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COMPLIANCE MEASUREMENTS OF THE UPPER AIRWAY IN PEDIATRIC DOWN SYNDROME SLEEP APNEA PATIENTS

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Abstract

Compliance of soft tissue and muscle supporting the upper airway are two of several factors contributing to pharyngeal airway collapse. We present a novel, minimally invasive method of estimating regional variations in pharyngeal elasticity. Magnetic resonance images for pediatric sleep apnea patients with Down syndrome (9.5 ± 4.3 years (mean age $\pm$ standard deviation)) were analyzed to segment airways corresponding to baseline (no mask pressure) and two positive pressures. A three dimensional map was created to evaluate axial and circumferential variation in radial displacements of the airway, dilated by the positive pressures. The displacements were then normalized with respect to the appropriate transmural pressure and radius of an equivalent circle to obtain a measure of airway compliance. The resulting elasticity maps indicated the least and most compliant regions of the pharynx. Airway stiffness of the most compliant region (403 ± 204 (mean $\pm$ standard deviation) Pa) decreased with severity of OSA. The non-linear response of the airway wall to CPAP was patient specific and varied between anatomical locations. We identified two distinct elasticity phenotypes. Patient phenotyping based on airway elasticity can potentially assist clinical practitioners in decision making on the treatments needed to improve airway patency.

Keywords

sleep apnea; CPAP; radial displacements; airway elasticity; non-linearity; anisotropy

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1. Introduction

Obstructive sleep apnea (OSA) is an airway disorder that is prevalent in almost 1–10 % of children⁸ and in about 2–4 % of adult population⁴⁰. It is characterized by intermittent pharyngeal airway collapse during sleep, due to loss of muscle tone surrounding the airway and anatomical abnormalities⁴. Pharyngeal airway collapse is likely to occur in OSA patients, when the forces in the soft tissue that cause airway narrowing exceed the ones tending to dilate the airway³. The degree of physiologic relaxation of muscle and soft tissue determines the severity of the disorder. Clinical diagnosis of OSA includes polysomnography⁷, acoustic pharyngometry and rhinometry^{5, 17, 21}, tracheal breath sound analysis^{25, 39} and imaging methods such as cephalometric measurement and Magnetic Resonance (MR) images¹. Acoustic markers such as an increase in the first formant snoring frequency resulting from reduction in airway area have also been proposed to identify sleep apnea²⁸.

Factors influencing pharyngeal airway collapse in pediatric OSA patients with Down syndrome (DS) include obesity, hypotonia, midface hypoplasia, macroglossia, large tonsils and adenoids. Reduced airway muscular tone associated with sedation and supine position is more evident in children with DS^{9, 35}. Medical treatment options include surgeries such as Tonsillectomy & Adenoidectomy (T&A), mandibular advancement, glossectomy and non-surgical methods such as Continuous Positive Airway Pressure (CPAP) and weight loss¹. The success rates of these aforementioned procedures is not ideal³⁵ thereby emphasizing the need to improve the understanding of upper airway physiology and provide better OSA treatment.

Elastic properties of tissue surrounding the upper airway have been determined by mechanical testing of excised cadaver specimens¹⁹. Elastography, which involves either ultrasound (US) or MR, is capable of quantifying small tissue displacements (1 μm or less)¹¹. Bilston and Gandevia reported viscoelastic properties of the tongue and soft palate using in-vivo MR elastography³. Airway wall stiffness has been characterized previously using the Starling resistor or 'tube law' model^{6, 10}. Localized estimates of change in airway elasticity at two arbitrary locations in the velopharynx and oropharynx have been described using patient-specific compliance curves^{13, 14}. A major limitation of the tube law model is its inability to account for variations in airway elasticity along its periphery.

The objective of the current study is to describe a novel method to estimate patient specific elasticity of the upper airway using medical image analysis. The method involves upper airway segmentation of MR images, estimating radial displacements of the airway wall (interface between the airway lumen and soft tissue) in discrete angular sectors, and normalizing the computed displacements by the appropriate transmural pressure difference and radius of equivalent circle³⁷. The novelty of the proposed method is that it is non-invasive, requires less patient interaction, and its ability to determine the least and most compliant regions of the upper airway. It can also predict the nature of non-linearity in the airway wall response to different pressures. In our study, we test the hypothesis that the severity of OSA is greater for subjects with elastic upper airways.

2. Methods

2.1 MR Imaging and Airway Segmentation

Ten pediatric OSA patients with DS were used to demonstrate the method to evaluate the elasticity of the upper airway wall using medical image analysis. The patients were anesthetized using dexmedetomidine, a sedative shown to parallel natural sleep²⁷. Dexmedetomidine has a less effect on airway tone and collapsibility compared to propofol²² and is more favorable for dynamic MR imaging of the pharynx. The sedative dose was subject specific and dependent on the patient's BMI¹². Time was allocated following infusion of the sedative to allow for steady-state conditions before imaging. The level of anesthesia was assessed using the University of Michigan Sedation Scale (UMSS)²³. The patient's head and neck were placed in a vascular coil and the subject was transferred to the MRI scanner, once adequate level of sedation was attained (UMSS target score of 2 for all subjects). Lateral motion of the patient's head was minimized by securing the vascular coil to the subject's head using adhesive tape²³. MR imaging was performed using a 1.5-THDxt scanner (software version 16; General Electric) in supine position. A 3-dimensional (3D) fast spin echo with proton density weighting (CUBE) with end inspiratory respiratory triggering was the imaging sequence adopted in this study. The adopted imaging sequence ensured that images were acquired when the airway was open. Imaging parameters included slice interval 0.8 mm; slice thickness 1.6mm; acquisition matrix 256 by 256 and echotrain length 64. Positive airway pressures (CPAP) were applied using a modified face mask approved by the Institutional Review Board (IRB), to maintain airway patency. MR static images were taken at baseline (zero mask pressure) and two positive pressures (CPAP1, CPAP2) during the peak expiratory phase of the breathing cycle. It should be noted that airway size and collapsibility influenced the choice of CPAP2. A higher mask pressure was needed to maintain the patency of narrow or extremely floppy airways¹⁵. CPAP1 was a value of mask pressure greater than zero and lower than CPAP2. Collapsed baseline airways, subjects with open oral airways, patients who breathed paradoxically, moved or awoke during imaging, and low quality scans, were excluded from this study. Patients included in our study breathed with minor phase changes in abdominal and thoracic motion. On the other hand, patients who breathed paradoxically had large phase shifts in thoracic and abdominal movement signals. Furthermore, patient arousal was considered to be clinically significant, only when it followed an apneic event. Besides, patients who exhibited movement of the spine and mandible in excess of 2 mm were excluded from this study. The analysis was limited to subjects whose airway caliber changes resulted from soft tissue compression. The severity of OSA is typically quantified using the Apnea Hypopnea Index (AHI)³¹ and the value of transmural pressure at which the pharyngeal airway collapses completely (P_{crit}). Patient demographics, AHI, P_{crit} and the positive pressures at which the scans were obtained are summarized in Table 1. In order to estimate P_{crit} , the mask pressure was gradually decreased, approaching conditions of no flow. The linear portion of the curve relating the negative pressure to flow rate was extrapolated to zero to evaluate the airway closing pressure^{29, 36}.

Anatomical features in medical images can be identified using one of the following segmentation techniques: Thresholding, Region-Growing, Classifiers, Clustering, Markov

Random Field Models, Artificial Neural Networks, Deformable Models or Atlas Guided approach³⁰. Geometric quantities including airway diameter (anterior-posterior and lateral walls), area and soft-tissue volume have been evaluated for patients suffering from sleep-disordered breathing using commercial segmentation software³⁸, that employ variants of the thresholding method or by proprietary codes based on region-growing and fuzzy connectedness²⁰. Boundaries of the baseline, CPAP1 and CPAP2 airways were identified in MRI scans using an in-house MATLAB based thresholding algorithm. The intensity values in an image were mapped to new values such that 1% of the data were saturated at low and high intensities and the output image was cropped to the region of interest. A normalized threshold level of around 0.05 was used to convert the grayscale image to a binary image. The threshold value varied only slightly between images and enabled identification of the airway boundary without addition of irrelevant data. Pixels in the output binary image with luminance greater than the threshold value were replaced with the value 1 and the remaining pixels were assigned a value of 0, to identify the airway boundary.

Airway shapes were segmented using axial scans from the hard palate to base of tongue. Appropriate transformation equations were used to convert pixel values to their corresponding Cartesian co-ordinates. Variation in airway shapes along the length of the pharynx was obtained by repeating the process for each axial image slice that is part of the upper airway. Spurious values of airway profile changes may result from variation in the angulation of the airway with respect to image slices. The airway area and co-ordinates of the airway outlines were thereby corrected for angulation using the slice orientation. In order to illustrate the efficiency of the segmentation routine, we employed a modified Shepp-Logan phantom³⁴. The absolute error in the computed areas of the ellipses in the phantom was found to vary from 0.2 to 6%. The error was higher for the smaller sized ellipses. The airways analyzed in our study were similar in size to the large and medium sized elliptical profiles and the largest error in the calculation of their areas was approximately 2 percent. The segmentation algorithm consistently reproduced the airway outlines when the analysis was repeated on the same subject and the precision error in the estimation of airway co-ordinates was less than 1 percent. We also employed the segmentation algorithm to identify boundaries of the patient's head and mandible for baseline, CPAP1 and CPAP2 configurations. We superposed the outlines to verify that lateral displacement of the mandible and change in head and neck position was negligible between pressures.

2.2 Quantifying Airway Wall Motion

In order to compute the circumferential variation in the elasticity of the airway wall, the airway boundaries corresponding to the baseline (zero pressure) and dilated (CPAP level 1, 2) configurations are plotted in a polar co-ordinate system. In order to achieve this, we identified a suitable reference point based on the shape of the baseline airway outline (Fig. 1a, b, c, d). The first method (mean) involves averaging the maximum co-ordinates in the anterior-posterior (Y) and lateral (X) directions.

$$\begin{aligned} X_p &= 0.5 * (\max(X) + \min(X)) \\ Y_p &= 0.5 * (\max(Y) + \min(Y)) \end{aligned} \quad (1)$$

An alternative method is to identify the centroid of the airway, approximated as an n-sided, non-self-intersecting closed polygon.

$$\begin{aligned} X_p &= \frac{1}{6A_p} \sum_{i=0}^{n-1} (X_i + X_{i+1})(X_i Y_{i+1} - X_{i+1} Y_i) \\ Y_p &= \frac{1}{6A_p} \sum_{i=0}^{n-1} (Y_i + Y_{i+1})(X_i Y_{i+1} - X_{i+1} Y_i) \quad (2) \\ A_p &= \frac{1}{2} \sum_{i=0}^{n-1} (X_i Y_{i+1} - X_{i+1} Y_i) \end{aligned}$$

where A_p is the area of the polygon. As can be seen from Figure 1a, b and c, the first two methods are suitable for airways with a square, figure-8 or a 'T' shape. However for a horseshoe shape (Fig. 1d), the reference point computed using the aforementioned methods lies outside the airway outline. A third method estimates the center of the maximum inscribed circle and is suitable for most airway shapes. The fourth method involves identifying the X (or Y) coordinate based on the first method and computing the Y (or X) co-ordinate by evaluating the average of intersections between the airway outline and a constant X (or Y) line. For the purpose of the current study, we employed method 1 (average) and method 4 (average of intersections) to identify the reference point (X_p, Y_p). The reference point was then used to transfer the global Cartesian co-ordinates to local polar co-ordinates (R, θ) at every axial location along the airway length.

Figure 1e shows a polar plot of the baseline (blue) and airway shapes following deformation (CPAP level 1 - red, CPAP level 2 - black). We divide the airway boundary into discrete angular sectors subtending an angle $d\theta$ as shown in Figure 1e. The average radial distance within a sector with 'P' pixels or points is computed for the reference ($R_{o(avg)}$) or deformed configuration ($R_{d(avg)}$). It should be noted that the reference configuration can refer to either the baseline airway or the airway corresponding to CPAP level 1. The absolute radial displacement corresponding to each sector can be defined as,

$$\delta R = |R_{d(avg)} - R_{o(avg)}| \quad (3)$$

The circumferential variation in radial displacements over the entire length of the airway is obtained by repeating the process outlined earlier at each axial location. The airway wall was discretized into 24 angular sectors and the procedure was repeated for the three patients analyzed in this study, for CPAP level 1 and 2. The resulting three-dimensional color map indicating the peripheral and axial variations in displacement is given in Figure 1f.

A cutting plane is now chosen on the posterior wall to unfold the 3D map and project it onto a 2D plane (Fig. 2a). The projected map enhances visual clarity of the most relevant regions of interest, namely the anterior and lateral walls. The circumferential locations namely anterior (A), right (R), posterior (P) and left (L) are labelled on the abscissa in Fig. 2a. These maps account for the airway wall displacements in three significant anatomical regions (Fig. 2b), namely the hard palate to soft palate (RP - retropalatal airway), soft palate to the tip of epiglottis (RG1 - retroglossal airway) and tip of epiglottis to base of tongue (RG2 -

retroglottal airway). Three sets of displacement maps (baseline to CPAP level 1, baseline to CPAP level 2 and CPAP level 1 to level 2) are generated for the ten patients included in our study. Displacement maps corresponding to patient no. 3 and patient no. 10 are shown in Fig. 3b, c, d and Fig. 3f, g, h respectively. We chose these two patients based on the observations of airway wall elasticity (as described in the following section). Three-dimensional geometries of the baseline, CPAP1 and CPAP2 airways were generated using the MIMICS (Materialise NV, Belgium) image processing software. Figure 3a and 3e indicate the superposed baseline, CPAP1 and CPAP2 airway geometries for patient nos. 3 and 10 respectively (green-baseline, yellow-CPAP1 and blue-CPAP2). In patient 3, significant airway wall movement was observed only on the right wall, upon application of CPAP level 1 (Fig. 3b). The anterior, right and left walls of the airway displaced following an increase in mask pressure to CPAP level 2 (Fig. 3c, d). For patient 10, application of CPAP level 1 resulted in lateral wall displacements in the RG1 airway (Fig. 3f). Furthermore, the increased pressure caused the lateral walls to dilate further in the same anatomical region (Fig. 3g, h). It should be noted that superimposed models of the airways and corresponding displacement maps are aligned with the patient's anterior direction.

2.3 Evaluating Airway Wall Elasticity

Pressure-flow/area relations of the upper airway have been described using the Starling resistor or tube law model^{6, 18, 33}. The specific compliance (i.e., the normalized change in cross-sectional area divided by change in transmural pressure) is an index that has been used to describe the local elasticity of the pharyngeal airway^{10, 13, 14}.

$$\frac{\delta A}{A} = \frac{\delta P}{S} \quad (4)$$

where $\delta A/A$ is the area strain, δP is the transmural pressure and S is the airway wall stiffness. Equation 4 can be rearranged to obtain an expression for localized airway stiffness.

$$S = \frac{A \delta P}{\delta A} \quad (5)$$

We evaluate the compliance and the elasticity in a manner analogous to the tube law. The equivalent radius of circle R_c at a given axial location in the pharynx is defined by,

$$R_c = \sqrt{\frac{A}{\pi}} \quad (6)$$

where A is the axially varying airway cross-sectional area. The area strain term ($\delta A/A$) in equations 4 and 5 can be expressed in terms of the area of a circle,

$$\frac{\delta A}{A} = \frac{\delta(\pi R_c^2)}{\pi R_c^2} \quad (7)$$

Replacing the differential term 'δ' by a derivative,

$$\frac{\delta A}{A} \approx \frac{d(\pi R_c^2)}{\pi R_c^2} \quad (8a)$$

$$\text{i. e. } \frac{\delta A}{A} \approx \frac{2\pi R_c dR_c}{\pi R_c^2} \quad (8b)$$

$$\text{i. e. } \frac{\delta A}{A} \approx \frac{2dR_c}{R_c} \quad (8c)$$

The term dR_c in equation 8c is replaced by the differential radius δR (equation 3), that varies along the airway periphery and length. Accordingly, the specific compliance (C) is defined as follows,

$$C = \frac{1}{S} = \frac{2\delta R}{R_c \delta P} \quad (9)$$

Using equation 9, the displacements at every circumferential and axial location (Fig. 3b, c, d, f, g, h) are normalized by the appropriate circle radius of the reference airway at the respective axial location (Fig. 4a, e) and by the CPAP pressure differences relevant to each map, in order to generate a compliance map (Fig. 4b, c, d, f, g, h). Since the change in head and neck position was negligible between CPAP levels, extraluminal tissue pressure (ETP) distribution¹⁶ was assumed to remain the same for baseline, CPAP1 and CPAP2 configurations. Variations in transmural pressure were influenced only by changes in CPAP.

It should be noted that the unit of compliance employed in this study is mm/cm-mm or 1/cm. A higher value indicates that the airway wall is more flexible and the surrounding tissue is softer. For patient 3, the compliance of the right wall was higher for $\delta P = \text{CPAP1} - \text{CPAP0}$ (Fig. 4b) than for $\text{CPAP2} - \text{CPAP1}$ (Fig. 4d). Conversely, for patient 10, the compliance of the lateral walls in the RG1 airway is comparable for changes in CPAP levels corresponding to $\text{CPAP1} - \text{CPAP0}$ and $\text{CPAP2} - \text{CPAP1}$ (Fig. 4f, h). The axial variation in compliance computed using the tube law (Eqn. 4) is also plotted (Fig. 4a, e) to illustrate the novelty of the proposed method. As can be seen, the proposed mapping method captures circumferential and axial changes in compliance compared to the tube law. An overall value of patient specific stiffness can be obtained for each of the three maps, by computing the average of compliance values at every location and inverting the resulting value. It should be noted that we have chosen to express the stiffness in terms of Pa (1 cm of water ~ 100 Pa). The compliance maps are also simplified by evaluating the average compliance in the anterior, posterior, right and left walls corresponding to the RP, RG1 and RG2 anatomical regions. For the purpose of this analysis, we have assumed that the anterior, posterior and lateral walls subtend equal angles of 90° each, at every axial location. The resulting 4×3 maps of average compliance for patient nos. 3 and 10 are inverted to generate 4×3 maps of average elasticity as indicated in Figure 5. The simplified maps indicate that although the posterior

wall is most likely much stiffer than the other sections of the airway, there are some instances where the posterior wall stiffness is comparable or smaller than that of the anterior and lateral walls (Fig. 5a, b). The maps also indicate that the lateral walls could be significantly softer than the anterior wall in some patients, particularly in the RG1 airway (Fig. 5a, b, d, e, f). The compliance of the anterior wall in the RP airway is found to be greater than the compliance of the lateral walls for patients 3 and 10.

3. Results

3.1 Elasticity based Patient Phenotyping

The overall airway stiffness corresponding to pressure changes from baseline to CPAP level 1 (blue bar) and CPAP level 1 to level 2 (red bar) are then plotted as a bar graph (Fig. 6) to illustrate the nature of non-linear behavior of the individual airways. As can be seen in GROUP 1 (patient nos. 5, 8, 9, 10), the stiffness is higher between baseline and CPAP1 and lower between CPAP1 to CPAP2, and indicates a ‘strain-softening’ behavior. On the other hand, the stiffness is higher between CPAP1 and CPAP2 than from baseline to CPAP1 for GROUP 2 (patient nos. 1, 2, 3, 4, 6, 7) and represents a ‘strain-hardening’ behavior.

Patient phenotyping based on circumferential and axial variations in elasticity with CPAP (i.e. change in airway wall stiffness in the anterior, posterior and lateral section corresponding to the RP (hard palate to tip of soft palate), RG1 (tip of soft palate to tip of epiglottis) and RG2 (tip to base of epiglottis) airways), was achieved using the simplified 4×3 maps of average elasticity. The elasticity phenotypes (overall, circumferential and axially varying) for patients analyzed in the study are summarized in Table 2.

Retro-palatal (RP) Airway—For the anterior section, the airway stiffness decreases with CPAP for patient nos. 4, 5, 7, 8, 9, 10 and increases with CPAP for patients 1, 2, 3 and 6. Patient nos. 5, 6, 8 and 9 exhibit a strain-softening behavior (GROUP 1) and patients 1, 2, 3, 4, 7 and 10 depict a strain-hardening response in the lateral right section (GROUP 2). For the posterior section, airway stiffness decreases with CPAP for patients 5, 8 and increases with CPAP for patients 1, 2, 3, 4, 6, 7, 9 and 10. Patient nos. 1, 4, 5, 8 and 10 exhibit a strain-softening behavior (GROUP 1) and patients 2, 3, 6, 7 and 9 depict a strain-hardening response in the lateral left section (GROUP 2). The elasticity phenotypes for patient nos. 2, 3, 5 and 8 were unchanged along the airway periphery within the RP airway.

Retro-glossal (RG1) Airway—For the anterior section, the airway stiffness decreases with CPAP for patient nos. 1, 2, 4, 5, 6, 8, 9, 10 and increases with CPAP for patients 3 and 7. Patient nos. 2, 5, 6, 8 and 9 exhibit a strain-softening behavior (GROUP 1) and patients 1, 3, 4, 7 and 10 depict a strain-hardening response in the lateral right section (GROUP 2). For the posterior section, airway stiffness decreases with CPAP for patients 5, 8 and increases with CPAP for patients 1, 2, 3, 4, 6, 7, 9 and 10. Patient nos. 1, 3, 4, 5, 8 and 9 exhibit a strain-softening behavior (GROUP 1) and patients 2, 6, 7 and 10 depict a strain-hardening response in the lateral left section (GROUP 2). The elasticity phenotype of patient nos. 5 and 8 did not change with the circumferential location in the RG1 airway.

Retro-glossal (RG2) Airway—For the anterior section, the airway stiffness decreases with CPAP for patient nos. 1, 5, 7, 9, 10 and increases with CPAP for patients 2, 3, 4, 6 and 8. Patient nos. 5, 8 and 9 exhibit a strain-softening behavior (GROUP 1) and patients 1, 2, 3, 4, 6, 7 and 10 depict a strain-hardening response in the lateral right section (GROUP 2). For the posterior section, airway stiffness decreases with CPAP for patients 8, 10 and increases with CPAP for patients 1, 2, 3, 4, 5, 6, 7 and 9. Patient nos. 2, 5, 9 and 10 exhibit a strain-softening behavior (GROUP 1) and patients 1, 3, 4, 6, 7 and 8 depict a strain-hardening response in the lateral left section (GROUP 2). The elasticity based phenotypes for all 10 patients varied along the airway circumference within the RG2 airway.

Moreover, no patient exhibited the same phenotype across all circumferential and axial locations. Patients 3, 5 and 8 exhibited a different phenotype at only one location.

3.2 Correlations with Clinical Parameters

The softest section in the 4×3 simplified maps of elasticity (Fig. 5) is obtained by evaluating the minimum of the 12 airway stiffness values. The ‘representative’ softest section of a patient’s airway is then obtained by computing the least of the three minimum values obtained from the 4×3 maps of stiffness (i.e. baseline to CPAP1, baseline to CPAP2 and CPAP1 to CPAP2). The ten patients were grouped according to the severity of OSA (Fig. 6) and average airway stiffness was estimated for each group, corresponding to the softest section. As indicated in Figure 7, the group averaged airway stiffness values decreased with increasing severity of OSA. Table 3 summarizes the locations of the representative softest sections for each airway and the corresponding values of localized airway wall stiffness.

4. Discussion

The nature of non-linearity in the airway wall response to CPAP for the ten patients analyzed in our study was found to be patient specific and varies along the periphery and length of the airway (Table 2). This highlights the anisotropy in elasticity of the airway and tissue supporting the pharynx. Two types of non-linearity were observed; a strain softening (decreasing airway stiffness with CPAP – GROUP 1) and strain-hardening behavior (increasing stiffness with CPAP – GROUP 2). This implies that in some OSA patients with DS, the increments in compliance decrease with increasing CPAP while in others the compliance increments increase with CPAP. The smallest and largest values of overall airway stiffness for the 10 subjects analyzed in our study differed by one order of magnitude. Patient 7 exhibited a very dynamic baseline airway, as observed from cine MR images. Small changes in pressure were sufficient to produce large variations in airway caliber. This resulted in the baseline airway to remain wide open at peak expiration. The high overall airway stiffness for patient 7 can be attributed to minimal changes in airway caliber at peak expiration, upon application of mask pressure. The spread corroborates the patient-specific nature of CPAP levels needed to maintain airway patency. Furthermore, the elasticity phenotypes based on the overall stiffness corresponded well with those obtained from the 4×3 maps of elasticity for patient nos. 3, 5, 7 and 8 (as indicated in Table 2). Although the proposed method is derived from a tube law model (i.e. pressure-area relationships), it provides an improvement over the simplified Starling resistor theory. It accounts for circumferential changes in localized airway elasticity in addition to changes in

pharyngeal stiffness along the airway length. With the exception of patients 1, 2, 6 and 7, the lateral walls were observed to be more elastic than the anterior and posterior walls. This observation confirms the importance of assessing lateral tissue stiffness in apneic patients ³².

The methodology was demonstrated on ten pediatric OSA patients with DS. Exclusion criteria described in section 2.1 resulted in several patient scans being not usable for the analysis. The group-averaged stiffness at the softest location was found to decrease with increasing severity of OSA. The inverse relationship between airway stiffness and OSA severity suggests that localized airway compliance can supplement clinical measures such as AHI and P_{crit} . Conclusive evidence of this inverse relationship would be obtained in future studies by performing multivariate analysis, with adjustments for gender and BMI. Furthermore, a larger sample size and incorporation of controls would significantly enhance our study. The static MRIs employed in this study are acquired during the peak expiratory phase of the breathing cycle. The shapes of the airways and subsequently the elasticity values computed in this study are averaged over multiple breathing cycles. Elasticity calculation during the inspiratory phase is challenging since the baseline airway may be partially or fully occluded ¹⁵. Besides, imaging of the airway during natural sleep would necessitate acoustic scanner noise attenuation and real time imaging that does not induce signal image artifacts ². Although the segmentation algorithm was demonstrated to be fairly accurate, coarse angular discretization of the airway boundary and averaging reduce the accuracy of the elasticity computations. The present study discretizes the airway cross-section into 24 angular segments, each subtending an angle of 15 degrees. Finer discretization, although possible, are limited by the number of pixels per sector. A non-uniform angular discretization is also relatively simple to implement in the current algorithm. The simplified compliance maps (Fig. 5) assume that the anterior, posterior and lateral walls subtend equal angles of 90 degrees over the entire length of the pharyngeal airway. Although patient-specific, non-uniform, axially varying angular extents of the circumferential sections would improve the accuracy of the 4×3 maps of stiffness, identifying the extents of individual tissue from MR images is quite challenging. The presented methodology assumes a uniform airway wall pressure distribution along the airway length and periphery. This assumption was validated using computational fluid dynamics (CFD) ^{24, 26} of the upper airway. Results from the CFD simulations indicated that with application of CPAP, the intraluminal pressure was uniformly distributed circumferentially and axially. We propose a combination of ETP measurements with specialized IRB approved catheters and CFD or the use of IRB approved cannula and pressure transducers ¹³, in order to accurately estimate the transmural pressure difference.

The overall and local compliance estimates reported in this study are within the range of values evaluated previously. Phenotyping of patients based on localized variations in airway stiffness can potentially influence the treatment needed to reduce the severity of the disorder. The stiffness estimates could serve as an input to a virtual, bed-side computational tool that is being developed by our research group to assess the success or failure of different surgeries prior to their application. The present approach is suitable to estimate the static or passive compliance of the airway wall, a quantity that can significantly vary from the dynamic or active compliance. The active compliance stems from muscle activity and temporal variations in pressure during breathing ³. The same can be estimated from cine

MRIs that also serve to improve the patient specific aspects of sleep disordered breathing including neck movement, jaw thrusting, independent and coupled behavior of soft-tissue components such as the tongue, soft palate, etc.

5. Conclusions

We presented a minimally invasive method to evaluate the passive compliance and elasticity of the pediatric upper airway by comparing static MRIs in the dilated and baseline configurations. A series of complex radial displacement and compliance maps were obtained by normalizing the airway wall displacements by the difference in CPAP levels and the equivalent radius of the lumen in a manner analogous to the tube law. Not only does this approach model the non-linear response of the airway wall to CPAP, but also accounts for anisotropy, i.e. directionality in the mechanical properties. The proposed method has several advantages including its simplicity and ability to evaluate patient specific compliance. The method can be further refined by overcoming some of the pitfalls and sources of error, highlighted in the previous section. Our future direction would involve estimating the optimized, passive mechanical properties of individual tissue structures iteratively using prior knowledge of the airway collapsibility and airway wall pressure distribution from MR images and CFD, respectively.

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Figure 1. Representative outlines of upper airway a) Square shape b) Figure-eight Shape c) T shape d) Horseshoe shape. Reference point is determined by either the mean of extreme coordinates (Method 1), centroid (Method 2), center of inscribed circle (Method 3) or average of intersections (Method 4) e) Approximation of an angular segment of the airway as a cylindrical element subtending an angle $d\theta$, arbitrarily chosen to be 15° f) Three-dimensional map of variation in radial displacement (patient 3, CPAP1 to CPAP2) along the airway periphery and length.

Figure 2.

a) Unwrapped displacement map (patient 3, CPAP1 to CPAP2) quantifying airway wall displacements circumferentially (A,R,P,L) and axially (RP,RG1,RG2) b) Mid-sagittal airway profiles for patient 3 (blue – Baseline, red – CPAP1, black – CPAP2) indicating axial extents of relevant anatomical regions. (Note: A-Anterior, R-Right, P-Posterior, L-Left, RP-Retropalatal Airway (Hard palate to tip of soft palate), RG1-Retroglossal Airway (Tip of soft palate to tip of epiglottis), RG2-Retroglossal Airway (Tip of epiglottis to base of tongue)).

Figure 3.

Unwrapped displacement maps for patient 3 (b, c, d) and patient 10 (f, g, h) corresponding to changes in CPAP levels (0 (baseline) to pressure 1, 0 (baseline) to pressure 2, pressure 1 to pressure 2). Superposed three-dimensional geometric models of the baseline (green), CPAP1 (yellow) and CPAP2 (blue) also indicated for reference (a – patient 3, e – patient 10). (Note: All displacements are in mm).

Figure 4.

Compliance maps obtained by normalizing radial displacements by CPAP pressure difference (δP) and axially varying equivalent radius of circle (R_c) (a, e (baseline – solid blue line, CPAP1 – solid red line)) for patient 3 (b, c, d) and patient 10 (f, g, h), corresponding to changes in CPAP levels (0 to pressure 1, 0 to pressure 2, pressure 1 to pressure 2). Axial variations in compliance (blue dashed line – 0 to pressure1, red dashed line – 0 to pressure 2, black dashed line – pressure 1 to pressure 2) computed using the tube law (Eqn. 4) are also indicated in Fig. 4a, e. (Note: Units for compliance are mm/cm-mm (compliance maps) or mm²/cm-mm² (tube law). For 0 to pressure 1 and 0 to pressure 2, the displacements are normalized by the equivalent circle radius corresponding to baseline airway. For pressure 1 to 2, the corresponding displacements are normalized by the equivalent circle radius corresponding to the airway dilated by pressure 1).

Figure 5.

4×3 maps of average stiffness for patient 3 (a, b, c) and patient 10 (d, e, f). (Note: Units of stiffness is Pa. A-Anterior, R-Right, P-Posterior, L-Left, RP-Retropalatal Airway (Hard palate to tip of soft palate), RG1-Retroglossal Airway (Tip of soft palate to tip of epiglottis), RG2-Retroglossal Airway (Tip of epiglottis to base of tongue)).

Figure 6.

Variation in overall stiffness with CPAP, for the 10 patients considered in this study. Patients in GROUP 1 (patient nos. 5, 8, 9, 10) exhibit a 'strain-softening' behavior and patients in GROUP 2 (patient nos. 1, 2, 3, 4, 6, 7) depict a 'strain-hardening' response. Patients within each group are arranged in the order of increasing AHI.

Figure 7.

Variation in group averaged airway stiffness at softest location with a) AHI (GROUP 1 – Mild OSA (AHI values 1 to 6), GROUP 2 – Moderate OSA (AHI values 6 to 21), GROUP 3 – Severe OSA (AHI values above 21)) b) P_{crit} (GROUP 1 – Mild OSA (P_{crit} values from -11 to -8 cm), GROUP 2 – Moderate OSA (P_{crit} values from -8 to +1.25 cm), GROUP 3 – Severe OSA (P_{crit} values above +1.25 cm). The trend indicates an inverse relationship of group averaged airway stiffness with AHI and P_{crit} .

Summary of patient clinical history (Note: Pressure (P_{crit} , CPAP1 and CPAP2) is in cm of water, 1 cm of $H_2O \sim 100$ Pa)

Table 1

Patient No.	Age (years)	Gender	AHI	BMI	P_{crit}	CPAP1	CPAP2
1	11	F	20.2	24.7	1.3	4	10
2	14	M	6.4	20.6	-4.3	3	7
3	4	M	9.3	20.4	-8.1	2	8
4	7	M	8.7	18.9	1.3	7	12
5	9	F	9.1	16.8	-3.8	4	6
6	3	F	5.9	22.1	-10	2	6
7	10	M	4	17.3	-10.8	4	10
8	17	M	21.3	30.5	N/A	10	15
9	12	M	5.9	27.1	-0.2	4	8
10	8	M	7.5	16.5	-0.8	8	14

Table 2

Summary of elasticity phenotypes (Note: 1 indicates softening, 0 depicts hardening)

Patient	Overall	Anterior			Right			Posterior			Left		
		RP	RG1	RG2	RP	RG1	RG2	RP	RG1	RG2	RP	RG1	RG2
1	0	0	1	1	0	0	0	0	0	0	1	1	0
2	0	0	1	0	0	1	0	0	0	0	0	0	1
3	0	0	0	0	0	0	0	0	0	0	0	1	0
4	0	1	1	0	0	0	0	0	0	0	1	1	0
5	1	1	1	1	1	1	1	1	1	0	1	1	1
6	0	0	1	0	1	1	0	0	0	0	0	0	0
7	0	1	0	1	0	0	0	0	0	0	0	0	0
8	1	1	1	0	1	1	1	1	1	1	1	1	0
9	1	1	1	1	1	1	1	0	0	0	0	1	1
10	1	1	1	1	0	0	0	0	0	1	1	0	1

Table 3

Summary of softest sections in the pharyngeal airway

Patient No.	Axial Location	Peripheral Section	Airway Stiffness (Pa)
1	RG1	Anterior	545
2	RG2	Posterior	335
3	RG1	Right	145
4	RP	Right	370
5	RG1	Right	165
6	RG2	Posterior	375
7	RP	Posterior	835
8	RP	Right	270
9	RG2	Right	540
10	RG1	Right	445