Assessing the Diagnostic Power of a Hybrid Combination of Hyperpolarized ^{3}He MRI derived ADC, Specific Ventilation and Alveolar Oxygen Tension in COPDs

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INTRODUCTION: The hybrid multibreath ^{3}He imaging technique has been previously used to measure regional lung parameters such as p_AO_2, specific ventilation (SV) and ADC measurements simultaneously [1]. 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 current clinical measurements. The obtained measurements are highly correlated with conventional pulmonary tests (pulmonary function test (PFT), six-minute walk test (6MWT), and the St. George's Questionnaire (SGRQ). In this study, the p_AO_2, SV and ADC measurements acquired using the hybrid technique were assessed for their viability as markers for distinguishing between smokers and nonsmokers.

METHODS: 10 subjects (5 Smokers, 5 Nonsmokers) were imaged using the hybrid multibreath imaging technique. Hyperpolarized ^{3}He imaging was performed during a sequence of 7 breath holds (6 short (~1s) breath holds followed by a 12s breath hold). A normoxic mixture of HP ^{3}He:N_2:O_2 (3:1:1) based on subjects' total lung capacity (12% TLC) was administered in a multi-breath regime, as shown in Fig.1. Subjects breathed through a passive patient-driven gas delivery device presented before [2], which maintains the gas mixture concentration (F_iO_2=21%) and the tidal volume for each breath. Subjects completed sufficient practice 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 evaluate the fractional ventilation 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, r, defined as the ratio of the inspired gas volume to the total end-inspiratory volume, was computed by fitting the signal buildup in multiple back-to-back breaths to a dynamic recursive model (a manner analogous to [4]). Accelerated imaging was performed using the well-established GRAPPA method with a factor of four and reference-line = 16. Six coronal slices (20-25 mm) with spatial 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. A total of six time-points were acquired in a ~30s multi-breath maneuver. The simultaneous p_AO_2-ADC-imaging occurred during the final 12-s breath-hold, at which time the signal is at its highest level, and filling all the ventilated parts of the parenchyma. The mean and standard deviation of each measurement were calculated for all the voxels in the lung (M_{ADC}, D_{ADC}; M_{SV}, D_{SV}; Mp_AO_2, Dp_AO_2). A stepwise multivariate logistic regression was used to predict the smokers and nonsmokers in the study. An α=0.05 was considered significant and a p_R=0.25 was considered for a predictor to retain in the multivariate regressions.

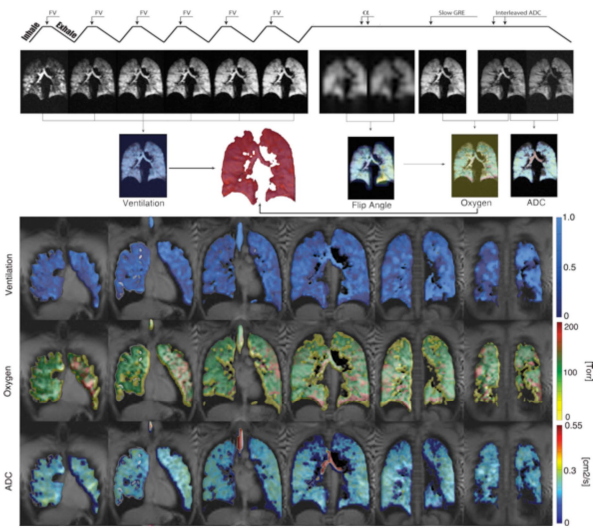

Figure 1- (a) Spin-density maps for one of the middle slices **(b)** ADC maps **(c)** p_AO_2 Maps and **(d)** fractional ventilation maps for a representative smoker.

RESULTS AND DISCUSSION: Figure 1 shows the series of acquired images (n=11), as well as the resultant ADC, p_AO_2 and FV for a representative subject. The results of the three measurements for all the subjects are listed in **Table 1**. The variables entered in the multivariate model were average ADC, average SV, and standard deviation of p_AO_2. Leave-one-out cross validation was used to plot the receiver operating characteristic (ROC) curve. The odds-ratios for the variables were M_{ADC} (OR=2.23), M_{SV} (OR = 1.05), and D_{PAO2} (OR=118). The area under the ROC curve (AUC) was 0.821. **Figure 2** shows the prediction quality of the regression model detect small, hard-to-assess functional alterations in the asymptomatic smokers.

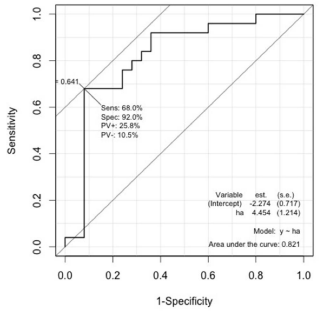

Figure 2- ROC plot for the Regression

CONCLUSION: In this preliminary study we showed that hybrid multi-breath hyperpolarized ^{3}He imaging derived SV, ADC and p_AO_2 measurement can be used to parse otherwise hard to detect differences between smokers and nonsmkers.

Table2- Multivariate Regression Model Statistics

Variable	*Coeff.*	SE	OR*	95% CI*	z	P > |z|
M_{ADC}	-28.570	8.970	1.33	(1.047 , 4.34)	-3.19	**0.001**
M_{SV}	-9.747	4.993	1.05	(0.776 , 1.21)	1.95	**0.051**
D_{pAO2}	0.163	0.054	1.18	(0.697 , 1.44)	3.00	**0.003**

Abbreviations: *Coeff.* (Coefficient), SE (standard error), OR (odds ratio), CI (confidene - interval), G-statistic (likelihood ratio test), z-statistic (Wald test).

Table 1- The Results Of Three Meaurements In All the Subject

Subjects #	ADC	SV	p_AO_2
H1	0.187 ± 0.230	0.344 ± 0.174	118.895 ± 7.517
H2	0.164 ± 0.062	0.312 ± 0.158	99.055 ± 10.248
H3	0.209 ± 0.062	0.366 ± 0.212	85.966 ± 13.914
H4	0.222 ± 0.062	0.235 ± 0.156	87.114 ± 11.554
S1	0.213 ± 0.078	0.321 ± 0.160	110.109 ± 15.223
S2	0.194 ± 0.050	0.355 ± 0.135	106.862 ± 20.034
S3	0.227 ± 0.122	0.454 ± 0.213	105.482 ± 17.718
S4	0.228 ± 0.048	0.456 ± 0.195	102.166 ± 19.631
S5	0.194 ± 0.072	0.398 ± 0.162	107.367 ± 14.739

REFRENCES:

[1] Hamedani H et al., ATS 2013. [2] Emami K et al., ISMRM 2012