Measuring dynamic changes in liver perfusion and blood flow following a meal challenge

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Target Audience: The ability to stratify liver disease is important for clinicians to assess disease severity and ascertain prognosis in patients. The current reference tests have limitations including sampling error (liver biopsy) or availability in specialist centres (hepatic venous pressure gradient).

PURPOSE: Liver disease is one of the five commonest causes of death in the UK and its prevalence is increasing. Liver fibrosis and cirrhosis are asymptomatic until the latter stages of disease and the current tools to stratify liver disease either lack sensitivity and specificity (e.g. liver function tests and ultrasound) or are invasive (liver biopsy). It is known that meal ingestion causes changes in splanchnic blood flow [1], and the postprandial liver response to a meal may provide a non-invasive MRI method to stratify liver disease. Prior human studies in cirrhosis report an increase in hepatic blood flow 30 minutes following meal ingestion and elevated portal pressure [1]. We hypothesise that the dynamic postprandial hyperaemia response will improve the stratification of chronic liver injury.

AIM: To assess the dynamic postprandial change in hepatic blood flow and perfusion to a meal challenge in healthy subjects.

METHODS: The study was approved by the local Ethics Committee, and volunteers gave written consent. Four healthy subjects were scanned (2M/2F, age 22-56 yrs) following an overnight fast.

Image Acquisition: Imaging was performed on a 3T Philips Achieva scanner (multi-transmit body coil, 16-channel SENSE torso receive coil). Multi-slice bTFE data were acquired in 3 orthogonal planes to locate the liver and vessels. Baseline blood flow and ASL (3 repeats) data were acquired prior to ingestion of a standard meal (440 ml Ensure plus, 660 kcal, 22 g fat, 89 g carb, 28 g protein) [1] (T = 0 min). Scans were repeated at 5-6 min intervals from T = 20 - 62 min. *Blood Flow*: Phase contrast (PC) data were collected for the portal vein (PV) and hepatic artery (HA) [2]. A single slice TFE sequence, with the imaging slice perpendicular to each vessel, was used to collect *N* phases across the cardiac cycle. (PV: $N = 20$, TR/TE = 8.4/3.7 ms, V_{ENC} = 50 cm/s. HA: $N = 30$, TR/TE = 5.6/3.2 ms, baseline/post-meal V_{ENC} = 100/150 cm/s. Both: FA 25°, NEX 2, recon. voxel 1.17x1.17x6 mm^3, TFE factor 4-6 (dependent on subjects' heart rate)). Each PC measurement was acquired during a single 15-20 s breath hold. *ASL*: Multiphase FAIR ASL (3x3x5 mm voxel, 18 pairs) was collected with a bTFE readout (TE/TR 1.45/2.9 ms, SENSE 2, flip angle 45º, half-Fourier acquisition, shot duration 130 ms). Data were collected whilst free breathing by introducing a respiratory trigger delay of 500 ms prior to ASL labeling. Labeling was followed by multiphase Look-Locker sampling with an initial delay of 100 ms, and subsequent readout spacing of 350 ms with 6 readout phases (spanning post-label delay times (TI) of 100 - 1850 ms) [3]. A base magnetization (M_0) image was also collected.

Data Analysis: *Blood Flow:* Q-flow software (Philips Medical Systems) was used to estimate PV and HA blood flow (ml/min) over the cardiac cycle, and total hepatic blood flow (THBF) calculated from (PV+HA) flow. *ASL*: Individual difference images (control-label) were calculated and averaged to form perfusion weighted (PW) difference maps (ΔM) for each phase. A liver mask was formed from the base M_0 image, excluding major vessels. Mean values of ΔM and M_0 were used in an iterative model [4] to calculate tissue perfusion (f), assuming $T_{1tissue}$ = 0.8 s and T_{1blood} = 1.6 s.

RESULTS: In all subjects PV flow increased following meal ingestion (T = 0 min: 730 ± 80 ml/min, T = 25 min: 1593 ± 312 ml/min (mean ± SD)), in 3 subjects HA flow decreased by at least 30 % reflecting the HA buffer response (HABR) (T = 0 min: 295 ± 59 ml/min, T = 50 min: 171 ± 49 ml/min), see *FIG 1*. *FIG 2A* shows example PW images ($\Delta M/M_0$) for each ASL phase at 20 min and 50 min after meal ingestion, when perfusion weighting is increased. *FIG 2B* shows the corresponding ASL ($\Delta M/M_0$) signal change curves. *FIG 3* shows the absolute change in perfusion (Δf) from baseline of 163 ± 53 ml/100g/min following meal ingestion. Baseline perfusion and THBF were closely correlated.

DISCUSSION: In response to meal ingestion we show an increase in PV flow and a later reduction in HA flow, reflecting the HABR. Perfusion, as measured by multiphase ASL, was found to increase significantly with the time course of this response following the meal being inversely related to the HA time course. Since for the multiphase ASL data no vascular crushing was used, it is likely that the measure includes contributions from increased blood volume (BV) in response to the meal, due to the mechanism of vasodilation, to reduce resistance that occurs in healthy subjects.

CONCLUSION: Future studies will separate *f* and BV components, and assess dynamic alterations in blood flow and perfusion in liver disease.

References: [1] Albillos A *et al*. Gut. 2007; 56(2): 259-64 [2] Debatin, JF. Abdom. Im. 1998; 23: 485-95, [3] Liss P *et al*. Clin. Exp. Pharm. Physiol. 2013; 40 (2): 158-67, [4] Francis ST *et al*. MRM 2008; 59: 316-25. **Acknowledgement**: Funded by the MRC Confidence in Concept Award.

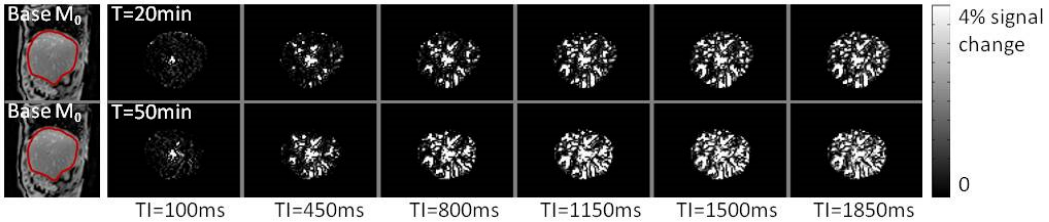

FIG 2A: Base M_0 image showing the ROI of liver (red outline) and multiphase PW images across the 6 LL readouts (post-label delay times (TI) shown below) at 20 and 50 mins following meal ingestion

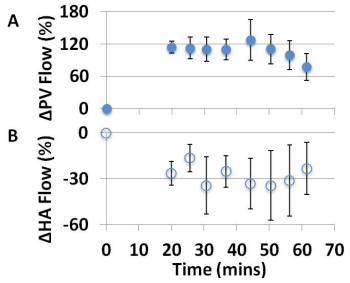

FIG 1: Percentage change in flow in the (A) portal vein (PV) and (B) hepatic artery (HA) (Mean ± SD across subjects)

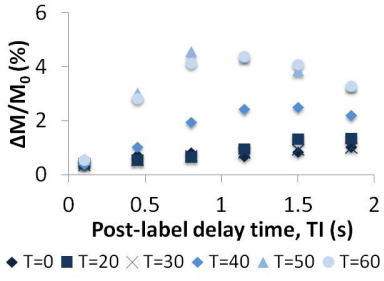

FIG 2B: Tissue $\Delta M/M_0$ at each ASL phase (TI) at selected time points (T, mins) following the meal

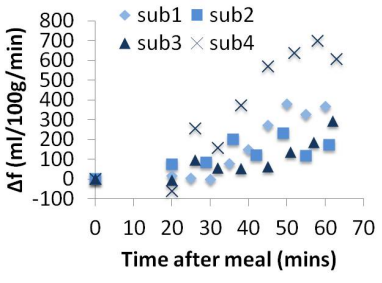

FIG 3: Absolute change in perfusion (Δf) for each subject following the meal