Short-breath-hold pO2 imaging with 3He: Initial experience in lung disease

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Introduction: We recently described a method for generating lung pO_2 maps during a single breath hold of less than 6 seconds using hyperpolarized ^{3}He MRI [1]. Relatively homogeneous pO_2 maps were obtained in healthy human subjects, with mean values (84-112 mm Hg) consistent with the steady state value of 100 mm Hg reported by West [2]. Although the short-breath-hold method does not measure rates of oxygen uptake, it should be able to provide information about regional ventilation-perfusion ratios (V/Q), since areas of elevated V/Q will have higher oxygen concentration (and conversely) at steady state. The motivation behind the short-breath-hold method is to permit pO_2 measurements in subjects with impaired lung function that cannot sustain an extended breath hold. In the present work, we report on initial experience applying this technique in patients with lung disease and explore implications for pO_2 measurements in patients with chronic obstructive pulmonary disease (COPD).

Methods: The short-breath-hold technique allows a pO_2 "snapshot" to be calculated directly from the pixel-by-pixel ratio of two ^{3}He spin density images separated by a time delay of a few seconds ("oxygen-sensitization" time) during which oxygen-induced T_1 relaxation occurs. The first image is acquired in reverse-centric phase-encoding order and the second with centric ordering, so that by a judicious choice of imaging parameters the RF contribution to the oxygen-weighted magnitude ratio can be made negligible. Asymmetry between the *k*-space filters is minimized by using variable-flip-angle excitation RF pulses with a terminal flip angle of 10°. Two COPD patients (male, ages 66 and 60), both with single-lung transplants, were imaged using the short-breath-hold pulse sequence. Sequence parameters included: FOV, 315×420 mm; matrix, 48×64 or 30×64; TR/TE, 7.5/1.9 ms; readout bandwidth, 390 Hz/pixel; oxygen-sensitization time, 2.7 or 3.0 s. To avoid complications resulting from diffusion perpendicular to the imaging plane, all images were obtained as coronal projections. Subjects inhaled ~150-220 ml hyperpolarized ^{3}He gas plus enough room air to reach full inspiration, and ^{3}He MR imaging was performed during the subsequent breath hold lasting approximately 5 seconds. Spirometry was also performed in each subject. The ^{3}He gas was polarized to ~35% by collisional spin exchange with an optically pumped rubidium vapor using a commercial system (Model 9600, MITI), and all MR imaging was performed using a 1.5 T commercial scanner (Sonata, Siemens). In addition to the generation of pO_2 maps, the bulk average pO_2 within each lung was calculated from the underlying spin density images by comparing the total ^{3}He signal in each lung before and after the oxygen-sensitization time.

Results: MR images from patient #2 (right-lung transplant, FEV_1 26% predicted) are shown in the figure. The axial and coronal ^{1}H scout images in **(A)** illustrate the degree of asymmetry between the transplanted lung (on the left in the figure) and native lung. Both ^{3}He spin density images from the short-breath-hold pO_2 acquisition are shown in **(B)** along with the calculated pO_2 map. Measured values in the transplanted lung are fairly homogeneous except for markedly elevated values near the diaphragm. The likely explanation for these elevated values can be seen by carefully comparing the two ^{3}He images: the patient apparently relaxed his breath hold between the first and second images. The gas near the diaphragm did not depolarize rapidly, but rather moved up in the field of view. However, the loss of signal in this region of the image leads to anomalously high values on the pO_2 map. Interestingly, the same phenomenon is not seen in the native lung. As can be inferred from its large size, there is a significant loss of compliance in the native lung, so this side of the diaphragm does not easily move. Focal regions with elevated pO_2 values are also apparent in the native lung (arrows). Despite their presence, the bulk pO_2 is actually lower in the native lung (94 mm Hg) than in the transplanted lung (115 mm Hg). Closer inspection of the pO_2 map reveals that neighboring pO_2 values are negative. These negative values can be explained if there is significant diffusion of the gas during the oxygen-sensitization time from well-ventilated to poorly-ventilated regions, such that the ^{3}He signal actually increases in these regions. Thus it is reasonable to suppose that at least some of the apparent pO_2 variation is an artifact of gas motion within the non-uniformly ventilated regions. Similar effects were observed in the native lung of patient #1 (left-lung transplant, FEV_1 51% predicted), and the bulk pO_2 was also lower in the native lung (84 mm Hg) than in the transplanted lung (103 mm Hg).

Discussion: These initial results demonstrate both the promise and potential limitations of the pO_2 measurement technique. Although pO_2 maps were obtained in a short breath hold from patients with impaired lung function, artifacts were present due to motion of the inhaled ^{3}He gas. We contend that this effect is not unique to our particular implementation but is a limitation of the underlying pO_2 measurement technique, in which subtractions are made between images acquired at substantially different times within a breath hold. Furthermore, it is possible that such effects may be masked in longer breath hold implementations and oxygen uptake measurements. Since there are more free parameters to be fit in these analyses, gas motion could be mistakenly attributed to variations in either pO_2 or oxygen uptake rates. In conclusion, since non-uniform ventilation and difficulty sustaining a breath hold are intrinsic to COPD, the effects of gas motion on measured pO_2 values must be carefully considered in the interpretation of pO_2 measurements in obstructive lung disease using hyperpolarized ^{3}He.

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References: [1] GW Miller *et al*., Abstract #243, ESMRMB, 2005. [2] J West, *Respiratory Physiology* (6th Ed.), 2000.

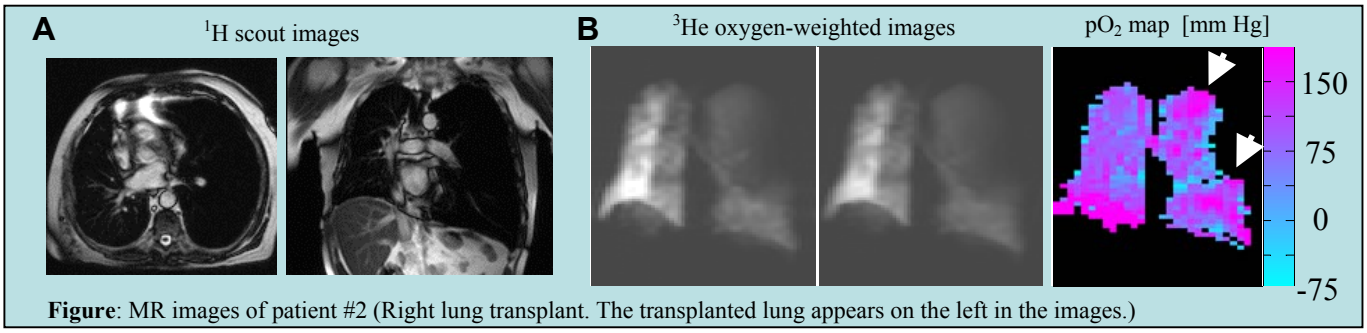

Figure: MR images of patient #2 (Right lung transplant. The transplanted lung appears on the left in the images.)