Anatomical Distribution of Fractional Ventilation and Oxygen Uptake Imaged by Multibreath Wash-in Helium-3 MRI in Human Subjects

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TARGET AUDIENCE: Hyperpolarized noble gas MRI researchers, pulmonary physiologists, clinicians.

PURPOSE: It is known due to the effect of gravity that the greatest regional volume change occurs in the dependent regions of the lung. It is also known that blood flow increases in the dependent zones due to decreasing vascular resistance. This resultant ventilation-perfusion match passively keeps the oxygen uptake efficient in the whole lung [1]. It was shown in many studies that this vital mechanism will be altered in diseased lungs. Specifically, smoking, which can lead to chronic obstructive pulmonary disorder (COPD) has been shown to increase perfusion heterogeneity and lung compliance. Hyperpolarized ^{3}He imaging has been shown to be sensitive to detect these gravitational effects in lung function. In an earlier study we have shown that the absence of gravitational effects in alveolar oxygen tension (P_AO_2) may be a sign of subclinical changes that are hidden from other clinical tests [2]. In this study, the effects of the gravitational gradient on fractional ventilation (FV) and oxygen uptake were measured via a ^{3}He multibreath imaging in the lungs of healthy, smokers and COPD patients.

METHODS: The experiment was performed on 15 subjects: 5 healthy subjects with no history of smoking (HN: 2 Males, 43±11 years old), 5 asymptomatic smokers (AS: 5M, 48±5 years old, 25±5 pack-years), and 5 smokers diagnosed with COPD (COPD: 5M, 58±5 years old, 35±10 pack-years). A gas delivery system presented in [3], was used to deliver the gas for 6 time points for FV and the seventh breathing time-point for the oxygen tension measurement (breath-holds 1.6 and 12 seconds, respectively). The volume, FiO_2 and the duration of inspiration were kept constant for each breath. Both the FV and P_AO_2 maps were constructed via a previously described iterative fitting model [4]. Oxygen uptake then were calculated from $R = (F_iO_2 - P_AO_2) \times FV/BR$ for each pixel. End-inspiratory slice-selective images were acquired covering the entire lung volume in < 2s on a 1.5-T Sonata MRI scanner (Siemens Healthcare) using an 8-channel phase array chest coil (Stark Contrast). **Figure 1** shows the imaging protocol, the gas delivery device, imaging parameters and representative functional maps.

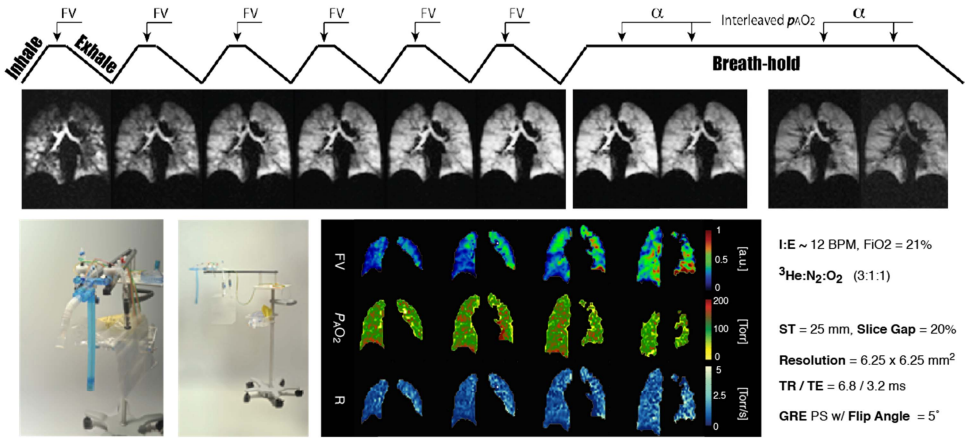

Figure 1- A) the multibreath regime for fractional ventilation (FV) and oxygen tension imaging (*PAO2*). **B)** The gas delivery device for multibreath imaging. **C)** representative maps of FV, *PAO2* and the resulting oxygen uptake (R). **D)** imaging and gas delivery parameters.

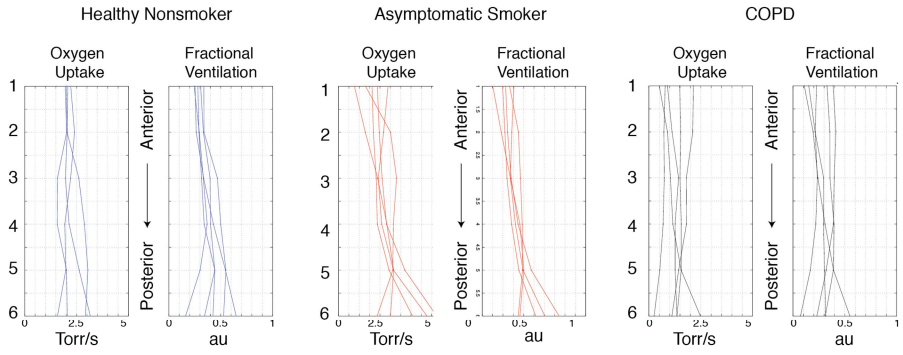

Figure 2) The summary plots of oxygen uptake and fractional ventilation from anterior to posterior in three cohorts. From top to bottom six slices were images and each slice is 20 cm.

RESULTS: The overall FV were 0.30±0.06 in healthy subjects, and were 0.28±0.17 and 0.29±0.12 in smokers and COPD subjects. The oxygen uptakes were 2.18±0.98, 2.02±1.20 and 1.69±0.83 in HN, AS and COPD subjects. COPD and healthy subjects were significantly different in the oxygen uptake level ($p < 0.01$). **Figure 2** shows the fractional ventilation and oxygen uptake along the anterior posterior direction. In both healthy nonsmoker and smoker groups, a vertical gradient was observed in the fractional ventilation (slope: 0.04±0.04 and 0.06±0.03), but the gradients were lost in COPD subjects (slope:0.01±0.04). The resulting oxygen uptake was constant along the anterior-posterior direction in healthy subjects and no gradient was observed in the gravity direction (slope:0.15±0.30). The COPD subjects showed significantly lower oxygen uptake with no gravitational gradients (slope: 0.04±0.37), while in healthy smokers a gradient was observed both in FV (slope: 0.06±0.03) and oxygen uptake (slope: 0.66±0.40) along the anterior-posterior direction.

CONCLUSION: In our previous studies we have shown an anterior-posterior gradient in P_AO_2 in human subjects when imaged in supine position. In this study, we present the vertical gradients in fractional ventilation and oxygen uptake. While all the healthy subjects showed higher ventilation in the posterior slices, the oxygen uptake was always constant in the gravity direction. Smokers on the other hand showed higher uptake in the dependent regions and gravitational gradients in FV were lost in COPD subjects.

REFERENCE: [1] Glenny RW and Roberston T, Comprehensive Physiology, volume 1 Jan 2011. [2] Hamedani H, et al NMR in bio, 2014. [3] Emami K, et al ISMRM 2012. [4] Hamedani H, et al, ISMRM 2014.