VOLUMETRIC AIRWAY ANALYSIS FOLLOWING MAXILLOMANDIBULAR ADVANCEMENT FOR THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA

by

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ABSTRACT

Purpose: The aim of this study was to quantify pharyngeal airway changes in patients undergoing MMA surgery and determine if there was a relationship between airway parameters and sleep parameters.

Methods and Materials: Patients undergoing MMA for the treatment of moderate to severe OSA between October 2014 and January 2018 were included in this prospective study. Patients underwent both a standardized CBCT of their upper airway and polysomnography preoperatively and a minimum of 6 months postoperatively. The preoperative and postoperative DICOM files were processed using Dolphin 11.8 for airway analysis using a standardized protocol to measure the retropalatal and retroglossal regions. Data was collected on airway volume, minimum axial cross-sectional area, AHI, and ESS both preoperatively and post-operatively. A student paired t-test was used to look at the effect of surgical intervention on the airway parameters and sleep parameters and a Pearson bivariate analysis was used to assess for a relationship between airway parameters and sleep parameters.

Results: 30 patients had preoperative and postoperative CBCT imaging of their airway, and 22 patients underwent postoperative polysomnography. There were statistically significant increases in airway volume (75%) and minCSA (145%) with MMA surgery. The airway increased in both the lateral (5.1 mm) and AP (3.2 mm) dimension, with a decrease in LAT/AP dimension, which is associated with a change to a rounder airway. 82% of patients experienced surgical success and 50% of patients experienced surgical cure. The magnitude of the increases in airway parameters following MMA surgery did not correlate to decreases in the sleep parameters. However, the magnitude of mandibular advancement was correlated to both increases in the minCSA as well as decreases in the AHI following surgery.

Conclusion: Maxillomandibular advancement surgery is a successful procedure that results in statistically significant increases in measured airway parameters and improvement in sleep parameters.

LIST OF ABBREVIATIONS USED

AASM – American Academy of Sleep Medicine

AHI – Apnea-Hypopnea Index

AP – Anterior-Posterior dimension of the minimum axial cross sectional area (minCSA)

ASDA – American Sleep Disorders Association

BMI – Body Mass Index

CBCT – Cone Beam Computed Tomography

CPAP – Continuous Positive Airway Pressure

CT – Computed Tomography

ECG – Electrocardiogram

EDS – Excessive Daytime Sleepiness

EEG – Electroencephalogram

EMG – Electromyogram

ENT – Ear Nose and Throat

EOG – Electrooculogram

ESS – Epworth Sleepiness Scale

LAT – Lateral dimension of the minimum axial cross sectional area (minCSA)

minCSA – Minimum axial cross sectional area

MMA – Maxillomandibular Advancement

MP-H – Mandibular Plane to Hyoid

MRI – Magnetic Resonance Imaging

OSA – Obstructive Sleep Apnea

PAS – Posterior Airway Space

PSG – Polysomnography

RDI – Respiratory Disturbance Index

RERA – Respiratory Event Related Arousal

SDB - Sleep Disordered Breathing

UPPP – Uvulopalatopharyngoplasty

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CHAPTER 1 – INTRODUCTION

1.1 Preamble

Obstructive sleep apnea syndrome (OSA) is the most common type of sleep disordered breathing (SDB).[1] Although obesity is the most common cause of OSA, many people have a predisposition because of the position of their jaws.[2] There are different treatment options available to patients diagnosed with OSA, including nonsurgical and surgical options. Continuous Positive Airway Pressure (CPAP) is an effective nonsurgical option that involves wearing a facemask to bed that delivers continuous air to prevent the airway from collapsing. However, many patients cannot tolerate CPAP and are non-adherent, limiting the efficacy of CPAP therapy.

Maxillomandibular advancement (MMA) surgery has been found to be the most effective surgical option. With MMA or 'jaw advancement surgery', the upper and lower jaws are moved into a more forward position. This opens up the airway and helps to prevent its collapse during sleep. In the past, plain film x-rays have been used to evaluate the airway before and after surgery, but these only show the airway size in two dimensions. Cone-beam computed tomography (CBCT) is a relatively new technology that is being used to image the head and neck region. It can provide three dimensional images of the structures of the head and airway at a much lower radiation dose than conventional CT scans. CBCT has become the standard of care in patients undergoing MMA surgery prior to their procedure to evaluate the position of their facial bones and size of their airway. A repeat CBCT scan 6 months following MMA is used to assess proper healing of the surgery sites, and to assess the outcome of the surgery and elimination of anatomic abnormalities.

By comparing the preoperative and postoperative airway CBCT scans, we can determine how MMA surgery changes the size and shape of the airway, and why it is effective for the treatment of OSA. This may help clinicians to make future treatment recommendations to patients based on their three-dimensional airway anatomy.

1.2 Health impact of OSA

OSA is characterized by recurrent upper airway collapse during sleep, resulting in the complete or partial cessation of airflow despite adequate respiratory efforts. This results in oxygen desaturations and associated arousals from sleep. Due to sleep fragmentation and deprivation, patients with OSA may present with symptoms such as excessive daytime sleepiness (EDS), fatigue, and impaired concentration and memory.[3] Individuals with OSA may have deficits in attention, vigilance, and executive function and successful treatment of a patient's sleep apnea improves these deficits.[4,5] Other symptoms include snoring, witnessed apneas, morning headaches, mood disorders, and depression.[6] This can have a devastating impact on a patient's health and interpersonal relationships.

Research has linked the chronic hypoxemia resulting from OSA to neurocognitive, behavioral, cardiovascular, and cerebrovascular complications.[7] In addition, excessive daytime sleepiness places these individuals at a significantly increased risk for occupational accidents and motor vehicle crashes that ultimately can result in their death .[8,9] When you consider all causes of mortality, there is evidence that patients with severe OSA die at twice the rate of controls.[10]

1.3 *Epidemiology*

Large population studies have demonstrated that the incidence of OSA is increasing with an estimated prevalence in North America of 20 to 30 percent in males and 10 to 15 percent in females with at least mild OSA (AHI>5).[1,11–13] This is likely related to increasing rates of obesity in our society, which is a strong causal risk factor for OSA. However, 30% of patients with OSA are not obese, and these patients often have an underlying craniofacial abnormality contributing to their sleep-disordered breathing.[14] Young et. al have reported that 93% of women and 82% of men with moderate to severe OSA in adults aged 30-60 years go undiagnosed.[15] These undiagnosed patients are may be predisposed to the harmful effects of OSA resulting in their premature death. Moreover, patients who are appropriately diagnosed often do not appreciate the serious harm that can result from having sleep apnea. As a result, they are often ambivalent about seeking treatment or seeking the appropriate treatment.

The prevalence of OSA in children is not as well established. The available evidence suggests a prevalence based on varying diagnostic criteria between 1-4% and is more common among boys with higher BMI's.[16] Because of anatomic factors, children with craniofacial syndromes such as Treacher Collins syndrome, Crouzon syndrome, Apert syndrome, and Pierre Robin sequence are at higher risk of having OSA.[17] However, the most common contributing factor to pediatric OSA is adenotonsillar hypertrophy. The standard treatment for pediatric OSA is adenotonsillectomy, however, the resolution of obstructing events is not always predictable post-operatively.[18] With increasing age, the size of the pharyngeal airway increases and the adenotonsillar lymphoid tissue decreases, resulting in a large proportion of children outgrowing their obstructing events without intervention if adenotonsillar hypertrophy was the main contributing factor.[17]

1.4 Airway Anatomy and Physiology in Obstructive Sleep Apnea

The human pharynx is a musculomembranous tract that connects the nasal cavity to esophagus and larynx and can be divided into three anatomic subdivisions. The nasopharynx extends from the base of skull behind the nasal cavity to the upper surface of the soft palate. The oropharynx extends from the soft palate to the superior border of the epiglottis. The hypopharynx extends from the epiglottis to the lower border of the cricoid cartilage. The oropharynx can further be divided into retropalatal and retroglossal regions, and it has been shown that the majority of patients with obstructive sleep apnea have airway collapse in these regions (Figure 1).[19,20]

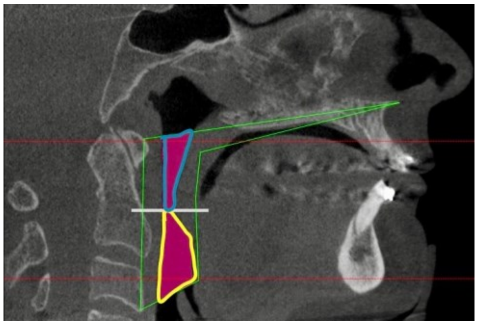


Figure 1 CBCT midsagittal slice of patient with OSA. Oropharynx coloured in pink from soft palate to epiglottis. This can be further divided into retropalatal (blue outline) and retroglossal (yellow outline) regions.

The pharynx acts as a conduit for air passing from the nose to the lungs, and also has roles in phonation and deglutition. There are over 20 muscles that form the pharynx that assist in dilation or constriction depending on the function at hand (Figure 2).[21]

Broadly, they can be categorized into four groups including muscles of the soft palate, tongue, hyoid, and posterolateral pharyngeal walls. Complex interplay between these muscles is involved in changing the shape and patency of the airway. The size and shape of the mandible and maxilla, as well as the position of the hyoid bone are the main craniofacial bony structures that help to determine the shape of the pharynx and airway by acting as anchoring structures to which the muscles and soft tissues attach.[22] However, the pharynx is largely unsupported by bony structures which makes it susceptible to collapse from the negative pressures created during inspiration.

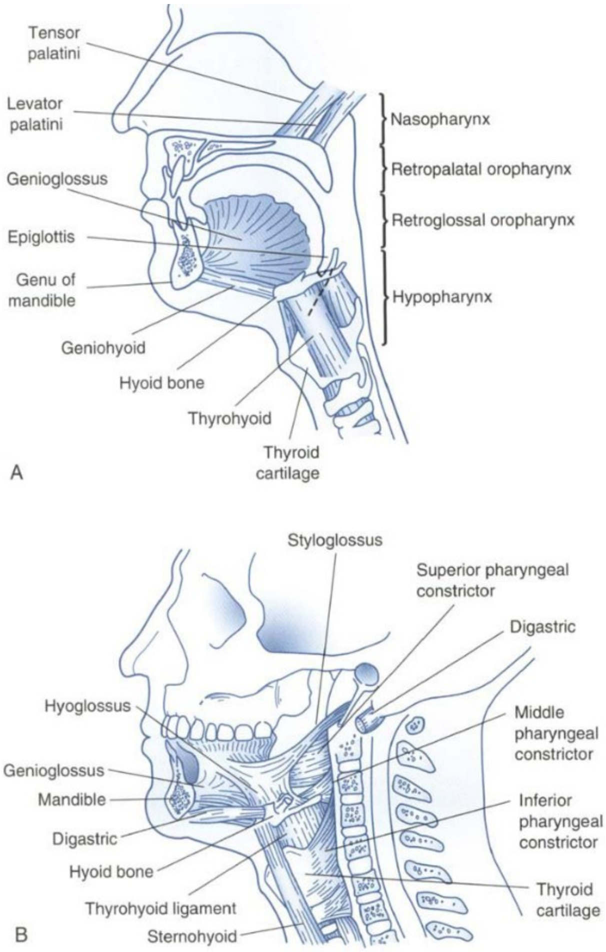


Figure 2 Upper Airway Anatomy. Over 20 muscles contribute to the many functions of the pharynx. Reprinted with permission; Schwab RJ, Kuna ST, Remmers JE. Anatomy and Physiology of Upper Airway Obstruction. In: *Principles and Practice of Sleep Medicine*. ; 2005.

The patency of the airway is maintained by two counteracting forces including the activity of the upper airway muscles described above, and the negative intraluminal pressure. The balance between these two forces can be disrupted by abnormalities in upper airway anatomy as well as neural control.[21]

Studies have shown the upper airway of patients with sleep apnea is smaller than normal controls due to enlargement of the surrounding soft tissues and differences in the craniofacial structures.[23] Cephalometric studies have shown evidence that patients with obstructive sleep apnea demonstrate a retropositioned maxilla, an inferiorly positioned hyoid bone, increased anterior facial height, reduced pharyngeal airway space, and a retrognathic mandible.[24,25] Of all of these craniofacial risk factors, reduced mandibular body length is the most important due to the insertion of the tongue musculature to the mandible.[26] CT and MRI studies have shown increased cross-sectional areas of the tongue, soft palate, parapharyngeal fat pads, and lateral pharyngeal walls in patients with OSA.[24,27] It is know that obesity leads to increased neck circumference and increased levels of parapharyngeal fat which can narrow the pharyngeal space and predispose to obstruction during sleep.[28] However, even when BMI and neck circumference are adjusted for, patients with sleep apnea show significantly increased volume of the lateral pharyngeal walls, tongue, and total upper airway soft tissue compared with controls (Figure 3). [23]

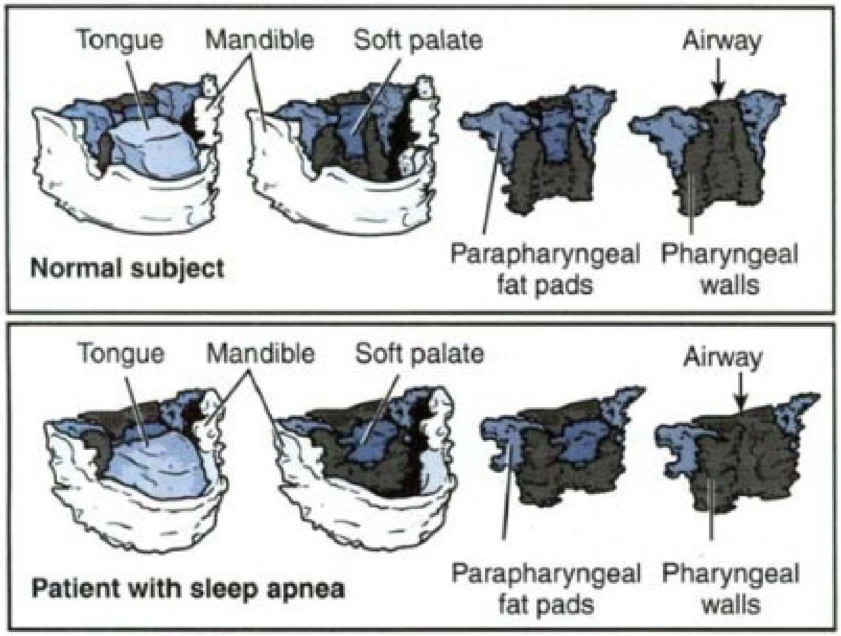
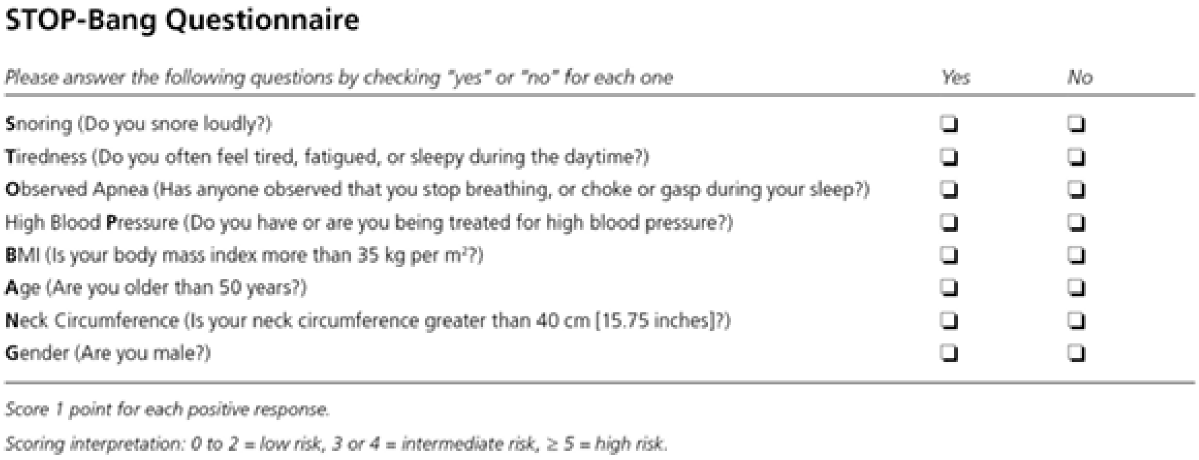


Figure 3 Volumetric reconstruction of MRI images in a normal subject and a patient with sleep apnea. The sleep apnea patient has a larger tongue, soft palate, and lateral pharyngeal walls than the normal subject. The BMI of both subjects was elevated at 32.5 kg/m^2. Reprinted with permission; Schwab RJ, Kuna ST, Remmers JE. Anatomy and Physiology of Upper Airway Obstruction. In: *Principles and Practice of Sleep Medicine*. ; 2005.

A reduction in upper airway dilator muscle activity also contributes to obstruction during sleep. The main pharyngeal dilator is the genioglossus muscle and contraction leads to anterior movement of the tongue and increase in the oropharyngeal airway space. Genioglossus activity is increased during inspiration when negative pressures rise to prevent airway collapse. It is also active during expiration but to a lesser degree. This variation in muscle activity is controlled by both the respiratory central pattern generator as well as negative pressure input from the larynx.[29] In OSA patients, upper airway dilator muscle activity is reduced compared to controls.[30] Decreased genioglossus activation along with the anatomical deficits described above leads to obstruction of the upper airway. Carbon dioxide and negative pressure in the upper airway continue to build until an arousal from sleep occurs. Increased activity of the airway muscles opens the airway, ventilation increases to reverse blood gas disturbances, and central respiratory drive is eventually reduced as sleep is re-initiated and the cycle begins again.[29]

1.5 Quantifying Obstructive Sleep apnea severity

The STOP-BANG questionnaire was developed in 2008 and originally validated to screen for OSA in the undiagnosed surgical population (Figure 4).[31] However, due to its simplicity, it has since been adopted in preoperative clinics and sleep clinics to determine those at high risk for OSA.[32,33] A recent systematic review and meta-analysis found that a questionnaire score of ≥ 3 demonstrated a sensitivity of 94% in sleep clinic patients and 91% in surgical patients to detect moderate to severe OSA.[34]



STOP-Bang Questionnaire

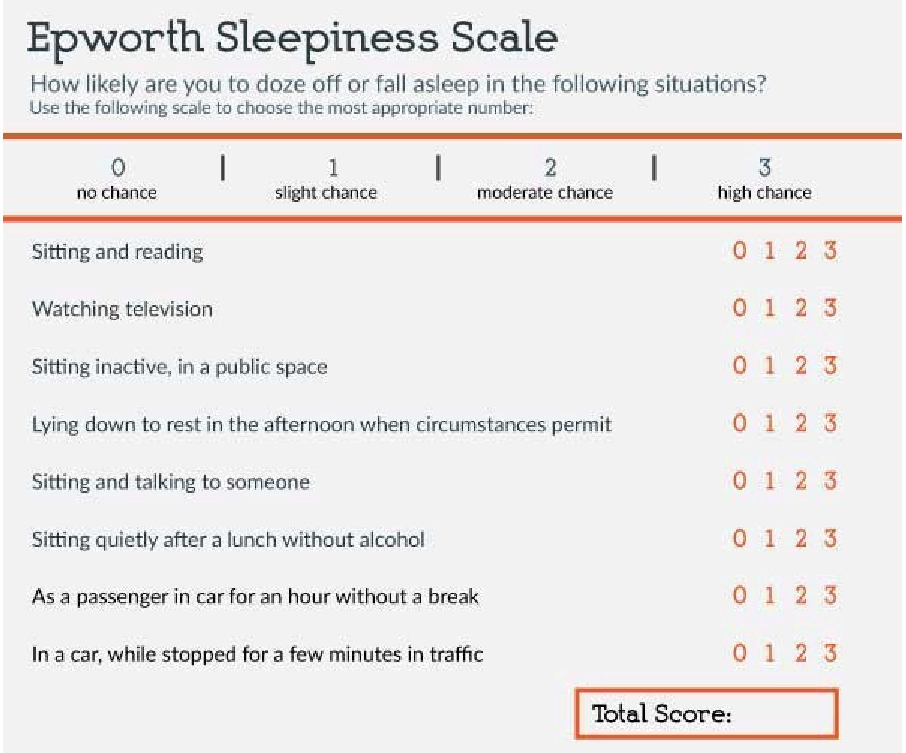
Please answer the following questions by checking "yes" or "no" for each one	*Yes*	*No*
Snoring (Do you snore loudly?)	☐	☐
Tiredness (Do you often feel tired, fatigued, or sleepy during the daytime?)	☐	☐
Observed Apnea (Has anyone observed that you stop breathing, or choke or gasp during your sleep?)	☐	☐
High Blood **P**ressure (Do you have or are you being treated for high blood pressure?)	☐	☐
BMI (Is your body mass index more than 35 kg per m^2?)	☐	☐
Age (Are you older than 50 years?)	☐	☐
Neck Circumference (Is your neck circumference greater than 40 cm [15.75 inches]?)	☐	☐
Gender (Are you male?)	☐	☐

Score 1 point for each positive response.

Scoring interpretation: 0 to 2 = low risk, 3 or 4 = intermediate risk, ≥ 5 = high risk.

Figure 4 STOP-Bang Questionnaire.

The Epworth Sleepiness Scale (ESS) is a self-administered questionnaire that is a tool used to quantify excessive daytime sleepiness (EDS) (Figure 5).[35] The ESS asks patients to grade their likelihood of falling asleep in 8 different situations on a scale of 0 to 3. A score greater than 10 indicates excessive daytime sleepiness, with a maximum score of 24. ESS scores have been shown in the literature to correlate with the RDI obtained from polysomnography.[36,37]



Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations?

Use the following scale to choose the most appropriate number:

0 no chance	1 slight chance	2 moderate chance	3 high chance

Sitting and reading	0 1 2 3
Watching television	0 1 2 3
Sitting inactive, in a public space	0 1 2 3
Lying down to rest in the afternoon when circumstances permit	0 1 2 3
Sitting and talking to someone	0 1 2 3
Sitting quietly after a lunch without alcohol	0 1 2 3
As a passenger in car for an hour without a break	0 1 2 3
In a car, while stopped for a few minutes in traffic	0 1 2 3

Total Score:

Figure 5 Epworth Sleepiness Scale.

Polysomnography (PSG) is the gold standard in accurately diagnosing OSA as well as appropriately assessing treatment responses.[38] Sleep studies are classified from levels 1 to 4 depending on the setting and parameters measured. A level 1 study is takes place at a sleep laboratory with a trained health care professional in attendance. The

American Academy of Sleep Medicine (AASM) has published standard protocols for PSG as well as scoring sleep related events. Sleep stages are recorded via an electroencephalogram (EEG), electrooculogram (EOG), and chin electromyogram (EMG). Heart rhythm is monitored with an ECG and leg movements are recorded with an anterior tibialis EMG. Airflow is measured at the nose and mouth using a thermal sensor and/or a nasal pressure transducer and respiratory effort is monitored using inductance plethysmography. Pulse oximetry is used to monitor oxygen saturation and breathing pattern is analyzed for the presence of apneas and hypopneas which determined according to definitions standardized by the AASM.[39–41] A level 2 study uses the same equipment and monitors, but takes place outside of a sleep laboratory with no sleep technician in attendance. A level 3 study takes place at the patient's home and measures less parameters (two respiratory, one cardiac, oxygen saturation) , and a level 4 study only measures a single parameter.[41] A level 3 study is convenient for patients and has shown good diagnostic performance in those with a high pretest probability of having moderate to severe sleep apnea. However, level 1 studies remain the gold standard in patients with sleep disorders not related to breathing, or unstable medical comorbidities.[42]

OSA is diagnosed and categorized into different severities based on the number of apnea and hypopnea events per hour of sleep (apnea-hypopnea index, AHI) as determined by overnight polysomnography. An obstructive apnea is a cessation (≥ 90% reduction) of airflow for at least 10 seconds duration in the presence of continued or increased respiratory effort. The AASM recommends scoring a hypopnea when there is a reduction in airflow of greater than 30% for at least 10 seconds that is associated with an oxygen desaturation of 3% or an arousal.[43] An AHI of 5 to 15 is classified as mild OSA, 16 to 30 as moderate, and an AHI greater than 30 events per hour constitutes severe obstructive sleep apnea. The Respiratory disturbance index (RDI) is another measure commonly used to diagnosis OSA. The RDI includes respiratory-effort related arousals (RERAs) in addition to apneas and hypopneas. RERAs are arousals from sleep greater than 10 seconds that do not meet the criteria for apneas or hypopneas. [44]

1.6 Treatment of Obstructive Sleep Apnea

The management of OSA can be divided into nonsurgical and surgical therapies. Nonsurgical therapies include weight loss and behavior modification, oral appliance therapy, and continuous positive airway pressure (CPAP). Surgical therapies include tracheostomy, uvulopalatopharyngoplasty (UPPP) and maxillomandibular advancement surgery (MMA), as well as adjunctive surgeries such as nasal surgery, hyoid suspension, partial glossectomy, and hypoglossal nerve stimulation.

According to the guidelines published by the American Academy of Sleep Medicine (AASM), the major role for oral appliance therapy appears to be the treatment of patients with mild-to-moderate OSA who cannot tolerate CPAP.[45] The most common oral appliance prescribed is a mandibular advancement splint which acts by inducing mandibular protrusion and helping to maintain a patent airway. A review of the literature by the American Sleep Disorders Association (ASDA) found that oral appliances were more likely to be successful in patients with low BMIs and a small neck circumference, a short soft palate, and a small oropharynx.[46] Adverse side effects related to oral appliances include dental pain, temporomandibular joint pain and dysfunction, dry mouth, excessive salivation, gingival irritation, and bruxism.[47] However, one of the biggest long term sequelae can include adverse changes in dental occlusion.[48]

CPAP is considered the nonsurgical gold standard in the treatment of OSA as randomized controlled trials have shown that CPAP improves symptoms, cognitive function, mood, and quality of life in these patients.[49] A sealed nasal mask pneumatically splints open the upper airway, preventing collapse of the soft palate and tongue onto the posterior pharyngeal mucosa. However, the efficacy of CPAP is dictated by patient adherence, which can be poor due to physical discomfort associated with wearing the unit, drying of mucous membranes, dislodgement, noise, and the inconvenience of transporting the unit. When adherence is defined as greater than four hours of nightly CPAP use, up to 83 percent of patients have reported to be non-adherent.[50] A recent symposium at the 2015 meeting of the Canadian Sleep Society acknowledged that most sleep centers take a 'one size fits all' approach, prescribing CPAP even though the poor compliance rate means that a sizable proportion of the patient population will not receive adequate therapy.[51] Surgical treatments can eliminate the need for CPAP and circumvent the associated adherence issues.

Uvulopalatopharyngoplasty (UPPP) is a surgical treatment that involves excision of the tonsils and posterior soft palate and uvula, and closure of the tonsillar pillars. It was originally described by Fujita in 1981 and gained initial popularity among ENT surgeons for the treatment of OSA. Surgical success rates are as low as 40% in some series, with many patients developing worsening of their sleep apnea following surgery.[52,53] This low success rate is due to the fact that a UPPP only addresses the obstruction of the palate and tonsils at a single level of the airway. Most patients with OSA have a multilevel expression of the disease with obstructions in the oropharynx and hypopharynx; therefore, the appropriate surgical treatment should be multilevel. Unfortunately, many physicians and healthcare providers still associate OSA surgery with UPPP, which is painful and of poor efficacy, therefore limiting referrals for other more efficacious procedures such as MMA.[54]

Maxillomandibular advancement surgery (MMA) surgery has been shown in the literature to be the most highly effective surgical treatment for OSA.[55–60] MMA enlarges the pharyngeal airway space by advancing the maxilla, mandible, and hyoid bone in an anterior position, thereby resulting in increased tension on suprahyoid and velopharyngeal musculature, preventing its collapse.[61] Many patients who undergo MMA for treatment of OSA are able to discontinue CPAP use after surgery.[56]

A 2010 meta-analysis included 21 unique cohorts of patients with a total of 621 patients undergoing maxillomandibular advancement for the treatment of obstructive sleep apnea.[58] Surgical success was defined as an AHI <20 events per hour and reduced by at least 50 percent from baseline. Surgical cure of OSA was defined as an AHI of less than 5 events per hour. Using these definitions, the surgical success rate was 86% and the surgical cure rate was 43%. Lower baseline BMI and greater maxillary advancement were the only independent predictors of success or cure.

Boyd evaluated a cohort of 37 patients with OSA who used CPAP and then went on to have MMA surgery. He looked at the level of CPAP adherence necessary to reach the same level of effectiveness as MMA. It was found that an 86% adherence rate with CPAP would be necessary to equal MMA in this group. When you take into account adherence issues with CPAP, recent evidence suggests MMA may be more efficacious than CPAP for treatment of obstructive sleep apnea.[62,63]

1.7 Maxillomandibular Advancement Surgery

Maxillomandibular Advancement Surgery was first suggested as an alternative to tracheostomy for the treatment of OSA in the late 1970's when it was noted that the surgical advancement of the retrognathic patient's underdeveloped mandible corrected their sleep apnea symptoms.[64] The surgery entails advancing the maxilla forward using a Lefort 1 osteotomy and advancing the mandible forward using a bilateral sagittal split osteotomy (Figure 6).[65] A concomitant genioplasty may also be performed which involves forward repositioning of the anterior mandibular segment including the genial tubercles and associate tongue musculature, which further helps to expand the pharyngeal airway.

Figure 6 Cephalometric changes following MMA surgery. Left: Preoperative cephalometric radiograph showing narrowed posterior pharyngeal airway space associated with convex and retrognathic facial profile. Preoperative AHI was 27.3 events/hour. Right: Postoperative MMA cephalometric radiograph of same patient showing improved posterior pharyngeal airway space and appropriate facial balance. Postoperative AHI was 1.5 events/hour.

The cephalometric radiographic analysis has a vital role in aiding the clinician in formulating the appropriate treatment plan by optimizing the advancement of the deficient structures while maintaining normal facial balance for each individual patient. The architectural and structural craniofacial analysis of Delaire is based on mutual balance of the cranial and facial bony structures and allows the face to be studied in relation to the cranium and cranial spinal articulation rather than statistical averages (Figure 7).[66] The surgeon can predict the movements of the maxilla, mandible, and chin that can be achieved to enlarge the pharyngeal airway while staying within the range of normal facial balance for each individual.

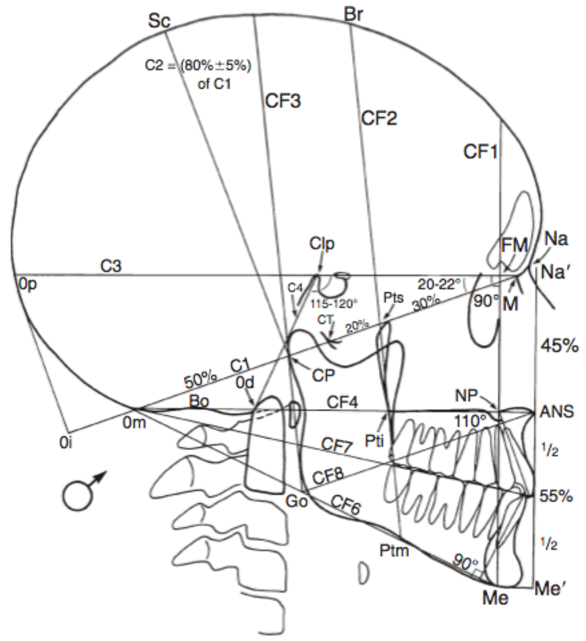


Figure 7 Delaire’s Architectural and Structural Craniofacial Cephalometric Analysis.

1.8 Airway Imaging Techniques

Previous studies have analyzed patient’s airways following maxillomandibular advancement surgery using a variety of modalities such as lateral cephalometric radiographs, magnetic resonance imaging (MRI), spiral CT, and nasopharyngoscopy.[24,61,67–69] Unfortunately, there are limitations with all of these techniques for airway evaluation. Lateral cephalometric measurements are useful for analyzing airway size in the sagittal plane, however, they do not accurately reflect the three-dimensional airway anatomy, including the lateral dimension. Spiral CT allows three-dimensional analysis at the expense of higher radiation doses. MRI is often difficult to obtain, and difficult to analyze the images afterwards because of lack of proper software.

1.8.1 Nasopharyngoscopy (NPG)

Nasopharyngoscopy is a high-resolution imaging technique used to observe the soft tissue of the pharyngeal airway during respiration. A flexible endoscope is inserted through the nasal cavity, into the pharyngeal airway to the tip of the epiglottis.[70] During both insertion and removal, soft tissue anatomic structures that may play a role in pharyngeal narrowing and airway obstruction are well visualized.[67] Identification of the site of airway obstruction during sleep is useful to OSA diagnosis and recommended treatment for the patient. However, with many OSA cases, the shape changes that occur in the airway leading to obstruction during sleep, can only be detected during sleep itself. The Muller maneuver is when a patient is asked to inhale with their mouth closed and nostrils plugged, creating a negative pressure which causes a collapse of the airway. The Muller maneuver was designed to predict the site of airway collapse in the absence of sleep, but has not been proven to accurately represent its counterpart event during sleep.[71,72]

Flexible nasopharyngoscopy has been used as an OSA research tool to compare pre-operative and post-operative airways following MMA surgery. Studies using NPG have shown that MMA surgery leads to an enlarged pharyngeal airway and an increased airway volume.[73–75]. Postoperative nasopharygoscopy has also shown decreased collapsibility of the airway, especially at the level of the lateral pharyngeal walls.[67]

1.8.2 Cephalometric Radiographs

Cephalometric radiographs obtained from a lateral or anterior-posterior perspective provide good visualization of the hard tissue relationships of the head and neck. Most importantly, cephalometric measurements are made using these x-rays to relate the maxilla and mandible to each other as well as nearby anatomical structures. This technique is an important step in the process of treatment planning for OSA patients. [76,77]

The use of cephalometric radiographs has led to a greater comprehension of the anatomical differences between OSA patients and normal control subjects. In 1984, Guilleminault et al found that OSA patients have a greater mandibular plane to hyoid bone (MP-H) distance and a small posterior airway space (PAS) in comparison to controls.[77] A review by Poirrier et al noted an inferior position of the hyoid bone in OSA patients, as well as a retro-positioned mandible, and a long soft palate.[71] A recent meta-analysis by Neelapu et al[78] including 25 studies demonstrated that patients with OSA had longer lower anterior facial heights and longer total anterior facial heights. The authors also noted a reduced SNB angle, reduced mandibular length and clockwise rotation of mandible in OSA subjects. The metanalysis also exhibited increase in all soft palate and tongue dimensions in OSA patients. The hyoid bone was more inferiorly positioned and the pharyngeal airway space was significantly decreased in patients with OSA.

These findings became important in understanding the reason behind MMA surgery success for OSA patients and helped to outline the expected advancement goals of surgical cases to reduce their apnea hypopnea index (AHI).[79]

There are many benefits to using cephalometrics to analyze airways of OSA patients. One of the major advantages is the reproducibility of images. Studies that use cephalometrics may be more easily compared as there are several standard points on the radiographs used for reliable measurements. Unlike the use of a scope, cephalometry does expose patients to radiation, however the risks are evaluated at 0.005mSv or less which can be said to be an insignificant dose.[71]

There are also several limitations to cephalometric radiographs, mainly that the image cannot accurately reflect the complex three-dimensional anatomy of the pharyngeal airway. As a consequence of a two-dimensional image, measurements are limited to linear and angular values and thus, the minimal cross-sectional area of the patient's airway cannot be measured.[80] The minimal cross-sectional area is an important parameter relating to collapsibility of the airway. Furthermore, cephalometric radiographs are obtained while the patient is seated in an upright position. Measurements obtained in this orientation are used to predict obstructive events that occur in supine position during sleep. However, the pharyngeal airway does not remain static between these two positions. The force of gravity while in supine position pulls down on musculature, narrowing the lateral walls of the pharyngeal space causing the airway to become even smaller.[81,82]

1.8.3 Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging is a technique that involves the use of a magnetic field in combination with radio wave energy to generate head and neck images while the patient is positioned supinely. MRIs are the first imaging technique used in OSA research that involved patient positioning equivalent to that of sleeping to provide a more accurate image of the pharyngeal airway during rest.[83]

In 2013, Faria et al[73] used MRI scans to analyze the change in airway volume pre- and post-operatively following MMA surgery. Both the retropalatal (RP) and retrolingual (RL) airway sections experienced a significant increase in airway volume (26% and 27% respectively). It was noted that in comparison to other airway imaging techniques, MRIs were beneficial in providing excellent contrast between the soft tissues of the airway without the harms of ionizing radiation.

Magnetic resonance imaging is not as often used in recent OSA research, as current topics of interest in the field involve several measurements of the airway. The use of MRI scans to obtain these measurements have proven to be difficult due to the lack of adequate analyzing software. From a patient perspective, MRIs are not an ideal choice of imaging for those who suffer from claustrophobia. Additionally, many clinicians have reported patient movement in the MRI machine to be an issue, resulting in the lack of a clear image.[73]

1.8.4 Computed Tomography (CT)

Computed tomography scans use x-rays to create images of internal structures as opposed to radio waves used by MRIs. Computed tomography scanning became increasingly popular in airway analysis in the last decade, mostly for its ability to represent anatomic structures in three dimensions. A three-dimensional representation of the airway is a revolutionary advancement in obstructive sleep apnea research allowing for analysis of airway parameters in all three spatial orientations from a single scan, overcoming the limitations of a two-dimensional image. With increased airway measurement diversity, OSA research has progressed in determining how the pharyngeal airway size and shape changes following MMA surgery. Studies have found an increase in airway volume, lateral and anterior-posterior dimensions as well as minimal cross-sectional area in the post-operative airway. A decrease was observed in the airway length. These physical changes in the morphology of the airway led to a notable reduction in obstructive events during sleep measured by RDI. [80,84,85]

The combination of three-dimensional imaging as well as supine patient positioning has attracted researchers to the use of computed tomography. The main drawback to the use of CT scans is their high levels of radiation exposure to patients. A conventional CT scan is evaluated at 2,270 μSv.[86,87]

1.8.5 Cone Beam Computed Tomography (CBCT)

Cone beam computed tomography has become the standard airway imaging technique in recent years due to its reduced radiation exposure (20-200 μSv) and cost, while maintaining the same benefits as a conventional CT scan.[86–88] The effective radiation dose is dependent on the device as well as the parameters outlined in the protocol for scanning. As spatial resolution is enhanced, and field of view is increased, the effective radiation dose will increase as well. CBCTs have been documented to be a reliable method of airway measurement, with no statistically significant difference between CBCT and manual measurements.[89] Scans have been found to be of great benefit in discriminating borders between soft tissues and air spaces, specifically in airway analysis.[90]

CBCT scanning is still a fairly novel method of airway imaging in comparison to the previously discussed techniques. Researchers have found there to be some inconsistency in how published studies report CBCT device settings as well as patient instructions during scanning. A standard method of reporting these parameters must still be developed to allow for true comparison between studies. Factors such as swallowing, mandibular position and head posture can all influence the morphology of the airway between patient scans.[91]

CHAPTER 2 – REVIEW OF LITERATURE

Three dimensional imaging has created a new era in the assessment of craniomaxillofacial structures and the airway.[28,29] Compared with cephalometric assessments of the airway, parameters such as minimum cross sectional area (minCSA), lateral measurements (LAT), anterior-posterior measurements (AP), as well as volume of the airway can now be elucidated. Software has been developed that is accurate and reliable in capturing this information. This has given new tools for clinicians and researchers to evaluate the airway in patients with obstructive sleep apnea.

2.1 OSA Patient vs. Normal Controls

Schwab et al[23] used MRI to study the upper airway and surrounding soft tissue structures in 21 normal subjects, 21 snorer/mild apneic subjects, and 26 patients with obstructive sleep apnea. They found that the minimum airway area was significantly smaller in apneic compared with normal subjects and occurred in the retropalatal region. They also noted that airway narrowing in OSA patients was significant in the lateral dimension (Figure 8). Li et al[92] looked at 59 patients with OSA and 57 normal adults to compare the lingual region of the upper airway on CT scan. They also noted no differences in AP dimension but significant decrease in the LAT dimension of the oropharynx comparing normal controls to those with OSA. In another CT series, Li et al[92] studied 194 consecutive patients with sleep disordered breathing (SDB). They found the smaller the retropalatal area, the higher is the RDI. The LAT dimension was also correlated to RDI in a similar manner. Fogel et al[30] looked at 14 morbidly obese patients to look for anatomic and physiologic predictors of apnea severity. They found that airways with lower LAT/AP ratios demonstrated more compliance and were less effective at maintaining their patency. Lower LAT/AP ratios are associated with rounder airways.

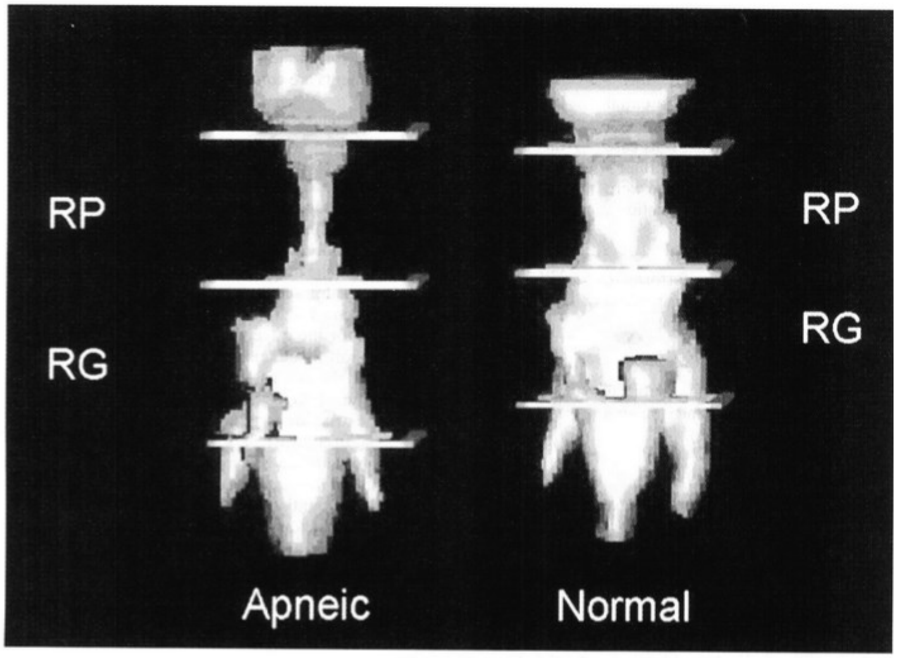
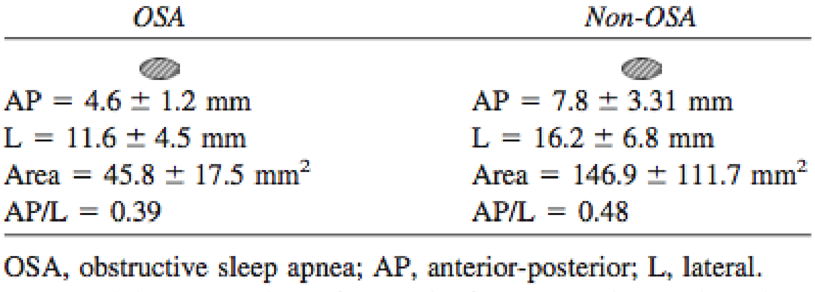


Figure 8 Airway volume in patient with sleep apnea (left) and normal subject (right). Upper airway volume is small in the retropalatal region and the lateral dimension is significantly reduced in the subject with OSA. Reprinted with permission; Schwab RJ, Pasirstein M, Pierson R, et al. Identification of upper airway anatomic risk factors for obstructive sleep apnea with volumetric magnetic resonance imaging. *Am J Respir Crit Care Med*. 2003;168(5):522-530

Vos et al[93] looked at CT scans of 20 patients with obstructive sleep apnea. A 3D model of the upper airway geometry was reconstructed and this was used to evaluate the anatomical properties of the upper airway in OSA patients as well as to perform computational fluid dynamics (CFD) computations to evaluate the airflow and resistance of this upper airway. The authors confirmed the existence of a relationship between the smallest cross-sectional area of the upper airway and the AHI in OSA patients, independent of its location in the airway. The average minimum cross sectional area in this subset of patients was 38.88 mm^2.

Ogawa et al[94] compared the airways of ten patients with OSA to ten controls using CBCT imaging. The OSA subjects presented with a lower total volume of the airway as well as differences in minimum cross sectional area (Figure 9). These results correlated with the data collected by Cosentini et al[95], who examined 28 obese, severe OSA patients with MRI imaging during wakefulness and reported that the subjects had a very small minimal cross-sectional area (35 mm^2), which was usually positioned retropalatally. These results show that the minimum cross sectional area is an important parameter in evaluating the airway of patients with obstructive sleep apnea.



OSA	*Non-OSA*
AP = 4.6 ± 1.2 mm	AP = 7.8 ± 3.31 mm
L = 11.6 ± 4.5 mm	L = 16.2 ± 6.8 mm
Area = 45.8 ± 17.5 mm^2	Area = 146.9 ± 111.7 mm^2
AP/L = 0.39	AP/L = 0.48

OSA, obstructive sleep apnea; AP, anterior-posterior; L, lateral.

Figure 9 Comparison of airway shape and size at the minimal axial cross-sectional area in controls and patients with OSA. Reprinted with permission; Ogawa T, Enciso R, Shintaku WH, Clark GT. Evaluation of cross-section airway configuration of obstructive sleep apnea. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103(1):102-108.

Tikku et al[96] completed a retrospective cohort study measuring the CBCT airway volume of 32 patients divided into a control group and an OSA group. The authors found that the OSA subjects had significantly lower oropharyngeal volume, minimum axial cross sectional area, and the anteroposterior and lateral width of the airway at the MinCSA. The mean minCSA in the control group was 145.6 mm^2 and in the OSA group was 52.9 mm^2.

OSA patients undergoing MMA

Fairburn et al[61] evaluated 20 consecutive patients treated with MMA with pre and postoperative helical CT scans. They evaluated the lateral/AP ratios of the airway both before and after surgery from the hard palate to the hyoid bone. They found that there was enlargement of LAT and AP diameters for all patients at all levels. LAT dimensions were enhanced greater than AP in the retroglossal region.

Zinser et al[97] performed a retrospective CT analysis on 17 patients who underwent 'rotation advancement' for the treatment of obstructive sleep apnea. The total airway volume and the lateral dimension of the cross-sectional airway increased significantly. The total length of the airway became shorter. The airway volume increased post-operatively by 45% and the minimal CSA (min CSA) of the entire airway increased postoperatively by 38%. The authors found the LAT/AP ratio increased after surgery, and this indicated a significant geometric change of the shape of the airway from round to more elliptical. The authors felt this new shape of the airway had a lower probability of collapse.

Raffaini et al[98] conducted a retrospective analysis on 10 patients without sleep apnea to evaluate three-dimensionally the changes that occur in the pharyngeal airway space after maxillo-mandibular advancement surgery. In all patients, the amount of mandibular advancement was greater than 10 mm. The average increase in the PAS volume was 56%; and the average increase in the PAS minimum axial area was 112%, which were both statistically significant. As part of the study the authors also included a subjective patient evaluation using a self-assessment questionnaire, which showed the parameters with the highest degree of perceived improvement were snoring during the night, the quality of breathing while sleeping and respiratory efficiency while awake and during sport activities.

Hernández-Alfaro et al[99] evaluated pharyngeal airway changes using CBCT with a retrospective evaluation of 30 patients who underwent maxillomandibular advancement, maxillary advancement, or mandibular advancement. Three groups of 10 subjects each were established. The average increase was 69.8% in the bimaxillary advancement group and 78.3% in the mandibular advancement group. The authors concluded that the influence of mandibular advancement on the pharyngeal airway volume is greater than the effect of the forward movement of the maxilla.

Butterfield et al[100] looked at a series of 15 consecutive patients undergoing MMA for OSA. They reviewed the airway CBCT images pre and post operatively. The total AV had increased by 80% and the minCSA by 212%. Despite significant airway volumetric increases in the their study, the AV was not associated with improvement in the AHI.

However, a postoperative increase in the minCSA was associated with reductions in AHI. Interestingly, the authors found that Maxillary advancement correlated significantly with the reduction in AHI but mandibular advancement did not. Shortcomings of this study include a retrospective study design with lack of stringent protocol, as well as small sample size with little standardization of the timing of PSG and CBCT scans.

CHAPTER 3 - PURPOSE

The primary objective of this prospective study was to quantify pharyngeal airway changes in patients undergoing maxillomandibular advancement surgery for the treatment of obstructive sleep apnea.

The Secondary objective was to determine if the airway parameters are correlated with AHI and ESS, and if the magnitude of airway changes following surgery correlates to changes in postoperative AHI and ESS.

CHAPTER 4 - METHODS

4.1 Subject Selection

Potential patients were referred to the Department of Oral and Maxillofacial Surgery at the Victoria General Hospital for treatment of their obstructive sleep apnea with maxillomandibular advancement surgery. The study was approved by the Nova Scotia Health Authority Research Ethics Board. Participants were recruited from October 2014 until January 2018. Study participants had to meet the following criteria listed below.

Inclusion criteria:

a) Patient scheduled for maxillomandibular advancement (MMA) surgery for treatment of obstructive sleep apnea

b) Diagnosis of moderate to severe Obstructive sleep apnea (AHI>15) confirmed by polysomnography

c) 18 years of age or older

d) Has received a preoperative CBCT scan of the pharyngeal airway apparatus and maxillofacial structures, as well as a postoperative CBCT scan at least 6 months following MMA surgery

Exclusion criteria:

a) Diagnosis of central sleep apnea or mixed sleep apnea

b) Diagnosis of a craniofacial syndrome

4.2 Surgical Protocol

A head and neck examination was performed by a staff oral and maxillofacial surgeon and standardized lateral cephalometric radiographs were used to assess the patient's anatomy. Cephalometric analysis using the architectural and structural craniofacial analysis of Delaire determined which patients would benefit from advancement of their maxilla and mandible from an anatomical standpoint, while remaining within the limits of normal facial balance. Patients who were deemed candidates for maxillomandibular advancement surgery for the treatment of obstructive sleep apnea syndrome were explained the risks and benefits of surgery during the informed consent process. A standardized pre-operative questionnaire was filled out that included information such as the Epworth Sleepiness Scale (ESS) score.

Prior to their surgery date, patients underwent a cone beam computed tomography scan (CBCT) using the i-CAT FLX unit in the oral and maxillofacial surgery department using a standardized protocol. A 16 cm x 10 cm field of view was utilized to capture the maxillomandibular complex and pharynx from the level of the soft palate to the base of the epiglottis (Voxel size 0.25mm, Exposure time 7.4 seconds). The patients had the scans taken sitting upright with the head in natural head position. A laser beam on the CBCT unit was used to aid in positioning. The teeth were in maximum intercuspation and the patients were asked to hold their tongue in a relaxed position while breathing lightly and avoiding any other movements as described by Guijarro-Martínez in a validation study.[91] Calibration of the CBCT unit takes place weekly.

Staff surgeons in the VG Oral and Maxillofacial surgery department carried out all of the MMA procedures with the assistance of residents. The magnitude of the maxillomandibular advancement was predetermined from cephalometric analysis, CBCT evaluation, and clinical examination. Surgical intermediate splints were fabricated via traditional orthognathic model surgery for intraoperative control of the planned advancement. Both mandible first and maxilla first approaches were utilized, depending on the case.

Maxillary advancement was achieved using Lefort I osteotomies and mandibular advancement was achieved using bilateral sagittal split osteotomies (BSSO). If the cephalometric tracing and clinical examination demonstrated anterior mandibular deficiency, a functional genioplasty was performed in conjunction. Semi-rigid fixation was obtained following the osteotomies using 2.0 mm KLS fixation plates and wire fixation. Intermaxillary fixation was applied for 2 to 4 weeks following the surgery using orthodontic elastics. Patients typically spent three nights in hospital prior to discharge home. Normal post-operative follow up was commonly performed at 2, 4 and 6 weeks.

As part of standard protocol following maxillomandibular advancement surgery, patients underwent postoperative polysomnography at least 6 months following surgery to assess changes in AHI. A post-operative questionnaire was filled out that included their new Epworth Sleepiness Scale score. A postoperative CBCT scan was taken at least 6 months following surgery, utilizing the same field of view, resolution, and protocol as their pre-operative scan. Lateral cephalometric and panoramic radiographs were also repeated at 6 months following surgery as per standard protocol. This allowed the surgeon to assess healing at the osteotomy sites, adequacy of fixation, the outcome of the surgery, and the elimination of anatomic abnormalities.

4.3 Defining the airway

The preoperative and 6 month postoperative DICOM (Digital Imaging and Communications in Medicine) data from the CBCT scans were processed using third-party software (Dolphin Imaging 11.8, Chatsworth, CA, USA). The accuracy and reliability of airway volume analysis using dolphin software has been previously validated in the literature.[89] The scans were evaluated separately by two investigators. Each investigator examined each data set (preoperative and postoperative) 2 times using separate spreadsheets at different time periods to determine intra-observer and inter-observer error.

The presurgical and postsurgical DICOM files were reviewed independently by the examiners and the parameters of the upper airway defined by each examiner using the Dolphin software based on predetermined anatomical limits described by Guijarro-Martínez.[91] Within the Dolphin software, the images were reoriented prior to demarcating the airway using the following guidelines:

i) In the coronal view, the mid-sagital plane was set through the anterior nasal spine and the axial plane bisected the mid-body of both the right and left zygomas.

ii) In the axial view, the mid-sagital plane was set through a line that bisected the anterior nasal spine and posterior nasal spine.

iii) In the mid-sagittal view, the anatomic limits to be evaluated were defined between two axial planes.

iv) The superior limit axial plane was set through a line that bisected the anterior nasal spine and posterior nasal spine and projected onto the posterior pharyngeal wall.

v) The inferior limit axial plane was set through a line between the most inferior-anterior point of the C3 vertebrae that ran tangential to the tip of the epiglottis.

vi) A virtual marker referred to as a ‘seed point’ was be placed between the lines described in iv) and v) which outlined the area of interest

vii) The examiner inspected the sagittal cuts to ensure the oral cavity was not included in the area of interest. If the oral cavity was included, the examiner redefined the anterior limit of the airway by outlining the contour of the soft palate, uvula, and base of tongue.

The Dolphin 11.8 software was then used to calculate the total airway volume (mm^3) and minimum cross sectional area (mm^2) of the region of interest between the superior and inferior limits defined above (figure 10). Each examiner redefined the points on the software during each measurement to ensure reliability. The examiner recorded the preoperative values on an excel spreadsheet and the same examiner repeated the airway measurements at least one week later and recorded the values on a separate excel spreadsheet. Postoperative airway volumes were collected and recorded in the same manner as the preoperative values. The two independent examiners reviewed the same preoperative and postoperative airway volumes.

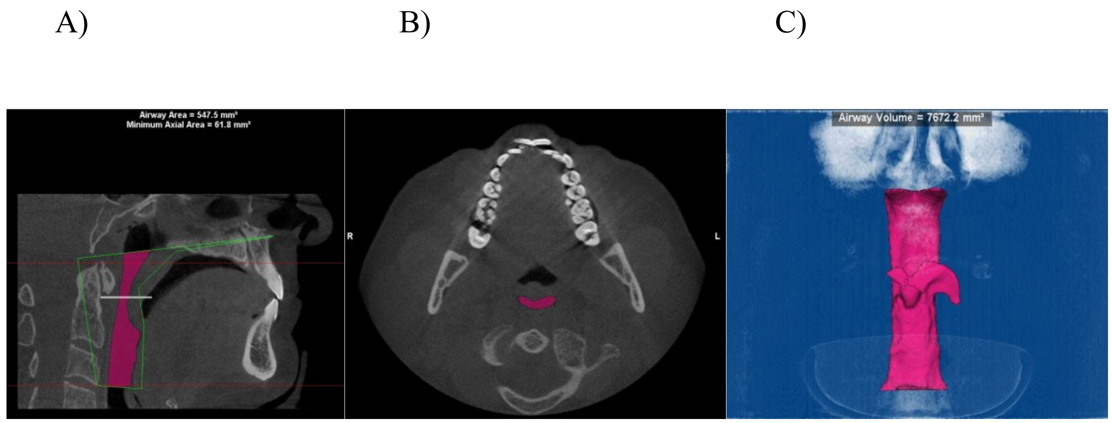


Figure 10 Preoperative airway of patient undergoing MMA surgery. A) Dolphin 11.8 software used to set airway limits and calculate the minimum axial cross sectional area (minCSA). B) minCSA seen from axial view C) Airway seen from frontal view with total airway volume calculated.

For each patient, the axial slice with the minimum cross sectional area (mCSA) was further analyzed. A measuring tool within the software allowed measurement of the mid anterior-posterior (AP) distance as well as the mid lateral distance between the pharyngeal walls. This allowed for comparison of airway shape at the most constricted point to analyze how surgery changes the morphology of the patients' airways (Figure 11).

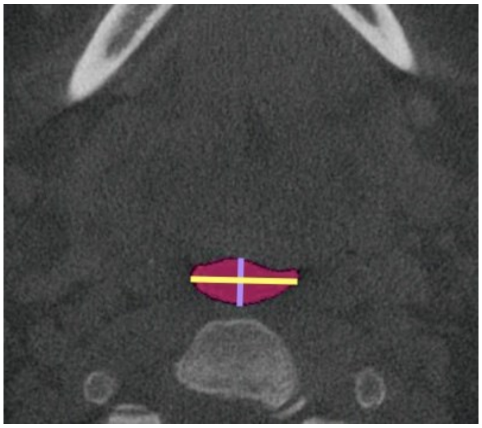


Figure 11 Axial view of the minimum cross sectional area (minCSA). Purple line represents the anterior posterior (AP) dimension of the minCSA. Yellow line represents the lateral (LAT) dimension of the minCSA.

Airway length was collected by measuring a line from the mid-sagittal plane projecting from the tip of the epiglottis to the projection of the upper airway limit on the posterior pharyngeal wall. The most constricted airway point was also measured on this line so that a ratio could be created to compare how the location of the most constricted point changes with surgery (Figure 12).

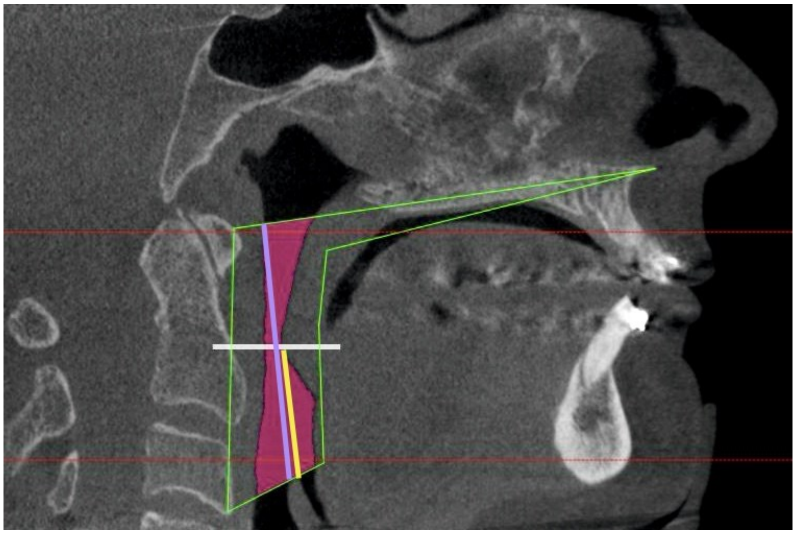


Figure 12 Mid sagittal view of the airway. Horizontal white line represents minimum axial cross sectional area (mCSA). Airway length is measured from tip of epiglottis to posterior pharyngeal wall and is represented by purple line. Yellow line represents distance from tip of epiglottis to mCSA point. This allows a ratio to be created (yellow line:purple line) to quantitatively assess how the position of the most constricted airway point changes with surgery.

The magnitude of surgical movement was collected by comparing the lateral cephalometric radiographs preoperatively (T1) and 6 months post-operatively (T2). Vertical and horizontal tracing measurements were documented using cephalometric landmarks described in the Delaire analysis (Figure 7).[66] An X-axis was established by a line passing from Nasion (N) to the posterior clinoid process (Clp). The Y axis was drawn perpendicular to the X axis from a line projecting from the Clp point. Horizontal measures were taken perpendicular to the Y axis to the A point, B point, and Pogonion (Pg). A point measurements represent maxillary position, B point measurements represent mandibular position, and Pogonion measurements represent chin position. T1 measurements could then be subtracted from T2 measurements to determine the magnitude of advancement of the craniofacial skeleton at least 6 months postoperatively.

4.4 Analysis of Data

The following data was collected from preoperative and postoperative (>6 month) records:

i) Age of patient
ii) Gender of patient
iii) Body Mass Index (BMI)
iv) Apnea Hypopnea Index (AHI)
v) Epworth Sleepiness Scale (ESS) Score
vi) Amount of skeletal movement
vii) Airway Volume (AV)
viii) Airway Length (AL)
ix) Minimum axial cross sectional area (minCSA)
x) Lateral dimension of the minimum axial cross sectional area (LAT)
xi) Anterior-Posterior dimension of the minimum axial cross sectional area (AP)
xii) LAT/AP ratio of the minimum cross sectional area

Statisical analysis was performed using SPSS software (version 23.0). Consultation with a statistician was sought before and after statistical analysis. The main independent variable was the timing of treatment (preoperative vs. postoperative). The main dependent variable was the airway measurements. The student paired t-test was used to evaluate the effect of surgical intervention on airway volume, minimum cross sectional area, and other airway parameters. This enabled us to answer the primary objective of quantifying pharyngeal airway volume changes in patients undergoing MMA surgery for treatment of OSA.

Our secondary objective was to determine if the airway parameters were correlated with AHI and ESS, and if the magnitude of airway changes following surgery correlates to changes in postoperative AHI. Both preoperative and postoperative airway parameters and sleep parameters (AHI, ESS) were analyzed using Pearson bivariate tests to determine if there was any correlation. The following statistical analyses were performed:

i) Preoperative airway parameters vs. preoperative sleep parameters
ii) Postoperative airway parameters vs. postoperative sleep parameters
iii) Change in airway parameters vs. change in sleep parameters
iv) Surgical movements vs. airway parameters
v) Surgical movements vs. sleep parameters

Student paired t-tests were used to study the effect of a functional genioplasty on the airway parameters, as well as the airway differences between patients who experienced surgical success vs. non-responders to treatment. Statistical significance was defined as a P value of less than 0.05.

CHAPTER 5 – RESULTS

5.1 Preoperative Airway parameters and preoperative sleep parameters

Between October 2014 and January 2018, a total of 35 patients who were undergoing MMA for the treatment of OSA had preoperative CBCT scans. Three patients were excluded because they did not meet the inclusion criteria of a diagnosis of moderate to severe OSA (AHI>15) with polysomnography. One patient was lost to follow-up and never returned for post-operative imaging. One patient was excluded because of head movement during the pre-operative scan. A total of 30 patients were included in the study and their demographics, sleep parameters, and airway parameters are listed below (Table 1).

The average age of patients was 51.7 years at the time of surgery (range 39 to 62). There were 21 male patients and 9 female patients. The BMI ranged from 23.3 to 46.8 with a mean of 31.4. The mean pre-operative AHI was 40.0 events/hr with a range of 16.7 to 104. The mean pre-operative ESS score was 12.0 with a range of 0 to 22. The mean preoperative airway volume was 8303 mm^3 and the mean preoperative minimum axial cross sectional area was 72.0 mm^2.

A Pearson bi-variate correlation test was used to analyze any correlation between BMI, pre-operative sleep parameters, and pre-operative airway parameters (table 2). There was no correlation noted between BMI and pre-operative AHI. There was also no correlation between BMI and pre-operative airway volume, or BMI and pre-operative minCSA. A statistically significant correlation was found between BMI and pre-operative Epworth Sleepiness Scale scores (r=0.37, p=0.04).

Table 1 Preoperative Demographics, Sleep parameters, and Airway parameters of patients undergoing MMA for the treatment of OSA.

Pt #	Age	Gender	AHI (events/hr)	ESS	BMI	AV (mm^3)	minCSA (mm^2)
1	46	M	17.1	3	25.6	16691	206.9
2	39	M	17.0	4	23.7	8726	110.4
3	67	M	29.1	13	31.4	9345	129.8
4	57	F	27.3	9	18.1	7391	59.4
5	52	F	16.7	14	36.2	7519	112.1
6	50	M	47.4	7	31.8	6363	81.6
7	50	M	17.3	10	28.4	7076	80.6
8	49	M	26.0	7	35.1	7484	60.7
9	56	F	28.3	17	27.3	8800	93.5
10	44	M	44.3	0	28.4	7490	60.3
11	50	M	51.0	18	30.8	7222	38.1
12	47	F	29.0	21	46.8	5542	20.9
13	42	M	17.8	7	27.2	10204	79.2
14	59	F	68.0	13	31.4	7048	31.2
15	51	M	41.0	18	32.9	7999	94.7
16	55	M	42.7	16	34.0	5932	30.9
17	56	F	46.0	14	27.5	8454	35.9
18	48	M	17.1	4	38.3	8528	62.0
19	62	M	104.0	5	37.2	7392	63.8
20	46	M	32.0	12	32.2	13694	73.2
21	60	F	58.5	21	35.7	4075	28.7
22	46	M	47.0	18	33.0	5541	46.5
23	47	M	72.5	22	31.9	6857	36.0
24	54	M	37.0	11	33.5	8718	45.1
25	52	F	89.0	16	28.5	3458	26.8
26	61	F	37.0	2	23.3	9908	81.2
27	35	M	30.0	11	37.2	7031	81.7
28	58	M	50.0	7	34.3	10332	129.3
29	56	M	17.1	2	26.1	11466	66.3
30	56	M	41.8	22	32.8	15969	94.5
MEAN	**51.7**	**21M, 9F**	**40.0**	**12**	**31.4**	**8303**	**72.0**

Table 2 Correlation of sleep and airway parameters to BMI. * Significant correlation at p<0.05.

	R value	P value
BMI vs. pre-op AHI	0.18	0.35
BMI vs. pre-op ESS	0.37	0.04*
BMI vs. pre-op AV	-0.27	0.15
BMI vs. pre-op minCSA	-0.26	0.17

Airway volume was correlated with mimimum axial cross-sectional area of the airway with an R value of 0.68 and $p<0.0001$ (Figure 13).

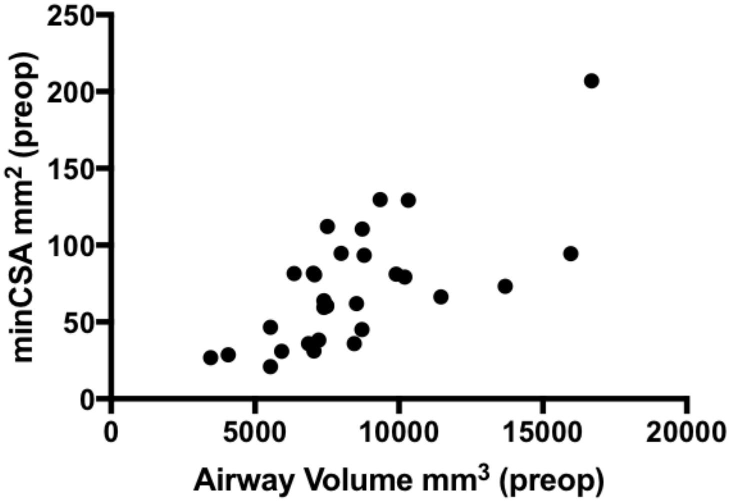


Figure 13 Correlation between Airway volume and Minimum axial cross sectional area (minCSA).

Pearson bivariate correlation tests were used to assess for correlation between preoperative AHI and ESS, and preoperative airway parameters (Table 3, Table 4). Higher pre-operative AHI's were correlated with lower total airway volumes and minimum axial cross sectional areas, and this was statistically significant (Figure 14). Epworth sleepiness scale scores were found to have a statistically significant correlation to the minCSA, but not the total airway volume. Higher ESS scores were correlated with lower minCSAs and smaller AP dimension of the minCSA.

Table 3 Correlation between preoperative AHI and preoperative airway parameters. * Significant correlation at $p<0.05$.

	R value	P value
Airway Volume (AV) (mm^3)	-0.40	0.028*
minCSA (mm^2)	-0.44	0.014*
LAT (mm)	-0.35	0.056
AP (mm)	-0.36	0.050
LAT/AP	-0.01	0.974
Airway Length (AL) (mm)	0.19	0.321

Table 4 Correlation between preoperative ESS and preoperative airway parameters. * Significant correlation at $p<0.05$.

	R value	P value
Airway Volume (AV) (mm^3)	-0.31	0.090
minCSA (mm^2)	-0.40	0.031*
LAT (mm)	-0.17	0.374
AP (mm)	-0.44	0.016*
LAT/AP	0.25	0.177
Airway Length (AL) (mm)	-0.29	0.127

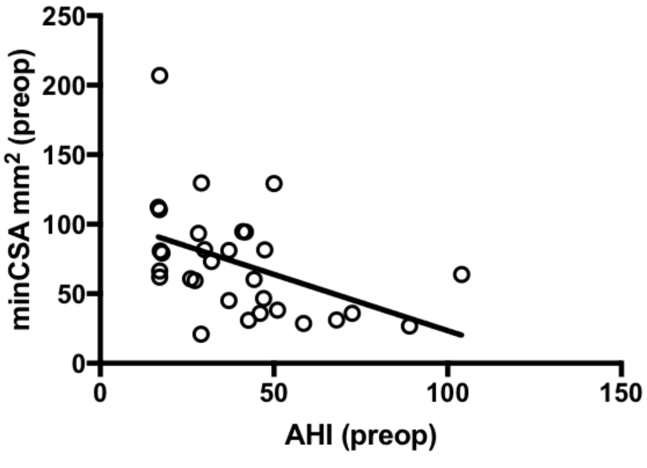


Figure 14 Correlation between preoperative AHI and preoperative minimum axial cross sectional area.

5.2 Reliability of airway measurements

Two independent examiners defined the parameters of the upper airway both preoperatively and postoperatively using the Dolphin 11.8 software as described in the methods section. Each examiner made airway measurements at two different time points. Intra-observer and inter-observer reliability were calculated using intraclass correlation tests. The intraexaminer and interexaminer reliability was extremely high ($r>0.9$) for all airway measurements recorded (Table 5).

Table 5 Reliability using intraclass correlation coefficients.

	Timing	AV	AL	AV/AL	MCSA	LAT	AP	LAT/AP
Observer #1	Pre-op	0.966	0.922	0.991	0.999	0.994	0.992	0.989
	Post-op	0.996	0.985	0.921	0.998	0.997	0.996	0.946
Observer #2	Pre-op	0.993	0.992	0.997	0.995	0.992	0.991	0.994
	Post-op	0.996	0.938	0.999	0.999	0.996	0.996	0.989
Inter-observer	Pre-op	0.965	0.932	0.985	0.988	0.979	0.993	0.989
	Post-op	0.994	0.892	0.947	0.996	0.993	0.965	0.958

5.3 Change in Airway parameters with MMA surgery

A paired-samples T test was used to compare the means of the preoperative and postoperative airway values (Table 6). There was a statistically significant increase in airway volume from 8303 mm^3 to 14 520 mm^3 representing an overall increase in the size of the oropharyngeal airway by 75% ($p<0.001$) (Figure 15). The minimum axial cross sectional area (minCSA) increased from a mean of 72.0 mm^2 to 175.5 mm^2 which is an increase of 145% ($p<0.001$) (Figure 16). There was a mean increase in the lateral dimension of the mCSA by 5.1 mm and an increase of the AP dimension by 3.2 mm, both of which were significant ($p<0.001$). There a statistically significant decrease in airway length from 55.0 mm to 53.2 mm postoperatively ($p=0.005$). The LAT/AP ratio decreased from 5.1 preoperatively to 3.7 post-operatively ($p=0.007$) which represents a change to a rounder airway.

Table 6 Preoperative and Postoperative airway parameters. * Significant difference at $p<0.05$.

	Pre-operative mean	Post-operative mean	P value
Airway Volume (AV) (mm^3)	8303	14 520	<0.001*
minCSA (mm^2)	72.0	175.5	<0.001*
LAT (mm)	16.8	21.9	<0.001*
AP (mm)	4.1	7.3	<0.001*
LAT/AP	5.1	3.7	0.007*
Airway Length (AL) (mm)	55.0	53.2	0.005*

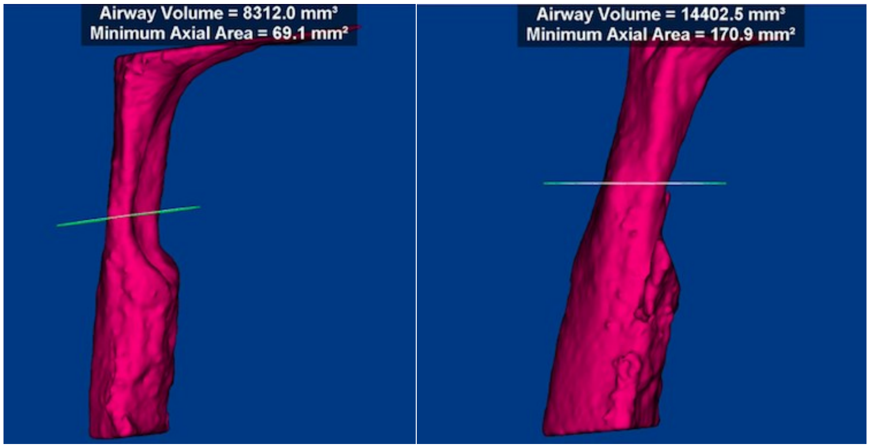


Figure 15 Airway volumes increased from an average of 8303 mm^3 to 14 520 mm^3 representing an overall increase in the size of the oropharyngeal airway by 75%.

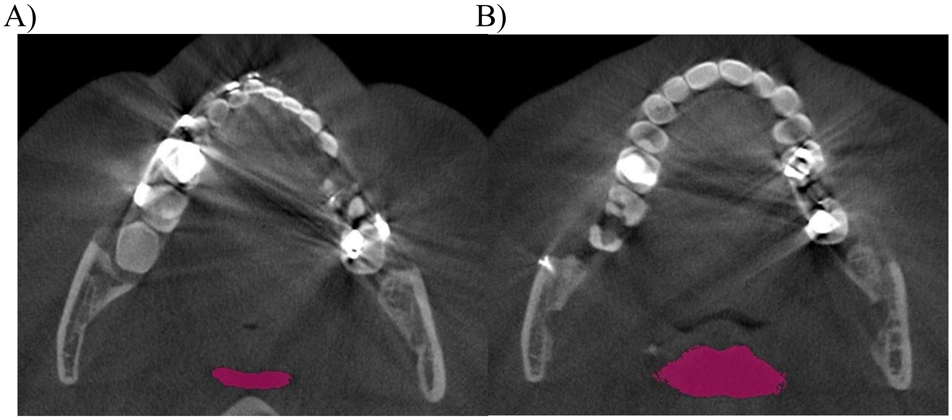


Figure 16 A) Preoperative axial view of minimum cross sectional area (mCSA)
B) Postoperative axial view of mCSA of same patient showing enlargement in all dimensions. On average, the minCSA increased by 145%. The lateral dimension of the mCSA increased by a mean of 5.1 mm and the AP dimension by 3.1 mm.

The position of the most constricted airway point (minCSA point) was represented by a ratio in the lateral view as described in the methodology. It was found that the position of the most constricted airway point moved superiorly by an average of 8% and this was found to be statistically significant ($p=0.033$) (Figure 17).

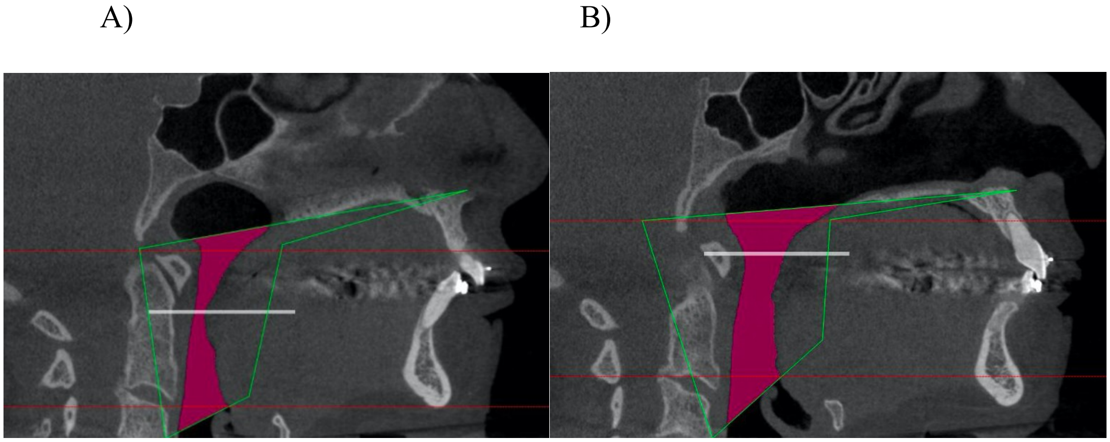


Figure 17 A) Preoperative Lateral view of the airway with minimum cross sectional area point (minCSA) represented by horizontal white line
B) Postoperative Lateral view of the same patient with min CSA point moving superiorly. The minCSA point was found to move superiorly by an average of 8%.

5.4 Change in Sleep parameters with MMA surgery

There was no statistically significant difference between preoperative and postoperative BMI. Twenty-two patients obtained 6 month post-operative polysomnography. The mean AHI was 41.3 events/hour preoperatively and that decreased to 12.4 events/hour post-operatively($p<0.001$) (Table 7). 18/22 patients (82%) were deemed to have had surgical success as defined by the criteria outlined in the methodology.11/22 patients (50%) obtained surgical cure of their sleep apnea. 4/22 patients (18%) were non-responders (Figure 18). The ESS scores decreased from a mean of 12 preoperatively to 5.4 postoperatively ($p<0.001$). 17 patients were sleep preoperatively (ESS > 10) and 3 patients were sleepy post-operatively. Preoperative and postoperative airway volumes, minCSA, AHI, and ESS are listed below (Table 8).

Table 7 Mean Preoperative and Postoperative sleep parameters. * Significant difference at $p<0.05$.

	Preoperative	Post-operative	P value
BMI (n=30)	31.3	30.6	0.204
AHI (n=22)	41.3	12.4	<0.001
ESS (n=30)	12.0	5.4	<0.001

Table 8 Preoperative and Postoperative Sleep and airway parameters. AHI post values; green – surgical success, red – non responder. *no post-operative polysomnography.

	AV pre (mm^3)	AV post (mm^3)	minCSA pre (mm^2)	minCSA post (mm^2)	AHI pre	AHI post	ESS pre	ESS post
1	16691	19986	206.9	290.0	17.1	2.7	3	6
2	8726	14507	110.4	164.4	17.0	0.7	4	4
3	9345	21398	129.8	355.5	29.1	4.5	13	7
4	7391	12197	59.4	130.9	27.3	1.5	9	3
5	7519	7861	112.1	92.1	16.7	1.4	14	3
6	6363	8178	81.6	107.9	47.4	6.1	7	0
7	7076	13436	80.6	109.5	17.3	4.5	10	7
8	7484	14280	60.7	157.3	26.0	9.5	7	9
9	8800	17466	93.5	229.5	28.3	1.3	17	4
10	7490	15638	60.3	113.9	44.3	35.1	0	2
11	7222	6188	38.1	41.3	51.0	27.3	18	11
12	5542	5256	20.9	82.6	29.0	*	21	
13	10204	16531	79.2	202.5	17.8	0.7	7	4
14	7048	12740	31.2	135.1	68.0	*	13	2
15	7999	24073	94.7	392.1	41.0	18.1	18	6
16	5932	10248	30.9	43.1	42.7	43.2	16	16
17	8454	9890	35.9	73.7	46.0	2.1	14	5
18	8528	16261	62.0	198.2	17.1	*	4	5
19	7392	11100	63.8	80.2	104.0	65	5	5
20	13694	22082	73.2	310.6	32.0	2.2	12	1
21	4075	9460	28.7	150.5	58.5	7.8	21	16
22	5541	12880	46.5	192.2	47.0	13.0	28	6
23	6857	19601	36.0	251.9	72.5	2.1	22	5
24	8718	11010	45.1	76.7	37.0	*	11	5
25	3458	6244	26.8	60.9	89.0	13.5	16	0
26	9908	15578	81.2	167.7	37.0	11.7	2	6
27	7031	8474	81.7	120.1	30.0	*	11	6
28	10332	15372	129.3	225.1	50.0	*	7	9
29	11466	22668	66.3	311.8	17.1	*	2	1
30	15969	34995	94.5	397.4	41.8	*	22	3
Mean	**8303**	**14520**	**72.0**	**175.5**	**41.3**	**12.4**	**12.0**	**5.4**

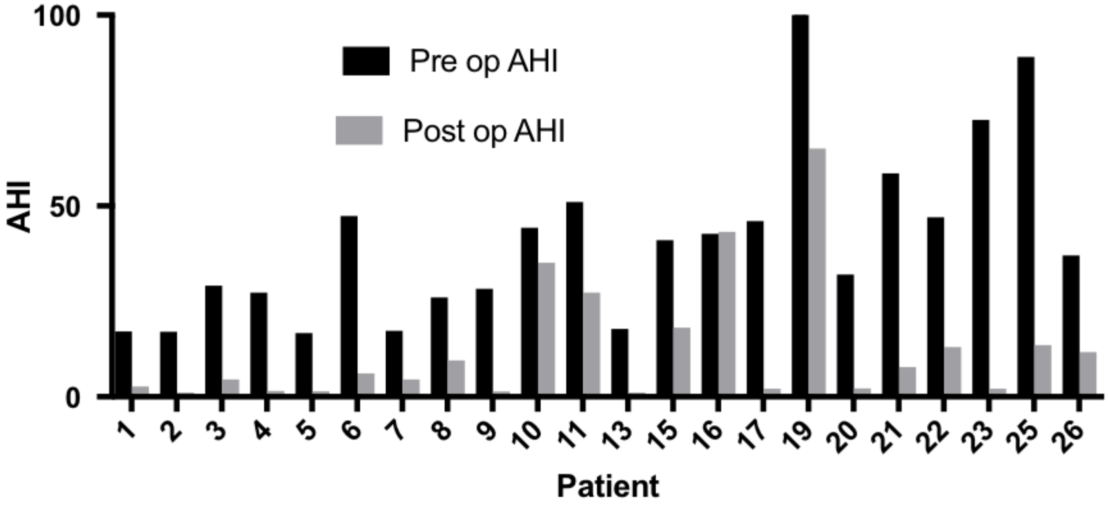


Figure 18 Preoperative and Postoperative AHI following MMA surgery

5.5 Surgical Advancement

The amount of surgical advancement of the maxilla, mandible, and chin was obtained from 6 month post-operative lateral cephalograms as described in the methodology (Table 9). A point measurements represent maxillary movement and B point measurements represent mandibular movement. Pogonion (Pg) measurements were dependent on whether a concomitant functional genioplasty was performed as well as any rotation of the maxillomandibular occlusal plane. A genioplasty was performed in 15 of 30 patients (50%). The mean maxillary advancement was 7.5 mm with a range of 0 mm to 13 mm. The mean mandibular advancement was 9.25 mm and ranged from 3 mm to 14.5 mm. The mean advancement measured at pogonion was 11.5 mm with a range of 5 mm to 18.5 mm.

Table 9 Surgical advancement, Airway change, and AHI change. *no post-operative polysomnography.

Patient	Procedure	A point (mm)	B point (mm)	Pg (mm)	% change mCSA	% change AHI
1	BSSO, FG	0	9.5	13.5	40.15	-75.68
2	LF, BSSO	10	11.5	13.5	48.79	-95.88
3	LF, BSSO	12.5	10	10	173.90	-84.85
4	LF, BSSO, FG	3	10	18.5	120.46	-94.91
5	LF, BSSO, FG	8	8.5	12	-17.89	-91.62
6	LF, BSSO	9	9.5	8	32.23	-87.13
7	LF, BSSO	9.5	8.5	9	35.84	-73.99
8	LF, BSSO	4.5	9	9.5	158.89	-63.46
9	LF, BSSO	5	9	10	145.52	-95.41
10	LF, BSSO, FG	9.5	9	13.5	88.81	-20.77
11	LF, BSSO, FG	3	4.5	8.5	8.33	-46.47
12	LF, BSSO	8	8	8.5	295.22	*
13	LF, BSSO	10	12	13	155.60	-96.07
14	LF, BSSO	8.5	10	10	333.71	*
15	LF, BSSO	7.5	6	7	314.15	-55.85
16	LF, BSSO, FG	5	8	11	39.48	+1.17
17	LF, BSSO, FG	8	9	15	105.10	-95.43
18	LF, BSSO, FG	8.5	10.5	15	219.68	*
19	LF, BSSO, FG	10.5	4.5	7	25.80	-37.50
20	LF, BSSO, FG	11.5	11.5	14	324.39	-93.13
21	LF, BSSO	8.5	10.5	10.5	424.22	-86.67
22	LF, BSSO	9.5	10	9.5	313.33	-72.34
23	LF, BSSO, FG	9	14	18	599.58	-97.10
24	LF, BSSO, FG	5	8	12	69.86	*
25	LF, BSSO, FG	5	10	15	127.76	-84.83
26	LF, BSSO	13	14.5	14	106.53	-68.38
27	LF, BSSO, FG	4	3	5	46.94	*
28	LF, BSSO, FG	4	8	10	73.99	*
29	LF, BSSO	6	10	12	370.64	*
30	LF, BSSO	7	11	12	320.53	*
Mean	**15 - Genioplasty** **15 - No Genioplasty**	**7.5 mm**	**9.25 mm**	**11.5 mm**	**163%**	**-73.5%**

There was a statistically significant correlation between advancement measured at B point and percent change of the minCSA (Table 10, Figure 19-A). There was no statistical significance between A point movement or Pg movement and % change in minCSA. B point advancement was also significantly correlated with % decrease in AHI post-operatively (Figure 19-B). There was no correlation between A point movement or Pg movement and % change in post-operative AHI.

Table 10 Correlation between surgical movements, AHI, and minimum cross sectional area changes.

	R value	**P Value**
% change minCSA vs. A point	0.283	0.137
% change minCSA vs. B point	0.456	0.013*
% change minCSA vs. Pg	0.219	0.253
% change AHI vs. A point	-0.126	0.577
% change AHI vs. B point	-0.532	0.011*
% change AHI vs. Pg	-0.389	0.074

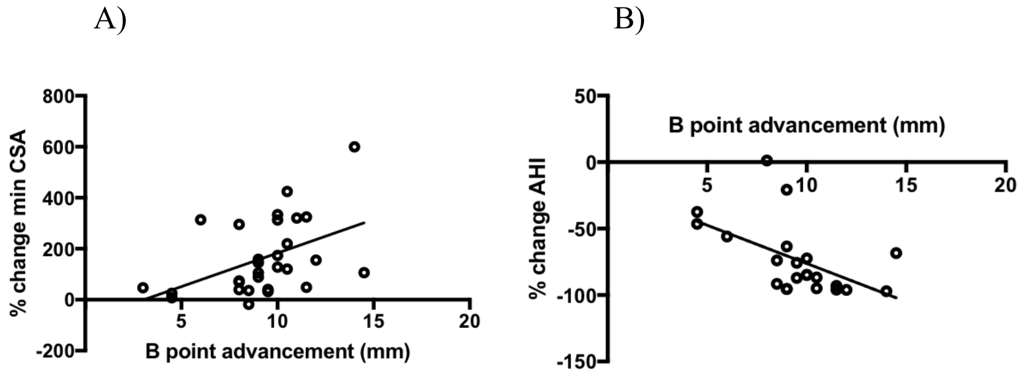


Figure 19 A) Increased B point advancement is correlated with a larger increase in minimum cross sectional area (minCSA) following surgery (p=0.013)
B) Increased B point advancement is correlated with a larger decrease in AHI following surgery (p= 0.011)

5.6 Effect of Functional Genioplasty

In the study population, 15 patients out of 30 underwent a concomitant genioplasty procedure. The mean airway preoperative and postoperative airway parameters in both groups are listed below (table 11). A one-way ANOVA was used to assess for differences between groups. There was no statistically significant difference in any airway parameter between patients who underwent the genioplasty procedure and those who didn’t.

Table 11 Airway changes in patients who underwent MMA with and without concomitant genioplasty. Significance at $p<0.05$.

	No Genioplasty	With Genioplasty	P value
Pre AV	8149	8447	0.793
Post AV	15770	12810	0.217
Pre minCSA	73.8	70.8	0.842
Post minCSA	203.1	140.6	0.096
Pre LAT	17.2	16.7	0.816
Post LAT	23.3	20.4	0.220
Pre AP	3.9	4.3	0.596
Post AP	8.1	6.3	0.116
Pre LAT/AP	5.1	5.1	0.995
Post LAT/AP	3.4	4.0	0.458
Pre AL	51.9	55.0	0.210
Post AL	54.9	53.7	0.736

5.7 Postoperative Sleep parameters and postoperative airway parameters

A pearson bivariate test showed that there was no statistical significant correlation between the magnitude of changes in minCSA and percent reduction in AHI following MMA surgery ($r=0.30$, $p=0.18$). There was also no correlation noted between changes in airway volume and changes in AHI.

Pearson bivariate correlation tests were used to assess for any correlation between postoperative AHI and postoperative airway parameters (Table 12). Larger lateral dimension of the minCSA (LAT) was correlated with lower post-operative AHIs, and this was statistically significant ($p=0.043$). There was also a trend towards larger minCSA and larger AP dimensions correlating with lower post-operative AHIs, but this did not meet statistical significance. Postoperative ESS scores did not show any correlation to postoperative airway parameters (Table 13).

Table 12 Correlation between postoperative AHI and postoperative airway parameters. * Significant correlation at $p<0.05$.

	R value	P value
Airway Volume (AV) (mm^3)	-0.24	0.275
minCSA (mm^2)	-0.38	0.079
LAT (mm)	-0.44	0.043*
AP (mm)	-0.38	0.084
LAT/AP	0.12	0.585
Airway Length (AL) (mm)	0.08	0.712

Table 13 Correlation between postoperative ESS and postoperative airway parameters. * Significant correlation at $p<0.05$.

	R value	P value
Airway Volume (AV) (mm^3)	-0.17	0.379
minCSA (mm^2)	-0.14	0.491
LAT (mm)	-0.13	0.518
AP (mm)	-0.13	0.499
LAT/AP	0.08	0.700
Airway Length (AL) (mm)	-0.07	0.735
AV/AL	-0.14	0.491

5.8 Airway differences in patients with surgical success vs. non-responders

A student paired t-test was used to compare the preoperative and postoperative airway parameters of patients who experienced surgical success (n=18) as well as those who were non-responders (n=4) (Table 14). Of note, the minCSA increased by 139.5% in the surgical success group and by 44% in the non-responder group. There was relatively less change in all airway parameters in the non-responder group. Student paired t-tests were also used to assess change in sleep parameters between the surgical success group and the non-responder group (Table 15).

Table 14 Preoperative and postoperative airway parameters in patients who had surgical success vs. patients who were non-responders.

	Surgical Success			**Non-Responders**		
	Mean	% change	P value	Mean	% change	P value
Pre AV **Post AV**	8310 14758	77.6%	<0.001*	7009 10793	54.0%	0.138
Pre minCSA **Post minCSA**	79.8 191.1	139.5%	<0.001*	48.3 69.6	44.1%	0.150
Pre LAT **Post LAT**	18.3 22.6	23.5%	0.002*	13.6 15.9	16.9%	0.445
Pre AP **Post AP**	4.1 8.1	97.6%	<0.001*	3.5 4.0	14.3%	0.024*
Pre LAT/AP **Post LAT/AP**	5.3 3.2	-39.6%	0.003*	6.2 5.0	-19.4%	0.554
Pre AL **Post AL**	50.4 52.9	4.9%	0.257	60.1 58.1	-3.3%	0.305
Pre AV/AL **Post AV/AL**	165.6 282.2	70.4%	<0.001*	116.8 185.3	58.64%	0.122

Table 15 Preoperative and postoperative sleep parameters in patients who had surgical success vs. patients who were non-responders.

	Surgical Success			**Non-Responders**		
	Preop	% change	P value	Pre-op	% change	P value
AHI pre **AHI post**	37.1 5.7	-84.6%	<0.001*	60.5 42.6	-29.6%	0.130
ESS pre **ESS post**	12.4 5.1	-58.9%	<0.001*	9.8 8.5	-13.26%	0.572
BMI pre **BMI post**	29.6 28.7	-3.0%	0.215	32.6 31.6	-3.1%	0.606

CHAPTER 6 – DISCUSSION

6.1 Changes in airway parameters with MMA surgery

The primary objective of our study was to quantify pharyngeal airway changes in patients undergoing maxillomandibular advancement surgery for the treatment of obstructive sleep apnea. Our results clearly demonstrate that there is a statistically significant increase in airway volume, minCSA, LAT, AP, and a statistically significant decrease in airway length and LAT/AP ratio following MMA surgery (Table 6).

A recent metaanalysis by Rosario et al[101] assessed the efficiency of bimaxillary surgery in increasing the volume of the upper airways. In total, six studies representing 83 patients were included for analysis. Heterogeneity of airway volumes resulted from differences in anatomic limits set by each author. Some studies included nasopharyngeal and hypopharyngeal airway changes, while others were limited to the oropharynx. The mean increase in total airway volume was 7860 mm^3 following maxillomandibular advancement surgery with mean increases from 28.5% to 80%. [84,98,99,102–104] However, the majority of airway obstruction occurs in the retropalatal and retroglossal region of the oropharynx, making it the most important area of interest with regards to volume change. Veys et al[105] studied a cohort of 11 consecutive patients who underwent MMA for OSA. Similar to our study, they used airway limits that were outlined in a validation study by Guijarro-Martinez.[91] The oropharyngeal volume increased from a preoperative value of 7641 mm^3 to 13770 mm^3 postoperatively. Butterfield[100] showed oropharyngeal changes in 12 patients undergoing MMA from 8680 mm^3 preoperatively to 13350 mm^3 postoperatively. In our study population, the oropharyngeal volume increased from 8303 mm^3 to 14520 mm^3 which was a mean increase of 6217 mm^3 or 75%. Maxillomandibular advancement surgery significantly increases oropharyngeal airway volume in patients with obstructive sleep apnea.

As discussed previously, smaller minimum axial cross sectional areas of the oropharyngeal airway have been shown to correlate with both the presence and severity of obstructive sleep apnea. However, there has been no study to date which determines a threshold minCSA that increases the risk of having OSA. Review of the current literature demonstrates that OSA populations always have mean minCSA of less than 100 mm^2, with mean values of the minimum axial cross sectional area ranging from 35 mm^2 to 82 mm^2.[93,95,96,100,103] In our study population, the mean preoperative minCSA was 72.0 mm^2. Postoperatively, the mean minCSA increased to 175.5 mm^2 which was an increase of 145%. Other authors have shown increases of the minCSA from 38% to 212% postoperatively following MMA surgery.[97–99,103] The postoperative airway parameters of patients who underwent MMA surgery resemble those of healthy non-OSA patients outlined in the literature.

The lateral dimension of the mCSA increased by an average of 5.1 mm and the AP dimension increased by 3.2 mm following surgery, both of which were statistically significant. As Schwab et al. noted in their MRI study, OSA patients demonstrate significant airway narrowing in the lateral dimension. Previously, only AP airway changes could be appreciated on lateral cephalometric radiographs. With CBCT imaging, it is apparent that MMA surgery helps to increase the lateral dimension of the minimum cross sectional area, especially in individuals who present with a narrowed hourglass shape in coronal view (Figure 20). The airway also tends to change from an hourglass shape to a wider column shape in the sagittal view (Figure 21). This also accounts for the narrowest portion of the minCSA moving slightly superiorly by 8% on average as demonstrated below.

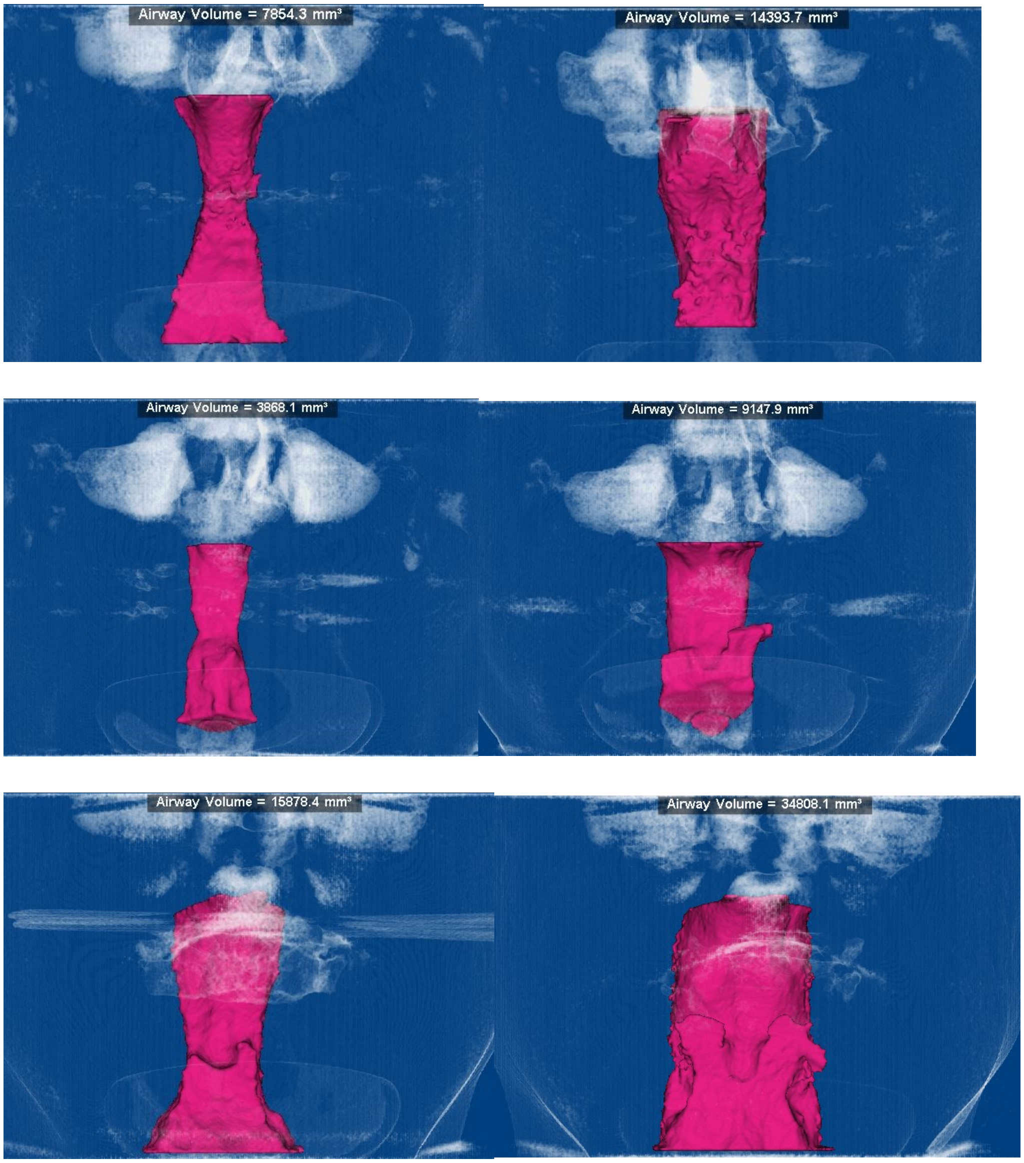


Figure 20 Preoperative and postoperative AP coronal views of the airway showing a narrowed preoperative hourglass shape and a widened postoperative column shape of the airway.

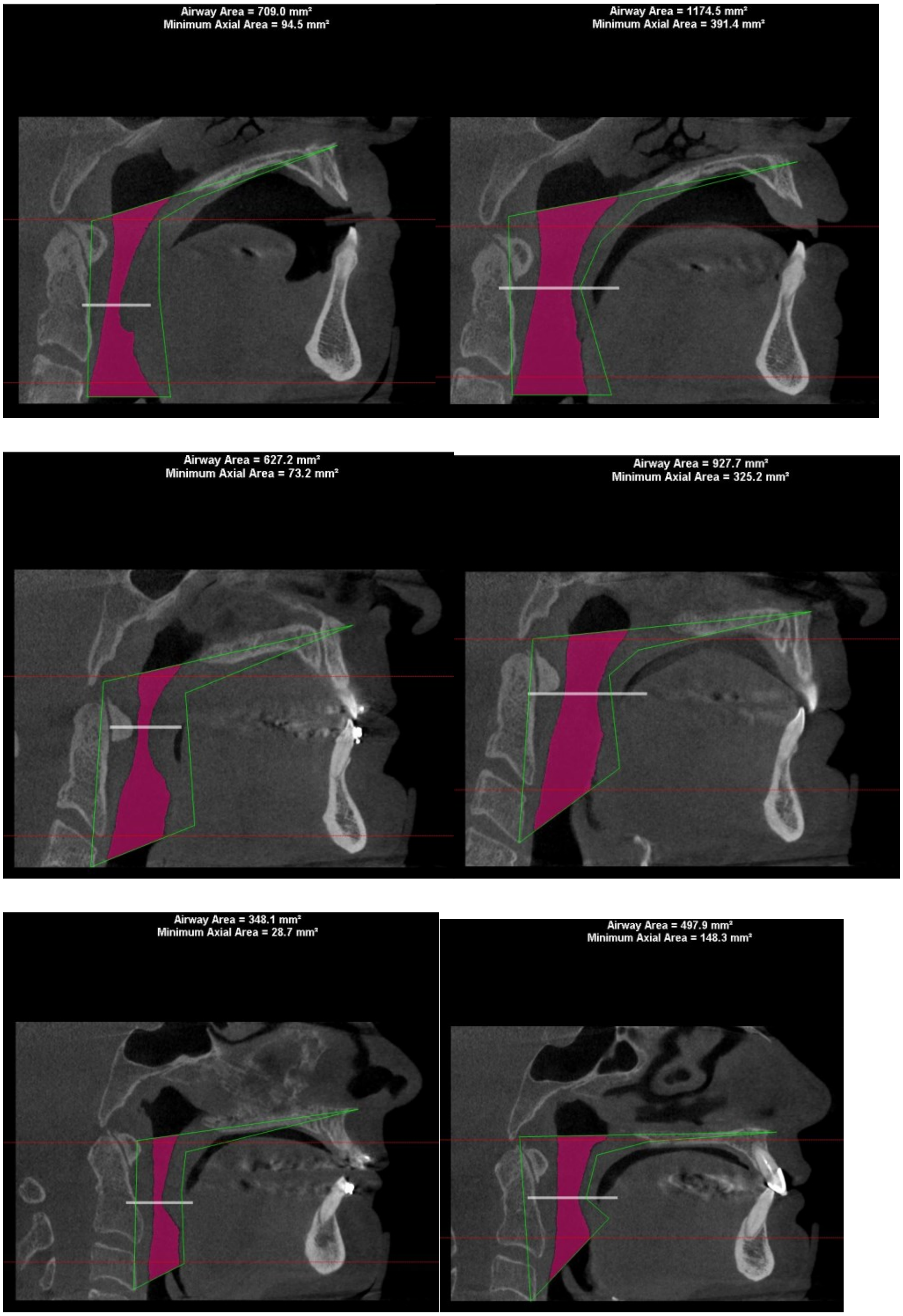


Figure 21 Sagittal view showing narrowed hourglass shape with minCSA point in retropalatal region (left). Postoperative images of same patient show a widened airway with the minCSA point moving superiorly (right).

In our study population, airway length decreased on average by 1.8 mm following MMA which was statistically significant (p=0.005). It has been proposed that a shorter airway decreases airway resistance according to Poiseulle's law, and this contributes to improvements with AHI following MMA surgery (Figure 22). Other authors have shown similar decreases in airway length following MMA surgery.[84,85,97,106]

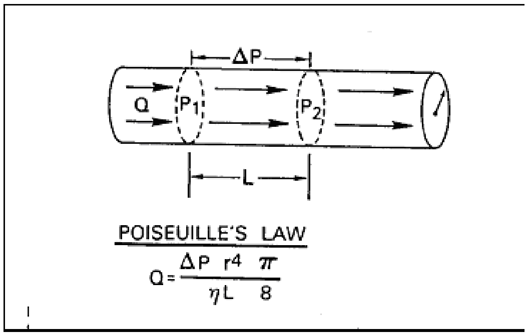


Figure 22 Poiseuille's Law. Flow is proportional to the 4th power of the radius and inversely proportional to the length.

The LAT/AP ratio represents the relative shape of the minCSA. Larger values are associated with more elliptical airways and previous authors have postulated that an elliptical shape is more favourable and less prone to collapse.[80,97,107] However, in our study population, the LAT/AP ratio decreased postoperatively. This is due to the fact that there was a global increase in both the lateral and AP dimensions, with a proportionally greater increase in the AP dimension. In all patients, the preoperative AP dimensions were much smaller than the LAT dimensions of the minCSA. Therefore, a uniform linear increase in both these parameters would cause a decrease in the LAT/AP ratio. In our study population, even though LAT increased more than AP (5.1 mm vs. 3.2 mm), the LAT/AP ratio decreased because of this phenomenon. We suspect that the LAT/AP ratio is not as important as the overall surface area of the minCSA. This is also demonstrated by the fact that there was no correlation between preoperative LAT/AP ratio and AHI, however, a strong correlation exists between preoperative minCSA and AHI. According to Poiseulle's law, a small minCSA with a large LAT/AP ratio would have increased resistance compared to an airway with a large minCSA and a small LAT/AP ratio. Examples of changes in the minCSA can be seen below (Figure 23).

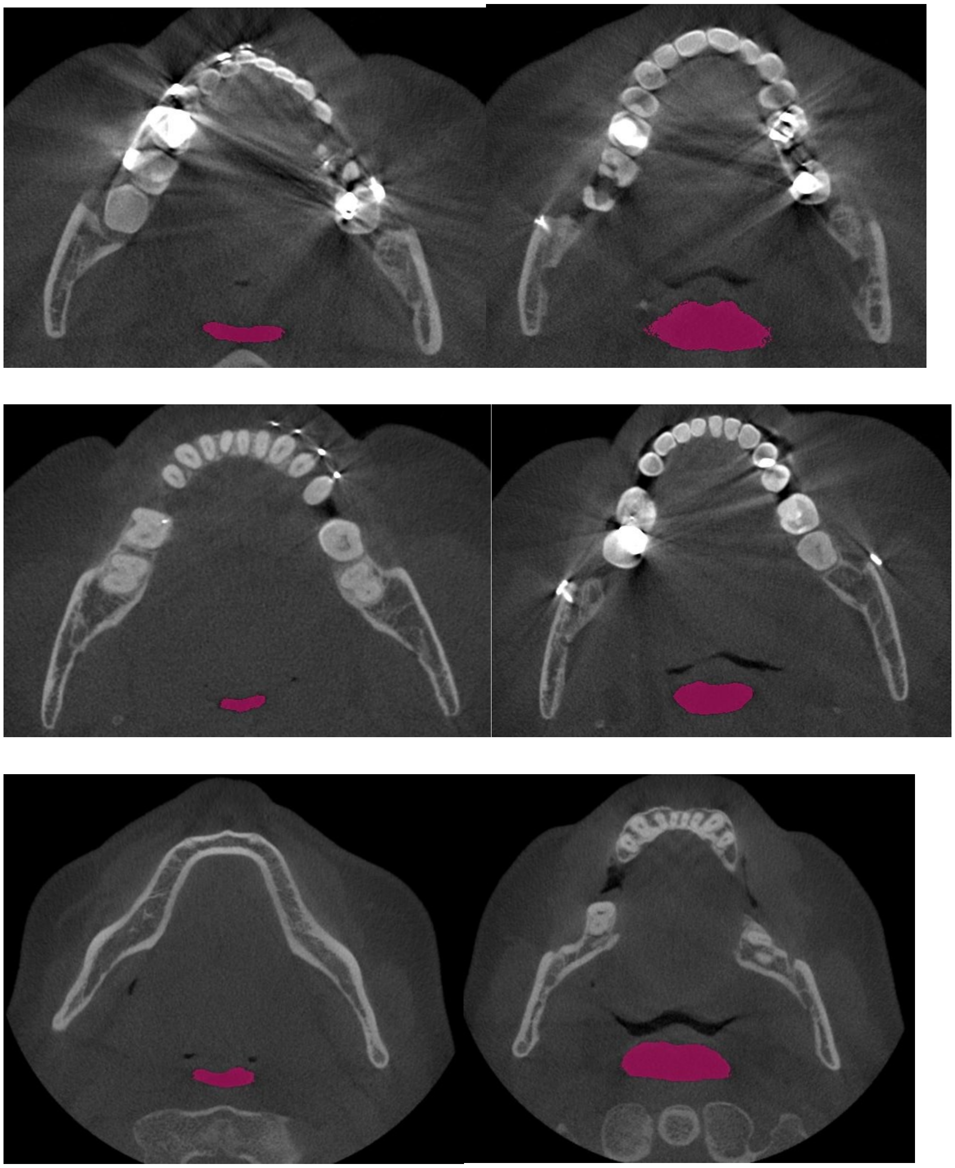


Figure 23 minCSA preoperatively (left) and postoperatively (right). Both the lateral and AP dimensions increased significantly which changes the airway from a more elliptical shape to more circular shape.

6.2 Preoperative airway parameters compared with preoperative sleep parameters

Previous studies have shown that the BMI is increased in patient with EDS [37,108] Lee et al. compared a cohort of obstructive sleep apnea patients with and without excessive daytime sleepiness. The mean BMI in 59 patients without EDS was 24.68, and in 37 patients with EDS was 27.24, which was statistically significant ($p<0.001$). In our study population, the BMI showed a significant positive correlation to the preoperative ESS score ($r=0.37$, $p=0.04$). The mean BMI in the 13 patients without EDS was 29.04 and the BMI in the 17 patients with EDS was 33.12 ($p<0.001$). Obesity is a known risk factor for excessive daytime sleepiness and our study corroborates this finding.

Different landmarks have been used in the literature to delineate airway boundaries and this has created a wide range of preoperative airway volumes reported in both patients with OSA, and normal controls. In our study, preoperative airway volumes ranged from 3458 mm^3 to 16691 mm^3 with a mean of 8303 mm^3. It was found that preoperative airway volume was significantly negatively correlated with preoperative AHI ($r=-0.40$, $p=0.028$).

Schwab[109] used an MRI study to show that the minimum axial cross sectional airway area was significantly smaller in apneic compared with normal subjects and occurred in the retropalatal region. Other three-dimensional imaging studies have found the most constricted airway point in patients with obstructive sleep apnea is in the retropalatal region.[92,93,96,109] Our study corroborated these findings with 27/30 (90%) of patients having their minCSA point in the retropalatal area. Enciso et al[110] found the minimum axial cross sectional area was 73.3 mm^2 in a group of 46 patients with OSA which was significantly lower than the control group. Li et al[92] used CT imaging and found smaller retropalatal areas are correlated with higher RDIs. The average preoperative minCSA in our study was 72.0 mm^2. Higher pre-operative AHI's were significantly correlated with smaller minimum axial cross sectional areas (r=-0.44, p=0.014). Previous authors have demonstrated a similar relationship between a smaller minCSA and worsening OSA severity.[93–96]

Previous studies have shown a smaller lateral dimension[92,96,100,110] and anterior-posterior dimension[94,96,111] of the minimum axial airway in subjects with OSA compared to controls. Schwab et al[109] found that a smaller lateral dimension of the airway is correlated with higher AHIs. Within our study population, smaller lateral dimension of the minimum cross sectional area was associated with higher AHIs, but this did not meet statistical significance (r=-0.35, p=0.056). The AP dimension of the minimum cross sectional area showed a similar trend, but did not meet statistical significance (p=0.05). With higher sample sizes, it is likely that both these parameters would be statistically significant.

Previous authors have shown an association between increased airway length and OSA severity.[80,106,112] Susarla et al[106] used lateral cephalograms to evaluate 96 individuals with OSA and 56 controls without OSA and found a strong correlation between upper airway length and RDI. They found that upper airway lengths greater than 72 mm in males, and greater than 62 mm in females were significantly associated with the presence of OSA. In contrast, Enciso et al[110] found no differences in airway length in 46 OSA patients, and 34 snorers without OSA.

In our study population, there was no correlation noted between preoperative airway length and preoperative AHI. The preoperative airway lengths ranged from 45.9 mm to 67.5 mm with a mean of 55.0 mm. These results agree with a comparative study by Butterfield et al[100] where the airway length in a group of 12 OSA patients had a mean of 55.8 mm, which showed no statistical difference from the 12 patient control group mean of 56.1 mm. This suggests that an elongated airway may not be a large contributing factor to the severity of OSA.

No literature exists comparing ESS scores to three dimensional airway parameters. In our study population, higher preoperative ESS scores were correlated to smaller minCSAs ($r=-0.4$, $p=0.031$). Higher ESS scores were also correlated to smaller AP dimensions ($r=-0.44$, $p=0.016$) of the minCSA, but not the lateral dimension ($p=0.374$). Airway volumes did not show a statistically significant correlation to ESS scores, but a trend was present ($r=-0.31,p=0.09$). These results suggest that a narrowed oropharyngeal airway could be a risk factor for excessive daytime sleepiness.

It is clear from our study population that smaller preoperative airways are associated with more severe OSA. It is therefore logical to postulate that improvement in airway parameters with MMA surgery would also help to reduce the number of obstructive events that a patient experiences.

6.3 Changes in sleep parameters following MMA Surgery

A meta-analysis by Holty et al.[58] included 21 unique cohorts of patients (n = 627) undergoing maxillomandibular advancement for OSA. The overall surgical success rate of MMA was 86% and the surgical cure (AHI<5) was 43%. Our study population showed a surgical success rate of 82%, and a surgical cure rate of 50%. The Holty metanalysis cited the amount of maxillary advancement as a predictor of surgical success. In our study, there was no statistical association between maxillary advancement (A point) and changes in minCSA or AHI postoperatively. However, mandibular advancement (B point) was significantly correlated with changes in minCSA (r=0.456, p=0.013) and reduction in AHI (r=-0.532, p=0.011). This may suggest that mandibular advancement may be more important than maxillary advancement for improved airway characteristics as well as surgical outcomes. Many clinician's attempt to achieve a mandibular advancement of at least 10 mm with MMA, but this is not based on sound evidence. These findings may help to guide clinicians to maximize mandibular advancement when performing MMA surgery. However, in patients with a small preoperative overjet, maxillary position can limit the amount of mandibular advancement that is achievable. In this population, a larger maxillary advancement will allow the clinician to maximize mandibular advancement, as it provides more space for the mandible to be positioned anteriorly into the desired postoperative occlusion.

Almost all patients had significant increases in their airway volume and minCSA, as well as significant decreases in their AHI following surgery. However, there was no statistically significant correlation between the magnitude of the airway changes and improvement in sleep parameters. A larger increase in a patient's airway didn't correlate with a larger reduction in their AHI. With a larger sample size, it is likely that statistical significance would have been reached between increases in minCSA and reduction in AHI following surgery, as a trend was noticed with our data (r=-0.30, p=0.18). Regardless, there was a significant negative correlation between preoperative minCSA and AHI, and our results also show significant improvements in minCSA and other airway parameters following MMA surgery. We can infer that the improvement in the sleep parameters are related to increases in the airway parameters. With a larger study, one may be able to determine a threshold minCSA that significantly reduces the risk of having OSA.

When assessing postoperative airway parameters, there was a statistically significant correlation found between larger lateral dimensions of the postoperative minCSA (LAT) and decreased post-operative AHIs (r=-0.44, p=0.043) (Table 12). This could help to explain the fact that patients who have underwent MMA surgery have been found to have reduced collapsibility of their lateral pharyngeal walls after surgery. Patients who respond less in the lateral dimension with MMA surgery may be more prone to airway collapse and residual OSA following surgery.

When we compare airway changes of patients who experienced surgical success vs. non-responders, it becomes apparent that the non-responders had less favourable changes in their airway parameters (Table 15). The surgical success group had a minCSA change from 79.8 mm to 191.1 mm which was an increase of 140% following MMA. The non-responder group had an increased minCSA from 48.3 mm to 69.6 mm, which was an increase of 44% following surgery. The non-responders had smaller preoperative airway parameters and higher preoperative AHI's than the surgical success group. However, there were many patients in the surgical success group with similar preoperative airway and sleep parameters that exhibited large improvements following surgery. Of note, average B point movements were 10.2 mm in the success group, and 6.5 mm in the non-responder group. It is possible that some degree of mandibular relapse or inadequate advancement at the time of surgery could be responsible for less than ideal outcomes in the non-responder group. This lack of B point movement is likely related to smaller increases in the airway parameters, and subsequently less improvement with their AHI following surgery.

6.4 Limitations

The largest limitation with this study is sample size. 8 of 30 patients were not able to undergo 6 month post-operative polysomnography. Limiting factors to obtaining post-op sleep studies include patient refusal once OSA symptoms have resolved, as well as long waitlists to undergo Level 1 overnight PSG. It is possible that with an increased sample size there would be a correlation noted between the magnitude of airway changes and changes in post-operative AHI.

CBCT represents a static capture of a patient’s airway morphology, and the image is partially dependent on the respiratory cycle, swallowing, and positioning of the patient. Error from these factors are ideally minimized with a standardized imaging protocol, but it is likely that some degree of error still exists. OSA also represents a dynamic multifactorial process. The fact that patients can still present with some degree of residual OSA following anatomic normalization of their supine airway implies that neuromuscular influences also play a role in the pathophysiology of OSA.

Future advancements in the field of imaging will likely involve faster scanning times at an attempt to eliminate confounding factor of respiration.[113] Ideally, future pharyngeal airway imaging will have the ability to capture respiration in motion in a supine position. This would provide the most accurate representation of breathing and obstructive events during sleep. A newer form of imaging called cine magnetic resonance imaging (cineMRI) is able to gather information throughout the various phases of the breathing cycle, however, the availability of this technology is greatly limited at this point in time.[100]

CHAPTER 7 – CONCLUSION

Maxillomandibular advancement surgery results in significant increases in total airway volume, the minimum axial cross sectional area, lateral dimension of the minimum cross sectional area, and anterior-posterior dimension of the minimum cross sectional area. MMA also results in a decrease in airway length and moves the minCSA point superiorly by 8%. All of these factors work to decrease airway resistance and help prevent its collapse during sleep.

MMA surgery is correlated with a decrease in the LAT/AP dimension which is associated with a change from an elliptical to a rounder airway. A smaller LAT/AP dimension is not associated with increased airway collapsibility, because it does not take into account the area of the minimum axial slice. The minCSA is more predictive than the LAT/AP dimension in determining airway collapsibility in patients with OSA.

The severity of a patient's OSA is correlated to both their airway volume as well as their minCSA. Patient's with smaller total airways and smaller minCSA have more obstructive events per hour. Patient's with residual OSA after MMA surgery are noted to have a smaller lateral dimension of their minimum cross sectional area. This could point to the importance of increasing the lateral dimension with MMA surgery.

MMA is a highly successful procedure that results in significant decreases in AHI and ESS. The magnitude of increases in airway parameters following MMA surgery showed no correlation to the decreases in sleep parameters. However, the magnitude of mandibular advancement is correlated to both increases in the minCSA as well as decreases in the AHI following surgery. This points to the importance of maximizing mandibular advancement with MMA surgery.

Future studies would benefit from an increased sample size to help determine a threshold minCSA and airway volume that reduces the risk of residual obstructive events following surgery.

Bibliography

1. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The Occurrence of Sleep-Disordered Breathing among Middle-Aged Adults. *N Engl J Med*. 1993. doi:10.1056/NEJM199304293281704

2. Schwartz AR, Patil SP, Laffan AM, Polotsky V, Schneider H, Smith PL. Obesity and Obstructive Sleep Apnea: Pathogenic Mechanisms and Therapeutic Approaches. *Proc Am Thorac Soc*. 2008. doi:10.1513/pats.200708-137MG

3. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: A population health perspective. *Am J Respir Crit Care Med*. 2002. doi:10.1164/rccm.2109080

4. Bucks RS, Olaithe M, Eastwood P. Neurocognitive function in obstructive sleep apnoea: a meta-review. *Respirology*. 2013. doi:10.1111/j.1440-1843.2012.02255.x

5. Beebe DW, Groesz L, Wells C, Nichols A, McGee K. The neuropsychological effects of obstructive sleep apnea: A meta-analysis of norm-referenced and case-controlled data. *Sleep*. 2003. doi:10.1093/sleep/26.3.298

6. Bonnet MH, Arand DL. Clinical effects of sleep fragmentation versus sleep deprivation. *Sleep Med Rev*. 2003. doi:10.1053/smrv.2001.0245

7. Young T, Skatrud J, Peppard PE. Risk Factors for Obstructive Sleep Apnea in Adults. *Jama*. 2004. doi:10.1001/jama.291.16.2013

8. Garbarino S, Guglielmi O, Sanna A, Mancardi GL, Magnavita N. Risk of Occupational Accidents in Workers with Obstructive Sleep Apnea: Systematic Review and Meta-analysis. *Sleep*. 2016. doi:10.5665/sleep.5834

9. Tregear S, Reston J, Schoelles K, Phillips B. Obstructive sleep apnea and risk of motor vehicle crash: Systematic review and meta-analysis. *J Clin Sleep Med*. 2009.

10. Jonas DE, Amick HR, Feltner C, et al. Screening for Obstructive Sleep Apnea in Adults Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA*. 2017. doi:10.1001/jama.2016.19635

11. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol*. 2013;177(9):1006-1014. doi:10.1093/aje/kws342

12. Bixler EO, Vgontzas AN, Ten Have T, Tyson K, Kales A. Effects of age on sleep apnea in men. I. Prevalence and severity. *Am J Respir Crit Care Med*. 1998. doi:10.1164/ajrccm.157.1.9706079

13. Bixler EO, Vgontzas a N, Lin HM, et al. Prevalence of sleep-disordered breathing in women: effects of gender. *Am J Respir Crit Care Med*. 2001. doi:10.1164/ajrccm.163.3.9911064

14. Strelzow V V, Blanks RH, Basile A, Strelzow AE. Cephalometric airway analysis in obstructive sleep apnea syndrome. *Laryngoscope*. 1988. doi:10.1001/archotol.1987.01860050019002

15. Young T, Evans L, Finn L, Palta M. Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. *Sleep*. 1997. doi:10.1093/sleep/20.9.705

16. Lumeng JC, Chervin RD. Epidemiology of pediatric obstructive sleep apnea. *Proc Am Thorac Soc*. 2008. doi:10.1513/pats.200708-135MG

17. Tauman R, Gozal D. Obstructive sleep apnea syndrome in children. *Expert Rev Respir Med*. 2011. doi:10.1586/ers.11.7

18. Tauman R, Gulliver TE, Krishna J, et al. Persistence of obstructive sleep apnea syndrome in children after adenotonsillectomy. *J Pediatr*. 2006. doi:10.1016/j.jpeds.2006.08.067

19. Schwab RJ, Goldberg AN. Upper Airway Assessment. *Otolaryngol Clin North Am*. 1998. doi:10.1016/S0030-6665(05)70100-6

20. Suto Y, Matsuo T, Kato T, et al. Evaluation of the pharyngeal airway in patients with sleep apnea: Value of ultrafast MR imaging. *Am J Roentgenol*. 1993. doi:10.2214/ajr.160.2.8424340

21. Schwab RJ, Kuna ST, Remmers JE. Anatomy and Physiology of Upper Airway Obstruction. In: *Principles and Practice of Sleep Medicine*. ; 2005. doi:10.1016/B0-72-160797-7/50089-6

22. Ayappa I, Rapoport DM. The upper airway in sleep: Physiology of the pharynx. *Sleep Med Rev*. 2003;7(1):9-33. doi:10.1053/smrv.2002.0238

23. Schwab RJ, Pasirstein M, Pierson R, et al. Identification of upper airway anatomic risk factors for obstructive sleep apnea with volumetric magnetic resonance imaging. *Am J Respir Crit Care Med*. 2003;168(5):522-530. doi:10.1164/rccm.200208-866OC

24. Lowe AA, Fleetham JA, Adachi S, Ryan CF. Cephalometric and computed tomographic predictors of obstructive sleep apnea severity. *Am J Orthod Dentofac Orthop*. 1995. doi:10.1016/S0889-5406(95)70101-X

25. Neelapu BC, Kharbanda OP, Sardana HK, et al. Craniofacial and upper airway morphology in adult obstructive sleep apnea patients: A systematic review and meta-analysis of cephalometric studies. *Sleep Med Rev*. 2017. doi:10.1016/j.smrv.2016.01.007

26. Miles PG, Vig PS, Weyant RJ, Forrest TD, Rockette HE. Craniofacial structure and obstructive sleep apnea syndrome--a qualitative analysis and meta-analysis of the literature. *Am J Orthod Dentofacial Orthop*. 1996;109(2):163-172. doi:10.1016/S0889-5406(96)70177-4

27. Schwab RJ. Upper airway imaging. *Clin Chest Med*. 1998. doi:10.1016/S0272-5231(05)70430-5

28. Patil SP, Schneider H, Schwartz AR, Smith PL. Adult Obstructive Sleep Apnea: Pathophysiology and Diagnosis. *Chest*. 2010;132(1):1-21. doi:10.1378/chest.07-0040.Adult

29. Jordan AS, White DP. Pharyngeal motor control and the pathogenesis of obstructive sleep apnea. *Respir Physiol Neurobiol*. 2008;160(1):1-7. doi:10.1016/j.resp.2007.07.009

30. Fogel RB, Trinder J, White DP, et al. The effect of sleep onset on upper airway muscle activity in patients with sleep apnoea versus controls. *J Physiol*. 2005. doi:10.1113/jphysiol.2005.083659

31. Chung F, Yegneswaran B, Liao P, et al. STOP Questionnaire. *Anesthesiology*. 2008. doi:10.1097/ALN.0b013e31816d83e4

32. Doshi V, Walia R, Jones K, Aston CE, Awab A. STOP-BANG questionnaire as a screening tool for diagnosis of obstructive sleep apnea by unattended portable monitoring sleep study. *Springerplus*. 2015. doi:10.1186/s40064-015-1588-0

33. Vana KD, Silva GE, Goldberg R. Predictive abilities of the STOP-Bang and Epworth Sleepiness Scale in identifying sleep clinic patients at high risk for obstructive sleep apnea. *Res Nurs Heal*. 2013. doi:10.1002/nur.21512

34. Nagappa M, Liao P, Wong J, et al. Validation of the stop-bang questionnaire as a screening tool for obstructive sleep apnea among different populations: A systematic review and meta-Analysis. *PLoS One*. 2015. doi:10.1371/journal.pone.0143697

35. Johns MW. A new method for measuring daytime sleepiness: The Epworth sleepiness scale. *Sleep*. 1991. doi:10.1093/sleep/14.6.540

36. Gottlieb DJ, Whitney CW, Bonekat WH, et al. Relation of sleepiness to respiratory disturbance index: The sleep heart health study. *Am J Respir Crit Care Med*. 1999. doi:10.1164/ajrccm.159.2.9804051

37. Lee SJ, Kang HW, Lee LH. The relationship between the Epworth Sleepiness Scale and polysomnographic parameters in obstructive sleep apnea patients. *Eur Arch Oto-Rhino-Laryngology*. 2012. doi:10.1007/s00405-011-1808-3

38. Sateia MJ. International classification of sleep disorders-third edition highlights and modifications. *Chest*. 2014. doi:10.1378/chest.14-0970

39. Iber C, Ancoli-Israel S, Chesson AL Jr. QS for the AA, Medicine. of S, Iber CC, et al. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. In: *AASM Manual for Scoring Sleep*. ; 2007. doi:10.1002/ejoc.201200111

40. Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: Update of the 2007 AASM manual for the scoring of sleep and associated events. *J Clin Sleep Med*. 2012. doi:10.5664/jcsm.2172

41. Richard B. Berry, MD; Rita Brooks, MEd, RST, RPSGT; Charlene E. Gamaldo M, Susan M. Harding, MD; Robin M. Lloyd MCLM. American Academy of Sleep Medicine. The AASM Manual for the Scoring of Sleep and Associated Events : Rules, Terminology, and Technical Specifications, Version 2.2. *Am Acad Sleep*. 2016;28(3):391-397. doi:10.1017/CBO9781107415324.004

42. Shayeb M El, Topfer LA, Stafinski T, Pawluk L, Menon D. Diagnostic accuracy of level 3 portable sleep tests versus level 1 polysomnography for sleep-disordered breathing: A systematic review and meta-analysis. *CMAJ*. 2014. doi:10.1503/cmaj.130952

43. Berry RB, Brooks R, Gamaldo C, et al. AASM scoring manual updates for 2017 (version 2.4). *J Clin Sleep Med*. 2017. doi:10.5664/jcsm.6576

44. AASM. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. *Sleep*. 1999. doi:10.1378/chest.97.1.27

45. Clark GT, Blumenfeld I, Yoffe N, Peled E, Lavie P. A crossover study comparing the efficacy of continuous positive airway pressure with anterior mandibular positioning devices on patients with obstructive sleep apnea. *Chest*. 1996. doi:10.1378/chest.109.6.1477

46. Kushida CA, Morgenthaler TI, Littner MR, et al. Practice parameters for the treatment of snoring and obstructive sleep apnea with oral appliances: An update for 2005. *Sleep*. 2006. doi:10.1093/sleep/29.2.240

47. Cistulli PA, Gotsopoulos H, Marklund M, Lowe AA. Treatment of snoring and obstructive sleep apnea with mandibular repositioning appliances. *Sleep Med Rev*. 2004. doi:10.1016/j.smrv.2004.04.002

48. Pliska BT, Nam H, Chen H, Lowe AA, Almeida FR. Obstructive sleep apnea and mandibular advancement splints: Occlusal effects and progression of changes associated with a decade of treatment. *J Clin Sleep Med*. 2014. doi:10.5664/jcsm.4278

49. Jenkinson C, Davies RJ, Mullins R, Stradling JR. Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. *Lancet*. 1999. doi:10.1016/S0140-6736(98)10532-9

50. Weaver TE, Grunstein RR. Adherence to Continuous Positive Airway Pressure Therapy: The Challenge to Effective Treatment. *Proc Am Thorac Soc*. 2008. doi:10.1513/pats.200708-119MG

51. Baltzan M SC. *OSA Management in the Era of Individualized Care: Evidence Based Methods for Selecting Treatment Alternatives*.

52. Sher AE, Schechtman KB, Piccirillo JF. The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnea syndrome. *Sleep*. 1996. doi:10.1093/sleep/19.2.156

53. Caples SM, Rowley JA, Prinsell JR, et al. Surgical modifications of the upper airway for obstructive sleep apnea in adults: A systematic review and meta-analysis. *Sleep*. 2010. doi:10.1093/sleep/33.10.1396

54. Boyd SB. Comparative Effectiveness of Maxillomandibular Advancement and Uvulopalatopharyngoplasty for the Treatment of Moderate to Severe Obstructive Sleep Apnea. 2014;71(4):743-751. doi:10.1016/j.joms.2012.10.003.Comparative

55. Goodday R, Bourque S. Subjective outcomes of maxillomandibular advancement surgery for treatment of obstructive sleep apnea syndrome. *J Oral Maxillofac Surg*. 2012. doi:10.1016/j.joms.2011.02.122

56. Goodday RH, Bourque SE, Edwards PB. Objective and Subjective Outcomes Following Maxillomandibular Advancement Surgery for Treatment of Patients With Extremely Severe Obstructive Sleep Apnea (Apnea-Hypopnea Index >100). *J Oral Maxillofac Surg*. 2016. doi:10.1016/j.joms.2015.07.016

57. Zaghi S, Holty JE, Certal V, et al. Maxillomandibular Advancement for Treatment of Obstructive Sleep Apnea: A Meta-analysis. *JAMA Otolaryngol Head Neck Surg*. 2016. doi:10.1001/jamaoto.2015.2678

58. Holty JEC, Guilleminault C. Maxillomandibular advancement for the treatment of obstructive sleep apnea: A systematic review and meta-analysis. *Sleep Med Rev*. 2010;14(5):287-297. doi:10.1016/j.smrv.2009.11.003

59. Li KK. Surgical management of obstructive sleep apnea. *Clin Chest Med*. 2003.

60. Pirklbauer K, Russmueller G, Stiebellehner L, et al. Maxillomandibular advancement for treatment of obstructive sleep apnea syndrome: A systematic review. *J Oral Maxillofac Surg*. 2011;69(6):e165-e176. doi:10.1016/j.joms.2011.01.038

61. Fairburn SC, Waite PD, Vilos G, et al. Three-Dimensional Changes in Upper Airways of Patients With Obstructive Sleep Apnea Following Maxillomandibular Advancement. *J Oral Maxillofac Surg*. 2007;65(1):6-12. doi:10.1016/j.joms.2005.11.119

62. Boyd SB, Walters AS, Waite P, Harding SM, Song Y. Long-Term Effectiveness and Safety of Maxillomandibular Advancement for Treatment of Obstructive Sleep Apnea. *J Clin Sleep Med*. 2015. doi:10.5664/jcsm.4838

63. Boyd SB, Walters AS. Effectiveness of treatment apnea-hypopnea index: A mathematical estimate of the true apnea-hypopnea index in the home setting. *J Oral Maxillofac Surg*. 2013. doi:10.1016/j.joms.2012.05.009

64. Kuo PC, West RA, Bloomquist DS, William McNeil R. The effect of mandibular osteotomy in three patients with hypersomnia sleep apnea. *Oral Surgery, Oral Med Oral Pathol*. 1979. doi:10.1016/0030-4220(79)90063-X

65. Goodday RH, Percious DS, Morrison AD, Robertson CG. Obstructive sleep apnea syndrome: diagnosis and management. *J Can Dent Assoc*. 2001.

66. Delaire J, Schendel SA, Tulasne JF. An architectural and structural craniofacial analysis: A new lateral cephalometric analysis. *Oral Surgery, Oral Med Oral Pathol*. 1981. doi:10.1016/0030-4220(81)90252-8

67. Li KK, Guilleminault C, Riley RW, Powell NB. Obstructive sleep apnea and maxillomandibular advancement: An assessment of airway changes using radiographic and nasopharyngoscopic examinations. *J Oral Maxillofac Surg*. 2002;60(5):526-530. doi:10.1053/joms.2002.31849

68. Meisami T, Musa M, Keller MA, Cooper R, Clokie CML, Sàndor GKB. Magnetic resonance imaging assessment of airway status after orthognathic surgery. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007. doi:10.1016/j.tripleo.2006.07.006

69. Sears CR, Miller AJ, Chang MK, Huang JC, Lee JS. Comparison of pharyngeal airway changes on plain radiography and cone-beam computed tomography after orthognathic surgery. *J Oral Maxillofac Surg*. 2011. doi:10.1016/j.joms.2011.03.015

70. Strauss RA. Flexible Endoscopic Nasopharyngoscopy. *Atlas Oral Maxillofac Surg Clin North Am*. 2007. doi:10.1016/j.cxom.2007.05.004

71. Poirrier AL, Fanielle J, Bruwier A, Chakar B, Poirrier R. Upper airway imaging in sleep-disordered breathing. *Acta Neurol Belg*. 2014. doi:10.1007/s13760-013-0278-3

72. Katsantonis GP, Maas CS, Walsh JK. The predictive efficacy of the Muller maneuver in uvulopalatopharyngoplasty. *Laryngoscope*. 1989.

73. Faria AC, Da Silva-Junior SN, Garcia LV, Dos Santos AC, Fernandes MRF, De Mello-Filho FV. Volumetric analysis of the pharynx in patients with obstructive sleep apnea (OSA) treated with maxillomandibular advancement (MMA). *Sleep Breath*. 2013. doi:10.1007/s11325-012-0707-1

74. Schendel SA, Broujerdi JA, Jacobson RL. Three-dimensional upper-airway changes with maxillomandibular advancement for obstructive sleep apnea treatment. *Am J Orthod Dentofac Orthop*. 2014;146(3):385-393. doi:10.1016/j.ajodo.2014.01.026

75. Hsieh YJ, Liao YF. Effects of maxillomandibular advancement on the upper airway and surrounding structures in patients with obstructive sleep apnoea: A systematic review. *Br J Oral Maxillofac Surg*. 2013. doi:10.1016/j.bjoms.2012.11.010

76. Goodday R. Diagnosis, Treatment Planning, and Surgical Correction of Obstructive Sleep Apnea. *J Oral Maxillofac Surg*. 2009. doi:10.1016/j.joms.2009.03.035

77. Guilleminault Ch., Riley R, Powell N. Obstructive sleep apnea and abnormal cephalometric measurements. Implications for treatment. *Chest*. 1984. doi:10.1378/chest.86.5.793

78. Neelapu BC, Kharbanda OP, Sardana HK, et al. Craniofacial and upper airway morphology in adult obstructive sleep apnea patients: A systematic review and meta-analysis of cephalometric studies. *Sleep Med Rev*. 2017;31:79-90. doi:10.1016/j.smrv.2016.01.007

79. Partinen M, Guilleminault C, Quera-Salva MA, Jamieson A. Obstructive sleep apnea and cephalometric roentgenograms. The role of anatomic upper airway abnormalities in the definition of abnormal breathing during sleep. *Chest*. 1988. doi:10.1378/chest.93.6.1199

80. Abramson Z, Susarla S, August M, Troulis M, Kaban L. Three-Dimensional Computed Tomographic Analysis of Airway Anatomy in Patients With Obstructive Sleep Apnea. *J Oral Maxillofac Surg*. 2010;68(2):354-362. doi:10.1016/j.joms.2009.09.087

81. Van Holsbeke CS, Verhulst SL, Vos WG, et al. Change in Upper Airway Geometry Between Upright and Supine Position During Tidal Nasal Breathing. *J Aerosol Med Pulm Drug Deliv*. 2014. doi:10.1089/jamp.2012.1010

82. Sutthiprapaporn P, Tanimoto K, Ohtsuka M, Nagasaki T, Iida Y, Katsumata A. Positional changes of oropharyngeal structures due to gravity in the upright and supine positions. *Dentomaxillofacial Radiol*. 2008. doi:10.1259/dmfr/31005700

83. Maurer JT, Stuck B a. Update on upper airway evaluation in obstructive sleep apnea. *HNO*. 2008. doi:10.1007/s00106-008-1758-2

84. Abramson Z, Susarla SM, Lawler M, Bouchard C, Troulis M, Kaban LB. Three-dimensional computed tomographic airway analysis of patients with obstructive sleep apnea treated by maxillomandibular advancement. *J Oral Maxillofac Surg*. 2011;69(3):677-686. doi:10.1016/j.joms.2010.11.037

85. Hsieh YJ, Liao YF, Chen NH, Chen YR. Changes in the calibre of the upper airway and the surrounding structures after maxillomandibular advancement for obstructive sleep apnoea. *Br J Oral Maxillofac Surg*. 2014. doi:10.1016/j.bjoms.2014.02.006

86. Mah JK, Danforth RA, Bumann A, Hatcher D. Radiation absorbed in maxillofacial imaging with a new dental computed tomography device. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2003. doi:10.1016/S1079-2104(03)00350-0

87. Wortche R, Hassfeld S, Lux CJ, et al. Clinical application of cone beam digital volume tomography in children with cleft lip and palate. *Dentomaxillofac Radiol*. 2006. doi:10.1259/dmfr/27536604

88. Ludlow JB, Walker C. Assessment of phantom dosimetry and image quality of i-CAT FLX cone-beam computed tomography. *Am J Orthod Dentofac Orthop*. 2013;144(6):802-817. doi:10.1016/j.ajodo.2013.07.013

89. Ghoneima A, Kula K. Accuracy and reliability of cone-beam computed tomography for airway volume analysis. *Eur J Orthod*. 2013;35(2):256-261. doi:10.1093/ejo/cjr099

90. Guijarro-Martínez R, Swennen GRJ. Cone-beam computerized tomography imaging and analysis of the upper airway: A systematic review of the literature. *Int J Oral Maxillofac Surg*. 2011;40(11):1227-1237. doi:10.1016/j.ijom.2011.06.017

91. Guijarro-Martínez R, Swennen GRJ. Three-dimensional cone beam computed tomography definition of the anatomical subregions of the upper airway: A validation study. *Int J Oral Maxillofac Surg*. 2013;42(9):1140-1149. doi:10.1016/j.ijom.2013.03.007

92. Li HY, Chen NH, Wang CR, Shu YH, Wang PC. Use of 3-dimensional computed tomography scan to evaluate upper airway patency for patients undergoing sleep-disordered breathing surgery. *Otolaryngol - Head Neck Surg*. 2003;129(4):336-342. doi:10.1016/S0194-5998(03)00629-6

93. Vos W, De Backer J, Devolder A, et al. Correlation between severity of sleep apnea and upper airway morphology based on advanced anatomical and functional imaging. *J Biomech*. 2007;40(10):2207-2213. doi:10.1016/j.jbiomech.2006.10.024

94. Ogawa T, Enciso R, Shintaku WH, Clark GT. Evaluation of cross-section airway configuration of obstructive sleep apnea. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;103(1):102-108. doi:10.1016/j.tripleo.2006.06.008

95. Cosentini T, Le Donne R, Mancini D, Colavita N. Magnetic resonance imaging of the upper airway in obstructive sleep apnea. *Radiol Med*. 2004.

96. Tikku T, Khanna R, Sachan K, Agarwal A, Srivastava K, Lal A. Dimensional and volumetric analysis of the oropharyngeal region in obstructive sleep apnea patients: A cone beam computed tomography study. *Dent Res J (Isfahan)*. 2016;13(5):396-404. doi:10.4103/1735-3327.192273

97. Zinser MJ, Zachow S, Sailer HF. Bimaxillary “rotation advancement” procedures in patients with obstructive sleep apnea: A 3-dimensional airway analysis of morphological changes. *Int J Oral Maxillofac Surg*. 2013;42(5):569-578. doi:10.1016/j.ijom.2012.08.002

98. Raffaini M, Pisani C. Clinical and cone-beam computed tomography evaluation of the three-dimensional increase in pharyngeal airway space following maxillo-mandibular rotation-advancement for Class II-correction in patients without sleep apnoea (OSA). *J Cranio-Maxillofacial Surg*. 2013. doi:10.1016/j.jcms.2012.11.022

99. Hernández-Alfaro F, Guijarro-Martínez R, Mareque-Bueno J. Effect of mono- and bimaxillary advancement on pharyngeal airway volume: Cone-beam computed tomography evaluation. *J Oral Maxillofac Surg*. 2011;69(11):e395-e400. doi:10.1016/j.joms.2011.02.138

100. Butterfield KJ, Marks PLG, McLean L, Newton J. Pharyngeal airway morphology in healthy individuals and in obstructive sleep apnea patients treated with maxillomandibular advancement: A comparative study. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2015. doi:10.1016/j.oooo.2014.11.016

101. Rosário HD, Oliveira GMS, Freires IA, de Souza Matos F, Paranhos LR. Efficiency of bimaxillary advancement surgery in increasing the volume of the upper airways: a systematic review of observational studies and meta-analysis. *Eur Arch Oto-Rhino-Laryngology*. 2017. doi:10.1007/s00405-016-4015-4

102. Brunetto DP, Velasco L, Koerich L, Araújo MTDS. Prediction of 3-dimensional pharyngeal airway changes after orthognathic surgery: A preliminary study. *Am J Orthod Dentofac Orthop*. 2014. doi:10.1016/j.ajodo.2014.05.024

103. Butterfield KJ, Marks PLG, McLean L, Newton J. Linear and volumetric airway changes after maxillomandibular advancement for obstructive sleep apnea. *J Oral Maxillofac Surg*. 2015. doi:10.1016/j.joms.2014.11.020

104. Valladares-Neto J, Silva MAG, Bumann A, Paiva JB, Rino-Neto J. Effects of mandibular advancement surgery combined with minimal maxillary displacement on the volume and most restricted cross-sectional area of the pharyngeal airway. *Int J Oral Maxillofac Surg*. 2013. doi:10.1016/j.ijom.2013.03.018

105. Veys B, Pottel L, Mollemans W, Abeloos J, Swennen G, Neyt N. Three-dimensional volumetric changes in the upper airway after maxillomandibular advancement in obstructive sleep apnoea patients and the impact on quality of life. *Int J Oral Maxillofac Surg*. 2017;46(12):1525-1532. doi:10.1016/j.ijom.2017.06.020

106. Susarla SM, Abramson ZR, Dodson TB, Kaban LB. Cephalometric measurement of upper airway length correlates with the presence and severity of obstructive sleep apnea. *J Oral Maxillofac Surg*. 2010;68(11):2846-2855. doi:10.1016/j.joms.2010.06.196

107. Mayer P, Pépin JL, Bettega G, et al. Relationship between body mass index, age and upper airway measurements in snorers and sleep apnoea patients. *Eur Respir J*. 1996. doi:10.1183/09031936.96.09091801

108. Vgontzas AN, Bixler EO, Chrousos GP. Obesity-related sleepiness and fatigue: The role of the stress system and cytokines. In: *Annals of the New York Academy of Sciences*. ; 2006. doi:10.1196/annals.1367.023

109. Schwab RJ. Identification of Upper Airway Anatomic Risk Factors for. 2003;(C). doi:10.1164/rccm.200208-866OC

110. Enciso R, Nguyen M, Shigeta Y, Ogawa T, Clark GT. Comparison of cone-beam CT parameters and sleep questionnaires in sleep apnea patients and control subjects. *Oral Surgery, Oral Med Oral Pathol Oral Radiol Endodontology*. 2010;109(2):285-293. doi:10.1016/j.tripleo.2009.09.033

111. Butterfield KJ, Marks PLG, McLean L, Newton J. Pharyngeal airway morphology in healthy individuals and in obstructive sleep apnea patients treated with maxillomandibular advancement: A comparative study. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2015;119(3):285-292. doi:10.1016/j.oooo.2014.11.016

112. Heo JY, Kim JS. Correlation between severity of sleep apnea and upper airway morphology: Cephalometry and MD-CT study during awake and sleep states. *Acta Otolaryngol*. 2010. doi:10.3109/00016489.2010.514007

113. Zinsly S dos R, Moraes LC de, Moura P de, Ursi W. Assessment of pharyngeal airway space using Cone-Beam Computed Tomography. *Dental Press J Orthod*. 2010;15(5):150-158. doi:10.1590/S2176-94512010000500018