Heterogeneity of the ventilation–perfusion ratio in lung disease using OE-MRI

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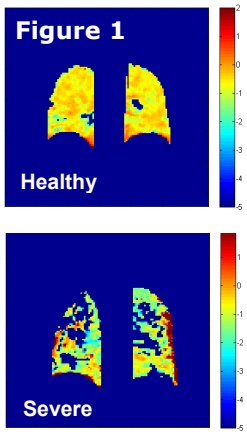
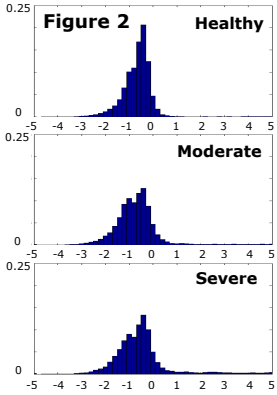
Introduction We present the results of an oxygen-enhanced (OE-) MRI study in subjects with Chronic Obstructive Pulmonary Disease (COPD) and age-matched healthy subjects. COPD refers to two generally co-existing lung diseases, chronic bronchitis and emphysema, in which the airways become narrowed and the parenchyma destroyed. COPD is commonly diagnosed and monitored using standard spirometric tests which provide only global measures of lung function. Previously the relative effects of ventilation (V) and perfusion (Q) have been calculated as the "V/Q ratio" using SPECT [1,2], PET [3], ^{19}F MRI [4] and MIGET [5]. Our approach allows quantitative maps of V/Q ratio to be determined using a novel two-compartment physiological model, applied to dynamic the OE-MRI data[6,7].



Methods Dynamic OE-MRI imaging was carried out on a 1.5 T Philips Achieva system (Philips Medical Systems, Best, NL) on a group of 12 subjects with moderate COPD (GOLD Stage 1-2 [8]), 12 with severe COPD (Gold stage 3-4) and 12 age-matched healthy subjects. Written informed consent was obtained. A 10 mm thick coronal slice was positioned posterially with a 450 x 450 mm^2 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, 1100, 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 gas supply to the mask was switched to 100% oxygen and a further 76 images acquired, then back to medical air for a further 61 image acquisitions. 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 perform motion correction, as described in [9]. Breathing 100% oxygen increases the concentration of dissolved paramagnetic molecular oxygen in the lung tissue and produces a decrease in T_1. Changes in T_1 due to inhalation of oxygen were converted to changes in partial pressure of oxygen (ΔPO_2) for each registered image in the dynamic series, on a voxel-by-voxel basis. Maps of V/Q were generated via the application of a compartmental model to the time series, on a voxel-by-voxel basis [6]

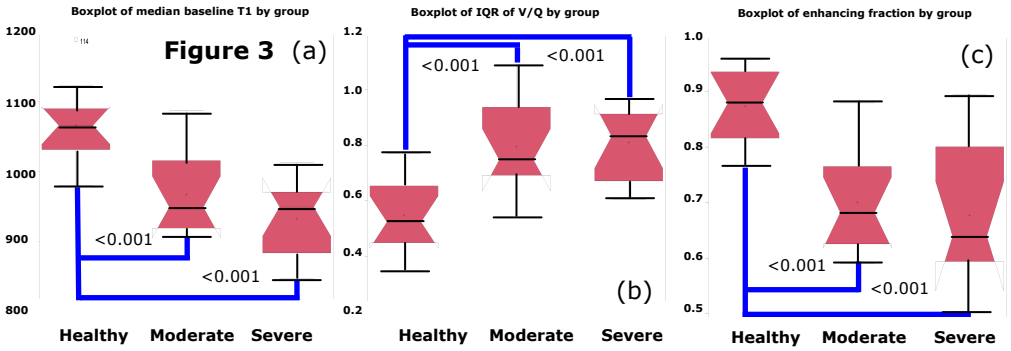


Results & Discussion Figure 1 shows $\log_{10}$ V/Q maps for a representative healthy subject and a subject with severe COPD. The healthy lung shows a relatively homogeneous map, whereas in COPD considerable heterogeneity is apparent, with some regions of low and some regions of high V/Q. The data are only shown for voxels in which the model was preferred over a flat line fit, according to the Akaike information criterion [10], thresholded at p=0.5.

Figure 2 shows the group-average histograms for the healthy, moderate COPD and severe COPD groups. A narrow peak, just below V/Q of 1 ($\log_{10}$ V/Q = 0), is observed in the healthy group; this peak broadens and a second peak becomes evident at lower V/Q for both the moderate and severe COPD groups. Some evidence of a high V/Q tail to the histogram is also evident.

Group parameter boxplots are presented in figure 3. The first of these is compatible with the findings of [11,12], who demonstrated a statistically significant difference is observed in the median baseline (on air) T_1 when comparing the healthy and COPD lungs. Secondly, the heterogeneity apparent in the maps and histograms is captured by the interquartile range of $\log_{10}$ V/Q and shows significant differences between the healthy and COPD groups. Finally, the fraction of the lung in which there is a sufficient signal change to fit the model (the enhancing fraction, as detailed above) is significantly lower in the moderate and severe COPD groups than in the healthy subjects.

Figure 1 Comparison of $\log_{10}$ V/Q maps for healthy and severe COPD.
Figure 2 Group $\log_{10}$ V/Q histograms for healthy, moderate COPD and severe COPD
Figure 3 Group boxplots of (a) median baseline T_1 (b) interquartile range (IQR) of $\log_{10}$ V/Q and (c) enhancing fraction calculated from the V/Q model. Groups were compared by taking the mean of the 2 visits per subjects and performing a mixed model ANOVA.



Conclusions The heterogeneity and shape of the $\log_{10}$ V/Q histograms presented in figure 2 show similarities to those previously published in the SPECT and PET literature [1,2,3], with the increased heterogeneity being represented by a broadening and appearance of an extra peak/s. The lack of statistical significance between the moderate and severe COPD groups agrees with the conclusions of a recent paper using MIGET [5] and may be evidence of pathogenic processes that decrease V and Q concurrently at a local level.

References **1.** Suga K *et al. Nuc Med Com* **30**:881–889, 2009; **2.** Suga K *et al*, *Ann Nucl Med* **24**:269–277, 2010; **3.** Vidal Melo MF *et al. J Nucl Med* **51**(1):57–65, 2010; **4.** Adolphi N *et al. MRM* **59**:739–746, 2008; **5.** Rodríguez-Roisin R *et al*, *J Appl Physiol* **106**:1902–1908, 2009; **6.** Naish JH and Parker GJM, *Proc. ISMRM.* **18**:2516, 2010; **7.** Hubbard PL *et al*, *Proc. ISMRM* **18**:2515, 2010; **8.** www.goldcopd.com; **9.** Naish JH *et al. MRM* **54**: 464–469, 2005; **10.** Akaike H, *IEEE T Autom Contr* **19**, 716–723, 1974; **11.** Stadler A. *et al. MRM* **59**: 96–101, 2008; **12.** Stadler A. *et al. JMRI* **21**:759–764, 2005.

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