Investigating the dependence of R1 and R2* of Gadofosveset concentration and magnetic field strength

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INTRODUCTION

Gadofosveset (Vasovist™, Schering) is a gadolinium based blood pool agent which acts by reversibly binding to human serum albumin in plasma. For contrast enhanced MR angiography (CE-MRA), this offers the opportunity of increased signal enhancement, and a prolonged imaging window facilitating both high quality venous imaging and longer acquisition windows to enhance spatial resolution. The advantages of these agents lie not only in their pharmacokinetics but also in their enhanced relaxivities, although this advantage becomes less pronounced with increasing field strength. We are investigating CE-MRA at ultra-high field and therefore we have undertaken a study of the R_1 and R_2* relaxivities of Gadofosveset in whole human blood at 37°C, at a range of field strengths including 7.0 T. Previous work has studied the field strength dependence of the R_1 and R_2 relaxivity of this agent in plasma from 0.47–4.7 T and in whole blood only at 1.5 T. We have measured R_1 and R_2* since R_2* is the significant parameter in the spoiled gradient echo sequences generally used in CE angiography.

METHOD

Two healthy adult volunteers gave informed consent and donated 50 ml of blood on a different day each. Blood was collected in lithium heparinised blood tubes to prevent clotting. Small amounts of Gadofosveset were added to each tube to give contrast agent concentrations ([Gadofosveset]) ranging 0 mM to 1.688 mM (day 1) and from 0 mM to 3.425 mM (day 2) (confirmed by weighing the tubes). Blood oxygenation was measured using a blood gas analyser before and after scanning. Prepared samples were transferred to spherical containers (to preserve B_o homogeneity for T_{2*} measurements) with an external diameter of 19 mm. Samples were maintained at 37°C and agitated prior to imaging. Imaging was performed on whole-body Philips Achieva systems at 1.5 T, 3.0 T and 7.0 T on the same day, samples were placed in an insulating box whilst in the magnet. First T_1 measurements were made for each sample in turn, using an inversion recovery sequence, with single shot EPI image acquisition (64x64 matrix, 1.0 x 1.0 x 3.3 mm^3 resolution, only 30% of the phase encode steps acquired due to the small sample size, TR = 10 s). A set of 10 inversion times (TI) were acquired, ranging from 50 ms to 7000 ms but tailored to the field strength and contrast agent concentration. Subsequently R_2* maps were obtained using a single RF excitation pulse followed by an EPI switched gradient acquisition module, in which the blipped gradient was removed and an initial phase encoding gradient added which was increased between repeats of the sequence, so that a series of images at different gradient echo times could be reconstructed [1] (matrix size is 128x128, 1.0 x 1.0 x 3.3 mm^3 resolution, 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, TR= 267 ms). The total acquisition time for R_1 was only 100 s and R_2* was only 35 s, so heating and stirring were not performed for samples inside the scanner and no evidence of blood separation was observed on the images. Fitting was performed on a pixel-by-pixel basis, using least squares minimisation for T_1 and a linear fit for T_2 excluding data below a noise threshold.

RESULTS

The samples' fractional oxygenations varied from 0.104 ± 0.023 to 0.133 ± 0.018 (day 1) and 0.194 ± 0.010 to 0.272 ± 0.020 (day 2). A small trend for R_2* to vary with oxygenation was detected using multivariate analysis. Figure 1 shows the dependence of R_1 on [Gadofosveset] and Figure 2 shows the dependence of R_2* on [Gadofosveset]. Table 1 shows the relaxivities measured at different field strengths, and also the relaxation times of blood measured for no contrast agent in the sample.

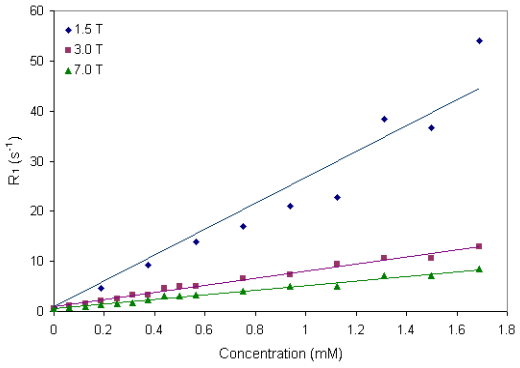

Figure 1: R_1 versus [Gadofosveset]

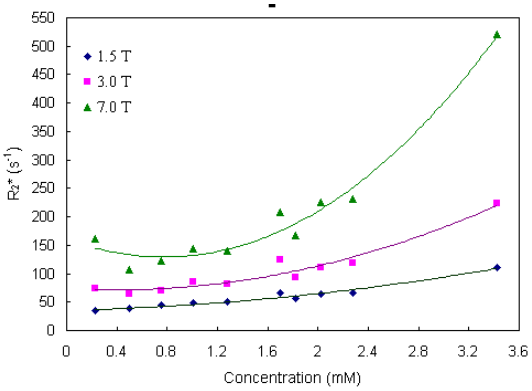

Figure 2: R_2^* versus [Gadofosveset]

B_0 (T)	R_{1blood} (s^{-1})	r_1 ($mM^{-1}s^{-1}$)	R_{2blood}^* (s^{-1})	r_2^* ($mM^{-1}s^{-1}$)
1.5	0.68	26.0 ± 1.8	36.8	6.2 ± 2.9
3.0	0.62	7.1 ± 0.2	69.2	-3.9 ± 4.7
7.0	0.58	4.6 ± 0.1	324.3	-90.5 ± 8.9

Table 1 Relaxivities of blood at different field strengths

DISCUSSION

The R_1 relaxivity of Gadofosveset at 1.5 T and 3.0 T compared well to the literature values in plasma [2]. As expected they were greater than the reported R_1 relaxivities of standard Gd-chelates measured using similar methods [3] even at 7.0 T although the relaxivities of Gadofosveset and Gd-DTPA do start to converge with increasing field strength. The trend of R_2* relaxivity is less clear at high field. At greater concentrations there is a point of inflection in Figure 2, beyond which the 7.0 T relaxivity changes from negative to positive. For all paramagnetic contrast agents, the contribution to T_2* from local field gradients depends on the relative susceptibilities of the plasma and paramagnetic deoxygenated red blood cells. Therefore the T_2* relaxivity at 7.0 T is not monotonic, but reaches a minimum when the susceptibility of the red blood cells is matched to that of the plasma, and therefore also depends on the oxygenation of the red blood cells. This effect is less pronounced at lower fields, and diamagnetic effects in the plasma dominate. The variability in the data is likely to result mainly from blood handling leading to cell damage or blood clotting, and variations in temperature and oxygenation, although some of the noise in Figure 1 also arises from the non optimal choice of inversion times for the very short relaxation times achieved at 1.5 T. This data will be useful not only in optimizing CE-MRA sequences but also in other CE MRI studies using this blood pool agent.

REFERENCES

[1] Dahnke *et al*., MRM, 53: 1202-1206 (2005) [2] Rohrer *et al*,. Invest. Radiol 40(11): 715-724 (2005)
[3] Blockley et al., Proc. ISMRM #2516 (2006)

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