Multi-Nuclear MR Imaging of Ventilation and Perfusion Distribution Response to Bronchodilator in Asthma

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Target Audience: Respiratory clinicians, hyperpolarised gas MRI community, pharmaceutical scientists

Purpose: ^{3}He MRI is sensitive to regional ventilation changes after bronchodilator administration in patients with asthma [1]. Imaging of blood perfusion distribution [2] in the same exam provides information on perfusion matching and insight into which parts of the lung contribute to gas exchange. The aim of this study was to image regional ventilation and perfusion (VQ) distributions at baseline and post-bronchodilator (post-BD) in patients with moderate-to-severe asthma using ^{3}He ventilation and ^{1}H perfusion MRI.

Methods: 5 patients with moderate-to-severe asthma (GINA 2-5) incompletely controlled on their current therapy, were scanned using a 1.5T MRI system (GE HDx). The following data acquisition was carried out at baseline and after bronchodilator treatment:

^{3}He MRI: Patients were positioned in a ^{3}He transmit-receive vest coil (CMRS). A mix of 350ml hyperpolarized ^{3}He (25% polarisation) and 650ml N_2 was inhaled from functional residual capacity (FRC) and ventilation-weighted images were acquired during breath-hold. Sequence parameters were; 2D coronal spoiled gradient echo (SPGR), full lung coverage, voxel size =3x3x10mm, θ=8º, TE / TR =1.1 / 3.6ms and bandwidth =63kHz.

^{1}H MRI: In order to calculate baseline pre-contrast T_1 maps three whole lung volumes were acquired with flip angles of 2º, 10º and 30º respectively. A 3D coronal SPGR sequence was used with voxel size =2.4x6x4mm, TE / TR = 0.9 / 2.9ms and bandwidth =125kHz. Perfusion-weighted images of the whole lung were then acquired after intravenous injection of gadolinium contrast agent (Gadovist). Sequence parameters were; 3D coronal SPGR with TRICKS [3] and SENSE [4] factor 2, voxel size =2.4x6x10mm, TE / TR = 0.8 / 2.3ms, bandwidth = 250kHz and 36 time-frames of 0.5s each. Contrast dose was 0.05ml/kg Gadovist at 4ml/s with 20ml saline flush.

Data processing: T_1 maps were calculated and used to determine the concentration of contrast at each time-point [5, 6]. Maps of maximum perfusion concentration (perfusion) and the time taken to reach maximum perfusion (time to peak perfusion) were also generated. ^{3}He ventilation images and perfusion maps were normalised by the mean signal in the trachea and pulmonary artery respectively. Histograms of normalised ventilation and perfusion distributions were plotted with frequency normalised to the total number of voxels in the lung.

Results and Discussion: The patients imaged had a mean±SD age of 54±7 years, TLCO =92±7% predicted and mean FEV_1 predicted at baseline / post-BD = 91±29% / 96±30%. Regional ventilation and perfusion distributions were visualized with high spatial resolution. Individual patient VQ response to bronchodilator differed but tended towards increased and more homogeneous ventilation and perfusion post-bronchodilator.

Example data are shown in figure 1 from an asthma patient with TLCO =95% and FEV_1 at baseline / post-BD =121 / 129%. At baseline ventilation (a) and perfusion (b) distributions were well matched, with poor VQ and increased time to peak perfusion (c) in the lower lobes. Post-bronchodilator, ventilation to the lower lobes was increased (e) but perfusion remained poor (f, g) which is reflected by the VQ mis-match seen in the VQ distribution histogram (h). Increased ventilation to a region which remains poorly-perfused post-bronchodilator contributes less to gas exchange, and diversion of inhaled gas away from areas of functional lung may be detrimental to the overall ability of the lung to carry out gas exchange. Also of interest is the consistent elevated time to peak perfusion in the base of both lungs indicative of longer pulmonary perfusion transit times and elevated pulmonary vascular resistance to flow in these initially obstructed regions of the lung.

Ventilation perfusion mis-match directly results in reduced arterial pO_2 (hypoxemia), with alveolar units of low V/Q contributing relatively more to reduced arterial pO_2 than those of high V/Q due to the relative blood flow present [7]. Multi-nuclear MRI provides a technique to assess regional distributions of V/Q present in lung disease and monitor how they change in response to therapy.

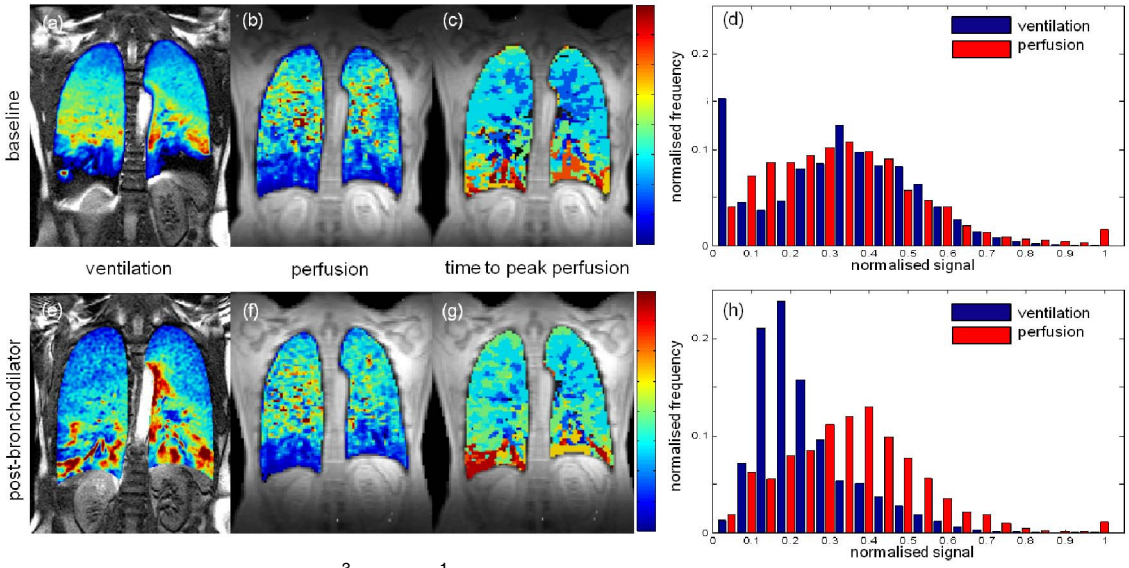

Figure 1; baseline (top) and post-bronchodilator (bottom) VQ distributions in a patient with asthma. Ventilation (a, e), peak perfusion concentration (b, f), time to peak perfusion (c, g) and histograms of VQ distributions (d, h).

Conclusions: Hyperpolarised ^{3}He and ^{1}H MRI provide high resolution images of regional ventilation and perfusion distributions, and are sensitive to changes in V and Q following bronchodilator administration in asthmatic patients. Multi-nuclear lung MRI is a non-ionizing tool for assessment of regional V and Q, which could be used to investigate the bronchodilatory and vasodilatory effects on the lungs with different mechanistic therapeutics in a range of obstructive and vascular lung diseases.

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