Hyperpolarized 3He Magnetic Resonance Imaging of Cystic Fibrosis :Initial Findings in Adults with Moderate and Good Lung Function and Comparison to Spirometry

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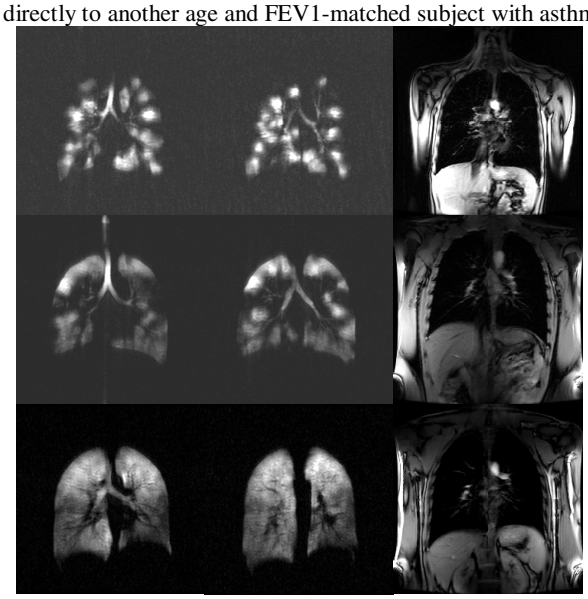
INTRODUCTION: The use of hyperpolarized helium-3 magnetic resonance imaging (^{3}He MRI) to measure regional ventilation defects in pediatric and adult cystic fibrosis (CF) has been undertaken by a number of research groups (1-4). It has been previously established in other respiratory diseases that regional ventilation defects can be visualized using ^{3}He MRI and a number of attempts have been made to quantify regional ventilation defects by objective scoring (5) and volumetric analysis (6). The overarching goal of this research is to identify new imaging intermediate endpoints of cystic fibrosis (CF) and then validate these as outcome measures for CF clinical trials. While lung function parameters typically have been used as the primary endpoints in therapy development studies, the specific improvement in lung function in patients with CF (as a result of mucolytic therapy) has rendered these measurements less sensitive to potential effects of novel therapies. Therefore, the aim of this observational pilot study is to assess the precision and specificity of candidate intermediate endpoints of CF measured using hyperpolarized helium-3 (^{3}He) magnetic resonance imaging (MRI). We hypothesized that for adult CF patients with moderate-to-good lung function (FEV_1 >60%predicted), ventilation patterns and ventilation defects or the normalized percent ventilation volume would be predictive of disease severity (measured using FEV_1) as is the case in asthma and COPD and that short term reproducibility of ventilation defect or percent ventilation volumes would be high. Here we present initial findings of adult CF patients with good to moderate lung function. We compare results of ^{3}He MRI center-slice ventilation defects in adult CF patients with an asthma subject with similar spirometry results as both types of subjects are typical of subjects currently being enrolled in treatment clinical trials. **METHODS:** Imaging was performed at 3.0 Tesla (General Electric Health Care GEHC) as previously described (5) using hyperpolarized helium (35%) provided by a turn-key spin-exchange polarizing system (Helispin®, GEHC). 2D and 3D T1-weighted imaging was performed to enable ventilation defect analysis and T1/PAO2 calculations.

RESULTS: Images for two representative CF subjects are shown and compared directly to another age and FEV1-matched subject with asthma.



Row 1: CF Patient 001, Female 23 yr FEV_1 61%, FEV_1/FVC 65% Visit 1. L to R, ^{3}He MRI center coronal slice, ^{3}He one slice posterior to center slice and, ^{1}H center slice.

Row 2: CF Patient 002, Male 26 yr FEV_1 78%, FEV_1/FVC 73% Visit 1. L to R, ^{3}He MRI center coronal slice, ^{3}He one slice posterior to center slice and, ^{1}H center slice. Center slice, one slice posterior to center, center proton.

Row 3: Asthma Patient 003, Male 21 yr FEV_1 79%, FEV_1/FVC 62% L to R ^{3}He MRI center coronal slice, ^{3}He one slice posterior to center slice and, ^{1}H center slice.

DISCUSSION: The longitudinal assessment of CF patients using spirometry suggests that in stable patients with moderate to good lung function, global lung function measurements do not vary over short periods of time. ^{3}He MRI offers another indirect but regional measure of ventilation volume and ventilation defects. Here we provide initial findings of a pilot observational study to assess ventilation defects and percent ventilation volume in CF subjects with moderate-to-good lung function. Initial results suggest that spirometry results are not predictive of the ventilation pattern observed in CF, and very different from the findings in an asthma subject with similar spirometry results. The initial results of this study suggest that there is a discordance between ventilation patterns and FEV1 in adult subjects with CF as compared to subjects with asthma and similar pulmonary function results which has implications for the etiology of these defects in CF and asthma.

REFERENCES:

1. Altes, TA, deLange, EE. Topics in Mag Res Imaging 2003: 14, 231-236.
2. Koumellis P, et al. *J Magn Reson Imaging* 2005; 22(3):420-426.
3. Mentore, K, et al. Acad Radiol 2005: 12, 1423-1429.
4. vanBeek EJR, et al, Eur Radiol. 2006, Aug 29
5 de Lange EE, Altes TA et al. J Allergy Clin Immunol 2007; 119:1072-8.
6. Parraga G, et al, *Invest Radio 2007, 42, 384-391.*

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