Multi-slice cardiac arterial spin labelling using improved myocardial perfusion quantification with simultaneously measured blood pool input function

Adrienne E Campbell-Washburn[1,2], Hui Zhang[3], Bernard M Siow[1,3], Anthony N Price[4], Mark F Lythgoe[1], Roger J Ordidge[5], and David L Thomas[6]

[1]Centre for Advanced Biomedical Imaging, Division of Medicine and Institute of Child Health, University College London, London, United Kingdom, [2]Department of Medical Physics and Bioengineering, University College London, London, United Kingdom, [3]Centre for Medical Image Computing, Department of Computer Science, University College London, London, United Kingdom, [4]Division of Imaging Sciences and Biomedical Engineering, King's College London, London, United Kingdom, [5]Centre for Neuroscience, University of Melbourne, Melbourne, Victoria, Australia, [6]Brain Repair and Rehabilitation, Institute of Neurology, University College London, London, United Kingdom

TARGET AUDIENCE: This study is aimed at researchers interested in non-invasive MRI methods to measure myocardial perfusion

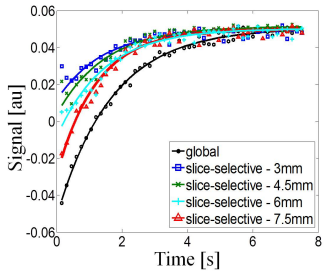
PURPOSE: Cardiac arterial spin labelling (ASL) has previously been applied to measure myocardial blood flow (MBF) in a single slice.[e.g.1,2] This work develops a new method of MBF quantification for ASL data (named "bpMBF quantification"), using blood pool magnetization sampling, to achieve the first multi-slice cardiac ASL.

THEORY: The myocardium is perfused by the coronary arteries which branch from the aorta. ASL uses the difference between T_1 recovery following global and slice-selective inversions to quantify MBF, typically with the assumption that fresh non-inverted blood perfuses the myocardium after slice-selective inversion (Eqn 1)[3]

$$MBF = \frac{\lambda}{T_{1blood}}\left(\frac{T_{1global}}{T_{1slice-selective}} - 1\right) \quad \text{Eqn 1}$$

with λ=0.95 ml/g[4]. However, the assumption that all inflowing blood is fresh following slice-selective inversion is not always valid, since a large volume of blood in the heart is simultaneously inverted and the ejection fraction is <1. Therefore, for many heartbeats following slice-selective inversion, some non-negligible fraction of the blood perfusing the myocardium will be labelled, particularly when using a multi-slice acquisition which requires widening the slice-selective inversion thickness.

Fig 1: Blood pool recovery curves from a mid ventricle slice with varying slice-selective thickness



METHODS: A multi-slice segmented ECG-gated Look-Locker T_1 mapping sequence was implemented for the mouse heart.[5,6] Scan parameters were: TE/TR(inv)/TR(RF)= 1.18ms/13.5s/3ms, 4 lines of k-space per slice per heart beat, flip angle=5°, FOV = 25.6 x 25.6 mm, matrix = 128x128, slice thickness=1.5 mm, inversion thickness = 3 – 12 mm (slice-selective) or 150 mm (global), number of slices = 1 or 3, gap = 0 mm, points in T_1 curve= 50, acquisition order = centric, T_1 acquisition time = 8 min.

bpMBF quantification uses a direct measurement of the left-ventricle blood pool magnetization to approximate the blood input function ($M_{blood}(t)$)in the Bloch equations (Eqn 2)[7]. Numerical integration of Eqn 2 generates $M_{tissue}(t)$ and the mean-squared difference between the experimental T_1 data and the synthesized $M_{tissue}(t)$ was minimized to fit for MBF, $T_{1tissue}$ and $M_{0tissue}$.

$$\frac{dM_{tissue}(t)}{dt} = \frac{M_{0tissue}}{T_{1tissue}} - \left(\frac{1}{T_{1tissue}} + \frac{MBF}{\lambda}\right)M_{tissue}(t) + MBF \cdot M_{blood}(t) \quad \text{Eqn 2}$$

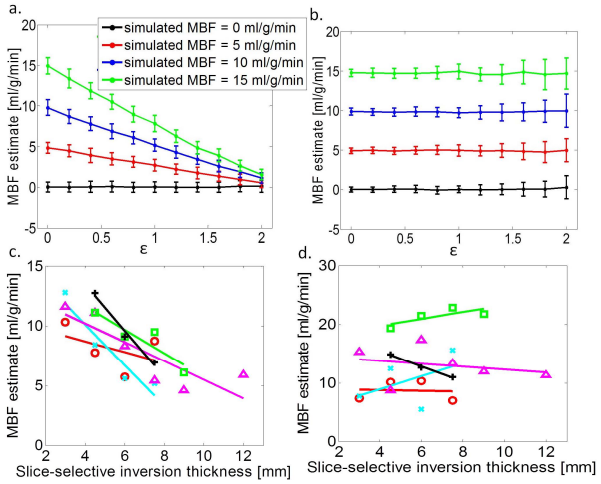
Simulations of $M_{tissue}(t)$ were performed to test quantification methods for a range of slice-selective inversion thicknesses and MBF values. For simulation, $M_{blood}(t)$ was modelled by:

Slice-selective: $M_{blood}(t) = M_{0blood}(1 - \varepsilon\exp(-t/T_{b,ss}))$ Eqn 3

Global: $M_{blood}(t) = M_{0blood}(1 - 2\exp(-t/T_{1blood}))$

where $T_{b,ss}$ describes the recovery of the left-ventricle blood after slice-selective inversion, and ε indicates the initial fraction of inverted blood in the left ventricle. *MBF* and ε were varied in simulations (varying ε represents varying slice-selective inversion thickness). Other parameters were fixed as follows: $M_{0tissue}$ = 0.07au, $T_{1tissue}$ = 1.7s, M_{0blood} = 0.08au, $T_{b,ss}$ = 1.4s, T_{1blood} = 2s. Simulations were repeated 100 times with Gaussian noise for each MBF and ε value to calculate mean MBF estimation. Quantification methods were also compared *in vivo* in the mouse heart for a range of slice-selective inversion thicknesses in a mid-ventricle slice (n = 5).

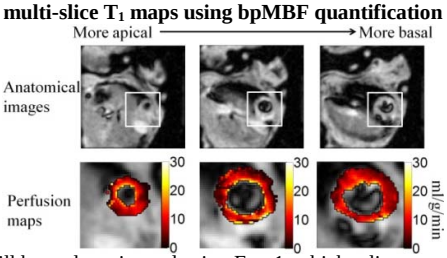
Fig 2: Mean ± standard deviation MBF estimated from simulated $M_{tissue}(t)$ curves with given MBF input (a,b), and *in vivo* MBF estimation (c,d) for range of slice-selective inversion thicknesses. Quantification using Eqn 1 (a,c) and bpMBF (b,d) are compared.



RESULTS: The blood pool magnetization throughout recovery for a single slice acquired with a range of slice-selective thicknesses (from one mouse) is demonstrated in Fig 1. Even for the smallest inversion thickness, the blood magnetization is not at equilibrium at short inflow times. Typical fitted values of ε (Eqn 3) from the blood pool of a mid-ventricle slice are 0.75-1 and 1.25-1.5 for single (3 mm) and multi-slice (7.5mm) slice-selective inversion thicknesses, respectively (the ideal ε value for 'perfect' equilibrium blood magnetization is 0).

Simulations of $M_{tissue}(t)$ show that unless the assumptions of Eqn 1 are satisfied (ε=0) or MBF = 0ml/g/min, Eqn 1 underestimates MBF. However, using bpMBF quantification, MBF is well estimated regardless of ε (Fig 2a,b). This finding was validated *in vivo* (Fig 2c,d) where Eqn 1 MBF quantification shows a negative trend with slice-selective inversion thickness for a mid-ventricle slice (R^2=0.72), and bpMBF quantification generates consistent MBF estimates for the same data sets (R^2=0.37). Fig 3 shows MBF maps of three contiguous mid-ventricle slices (1.5mm slice thickness, 7.5mm slice-selective inversion thickness) from the mouse heart generated using multi-slice T_1 mapping and bpMBF quantification.

Fig 3: MBF maps of 3 contiguous slices generated from multi-slice T_1 maps using bpMBF quantification



DISCUSSION: The novelty of the bpMBF quantification method comes from the direct measurement of the left-ventricle blood pool magnetization at each time point of the Look-Locker T_1 acquisition *in vivo*, such that MBF measurements are independent of slice-selective inversion thickness. This study demonstrated that MBF will be underestimated using Eqn 1, which relies on incorrect assumptions about the blood magnetization input function, particularly in the multi-slice case, but bpMBF quantification using Eqn 2 reliably quantifies perfusion. Multi-slice acquisition was limited to 3 slices for this study, to account for decreased fitting sensitivity with larger volumes of inverted blood. If full heart coverage is required, two separate acquisitions of three 1.5mm slices (to achieve 9mm coverage) are recommended.

CONCLUSION: This study presents a new method of perfusion quantification using direct measurements of blood pool magnetization. This method has been used to generate the first multi-slice MBF maps with cardiac ASL. This work will be useful for the future application of multi-slice ASL perfusion studies of the heart.

REFERENCES:[1] Vandsburger et al, MRM 2010; 63:648-657 [2] Kober et al, MRM 2004; 51:601-606 [3] Belle et al, MRM 1998; 8:1240-1245 [4] Kober et al, MRM 2005; 53:601-606 [5] Campbell-Washburn et al, MRM 2012; DOI:10.1002/mrm.24243 [6] Campbell et al ISMRM 19(2011): 4463 [7] Detre et al, MRM 1992; 23:37-45