Measuring Septal Wall Thickening in Human Lung Disease Using Xe129 CSSR Spectroscopy
Kai Ruppert1, Talissa A. Altes1, Jaime F. Mata1, Julian Ruset1, F. William Hersman2,3, and John P. Mugler III1
1University of Virginia, Charlottesville, VA, United States, 2Xemed, LLC, Durham, NH, United States, 3University of New Hampshire, Durham, NH, United States


Purpose: Several lung diseases, including chronic obstructive pulmonary disease (COPD) (1) and asthma (2), are characterized by a strong inflammatory component. “Chemical Shift Saturation Recovery” (CSSR) MR spectroscopy is a method for monitoring the uptake of hyperpolarized xenon-129 (Hxe) by the lung parenchyma (3-9). This technique has been shown to be sufficiently sensitive for the detection of septal wall thickening due lipopolysaccharide (4), fungal spores (5) or bleomycin (6). The purpose of our studies was to investigate whether CSSR can also detect alveolar wall thickening in subjects with heavy smoking exposure or asthma.

Methods: Gaussian RF pulses (2-ms duration) were applied to saturate the tissue/plasma (TP; 198 ppm) and red blood cell (RBC; 218 ppm) dissolved-phase resonances. Following a delay time \( \tau \), a 1.2-ms Gaussian RF excitation pulse was used to generate a free induction decay. This sequence was repeated 32 times during a single breath hold with \( \tau \) ranging from 3 ms to 900 ms. The signal was sampled for 30.72 ms with 1024 sampling points, apodized by a squared cosine function, zero-filled to 2048 points, Fourier transformed and phased. The gas-phase and TP resonances were integrated numerically and their ratio was calculated as a function of \( \tau \). Fitting this data to the model described in (9) and assuming an Hxe diffusion constant in tissue of 3.3x10^{-6} cm^2/s (10) permitted the calculation of the alveolar wall thickness. All MR studies were performed at 1.5T (Avanto; Siemens), using a flexible (Clinical MR Solutions) or rigid (custom built) XeBox-E10, Xemed). The study group included 8 healthy nonsmoking subjects, 3 asthmatics, 1 subject with heavy second-hand smoke (SHS) exposure and 3 smokers with COPD (1 Gold stage (GS) 0, 2 GS 3) who were asked to inhale 0.5L of HXe starting from residual volume (RV), continue inhalation of room air, and hold their breath at total lung capacity (TLC). Five of the healthy subjects were also studied at RV and 50% forced vital capacity (FVC).

Results and Discussion: Figure 1 depicts the average septal wall thickness in 5 healthy subjects at RV (7.1 ± 0.56 \( \mu m \)), 50% FVC (7.3 ± 0.53 \( \mu m \)) and TLC (6.6 ± 0.42 \( \mu m \)). Since the relative error was found to be smallest at TLC, all subsequent studies were performed at this inflation level. Figure 2 illustrates the distribution of the measured alveolar wall thicknesses across the study population. In healthy subjects, the alveolar walls were about 6-8 \( \mu m \) thick. Subjects with lung disease or heavy exposure to cigarette smoke tended to have an elevated septal wall thickness relative to the healthy subjects, possibly due to the presence of inflammatory processes. The alveolar wall thickness as quantified by CSSR spectroscopy is a parameter that is independent of the lung tissue density as assessed by CT or hyperpolarized-gas diffusion measurements. In particular, our measurements seem to confirm the biopsy-based findings of inflammatory wall thickening in the presence of emphysematous lesions (1).

Conclusion: We demonstrated that the CSSR technique detects elevated septal-wall thicknesses in subjects with asthma or heavy cigarette-smoke exposure, likely due to inflammatory processes in the pulmonary interstitium.


Acknowledgements: Supported by NIH grant R01 HL109618 and Siemens Medical Solutions.