Mapping the ventilation–perfusion ratio in chronic obstructive pulmonary disease using oxygen-enhanced MRI

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Introduction We present a preliminary analysis of oxygen-enhanced (OE-) MRI data in subjects with Chronic Obstructive Pulmonary Disease (COPD) and age-matched healthy subjects, using a novel two-compartment physiological model. COPD refers to two generally co-existing lung diseases, chronic bronchitis and emphysema, in which the airways become narrowed and the parenchyma destroyed. COPD is commonly diagnosed and monitored using standard spirometric tests which provide only global measures of lung function. Previous authors have semi-quantitatively mapped the relative effects of ventilation (V) and perfusion (Q) by calculating a "V/Q signal intensity ratio" using OE-MRI and Arterial Spin Labelling [1]. Our new approach allows parameters directly related to V and Q to be extracted from OE-MRI data and quantitative maps of the V/Q ratio to be obtained.

Molecular oxygen is paramagnetic and acts a contrast agent when dissolved in parenchymal water. Breathing 100% oxygen increases the concentration of dissolved oxygen in the lung tissue and produces a decrease in T_1. Using a mathematical compartmental model that considers gas exchange processes in the lung in one compartment consisting of the alveolar gas space and second consisting of parenchymal water within tissues and blood within capillaries, we are able to relate the T_1 change in the OE-MRI data directly to physiological parameters indicative of lung function for the first time in the diseased lung.

Methods Dynamic OE-MRI imaging was carried out on a 1.5 T Philips Intera system (Philips Medical Systems, Best, NL) on a small group of age-matched healthy subjects and subjects with COPD. Written informed consent was obtained. A 10 mm thick coronal slice was positioned posterially with a 450 x 450 mm field of view. A measure of T_1 was acquired from this volume using the half Fourier acquisition single shot turbo spin echo (HASTE) sequence (TR 5500 ms, TE 3 ms, 68 phase-encoding steps, flip angle 90°, matrix 128 x 128) at a range of inversion times (TI 50, 300, 110, 2000 and 5000 ms). This measurement preceded a dynamic series of images acquired at TI=1100 ms and was used to infer T_1 for this series. During the inversion recovery T_1 measurement the volunteers breathed medical air (21% oxygen) via a high concentration non-rebreathing mask (Intersurgical, Wokingham, UK). After the first 15 images of the dynamic series the supply to the mask was switched to 100% oxygen and a further 61 images acquired. Gas was delivered at 15 L/min and the subject breathed freely throughout. The data collection was repeated on the same subjects after 7-10 days to investigate reproducibility.

Due to diaphragm motion and volume changes during free breathing it is necessary to register the images, as described in [2]. The outline of the lung was manually marked up for a sub-set of the images and used to build an active shape model [3] to automatically locate the outline of the lung on the remaining images. The registration procedure was based on the observation that during breathing the lung stretches mainly in the longitudinal direction due to motion of the diaphragm. Images were transformed onto a reference image chosen from the set using a simple linear transformation on each column of voxels. Changes in T_1 due to inhalation of oxygen were then converted to changes in partial pressure of oxygen (ΔPO_2) using relaxivity constant (2.49×10^{-4} [4]) for each registered image in the dynamic series, on a voxel-by-voxel basis.

In applying the compartmental model we assume that the diffusion across the alveolar membrane between the two compartments is rapid. This allows, for a known change in fractional inspired oxygen (79%) and an assumed change in systemic O_2 concentration, ΔPO_2 to be related to ventilation, perfusion and the time average of the blood-gas partition coefficient for oxygen. The model was fitted voxel-by-voxel to obtain these 3 fit parameters and maps of V/Q were generated. The derivation of this model is described in detail in Naish and Parker ISMRM 2010 (submitted).

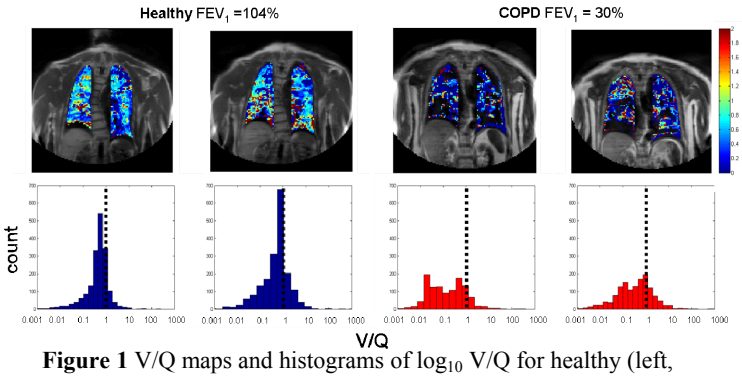

Figure 1 V/Q maps and histograms of $\log_{10}$ V/Q for healthy (left, blue) and COPD (right, red) subjects, both scan and re-scan. Dotted line, V/Q=1.

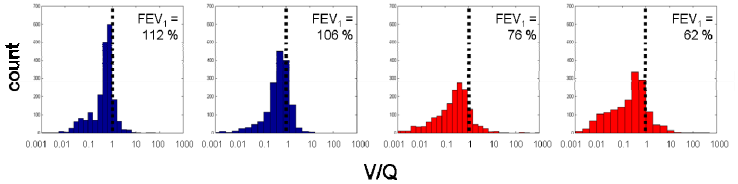

Figure 2 Histograms of $\log_{10}$ V/Q for 2 other healthy subjects (left, blue) and 2 other COPD subjects (right, red).

Results Figure 1 shows a representative V/Q map for one healthy (FEV_1 = 104% predicted) and one severe COPD (FEV_1 = 30% predicted) subject, both scanned and re-scanned. A relatively homogenous V/Q is observed in the healthy subject, in the physiological normal range (~0.8). In COPD, regions of high and low V/Q are apparent and ventilation appears generally lower throughout the imaging plane. Histograms clearly support this. A narrow peak is observed in the healthy subject and a broad peak centred at lower V/Q observed in subject with COPD. For each subject the reproducibility of both maps and histograms is generally good, although there are noticeable differences between scans. This is primarily due to the difficulties in positioning the slice in exactly the same location in each scan. The development of a 3D protocol will negate such issues and is currently under investigation. Figure 2 shows histograms for a further 2 healthy subjects and 2 subjects with moderate COPD, reproducibility data is not shown. A similar, but less pronounced, peak broadening and shift to low V/Q is observed in the moderate COPD subjects compared to that seen in severe COPD in Figure 1.

Conclusions We present a regional characterisation of the ventilation-perfusion ratio via in a one-step process. Using a physiological model-based analysis of the time-varying OE-MRI signal, detailed, quantitative information about the regional changes to the lung in COPD has been obtained. This novel MR method is minimally-invasive and repeatable. It is of significant interest to the respiratory community as it is likely to be more sensitive to early onset of disease than the more traditional global lung function measures because of the spatial information obtained.

References 1. Mai VM *et al. Magn Reson Med* **48**,341–350, 2002; 2.Naish JH *et al. Magn Reson Med* **54**, 464–469, 2005; 3. Cootes TF *et al. Comput Vis Image Understand* **61**, 38–59, 1995; 4. Zaharchuk G *et al. Acad Radiol* **13**, 1016–1024, 2006.

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