

Regional Quantification of Lung Function in Cystic Fibrosis using 3D Single-Breath CSI

Steven Guan¹, Kun Qing¹, Talissa Altes¹, John Mugler III¹, Carolina Fernandes¹, Kai Ruppert¹, Julian Ruset^{2,3}, F. William Hersman^{2,3}, Deborah Froh¹, William Teague¹, Grady Miller¹, James Brookeman¹, and Jaime Mata¹

¹University of Virginia, Charlottesville, VA, United States, ²University of New Hampshire, Durham, NH, United States, ³Xemed, LLC, Durham, NH, United States

Introduction: Cystic fibrosis (CF) is the most common, fatal, single gene defect in the Caucasian population. Mutations in the CF gene lead to the production of unusually thick mucus that clogs the airways and creates an ideal breeding ground for chronic airway infections [1]. For diseases like CF that have both obstructive and restrictive characteristics, standard pulmonary function tests can only provide a limited global assessment of ventilation parameters [2]. Three-dimensional Single-Breath Chemical Shift Imaging (3D SB-CSI) is capable of non-invasively assessing regional ventilation and multiple compartment gas uptake/exchange, which permits a more comprehensive understanding of the disease and treatment efficacy [3,4].

Methods: A total of 17 subjects (Table 1) underwent hyperpolarized Xe-129 3D SB-CSI: eight healthy (n=8) and nine CF (n=9) subjects. All scans were performed on a 1.5T clinical system (Avanto, Siemens Medical Solutions, USA) using a transmit/receive RF coil (Clinical MR Solutions, WI) tuned to the frequency of Xe-129. Isotopically enriched (~87%) Xe-129 was polarized to ~30-40% using a commercial prototype polarizer (Xemed LLC, NH). The parameters for the 3D SB-CSI sequence were as follows, TR/TE: 24.6 ms/2.3 ms, matrix: 18x18x8 interpolated to 32x32x8 voxels, FOV: 280-320 mm², and slice thickness: 25 mm. Matlab (Mathworks, Natick, MA) was used to perform the 3D SB-CSI post-processing, in which the acquired FIDs were filtered, zero-filled, and phase corrected automatically. Subsequently, the gas and dissolved peaks were integrated and used to generate CSI maps that represents the distribution of Xe-129 in the alveolar spaces (ventilation), as well as the Xe-129 dissolved in the parenchyma tissue and red blood cells (RBC).

Results: The tissue/RBC ratio maps revealed that CF subjects typically exhibit a heterogeneous ratio distribution that features bright and dark spots dispersed throughout the lung (Fig. 1). CF subjects had a higher average tissue/RBC ratio and standard deviation, 2.96 ± 0.74 , compared to that of healthy subjects, 2.39 ± 0.53 (Fig.2). Using a two-tailed T-test, there was a statistical difference between the tissue/RBC ratios of CF and healthy subjects, $p = 0.0003$. There also appears to be a good correlation ($R = 0.71$) between the tissue/RBC ratio and the %predicted FEV₁ (Fig. 3).

Table 1: Subject Data

Subject #	H-1	H-2	H-3	H-4	H-5	H-6	H-7	H-8	CF-1	CF-2	CF-3	CF-4	CF-5	CF-6	CF-7	CF-8	CF-9
Age	19	21	21	18	18	27	51	33	19	24	37	26	19	12	13	13	13
Sex	F	F	F	M	F	F	F	F	F	F	M	M	M	F	F	F	F
FEV ₁ % Pred.	104	112	106	88	119	129	107	99	55	71	87	80	55	54	74	64	71

Conclusion: This pilot clinical study has demonstrated that 3D SB-CSI is capable of assessing regional ventilation and multiple compartment gas uptake/exchange. CF subjects showed an elevated tissue/RBC ratio, most likely due to the inflammation and thickening of the parenchyma walls. The ratio maps also reveal that their lungs have significant regional defects and abnormalities, which reflects the highly focal nature of the disease [2]. The bright yellow spots indicate impaired gas transfer from the pulmonary tissue to the RBC, while the black spots indicate poor ventilation. Detection of these regional changes may be useful in characterizing disease progression and evaluating treatment efficacy.

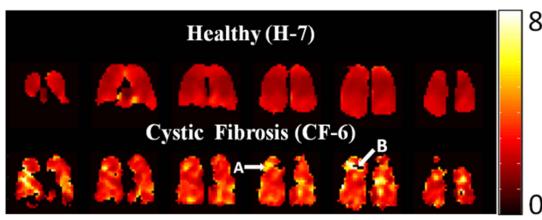


Figure 1: Coronal tissue/RBC ratio maps for subjects H-7 and CF-6. Healthy subjects (top row) typically have a homogenous ratio distribution across the lungs, while CF subjects (bottom row) have bright spots (A) and ventilation defects (B).

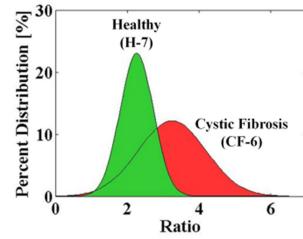


Figure 2: Example tissue/RBC ratio histogram for a healthy and CF subject (H-7 and CF-6). Histograms were fitted with a Gaussian for better visualization of the distribution.

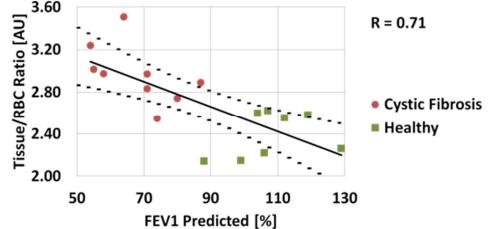


Figure 3: There is a good correlation between the average tissue/RBC ratio of each subject and their %predicted FEV₁ ($R=0.71$). The dotted line represents a 95% confidence interval for the regression.

References: [1] Flume, P.A., Respir Care, 2009. [2] Fain, S.B., et al. JMRI, 2007. [3] Mata J. ISMRM, Stockholm, 2010. [4] Reis et al. ISMRM, Melbourne, 2012 (abstract #5451).

Acknowledgements: Supported by NIH grant R01 CA172595-01 and Siemens Medical Solutions.