^{129}Xe as an in vivo probe for MR oximetry

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Target Audience MRI Oximetry, Lung Imaging

Purpose Demonstrate the use of ^{129}Xe as an *in vivo* probe of red blood cell oxygen saturation in the lungs

Introduction Non-invasive, direct measurement of hemoglobin oxygenation could be of interest in many clinical settings. Xenon has been used as a perfusion tracer for many years, and after hyperpolarization, MRI can detect ^{129}Xe in small quantities. Furthermore, Xe dissolves into various biological tissues, such as plasma and blood, making it an interesting reporter of physiology. The highly polarizable electron cloud of ^{129}Xe generates a chemical shift that is very sensitive to its local environment. When ^{129}Xe dissolves in red blood cells (RBCs), the resonance frequency has been shown to be sensitive to blood oxygen saturation (sO_2) *in vitro*[1], changing by 4 ppm over the entire range of RBC oxygenation. In this work we demonstrate a method of using this change in frequency of dissolved ^{129}Xe-RBC as an estimate of RBC oxygenation *in vivo* in the human pulmonary vasculature.

Methods Whole lung spectroscopy was performed on a 3T Philips Achieva (Philips Healthcare, Netherlands), using a flexible quadrature transmit/receive coil (Clinical MR Solutions, USA). Volunteers (n=3) inhaled 400 mL of hyperpolarized ^{129}Xe gas topped up with N_2 to 1 L. Data were acquired every 3 seconds with a 4 kHz readout bandwidth. RBC peak position was extracted by fitting a Lorentzian to the spectra. To generate phase imaging data, one volunteer was imaged on a 1.5T GE MRI (14M4, USA). A six element composite binomial pulse 0.8ms long was used for selective excitation of the dissolved ^{129}Xe. An Archimedean spiral readout trajectory was designed with maximum gradient of 33 mT/m and maximum slew rates of 110mT/m/ms. 512 data points on 128 spiral arms were acquired with a read bandwidth of 250 kHz for a total readout window of 2 ms. The effective echo time was 590us, TR was 100 ms to allow for replenishment of signal from gas phase ^{129}Xe. The 128 arm spiral was repeated twice to collect enough data for a sliding window reconstruction. Data were regridded after density and intensity correction to account for sampling density and RF depolarization[2]. Phase images were reconstructed using a 128 TR sliding window, updating a spiral arm each reconstruction. The lung boundary was calculated from a magnitude threshold and mean phase was calculated over this ROI. Phase difference was calculated by subtracting the first fully sampled phase image and converted to frequency by dividing by the the echo time.

Results The change in ^{129}Xe-RBC resonance frequency from whole lung spectroscopic data are plot in Figure 1 from three volunteers showing an exponential change as a function of time. Converting this value to sO_2 from previously calibrated *in vivo* data[3], the saturation asymptotically approaches clinically accepted values of mixed venous sO_2. Figure 2 shows an overlay of the magnitude of dissolved ^{129}Xe signal on a ^{1}H proton image and to the right, the phase of this image with the ROI generated from the threshold magnitude data. Mean phase over the whole lung is plot in purple in Figure 3. Also plot on the same graph is the spectroscopy data from the same individual. Both curves follow the same pattern, indicating that the phase of the signal follows the evolution of frequencies from the shifting RBC peak.

Discussion. We observe a shift in ^{129}Xe-RBC resonance frequency that declines exponentially as a function of breath hold. It was shown previously with ^{3}He that partial pressure of oxygen (pO_2) also declines exponentially as a function of apnea time[4]. Assuming adequate capillary/alveolar gas transfer in these healthy volunteers, blood sO_2 will follow the same trend.

Phase evolution over a number of identical NMR excitations occurs due to two reasons: drift in B_o field & change in the constituent resonant frequencies. The ^{129}Xe gas peak shows no change in resonance frequency over the breath hold and suggests that the change of phase seen in this data is related to the changing frequency of the dissolved ^{129}Xe-RBC owing to deoxygenation. The phase change in the dissolved ^{129}Xe spectra follows closely the change in frequency of the ^{129}Xe-RBC observed during breath hold apnea measured using whole lung spectroscopy. Quantitating this phase change, using a Dixon imaging technique[5], may provide insights into spatially localizing this RBC resonance shift, and in turn, measuring RBC oxygenation non-invasively.

References 1. Wolber J *Magnetic Resonance in Medicine*. 2000;43(4):491–496.2. Marshall H, *NMR Biomed*. 2012;25(2):389–399.3. Leung G, *Proceedings of the European Respiratory Society,* 2012 Vienna.4. Cieślar K, *NMR in Biomedicine*. 2007;20(3):383–391.5. Dixon WT. *Radiology*. 1984;153(1):189–194.

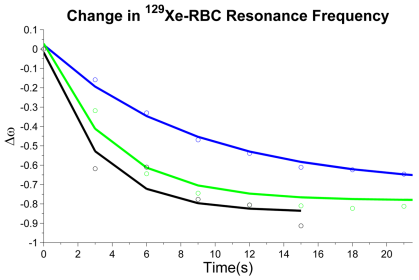

Figure 1: Change in RBC peak position as a function of breath hold measured using whole lung spectroscopy. Apnea is known to cause a drop in pO_2 which will translate into a drop in RBC O_2 saturation. We observe an exponential change in ^{129}Xe-RBC resonance frequency as a function of breath hold time in n=3 volunteers.

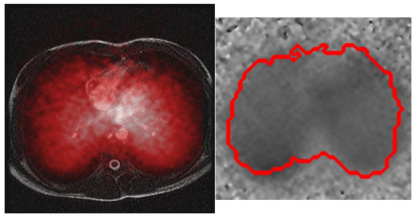

Figure 2: ^{129}Xe dissolved imaging, magnitude and phase. Left shows a dissolved ^{129}Xe magnitude image overlay on a ^{1}H proton localizer acquired with the T/R body coil. Right is the phase image from the same data with the threshold region, derived from the magnitude data, drawn as a red ROI.

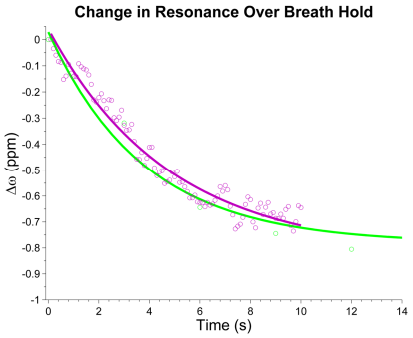

Figure 3: Mean phase data from whole lung as a function of breath hold. Plot is data (green) from one individual from figure 1 (also green). The mean phase calculated over the entire lung, divided by the echo time to convert to frequency, is also plot (purple). The same relationship is seen as a function of time, suggestive that the phase of the dissolved ^{129}Xe follows the shift of frequency seen by the ^{129}Xe-RBC due to changing oxygen saturation.