A mathematical description of the morphology of the lung is necessary for modeling and analyzing the deposition of inhaled aerosols. A model of the lung boundary was generated from magnetic resonance images, with the goal of creating a framework for anatomically realistic morphological models of the human airway network. We used data visualization and analysis software to reconstruct the lung volume from a series of transverse magnetic resonance images collected at many vertical locations in the lung, ranging from apex to base. The lung model was then built using isosurface extraction techniques. These modeling methods may facilitate the creation of customized morphological models for individual subjects, resulting in improved interpretation of aerosol distribution data from single-photon-emission computed tomography (SPECT). Such customized models could be developed for children and for patients with respiratory diseases, thus aiding in the study of inhaled medications and environmental aerosols in these sensitive populations. Key words: magnetic resonance imaging; single-photon-emission computed tomography; lung, modeling; computer simulation; models, theoretical; models, anatomical. [Respir Care 2004;49(2):180–185. © 2004 Daedalus Enterprises]

Introduction

Three-dimensional models of the morphology of the human airway network are of great use in the study of lung deposition patterns of inhaled aerosols. In these models the diameters, lengths, and branching angles of the individual lung airways are defined (using values from published anatomic or morphological studies1–6) and then the 3-dimensional spatial arrangement of the branches are calculated and visualized in a recursive manner. The airways of the model may be represented digitally as either solid cylinders (cylindrical model) or as hollow tubes (tubular model). Cylindrical morphological models have been used to analyze and interpret experimental aerosol distribution data obtained from gamma scintigraphy imaging studies.7–10 These models have been used to predict which lung airways are associated with a particular region of a scintigraphy image. Tubular branching models11 have the potential to provide a framework for computational fluid dynamics simulations of flow and parti-
cle deposition in the lung, since they can be used to define the spatial geometry of the region of airflow.

Though several early morphological models were based on symmetric, dichotomously bifurcating systems, such as those developed by Weibel,¹ lung images obtained by gamma scintigraphy showed that such symmetrical models lack anatomical realism.¹²–¹⁴ Subsequently, Martonen et al developed tubular and cylindrical models¹¹,¹⁴–¹⁷ based on qualitative observations of lung images obtained from single-photon-emission computed tomography (SPECT), which is a 3-dimensional gamma scintigraphy imaging method based on measuring the spatial distribution of a radiolabeled aerosol within the lung.¹⁸ These models, which were based on morphometric information from the literature, incorporated developments such as a spatial separation of the left and right lungs and a distinct lung boundary. This mathematically defined boundary was characterized by volumetric, elliptic cones that were truncated at the top and bottom to simulate the apical and basal lung surfaces. Though that boundary approximated the shape of the lungs, it was not anatomically realistic, since it accounted for neither asymmetry about the lung midline nor nonuniformity in transverse cross-sectional shape.

We now present a method for generating a model of the lung boundary, derived from transverse magnetic resonance (MR) images of human lungs. The model is reconstructed from the images using advanced data visualization and modeling techniques. The model provides an anatomically realistic framework for the generation of morphological branching airway models.

Methods

Magnetic Resonance Images

Transverse MR images of the lung, at 8-mm intervals, were obtained from a normal adult male. The MR images were then aligned to SPECT images obtained at 4.67-mm intervals in the same subject, following inhalation of a radiolabeled aerosol, the particles of which had a mass median diameter of 6.5 μm. The image collection methods were previously described.⁹,¹⁹,²⁰ Both the MR and SPECT image collection spanned a vertical distance of approximately 24 cm, covering the full extent of both the right and left lungs.

Model Reconstruction

The morphological model was reconstructed from the MR images using IBM Visualization Data Explorer, which is a general-purpose data visualization and analysis program that is free, and its source code is open. Data Explorer can run in either Unix or Windows systems. We used Data Explorer version 3.1.4B with a Silicon Graphics Onyx 2000 workstation that has eight 300-MHz central processing units, 6 gigabytes of main memory, and SGI Infinite Reality 2 graphics hardware. The details of the image data manipulation and the reconstruction program are given below.

Image Data Manipulation. The right and left lungs were defined on each transverse MR image using a semi-automatic segmentation algorithm that is part of the Analyze software package (Mayo Clinic, Rochester, Minnesota). Two-dimensional binary images of each transverse slice were then derived, in which the pixel values were transformed to either a 0 (outside the lung) or 1 (inside the lung). The binary image data were then interpolated to produce images having the same vertical resolution as the collected SPECT images. This produced a total of 52 transverse images, which were then concatenated into a single 3-dimensional data file. The file therefore defined a volume of isotropic 3-dimensional pixels (or “voxels”) representing both lungs, in which each voxel was associated with a corresponding 2-dimensional SPECT image pixel. Data Prompter, a stand-alone program used within the Data Explorer environment, was used to create a corresponding header file for the image data, enabling it to be imported into Data Explorer. The header file contained information needed by Data Explorer for correct interpretation of the image data, such as data size, format, and organization.

Visualization Network. The Visual Program Editor, another utility within the Data Explorer environment, was used to create a custom Data Explorer program for the analysis of the lung volume images. The custom analysis program (or “network,”” in Data Explorer terminology) was constructed from intrinsic Data Explorer file operation and analysis modules. The network program used the following Data Explorer modules:

1. A file selector module was used to select the lung volume image file to analyze.
2. An import module was used to load the voxel data into an appropriate internal Data Explorer data structure.
3. An isosurface module then extracted the surface of the lung boundary from the data.
4. An autocolor module then colored the resulting lung geometry for visualization.
5. An image module was then used to render the resulting model on the screen.

From the binary volume data set, the isosurface module extracted a surface from the points at which the data transitioned from 0 (outside the lung tissues) to 1 (inside the lung tissues). The isosurface module used a variation of the marching cubes surface extraction algorithm.²¹ The resulting lung boundary surface was saved in Data Explorer as a mesh of 3-dimensional spatial points. The re-
sulting surface data set can be exported in various data formats for use in defining a limiting boundary for the branching airway model generator. No smoothing of the surface was performed in Data Explorer; that is, all the features of the lung surface are due to the shapes of the contours derived from the MRI images. However, if necessary, smoothing could be carried out on the contours prior to the creation of the binary data set. Further details of the Data Explorer software modules are available.22,23

Results

Figure 1 shows the resampled, transverse, MR lung volume images. Though the general shape of the transverse cross-section is relatively stable through the middle section of the lungs, we note a marked deviation in transverse cross-sectional shape in the apical and basal regions. We also note more asymmetry about the lung midline in the basal region.

Figure 2 shows a perspective view of the reconstructed morphological lung model, including a coordinate system. Figure 3 shows additional views of the model. These figures clearly demonstrate the asymmetric geometry of the model about the lung midline. Figure 4 shows 8 examples of the transverse model cross-section, in which the asymmetry of the cross-sectional shape, particularly near the base of the lung, is evident.

Figure 5 shows sagittal and Figure 6 shows orthogonal sections of the lung morphology model. These sections demonstrate our ability to reconstruct other views of the morphological model not represented in the original images. Though the sectioning is demonstrated here using the volume generated from the binary data, the isosurfacing and sectioning methodologies could be used to generate volume and section visualizations of 3-dimensional regions associated with a particular level of aerosol deposition (ie, radioactivity) using data from the SPECT images (Fig. 7) from the same subject. Such 3-dimensional visualizations would facilitate understanding of the spatial distribution of aerosols within the lung.

Discussion

The model presented here is much more anatomically realistic than our previous lung boundary models used in the generation of branching airway models. Our previous methods used idealized, geometrically regular lung boundaries to define the spatial extent of 3-dimensional airway models derived using airway lengths, diameters, and angles from various morphological studies. We can now use the MRI-based boundaries to more realistically define the spatial extent of both cylindrical and tubular branching models. Specifically, the models could be instructed to position the trachea between the left and right lungs and to situate the entrance of the main bronchi into each lung at an anatomically correct location. The branching models could then be configured to restrict all further airway generations to lie solely within the MR-based lung boundary. Thus, the description of the boundary would have a large impact on the shape of the branching airway network, resulting in an asymmetric, anatomy-based airway model. Particle deposition in each airway of the model could then be estimated by associating SPECT images (see Fig. 7) with the model (Fig. 8).

Recently, 3-dimensional morphological models of actual lung airways have been developed by reconstructing airway surfaces from high-resolution computed tomography images.24–27 However, such CT-based imaging and reconstruction methods are unable to resolve the geometry of very small airways. The insertion of an airway network model into the lung boundary morphology model will allow us to model every generation of lung airway within an anatomy-based foundation. In addition, the boundary model could be used in conjunction with 3-dimensional airway models derived from CT images obtained from the same subject. That is, the 3-dimensional airway models of the first several airway generations could be placed within the lung boundary, and then a branching model could be used to “fill in” the higher generations.
The MR-based morphological model, in conjunction with an associated tubular branching airway model, could be used as a foundation for accurate computational fluid dynamics simulation of airway flow, particle transport, and particle deposition. Such research would allow us to study the fate of inhaled particles with a wide variety of particle sizes and respiratory conditions. Such modeling efforts have potential use in the study of inhaled pollutants and development of aerosol therapies. In addition, the morphological model would

Fig. 2. Perspective view of the lung boundary model.

Fig. 3. Top, perspective, front, and side views of the lung boundary model.

Fig. 4. Transverse cross-sections in relationship to the lung boundary model. Note asymmetry about the lung midline and differences in the shape of the cross-sections.
facilitate the development of methods for validating computational fluid dynamics studies with SPECT data.

Our methods could be used to generate customized morphological models for people of various ages, physical characteristics, and lung pathologies, allowing creation of an airway model for each individual, which could aid interpretation of SPECT data, enabling us to better study the effect of lung morphology differences on particle deposition. In particular we hope to create specific dosimetry models of the deposition of aerosolized drugs and environmental pollutants in children and in people with respiratory disease.

We believe the methods presented here represent an important advance toward our goal of rapidly creating realistic, customized models of the branching airway struc-

Fig. 5. Sagittal section of the lung boundary model.

Fig. 6. Various orthogonal sections of the lung boundary model.

Fig. 7. Single-photon-emission computed tomography (SPECT) images obtained at transverse locations approximately (A) 19 cm, (B) 13 cm, and (C) 5 cm from the base of the lungs.

Fig. 8. Relationship of the single-photon-emission computed tomography (SPECT) images with the lung boundary model. Airways of a branching model inserted within the boundary could be associated with a particular region of a SPECT image.
ture. The modeling procedure is very quick (the image manipulation and surface extraction algorithms are not exceedingly computationally intensive) and the cost is low, since the Data Explorer software is free. However, the anatomical accuracy of the lung boundary depends on both the accuracy of the collected MRI images and the details of the boundary creation. Noise or motion artifacts in the images may result in incorrect lung model boundaries. However, an inappropriately high degree of smoothing of the lung contours may mask important real anatomical features of the lung shape.

Conclusions

We believe we have created an anatomically realistic model of the human lung boundary from magnetic resonance images. The model provides a mathematical description of the boundary, which can be used in conjunction with computational models of the branching structure of human airways to produce realistic, asymmetrical models of the entire lung airway system. These models have immediate use in aerosol therapy and inhalation toxicology research, as they could be applied both to the computational fluid dynamics modeling of drug or pollutant deposition in the lungs and to the interpretation of experimental SPECT data.

References