Differential portal venous flow response to terlipressin in normal and cirrhotic rats – non-invasive assessment using phase-contrast MRI

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

Purpose: Total liver blood flow is closely regulated by relative contributions from the hepatic artery and portal vein (PV). While it is recognised that profound haemodynamic changes underpin liver disease,[1] limited techniques for repeated measurement of liver blood flow have restricted our understanding of the vascular pathophysiology of liver disease and the development of therapeutic strategies to address these changes. The measurement of PV flow using phase-contrast (PC) MRI is feasible at 9.4T, but has never been applied to study changes in PV flow in rodent models of liver disease. Terlipressin is a clinically used agent known to reduce PV blood flow [2]. Reductions in PV flow are typically met with rises in hepatic arterial flow, thereby maintaining perfusion in healthy subjects. This response is known to be impaired in chronic liver disease [3]. In this study we test the ability of PCMRI to detect expected changes in portal flow after terlipressin administration and study any differences in response between normal and cirrhotic rats.

Methods: Eight healthy male Sprague-Dawley rats were randomised to bile duct ligation (BDL) procedure (n=4) or sham laparotomy (n=4). Studies were conducted after 4 weeks, based on experience of established liver cirrhosis in BDL models at this time. Animals were anaesthetised with isoflurane. PCMRI was performed using a 9.4T Agilent scanner. After anatomical imaging, PCMRI

Results: An example of a PCMRI acquisition is shown in Figure 1. After 4 weeks, sham vs BDL body weight (530.5±37.5g vs 427.0±41.5g) and liver weight (19.4±1.38g vs 32.4±2.18g) was expectedly significantly different (p<0.05). Pre-terlipressin baseline mean PV flow in sham (143.53±14.42 ml/min/100g) vs BDL (79.51±44.74 ml/min/100g) rats approaches significance (p=0.059). Trends in changes in PV flow are shown in Figure 2, with terlipressin administered at a relative time of zero minutes. The reduction in PV flow post-terlipressin was significant in sham (mean reduction of 63.48±14.28 ml/min/100g; p<0.05), and close to statistical significance in BDL rats (mean reduction of 55.44±35.71 ml/min/100g; p=0.053). Significant differences in post-terlipressin nadir PV flow in sham (80.05±20.18 ml/min/100g) vs BDL (24.07±14.66 ml/min/100g) rats were demonstrated (p<0.05).

Discussion: Expected reductions in PV flow were detected non-invasively using PCMRI in both normal and cirrhotic rats. Data is suggestive of a lower baseline PV flow in BDL rats, which go on to demonstrate an altered more labile haemodynamic response to terlipressin compared to sham-operated animals. Profound haemodynamic differences are identifiable even with the small number of subjects included in this study. Additionally, our preliminary experience of repeatability, reproducibility and validation of PCMRI is encouraging. Further studies with larger numbers of subjects are planned.

Conclusion: This is the first work to our knowledge of PCMRI comparative quantification of PV flow in cirrhotic and control rats at 9.4T. Differences in baseline PV flow and haemodynamic response to terlipressin using PCMRI are encouraging and beg more comprehensive haemodynamic studies in these cohorts.


Figure 1: Example of a PCMRI acquisition

Figure 2: Scatter plot of PV flow measurement in shams and cirrhotics

Trendlines (solid lines) with standard error limits (dashed lines) for sham versus BDL animals demonstrate marked differences in response both in terms of baseline and nadir PV flow.