Regional ventilation assessed by conventional MRI in health and pathology

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Introduction The evaluation of regional ventilation is of major importance in investigating lung function in health and disease. Hyperpolarized-gas magnetic resonance imaging (MRI) has proven useful in imaging lung function and microstructure (1-2), but its designation as a drug has thus far restricted translation to the clinic. Conventional MRI has been hampered by the combination of low proton density and short T_2* of lung tissue (3-4), but it has recently regained attention with the development of short acquisition time techniques (5) and frequency-sweep NMR (6-8). We hypothesize that proton signal change within the lung between different lung volumes (9) is a reliable estimate of regional lung function. In this IRB-approved study proton difference images were compared with the corresponding ^{3}He ventilation images in health and obstructive lung disease.

Methods Healthy volunteers (six) and patients with asthma (six), mild emphysema (six), and severe emphysema (four) were imaged with a Siemens 1.5 T whole-body scanner at 4 lung volumes (RV – residual volume; FRC – functional residual capacity; FRC+1 L; TLC – total lung capacity) with breath-holds of 10-11 s, using volumetric interpolated breath-hold examination (VIBE) with the integrated body coil. Imaging parameters were: TR/TE = 3.1/0.8 ms, 5 mm slice thickness, 450x270 field of view, 2.3x2.3 mm^2 in-plane resolution. Signal intensities in parenchymal areas were normalized to heart signal (tissue+blood) to eliminate the effect of sensitivity changes due to volume differences. Each volume was registered onto the reference (FRC) using the Demons algorithm (10) and the image subtracted from the reference, resulting in maps of density change between the two lung volumes. ^{3}He ventilation images of the six asthmatic subjects were also acquired at FRC+1L with 12-mm thick slices within-plane resolution of 3.125x3.125 mm^2 for comparison with the proton difference images at four lung levels (^{3}He polarization ~40%, using a commercial device [GE Healthcare]). Data are reported in normalized units as median (25th - 75th percentile).

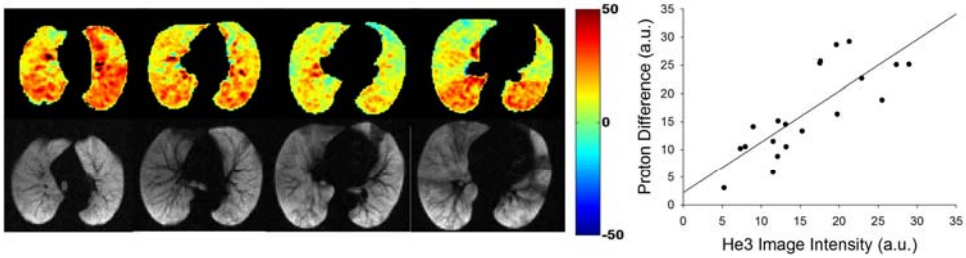

Figure 1 Proton difference images (top) and corresponding 3He ventilation images (bottom) are shown at four lung levels (columns) in a representative asthmatic subject (FEV_1=85% predicted). On the right, correlation between the intensities of 20 regions (5 within each level).

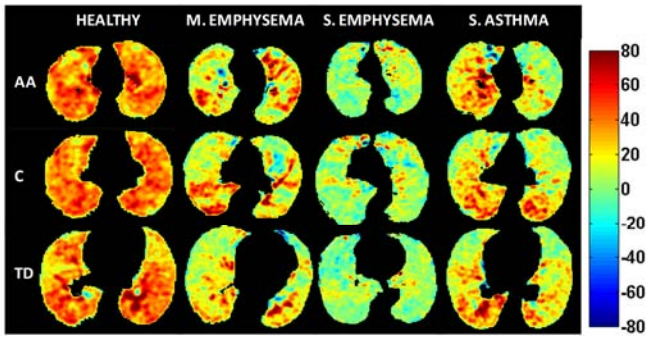

Figure 2 In each column representative Healthy (never-smoker), Mild emphysematous (FEV_1=50% predicted), Severe Emphysematous (FEV_1=24% predicted) and Severe Asthmatic (FEV_1=67% predicted) subject is shown at representative lung levels: Aortic arch (top,AA), Carina (middle,C) and top diaphragm (bottom,TD).

		HEALTHY	M. EMPHYSEMA	S. EMPHYSEMA	S. ASTHMA
RV-FRC	Median	8.3(5.5-11.4)	5.5(2.9-7.4)	4.0(2.0-4.9)	7.8(-4.0-19.2)
	IQ	14.3(12.4-16.8)	15.6(13.6-16.3)	11.4(10.2-12.8)**	15.3(13.9-17.0)
FRC-(FRC+1)	Median	12.4(7.9-15.4)	6.3(5.4-12.5)**	1.4(-0.2-3.3)***	13.0(8.6-15.5)
	IQ	13.0(11.2-14.9)	12.9(11.1-15.5)	9.9(9.2-11.2)*	17.2(14.7-21.6)***
FRC-TLC	Median	14.7(10.5-18.6)	13.4(12.1-18.7)	2.8(0.9-4.0)***	17.0(11.3-21.5)
	IQ	14.3(13.0-17.3)	15.9(14.0-19.7)	10.1(9.0-11.7)***	20.3(17.3-22.7)***

Table 1 Median and interquartile range (IQ, in arbitrary units) of proton difference images in health and pathology computed during the different phases of the respiratory cycle (RV-FRC, FRC-(FRC+1), FRC-TLC). *p<0.05, **p<0.01, ***p<0.001 vs healthy.

Results In Figure 1 proton difference images between RV and TLC (top) with corresponding ^{3}He MR ventilation images (bottom) and their correlation (right) are shown in a representative asthma subject at four lung levels. The correlation between the two modalities is computed by selecting five corresponding regions at each slice-level to uniformly cover the overall lung. Data were fitted linearly which resulted in R^2 of 0.62 ($p<0.001$). In the six asthmatic patients the correlation coefficient was 0.60 (0.58-0.64) ($p<0.001$). Lower R^2 was found between ^{3}He ventilation images and proton difference images computed as FRC-FRC+1 and FRC-TLC [respectively 0.55 (0.49-0.58) and 0.47 (0.41-0.64)] due to the lower contrast when lower volume change occurs. In Figure 2 representative proton difference images (TLC-RV) are shown in health, mild and severe emphysema and severe asthma at levels corresponding to the aortic arch (AA), carina (C) and top diaphragm (TD). Table 1 reports the median and inter-quartile range (IQ) of the frequency distribution of proton difference images in volunteers and patients for each respiratory phase. In emphysema proton density difference is lower than healthy volunteers (in both median and IQ), reflecting tissue destruction and lower gravity dependence as expected; in asthma the higher IQ is indicative of the presence of both obstructed and healthy regions within slices.

Discussion and Conclusions Positive correlations were found between proton density difference and ^{3}He ventilation images; we attribute the less-than-perfect correlation (R^2=0.6) to the low signal-to-noise ratio of the proton images (TE=0.8 ms and T_{2_lung}≈0.5 ms at 1.5 T). Nevertheless, proton MRI with VIBE was able to identify ventilation defects and to differentiate health and pathology in terms of median signal difference and variability (IQ) during inspiration, demonstrating the feasibility of conventional proton MRI, combined with image registration, to quantify regional ventilation. This suggests that proton MRI, perhaps with UTE sequences, is likely to emerge as a new clinical and research tool to identify structure-function relationships with no need for special equipment and with no ionizing radiation.

References: (1) Yablonskiy DA et al. *J Appl Physiol* 2009;107:1258 (2) Mugler III JP et al. *PNAS* 2010;1011912107 (3) Bergin CJ et al. *Radiology* 1991;179:777 (4) Wielpütz M et al. *Diagn Interv Radiol* 2012; 18:344 (5) Kuethe DO et al. *MRM* 2007;57:1058 (6) Garwood M et al. *J Magn Reson* 2001;153 (7) Idiyatullin D et al. *ISMRM* 2006:2433 (8) Corum CA et al. *ISMRM* 2010:204 (9) Bankier AA et al. *J Magn Reson* 2004;20:961 (10) Thirion JP. *Med Image Anal* 1998; 2:243.