A two-stage general kinetic model for improved estimation of brain tumour perfusion using arterial spin labeling

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Target audience Clinicians and scientists interested in neuro-oncology and perfusion quantification.

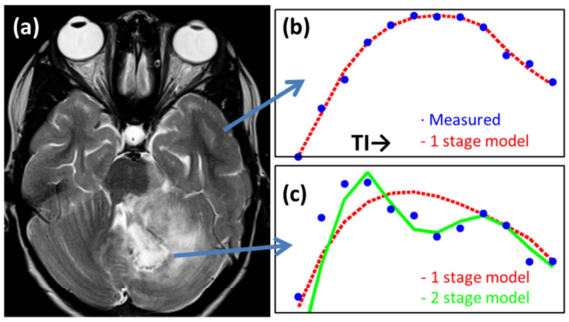

Fig 1 (a) T2w image from a ganglioglioma patient. ASL data in healthy grey matter (b) show good agreement with a 'single-stage' model, however, data taken from the tumour region (c) are better described by a 'two-stage' dynamic model

Purpose Arterial spin labeling (ASL) is an emerging technique for non-invasive quantification of cerebral blood flow (CBF). When dynamic data are acquired over a range of inflow times (TI's), a 'single-stage' general kinetic model such as [1] is often used for CBF quantification. However, these models assume labelled blood instantaneously exchanges with tissue on arrival. This results in an overestimation of CBF in voxels containing large arteries, the blood in which is destined to perfuse more distal tissue. Furthermore, this model often fails to describe the irregular perfusion kinetics in paediatric brain tumours (Fig 1). We introduce here a 'two-stage' general kinetic model, which describes the passage of blood in both non-exchanging arteries and the capillary bed, and is better suited to modelling the irregular flow dynamics found in brain tumours.

Methods *Theory:* Similar to [1], our model is derived from three basis functions: the delivery term, $c(t)= exp(-t/T_1)$ [1] (for $BAT<t<BAT+T$, BAT=bolus arrival time, T=bolus duration) the magnetization relaxation function, $m(t)=exp(-t/T_1)$ [2], and the tissue residue function, $r(t)$. In our model we relaxed the assumption of single-compartment kinetics, allowing labelled water to remain in the larger arterial vessels up to time $t=t_A$, after which it is free to exchange with surrounding tissue ($t>t_A$). The tissue residue function is therefore: $r(t) = 1*aBV$ for $t<t_A$, and $r(t) = (1-aBV)\cdot exp(-cbf\cdot t/\lambda)$ $t>t_A$ [3], where aBV=local arterial blood volume fraction, cbf=cerebral blood flow (ml/100g/min), and λ=equilibrium tissue/blood partition coefficient of water (0.9). As described in [1], the dynamic ASL difference signal is then: $dM(t) = 2M_{0b}cbf\cdot[c(t) \times (r(t)\cdot m(t))]$ [4], where '$\times$' denotes convolution, and dM=control-label signal intensity. *Data Acquisition:* Six paediatric brain tumour patients (2 gangliogliomas, 2 pilocytic astrocytomas, 1 meningioma, 1 pituitary adenoma, mean age 12.5 yrs) and 5 healthy subjects (mean age 28 yrs) were imaged at Great Ormond Street hospital using a 1.5T Siemens MR system. ASL was performed using a FAIR sequence with 3D GRASE readout and background suppression (details in [2]), with 12 TI times (0.2 to 2.4 s) and 3.6x3.6x5.0 mm resolution. Voxel-wise dM values were fit to equation [4], with BAT, cbf, t_A and aBV as fitted parameters (T was fixed at 0.7 s). Data were also fit to the standard 'single-stage' Buxton model[1], and the Bayesian Information Criterion (BIC) was used for model comparison.

Results Mean CBF in the healthy subject's grey matter was 42±4 ml/100g/min (mean±SD) using the two-stage model, compared to 75±9 ml/100g/min derived from the standard Buxton model[1]. Across the tumour cohort, mean CBF within the tumour was 16±6 ml/100g/min, and mean aBV was 0.42±0.11. The mean BIC value within tumour voxels was -2.65 using our arterial model, compared to -2.61 using the standard model.

Discussion & Conclusion Healthy grey matter CBF values derived from our two-stage model showed improved agreement with previously reported values derived from PET [3], suggesting CBF quantification may be more accurate using our model, due to reduced large vessel artefacts. Furthermore, the lower voxel-wise BIC values within tumour regions suggest dynamic ASL data is better described by our two-stage ASL model in this pathology. This is because our model is able to capture the 'dual peaks' seen in the dM time series observed in some tumour voxels (Fig 1), which may be due to tortuous vasculature in the tumour region. The novel contrast seen in aBV maps (Fig 2) suggests new information regarding the vasculature surrounding brain tumours may be obtained from our two-stage ASL model, which may be important in the classification and assessment of treatment response in brain tumours.

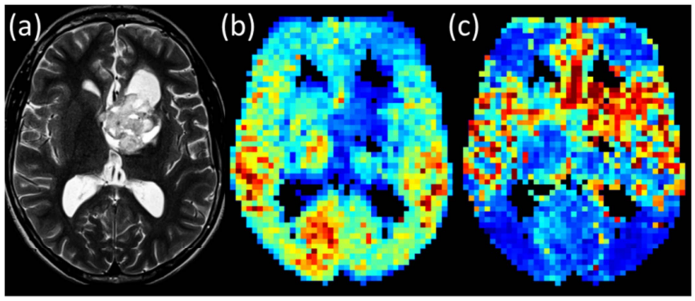

Fig 2 (a) T2w image from a ganglioglioma patient. (b) CBF and (c) aBV map from two-stage model fitting in the same patient.

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References 1. Buxton RB, Frank LR, Wong EC, Siewert B, Warach S, Edelman RR. A general kinetic model for quantitative perfusion imaging with arterial spin labeling. *Magnetic Resonance in Medicine*. 1998;40(3):383–396. 2. Günther M, Oshio K, Feinberg DA. Single-shot 3D imaging techniques improve arterial spin labeling perfusion measurements. *Magnetic Resonance in Medicine*. 2005;54(2):491–498. 3. Calamante F, Thomas DL, Pell GS, Wiersma J, Turner R. Measuring Cerebral Blood Flow Using Magnetic Resonance Imaging Techniques. *J Cereb Blood Flow Metab*. 1999;19(7):701–735.