A Simultaneous Multi-breath Scheme for Measurement of ADC, p_AO_2 and Fractional Ventilation Using ^{3}He MRI in Human

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INTRODUCTION: The majority of clinical lung evaluation methods currently in use fail to provide enough information to detect the regional and small changes in patient's response to therapeutic procedures. Hyperpolarized (HP) gas magnetic resonance imaging (MRI) has emerged as a technique that can fill this void. HP MRI, which is both safe and sensitive, enables direct imaging of gas in the airways and parenchyma. The use of ^{3}He gas in particular has enabled imaging of both structural and functional aspects of the lung. This work introduces a recently developed scheme for imaging the regional ventilation, partial pressure of oxygen (p_AO_2) and lung microstructure (ADC) in human lungs using a single protocol with a multi-breath regimen, achievable by use of a patient-driven gas delivery device previously presented in [1]. These measurements can be used simultaneously in an iterative method introduced in [2] to achieve a more accurate regional alveolar assessment. Thus, the combination of these three imaging measurements, acquired using a short multi-breath sequence, effectively probes the different aspects of lung disease in a manner analogous to measurements of DLCO, CT% air-trapping, CT % emphysema, and airway wall thickness (AWT).

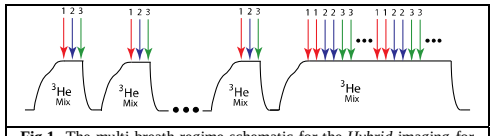

Fig.1- The multi-breath regime schematic for the *Hybrid* imaging for the case of three slices. Each arrow stands for one slice acquisition.

METHODS: So far four (n = 4) subjects have participated in this study, two healthy nonsmokers (F, 47 ± 3 yrs.) and two asymptomatic smokers (1 M, 44 ± 3 yrs.). A normoxic mixture of HP ^{3}He:N_2:O_2 (1:3:1) based on subjects' total lung capacity (12% TLC) was administered in a multi-breath regimen, as shown in Fig. 1. Subjects breathed through a passive patient-driven gas delivery device, which regulates the gas mixture concentration (F_iO_2=21%) and the tidal volume for each breath. Subjects completed sufficient practice prior to MRI session in order to ensure a repeatable breathing pattern. An end-inspiratory slice-selective gradient-echo was acquired for six coronal slices spanning the entire lung in a ~2s breath-hold. This scheme was repeated six times to yield the fractional ventilation distribution resulting from the regional signal buildup. Prior to the last breath, the subject is informed to hold her breath for an extended 12-sec breath-hold, during which the simultaneous p_AO_2-ADC imaging occurs. Fractional ventilation was computed by fitting the signal buildup in multiple back-to-back breaths to a dynamic recursive model (a manner analogous to [3]). Accelerated imaging was performed using the well-established GRAPPA method with an undersampling factor of four and 16 auto-correlating reference lines. Six coronal slices (20-25 mm) with planar resolution of 6.25×6.25 mm^2 (TR/TE = 6.7/3.2 ms, FOV = 30×40 cm^2, flip-angle = 5˚, Slice Gap = 20%) were acquired over a ~2s time span. The simultaneous p_AO_2-ADC-imaging occurred during the final breath-hold, at which time the ^{3}He signal is at its highest level, and uniformly distributed in the lung parenchyma. Fig. 2 illustrates the imaging-scheme used for the simultaneous imaging of oxygen-weighted and diffusion-weighted signal decay, from which p_AO_2 and ADC maps can be constructed. Both ventilation and p_AO_2 measurements require the flip-angle maps in order to decouple the contribution of the radio-frequency pulses in depolarization. Low-resolution (25×25 mm^2, TR/TE = 6.7/3.2ms, FOV = 30×40cm^2, flip-angle = 5˚, Slice-Gap = 20%), consecutive images were acquired for each slice in the first second of the 12-s breath-hold in order to estimate a smooth flip-angle map (refer to Fig. 3 and 4). Using this flip-angle map, p_AO_2 computation needs at least another two time-points. A slice-selective GRE (6.25×6.25 mm^2, TR/TE = 9.1/5.8ms, FOV = 30×40cm^2, flip-angle = 5˚, Slice-Gap = 20%) was acquired for each slice as the first time-point of p_AO_2 scheme. The second p_AO_2 time-point comes from the ADC-sequence with b = 0 cm^2/s after a ~5-s waiting time. The ADC-sequence (6.25×6.25 mm^2, TR/TE = 8.9/15.2ms, FOV = 30×40cm^2, flip-angle = 5˚, Slice-Gap = 20%) was acquired for two diffusion b-values = [0 1.6] cm^2/s at the end of the breath-hold.

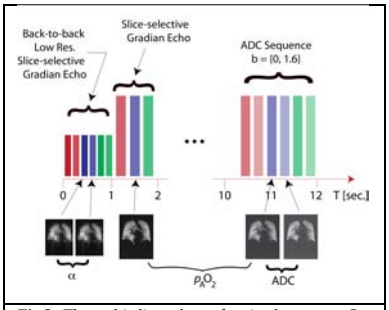

Fig.2- The multi-slice scheme for simultaneous p_AO_2-ADC imaging in the last long breath-hold of the multi-breath maneuver in Fig. 1.

Subjects	Weight [Lbs]	Smoked [Pck/Yrs.]	ADC [cm^2/s]	p_AO_2 [Torr]	Frac. Vent. [-]
Healthy	110	-	0.16 ± 0.05	120.7 ± 28.2	0.28 ± 0.26
	150	-	0.18 ± 0.06	123.4 ± 25.8	0.30 ± 0.25
Smoker	153	30	0.19 ± 0.23	127.1 ± 34.3	0.35 ± 0.18
	181	35	0.22 ± 0.13	120.4 ± 33.1	0.35 ± 0.21

Table 1- The whole-lung averages and standard deviations for the 3 measurements and subject's smoking history and weight.

RESULTS: Fig. 3 shows the spin-density maps for a representative middle slice and the resulting fractional ventilation, oxygen tension and ADC maps for all the slices of a representative smoker subject. Table 1 lists the whole-lung averages and standard deviations for all subjects entered this study. This is an ongoing study and more subjects will be recruited.

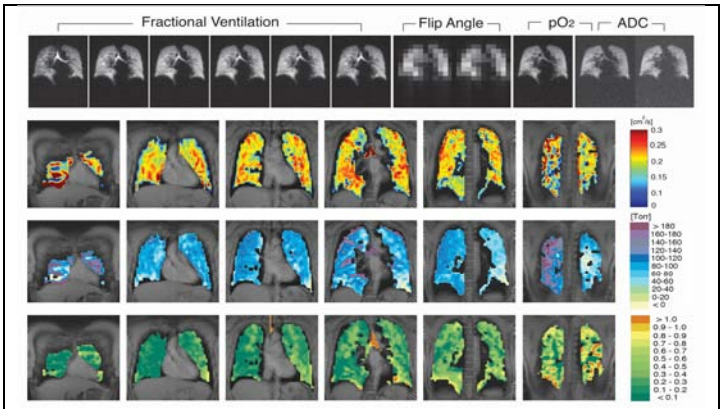

Fig.3- (a) Spin-density maps for one of the middle slices **(b)** ADC maps **(c)** p_{AO_2} Maps and **(d)** fractional ventilation maps for a representative smoker.

CONCLUSION: A hybrid imaging scheme presented, allowing for simultaneous measurement of ADC, oxygen tension and fractional ventilation performed on human subjects. The introduced method utilizes the minimum possible amount of hyperpolarized gas while still achieving the highest signal-to-noise possible with a multi-breath maneuver. This multi-breath ^{3}He wash-in sequence improves the quality of spin-density maps from which the p_AO_2 measurements can be made, which in turn can help to produce a more accurate calculation of fractional ventilation from the p_AO_2 maps themselves. An iterative method of simultaneous fractional ventilation and p_AO_2 analysis is presented in [2], which is shown to enhance the estimations and which can be used to compute regional oxygen uptake.

REFERENCES: [1] Emami K, Proc 20th ISMRM 2012 May. [2] Kadlececk S,Proc 21th ISMRM 2013 April. [3] Emami, MRM. 2010 Jan;63(1):137-50.