A multiscale analytical model of bronchial airway acoustics

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Sound transmission and resulting airway wall vibration in a complex multiscale viscoelastic model of the subglottal bronchial tree was calculated using a modified one-dimensional (1D) branching acoustic waveguide approach. This is an extension of previous work to enable use of complex airway trees that are partially derived from subject-specific medical images, without the need for self-similarity in the geometric structure. The approach was validated numerically for simplified airway geometries, as well as experimentally by comparison to previous studies. A comprehensive conducting airway tree with about 60 000 branches was then modified to create fibrotic, bronchoconstrictive, and pulmonary infiltrate conditions. The fibrotic case—systemic increase in soft tissue stiffness—increased the Helmholtz resonance frequency due to the increased acoustic impedance. Bronchoconstriction, with geometric changes in small conducting airways, decreased acoustic energy transmission to the peripheral airways due in part to the increased impedance mismatch between airway orders. Pulmonary infiltrate significantly altered the local acoustic field in the affected lobe. Calculation of acoustic differences between healthy versus pathologic cases can be used to enhance the understanding of vibro-acoustic changes correlated to pathology, and potentially provide improved tools for the diagnosis of pulmonary diseases that uniquely alter the acoustics of the airways. © 2017 Acoustical Society of America. <https://doi.org/10.1121/1.5005497>

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I. INTRODUCTION

A. Background and motivation

The lungs are a unique multiscale and multiphase porous structure that has challenged conventional noninvasive medical diagnostic and imaging methods and our ability to precisely locate and quantify changes in macroscopic functional and structural properties indicative of pathology that are often fundamentally linked to biomechanical changes at the microscopic scale. Patients suffer from a wide range of pulmonary ailments that cause unique and significant changes, focally or diffusely, to the geometry, material composition, and intrinsic mechanical properties—stiffness, viscosity and density—of the lungs; all of these changes can alter lung acoustics in unique ways.

Sound within the subglottal bronchial airways, whether generated internally by the respiratory process or introduced externally as part of a noninvasive diagnostic^{1–3} or therapeutic tool,⁴ will cause the airway walls to vibrate, which in turn will disperse acoustic energy throughout the lung parenchyma, and ultimately to the torso surface, where its motion can be measured noninvasively via contacting or noncontacting (optical) methods. Internal lung tissue oscillatory motion initiated from sound in the airways or other internal or external sources may also be measureable noninvasively utilizing dynamic elastographic methods, such as magnetic resonance elastography.^{5,6} Improved understanding of the acoustic propagation path and how it is altered by disease and injury

may lead to improvements in these diagnostic and therapeutic methods that are based on sound.

Previous analytical and numerical studies of our group focusing on acoustic transmission in the lungs have utilized thoracic cavity and lung models with no^{7–10} or simplified subglottal airway structures.^{11,12} Dai *et al.*¹³ advanced a one-dimensional (1D) branching waveguide analytical approach for efficiently calculating airway acoustic transmission and experimentally validated it in a simple phantom model with several bifurcating pathways. Implicit to that approach was an assumption of self-similarity in airway tree structure with geometric ratios between mother and bifurcating daughter branches repeated at multiple bifurcating orders throughout the tree. In the present study, we modify and extend this approach to more complex airway tree models, including a full conducting airway tree model that does not explicitly obey self-similarity. The goal is to gain insight into changes in acoustic propagation within the airways associated with geometric and mechanical property changes brought on by specific respiratory pathologies. As illustrative examples, three pathological conditions are considered that alter the bronchial tree in distinctly different ways: pulmonary fibrosis, bronchoconstriction, and pulmonary infiltrate.

Pulmonary fibrosis (PF), which can cause a global stiffening of the lung parenchyma and airway walls, has a poor prognosis in part because a definitive diagnosis often requires a dangerous invasive lung biopsy. The growth of fibrous tissue is a regenerative process associated with healing; however, it can be excessive or uncontrolled, as a secondary chronic effect of various conditions, including cystic fibrosis and numerous connective tissue diseases, or as a result of exposure to environmental hazards or radiation

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therapy. It also is often idiopathic.^{14,15} PF prevalence in the United States may be as high as 132 000, based on the population in 2000. The actual numbers may even be higher due to under or misdiagnosis. While most patients are in their forties and fifties when diagnosed, the incidence of idiopathic PF in particular increases dramatically after the age of fifty.¹⁵

While evidence indicates that there is a direct relationship between the regional mechanical properties of the lung parenchyma and the disease stage and progression of PF,¹⁵ a noninvasive means of assessing these regional mechanical properties has been lacking. Although there are several organ-level parameters that can be derived from standard lung function tests such as lung resistance, compliance, hysteresis, and bulk modulus, none of these measures directly assesses or spatially resolves the intrinsic mechanical properties of the lung parenchyma. Noninvasive and reproducible techniques to quantify lung tissue fibrosis would accelerate research and potentially lead to improved evaluation and management of patients who suffer from PF and related interstitial lung diseases. Dynamic elastography imaging methods could potentially address this need.^{5,6} In addition, more detailed patient-specific models of airway acoustics, throughout the conducting airways, could aid in interpretation and reconstruction of airway elastography measurements using ultrasonic or noninvasive hyperpolarized gas magnetic resonance elastography methods, with potentially sufficient sensitivity to quantify bronchi and bronchiole health deterioration caused by fibrotic and other lung conditions.

Bronchoconstriction, a narrowing of the airways in the bronchi and/or bronchioles, may result from a spasmodic state of the airway wall smooth muscles, an inflammation in the airway wall middle layers, or excessive mucous in the lumen. There are many potential causes, including the obstructive lung diseases of emphysema and asthma, as well as an allergic reaction. Asthma afflicts 1 in 13 Americans and is one of the costliest health conditions in the United States.¹⁶ Despite its prevalence, the pathogenesis of asthma is not fully understood. Some of the symptoms are quantifiable; for example, patients with asthma typically have an inflammatory bronchoconstrictive response in small airways (airways smaller than 2 mm), causing the diameter of those airways to reduce and the airway walls to thicken. In addition, mucous plugs made up of glycoproteins generated from epithelial cells in pulmonary vasculature clog the airways, leading to bouts of severe wheezing and sometimes death, as revealed in post-mortem examination. Understanding how bronchoconstriction affects generation and propagation of respiratory sounds, such as wheezing, may lead to an improved ability to differentiate the severity and root cause of this potentially life-threatening condition.

A pulmonary infiltrate can occlude airways and reduce lung capacity. It can stem from a variety of sources, including acute chest syndrome (ACS), a leading cause of death for those with sickle cell disease (SCD), which affects 30 million people worldwide.¹⁷ ACS is classically defined by the development of a new pulmonary infiltrate on chest x-ray, with fever, and respiratory symptoms. Typically, it is

confined to one or a few lobes of the lung. About half of those with SCD will have at least one episode of ACS in their lifetime. For adults, it generally occurs one to three days after admission to the hospital for a severe painful vaso-occlusive episode, suggesting that the process may have already started while the patient was at home, but before there are findings consistent with the diagnosis upon admission. Efforts have been made to apply various technologies in the hospital setting to diagnosis or predict it sooner than an x-ray, but many of them are expensive, increase radiation exposure to the patient, and are not technologies that are easily transferrable for home use to help with early diagnosis.

Acoustic crepitations have been noted when performing chest auscultation during ACS. Frequent severe wheezing episodes have also been correlated with SCD and ACS, and are considered a potential marker of the severity of the disease progression. Also, enhanced respiratory sound coupling to the chest wall has been noted over regions of consolidation within the lung.¹⁸ Inexpensive acoustical measurements recorded quantitatively with contact sensors and analyzed with a better understanding of how respiratory sounds are altered during ACS could potentially provide an earlier diagnostic indicator of its onset.

B. Objectives and structure

The objectives of the current study are to: (1) advance the analytical approach of Dai *et al.*¹³ to enable the efficient calculation of airway acoustic transmission for a complete model of the conducting airway tree with up to 15 generations (about 60 000 airway segments) that is not explicitly self-similar in structure; and, (2) using this model, explore acoustic differences introduced by three specific pathological responses that alter airway geometry and/or material properties in unique ways. In Sec. II, the theory behind the analytical approach is introduced. In Sec. III, validation of the analytical approach through comparison to previous studies is presented. Analytical calculation of sound transmission in a complete conducting airway network is presented in Sec. IV for healthy and pathological conditions. Discussion and conclusions are provided in Secs. V and VI, respectively.

II. THEORY

A. Subglottal airway geometry

In the past, the Horsfield self-similar model of subglottal airway tree geometric properties has been used to develop an efficient analytical means of calculating acoustic impedance throughout the tree.^{1,11,13} Per the Horsfield model, the human airway tree is divided into 35 orders with consistent linkages between different orders and consistent geometric properties within an order—diameter, length, wall thickness, cartilage fraction, degree of asymmetry in daughter branches—ranging from the trachea down to the millions of alveoli. Accompanying that geometric model is a mathematical description of the acoustic properties for those airway segments that can sufficiently describe wave propagation in

a bifurcating geometry structure. Each n th order segment, depending on the level of asymmetry given by a recursion index Δ , bifurcates into $(n-1)$ th order and a $(n-1-\Delta^n)$ th order segments.

However, human airway trees do not strictly adhere to the Horsfield self-similar structure; thus, a modified analytical approach has been developed that does not require self-similarity and can be applied to subject-specific airway geometry derived from medical images and/or grown algorithmically. In this study, a healthy human male model of the conducting airways was obtained from Miyawaki *et al.*,¹⁹ which was generated from a combination of medical image-based segmentation combined with algorithmic generation of segments that are beyond x-ray computed tomography (CT) image resolution.²⁰

The hybrid image-derived/algorithmically grown tree was developed using a fractal quasi-volume halving approach developed by Tawhai *et al.*²¹ The algorithm grows additional airway segments based on a partial centerline airway tree generated from segmentation from medical image data, at which point the rest of the conducting airways are generated from an airway generation algorithm. This method has produced physiologically similar complex bronchial trees, which exhibit similar diameter ratios, lengths, bifurcation angles, and numbers of airway segments per lobe for a grown bronchial tree. There are some assumptions (diameter to branching order) that limit the use and classification of the grown bronchial tree as a physiologically accurate airway tree; the evidence for the fidelity of the approach in developing bronchial trees with geometrical parameters similar to published literature is quantified in Ref. 21.

B. Acoustic and diagrammatic description of modified analytical approach

Using the 1D branching waveguide governed by the Horsfield self-similar (fractal) tree structure, calculations of acoustic impedance in the frequency domain are extremely efficient requiring only 35 steps to proceed from the terminal alveoli ($n = 1$) to the trachea ($n = 35$). With additional effort, this can be used to determine the pressure distribution in the airway tree. In the present study, modifications were made to the 1D branching waveguide to calculate acoustic properties recursively, without requiring Horsfield's fractal airway ordering.

Previously,¹³ inlet impedance Z_{in} , referring to Fig. 1, was calculated using the following expression:

$$Z_{in}^n[\omega] = \frac{Z_T^n[\omega] + Z_0^n[\omega] \tanh(\gamma_0^n[\omega] l^n)}{1 + \left(\frac{Z_T^n[\omega]}{Z_0^n[\omega]} \right) * \tanh(\gamma_0^n[\omega] l^n)}, \quad n = 1, \dots, 35. \quad (1)$$

The terms $Z_0^n[\omega]$ and $\gamma_0^n[\omega]$ are the characteristic impedance and propagation coefficient of the n th airway segment, and can be calculated via the following equations.

$$Z_0^n[\omega] = \sqrt{\frac{Z^n[\omega]}{Y^n[\omega]}}, \quad (2)$$

FIG. 1. An airway model with a single bifurcation.

$$\gamma_0^n[\omega] = \sqrt{Z^n[\omega] Y^n[\omega]}, \quad (3)$$

$$Z^n[\omega] = \frac{j\omega\rho_g}{A^n(1 - F_v^n[\omega])}, \quad (4)$$

$$Y^n[\omega] = \frac{j\omega A^n}{p_g c_g^2} (1 + 0.402 F_t^n[\omega]) + \frac{1}{Z_w^n[\omega] l^n}, \quad (5)$$

$$F_v^n[\omega] = \frac{2}{a^n(-j\omega\rho_g/\eta_g)} \frac{J_1 \left[a^n \sqrt{-j\omega\rho_g/\eta_g} \right]}{J_2 \left[a^n \sqrt{-j\omega\rho_g/\eta_g} \right]}, \quad (6)$$

$$F_t^n[\omega] = \frac{2}{a^n(-j\omega C_g/\kappa_g)} \frac{J_1 \left[a^n \sqrt{-j\omega C_g/\kappa_g} \right]}{J_2 \left[a^n \sqrt{-j\omega C_g/\kappa_g} \right]}, \quad (7)$$

$$Z_w^n[\omega]^{-1} = \frac{c^n}{Z_{w,c}^n[\omega]} + \frac{1 - c^n}{Z_{w,s}^n[\omega]}. \quad (8)$$

Here, ω is the circular frequency and $Z^n[\omega]$ and $Y^n[\omega]$ are, respectively, the series impedance and shunt admittance of the n th airway segment. The terms ρ_g , η_g , and c_g are the air density, viscosity, and speed of sound, respectively. C_g and κ_g are the air specific heat and thermal conductivity, and A^n and l^n are the cross-sectional area and length of the n th order segment. The terms $F_v^n[\omega]$ and $F_t^n[\omega]$ account for sound attenuation via air viscosity and thermal dissipation, respectively. In addition, $Z_w^n[\omega]$ is the effective volumetric wall compliance of the n th order segment composed of two material types, cartilage and soft tissue, with c^n and $1 - c^n$, respectively, denoting the cartilage and soft tissue fractions of the n th order segment. Cartilage components are mainly present in orders $n = 35$ down to $n = 17$, after which the airway wall is composed entirely of soft tissue. The volumetric wall compliance of the cartilage or soft tissue can be computed via a series resistance (R_w), inertance (I_w), and compliance (C_w) representation of each wall compartment:

$$Z_{w,ors}^n[\omega] = R_w^n + j(\omega I_w - 1/\omega C_w^n), \quad (9)$$

where

$$R_{w,ors}^n = \frac{4h^n E_{I,ors}}{\pi(d^n)^3 l^n \omega}, \quad (10)$$

$$I_{w,cor s}^n = \frac{h^n \rho_{cor s}}{\pi(d^n)^3 l^n}, \quad (11)$$

$$C_{w,cor s}^n = \frac{\pi(d^n)^3 l^n}{4h^n E_{R,cor s}}. \quad (12)$$

Here, $\rho_{cor s}$ denotes the density of the cartilage or soft tissue, respectively, $E_{R,cor s}$ and $E_{I,cor s}$ denote the real and imaginary part, respectively, of the Young's modulus.

Previously,¹³ the terminal (distal) impedance of each order of airway segment was calculated via the following equation:

$$Z_T^n[\omega] = \begin{cases} \frac{N_T}{j\omega C_g + 1/[R_t + j(\omega I_t - 1/[\omega C_t])] } & \text{for } n=1 \\ \frac{1}{1/Z_T^{n-1}[\omega] + 1/Z_T^{n-1-\Delta[n]}[\omega]} & \text{for } n=2, \dots, 35, \end{cases} \quad (13)$$

where C_g is the alveolar gas compression compliance based on the Dubois six-element airway model.²² R_t , I_t , and C_t are

the Dubois model resistance, inertance, and compliance, and $Z_T^{n-1}[\omega]$ along with $Z_T^{n-1-\Delta[n]}[\omega]$ are described as the lumped downstream impedance. N_T denotes the total number of bronchiole segments, which is $\sim 2.35 \times 10^6$.

As seen in Eq. (13), the terminal impedance for order number n is dependent on the orders of $n-1$ and $n-1-\Delta(n)$, where $\Delta(n)$ is the recursion index. For non self-similar geometric models, this equation is turned into a recursive calculation based on airway connectivity, shown in Eq. (14):

$$Z_T^{parent}[\omega] = \left\{ \frac{1}{1/Z_{in}^{daughter1}[\omega] + 1/Z_{in}^{daughter2}[\omega]} \right\}. \quad (14)$$

Here, $Z_{in}^{daughter1}[\omega]$ and $Z_{in}^{daughter2}[\omega]$ are the input impedances of the two daughter segments at each bifurcating segment.

From this point, calculating the acoustic pressure at each segment as a component of the frequency is done through calculation of a pressure ratio ($P_{rat}[\omega]$), a predefined inlet pressure, and a recursive calculation from the source of the excitation (the trachea) down to the terminal segments. The calculation of the pressure ratio is given in Eq. (15):

$$P_{rat}[\omega] = \frac{P_T[\omega]}{P_{in}[\omega]} = \frac{Z_T[\omega]Z_0[\omega]}{Z_{in}[\omega](Z_T[\omega]\sinh[\gamma_0[\omega]l] + Z_0[\omega]\cosh[\gamma_0[\omega]l])}. \quad (15)$$

Here, $P_{in}[\omega]$ and $P_T[\omega]$ are the inlet and distal pressure for each cylindrical airway segment, respectively.

Given an acoustic input at the top of the trachea, the pressure distribution of the airway tree can then be solved using the pressure ratio of each segment in a series of calculations from the trachea down to the terminal segments via Eqs. (16) and (17):

$$P_{in}^{daughter}[\omega] = P_T^{parent}[\omega], \quad (16)$$

$$P_T^{segment}[\omega] = P_{in}^{segment}[\omega] * P_{rat}^{segment}[\omega]. \quad (17)$$

Additionally, once the terminal pressure has been calculated per segment, acoustic pressure can be solved for at any location x within the airway segment from $x=0$ at the inlet and $x=l$ at the outlet per Eq. (18):

$$P[x, \omega] = \frac{Z_0[\omega]}{\sinh(\gamma_0[\omega]l)} \left(\frac{P_{in}[\omega]}{Z_{in}[\omega]} \cosh(\gamma_0[\omega](x-l)) - \frac{P_T[\omega]}{Z_T[\omega]} \cosh(\gamma_0[\omega]x) \right). \quad (18)$$

In this study, an acoustic point source is introduced as a non-homogeneous boundary condition at the top of the trachea in order to mimic experimental airway insonification from an external source. However, the acoustic source can be moved anywhere in the tree. In addition, many respiratory sounds—for example, normal breathing, wheezing, stridor, crackles,

etc.—can be approximated as a distribution of point sources throughout certain regions of the airway trees. Given the assumption of linearity, the response to a sum of sources is equal to summing the responses to each individual source.

III. VALIDATION

In Ref. 13, the 1D branching waveguide theory, which assumes a self-similar (fractal) airway tree, was validated by experiment and numerical finite element (FE) simulations of an airway (branching waveguide) phantom. The modified waveguide theory introduced in the present study, which does not require but can still accommodate self-similar structure, is applied to this same phantom for validation (Sec. III A). Validation via comparison to numerical FE simulation is then extended to a more complex and realistic airway tree that is not self-similar (Sec. III B).

A. Validation by comparison to fractal-based approach for simple airway tree phantom

Per the recursive algorithm presented in Sec. II B, the modified algorithm uses parent–daughter connectivity instead of Horsfield order numbers. Figure 2(a) shows the phantom used in this experimental validation study detailed in Ref. 13, with its internal geometry provided in Fig. 2(b). The terminal acoustic pressure at locations A, C, E, and G (and thus also B, D, F, and H, respectively, by symmetry) was analytically determined via Eq. (18). Shown in Fig. 3 is

FIG. 2. (Color online) Airway phantom: (a) photograph; (b) schematic with locations A–H labeled.

the acoustic pressure amplitude calculated by the unmodified self-similar (fractal) waveguide approach and the modified waveguide approach, which does not require, but can accommodate, a fractal structure.

As seen in Fig. 3, calculations of the acoustic pressure using the modified versus unmodified waveguide models are identical across all frequencies. For every cylindrical segment, the calculation of Z_T via Eq. (14) in the modified waveguide yielded the same impedances compared to the unmodified waveguide based on Eq. (13). As noted in Ref. 13, this analytical calculation matched the experiment reasonably well above 600 Hz, but showed some discrepancy at lower frequencies. A possible reason for this discrepancy is that the airway walls are assumed to be annular in the theory, while experimentally the airway tree was embedded in the phantom. Thus, the effective airway wall thickness varied circumferentially, being its thinnest in the direction towards the top surface of the phantom. At lower frequencies, wall compliance plays a larger role in affecting airway acoustics. Since the model for wall compliance is not accurate due to the nonuniform thickness, this may result in greater discrepancies as frequency decreases.

B. Validation by comparison to numerical FE simulation of larger branches of realistic airway tree

A geometric model of a conducting human airway tree was provided by Miyawaki *et al.*¹⁹ The airway tree geometry was developed via a hybrid segmentation/algorithmic approach where CT provided a patient-specific backbone up to the limit of clinical CT resolution, and the quasi-volume halving fractal algorithm generated the rest of the airways

FIG. 3. (Color online) Acoustic pressure magnitude at locations A–H (see Fig. 2) referenced to acoustic pressure at inlet.

down to the limit of the conducting tree.^{19,20} Shown below in Fig. 4(a) is a graphical depiction of the full conducting tree with coloring per Horsfield order, and Fig. 4(b) depicts the partial conducting tree modeled to Horsfield order 15.

The human subject conducting airway tree model based on medical imaging combined with algorithmically-developed smaller airways included multiscale diameter ranges spanning centimeters in the trachea to hundreds of microns in the terminal conducting segments. The airway segment thickness, cartilage, and soft tissue fractions were assigned based on determining the closest Horsfield order segment referring to the values provided in Ref. 1.

FIG. 4. (Color online) Full conducting model used in this study (a) colored by its Horsfield order. Partial tree modeled to Horsfield order $n = 15$ (b) used for validation by comparison to numerical FE simulation, colored by Horsfield order.

To further validate the modified waveguide model, it was compared to a FE simulation of the acoustic pressure and airway wall radial velocity for the partial airway tree in Fig. 4(b). Due to computational limitations, FE simulation of the full tree [Fig. 4(a)] is impractical. FE models were produced in ANSYS ICEM CFD.²³ The hollow tube network was developed in ANSYS via a series of tcl (tool command) script files, which had the instructions to automatically generate the cylinder geometry segment by segment. Spheres were inserted at the bifurcation junctions to make the connectivity smoother. Two separate sets of scripts were written from MATLAB 2016a²⁴ to depict the inner and outer radius of the hollow tube network, which were merged and volume meshed to provide the hollow tube FE model. The final FE model had two volumes, denoted by the inner (air volume) and outer radius (airway wall thickness) for the hollow tube model to replicate as closely as possible the conducting tree geometry.

Shown in Table I are the material properties used in the analytical and numerical studies. The material properties

TABLE I. Material properties of the human airway tree.

Variable	Units	Value
Air density	ρ_g (kg/m ³)	1.14
Air viscosity	η_g (Pa s)	1.86×10^{-5}
Speed of sound in air	c_g (m/s)	343.0
Airway Wall Elastic Modulus	E_w (Pa)	5.81×10^4 soft tissue
		3.92×10^5 cartilage
Airway Wall Viscosity	η_w (Pa s)	102.0 soft tissue
		688.0 cartilage
Airway Wall Poisson's Ratio		0.4995

used were obtained from literature, and represent physiological values.^{1,11,12} Lung parenchyma values were used for the airway soft tissue component. Additionally, to simulate the acoustic structure interaction accurately, the airway wall was modeled with the complex Young's modulus, Poisson's ratio, and density of material.

The post processing of the acoustic pressure as a response to a sinusoidal acoustic source at the top of the trachea was conducted in MATLAB. To do this, the solution of the internal acoustic pressure from the numerical COMSOL Multiphysics²⁵ experiment was output and brought into MATLAB alongside the analytical calculations. As an input boundary condition, a 1 Pa planar wave was applied at the entrance to the trachea, with spectral content between 100 and 800 Hz in 100 Hz increments. Analytical calculations of the pressure were obtained within each segment as each cylindrical segment was subdivided into 9 points, from $l = 0$ to $l = x$, where x refers to the length of the segment, and internal acoustic pressures were solved via Eq. (18). Numerical results for the internal acoustic pressure from COMSOL were taken at those identical points and exported. Shown in Fig. 5 are the MATLAB and COMSOL plots of the acoustic pressure at 400 Hz in dB ref. 1 Pa. In each plot, the scale of the color bars was matched, with the units in dB with respect to m/s/Pa.

Figures 5 show a good match for the pressure distribution at 400 Hz between the analytical solution and numerical (FE) simulation results for the partial conducting tree. The error in the first few generations of airway segments is minimal, ranging from 0 to 10%, with downstream errors rising. One possible source of error in the smaller terminal segments can stem from the segments that do not bifurcate because of the break-off point at Horsfield order $n = 15$ in the partial model. Since further downstream segments were not considered in this tree, wave propagation changes, and this influences the numerical model. Per the modified 1D waveguide, when a non-bifurcating segment is encountered, the downstream segments until bifurcation or airway termination are taken to be a single segment with tortuosity. This enables the valid use of the 1D waveguide approach. In the full conducting tree used in Sec. IV, the number of non-bifurcating segments is minimal (3 total non-bifurcating segments out of 59 834 total segments, located at the terminals). The partial tree used here for FE validation is a balance between an exponentially increasing node count and adequate geometric complexity. Good agreement between analytical and numerical models can be seen in the first several generations, and the trend in the trachea and first

FIG. 5. (Color online) Magnitude of the acoustic pressure at 400 Hz in dB (a) solved analytically in MATLAB (0.35 s computation time) and (b) solved numerically using FE analysis via COMSOL (3861 s computation time). Shown in (c) is the difference between the two plots in dB, and (d) shows the % error.

few generations where bifurcations were always present, shows close agreement with regard to airway lumen acoustic pressure.

The error was calculated via the following equation:

$$\%error = \left(\frac{dBPressure_{FE} - dBPressure_{analytical}}{dBPressure_{analytical}} \right) * 100, \quad (19)$$

where MATLAB was used for post-processing.

IV. ANALYTICAL STUDIES OF PATHOLOGICAL EFFECTS ON AIRWAY TREE ACOUSTICS

A. Pathology simulations

A combination of geometric, material property, and boundary condition changes were implemented to mimic the pathological conditions described in Sec. I. While a broad range of frequencies can be quickly calculated, for succinctness we choose here to present results at one frequency, 400 Hz, because of its relevance in respiratory sounds and possible application in dynamic elastography methods. Trends seen at 400 Hz were similar at other comparable frequencies.

To simulate pulmonary fibrosis, a global material property for the airway wall stiffness was changed to be five times its original value.^{26,27} This was done in the algorithm

setup by multiplying the real part of Young's modulus by a factor of five. There were no geometric changes in this pathological case. To simulate bronchoconstriction in asthma, several geometric changes were made per Ionescu *et al.*²⁸ In airways smaller than 2 mm, to model the airway wall thickening, the thickness of the soft tissue component of the segments was multiplied by 1.5, and the airway radius was reduced by 50% of the soft tissue component of the thickness. The change in airway radius was made to model the presence of mucous, and due to airway remodeling, the thickness of these segments increases. To simulate pulmonary infiltrate in the lower left lobe, the terminal impedance in this lobe was made infinite, meaning a rigid boundary was introduced to the terminal conducting airway segments in the afflicted lobe. All other lobes were healthy and had no other change. No other geometry or material properties were changed.

B. Results

Shown below in Fig. 6 is the airway wall acoustic radial velocity in dB ref. 1 m/s for the full conducting tree model for 400 Hz for the healthy, fibrotic, bronchoconstrictive, and pulmonary infiltrate cases. Airway wall radial velocity from 10 to 1600 Hz in 10 Hz increments for healthy and pathological cases is shown in Fig. 7 for different locations within the airway tree. For these simulations, the acoustic pressure source was located at the top of the trachea, which itself was 8.39 cm in length. For a rigid tube of this length with one end closed and one end open, there will be a resonance for acoustic wavelengths that are four times the length of the tube. With both ends open or both ends closed the resonance would be for acoustic wavelengths that are two times the length of the tube. With a speed of sound in air of 343 m/s, this corresponds to resonances of about 1000 and 2000 Hz, respectively. Given the more complex end conditions for the trachea, this resonance peak has shifted to about 1200 Hz, which is consistent with what has been reported in previous experimental measurements on *in situ* and excised dog lungs, with this first resonance occurring at 1.2 times the lower predicted resonance.³ Note, the frequency of the peak is not altered by the change in tracheal wall stiffness due to fibrosis. This amplified response and greater coupling efficiency to the acoustic source at the resonance propagates through the airway system even down to the terminal conducting segments.

V. DISCUSSION

Sound transmission in a complex airway network was solved analytically using a modified 1D branching waveguide. The analytical approach was validated by comparison to previous analytical methods, as well as numerical FE analysis of much-simplified airway trees. Validation was conducted over a broad frequency range relevant to both respiratory sounds and externally introduced acoustic stimuli. The new analytical approach could calculate the acoustic response distribution at a fraction of the memory requirements and computation time compared to numerical FE simulations: 0.0857 s versus 3261 s for a single frequency;

FIG. 6. (Color online) Airway wall radial velocity in dB ref. 1 m/s at 400 Hz for healthy, fibrotic, bronchoconstrictive, and pulmonary infiltrate cases shown in (a), (b), (c) and (d), respectively.

0.1180 s versus 32 610 s for 10 frequencies using a quad-core workstation computer with 256 GB of memory for a partial airway tree ending at Horsfield order $n = 15$. The runtime for one frequency versus ten frequencies for the full conducting tree was 44.172 and 70.833 s, respectively. Increasing the number of frequencies in both cases could be streamlined through parallel processing on multiple cores. Numerically (FE), creating a broadband simulation with 160 frequencies at once was impossible as it required too much memory. Figure 7

FIG. 7. (Color online) Comparisons of healthy and pathological cases: (a), (b) airway wall radial velocity in dB ref. 1 m/s at the midpoint of the trachea and mean terminal segment for the healthy, fibrotic, and bronchoconstrictive cases; (c), (d) airway wall radial velocity at the midpoint of the trachea and mean terminal segment for the healthy and pulmonary infiltrate cases.

depicts the simulated analytical case, which was done on a wideband frequency range from 10 to 1600 Hz in 10 Hz increments, and it required on average 600 MB of memory to solve, and computation time averaged around 300 s.

Previous analytical approaches have used a 1D branching waveguide limited to self-similar Horsfield models of the airway geometry that are less realistic. By modifying the Horsfield level of bifurcation asymmetry, or the way a parent bifurcates from order number n to order number $n - 1$ and $n - 1 - \Delta(n)$, into a recursive parent-daughter relationship, an algorithmic change was made possible to solve for acoustic transmission in a complex airway tree not bound by self-similarity. Furthermore, algorithmic changes allowed for non-bifurcating segments to be included near terminal segments. Additionally, the method of generation allows for patient-specific modeling. This hybrid image segmentation/algorithmic approach to airway tree generation has the potential to provide both a more physiologically comprehensive and patient-specific simulation capability. However, testing the sensitivity of the predictions to variations in the algorithmically-generated portion of the geometry is a possible important step in the future.

Airway acoustic pressure and wall radial velocity trends between healthy and simulated pathological conditions provided insight into possible diagnostic markers. Each pathologic case considered showed local and global differences in calculated acoustic pressure and wall radial velocity. The fibrotic case predicted a doubling of what is believed to be the Helmholtz resonant frequency to about 250 Hz [Fig. 7(a)] due to increased airway wall stiffness, and thus acoustic impedance, throughout the system. Bronchoconstrictive subjects showed a decrease in mean terminal wall radial velocity across frequencies [Fig. 7(b)], possibly because there is a significant increase in wall impedance for airways smaller than 2 mm. This also creates a larger radius disparity between larger and smaller airway segments, which may result in less acoustic energy reaching the lumen of the smaller airways in the first place.

In comparing the healthy versus pulmonary infiltrate case [Figs. 7(c) and 7(d)], there is a significant increase in mean terminal airway wall radial velocity at all frequencies. This may be due to the rigid acoustic boundary condition within the terminal segments in the affected (lower left) lobe. Pulmonary infiltrate creates an airway blockage, causing the downstream gas exchange segments to be inaccessible. This blockage causes an increased acoustic impedance, and thus increased acoustic load on the surrounding airway walls leading to increased wall radial velocity in those segments.

In all cases, both the airway acoustic pressure and wall radial velocity attenuate typically more than 50–60 dB (3 orders of magnitude) as one travels beyond 5 or 6 bifurcations from the acoustic source placed at the top of the trachea. This suggests that changes that occur in the peripheral smaller airways further downstream may have a negligible effect on the sound that ultimately reaches the torso surface. Thus, for respiratory sounds originating from the central (larger) airways, a simplified airway tree may be sufficient to simulate auscultative sounds. However, adventitious lung sounds, such as crackles and wheezes, may originate in the smaller conducting airways. For these sounds, detailed modeling of the small airway structure may be necessary to

simulate the spatial and spectral distribution of the propagated sound and its auscultative profile.

The developed analytical model can simulate the response to an array of simple (monopole) acoustic sources located anywhere in the airway tree and for any frequency. As noted previously, typical respiratory sounds will have distributed origin and broad spectral content that attenuates beyond a few kHz. The response to broadband, distributed sources can be calculated by superposition of the types of response calculations shown in this article, taking only a few minutes for the model to perform these calculations in MATLAB on a laptop computer. In addition, via an inverse Fourier transform, time domain studies with arbitrary temporal and spatial source distribution can also be conducted.

Compared to previous studies, the current analytical approach can be extended to a complete conducting airway tree that is partially based on geometry derived from a human subject CT scan merged with algorithmically developed conducting airways that are beyond CT image resolution. However, the current model does not explicitly account for the millions of microscopic alveolar segments in the gas conducting part of the tree. For small-amplitude mechanical motion in the conducting tree model where the wavelength is significantly longer than the alveolar dimensions, a Biot theory-based approach has been developed and experimentally validated previously.²⁹ This may be integrated with the analytical model for the conducting airways to extend calculations from the trachea to the alveoli.

Even with the above-noted extensions the presented modeling approach still does not account for all potential acoustic wave propagation modes within the subglottal pulmonary system. The approach neglects other wave types, such as shear or other transverse waves that may arise at structural interfaces within and on the surface of the lung parenchyma. However, shear wave propagation may only be significant at frequencies below or at the very low end of the range of interest in the current study.³⁰ As frequency increases, shear waves are expected to rapidly attenuate within the vicinity of the source. Additionally, our means of acoustic stimulation, which causes purely radial expansion of the airway walls, may not be a strong driver of shear or other types of transverse wave motion in the surrounding parenchyma, as compared to, for example, normal or shear perturbation of the surface of the parenchyma³⁰ or the torso surface.^{5,6}

VI. CONCLUSION

Sound transmission in a complex multiscale viscoelastic model of the subglottal airway tree based on a hybrid patient-specific image segmented/algorithmically grown conducting bronchial airway tree comprised of nearly 60 000 distinct airway segments was calculated using a modified 1D branching acoustic waveguide model. The new approach was validated numerically for simplified airway geometries, as well as experimentally by comparison to previous studies. The conducting airway tree was then modified to create fibrotic, bronchoconstrictive, and pulmonary infiltrate conditions. Each pathologic case resulted in local and global

differences in calculated acoustic pressure and wall radial velocity.

Future directions of development include integration of the bronchial airway model with a model of the surrounding lung parenchymal and chest wall structures to enable simulation of other acoustic wave types that may exist and be of diagnostic value and to simulate the resulting sound field that reaches the torso surface and can be measured by auscultation. More in-depth simulation studies of specific pathological conditions, supported by human subject studies, are needed to fully assess the capability of the model's potential to aid in interpretation of diagnostic measurements and design of therapeutic strategies that utilize sound.

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