# DYNAMIC OE-MRI OF THE LUNG IN ASTHMA

Weijuan Zhang[1,2], Robert M Niven[3,4], Simon S Young[5], Yuzhen Liu[5], Penny L Hubbard[1,2], Geoffrey JM Parker[1,2], and Josephine H Naish[1,2]

*[1]Centre of Imaging Sciences, The University of Manchester, Manchester, United Kingdom, [2]Biomedical Imaging Institute, The University of Manchester, Manchester, United Kingdom, [3]North West Lung Centre, University Hospital of South Manchester, Manchester, United Kingdom, [4]Department of Respiratory Medicine, University Hospital of South Manchester, Manchester, United Kingdom, [5]Personalised Healthcare and Biomarkers, AstraZeneca, Alderley Park, United Kingdom*

**INTRODUCTION** Dynamic oxygen-enhanced (OE-) MRI can obtain spatial information on regional oxygen delivery and uptake in the lung by using paramagnetic oxygen ($^{16}O_2$) as a contrast agent. The aim of this study was to estimate the feasibility of dynamic OE-MRI in the assessment of lung functional changes in asthmatic patients and to explore the correlation between dynamic OE-MRI and spirometry.

**METHODS** Dynamic OE-MRI was performed on 4 mild asthmatic patients (the percent of predicted forced expiratory volume in 1 s ($FEV_1$% Pred norm, pre-bronchodilator)> 85%; treatment requirement is consistent with BTS/SIGN asthma guideline step 1 or step 2) and 6 severe asthmatic patients ($FEV_1$% Pred norm=50%-80%; treatment requirement is consistent with BTS/SIGN asthma guideline step 4 or step 5) twice at 1 month apart using a 1.5 T Philips Achieva MR system. Spirometry was carried out within 7 days prior to MR scans. Ethical approval and written informed consent were obtained. All patients withheld short-acting $\beta_2$-adrenergic receptor agonists for 6 hours and long-acting $\beta_2$-adrenergic receptor agonists for 12 hours prior to each visit. Baseline $T_1$ mapping was performed while subjects breathed medical air (21% $O_2$) using a 2D inversion-recovery turbo spin echo sequence (IR-TSE) with a range of inversion times (TI=60, 300, 1100, 2000 and 5000 ms). This was followed by a $T_1$-weighted dynamic acquisition to monitor the change in $T_1$ during gas switchover from medical air to 100% $O_2$ using the same sequence but with a single TI=1100 ms. Other parameters were: TR/TE 6000 ms/3.2 ms, 128 x 128 matrix, 10 mm thickness, pixel size 3.52 mm x 3.52 mm, free breathing, no respiratory or cardiac triggering. A single coronal slice was acquired. All images were registered to the end inspiration position [1]. The dynamic measurements of $T_1(t)$ were then converted to the changes in the partial pressure of $O_2$ ($\Delta PO_2(t)$) in the lung parenchyma. The $\Delta PO_2(t)$ curve was fitted pixel-by-pixel according to $\Delta PO_2(t) = \Delta PO_{2max}(1-\exp(-t/\tau_{up}))$ and $\Delta PO_2(t) = \Delta PO_{2max}\exp(-t/\tau_{down})$ for the calculation of $O_2$ wash in ($\tau_{up}$ in min) and wash out ($\tau_{down}$ in min) time constants and the plateau $\Delta PO_2$ value ($\Delta PO_{2max}$ in mmHg) [2].

**RESULTS** As can be seen in the examples in Figure 1, the severe asthmatic patient shows more low value regions of $\Delta PO_{2max}$ (in blue). The $\tau_{up}$ and $\tau_{down}$ maps show more heterogeneity in severe asthmatic lungs than mild asthmatic lungs. The group averaged $\Delta PO_2$ time course curve of the mild group shows a steeper $O_2$ wash-in slope and a higher plateau than that of the severe group (Figure 2). There was a statistically significant difference between the plateau $\Delta PO_2$ values for the two groups (Table 1), although not in the mean value of $\tau_{up}$ and $\tau_{down}$. The inter quartile range of $\tau_{up}$ was significantly wider in the severe asthma group than in the mild asthma group, while the inter quartile range of $\tau_{down}$ between the two groups were not significantly different. Table 2. shows the Spearman's rank correlation between the mean values of $\Delta PO_{2max}$, inter quartile range of $\tau_{up}$ and spirometric parameters. $\Delta PO_{2max}$ had a borderline correlation with age and $FEV_1$% Pred norm, a moderate correlation with the actual value of post-bronchodilator $FEV_1$ and $FEV_1$/FVC (forced vital capacity) and a strong correlation with actual value of pre-bronchodilator $FEV_1$. The mean value of $\tau_{up}$ and $\tau_{down}$ showed no linear correlation with age and spirometric parameters, while the inter quartile range of $\tau_{up}$ was significantly correlated with $FEV_1$ % Pred norm., pre bronchodilator $FEV_1$, post bronchodilator $FEV_1$ and $FEV_1$/FVC.

**CONCLUSION** Quantitative dynamic OE-MRI outputs are sensitive to disease sensitivity in asthma and are correlated with spirometry. The spatial information of oxygen delivery and uptake of the lung available from dynamic OE-MRI using a non-ionising source of contrast makes it an attractive option in the assessment of asthma.

**REFERENCES** 1. Naish, J.H., et al., *Magn Reson Med*, 2005. 54(2): p. 464-469. 2. Kershaw, L.E., *et al. Magn Reson Med*; 2010; 64: p 1838–1842.

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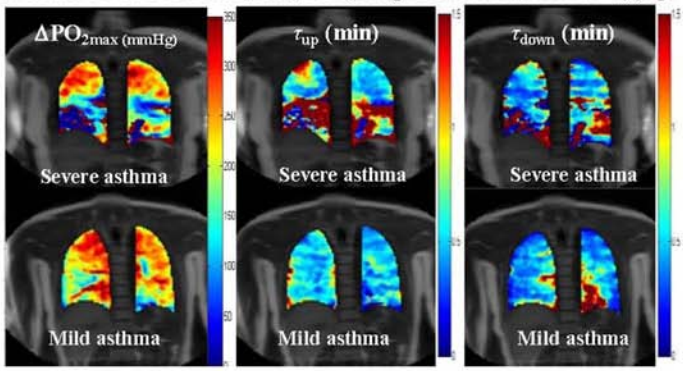


Figure 1. The OE-MRI parameter maps of a severe asthmatic participant (F, 19yrs, $FEV_1$ % Pred norm. =63.5%) and a mild asthmatic participant (F, 19yrs, $FEV_1$ % Pred norm.=99.0%).

Table 1. Comparison of OE-MRI parameters in two groups

| | Mild asthma | Severe asthma | p-value |
|---|---|---|---|
| Mean $\Delta PO_{2max}$ (mmHg) | 288.7±43.8 | 172.4± 37.2 | p=0.002** |
| Mean $\tau_{up}$ (min) | 0.86±0.14 | 1.77±1.14 | p=0.159 |
| Mean $\tau_{down}$ (min) | 1.17± 0.87 | 2.67±2.16 | p=0.257 |
| p-value† | p=0.477 | p=0.502 | |
| IQR_$\Delta PO_{2max}$ | 138.6± 53.2 | 126.0± 25.3 | p=0.622 |
| IQR_$\tau_{up}$ | 0.24± 0.10 | 0.90± 0.35 | p=0.008** |
| IQR_$\tau_{down}$ | 0.72± 0.75 | 1.37± 1.12 | p=0.171 |

†p-value between $\tau_{up}$ and $\tau_{down}$; ** The difference is significant at 0.05, 0.01 level.

Table 2. Spearman's rank correlation between OE-MRI and spirometry

| | | Age | $FEV_{1preBD}$ | $FEV_1$%$_{Pred\ norm}$ | $FEV_1$/FVC | $FEV_{1post\ BD}$ |
|---|---|---|---|---|---|---|
| Mean $\Delta PO_{2max}$ | CC§ | -0.638 | 0.830 | 0.636 | 0.721 | 0.767 |
| | p | 0.047* | 0.003** | 0.048* | 0.019* | 0.016* |
| IQR_$\tau_{up}$ | CC | 0.438 | -0.673 | -0.745 | -0.685 | -0.767 |
| | p | 0.206 | 0.033* | 0.013* | 0.029* | 0.016* |

§Spearman's rank correlation coefficient. *,** The correlation is significant at 0.05, 0.01 level.

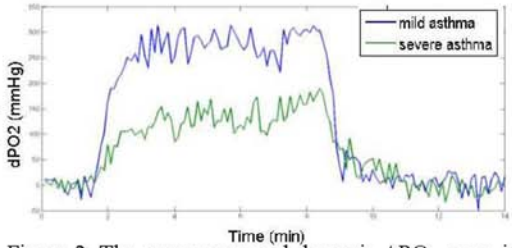


Figure 2. The group averaged dynamic $\Delta PO_2$ curve in mild asthma (blue) and severe asthma (green).