# Measuring Septal Wall Thickening in Human Lung Disease Using Xe129 CSSR Spectroscopy

Kai Ruppert[1], Talissa A. Altes[1], Jaime F. Mata[1], Iulian Ruset[2,3], F. William Hersman[2,3], and John P. Mugler III[1]

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

**Target Audience:** MR scientists and physicians interested in hyperpolarized-gas MRI and the assessment of pulmonary function.

**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 lipopolysaccaride (4), fungal spores (5) or bleomycin (8). 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 $3.3\times10^{-6}$ $cm^2/s$ (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) Xe129 chest RF coil, under a physician's IND for HXe MRI. Informed consent was obtained in all cases and a physician supervised each study. Enriched xenon gas (87% Xe129) was polarized to approximately 50% using a prototype commercial system (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).

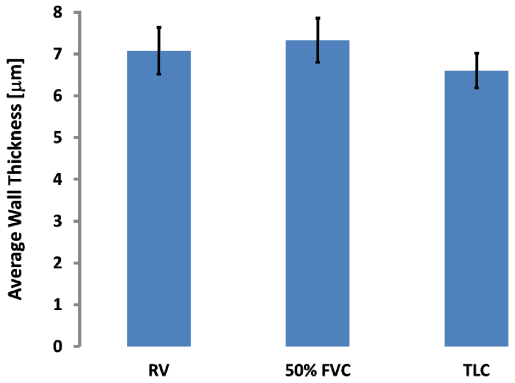


***Figure 1. Average septal wall thickness and standard deviation in 5 healthy volunteers at three different lung inflation levels.***

**Results and Discussion:** Figure 1 depicts the average septal wall thickness in 5 healthy subjects at RV (7.1 ± 0.56 μm), 50% FVC (7.3 ± 0.53 μm) and TLC (6.6 ± 0.42 μm). 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 μm 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).

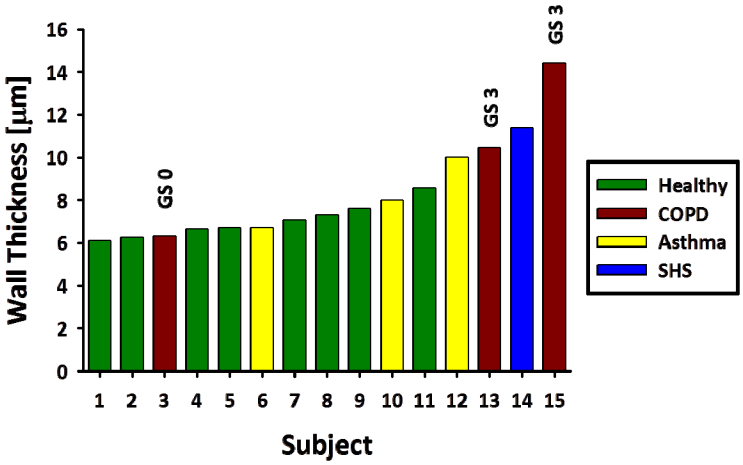


***Figure 2. Septal wall thickness in the 15 studied subjects in increasing order. The thickest walls were found in asthmatics and subjects with heavy exposure to cigarette smoke.***

**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.

**References:** **[1]** Vlahovic G et al. Am J Resp Crit Care Med 1999;160(6):2086-2092. **[2]** Cazzola M et al. Curr Opin Pulm Med 2012;epub. **[3]** Butler JP et al. J Phys Condens Matter 2002;14:L297-L304. **[4]** Mansson S et al. MRM 2003;50:1170-1179. **[5]** Abdeen N et al. MRM 2006;56:255-264. **[6]** Patz S et al. Acad Rad 2008;15:713-727. **[7]** Ruppert K et al. NMR Biomed 2000;13:220-228. **[8]** Driehuys B et al. PNAS 2006;103(48):18278-18283. **[9]** Patz S et al. New J Physics 2011;13:015009. **[10]** Ruppert K et al. MRM 2004;51:676-687.

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