Detection of a New Pulmonary Gas-exchange Component for Hyperpolarized Xenon-129

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Introduction: Over the past several years numerous studies have documented the use of hyperpolarized xenon-129 (HXe-129) MRI or MRS to characterize uptake and exchange of xenon gas in the lungs of humans and animals. However, these studies revealed a puzzling and little explored discrepancy in the same subject between the time constant for xenon entering the lung tissue (50-120 ms) (1-4) and that for xenon returning to the alveoli through exchange (~10 ms in rabbits) (5). By employing an uptake MRS pulse sequence with finely spaced delay times and comparing it, for short delay times, to an equivalent exchange MRS sequence (5,6), we investigated in rabbits the origins of this apparent difference in time constants.

Methods: For the uptake studies three 90° 900-µs Gaussian RF saturation pulses, centered at the dissolved-phase frequency (i.e., 202 ppm downfield from the resonance frequency of HXe-129 gas residing in the lung airspaces) and separated by gradient spoilers, were applied to destroy any xenon signal originating from within the lung parenchyma. After a variable delay time that controlled how much HXe-129 gas can enter the lung parenchyma and the blood from the alveolar airspaces, a 900-µs Gaussian RF excitation pulse was applied and a free induction decay was collected (TR 100 ms, TE 0.55 ms, Bandwidth 32.6 Hz, 1024 data points). This process was repeated 32 times during the same breath hold with delay times ranging from 2 ms to 900 ms. Exchange data for 32 delay times (2-55ms) was collected during a single breath hold with a pulse sequence similar to the one described in (6). Experiments were performed on a 1.5-T commercial whole-body imager (Sonata, Siemens Medical Solutions, Malvern, PA) using a custom-made transmit-receive birdcage RF coil (IGC Medical Advances, Milwaukee, WI). New Zealand rabbits (approximately 5 kg) were anesthetized with a mixture of Xylazine 5 mg/kg and Ketamine 50 mg/kg. The animals were then intubated and placed in the xenon RF coil. The rabbits were ventilated with 30 cc of isotopically enriched (85% ^{129}Xe) xenon gas, polarized to approximately 10-15% via spin exchange with an optically pumped rubidium vapor (Model IGI 9600Xe Xenon Polarizer, MITI, Durham, NC). The protocol was approved by our Institutional Animal Care and Use Committee.

In rabbits the difference between the xenon resonance frequency in red blood cells (RBCs) and that in tissue/plasma is only about 5.5 ppm, which is small compared to that in other species (1,3) and, coupled with the broadness of the peaks, makes an accurate separation at short delay times difficult. However, using the more distinct peak appearance at delay times longer than 500ms, we were able to identify the peak locations and fit the dissolved-phase signal with two Lorenzian line shapes. The xenon signal for each compartment at a given delay time was assumed to be the integral under the associated Lorenzian. Two different models were attempted to fit to the experimental data: (1) $S(t) = a(1-\exp(-t/\tau)) + ct$ [1], where $S(t)$ is the peak integral as a function of delay time t, a is the asymptotically approached saturation value, τ is the time constant for the gas uptake and c characterizes the blood flow (3); and (2) The biexponential form of the previous equation: $S(t) = a_1(1-\exp(-t/\tau_1)) + a_2(1-\exp(-t/\tau_2)) + ct$ [2]. The gas-phase depolarization f_D was fitted with a function of the type $f_D = a_1 + a_2(1-\exp(-t/\tau))$ [3], as in (5).

Results: Figure 1a shows the dissolved-phase signals obtained with the uptake sequence as a function of the delay time. While the RBC signal could be fitted with Eq. 1 ($\tau_{RBC} = 57 \pm 10$ms) this was not possible for the tissue/plasma peak. Instead, a bi-exponential fit with two very different time constants was required ($\tau_{Plasma} = 72 \pm 12$ms and $\tau_{Tissue} = 4.2 \pm 1$ms). Figure 1b displays the data in Fig. 1a for short delay times and Fig. 1c depicts the results from the exchange experiment. The latter was fitted with Eq. [3] and yielded a time constant $\tau_{Exchange} = 9.7 \pm 2.3$ms .

Conclusion: HXe-129 uptake spectroscopy with a high temporal resolution permitted the detection of a heretofore unidentified dissolved-phase component that is saturated with a time constant of just a few milliseconds. Tentatively we assigned this rapidly-filling component to the tissue compartment (or maybe just the membranes) and the more slowly-filling component to the plasma compartment due to its similarity with the RBC time constant. Clearly, the rapidly-filling component dominates the exchange measurement and explains the apparent discrepancy in time constants between uptake and exchange. The detection of this new component will probably require a revision of all existing pulmonary xenon uptake and exchange models (1-6).

References

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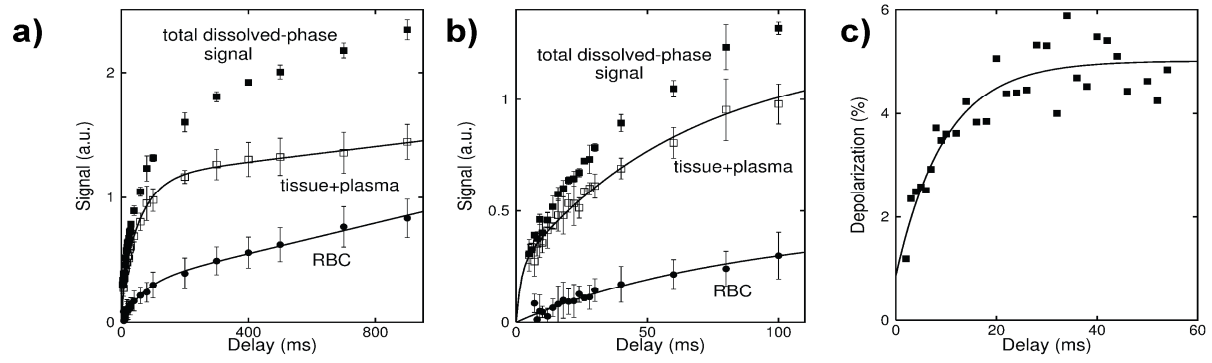

Figure 1. (**a**) Delay-time dependence of the dissolved-phase peaks as well as their composite. (**b**) Same as (**a**) but only delay times shorter than 100ms are displayed. (c) Delay-time dependence of gas-phase depolarization.