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=160x160x11mm. Parameters for acquisition of spin-echo were TE1/ΔTE/TR=4.85/4.85/600 and for 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}.

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.

Conclusions
The R_{2} and R_{2*} parameters show greater sensitivity to increases in methaemoglobin when compared to R_{2} relaxation rate. R_{2*}, 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