# Initial experiences evaluating the hepatic arterial buffer response with DCE-MRI in healthy rats at 9.4T

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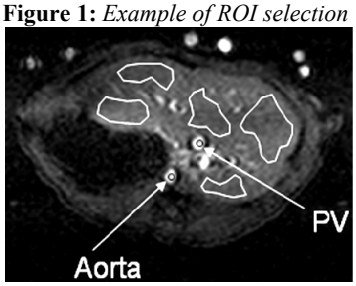
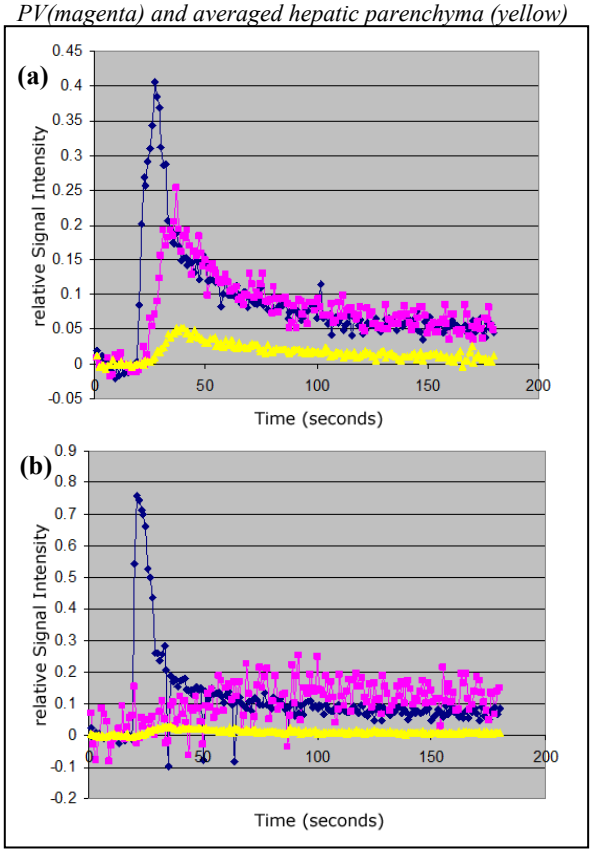
**Introduction:** In health, maintenance of total hepatic blood flow is achieved via close regulation of the relative contributions from the hepatic artery (HA) and portal vein (PV). Reductions in portal flow are matched with compensatory increases in hepatic arterial flow – the hepatic arterial buffer response (HABR)[1]. In cirrhotic patients this homeostatic mechanism is compromised, resulting in failure to maintain adequate hepatic blood supply[1-3]. Recent work has shown that dynamic contrast enhanced MRI maybe used to assess liver haemodynamics[4,5]. An animal model of cirrhosis in which liver haemodynamic changes could be non-invasively assessed following therapeutic interventions is of significant clinical value and would also allow validation of DCE MR parameters using invasive Doppler ultrasound. This study reports the feasibility of DCE imaging for liver haemodynamic assessment within a rat model at 9.4T, before and after modulation of the portal venous flow.

**Figure 1:** *Example of ROI selection*




**Methods:** Experiments were performed on healthy male Sprague-Dawley rats ($n$=5, mean weight 280.3g). Animals were anaesthetised with halothane. Intravascular access was sited in a carotid vessel. Laparotomy was performed and a silk ligature was placed loosely around the PV. DCE MR imaging was conducted on a 9.4T Varian scanner. Data were acquired using a respiratory-gated T1-weighted saturation-recovery spoiled gradient-echo sequence with centric-ordered k-space coverage. A slice was selected from scout images that enabled good visualisation of the portal vein, aorta and a large volume of hepatic parenchyma. The slice was acquired at each trigger point. The saturation-recovery time (TS) was set to enable the acquisition to be completed within a single respiratory cycle. Inflow effects into the slice were minimised by using a global saturation pulse. Flow artefacts in vessels perpendicular to the acquisition slice were minimised by using velocity-compensated slice-select gradients. For the dynamic acquisition, the following parameters were used: TR = 6.2 ms, TE = 3.4 ms, α = 15°, 128 x 96 (frequency encoding x phase encoding) acquisition matrix and TS = 250 ms. An initial T1 measurement was obtained at baseline. As soon as dynamic imaging began, a 500μL bolus of 0.025 mmol/L Gd-DTPA was administered over 5-10 seconds by hand injection. Following DCE MR imaging with the portal vein patent, the animal was removed from the scanner, the previously placed ligature was tightened around the portal vein and the animal was replaced for a second dynamic acquisition. A 45 minute delay was adhered to between the first and second DCE studies to allow adequate washout and recovery of T1. Images were analysed using in house developed MatLab modules. Regions of interest (ROI) were selected within the aorta, PV and hepatic parenchyma (avoiding intrahepatic vessels) (Figure 1). Signal intensity – time curves were generated for pre and post PV ligation DCE studies. A dual input single compartment model of liver blood flow was applied to derive physiological parameters [6] using MatLab.

**Figure 2:** *Temporal MRI signal intensity changes (a) pre-ligation and (b) with ligated PV. Signal intensity changes derived from ROIs over the aorta(dark blue), PV(magenta) and averaged hepatic parenchyma (yellow)*




**Results:** Gd-DTPA signal intensity changes were derived for ROIs over the aorta, PV and hepatic parenchyma both pre (Figure 2a) and post (Figure 2b) portal vein ligation. There was a significant reduction but not complete loss of portal venous flow, portal fraction and hepatic venous outflow following PV ligation ($p<0.05$). There was no significant change in hepatic arterial flow ($p=0.75$) or distribution volume ($p=0.30$). There was an approximately 4-fold significant increase in mean transit time ($p<0.05$) (Table 1).

**Table 1:** *Estimated parameters from the dual input single compartment model.* †(P<0.05)

| | Pre-PV ligation | Post-PV ligation |
|---|---|---|
| HA flow (ml/100g/min) | 82.7 | 68.9 |
| PV flow (ml/100g/min)† | 175.7 | 27.5 |
| HV outflow (ml/100g/min)† | 1371.7 | 425.2 |
| Portal fraction (%)† | 58.6 | 15.8 |
| Distribution volume (%) | 20.4 | 15.7 |
| Mean transit time (seconds)† | 6.5 | 24.1 |

**Discussion:** Our results suggest that DCE MR may be utilized in a rat model for assessment of liver blood flow. We recorded changes in liver haemodynamics which were generally in keeping with those expected following portal vein ligation. However, we did not observe any significant increase in hepatic arterial flow following portal venous ligation. Whilst this maybe due to the rat model itself, errors in estimation of physiological parameters using the dual input single compartment model should also be considered. In particular whilst we used a dilute slow injection protocol, at 9.4T estimation of arterial input function may still have been influenced by T2* clipping effects. Further work is underway to refine the acquisition protocol and validate the MR derived flow changes with ultrasound Doppler measurements. In conclusion, our preliminary study confirms that liver haemodynamic changes can be estimated using DCE MR imaging within a rat model at 9.4T.

**References: 1.** Lautt WW. Hepatol Res 2007;37(11)891-903. **2.** Jalan R, Williams R. Blood Purif 2002;20:252-261. **3.** Aoki T et al. Liver Transpl 2005;11(6):684-691. **4.** Hagiwara M et al. Radiology 2008;264(3):926-934. **5.** Kim H et al. Radiology 2008;247(3):696-705. **6.** Materne R et al. Clin Sci 2000; 99:517–525.