EVALUATION OF AIRWAY MORPHOLOGY IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE OF HYPERPOLARIZED HELIUM-3 MAGNETIC RESONANCE IMAGING AND COMPUTED TOMOGRAPHY

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Target Audience: Scientists and clinicians that are interested in using hyperpolarized helium-3 (^{3}He) magnetic resonance imaging (MRI) to evaluate lung disease.

Purpose: Computed Tomography (CT) has been widely used to investigate airway structure in patients with chronic obstructive pulmonary disease (COPD) and hyperpolarized ^{3}He MRI has been used to investigate lung function. Although ^{3}He MRI allows direct visualization of the lung regions that participate in ventilation as well as those regions that do not participate in ventilation, known as ventilation defects, we still do not have a clear understanding of the exact etiology of noble gas MRI ventilation defects. Although it is assumed that narrowed or constricted/occluded small airways, mucous plugs, or bullous disease are responsible for the ventilation abnormalities and heterogeneity observed in COPD, until regional CT-MRI comparisons are performed, this cannot be ascertained. A model that has both the CT airway tree and ^{3}He MRI static ventilation (SV) registered in three dimensional space would allow us to see which airways lead to regions of lung ventilation defects and allow us to evaluate how airway morphology is altered in these regions. In this study, our objective was to volumetrically register the CT-derived airway tree with ^{3}He MRI to evaluate the airway morphology and lung ventilation structure-function relationships.

Methods

Subjects: All subjects provided written informed consent to a study protocol approved by the local research ethics board and Health Canada. Ex-smokers with a clinical diagnosis of COPD between the ages of 50-85 and a smoking history of ≥10 pack-years were enrolled. Elderly never-smokers were also enrolled who had no history of previous chronic or current respiratory disease. Spirometry and plethysmography were performed and the diffusing capacity of carbon monoxide (D_{LCO}) was measured according to the American Thoracic Society guidelines.

Image Acquisition: MRI was performed on a whole body 3.0 Tesla Discovery 750MR (General Electric Health Care, Milwaukee, WI) with broadband imaging capability as previously described[1]. ^{1}H images were acquired prior to ^{3}He imaging with subjects scanned during a 1L breath-hold of N_2 using the whole body RF coil and proton fast spoiled gradient-echo (16s total data acquisition, relaxation time (TR)/echo time (TE)/flip angle = 4.7 ms/1.2 ms/30°, field-of-view (FOV) = 40 x 40 cm, matrix 256 x 256, 14 slices, 15 mm slice thickness, 0 cm gap). For ^{3}He MRI, a polarizer system (HeliSpin™) was used to polarize ^{3}He gas. Hyperpolarized ^{3}He MRI coronal SVimages were acquired during breath-hold of a 1L ^{3}He/N_2 mixture (14s data acquisition, TR/TE /flip angle = 4.3 ms/1.4 ms/7°, bandwidth = 31.25, FOV = 40 × 40 cm, matrix 128 × 128, 14 slices, 15 mm slice thickness, 0 gap). Thoracic CT was performed using a 64-slice Lightspeed VCT scanner (General Electric Health Care, Milwaukee, WI) using a detector configuration of 64x0.625 mm, 120 kVp, 100 effective mA, tube rotation time of 500ms and a pitch of 1.0. CT was acquired similar to MRI with subjects in breath hold after inhalation of a 1.0L bag of N_2.

Analysis: Thoracic CT was evaluated using automated software (Pulmonary Workstation 2.0, VIDA Diagnostics; Iowa City, IA). Airway wall area percent (WA%) was segmented up to the seventh generation airways. The airway tree was reconstructed in 3D Slicer (Version 3.6.3, Boston, MA). A dynamic threshold range of 5 to 255 was used to isolate the CT signal and the model was then constructed using 3D Slicer's interactive Model Maker module. ^{3}He MRI SV images were segmented using semi-automated image segmentation/registration software as previously described[2]. ^{3}He ventilation defect percent (VDP) was generated as the ventilation defect volume normalized to the thoracic cavity volume. ^{3}He apparent diffusion coefficient (ADC) maps were generated using in-house software. Three dimensional ^{3}He MRI SV models were constructed using similar dynamic threshold values CT airway tree.

Registration of CT and ^{3}He MRI volumes: Using 3D Slicer's Fiducials module, two separate fiducial lists were created, one for the airway tree model and one ^{3}He ventilation model. Each fiducial list had between two and four points. The number of fiducials in each list was determined based on visibility of landmarks in each model. Fiducial landmarks were; the trachea, the carina and left and right main branches of each model. Once the fiducial markers were placed, two transformation nodes were made; one for the airway tree model and one for the ^{3}He MRI SV model. Models were registered using the Transforms module in 3D Slicer. A transformation range of -400 to 400 was used and corresponding fiducial points were manually aligned and 3D coordinates matched. Once registered ^{3}He MRI SV models were adjusted to opacity of 0.3 to visualize the airway tree within them.

Results*:* Figure 1 shows the CT derived airway tree model, ^{3}He MRI SV model and the volumetrically registered CT-MRI model. Table 1 shows spirometry, ^{3}He MRI and CT measurements for a healthy volunteer and three representative COPD subjects. In comparison with the healthy volunteers, the COPD subjects have greater ^{3}He ADC and VDP as well as greater CT WA%.

Conclusions*:* Registration of a CT derived airway tree model with a ^{3}He MRI SV model in 3D Slicer allows three dimensional view of airway tree anatomy and regional ^{3}He MRI gas distribution. These models can be used to assess airway morphology in lung regions with high VDP. Preliminary results suggest that the airways of subjects with lung disease are inflamed and have greater WA% than healthy subjects without lung disease. Future work with these models will be focused on tracing specific airway paths into ventilation defective regions. This will allow us to evaluate the alterations in airway morphology that occur in lung disease.

Table1. Spirometry, ^{3}He MRI and CT Measurements

	Healthy (i)	COPD S1 (ii)	COPD S2 (iii)	COPD S3 (iv)
FEV_1(%pred)	103	23	52	52
VDP (%)	5	26	43	36
ADC (cm^2)	0.30	0.61	0.45	0.63
5^{th} gen.WA (%)	57	64	59	63

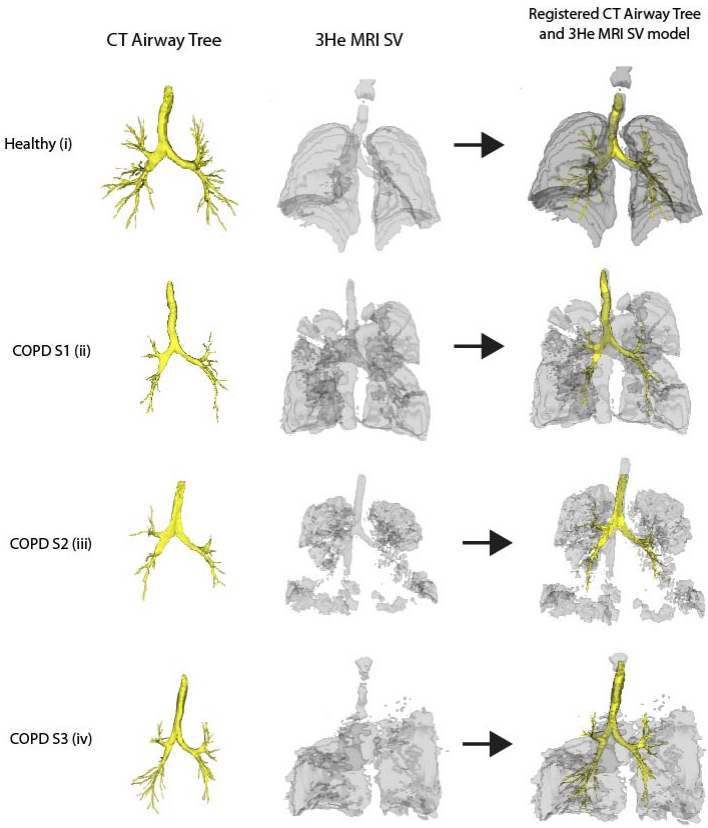

Figure 1. CT Airway Tree, 3He MRI SV and Registered CT and MRI SV Lung Models

References

1. Parraga, G. *et al. Invest Radiol.* (2007).
2. Kirby, M. *et al. Acad Radiol.* (2011).