Systematic Segmental Analysis of Ventilated Lung Volumes in Severe Asthma using 3-Helium MRI Pre and Post Bronchodilator Therapy: Comparison with Spirometric Indices and HRCT

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Introduction

3-Helium (3-He) MRI of the lungs has the potential to become a powerful tool for assessing the regional ventilation of the lungs. Asthma is a disease characterised by airway hyper-responsiveness and bronchoconstriction, which narrows the airways and limits airflow. 9% of the UK population have asthma, with 1400 fatalities per year, 33% of these are <65 years of age. In the USA 8% of the population are asthmatic with 5000 deaths annually. Regional assessment of ventilation change is important in determining different phenotypes of asthma and in understanding the effects of bronchodilator therapy.

Methods

Six patients with steroid resistant or dependent asthma (mean prednisolone equivalent daily dose 24.4mg) were assessed with spirometry and 3-He ventilation MRI pre and 15 minutes post bronchodilator therapy (nebulized ventolin/terbutaline 5mg). MR images were acquired on a 1.5 T Eclipse system*, (Philips Medical Systems*). 24x 10mm slices were produced in 20s using a 3D gradient recalled echo sequence [1] after inhaling a mixture of 300ml hyperpolarized 3-He / 500ml N_2, followed by room air to fully inflate the lungs. 3-He was hyperpolarized on site using a spin exchange polarizer (*GE-Health)*. The images from the 3-Helium scans were systematically segmented into 6 regions of interest for each lung using the bifurcation of the bronchi as a reference point. Each region was then thresholded (Fig 1) and the pixels counted to calculate a volume. The changes in total ventilated volume were compared to the changes in spirometric indices. All patients were also imaged with high-resolution CT (HRCT) as part of their routine clinical care.

Results

Two patients were unable to hold their breath long enough pre-therapy to produce adequate images for full evaluation, the images from the remaining four patients were segmented and thresholded and the regional lung volumes were calculated. All patients showed an increase in total ventilated volume post bronchodilator, with some resolution of ventilation defects seen pre-therapy. The percentage increases in ventilated volumes, forced expiratory volume in one second (FEV1), and forced vital capacity (FVC) are displayed below (table 1), the Pearson correlation coefficients with the increase in ventilated volume were 0.995 and 0.987 respectively.

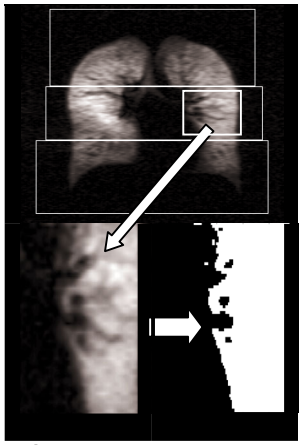

Fig 1.
Segmentation & Threshold

Patient	%Increase 3-He Volume	%Increase FEV_1	%Increase FVC
1	30	20	13
2	6	10	11
3	10	17	6
4	130	97	48

Table 1: Changes in ventilation post bronchodilator therapy

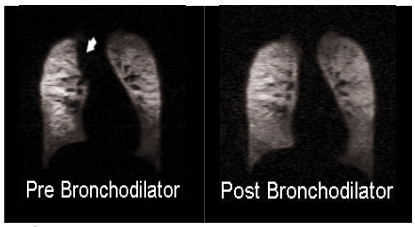

Fig 2.
Resolution of ventilation defect

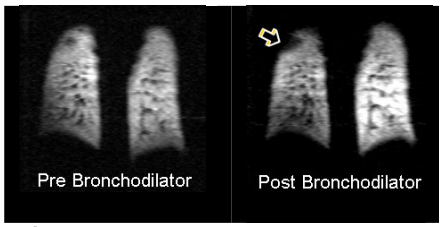

Fig 3.
Extension of ventilation defect

There was a marked difference in the distribution of ventilation changes between patients, and this was confirmed in the segmental analysis; patient 1 showed a wide range of changes from a 288% increase in the right posterior basal region to a 6% reduction in the left posterior medial region. Whereas patient 2 showed a much more uniform distribution in ventilated volume changes Ranging from a 12% reduction in the left posterior basal region to a 12% increase in the right posterior apical region. Visual review of the ventilation changes in all 6 patients showed that while all of the patients had resolution of some ventilation defects (Fig 2), 4 patients developed new and/or extended existing ventilation defects post bronchodilator (Fig 3). The HRCT scans were independently assessed, and each region was scored. No correlation between the CT scores and the changes in ventilated volume was demonstrated.

Discussion

Patients with severe asthma requiring similar levels of steroid therapy exhibit large variations in the distribution of ventilation changes following bronchodilator therapy. The changes in total ventilated volume seem to be directly related to the reversibility of asthma symptoms as measured by spirometry, and the regional assessment of ventilated volume indicates precisely where the changes occur. The fact that the regional assessment of the HRCT scans did not correlate with the changes seen at MRI may indicate that the ventilation changes occur distal to the CT manifestations of asthma. The systematic, and visual approaches to image evaluation reveal that a number of processes are occurring; the resolution of ventilation defects, the extension of existing defects, new defects appearing and increased expansion of the lungs. The first and last effects can be put down largely to the bronchodilatory effect of the inhaled steroid, and the variability of ventilation defects may be due to the shifting around of mucus plugs. Regional evaluation of ventilation changes using 3-He may prove to be an ideal tool for the assessment of new and existing inhaled therapies.

[1] Wild JM, Woodhouse N, Paley MN, Fichele S, Said Z, Kasuboski L, vanBeek EJ. *Comparison between 2D and 3D gradient-echo sequences for MRI of human lung ventilation with hyperpolarized 3He.* Magn Reson Med. 2004 Sep;52(3):673-8