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

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Introduction: Pulmonary functional imaging using helium-3 (3He) 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. 3He 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 3He 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 3He 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 (PC20) in the forced expiratory volume at 1 s FEV1 but the number of defects would not significantly change. We also hypothesized that upon salbutamol rescue, the relationship between the change in FEV1 and VDP would not be significant because of anecdotal evidence of incomplete resolution of ventilation defects (with return to normal FEV1) 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 3He MRI and a semi-automated ventilation defect segmentation and defect counting algorithm.

Methods: Hyperpolarized 3He MRI was performed at 3.0 T using a fast gradient-recalled echo (FGRE) method with centric k-space sampling to acquire 3He 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 PC20 and 30 minutes after salbutamol administration). Semi-automated segmentation using a modified k-means cluster algorithm was used to generate 3He 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 PC20 and post-salbutamol recovery (p = 0.011). With respect to the relationship of FEV1 and ventilation defect percentage (VDP) between PC20 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: 3He 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 FEV1 that occur at PC20 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:

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<thead>
<tr>
<th>Mean Defect Area</th>
<th>Defect Count</th>
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<tr>
<td>Base v. Meth</td>
<td>p &lt; 0.05</td>
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<tr>
<td>Meth v. Recovery</td>
<td>p &lt; 0.001</td>
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<tr>
<td>Recovery v. Base</td>
<td>p &lt; 0.05</td>
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Table 1: relationship between time points with mean defect area and count.

Figure 1: Relationship between change in FEV1 and change in VDP at PC20 and after salbutamol recovery.

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