Dependence of R_2^* on oxygenation and contrast agent concentration in human blood at 3T

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INTRODUCTION

There is currently considerable interest in modelling the BOLD response based on the changes in blood volume (CBV) and deoxyhaemoglobin ([dHb]) concentration during neural activity [1]. The BOLD signal can be simulated as a weighted sum of the intra- and extra-vascular signals which are functions of CBV and [dHb]. The extra-vascular signal is usually represented by numerical [2] or analytic [3] results. However the intravascular signal is generally characterised by empirical results [4] relating the transverse relaxation rate, R_2^* of blood to its oxygenation, Y. Previously these measurements have been performed at 1.5T [4]. This work extends this to 3T. In addition the relationship between contrast agent (CA) concentration and blood R_2^* is also investigated, with a view to modelling its effect on the BOLD signal [5].

METHOD

Informed consent was obtained from 10 volunteers who each donated 20 ml of blood. The oxygenation or CA concentration ([CA]) of the blood samples was adjusted to produce five evenly spaced concentrations. Blood oxygenation was increased by bubbling oxygen through the sample or decreased by bubbling a nitrogen/carbon dioxide mix through it. In the CA experiments small amounts (0µl, 10µl, 30µl, 50µl, 70µl) of a 50mM gadolinium-chelate (Prohance) were added to each of the five samples and the blood oxygenation levels held at approximately resting levels. Prepared samples of blood were then transferred to spherical phantoms to be scanned on a 3T whole-body scanner at 37°C [6]. A quadrature head coil was used for both transmission and reception. R_2^* maps were obtained using a single RF excitation pulse followed by an EPI switched gradient and acquisition module. The blipped gradient was replaced and an initial phase encoding gradient added. This was then stepped 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 128mm and a slice thickness of 3.3mm was used, collecting images at 63 different echo times from 1.1-70.3ms. The data were fitted simultaneously for R_2^* and first-order macroscopic inhomogeneities, assuming a linear field variation ΔB_0 in the slice select direction [7].

RESULTS

Figure 1 shows a plot of R_2^* versus fractional deoxyhaemoglobin content. A least squares fit to the data was performed, weighted by the inverse of the variance in R_2^*. A second order fit to this data produced a function of the following form: $R_2^* = 122.6\,(1\text{-}Y)^2 + 24.0\,(1\text{-}Y) + 21.2$. A linear fit was also performed yielding a function $R_2^* = 122.0\,(1\text{-}Y) + 7.0$. The correlation coefficients, r, for these relations were 0.97 and 0.93, respectively. Figure 2 shows a plot of blood R_2^* versus [CA]. A linear least squares fit was performed for each subject yielding a mean relaxivity of $(-2.74\pm1.23)\times10^{-4}$ $s^{-1}M^{-1}$. It was observed that R_2^* decreased with [CA]. Therefore a further experiment was performed, gradually adding contrast agent to achieve a wider range of [CA]. The blood oxygenation changed from 0.6 to 0.8 during this experiment. Figure 3 shows that at low CA concentrations R_2^* is reduced until a turning point is reached at approximately 1mM concentration. From then on the expected behaviour returns, with R_2^* tending to increase.

DISCUSSION AND CONCLUSION

Previous studies at 1.5T have also found a quadratic dependence of R_2^* on oxygenation, albeit with a smaller magnitude of effect. The decrease in R_2^* with [CA] was unexpected but might be explained by considering the susceptibilities (relative to plasma) of oxygenated red blood cells ($\Delta\chi = -0.26\ 10^{-7}$(cgs)) (RBC) and deoxygenated RBC ($\Delta\chi = +1.57\ 10^{-7}$) [8]. (It should be noted that there is some variation in these values in the literature). Unless the blood is more than 86% oxygenated, adding paramagnetic contrast agent to the plasma ($\chi = 2.5\ 10^{-5}\ M^{-1}$) [9] will initially reduce the susceptibility difference between the red blood cells and surrounding plasma, thus reducing the internal magnetic field gradients within the blood, and increasing R_2^*. The implications of this observation would be that for most arterial blood, the relaxivity of a paramagnetic contrast agent will be positive, but for most venous blood and normally accessible [CA] the relaxivity will be negative. Further studies using lysed blood, and blood of different oxygenations are underway, to further investigate this effect.

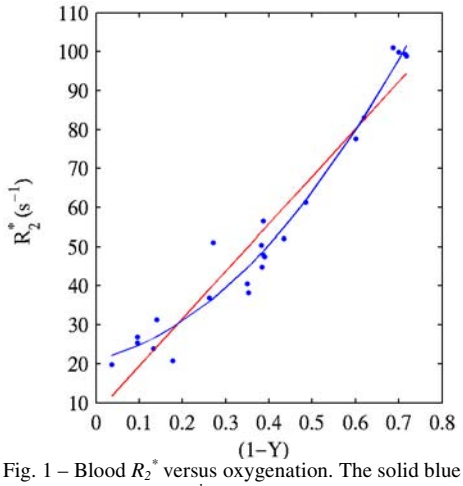

Fig. 1 – Blood R_2^* versus oxygenation. The solid blue curve represents the 2nd order fit to the data and the solid red line is the linear fit.

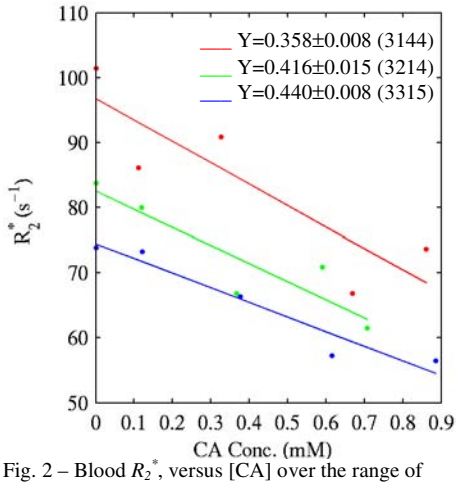

Fig. 2 – Blood R_2^*, versus [CA] over the range of expected in-vivo concentrations. The oxygenation of the samples is indicated in the legend. Subject number quoted in brackets.

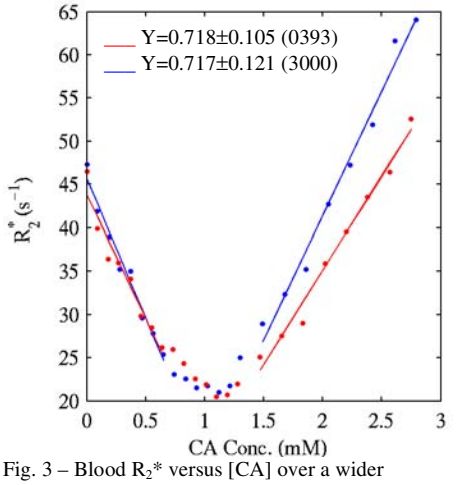

Fig. 3 – Blood R_2^* versus [CA] over a wider concentration range and at higher oxygenation. Subject number quoted in brackets.

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