Imaging of Structural and Functional Changes in Early Stage CF with ^{3}He MRI, ^{1}H MRI and CT

Helen Marshall[1], David Hughes[2], Felix Horn[1], Juan Parra-Robles[1], Alex Horsley[3], Laurie Smith[2], Leanne Armstrong[1], Ina Aldag[2], Chris Taylor[2], and Jim M Wild[1]
[1]Academic Radiology, University of Sheffield, Sheffield, United Kingdom, [2]Sheffield Children's Hospital, Sheffield, United Kingdom, [3]Manchester Adult CF Centre, University of Manchester, Manchester, United Kingdom

Target Audience: CF clinicians, hyperpolarised gas MRI community, MRI and CT radiologists

Purpose: Early detection of lung disease is of upmost importance in cystic fibrosis (CF), in order to intervene before lung disease becomes irreversible [1]. Hyperpolarized ^{3}He ventilation MRI (^{3}He MRI) and CT are both sensitive to early changes in the lungs before spirometry, and have been shown to correlate well with each other in adult CF patients with substantial lung disease [2]. ^{3}He MRI is sensitive to peripheral airway obstruction in paediatric CF patients with normal spirometry [3] and ^{1}H MRI has been proposed as a radiation-free alternative to CT for imaging the CF lung [4]. The aim of this study was to investigate the relative sensitivity of ^{3}He MRI, ^{1}H MRI and CT alongside each other for detection of early stage lung disease in children with mild CF.

Methods: 7 CF patients and 5 healthy controls were assessed with ^{3}He and ^{1}H MRI, CT (patients only) and pulmonary function tests including multi-breath washout. All subjects had normal spirometry (forced expiratory volume in 1s (FEV1) >80%) when recruited to the study and were aged 8 to 16 years old.

^{3}He MRI: Subjects were scanned using a 1.5T whole body MRI system (GE HDx) and a ^{3}He transmit-receive vest coil. Hyperpolarized ^{3}He dose was determined empirically according to the subject's predicted functional residual capacity (FRC) [5], and ranged from 150-350ml of ^{3}He (25% polarisation). A gas mixture of equal parts ^{3}He and N_2 was inhaled from FRC and ventilation images were acquired during breath-hold. Sequence parameters were; 2D coronal spoiled gradient echo, full lung coverage, θ=8º, voxel size =2.7x2.7x10mm, TE / TR =1.1 / 3.6ms and bandwidth =63kHz. Ventilated lung volume percentage (Vv%) was calculated by manual segmentation of the ^{3}He images [6].

^{1}H MRI: Subjects were repositioned into a ^{1}H 8-element chest array. A volume of air equal to the total gas volume inhaled for ^{3}He MRI was inhaled from FRC, and anatomical ^{1}H images were acquired during breath-hold. Sequence parameters were; 2D coronal steady state free precession, full lung coverage, θ =50º, voxel size =1.4x1.4x10mm, TE / TR =0.9 / 2.9ms and bandwidth =250kHz.

CT: Low dose inspiratory and ultra-low dose expiratory non-contrast volume CT images [7] were acquired from patients only. Parameters were; 80kV for <35kg patient, 100kV for >35kg patient, auto mAs for inspiratory scans, fixed 25mAs for expiratory scans and 5mm collimation reconstructed to 0.625mm isotropic spatial resolution.

All images were read by an experienced paediatric chest radiologist.

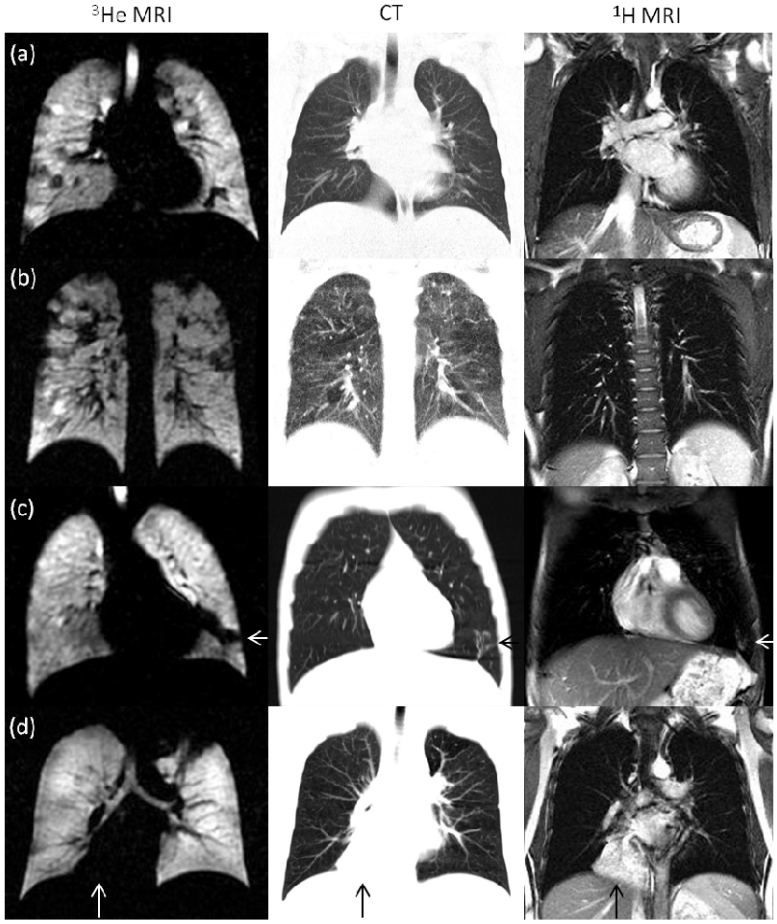

Figure 1; Images from 4 different patients, (a) FEV_1=94%, Vv=94.5% , (b) FEV_1=78%, Vv=94.3% (c) FEV_1=110%, Vv=95.7% and (d) FEV_1=84%, Vv=92.2%

Results and Discussion: Table 1 summarises the numerical results from CF patients and healthy controls.

Value	*CF Patients*	*Healthy Controls*
Age (years)	11.8 ± 2.9	10.1 ± 2.8
Vv%	95.4 ± 2.2	97.9 ± 1.1
FEV1% predicted	94.8 ± 11.1	94.7 ± 10.1
Lung clearance index	7.2 ± 1.0	6.7 ± 0.5

Table 1; summary values given as mean ± SD

Abnormalities were detected in the ^{3}He MR and CT images of 6 patients (see fig 1). Ventilation defects and heterogeneity visualized with ^{3}He MRI generally corresponded to regions of air-trapping, mucus plugging of small airways and atelectasis on CT. In some patients, abnormalities were more obvious on ^{3}He MRI than CT, e.g. (a) and (c), which may be due to its inherent sensitivity to ventilation heterogeneity related to small airways obstruction. Patient Vv% was significantly less (p=0.04) than in healthy controls. One patient had mild variant disease with the dF508/R117H genotype and normal MRI, CT and LCI. ^{1}H MRI showed abnormalities in 3 patients; lingular atelectasis in 3 patients e.g.(c) and segmental lobar collapse in 1 patient (d).

Conclusions: ^{3}He MRI is more sensitive to early ventilation changes in CF than ^{1}H MRI and pulmonary function tests. ^{3}He MRI and CT both have sensitivity to lung abnormalities in this patient population and provide complementary information about lung structure and function, however the non-ionizing nature of MRI makes it more suitable for repeated evaluation of young CF patients.

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References: [1] Boucher et al, Annu Rev Med 2007 58;157-70; [2] McMahon et al, Eur Radiol 2006,16(11):2483-90; [3] Bannier et al, Radiology 2010 255(1):225-32; [4] Purderbach et al, Eur Radiol 2007 17(3):716-24; [5] Rosenthal et al, Thorax 1993 48(8):803-8; [6] Niles et al, Radiology 2013 266(2):618-25; [7] Loeve et al, Radiology 2009,253(1):223-9;