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

P. L. Hubbard1,2, G. J. Parker1,2, D. Singh1, E. Bondesson1, L. E. Olsson1, L. Wigström1, S. S. Young2, and J. H. Naish1,2

1Imaging Sciences and Biomedical Engineering, The University of Manchester, Manchester, United Kingdom, 2The Biomedical Imaging Institute, The University of Manchester, Manchester, United Kingdom, 3Airway Pharmacology Group, School of Translational Medicine, University Hospital of South Manchester Foundation Trust, Manchester, Greater Manchester, United Kingdom, 4AstraZeneca R & D, Lund, Sweden, 5AstraZeneca R & D, Möndal, Sweden, 6AstraZeneca R & D, Charnwood, United Kingdom

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]. 19F MRI [4] and MIGET [5]. Our approach allows quantitative maps of V/Q ratio to be determined using a novel two-component physiological model, applied to dynamic 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 posteriorly with a 450 x 450 mm² field of view. A measure of T₁ 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 T₁ for this series. During the inversion recovery T₁ 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 T₁. Changes in T₁ due to inhalation of oxygen were converted to changes in partial pressure of oxygen (PO₂) 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 log₁₀ 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 (log₁₀ 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 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) T₁ when comparing the healthy and COPD lungs. Secondly, the heterogeneity apparent in the maps and histograms is captured by the interquartile range of log₁₀ 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.

Conclusions

The heterogeneity and shape of the log₁₀ 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


Acknowledgements

This study was funded by AstraZeneca.