

Diurnal Variation of Portal Hemodynamics with 4D flow MRI

Alejandro Roldán-Alzate¹, Camilo A Campo¹, Kevin M Johnson², Oliver Wieben¹, and Scott B Reeder¹

¹Radiology, University of Wisconsin, Madison, Wisconsin, United States, ²Medical Physics, University of Wisconsin, Madison, Wisconsin, United States

Target audience: Researchers and clinicians interested in 4D flow for non-invasive assessment of mesenteric circulation and portal hypertension.

Introduction: Portal hypertension is an end-stage complication of cirrhosis that leads to dramatic and complex alterations in the hemodynamics of the hepatic and the mesenteric circulation. Currently, there are few valid quantitative biomarkers to assess blood flow to and from the liver. Phase contrast 4D-flow MRI methods hold great promise to overcome the challenges associated with comprehensive non-invasive flow measurements in the abdomen [1,2,3]. However, portal flow is well known to have a strong diurnal dependence with slow variation in flow [4]. **The purpose of this study** was to evaluate diurnal changes in mesenteric blood flow in normal subjects and patients with portal hypertension using 4D-flow MRI [5].

Methods: In this IRB-approved and HIPAA-compliant study, 7 subjects with no history of liver disease (36±9 years, 88±8 kg) and 3 patients with known portal hypertension (53±8 years, 94±14 kg) were imaged after written informed consent was obtained.

Diurnal protocol: The first MR scan (pre breakfast – 8 am) was performed after at least 5 hours of fasting. Subsequently, subjects ingested 574mL EnSure Plus® (Abbot Laboratories, Columbus, OH; 700cal, 28% from fat, 57% from carbohydrates) orally. A second acquisition (post breakfast – 9 am) was started 20min after the meal challenge. A third scan was performed before lunch (pre lunch - noon). Subjects were asked to have a normal lunch at the cafeteria, 20 minutes after which a fourth acquisition took place (post – lunch - 1:30 pm). Finally, a fifth scan was performed (afternoon - 4 pm).

MR-Imaging. Studies were conducted on a clinical 3T scanner (Discovery MR 750, GE Healthcare, Waukesha, WI) with a 32-channel body coil (NeoCoil, Pewaukee, WI). 4D velocity mapping was achieved using a radially undersampled phase contrast acquisition (5-point PC-VIPR) with increased velocity sensitivity performance [6,7] and comprehensive coverage of the upper abdomen. Radial 4D flow MRI image parameters included: imaging volume: 32x32x24cm spherical, 1.25mm acquired isotropic spatial resolution, TR/TE=6.4/2.2ms, retrospective ECG gating. All subjects received 0.03mmol/kg of gadofosveset trisodium (Lantheus, N. Billerica, MA), an intravascular gadolinium based contrast agent used to maximize SNR performance and injected prior to the first scan. The venous was adjusted for pre- and post-meal acquisitions to provide optimal velocity encoding with expected increases in flow velocities.

4D flow MRI Data Analysis: Vessel segmentation was performed in MIMICs (Materialize, Leuven, Belgium) from PC angiograms while flow visualization and quantification was performed in EnSight (CEI, Apex, NC). Flow data were measured at the supraceliac Aorta (SCAo), Portal Vein (PV), Superior Mesenteric Vein (SMV) and Splenic Vein (SV)

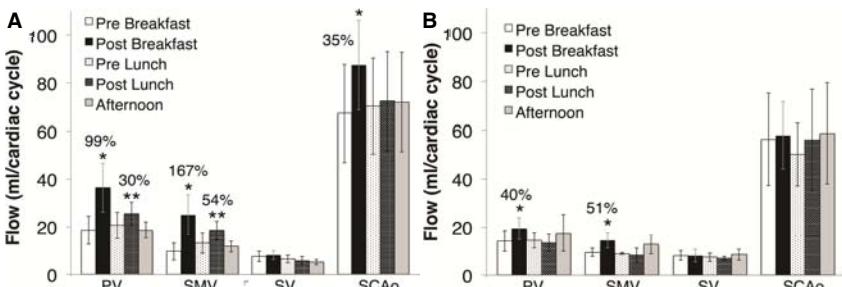


Figure 2 – Diurnal blood flow changes in the portal circulation. A. Healthy controls. B. Portal hypertension patients. (*) Represents significant increase induced by breakfast. (**) Represents significant increase induced by lunch. Reduced meal effect and diurnal changes are seen in patients compared to healthy controls.

significant increase in SMV and PV in response only to breakfast, however these increases in flow were much smaller than those in healthy controls. In general patients showed reduced response to meals compared to that in healthy controls. Interestingly aortic flow in patients had the highest value in the afternoon scan with PV, SMV and SV being also elevated compared to the fasting scan in the morning. However this increase in blood flow was not statistically significant. Reduced flow response in patients may be due to structural and functional vascular changes resulting from cirrhosis.

Summary: Radial 4D-flow MRI was used to characterize the diurnal portal hemodynamic changes in patients with portal hypertension and healthy controls. In previous studies healthy controls had shown larger changes in response to meal challenge [8]. Results here suggest that meal challenge for evaluating mesenteric circulation should be done in the morning to maximize hemodynamic response. Finally, comprehensive characterization of portal hypertension hemodynamics using 4D-flow MRI would provide valuable information for stratification of variceal bleeding risk in patients.

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References: [1] Stankovic JMRI 2010; [2] Frydrychowicz JMRI 2011; [3] Roldán-Alzate JMRI 2012; [4] Alvarez D Hepatology 1997 [5] McCormick J Hepatol 1990 [6] Gu AJNR 2005; [7] Johnson MRM 2010; [8] Bosch J Hepatol 1985; [8] Roldán-Alzate ISMRM 2013.

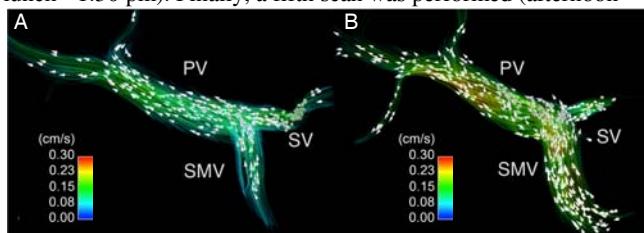


Figure 1 – Portal blood flow increase in response to breakfast in a healthy volunteer. A. Pre breakfast B. Post breakfast. Velocity color-coded streamlines show increased velocities in the post case. Enlarged PV and SMV can also be seen in the post case. With arrows show the direction of the flow revealing homogeneous flow in the pre case and unsteady vortical flow in the post case induced by the SMV flow increase.

Statistics: For each vessel, flow values were compared before and after breakfast using a paired Student t-test. Similarly, a paired t-test was used to compare values before and after lunch. Finally, the same analysis was performed between the three fasting conditions. A p-value of 0.05 was chosen to indicate statistical significance. This analysis was performed for patients and healthy controls.

Results and Discussion: In healthy controls statistically significant increase in blood flow were seen in the PV, SMV and SCAo in response to breakfast but only the SMV and PV had a significant response to lunch. No significant changes in SV flow were seen in response to any of the meals. Additionally, no differences between measurements at the three fasting conditions were found for any of the vessels. Patients with portal hypertension showed