Deflation-induced changes in alveolar-duct geometry via ^{3}He lung morphometry, with histological validation

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Introduction

^{3}He lung morphometry [1] is quickly becoming an established technique for studying pulmonary microstructure. This method relates the anisotropic diffusion coefficients D_T and D_L within cylindrical acinar airways, measured via ^{3}He diffusion MRI [2], to airway radii, R, and alveolar depth, h [3]. ^{3}He morphometry results from canine lungs at varying levels of deflation have previously been reported using a set of empirical relationships between anisotropic diffusivity and acinar geometry that had been optimized for morphometric measurements in human lungs (values of R between 300 and 500 μm) [1,3,4]. Because the average size of canine acinar airways falls just outside this range, we have adjusted the empirical relationships between diffusion and airway geometry to be specific to dog lungs (R between 140 and 260 μm). We compare the new ^{3}He morphometry results from dog lungs with histological morphometry from the same lungs frozen at different levels of inflation after imaging.

Methods

Normal lungs were excised from six dogs after sacrifice following unrelated cardiac experiments; approval was obtained from the Washington University Animal Studies Committee. For each experiment a mixture of hyperpolarized ^{3}He and N_2 was injected into the lung via syringe to a maximum transpleural pressure of 23 cm H_2O and homogenized to ensure that gas was uniformly distributed throughout the lung. The gas mixture was then partially evacuated by free collapse to obtain one of three desired pressures (approximately 18, 7.5, or 2.5 cm H_20) and imaged at near-static pressure for between 15 and 50 seconds. 2-D FLASH images at 9 b-values (0 to 14 s/cm^2) were obtained on a 1.5-T Siemens Magnetom Sonata scanner. At each inflation pressure a complete set of multiple-b-value diffusion-weighted images was acquired consisting of 9 images for each slice, each with a diffusion time of 1.8 ms and a different diffusion weighting parameter using the diffusion sensitizing pulse gradient waveform described in Ref. 2. Each lung was assumed to be at total lung capacity (TLC) at high inflation levels (approximately 18 cm H_20), and all other volumes are reported as a percentage of TLC as measured by counting pixels from the ^{3}He MR images. Signal attenuation was related to acinar geometry by equations [A1] and [A3]-[A5] from Ref. 4 in addition to the following set of equations determined from new computer simulations in canine-sized acinar airways:

$$D_{T0} = D_0 \cdot 7/16 \cdot (R/L_2)^{(4-3.61\cdot(R/L_2)^{0.63})}\left[1+f(R,h)\right]$$

$$f(R,h) = \exp[-A\cdot(h/R)^2\cdot[\exp(-5\cdot(h/R)^2)+5\cdot(h/R)^2-1]$$

$$A = -6.55 + 6.44\cdot\exp[2.68\cdot(R/L_2)^2]$$

Here D_0 is ^{3}He diffusion coefficient, $L_2 = \sqrt{4D_0\Delta}$ is diffusion length, and Δ is diffusion time. These equations are valid for Δ of 1.8 ms, values of R from 140 and 260 μm, and h/R less than 0.75. After imaging, the right and left lungs from Dog 5 and Dog 6 were frozen at different levels of inflation for quantitative histological studies. Each lung was cut, sampled, and sectioned at 6 microns. Low resolution (5X) microscope images were acquired across the entire slide, and all airways deemed perpendicular to the slides by serial section were measured for morphometric parameters R and h.

Results

Data were analyzed on a pixel-by-pixel basis. For each lung, R and h values were obtained from all pixels with sufficiently high fitting confidence and S/N greater than 100. On average a 37% decrease in lung volume led to a 17% decrease in R (from 240 to 200 μm) and an 8% increase in the alveolar wall depth h (from 110 to 120 μm). Regional variation (on average about 15% for R and 24% for h) was seen in each case but was consistent across all volumes, implying the spatial variations were physiological. Figure 1 shows histograms of R and h at three levels of deflation for all pixels included in the analysis in all six lungs. A comparison of the histology and MR measurements from Dogs 5 and 6 is shown in Table 1. The comparison is quite favorable, and in each case the difference between histology and MRI was well within one standard deviation of either average measurement.

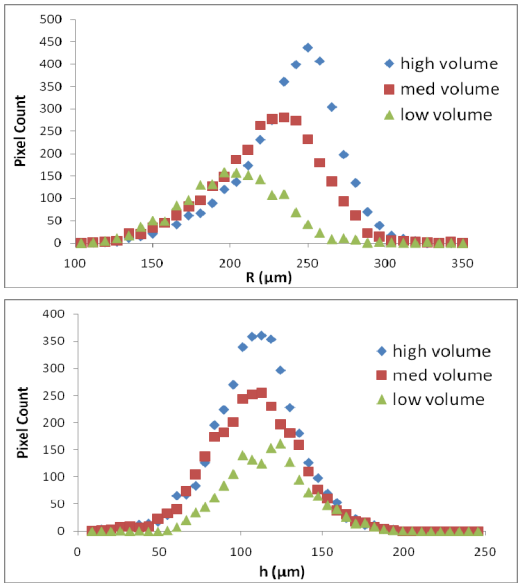

Figure 1: Histograms of geometrical parameters R (top) and h (bottom) for all six dog lungs at 3 different levels of deflation.

		Histology		^{3}He MRI	
	Volume	R (μ)	h (μ)	R (μ)	h (μ)
Dog 5	High	224 ± 27	138 ± 21	228 ± 29	119 ± 29
	Low	173 ± 24	116 ± 31	184 ± 38	124 ± 34
Dog 6	High	243 ± 35	121 ± 44	249 ± 33	120 ± 34
	Low	202 ± 25	107 ± 31	205 ± 40	133 ± 42

Table 1: Comparison of histology and MR results from Dog 5 and Dog 6. Results are average ± std. dev.

Conclusions

On average the ^{3}He morphometry results presented here for R are about 20% smaller than previously reported results, and are in better agreement with our histological findings shown in Table 1. These imaging data indicate that changes in alveolar duct volume contribute significantly to changes in total lung volume; this is validated via histological finding in the same lungs. Further, the 9% increase in h during deflation, is similar to changes in h measured by ^{3}He morphometry in human lungs where a 50% increase in lung volume led to a 22% decrease in h [5].

References

[1] Yablonskiy *et al., J Appl Physiol*, 107: 1258-1265, 2009 . [2] Yablonskiy *et al., Proc Natl Acad Sci USA* 99: 3111-3116, 2002 [3] Sukstanskii, Yablonskiy, *J Mag. Reson*. 190: 200-210, 2008. [4] Hajari *et al*. ISMRM 2009. [5] Hajari *et al*. ISMRM 2010.