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LONGITUDINAL AIRWAY CHANGES IN ADOLESCENTS USING CBCT

By

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Submitted in partial fulfillment of the requirements for the degree of Master of Science in Dentistry

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January 2010

DEDICATION

I would like to dedicate this thesis to:

My parents and brothers; you have always given me love and support no matter when, why, or where. Without a doubt, none of my accomplishments were possible without your help, advice, and encouragement. Thank you for being the best family I could ask for. I love you all from the bottom of my heart.

Clay Damon; you have always been my mentor in orthodontics. I owe so much to you for your inspiration and support. You have helped me strive to become the best I can be. Most importantly, though, you have always been such a great friend. Thank you.

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Thank you to all my co-residents for the assistance, friendship, and good times we had together. I thoroughly

enjoyed my years in residency with each and every one of you.

LONGITUDINAL AIRWAY CHANGES IN ADOLESCENTS USING CBCT

Abstract

By

DAVID JOSEPH SULLIVAN

The purpose of this study is to utilize Cone Beam Computed Tomography (CBCT) imaging to examine volume changes of the nasopharynx and oropharynx in young subjects who are treated with comprehensive orthodontics. The volume of both the nasopharynx and oropharynx was measured at pre- and post-treatment for the 50 most recently treated individuals under the age of 18 at the Case Western Department of Orthodontics. Ortho Segment, a custom program written for the orthodontic department, was used to reconstruct the raw data from the CBCT. Using the method developed my Peters (2007), the software was used to paint the airway slice-by-slice, rendering the total volume by calculating the number of painted voxels.

The mean and standard deviation for initial and final volumes of both oropharynx and nasopharynx were measured. The initial volume measurements were subtracted from the final in order to calculate the amount of

change. Due to varying durations of treatment time, a rate of volume change per year was also calculated and reported. To test reliability, 15 randomly selected airways were remeasured for volume of both oropharynx and nasopharynx.

Intra-operator analysis showed good reliability for airway volume measures ($r > 0.96$). Before orthodontic treatment, the average volume of the oropharynx was 6.57 ± 2.15 CC, and the nasopharynx was 5.98 ± 3.31 CC. At the end of treatment, both the oropharynx and nasopharynx volumes increased to statistically significant measures of 8.55 ± 2.78 CC and 7.89 ± 3.45 CC, respectively. The average change in oropharynx volume throughout orthodontic treatment was 1.97 ± 1.99 CC, and the average change for the nasopharynx was 1.91 ± 1.65 CC. Age, gender, duration of treatment, ethnicity, and the use of a RME caused no significant differences for either the oropharynx or the nasopharynx volume changes. The sample's average rate of volume increase was 0.98 ± 1.17 CC/Yr for the oropharynx and 1.05 ± 0.89 CC/Yr for the nasopharynx; both statistically insignificant. Age, gender, duration of treatment, ethnicity, and the use of

a RME in treatment did not produce any significant differences in rate of volume change.

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LITERATURE REVIEW

The literature has thoroughly revealed the association of the airway passageways with craniofacial development. The "long face syndrome," as characterized by an increased lower facial height, open bite tendency, lip incompetency, maxillary transverse deficiency, and vertical maxillary excess, is believed to be a developmental result of mouth breathing (O'Ryan, 1982). Furthermore, the underlying cause of mouth breathing is primarily chronic nasal obstruction. It has been shown in individuals suffering from obstructive sleep apnea (OSA) that the upper airway volume is chronically constricted or reduced, ultimately influencing the development of the dentofacial pattern as described previously.

Seto et al (2001) compared the maxillary morphology between 40 OSA patients and 21 non-snoring, non-apnoeic, control subjects. Inter-molar, inter-premolar, and inter-canine measurements were performed on dental casts.

Maxillary depth and palatal height were also measured. Using posterior-anterior cephalographs, ratios of maxillary-to-mandibular widths and maxillary-to-facial widths were determined in a sub-group of patients (n = 29) and controls. They found the OSA patients to be significantly constricted in all inter-dental measurements and shallower in maxillary depths ($P < 0.05$), but no difference in palatal height. Also, OSA patients demonstrated significantly smaller ($P < 0.01$) maxillary-to-mandibular widths and maxillary-to-facial widths. This evidence suggests a causative association between maxillary dimensions and facial morphology.

Prior to the recent advent and clinical use of cone beam computed tomography (CBCT), the majority of previous literature concerning craniofacial pattern and airway configurations have been analyzed with traditional two-dimensional radiographs, such as lateral and anterior-posterior (AP) cephalographs. From most of these studies, conclusions about the three-dimensional airway have been derived from limited linear measurements of length and width. A few studies (Martin et al 2006; Warren et al 1987) calculated area measurements of the airway in

either the sagittal or frontal plane on radiographs. Furthermore, methods such as rhinometry and rhinomanometry have been utilized for measurements of the airway, albeit limited to the nasopharynx. These methods are inherently insufficient to evaluate the airway and its three-dimensional configuration. Thus, the idea of studying both the nasopharynx and oropharynx three-dimensionally with CBCT seems very compelling in order to determine if the conclusions drawn from previous literature remain valid and applicable.

Airway and Associated Growth

Taylor et al (1995) described the pattern of bony and soft tissue growth of the oropharynx in healthy, orthodontically untreated children. Using lateral cephalographs from the Broadbent Bolton Study, they traced multiple hard and soft tissue points for 16 males and 16 females at the ages 6, 9, 12, 15, and 18 years. They reported two soft tissue measurements within the oropharynx to be significantly increasing over certain time periods: one - PNS to the posterior pharyngeal wall, and two - posterior soft palate to the posterior pharyngeal wall. This acceleration of change for the

oropharyngeal soft tissue occurred during the 6-9 and 12-15 age periods. These same measures showed very little change within the 9-12 and 15-18 year periods. Taylor et al (1995) attribute the airway increase in size during the 6-9 period to three possible reasons: 1) surgical removal of adenoid tissue, 2) possible continued growth of the pharynx, and 3) the onset of adenoidal regression around age 8. Again, they reason that the increase seen in the 12-15 period is due to three possibilities: 1) this time period encompasses the pubertal growth spurt, 2) this is the time of complete adenoid regression, and 3) 24 of the 32 individuals studied had tonsillectomies and adenoidectomies by the age of 15.

Airway and Orthodontic Treatment

Multiple treatment modalities exist to alleviate the signs and symptoms related to upper airway constriction. Of these modalities, rapid maxillary expansion (RME) is of particular interest to the orthodontist. Villa et al. (2007) demonstrated that early treatment of obstructive sleep apnea syndrome (OSAS) with a rapid maxillary expander alone reduced the symptoms of OSAS immediately after expansion in 71.4% of their study subjects. Results

were gathered from a polysomnography, and the subject responses to a Brouillette questionnaire eliciting OSAS symptoms such as sleepiness, irritability, headache, oral breathing, habitual snoring, apneas, restless sleep, and nightmares were assessed. They also reported that after 12 months of post-expansion therapy, only 2 of the 13 subjects who initially breathed through the mouth continued to do so. Such results shed light on the use of RME to decrease upper airway constriction. Then again, a major limitation of this study is the small amount of subjects (n=14) and the lack of a control group.

A considerable amount of attention has been given to evaluating changes in airway resistance in individuals treated with RME. Hartgerink et al (1987) measured nasal resistance in a group of 38 patients before, immediately following, and 9-12 months after RME. They also utilized a control group of 18 undergoing no treatment. A significant reduction in nasal resistance was found in the expansion group immediately after treatment as well as at the 1-year follow-up. It must be noted, however, that the treated group initially possessed much greater nasal resistance measurements (6.4 cm H_2O/L/sec) than the

control group (3.8 cm H_2O/L/sec). As a result of the expansion, the nasal resistance was in fact improved, but not to a value significantly different than that of the control group. In order to dismiss this limitation of the study, Phoenix et al (2008) suggested that the expansion group be compared to more comparable subjects with narrow maxillae not receiving rapid maxillary treatment.

The previous study included a control group receiving no treatment with expansion or orthodontic fixed appliances. Warren et al (1987) conducted a similar study, but compared orthodontic patients treated with either RME or surgical expansion to that of a control group of orthodontic patients. Their expansion group had the mean age of 12.5 years, and the control group had the mean age of 12.6 years. Within the RPE group, all the subjects had skeletal maxillary constriction and, in most cases, a posterior crossbite existed. Again, the experimental group demonstrated a drop in nasal resistance. Furthermore, an increase in the expansion subjects' airway cross-sectional area from 0.29 cm^2 to 0.46 cm^2 was significant; however, they were not

significantly larger than the control group's area. There was no statistical difference in nasal airway size between the RPE and control groups at the one-year post treatment time. Again, the limitation of this study is the fact that the study group differed initially from the control group with the presence of maxillary constriction.

Measuring nasal resistance and intermolar width in a group of seventeen patients before and after RPE treatment, Hershey et al (1976) found that RPE produced a significant reduction in nasal resistance. They also found after three months of retention that this reduction remained persistent. Despite these positive findings, the correlation between the amount of maxillary first molar expansion and change in nasal resistance was very low. This study also found that patients requiring RPE for a constricted maxilla had significantly higher nasal resistance before the treatment, and as result of RPE treatment, the nasal resistance was reduced to the level of normal subjects.

The dimensions of the upper airway have been analyzed with RME treatment. Utilizing the measuring

methods of rhinomanometry and acoustic rhinometry, Compadretti et al (2006) examined 27 children (mean age 9.5 yrs, range 5-13 yrs) before expansion and 1 year after completion of the expansion. The inclusion criteria identified children with maxillary constriction and the absence of ear, neck, and throat criteria attributing to nasal breathing impairment, such as enlarged adenoids or obstructive septum deformities. A control group consisted of untreated children (24 subjects, mean age 10.2 yrs, range 8-12 yrs) who presented with maxillary constriction. Any patients with nasal obstruction, as previously stated, were identified with flexible nasopharyngoscopy and excluded. Not only did their results find a statistically significant reduction in nasal airway resistance during both inspiration (0.20 Pa/mm^3 per sec, SD ± 0.44) and expiration (0.16 Pa/mm^3 per sec, SD ± 0.33), but also an increase in all dimensional measurements they investigated, such as total minimum cross-sectional areas (TMCA), total nasal volume (TNV), nasal cavity width (NCW), and interzygomatic distance (IZD) was reported. A significant increase was apparent in TMCA (0.17 cm^2, SD ± 0.35), TNV (1.442 cm^2, SD ±

2.292), NCW (2.2 mm, SD ± 2.1), and IZD (7.0 mm, SD ± 8.6) in the expansion group as compared to the control group. According to the authors, RME may improve nasal breathing by way of increasing internal nasal dimensions. A limitation of the study is the fact that the exposed group and control group differed in mean age. This fact could subject the two groups to different amounts of growth during the treatment time that may attribute to the increases in measurements.

Similarly, Bicakci et al (2005) reported an increase in the nasal minimum cross-sectional area (MCA) immediately after treatment with RME and three months after retention. In this study, acoustic rhinometry was used to measure an experimental group of 29 patients exhibiting maxillary constriction with no nasal pathology and a control group of 15 patients undergoing orthodontic treatment alone. Emphasis was in the timing of the delivered treatment, being either before or after the pubertal growth spurt. This was accomplished by dividing both the experimental and control groups into two groups consistent with their respective skeletal maturation as assessed by the cervical vertebral maturation (CVM)

method. Thus, the early-treated group (mean age 11 years 8 months) contained 16 patients; the early-control group (mean age 12 years 6 months) contained 16 patients; the late-treated group (mean age 14 years 1 month) contained 13 patients, and the late-control group (mean age 13 years 4 months) contained 13 subjects. Both early and late expansion groups showed statistically significant increases in MCA (0.34 cm^2, SD ± 0.26 and 0.19 cm^2, SD ± 0.16, respectively) in comparison to the early and late groups of the non-expansion controls. Additionally, the increase in MCA was greater in the early treated group than in the late treated group, but not statistically significant ($P > .05$). There was no mention of clinical significance.

Most of the literature concerning airway dimensions and expansion focus on the nasopharyngeal space with very limited insight of the oropharyngeal space. Buccheri et al (2004) assessed cephalometrically the influence of RME on the entire upper respiratory airway dimensions in 24 children between the ages of 5-9 years (7.2 ± 1.1 years). The subjects all presented as mouthbreathers with radiographically-determined (lateral cephalographs)

adenotonsillar hypertrophy and were all inquired about their ability to breath nasally. Five months after treatment with RME, upper airway measurements showed an increase in width and significantly correlated with the subjects' reports of improved nasal breathing. The authors of this study noted that the increase in the upper respiratory airway and associated improved breathing were results of the expansion and not attributed to any reduced volume of the adenoid tissue. As seen before, a limitation of this study is the use of 2-dimensional cephalometric imaging to examine and report on a 3-dimensional entity.

Airway and CT Imaging

In an attempt to better evaluate volume, Palaisa et al (2007) compared nasal airway anatomic changes before, immediately after, and 3 months after RME using conventional tomography. Reported volume measurements were the outcome of a formula that accounted airway areas and tomographic slice thicknesses. Measurements of total volume and areas for left and right anterior, middle, and posterior nasal cavities (ANC, MNC, and PNC, respectively) were compared among 19 subjects (age 8-15

years) who underwent RME (minimum of 4 mm of expansion, mean 6.1 ± 1.7 mm) as part of their comprehensive orthodontic treatment. There was no control group. Palaisa et al (2007) reported a 10% increase in area (ANC mean area change 0.85 cm^2 ± 1.2; MNC mean area change 0.81 cm^2 ± 1.36; PNC mean area change 1.13 cm^2 ± 1.6) and 10% increases in volume (total nasal cavity volume change mean 2.08 cm^3 ± 2.66) in the anterior, middle, and posterior nasal cavities immediately after expansion. After retaining the expansion for 3 months, further increases of 25% in area (ANC mean area change 1.78 cm^2 ± 1.2; MNC mean area change 2.4 cm^2 ± 1.03; PNC mean area change 2.05 cm^2 ± 1.85) and 15% in volume (total nasal cavity volume change mean 4.9 cm^3 ± 2.3) were observed. The authors concluded that the areas and the volumes increased significantly for all parts of the nasal cavity between the times of appliance removal and after 3 months of retention. The lack of a control group to make comparisons relative to area and volume increases is a limitation of this study. These conclusions indicate that RME is associated with increases in area and volume of the nasal cavity.

In a study by Shigeta et al (2008), the upper and lower oropharynx configuration was evaluated for changes influenced by aging in Japanese patients. CT images of 19 men (age 26 to 80 years) and 19 women (age 24 to 84 years) were utilized to measure the upper oropharynx length (superior border being the posterior nasal spine and inferior border as the occlusal plane) and the lower oropharynx length (superior border being occlusal plane and the inferior border as the tip of the epiglottis). After normalizing the measures by height, Shigeta et al (2008) found no significant changes in upper oropharyngeal length (UOL) with age, height, or BMI in men or women. However, they did conclude age as a significant predictor of lower oropharyngeal length (LOL), which increases 0.49 mm in men (P = .0004) and 0.20 mm in women (P = .047) per year of age increase, after adjusting for height, OSA status, and BMI. They hypothesized the length increase seen only in LOL with age was due to the lack of anatomical hard tissue support in this area, as opposed to that seen in the UOL. This would lend the LOL to stretching, and its increased potential for pharyngeal collapse. This may be possible

evidence as to why men are more susceptible to OSA disorders.

A study conducted by Aboudara et al (2003) investigated the 2-dimensional representation of the airway on lateral headfilms and the 3-dimensional airway structure from computed tomography (CT) scans. The headfilms and CT scans were both taken at the same point in time on 11 adolescents aged between 7 and 16 years. Within the nasopharynx superior to the hard palate, the airway area on the headfilm was evaluated for how well it depicted the volume measured for the same anatomical area on the CT scans. Aboudara et al (2003) found moderate variability between intra-subject proportion of airway volume on CT scans to the area on lateral headfilms. Furthermore, they showed considerably more variability on the CT volumes compared to the area measurements on the lateral headfilms. They concluded that information derived from 2-dimensional lateral headfilms regarding the 3-dimensional airway may be inaccurate.

Utilizing CBCT, Ogawa et al (2007) investigated oropharynx volume and area of greatest constriction differences between obstructive sleep apnea (OSA) and

non-OSA individuals. The boundaries defining the oropharynx on the CBCT reconstruction are the same as those used in our present study. In Ogawa's retrospective study, 10 OSA patients (2 females, 8 males) and 10 non-OSA (4 females, 6 males) had been evaluated for OSA at the University of Southern California's Orofacial Pain/Oral Medicine Center. The OSA group did possess a more constricted oropharynx. The smallest cross-section area (P = .011) and AP dimension (P = .009) were significantly smaller in OSA patients than non-OSA patients. However, Ogawa's group found no statistically significant differences between the two groups in total median volume (P = .054) and median lateral dimension (P = .104). Furthermore, using the Spearman correlation coefficient, they reported no correlation between body mass index (BMI) and the volume of the airway (r = -0.39, P = .09), or BMI and AP measurement of the area of greatest constriction (r = -0.32, P = .17). There was a significant correlation between BMI and the minimum cross-section area (r = -0.48, P = .034) and the BMI and lateral dimension (r = 0.50, P = .03).

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STATEMENT OF THESIS

Prior to CBCT's introduction into orthodontic research, the studies concerning the airway have been limited to 2-dimensional cephalometrics, subjective questionnaires, and methods for the nasopharynx exclusively. Although the studies were valiant in their effort, it is difficult to draw important conclusions about the 3-dimensional airway that are derived from methods possessing such restricted capabilities. These restrictions have been removed with the advantages of CBCT's ability to reliably and accurately obtain information in three dimensions. A reliable method for measuring and reporting airway volumes in orthodontic patients has been established recently by Peters et al (2008). The pre-treatment and post-treatment CBCT records of orthodontically treated individuals have never been measured for volume changes before.

The purpose of this study is to utilize Cone Beam Computed Tomography (CBCT) imaging to examine volume changes of the nasopharynx and oropharynx in young subjects who are treated with comprehensive orthodontics.

LONGITUDINAL AIRWAY CHANGES IN ADOLESCENTS USING CBCT

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Keywords: Cone beam computed tomography, airway volume.

Objectives: to utilize Cone Beam Computed Tomography (CBCT) imaging to examine volume changes of the nasopharynx and oropharynx in young subjects who are treated with comprehensive orthodontics. **Methods:** The sample consisted of 50 adolescents (mean age 13.80 ± 1.2 years) who had started and completed orthodontic treatment at the CWRU Dept. of Orthodontics. Oropharyngeal and nasopharyngeal volumes were measured on each patient using reconstructed data from cone beam CT images taken at initial and final records. Changes in airway volume and rate of airway volume changes were calculated. **Results:** The orophaynx and nasopharynx increased significantly in volume by 30% and 32%, respectively. The upper airway of males was larger and increased more than those of females, however, to statistically insignificant levels. No difference was found in airway change for the following variables: gender, age, duration of treatment, and treatment with or without an expander. **Conclusions:** Adolescents treated orthodontically do experience increases in volume of both the oropharynx and nasopharynx. Gender, age, duration of treatment, ethnicity, and treatment with an RME did not affect volume of the airway in this study. Further studies with larger samples and better group-matching are needed to evaluate the airway using 3-dimensional imaging.

INTRODUCTION:

The literature has thoroughly revealed the association of the airway passageways with craniofacial development. The "long face syndrome," as characterized by an increased lower facial height, open bite tendency, lip incompetency, maxillary transverse deficiency, and vertical maxillary excess, is believed to be a developmental result of mouth breathing[1]. Furthermore, the underlying cause of mouth breathing is primarily chronic nasal obstruction. It has been shown in individuals suffering from obstructive sleep apnea (OSA) that the

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complete adenoid regression, and 3) 24 of the 32 individuals studied had tonsillectomies and adenoidectomies by the age of 15.

Airway and Orthodontic Treatment

Multiple treatment modalities exist to alleviate the signs and symptoms related to upper airway constriction. Of these modalities, rapid maxillary expansion (RME) is of particular interest to the orthodontist. Villa et al[4] demonstrated that early treatment of obstructive sleep apnea syndrome (OSAS) with a rapid maxillary expander alone reduced the symptoms of OSAS immediately after expansion in 71.4% of their study subjects. Results were gathered from a polysomnography, and the subject responses to a Brouillette questionnaire eliciting OSAS symptoms such as sleepiness, irritability, headache, oral breathing, habitual snoring, apneas, restless sleep, and nightmares were assessed. They also reported that after 12 months of post-expansion therapy, only 2 of the 13 subjects who initially breathed through the mouth continued to do so. Such results shed light on the use of RME to decrease upper airway constriction. Then again, a major limitation of this study is the small amount of subjects (n=14) and the lack of a control group.

A considerable amount of attention has been given to evaluating changes in airway resistance in individuals treated with RME. Hartgerink et al[5] measured nasal resistance in a group of 38 patients before, immediately following, and 9-12 months after RME. They also utilized a control group of 18 undergoing no treatment. A significant reduction in nasal resistance was found in the expansion group

immediately after treatment as well as at the 1-year follow-up. It must be noted, however, that the treated group initially possessed much greater nasal resistance measurements (6.4 cm H_20/L/sec) than the control group (3.8 cm H_20/L/sec). As a result of the expansion, the nasal resistance was in fact improved, but not to a value significantly different than that of the control group. In order to dismiss this limitation of the study, Phoenix et al[18] suggested that the expansion group be compared to more comparable subjects with narrow maxillae not receiving rapid maxillary treatment.

The previous study included a control group receiving no treatment with expansion or orthodontic fixed appliances. Warren et al[6] conducted a similar study, but compared orthodontic patients treated with either RME or surgical expansion to that of a control group of orthodontic patients. Their expansion group had the mean age of 12.5 years, and the control group had the mean age of 12.6 years. Within the RPE group, all the subjects had skeletal maxillary constriction and, in most cases, a posterior crossbite existed. Again, the experimental group demonstrated a drop in nasal resistance. Furthermore, an increase in the expansion subjects' airway cross-sectional area from 0.29 cm^2 to 0.46 cm^2 was significant; however, they were not significantly larger than the control group's area. There was no statistical difference in nasal airway size between the RPE and control groups at the one-year post treatment time. Again, the limitation of this study is the fact that the study group differed initially from the control group with the presence of maxillary constriction.

Measuring nasal resistance and intermolar width in a group of seventeen patients before and after RPE treatment, Hershey et al[7] found that RPE produced a significant reduction in nasal resistance. They also found after three months of retention that this reduction remained persistent. Despite these positive findings, the correlation between the amount of maxillary first molar expansion and change in nasal resistance was very low. This study also found that patients requiring RPE for a constricted maxilla had significantly higher nasal resistance before the treatment, and as result of RPE treatment, the nasal resistance was reduced to the level of normal subjects.

The dimensions of the upper airway have been analyzed with RME treatment. Utilizing the measuring methods of rhinomanometry and acoustic rhinometry, Compadretti et al[8] examined 27 children (mean age 9.5 yrs, range 5-13 yrs) before expansion and 1 year after completion of the expansion. The inclusion criteria identified children with maxillary constriction and the absence of ear, neck, and throat criteria attributing to nasal breathing impairment, such as enlarged adenoids or obstructive septum deformities. A control group consisted of untreated children (24 subjects, mean age 10.2 yrs, range 8-12 yrs) who presented with maxillary constriction. Any patients with nasal obstruction, as previously stated, were identified with flexible nasopharyngoscopy and excluded. Not only did their results find a statistically significant reduction in nasal airway resistance during both inspiration (0.20 Pa/mm^3 per sec, SD $\pm$ 0.44) and expiration (0.16 Pa/mm^3 per sec, SD $\pm$ 0.33), but also an increase in all dimensional measurements they investigated, such as total

minimum cross-sectional areas (TMCA), total nasal volume (TNV), nasal cavity width (NCW), and interzygomatic distance (IZD) was reported. A significant increase was apparent in TMCA (0.17 cm^2, SD ± 0.35), TNV (1.442 cm^2, SD ± 2.292), NCW (2.2 mm, SD ± 2.1), and IZD (7.0 mm, SD ± 8.6) in the expansion group as compared to the control group. According to the authors, RME may improve nasal breathing by way of increasing internal nasal dimensions. A limitation of the study is the fact that the exposed group and control group differed in mean age. This fact could subject the two groups to different amounts of growth during the treatment time that may attribute to the increases in measurements.

Similarly, Bicakci et al[12] reported an increase in the nasal minimum cross-sectional area (MCA) immediately after treatment with RME and three months after retention. In this study, acoustic rhinometry was used to measure an experimental group of 29 patients exhibiting maxillary constriction with no nasal pathology and a control group of 15 patients undergoing orthodontic treatment alone. Emphasis was in the timing of the delivered treatment, being either before or after the pubertal growth spurt. This was accomplished by dividing both the experimental and control groups into two groups consistent with their respective skeletal maturation as assessed by the cervical vertebral maturation (CVM) method. Thus, the early-treated group (mean age 11 years 8 months) contained 16 patients; the early-control group (mean age 12 years 6 months) contained 16 patients; the late-treated group (mean age 14 years 1 month) contained 13 patients, and the late-control group (mean age 13 years 4 months) contained 13 subjects. Both early and late expansion groups showed statistically

significant increases in MCA (0.34 cm^2, SD ± 0.26 and 0.19 cm^2, SD ± 0.16, respectively) in comparison to the early and late groups of the non-expansion controls. Additionally, the increase in MCA was greater in the early treated group than in the late treated group, but not statistically significant ($P > .05$). There was no mention of clinical significance.

Most of the literature concerning airway dimensions and expansion focus on the nasopharyngeal space with very limited insight of the oropharyngeal space. Buccheri et al[13] assessed cephalometrically the influence of RME on the entire upper respiratory airway dimensions in 24 children between the ages of 5-9 years (7.2 ± 1.1 years). The subjects all presented as mouthbreathers with radiographically-determined (lateral cephalographs) adenotonsillar hypertrophy and were all inquired about their ability to breath nasally. Five months after treatment with RME, upper airway measurements showed an increase in width and significantly correlated with the subjects' reports of improved nasal breathing. The authors of this study noted that the increase in the upper respiratory airway and associated improved breathing were results of the expansion and not attributed to any reduced volume of the adenoid tissue. As seen before, a limitation of this study is the use of 2-dimensional cephalometric imaging to examine and report on a 3-dimensional entity.

Airway and CT Imaging

In an attempt to better evaluate volume, Palaisa et al[14] compared nasal airway anatomic changes before, immediately after, and 3 months after RME using

conventional tomography. Reported volume measurements were the outcome of a formula that accounted airway areas and tomographic slice thicknesses. Measurements of total volume and areas for left and right anterior, middle, and posterior nasal cavities (ANC, MNC, and PNC, respectively) were compared among 19 subjects (age 8-15 years) who underwent RME (minimum of 4 mm of expansion, mean 6.1 ± 1.7 mm) as part of their comprehensive orthodontic treatment. There was no control group. The authors reported a 10% increase in area (ANC mean area change 0.85 cm^2 ± 1.2; MNC mean area change 0.81 cm^2 ± 1.36; PNC mean area change 1.13 cm^2 ± 1.6) and 10% increases in volume (total nasal cavity volume change mean 2.08 cm^3 ± 2.66) in the anterior, middle, and posterior nasal cavities immediately after expansion. After retaining the expansion for 3 months, further increases of 25% in area (ANC mean area change 1.78 cm^2 ± 1.2; MNC mean area change 2.4 cm^2 ± 1.03; PNC mean area change 2.05 cm^2 ± 1.85) and 15% in volume (total nasal cavity volume change mean 4.9 cm^3 ± 2.3) were observed. The authors concluded that the areas and the volumes increased significantly for all parts of the nasal cavity between the times of appliance removal and after 3 months of retention. The lack of a control group to make comparisons relative to area and volume increases is a limitation of this study. These conclusions indicate that RME is associated with increases in area and volume of the nasal cavity.

In a study by Shigeta et al[19], the upper and lower oropharynx configuration was evaluated for changes influenced by aging in Japanese patients. CT images of 19

men (age 26 to 80 years) and 19 women (age 24 to 84 years) were utilized to measure the upper oropharynx length (superior border being the posterior nasal spine and inferior border as the occlusal plane) and the lower oropharynx length (superior border being occlusal plane and the inferior border as the tip of the epiglottis). After normalizing the measures by height, Shigeta et al (2008) found no significant changes in upper oropharyngeal length (UOL) with age, height, or BMI in men or women. However, they did conclude age as a significant predictor of lower oropharyngeal length (LOL), which increases 0.49 mm in men ($P = .0004$) and 0.20 mm in women ($P = .047$) per year of age increase, after adjusting for height, OSA status, and BMI. They hypothesized the length increase seen only in LOL with age was due to the lack of anatomical hard tissue support in this area, as opposed to that seen in the UOL. This would lend the LOL to stretching, and its increased potential for pharyngeal collapse. This may be possible evidence as to why men are more susceptible to OSA disorders.

A study conducted by Aboudara et al[20] investigated the 2-dimensional representation of the airway on lateral headfilms and the 3-dimensional airway structure from computed tomography (CT) scans. The headfilms and CT scans were both taken at the same point in time on 11 adolescents aged between 7 and 16 years. Within the nasopharynx superior to the hard palate, the airway area on the headfilm was evaluated for how well it depicted the volume measured for the same anatomical area on the CT scans. Aboudara et al (2003) found moderate variability between intra-subject proportion of airway volume on CT scans to the area on lateral

headfilms. Furthermore, they showed considerably more variability on the CT volumes compared to the area measurements on the lateral headfilms. They concluded that information derived from 2-dimensional lateral headfilms regarding the 3-dimensional airway may be inaccurate.

Utilizing CBCT, Ogawa et al[21] investigated oropharynx volume and area of greatest constriction differences between obstructive sleep apnea (OSA) and non-OSA individuals. The boundaries defining the oropharynx on the CBCT reconstruction are the same as those used in our present study. In Ogawa's retrospective study, 10 OSA patients (2 females, 8 males) and 10 non-OSA (4 females, 6 males) had been evaluated for OSA at the University of Southern California's Orofacial Pain/Oral Medicine Center. The OSA group did possess a more constricted oropharynx. The smallest cross-section area (P = .011) and AP dimension (P = .009) were significantly smaller in OSA patients than non-OSA patients. However, Ogawa's group found no statistically significant differences between the two groups in total median volume (P = .054) and median lateral dimension (P = .104). Furthermore, using the Spearman correlation coefficient, they reported no correlation between body mass index (BMI) and the volume of the airway (r = -0.39, P = .09), or BMI and AP measurement of the area of greatest constriction (r = -0.32, P = .17). There was a significant correlation between BMI and the minimum cross-section area (r = -0.48, P = .034) and the BMI and lateral dimension (r = 0.50, P = .03).

Prior to CBCT's introduction into orthodontic research, the studies concerning the airway have been limited to 2-dimensional cephalometrics, subjective questionnaires, and methods for the nasopharynx exclusively. Although the studies were valiant in their effort, it is difficult to draw important conclusions about the 3-dimensional airway that are derived from methods possessing such restricted capabilities. These restrictions have been removed with the advantages of CBCT's ability to reliably and accurately obtain information in three dimensions. A reliable method for measuring and reporting airway volumes in orthodontic patients has been established recently by Peters et al.[17] The pre-treatment and post-treatment CBCT records of orthodontically treated individuals have never been measured for volume changes before.

The purpose of this study is to utilize Cone Beam Computed Tomography (CBCT) imaging to examine volume changes of the nasopharynx and oropharynx in young subjects who are treated with comprehensive orthodontics.

MATERIALS AND METHODS

Approval to conduct this study was obtained from the Case Western Reserve University Institutional Review Board. The investigation was a retrospective descriptive study. All patients had been treated and drawn from Case Western Reserve University Department of Orthodontics.

Using ViewPoint software (Ortho Computer Systems, Inc. – Ames, Iowa), a list of the 50 most recently treated individuals under the age of 18 was compiled.

Each individual had an initial and final CBCT scan obtained from the department's Hitachi CB Mercuray (Hitachi Medical Systems America Co. – Twinsburg, OH), as is every patient treated at the Orthodontic Department. All records are standardized to a 2mA, 120 kVp, and a 9-inch field of view.

Ortho Segment, a custom program written for the Orthodontic department, was used to reconstruct the raw data from the CBCT. The superior and inferior boundaries of the airway as defined by Ogawa et al[21] were used. Oropharyngeal airway was defined as the area inferior to a plane drawn parallel to the Frankfort plane and going through the most distal point of the bony hard palate and superior to a plane drawn parallel to Frankfort plane and going through the most anterior-inferior point of the second cervical vertebrate. The inferior limit of the nasal passage airway was defined as the area superior to the oropharyngeal airway. The superior limit was defined as the last slice before the nasal septum fused with the posterior wall of the pharynx. To preserve consistency, volume of the nostrils was not included because many were partially out of the CBCT field of view.

The airway was painted in Ortho Segment slice-by-slice and the program rendered the total volume by calculating the number of pixels painted. The volumes were then entered into Microsoft excel spreedsheets (Microsoft Corporation – Redmond, WA) manually. The primary author performed all measurements. The measuring method used has been shown to be reliable. With a confidence interval of 95%, Peters et al[17] determined the intraclass correlation is 0.978 for the oropharyngeal measures and 0.967 for the nasopharyngeal measures.

The inclusion criteria for the sample were as follows: 1) patients under the age of 18 years at the beginning of treatment with 2) a complete medical history form and 3) complete pre-treatment and post-treatment CBCT records. The exclusion criteria for the sample were as follows: 1) patients who did not complete their orthodontic treatment, 2) had tonsillectomy/adenoidectomy or any other surgical procedure before or during the orthodontic treatment, and 3) received any treatment other than RME and/or full fixed appliances, such as functional appliances, headgear, surgery, etc.

The total sample of 50 individuals consisted of 22 males and 28 females. The average age at the start of treatment was 13 years 9 months ± 1 year 2 months. The average age at the end of treatment was 15 years 8 months ± 1 year 1 month. The average length of treatment was 1 year 10 months ± 0 years 4 months.

The patient medical history and the treatment record were used to collect the following information:

- Gender and race
- Patients' age at initial record
- Patients' age at final record
- The use of an expander during treatment
- Duration of orthodontic treatment

According to Allhaija et al[15], until the age of 13 years the dimensions of the nasopharynx increase rapidly due to growth. Thus, age and the associated growth during treatment is believed to be an important confounder that must be taken into account. A younger group was defined as those <14 years of age at the start of

treatment, and an older group was defined as those ≥14 years of age at the start of treatment. To standardize everyone, a rate of volume change was calculated by dividing airway change by duration of treatment. All variables were extracted from treatment records using ViewPoint software.

All descriptive statistics were calculated using Excel spreadsheets. For further statistical analysis, data was entered in SPSS 17.0 (SPSS Inc., Chicago, IL). The mean and standard deviation for initial and final volumes of both oropharynx and nasopharynx were measured. The initial volume measurements were subtracted from the final in order to calculate the amount of change. Due to varying durations of treatment time, a rate of volume change per year was also calculated and reported. Independent sample T-tests for the comparison of means between groups were used to evaluate the changes. Dependent T-tests were used for comparison of means within the groups. To test reliability, 15 randomly selected airways were remeasured for volume of both oropharynx and nasopharynx. All remeasurements were performed after 2 weeks or more of initial data collection. Intraclass correlation coefficients were calculated using SPSS 17.0.

Using means and standard deviations reported by Peters et al[17] a standardized effect size was calculated for both the nasopharynx and oropharynx. An effect size of 30% was chosen. The confidence interval was set at 95% and the power was designated at 80%. With these parameters, a sample size of at least 44 was required in order to use t-tests to compare means and standard deviations for continuous variables. 50 subjects were included in the study.

RESULTS

A descriptive summary is given in Table 1, showing the distribution of age, sex, treatment with or without RME, ethnicity, and duration of treatment within the sample group. Table 2 displays the average initial and final volumes of both oropharynx and nasopharynx for the entire group. Before orthodontic treatment, the average volume of the oropharynx was 6.57 ± 2.15 CC, and the nasopharynx was 5.98 ± 3.31 CC. At the end of treatment, both the oropharynx and nasopharynx volumes increased to statistically significant measures of 8.55 ± 2.78 CC and 7.89 ± 3.45 CC, respectively. The average change in oropharynx volume throughout orthodontic treatment was 1.97 ± 1.99 CC, and the average change for the nasopharynx was 1.91 ± 1.65 CC. Age, gender, duration of treatment, ethnicity, and the use of a RME caused no significant differences for either the oropharynx or the nasopharynx volume changes.

In order to account for variable durations of treatment, the rate of airway volume change per year in treatment was calculated and reported in Tables 3. This was done by dividing the average airway volume change by the total time in treatment for each individual. The sample's average rate of volume increase was 0.98 ± 1.17 CC/Yr for the oropharynx and 1.05 ± 0.89 CC/Yr for the nasopharynx. These were not significantly different. Age, gender, duration of treatment, ethnicity, and the use of a RME in treatment did not produce any significant differences in rate of volume change.

DISCUSSION

The main purpose of this retrospective longitudinal study was to evaluate changes in upper airway volume in adolescents who underwent orthodontic treatment using a reliable 3D method of measuring volumes from CBCT records. Overall, after orthodontic treatment there was a 30% increase in oropharyngeal volume and a 32% increase in nasopharyngeal volume. The average length of treatment was 1 year 10 months ± 0 years 4 months and the average initial age was 13 years 9 months ± 1 year 2 months. Taylor et al[3] did find significant increases in linear measurements within the AP dimension of the oropharynx during the age period of 12-15 years. Thus, it would seem logical to expect the volume of the oropharynx to increase since the majority of our subjects fell within this critical age range throughout their orthodontic treatment. The increase in nasopharygeal volume is very similar to the oropharyx, which is, also, consistent with a pattern that Taylor reported.

Possible reasons as to why the upper airway is increasing in volume are similar to those reported by Taylor[3]. First, our sample's average age coincides with the peak pubertal growth spurt. Second, total regression of the adenoid tissue usually occurs between 12 and 14 years of age. Thus, shrinking adenoid tissue within the oropharynx and nasopharynx may be a factor in increasing airway volume. No subjects in this study had a history of adenoidectomy or tonsillectomy before or during orthodontic treatment.

Gender, race, length of treatment, and age did not induce any statistically significant differences in either oropharyngeal nor nasopharyngeal volume change. What may be more surprising is that there was no difference between adolescents treated with an RME and those without. This disagrees with many previous studies that use two-dimensional measures to conclude that treatment with an RME may significantly increase airway dimensions[6,8,12,13]. However, our lack of detecting a difference may be due to such large variability in the sample. This is evident by the standard deviations being as large or larger than the means. A larger sample size would reduce such variability. Our sample only consisted of 10 individuals treated with a RME.

An attempt to eliminate varying treatment durations as a possible confounder was made by calculating rates of airway volume change per year. The amount of volume change was divided by the duration of treatment time for each individual. Again, no significant differences were detected in airway volume rate of change due to differences in gender, age, ethnicity, or treatment with an expander. Allhaija et al[15] noted that the nasopharynx increases in dimension rapidly into the age of 13 years. Our study does not support this claim. Individuals under the age of 14 years showed a rate of nasopharyngeal volume increase of 1.11 ± 0.91 CC/Yr. Similarly, individuals 14 years and older increased at a rate of 0.97 ± 0.89 CC/Yr. It is possible there is a difference in rates of airway volume increases between different age groups if better group matching is used.

CONCLUSIONS

The objective of the study was to investigate changes in upper airway volume in orthodontically-treated adolescents using a reliable 3D method. Age, gender, ethnicity, duration of treatment, and the use of a RME had no significant effect on airway volume change. Many studies have examined the airway, however, using 2D methods that have obvious and inherent limitations. With the availability and accuracy of CBCT, further studies are needed to either reject or confirm what has been previously established about the airway.

Table 1.-- Descriptive summary of socio-demographic factors, gender, treatment duration, and treatment with RME (T=50).

Variables	**N**
Age (Initial)	
11-0 – 13-11	30
14-0 – 16-8	20
Gender	
Male	22
Female	28
Rapid Maxillary Expander	
Expander	10
No Expander	40
Ethnicity	
White	41
Non White	9
Treatment Duration	
Short ≤ 2 Years	32
Long > 2 Years	18

Table 2.-- Means, standard deviations and P values for initial and final airway

	Initial **N = 50**	**Final** **N = 50**	**Mean Volume** Δ	***P***
Oropharyngeal Volume (CC)	6.57 ± 2.15	8.55 ± 2.78	1.97 ± 1.99	**< .001***
Nasopharyngeal Volume (CC)	5.98 ± 3.31	7.89 ± 3.45	1.91 ± 1.65	**< .001***

CC denotes cubic centimeter.

* denotes $P < 0.05$

Table 3.—Means and standard deviations for rate of airway volume change.

	Rate of Volume Change (CC/Yr)
Oropharynx **N = 50**	0.98 ± 1.17
Nasopharynx **N = 50**	1.05 ± 0.89

CC/Yr denotes cubic centimeters per year.

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Figure 1. Inferior and superior limit of oropharynx.

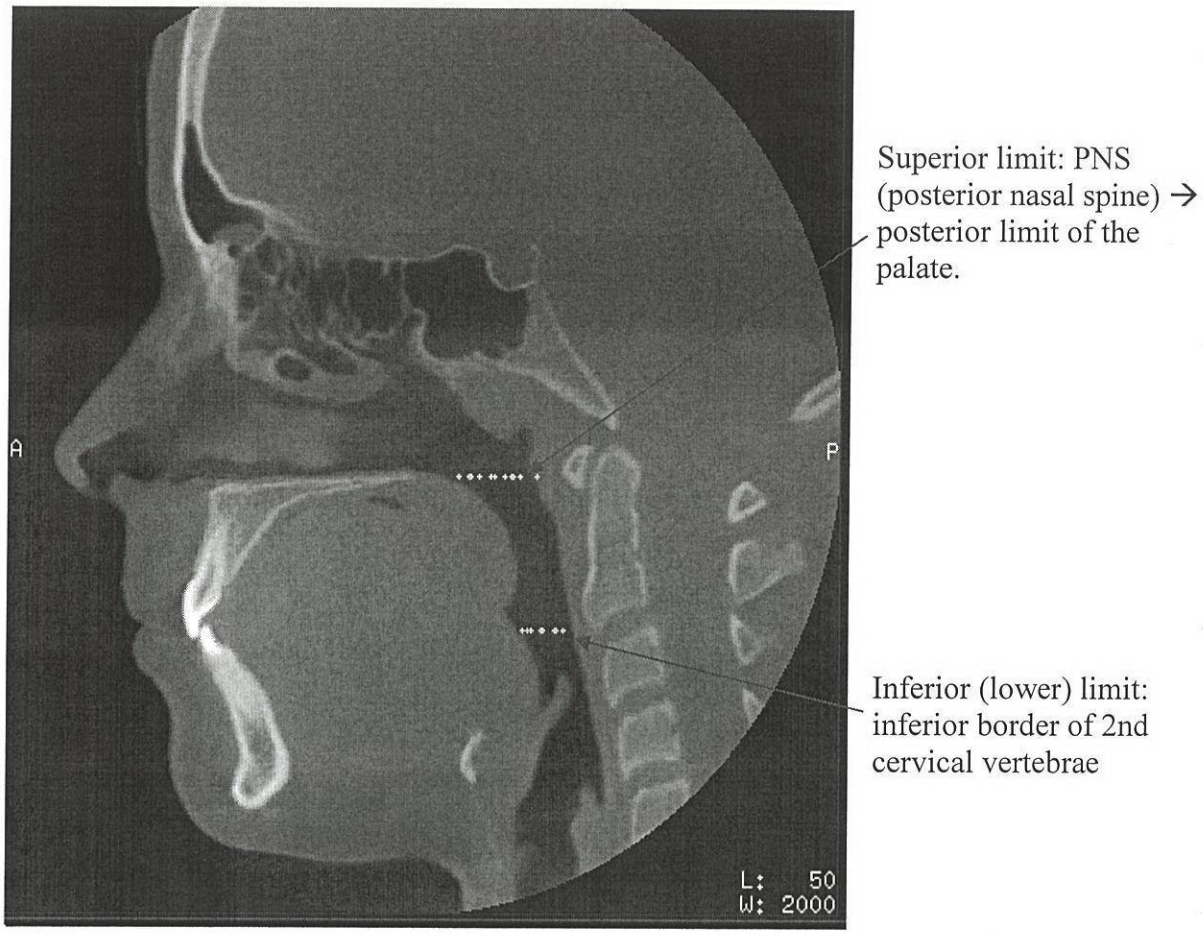


Figure 2. Superior limit of nasal passage.



The nasal septum has fused with the posterior wall of the pharynx. The slice inferior to this marks the superior limit of the nasal passage.

Figure 3. Painting of the airway slice-by-slice.



Figure 4. Volume rendered of the oropharynx (sagittal view).



Figure 5. Volume rendered of the oropharynx (coronal view).

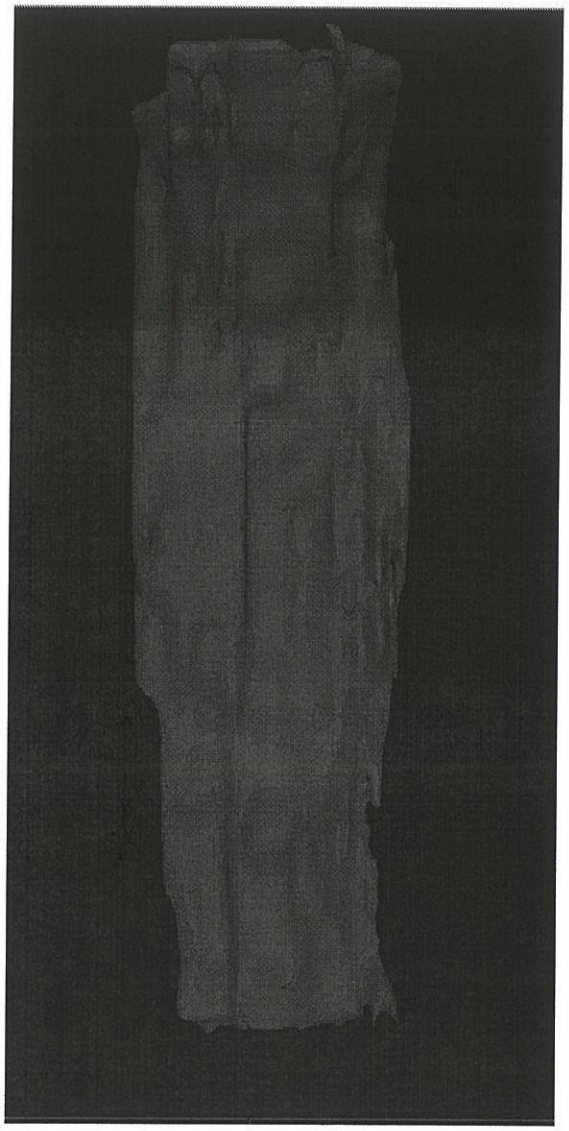


Figure 6. Volume rendered of the nasopharynx (sagittal view).

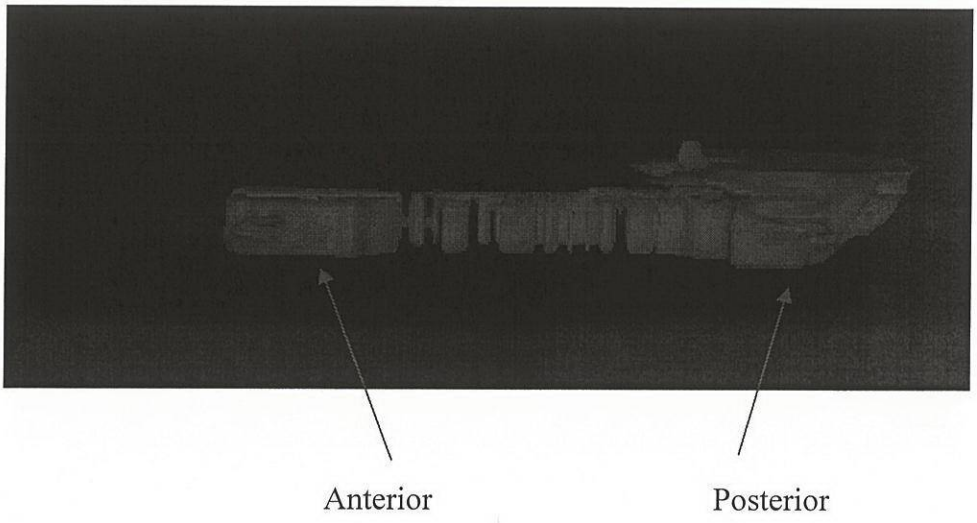
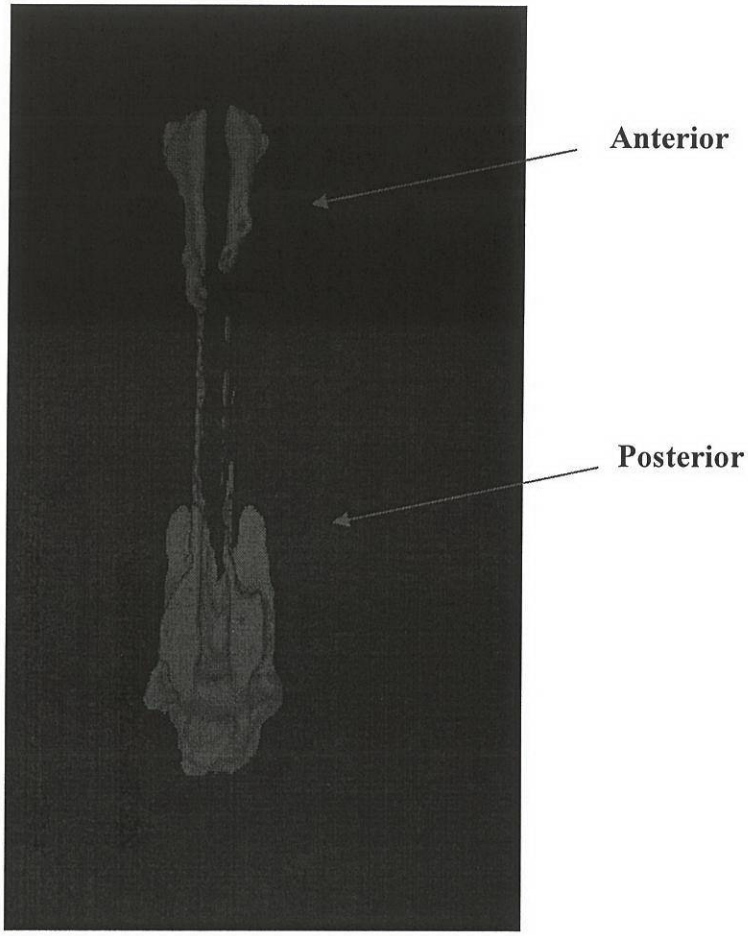


Figure 7. Volume rendered of the nasopharynx (axial view).



APPENDICES

APPENDIX 1

IRB APPROVAL

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.

This protocol is exempt under the #4 category because this involves existing retrospective de-identified data. Prospective data are NOT included in this exemption. De-identified pre-existing data to be collected on 02/10/2009 and after are NOT covered by this exemption.

PLEASE NOTE THAT THIS ONLY APPLIES TO EXISTING DATA. THE RI MUST ENSURE DATA REMAIN COMPLETELY DE-IDENTIFIED.

If you wish to change the protocol in any way, you must an addendum request PRIOR to implementing any protocol change.

Responsible Investigator: **J. Martin Palomo**
Department: **Dental Orthodontics**
IRB Protocol Number: **20090201**
Title: ***Changes in upper respiratory airway volume associated with rapid maxillary expansion***
Co-Investigator: **David Sullivan**

Exemption Date: February 9, 2009

The Institutional Review Board (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.

Any changes to the protocol that put it under the purview of the IRB would require a formal application to, and approval of, the IRB prior to implementation of the change IRB applications are available at the CWRU IRB Pages, or from the Office of Research Compliance (ORC) at Sears Library Building, #657.

Questions? Please visit our website:
http://ora.ra.cwru.edu/orc_humansubjects_CWRU_IRB.asp
OR□contact our administrative office...
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MATERIALS AND METHODS

Approval to conduct this study was obtained from the Case Western Reserve University Institutional Review Board. The investigation was a retrospective descriptive study. All patients had been treated and drawn from Case Western Reserve University Department of Orthodontics.

Using ViewPoint software (Ortho Computer Systems, Inc. - Ames, Iowa), a list of the 50 most recently treated individuals under the age of 18 was compiled. Each individual had an initial and final CBCT scan obtained from the department's Hitachi CB Mercuray (Hitachi Medical Systems America Co. - Twinsburg, OH), as is every patient treated at the Orthodontic Department. All records are standardized to a 2mA, 120 kVp, and a 9-inch field of view.

Ortho Segment, a custom program written for the Orthodontic department, was used to reconstruct the raw data from the CBCT. The superior and inferior boundaries of the airway as defined by Ogawa et al (2007) were used. Oropharyngeal airway was defined as the area inferior to a plane drawn parallel to the Frankfort plane and going through the most distal point of the bony hard palate and

superior to a plane drawn parallel to Frankfort plane and going through the most anterior-inferior point of the second cervical vertebrate. The inferior limit of the nasal passage airway was defined as the area superior to the oropharyngeal airway. The superior limit was defined as the last slice before the nasal septum fused with the posterior wall of the pharynx. To preserve consistency, volume of the nostrils was not included because many were partially out of the CBCT field of view.

The airway was painted in Ortho Segment slice-by-slice and the program rendered the total volume by calculating the number of pixels painted. The volumes were then entered into Microsoft excel spreedsheets (Microsoft Corporation - Redmond, WA) manually. The primary author performed all measurements. The measuring method used has been shown to be reliable. With a confidence interval of 95%, Peters et al (2008) determined the intraclass correlation is 0.978 for the oropharyngeal measures and 0.967 for the nasopharyngeal measures.

The inclusion criteria for the sample were as follows: 1) patients under the age of 18 years at the

beginning of treatment with 2) a complete medical history form and 3) complete pre-treatment and post-treatment CBCT records. The exclusion criteria for the sample were as follows: 1) patients who did not complete their orthodontic treatment, 2) had tonsillectomy/adenoidectomy or any other surgical procedure during the orthodontic treatment, and 3) received any treatment other than RME and/or full fixed appliances, such as functional appliances, headgear, surgery, etc.

The total sample of 50 individuals consisted of 22 males and 28 females. The average age at the start of treatment was 13 years 9 months ± 1 year 2 months. The average age at the end of treatment was 15 years 8 months ± 1 year 1 month. The average length of treatment was 1 year 10 months ± 0 years 4 months.

The patient medical history and the treatment record were used to collect the following information:

- Gender and race
- Patients' age at initial record
- Patients' age at final record
- The use of an expander during treatment
- Duration of orthodontic treatment

According to Allhaija et al (2005), until the age of 13 years the dimensions of the nasopharynx increase rapidly due to growth. Thus, age and the associated growth during treatment is believed to be an important confounder that must be taken into account. A younger group was defined as those <14 years of age at the start of treatment, and an older group was defined as those ≥14 years of age at the start of treatment. To standardize everyone, a rate of volume change was calculated by dividing airway change by duration of treatment. All variables were extracted from treatment records using ViewPoint software.

All descriptive statistics were calculated using Excel spreadsheets. For further statistical analysis, data was entered in SPSS 17.0 (SPSS Inc., Chicago, IL). The mean and standard deviation for initial and final volumes of both oropharynx and nasopharynx were measured. The initial volume measurements were subtracted from the final in order to calculate the amount of change. Due to varying durations of treatment time, a rate of volume change per year was also calculated and reported. Independent sample T-tests for the comparison of means between groups were used to evaluate the changes.

Dependent T-tests were used for comparison of means within the groups. To test reliability, 15 randomly selected airways were remeasured for volume of both oropharynx and nasopharynx. All remeasurements were performed after 2 weeks or more of initial data collection. Intraclass correlation coefficients were calculated using SPSS 17.0.

Using means and standard deviations reported by Peters et al (2008), a standardized effect size was calculated for both the nasopharynx and oropharynx. An effect size of 30% was chosen. The confidence interval was set at 95% and the power was designated at 80%. With these parameters, a sample size of at least 44 was required in order to use t-tests to compare means and standard deviations for continuous variables. 50 subjects were included in the study.

APPENDIX 2

Raw Data

Table 1. --Abbreviations

ID	Subject Identification Number
AGE1	Age at initial
AGE2	Age at final
DUR	Duration of treatment
IOPM1	First measurement of oropharyngeal volume at initial
FOPM1	First measurement of oropharyngeal volume at final
INPM1	First measurement of nasopharyngeal volume initial
FNPM1	First measurement of nasopharyngeal volume at final
RACE	Race: Caucasian = 1, Not Caucasian = 2
SEX	Sex: Male = 1, Female = 2
RME	Treated with RME: 0 = no, 1 = yes
EXT	Treated with extractions: 0 = no, 1 = yes
OPR	Oropharyngeal rate of volume change
NPR	Nasopharyngeal rate of volume change
R1	Reliability measure: first measure
R2	Reliability measure: second measure
CC	Cubic centimeter

APPENDIX 2

Raw Data

Table 2. --Demographics and potential explanatory variables

ID	AGE1	AGE2	DUR	IOPM1	FOPM1	INPM1	FNPM1
1	6092	6555	353	4.42	7.22	4.13	4.94
2	4757	5329	572	11.22	11.46	8.91	11.92
3	4567	5112	545	4.21	6.01	1.86	2.75
4	5936	6642	706	4.61	5.55	4.29	6.81
5	5414	6159	745	6.15	8.96	2.00	5.79
6	5397	6078	681	7.26	7.65	4.75	6.71
7	6065	6694	629	9.08	10.84	8.03	7.29
8	5151	6014	863	7.16	7.72	9.41	10.71
9	4703	5327	624	8.12	13.92	4.57	5.81
10	5106	5713	607	5.01	6.97	4.10	4.50
11	4910	5595	685	6.00	7.45	2.13	4.70
12	5484	6022	538	5.74	7.61	5.05	6.00
13	5571	6394	823	2.58	7.41	14.50	16.13
14	5228	5884	656	5.48	5.28	3.35	4.90
15	5528	6286	758	4.06	3.71	3.52	11.30
16	5452	5929	477	6.87	9.53	9.10	9.82
17	5068	5606	538	5.53	7.78	16.14	16.90
18	5517	6234	717	6.21	7.76	3.04	4.18
19	5088	5756	668	7.67	8.62	3.78	5.01
20	5269	6048	779	6.25	8.41	12.65	14.50
21	5531	5939	408	4.87	5.52	8.69	11.34
22	4514	5123	609	7.26	10.39	4.76	7.94
23	4878	5505	627	4.43	3.99	4.06	4.96
24	4760	5498	738	10.78	14.48	9.47	9.58
25	5308	5940	632	6.51	8.78	5.14	7.63
26	4794	5414	621	11.88	13.52	4.66	6.19
27	4127	4893	766	6.65	8.34	2.74	5.06
28	4127	4811	684	4.45	13.03	2.81	5.19
29	4951	5750	799	6.55	7.35	9.33	10.37
30	4949	5506	557	7.27	7.47	4.53	9.89
31	5142	5925	784	3.40	3.58	4.20	5.54
32	4309	4957	648	10.20	11.73	4.34	6.13
33	5175	5881	706	9.09	11.54	12.95	14.51
34	4374	5104	730	7.43	12.82	8.37	8.87
35	5033	5457	424	8.75	8.15	6.63	8.20
36	4910	5617	707	5.08	8.36	2.75	2.20
37	4382	5119	737	5.15	7.41	4.48	7.01
38	4662	5372	710	6.73	12.46	4.79	7.50
39	5400	5966	566	6.90	12.53	3.48	4.10
40	5127	5912	785	6.78	8.02	7.21	7.82
41	4862	5675	813	4.50	8.11	4.92	6.27
42	4449	5081	632	5.74	7.85	4.93	5.02
43	5051	5786	735	4.48	4.58	4.51	7.43
44	4794	5537	744	5.98	6.96	5.59	10.72
45	5081	5745	664	4.36	5.34	9.07	10.20
46	5319	6084	765	5.24	6.18	4.82	5.40
47	4588	5332	744	12.06	13.80	1.72	5.11
48	4998	5830	832	6.69	8.48	6.00	7.28
49	4904	5643	739	6.85	7.87	10.05	13.16
50	4970	5648	678	9.00	8.76	6.51	13.11

APPENDIX 2

Raw Data

Table 2 (cont). --Demographics and potential explanatory variables

ID	RACE	SEX	RME	EXT	OPR	NPR
1	2.00	2.00	0.00	0.00	-2.89	0.84
2	2.00	2.00	0.00	0.00	0.15	1.92
3	1.00	2.00	1.00	0.00	1.21	0.60
4	1.00	2.00	0.00	0.00	0.49	1.30
5	1.00	1.00	0.00	0.00	1.38	1.86
6	1.00	2.00	0.00	0.00	0.21	1.05
7	1.00	2.00	0.00	0.00	1.02	-0.43
8	1.00	2.00	0.00	0.00	0.24	0.55
9	1.00	2.00	0.00	0.00	3.39	0.73
10	1.00	1.00	0.00	0.00	1.18	0.24
11	2.00	2.00	0.00	0.00	0.77	1.37
12	1.00	2.00	1.00	0.00	1.27	0.64
13	1.00	1.00	1.00	0.00	2.14	0.72
14	1.00	2.00	0.00	0.00	-0.11	0.86
15	2.00	1.00	0.00	0.00	-0.17	3.74
16	1.00	1.00	0.00	0.00	2.04	0.55
17	1.00	1.00	0.00	0.00	1.53	0.52
18	1.00	1.00	0.00	1.00	0.79	0.58
19	1.00	2.00	0.00	0.00	0.52	0.67
20	1.00	1.00	0.00	0.00	1.01	0.87
21	1.00	2.00	0.00	0.00	0.58	2.37
22	1.00	2.00	1.00	0.00	1.88	1.91
23	1.00	2.00	1.00	0.00	-0.26	0.52
24	1.00	1.00	0.00	0.00	1.83	0.05
25	1.00	2.00	0.00	0.00	11.31	1.44
26	2.00	1.00	1.00	0.00	0.96	0.90
27	1.00	2.00	0.00	0.00	0.81	1.11
28	1.00	1.00	0.00	0.00	4.58	1.27
29	1.00	1.00	0.00	0.00	0.37	0.48
30	1.00	1.00	0.00	0.00	0.13	3.51
31	1.00	1.00	0.00	0.00	0.08	0.62
32	1.00	2.00	0.00	0.00	0.86	1.01
33	1.00	1.00	1.00	1.00	1.27	0.81
34	1.00	1.00	0.00	0.00	2.70	0.25
35	2.00	1.00	0.00	0.00	-0.52	1.35
36	2.00	1.00	1.00	0.00	1.69	-0.28
37	1.00	2.00	0.00	0.00	1.12	1.25
38	2.00	1.00	0.00	1.00	2.95	1.39
39	1.00	2.00	0.00	0.00	3.63	0.40
40	1.00	2.00	0.00	0.00	0.58	0.28
41	1.00	2.00	0.00	0.00	1.62	0.61
42	1.00	1.00	0.00	0.00	1.22	0.05
43	1.00	2.00	0.00	0.00	0.05	1.45
44	1.00	2.00	1.00	0.00	0.48	2.52
45	2.00	2.00	0.00	0.00	0.54	0.62
46	1.00	2.00	1.00	0.00	0.45	0.28
47	1.00	1.00	0.00	0.00	0.85	1.66
48	1.00	2.00	0.00	0.00	0.79	0.56
49	1.00	2.00	0.00	0.00	0.50	1.54
50	1.00	1.00	0.00	0.00	0.13	3.55

APPENDIX 3

Raw Data

Table 1. --Oropharyngeal and nasopharyngeal volumes and rates of change

	Oropharynx				Nasopharynx			
	Pre	Post			Pre	Post		
ID	CC	CC	Rate (CC/Yr)	T1-T0 (CC)	CC	CC	Rate (CC/Yr)	T1-T0 (CC)
1	4.42	7.22	-2.89	**-2.80**	4.13	4.94	0.84	**0.81**
2	11.22	11.46	0.15	**0.24**	8.91	11.92	1.92	**3.01**
3	4.21	6.01	1.21	**1.80**	1.86	2.75	0.60	**0.89**
4	4.61	5.55	0.49	**0.94**	4.29	6.81	1.30	**2.52**
5	6.15	8.96	1.38	**2.81**	2.00	5.79	1.86	**3.79**
6	7.26	7.65	0.21	**0.39**	4.75	6.71	1.05	**1.96**
7	9.08	10.84	1.02	**1.76**	8.03	7.29	-0.43	**-0.74**
8	7.16	7.72	0.24	**0.56**	9.41	10.71	0.55	**1.30**
9	8.12	13.92	3.39	**5.80**	4.57	5.81	0.73	**1.24**
10	5.01	6.97	1.18	**1.96**	4.10	4.50	0.24	**0.40**
11	6.00	7.45	0.77	**1.45**	2.13	4.70	1.37	**2.57**
12	5.74	7.61	1.27	**1.87**	5.05	6.00	0.64	**0.95**
13	2.58	7.41	2.14	**4.83**	14.50	16.13	0.72	**1.63**
14	5.48	5.28	-0.11	**-0.20**	3.35	4.90	0.86	**1.55**
15	4.06	3.71	-0.17	**-0.35**	3.52	11.30	3.75	**7.78**
16	6.87	9.53	2.04	**2.66**	9.10	9.82	0.55	**0.72**
17	5.53	7.78	1.53	**2.25**	16.14	16.90	0.52	**0.76**
18	6.21	7.76	0.79	**1.55**	3.04	4.18	0.58	**1.14**
19	7.67	8.62	0.52	**0.95**	3.78	5.01	0.67	**1.23**
20	6.25	8.41	1.01	**2.16**	12.65	14.50	0.87	**1.85**
21	4.87	5.52	0.58	**0.65**	8.69	11.34	2.37	**2.65**
22	7.26	10.39	1.88	**3.13**	4.76	7.94	1.91	**3.18**
23	4.43	3.99	-0.26	**-0.44**	4.06	4.96	0.52	**0.90**
24	10.78	14.48	1.83	**3.70**	9.47	9.58	0.05	**0.11**
25	6.51	8.78	1.31	**2.27**	5.14	7.63	1.44	**2.49**
26	11.88	13.52	0.96	**1.64**	4.66	6.19	0.90	**1.53**
27	6.65	8.34	0.81	**1.69**	2.74	5.06	1.11	**2.32**
28	4.45	13.03	4.58	**8.58**	2.81	5.19	1.27	**2.38**
29	6.55	7.35	0.37	**0.80**	9.33	10.37	0.48	**1.04**
30	7.27	7.47	0.13	**0.20**	4.53	9.89	3.51	**5.36**
31	3.40	3.58	0.08	**0.18**	4.20	5.54	0.62	**1.34**
32	10.20	11.73	0.86	**1.53**	4.34	6.13	1.01	**1.79**
33	9.09	11.54	1.27	**2.45**	12.95	14.51	0.81	**1.56**
34	7.43	12.82	2.70	**5.39**	8.37	8.87	0.25	**0.50**
35	8.75	8.15	-0.52	**-0.60**	6.63	8.20	1.35	**1.57**
36	5.08	8.36	1.69	**3.28**	2.75	2.20	-0.28	**-0.55**
37	5.15	7.41	1.12	**2.26**	4.48	7.01	1.25	**2.53**
38	6.73	12.46	2.95	**5.73**	4.79	7.50	1.39	**2.71**
39	6.90	12.53	3.63	**5.63**	3.48	4.10	0.40	**0.62**
40	6.78	8.02	0.58	**1.24**	7.21	7.82	0.28	**0.61**
41	4.50	8.11	1.62	**3.61**	4.92	6.27	0.61	**1.35**
42	5.74	7.85	1.22	**2.11**	4.93	5.02	0.05	**0.09**
43	4.48	4.58	0.05	**0.10**	4.51	7.43	1.45	**2.92**
44	5.98	6.96	0.48	**0.98**	5.59	10.72	2.52	**5.13**
45	4.36	5.34	0.54	**0.98**	9.07	10.20	0.62	**1.13**
46	5.24	6.18	0.45	**0.94**	4.82	5.40	0.28	**0.58**
47	12.06	13.80	0.85	**1.74**	1.72	5.11	1.66	**3.39**
48	6.69	8.48	0.79	**1.79**	6.00	7.28	0.56	**1.28**
49	6.85	7.87	0.50	**1.02**	10.05	13.16	1.54	**3.11**
50	9.00	8.76	-0.13	**-0.24**	6.51	13.11	3.55	**6.60**
Average	**6.57**	**8.55**	**0.98**	**1.97**	**5.98**	**7.89**	**1.05**	**1.91**
SD	**2.15**	**2.78**	**1.17**	**1.99**	**3.31**	**3.45**	**0.89**	**1.65**

APPENDIX 4

Raw Data: Distribution

Figure 8. Initial Oropharyngeal Volume (CC)

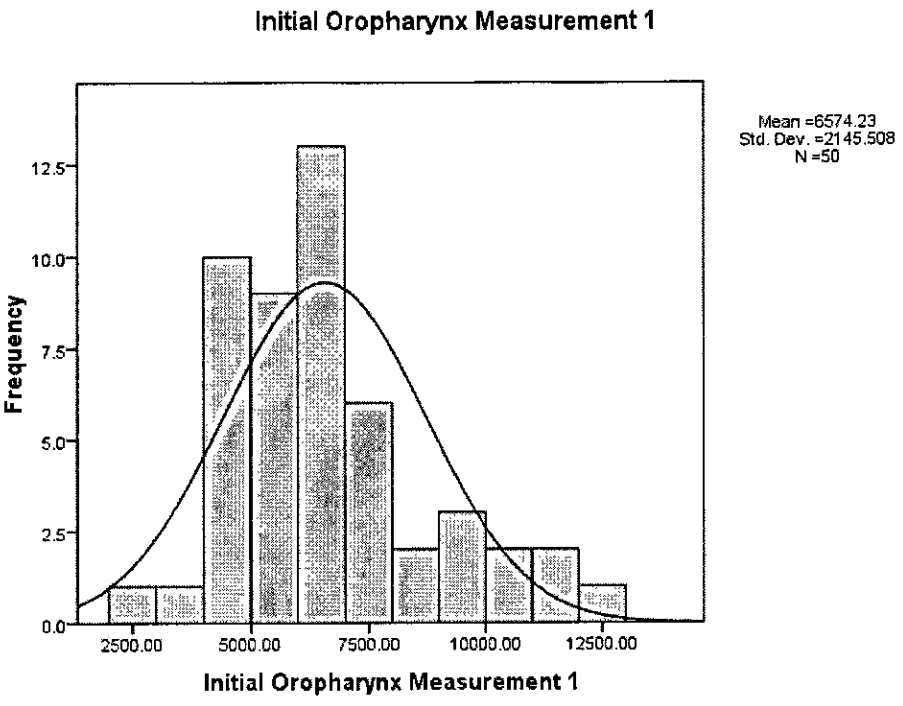


Figure 9. Final Oropharyngeal Volume (CC)

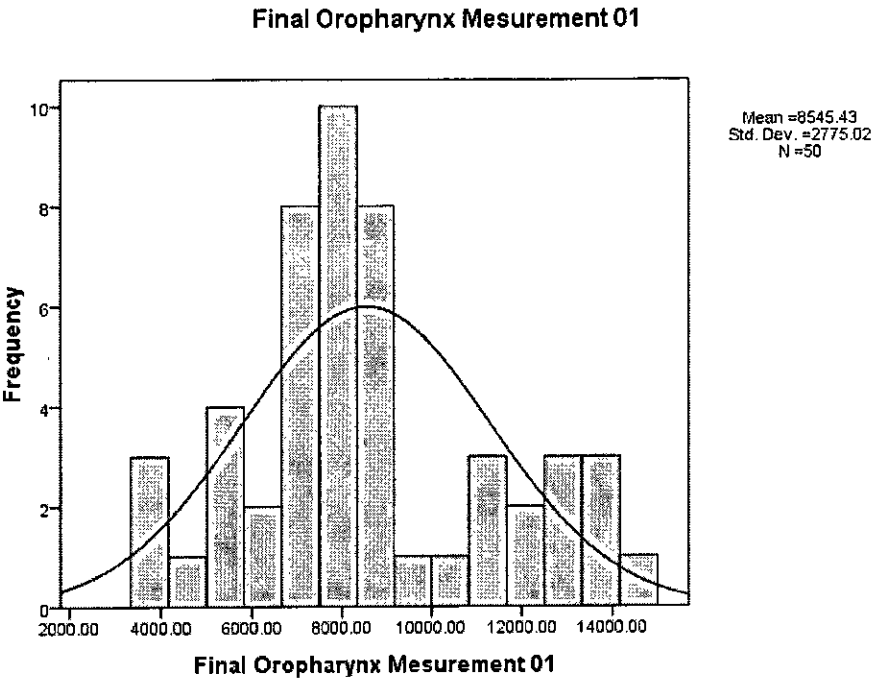


Figure 10. Initial Nasopharyngeal Volume (CC)

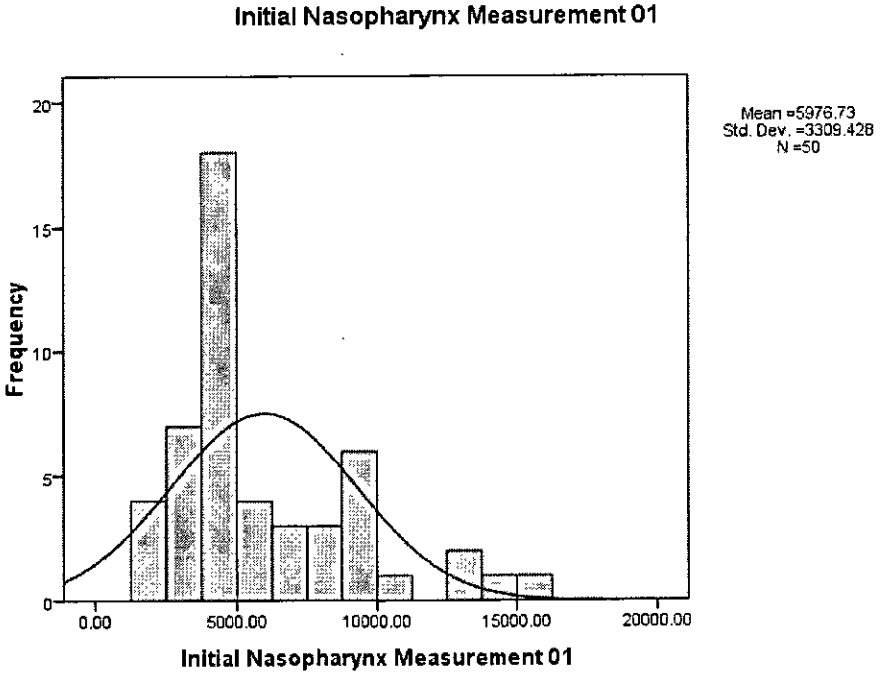


Figure 11. Final Nasopharyngeal Volume (CC)

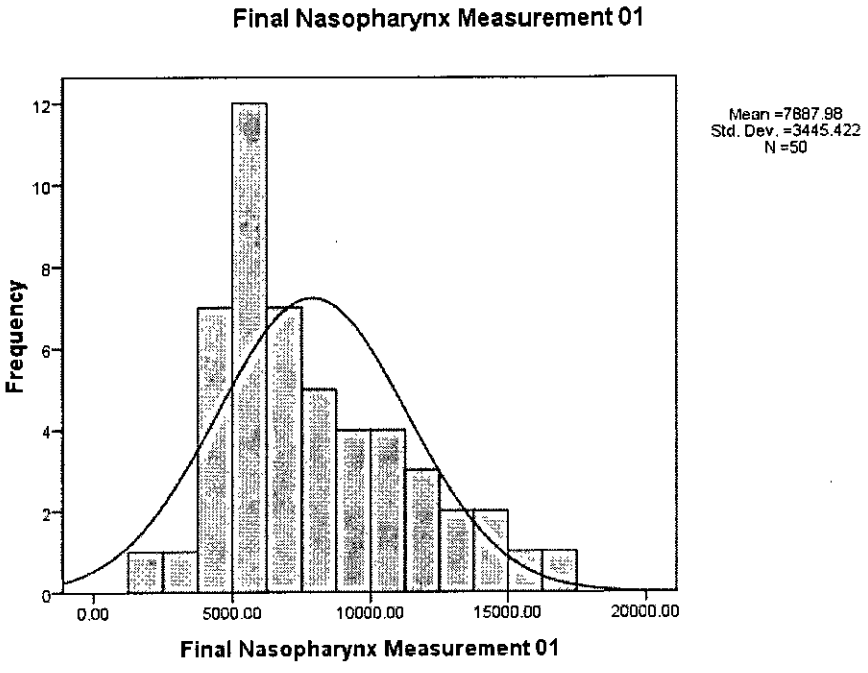


Figure 12. Age at Initial Records (Days)

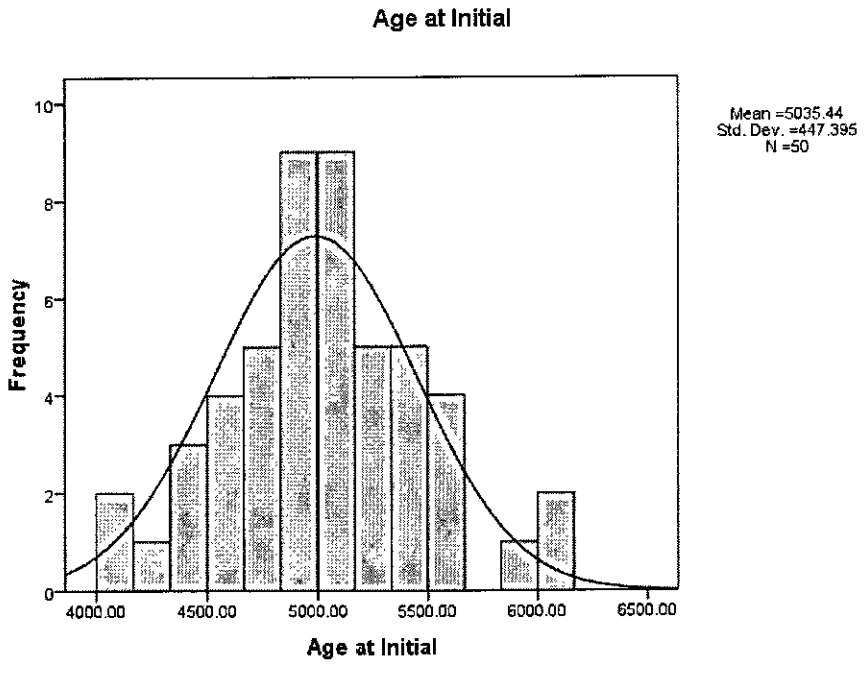


Figure 13. Duration of Treatment (Days)

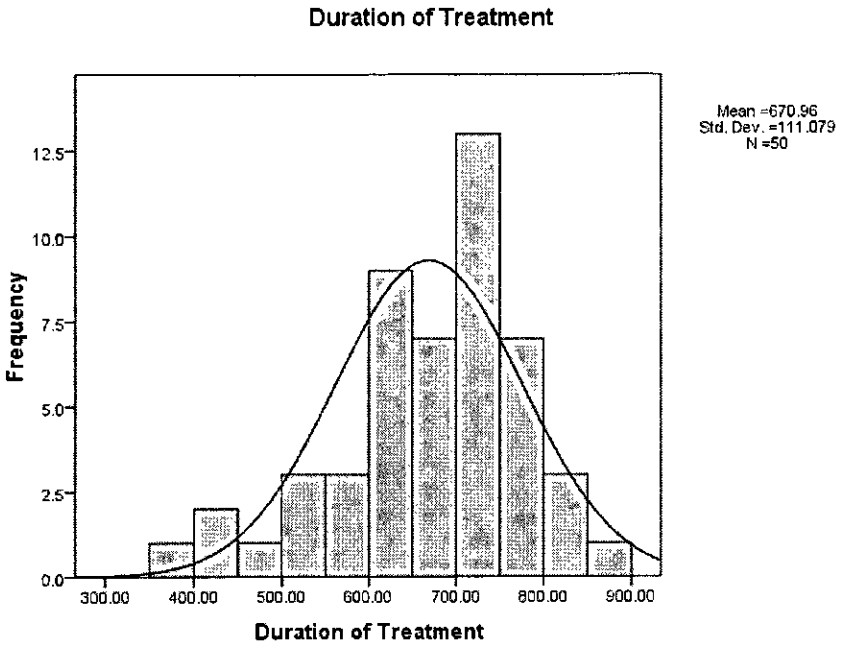


Figure 14. Oropharyngeal Volume Rate of Change (CC/Yr)

