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 $\mu$s) 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.

Results and discussion: The $^{129}$Xe-RBC $T_1$s 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$_d$ and Hb$_o$O$_2$, which have electron spin $S = 2$ (paramagnetic deoxyhaemoglobin) 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: