Reproducibility Assessment of High Resolution Imaging of Alveolar Oxygen Tension in Human Subjects

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INTRODUCTION: Pulmonary alveolar partial pressure of oxygen (P_AO_2) is closely related to the regional ventilation-perfusion ratio and therefore to alveolar gas exchange. Thus, a reproducible and noninvasive measurement of regional P_AO_2 can be of significant investigational and diagnostic value, especially since no other probe of localized alveolar oxygen tension information is currently available in clinical practice. Several techniques based on hyperpolarized helium-3 (HP ^{3}He) MRI have been developed for this purpose in animals, as well as in humans. Reproducibility studies, however, are rare. The handful of reported experiments on human subjects also suffer from low spatial resolution. For the first time, we present the short-term reproducibility results of a longitudinal study of high-resolution P_AO_2 measurements in human subjects.

METHODS: A total of 21 measurements on seven volunteers were performed. Four healthy non-smokers (50-60 yrs, 2M, 2F), two asymptomatic smokers (47 yr M, 64 yr F), and one level-2 COPD subject (65 yr M) underwent P_AO_2 imaging, repeated three times within 15 days. The experiments were performed under IRB-approved protocols for HP ^{3}He MRI after obtaining subjects' informed written consent prior to each experiment. All the human data and their demographics were anonymized. The volunteers' Body Mass Index (BMI), total smoking pack/years and Total Lung Capacity (TLC) are listed in **Table 1**. For each measurement, subjects inhaled a mixture of ^{3}He:N_2:O_2 ($FiO_2 \approx 21\%$), with the total volume of 12%TLC. P_AO_2 imaging was performed using an improved high-resolution interleaved technique (as described in Hamedani, H. *et al.* in this conference) during a 12-sec breath-hold. Four images of the entire lung (consisting of 12 coronal slices in supine position) were acquired with an interslice time delay of [0.00, 0.24, 5.79, 6.03] sec, with an approximately 2-sec pre-acquisition delay. The end-expiratory O_2 was measured for technique validation. Images were acquired using a multi-slice gradient echo imaging pulse sequence with the following imaging parameters: TR/TE= 6.7/3.2ms, FOV = 300×400mm^2, NS = 12, ST = 13 mm, $\alpha = 5^\circ$ and a matrix size = 48×36 (L–R phase encode). The overall mean and standard deviation of P_AO_2 distribution within each lung were calculated and the variation δ of mean P_AO_2 among each three measurements was calculated according to: δ= (max−min)/mean.

Subject	BMI	Smoking Pck/Yrs	TLC (L)	Inhaled Gas [mL] [3He+N2]	[O2]	Exhaled [%] [O2]	Overall pO2 [mmHg] Mean	SD	Variation of Means
Healthy	23	0	5.9	390 + 170	140	-	117.6	22.8	2.9%
						-	114.3	19.2	
						-	115.2	21.3	
Healthy	23	0	6.8	440 + 200	180	18.6	110.8	22.4	3.4%
						16.6	109	25	
						19.4	112.8	23.9	
Healthy	26	1	7	470 + 200	170	14.4	102.6	27.4	6.4%
						15.0	108.4	30.1	
						15.6	101.7	35.8	
Healthy	30	0	3.6	310 + 120	120	12.7	87.7	30.7	6.8%
						16.5	93.9	34.3	
						16.0	93.5	42.2	
Smoker	27	25	6	400 + 170	150	12.0	75.2	42	6.8%
						12.4	70.2	70.2	
						12.5	74	37	
Smoker	20	40	4.4	320 + 120	110	17.5	98.2	37.5	11.6%
						17.6	100.6	40.6	
						16.6	89.5	37.5	
COPD	22	50	7	470 + 200	170	16.4	95.8	36.7	4.1%
						16.7	95.3	35.9	
						15.4	91.9	35.9	

Table 1. Volunteer's data and overall P_AO_2 values from repeated measurements in the HP ^{3}He pulmonary oxygen reproducibility study. Values are listed as [mean ± standard deviation] (Torr). The last column is the variation δ of the global mean.

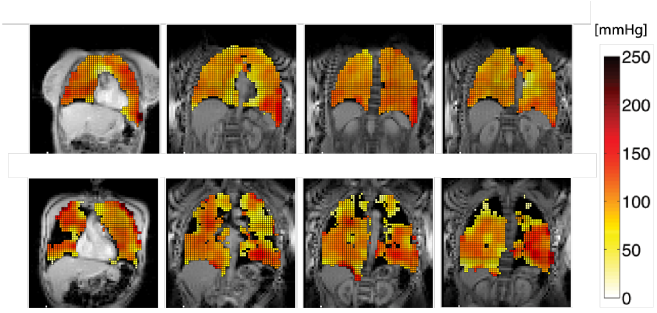

Figure 1. The PAO2 maps for healthy #2 (top) and COPD (bottom) volunteers.

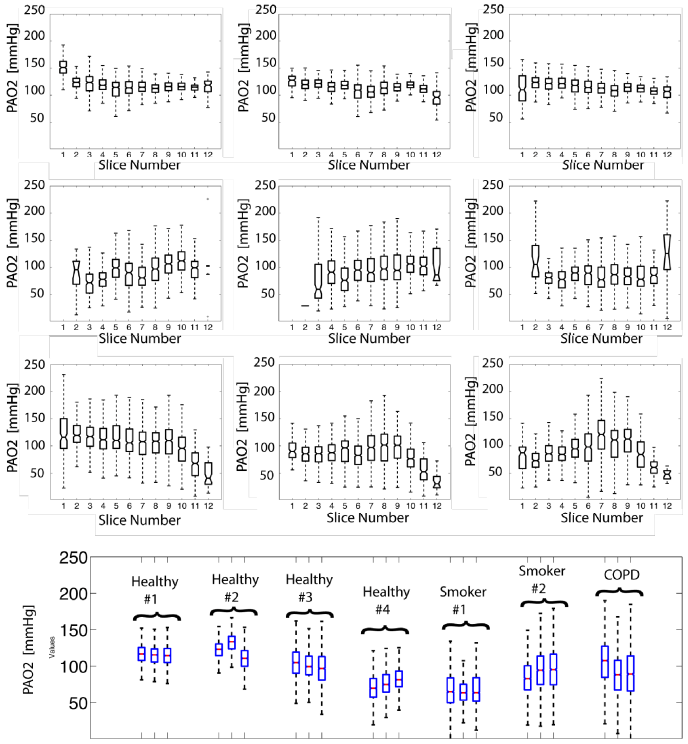

Figure 2. Box plot representation for PAO2 measurements of all slices in three experiments (left to right), for three representative subjects of each group (1st row: healthy #1, 2nd row: smoker #2 and 3rd row: COPD).
Bottom row: the overall distributions in all the measurements for all the subjects.

RESULTS AND DISCUSSION: Figure 1 shows four P_AO_2 maps from representative healthy #2 and COPD subjects. The P_AO_2 distribution is significantly more heterogeneous in the COPD subject. **Table 1** lists the overall mean±standard deviation values for all subjects, as well as the variation δ of mean P_AO_2 (δP_AO_2) of the three repeated measurements. δP_AO_2 did not exceed 7.0% among the three measurements except for one experiment (smoker #2), where it had the maximum value of 11.6%. The average δP_AO_2 was 6.0% across all the reproducibility measurements. The mean P_AO_2 obtained from imaging correlated well with the end-tidal O_2 concentration (r = 0.79). The standard deviations of P_AO_2 distribution in healthy subjects were generally smaller than those in smokers and COPD subjects. **Figure 2** (top) shows the variation of P_AO_2 distribution as a function of vertical position in the lungs of three representative subjects. Also shown in **Figure 2** (bottom) is the results summary for the entire study in box-plot format (centerlines are the P_AO_2 medians). As can be seen, the P_AO_2 distribution in healthy lungs has a smaller intrasubject variability as well as a smaller lung-position dependence compared to the smoker and COPD counterparts.

CONCLUSIONS: Results show that our improved interleaved P_AO_2 imaging technique provides a well-reproducible estimate of regional oxygen tension in healthy and diseased subjects. With its unprecedented spatial resolution it can serve as a potentially sensitive marker for diagnosis and assessment of pulmonary diseases