

# A novel MRI protocol to examine haemodynamic compartments in compensated liver cirrhosis

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**Target Audience:** Monitoring early haemodynamic changes in compensated cirrhosis patients provides clinicians with important information about the prognosis of developing future complications. The ability to detect these changes using non-invasive imaging techniques in a contemporaneous fashion will allow a greater understanding of pathophysiology and provide an important tool to assess novel drug therapies.

**BACKGROUND** The hyperdynamic circulation in cirrhosis is thought to result from changes in the liver, splanchnic, cardiac and renal compartments; and underpin the clinical consequences of portal hypertension. We present a novel MRI protocol that provides non-invasive haemodynamic measurements in each of these compartments in a single MR assessment of under 1 hour. Arterial spin labeling (ASL) with respiratory triggering is used to measure perfusion in abdominal organs (kidney, liver and spleen) without the need for contrast agent<sup>1,2</sup>, whilst phase contrast (PC) MRI is used to assess the velocity (in cm/s), area, and hence flux (=velocity\*area (in ml/s)) in a given feeding vessel to each organ<sup>3</sup>.

**AIM** To use PC and ASL MRI measures, in addition to MR measures of cardiac function, to assess haemodynamic changes in early, compensated cirrhosis and compare to an age matched healthy volunteer group.

## METHODS

**Subjects** The study was approved by the NHS ethics committee, and all volunteers gave informed, written consent. Patients were recruited to this study which forms part of a prospective, longitudinal study of compensated cirrhosis (CC) (Child Pugh A). 30 CC patients (18M/12F, age 59 ± 1 yrs (mean±SEM), aetiology 9 ALD/ 8 HCV/ 7 NAFLD/ 2 Haemochromatosis/ 1 PBC/ 1 PSC/ 1 HBV, 1 Autoimmune, MELD 6–10.79) were studied. In addition, 30 age and sex matched healthy volunteers (HV) were also assessed: 18M/12F, age 61 ± 1 yrs.

**Image Acquisition** All imaging was performed using a 1.5T Philips Achieva scanner (body transmit coil, 16-channel SENSE torso receive coil) in a single 60 minute scan session. Multi-slice True-FISP data was acquired in 3 orthogonal planes to locate organs and vessels, and for volume analysis.

**Perfusion:** Two ASL data sets were acquired to evaluate (a) liver (Fig 1a, 3 sagittal slices, 60 pairs, TE/TR = 1.2/2.4 ms) and (b) spleen/ renal cortex perfusion (Fig 1b, 5 coronal oblique slices, 30 pairs, TE/TR = 2.1/4.2 ms) using respiratory-triggered FAIR ASL data (3x3x8 mm voxel, post-label delay (TI) = 1100 ms, in-plane pre-saturation) with a True-FISP readout (SENSE 2, FA 60°, centric acquisition, half-Fourier acquisition). Base magnetization (M<sub>0</sub>) images and an inversion recovery series (Liver: 13 TIs 100-1500 ms, Spleen/Renal Cortex: 9 TIs 100-1476 ms) were acquired to form M<sub>0</sub> and T<sub>1</sub> maps. Transit time was also estimated from 4 pairs of label/control images acquired at TI = 300, 500, 700, 900 ms.

**Vessel Flow:** PC data were collected for the superior mesenteric artery (SMA), splenic artery (SA), hepatic artery (HA), renal artery (RA), portal vein (PV) and aorta (AO). A single slice TFE sequence, with the imaging slice placed perpendicular to each vessel, was used to collect 15 phases (30 for AO) across the cardiac cycle (TR/TE 6.9/3.7 ms, FA 25°, NEX 2, reconstructed resolution 1.17 x 1.17 x 6 mm<sup>3</sup>, TFE factor 4-6 (dependent on the subjects' heart rate), V<sub>ENC</sub> (cm/s) = 140/100/100/100/50/200 for SMA/SA/HA/RA/PV/AO). Each PC measurement was acquired during a single 15-20 s breath hold (free breathing for AO).

**Cardiac:** Cardiac MR consisted of short axis cine images to measure left ventricular ejection fraction (EF) and cardiac output (CO) using a multi-slice TFE sequence with 30 phases (12 slices, 1.6x1.6x10 mm<sup>3</sup> voxel, TR/TE = 2.9/1.45 ms, FA 60°).

## Data Analysis

**Vessel flow:** Q-flow software (Philips Medical Systems) was used to draw a region of interest (ROI) over the vessel of interest, from which to estimate vessel area, and the mean velocity and flux of blood flow (ml/s) over the cardiac cycle, across the vessel.

**Perfusion:** The time series of ASL label and control image was motion corrected to the base M<sub>0</sub> image (using in house IDL software for liver and FSL (FMRIB Software Library) for spleen/cortex) and individual difference images (label-control) calculated [7] and averaged to create a single perfusion weighted difference map (ΔM). A mask was formed from the base M<sub>0</sub> image for each organ, taking care to avoid major vessels. Mean values of ΔM, M<sub>0</sub> and T<sub>1</sub> were then used in the kinetic model [8] to calculate tissue perfusion (f).

**Cardiac:** Philips LV analysis software (Philips Medical Systems) was used to draw epi- and endo-cardial wall contours over the left ventricle, and the left ventricular ejection fraction (EF) (%) and cardiac output (l/min) calculated. Both values were corrected for body surface area (BSA) to allow for subject size variations.

## RESULTS AND DISCUSSION

**Liver** (Fig 2): The PV was dilated (p=0.0001) with a trend for a reduced PV velocity in CC compared to the HV group; there was no significant differences in HA velocity, flux or area between groups. In CC, liver perfusion was found to be significantly reduced (p=0.002) (Figure 1a shows example liver perfusion maps).

**Splanchnic** (Fig 3): The SMA and SA, were dilated in the CC group compared to the HV group (p=0.047 and p=0.022 respectively) with no change in flow velocity, resulting in increased flux (p=0.034 and p=0.023 respectively) in CC compared to HV. However the CC group had significantly enlarged spleens (spleen volume in CC: 493 ± 44 ml, HV: 203 ± 18 ml, p<0.0001). Reduced spleen perfusion was found in CC compared with the HV group (p=0.002) (Figure 1b).

**Cardiac** (Fig 4): The BSA corrected ejection fraction and cardiac output were significantly higher in CC compared to the HV (p=0.046 and p=0.014 respectively). Aortic flux and velocity were higher in CC (p=0.016 and p=0.029 respectively) compared with HV, with no change in area.

**Renal:** No changes in renal cortical perfusion, renal artery flux, velocity or area were found between the CC and HV groups (Figure 1b shows renal perfusion maps).

**CONCLUSIONS** Using a non-invasive MRI protocol, we have measured haemodynamics in four compartments contemporaneously in cirrhosis. The detection of significant changes in early cirrhosis, suggests this technique has potential to a) study the evolution of portal hypertension with accompanying changes in splanchnic, renal and cardiac circulation and b) potential to assess the haemodynamic response to novel therapeutic agents in cirrhosis.

**References:** [1] P Martirosian et al. MRM 2004; 51(2): 353-361, [2] Gardener et al. MRM 2010; 63:1627-36, [3] Debatin, JF. Abdom. Im. 23:485-95 (1998)

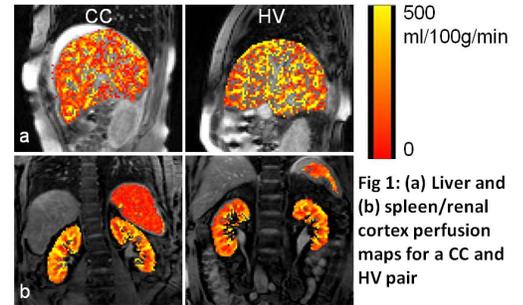


Fig 2: Liver

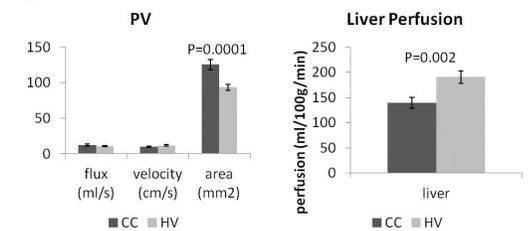


Fig 3: Splanchnic

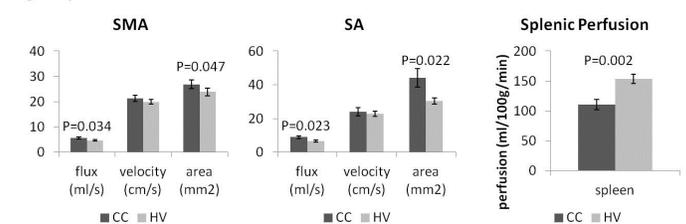


Fig 4: Cardiac

