Characterising the Origin of the Arterial Spin Labelling Signal in MRI using Multi-Echo Acquisitions

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Introduction: Arterial spin labelling (ASL) MRI [1] is increasingly being used to measure cerebral blood flow (CBF) non-invasively with good spatial and temporal resolution. However, it suffers from poor SNR and struggles to produce robust, reliable CBF estimates given the complexity of cerebral anatomy and the multifaceted nature of neuropathology. Understanding the complicated mechanisms underlying blood delivery and exchange will aid the progression of an ASL CBF quantification model to more accurately characterize cerebral physiology. This will enable more reliable perfusion estimates over a broad range of flow values and will help reduce the possible confounding effects of pathology. In this study we present a novel approach to help understand the origin of the ASL perfusion-weighted signal. We aim to take advantage of the different transverse decay rates associated with spins situated in the blood and in the extra- and intracellular space within the grey matter to characterise the passage of blood water as it flows up the vascular tree, into the brain tissue, by calculating the T2 of the ASL perfusion-weighted signal (ΔM) at a variety of post labelling delays (PLD) and tagging durations, τ, with and without bipolar crusher gradients (BCGs), in the rat brain.

Methods: MRI studies were performed on 9 anaesthetised male Sprague Dawley (162-226g) rats using a 2.35T horizontal bore magnet interfaced to a SMIS console, with a volume coil transmitter and a passively decoupled surface coil for signal reception. A continuous arterial spin labelling (CASL) sequence [2] was implemented with an alternating adiabatic spin tagging pulse applied to a plane 2mm caudal to the cerebellum. In order to monitor the progression of labelled blood water within the cerebral vessels and tissue, the tagging duration was varied, with values of 500, 750, 1000, 1500 and 3000ms (see Fig. 1). Single slice coronal images, 0.3mm caudal to the bregma, were then acquired using a multi-echo half-Fourier EPI sequence, after a PLD to produce 4 images in a single shot. This was twice repeated for a total of 12 echo times (25, 37, 49, 64.2, 78.2, 90.2, 107.4, 119.4, 131.4, 148.6, 160.6, and 172.6ms). The PLD was 50 ms but was extended for additional acquisitions to 300 and 500 ms after the 3 second labelling pulse (see figure 1) to investigate the provenance of the ASL signal further downstream, an approach commonly used to negate possible confounding transit time effects [2]. The protocol was then repeated with the addition of BCGs around the first 180 refocusing pulse giving a *b* value of approximately 30s/mm^2. These are frequently used to attenuate signal from the labelled spins in the vasculature to avoid overestimating the measured perfusion [3,4]. The entire set of interleaved acquisitions were then repeated for a total of 36 averages at each echo time, τ /PLD combination, BCGs on and off, control and tag acquisition. Other acquisition parameters were: inter-experiment delay time = 6s; matrix size =36x64; FOV = 32mm x 32mm; slice thickness = 2mm. Images were first averaged in k-space and then reconstructed to 64 x 64 using the POCS algorithm [5]. The mean signal within a large ROI in the cortex was taken and fitted to a mono-exponential model to calculate the T2 of both the ASL ΔM signal and the control signal. The extraction fraction (EF –using the definition in [7] and [8]) was estimated by calculating $\Delta M_{BCGs\text{-}on}/\ \Delta M_{BCGs\text{-}off}$, assuming the BCGs act to crush all the vascular signal [4]. Assuming the T2's of the intra- and extracellular compartments to be 57ms and 174ms respectively [6] and fitting to a biexponential model, the proportion of extracellular signal contributing to ΔM relative to the proportion in the control, $F_{\Delta M}^{EC}/\ F_{Mctrl}^{EC}$ is reported for the data acquired with BCGs.

Results: Figure 1 shows typical perfusion weighted images (Nav=36) acquired at the first echo time (25ms) at the PLD/ τ combinations below the respective images. Also shown are the estimated values of EF and and $F_{\Delta M}^{EC}/\ F_{Mctrl}^{EC}$. The left-most image is an anatomical reference with a typical ROI in the left and right cortex. The images presented were acquired without BCGs so the reader may observe the progression of labelled blood in the vessels.

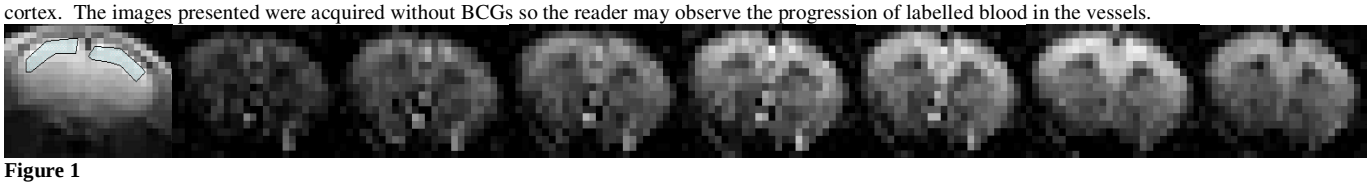


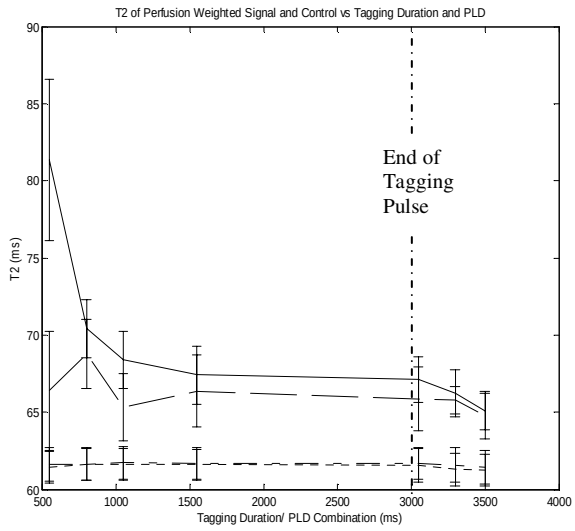
Figure 1

τ (ms)	500	750	1000	1500	3000	3000	3000
PLD(ms)	50	50	50	50	50	300	500
EF±sem	0.67±0.08	0.73±0.03	0.77±0.01	0.81±0.04	0.81±0.01	0.85±0.02	0.94±0.06
$F_{\Delta M}^{EC}/\ F_{Mctrl}^{EC}$±sem	3.2 ± 0.2	3.0 ± 0.2	2.1 ±0.4	2.2 ±0.3	2.0 ± 0.5	1.9 ± 0.2	1.6 ± 0.3

Figure 2 shows the mean T2 of the subtracted signal with BCGs (dashed line) and without BCGs (solid line) and of the control data with crushers (dash dot) and without (dotted) at different PLD and τ times. Error bars denote the standard error across the 9 experiments.

Discussion: The measured extraction fraction is in good agreement with reported values using similar imaging parameters and increases with τ and PLD [7,8]. By fitting a biexponential model to the measured T2(ΔM, BCGs-off) against τ and assuming an arterial T2 of 150ms, the arterial transit time is estimated to be 220ms, in very good agreement with previous measurements [9]. Visual inspection of figure 2 reveals a trend of decreasing T2(ΔM, BCGs-off) as the tagging duration increases from 500ms to 1000ms which is likely to reflect the shift of the source of the ASL signal from the intravascular space into the tissue. The subsequent stability of the T2(ΔM, BCGs-off) and T2(ΔM, BCGs-on) as a function of τ and PLD provides some evidence that a steady state between labelled water in the vasculature and in the intra- and extra- cellular tissue space is rapidly established relative to the τ and PLD timescale, given the expected difference in T2 between these compartments. The similarity of T2(ΔM, BCGs-off) to T2(ΔM, BCGs-on) at tagging durations greater then 500ms, despite significant vascular contribution to $\Delta M_{BCGs\text{-}off}$ (ie EF<1), suggests that the vascular signal is made up of both arterial and venous blood (supporting recent findings [10]). The raised T2(ΔM, BCGs-on) in comparison to the control T2 suggests that the ΔM signal is weighted towards the extracellular space even at 3 second τ and extended PLD, as found in [11]. However, contrary to [11], the rapid mean residence time (120ms [12]) of the extracellular spins relative to the τ and PLD timescale as well as the aforementioned evidence for rapid establishment of a steady state, suggests this is due to the greater T1 decay of the labelled spins that have exchanged into the cells rather than slow exchange between the intra- and extra-cellular water.

Figure 2



References: [1]Detre, et al. Magn Reson Med 1992; 23:37-45. [2] Alsop, Detre. JCBFM 1996; 16:1236-49. [3] Wang, et al Magn Reson Med 2003; 50(3):599-607. [4] Wang et al. JCBFM 2007 Apr;27(4):839-49 [5] Liang, Lauterbur. Principles of Magnetic Resonance Imaging 325-326; IEEE press 2000 [6] Haida, et al JCBFM 1987; 7:552-556 [7] Silva, et al. Magn Reson Med 1997; 37:58-68 [8]Zaharchuk, et al. Magn Reson Med 1998 Nov;40(5):666-78 [9] Thomas, et al. JCBFM. 2006 Feb;26(2):274-82. [10] He, Yablonskiy. Proc Intl. Soc. Mag. Reson. Med. 2007; 15; 371; [11] He, Yablonskiy ISMRM Perfusion Workshop Brazil 2007 'Transverse relaxation of the perfusion MRI signal' [12] Quirk, et al Magn Reson Med 2003; 50(3):493-9.