Quantifying Blood Flow and Perfusion in Liver Tissue using Phase Contrast Angiography and Arterial Spin Labelling.

C. Hoad[1], C. Costigan[1], L. Marciani[2], P. Kaye[3], R. Spiller[2], P. Gowland[1], G. Aithal[2], and S. Francis[1]

[1]School of Physics and Astronomy, University of Nottingham, Nottingham, Nottinghamshire, United Kingdom, [2]Nottingham Digestive Diseases Centre, NIHR Biomedical Research Unit, University Hospitals NHS Trust, Nottingham, Nottinghamshire, United Kingdom, [3]Department of Cellular Pathology, University Hospitals NHS Trust, Nottingham, Nottinghamshire, United Kingdom

Introduction: Chronic liver disease can cause persistent liver injury leading to fibrosis and cirrhosis. Architectural changes associated with cirrhosis lead to hemodynamic changes with increased hepatic resistance and portal hypertension [1]. These effects can only be assessed accurately using invasive techniques such as hepatic venous portal pressure gradient measurements (HVPG). Alternative non-invasive methods to assess and monitor the degree of fibrosis and portal hemodynamic changes associated with chronic liver disease are highly desirable [2,3]. A small number of studies [4-6] have measured liver tissue perfusion with MRI using contrast enhanced (CE) dynamic MRI. However, contrast agents have their own disadvantages including adverse reactions, cost and inability to repeat the measurement. Phase contrast angiography (PCA) [7] and True-FISP arterial spin labelling (ASL) [8] provide non-invasive alternative methods for monitoring hemodynamic changes to liver tissue. The aim of this study was to determine whether PCA of the portal vein (PV) and ASL of liver could be used to monitor liver hemodynamics.

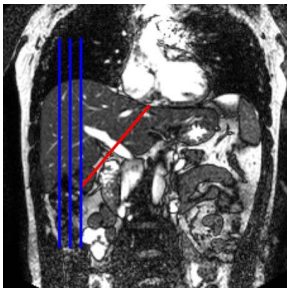

Figure 1. *Coronal True-FISP image showing positioning of PCA slice perpendicular to portal vein (red line) and sagittal ASL slices (blue lines)*

Methods: *Main Study*: The study was approved by the local NHS Ethics Committee and all patients gave written informed consent. Patients (n=36, 26 male) with chronic liver disease confirmed on liver biopsy were scanned after an overnight fast on a 1.5 T Philips Achieva whole body scanner using a 5-element SENSE cardiac coil. A series of multi-slice True-FISP (bTFE) images were acquired in 3 orthogonal planes to locate the liver and main feeding vessels (PV and hepatic artery (HA)) to aid planning the PCA data and ASL labelling (figure 1). PCA on the PV was performed using a single slice TFE technique with the imaging slice placed perpendicular to the vessel (15 phases collected across the cardiac cycle, TR/TE 6.9/3.7 ms, FA 25°, NEX 2, acquired resolution 2.7x2.7x6 mm^3 interpolated to 1.17x1.17x6 mm^3, TFE factor depended on the subjects' heart rate, VENC 50 cm/s). Data were acquired during a single 20-25 s breathhold. ASL was performed using the FAIR technique (with pre- and post- in-plane saturation pulses and FOCI labelling inversion pulse) followed at a post-label delay time (TI) by a multi-slice True-FISP readout (TR/TE 2.4/1.2 ms, FA 60º, SENSE 2, total slice acquisition time 138 ms). Three sagittal slices (positioned lateral to the end of the main portal vein) were acquired (lateral to medial) with 3 mm in-plane resolution and 8 mm slice thickness with a 5 mm slice gap. To measure the approximate transit time of the labelled blood to the tissue, an ASL experiment with 4 pairs of tag/control images acquired at TI=300, 500, 700, 900 ms was performed. To measure perfusion, 60 pairs of tag/control images were acquired at TI=1100ms. In addition, a base image (with no inversion pulse) and an inversion recovery (IR) series (13 TIs 100-1500ms) were acquired to form M_o and T_1 maps. All datasets were acquired using respiratory triggering. For the T_1 map and transit time data (which use variable TIs), an additional delay (T_v) was introduced after the respiratory trigger so that all slices were collected at a constant time in the respiratory cycle, TI + T_v =1500 ms, following the trigger for all data sets. *Reproducibility:* To assess the reproducibility of the measurements, 5 healthy volunteers (1 male) were each scanned on two separate occasions, after an overnight fast.

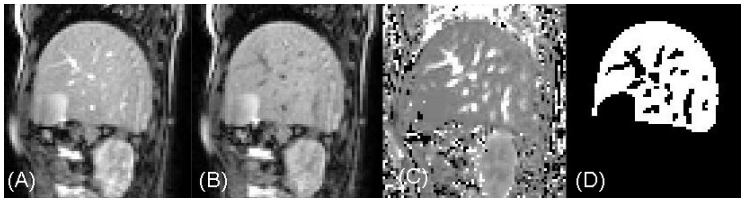

Figure 2. Typical ASL images: (A) Tag (B) Control (C) Perfusion weighted image (D) Parenchyma Mask

Data Analysis: The PCA data was analysed using the Philips Q-flow software. An ROI was drawn over the vessel of interest and mean flux and velocity (over the cardiac cycle) were calculated. ASL tag and control images were motion corrected to the base image using FSL and difference images (label-control) calculated. Any difference images which showed poor motion correction (as a result of poor respiratory triggering) were discarded from subsequent analysis. Individual difference images were then averaged to create a single perfusion weighted (ΔM) difference map for each TI. Data from the averaged difference maps was used to create an automated mask of liver parenchyma, by segmenting those voxels whose signal was 3 times larger than the median value (corresponding to the portal vein and its branches and hepatic veins). A transit time map (Δ) of the time for the label to arrive at the parenchyma was estimated from fitting the transit time data, and T_1 maps generated from the IR series. The mean vessel transit times to each slice were calculated, and an additional 100 ms added to allow blood flow into the parenchyma. A perfusion (*f*) map was then formed using a kinetic model [9] taking into account individuals' inflow time and tissue T_1.

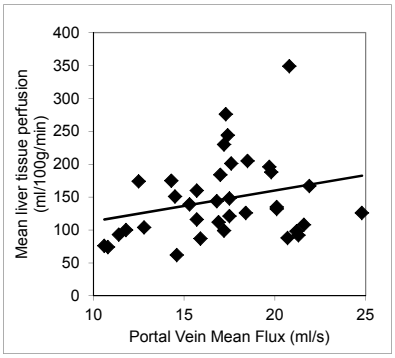

Figure 3. Chronic liver disease patient data.

Results: Figure 2 shows a typical example of the sagittal ASL images (A – C) and the parenchyma mask (D). Mean (± std. dev.) vessel transit times to each slice were found to be 327±113 ms, 528±97 ms, 678±54 ms for medial to lateral slices. Mean (± std. dev.) liver perfusion across all patients was found to be 146±62 ml/100g/min. Figure 3 shows a graph of mean portal vein flux versus mean liver tissue perfusion for the chronic liver disease patients. Table 1 shows the intra-subject reproducibility of these two measurements for the healthy volunteers.

Discussion: Mean liver tissue perfusion and portal vein flux show a wide inter-subject variation between the chronic liver disease patients. However, the reproducibility data shows that the intra-subject variability was much smaller than inter-subject variability, suggesting that these measurements reflect actual differences in the hemodynamics of the liver tissue. Indeed inter-subject variability across the chronic liver patients is expected due to their varying degree of fibrosis. The good intra-subject repeatability suggests that it would be possible to use these techniques to monitor hemodynamic changes in the liver over a period of time to assess progression of fibrosis or the effect of interventions. Mean perfusion values (excluding larger vessels) in the chronic liver disease patients were within the range reported using CE-MRI, where total liver perfusion was also shown to display large variance at 111 ± 119 ml/100g/min (mean ± stdev) [6]. In the current implementation our perfusion rates reflect total flow from both the hepatic artery and portal vein. Future studies will assess the feasibility of labelling each supply separately and further interrogating transit times.

	PV mean flux (ml/s)		Tissue Mean perfusion (ml/100g/min)	
Volunteer	Visit 1	Visit 2	Visit 1	Visit 2
1	11.0	12.3	38	41
2	15.5	12.8	178	195
3	12.2	11.4	158	130
4	16.5	12.3	45	59
5	24.6	21.9	155	141

Table 1. PV mean flux and mean liver tissue perfusion data from the reproducibility study.

References: [1] Bosch J. et al. J Hepatol 2000;32;141-156 [2] Talwalkar J. et al. Hepatology 2008;47;332-342. [3] Bonekamp S. et al. J Hepatol 2009;50;17-35 [4] Annet L. et al. Radiol. 2003;229;409-414 [5] Aguirre D. et al. Radiol. 2006;239;425-437 [6] Hagiwara M. et al. Radiol. 2008;246;926-934 [7] Yzet T. et al Eur J Radiol. 2010;73;119-124 [8] Gardener A. et al MRM 2010;63;1627-1636 [9] Buxton R. et al. MRM 1998;40;383-396

Acknowledgements: This work was funded by a Strategic Funding Initiative from the Biomedical Research Committee at the University of Nottingham.