Imaging morphometric changes in the human pulmonary acinus *in vivo* via ^{3}He diffusion MRI

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Introduction

It has been established that hyperpolarized ^{3}He diffusion MRI is capable of quantifying microstructual changes of terminal airspaces in the lung [1-4]. This technique holds advantages over other morphometric techniques for studying lung microstructure—in particular it enables rapid three-dimensional measurements over the entire human lung *in vivo*. Using this method we were able to measure changes in acinar airspaces at different points in the inspiratory cycle *in vivo* in human lungs. Herein we employ a 6 b-value diffusion pulse sequence for imaging at three different levels of inspiration. The results were used to determine average alveolar depth, *h*, and alveolar duct radii, *R* (Figure 1), at each of the three lung volumes.

Materials and Methods

Five healthy volunteers were each instructed to perform three inspiratory maneuvers that ended in a 10-second breath hold: (1) exhale to residual volume and then inhale a 1L gas mixture, (2) inhale a 1L gas mixture from functional residual capacity (FRC), and (3) inhale a 1L gas mixture from FRC and continue to inhale until total lung capacity (TLC) is reached. Each maneuver was performed twice: once with a liter of air followed immediately by a proton scan of the entire lung (matrix=128 x 128; resolution = 3.5 x 3.5 x 15 mm; 21 slices) and a second time with a mixture of 0.3 L of hyperpolarized ^{3}He and 0.7 L of nitrogen followed immediately by a diffusion-weighted ^{3}He scan (matrix=64 x 40; resolution = 7 x 7 x 30 mm; diffusion time = 1.8 ms; 3 slices; b-values = 0, 2, 4, 6, 8, 10 s/cm^2). All images were obtained on a 1.5-T Siemens Magnetom Sonata scanner. ^{3}He images were acquired using a custom-built ^{3}He volume-transmit/8-channel receiver pair. Hyperpolarized ^{3}He gas was prepared using spin-exchange optical pumping on a commercial He polarizer (General Electric). Total lung volume at each breath hold was determined from the proton images. An established mathematical model relating signal attenuation from the diffusion gradients to the physical parameters *h* and *R*, corresponding to alveolar depth and alveolar duct radius (Figure 1), was fit voxel-by-voxel to ^{3}He diffusion images [1].

Results

All images demonstrated sufficient signal-to-noise to confidently fit the mathematical model to the data in order to obtain the physical parameters *R* and *h*. A summary of the results for both *R* and *h* averaged over each lung is shown in Table 1; typical images are presented in Figure 2. On average a 50% increase in lung volume led to a 9% increase in average alveolar duct radius and a 22% decrease in average alveolar depth.

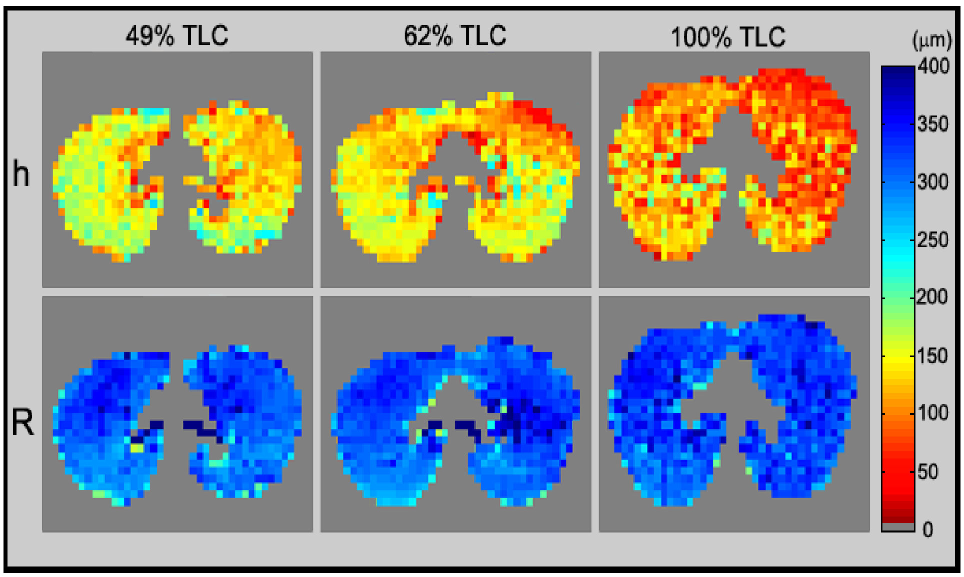
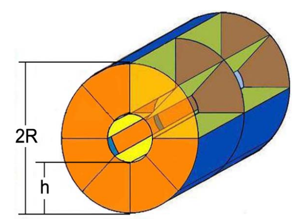


Figure 2: Axial images of h and R from slice 2 of subject 1 at multiple volumes. Top row: h-map in microns at 49%, 62%, and 100% TLC (L to R). Bottom Row: R-map at identical volumes

Figure 1: Model of an acinar airway. Two segments of the periodic structure are shown. Part of the outer wall has been made transparent for illustrative purposes.



Subject #	%Max Vol.	R(μm)	h(μm)
1	100%	317	109
	62%	309	137
	49%	302	149
2	100%	298	110
	73%	282	125
	51%	282	143
3	100%	316	149
	69%	285	153
	47%	282	173
4	100%	317	133
	64%	306	141
	51%	289	154
5	100%	316	141
	77%	301	152
	46%	269	162

Table 1: Data for R and h for each lung, averaged over all voxels

Conclusions

Using ^{3}He diffusion MR imaging we have, for the first time, imaged precise *in-vivo* morphological changes at the alveolar level during inspiration in humans. While the total lung volume increased by 50%, alveolar duct radius increased by only 9%, implying that the bulk of the volume change at the alveolar level occurs by lengthening of alveolar ducts. This and the decrease in alveolar depth during lung inflation support an accordion-like model of acinar airway expansion, where the bellows of the accordion represent the alveoli lining the duct walls. Such models have previously been proposed by Macklin and, more recently, by Kitaoka *et al* [5,6].

References

[1] Yablonskiy *et al., J Appl Physiol* , 2009. [2] Yablonskiy et al., PNAS 2002; 99: 3111. [3] Sukstanskii, Yablonskiy, *J Mag. Reson*. 2008; 190: 200. [4] Hajari *et al*. ISMRM 2009 [5] Macklin, *Proc Inst Med*, 1950: 78-95 [6] Kitaoka *et al*., *J. Physiol. Sci.* 2007: 175-185