Detection of a Long-T2 Dissolved-phase Xe129 Component in the Human Chest

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Introduction: Compared to helium-3, the solubility of xenon-129 in the lung parenchyma is relatively high. Also, the associated large chemical-shift difference of ~200 ppm between this so-called "dissolved phase" and the xenon gas phase makes it feasible to directly image the dissolved phase using hyperpolarized xenon-129 (HXe) MRI [1,2]. Nevertheless, the overall dissolved-phase signal is only about 1-2% of the gas-phase signal. To make matters worse, the T2* of the dissolved phase is also just on the order of 2 ms [1], which greatly reduces the resulting signal amplitude for most gradient-echo pulse sequences. In this work, we measured the T2 of the dissolved-phase compartment using a global (whole-lung) CPMG echo-train spectroscopic pulse sequence, and evaluated the potential for imaging the dissolved phase using a spin-echo pulse sequence.

Methods: Measurements were performed at 1.5T (Avanto, Siemens Medical Solutions, Malvern, PA) using a rigid chest RF coil (custom built). Enriched xenon gas (87% Xe129) was polarized by collisional spin exchange with an optically-pumped rubidium vapor using a prototype commercial system (XeBox-E10, Xemed LLC, Durham NH). Each subject inhaled a gas mixture having a total oxygen concentration of 21% and containing 0.5-L of hyperpolarized Xe129 polarized to 30-50%, room air and oxygen. All experiments were performed under a Physician's IND for imaging with HXe using a protocol approved by our institutional review board. Informed consent was obtained in all cases.

Spin-echo-train data were obtained in two healthy subjects (#1, female, 23 yrs; #2, female 22 yrs) using the following sequence parameters: echo spacing, 18 ms; number of echoes, 16; data sampling period, 5 ms; and RF-pulse duration, 8 ms. The RF pulse waveform was designed such that application at the frequency corresponding to a given dissolved-phase component (red blood cells [RBC] or parenchyma/plasma) would yield negligible (a few percent) signal contribution from the other component. Following initiation of the breath-hold period, a given component was excited every 3 (subject 1) or 4 (subject 2) seconds. Bi-exponential decay functions were fitted to the dissolved-phase peak areas from the 16 echoes collected in each echo train.

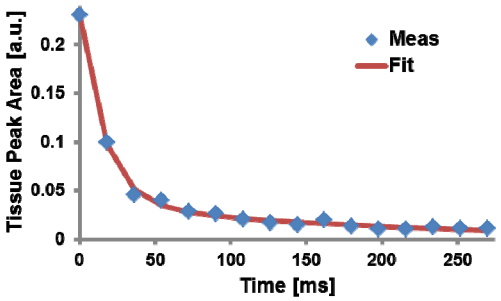

Figure 1. Tissue peak area in spectra acquired with a spin-echo train sequence and the resulting bi-exponential fit.

Results and Discussion: Figure 1 depicts the measured peak area for each spectrum in a representative tissue echo-train (i.e., at the frequency corresponding to the parenchyma/plasma resonance), and the corresponding bi-exponential fit. Table 1 summarizes the resulting short and long T2 values, and the fraction of the long-T2 component in the total tissue signal. Based on these findings, ~85% of the measured tissue signal is comprised of a component that decays quickly, with a T2 of about 18 ms. It also contains a much smaller second component with a T2 that is at least about 10 times longer. While the exact T2 of this second component was difficult to determine due to the low signal-to-noise ratio (SNR) in the late echoes, it remained clearly apparent even in the final echo, 270 ms after the first. Interestingly, echo trains at the RBC frequency yielded almost no discernible dissolved-phase peaks. Therefore, we hypothesize that rapid exchange of xenon atoms between the RBC and blood plasma results in a complete dephasing of these two signal components within 18 ms; the time of the first echo. Only more slowly exchanging HXe dissolved in the lung tissue or some compartment further downstream contributes to the signal measured during the echo train. We further hypothesize that, in particular, the long T2-signal component could be attributed to HXe accumulation in a more magnetically-homogenous environment than that within the pulmonary gas-exchange regions. Although the long T2 of part of the dissolved-phase signal would make it a very promising target for suitably designed spin-echo imaging sequences, the amplitude is at least another factor of 10 lower than the already small total dissolved-phase signal measured by the currently employed gradient-echo-based pulse sequences [1,2].

Subject	Train #	T2 (short) [ms]	T2 (long) [ms]	Long-short component ratio [%]
1	1	16.2	190	16
	2	19.2	1110	6
2	1	19.6	480	15
	2	16.3	130	4
Mean		**17.8**	**480**	**12**
Median		**17.8**	**330**	**14**
Std. Dev.		**1.8**	**450**	**5**

Table 1. T2 values and their relative contribution to the signal total for both subjects. Additional echo trains were collected but their SNR was too low for analysis.

Conclusion: Using a CPMG-based spectroscopy pulse sequence we identified short (~18 ms) and long (~400 ms) T2 components of the HXe dissolved-phase signal at the frequency corresponding to parenchyma/plasma. Although the long T2 component is of currently unassigned origin, it would be most suitable for direct imaging using a spin-echo pulse sequence. However, due to its small amplitude, an improvement in image quality over that of existing gradient-echo pulse sequences remains doubtful.

References: **[1]** Cleveland ZI et al. PLoS ONE 5(8): e12192. **[2]** Mugler JP 3rd et al. PNAS USA 2010; 107(50):21707-21712

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