Differentiating haematoma with the R_2' relaxation rate

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Introduction

Subdural haematoma (SDH) is a form of traumatic brain injury that can be classified as acute, subacute or chronic, based upon time from injury. When acute, it is a medical emergency in which surgical decompression is the only option to prevent mortality. Small subdurals and those that are no longer actively bleeding may be left to re-absorb spontaneously and clinical decision-making is aided by an accurate assessment of size and age of the haematoma. MR could potentially be used to differentiate the stages of SDH based on the accumulation and spatial position of methaemoglobin. The acute phase of SDH may be characterised by increasing concentrations of intracellular methaemoglobin, while in the subacute phase, methaemoglobin is released as red cells begin to lyse [1]. Methaemoglobin provides a magnetic susceptibility effect through dipole-dipole interaction. *In vitro* studies using canine blood show that an increase R_2 ($=1/T_2$) relaxation rate correlates with increased methaemoglobin accumulation within clot. We hypothesise that the local field inhomogeneity created by methaemoglobin (containing Fe^{3+}) compartmentalised by intact red blood cells demonstrates a greater effect in R_2*. This is based on literature demonstrating the compartmentalisation of iron-oxide contrast agents into the static dephasing regime [2]. It follows from this effect that intracellular methaemoglobin can be differentiated from extracellular methaemoglobin with R_2' imaging [3]. In the subacute phase, when red cells containing methaemoglobin begin to lyse, R_2 becomes low [4]. We examine this phenomenon in an *in vitro* system of SDH using human blood, and show potential for a more accurate method to diagnose onset of the subacute phase.

Method

Blood was obtained from 3 volunteers using standard venepuncture techniques with appropriate consent. Varying concentrations of a nitric oxide (NO) donor was added to venous blood to create methaemoglobin, determined using a blood gas analyser and validated with the method of Evelyn and Malloy. Duplicate samples of each concentration were placed in a phantom and imaged. Following this, one set of samples was lysed by repeated cycles of freeze thawing to disrupt the red blood cells by ice crystal formation before further imaging. Multi-echo spin-echo and gradient-echo images were acquired on a 3.0T MR scanner (Philips, Achieva) using a quadrature transmit/receive head coil and 1mm isotropic resolution; FOV=160x160x1mm^3. Parameters for acquisition of spin-echo were TE1/ΔTE/TR=4.85/4.85/600 and gradient-echo were TE1/ΔTE/TR=2.3/2.3/80. A pixel-by-pixel mono-exponential fit was applied to spin-echo and gradient-echo data using the images at different TEs to form a map of the R_2 and R_2^* parameters. The R_2' relaxation rate was recovered by subtraction of the two parameter maps from similar positions: $R_2'=R_2^*-R_2$.

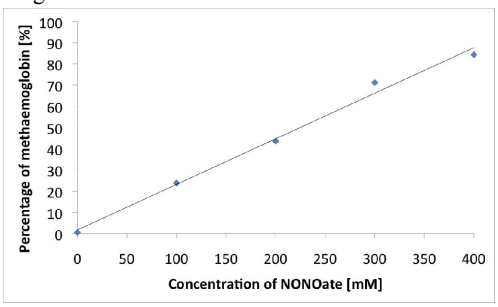

Figure 1. Plot of percentage methaemoglobin measured by blood gas analyser with addition of NO donor at different concentrations.

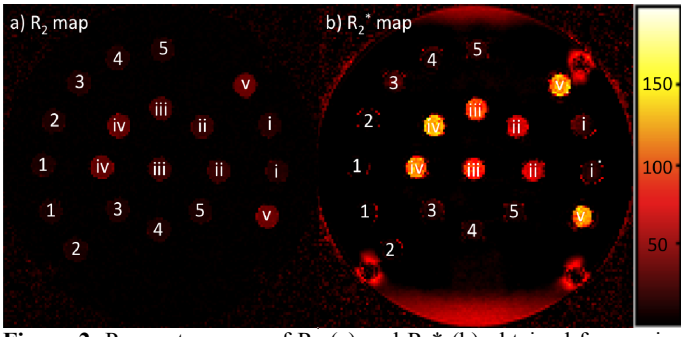

Figure 2. Parameter maps of R_2 (a) and R_2* (b) obtained from spin- and gradient-echo data respectively. The colour-bar shows relaxation rates in units [s^{-1}].

Results and Discussion

Methaemoglobin increases proportionally (R^2=0.99, Fig.1) with concentration of NO donor. This represents the progression of haematoma during the acute stage of SDH. Maps of the relaxation rates R_2 (Fig.2a) and R_2* (Fig.2b) both show a visual distinction between blood samples with NO donor before (ii-v) and after (2-5) lysis of red cells. However, quantification of R_2* is more sensitive at detecting changes in the concentration of methaemoglobin (Fig.3a). This is due to the increase in local field inhomogeneity created by an increase in compartmentalised methaemoglobin. Plots of the R_2 and R_2* relaxation rates in the pre-lysis (Fig.3a) and post-lysis (Fig.3b) samples illustrate the difference in R_2'. The transition from intracellular to extracellular methaemoglobin thus resulted in the R_2' dropping to low-level values, as methaemoglobin was no longer compartmentalised. In particular, measurement of the r_2' relaxivity, given by the gradient of R_2' against concentration of methaemoglobin, was 1.12s^{-1}%$^{-1}$ in the pre-lysis sample and dropped to r_2'=0.06s^{-1}%$^{-1}$ following lysis.

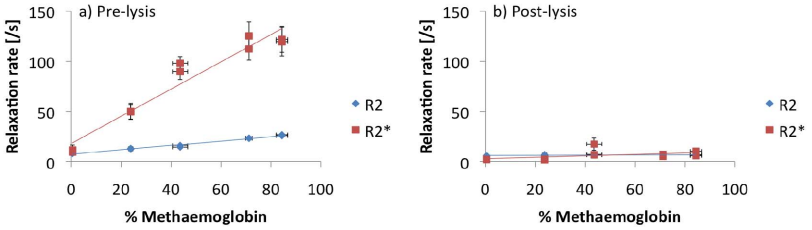

Figure 3. R_2 and R_2* relaxation rates plot for increasing methaemoglobin concentration. The plot pre-lysis (a) infers a larger R_2' values, from the difference between the R_2 and R_2, than for extracellular methaemoglobin.

Conclusions

The R_2' and R_2* parameters show greater sensitivity to increases in methaemoglobin when compared to R_2 relaxation rate. R2', however, can also distinguish between intra- and extracellular methaemoglobin within a closed system. This parameter could therefore be used to quantify changes in the acute and subacute phases of SDH and help direct therapy.

References

[1] Bradley *et al*. Radiology 1993 189:15:26; [2] Bowen *et al*. MRM 2002 48:52-61; [3] Kuhlpeter *et al*. Radiology 2007 245:449-457; [4] Bass *et al*. Investigate Radiology 1990 25:1232-1237