al. developed and validated a pediatric sleep questionnaire (PSQ) which provides practitioners with a screening tool for their patients.[48]

Using sleep questionnaires, studies have begun to analyze the airway of patients with obstructive sleep apnea. Lavanya et al. divided 206 patients into either a high-risk group or a control group based on results from the Berlin questionnaire.[21] They then analyzed digital cephalograms to measure both the upper airway diameter and mandibular-to-hyoid bone distance. Their results showed a significantly lower upper airway diameter and a significantly higher mandibular-to-hyoid bone distance in the high risk patients based on the Berlin questionnaire results. They suggested that utilizing these simple measurements to assess patients at a high risk of obstructive sleep apnea may play a vital role in the early diagnosis of this disease.[21] Enciso et al. compared airway volumes using CBCT data from 46 OSA patients with AHI >10 and 34 known snores with AHI <10.[9] The OSA patients were predominantly male and older who had larger neck size and larger body mass index than the snorers. The minimum cross-sectional area of the upper airway and its lateral dimension were significantly smaller in the OSA patients. They found that males over the age of 57, scoring “high risk” on the Berlin questionnaire and had a narrow upper airway lateral dimension (<17 mm) were identified as significant risk of OSA. They concluded that 3-dimensional CBCT airway analysis could be used as a tool to assess the presence and severity of OSA.

A recent study by Adisen et al. compared radiographic measurements of the upper airway in young adult patients with different risk levels for

obstructive sleep apnea syndrome.[49] Using 50 patients between 18-30 years of age who were referred for evaluation of impacted third molars, 25 high and 25 low risk patients were identified. Risk levels were determined by case record forms, which included habit history, a Berlin Questionnaire and the Epworth Sleepiness Scale. They found significant differences between risk groups for BMI, neck circumference, Epworth score, smoking status and both area and volume measurements of the upper airway. Hyoid to third cervical vertebra distance, hyoid to mandibular plane distance and tongue length were not statistically different between risk groups. Patients classified as high risk for OSA by the Berlin Questionnaire and the Epworth Sleepiness Scale showed significantly more constricted upper airways compared to the low risk group with the velopharynx having the most significant difference between the two groups. Adisen et al. suggest that radiographic measurements of the upper airway may be used as a predictor for OSA risk in a young population.[49]

Structural narrowing of the upper airway has been well reported in patients with obstructive sleep apnea.[9, 17, 19-21, 26, 27] Extensive cephalometric evaluations have been evaluated in an effort to aid in the diagnosis of this disease. Most of these studies, while sound, lack the three dimensional quality that represent the upper airway. CBCT studies have illustrated the importance of not only airway volume, constriction and length, but also morphology of the upper airway as it relates to OSA.

Sleep disordered breathing is a complex, multi-factorial disease in which there is a documented relationship between OSA and constriction of the upper airway. Currently, there are no studies evaluating the airway of adolescent patients using CBCT and the pediatric sleep questionnaire to evaluate the upper airway morphology associated with increased risk for OSA.

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STATEMENT OF THESIS

Our objective is to determine if there is an anatomical difference in the upper airway of adolescents who were deemed to be high risk on the Pediatric Sleep Questionnaire (PSQ) compared to their low risk counterparts. The anatomical variations between these two groups were explored.

Null Hypothesis: There is no anatomical difference in the upper airway of high and low risk adolescent patients using the Pediatric Sleep Questionnaire.

Alternative Hypothesis: There are anatomical differences in the upper airway of high and low risk adolescent patients using the Pediatric Sleep Questionnaire.

A 3-D Airway Comparison Between High and Low Risk Pediatric Sleep Disordered Breathing Patients

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ABSTRACT

Introduction: Our objective was to determine if there is an anatomical difference in the upper airway of high risk adolescent patients compared to their low risk counterparts. **Methods:** Using the Pediatric Sleep Questionnaire (PSQ), Cone Beam Computed Tomography (CBCT) data was retrospectively analyzed for 20 high risk and 20 low risk patients. The high risk patients were matched for sex, BMI and age. Airway volumes were calculated for the nasal passage, nasopharyngeal airway and oropharyngeal airway. Maximum constriction was also measured for the nasopharyngeal and the extended oropharyngeal airway, which was measured from posterior nasal spine (PNS) to the inferior boarder of CV4. Linear measurements were also gathered for the nasopharynx length, retropalatal length, oropharynx length and the sagittal and vertical position of the hyoid bone. **Results:** A statistically significant difference was found for the nasal cavity volume (p=.001), nasopharyngeal volume (p=.001), oropharyngeal volume (p=.034), constriction of the nasopharyngeal airway (p=.024) and the linear nasopharynx measurement (p=.026). No differences were found with the constriction of the upper airway, retropalatal linear, retrolingual linear, hyoid to mandibular plane or hyoid horizontal.

Conclusions: High risk patients for SDB exhibit a reduced upper airway volume and a constricted nasopharyngeal airway and nasal

passage. Orthodontic records taken with CBCT can aid in identification of an airway obstruction and help inform patients of a possible problem.

Keywords: Pediatric Sleep Questionnaire, Sleep disordered breathing, Cone Beam Computed Tomography

INTRODUCTION

Craniofacial anatomy plays a role in sleep disordered breathing (SDB), and screening for anatomical abnormalities is an important tool in its diagnosis.[1] Sleep disordered breathing is a complex, multi-factorial disease in which there is a documented relationship between obstructive sleep apnea (OSA) and constriction of the upper airway. Currently, there are no studies comparing the airway anatomy of adolescent patients based on their pediatric sleep questionnaire results using CBCT.

Sleep disordered breathing (SDB), a term which includes obstructive sleep apnea (OSA) and upper airway resistance syndrome, affects between one and four percent of young children.[2] SDB disrupts normal ventilation during sleep due to collapse of the airway by the pharyngeal and tongue muscles leading to increased resistance to airflow.[3] These disturbances can lead to behavioral, neurocognitive and cardiovascular complications as well as disturbances in growth and mood.[2, 4]

Most children affected by OSA breathe normally while awake, but sleep induces changes in the respiratory system. These changes may result in clinically significant abnormalities in the upper airway function and gas exchange. OSA is a disorder of breathing during sleep that is characterized by episodic upper airway obstruction that interferes with normal respiratory gas exchange.[5] Clinical manifestations of OSA in children includes continuous heavy snoring, excessive daytime somnolence, hyperactivity,

failure to thrive, frequent upper airway infections and restlessness during sleep.[6]

In children, OSA is thought to be secondary to a combination of enlargement of the lymphoid tissues (tonsils and adenoids) and sometimes, obesity, as well as the reductions in neuromuscular tone.[7] Decreased mandibular and maxillary lengths, skeletal retrusion, increased lower facial height, small posterior airway space and inferiorly positioned hyoid bone are all predisposing factors for OSA.[1] The leading anatomic factor associated with OSA is adenotonsillar hypertrophy, which may increase airway resistance. [8-10] Consequently, adenotonsillectomy (AT) is the first-line surgical treatment for pediatric OSA patients.[11] Chervin et al. demonstrated significant improvement in neurobehavorial issues following AT.[12] Marus et al. suggested children with SDB had a structurally narrow airway which predisposed them to airway obstruction, typically from adenotonsillar hypertrophy.[13]

While AT is the first-line surgical treatment for pediatric OSAS, the gold standard for diagnosing OSA is the nocturnal polysomnography (PSG).[1, 14] However, PSG can be expensive, time consuming and intrusive for some children. [10, 15]

Craniofacial anatomy plays a role in OSA, and screening for anatomical abnormalities is an important tool in its diagnosis.[1] Over the years, studies

have been conducted to evaluate risk factors for OSA using radiographs. Radiographic evaluations have shown the presence of airway narrowing to increase the probability of predicting OSA on PSG.[14] Pracharktam et al. evaluated 2D lateral cephalograms to identify subjects with OSA and found hyoid bone to mandibular plane, body mass index and soft palate length had the highest predictive value.[16] Graf et al. found posterior airway dimensions were significantly reduced in orthodontic adolescent patients that snored compared to the non-snoring controls while finding no difference in the hyoid position.[17] Banhiran et al. found patients who had long mandibular plane to hyoid bone lengths, narrower posterior airway space and skull base angle increased the risks of moderate to severe OSA.[18]

A cross sectional study by Banhiran et al. was aimed at comparing lateral cephalometric measurements of varying degrees of obstructive sleep disordered breathing and determine if there were radiographic variables that increased the risk of obstructive sleep apnea.[18] Using ten linear and five angular parameters from cephalograms collected from 188 adjust subjects, 47 controls and 141 patients with OSA, they found patients who had long mandibular plane to hyoid bone lengths, narrower posterior airway space and skull base angle increased the risks of moderate to severe OSA. Other imaging studies have shown obstructive sleep apnea patients to have a smaller pharyngeal airway and increased upper-airway soft tissues than normal subjects when assessed during wakefulness.[19-22]

The airway is a three dimensional image. Traditional cephalograms which have been used to measure airway depth cannot be accurately evaluated without a 3-D image.[23] Lateral cephalograms have many limitations. There are inherent errors in a 3D structure being distorted, magnified or superimposed on a 2D image. There is also a lack of cross-sectional area and volume on a 2D image.[23] Tsolakis et al. studied the accuracy of cone beam computed tomography (CBCT) volumetric measurement. Using a sample of 59 subjects (mean age, 15± 3.8 years), they found that CBCT airway volumetric measurement was as accurate as the gold standard-acoustic reflection.[24]

As CBCT usage is becoming increasing more common, studies have begun evaluating upper airway volumes in patients diagnosed with OSA. El et al. presented a case report of a 32 year-old female showing significant changes in both the apnea-hypopnea index (AHI) and oropharyngeal volume following maxillomandibular advancement.[25] Post-surgical AHI fell from 33.7 to 6.7 while also seeing a significant increase in airway volume. Suleiman et al. evaluated the validity of CBCT as one of the many predictive tools to help identify high risk cases of OSA in adults.[26] They found that while patients with OSA had larger body mass index and neck circumferences, they also showed significantly smaller airway narrowest cross-sectional areas and larger posterior nasal spine and second cervical vertebrae distances compared to non-OSA controls. They concluded that CBCT can provide findings that entail

earlier referral of suspected adult patients with OSA for further assessment from a sleep physician.

Sleep disordered breathing is a multi-factorial disease.[8] As such, attempts have been made to develop questionnaires to aid in the screening of OSA and SDB. The Berlin questionnaire and STOP questionnaire have both demonstrate moderately high levels of sensitivity for OSA screening in adults.[27] Chervin et al. developed and validated a pediatric sleep questionnaire (PSQ) which provides practitioners with a screening tool for their adolescent patients.[28]

Using sleep questionnaires, studies have begun to analyze the airway of patients with obstructive sleep apnea. Enciso et al. compared airway volumes using CBCT data from 46 OSA patients with AHI >10 and 34 known snores with AHI <10.[3] They found that males over the age of 57, scoring “high risk” on the Berlin questionnaire and had a narrow upper airway lateral dimension (<17 mm) were identified as significant risk of OSA. They concluded that 3-dimensional CBCT airway analysis could be used as a tool to assess the presence and severity of OSA.

A recent study by Adisen et al. compared radiographic measurements of the upper airway in young adult patients with different risk levels for obstructive sleep apnea syndrome.[29] Using 50 patients between 18-30 years of age who were referred for evaluation of impacted third molars, 25 high and

25 low risk patients were identified. Risk levels were determined by case record forms, which included habit history, a Berlin Questionnaire and the Epworth Sleepiness Scale. They found significant differences between risk groups for BMI, neck circumference, Epworth score, smoking status and both area and volume measurements of the upper airway. Hyoid to third cervical vertebra distance, hyoid to mandibular plane distance and tongue length were not statistically different between risk groups. Patients classified as high risk for OSA by the Berlin Questionnaire and the Epworth Sleepiness Scale showed significantly more constricted upper airways compared to the low risk group with the velopharynx having the most significant difference between the two groups. Adisen et al. suggest that radiographic measurements of the upper airway may be used as a predictor for OSA risk in a young population.[29]

Sleep disordered breathing is a complex, multi-factorial disease in which there is a documented relationship between OSA and constriction of the upper airway. Currently, there are no studies evaluating the airway of adolescent patients using CBCT and the pediatric sleep questionnaire to evaluate the risk for OSA.

Materials and Methods

The Case Western Reserve University (CWRU) Institutional Review Board (IRB) approved this study (IRB-2016-1640). Data was collected retrospectively from records of patients being treated at Case Western Reserve School of Dental Medicine, Orthodontic Department. Records were used to identify the 20 high risk patients, as found using their Pediatric Sleep Questionnaire (Figure 1). The Pediatric Sleep Questionnaire (PSQ) is a 22 question survey. Any individual answering “yes” to more than .33 of all the responses is deemed high risk. Height, weight and date of birth gathered at the initial screening were later used to facilitate matching of the high and low risk groups. Diagnostic pre-treatment Cone Beam Computed Tomography (CBCT) scans (Hitachi CB MercuRay, Hitachi Medical Systems America) were used for evaluation of upper airway anatomy.

The following inclusion criteria was used:

1. Completed Pediatric Sleep Questionnaire (PSQ)
2. Cone Beam Computed Tomography (CBCT) taken
3. Height, weight and date of birth recorded
4. No craniofacial syndromes

All measurements were performed on de-identified CBCT scans using version 11.9.7.20 Dolphin3D imaging (Patterson Dental Supply, Inc., St. Paul, MN) software. One examiner performed all measurements (B.J.) and intra-rater reliability was performed on 10 randomly selected patients using alpha-

intraclass correlation 20 days following initial collection. All high risk patients identified were randomly matched to a low risk group for sex, age, and BMI.

3-D airway regions

Four regions were used to determine airway volume and constriction of the upper airway. The nasal passage (Figure 2), nasopharyngeal airway (Figure 3), oropharyngeal airway (Figure 4) and the upper airway (Figure 5) were all measured. Nasal passage was defined as the inferior boarder as a horizontal line through the palatal plane (anterior nasal spine- posterior nasal spine), extending to the posterior wall of the pharynx to the superior boarder where the nasal septum first fuses with the posterior wall of the pharynx anteriorly to the nares. The nasopharyngeal airway was defined by a triangular region extending horizontally from posterior nasal spine to the posterior wall of the pharynx, then to sella and back to posterior nasal spine. The oropharyngeal airway was defined superiorly by the palatal plane (anterior nasal spine-posterior nasal spine) to the posterior wall of the pharynx and inferiorly by a horizontal line through the most anterior-inferior point of the second cervical vertebrae. The upper airway was defined as the region extending from posterior nasal spine to the inferior border of the fourth cervical vertebrae.

3-D airway measurements

Using version 11.9.7.20 Dolphin3D imaging (Patterson Dental Supply, Inc., St. Paul, MN) software, total airway volume was measured for the nasal passage, nasopharyngeal airway and oropharyngeal airway. Minimal axial area was measured for the nasopharyngeal airway, oropharyngeal airway and the upper airway.

2-D airway measurements

A lateral cephalogram was constructed from the Cone Beam Computed Tomography and linear measurements were collected. Nasopharynx length was measured as the distance from PNS to posterior pharyngeal wall. Retropalatal length was measured as the distance between the most posterior point of the soft palate and the posterior pharyngeal wall. Oropharynx length was measured as the distance from the mandibular inferior boarder in the posterior area of the tongue to the posterior pharyngeal wall. The sagittal and vertical position of the hyoid bone was calculated by the most anteriorsuperior point of the hyoid bone (Hyoidale) to the posterior pharyngeal wall and mandibular plane, respectively (Figure 6 and Figure 7).

Statistical Analysis

Statistical analysis was performed with SPSS version 17.0 for Windows (Statistical Package for the Social Sciences, SPSS 17.0, Inc- Chicago, IL, USA). Intra-rater reliability was tested using 10 randomly selected patients, 20

days after initial measurements. Using alpha-intraclass correlation, all measurements were found to have high reliability, greater than 0.90 (table III). Shapiro-Wilk analysis was used to determine normality for each data point (table IV). A Mann-Whitney-U test was used to determine significance of non-normally distributed data (table V). A one tailed paired sample T-test was used to evaluate normally distributed data (table VI). The significance level, alpha, was set at 0.05 for each test.

Results

A statistically significant difference was found for the nasal cavity volume, nasopharyngeal volume, oropharyngeal volume, constriction of the nasopharyngeal airway (figure 8) and nasopharynx linear. No difference was found for upper airway constriction, retropalatal linear, retrolingual linear, hyoid to mandibular plane or hyoid horizontal.

Discussion

The pediatric sleep questionnaire (PSQ) is a tool which is becoming a common addition to our orthodontic evaluation process. While the polysomnography (PSG) is the gold standard for diagnosis of SDB, the PSQ is easy to administer, score and has little expense associated; making it an attractive option to detect patients with a high risk for sleep disordered breathing. The PSQ has a sensitivity of 0.85 and specificity of 0.87, making it

a reliable instrument to identify sleep issues in children when a PSG is not available.[28]

Obesity is factor that is often attributed to increased risk of adult OSA. [16, 26, 30] Obesity is not often identified as a common cause of SDB in children; however, the prevalence of OSA in obese children is higher than in non-obese children. In children with a body mass index >28, there is a four to five fold increase in risk of OSA.[30] In our study, we had two individuals in the high risk group and one in the low risk group with BMI's >28. Matching for age, sex and BMI, we still found a statistically significant difference in upper airway measurements. While BMI is clearly a risk factor for adult OSA, it is unclear the influence BMI places in a child's risk of OSA.

Evaluation of hyoid bone position is another radiographic landmark used in OSA risk determination. A relationship between lower positioned hyoid bones and increased risk of OSA has been well documented. [16, 31] However, other studies fail to show such a relationship.[17, 29, 32] In our study, we did not find a horizontal or a vertical difference in hyoid position between the high and low risk groups.

Cone beam computed tomography has many advantages compared to traditional 2D lateral cephalograms. Lateral cephalograms have inherent errors in a 3D structure being distorted, magnified or superimposed to create a 2D image. There is also a lack of cross-sectional area and volume

information on a 2D image.[23] Tsolakis et al. studied the accuracy of CBCT volumetric measurement compared to acoustic reflection- an accepted method to measure upper airway volume.[24] Using 59 patients, they compared volumes and minimal cross-sectional areas from both modalities. They found no statistical difference in airway measurements between CBCT and acoustic reflection. They concluded that CBCT is an accurate method for measuring anterior nasal volume, nasal minimal cross-sectional area, pharyngeal volume and pharyngeal minimal cross sectional area.

Using CBCT data, evaluation of upper airway volumes and minimal axial areas are a luxury we did not have with 2D lateral cephalograms. Using this technology, studies have found significantly smaller average airway area, average airway volume, total airway volume, cross-sectional areas and mean airway width. [26, 32] While their study was on adults, our adolescent sample showed similar findings- high risk patients had a smaller upper airway volume. In addition to decreased volumes, our high risk sample also displayed a smaller minimal axial area for the upper airway and nasopharyngeal airway.

The prevalence of SDB in an orthodontic seeking population is 7%.[33] As orthodontic professionals, we routinely take x-rays as part of our initial new patient exam. Evaluation of the upper airway and PSQ to help identify at risk patients could have a profound impact on facial growth and overall health.

Conclusions

Sleep disordered breathing is a complex and multi-factorial disease in which there is a documented relationship between OSA and constriction of the upper airway. High risk patients for SDB exhibit a reduced upper airway volume and a constricted nasopharyngeal airway and nasal passage. Orthodontic records taken with CBCT can aid in identification of an airway obstruction and help inform patients of a possible problem. SDB can not only affect the facial growth and development of the patient, but also impact the patients' overall health.

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APPENDIX A: TABLES

Table I. Descriptive summaries of high and low risk groups

	High Risk	Low Risk
Nasal Cavity (CC) *	15.8 +/- 3.0 (10.9-22.6)	19.6 +/- 3.9 (12.5-29.2)
Nasopharyngeal Airway (CC) *	3.7 +/- 1.6 (1.5-7.1)	5.7 +/- 2.1 (2.8-9.6)
Oropharyngeal Airway (CC) *	8.7 +/- 1.6 (4.1-14.9)	10.2 +/- 3.6 (5.2-19.7)
Nasopharyngeal Airway (mm2) *	136.4 +/- 79.4 (48.0-309.0)	195 +/- 94.3 (81.3- 389.9)
Upper Airway (mm2)	131.4 +/- 64.7 (31.0-269.0)	173.3 +/- 99.3 (56.0-414.0)
Nasopharynx (mm) *	15.0 +/- 5.2 (2.9-24.2)	18.0 +/- 3.4 (13.7-24.1)
Retropalatal (mm)	7.8 +/- 2.2 (3.3-10.3)	8.4 +/- 2.9 (4.7-16.8)
Retrolingual (mm)	10.3 +/- 2.4 (6.1-15.4)	9.3 +/- 3.4 (3.5-17.6)
Hyoid to Mandibular Plane (mm)	14.2 +/- 7.1 (4.1-27.3)	13.1 +/- 4.2 (6.2-22.0)
Hyoid Horizontal (mm)	28.8 +/- 3.2 (23.2-34.3)	28.8 +/- 3.2 (23.2-33.7)

*denotes statistical significance at α=.05

Table II. Sample Distribution

	High Risk	Low Risk
Age	14.04	14.07
Males	10	10
Females	10	10
BMI	20.6	20.5
PSQ	.43	.003

Table III. Intra-Rater Reliability

Nasal Cavity	Nasopharyngeal	Nasopharyngeal	Oropharyngeal	Oropharyngeal	Nasopharynx	Retropalatal	Retrolingual	Hyoid to mand	Hyoid horizontal
0.964	0.991	0.939	0.991	0.999	0.975	0.905	0.937	0.995	0.95

Table IV. Shapiro-Wilk Normality Testing

Variable	P-Value
Nasal Cavity Volume	.216
Nasopharynx Volume	.046 *
Nasopharynx Constriction	.002 *
Oropharynx Volume	.051
Upper airway Constriction	.001 *

Variable	P-Value
Nasopharynx Linear	.071
Retropalatal Linear	.044 *
Retrolingual Linear	.930
Hyoid to Mandible Linear	.097
Hyoid Horizontal Linear	.287

*denotes statistical significance at α=.05

Table V. MANN-WHITNEY U TEST

Variable	P-Value
Nasopharynx Volume	.001 *
Nasopharynx Constriction	.024 *
Upper airway Constriction	.201
Retropalatal Linear	.862

*denotes statistical significance at α=.05

Table VI. PAIRED SAMPLES T-TEST

Variable	P-value
Nasal Cavity Volume	.0007 *
Oropharynx Volume	.0338 *
Nasopharynx Linear	.0259 *
Retrolingual Linear	.1475
Hyoid to Mandible Linear	.2460
Hyoid Horizontal Linear	.5000

*denotes statistical significance at α=.05

APPENDIX B: FIGURES

Figure 1. Pediatric Sleep Questionnaire



SCHOOL OF DENTAL MEDICINE
CASE WESTERN RESERVE UNIVERSITY

DEPARTMENT OF ORTHODONTICS

PEDIATRIC SLEEP QUESTIONNAIRE
PATIENTS UNDER 18 YEARS OF AGE

Last Name ..... First Name ..... Age ..... Date .....

Please answer on behalf of your child for the past month.
If you don't know, circle "?"

While sleeping, does your child . . .

1. snore more than half the time? ..... Yes / No / ?
2. always snore? ..... Yes / No / ?
3. snore loudly? ..... Yes / No / ?
4. have trouble breathing, or struggle to breathe? ..... Yes / No / ?
5. have "heavy" or loud breathing? ..... Yes / No / ?
6. have you ever seen your child stop breathing during the night? ..... Yes / No / ?

Does your child . . .

7. tend to breathe through the mouth during the day? ..... Yes / No / ?
8. have a dry mouth on waking up in the morning? ..... Yes / No / ?
9. occasionally wet the bed? ..... Yes / No / ?
10. wake up feeling unrefreshed in the morning? ..... Yes / No / ?
11. have a problem with sleepiness during the day? ..... Yes / No / ?
12. has a teacher commented that your child appears sleepy during the day? ..... Yes / No / ?
13. is it hard to wake your child up in the morning? ..... Yes / No / ?
14. does your child wake up with headaches in the morning? ..... Yes / No / ?
15. did your child stop growing at a normal rate at any time since birth? ..... Yes / No / ?
16. is your child overweight? ..... Yes / No / ?

My child often . . .

17. does not seem to listen when spoken to directly. ..... Yes / No / ?
18. has difficulty organizing task and activities. ..... Yes / No / ?
19. is easily distracted by extraneous stimuli. ..... Yes / No / ?
20. fidgets with hands or feet or squirms in seat. ..... Yes / No / ?
21. is 'on the go' or often acts as if 'driven by a motor'. ..... Yes / No / ?
22. interrupts or intrudes on others (e.g. butts into conversations or games) ..... Yes / No / ?

Figure 2. Nasal Cavity Volume Measurement

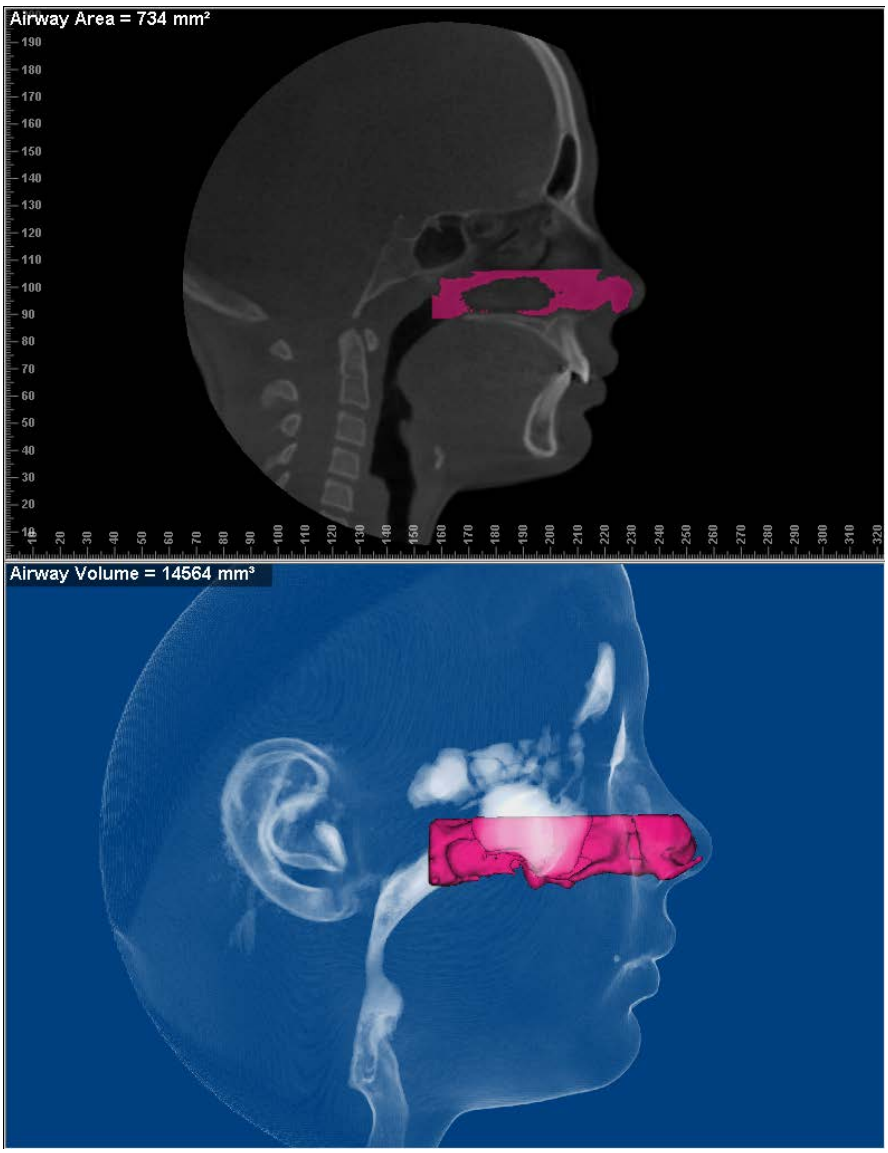


Figure 3. Nasopharyngeal Airway Volume Measurement

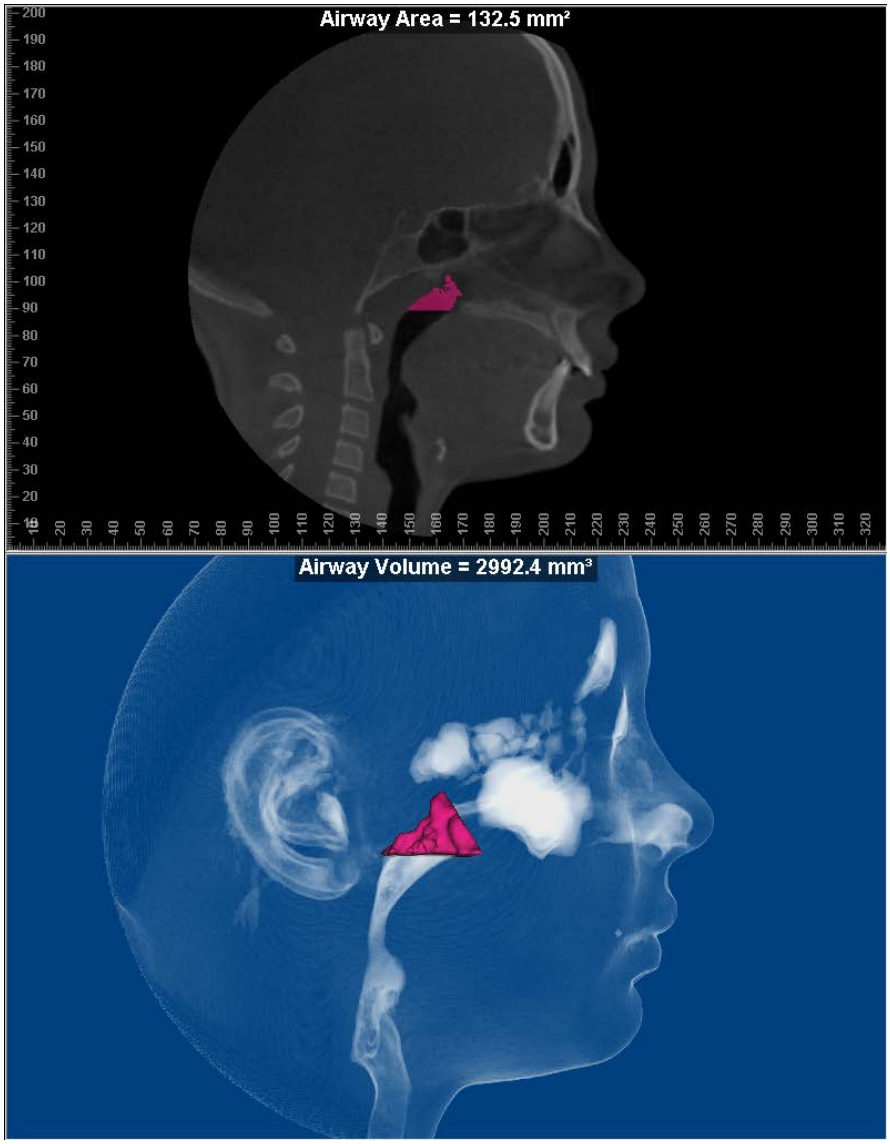


Figure 4. Oropharyngeal Airway Volume Measurement

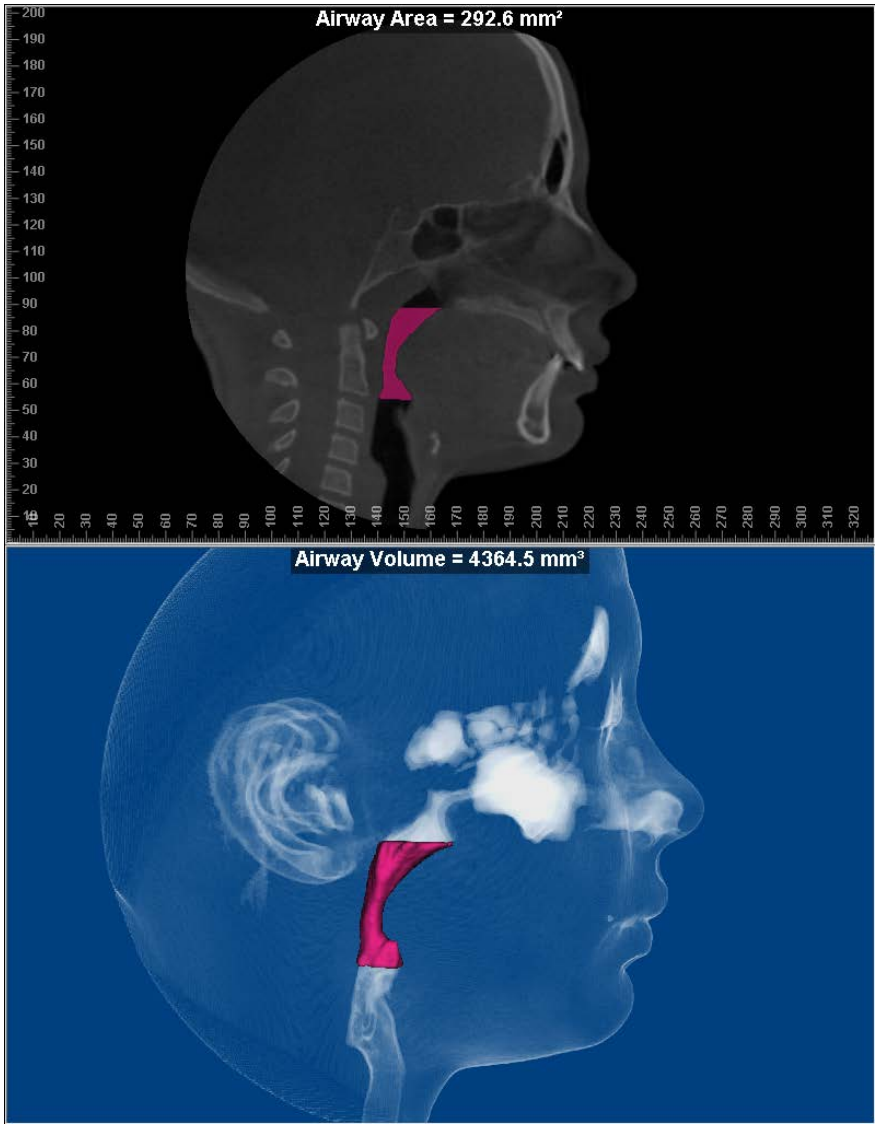


Figure 5. Upper Airway Constriction Measurement

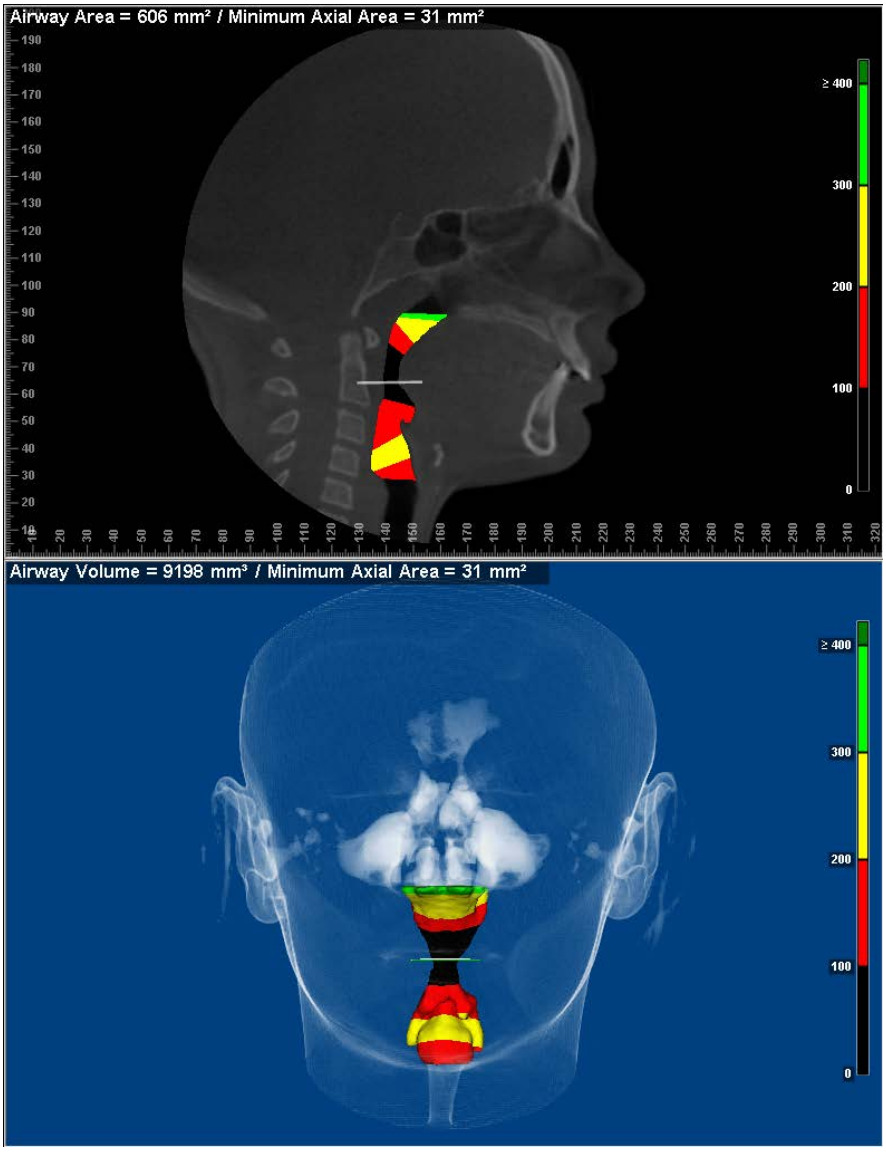


Figure 6. Linear Cephalometric Measurement Points

Measurement	Landmarks	Definition
Nasopharynx length	**PNS-PPW (mm)**	**Measured as the distance from Posterior Nasal Spine (PNS) to posterior pharyngeal wall (PPW).**
Retro-palatal length	**PSP-PPW (mm)**	**Measured as the distance between the most posterior point of the soft palate (PSP) and the posterior pharyngeal wall (PPW).**
Retro-lingual length	**PTO-PPW (mm)**	**Measured as the distance from the mandibular inferior border in the posterior area of the tongue (PTO) to the posterior pharyngeal wall (PPW), which can be defined as retro-lingual region.**
Hyoid bone horizontal position	**H-PPW (mm)**	**Measured as the distance between the most anterosuperior point of hyoid bone (H) and PPW.**
Hyoid bone vertical position	**H-MP (mm)**	**Measured from the most anterosuperior point of hyoid bone (H) to the mandibular plane (MP).**

Figure 7. Linear Cephalometric Data Points

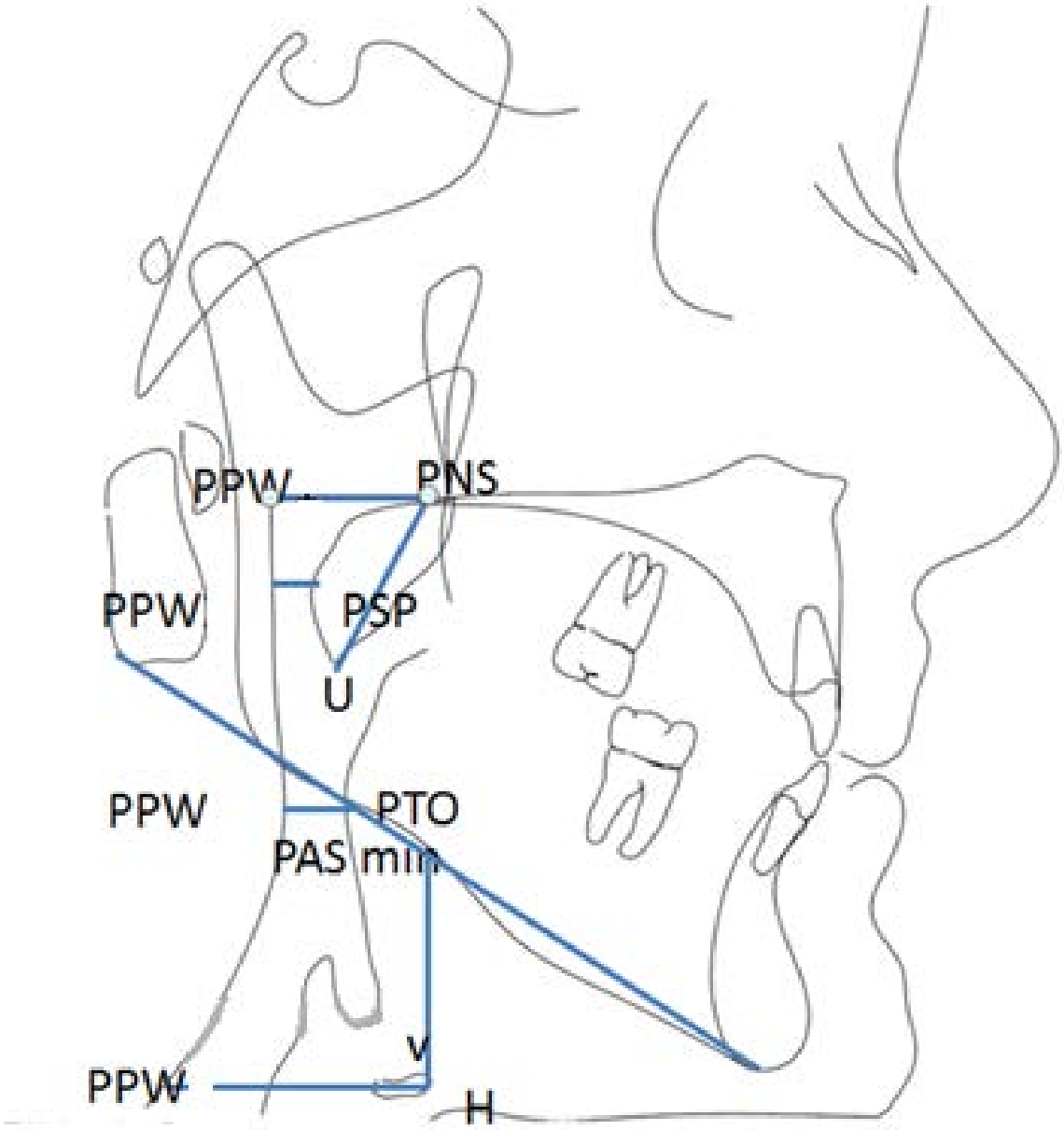
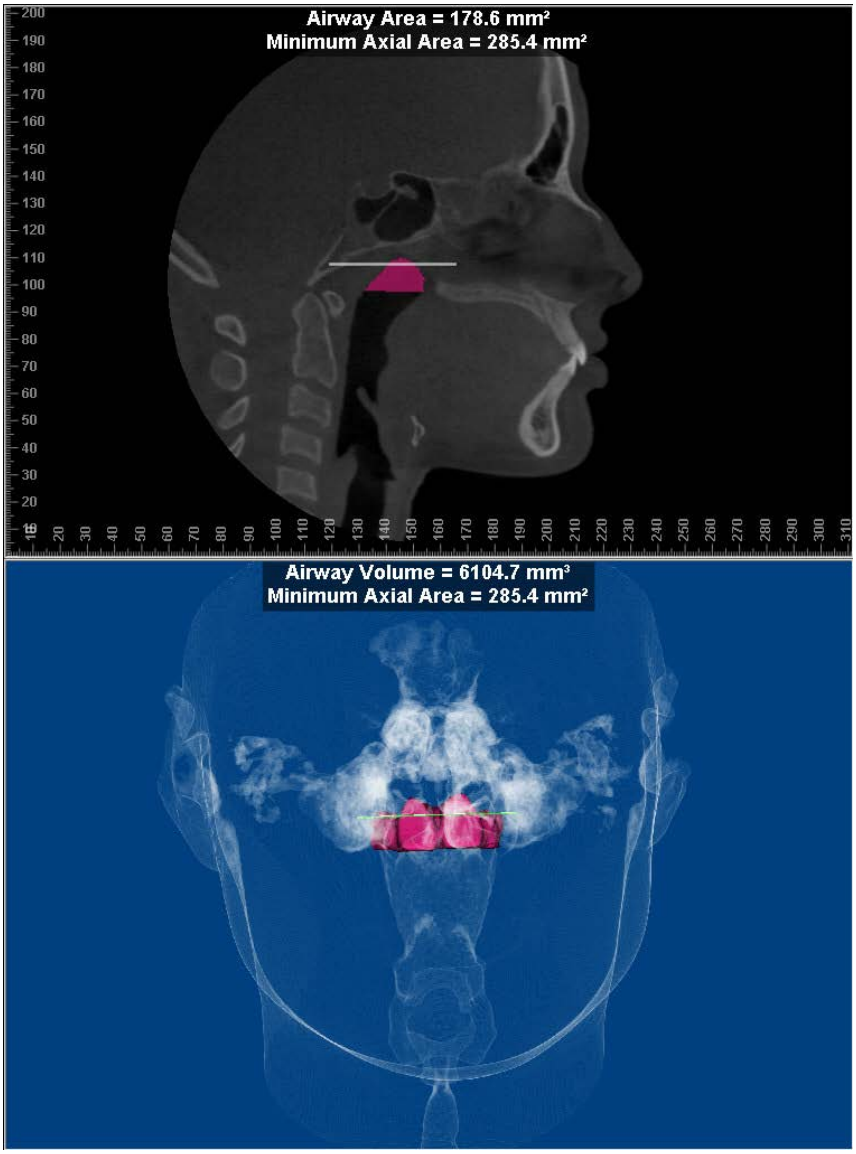
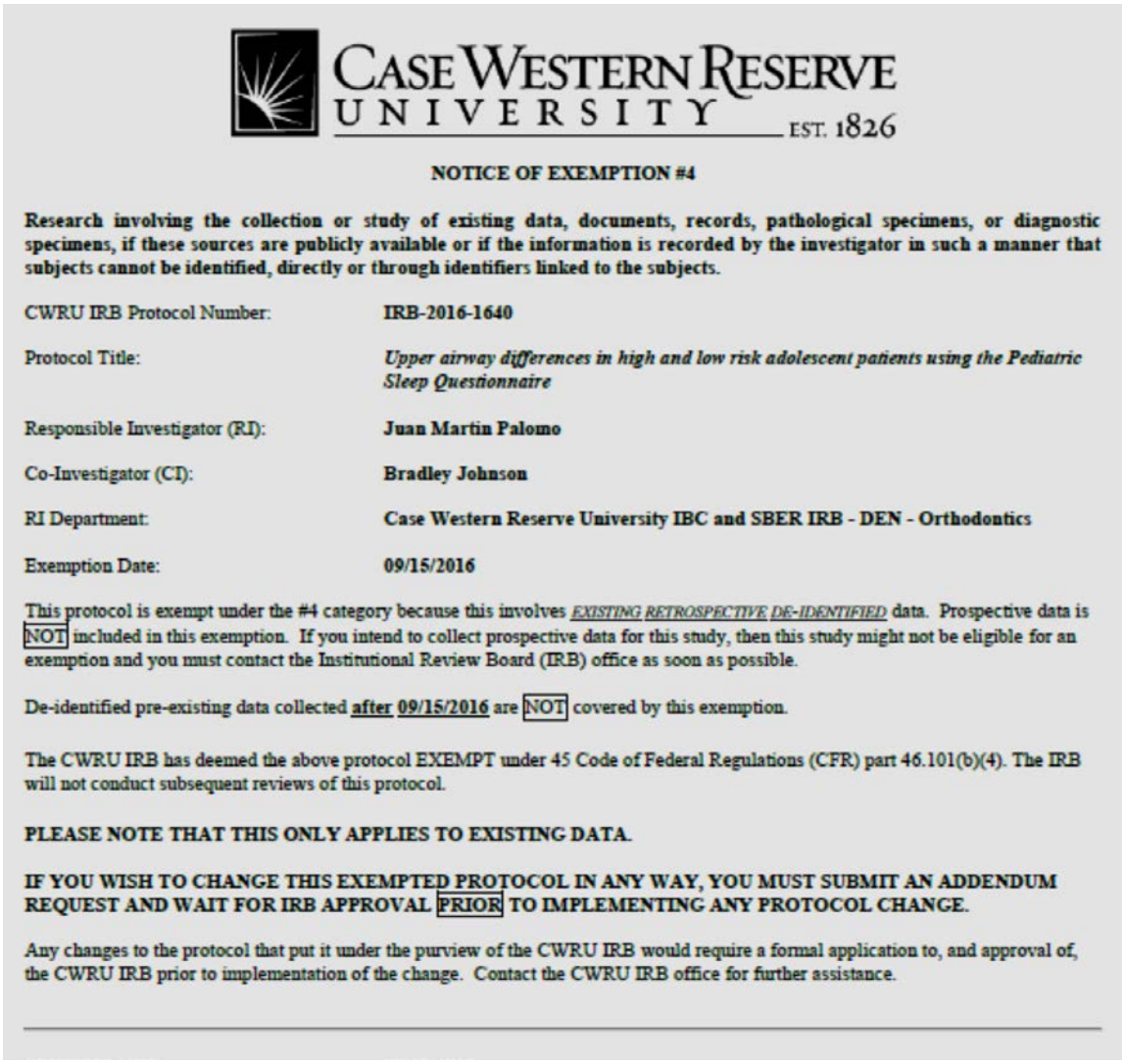


Figure 8. Nasophargneal Airway Constriction



APPENDIX C: IRB APPROVAL

Appendix C. IRB Approval



CASE WESTERN RESERVE UNIVERSITY EST. 1826

NOTICE OF EXEMPTION #4

Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

CWRU IRB Protocol Number:	**IRB-2016-1640**
Protocol Title:	***Upper airway differences in high and low risk adolescent patients using the Pediatric Sleep Questionnaire***
Responsible Investigator (RI):	**Juan Martin Palomo**
Co-Investigator (CI):	**Bradley Johnson**
RI Department:	**Case Western Reserve University IBC and SBER IRB - DEN - Orthodontics**
Exemption Date:	**09/15/2016**

This protocol is exempt under the #4 category because this involves *EXISTING RETROSPECTIVE DE-IDENTIFIED* data. Prospective data is NOT included in this exemption. If you intend to collect prospective data for this study, then this study might not be eligible for an exemption and you must contact the Institutional Review Board (IRB) office as soon as possible.

De-identified pre-existing data collected **after 09/15/2016** are NOT covered by this exemption.

The CWRU IRB has deemed the above protocol EXEMPT under 45 Code of Federal Regulations (CFR) part 46.101(b)(4). The IRB will not conduct subsequent reviews of this protocol.

PLEASE NOTE THAT THIS ONLY APPLIES TO EXISTING DATA.

IF YOU WISH TO CHANGE THIS EXEMPTED PROTOCOL IN ANY WAY, YOU MUST SUBMIT AN ADDENDUM REQUEST AND WAIT FOR IRB APPROVAL PRIOR TO IMPLEMENTING ANY PROTOCOL CHANGE.

Any changes to the protocol that put it under the purview of the CWRU IRB would require a formal application to, and approval of, the CWRU IRB prior to implementation of the change. Contact the CWRU IRB office for further assistance.

APPENDIX D: RAW DATA

Appendix D. Raw Data

PTID	Age	Height	Weight	BMI	Sex	PSQ	Nasopharynx	Oropharyngeal	Oropharynx	nasopharynx	nasopharynx const	Nasopharx	retropalatal	retrolingual	hypopharynx	hyoid- mand	hyoid horizon
							(mm3)	(mm3)	(mm2)								
MC 284	9.05	5'2"	97 lbs	17.7	1	0.77	21577	8557	154	2469.00	50.40	15	8.5	15.4	14.6	11.7	26.2
TO 121	11	5'1"	140 lbs	26.5	1	0.55	15174	8855	108	2426.70	48.00	17.9	8.1	11.9	15	15	34.3
CL 105	12	4'11"	87 lbs	17.6	1	0.5	17374	4134	46	2496.5	80.3	20.8	3.3	7.9	11.6	8.2	24.1
NI 64	12	5'4"	110	18.9	2	0.33	15818	7736	152	7076.2	289.4	16.4	9	10	14.8	9.2	29.1
BR 324	13	5'2"	90 lbs	16.5	2	0.36	18793	7943	128	2754.7	148.2	22.9	8.5	8.1	12.3	4.7	24.1
GO209	13	5'1"	150	28.3	2	0.47	19975	7470	110	5101.5	214.2	15.9	10.3	12.2	10.2	8.6	31.1
OW25	13	5'4"	110 lbs	18.9	1	0.35	16620	7314	90	2308.4	91.9	9.1	8.5	13.8	13.4	8	31.9
LI 126	13	4'6"	75	18.1	1	0.33	14564	4365	31	2700.9	96.8	16	3.7	6.1	11.2	13.5	26.6
FA 73	14.1	4'11"	85 lbs	17.2	2	0.49	15921	9908	91	2929.10	142.00	13.1	9.8	9.6	13.9	16.7	26.4
MC 290	14.1	5'11"	120 lbs	16.7	2	0.38	14568	10905	121	4,302.00	85.40	12.5	9	12.3	14.8	10.7	33.7
JA 194	14.1	4'10.5"	91 lbs	18.4	1	0.36	14271	8600	154	5792	309	18.3	10	8.5	16.1	13.2	29.5
KA 192	15	4'9"	112 lbs	24.2	1	0.45	22604	10864	190	4799.8	175.5	24.2	10	9.8	12.4	11.1	23.2
BU 196	15.1	5'11"	210	29.3	2	0.36	10904	14969	76	1929.7	80	2.9	6.5	12.4	13.8	27.1	32.9
ME 166	15.1	5'2"	108 lbs	19.8	1	0.5	16255	11549	269	5001	103	12	9.2	11.7	11.9	23	30.2
MU 119	15.1	4'11"	93 lbs	18.8	1	0.54	14269	7255	112	2163.6	99	15.5	4.7	8.6	15.5	20.1	27.7
BA 358	16	6'0"	160 lbs	21.7	2	0.42	15587	11775	248	6211.5	271.6	15.5	9.4	9.6	16.7	21.6	29.8
SZ 24	16	5'1"	104 lbs	19.6	2	0.33	14040	5568	68	2622.3	133.2	8.5	3.9	12.9	13.7	21.4	31.2
CH 159	16.1	5'8"	170 lbs	25.8	2	0.368	13194	6813	88	1517.4	58.6	8	6.3	7.1	13.4	27.3	28.2
CZ 7	17	5'2"	100 lbs	18.3	2	0.45	12385	7403	158	5166.4	81.5	18	8.7	8.8	14.4	4.1	28.2
CO 291	17	5'4"	110 lbs	18.9	1	0.375	12394	10838	233	4197.2	170.6	16.9	7.9	8.5	15.2	8.4	26.7
PTID	Age	Height	Weight	BMI	Sex	PSQ	Nasopharynx	Oropharyngeal	Oropharynx	nasopharynx	nasopharynx const	Nasopharx	retropalatal	retrolingual	hypopharynx	hyoid- mand	hyoid horizon
							(mm3)	(mm3)	(mm2)								
KO 191	9.03	4'8"	70	15.7	1	0.05	18593	12695	117	2762.4	81.3	13.7	5.6	13.3	17.9	16.7	29.1
BR 411	11.1	5'1"	145.4	27.4	1	0	16448	6291	68	3471.5	100.5	15.2	6.9	3.5	11	11.3	23.2
DA 280	12	5'4"	130	22.3	1	0	16866	8834	77	3876.8	101.7	14.2	6.7	10.8	7.7	9.9	28.4
SH 231	12.1	5'5"	153	25.5	2	0	16536	6918	108	6064.9	135.7	15.1	4.7	5.5	7.1	13.1	24.6
JI 15	13	5'5"	108	18	2	0	15369	8869	164	5155.7	87.5	18.3	9.7	11.7	15.8	6.2	32.5
BU 224	13.1	5'4"	168	28.8	2	0	23486	7673	147	8365.4	303	17.5	7.5	7.5	14.2	12.7	33.3
ME 175	13.1	4'10"	91	19	1	0.09	20213	6668	112	3566.3	117.3	15.4	6.9	11.4	12.2	10.3	28.6
NA 87	13.1	5'4"	102	17.5	1	0	19178	8818	190	3076.4	158.5	14.1	8.7	8.7	11.6	14	24.3
RA 120	14	4'9"	79	17.1	2	0	18902	5169	56	5481.2	164	15.4	5.5	6.9	6.1	22	25.4
FR 181	14.1	5'3"	93	16.5	2	0	21988	11110	135	5693.2	214.1	16.6	10	8.5	16.2	10.7	27.5
LE 228	14.1	5'3"	105	18.6	1	0.05	17644	7842	182	3006.6	110.5	16.2	7.9	9.2	13.5	14.8	24.5
FI 76	15	6'0"	163	22.1	1	0	24923	11822	94	8391.8	221.4	23.1	7.5	4.4	10.6	18.3	27.9
DA 272	15.1	5'6"	113	18.2	1	0	14967	13130	251	6104.7	285.4	24.1	11.9	11.4	15.8	9.1	29.4
CO 408	15.1	5'4"	117	20.1	1	0.09	19107	19364	414	8053.1	302	21.5	16.8	17.6	16.3	11.8	30.1
KR100	15	5'10"	133	19.1	2	0	19089	16577	364	9589.4	295.3	23.2	8.5	10.1	19.1	20.1	30.7
JO 366	15.1	5'7"	140	21.9	2	0.05	20477	9699	148	5889.8	144.5	20.6	5.8	6.7	14.8	12.8	31.2
ME 174	16	5'7"	128	20	2	0.09	23278	7854	152	6696	262.2	18.7	7.7	7.1	10	9.7	29.8
HY 5	16.1	5'7"	135	21.1	2	0.09	29164	11231	210	4810.9	120.7	15.8	9.1	8	10.3	16.3	32.9
WA346	17.1	5'10"	134	19.2	2	0	22981	13234	343	8909.1	389.9	23.1	13.1	12.7	20	6.6	33.7
HA657	16.1	5'2"	120	21.9	1	0.05	12457	10801	134	5401.3	316.3	17.3	7.1	11.4	10.6	14.8	28