Quantitative evaluation of Ventilation Dynamics in Asthma during methacholine challenge using Hyperpolarized 3He Magnetic Resonance Imaging

S. Costella[1,2], A. Wheatley[1], D. McCormack[3], and G. Parraga[1,2]

[1]Imaging Research Laboratories, Robarts Research Institute, London, Ontario, Canada, [2]Graduate Program in Biomedical Engineering, University of Western Ontario, London, Ontario, Canada, [3]Medicine, Division of Respirology, University of Western Ontario, London, Ontario, Canada

Introduction: Pulmonary functional imaging using helium-3 (^{3}He) magnetic resonance imaging (MRI) has provided us with a way to quantitatively evaluate the spatial and temporal functional changes in a variety of respiratory conditions. ^{3}He MRI ventilation abnormalities in particular have identified those specific regions of the lung that function poorly in obstructive airway diseases such as asthma and COPD [1]. In previous work, deLange *et al* compared pre- and post-methacholine MRI measurements of pulmonary function [2] and they also showed the longitudinal persistence of ^{3}He ventilation abnormalities in asthma over relatively long periods of time [3]. In both cases, MRI indicated that the size and number of focal ventilation defects changed upon challenge, but these were relatively unchanged over time under non-asthmatic exacerbation conditions. In an extension of this previous work, we hypothesized that 3D acquisitions of ^{3}He MRI ventilation defect volume (VDV) and ventilation defect percent ((VDP) –the VDV normalized by the 1H thoracic cavity volume) would be significantly increased at the concentration of methacholine that induced a 20% change (PC_{20}) in the forced expiratory volume at 1 s FEV_1) but the number of defects would not significantly change. We also hypothesized that upon salbutamol rescue, the relationship between the change in FEV1 and VDV would not be significant because of anecdotal evidence of incomplete resolution of ventilation defects (with return to normal FEV_1) after asthmatic exacerbation using either exercise or methacholine. Therefore, the objective of this study was to evaluate the volume and number of ventilation defects in asthma before and after methacholine challenge as well as post recovery with salbutamol using hyperpolarized ^{3}He MRI and a semi-automated ventilation defect segmentation and defect counting algorithm.

Methods: Hyperpolarized ^{3}He MRI was performed at 3.0 T using a fast gradient-recalled echo (FGRE) method with centric k-space sampling to acquire ^{3}He spin density images. Plethysmography and spirometry were also performed for 16 asthmatic subjects (mean age = 32.3 ± 10.6 years) three times within an hour (just prior to methacholine challenge, 5 minutes after achieving PC_{20} and 30 minutes after salbutamol administration). Semi-automated segmentation using a modified k-means cluster algorithm was used to generate ^{3}He VDV and VDP as well as to obtain defect counts and defects sizes on a 3D model of the 2D image slices. Ventilation defects were scored based on the clustering of ≥20 connected pixels with the lowest cluster value pixel intensity.

Results: As shown in Table 1, there was a significant interaction between mean defect volume and time point. There was no significant interaction between defect count and time point except for PC_{20} and post-salbutamol recovery ($p = 0.011$). With respect to the relationship of FEV_1 and ventilation defect percentage (VDP) between PC_{20} and post-salbutamol, Figure 1 shows that no significant results are present due to the presence of two outliers who exhibit large changes in VDP.

Discussion and Conclusion: ^{3}He MRI provides a way to quantitatively measure defect changes before and after methacholine challenge and post-recovery in the asthmatic lung. Our results suggest that mean defect size is the dominant mechanism for the changes in FEV_1 that occur at PC_{20} as compared to defect count. This provides important new information on the mechanisms involved in asthma exacerbations and insights on prophylaxis to avoid exacerbations.

References:

[1] Altes, T. *et al. J. MRI*. **13**, 378-384 (2001).
[2] de Lange, E. *et al. J Allergy Clin Immunol.* **119**, 1072-1078 (2007).
[3] de Lange, E. *et al. Radiology*. **250,** 567-575 (2009).

	Mean Defect Area	Defect Count
Base v. Meth	$p < 0.05$	$p > 0.05$
Meth v. Recovery	$p < 0.001$	$p < 0.05$
Recovery v. Base	$p < 0.05$	$p > 0.05$

Table 1: relationship between time points with mean defect area and count .

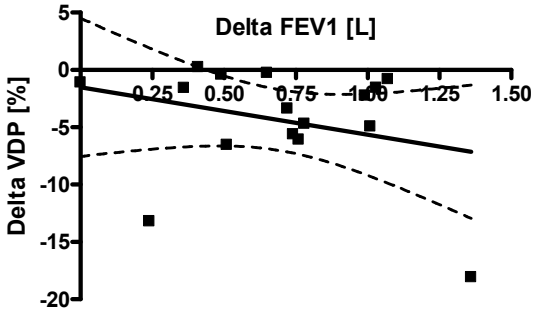

Figure 1: Relationship between change in FEV_1 and change in VDP at PC_{20} and after salbutamol recovery.

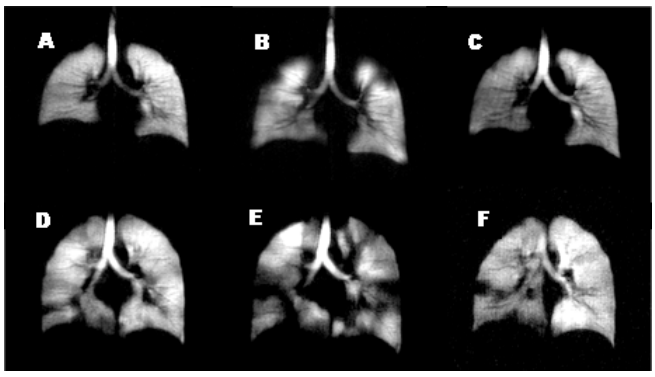

Figure 2: Hyperpolarized ^{3}He MRI of asthmatic lungs of two subjects at baseline (A and D), after methacholine challenge (B and E) and after recovery (C and F).