Detecting Simulated Pulmonary Embolism in a Rabbit Model with Hyperpolarized Xenon-129 Uptake Spectroscopy

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Introduction: Previous studies have demonstrated the feasibility of indirectly detecting a pulmonary embolism (PE) using hyperpolarized helium-3 (HHe-3) MRI by tracing the gas-signal depletion following the injection of a paramagnetic contrast agent (1), quantifying the regional oxygen depletion rate in the lung (2) or by combining HHe-3 ventilation images with proton perfusion measurements (3). Hyperpolarized xenon-129 (HXe-129) uptake spectroscopy has been used to measure how quickly xenon gas enters the dissolved-phase compartments in the lung (4-7). We hypothesized that this gas uptake would be affected by lung pathologies such as a PE and we investigated the impact of a PE using a previously described PE rabbit model (3).

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. 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). Six New Zealand rabbits (4.2-5.2 kg) had a non-detachable occlusion balloon catheter placed in their left pulmonary artery under fluoroscopic guidance. This balloon permitted full occlusion of the left lower lobe pulmonary artery, blocking the blood supply to the associated lung. Data was acquired with the balloon initially deflated. The studies were repeated after the balloon had been inflated. The animals were ventilated with 30cc 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 used 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]. Equation 1 was then applied to fit the RBC uptake and Eq. 2 to fit the tissue + plasma (T + P) uptake.

Results: Figure 1 shows the uptake curves for the xenon dissolved-phase compartments in the lung of one of the rabbits before and during the inflation of the balloon in the pulmonary artery. While the RBC signal drops substantially during the inflation of the balloon the T+P signal remains largely unchanged. Table 1 summarizes the average values for the fitting parameters for all six rabbits. Unfortunately the signal-to-noise ratio of our method proved to be too low for a reliable quantification of the parameters c and c_1, which, according to our model, should be proportional to the global lung perfusion.

Conclusion: Although xenon uptake spectroscopy is a global technique it appears to be sufficiently sensitive to detect the impact of a simulated PE. However, the responses in the individual animals differed vastly (as indicated by the large standard deviations of the fitted parameters). Additional studies will show whether this variability can be correlated with different systemic responses in the animals.

References

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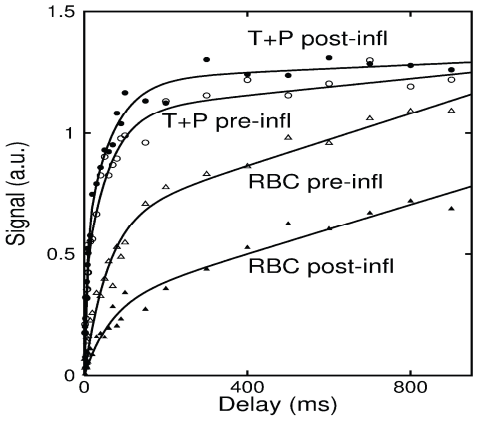

Figure 1. Xenon uptake curves for the RBC and tissue/plasma dissolved-phase compartments in the lung of a rabbit before and after inflation of the balloon in the left pulmonary artery.

	Pre-inflation	During inflation
a (a. u.)	0.36±0.30	0.26±0.20
τ (ms)	42±29	35±22
c (a. u. / ms)	0.0006±0.0004	0.00050±0.00001
a_1 (a. u.)	0.58±0.19	0.62±0.14
τ_1 (ms)	9.3 ± 5.6	9.1 ±3.7
a_2 (a. u.)	0.71± 0.33	0.55 ±0.20
τ_2 (ms)	162 ±160	122 ±56
c_1 (a. u. / ms)	0.00002 ±0.00004	0.00003 ±0.00015

Table 1. Fitted parameter values for xenon uptake by the dissolved-phase compartments before and during inflation of the balloon that occluded the left pulmonary artery.