A Pilot Fractional Ventilation Imaging Study in Healthy Subjects, Asymptomatic Smokers and Obstructive Pulmonary Disease Patients

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INTRODUCTION: Pulmonary ventilation is a key aspect of lung function. Together with parenchymal perfusion it makes up half of the gas exchange equation. Almost all pulmonary disorders alter ventilation in one way or the other, either on a localized or global basis. Therefore quantitative ventilation imaging provides pulmonary researchers with a potentially sensitive tool to investigate the severity and distribution of disease, as well as patient's response to therapy. The ability of Hyperpolarized (HP) gas MRI to directly and noninvasively visualize the distribution of respiratory gas has gradually found more acceptance among researchers as a suitable tool for this purpose. Fractional ventilation imaging techniques have been developed as a means to quantify respiratory gas distribution [1] in a complementary fashion to the more established single-breath ventilation scans. These techniques however rely on multiple consecutive HP gas breaths delivered to the subject and their implementation has been until very recently limited to mechanically ventilated animals. The advent of a patient-driven HP gas delivery device recently enabled translation of fractional ventilation imaging technique to conscious human subjects [2]. Based on this demonstrated feasibility, we have started investigating the distribution of fractional ventilation in lungs of healthy volunteers in comparison to asymptomatic smokers and those exhibiting obstructive pulmonary disease. This work presents preliminary results of this ongoing study.

METHODS: So far two (n = 2, F, 51±4 yrs.) healthy subjects, four (n = 4, 1×F, 3×M, 46±3 yrs.) asymptomatic smokers and two (n = 2) COPD subjects (one mild M 63 yrs. and one moderate M 58 yrs.) have enrolled in this study. A normoxic mixture of HP ^3He:N_2:O_2 (3:1:1) based on subjects' total lung capacity (12% TLC) was administered in a multi-breath sequence, as shown in **Figure 1**. HP gas mixture was administered through a passive patient-driven delivery device described earlier [3], which regulated the inspired gas F_iO_2 at around 21% and the prescribed tidal volume (I:E~3:4, ~10 BPM). End-inspiratory slice-selective images were acquired covering the entire lung volume with six coronal slices in < 2s on a 1.5-T Sonata MRI scanner (Siemens Healthcare) using an 8-channel phase array chest coil (Stark Contrast) and with parameters: ST = 20–25 mm, planar resolution = 6.25×6.25 mm^2, TR/TE = 6.7/3.2 ms, FOV = 30×40 cm^2, flip angle ~ 5°, slice gap = 20% ST. This process was repeated six times to drive signal buildup in the airways, which was then use to calculate the fractional ventilation distribution according to [4]. At the end of the sequence the subject was instructed to hold her breath for approximately 5 s during which a series of consecutive images were acquired to estimate the flip angle distribution. Accelerated imaging was performed using GRAPPA [5] with an undersampling factor of four and 16 auto-correlating reference lines.

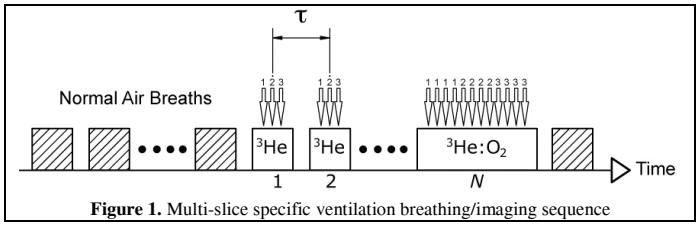

Figure 1. Multi-slice specific ventilation breathing/imaging sequence

RESULTS & DISCUSSION: Multi-breath ventilation imaging protocol was fairly well tolerated by all subjects including the severe COPD patient. A few practice runs using room air while subject was positioned inside the MRI scanner proved to be very beneficial in synchronizing the patient's expectation of the device gas delivery pattern and image acquisition. Representative fractional ventilation maps for each subject is shown in **Figure 2** overlaid on corresponding ^1H images of thorax. Lungs of COPD subjects show areas of complete ventilation defect – as demonstrated in earlier single breath ventilation scan studies – and simultaneously show a more heterogeneous distribution of fractional ventilation. Healthy subjects on the other hand show a very uniform fractional ventilation distribution as expected from normal physiology. Contrary to the other two groups, asymptomatic smokers although not showing any detectable ventilation defects, do show a more heterogeneous fractional ventilation distribution. The degree of heterogeneity of fractional ventilation is somewhat different among the smokers likely due the variability of the effect of chronic smoke exposure on each subject. A common observation to both smokers and COPD subjects is that regions which are in the proximity of very poorly ventilated regions (or complete defects in the case of COPD lungs) exhibit an unusually high fractional ventilation value. This is likely due to the transport of gas between the well-ventilated and poorly-ventilated regions, and the fact that this distribution takes place at different time constants among various regions in the lung, especially those afflicted by airway obstruction, air trapping, or pulmonary shunt.

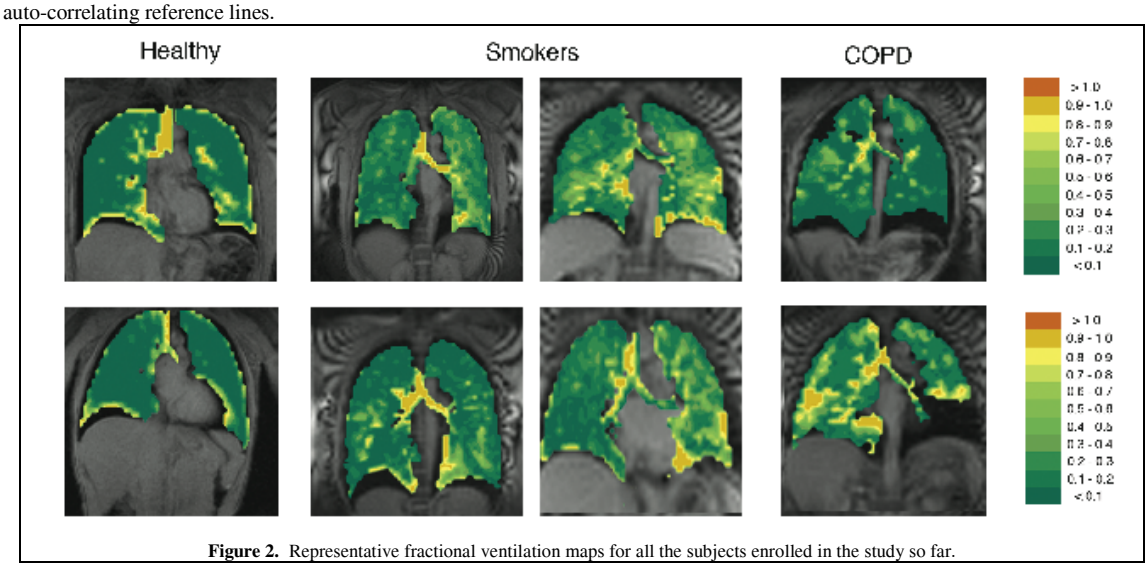

Figure 2. Representative fractional ventilation maps for all the subjects enrolled in the study so far.

CONCLUSION: This work presents the first study of its kind to investigate the distribution of fractional ventilation in lungs of human subjects with different pulmonary conditions. Although larger data points need to be acquired in order to draw any statistically significant conclusions, preliminary results indicate the potential utility of quantitative fractional ventilation maps complementing gross ventilation defects only observable in severe lung disease conditions. Multi-breath ventilation imaging protocols therefore may provide richer information about respiratory gas distribution and the associated effect of disease progression and stage. Multi-breath HP gas MRI protocols are now substantially more accessible by use of newly developed devices which not only streamline delivery of multiple identical breaths to the subject, but also help with enhancing uniformity and reproducibility of clinical studies on different days and across different sites.

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