Look-Locker Arterial Spin Labelling (ASL) of Liver Metastases
Rajiv Ramasawmy1,2, Simon Walker-Samuels1, Adrienne Campbell1, Sean P Johnson1, Jack Wells1, Rosamund B Pedley2, and Mark F Lythgoe3
1UCL Centre for Advanced Biomedical Imaging, Division of Medicine and Institute of Child Health, University College London, London, United Kingdom, 2Cancer Institute, University College London, London, United Kingdom

Equal contribution from RR and SW-S

Introduction
Liver metastases are a significant cause of mortality from colorectal cancer [1]. A number of therapeutic strategies are under investigation for the treatment of metastases, including drug therapies that specifically target tumour blood vessels. With the development of novel therapies, there is a clear need for accessible, non-invasive methods for evaluating the efficacy of such treatments. Arterial spin labelling (ASL) has been developed for use in the normal liver (2.4 ± 0.6 ml/g/min) [3]. As there is limited published literature on hepatic ASL, a blood-particle constant of 0.9 was interpolated from existing literature on renal [4] and cardiac [3] perfusion. The liver and tumour capillary blood T1 was assumed to be 1900ms [6], from previous measurements of the ventricular blood pool T1 in the mouse heart. Liver metastases were assumed to be arterially perfused [7].

Methods
ASL acquisition: Perfusion measurements were obtained using a respiratory-triggered segmented FAIR Look-Locker ASL sequence with a single slice spoiled gradient-echo readout [5]. Sequence parameters were: FOV, 30 x 30 mm2; matrix size, 128 x 128; TE, 1.18 ms; Ti, 110 ms; TR1, 2.3 ms; TR2, 13 s; 50 inversion recovery readouts. A localised inversion thickness of 6 mm was used followed by a global inversion slice thickness of 200 mm; the imaging readout slice thickness was 1 mm. Scans were performed on a 9.4T Agilent VNMRS 20 cm horizontal-bore system, using a 39 mm birdcage coil. Inversions were triggered at the end of the inspiration phase using respiratory gating apparatus (SA Instruments, New York, US).

In vivo measurements: Liver metastases were induced by an intrasplenic injection of 1x106 SW1222 human colorectal tumour cells into nude mice, followed by a splenectomy. Mice were anaesthetised using 1.5% isoflurane in 100% O2 and positioned in the centre of the magnet. Core body temperature was monitored and maintained using a warm air blower. Respiratory-gated fast spin echo images were used to define a suitable axial imaging slice within the liver. Post-processing: Perfusion maps were calculated using the quantitative model as described by Belle et al [3]. As there is limited published literature on hepatic ASL, a blood-particle constant of 0.9 was interpolated from existing literature on renal [4] and cardiac [3] perfusion. The liver and tumour capillary blood T1 was assumed to be 1900ms [6], from previous measurements of the ventricular blood pool T1 in the mouse heart. Liver metastases were assumed to be arterially perfused [7].

Results
Fig. 1 shows two examples of metastatic burden in a murine liver: for each there is an anatomical T2-weighted image (1A,C) of the liver alongside its concomitant perfusion map (1B,D). On the anatomical images, the metastases appear as hyper-intense (examples outlined) compared to the normal liver, and the stomach and blood vessels appear hypo-intense. The metastases in 1C are more pervasive than in 1A having grown for a week longer. The mean perfusion values within the metastases (1.1 ± 0.5 mlg·min⁻¹) were significantly lower (n=6, p<0.01) than in the normal liver (2.4 ± 0.6 mlg·min⁻¹). Blood vessels including the inferior vena cava (IVC) can be visualised in figure 1B & 1D due to a large, but non-quantitative perfusion signal. The perfusion values of the liver and the metastases are comparable with Dynamic Contrast Enhanced (DCE) MRI measurements with gadolinium chelates [8].

Discussion and Conclusion
Arterial spin labelling has been principally used for measuring brain perfusion [2], with more recent application to cardiac [3] and renal [4] imaging. We have shown that localised measurements of perfusion in mouse liver are feasible using FAIR-ASL, an application that has not been extensively reported in the literature. Furthermore, we have shown that we can measure blood flow in liver metastases and that the flow values are significantly lower than normal liver tissue. The ability to measure regional perfusion within metastases can further inform on therapy delivery and efficacy, as previous vascular targeting studies have shown that a rim of viable cells remain 24 hours post-therapy [9]. Further work is required to evaluate the respective contributions of arterial and portal contributions of blood flow into the liver. Using this technique, we aim to investigate perfusion changes in colorectal cancer metastasis induced by novel anti-cancer therapies. Furthermore, given the non-invasive nature of the technique, we anticipate that hepatic ASL could also find utility in a clinical setting.

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References: