Ventilation heterogeneity in obstructive airways disease – comparing multi-breath washout-imaging with global lung measurements

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Purpose: Multiple breath washout as measured in the pulmonary function lab (MBW-PFT) has been proven to be a sensitive tool for detection of early changes in obstructive lung diseases [1,2]. By measuring regional signal intensity decay during gas washout using hyperpolarised ^{3}He MRI this method can be extended to a regional measure – MBWI [3,4]. Using this regional information an insight into ventilation heterogeneity can be obtained as an early marker for lung disease detection. In this work, ventilation heterogeneity derived from imaging (MBWI) is compared to parameters from MBW-PFT and spirometry in healthy normal subjects and patients with CF and asthma.

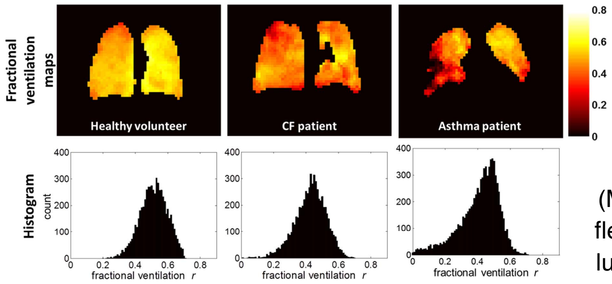

Figure 1: Whole lung histograms and fractional ventilation maps from a healthy volunteer, a CF and an asthma patient.

Methods: A total of 6 healthy volunteers age matched with 10 CF patients (6-16 years, with normal spirometry) and 30 asthma uncontrolled patients (21-65 years, FEV1%predicted = 75±26%) were studied. **Imaging:** Multiple breath washout imaging (MBWI) was performed on a 1.5T scanner (GE HDx) with a quadrature ^{3}He flex coil. A gas mixture of ^{3}He (~25% polarisation, 150-250ml depending on lung size to achieve similar average concentrations, depending on height and weight) topped up with N_2 was inhaled . Sequence parameters were: 3D coronal spoiled gradient echo covering the whole lung with a resolution of 1cm^3, FA = 1°, 5 acquisitions at a fixed interval (4s for children, 5s adults). Two volume images were acquired at breath-hold to correct for non-washout related signal decay of the HP-^{3}He (RF depolarisation and T_1 decay). The next three image volumes were acquired during washout with free breathing synchronized with image acquistion. The images were segmented and registered for inter-breath motion [5] before calculating maps of fractional ventilation (*r*), the gas turned over per breath on a voxel-by-voxel basis. The standard deviation of the volumetric MBWI *r* maps was used as a measure of ventilation heterogeneity (VH-MBWI). Spearman's correlations were performed between VH-MBWI, LCI and FEV1. ANOVA was used to test for differences between groups. **PFT:** Spirometry was performed according to ATS/ERS guidelines [5]. MBW-PFT was performed according to guidelines using a modified Innocor (Innovision, Denmark) SF_6 photoacoustic gas analyser [6]: Following a wash in of 0.2% SF_6 gas to equilibrium concentration, washout was monitored over multiple breaths. The lung clearance index (LCI) as the number of lung-turnovers to reduce end-expiatory tracer gas concentration to 0.005% was derived from MBW.

Results and Discussion: Representative MBWI coronal slices from; a healthy volunteer, CF patient and asthma patient are shown in Fig. 1 with the corresponding whole-lung histograms of fractional ventilation *r*. The histograms of fractional ventilation (Fig. 1)show a broadening with increase of disease (resulting in a higher standard deviation). A significant positive correlation was observed between the MBW-PFT parameter lung clearance index (LCI) and the VH-MBWI (r = 0.7) showing increased ventilation heterogeneity with severy of disease (Fig 2A). in contrast, there was a significant negative correlation between FEV1 and VH-MBWI (r = -0.6) (Fig 2B). The ANOVA test showed significant differences between all groups based upon VH-MBWI (Fig 2C), but not for LCI or FEV1.

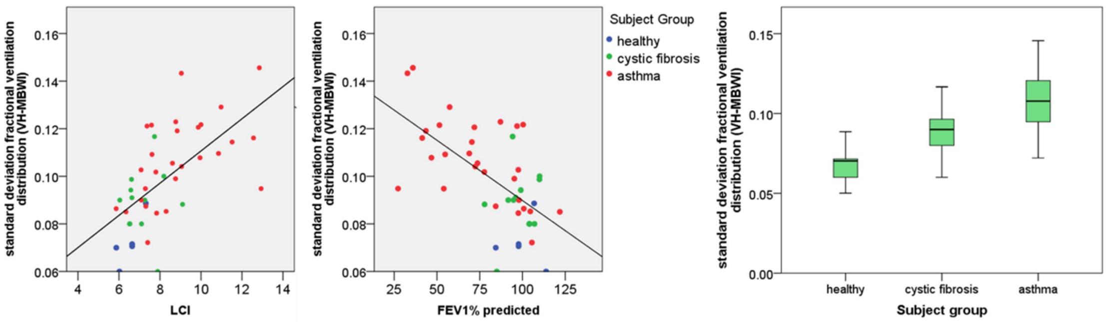

Fig 2: Correlation of standard deviation of *r* as measure of ventilation heterogeneity (VH-MBWI) with (A) lung clearance index (LCI) r = 0.7 (p<0.01) and (B) forced expiratory flow in 1s (FEV1) r = -0.6 (p<0.01). (C) Comparison of VH-MBWI using ANOVA testing shows significant difference between all groups.

Conclusion: MBW-imaging derived metrics were shown to correlate significantly with pulmonary function tests. MBW-imaging was more sensitive to increased ventilation heterogeneity in CF and asthma than LCI or spirometry, even in a group of mild CF patients. Imaging of MBW can provide regional insight for understanding measurements and models of ventilation heterogeneity from global lung MBW.

References: [1] Horsley, Thorax,2008,(63(2):135-14) [2] Lutchen, JAP, 1990,(68:2139-2149) [3] Deppe, Mag. Res. Med., 20111(65:1076-1084) [4] Horn et a., JAP, 2014, (116(2):129-139) [5] Miller et al., ERJ, 2005,(26:319-338) [6] Robinson, ERJ, 2013,(41(3):507-522);

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