Investigating the dependence of R_2^* of whole blood on oxygenation, contrast agent concentration and magnetic field strength

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INTRODUCTION

The transverse relaxation properties of blood are an important factor in determining the BOLD signal. Furthermore contrast agents can be used to modulate the BOLD signal, for instance to measure changes in CBV on activation [1]. In this experiment we measured the transverse relaxation rate, R_2^*, of whole blood and its dependence on blood oxygenation (Y), paramagnetic contrast agent (ProHance) concentration ([CA]) and magnetic field strength (B_0). These results will be useful in the interpretation of BOLD fMRI data and also in the optimisation of contrast enhanced angiography sequences [2].

METHOD

Informed consent was obtained from a single volunteer, who donated 100 ml of blood. Blood was collected in lithium heparinised blood tubes in order to prevent clotting. Samples were stored at 5°C and used within 48 hours. Blood oxygenation was modulated by slowly bubbling oxygen through the sample. Using this technique it was possible to obtain a physiological range of oxygenations between 48% and 84%. In order to investigate [CA] dependence small amounts of ProHance were added giving a concentration range between 0.3 mM and 3 mM, whilst maintaining static oxygenation. Throughout this process blood oxygenation was measured using a blood gas analyser. The mean and standard deviation of the haematocrit of all the samples was 43.2±2.0%. The percentage oxygen saturation of the CA samples was 66.3±4.8%. Prepared samples were transferred to spherical containers with an external diameter of 19 mm. Samples were maintained at 37°C and agitated prior to scanning. Imaging was performed on whole body Philips Achieva systems at 1.5 T, 3.0 T and 7.0 T. R_2^* maps were obtained using a single RF excitation pulse followed by an EPI switched gradient and acquisition module, in which the blipped gradient was removed and an initial phase encoding gradient added. This was then increased between repeats of the sequence. This causes the same phase encoding to be applied to each of the gradient echoes, and therefore a series of images at different gradient echo times could be reconstructed. A matrix size of 128x128 with a FOV of 128 mm and a slice thickness of 3.3 mm was used, collecting 63 gradient echoes with echo spacings of 1.39 ms, 1.12 ms and 1.16 ms for 1.5 T, 3.0 T and 7.0 T, respectively. The repetition time (TR) was 267 ms giving a total scan duration of 35.2 s. Due to this short scan duration heating and stirring were not performed inside the scanner with no adverse effects. Fitting was performed, using least squares minimisation, on a pixel-by-pixel basis.

RESULTS

Figure 1 plots blood R_2^* as a function of deoxyhaemoglobin (dHb) content, 1-Y. A quadratic fit to this data would normally be performed. However Li *et al.* [3] showed that for a narrow physiological range of oxygenations R_2^* is linearly dependent on dHb content. This approach allows us to calculate the relaxivity of dHb. As expected the relaxivity of dHb increases with magnetic field strength, figure 2. Figure 3 shows the dependence of R_2^* on [CA] and exhibits a point of inflection at approximately 1 mM. This effect becomes more pronounced at higher field, but is present at all 3 field strengths. The relaxivity of CA in blood was calculated from the rising edge of the curve and all 3 values are plotted in figure 4. Table 1 lists the measured values of relaxivity.

B_0 (T)	1-Y r_2^* (ms^{-1})	[CA] r_2^* ($ms^{-1}mM^{-1}$)
1.5	$(6.23\pm0.97)\times10^{-2}$	$(1.45\pm0.16)\times10^{-2}$
3.0	$(17.45\pm2.06)\times10^{-2}$	$(3.79\pm0.48)\times10^{-2}$
7.0	$(37.86\pm5.68)\times10^{-2}$	$(8.36\pm2.32)\times10^{-2}$

Table 1 – Relaxivity measurements

DISCUSSION

Blood dHb relaxivity measurements confirm the expected increase in sensitivity of blood T_2^* to blood oxygenation with field strength and decrease in blood T_2^* with field strength. Similarly the blood CA relaxivity (as defined above) increases with magnetic field strength. A negative relaxivity is observed for the physiological range of [CA] in humans. Red blood cells (RBC) contain the majority of the dHb in the blood, giving rise to an inhomogeneous susceptibility distribution, leading to local field gradients. The addition of CA to the plasma space reduces the field inhomogeneity and hence reduces the rate of transverse dephasing. The point of inflection represents the plasma [CA] required to match the susceptibility of plasma to RBC dHb. We have confirmed this by Monte Carlo simulations (not shown) using the method of Weisskoff *et al.* [5]. These simulations also confirmed the quadratic dependence of R_2^* on [CA] and the increasing magnitude of this effect with field strength. Experiments and simulations are ongoing to ascertain whether this effect can be used to measure oxygenation in vivo. These results will be used in experiments designed to test models of the BOLD effect, but will also be useful in optimizing pulse sequences for contrast enhanced imaging.

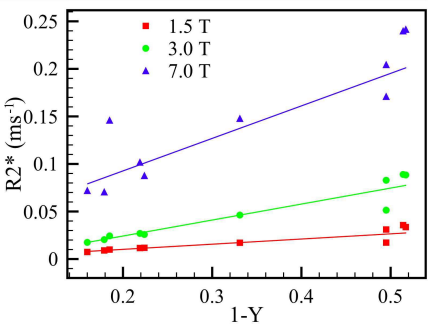

Fig. 1 – R_2^* versus dHb content

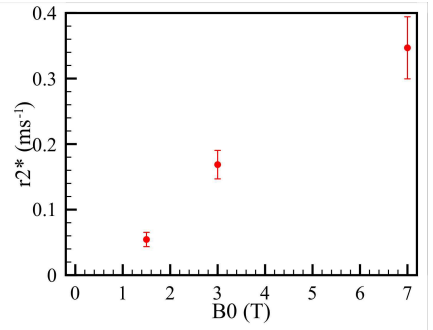

Fig. 2 – Relaxivity versus field strength

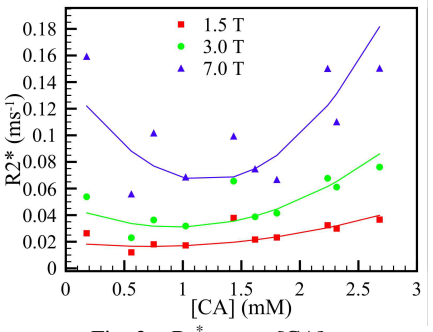

Fig. 3 – R_2^* versus [CA]

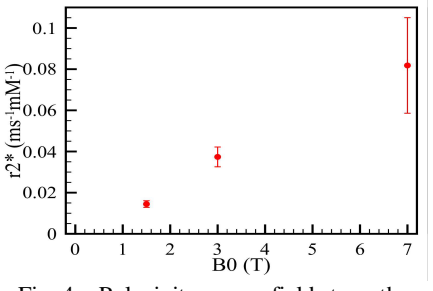

Fig. 4 – Relaxivity versus field strength

REFERENCES

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