Effects of Mandibular Advancement Device (MAD) on Airway Dimensions Assessed With Cone-Beam Computed Tomography

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Upper airway constriction is an important contributing factor to obstructive sleep apnea (OSA), which may be treated in a palliative manner with mandibular advancement devices (MADs) to increase patency of the airway. It may be the treatment of choice for affected individuals who cannot use a continuous positive airway pressure device or who are not candidates for surgical correction of OSA. The specific distance applied during mandibular advancement, however, is often arbitrarily determined. This project uses cone beam computed tomography imaging in patients with OSA to determine a quantifiable relationship between airway patency and mandibular advancement. This correlation may be the basis to create an ideal technique to diagnose and treat patients having OSA. Twenty-six subjects successfully treated for OSA with a MAD received 2 cone beam computed tomography scans; 1 with and 1 without the MAD. Volumetric, cross-sectional, and cephalometric measurements were gathered from these scans. With the use of linear regression statistical analysis, specific predictor parameters have been identified for volumetric and cross-sectional airway information. An average oropharyngeal volume increase of approximately 2800 mm^3 was achieved with MAD therapy. (Semin Orthod 2009;15:132-158.) © *2009 Elsevier Inc. All rights reserved.*

In the present study, the authors sought to determine a quantifiable relationship between mandibular advancement performed with a removable orthotic device and the resulting upper respiratory airway dimensions and volume. Upper airway dimension has been considered a contributing factor to obstructive sleep apnea (OSA). This condition has been treated by continuous positive airway pressure (CPAP), soft-tissue surgery, orthognathic surgical advancement of the mandible or removable oral appliances directed at mandibular protrusion, and patency of the pharyngeal airway to prevent the lumen from collapsing during sleep. Traditionally, upper respiratory airway space has been evaluated by the use of cephalometric radiographs; however, this method results in superimposition of all bilateral structures of the skull and only provides a 2-dimensional (2D) anteroposterior (AP) linear dimension. In this study, we analyzed a series of images obtained from 2 volumetric data sets generated with the use of cone beam computed tomography (CBCT): with

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The present study is currently under IRB approval at the University of Louisville as of April 20, 2006. It has undergone 2 annual reviews and is not due for another annual review until April 21, 2009. Risk to the subjects is from radiation exposure using a FDA/CDRH approved device. The short and long-term risks of somatic and genetic damage at the level used in this study are considered negligible.

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1073-8746/09/1502-0$30.00/0
doi:10.1053/j.sodo.2009.02.001

and without the use of a mandibular orthotic advancement device. All images used in this study were generated with the i-CAT® CBCT (Xoran Technologies, Ann Arbor, MI/Imaging Sciences International, Hatfield, PA). This modality allows an identification of skeletal landmarks seen in 2D cephalometry and also permits measurements of airway space as a 3D volume.

Overview of OSA

Sleep apnea is defined as a decrease in respiration, yielding hypoxia and hypercapnia during sleep. It can be caused by many factors, including those of either neurologic origin or physical blockage of the airway. This study focused on the latter, more common, OSA. OSA physically limits the amount of air that a person can inhale during sleep. It occurs in 4% of men and 2% of women. Many authors agree that polysomnographic data are needed for definitive diagnosis of OSA; however, there are several diagnostic symptoms and consequences of the disease, including snoring as a very major indicator.

OSA causes episodic apneic or hypopneic events during sleep, defined by the American Academy of Sleep Medicine as 10 seconds of absent or decreased airflow. These events are frequently characterized by electroencephalographic arousal and decreased oxygen saturation of hemoglobin. Severity of OSA is determined by an apnea/hypopnea index (AHI), which measures the average number of these apneic events per hour. Mild OSA is defined as an AHI between 5 and 15, moderate between 15 and 30, and severe OSA is defined as an AHI >30. Although OSA is caused by an occlusion of the upper airway, the level of obstruction in most OSA cases is the oropharynx.[2] This is caused by sleep-induced relaxation of the muscles attached to the soft tissues that make up the lumen of the oropharynx. It is now thought that patency of this region is dependent on the action of the oropharyngeal dilator and abductor muscles. The airway is subject to collapse when subatmospheric intraluminal pressure during inspiration overwhelms the stabilizing force produced by these muscles.[3] In OSA, the apneic events are accompanied by a physical effort to breathe better, whereas in central sleep apnea, there is no such effort to overcome the apnea.

Consequences of OSA

The most serious and deadly consequences are the cardiovascular diseases that can arise from OSA. Hypertension, tachycardia, increased risk of cerebrovascular accidents, daytime hypercapnia, atrial fibrillation, and even coronary artery disease all have been associated with OSA. Hypertension is more prevalent in younger or middle-aged OSA sufferers than those aged 60 years or older.[4] The pathogenesis of these effects of OSA is still being researched, but it is generally accepted that the intermittent hypoxia and hypercapnia that is caused by the apneic episodes triggers homeostatic compensation events in the body that lead to cardiovascular disease over time.

Many authors have investigated the characteristics, incidence, and pathophysiology of the cardiovascular consequences of OSA. Hypertension is found in 50-90% of OSA patients.[5] It has been shown that nocturnal blood pressures of patients with severe OSA can reach up to 240/120 mm Hg.[5] This increase in blood pressure at night is a specific characteristic of OSA, because most normally functioning individuals will have a decrease in blood pressure during sleep. Another characteristic of OSA-related hypertension is that the organs affected are more often the brain and heart, whereas the kidneys tend to be spared, unlike in other forms of hypertension.[6] It has also been noted that OSA hypertensive patients have a greater blood plasma volume than other hypertensive patients. Kawata et al.[7] found that daytime hypercapnia, an unexpected consequence, has an incidence approximately equal to 14% of OSA patients.

The Wisconsin Sleep Cohort Study showed that there is a statistical relationship between OSA severity and hypertension severity, and Kawata et al.[6] showed that AHI and, to a lesser extent, body mass index (BMI) are predictors of daytime hypercapnia severity.

Beyond hypertension and its related cardiovascular damage, atherosclerosis is also a sequela of OSA. Patients with OSA have an increase of oxidative stress and a decrease in antioxidant capabilities.[7,8,9] Oxidative stress also may be associated with the increased amounts of inflammatory cytokines and interleukins found in OSA, which in turn lead to an enhanced rate of vascular damage, atherosclerosis and coronary artery disease.[4]

Airway obstruction can be caused by a multitude of different types of blockages on any of the different levels of the upper or lower airway. This study focused upon the anatomy of the oro and velopharyngeal areas.[9]

Diagnostic Problems in OSA

Polysomnography is a sleep study that measures many physiological variables associated with sleep and is used to diagnose OSA. Common measurements include oxygen saturation, electrocardiography, air flow, respiratory effort, limb movement, eye and jaw muscle movement, and brain electrical activity. Although polysomnography is considered the gold standard for OSA diagnosis, there are preliminary techniques that often go ignored to determine whether to send a patient for a sleep study.

Although OSA is a common disease, it has been estimated that between 80% and 90% of those with it go undiagnosed. In fact, many cases of what were initially thought to be "primary hypertension" were later found to be secondary hypertension caused by OSA. Rahaghi and Basner[10] investigated the cause of this great deficiency by interviewing known OSA patients. They found that there was an average of 87 months that elapsed between the patient first noticing a symptom of OSA, and being diagnosed with this condition.

Because of the large percentage of undiagnosed sufferers, preliminary examinations of patients should include screening for sleep apnea to help reduce the number of OSA patients going untreated. There are several ways this can be done with varying ease and efficiency. Faber and Grymer[11] reviewed several techniques for diagnosis of OSA and rated them for ease, accuracy, ability to be standardized, and cost-effectiveness. One technique includes visual inspection of the nose and pharynx to asses any obvious anatomic discrepancies. This method, however, does not allow visualization inferior to the oropharynx, so will not identify all cases of OSA. A more telling review of anatomic structures can be done with fiberoptic endoscopy during wakefulness for a more detailed view.

The problem with both of these latter techniques is that the patient is awake, and the structures may change position during sleep causing an obstruction that goes unnoticed during wakefulness. This is why a definitive diagnosis cannot be made without a sleep study.[11]

Obesity is one of the most important risk factors of OSA. Obesity is defined as a BMI of 30 or greater by the National Institute of Health. BMI is calculated by dividing one's weight in kilograms by the square of height in meters to give a normalized measure a person's body mass. Although obesity is a very important risk factor, the direct relationship between BMI and severity of OSA is poorly understood. One study found that the correlation between BMI and AHI is very low ($r = 0.23$).[12]

Fogel et al.[12] set out to determine more specific predicting factors than BMI within the obese population. They found that several variables were positively correlated with severity of sleep apnea, such as airway collapsibility, and a more AP-oriented than laterally oriented airway. The latter finding is likely related to the resultant mechanical disadvantage of the genioglossus muscle. The function of this muscle is to pull the tongue anteriorly, which increases patency of the airway. If the length of the muscle is shortened, it does not have as great of an ability to perform this function, thus allowing the tongue to stay in a retruded position (i.e., blocking the airway). This is an example of the obstruction in OSA at the level of the oropharynx. Additionally, Fogel et al.[12] found that the pharyngeal volume of an individual experiencing more severe OSA is lower when the lungs are at residual volume or when there is less air in the lungs. This means that, just after exhalation, the danger of an apneic event is greatest and that there is a negative correlation between lung volume and OSA severity.

Most Common Types of Obstruction

Although most obstructions in OSA occur at the oropharynx, another common point of airway blockage is the nasopharynx. Hypertrophied adenoids are a common source of obstruction of the upper airway. This type of obstruction may directly cause OSA if the individual is not able to breathe through the mouth during sleep, or it can result in mouth-breathing. If a patient is still growing, mouth breathing can alter the development of skeletal structures in a growing individual.[13] Major et al.[13] found that there was at best, an $r = 0.68$ correlation between linear measurements of the upper airway in a 2D cephalometric film and the diagnosis of upper airway blockage. They suggest that the cephalogram should be used only as a screening tool for airway obstruction.

The mechanism that decreases oropharyngeal patency in cases with those skeletal anomalies associated with OSA has been highly debated and researched. A skeletal Class II configuration is caused by the maxilla being too far anterior relative to the mandible. It may be caused by the mandible being positioned too far posteriorly, or simply underdeveloped. It may also be due to the maxilla being positioned too far anteriorly, or any combination of these problems in either jaw. In skeletal Class II patients with OSA, the problem is likely caused by a posteriorly-oriented mandible that is displacing the soft tissues attached to it, impinging on the airway space.[1]

Johal et al.[14] investigated the specific anatomical anomalies statistically contributing to OSA. Retrognathia was found a contributing factor in OSA, with patients having a shorter mandibular body length, with a significantly shorter distance from their posterior pharyngeal wall to the lingual surface of their lower incisors. A shorter AP face length in general also was a contributing factor. Therefore, their findings support bimaxillary surgical advancement as treatment for OSA, a treatment successfully used in severe cases of OSA for the last decade.[15] Many investigators also agree that a lower-positioned hyoid is also a contributing factor.[12,15,16] This anomaly is related to posteriorly-displaced tongue because the muscles that connect the tongue to the hyoid, such as the hyoglossus, would pull the tongue posteriorly when the hyoid is more inferior.

Soft tissue anomalies can also be a contributing factor to OSA. Johal et al.[16] found that a larger soft palate, a smaller pharynx, and a larger tongue were soft-tissue contributors. An increase in palate length was significant in subjects with OSA. The distance between the posterior aspect of the soft palate and the posterior pharyngeal wall was on average two-thirds that of the control subjects. A large tongue size is another contributing factor as it also decreases the size of the pharynx by causing the tongue to be placed posteriorly.[15]

The pharyngeal dilator muscles seem to be less effective in preventing pharyngeal lumen collapse in these soft-tissue anatomical anomalies. Sher et al considered etiological factors by regions of the pharynx, the retropalatal region and the retrolingual region.[17] There may be an obstruction in either or both of these regions of the pharynx.

Treatment of OSA

Continuous Positive Airway Pressure (CPAP)

The general aim of all treatment modalities in sleep-breathing disorders is to facilitate breathing and thereby reduce the risk of increased morbidity. Because there can be many causes of OSA, there are also several different treatment types. They all focus on preventing collapse of the lumen of the pharynx during sleep. The gold standard for initial treatment is home use of a device called CPAP[18] because it seems to be somewhat of a "cure-all" OSA treatment. No matter where the obstruction in the pharynx occurs, this treatment has been shown to be very effective in most OSA patients. In this treatment method, the patient wears a mask at night (Fig 1) that is attached to a machine that continuously forces air through the entire airway. This keeps the pharynx patent due solely to increased air pressure as if it is being blown up like a balloon.

This method has been shown to be highly effective, but there are several negative aspects of this type of treatment. The most important is that many patients cannot tolerate the treatment.[18] Many complain of not being able to sleep with a mask on their face or that it feels unnatural to have air blown down their throat all


[redacted]

Figure 1. CPAP treatment during sleep. (Color version of figure is available online.)

the time. Still others, who can fall asleep with the CPAP in place, will rouse in the middle of the night and remove the device. Other reasons for discontinuing CPAP therapy have been primarily related to issues of nasal dryness and congestion, and difficulty adapting to the pressure.

Surgical Treatments

Although it has proven to be very effective in many cases of OSA, not all patients who are able to tolerate CPAP will respond to the treatment. These are often more severe OSA sufferers. For these patients, another treatment option is surgery. The guidelines for OSA surgery state that a prerequisite for surgery candidates is that they must be nonresponsive to CPAP or other nonsurgical OSA treatments.[19]

There are many different types of surgery that have been used to treat OSA. They range from soft tissue to osteotomy surgeries. The older of the 2 is soft-tissue surgery. The uvulopalatopharyngoplasty (UPPP) was introduced in 1981 and has been the most popular form of soft tissue surgical treatment of OSA. In this type of treatment, part of the soft palate and surrounding oropharyngeal tissues are surgically resected to reduce their potential for obstructing the upper airway during sleep. This type of treatment has had about a 50% success rate.[17,20] Sher, et al.[17] concluded that a low success rate is likely if the etiology of the problem is a pharyngeal narrowing or collapse. The OSA may simply not respond to a reduction of the soft palate alone. It has also been anecdotally reported that this treatment, even with postsurgical success, has lead to relapse after several years when the soft tissue has grown back, or the patient has gained weight.

Because of the limitations of soft-tissue surgery in the treatment of OSA, orthognathic treatments have been used. Placing the anterior aspect of the mandible more anteriorly pulls the tongue forward and away from the posterior wall of the oropharynx, thus opening the airway. These procedures include inferior sagittal mandibular osteotomy and maxillomandibular osteotomy and advancement. Much more recently, maxillary and mandibular expansion has also been found to be effective in the treatment of sleep apnea.[1,19]

An orthognathic surgical treatment for OSA is bimaxillary, or maxillomandibular, advancement. This procedure advances both jaws anteriorly with the use of bilateral sagittal split osteotomy on the mandible and a Le Fort I procedure on the maxilla.

Bimaxillary surgical advancement of the jaws brings forward all soft tissue attached to them and the hyoid bone. MAD devices only advance the mandible. The difference is that the dental occlusion can be controlled in the surgically bimaxillary advancement because both jaws are being moved. This way, the original occlusion can be maintained, or a malocclusion of skeletal origin corrected. This procedure is aggressive and it can correct OSA due to obstructions at many different levels of the oropharynx. It also prevents the immediate postoperative period of worsening OSA that is found in soft-tissue pharyngeal surgeries. Because this area has not been operated upon, there is no edema that can cause further obstruction. Rather, the swelling is confined to the soft tissue of the face.[19]

Another surgical treatment that has been found to coincidentally improve OSA but was not initially used as a primary OSA treatment is mandibular and maxillary transverse distraction osteogenesis. When used in conjunction with bimaxillary advancement, this treatment can result in a significant increase effect on the dimensions of the oropharynx,[1] as a decreased lateral dimension of the airway is a very common etiology of OSA in obese patients.

Mandibular Repositioning

For patients with mild-to-moderate OSA who cannot tolerate CPAP treatment, orthognathic surgery may be too aggressive a form of treatment. An option for these patients is a removable oral appliance that repositions the mandible forward. The success of this type of treatment is based on a somewhat similar response of the tissues to that of orthognathic surgery. These devices have their effect because of the attachment of the mandible to the tongue, pharyngeal dilator muscles, and indirectly the soft palate. By moving the mandible forward, it brings these structures that make up the lumen of the oropharynx forward as well, thereby increasing the airway space.[21-28]

Many authors now agree that mandibular repositioning treatment with an oral appliance has many advantages and should be among the first considered choices for treatment on a wide variety of patients, including patients with severe OSA, if an optimal amount of advancement is possible.[22,29-31] Fransson et al.[30] reported a great capacity for the patient to adapt to usage, with minimal negative temporomandibular disorders or dental changes after a 2-year period.

The Food and Drug Administration has approved the use of these devices only for individuals 18 years and older. There are many different types of appliance design, but no definitive criteria exist either for the ideal amount of mandibular protrusion or for the amount of vertical opening associated with it. The success rates of these devices vary. Most often, a patient must be titrated to the amount of protrusion that is optimal for that individual. This process involves much trial and error.

The removable Herbst appliance (Figs 2 and 3) is one type used for mandibular advancement in patients with OSA. This appliance is composed of 2 acrylic splints, one that fits over the teeth in each arch, which are attached to each other by a pistonlike connector. This piston serves to push the mandible forward relative to the maxilla, while a rod slides inside a tube to allow the patient to open and close. This device can be adjusted by the patient to more or less forward extension, which is called titrating to effectiveness. Movement of the mandible forward is done in small increments with the patient is instructed to continue until the OSA symptoms have diminished, or to stop the activation it if too much discomfort in the temporomandibular joint is felt.

Figure 2. Herbst appliance: anterior view. (Color version of figure is available online.)

Figure 3. Herbst Appliance: posterosuperior view. (Color version of figure is available online.)

A study conducted with removable Herbst in patients with OSA compared the before-treatment and after-treatment AHI values in OSA sufferers and found that the Herbst significantly improved the AHI by up to 34 apneic events. The cephalometric analysis of these patients revealed that those who responded the most had a shorter mandible-to-hyoid distance.[21,22,23,30,31,32,33]

Radiographic and Other Imaging of the Oropharynx

Cephalometrics in OSA Imaging

The imaging of the upper airway space has traditionally been accomplished with the use of lateral cephalometric radiography (Fig 4). An advantage of this type of imaging is that it is widely used and readily available. It also uses a relatively low radiation dosage. However, images taken from a lateral viewpoint give only 2D information. This information is valuable because the AP dimension is that which is most likely to be changed with mandibular protrusion. It is not an ideal imaging technique for an OSA study because any changes in the medial-lateral dimension cannot be measured. This is an important dimension because previous researchers have found that a decreased lateral dimension is often present in patients with OSA.[12] The only useful measurements that can be made in ceph-

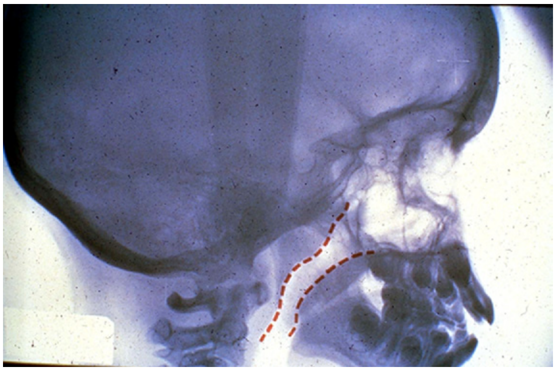


Figure 4. Lateral cephalometric skull radiograph with airway outlined in red (with permission from RMO, Corp., Denver, CO). (Color version of figure is available online.)

alometry for OSA and all other 2D imaging methods are linear or angular, and therefore volume cannot be accurately assessed. Furthermore, cephalometry produces problems with magnification, distortion, and superimposition of structures.[21] Another limitation of cephalometry in diagnosing and treating OSA is that the patient must be upright. Observation of the pharynx when the patient is supine, as they are more likely to be during sleep, cannot be visualized.[9]

Johal and Conaghan[14] attempted to find a relationship between maxillary morphology in patients with OSA by using cephalometrics. They made cephalometric lateral radiographs of 13 OSA patients and 18 control subjects. They found that their population did not have a significant difference in frequency of Class II skeletal patterns. All subjects with OSA had reduced distance from the posterior nasal spine (PNS) to posterior pharyngeal wall, indicating a constriction in the airway by a retruded maxilla. The cranial base was shorter and the palatal angle was significantly more obtuse in male patients with OSA only. This finding indicates that the soft palate was further inclined into the airway space in these instances. In addition, there were significant differences in palatal height at the premolar and molar points, suggesting that palatal vaulting contributes to OSA.

Other OSA Imaging

To overcome the limitations of the static, upright images found in cephalometry, fluoroscopy has been used to observe changes in the pharynx on patients in a supine position.[21] Fluoroscopy also has the advantage of being able to record the dynamic changes in the pharynx as the mandible is moved, as opposed to static views of the pharynx in different positions.[21]

For volumetric and area measurements of the airway, the technique of acoustic reflection has also been used for nearly 25 years. In this technique a rhinometer and pharyngometer wave tube and nosepiece or mouthpiece generate sound which is reflected in the airway and recorded by microphones within the wave tube. In 2002, Viviano[34] published a review article on the accuracy, reproducibility, and usefulness of acoustic reflection in OSA airway assessment. Its accuracy has been compared favorably to radiographic and magnetic resonance (MR) 3D imaging and it has the unique ability to localize the minimum or maximum cross-sectional area of the airway. The limitation of acoustic reflection is that changes in the airway cannot be localized to specific anatomic structures as they can in 3D imaging.

In 2002, Sanner et al.[8] conducted an experiment using MR imaging (MRI) to image the etiology of pharyngeal obstruction in patients with OSA. They found that in the patients not responding to treatment, the area of obstruction was in the velopharynx only, whereas other patients who responded to treatment had obstructions in the glossopharynx (oropharynx) only or both the glossopharynx and velopharynx.

Although MRI may be more useful in understanding the role of soft-tissue in OSA than computed tomography (CT), it may be unwarranted because of the extremely high cost. In many cases, it would actually be less expensive to try different treatments for OSA than to use the MRI to predict effectiveness. An answer to 3D imaging of the airway may lie in CBCT technology, which does not show clear delineations between soft tissues, but clearly shows the airway space and related skeletal structures.

Conventional CT Versus CBCT

Both conventional CT and CBCT have a source of X-rays that spin around the subject, collecting information from all directions, which a computer then uses to compile a 3D image. A conventional CT has a fan-shaped beam originating from a high-output rotating anode generator

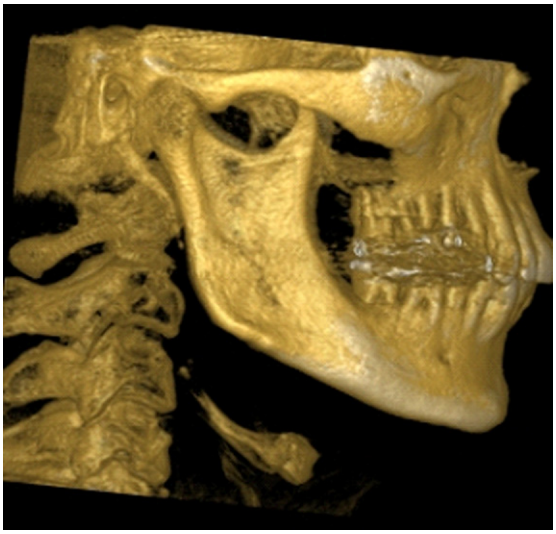


Figure 5. Lateral skull view of a 3D reconstruction made by 3DVR from the iCAT (Imaging Sciences International). (Color version of figure is available online.)

that moves around the subject many times in the form of a spiral, projecting through the subject onto a series of solid-state image detectors arranged in a 360° array to collect several slices of images that the computer later stacks to form a 3D image.[34] The CBCT has a cone-shaped beam originating from a low-energy fixed anode tube that is projected through the subject to an attached single solid-state or amorphous silicon 2D panel detector that rotates with the beam. CBCT can collect a much greater amount of information from the subject in a single rotation than the conventional CT.[34,35]

CBCT Technology

Radiation Dosage

A main advantage of using CBCT to image the oropharynx is the relatively low dosage of radiation. Several studies have been done to determine the exact radiation dosage to different parts of the body of different types of radiography.[36-38] It has been found that the general dosage of CBCT dosimetry is up to 50 times less than spiral CT. CBCT uses only minimal radiation, equal to 7 panoramic exposures, or approximately 3.5 days of background exposure. This is a huge reduction from spiral CT, which has a probability of causing stochastic effects in up to 145.6 examinations per million taken in the whole body, or up to 199 per million in the salivary glands.[36,37]

Image Quality and Accuracy

Although soft tissue is not clearly delineated from other soft tissue on CBCT, it clearly shows high contrast between bone, teeth, empty space, and soft tissue in general. It is ideal to show the patency of the airway, related to the position of the hard tissue structures of the skull.[17,34] The spatial resolution is also much greater than conventional CT, with a voxel resolution between 0.09 and 0.25 mm.[38] Some programs that can create these 3D images are 3DVR (Danaher/Imaging Sciences International, Hatfield, PA) (Figs 5 and 6), Anatomage (Anatomage Inc., San Jose, CA), and Dolphin 3D imaging (Dolphin Imaging/Patterson Dental, Chatsworth, CA).

CBCT images can be used to make accurate 2D simulations of lateral cephalometrics, AP cephalometrics, panoramic images, and arthrography.[40] The resulting images are more accurate than those traditionally made using lateral cephalometric radiographs. These CBCT images achieve this accuracy by isotropic images reconstructed with cone beam technology.[39]

Reconstructing and Measuring the Airway

Because the value of measuring the airway dimensions in patients with OSA has been recog-

Figure 6. Anterior airway space view of a 3D reconstruction made by 3DVR made by iCAT CBCT. (Color version of figure is available online.)

nized, there have been many studies that measure the airway in this population. The most common measurements comparing OSA patients with normal airways made in 3D imaging are minimum surface area of the oropharynx, and the AP and lateral lengths of this area.[41] Mayer et al.[42] found that the airway in OSA patients with greater BMI tends to be more spherical, with a shorter lateral length. Several morphometric techniques have been developed to obtain precise measurements on 3D images. Shi et al.[43] created an algorithm to calculate several parameters based on the contrast of the pixels of the airway to the surrounding soft tissue in CBCT images. They measured total airway volume, smallest trans-sectional area, largest sagittal view airway area, and smallest cross-areas and anterior-posterior distances of the retropalatal and retroglossal space.

Ogawa et al.[41] defined the upper and lower aspects of the airway by 2 lines parallel to the Frankfort Horizontal; 1 through the most distal point of the hard palate, and 1 through the most anterior-inferior point of the second vertebrae. Previous authors[41,43] measured the total airway volume, the smallest cross-sectional area, and anterior-posterior and lateral lengths of the smallest cross-sectional area. Ogawa et al. also noted the general shape of the smallest cross-sectional area as being closest to rounded, elliptical, square, or concave. They found that in 70% of OSA cases, the smallest cross-sectional area of the airway was below the occlusal plane, and more often had an elliptic shape of this area.

Peh et al.[44] measured the airways of Chinese OSA patients with conventional CT because they wished to assess the airway in a supine position. Most of the Asian OSA population (62%) is not obese. It is believed that craniofacial morphology plays a more major role in OSA etiology in this population than does soft-tissue morphology. There is also a higher incidence of severe OSA in the nonobese patients in this population.[45] Peh et al.[44] found statistically significant differences between OSA and control subjects in the hyoid position, the nasal cavity length, the tongue length (vallecula to tongue base distance), oropharyngeal airway space, posterior airway space, and the velopharyngeal and hypopharyngeal cross-sectional areas.

Effect of Mandibular Advancement on OSA

Previous studies have concluded that gradually advancing the mandible forward to an optimal level have yielded good responses from the supine patient via a reduced AHI, which is calculated upon the basis of electroencephalographic, elector-oculographic, and electromyographic measurements.[25-32]

There have been several studies that measured the oropharynx dimensions in patients with OSA, but most of the studies using 3D imaging, such as CBCT, conventional CT, or MRI have compared OSA airways to their non-OSA counterparts.[41] Of the studies evaluating actual changes in the pharynx caused by mandibular advancement, most of the studies have used cephalometry or other 2D imaging techniques that do not show the transverse or volumetric dimensions of the pharynx.

In 2004, Ogutcen-Toller et al.[2] conducted an experiment looking at changes in the airway in 15 snoring subjects who had not previously been diagnosed with OSA. They made a customized acrylic block for each subject that advanced each mandible 3 mm less than maximum protrusion to an average advancement of 2.39 mm and open 7 mm by interincisal distance. By using CT scans, 1 with and 1 without the mandibular advancement device, they measured the cross-sectional area of the airway. The only dramatically differing measurement between the appliance and nonappliance scans, was the minimum cross-sectional area of the airway, which increased by 60 mm^2 or 72%. It was not known if the subjects had OSA, as snoring by itself does not indicate sleep apnea.

The Present Study

The present study used CBCT to image the airway of successfully treated OSA patients with and without a mandibular advancement device in place, and measured parameters which address the patency of the oropharyngeal, velopharyngeal, and hypopharyngeal airway. It was intended to try to understand the effect of OSA orthotic appliances on airway dimensions, including cross-sectional areas and volume by finding cephalometric and 3D anatomical correlates for the efficacy of mandibular advancement treatment in specific cases of OSA.

Methods

Twenty-six patients diagnosed with OSA who had been previously treated with mandibular advancement device (MAD) therapy by a general dental practitioner with advanced training in the diagnosis and treatment of OSA patients (J.M.) were recruited for the study following guidelines designated by the intuitional review board of the University of Louisville. There were 17 men and 9 women in this study group. Each subject underwent polysomnography to diagnose their OSA, defined as an AHI greater than or equal to 5. Each subject was treated with the same type of MAD, specifically a removable Herbst appliance, to act as a constant. The MAD was titrated to effectiveness according to the patient feeling relief of symptoms. This was done by the patient adjusting the pistons to a greater and greater extent until the symptoms were no longer noticed. Each patient was referred to the Radiology and Imaging Science Division, University of Louisville School of Dentistry for CBCT, and informed consent was obtained.

Imaging

Two CBCT scans were performed with the Classic iCAT on each awake subject seated upright. For both scans, the 22 cm, extended field of view setting was used during a 20 + 20 seconds scan with a 0.4-mm resolution. One was made without the appliance, serving as a control and the second was made with the removable Herbst OSA appliance in place. The image detector and beam were positioned to maximize coverage of the upper airway to approximately the level of the fifth cervical vertebra.

Image Generation

The CBCT volumetric datasets were imported in the format of single-file DICOM files into a pre-alpha version 11.0 of Dolphin 3D Imaging (Dolphin Imaging and Management Solutions, Chatsworth, CA), a software package that reconstructs 3D images and facilitates making measurements. Once imported, the 3D reconstructions were oriented so the Frankfort horizontal plane was parallel to the axial plane. The mid-sagittal plane was oriented to the midline of the subject. The coronal plane was oriented so that it passed through both the left and the right porion points. In cases of asymmetry, the orientation was made as close as possible to these guidelines (Fig 7). Once the image was oriented properly, the software was used to create a 2D simulated

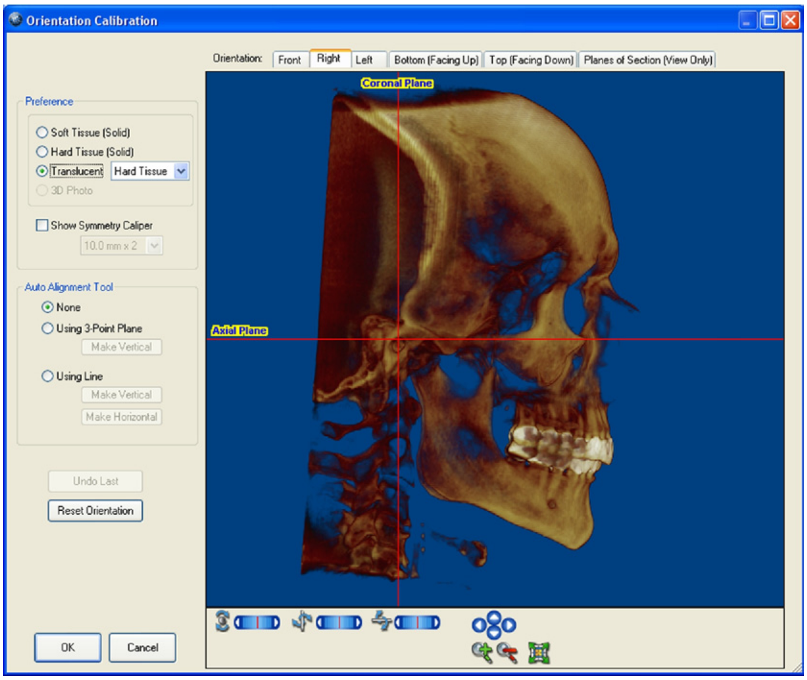


Figure 7. Orientation screen for Dolphin 3D Imaging. (Color version of figure is available online.)

lateral cephalometric image with the use of a ray-sum technique. The options were set to an orthogonal projection type and a 100-mm ruler was placed in the cephalometric image (Fig 8). The airway analysis tool was used to define the portion of the airway of interest. This portion is the velopharynx and the oropharynx, defined with the superior border being the edge of the soft palate to the posterior of the pharynx (parallel to FH). The inferior border is the tip of the epiglottis on a plane parallel to FH. The border between the velopharynx and the oropharynx is the occlusal plane. The area of interest was defined by a clipping box and seeds in the airway space (Fig 9).

Once the portion of the airway of interest was defined, the airway analysis tool calculated volume and cross-sectional areas of different slices of the airway. It also generated JPG files of cross-sectional areas of interest (Fig 10). Axial-view images of the smallest cross-sectional area (SmCa), largest cross-sectional area (LgCa), and area of the slice at the level of the anterior superior aspect of C2 (C2Ca) were saved and exported into Image J for analysis. This process was performed for all subjects for both CBCT files, with and without the device, i.e., S1-In and S1-OUT.

Image Analysis and Data Generation

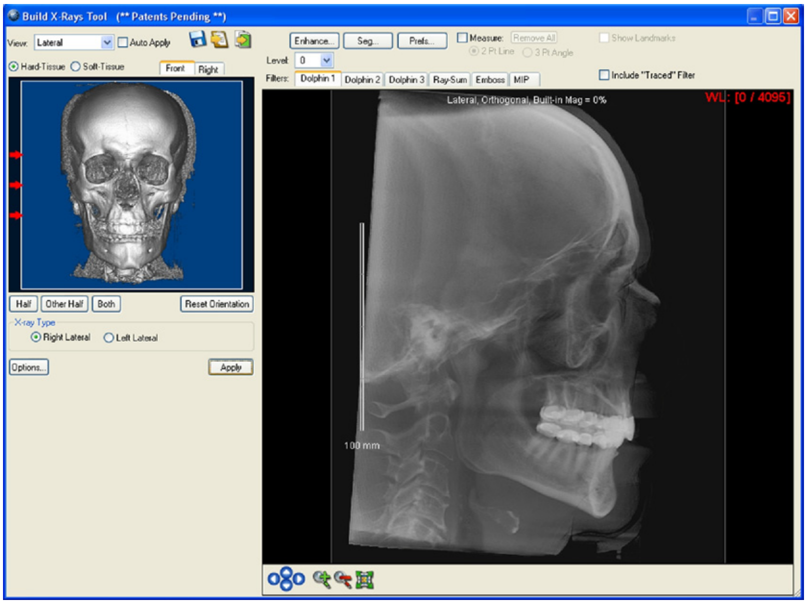
Cephalometric Measurements

The lateral cephalogram simulated image allowed the measurement of classic cephalometric measurements with the Dolphin Program. A custom cephalometric analysis was created for the purpose of this study. The measurements were tested by measuring the same image on another cephalometric analysis package, RMO Joe (Rocky Mountain Orthodontics, Inc., Denver, CO), and found to be the same.

Two series of cephalometric measurements were made. The first series described the anatomy of the subject on the non-moving aspect of the craniofacial complex. The second series had one or more points on the mandible that show change when the Herbst was in place. The following specific measurements were made due to the accompanying rationale:

Anatomic Descriptive Measurements

1. Cranial deflection N-S-Ba: this angle denotes the relative angulation of the posterior and anterior cranial base. The measurement of this kyphosis may impact upon the nasopharyngeal airway. A more acute angulation may compress the airway by having a skull shape



Build X-Rays Tool (** Patents Pending **)

View: Lateral ☐ Auto Apply

● Hard-Tissue ○ Soft-Tissue

Level: 0

Filters: Dolphin 1

☐ Measure: ● 2 Pt Line ○ 3 Pt Angle

☐ Show Landmarks

☐ Include "Traced" Filter

X-ray Type: ● Right Lateral ○ Left Lateral

Lateral, Orthogonal, Built-in Mag = 0%

WL: [0 / 4095]

Figure 8. "Build X-rays" tool in Dolphin 3D Imaging. (Color version of figure is available online.)

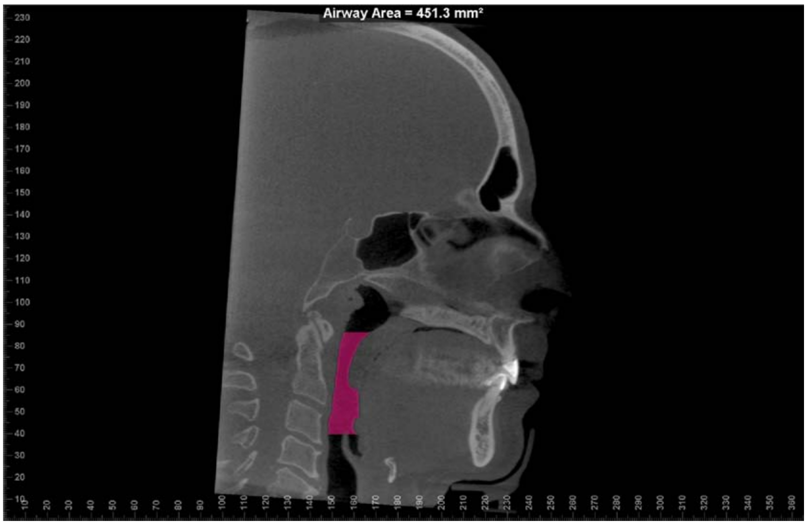


Figure 9. Pink area denotes defined airway portion of interest. (Color version of figure is available online.)

that is more vertical than elongated (norm: 129.6 degrees; standard deviation [SD]: 5 degrees).

2. Ba–S–PNS: this may be used to determine the horizontal position of the hard and soft palate. The more acute the angulation, the more potential for diminished airway the AP plane (norm: 63 degrees; SD: 2.5 degrees).
3. Linder-Aronson (Rocky Mountain Orthodontics, Diagnostic Services Handbook Course Syllabus, 1989, Denver, CO) (1): the distance from PNS to the nearest adenoid tissue in a line from PNS to basion. This is considered an excellent, but limited expression of airway availability in the horizontal AP plane. It is an indicator of potential airway obstruction (norm: dependent on age, sex, ethnic origins, size of tissue mass).
4. Linder-Aronson (2): another indicator of potential airway obstruction, measured by the distance from PNS to the nearest adenoid tissue in a line from PNS perpendicular to sella-basion (norm: Also dependent on age, sex, ethnic origins, size of tissue mass).

Figure 10. Axial slice of CBCT scan exported to Image J. Pink shows cross-sectional area of airway. (Color version of figure is available online.)

Measurements of Mandibular Change (With and Without MAD)

All of these were altered with the movement of the mandible forward and obliquely downward using the MAD.[2]

1. Lower facial height: ANS-Xi-PM: Describes the vertical relationship of the mandible and maxilla. Low values indicate a skeletal deepbite, a factor known to be contributory to OSA (norm: 45 degrees; SD: 4.0 degrees) (Xi is mandibular foramen).
2. Posterior facial Height: sella-gonion: Describes the vertical dimension of the ramus to the cranium (in mm).
3. Ramal height: From gonion to CF: measured from the posterior border of the pterygomaxillary fissure to the angle of the mandible (norm: 54.8-mm; SD 3.3 mm).
4. Anterior facial Height: nasion—menton (in mm).
5. Saddle angle: nasion-sella to sella-articulare: . Low values could indicate a forward position of the mandible. The relative position of the mandible in space may well have an influence on the airway patency and /or the relative advancement required for a MAD to be effective (norm: 123.0 degrees; SD: 3.0 degrees).
6. Facial axis: measured by the angle formed by the plane CC to gnathion and the basion—nasion plane. The placement of the Herbst will show the oblique change in angulation of the mandible. The degree of up and forward or down and back positioning may be important to evaluate effective OSA symptom reduction (norm: 90 degrees; SD: 3.5 degrees).
7. SNB: the angular position of the mandible to the cranium as measured from sella—nasion—B point (norm: 80 degrees; SD: 3.7 mm).
8. ANB: measured by the angle formed by the planes nasion—point A and nasion—point B (norm: 2.0 degrees).
9. Ramus–Xi position: measured by the angle formed by the planes CF—Xi (mandibular foramen) and Frankfort horizontal. It describes the horizontal position of the ramus unaffected by vertical change (norm: 76 degrees; SD: 3.0 degrees).
10. Horizontal movement: anterosuperior aspect of C- 3 to pogonion: the distance as measured in mm to show the forward displacement of the mandible using the MAD (Fig 11).

Each of the aforementioned cephalometric measurements was made 3 times for each image made from each subject.

Airway Measurements

The airway analysis tool in Dolphin 3D Imaging was used to find the volume (Fig 12) and cross-sectional areas of the airway. It is able to find the minimum cross-sectional area in the part of the airway that had been defined, and the other 2 cross sections were found by scrolling through the axial slices. The volume and cross-sectional areas from the smallest cross-sectional area (SmCa), largest cross-sectional area (LgCa), and cross-sectional area at C2 (C2Ca) were recorded. The airway was defined 3 times, and the volume and cross-sectional areas were found for each unique airway definition. Each defined airway space can vary based on the sensitivity settings, where the "clipping box" and the imaging "seeds" were placed.

Finally, for each airway definition, the location of the smallest cross-sectional area was

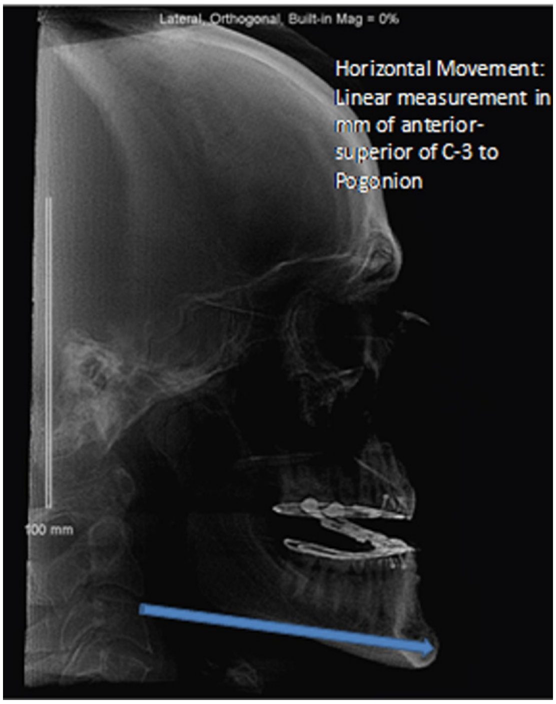


Figure 11. Horizontal movement. (Color version of figure is available online.)

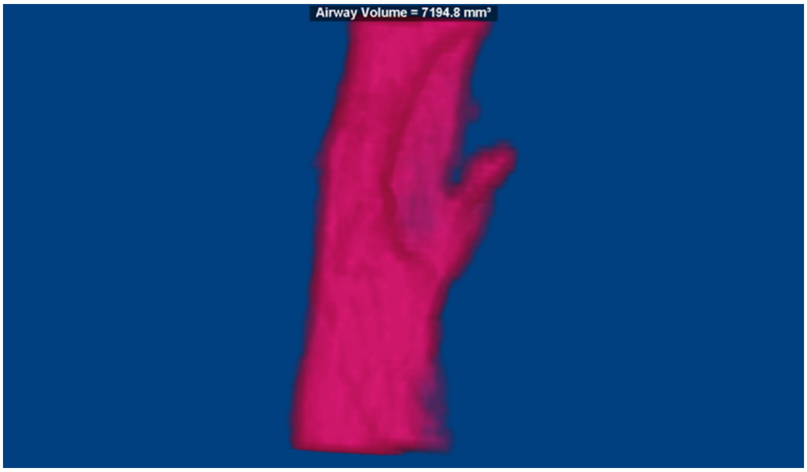


Figure 12. Airway volume reconstructed and measured in Dolphin software, version 11. (Color version of figure is available online.)

noted as either above or below the occlusal plane. The rationale for using these 3 cross-sections is explained below:

(SmCa): the smallest cross section (Fig 13) is the point where the airflow is theoretically most constricted. This point is a limiting factor in airflow.

(LgCa): the largest cross section shows the maximum amount the airway has expanded

(C2Ca): this cross section is measured at a constant level (Fig 14), whereas the location of the smallest and largest can shift. This measurement will show how the area at the same point will change.

It was noted for each scan whether the location of the smallest cross section is above or below the occlusal plane, as some authors have shown that patients are more likely to respond to MAD therapy if the smallest cross section of the oropharynx is located below the occlusal plane. A value of (1) is given if it is below, and a value of (2) is given if it is above. This is the only nonparametric data measured in the study.

The images exported to Image J, a public domain Java image processing program, at

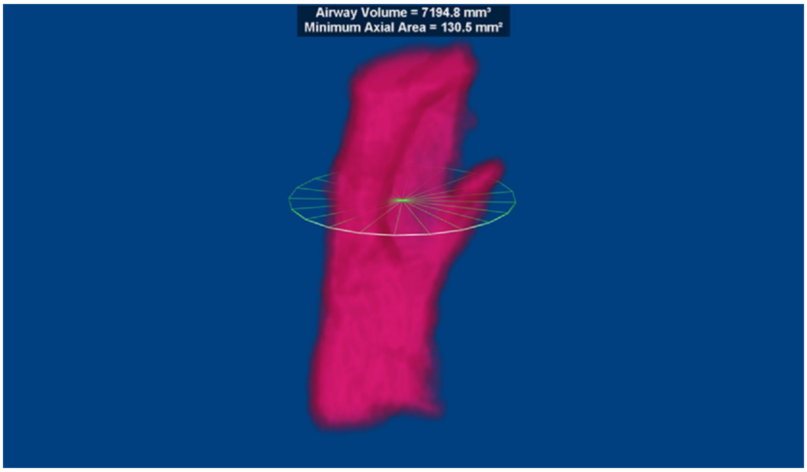


Figure 13. Smallest cross-sectional area marked on volumetric reproduction. (Color version of figure is available online.)

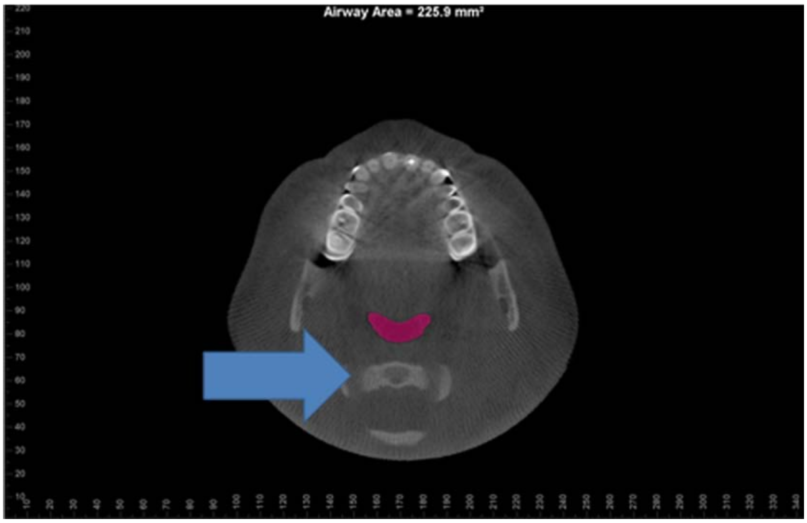


Figure 14. Arrow points to cross section of C-2. Pink area is (C2Ca). (Color version of figure is available online.)

http://rsbweb.nih.gov/ij/, are used to make linear measurements of airway cross-sections. The scale on Image J is calibrated to the ruler marks on the image. A linear measurement in mm is then made at the largest AP dimension and the largest lateral (L) or transverse dimension (Fig 15). Microsoft Excel (Microsoft, Seattle, WA) is then used to calculate the L:AP ratio to quantify the shape of the opening. The larger the ratio, the more elongated or elliptic is the shape of the cross section, while the smaller the ratio, the more circular. The shape of the airway is important because previous authors have described that it influences the collapsibility and expandability of the airway. In summary, each cross section has the following measurements:

1. area
2. lateral dimension in mm (L)
3. anteroposterior dimension in mm (AP)
4. L:AP ratio
5. Measurements of airway cross section

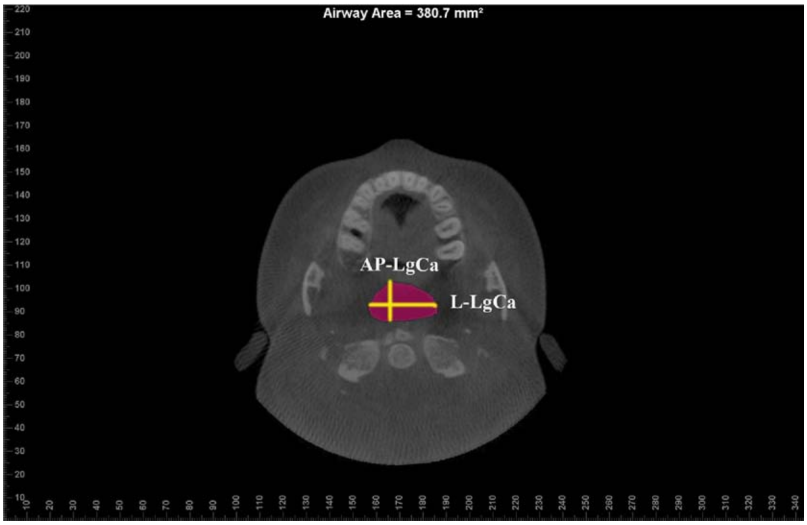


Figure 15. Airway area of largest cross section (LgCa) shown in pink. Anteroposterior (AP-LgCa) and lateral (L-LgCa) linear dimensions of this cross section shown in yellow. (Color version of figure is available online.)

Statistical Analysis

Once all 3 readings of each measurement were made, the mean was found, the difference calculated between the mean measurements made with and without the appliance in place, and the data were imported into SPSS, a statistical data analysis software package produced by SPSS Inc. (Chicago, IL). SPSS was used to perform linear regression statistical analysis. A reliability intraclass correlation was also computed using the raw data, and comparing the 3 measurements made, rather than using the averages. It was computed for all variables used in the linear regression analyses.

For the descriptive analysis, means, standard deviations, skewness, and kurtosis values were computed for all parametric variables. Multiple linear regression was then used to assess the contribution of each predictor in determining the value of the outcome measure for the parametric outcome variables. Linear regression was chosen to evaluate whether the changes in the cephalometric measurements based on the movement of the mandible with the Herbst could predict the outcomes of the changes in the pharynx.

The predictor variables in this study were the final changes measured in:

Posterior facial height,
Ramal height;
Anterior face height;
Saddle angle;
Facial axis;
Ramus position;
Horizontal movement.

the outcome measures were changes in:

Volume
SmCa: smallest cross-sectional area
AP-SmCa: AP linear dimension of the smallest cross-sectional area
L-SmCa: lateral linear dimension of the smallest cross-sectional area
L:Ap-SmCa: ratio of the lateral to the anterior-posterior linear dimensions of the smallest cross-sectional area
LgCa: largest cross-sectional area
AP-LgCa: AP linear dimension of the largest cross-sectional area
L-LgCa: lateral linear dimension of the largest cross-sectional area
L:AP-LgCa: ratio of the lateral to the AP linear dimensions of the largest cross-sectional area
C2Ca: cross-sectional area at the level of C2
AP-C2Ca: AP linear dimension of the cross-sectional area at the level of C2
L-C2Ca: lateral linear dimension of the cross-sectional area at the level of C2, and L:AP-C2Ca: ratio of the lateral to the anterior-posterior linear dimensions of the cross-sectional area at the level of C2.

The usefulness of the set of predictor variables was determined by testing the null hypothesis that R^2 was equal to zero. If the null hypothesis was rejected, the set of predictor variables was examined to determine which 1 or ones were statistically significant predictors. In this way, the predictor variables having an impact on the outcome measure were identified.

Results

The linear regression showed that there were 6 dependent, or "outcome," variables measured on the volumetric scan that were found to be predictable by independent variables. These outcome variables were Volume of the oropharynx, largest cross-sectional area (LgCa), the cross-sectional area at C2 (C2Ca), the lateral linear dimension of the cross section at C2 (L-C2Ca), the AP linear dimension of the cross section at C2 (AP-C2Ca), and the ratio of these 2 linear dimensions (L:AP-C2Ca). One predictor for each of these outcome variables was found.

For volume, largest cross-sectional area (LgCa), the cross-sectional area at C2 (C2Ca), and the lateral linear dimension of the cross section at C2 (L-C2Ca), the predictor was horizontal movement. This means that of all the cephalometrics measured, the only significant predictor was how far anteriorly the mandible had been pulled by the appliance. Therefore, an algorithm could be produced to predict each of these outcome measurements based on a given amount of mandibular advancement.

For the AP linear dimension of the cross section at C2 (AP-C2Ca), and the ratio of the lateral and AP linear dimensions, (L:AP-C2Ca), 2 different cephalometric predictor variables were found. Saddle angle was found to be able to

Table 1. Reliability or Consistency Values of Each Variable Used in the Linear Regression Analysis

	n	*Without Device*	*With Device*
Facial angle, FH-NPO	26	0.971	0.974
Facial axis Ricketts, NaBa-PtGn	26	0.992	0.984
Saddle-sella-angle, SN-Ar	26	0.952	0.967
Posterior face height, SGo	26	0.990	0.991
Anterior face height, NaMe	26	0.995	0.980
Total face height, N-Gn	26	0.995	0.979
Posterior facial height, Go-CF	26	0.990	0.975
horzMovmt	26	0.996	0.993
Volume(mm^3)	26	0.995	0.999
SmCa (mm^2)	26	0.990	0.995
AP-SmCa (mm)	26	0.981	0.986
L-SmCa	26	0.997	0.995
Ratio-SmCa	26	0.982	0.971
LgCa	26	0.978	0.996
AP-LgCa	26	0.946	0.962
L-LgCa	26	0.989	0.977
L:AP-LgCa	26	0.976	0.943
C2Ca	26	0.997	0.998
AP-C2Ca	26	0.983	0.989
L_C2Ca	26	0.995	0.993
L:AP-C2Ca	26	0.974	0.984

n is number of subjects. Reliability statistics show level of consistency of the measurements. All values being greater that 0.90 shows a very high level of consistency in the measurements made.

predict (AP-C2Ca) and facial axis was a significant predictor for (L:AP-C2Ca).

Table 1 shows the reliability or consistency values of each variable used in the linear regression analysis. This statistical analysis shows how consistently all the measurement in this study were made. It was computed by the use of the 3 measurements made of each variable. The value shown is the intraclass correlation of the average measures. The range of possible values is from 0 to 1, where 1 is the greatest amount of consistency.

Table 2 shows descriptive statistics for each variable used in this analysis in 26 subjects. All values reflect the measurements of difference between the "with device in place" and "without" measurements.

Table 3 shows the number of subjects that fell within a range of *Z* scores for some key variables.

Table 2. Descriptive Statistics of Change

	n	*Mean*	*SD*	*Skewness*	*Kurtosis**
Facial angle, FH-NPO	26	0.853846	1.6908138	0.582	0.471
Facial axis Ricketts, NaBa-PtGn	26	−1.091026	2.1843394	−0.632	0.103
Saddle-sella-angle, SN-Ar	26	−10.867949	5.2694548	−0.968	1.195
Posterior face height, SGo	26	3.596154	1.8280853	0.107	−0.488
Anterior face height, NaMe	26	7.485897	3.5100639	0.684	−0.157
Total face height, N-Gn	26	8.134615	3.8600343	0.699	0.198
Posterior facial height, Go-CF	26	3.421795	1.6987300	0.688	0.977
horzMovmt	26	3.993590	3.5692267	0.261	0.253
Volume(mm^3)	26	2792.794872	4380.9077	1.739	5.789
SmCa (mm^2)	26	43.157692	86.1480279	0.125	3.663
AP-SmCa (mm)	26	0.573077	2.5016975	−0.124	0.584
L-SmCa	26	2.464103	4.7274698	−1.043	4.089
L:AP-SmCa	26	0.165397	0.8896943	0.864	5.180
LgCa	26	71.419231	61.6807120	0.500	0.854
AP-LgCa	26	0.825641	2.0577940	−0.311	0.023
L-LgCa	26	3.656410	6.0296583	0.864	1.232
L:AP-LgCa	26	0.121319	0.5128242	0.320	2.253
C2Ca	26	77.638462	111.2364667	1.195	5.955
AP-C2Ca	26	1.027564	2.0505118	−0.534	2.028
L_C2Ca	26	4.269231	4.4366847	−0.416	2.173
L:AP-C2Ca	26	0.179047	0.5043837	0.714	1.474

*These values of Kurtosis are reported by SPSS where the norm equals zero.

Table 3. Distribution of Z Score Ranges

Variable	$-3 < Z \leq -2$	$-2 < Z \leq -1$	$-1 < Z \leq 0$	$0 < Z \leq 1$	$1 < Z \leq 2$	$2 < Z \leq 3$	$3 < Z \leq 4$
Horizontal movement	0	4	8	11	2	1	0
Volume	0	2	12	10	1	0	1
SmCa	1	1	15	6	2	1	0
LgCa	1	2	11	8	3	1	0
C2Ca	1	0	14	9	1	0	1

The Z score is the number of standard deviations the value is away from the mean. This table is illustrated in Figures 16, 17, and 18. They show the distribution of subjects for each range of Z scores. Specifically, Figures 16, 17, and 18 show change in volume of velopharynx and oropharynx, horizontal mandibular movement, and change in cross-sectional area at 3 different levels, respectively. The results of the linear regression analysis showed at least one statistically significant predictor variable only for the following outcome variables: volume, LgCa, C2Ca, L-C2Ca, AP-C2Ca, L:AP-C2Ca.

Table 4 shows the R^2 value of each significant regression test, and the P value found for the overall significance of the individual outcome to all the predictor variables. The overall test for significance of the predictors on an outcome variable showed a P value greater than 0.05 in 4 of these tests. However, a predictor variable in each of the 6 analyses was statistically significant ($P < 0.05$). This unexplained "fluke" in the analysis is likely due to the SPSS program rounding during the analysis of the variables. Table 5 shows which predictors were found to be significant in each linear regression test.

Discussion

This study was the first to show a sample of OSA patients successfully treated with a removable MAD in 3D imaging. The authors of previous work with MAD and 3D imaging[46,50] used subjects who only snored or had untreated OSA patients with conventional CT, and MRI.

This was also the first study to use CBCT volumetric imaging of OSA patients. Previous 2D studies were limited to cephalometrics, whereas previous CT and MRI studies were limited to cross-sectional area and linear measurements. These studies could not produce volumetric measurements.

Recent advances in CBCT technology in software packages has allowed these volumetric data to be collected from CBCT scans. This study used pre-released software from Dolphin (pre-alpha version 11). Technological advances such as these have allowed progress to be made in resolving and predicting the efficacy of OSA MAD treatment in this study.

This study was also the first to attempt to predict changes in airway from changes in cephalometric measurements before and after the

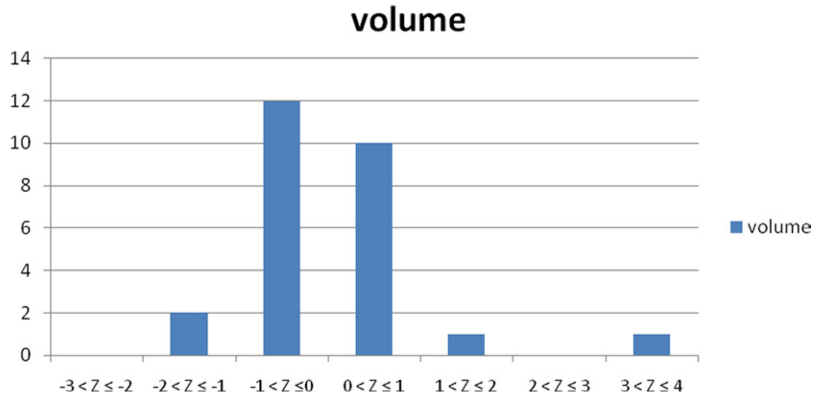


Figure 16. The z score distribution of volume change. This graph is similar to a bell-curve, but is presented in bars instead a smooth curve. (Color version of figure is available online.)

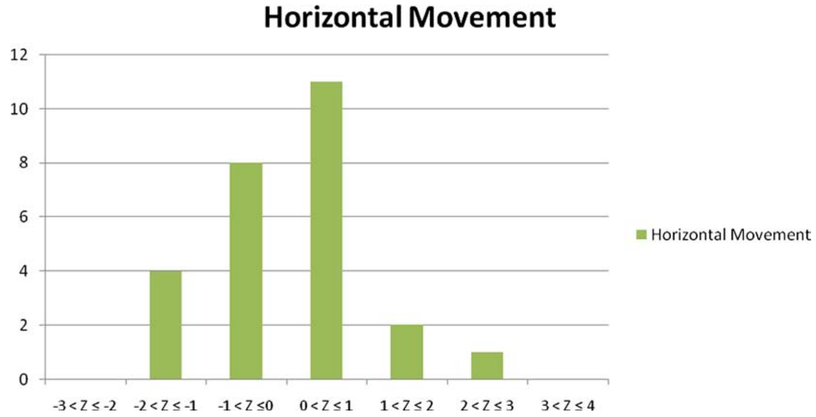


Figure 17. Z score distribution of change in horizontal movement. This shows how many subjects titrated their Herbst how many standard deviations away from the average amount titrated in this population. The mean was 4 mm. (Color version of figure is available online.)

MAD is used. All other cephalometric studies examined static anatomy as predictors of a diagnosis of OSA. This study found that it is possible to predict the volume gained, the amount of cross-sectional area gained at the largest cross section, the cross-sectional area gained at C2, and the lateral linear dimension gained at this level from the distance the mandible is advanced. It was also the first study to relate an established cephalometric measurement to changes in the airway. It found that the AP linear dimension gained at C2 is predictable by the saddle angle, and the amount of shape change (from elliptic to round, or vice versa) is predictable by the facial axis measurement.

Statistical Conclusions

The intraclass correlation for every variable analyzed in this study was equal or greater than $r = 0.95$. This result shows an extremely high reliability of the measurement process used in this study. This study related dynamic alterations in cephalometric measurements to specific changes in the airway. The distance the mandible is moved forward can be used to predict the gain in volume, largest cross-sectional area, and all parameters of the airway at C2. That is to say, this study has discovered that it is theoretically possible to predict the amount an airway will increase from the number of millimeters the MAD is activated.

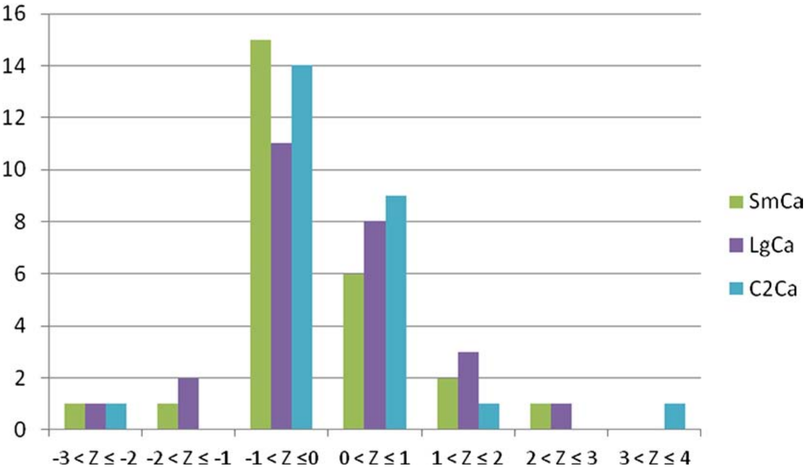


Figure 18. This shows the *Z* score distribution of change in cross-sectional area at the 3 levels measured: smallest cross section (SmCa), largest cross section (LgCa), and cross section at C2 (C2Ca). It compares how the different levels of the pharynx respond to a MAD. (Color version of figure is available online.)

Table 4. Significant Outcome Variables

Outcome Variable	R^2	*P Value*
Volume (mm^3)	0.556	0.043
LgCa (mm^2)	0.649	0.008
C2Ca (mm^2)	0.534	0.059
L-C2Ca (mm)	0.501	0.091
AP-C2Ca (mm)	0.468	0.132
L: AP-C2Ca	0.473	0.125

Only a limited number of outcome variables were found to be predictable, however. Nothing about the smallest cross-sectional area could be predicted, and only the area at the largest cross section could be predicted. It is likely that the C2 outcomes were the most predictable because each measurement of the C2 cross section remained at the same level before and after appliance placement. Because the smallest and largest cross-sections could be at any vertical level of the pharynx after the use of the appliance, the predictors in this study may have been insufficient for such complexly changing variables.

Two of the most interesting findings from the linear regression test involved preexisting cephalometric measures. The first is that of all the cephalometric changes measured in this experiment, only the change in saddle angle could predict the AP dimension of the airway changes at C2. The saddle angle is generally used as a measure of the location of the condyle in the glenoid fossa in relationship to the basion-nasion plane. In this study, however, it measures the change in the location of the condyle as it moves forward and downward with the mandible. The mean change in Saddle Angle in this experiment was approximately −11 degrees. Anatomically, this means that the mandible is moving both downward and forward. The result is an oblique movement, which has predicted the AP opening at C2, situated at the middle of the oropharynx.

The second significant predictor cephalometric measurement is facial axis, which was the only predictor of the change in the ratio of the L: AP at the level of C2. This ratio reveals the shape of the cross section of the airway rather than an absolute dimension. The larger the value, the more elongated or elliptic the shape, while the smaller the value, the shape is more spherical. Moving the jaw down the facial Axis with the appliance tended to predict an opening of the airway towards a more elliptic shape. This is in agreement to previous studies[46,47] in which the authors found that the increase in cross-sectional area was significant only because of the increase in transverse dimension, not the AP dimension. No one has previously related this particular observation of "roundness" of airway shape with a normalized oblique movement of the mandible.

Furthermore, the use of the appliance appeared to drive the facial axis in nearly every case towards a more normal measure, regardless of whether the patient was originally more open or closed in jaw orientation. This explains why the mean of the change appears small (−1), but is still significant.

The skewness of the volume and the area of the cross section at C2 have a positive value, which indicates that very few people responded negatively in the measured parameters to the MAD therapy.

Most of the airway outcome measurements showed a very high value of kurtosis. Kurtosis is a measure of "skinniness" of a bell-curve. A high level in this study means that the distribution of response to MAD therapy was close to the mean, and those who responded away from the mean did not stray very far. The authors have interpreted this to indicate that the change in the airway is highly predictable in response to MAD therapy. In addition, the mean values of airway change were overwhelmingly positive values, which further leads to the conclusion that most patients responded not only predictably, but positively (see distribution of the *Z* scores in Table 2 and the bar graphs in the Results section).

In accordance with the literature reported, this study has shown that MAD therapy increased the patency of the velopharynx and oropharynx. The mean increase of volume was 2792.7 mm^3. Although the average increase in horizontal movement of the mandible was 3.99

Table 5. Significant Predictor Variables

Outcome Variable	*Predictor Variable*	*P Value*
Volume (mm^3)	Horizontal movement	0.014
LgCa (mm^2)	Horizontal movement	0.001
C2Ca (mm^2)	Horizontal movement	0.044
L-C2Ca (mm)	Horizontal movement	0.011
AP-C2Ca (mm)	Saddle Angle	0.042
L: AP-C2Ca	Facial axis	0.042

mm with a standard deviation of approximately the same value, the average increase in total face height (or vertical change) was 8 mm with a smaller standard deviation. That is to say, despite a large variation in horizontal movement, when combined with a vertical increase, it yielded a significant and predictable volumetric improvement.

Visualizing Changes in the Airway and Understanding Nonresponders

The following images show comparisons of airway volume between an overresponder (Fig 19), a normal responder (Fig 20) and a subject who responded with a negative change in volume (Fig 21).

It is noted that the under-responder was one of the few subjects who had a worsening value of facial axis from 85 to 83 degrees (normal = 90), indicating a backwards or clockwise movement of the mandible. This may be contrasted with the example of the average responder, where the facial axis stayed within 1 degree of a positive change towards a normal cephalometric value. Both subjects had an average amount of mandibular advancement, whereas the superresponder was able to be advanced 12 mm (an atypical advancement range). Therefore, although the statistical analysis demonstrated that there was no significant correlation between facial axis and volumetric change in airway, a generalized perception by the authors showed that the worst responders had facial axis measurements outside the normal cephalometric values.

Although some patients appeared to worsen based on the parameters measured in this study, all subjects reported an improvement in OSA symptoms. There are several possible explanations, which may include:

1. Other anatomical parameters not yet described, related to the complex neuromuscular functions of the oropharynx
2. The wakefulness and uprightness of subjects in this study may have differed from the appearance of the airway on the image compared with the image of a patient taken in the supine position when asleep.
3. A placebo response was in effect.

Contrastingly, an anecdotal observation of this study supported the findings of Sanner et al.,[8] who found through MRI that if the most collapsible part of the airway is in the velopharynx alone, the patients would not respond well to MAD. In the present study's volumetric evaluation with CBCT, all the subjects found with the smallest cross-sectional area above the occlusal plane (with and without the device) either decreased or remained the same in volume. This finding, along with the findings of Sanner et al.,[8] implies that a MAD may only be partially effective or completely ineffective for OSA sufferers of this type. This strengthens the observation that a CBCT scan

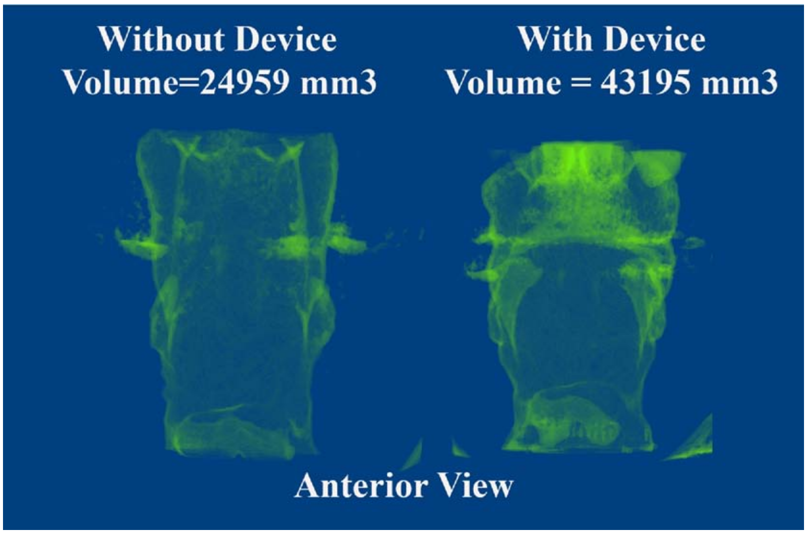


Figure 19. Subject 1 responded in volume change 4 standard deviations above the mean. (Color version of figure is available online.)

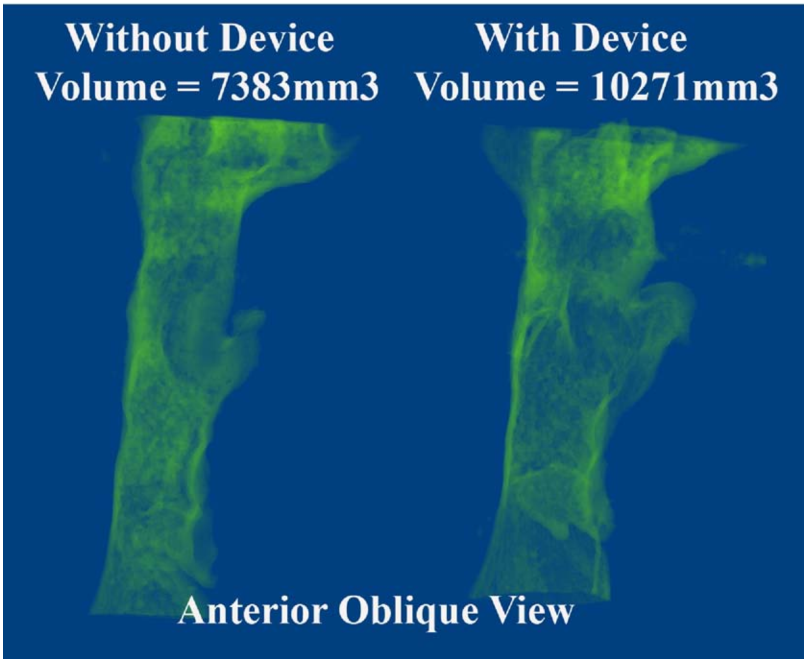


Figure 20. Subject 5 responded the mean amount in volume change. (Color version of figure is available online.)

and anatomical evaluation of the airway should be performed before initiating treatment on OSA patients with a MAD. Differentiating the morphology of each patient is critical to select the appropriate treatment, whether it be surgical correction, or the use of a removable orthotic appliance.

Another noteworthy finding in this study included the evaluation of an 18-year-old female subject who exhibited large tonsils. The first illustration (A) in Fig 22 shows the arrow pointing to the airway where the tonsils are impinging upon it. Although it had an overall increase, the volumetric change with the use of the appliance was less than half the average change, with no increase in smallest cross-sectional area with the use of the appliance. Another interesting finding was that the narrowest area as seen in part B of Fig 22, shifted

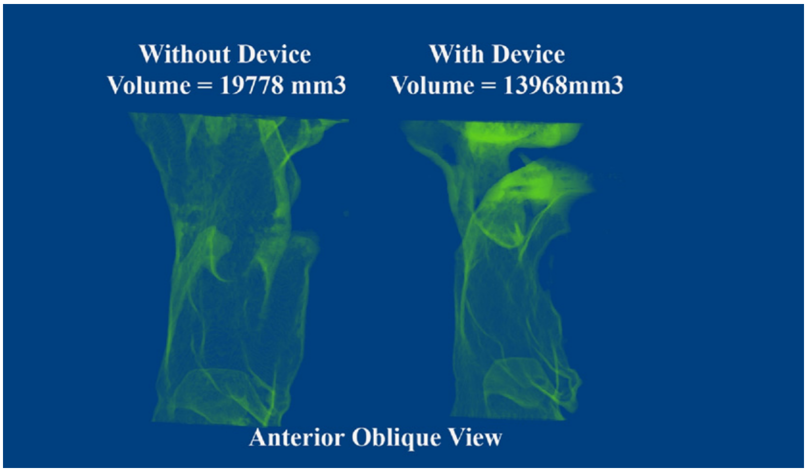


Figure 21. Subject 23 responded in volume change 2 standard deviations below the mean. (Color version of figure is available online.)

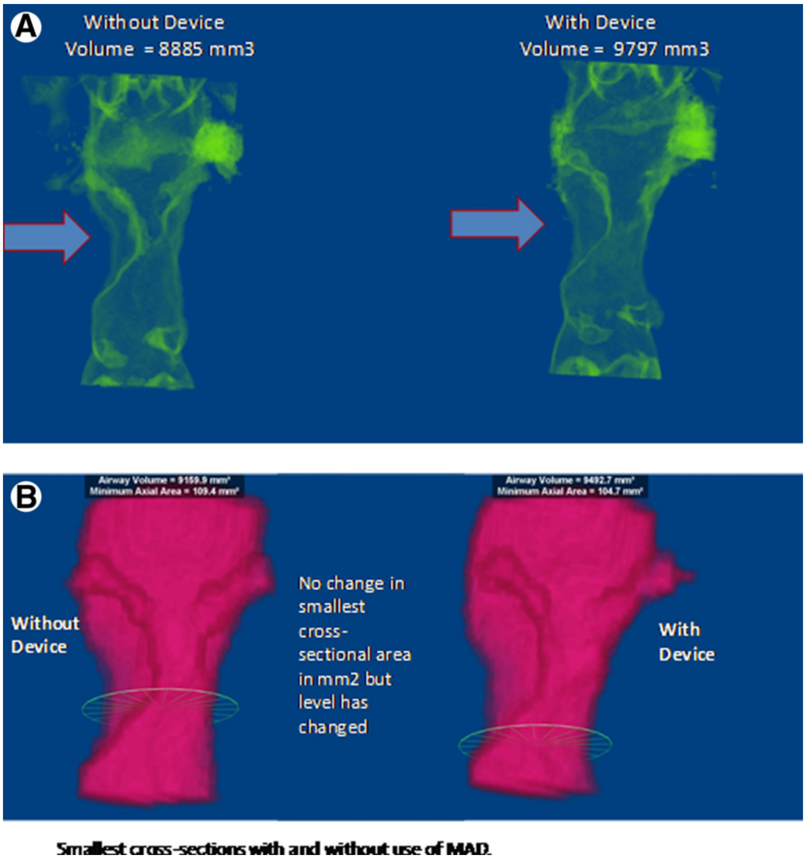


Figure 22. Volumetric representations of a subject with very large lingual tonsils. (A) Arrow points to site of tonsil impingement. (B) The wheel marks the level of smallest cross-sectional area, which has not changed in value, but shifted inferiorly. (Color version of figure is available online.)

inferiorly. The specific location change of the smallest cross-sectional area, vertically up or down, was unpredictable. This change is likely based upon the subject's individual morphology. This alteration in morphology of the airway with the use of an appliance could not have been predicted with previous 2D imaging modalities and could not be assessed without the use of 3D imaging such as CBCT.

To explain this subject's improvement in symptoms despite the apparent lack of volumetric change, it may be helpful to recall findings from other authors. Tsuiki et al.[48] found with electromyographic recordings that an increased neuromuscular tonicity of the genioglossus occurred with mandibular advancement in patients with OSA when they were awake. This reduced the tendency of the upper airway to collapse. If the same process occurred in patients during sleep, this could explain how a seemingly poor responder to MAD therapy based on below average increase in volumetric and cross-sectional area, could actually have an improvement in OSA signs and symptoms.

The subject with the largest airway change was advanced 12 mm. Patients with sufficiently dysplastic anatomy requiring a bimaxillary surgical advancement of the jaws as outlined by Conley and Legan,[1] often have jaw advancement surgery in this range. As the average volume change was in the order of 2800 mm^3, this patient increased in volume 18,000 mm^3! This large increase may be similar to that seen in surgical OSA corrective procedures, and could therefore explain the huge success of surgery for a permanent correction.

Anatomical Mechanisms

Previous authors have suggested that the improvement in volume in the oropharynx with a

MAD is caused by a forward repositioning of the soft palate.[25-28,43,45-50] The mandibular advancement theoretically stretches the soft palate with a concomitant stiffening of the wall of the oropharynx itself. This is accomplished through the bracing effect of the lateral wall of the soft palate in relation to the base of the tongue via the palatoglossal arch. A transverse widening of the airway with advancement is said to occur because of less movement of the hyoid bone forward than that of the mandible. This is explained because the posterior belly of the digastric muscle and the infrahyoid muscles mostly restrict this inferior bone. Another hypothesis is that the transverse widening effect is due to a reflex response of the stylopharyngeus muscle to the drag effect upon hyoid bone when using a mandibular advancing appliance.

The use of CBCT in depicting a mechanism for airway volume enhancement with an orthotic is also demonstrated in the present study through examination of the tonsillar area of the oropharynx. The presence of large tonsils illustrates the reduction of available airway and the possible limitation of the degree of volumetric increase. With MAD therapy and the absence of tonsils, a reconstructed 3D pharynx reveals a phenomenon not previously described in the literature. There is an area of expansion in the faucial pillar area that appears as appendages on the pharynx in Figure 23, but are actually depictions of a void. Figure 23 shows the enlargement and “ballooning” of the faucial pillar area using a lower jaw advancement appliance.

Figure 23 effectively demonstrates why removal of enlarged tonsils that can impinge upon this important area of expansion is a frequently

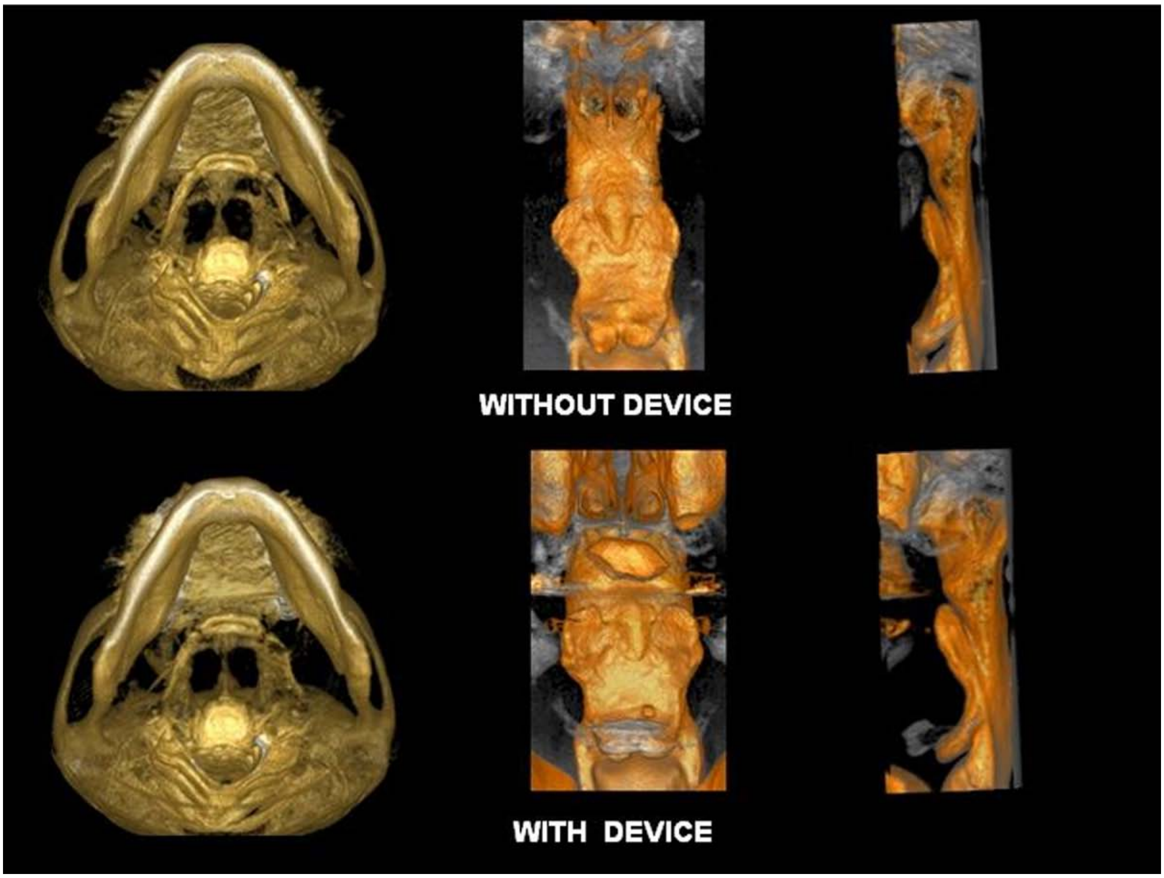


Figure 23. This reconstruction of the airway made with 3DVR shows a great expansion of the base of the tongue, tonsil, and faucial areas. It is illustrated here as what appears to be an appendage shaped like a bird with open wings. This is actually an empty space in the oropharynx surrounded by palatoglossus, palatopharyngeus, styloglossus and the base of the tongue. (Color version of figure is available online.)

used treatment modality for an improvement in airway patency in patients with OSA.[1]

The position of the smallest and largest cross-sectional areas before and after treatment was not able to be tracked. However, from a clinical standpoint, the greatest point at which the cross-sectional area increase occurs may not be as important as total volumetric change when treating OSA. Because most patients had an increase in volume, it is assumed that this gain in volume allowed more airflow, and thus improvement in OSA symptoms. Certain factors, such as airway tonicity, uprightness of posture, and awake-ness in an OSA sample could not be controlled.

Future Studies

Previous researchers and clinicians have reported that the gold-standard for permanent correction of OSA does not deal with surgical intervention of the soft tissues of the oropharynx, with the possible exception of excision of space-occupying pathognomonic tissue. Bimaxillary surgical advancement of both jaws is an absolute correction of OSA.[1] The present study indicated a 4-standard deviation above the mean increase in volume in one subject who was advanced the same degree as a normal orthognathic correction for OSA. There is a need for researchers to develop a prospective study evaluating at 3 dimensional changes occurring with surgery. Once a baseline value for normal volume is established in these patients, an algorithm that will predict the amount of volume gain from the amount of mandibular advancement might be developed.

There is some confusion as to which type of individual show a pharyngeal airway shape which is more elliptic than spherical. The literature reports that OSA patients have a more spherical shape than seen in normal patients. No one has yet described the reason for this differentiation in morphology in these 2 groups. With the data already collected in this study, it should be possible to relate a modified maxillofacial ratio index (akin to dolichocephalic vs. brachycephalic) to the shape of the airway. Clinicians have long reported that nasal airway obstruction leads to the greatest negative morphologic changes (openbite, adenoid facies) during growth in the dolichocephalic pattern.[11] Long-face people may well have a narrower or spherical airway than wide-headed individuals.

Understanding these relationships may also help to explain certain unusual findings related to the facial axis and volumetric change.

Conclusion

Lateral airway dimensions of the cross-section at C2, total volume, and cross-sectional area gained in the oropharynx can be predicted from the amount of mandibular forward movement. The saddle angle was a predictor of the linear anterior-posterior dimension, while the facial axis predicted the ellipticality of the airway at C2. With the placement of a MAD appliance, the smallest airway cross-section may move to an unpredictable position, superiorly or inferiorly along the length of the pharynx. No predictor variables could be found for this cross-section of the airway. Therefore, it may be advantageous that all patients wishing to receive MAD treatment for their OSA receive a CBCT scan in order to assess the individual appropriateness of this form of treatment. This is because when treating OSA, obtaining an improvement in a restrictive point in the airway may be just as or more important than achieving an overall volume increase.

References

1. Conley RS, Legan HL: Correction of severe obstructive sleep apnea with bimaxillary transverse distraction osteogenesis and maxillomandibular advancement. Am J Orthod Dentofac Orthop. 129:283-292, 2006
2. Ogutcen-Toller M, Sarac YS, Cakr-Ozkan N, et al: Computerized tomographic evaluation of effects of mandibular anterior repositioning on the upper airway: A pilot study. J Prosthet Dent 92:184-189, 2004
3. Abbott MB, Donnelly LF, Dardzinski BJ, et al: Obstructive sleep apnea: MR imaging volume segmentation analysis. Radiology 232:889-895, 2004
4. Sharabi Y, Dagan Y, Grossman E: Sleep apnea as a risk factor for hypertension (review). Curr Opin Nephrol Hypertens 13:359-364, 2004
5. Rey S, Valdés G, Iturriaga R: Pathophysiology of obstructive sleep apnea-associated hypertension. Rev Med Chil. 2007 October;135(10):1333-42. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18180843?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum. Epub December 20, 2007. In Spanish
6. Kawata N, Tatsumi K, Terada J, et al: Daytime hypercapnia in obstructive sleep apnea syndrome. Chest 132: 1832-1838, 2007

7. Barcelo A, Miralles C, Barbe F, et al: Abnormal lipid peroxidation in patients with sleep apnoea. Eur Repir J 16:644-647, 2000
8. Sanner BM, Heise M, Knoben B, et al: MRI of the pharynx and treatment efficacy of a mandibular advancement device in obstructive sleep apnoea syndrome. Eur Respir J 20:143-150, 2002http://my3.statcounter.com/project/
9. Yamachi M, Kimura H. Oxidative stress in obstructive sleep apnea: putative pathways to the cardiovascular complications. Antioxid Redox Signal. 2008 Jan 4; [Epub ahead of print]
10. Rahaghi F, Basner RC: Delayed Diagnosis of obstructive sleep apnea: Don't ask, don't tell. Sleep Breath 3:119-124, 1999
11. Faber CE, Grymer L: Available techniques for objective assessment of upper airway narrowing in snoring and sleep apnea (review). Sleep Breath. 7:77-86, 2003
12. Fogel RB, Malhotra A, Dalagiorgou G, et al: Anatomic and physiologic predictors of apnea severity in morbidly obese subjects. Sleep 26:150-155, 2003
13. Major MP, Flores-Mir C, Major PW: Assessment of lateral cephalometric diagnosis of adenoid hypertrophy and posterior upper airway obstruction: A systematic review. Am J Orthod Dentofac Orthop 130:700-708, 2006
14. Johal A, Conaghan C: Maxillary morphology in obstructive sleep apnea: A cephalometric and model study. Angle Orthod 74:648-656, 2004
15. Choi JK, Goldman M, Koyal S, et al: Effect of jaw and head position on airway resistance in obstructive sleep apnea. Sleep Breath 4:163-168, 2000
16. Johal A, Patel SI, Battagel JM: The relationship between craniofacial anatomy and obstructive sleep apnoea: A case-controlled study. J Sleep Res 16:319-326, 2007
17. Sher AE, Schechtman KB, Piccirillo JF: The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnea syndrome (review). Sleep 19: 156-177, 1996
18. Zozula R, Rosen R: Compliance with continuous positive airway pressure therapy: Assessing and improving treatment outcomes (review). Curr Opin Pulm Med 7:391-398, 2001
19. Rachmiel A, Aizenbud D, Pillar G, et al: Bilateral mandibular distraction for patients with compromised airway analyzed by three-dimensional CT. Int J Oral Maxillofac Surg 34:9-18, 2005
20. Aboussouan LS, Golish JA, Wood BG, et al: Dynamic pharyngoscopy in predicting outcome of uvulopalatopharyngoplasty for moderate and severe obstructive sleep apnea. Chest 107:946-951, 1995
21. Battagel JM, L'Estrange PR, Nolan P, et al: The role of lateral cephalometric radiography and fluoroscopy in assessing mandibular advancement in sleep-related disorders. Eur J Orthod 20:121-132, 1998
22. Clark GT, Arand D, Chung E, et al: Effect of anterior mandibular positioning on obstructive sleep apnea. Am Rev Respir Dis 147:624-629, 1993
23. Lowe AA: Can we predict the success of dental appliance therapy for the treatment of obstructive sleep apnea based on anatomic considerations? Sleep 16:S93-S95, 1993 (suppl)
24. Tsuiki S, Almeida FR, Lowe AA, et al: The interaction between changes in upright mandibular position and supine airway size in patients with obstructive sleep apnea. AJODO. 128:504-512, 2005
25. Tsuiki S, Hiyama S, Ono T, et al: Effects of titratable oral appliance on supine airway size. Sleep 24:554-560, 2001
26. Tsuiki S, Lowe AA, Almeida FR, et al: Effects of an anteriorly titrated mandibular position on awake airway and obstructive sleep apnea severity. Am J Orthod Dentofac Orthop. 125:548-555, 2004
27. Tsuiki S, Lowe AA, Almeida FR, et al: Effects of mandibular advancement on airway curvature and obstructive sleep apnoea severity. Eur Respir J 23:263-268, 2004
28. Rose EC, Staats R, Virchow C, Jr, et al: Occlusal and skeletal effects of an oral appliance in the treatment of obstructive sleep apnea. Chest 122:871-877, 2002
29. Schmidt-Nowara WW, Meade TE, Hays MB: Treatment of snoring and obstructive sleep apnea with a dental orthosis. Chest 99:1378-1385, 1991
30. Fransson AM, Tegelberg A, Johansson A, et al: Influence on the masticatory system in treatment of obstructive sleep apnea and snoring with a mandibular protruding device: A 2-year follow-up. Am J Orthod Dentofac Orthop. 126:687-693, 2004
31. Bonham PE, Currier GF, Orr WC, et al: The effect of a modified functional appliance on obstructive sleep apnea. Am J Orthod Dentofac Orthop. 94:384-392, 1988
32. O'Sullivan RA, Hillman DR, Mateljan R, et al: Mandibular advancement splint: An appliance to treat snoring and obstructive sleep apnea. Am J Respir Crit Care Med 151:194-198, 1995
33. Viviano JS: Acoustic reflection: Review and clinical applications for sleep-disordered breathing (review). Sleep Breath 6:129-149, 2002
34. Mah J, Hatcher D: Three-dimensional craniofacial imaging. Am J Orthod Dentofac Orthop. 126:308-309, 2004
35. Hashimoto K, Kawashima S, Araki M, et al: Comparison of image performance between cone-beam computed tomography for dental use and four-row multidetector helical CT. J Oral Sci 48:27-34, 2006
36. Ludlow JB, Davies-Ludlow LE, Brooks SL: Dosimetry of two extraoral direct digital imaging devices: NewTom cone beam CT and Orthophos plus DS panoramic unit. Dentomaxillofac Radiolol. 32:229-234, 2003
37. Schulze D, Heiland M, Thurmann H, et al: Radiation exposure during midfacial imaging using 4- and 16-slice computed tomography, cone beam computed tomography systems and conventional radiography. Dentomaxillofac Radiol 33:83-86, 2004
38. Farman AG, Scarfe WC, Sukovic P: Clinical applications of cone-beam computed tomography in dental practice. J Can Dent Assoc 72:75-80, 2006
39. Hilgers ML, Scarfe WC, Scheetz JP, et al: Accuracy of linear temporomandibular joint measurements with cone beam computed tomography and digital cephalometric radiography. Am J Orthod Dentofac Orthop. 128: 803-811, 2005

40. Cevidanes LH, Styner MA, Proffit WR: Image analysis and superimposition of 3-dimensional cone-beam computed tomography models. Am J Orthod Dentofac Orthop. 129:611-618, 2006
41. Ogawa T, Enciso R, Memon A, et al: Evaluation of 3D airway imaging of obstructive sleep apnea with cone-beam computed tomography. Stud Health Technol Inform 111:365-368, 2005
42. 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 9:1801-1809, 1996
43. Shi H, Scarfe WC, Farman AG: Upper airway segmentation and dimensions estimation from cone-beam CT image datasets. Int J Cars. 1:177-186, 2006
44. Peh WC, Ip MS, Chu FS, et al: Computed tomographic cephalometric analysis of Chinese patients with obstructive sleep apnoea. Australas Radiol 44:417-423, 2000
45. Vigg A, Vigg A, Vigg A: Obstructive sleep apnea in a referral population in India. Sleep Breath 7:177-184, 2003
46. Zhao X, Liu Y, Gao Y: Three-dimensional upper-airway changes associated with various amounts of mandibular advancement in awake apnea patients. AJODO. 20008:661-668
47. Kyung SH, Park YC, Pae EK: Obstructive sleep apnea patients with the oral appliance experience pharyngeal size and shape changes in three dimension. Angle Orthod 75:15-22, 2005
48. Sutthipraporn P, Tanimoto K, Ohtsuka M, et al: Positional changes of oropharyngeal structures due to gravity in the upright and supine positions. Dentomaxillofac Radiol 37:130-135, 2008
49. 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 9:240-243, 2006
50. Ogawa T, Enciso R, Memon A, et al: Evaluation of 3D airway imaging of obstructive sleep apnea with cone-beam computed tomography. Stud Health Technol Inform 111:365-368, 2005