Obstructive sleep apnea-hypopnea syndrome: Clinical applications of cone beam CT

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Sleep-Disordered Breathing (SDB) is a group of disorders characterized by disturbances in the normal respiratory pattern during sleep. Those are related to increased upper airway resistance and include snoring; upper airway resistance syndrome; and obstructive sleep apnea-hypopnea syndrome (OSAHS). OSAHS is the most common disorder and characterized by snoring, repetitive total or partial collapse of the pharyngeal airway during sleep terminated by oxygen desaturation or EEG arousal before ventilation resumes. Airway obstruction is manifested by a reduction in airflow, termed *hypopnea,* or a complete cessation of airflow, termed *apnea*, despite ongoing inspiratory effort. Hypopnea is defined in adults as a 10-second event where despite continued breathing, ventilation during sleep is reduced by at least 50% from baseline. Apnea is total cessation of airflow for at least 10 seconds. Apnea can be obstructive or due to failure in control centrally.

The early effects of repeated disrupted sleep are waking somnolence, impaired mental function, delayed reaction time and difficulty maintaining concentration. Long term effects of recurrent sleep arousal in association with intermittent hypoxia and hypercapnia have been associated with cardiovascular diseases including high blood pressure, depression, irritability, learning and memory difficulties, weight gain, impotence and headaches. In addition, there is evolving evidence that SDB may contribute to insulin resistance and other components of the metabolic syndrome. Population-based studies suggest that OSAHS is a relatively common disorder. In those aged 30 to 60 years, 24% of men and 9% of women are reported to have abnormal AHI indices.[1] The prevalence of symptomatic OSAHS is conservatively estimated to be 1% to 2% in middle-aged men and approximately 0.5% to 1%, in middle-aged women.[2]

Sleep apnea is not always easily diagnosed as symptoms might not be evident, either to the patient or others. Factors contributing to the presence and severity of SDB are multifactorial and include reduced airway anatomy, nasal blockage, the presence and distribution of body fat and muscle tone. Being even moderately overweight is the most common risk factor, especially a body mass index or BMI (weight in kilograms divided by height in meters squared) greater than 28. Other risk factors include collar size of snoring patients (greater than 17 inches for men, 15 inches for women), physical nasal obstruction, underactive thyroid and excessive fat around the neck area.

Diagnosis of OSAHS is made through a sleep study that is generally performed at a sleep laboratory. Various physiologic functions related to sleep are recorded using a polysomnogram, a compilation of tests including an electroencephalogram, electrooculogram, nasal pressure and flow, abdominal and chest excursions, electromyogram and pulse oximetry. The severity of the OSAHS is indexed using the Apnea/Hypopnea Index (AHI) calculated by adding the total number of apneas and hypopneas and dividing by the number of hours of observed sleep. Another metric is the Respiratory Disturbance Index (RDI) which also includes other respiratory disturbances such as respiratory event related arousals. Severity of OSAHS is generally defined using AHI or RDI. An AHI or RDI of 5-15 is considered mild; 16-25 moderate and; greater than 26 severe. A second study is usually performed while using a continuous positive airway pressure (CPAP) ventilation machine as therapy to prevent obstructive events)(Figure 1).

Therapies of OSAHS are primarily directed at pneumatically splinting the airway open or secondarily adjusting the airway in making it less apt to collapse. CPAP is the primary and most effective therapy initially offered for treatment of OSAHS.[3] It is usually provided in association with behavioral changes such as avoiding alcohol, smoking and medicines that cause sleepiness; and altered sleep posture or nutritional and dietary counseling to reduce weight. Unfortunately, CPAP is a cumbersome modality and hence approximately 25-50% of patients with OSAHS will either refuse the offer of CPAP therapy, or will not tolerate it.[4]

Secondary therapy for patients suffering from OSAHS who cannot tolerate CPAP is directed towards physically widening the pharyngeal airway. This can be performed reversibly by the use of removable oral appliances (OA) or permanently by surgery. OAs are categorized by the method used to improve the patency of the airway space. The most common OA appliances are mandibular advancement devices (MAD), which protrude the mandible anteriorly to pull the muscles of the oropharynx forward, and tongue retaining devices (TRD) that aim at holding the tongue in a protrusive position. These devices can be "titrated" to best fit the patient for comfort and efficiency (Figure 2). However, OA appliances are therapeutic only if selected appropriately for the specific site(s) of upper airway obstruction, which varies between individuals.[5,6] For patients with severe AHI and co-morbidities (e.g. significant bradycardia, severe hypercarbia, cor pulmonale and extreme hypersomnolence) on whom CPAP is not a viable option, surgery is usually the most appropriate alternative. Surgery options include upper airway soft tissue correction to enlarge the pharyngeal space and prevent airway collapse (e.g. removal of tonsils or adenoids, radiofrequency ablation of the tongue or soft palate (somnoplasty), uvulopalatopharyngoplasty and laser-assisted uvulopalatopharyngoplasty, and reduction in tongue size or movement of the mandible anteriorly (e.g. genioglossal advancement with hypoid myotomy, bimaxillary advancement, or maxillomandibular advancement). Procedures to improve upper airway patency are successful in certain subsets of patients, but some do not achieve desired relief.[7]

If secondary treatments are necessary, the site of the oropharyngeal obstruction must be identified such that appropriate therapy can be applied. Numerous supplemental tests can be performed to determine the site of reduction in airway caliber including fiberoptic nasopharyngoscopy with the Müller maneuver, sleep endoscopy, fluoroscopy, rhinomanometry and diagnostic imaging studies. The specific role of diagnostic imaging is to evaluate the

Figure 1. Example of CPAP device with patient wearing full face mask in sleep laboratory facility.

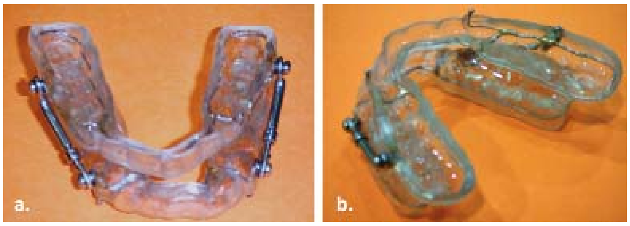

Figure 2. Example of Herbst MAD device allowing titratable mandibular advancement using a bilateral piston system comprised of rods and sleeves from the anterior (a) and posterior (b) views.

Figure 3. Patient seated in CBCT machine. For OSAHS patients scan technique is modified such that the chin support is removed and the patient is allowed to adopt habitual head position.

morphology of the upper airway, determine the site and degree of pharyngeal obstruction, identify potential causative conditions (Table 1) and anatomic characteristics that may be predictive of therapeutic efficacy. Lateral cephalometric radiography (LCR) has been long been used in clinical practice. Numerous authors have reported a variety of craniofacial anatomical abnormalities associated with OSAHS on LCR including reduced retroglossal airway linear dimensions, a long, bulky soft palate, an inferiorly placed hyoid bone and mandibular deficiency.[8-13] Computed tomography and magnetic resonance imaging have been used in the research environment to provide three-dimensional metrics of the naso-, oro- and hypo-pharyngeal regions such as minimal cross-sectional area, minimal antero-posterior/lateral dimensions and airway volumes. The results from these studies indicate that the upper airway is significantly narrowed among patients with OSA compared to controls, but that the site of narrowing varies among OSA patients.

Cone beam computed tomography (CBCT) scanners have been available for craniofacial imaging since 2001 in the United States (Figure 3). The CBCT has a cone- or pyramidal 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. In a single, rapid (5-20 sec) rotation, precise, accurate high resolution volumetric data is acquired. Reconstruction and subsequent viewing of the digital data is accomplished on a personal computer. Standard viewing layouts include the display of coronal, sagittal and axial data sets concurrently. A main advantage of using CBCT to image the oropharynx is the low dosage of radiation relative to conventional spiral computed tomography. Ludlow, *et al* reported large-field of view CBCT effective dose (E_{2007}) varied from 68 to 1,073µSv with most in the 100-200µSv range as compared to multi detector CT (range; 534-860µSv).[14] 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. The spatial resolution is also much greater than conventional CT, with a voxel resolution between 0.076 and 0.4 mm.

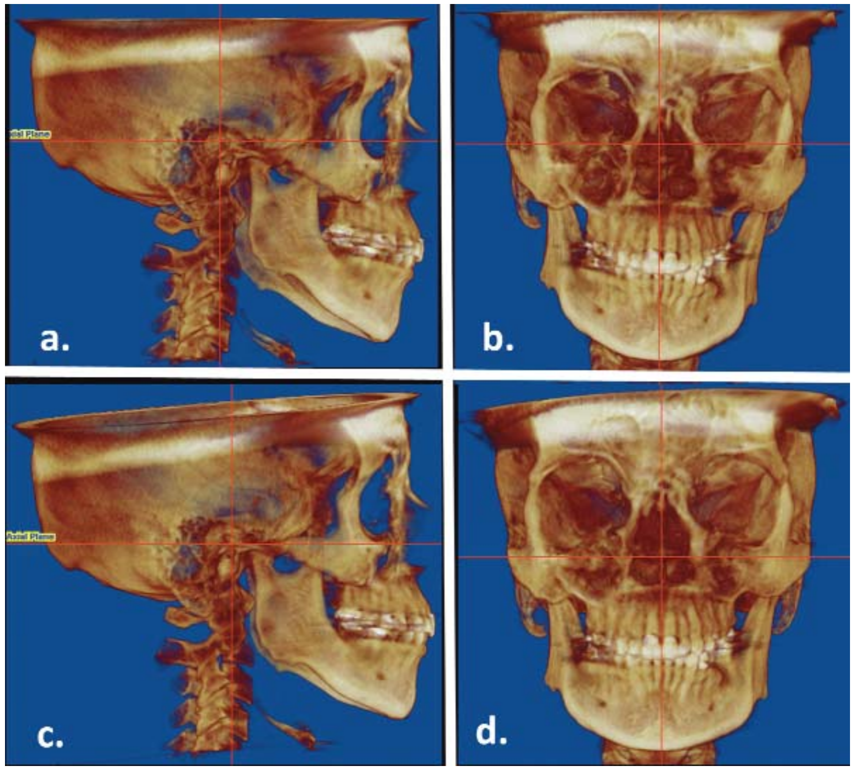

Figure 4. Reorientation of volumetric data to adjust patient head position during scan to anthropomorphic standard reference planes. Lateral (a) and frontal (b) volume rendering show that the patient was originally scanned with the head raised and tilted towards the right. Comparable lateral (c) and frontal (d) volumetric rendering with adjusted data to position Frankfort horizontal (FH) parallel to floor and mid-sagittal plane perpendicular to FH.

Table 1. Anatomic Abnormalities associated with OSAHS

Region	Structure	Condition
Nasal Cavity	Turbinate	Hypertrophy, polyps, mucosal thickening, hyper-secretion
	Septae	Deviated
Maxillofacial/Skeletal	Mandible	Relative hypoplasia, deficiency, cross-bite, mandibular tori
	Maxilla	Relative hypoplasia, deficiency, cross-bite
	Hyoid	Caudal displacement relative of the cervical spine and mandible
Upper Airway	Soft palate	Excessive length, low lying position
	Tongue	Macroglossia, short length, loss of muscle tone
	Nasopharynx	Hypertrophic adenoids, fatty lumen
	Oropharynx	Hypertrophic tonsils, lumen thickening, fat pad accumulation
	Hypopharynx	Lumen thickening
	Larynx	Abnormal vocal cord anatomy, paralysis of vocal cords

CBCT has particular application in the diagnosis and assessment of therapy in OSAHS patients and has the potential to eliminate the need for additional static imaging. The resulting volume of digital data can be manipulated to allow the clinician three-dimensional images that can be re-oriented in all three axes to correspond to anthropometric reference planes (Figure 4) and can be selectively contrasted, emphasized or reduced to visualize certain anatomical structures such as the craniofacial skeleton or airway (Figure 5). Data can exported as a DICOM (Digital Imaging and Communications in Medicine) format data set and imported into proprietary orthodontic image and analysis programs (e.g. InVivoDental by Anatomage or Dolphin 3D) which have specific modules capable of demonstrating and recording the airway and its surrounding structures. These programs offer practitioners opportunities to interact with the data and allow visualization of both untreated obstruction tendencies and potentially of changes in the airway by treatment modality. In this way, it may help identify those subsets of patients who may or may not benefit from a choice of treatment modalities. CBCT has been applied to describe significant differences in total airway volume and the antero-posterior dimension of the oropharyngeal airway between OSA and gender-matched controls, differences in airway shape between OSA (concave or elliptical) and non-OSA (concave, round, or square).[15,16] Recent research in the authors' clinic applied CBCT imaging to patients with and without OSA to determine a quantifiable relationship between airway patency and mandibular advancement using OA.[17] It was determined that custom titrated MAD devices repositioned the mandible on average horizontally 4mm and vertically 8mm and resulted in an average oropharyngeal volume increase of ~2800mm^3. It was possible to predict the airway volume gained, the amount of cross-sectional area gained at the narrowest 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.

In collaboration with colleagues of the University of Louisville Multidisciplinary Sleep Team, a specific CBCT imaging protocol has been developed that has proven particularly useful in the assessment of soft and hard tissue contributors to mechanical obstruction in patients with OSAHS. This involves:

a. Sequential axial and coronal images (1mm thickness/3mm interval). These conventional orthogonal images enable visualization of potential nasal obstructions (Figure 6) and anatomic anomalies, palatal and mandibular structures and provide an overview of the max-

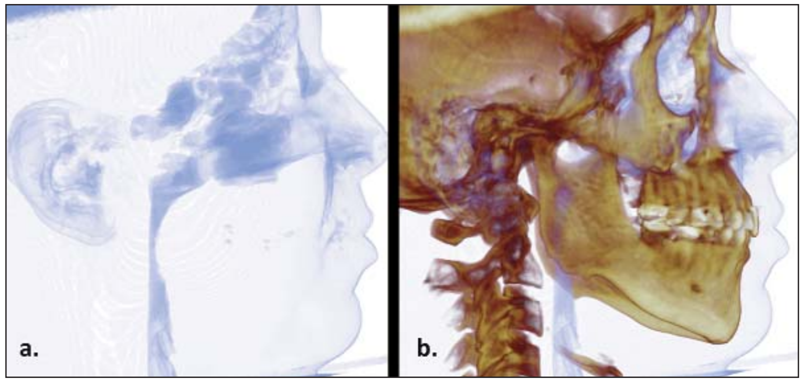

Figure 5. 3D volumetric image of the right side of an OSA patient demonstrating airway only (a) and with maxillofacial skeleton overlay (b). This is performed by selective segmentation procedures (Images created using Dolphin 3D V.11).

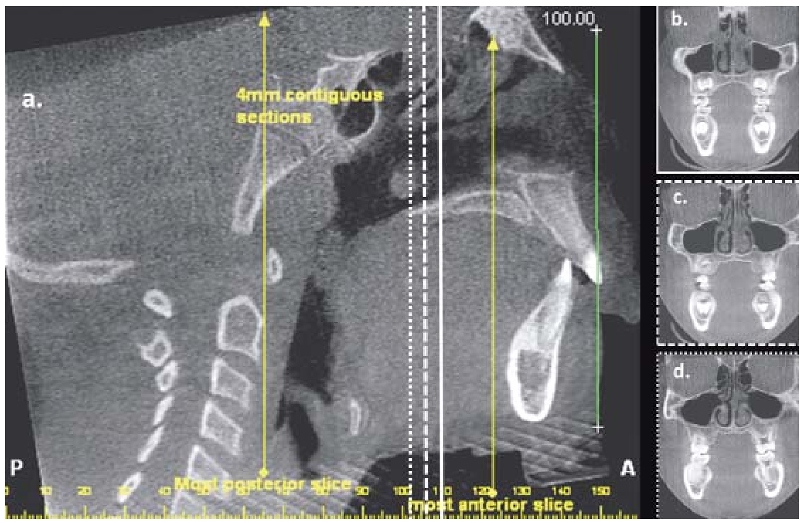

Figure 6. Reference sagittal orthogonal image at 0.4mm (a) of pediatric OSAHS patient demonstrating of coronal scans at progressively posterior locations. Note the generalized mucosal thickening of the turbinates of the right nasal fossa and marked reduction and partial occlusion in nasal cavity space.

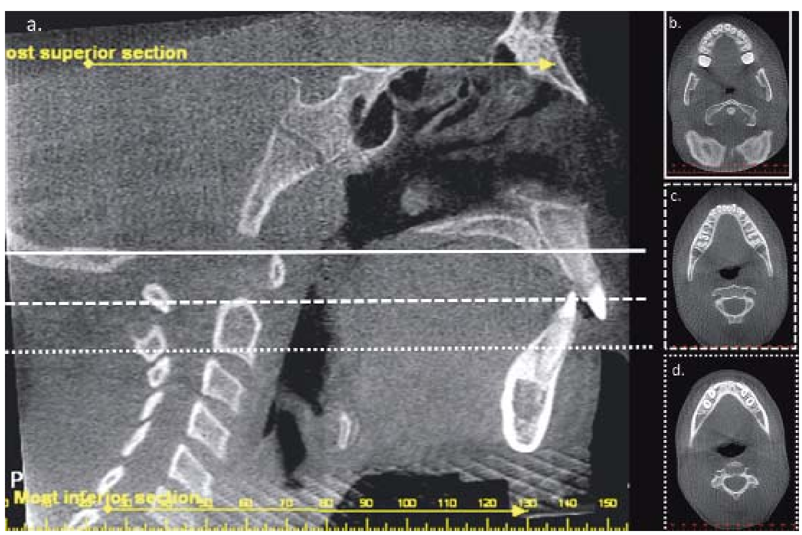

Figure 7. Reference sagittal CBCT image (a) and corresponding 0.4 mm axial cross sectional images of the upper (b) and lower retro-palatal (c), and retroglossal (d) airway.

imum and minimal (Figure 7) caliber of the airway space. Because of the relatively poor contrast resolution of CBCT imaging, potential specific soft tissue factors (e.g. muscular hypertrophy, redundant fat pads) are unable to be visualized.

b. Ray-sum and maximum intensity projection simulated panoramic, lateral cephalometric, postero-anterio and submentovertex images. Specific volumetric rendering of the CBCT data can be performed to produce conventional craniofacial skull images. These projections demonstrate global deficiencies of the maxillofacial skeleton in all three orthogonal planes that may contribute to the obstruction (e.g. retrognathia, maxillary cross-bite, mandibular asymmetry, palatal soft tissue) and allow visualization and measurement of parameters that have been reported to be associated with OSAHS (Figure 8).

c. Regionally corrected temporomandibular joint images. Visualization of the TMJ articulation provides information of the relative stability of morphology of this determinant of mandibular position. Active degenerative joint disease either osteoarthritic, autoimmune or idiopathic in nature can reduce mandibular ramal length resulting in an anterior open bite and produce substantial inferior and posterior positional changes in the location of the associated soft tissue (Figure 9).

d. Three dimensional analysis of upper airway anatomy. Concomitant segmentation of hard tissue maxillofacial skeleton, airway space and facial soft tissue surfaces from 3D CBCT data provides dynamic visualization of the interrelationship of these structures on airway obstruction. This facilitates identification and classification of the level of the obstruction (Table 2) and quantitative analysis of linear, area and volumetric parameters (Figures 10 and 11). Images also provide superior visualization of airway shape and caliber as well as soft tissue elements such as the epiglottis and soft palate.[18]

e. Comparison of pre- and post-therapy effects. Volumetric superimposition of CBCT datasets can be performed to produce colour-contrasted blended views of the mechanical and resultant airway changes as a result of specific therapies (Figure 12).

In addition to the imaging protocol presented above, it is possible to generate video frame of reference "fly through" reconstructions (e.g. Osiris imaging Software. V3.1, University Hospital of

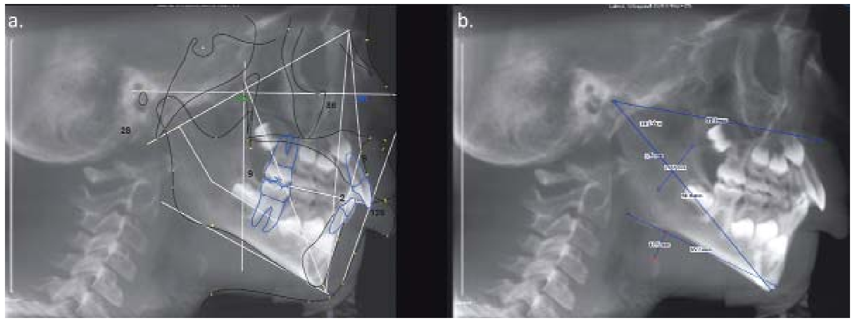

Figure 8. Ray sum simulated lateral cephalometric images demonstrating tracing of soft (a) and hard tissue (b) measurements using specific orthodontic analysis software (Images created using Dolphin 3D V.11).

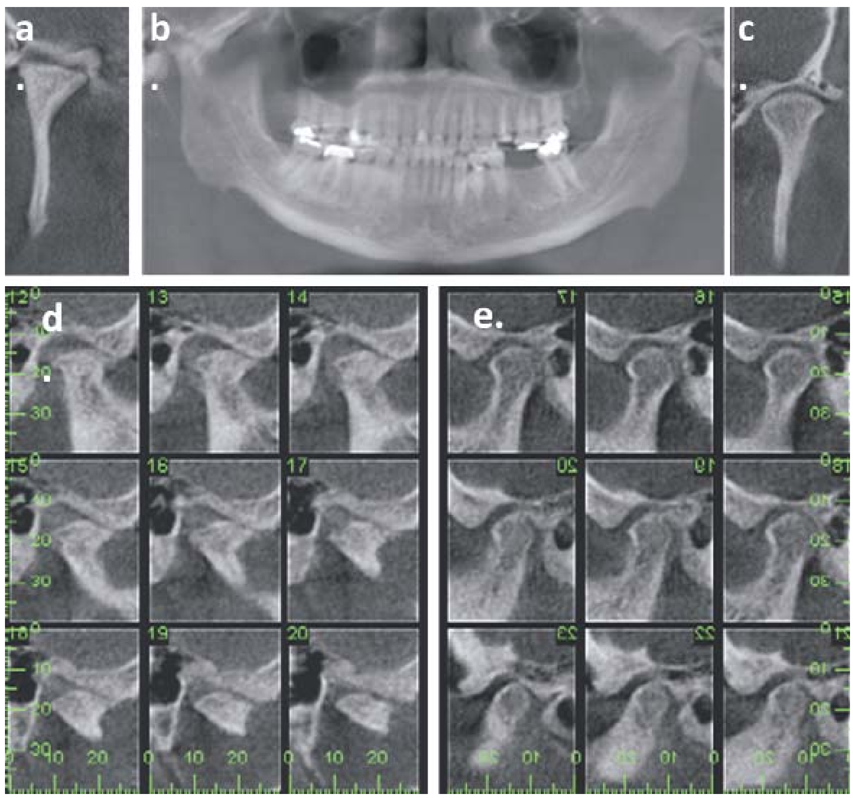

Figure 9. Temporomandibular image protocol demonstrating ray sum reformatted panoramic (b), 5mm thick sagittal (a and b) and sequential 1mm cross-sectional right (d) and left (e) images. Note the marked osteoarthritic degenerative joint disease of the right TMJ articulation in this OSAHS patient contributing to reduction in mandibular ramal length and asymmetry of the mandible.

Table 2. Classification of Velohypopharyneal Airway Obstruction[18]

Type	Sub-Type	Description
I		Retropalatal or velopharyngeal
II		Combined retropalatal and hypopharyngeal/retroglossal (base of tongue)
	IIa	Predominantly retropalatal
	IIb	Predominantly retroglossal
III		Isolated retroglossal or hypopharyngeal (base of tongue)

Geneva, Switzerland and OnDemand3D, CyberMed Inc., Seoul, Korea). While images produced by this technique demonstrate the static airway, this non-invasive approach serves as a potential method to create virtual fiberoptic nasopharyngoscopy visualizations (Figure 13).

OSAHS is an important public health concern because of under diagnosis and associated cardiovascular consequences. As upper airway constriction is an important contributing factor, CBCT technology provides a rapid low dose 3D imaging modality capable of providing simultaneous hard and soft tissue images facilitating visualization of upper airway characteristics. This, together with clinical information, may provide a valuable assessment tool of patients with OSAHS and assist in treatment modality choice based on predictable outcomes.

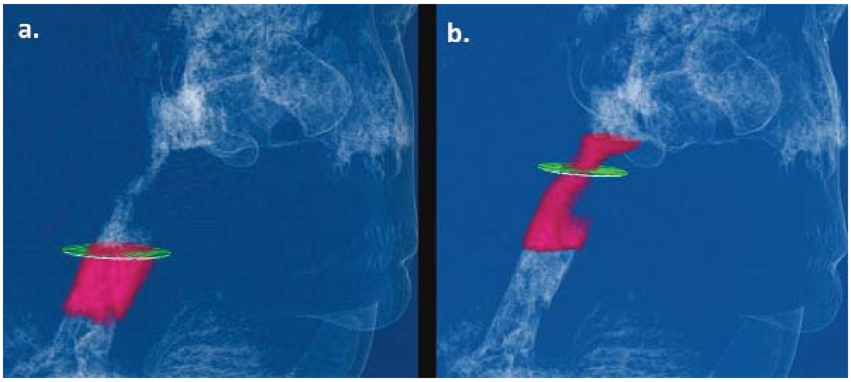

Figure 10. Lateral oblique 3D images of the segmented airway of an OSAHS patient after application of software algorithm to identify the volume of specific portions of the oro-pharyngeal airway. Retroglossal (a) and retropalatal (b) volumes are identified by a solid - the level of the minimum cross-sectional airway within the segment is identified as a radial disc (Images created using Dolphin 3D V.11).

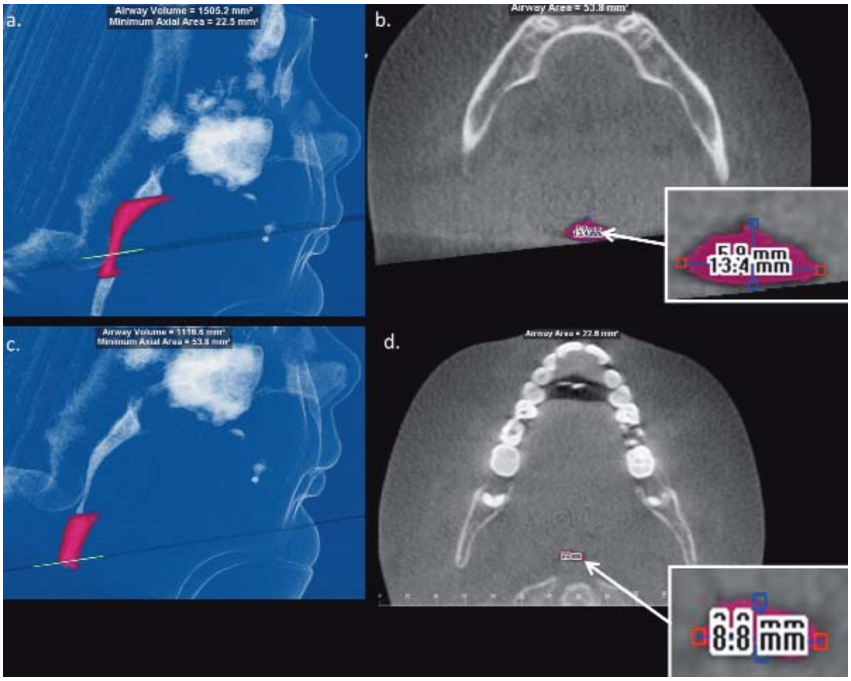

Figure 11. Lateral 3D images of the segmented airway of another OSAHS patient after demonstrating the specific volumes of retroglossal (a) and retropalatal (b) airway space. The software algorithm identifies and displays the axial images at which the minimum cross-sectional area is present (c and d) and allows for measurement of antero-posterior and transverse dimensions (Images created using Dolphin 3D V.11).

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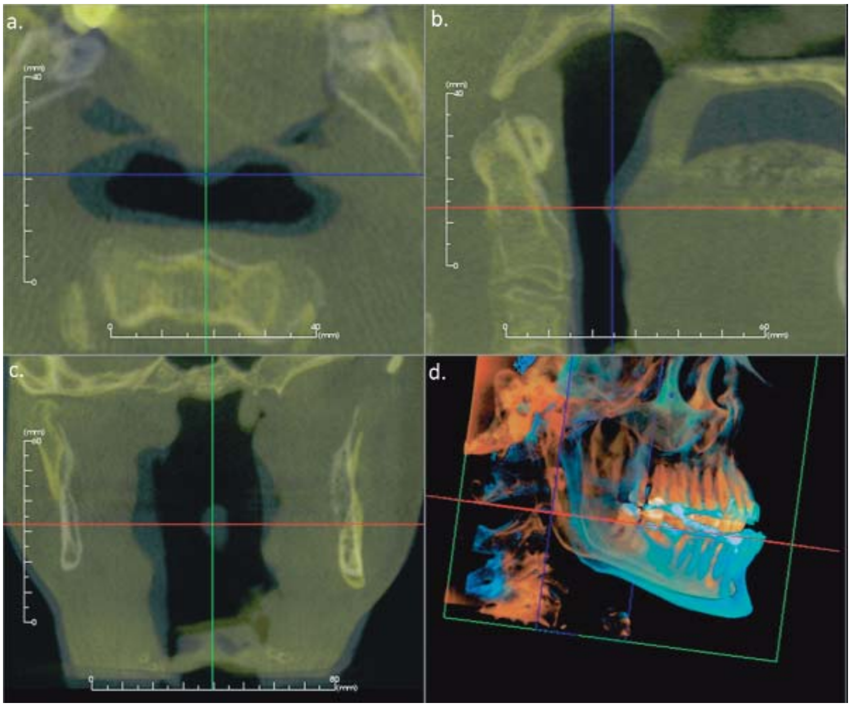

Figure 12. Superimposition of CBCT data sets using InVivoDental software (Anatomage) highlighting differences between CBCT scans. Axial (a), sagittal (b) and coronal (c) views of original (grey) and post-therapy images (yellow) using skeletal fiducial points to demonstrate improvement in airway patency following placement of a mandibular advancement device.

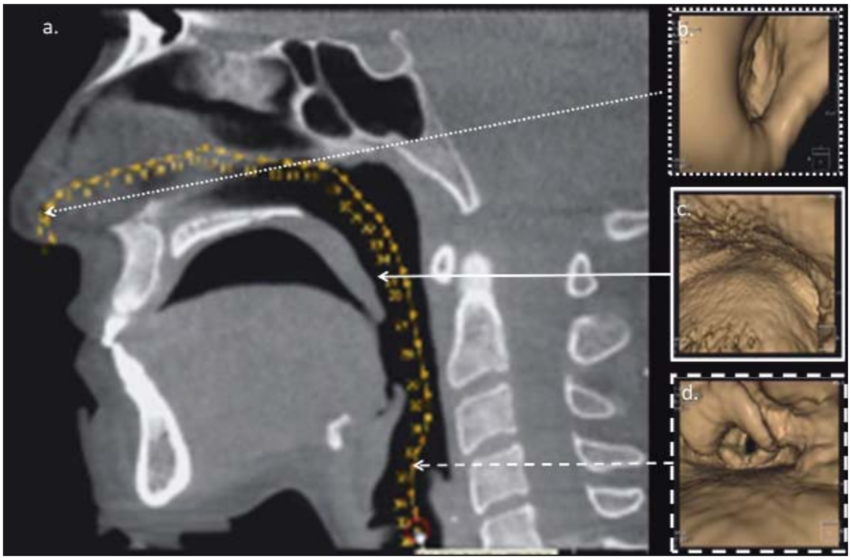

Figure 13. Initial sagittal reference image demonstrating "fly-through" path (a) and sequential screen capture of "Virtual" nasopharyngoscopy video at the level of the nares (b), velo- (c) and, hypo-pharyngeal (d) regions.