

Body

Flow Quantification in Portal Hypertension

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Chronic liver disease and liver cirrhosis are the 9th leading causes of death in the United States resulting in nearly 35,000 deaths per year (1,2). Complications from advanced liver cirrhosis include life-threatening variceal bleeding, ascites, hepatic encephalopathy and liver failure (1,2). In the clinical routine assessment of liver hemodynamics is performed by Doppler Ultrasound (US), contrast-enhanced low-dose multi-detector computed tomography (MDCT), 2D phase contrast (PC) MRI, contrast enhanced MR angiography (CE-MRA), or interventional wedged hepatic venous portography. All of these established diagnostic approaches, however, have specific limitations including poor observer variability (3), ionizing radiation and possible side effects of contrast application (4), limited anatomical coverage (5) or invasiveness (6).

MR imaging is an established clinical tool for morphologic and functional evaluation of the liver. In a single examination several clinically relevant questions can be answered:

- fat and iron quantification
- fibrosis assessment by elastography and diffusion weighted imaging
- liver function evaluation: contrast enhanced functional MR imaging

Flow quantification in portal hypertension and liver cirrhosis representing a further application is routinely performed using 2D PC-MRI. In the following presentation comprehensive 4D velocity mapping (time-resolved (CINE) 3D phase-contrast (PC) MRI with three-directional velocity encoding) is discussed as an emerging tool for flow quantification in portal hypertension.

4D velocity mapping provides a non-invasive method for the qualitative and quantitative characterization of blood flow in heart as well as thoracic and abdominal aorta. ECG synchronized 4D velocity mapping (also termed '4D flow MRI', 'flow sensitive 4D MRI', 'time-resolved 3D velocity mapping', or '4D PC-MRI') can be employed to detect and visualize global and local blood flow characteristics in entire targeted vascular regions of interest (Figure 1). For thoracic or abdominal applications the data acquisition needs to be synchronized with the subject's respiration using navigator or self-gating techniques.

Due to the acquisition of at least four data sets for three-directional velocity encoding, phase contrast MRI inherits a trade-off between spatial resolution, temporal resolution, and total scan time. Ongoing improvements using adaptive navigator gating with increased efficiency (7), time-optimized velocity encoding gradients (8), new spatio-temporal imaging acceleration techniques (9,10) or radial imaging with 3D PC VIPR (11,12) enable scan times of 4D velocity mapping data of the order of 10-15 minutes. An important benefit compared to traditional 2D PC-MR imaging is related to the possibility to flexibly quantify and visualize cardiovascular blood flow.

4D flow MRI with complete volumetric coverage of the liver arterial and portal venous vasculature has gained increasing interest in the last few years. This technique enables a comprehensive characterization of 3D blood flow patterns and quantification of liver hemo-

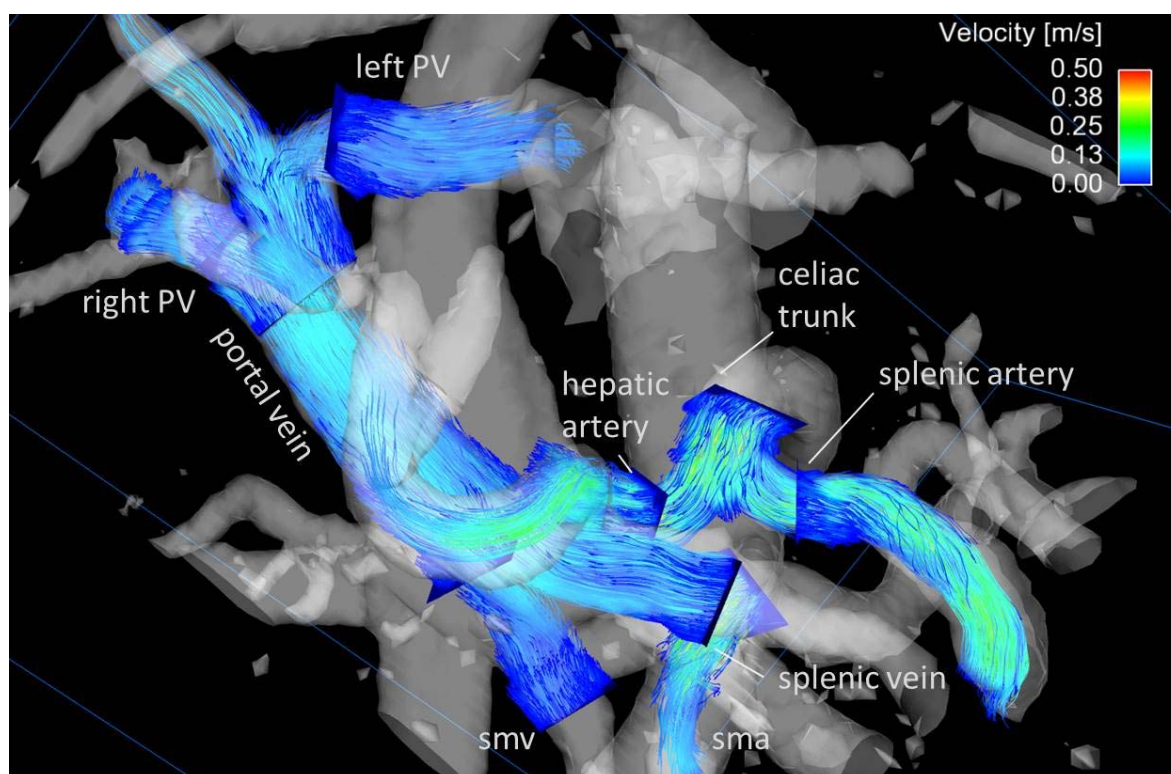


Figure 1: 4D flow MRI visualization with particle traces from emitter planes in the superior mesenteric and splenic vein, proximal and distal splenic-mesenteric confluence, right and left intrahepatic portal vein branch, celiac trunk, splenic, mesenteric and hepatic arteries. A regular physiological hepatic blood flow is shown in the arterial and portal venous systems.

dynamics in patients with liver cirrhosis. Initial studies in cirrhosis patients demonstrated the feasibility of the technique to visualize the complex blood flow patterns in portosystemic shunts. Quantification of the blood supply (peak and mean velocities, flow volume and vessel diameter) from the hepatic artery and the portal venous system revealed a moderate, but significant correlation compared to the clinical reference standard of Doppler US (13,14). Other investigators confirmed the feasibility of accelerated 4D flow MRI of the hepatic and splanchnic vasculature using an undersampled radial sequence (PC-VIPR) with a short time acquisition (15). Follow up studies validated the accuracy of the method demonstrating good internal consistency and inter- and intraobserver variability for quantifying hepatic and splanchnic hemodynamics in cirrhotic patients with portal hypertension (16,17).

Visualization of cardiovascular blood flow using 4D velocity mapping has improved and will likely continue to improve the understanding of normal and pathologically altered liver hemodynamics in patients with cirrhosis and portal hypertension. In addition to the retrospective quantification of blood flow parameters (vessel diameter, flow velocity and flow volume) further studies have also evaluated the value of 4D MRI in assessment of transstenotic pressure gradients (TSPG) in animal models for carotid, iliac and renal lesions. High correlation with good agreement to invasive pressure measurements was achieved (18,19). Promising future clinical applications include also the assessment of shunt function in patients with transjugular intrahepatic portosystemic shunt (TIPS) grafts, which are often difficult to assess with other non-invasive modalities (20). These initial results of 4D flow MRI in the liver indicate a potentially important role for the comprehensive analysis of hemodynamic changes based on 4D velocity mapping. However, the predictive and diagnostic value of the analyzed flow patterns and quantitative parameters are still limited. Clinical trials with prospective serial MR examinations in assessing the severity of liver disease and as a diagnostic test to determine response to therapy are needed to evaluate the clinical value of 4D velocity mapping of liver hemodynamics.

In addition to improved, but lengthy acquisition times, another limitation of 4D velocity mapping is related to the complex and often time-consuming data analysis. More automated methods for flow visualization and retrospective quantification are needed for applications within the clinical routine (21). New software tools with volumetric evaluation of 4D flow data might be a possible solution to streamline the clinical workflow and improve the accuracy of the obtained quantitative hemodynamic data.

In summary, 4D velocity mapping has demonstrated feasibility for the detailed visualization of complex liver blood flow patterns associated with pathologically altered hemodynamics. Within a single study, MR imaging with 4D velocity mapping offers a comprehensive diagnostic tool for the liver assessment potentially improving diagnosis and management of patients with cirrhosis.

References

1. Groszmann RJ. Hyperdynamic circulation of liver disease 40 years later: pathophysiology and clinical consequences. *Hepatology* 1994;20(5):1359-1363.
2. Pagliaro L, D'Amico G, Luca A, et al. Portal hypertension: diagnosis and treatment. *Journal of hepatology* 1995;23 Suppl 1:36-44.
3. de Vries PJ, van Hattum J, Hoekstra JB, de Hooge P. Duplex Doppler measurements of portal venous flow in normal subjects. Inter- and intra-observer variability. *Journal of hepatology* 1991;13(3):358-363.
4. Van Beers BE, Leconte I, Materne R, Smith AM, Jamart J, Horsmans Y. Hepatic perfusion parameters in chronic liver disease: dynamic CT measurements correlated with disease severity. *AJR Am J Roentgenol* 2001;176(3):667-673.
5. Yzet T, Bouzerar R, Allart JD, Demuynck F, Legallais C, Robert B, Deramond H, Meyer ME, Baledent O. Hepatic vascular flow measurements by phase contrast MRI and doppler echography: a comparative and reproducibility study. *J Magn Reson Imaging* 2010;31(3):579-588.
6. Ripoll C, Groszmann R, Garcia-Tsao G, Grace N, Burroughs A, Planas R, Escorsell A, Garcia-Pagan JC, Makuch R, Patch D, Matloff DS, Bosch J. Hepatic venous pressure gradient predicts clinical decompensation in patients with compensated cirrhosis. *Gastroenterology* 2007;133(2):481-488.
7. Markl M, Harloff A, Bley TA, Zaitsev M, Jung B, Weigang E, Langer M, Hennig J, Frydrychowicz A. Time-resolved 3D MR velocity mapping at 3T: improved navigator-gated assessment of vascular anatomy and blood flow. *J Magn Reson Imaging* 2007;25(4):824-831.
8. Johnson KM, Lum DP, Turski PA, Block WF, Mistretta CA, Wieben O. Improved 3D phase contrast MRI with off-resonance corrected dual echo VIPR. *Magn Reson Med* 2008;60(6):1329-1336.
9. Jung B, Stalder AF, Bauer S, Markl M. On the undersampling strategies to accelerate time-resolved 3D imaging using k-t-GRAPPA. *Magn Reson Med* 2011;66(4):966-975.
10. Carlsson M, Toger J, Kanski M, et al. Quantification and visualization of cardiovascular 4D velocity mapping accelerated with parallel imaging or k-t BLAST: head to head comparison and validation at 1.5 T and 3 T. *J Cardiovasc Magn Reson* 2011;13:55.
11. Gu T, Korosec FR, Block WF, Fain SB, Turk Q, Lum D, Zhou Y, Grist TM, Haughton V, Mistretta CA. PC VIPR: a high-speed 3D phase-contrast method for flow quantification and high-resolution angiography. *Ajnr* 2005;26(4):743-749.
12. Johnson KM, Lum DP, Turski PA, Block WF, Mistretta CA, Wieben O. Improved 3D phase contrast MRI with off-resonance corrected dual echo VIPR. *Magn Reson Med* 2008;60(6):1329-1336.
13. Stankovic Z, Frydrychowicz A, Csatari Z, et al. MR-based visualization and quantification of three-dimensional flow characteristics in the portal venous system. *J Magn Reson Imaging* 2010;32(2):466-475.
14. Stankovic Z, Csatari Z, Deibert P, et al. Normal and altered three-dimensional portal venous hemodynamics in patients with liver cirrhosis. *Radiology* 2012;262(3):862-873.
15. Frydrychowicz A, Landgraf BR, Niespodzany E, et al. Four-dimensional velocity mapping of the hepatic and splanchnic vasculature with radial sampling at 3 tesla: A feasibility study in portal hypertension. *J Magn Reson Imaging* 2011.
16. Roldan-Alzate A, Frydrychowicz A, Niespodzany E, et al. In vivo validation of 4D flow MRI for assessing the hemodynamics of portal hypertension. *J Magn Reson Imaging* 2013;37(5):1100-1108.

17. Stankovic Z, Jung B, Collins J, et al. Reproducibility study of four-dimensional flow MRI of arterial and portal venous liver hemodynamics: Influence of spatio-temporal resolution. *Magn Reson Med* 2013.
18. Lum DP, Johnson KM, Paul RK, et al. Transstenotic pressure gradients: measurement in swine--retrospectively ECG-gated 3D phase-contrast MR angiography versus endovascular pressure-sensing guidewires. *Radiology* 2007;245(3):751-760.
19. Bley TA, Johnson KM, Francois CJ, et al. Noninvasive assessment of transstenotic pressure gradients in porcine renal artery stenoses by using vastly undersampled phase-contrast MR angiography. *Radiology* 2011;261(1):266-273.
20. Stankovic Z, Blanke P, Markl M. Usefulness of 4D MRI flow imaging to control TIPS function. *The American journal of gastroenterology* 2012;107(2):327-328.
21. Heiberg E, Sjogren J, Ugander M, Carlsson M, Engblom H, Arheden H. Design and validation of Segment--freely available software for cardiovascular image analysis. *BMC medical imaging*. 2010;10:1.