Phase Velocity Imaging of Portal Pressure Gradients for Evaluating Liver Cirrhosis

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INTRODUCTION

Liver cirrhosis, a major cause of death worldwide, often leads to abnormal hemodynamic function in the portal vein. The current gold-standard to diagnose liver cirrhosis is an invasive biopsy. This work is aimed at providing a reproducible non-invasive MR measurement to assess liver cirrhosis by using a portal pressure gradient (PPG) model. We hypothesize that under cirrhotic conditions, either lower portal flow velocity or vessel dilation will lead to a decrease in PPG. This hypothesis is tested by comparing the PPG values in cirrhotic versus normal rats, and demonstrate its potential usefulness in diagnosis of liver cirrhosis.

METHODS

Theory: For fully-developed laminar flow in a circular tube (upper part of portal vein) under steady state, the velocity profile can be approximated as parabolic, and the pressure gradient can be written as: $dP/dx = 8\mu(V/A) = Const\cdot(V/A)$, ($\mu$ blood viscosity; V: the average flow velocity; A: vessel area) [1], such that PPG is proportional to the ratio of blood flow velocity to vessel area.

In order to maintain the physiological homeostasis, the blood supply ($Q=V\cdot A$) is conserved, therefore, the change of portal flow velocity (V) and the vessel area (A) is expected to be in opposite directions, which will enhance the sensitivity of the PPG (proportional to V/A) measurement.

Induction of liver cirrhosis in rats by CCl_4: Cirrhosis was induced by IP injection of a mixture of CCl_4 with vegetable oil (1.5 µl/g rat, 17% CCl_4 + 83% oil, both chemical purchased from Fisher Scientific) three times per week for 12 weeks [2]. Four of these five treated rats developed ascites. The sex- and age- matched rats in the control group were injected with 1.5 µl/g rat 100% vegetable oil. The difference in weight of two groups was not statically significant ($p>0.05$).

PC-MRI: The food and water were removed from the rats' cage three hours before each scan to minimize the prandial effect of portal flow [3]. The anesthetized (ketamine+xylazine) 5 cirrhotic rats and 5 normal rats were scanned on 1.5 T Siemens Sonata imaging system with a phase-array wrist coil (4 channels, USA Instruments, Inc, Aurora, OH). Velocity measurements were obtained using a FLASH sequence (fl_pc, Siemens) with (TR=45ms, TE=9.7ms, flip angle=15°, FOV=120mm, 512*512 matrix, 16 averages, one slice at upper portal vein with a thickness of 2.6 mm, total scan time ~ 5 min). Three interleaved velocity encoding gradients rather than the usual two were applied (zero, low and high gradient moments) with $Venc_1$ =10cm/s; $Venc_2$=50cm/s. During each scan, the slice was selected to be perpendicular to portal vein by referring to the coronal, sagittal and transverse images acquired using trueFISP (some examples shown in fig 1 (a)).

Data Analysis: Raw data were acquired and phase images were reconstructed. The velocity was calculated using three-point phase unwrapping algorithm [4] to increase the velocity-to-noise ratio in MATLAB. The vessel area was measured from the reconstructed magnitude image rather than the phase image to minimize the error of vessel definition, as shown in Fig1 (b) and (c).

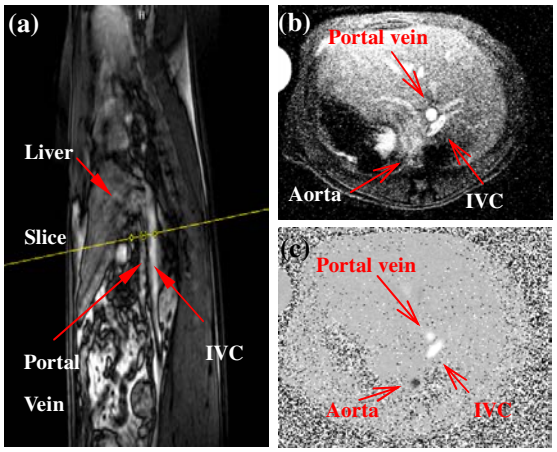

Fig 1. (a) Sagittal image acquired using trueFISP for slice selection; (b) The reconstructed magnitude image acquired using FLASH pc; (c) The reconstructed 3-point phase image acquired using FLASH pc.

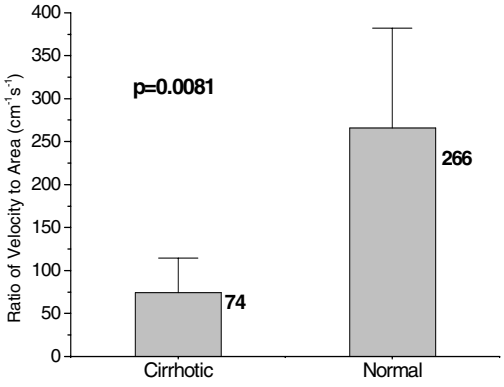

Fig 2. Ratio of Velocity to Area for cirrhotic and normal rats (p=0.0081).

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RESULTS

The ratio of velocity to area (V/A value), which represents the PPG (dP/dx) and hemodynamics of portal flow, is significantly different between cirrhotic and normal rats ($p<0.01$), as shown in fig 2. Average portal vein area in the cirrhotic rats was more than twice that of the control rats. Average portal blood velocity in cirrhotic rats was about two thirds that in the control rats.

DISCUSSION

This approach revealed statistically significant differences ($p<0.01$) in PPG along the portal vein between CCl4 induced cirrhotic rats and normal control rats. The difference in portal blood flow ($Q=V\cdot A$) was not significant ($p=0.22$) between cirrhotic and normal rats. Therefore, it is less sensitive to diagnose liver cirrhosis than PPG, because the multiplication of the decreased blood velocity and the increased vessel area in cirrhotic rats minimizes the total change in blood flow. In addition, unlike the portal blood flow measurement, the PPG model (V/A value) is not sensitive to the individual weight. In conclusion, PPG model is a useful indicator for non-invasive diagnosis of liver cirrhosis.

The fully-developed flow condition was verified in the rat portal vein (within 20 mm away from the entrance of the rat liver) by measuring velocities at different positions across the vessel. The flow is laminar with a Reynolds number less than 2000. No EKG gating was used as the pulsatility of portal vein is negligible. The slice must be chosen to be perpendicular to the vessel to satisfy the parabolic velocity profile assumption. The primary challenge to overcome with this approach is to increase the spatial resolution and SNR, perhaps by moving to a balanced SSFP sequence.