129Xe-RBC T1 dependence on blood oxygen saturation

Graham Norquay[1], General Leung[1], Jan Wolber[2], Gillian Tozer[1], and Jim Wild[1]
[1]*University of Sheffield, Sheffield, South Yorkshire, United Kingdom,* [2]*GE Healthcare, Amersham, Buckinghamshire, United Kingdom*

Target audience: NMR spectroscopy; Hyperpolarised gas MR

Purpose: Accurate knowledge of the ^{129}Xe T_1 in blood is vital for the design and optimisation of *in vivo* NMR experiments probing the exchange dynamics of Xe diffusing between intra- and extra-vascular compartments. In this study, the ^{129}Xe T_1 in red blood cells (RBCs) was measured as a function of blood oxygen saturation (sO_2). This knowledge may be used to develop *in vivo* MR spectroscopy/imaging techniques that provide a means to non-invasively measure regional oxygenation in tumour vasculature.

Methods: Approximately 200 ml of HP Xe (> 10 % polarisation) was acquired over 20 minutes using a home-built spin-exchange optical pumping polariser (SEOP) [1]. Human blood was extracted from two healthy male volunteers and was transferred into 6 ml lithium heparin test tubes (BD, Vacutainer, UK) ~ 1-4 hours prior to NMR measurements. For ^{129}Xe blood dissolution, Xe and blood were passed through a hollow-fiber membrane (Contactor G680, Membrana, United States), whereupon approximately ~ 2 ml of blood containing dissolved xenon was passed into a 3 ml syringe contained within a home-built solenoid coil with 2 cm diameter and a length of 4 cm. For NMR measurements, pulse-acquire acquisitions were made with rectangular hard pulses (500 µs) and a receive bandwidth of 2.5 kHz. T_1 measurements were made using small flip angle pulses (~ 15°), with an inter-pulse delay of 0.5 s. Signal intensities were corrected for depolarisation from RF pulses and the T_1 was calculated by fitting an exponential to these values using the non-linear Levenberg-Marquardt least squares method (Fig 1, inset). This was repeated for sO_2 values ranging from 0.4–1, where blood sO_2 was increased by passing oxygen through the membrane by the same method that was used for dissolving Xe into the blood. sO_2 values were determined using a blood gas analyser (Radiometer, ABL80) on ~ 1 ml samples of blood that were extracted from the membrane immediately after performing the NMR measurements.

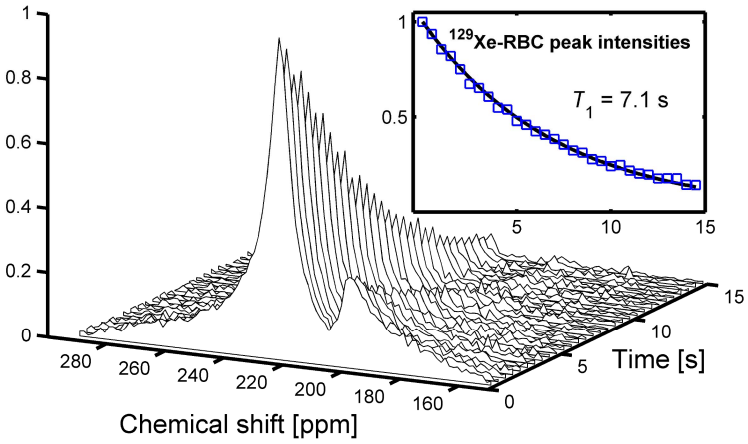

Figure 1: Decaying spectra from ^{129}Xe dissolved in blood acquired with 500 µs hard pulses (TR = 0.5 s) on a 1.5 T scanner. The peaks at ~ 196 and 220 ppm correspond to ^{129}Xe dissolved within plasma and RBCs, respectively. The inset shows an exponential fit performed on the decreasing ^{129}Xe-RBC NMR signal to establish a value for ^{129}Xe-RBC T_1 (fit is for a sample with 0.91 sO_2 and Hct of 57 %).

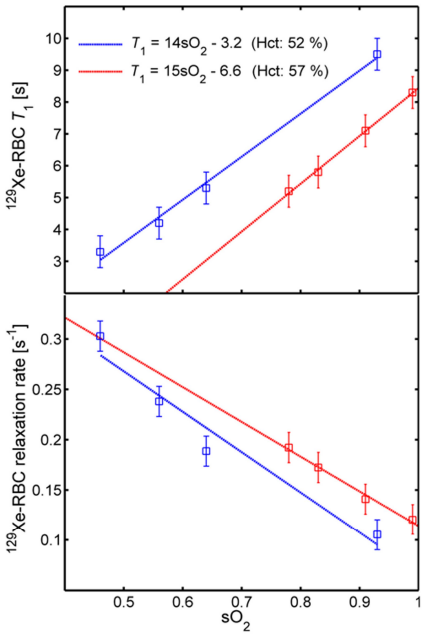

Figure 2: ^{129}Xe-RBC T_1 and relaxtion rates vs. blood oxygen saturation (sO_2). Blood samples were taken from two volunteers with different haematocrit (Hct) values.

Results and discussion: The ^{129}Xe-RBC T_1s for both blood samples increase linearly with increasing sO_2 and follow approximately the same slope (Fig. 2). In a previous study [2], an increase in ^{129}Xe-RBC T_1 with increasing sO_2 was also observed. However, the authors reported a non-linear relationship between ^{129}Xe-RBC T_1 and sO_2, where the mechanism believed to be responsible for the ^{129}Xe-RBC T_1 dependence on sO_2 was oxygenation-dependent conformational changes of haemoglobin. It has previously been observed [3] that blood sO_2 measurement is essentially an ensemble measure of the superposition of the two haemoglobin states, Hb_4 and and Hb_4O_8, which have electron spin S = 2 (paramagnetic deoxyhaemeoglobin) and S = 0 (diamagnetic oxyhaemoglobin), with a very small contribution from the three intermediate haemoglobin states. In addition, a linear relationship between magnetic susceptibility and sO_2 was found. Following from this, and from the linear relationship between ^{129}Xe-RBC T_1 and sO_2 observed in this study, we believe that the ^{129}Xe-RBC T_1 depends on the fraction of paramagnetic deoxyhaemoglobin molecules interacting with ^{129}Xe nuclei within RBCs. In addition, the baseline T_1 from the blood sample with a lower haematocrit (Hct) of 52 % is longer than that of the sample with a Hct of 57 %, which may be the result of fewer paramagnetic interaction sites for ^{129}Xe nuclei in the 52 % Hct blood sample. Further ^{129}Xe-RBC T_1 measurements with different Hct values are underway to investigate this further.

Conclusions: It has been reported for the first time a linear relationship between ^{129}Xe-RBC T_1 and blood sO_2. This has positive preclinical and clinical implications as it may open up the possibility of using HP ^{129}Xe *in vivo* as a non-invasive quantitative probe for blood oxygenation in tumours.

References: [1] Norquay G, et al. Optimized Production of Hyperpolarized129Xe at 2 bar for In Vivo Lung MRI *J Appl Phys.* 2012; (in press). [2] Wolber J, et al. Spin-lattice relaxation of laser-polarized xenon in human blood. *Proc Natl Acad Sci USA.* Mar 30 1999;96(7):3664-3669. [3] Coryell CD, et al.The Magnetic Properties of Intermediates in the Reactions of Hemoglobin. *The Journal of Physical Chemistry.* 1939/07/01 1939;43(7):825-839.