Quantification of 3D Arterial and Portal Venous Blood Flow Distribution in Liver Cirrhosis Patients using 4D Flow MRI

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Introduction: Patients with progressive liver cirrhosis typically develop a hyperdynamic syndrome characterized by increased splanchnic inflow and hepatic resistance, leading to portal hypertension and decreased portal flow velocity. As a noninvasive and user-independent method 3D phase contrast MRI with three-directional velocity encoding (4D flow MRI) have shown to be superior compared to traditional diagnostic method with Doppler Ultrasound which suffers from high inter-observer variability and limited anatomic coverage. Recent studies present promising application of 4D flow MRI for the quantitative analysis of flow velocity in liver vasculature [1-3].The aim of this study was to quantify and compare velocity distributions in arterial and portal venous blood supply of liver based on 4D flow MRI in healthy controls and liver cirrhosis patients.

Methods: MRI data were acquired in 5 healthy subjects (age=54±9years) and 7 liver cirrhosis patients (age=60±6years). Each subject underwent 4D flow MRI on 1.5T or 3.0T MR systems (Area and Skyra, Siemens, Germany). Pulse sequence parameters were as follows: venc=100m/s, spatial res.=2.1x3.0x2.5mm^3, flip angle=15°, temporal res.=40.8ms, TE=2.7ms, scan time=8.6min and 8.7min for volunteers and patients respectively, blood contrast agent: Ablavar© (Lantheus, N. Billerica, MA). After preprocessing with noise filtering, anti-aliasing and eddy current correction, a 3D PC-MR angiography was calculated from the 4D flow MRI data. The 3D PC-MRA data were imported to Mimics (Materialise NV, MI, USA) for manual 3D segmentation of portal venous, arterial and venous systems (fig.1) to isolate the velocity data in each vascular region. The resulting velocities for all voxels were arranged in a histogram and normalized by the total number of voxels in the segmented vessel to allow comparison across subjects. In addition, mean, median and the normalized number of voxels with velocities ranging from 0.05m/s to 0.3m/s (incidence) were calculated for each subject. A sensitivity analysis was conducted to identify which proportions of the velocity distribution (top 5%, 10%, 20%,…100%) were most sensitive to differences in flow distribution. At each value, the median, mean flow velocities and incidence of portal venous and arterial systems of each subject were calculated and t-test was conducted to evaluate the significance of difference between groups for each vascular system. Velocity thresholds were chosen respectively for portal venous and arterial systems on the basis of smallest P-value. Normalized histograms were averaged for all subjects with each group for comparison of cohort average flow distributions.

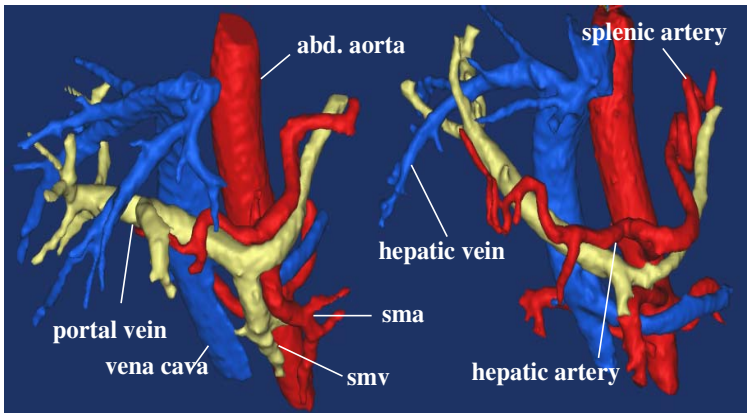

Figure 1: Segmentation of portal venous (yellow), arterial (red) and venous systems (blue) with Mimics (Left: healthy volunteer; Right: patient with liver cirrhosis).

	Control (n=5)		Patients (n=7)	
age	54±9y		60±6y	
	Portal Vein	**Artery**	**Portal Vein**	**Artery**
median velocity (m/s)	0.044± 0.015	0.048± 0.010	0.045± 0.012	0.055± 0.009
mean velocity (m/s)	0.080± 0.039	0.064± 0.014	0.048± 0.009	0.059± 0.009
standard dev. (m/s)	0.124	0.050	0.031	0.032
incidence (%)	>0.1m/s* 16.30±11.93	>0.15m/* 5.75±4.43	>0.1m/s* 3.09±2.00	>0.15m/s* 1.08±1.04

Table 1. Summary of the result of sensitivity test. The velocity threshold was chosen as 0.1m/s for the portal venous system and as 0.15m/s for the arterial system. (*=p<0.05)

Results: Sensitivity analysis showed that the top 20% of velocities was appropriate for quantitative analysis while providing most significant differences in flow parameters for both portal venous and arterial systems. Additionally, most pronounced differences for incidence were observed when the velocity threshold was chosen as 0.1m/s for the portal venous system (p=0.01) and as 0.15m/s for the arterial system (p=0.03) (table 1). The overall distributions of arterial and portal venous velocities were illustrated by the group-averaged velocity histogram analysis (fig.2). Compared to normal controls, patients with liver cirrhosis had a reduced mean blood flow in portal vein (0.048±0.009m/s, vs. 0.080±0.039m/s, p=0.07) and in arterial system (0.059±0.009m/s vs. 0.064±0.014m/s, p=0.55) which was not significant. Differences between normal and pathological conditions were most pronounced for incidence which showed a significantly increased fraction of high velocities >0.1m/s in normal controls compared to cirrhosis patients for both the portal venous (16.3% vs. 3.1%, p=0.014) and arterial systems (5.8% vs. 1.1%, p=0.034). Moreover, the blood flow velocities in pathologic groups were more widely and unevenly distributed while controls presented with a more homogeneous pattern with longer high velocity tails. Noticeably, there was even a trend towards a bimodal velocity distribution in portal vein in liver cirrhosis patients.

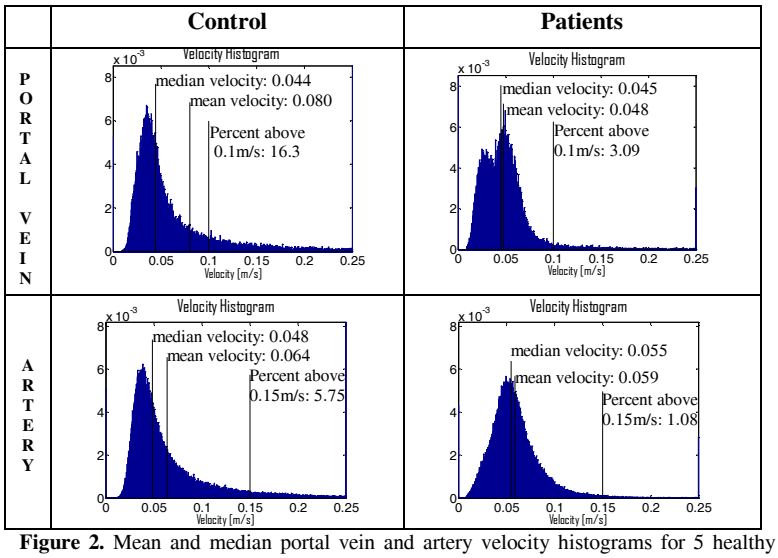

Figure 2. Mean and median portal vein and artery velocity histograms for 5 healthy volunteers and 7 patients with liver cirrhosis when including the top 20% of velocities. The median and mean velocities, and the percent of velocity values greater than 0.1 m/s in portal vein and greater than 0.15 m/s in artery are marked each panel. The area of each histogram is normalized to unity.

Discussion: Using 4D flow MRI, this study showed that mean velocities in portal venous and arterial systems of liver tended to be lower for liver cirrhosis patients. The result also revealed that the number of voxels with velocities exceeding a predefined threshold (incidence) was most sensitive to detect differences between normal and altered hemodynamics in the portal venous and arterial systems. An advantage of the presented methods is related to the potential to fully automate velocity histogram analysis once the 3D segmentation is performed and the inclusion of the full volumetric velocity data from 4D flow MRI instead of relying on manually positioned 2D analysis planes. Flow-sensitive 4D MRI may thus be a standardized method for quantitative analysis of liver blood flow hemodynamics. Future work will focus on analyzing velocity distribution at different branches of liver vascular systems in larger study cohorts.

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References: 1. Stankovic. Radiology. 2012;262:862-873. **2.** Roldán-Alzate. JMRI 2013;37:1100-1108. **3.** Stankovic. MRM 2013 *epub.*