

The Impact of Lung Disease on the Compartment-specific Uptake of Hyperpolarized ^{129}Xe

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

Purpose: Xenon uptake spectroscopy, commonly referred to as "Chemical Shift Saturation Recovery" (CSSR), is a method for monitoring the uptake of hyperpolarized xenon-129 (HXe) by the lung parenchyma¹⁻⁵. This is achieved through the acquisition of a free induction decay following a delay time τ after an RF saturation pulse that destroys the signal from all HXe currently residing in the lung tissue ("dissolved phase" HXe). In humans, this technique can be employed to quantify the xenon gas exchange dynamics for two discernible dissolved-phase resonances: red blood cells (RBCs) as well as a combination of tissue and plasma (TP). The purpose of our studies was to evaluate the relative volume of HXe dissolved in these two lung compartments in healthy subjects, asthmatics, and COPD patients.

Methods: Gaussian RF pulses (2-ms duration) were applied to saturate the TP (198 ppm) and RBC (218 ppm) dissolved-phase resonances. Following a delay time τ of 100 ms, 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. 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. Each of the two dissolved-phase resonances was integrated numerically and their average ratio from the 32 spectra was calculated. All MR studies were performed at 1.5T (Avanto; Siemens), using a flexible Xe129 chest RF coil (Clinical MR Solutions), 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 using a prototype commercial system (XeBox-E10, Xemed). The study group included 13 healthy nonsmoking subjects, 10 asthmatics and 10 COPD patients (4 GOLD Stage (GS) 1, 3 GS 2, 3 GS 3). All subjects were asked to inhale 0.5 L of HXe starting from residual volume (RV), then continue inhalation of room air and finally hold their breath at total lung capacity (TLC).

Results and Discussion: Figure 1 depicts the RBC-TP ratio (RTR) for all 33 subjects studied. The RTRs for 12 of the 13 healthy subjects (92%) were confined within a narrow band ranging from about 0.24 to 0.33 with an average value of 0.289 ± 0.035 . For all 20 subjects with lung disease, the RTRs fell outside this range. Interestingly, the RTRs for asthmatic subjects seemed to be either above (0.397 ± 0.041 , $p = 0.0004$) or below (0.183 ± 0.032 , $p = 0.002$) the normal value, while the RTRs for all COPD patients were below normal (0.152 ± 0.051 , $p < 0.00001$). All deviations were highly statistically significant. Although the number of subjects is still fairly small, our findings hint at the intriguing possibility that the RTR ratio could be used for the identification of two distinct asthma phenotypes. No correlation between RTR and GOLD Stage was apparent for the COPD subjects (not shown) but, again, too few subjects have been studied to draw conclusions. The physiologic origins for the measured differences in the RTR are currently unclear. Nevertheless, there are some indications that, at least in the case of the abnormally low RTRs in COPD, these changes appear to be due to a combination of low RBC volumes coupled with an elevated septal wall thickness⁶. Averaging the RTR over 32 separate measurements within the same breath hold not only greatly increased the signal-to-noise ratio but also minimized the impact of pulsatile variations in the HXe uptake rate, particularly for the RBC peak⁷.

Conclusion: We demonstrated that the RTR determined by the CSSR technique at TLC could be a valuable parameter for the assessment and phenotyping of lung disease.

References: [1] Butler JP et al. J Phys Condens Matter 2002;14:L297-L304. [2] Mansson S et al. MRM 2003;50:1170-1179. [3] Abdeen N et al. MRM 2006;56:255-264. [4] Patz S et al. Acad Rad 2008;15:713-727. [5] Ruppert K et al. NMR Biomed 2000;13:220-228. [6] Ruppert K et al. Proc. ISMRM 2013, 1455. [7] Ruppert K et al. Proc. ISMRM 2013, 817.

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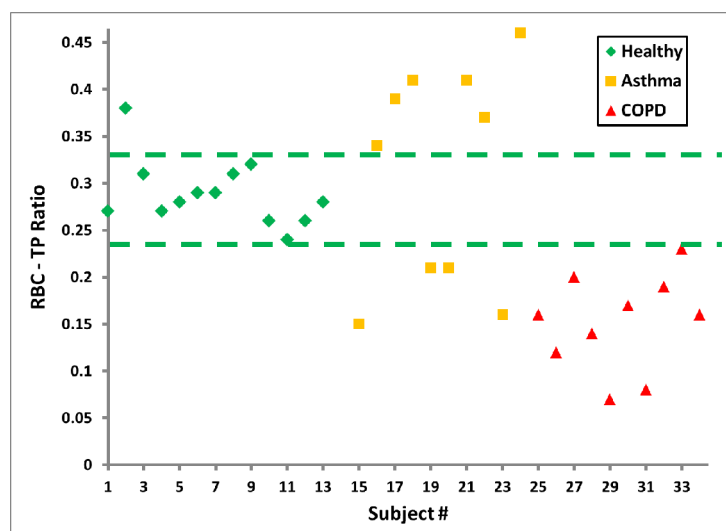


Figure 1. Averaged RBC-to-TP ratio for healthy (green), asthmatic (orange) and COPD (red) subjects at TLC. The dashed lines mark the "normal" RBC-TP ratio that encompasses 92% of the healthy subjects but does not contain a single subject with lung disease.