The Relationship between ^{3}He ADC and Lung Volume

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Introduction

Hyperpolarized ^{3}He diffusion MRI has been used for years in investigations of lung structural changes due to emphysematous tissue destruction [1-3]. The apparent diffusion coefficient (ADC) of ^{3}He gas at short (< 1 mm) and long length scales (1-3 cm) have both been shown to be sensitive to alveolar expansion in emphysematous lungs [4,5]. Recently, detailed comparison to morphometry in healthy and diseased human and canine lungs has more rigidly validated the ^{3}He ADC's as indicators of alveolar size [5-7]. The relationship between ^{3}He diffusivity and lung volume, however, is largely unknown. Differences in the ^{3}He ADC at different lung volumes in the same individual may confound longitudinal studies of disease progression. The purpose of the present study is to establish this relationship.

Materials and Methods

2-D imaging was performed *in vivo* in three healthy volunteers and *ex vivo* in four normal donor lungs (3 donors) that could not be used for transplantation (due to recipient mismatch or other technical reasons), all in transverse planes covering all or most of the lung(s). At least two and as many as four different inspiration volumes were used, ranging from well below functional residual capacity (FRC) to total lung capacity (TLC). The largest volume used was always TLC. Volumes were determined two ways: 1) by counting the total number of ^{3}He pixels where images covered the entire lung(s) (used for *ex-vivo* imaging), and 2) by segmenting the lung from proton images acquired at the same volume as the ^{3}He images (used for *in-vivo* imaging). Both methods were used in 2 of the 3 cases *in vivo*, with good agreement; *in-vivo* table values for volume are from proton images.

All imaging was performed with IRB approval; *in-vivo* imaging was performed under a ^{3}He IND FDA exemption. Healthy volunteers practiced breathing maneuvers with air before inhaling from a mixture of 350 mL of hyperpolarized gas and 1-2 L N_2, to reach approximately FRC and TLC for separate imaging acquisitions. Donor lungs were inflated with the ^{3}He/N_2 mixture via gas syringe. *Ex-vivo* imaging in donor lungs was performed at TLC (which we defined as 10-12 cm transpleural H_2O pressure) and subsequently at smaller volumes after releasing gas from TLC.

350-mL doses of ^{3}He gas at 40-50% polarization were prepared using spin-exchange optical pumping via a home-built apparatus and a commercial polarizer (G.E.). Each was mixed with N_2 for imaging at the desired inspiration volume. We used a single-turn solenoid rf coil with high sensitivity and a homebuilt Helmholtz pair for *ex-vivo* and *in-vivo* MR, respectively; both were at 48.47 MHz on a 1.5-T Siemens Magnetom Vision. Transverse, diffusion-weighted 10-mm-thick images (b = 1.38 s/cm^2, with an effective diffusion time of about 1.8 ms) were acquired using FLASH; in-plane resolution was 7 x 7 mm for *in-vivo* images and 5 x 5 mm for *ex-vivo* images.

Results

Results show some differences between these few individuals, as expected, with ADC results at TLC ranging from 0.17 to 0.23 cm^2/s. Modest changes in ADC were observed with changing volume within subjects; these results are summarized in the Table and graph. To compare ADC across individuals, we standardized each case's ADC as the fraction of the ADC value at TLC and the volume as a fraction of TLC volume. This analysis yielded a strong linear relationship between diffusivity and volume ($\%ADC_{TLC} = 0.46 * \%TLC + 55$; $R^2 = 0.91$). Thus, for a volume of 0.5 TLC, the ^{3}He ADC is only reduced to 78% of its value at TLC. We note that the unrestricted diffusivity of ^{3}He is a function of the fraction of total ^{3}He in the lung. The fractional volume of ^{3}He, however, never exceeded 14% of the total lung volume, ensuring that all measurements were in the dilute limit (0.9 cm^2/s max ADC).

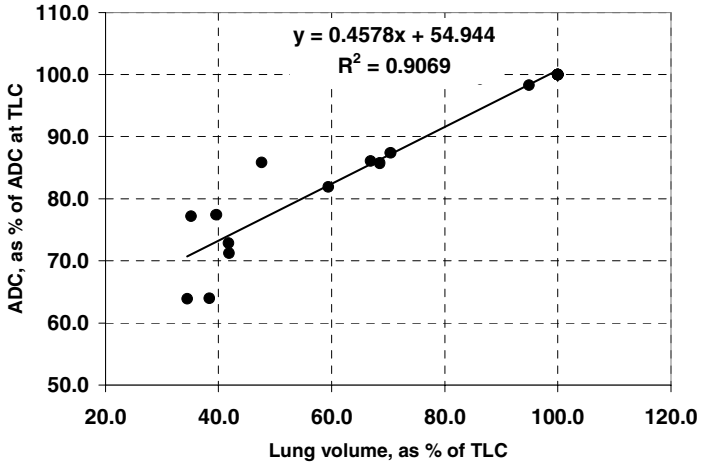

TABLE	volume (L)	Lung-avg. ADC (cm^2/s)	% of TLC	% of ADC at TLC
Volunteer1	2.5	0.149	34.5	63.9
age 43	3.5	0.200	47.6	85.8
	7.4	0.233	100.0	100.0
Volunteer2	2.6	0.107	38.4	64.0
age 24	6.7	0.167	100.0	100.0
Volunteer3	2.3	0.149	35.1	77.2
age 26	6.5	0.193	100.0	100.0
DonorLung1	1.5	0.150	41.7	72.9
	2.4	0.177	68.5	85.8
	3.1	0.205	86.2	99.3
	3.6	0.206	100.0	100.0
DonorLung2L	1.2	0.156	39.6	77.7
	1.5	0.165	59.4	82.6
	2.5	0.200	100.0	100.0
DonorLung2R	2.3	0.177	70.4	87.4
	3.3	0.202	100.0	100.0
DonorLung3	1.5	0.146	41.9	71.3
	2.3	0.177	66.9	86.1
	3.3	0.202	94.9	98.3
	3.5	0.206	100.0	100.0

Conclusions

According to our data, ^{3}He ADC is a linear function of human lung volume in the range of normal inspiration within individuals. Since ADC changes only modestly with lung volume, precise control of inspiratory volumes may not be critical in multi-center or longitudinal studies. Future studies of anisotropic ^{3}He diffusion at different volumes should be able to determine the relative contributions of transverse and longitudinal diffusivities [4], and thus what aspect of alveolar-duct geometry changes with inspiration.

Acknowledgments

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References

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