Quantifying Pulmonary Gas Transport Efficiency Using Hyperpolarized Xenon-129

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Introduction: Upon inhalation approximately 1-2% of hyperpolarized xenon-129 (HXe129) dissolves in the lung parenchyma and gives rise to several resonances that are chemically shifted by approximately 200 ppm relative to the alveolar gas phase. Such a large frequency difference makes it feasible to either exclusively image the dissolved HXe129 with selective excitation pulses [1] or to image both phases simultaneously, appearing side-by-side in the image [2,3]. However, the HXe129 distribution changes dynamically throughout the image acquisition due to gas exchange and transport by the blood. Thus, the image intensity in a pixel strongly depends on the history of the HXe129 magnetization. For known MR pulse sequence parameters it would seem plausible that information about xenon transport can be extracted from the images. In this work, we demonstrate the feasibility of measuring the transit time from xenon gas dissolving in the parenchyma until it reaches the left ventricle of the heart in healthy rabbits.

Methods: Experiments were performed on a 1.5-T commercial whole-body imager (Avanto, Siemens Medical Solutions, Malvern, PA) using a custom-made transmit-receive birdcage RF coil (IGC Medical Advances, Milwaukee, WI). The imaging sequence was a 2D-projection gradient-echo sequence that employed RF excitation pulses with a truncated-sinc waveform of 2.31 ms duration and centered 3,660 Hz downfield from the gas-phase resonance. The RF-pulse parameters were chosen such that they provided a high FA at the dissolved-phase resonance (~202 ppm) and a homogeneously low FA at the gas-phase resonance (0 ppm). The following sequence parameters were used: flip angle 10°, 20°, 40° or 80°; matrix size 36×80; TR 100 or 200 ms; TE 2.8 ms; FOV 280 mm; receiver bandwidth 110 Hz/pixel. Four New Zealand white rabbits (approximately 5 kg) were imaged. Each animal was anesthetized with a mixture of Xylazine 5 mg/kg and Ketamine 50 mg/kg, intubated, and placed in the xenon RF coil. Immediately before the pulse sequence was started the animal was ventilated with 30 cc of isotopically enriched xenon gas (~87% xenon-129), which was polarized to ~35% using a commercial prototype polarizer (Xemed LLC, NH). The protocol was approved by our Institutional Animal Care and Use Committee. Three regions of interest (ROIs) were analyzed in each image and their means calculated: a region encompassing the left ventricle in the dissolved-phase image (ROI 1) and two regions in the gas-phase image (see Fig. 1). All images were normalized using the two gas-phase ROIs. Since the images were projections, the mean signal in ROI 1 from an acquisition with an 80° flip angle, which did not contain HXe129 signal within the heart, was used to remove any background intensities from the mean signals in ROI 1 of all other acquisitions. Subsequently, the ratios of the ROI 1 means of two images obtained with different flip angles were calculated. Depending on the number of RF pulses n that the HXe129 in the dissolved phase experienced on its way to the heart this ratio is given by $\frac{S_1}{S_2} = \frac{\cos^{n-1}\alpha_1 \sin\alpha_1}{\cos^{n-1}\alpha_2 \sin\alpha_2}$, where S_1 and S_2 are the mean signal intensities in ROI 1 of the images acquired with flip angles of α_1 and α_2, respectively. When solving this equation, n was assumed to be a real number which, after multiplication with TR, yielded the xenon transit time from the alveolar spaces to the left ventricle of the heart.

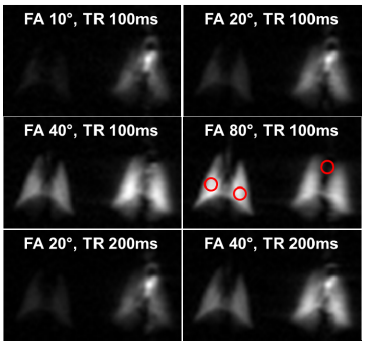

Figure 1. Representative images of simultaneous gas-phase (left side of image) and dissolved-phase (right side of image) acquisitions with different imaging parameters. The red circles mark the evaluated regions of interest.

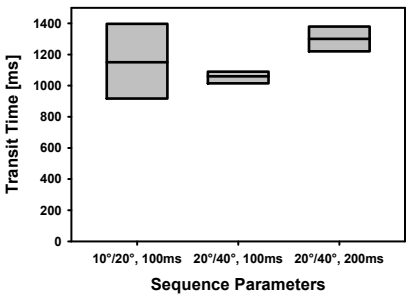

Figure 2. Calculated HXe129 transit times from the airspaces to the left ventricle for three different parameter combinations. Each gray box shows the mean (central line) as well as the 25th and 75th percentile of the parameter distribution.

Results and Discussion: Xenon transit times for the three flip-angle ratios and TR combinations investigated are shown in Fig. 2 and found to be: 1,160 ± 270 ms (10°/20°, 100 ms), 1,060 ± 40 ms (20°/40°, 100 ms) and 1,300 ± 90 ms (20°/40°, 200 ms). Given that the capillary transit time in rabbits is about 600 ms [4], the observed transit times all the way to the heart of around 1,200 ms seem very plausible. Within the investigated parameter space a flip angle combination of 20°/40° and a TR of 100 ms seemed to result in the smallest scatter. This might be due to the circumstance that, although the left ventricle is more conspicuous, the image signal-to-noise ratios at low flip angles are much lower as well. Since the number of flip angles HXe129 experiences on its way to the heart is relatively small (~10), part of the observed variability might be due to the circumstance that the image acquisitions were started at different points in the cardiac cycle. In the future, this variability will be minimized by cardiac triggering. Also, the absolute values of these transit times depend on the accuracy of the applied flip angles. For transit times around 1,100 ms and a flip angle error of 10%, we estimate the systematic error to be approximately 20%.

Conclusion: Simultaneous imaging of gas-phase and dissolved-phase xenon magnetization allows evaluation of lung function by quantifying HXe129 gas transport processes from the air spaces to the heart. Thus, any diseases that affect the uptake of xenon by the blood stream or the subsequent transport would in principle be detectable.

References: **[1]** Cleveland ZI et al. PLoS ONE 2010;5(8):e12192. **[2]** Mugler III JP et al. MRM 1997;37:809-815. **[3]** Mugler III JP et al. Proc Natl Acad Sci USA (in press). **[4]** Wang PM et al. J Appl Physiol 1990;69(6):2262-2268.

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