Combined Arterial Spin Labelling and Diffusion Weighted Imaging for Estimation of Capillary Volume Fraction and Permeability-Surface Product in the Human Brain

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Introduction Arterial spin labelling (ASL) is a non-invasive technique which can be used to measure cerebral blood flow (CBF) by magnetically labelling water molecules in the arterial blood supply, effectively eliminating the need for an exogenous tracer or contrast agent. Although the majority of ASL studies assume water is a freely diffusible tracer, nuclear [1] and MRI studies [2] have shown that there is limited exchange of water between the vascular and tissue space, particularly in the central nervous system, where the blood-brain barrier (BBB) reduces water permeability by an order of magnitude compared to systemic circulation. Two-compartment models, such as [3] and [4], account for this, allowing the time-dependent ASL difference signal to be modelled as a function of factors such as CBF and PS/ v_{bw}, where PS = permeability-surface area product of the capillary wall, and v_{bw} = fractional blood water volume per unit volume of tissue. Both PS and v_{bw} have the potential to provide clinically useful information, however, using the ASL signal alone only the PS/ v_{bw} ratio can be calculated. Here we demonstrate how, by combining ASL data with diffusion weighted imaging over a range of b-values (0 to 1000 s/mm^2), voxel-wise values of v_{bw} can be estimated independently using the intra-voxel incoherent motion (IVIM) method [5], which in turn can be used to determine PS values using the two-compartment ASL model developed by Parkes et al. [3].

Methods All experiments were performed using a Siemens 1.5 T Avanto MR system (max gradient strength 40 mT/m). Three healthy subjects (mean age 28 years) were imaged using a diffusion weighted single shot EPI sequence, with uni-polar diffusion gradients applied in three perpendicular directions, and the following imaging parameters: TR = 3.2 s, TE = 120 ms, in-plane resolution 4.7 x 4.7 mm, slice thickness = 5.0 mm, number of contiguous slices = 20, NEX = 4, b-value = 0,20,40,80,120,160,200,300,500,1000 mm^2/s, scan time = 6.4 minutes. This was followed by a FAIR pulsed-ASL sequence, with 3D single shot GRASE data acquisition (details in [6]), with the following imaging parameters: TR = 3.0 s, TE = 31.5 ms, NEX = 8. The FOV and resolution were identical to the diffusion weighted scan, and measurements were made at 12 inflow times (TI), ranging from 0.1 to 2.3 s in 0.2 s intervals, with total scan time = 9.6 minutes. ASL measurements were made with and without background suppression of static tissue. Following the method described in [7], an asymptotic fit was used to determine the fraction (f) of the diffusion signal linked to microcirculation, which appears as a fast-diffusion component at low b-values (b<200 s/mm^2). This was used to estimate local values of v_{bw}, using $v_{bw} = f * v_w^b$, where v_w^b = unit blood water content =0.7 [8]. The inversion-recovery data from the time-course of the non-background suppressed, un-labelled ASL signal was then used to fit *T1* and M_0 values in each voxel, and these, along with the v_{bw} maps, were used in Parkes' simplified two-compartment model (equation (20) in [9]) in order to calculate local PS values.

Results

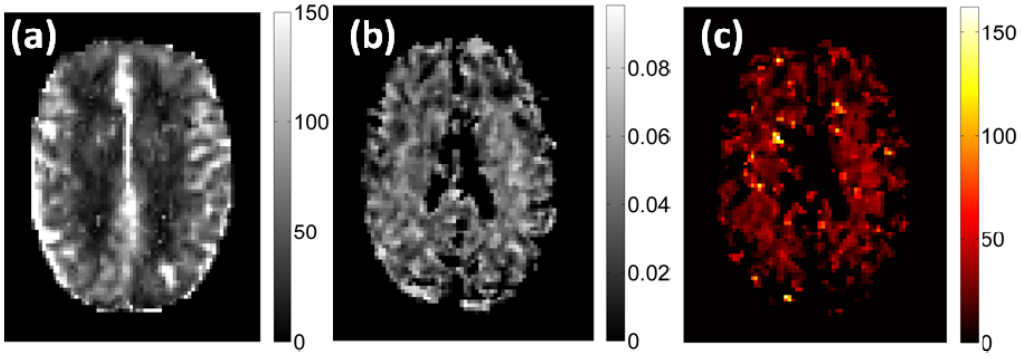

Figure 1 Axial maps of (a) CBF (ml/100g/min), (b) v_{bw} (au) and (c) PS (ml/100g/min) in one subject. The CSF has been masked in (b) and (c).

Maps of CBF, v_{bw}, and PS for an axial slice in one of the subjects are shown in Fig 1. The mean flow was 46.1 ± 4.4 and 39.1 ± 1.1 ml/100g/min in the grey and white matter respectively (all subjects mean ± SD). Voxels in or around CSF showed un-physiological, elevated values of v_{bw}, however, the modal value throughout the entire brain was 0.035 ± 0.004, indicating that both flow and capillary volume fractions agree well with literature values, in areas remote from the CSF. The mean PS in the brain was 58.6 ± 8.1 ml/100g/min, which is below the range reported in the literature (80-169 ml/100g/min, [4]), but shows a lower inter-subject variability than previous ASL measurements of PS/ v_{bw} [3].

Discussion The IVIM theory remains controversial, primarily due to the large uncertainties inherent in fitting the bi-exponential model, and unwanted bi-exponential signal decay caused by partial volume contamination from CSF. Our use of asymptotic fitting rather than a full bi-exponential fit should reduce the former error term, but due to the low spatial resolution of our data, CSF contamination remains an issue, and we suspect this is the cause of our under-estimation of PS values using the two-compartment model. Future work will focus on the effect of CSF suppression and increased spatial resolution on the calculation of PS maps in the brain. If this technique proves successful, it may provide a novel ASL-based methodology for measuring angiogenesis and BBB integrity in the progression of pathologies such as brain tumours.

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References

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