Ventilation-Perfusion Analysis with Co-registered Hyperpolarized Gas and CE ^{1}H Perfusion MRI

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Target Audience: Hyperpolarised gas MRI community, MR image processing community

Purpose: Many pulmonary diseases adversely affect both ventilation (V) and perfusion (Q) in different regions of the lung[1,2], and V/Q mismatch leads to poor gas exchange[1,3]. Quantification of the V/Q ratio in patients with respiratory disease using hyperpolarised gas MRI and contrast-enhanced(CE) ^{1}H perfusion MRI[4,5] is a key area of research but is often limited by the need to move patients between RF coils such that V and Q images are not spatially registered. The aim of this study was to produce a semi-automated workflow for quantitative measurement of V/Q from images acquired with the patient in different positions. The methodology is demonstrated on images from patients with moderate-to-severe asthma.

Methods: 2 patients with moderate-to-severe asthma were scanned using a 1.5T MRI system (GE HDx, Milwaukee, WI):

^{3}He / ^{1}H anatomical imaging: Patients were imaged with a ^{3}He transmit-receive vest coil (CMRS) after inhalation of a mix of hyperpolarised ^{3}He (polarised to 25%, 350ml) and N^{2} (650ml). Breath-hold ventilation-weighted images (e.g. fig 1b) were acquired using a 2D spoiled gradient echo sequence with full lung coverage and voxel size 3x3x10mm. ^{1}H anatomical images (e.g. fig 1a) were acquired during the same breath-hold with the body coil[6] using a 2D steady state free precession sequence with full lung coverage and voxel size 3x6x10mm.

^{1}H CE perfusion imaging: The patient was re-positioned in a ^{1}H 8-element chest receiver coil. CE perfusion-weighted images were acquired using a 3D spoiled gradient echo sequence with full lung coverage, voxel size 2.4x6x10mm and 36 time-frames of 0.5s each (e.g. fig 1c) following injection of 0.05ml/kg gadolinium contrast agent (Gadovist) at 4ml/s with 20ml saline flush.

Data processing: The proposed workflow is shown in figure 1. Peak perfusion enhancement (fig 1d) maps were generated from the 36 perfusion time points collected during ^{1}H CE imaging. Perfusion maps were registered to the ^{1}H anatomical images in order to align them to the ^{3}He ventilation images. Registration was carried out in two stages; (i) the perfusion time-course image with the most similar contrast to the proton anatomical image was chosen by visual inspection. (ii), this perfusion time-course image (fig 1c) was registered to the proton anatomical image (fig 1a) using a three-stage registration pipeline consisting of rigid, affine and diffeomorphic transforms applied using dedicated software[7]. The resulting deformation field was then applied to the perfusion maps. The ^{1}H anatomical images (fig 1a) were segmented semi-automatically in ITK-SNAP[8] using a seeded region-growing algorithm followed by manual adjustment to create a binary mask of the lung parenchyma (fig 1e). This mask was then applied to the ^{3}He ventilation images (fig 1f) and registered perfusion maps (fig 1g) in order to remove the large vessels and airways. Ventilation and peak perfusion image intensities were normalised by the mean intensity over the whole lung, and maps of V/Q ratio were then generated.

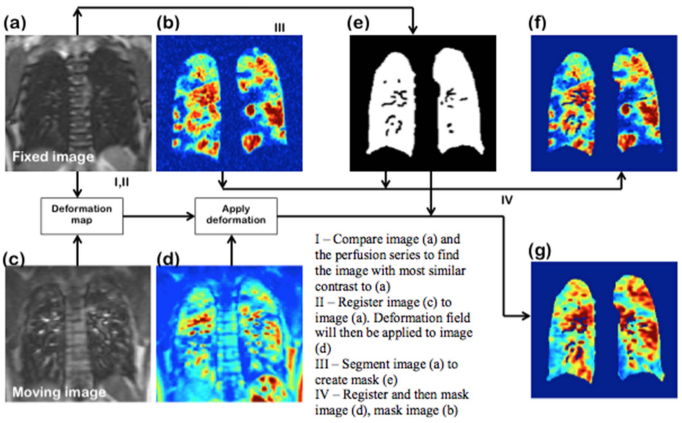

Figure 1 Image processing workflow. (a) ^{1}H anatomical image, (b) ^{3}He image, (c) perfusion time-course image, (d) peak perfusion map, (e) segmentation of ^{1}H anatomical image, (f) masked ^{3}He image and (g) post registration masked peak perfusion image

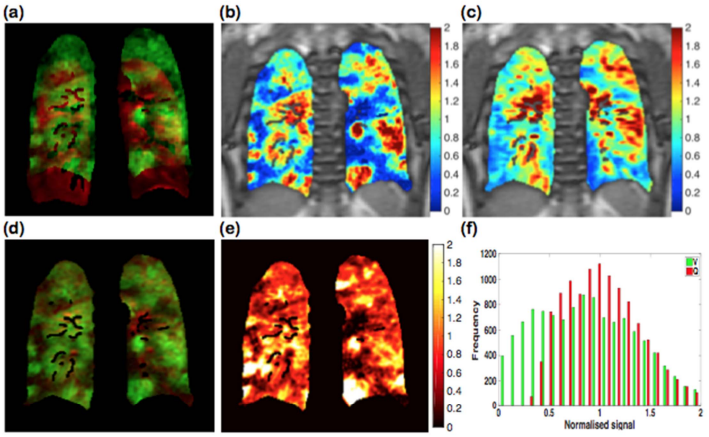

Figure 2 Output of workflow in figure 1. (a) Original V(green) and Q(red) note the mis-alignment, (b) ^{3}He image fused with ^{1}H anatomical image, (c) normalised, registered Q overlaid on ^{1}H anatomical image, (d) V(green) and Q(red) workflow outputs (e) V/Q map and (f) histogram plot of V(green) and Q(red)

Results and Discussion: Spatially registered images of V and Q output by the proposed data processing workflow are shown in figure 2 (b-e). Comparing the fusion of V and Q before (fig 2a) and after (fig 2d) the image processing workflow clearly demonstrates its utility, allowing voxel by voxel comparison of ventilation and perfusion which can be presented as V/Q maps (fig 2e) or V-Q histograms (fig 2f) to probe regional V-Q matching and gas exchange. The workflow produced well-registered V and Q images in the 2 datasets tested to date. Automation of image processing reduces the time required to analyse each dataset, removes user-bias and ensures consistency of analysis between datasets. Future development will focus on full-automation of steps I (image choice) and III (segmentation) of this workflow and validation of outputs in a larger patient population. Another approach to solving the problem of hyperpolarised gas and proton images being acquired in different positions is to use specialist RF coils to acquire multi-nuclear images with the patient in the same position[9], however the proposed image processing workflow provides a solution for V/Q quantitation using RF equipment currently commonly used by the lung imaging community.

Conclusions: A semi-automated image processing workflow for ventilation-perfusion analysis was proposed and demonstrated in patients with moderate-to-severe asthma. The methodology produced spatially registered, normalised images from which maps of V/Q ratio and V-Q histograms were generated. This technique could be applied to ventilation and perfusion images acquired at multiple time-points from patients with any respiratory disease to enable longitudinal monitoring and therapy assessment.

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References: **[1]** Hatabu et al. *MAGN RESON MED*, 1999, 42(6), 1033-1038; **[2]** Hartmann et al. *ACTA ANAESTH SCAND*, 2014, 58(8), 1032-1039; **[3]** Ohno et al. *AM J ROENTGENOL*, 188(1), 48-56, 2007; **[4]** Lipson et al, *MAGN RESON MED*, 47:1073-6 (2002); **[5]** Marshall et al, *AM J RESPIR CRIT CARE MED*, (5):e18-9 (2014); **[6]** Wild et al, *RADIOLOGY*, 267(1):251-5 (2013); **[7]** Avants et al. Advanced normalization tools (ANTS), *INSIGHT J*, 2009; **[8]** Yushkevich et al. *NEUROIMAGE*, 2006, 1;31(3):1116-28; **[9]** Rao et al *MAGN RESON MED*, 2014, DOI:10.1002/mrm.25384