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A Numerical Study of Heat and Water Vapor Transfer in MDCT-Based Human Airway Models

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Abstract

A three-dimensional (3D) thermo-fluid model is developed to study regional distributions of temperature and water vapor in three multi-detector row computed-tomography (MDCT)-based human airways with minute ventilations of 6, 15 and 30 L/min. A one-dimensional (1D) model is also solved to provide necessary initial and boundary conditions for the 3D model. Both 3D and 1D predicted temperature distributions agree well with available *in vivo* measurement data. On inspiration, the 3D cold high-speed air stream is split at the bifurcation to form secondary flows, with its cold regions biased toward the inner wall. The cold air flowing along the wall is warmed up more rapidly than the air in the lumen center. The repeated splitting pattern of air streams caused by bifurcations acts as an effective mechanism for rapid heat and mass transfer in 3D. This provides a key difference from the 1D model, where heating relies largely on diffusion in the radial direction, thus significantly affecting gradient-dependent variables, such as energy flux and water loss rate. We then propose the correlations for respective heat and mass transfer in the

airways of up to 6 generations: $Nu = 3.504 \left(Re \frac{D_a}{D_t} \right)^{0.277}$, $R = 0.841$ and $Sh = 3.652 \left(Re \frac{D_a}{D_t} \right)^{0.268}$, $R = 0.825$, where Nu is the Nusselt number, Sh is the Sherwood number, Re is the branch Reynolds number, D_a is the airway equivalent diameter, and D_t is the tracheal equivalent diameter.

Keywords

Thermodynamics; human airway temperature; water vapor; computed tomography

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CONFLICTS OF INTEREST

E. A. Hoffman is a shareholder in VIDA diagnostics, which is commercializing lung image analysis software derived from the University of Iowa lung imaging group.

1. INTRODUCTION

Thermodynamics is one of the fundamental processes in pulmonary physiology. The basic process has long been understood at the macroscopic level. During inspiration, air is heated and humidified by the airway wall until it reaches body core temperature and 100% relative humidity (RH). The location where air reaches this condition is called the isothermic saturation boundary (ISB). During expiration, the process reverses so that the exhaled saturated air cools and loses water. This partly compensates for the heat and water loss from the airway surface liquid (ASL) during inspiration. The bulk of normal air conditioning occurs in the nasal airway, but it also involves intrathoracic airways: the ISB has been reported to sit around 5cm distal to the carina during resting breathing,¹⁴ and during hyperventilation the ISB can move much further distally along the airway tree.^{15,16} At the microscopic level the heat and humidity can impact on the ciliated epithelial cells that line the airway wall (for example through evaporation of the ASL and entanglement of cilia within mucus) or can cause airway smooth muscle contraction via changes in the extracellular osmolarity of the epithelium.²⁵

Computational models for temperature and water vapor concentration have previously been developed to study thermodynamic characteristics in the human lungs. One-dimensional (1D) and two-dimensional (2D) models are the most popular methods due to their simplicity and efficiency, where temperature and water vapor concentration are obtained by solving 1D or 2D scalar transport equations^{1,2,20,24} or by solving energy balance equations based on control volume analysis.^{6,7,21} In general, temperature distributions along the airway axial direction that are predicted by 1D and 2D models agree with measurement data. However, assumptions and simplifications must be made to reduce three-dimensional (3D) governing equations and airway geometric models to 1D or 2D. The difference between 1D and 2D models is that 1D models assume radial profiles of scalars, while 2D models solve them. Because both models assume axisymmetric radial profiles of scalars, they cannot capture local variations of temperature and water vapor concentration whose local gradients are important in predicting local energy flux and water loss. Although 3D models are computationally more demanding than 1D and 2D models, they provide detailed distributions of velocities, temperature and water vapor concentration. For example, with a 3DRANS $k - \varepsilon$ model, Zhang et al.²⁹ showed asymmetric and skewed distributions of temperature and “Jet Propellant 8 fuel” vapor concentration in an idealized symmetric cylinder-based airway model.

For simulation of temperature and water vapor concentration in the human airways, an appropriate model for the wall boundary condition is crucial. The simplest approach is to assume that the airway wall remains at constant body temperature (e.g. Zhang et al.²⁹), however this cannot represent the airway wall cooling that occurs during inspiration due to evaporation and heat transfer, nor reheating of the airway wall and condensation that occurs during expiration.^{1,15,16} To represent the temperature change from the mouth to the deep lung, some studies have prescribed the airway wall temperature^{1,2,29} (or the outermost tissue layer temperature if tissue layers are considered^{6,7,21}), as a function of distance from the mouth. However, these distance-based models cannot predict temperature and humidity under different breathing conditions. Tawhai et al.²⁰ and Warren et al.²⁴ used a physics-

based approach to solve heat conduction equations through the airway wall while enforcing an energy balance at the interface between the lumen and the ASL, such that the interface temperature was determined by local energy flux (the rate of energy transfer per area). This approach allowed for a prediction of dynamic changes to the airway wall temperature during breathing, but was limited to a 1D model. The physics-based approach has not yet been used within a 3D thermo-fluid dynamics system.

Airway geometric models also influence local flow and thermodynamic variables, such as velocities, temperature and water vapor concentration. The importance and advantage of using subject-specific geometry and boundary conditions in simulation of pulmonary airflow have been discussed extensively in previous studies,^{10,12,13,27} however the impact of 3D airway geometry on airway thermodynamics has not yet been studied.

The dimensionless Nusselt (Nu) and Sherwood (Sh) numbers provide one means of characterizing the bulk heat and mass transfer in the human airways. For example, based on estimates from the first four generations of an idealized airway model, Zhang et al.²⁹ proposed that $Nu = 0.66(RePr)^{0.5}$, and $Sh = 1.727(ReSc)^{0.328}$, $Sc \approx 3$, where Pr is the Prandtl number and Sc is the Schmidt number of air. Improving the correlations of these parameters would allow better characterization of bulk heat and mass fluxes under various breathing conditions, for better design of physical and numerical experiments in studies of lung physiology and pathophysiology.

The objectives of this study are three-fold. First, we aim to develop a 3D computational thermo-fluid dynamic (CFD) lung model with a realistic wall boundary condition in a subject-specific airway geometric model. Second, the effect of asymmetric flow characteristics and the inter-subject variability of scalar transport are investigated. Finally, the dimensionless parameters of Nu and Sh for the airways up to six generations are computed and their correlations with airway branch diameter and local Re are derived. The ultimate goal is to integrate the above model with a model of epithelial cell fluid transport²⁴ for the study of periciliary liquid water homeostasis.¹²

2. MATERIALS AND METHODS

2.1. MDCT images and geometry modeling

Geometric models of the airways were reconstructed from volumetric multi-detector row computed-tomography (MDCT) imaging. Three healthy non-smoking subjects (see Table 1) that were recruited and imaged under previous studies (NIH grants HL064368 and EB005823) were used here. CT imaging was approved by the University of Iowa Institutional Review Board and Radiation Safety Committee. Subjects gave informed consent for the imaging study and subsequent use of their data for computational studies. Subjects were scanned using a Siemens Sensation 64-slice MDCT scanner (Forchheim, Germany) with scan parameters: 120 kV, 75-100 mAs, 0.75-0.13 mm slice thickness, 0.5-0.6 mm slice spacing, 1.00-1.25 pitch, and B35 reconstruction kernel. Subjects were imaged while supine during a breath-hold at near total lung capacity.

3D geometric models were reconstructed from MDCT using the ‘Apollo’ software (VIDA Diagnostics, Coralville, Iowa); this resolved up to six or seven generations of airways. At the ending segments of the MDCT-resolved central airways, anatomically-consistent 1D trees that extended as far as the terminal bronchioles (about 23 generations) were generated using the volume filling algorithm of Tawhai et al.²⁰, subject to the MDCT-resolved airways and lobar boundaries. For each subject, both 3D geometric models and their corresponding 1D skeletons are shown in Figs. 1 (a)-(c). The 1D airway models start from the top of the trachea, while the 3D models include the upper airways that start from the oral cavity.

2.2. Governing equations

The 3D CFD model solved the incompressible Navier-Stokes equations. Large-eddy simulation was adopted for modeling turbulent flow.^{10,12,13,27} The continuity and momentum equations read:

$$\frac{\partial u_i}{\partial x_i} = 0 \quad (1)$$

$$\frac{\partial u_i}{\partial t} + u_j \frac{\partial u_i}{\partial x_j} = -\frac{1}{\rho} \frac{\partial p}{\partial x_i} + g'_i + (\nu + \nu_T) \frac{\partial^2 u_i}{\partial x_j \partial x_j} \quad (2)$$

Here Einstein summation notation is invoked. u_i is the filtered velocity component in the i -direction ($i = 1, 2, 3$ or x, y, z), p is the pressure, and ν_T is the Vreman's subgrid-scale eddy viscosity²³, which reduces to zero if the flow is laminar. The buoyancy force is computed with Boussinesq approximation of constant density ρ , and $g'_i = -\beta T'_\nu g_i$, where $g_i = (0, 0, -g)$, g is the gravitational acceleration and β is the coefficient of volumetric expansion of air. T'_ν is the virtual temperature that dry air must have to have the same density as moist air at the same pressure, $T'_\nu = T' / (1 + 0.61\gamma)$. $T' = T - T_a$, where T_a is the atmospheric temperature. γ is the mixing ratio m_v/m_d , where m_v is the water vapor mass and m_d is the dry air mass. The pressure-Poisson equation that is derived by taking the divergence of Eq. (2) was solved to satisfy the continuity of Eq. (1).

The transport equations for temperature (T) and water vapor concentration (C) read:

$$C_p \rho \frac{\partial T}{\partial t} + C_p \rho u_i \frac{\partial T}{\partial x_i} = (k + k_T) \frac{\partial^2 T}{\partial x_i \partial x_i} \quad (3)$$

$$\frac{\partial C}{\partial t} + u_i \frac{\partial C}{\partial x_i} = (D + D_T) \frac{\partial^2 C}{\partial x_i \partial x_i} \quad (4)$$

where C_p is the thermal capacity of moist air and k_T is the turbulent conductivity, $\frac{k_T}{C_p \rho} = \frac{\nu_T}{Pr_t}$

D_T is the turbulent diffusivity of water vapor in air, $D_T = \frac{\nu_T}{Sc_t} \cdot Pr_t (Sc_t)$ is turbulent Prandtl (Schmidt) number of water vapor in air; both Pr_t and Sc_t are taken as 0.9.²⁹ The

characteristic Galerkin finite element method was used to discretize the above equations, and the fractional four step method was used to solve them. The validation of the solver can be found in a previous study.¹¹

2.3. Inlet and outlet boundary conditions

An image registration-based subject-specific flow boundary condition²⁷ was adopted. Two MDCT image datasets at different lung volumes from the same scanning session were matched using a mass-preserving image registration method to estimate the ventilation rate at the end of each terminal bronchiole of the 1D tree.²⁷ These ventilation rates were then used to derive flow conditions at the distal end of the terminal central airways for 3D CFD simulations. Parabolic profiles for velocity were prescribed at both inlets and outlets. A sinusoidal breathing waveform was used. The maximum flow rate was only a function of

minute ventilation (MV , L/min) as $\dot{V}_{max} = \frac{\pi}{t_T} \times tidal\ volume = \frac{MV \times \pi \times 10^{-3}}{60}$, in which t_T is the breathing period.

For temperature and water vapor concentration, the boundary conditions follow:

$$\left\{ \begin{array}{l} \Phi_0 = \Phi_1 \\ \frac{\partial \Phi_L}{\partial n} = 0 \end{array} \right. \quad (\text{Inspiration}); \quad \left\{ \begin{array}{l} \frac{\partial \Phi_0}{\partial n} = 0 \\ \Phi_L = \Phi_E \end{array} \right. \quad (\text{Expiration}) \quad (5)$$

where $\phi = T$ or C . The subscript o denotes the mouth cavity for the 3D model, or the top of the trachea for the 1D model, and L denotes the ending faces at the terminal airways in the 3D model or the 1D model. At the flow inlets, the air conditions were prescribed, where the subscript I represents inspired T or C at the mouth entrance for the 3D model, or the top of the trachea for the 1D model. The subscript E represents expired T or C at the ending faces of the terminal airways in 3D or 1D. Gradient-free conditions were prescribed at the flow outlets.

2.4. Airway wall boundary condition

For the momentum equation (2), the no-slip condition was imposed at the airway wall. For the T transport equation (3), energy balance was enforced across the wall boundary so that the energy exchange between the lumen and the ASL equals the heat conducted through the airway wall. For the C transport equation (4), 100% RH was assumed at the interface of the lumen and the ASL.

To provide the wall boundary conditions for T and C , a heat conduction equation through the airway wall tissues and the ASL (see Figs. 1 (e-g)) was solved. Two parameters need to be determined: 1. the thermodynamic properties of the airway wall tissues, and 2. the distance (or thickness) from the airway wall to a location that remains at body temperature during ventilation. Most of the tissues in the airway wall contain a high amount of water and their thermodynamic properties are close to those of water.⁵ Thus, a tissue of uniform water properties was assumed, which is the same as the ASL. In order to determine the thickness, the behavior of the 1D heat conduction equation was examined with boundary conditions of fixed temperature on one side and oscillating energy flux on the other side (see Fig. 1 (f)).

We found that after reaching quasi-steady state, only a small portion of the tissue undergoes temperature fluctuations, and the temperature of the other portion of the tissue remains unchanged. Therefore, a two-layer wall model was adopted with one layer capturing the transient response and the other layer representing the steady portion. The heat conduction equation for the two-layer wall model reads:

$$\frac{\partial T_i}{\partial t} = \alpha_i \left[\frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial T_i}{\partial r} \right) \right], \quad (6)$$

where the subscript $i=1$ (or 2) denotes the transient layer (or the steady layer). $\alpha_i = \frac{k_i}{C_{pi}\rho_i}$ is the thermal diffusivity of layer i . For the transient layer, which includes the ASL, the temperature fluctuation is caused by the oscillating energy flux during respiration. Its thickness is dependent upon the breathing period (estimated at 0.4 mm via the 1D model for 2s breathing period). For the steady layer, the temperature profile depends on the net energy flux during respiration. The temperature at its interface with the transient layer is denoted as T_m . With known net energy flux, T_m can be determined by the thermal resistance per area.

The thermal resistance is given by $R_{resist} = \frac{l_2}{k_2}$, where l_2 and k_2 are the thickness and the thermal conductivity of the steady layer, respectively. Because k_2 appears in Eq. (6) as

$\alpha_2 = \frac{k_2}{C_{p2}\rho_2}$, the parameter $R' = \frac{l_2}{\alpha_2}$ was calibrated using the 1D model against McFadden et al.'s data¹⁶ at 15 and 30 L/min with room air (27.6 °C, RH = 34.7%) and frigid air (−18.5 °C, RH = 5%).

Two boundary conditions are needed to solve Eq. (6). At the outer wall of the steady layer, body temperature was prescribed. At the ASL-lumen interface, the energy balance equation was enforced as in Tawhai et al.²⁰, where the energy flux by conduction at the ASL side of the interface equals the energy flux by conduction plus the latent heat of phase change at the lumen side.

$$k_{asl} \frac{\partial T}{\partial r} \Big|_{R^+} = (k + k_T) \frac{\partial T}{\partial r} \Big|_{R^-} + (D + D_T) \Delta H \frac{\partial C}{\partial r} \Big|_{R^-} \quad (7)$$

where k_{asl} is the thermal conductivity of the ASL. $k(k_T)$ is molecular (turbulent) conductivity for moist air. $D(D_T)$ is molecular (turbulent) diffusivity of water vapor in air. R^+ denotes the ASL side of the interface, while R^- denotes the lumen side. The finite element method was used to discretize Eqs. (6) and (7).

The water vapor concentration at the interface was assumed to be at 100% RH, and the saturated water vapor concentration was solely a function of temperature:

$$C_R = \frac{2.166 \times 10^{-3}}{T_R} \exp \left(\lambda_1 + \frac{\lambda_2}{T_R} + \lambda_3 \ln(T_R) + \lambda_4 T_R^2 \right) \quad (8)$$

where $\lambda_1 = 73.649$, $\lambda_2 = -7258.2$, $\lambda_3 = -7.3037$ and $\lambda_4 = 4.165 \times 10^{-6}$.²⁰ By solving Eqs. (6-8), the interfacial temperature and water vapor concentration were obtained, providing essential boundary conditions for the transport equations. Iteration was performed between the conduction equation and the scalar transport equations to yield a converged solution at any time step. Figure 2 shows the procedures of performing the 3D CFD thermodynamics simulation in the MDCT-based human airway model.

2.5. Simulation set-up and mesh sensitivity test

Three cases for each of three subjects with the room air condition of 27.6 °C and 34.7% RH (thus a total of nine cases) were simulated (Table 2). Minute ventilations for Cases 2 and 3 were chosen so that they could be validated against the measurement data of McFadden et al.,¹⁶ while minute ventilation of Case 1 corresponds to a resting breathing case. For each minute ventilation the breathing period may vary, but this has little influence on the final solution of temperature.²⁰

Since the airway geometry starts from the top of the trachea in the 1D model, on inspiration T_I (see Eq.(5)) is taken from the measurement data of McFadden et al.¹⁶ and C_I is calculated from Eq. (8) with 95% RH taken from the 3D CFD simulations. For the 3D model, the conditions of 27.6 °C and 34.7% RH reported in McFadden et al. were used at the mouth inlet. On expiration, at the ending branches of the 1D airway tree, body temperature of 36.5 °C and 100% RH were used.²⁰ Since the 3D model only has up to six or seven generations and the ISB can be located downstream of these branches, the 1D results on expiration at the corresponding 3D model distal branch locations were specified as time-varying boundary conditions. For the 1D model, the tissue temperature was uniformly initialized to body temperature, and after 200 breaths the tissue temperature reached a quasi-steady state. The 1D quasi-steady state tissue temperature at end expiration was then used as the initial condition for tissue temperature in the 3D model. The 3D upper airway was included to capture the laryngeal jet,¹³ and the wall temperature and humidity of 33.5 °C and 100% RH were adopted for the airway above the glottis.²¹

Tetrahedral meshes were used for 3D CFD simulations (see Table 1). First, a mesh sensitivity test was performed on subject A at 15 L/min using three meshes with densities of 21.4, 37.3 and 73.6 $\times 1000/\text{cm}^3$, and with average y^+ (a non-dimensional distance of the first grid point from the wall) = 5.6, 6.9 and 8.2, respectively, in the trachea at peak inspiration. Energy flux (Eq. (7)) was computed for assessment because of its dependence on the wall temperature gradient. As compared with the fine-mesh result, the differences of the overall energy flux integrated over the entire CT-resolved central airway during inspiration (expiration) were 4.17% (9.78%) for the coarse mesh and 2.77% (4.19%) for the medium mesh. The differences by generation for the medium mesh were (3.43, 3.35, 3.03, 3.32, 1.40, 2.16, 0.95) % on inspiration and (1.83, 6.84, 4.85, 3.90, 6.14, 6.27, 6.50) % on expiration for generations (0,1,2,3,4,5,6). The errors are greater at the inlets than the exits for both inspiration and expiration, which may be due to relatively large evaporative flux at generation 6 on inspiration and large condensation flux at generation 0 (trachea) on expiration. Then, the sensitivity test was performed on the same subject at 30 L/min on the medium and fine meshes to quantify the maximum error. The error was 6.44%, as compared

with 6.61% for the coarse mesh and 3.16% for the medium mesh at peak inspiration of 15 L/min.

For the ASL and the tissue layer, the 1D mesh was generated at each node on the airway wall along the wall-outward normal direction. As shown in Fig. 1 (g), the 1D mesh consists of seven nodes: nodes N1 and N2 (with a spacing of $10\ \mu\text{m}^{26}$) are for the ASL, nodes N2, N3, N4, N5 and N6 (with a uniform spacing of 0.1 mm) are for the transient tissue layer, and nodes N6 and N7 (with a spacing of 0.1 mm) are for the steady tissue layer. As the ASL is much thinner than the overall transient layer, the change of ASL depth is negligible. The temperature at node N1 is referred to as the interface temperature T_R , and the temperature at N6 is denoted as T_m , while the average lumen temperature is denoted as T_0 . Table 3 summarizes all of the model parameters.

3. RESULTS

3.1. Temperature and humidity distributions

The predicted 1D and 3D temperature distributions in the airway were validated against the measurement data of McFadden et al.¹⁶ In this previous study the authors inserted a probe with seven consecutive sensors, from the nasal cavity through the trachea and along the path marked by the landmarks in Fig. 1(d) into the right lower lobe (RLL). The spacing between sensors was about 4.3 cm, and the first sensor was placed about 2 cm below the glottis. Because the last sensor was placed beyond the most distal airways in two of our 3D models, and the fourth sensor malfunctioned, we compared the 1D and 3D CFD data along the same path using only the data measured from the first five normal sensor locations. Figures 3 (a)-(d) display the average values of temperature based on the three subjects. Both 1D and 3D data are generally consistent with the measurement data. A slight discrepancy was found between the most distal measurement point and the 3D data at end expiration for 30 L/min; the model predicted a temperature about 1 degree lower than the experiment. The 1D data shows very little difference between the three subjects before entering the AS (see Fig. 1 (d)), and the 3D data shows that the difference between these subjects is generally within 0.3 °C. The average discrepancies between the 1D model and the measurements are 0.28 °C for 15 L/min and 0.26 °C for 30 L/min. The average discrepancies between the 3D model and measurements are 0.24 °C for 15L/min and 0.27 °C for 30 L/min. Besides the measurement data of McFadden et al.¹⁶, Martonen et al.¹⁵ reported other measurement data that the temperature in the trachea mostly varies between 31.2 and 34.5 °C during inspiration, and between 32.6 and 37 °C during expiration, and the temperature after the carina mostly varies between 32.2 and 34.6 °C during inspiration, and between 33.7 and 36.0 °C during expiration. For our 3D CFD data, the temperature in the trachea varies between 31.4 and 34 °C during inspiration, and 32.8 and 35.0 °C during expiration, and the temperature after the carina varies between 32.1 and 34.4 °C during inspiration and between 33.5 and 35.8 °C during expiration. Thus, our CFD data agree with these measurement data as well.

Figures 3 (e)-(h) show the distributions of absolute humidity (water vapor concentration) and relative humidity along the same path as in (a)-(d). As both water vapor concentration and temperature are passive scalars, their distributions and characteristics are quite similar, only differing by the diffusion rate (2.2×10^{-5} for T and 2.7×10^{-5} for C). However, relative

humidity is quite different. During inspiration, the relative humidity is generally above 95% from the glottis, and quickly increases to 100%. The 1D model predicted saturation (100% RH) immediately after the carina, whereas the 3D model predicted that 100% RH was reached slightly beyond the ORLas marked in Fig. 1 (d), suggesting that unsaturated air penetrates deeper in the 3D airway model. During expiration, the relative humidity remained at ~100% in both 1D and 3D model data. As relative humidity is determined by local temperature, absolute humidity decreased on exhalation due to condensation of water on the ASL. For the same reason, even if both the interface and the lumen air were at 100% RH, evaporation or condensation may continue to occur because of local temperature and absolute humidity differences. Since absolute humidity and temperature exhibit similar distributions, only the temperature data are presented in later sections.

3.2. Lumen temperature in 1D trees and 3D central airways

The lumen temperature varies during ventilation. To illustrate this, the spatial distributions of 1D and 3D lumen temperatures of subject A for 15 L/min are shown in Figs. 4 and 5, respectively, at four time points: peak inspiration, end inspiration, peak expiration and end expiration. For the 1D model, the lumen temperature gradually increased until reaching the ISBs, which varied in location during ventilation. The ISB was located at approximately the 8th-9th generation in the upper lobes. As the lower lobes have higher ventilation rates, the ISBs in the lower lobes penetrated as far as the 10th-12th generations on peak inspiration.

For the 3D model, the iso-surfaces of 32 °C and 32.5 °C on inspiration and those of 34.5 °C and 35 °C on expiration are shown in Fig. 5. On peak inspiration or expiration, the temperature gradient at the ASL-lumen interface is much greater than that on end inspiration or expiration, since the airway wall has little time to warm or cool the air. The radial profile of temperature in 3D is not axisymmetric as assumed in 1D. The cold air tends to penetrate further into the lower lobes, particularly on peak inspiration, which may be attributed to the formation of secondary flows after the inspired air passes over the carina. All other cases exhibited similar lumen temperature distributions at the four time points.

3.3. Energy transfer at bifurcations

To inspect the features of secondary flows during inspiration, Fig. 6 (a) shows six streamlines near three bifurcations marked as B₁, B₂ and B₃ in the RLL. The streamline passing over B₁ is warmed by the inner surface of the bifurcation. The air pressing against B₁ then moves downstream toward the center of the lumen, impacts on bifurcations B₂ and B₃, and then flows along the surfaces of the respective daughter branches. Figure 6 (b) shows another example with three bifurcations marked as B₄, B₅ and B₆ in the left upper lobe (LUL) with several branches oriented upwards. Similar characteristics as in Fig. 6(a) are still observed. In fact, the same flow pattern begins at the carina where the cold high-speed air stream near the lumen center is split at the bifurcation to form secondary flows with its cold regions biased toward the inner wall. The cold air flowing along the wall is being warmed up much faster than the air in the lumen center. Unlike the 1D model that relies solely on diffusion in the radial direction of an axisymmetric profile to warm the central cold air, the repeated splitting and warming of cold airstreams acts as an efficient mechanism of enhancing energy transfer in the 3D airway branching structure.

3.4 Airway wall boundary model

Figure 7 (a) shows the time histories of the 1D ASL-lumen interface temperatures (T_R) at six selected locations along the path defined in Fig. 1 (d). T_R was initially set at body core temperature. The oscillations correspond to respiratory cycles. The phase-averaged T_R decreases with time until the net energy flux into the lumen is balanced by the energy flux through the tissue, when lumen temperature, energy flux and tissue temperature all reach quasi-steady states. T_R at a proximal location exhibits greater fluctuations than at a distal location. Figure 7 (b) shows the time histories of 1D instantaneous energy fluxes at three selected locations along the same path as before. The net energy flux at quasi-steady state decreases with increasing distance from the top of the trachea, with a net energy loss of 190, 112 and 34 J/m²/per cycle at $x = 4.3, 17.1$ and 27.0 cm, respectively. The higher net energy flux (or the net energy loss per cycle) results in lower T_R as shown in Fig. 7(a). Figures 7 (c) and (d) show that the 1D and 3D average lumen temperatures, T_θ , and their corresponding interface temperatures, T_R , oscillate with flow rate during respiration, agreeing with the measurement of Primiano et al.¹⁹ Figures 7 (e) and (f) show that the end inspiration (expiration) T_R is higher (lower) than the corresponding T_θ over the entire airways for both 1D and 3D models. The reverse in magnitude of these two temperatures ($T_R > T_\theta$ on inspiration vs. $T_R < T_\theta$ on expiration) is an important feature of air conditioning in the airways.

3.5. Dimensionless parameters

The Nu is the ratio of convective to diffusive heat transfer, and the Sh is its counterpart for mass transfer. Figures 8 (a) and (b) show the distributions of local Nu , Sh and $Re(D/D_t)$

along with the proposed correlations: $Nu = 3.504 \left(Re \frac{D_a}{D_t} \right)^{0.277}$, $R = 0.841$ and

$Sh = 3.652 \left(Re \frac{D_a}{D_t} \right)^{0.268}$, $R = 0.825$, during peak inspiration for the three subjects at three levels of minute ventilation. D_a is the local equivalent diameter computed as $D_a = (4A_L/\pi)^{1/2}$, where A_L = local cross-sectional area, D_t is the equivalent diameter of trachea, and $Re = 4flr/\pi\nu D_a$, where flr is the local flow rate at peak inspiration. The correlation proposed by Zhang et al.²⁹ is also displayed for comparison with $R = 0.641$ for Nu and $R = 0.624$ for Sh . Figures 8 (c) and (e) show that the Nu and Sh values predicted by the proposed correlations are overall more consistent with the 3D CFD computed values than those predicted by Zhang et al. in Figs. 8 (d) and (f).

4. DISCUSSION

4.1 1D vs. 3D

The main objective of this study was to develop a subject-specific 3D model for study of heat and mass transfer in the human airways. The corresponding 1D model was utilized to provide necessary initial and boundary conditions for the 3D model. Mathematically, the 1D model includes convection and diffusion in the axial direction, but it only includes diffusion in the radial direction with assumed radial velocity and scalar profiles. These

profiles take the axisymmetric form of $\Phi(r) = \Phi_R + (\Phi_0 - \Phi_R) \left(1 - \left(\frac{r}{R}\right)^\theta\right)$, $\phi = T, C, \text{ or } U$, where θ is empirically determined to fit measurement data. As the average lumen temperature strongly depends on the ASL-lumen interface temperature, with an interface temperature profile that lies between the temperature profiles at end inspiration and end expiration as shown in Figs. 7 (e) and (f), both 1D and 3D models can reasonably predict scalar transport along the axial direction as shown in Fig. 3. Nonetheless, the 3D model reveals local non-axisymmetric distributions of temperature and water vapor concentration due to secondary flows in a complex airway geometry, which are essential in accurate estimation of local energy flux and water loss rate. In particular, the 3D model creates relatively large gradients of temperature and water vapor concentration at bifurcations that enhance heat and mass flux. Therefore, as inspired air traverses down the airways it is heated and humidified at a faster rate than is represented by the 1D model, not only because airway surface area increases, but also because the central cold air streams are repeatedly split and effectively warmed up by the surface at the bifurcations. The above 3D mechanism is important in predicting water loss from the epithelia cells in different regions, which contributes to the overall energy loss as latent heat. This cannot be modeled using a standard 1D approach. For example, consider the water loss rate (defined as the net water loss per area per min) in the CT-resolved airways at 15 L/min. For the three 3D cases, the average water loss rates at generation (1,2,3,4,5,6) show an increase of (17.7, 25.0, 40.4, 33.4, 39.7, 40.9)% with respect to the rate at the trachea, due to the above mechanism. In contrast, for the three 1D cases the average water loss rates at generation (1, 2, 3, 4, 5, 6) show a decrease of (51.6, 60.0, 66.8, 71.1, 73.4)% with respect to the rate at the trachea. Note that the trachea is still responsible for most of the air conditioning compared with any other generation in both the 1D and 3D models due to its greater surface area, but the thermal input (or the net water loss) into local individual cells are much higher in the 2nd to 6th generations of the 3D model because of secondary flows. Without capturing this 3D phenomenon, the 1D model predicts the opposite trend. Moreover, as shown in Figs. 5 (a) and (b), the secondary flow at the carina also results in distributing a greater portion of cold air into the lower lobes. As a result, the lower lobes may condition more cold air in the 3D model than the 1D model.

4.2 Inter-subject variability

The subject-specific ventilation distribution influences the temperature and humidity distributions. The higher the local ventilation, the more air that needs to be conditioned in a given amount of time. As shown in Fig. 4 for the 1D results, the ISBs in the lower lobes are located more distally than in the upper lobes because of the higher local ventilation in the lower lobes. The 3D results show similar trends, as the lumen temperature in the upper lobes increases faster than in the lower lobes (see Fig. 5). However, as all three subjects have relatively large air ventilation to the lower lobes, the inter-subject differences in average temperature and humidity at end inspiration and expiration along the path are only ~0.3 °C and 1.5 g/m³. It is worth noting that even though the subject-specific geometry and boundary conditions might not have a significant influence on the bulk temperature and humidity distributions considered here, its importance is reflected in the local gradient terms

found in the calculation of heat and mass fluxes. For example, considering the water loss rate of the three 15 L/min cases, the inter-subject variability in each generation (up to the 6th generation) is around 10% to 20% for the 3D model and 5% to 10% for the 1D model. Thus, the distributions of average temperature and humidity are more sensitive to the interface temperature distribution than other factors, such as the specific mathematical model, ventilation distribution, or airway geometries. However, heat and mass fluxes across the interface are very sensitive to the local gradients of temperature and humidity, even for regions with only 0.3°C of average temperature difference at roughly 100% RH (e.g. 5th generation in RLL): the standard deviation in the water loss rate between the three subjects at 15 L/min is about 15% of the average value.

4.3 Dimensionless Correlations

We proposed new correlations for Nu and Sh with $Re(D_a/D_t)$, allowing estimation of bulk heat and humidity by airway generation under various breathing conditions. These correlations may be useful for understanding the role of heat and humidity in airway pathophysiology (e.g. as a trigger of asthmatic bronchoconstriction) and potentially for improving design of medical devices (e.g. humidification in mechanical ventilation). As compared with Zhang et al.'s study,²⁹ the proposed correlations were fitted to data from airways up to the 6th generation in three different subjects for three different flow rates, while Zhang et al.'s correlation was based on an idealized cylinder-based geometry with data points from the trachea to the 3rd generation. As subject-specific geometries and breathing conditions are used, the proposed correlations take into consideration the effects of both Re and local airway diameter, indicating that local flow rate is most likely to determine the Nu and Sh in the airways. Thus, this supports the importance of using subject-specific ventilation distribution. This also implies that if the local flow rate remains constant during airway constriction, both convective and diffusive heat and mass transfer may increase at constricted areas. Alternatively, if the local flow rate drops due to constriction, the Nu and Sh would decrease, resulting in more diffusive heat and mass transfer. When applying these correlations to asthmatics,²² the Nu and Sh could increase (decrease) in association with expanded (constricted) branches and altered ventilation, altering local heat and mass transfer. However, there are some data points that deviated from the correlations at the low Re region, with higher Sh or Nu , i.e. having high convective heat or mass transfer at even lower flow rate. These data points are usually found near the bifurcations. Thus, the proposed correlations could under-predict heat and mass transfer near the airway bifurcations.

4.4 Wall boundary conditions

The wall boundary condition is crucial in modeling airway thermodynamics. The ASL-lumen interface temperature is non-uniformly distributed in the airway and is not a simple function of the distance from the mouth. Moreover, the interface temperature must be able to oscillate with flow during ventilation. Because of these requirements, a two-layer wall model was adopted, in which one layer represents transient energy flux and the other represents net energy flux. The transient layer must allow fluctuation of the interface temperature in response to the oscillating energy flux for the model to agree with measurements,¹⁹ and to avoid over-prediction of instantaneous energy flux. The interface temperature has a smaller

fluctuation than the lumen temperature, ensuring that it is always higher (lower) than the lumen temperature during inspiration (expiration) to warm up (cool down) the air. As shown in Figs. 7 (e) and (f), the inspiratory and expiratory interface temperatures increase with distance into the airways, but they always stay between the inspiratory and expiratory lumen temperatures.

The important variable in the steady layer is the temperature T_m at the interface between the transient layer and the steady layer because the ASL-lumen interface temperature T_R usually fluctuates around a value close to the magnitude of T_m . The equilibrium value of T_m is determined by the net energy flux and the thermal resistance of the steady layer. As shown in Fig. 4, the upper lobes saturate at a shorter distance from the trachea than the lower lobes because of smaller energy flux in the upper lobes. Thus, T_m must be adjusted dynamically to increase more rapidly with distance in the upper lobes, which can only be achieved via simulating energy flux using the two-layer energy balance-based boundary condition rather than prescribing temperature.^{1,2,6,7,21,29}

4.5 Conclusions and limitations

In summary, the 3D model can provide detailed local temperature and humidity data, and the proposed correlations from the current model can be used to estimate local convective heat and mass fluxes. One potential source of error in the current model is that, when solving the water vapor concentration transport equation, it is possible for some small regions to exceed 100% RH. In these regions water vapor should condense into water droplets, however this is a complex phenomenon that was not considered in the model. In the current results, the liquid to vapor ratio was generally less than 0.05%, therefore the formation of droplets was neglected. Specifically, at the regions where RH exceeded 100% the water vapor concentration was set to 100% RH, meaning that only the vapor portion at these regions was considered. A further potential source of error is, the assumption of 100% RH at the ASL-lumen interface. Based on the human water activity coefficient $S = 0.995$,³ the RH at the interface could be 99.5%. A test case using subject C at 6 L/min gave differences of overall energy fluxes in the central airways of only 2.96% and 4.12% on inspiration and expiration, respectively, for 100% and 99.5% RH.

The current model could readily be coupled with particle tracking to study the deposition of hygroscopic aerosols whose sizes vary with humidity,⁴ and/or the predicted evaporative flux from the ASL could be coupled with an epithelial cell model²⁴ to predict the hydration state of the periciliary liquid.¹² While the 3D model could immediately be used for these applications, it has several limitations that limit its application to very generalized studies. First, the non-linear deformation of the airway^{8,28} and the change of regional ventilation distribution²² during respiration were not considered. Second, the tissue properties and the tissue and ASL thicknesses were assumed to be uniform over the entire lung, and only 1D heat conduction in the wall normal direction was considered in the tissue layer for simplicity and computational efficiency. Third, the study only considered air-water vapor, therefore the proposed correlations did not include Pr for use of different gases⁹ and could under-predict heat and mass transfer near bifurcations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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FIGURE 1.

3D CT-based airway geometric models overlapped with 1D airway models (up to the 5th Horsfield order) of: (a) subject A, (b) subject B and (c) subject C. (a) LUL, left upper lobe (blue); LLL, left lower lobe (green); RUL, right upper lobe (yellowish-green); RML, right middle lobe (yellow); RLL, right lower lobe (red). (d) Anatomical landmarks according to McFadden et al.¹⁶: ORL, orifice of RLL; AS, anterior segmental bronchus; Seg-1, sub-segmental bronchus. The temperature data measured by McFadden et al.¹⁶ along the path following these landmarks are compared with the both 1D and 3D CFD predictions. (e) Schematic of the cross section of the two-layer tissue model. (f) Schematic of the tissue temperature distribution. In the physical model, the radius of the interface is R . The radius of the transient layer is R_1 , where tissue temperature stays at T_m after reaching quasi-steady state. The radius of the steady layer is R_2 , where temperature is fixed at body temperature T_b . Solid line represents the tissue temperature profile at the end of inspiration where the interface temperature equals T_i , while dashed line represents the tissue temperature profile at the end of expiration where the interface temperature equals T_e . (g) Schematic of the 1D mesh for the tissue model. There are a total of seven nodes, denoted by N_i , where $i=1,2,3,4,5,6,7$.

FIGURE 2.

The flow chart illustrating the procedures to perform the 3D CFD thermodynamic simulation using a MDCT-based human airway model. Two MDCT scans were required at (a) close to the total lung capacity (TLC), and (b) close to the functional residual capacity (FRC). (c) 3D airway geometry was generated from the CT image at TLC by ‘Apollo’ software. (d) 1D tree was generated from 3D geometry by the volume filling method.²⁰ (e) The two images were used to generation regional ventilation by image registration.²⁷ (f) With the regional ventilation and 1D tree, the flow rate distribution of 1D airway can be computed. (g) 1D CFD was run to determine the quasi-steady state boundary conditions for temperature and water vapor. (h) 3D flow rate distribution at the outlets can be determined from the 1D airflow obtained from (f). (i) With all the inputs, 3D CFD simulation can be conducted.

FIGURE 3.

Validation of temperature distributions predicted by (a) and (c) 1D model, and (b) and (d) 3D model at 15 L/min and 30 L/min. Distributions of absolute humidity and relative humidity of (e) and (g) 1D model, and (f) and (h) 3D model at 15 L/min and 30 L/min. Experimental temperature data were taken from McFadden et al.¹⁶ along the path depicted in Fig. 1 (d). For the 1D CFD data, the error bars present the standard deviation between three subjects. For the 3D CFD data, the error bars present the standard deviation within the three spheres extracted from three subjects at the locations with same distances from the top of the trachea.

FIGURE 4.

Distributions of the 1D lumen temperature of subject A with 15 L/min at four time points: (a) peak inspiration, (b) end inspiration, (c) peak expiration, and (d) end expiration. Airway branches after ISB are blanked.

FIGURE 5.

Distributions of the 3D airway lumen and wall temperatures of subject A with 15 L/min at four time points: (a) peak inspiration, (b) end inspiration, (c) peak expiration, and (d) end expiration. The iso-surfaces of the lumen temperatures of 32 °C and 32.5 °C are plotted in (a) and (b). The iso-surfaces of the lumen temperatures of 34.5 °C and 35 °C are plotted in (c) and (d). Cross-sectional temperature contours are displayed at four locations at each time point.

FIGURE 6.

Cold air streams marked with streamlines color-coded with temperature at 6 L/min of subject A in: (a) RLL (the region with temperature above 34 °C is blanked); (b) LUL (the region with temperature above 34.5 °C is blanked).

FIGURE 7.

(a) Time histories of the ASL-lumen interface temperatures T_R at six locations in the 1D model along the path defined in Fig. 1 (d); (b) Time histories of energy fluxes across the ASL-lumen interface at three locations along the path as in Fig. 1 (d). The distance x of each location from the top of the trachea is labeled. The time histories of 1D (c) and 3D (d) interface temperatures T_R and average lumen temperature T_0 at the middle of trachea of subject C at 15 L/min. The interface temperature T_R and the average lumen temperature T_0 at end inspiration and end expiration of 1D (e) and 3D (f) as a function of distance along the path as in Fig. 1(d).

FIGURE 8.

The correlation between: (a) Nu and $Re (D_a/D_t)$, (b) Sh and $Re (D_a/D_t)$. The correlation proposed by Zhang et al.²⁹ is also plotted for comparison with $D_a/D_t = 1$ because their correlation does not depend on D_a ; (c) Nu predicted by the 3D CFD results are plotted against the values predicted by the proposed correlations for Nu (c) and Sh (e) and by Zhang et al.'s correlation for Nu (d) and Sh (f). The identity solid lines are plotted for comparison.

Table 1

Subject Information

	Age/Gender/Race	BMI	Total Volume(L)/Mesh Size (Million)	% Vital Capacity	Ventilation Distribution *	
Subject A	32/ Male/ White non-Hispanic	21.6	0.215/ 9.76	85	LUL	0.148
					LLL	0.348
					RUL	0.126
					RML	0.060
					RLL	0.319
Subject B	20.0/ Male/ White non-Hispanic	22.33	0.128/ 5.71	78	LUL	0.208
					LLL	0.279
					RUL	0.186
					RML	0.064
					RLL	0.264
Subject C	69.0/ Female/ White non-Hispanic	26.63	0.170/ 7.76	98	LUL	0.185
					LLL	0.281
					RUL	0.123
					RML	0.056
					RLL	0.355

* LUL, left upper lobe; LLL, left lower lobe; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe.

Table 2

Cases Set Up

	Minute Ventilation (L/min)	Period (s)	Tidal Volume (L)	Maximum Flow Rate (L/s)	Maximum Re in Trachea
Case 1	6	5	0.5	0.314	1180~1380
Case 2	15	2	0.5	0.785	2960~3450
Case 3	30	2	1	1.57	5910~6890

Table 3

Summary of Parameters

Parameter	Description	Value	Unit	Ref.
k	Molecular conductivity of moist air	2.68e-02	$\text{J m}^{-1}\text{s}^{-1}\text{K}^{-1}$	20
D	Molecular diffusivity of water vapor in air	2.7e-05	$\text{m}^2 \text{s}^{-1}$	20
Cp	Thermal capacity of moist air	1080	$\text{J kg}^{-1} \text{K}^{-1}$	20
ρ	Density of moist air	1.12	kg m^{-3}	20
α_1	Thermal diffusivity of layer 1 (water properties)	1.43e-07	$\text{m}^2 \text{s}^{-1}$	20
k_{asl}	Conductivity of ASL (water properties)	0.6	$\text{J m}^{-1} \text{s}^{-1} \text{K}^{-1}$	20
H	Latent heat of vaporization	2.41e06	J kg^{-1}	20
ν	Kinematic viscosity of moist air	1.65e-05	m^2s^{-1}	17
β	Coefficient of volumetric expansion of air	3.22e-03	K^{-1}	18
R'	Steady layer thermal property	1.67e05	s m^{-1}	-