In vivo dynamic measurement of pulmonary blood oxygenation and cardiac output using hyperpolarised ^{129}Xe

Graham Norquay[1], Neil Stewart[1], and Jim Wild[1]
[1]*University of Sheffield, Sheffield, South Yorkshire, United Kingdom*

Target audience: Pulmonary MR; hyperpolarised noble gases community.

Purpose: Lung hypoxia is of interest clinically, in lung diseases such as asthma and COPD, and in understanding disease mechanisms such as inflammation [1]. Real-time monitoring of pulmonary oxygenation is challenging and is typically performed indirectly via pulse-oximetry. Hyperpolarised (HP) ^{129}Xe NMR spectroscopy is a powerful tool for assessment of gas exchange in vivo, made possible by the solubility and high sensitivity of Xe to its chemical and physical surroundings. In this work, a method for direct, non-invasive dynamic measurement of pulmonary oxygenation in vivo using HP ^{129}Xe MR is demonstrated.

Method: ***In vitro calibration*****:** The relationship between the chemical shift of ^{129}Xe in plasma and red blood cells (RBCs), δ, and blood oxygenation, sO_2, was established in vitro using 1.5 T (GE, Signa, HDx) and 3 T (Philips, Achieva) scanners. 200 ml of HP Xe (> 10 % polarisation) was acquired using a home-built spin-exchange optical pumping polariser [2]. Xe was dissolved into human blood as described previously in ref. [3]. For NMR acquisition at 1.5 T and 3 T, pulse-acquire sequences, with block pulses (width 500 µs), receive bandwidths of 2.5 kHz (1.5 T) and 4 kHz (3 T) and an inter-pulse delay (TR) of 0.5 s were used. For spectral analysis, zero-order phase corrections were applied to the raw data and absorption spectra were fit in the chemical shift domain to a linear combination of two Lorentzians to calculate the ^{129}Xe-RBC and ^{129}Xe-plasma peak positions. ***In vivo lung spectroscopy***: Two healthy male subjects inhaled 600 ml of hyperpolarised ^{129}Xe (~ 40% polarisation [4]) and performed a 45 s breath-hold on a clinical 3 T scanner. Serial pulse-acquire MR measurements (FA = 90°, centered on the ^{129}Xe-RBC resonance) were made over the whole lungs (Fig. 2) with a receive bandwidth of 3 kHz, 2048 samples (frequency resolution = 0.04 ppm) and TR of 0.8 s. The experiment was repeated with increased temporal resolution (TR = 0.1 s), by reducing the sampling to 128 points (frequency resolution = 0.7 ppm). The detected ^{129}Xe-RBC and ^{129}Xe-tissue/plasma (TP) signals in vivo were normalised to the ^{129}Xe gas T_1 decay in the lungs (measured to be 18 s).

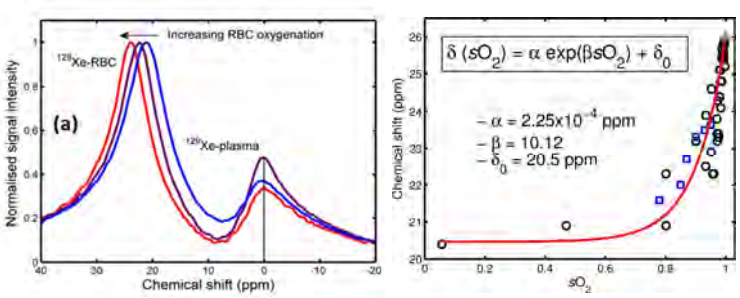

Fig. 1: *In vitro spectroscopy*. (a & b) Increasing ^{129}Xe-RBC chemical shift with increasing sO_2. (b) Empirical fit (red line) to 1.5 T (open black circles) and 3 T (open blue squares) data was used to calibrate blood oxygenation to chemical shift.

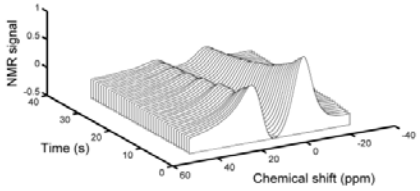

Fig. 2: *In vivo spectroscopy*. Time-series of dissolved ^{129}Xe spectra acquired from healthy lungs during breath-hold apnoea.

Results and Discussion: The in vitro calibration data showed that the ^{129}Xe-RBC chemical shift increases non-linearly with increasing sO_2, whilst the ^{129}Xe-plasma peak position was observed to remain fixed (Fig. 1). During in vivo experiments with TR = 0.8 s, it was found that the ^{129}Xe-RBC signal was modulated over the breath-hold period in an oscillatory manner with a non-constant frequency – the initial ^{129}Xe-RBC signal trough-peak time period was ~ 4 s, decreasing to a value of ~ 2 s at the breath-hold end (Fig 3, (a, b)). No modulation in the ^{129}Xe-TP signal was observed over the breath-hold period for TR = 0.8 s. In addition, the pulmonary blood oxygenation, calculated by converting the measured ^{129}Xe-RBC chemical shift into oxygenation using the boxed equation in Fig. 1 (b), was found to oscillate with the same frequency as the ^{129}Xe-RBC signal oscillations. Chemical shift maxima coincided with ^{129}Xe-RBC signal minima and the peak value gradually decreased (by ~ 4 %) over the breath-hold. Ruppert et al [5] previously observed ^{129}Xe-RBC (and ^{129}Xe-TP) signal modulations (peak-to-peak period of ~ 1 s, TR of 0.1 s), and attributed this behavior to cardiac pulsation. The dataset acquired at increased temporal resolution (TR = 0.1 s, see Fig. 3, (c)), confirmed the observations of Ruppert et al where the ^{129}Xe-RBC and ^{129}Xe-TP signals oscillated at rates of the same order as cardiac pulsation. For TR = 0.1 s, the frequency resolution (0.7 ppm) was too low to discriminate changes in the ^{129}Xe-RBC peak position (and hence oxygenation) over the breath-hold duration, therefore in future work, we endeavour to utilise cardiac gating to assess pulmonary oxygenation variability throughout the cardiac cycle.

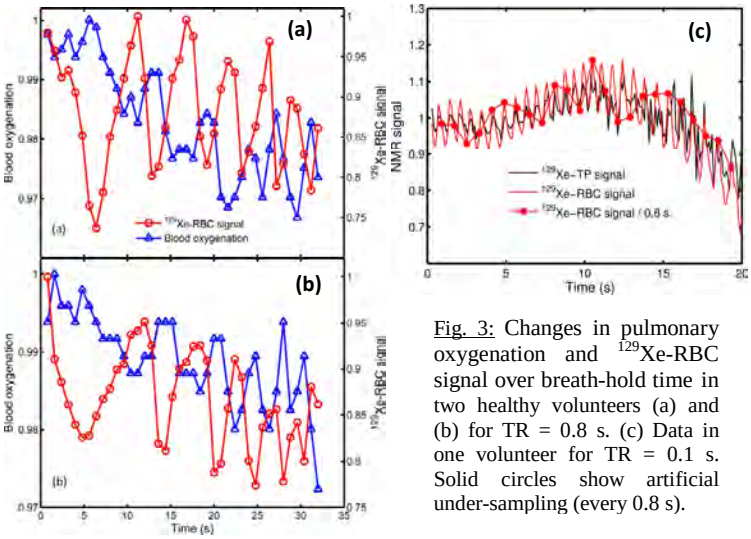

Fig. 3: Changes in pulmonary oxygenation and ^{129}Xe-RBC signal over breath-hold time in two healthy volunteers (a) and (b) for TR = 0.8 s. (c) Data in one volunteer for TR = 0.1 s. Solid circles show artificial under-sampling (every 0.8 s).

Conclusions: It has been shown that hyperpolarised ^{129}Xe MR is sensitive to dynamic pulmonary blood oxygenation changes in vivo during breath-hold apnoea. Oscillatory behaviour in ^{129}Xe-RBC signal and blood oxygenation has been observed during breath-hold, with a coincidence of blood oxygenation maxima and ^{129}Xe-RBC signal minima, indicating a common modulation frequency, suggestive of a link between pulmonary oxygenation and cardiac output, which is to be expected as deoxygenated blood from the body is circulated through the pulmonary vasculature during apnoea. Further work with cardiac gating acquisitions are thus underway to probe ^{129}Xe-RBC chemical shifts (blood oxygenations) at specific time points in the cardiac cycle, thereby enabling real-time monitoring of pulmonary oxygenation throughout the cardiac cycle.

References: [1] Hoenderdos et al., Am J Respir Cell Mol Biol, 48 (5), 2013. [2] Norquay et al., J. Appl. Phys, 113, 044908, 2013.[3] Norquay et al., MRM, doi: 10.1002/mrm.25417, 2014 [4] Norquay et al., Proc. PING, 2014. [5] Ruppert et al., Proc ISMRM, 2013, abstract 0817.

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