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Numerical simulations of aerosol delivery to the human lung with an idealized laryngeal model, image-based airway model, and automatic meshing algorithm

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ABSTRACT

The authors proposed a new method to automatically mesh computed tomography (CT)-based three-dimensional human airway geometry for computational fluid dynamics (CFD)-based simulations of pulmonary gas-flow and aerosol delivery. Traditional methods to construct and mesh realistic geometry were time-consuming, because they were done manually using image-processing and mesh-generating programs. Furthermore, most of CT thoracic image data sets do not include the upper airway structures. To overcome these issues, the proposed method consists of CFD grid-size distribution, an automatic meshing algorithm, and the addition of a laryngeal model along with turbulent velocity inflow boundary condition attached to the proximal end of the trachea. The method is based on our previously developed geometric model with irregular centerlines and cross-sections fitted to CT segmented airway surfaces, dubbed the "fitted-surface model." The new method utilizes anatomical information obtained from the one-dimensional tree, e.g., skeleton connectivity and branch diameters, to efficiently generate optimal CFD mesh, automatically impose boundary conditions, and systematically reduce simulation results. The aerosol deposition predicted by the proposed method agreed well with the prediction by a traditional CT-based model, and the laryngeal model generated a realistic level of turbulence in the trachea. Furthermore, the computational time was reduced by factor of two without losing accuracy by using the proposed grid-size distribution. The new method is well suited for branch-by-branch analyses of gas-flow and aerosol distribution in multiple subjects due to embedded anatomical information.

1. Introduction

A better understanding of the regional distribution of inhaled aerosols in the human lung improves targeted delivery of pharmaceutical drugs to the regions of interest in aerosol therapy [1]. Numerical (*in silico*) models based on computational fluid dynamics (CFD) are commonly used to study pulmonary aerosol delivery with, e.g., breathing patterns, carrier gases, inhalers, and aerosol types (e.g., Longest et al. [15] and Miyawaki et al. [17]). Realistic *in silico* models require image-based subject-specific airway geometry because aerosol transport is sensitive to air-flow structures in central airways, and the flow structures depend on local geometric features such as airway cross-sectional shape, transitions between parent and child branches (including bifurcations and trifurcations), bends, and constrictions.

One of the most important airway geometric features is the normal narrowing within the glottal region. This narrowing is responsible for generation of unsteady turbulent laryngeal jet during inspiration, which plays an important role in gas-flow and aerosol delivery in the human lung (e.g., Dekker [5], Lin et al. [14], and Miyawaki et al. [17]). Nonetheless, most of CT images do not include the extra-thoracic airway regions. Prior to CFD simulation, one needs to construct the geometry, generate a CFD mesh, and specify boundary conditions. After the simulation, one needs to count aerosol particle depositions in the regions of interest, e.g., branch-by-branch. Thus, it is time-consuming to perform subject-specific CFD analyses yet the strength of such analyses lies in the personalization of the methodologies.

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Geometric airway models have been presented by others. However, automated methods to construct the geometry are lacking (e.g., van Ertbruggen et al. [6], Gemci et al. [8], Tian et al. [21], and Walters et al. [22]). Tawhai et al. [20] proposed a centerline (CL)-based method to semi-automatically construct the three-dimensional (3-D) geometry using the skeleton and the associated branch diameters in the one-dimensional (1-D) tree. This CL-based 3-D geometry is a collection of cylinder-like branches corresponding to their respective branches in the 1-D tree. Thus, we can use the anatomical information obtained from the 1-D tree such as skeleton connectivity and branch diameters to facilitate pre- and post-processing. This method can represent the airway branch-scale geometry (e.g., direction and diameter), although sub-branch-scale geometry (e.g., bending and constrictions) and diameter-scale geometry (e.g., cartilage rings) are simplified and trifurcation geometry was not represented. Later Miyawaki et al. [18] improved this method to account for diameter-scale geometry and trifurcations by fitting cylindrical branches to CT-resolved airway surface, dubbed the "fitted-surface (FS) geometric model." Miyawaki et al.'s geometric model is not only subject-specific, but also directly associated with anatomical information, greatly facilitating data analysis, e.g., branch-by-branch. What remains to be developed is a convenient implementation for multi-subject CFD simulations.

The CFD meshes for airway geometries have been manually generated in most previous studies (e.g., Lin et al. [14]), but the meshes could have been generated automatically as follows. For example, in the CL-based geometric model proposed by Tawhai et al. [20], each branch is represented as a cylinder-like surface, which can define the volume for a 3-D CFD mesh. The optimal grid size in the volume can be roughly determined by the diameter and flow rate in the branch (e.g., Yin et al. [23]). Open source mesh-generation programs Gmsh [9] and TetGen [19] can automatically generate the mesh using the 3-D geometry and grid size distribution as input data. Therefore, the 3-D airway geometry could be discretized automatically and seamlessly from the trachea to the terminal bronchioles. Furthermore, boundary conditions on the top, bottom, and side wall of the cylinder-like volume can be systematically specified. Marchandise et al. [16] proposed a method to automatically mesh image-based geometry, but this method was not centerline-based as it required airway surface geometry for 3-D geometry construction.

The objectives of this study are three-fold. First, within the framework of the FS model [18], we propose a laryngeal model that can be attached to the FS central airway geometric model, and synthetic turbulence at the proximal end of the trachea can generate a realistic turbulent laryngeal jet during inspiration of CFD simulations, which is important to mix inhaled aerosols. Second, we propose grid-size distribution and automatic meshing algorithm to generate CFD meshes for the above airway models. Third, by performing CFD simulations we demonstrate that our proposed methods are able to accurately predict the regional aerosol distribution in the human lung and facilitate data analyses branch-by-branch with the embedded anatomical information.

The remainder of the paper is organized as follows. We first propose a laryngeal model and then describe in detail the methods to semi-automatically construct and mesh image-based subject-specific airway geometry. To assess the accuracy of the proposed method, we compare the prediction of aerosol deposition by the FS model with that of a traditional CT-based model. Finally, we discuss the performance, advantages, and potential improvements of the proposed methods.

2. Material and methods

A CFD-based numerical simulation of aerosol transport in the human lung consists of four major steps: construction of a geometric model, generation of the CFD mesh, simulation of gas-flow, and simulation of aerosol deposition. First, we constructed the geometric model as in Miyawaki et al. [18] and attached the geometric laryngeal model to the trachea. Second, we computed the grid size in each cross-section using the diameter and flow rate in each branch, automatically generated the CFD mesh using open-source mesh-generation programs Gmsh [9] and TetGen [19], and systematically specified boundary conditions using skeleton connectivity. Third, we performed gas-flow simulations with turbulent inflow boundary conditions designed for the geometric laryngeal model to produce inspiratory laryngeal jets with physiologically realistic turbulent intensities. Finally, we performed aerosol simulations and systematically post-processed the results using the skeleton connectivity. The four sub-sections below explain the four steps in detail.

2.1. Geometric human laryngeal and airway models

The CL-based geometric airway models proposed by Miyawaki et al. [18] consist of straight-CL, curved-CL, and fitted-surface (FS) models, in which a branch is a cylinder, a curved pipe, and a pipe with irregular CL and cross-sections, respectively. In this study we compared the FS model to the CT-based model used by Miyawaki et al. [17] in terms of air-flow field and aerosol distribution. In the CT-based model, a wall boundary was obtained from a CT-image, and inlet, outlet, and internal boundaries were defined manually. In contrast, the CL-based model is constructed in a way that anatomical information regarding branches are embedded and external and internal boundaries, surrounding each branch, can be easily defined (Fig. 1). As described in detail below, these features of the CL-based model greatly facilitate pre- and post-processing of the input and output data of gas-flow and aerosol deposition simulations.

When constructing the geometric model, we extended the 1-D tree from the trachea to larynx using the average imaged tracheal diameter. From the fluid mechanical point of view, the normal narrowing within the glottal region plays a crucial role in creating turbulent laryngeal jet during inhalation (Dekker [5], Lin et al. [14], and Miyawaki et al. [17]), but CT data usually do not include the region proximal to the trachea. Therefore, the geometry around the larynx needs to be modeled to replace missing extra-thoracic images. The geometry of larynx varies from subject to subject, so our goal is to devise a laryngeal model that can create a realistic level of turbulence in the trachea. We modeled the geometry of larynx using five parameters: location of the glottis L_g, (hydraulic) diameter at the glottis $D_{h,\,g}$, (hydraulic) diameter proximal to the glottis $D_{h,\,gu}$, length of the larynx proximal to the glottis l_{gu}, and length of the larynx peripheral to the glottis l_{gl} (Fig. 2). We normalized the five parameters by the subject-specific hydraulic diameters of their trachea $D_{h,\,t}$, e.g., $L_g^* = L_g/D_{h,t}$, thus facilitating the application of the developed methodologies to future subjects.

To empirically determine the five parameters, we used the data in the literature and the CT images of healthy subjects. We primarily used the data reported by Cheng et al. [2] together with CT images of two healthy subjects. The University of Iowa Institutional Review Board and radiation safety committee approved the associated prior human studies and the use of these data for the current purposes. Cheng et al. [2] did not report the inflation level, while the inflation levels for the CT images of the two healthy subjects were 90 percent vital capacity ("end inspiration"). In the previous imaging studies, the extra-thoracic airway was imaged during inhalation so as to assure that the glottis was fully open. Imaging of the lung itself was achieved with a linked spiral scan commencing after arrival at 90% vital capacity at which point the subject remained apneic (Choi et al. [3], Lin et al. [14], Yin et al. [24]). There is no precise definition of the beginning of trachea, and CT