Measurement of portal venous flow using phase-contrast MRI at 9.4T: preliminary repeatability, reproducibility and invasive validation studies

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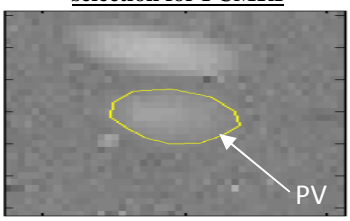
Target audience: Researchers studying phase-contrast MRI, liver perfusion and liver disease.

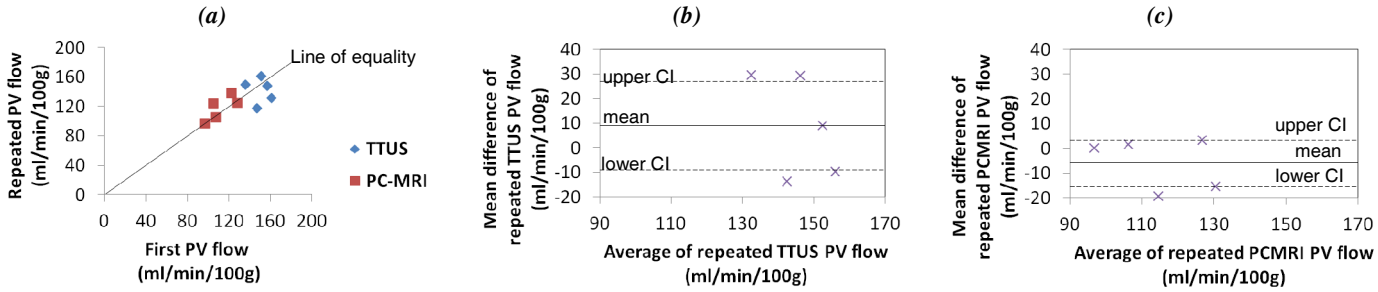
Purpose: Total liver blood flow is determined by contributions predominantly from the portal vein (PV). Profound haemodynamic changes underpin liver disease, but the lack of robust non-invasive techniques for repeated measurement of liver blood flow has restricted understanding of the vascular pathophysiology and the development of therapies to address these changes.[1] Phase-Contrast (PC) MRI has potential for portal venous flow quantification. In this study, we aim to, (i) assess the repeatability of PCMRI measurements relative to the repeatability of invasive transit-time ultrasound (TTUS) measurements in matched controls, (ii) assess the reproducibility of PCMRI measurements and (iii) compare PCMRI measurements with invasive TTUS data obtained from the same subjects.

Figure 1: Example of ROI selection for PCMRI



Methods: Healthy male Sprague-Dawley rats (n=13), were anaesthetised with isoflurane. PCMRI was performed using a 9.4T Agilent scanner. After anatomical imaging, PCMRI vessel orthogonality was determined using Varian's 3 point planning module. A respiratory-gated 2D PC sequence was used with the following acquisition parameters: 2 mm slice thickness, $\alpha = 10°$ and a 128 x 128 (FExPE) acquisition matrix. Velocity encoding settings of 16 and 22 cm/s were used, from plug flow simulations of reported values of PV bulk flow and vessel diameter.[2] Regions of interest (ROIs) were selected over the portal vein (Figure 1) and analysed using in house developed MatLab modules. Each recorded flow was the average of 3 measurements. For invasive flow measurements, a laparotomy was performed and a 2 mm TTUS probe (Transonic Systems, USA) was placed around the PV. Readings were taken after 10-15 minutes, once the subject was stable. For repeatability, naive rats (n=10, mean weight 383.3g) were randomised to PCMRI or TTUS. For PCMRI repeatability, each animal remained in the scanner for 30-45 minutes before a second PCMRI PV flow was recorded. For TTUS repeatability, the probe was removed after initial measurement and re-sited after 30-45 minutes for a second measurement. Repeatability flow measurements were normalised to estimated liver weight.[3] For reproducibility and invasive validation studies, rats 4 weeks post-sham operation (n=3, mean weight 546g) underwent initial PCMRI PV flow measurement. After removal from the scanner, TTUS PV flow was recorded for validation. The animal was then re-sited and a second PCMRI PV flow measurement was recorded for reproducibility. Reproducibility and validation PV flow measurements were normalised to explanted liver weight.

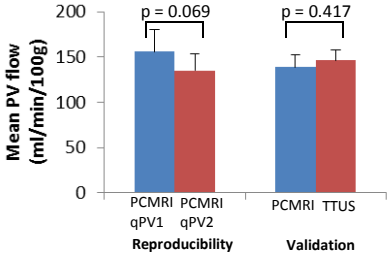
Figure 2: Repeatability of PV flow measurements with TTUS and PCMRI



Results: An example of a PCMRI acquisition is shown in Figure 1. Repeat PV flow measurements made using TTUS (n=5) were not significantly different, demonstrating a mean difference of 8.87±20.55 ml/min/100g (p=0.389). Similarly, repeat measurements with PCMRI (n=5) were also found to be not significantly different, demonstrating a mean difference of -5.91±10.58 ml/min/100g (p=0.280). The coefficient of variation of the difference between repeat measurements was higher using TTUS than for PCMRI (1.04 vs 0.80). Scatter plots of repeat flow measurements (Figure 2(a)) and Bland-Altman plots (Figures 2(b) and (c)) for repeatability are shown. PCMRI Reproducibility studies (Figure 2) demonstrated a mean difference of 21.29±10.21 ml/min/100g (p=0.069). PCMRI validation with TTUS PV flow measurement in the same subject (Figure 2) demonstrated a mean difference of -7.58±12.92 ml/min/100g (p=0.417).

Discussion: Invasive TTUS measurements of PV flow are well validated and considered a "gold-standard" measure of bulk vessel flow. Preliminary studies on repeatability are favourable for PCMRI, with a smaller coefficient of variation and narrower confidence interval of mean difference between repeat measurements tentatively suggesting that PCMRI may be more repeatable than TTUS. Reproducibility studies with PCMRI are just non-significant, and it is uncertain if this difference is attributable to physiological variation rather than measurement error. Initial validation with TTUS in the same subject is encouraging. Further studies with larger numbers are planned.

Figure 2: Reproducibility and validation of PV flow (n=3)



Conclusion: This is the first work to our knowledge of PCMRI for rat portal venous flow quantification at 9.4T. Preliminary PCMRI repeatability is comparable or better than invasive TTUS quantification, with encouraging early reproducibility and invasive validation data.

References: **1.** Iwakiri Y et al. Hepatology 2008;47(5):1754-63. **2.** D'Almeida et al. Am J Physiol 1996;271(40):H2701-09. **3.** Rikkers LF. and Moody FG. Gastroenterology 1974;67(4):691-9.