A Multiple-breath ^{3}He Wash-in Regimen to Reduce the Limitation of ^{3}He p_AO_2-Imaging Due to Delayed Ventilation and Slow Filling

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INTRODUCTION: Imaging of regional lung function has become a useful tool for studying the modified respiratory gas distribution in diseased lungs. Specifically, hyperpolarized ^{3}He alveolar oxygen tension (p_AO_2) measurements have proven to be a highly sensitive marker in lung functional imaging, clearly demonstrating smoking-induced alterations to the parenchyma [1]. The benefits of this method are somewhat diminished by its sensitivity to diaphragm movements, gas diffusion, and any abnormal gas flow that may occur during the required breath-hold, which can then result in implausible, non-physiologic values [1]. Slow-filling regions and collateral ventilation were reported in patients [2] during the ^{3}He imaging breath-holds (~15-25s). Such observed effects challenge the notion that gas is stationary during the imaging breath-hold, a simplifying and essential assumption underlying current models used to compute p_AO_2. Efforts have been made to account for these flow effects using dynamic model in rodents [3]. In this abstract, we present an alternative approach, aimed at mitigating artifacts by introducing a multi-breath regimen of ^{3}He wash-ins prior to the imaging. In contrast to the widely-recognized ventilation defects accompanying single-breath ^{3}He-images in COPD subjects, the proposed sequence of progressive breaths produces more reasonable p_AO_2 maps due to a more uniform spin-density map, improved signal-to-noise ratio and less sensitivity to heterogeneous time-constants.

METHODS: Two human subjects (2M, 47±3 yrs.) diagnosed with mild COPD, and three smokers (1M, 44 ±3 yrs.) participated in this study. The single- and multiple-breath regimes for p_AO_2 imaging were compared for each subject in order to demonstrate the effectiveness of the new breathing protocol in partial elimination of flow artifacts. The conventional multi-slice, four time-point scheme presented in [1] was performed across twelve 13-mm coronal slices after a single breath of HP gas. This method utilized an interleaved acquisition scheme with a gradient echo imaging pulse sequence at a spatial resolution of 8.3×8.3 mm^2 (TR/TE = 6.7/3.2 ms, FOV = 30×40 cm^2, flip-angle = ~5˚, Slice-Gap = 20%). A normoxic mixture of $^3He:N_2:O_2$ (3:1:1) based on subjects' total lung capacity was administered with images acquired during a 12-sec end-inspiratory breath-hold. An additional imaging session utilized the multi-breath protocol, shown schematically in Fig.1, which resulted in a gradually increasing hyperpolarized ^{3}He signal in the lung prior to the p_AO_2-acquisition (Fig. 3). Subjects breathed through a passive, patient-driven gas delivery device (described in [4]), which maintained the gas mixture concentration (FiO_2=21%) and volume (12% TLC) during each breath. After the final inhalation,, the subject performed a 12-sec breath-hold, during which the imaging occurred (six 25-mm coronal slices, imaging parameters otherwise unchanged). In order to observe the signal build-up, fast GRAPPA gradient echo images were also acquired during 1.6-sec breath-holds after each of the six breaths. The observed signal dynamics present in most of the voxels suggest that the signal reached steady state and that additional breaths would not have changed the initial signal distribution at breath-hold. We then compared the oxygen tension maps resulting from the single- and multiple-breath techniques.

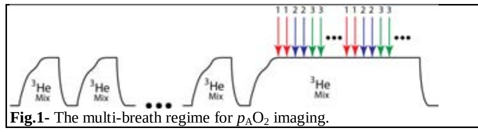

Fig.1- The multi-breath regime for p_AO_2 imaging.

RESULTS & DISCUSSION: Helium transport during the breath-hold, which can result from the slow filling, collateral ventilation and air trapping present in damaged lungs, can skew the p_AO_2 values upward or downward depending on the dynamics of transported polarized gas. This can result in negative p_AO_2 values in regions that fill slowly with polarized gas and manifest itself as a signal increase, while on the other hand can result in values higher than the FiO2 for regions in which the polarized gas escapes and replaces with lower polarization gas. Fig.2a shows the oxygen tension maps resulting from the conventional single-breath method for one of the two COPD subjects entered this study. These maps show adjacent regions of elevated and depressed p_AO_2 (shown in pink and yellow, respectively), as well as regions of supra- or superphysiological values. The presence of these regions highlights the difficulties with strict interpretation of ^{3}He signal dynamics as arising only from p_AO_2-induced relaxation, particularly in diseased lungs, but also suggests diagnostic potential in retaining sensitivity to this anomalous gas flow [1]. Fig. 3 illustrates the signal dynamics over the course of six wash-in breaths in a representative COPD subject. The lung is progressively being filled with HP gas in successive breaths. As with the single-breath technique, some regions remain unventilated even after the sixth breaths (green circle). However, others that appear unventilated in early breaths are gradually filled through collateral pathways (red circles). The quasi-steady state gas concentration achieved from this gradual filling reduces the errors present in the conventional single-breath p_AO_2 measurements, which would otherwise arise from gas redistribution during the breath-hold. Fig. 4 a, b shows the representative subject's spin-density maps for the first and last breaths, respectively, and Fig. 2b depicts the p_AO_2 maps that resulted from using the multi-breath protocol for the same subject. A visual comparison confirms the improved quality of the oxygen maps, as measured by the decreased presence of non-physiologic and negative values. Table 1 summarizes the measurements for all subjects in the study. The average and standard deviations are compared between the two methods for the subjects for all the valid and invalid computed p_AO_2 values. The standard deviation in the multi-breath regime dropped by ~30% for all the subjects. The supra- or superphysiological values were also reduced, as is noted in Table 1. The effect was most pronounced for the COPDs, and the average reduction across all subjects was ~35%.

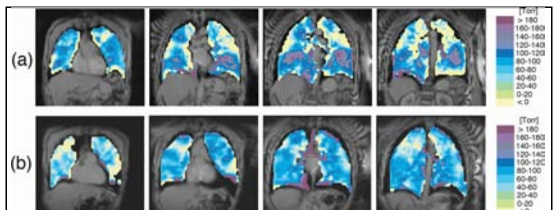

Fig.2- The p_AO_2 maps for the representative COPD subject **(a)** for the conventional single-breath regime and **(b)** for the presented multi-breath protocol.

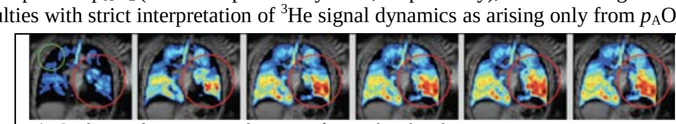

Fig. 3- The spin-density maps in the course of six washout breaths.

Subject	Smoking Hostory	Single-breath Maneuver				Multi-breath Maneuver				Decrease in Nonphysiologic Values
		p_AO_2			Invalid Voxels	p_AO_2			Invalid Voxels	
	[pack-yrs]	[Torr]			< 0 or > FiO2	[Torr]			< 0 or > FiO2	
COPD	50	92.6	±	75	1407	80.6	±	46	604	**42.9%**
COPD	48	73.7	±	80	366	81.4	±	59	231	**63.1%**
Smoker	38	91.9	±	44	77	80.4	±	38	23	**29.9%**
Smoker	35	111.5	±	55	112	115.1	±	26	29	**25.9%**
Smoker	25	95.6	±	46	88	108.4	±	33	19	**21.6%**

Table 1- The p_AO_2 results for single- and multiple-breath regimes (ave ± std) in the whole-lung and the success in reduction of invalid values in %.

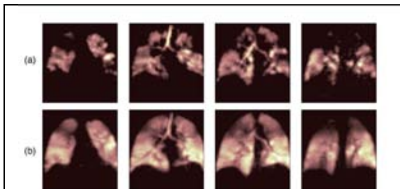

Fig.4- The spin-density maps **(a)** after the first breath and **(b)** after the last breath before the imaging.

CONCLUSION: Multiple inhalations of polarized gas prior to imaging not only improves the level of signal-to-noise, which is critical in the case of p_AO_2 imaging, but can also effectively reduce the flow artifacts present in the diseased lungs as reported here. In addition, filling the poorly ventilated regions of the lung by progressive washin breaths of HP gas provides information about these regions that is unavailable due to lack of signal when using the conventional single-breath protocols.

REFERENCES:
[1] Hamedani H. et al. Magn. Reson. Med. 2012; 67:1332–1345.
[2] Woods et al., FASEB J. 2008 March; 22, 763.9.
[3] Kadlecek S, et al. NMR Biomed 2011 Dec; 24(10):1253-63.
[4] Emami K et al., Proc 20th ISMRM 2012 May.