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Quantification of Hepatic Blood Flow Using a High-Resolution Phase-Contrast MRI Sequence with Compressed Sensing Acceleration

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Abstract

Purpose—To evaluate the performance of a high spatial resolution 2D phase-contrast (PC) MRI technique accelerated with compressed sensing for portal vein (PV) and hepatic artery (HA) flow quantification in comparison with a standard PC MRI sequence.

Patients and Methods—In this IRB approved prospective study, two sequences were compared, one with parallel imaging acceleration and low spatial resolution (PC-GRAPPA), and one with compressed sensing acceleration and high spatial resolution (PC-SPARSE). 76 patients were assessed, including 37 with cirrhosis. Two observers evaluated PC image quality. Quantitative analysis yielded mean velocity, flow and vessel area for PV and HA, and arterial fraction. PC techniques were compared using Wilcoxon test and Bland-Altman statistics. Flow parameter sensitivity to severity of cirrhosis was also assessed.

Results—Vessel delineation was significantly improved using PC-SPARSE ($p < 0.034$). For both in vitro and in vivo measurements, PC-SPARSE yielded lower estimates for vessel area and flow, with larger differences observed in the HA. PV velocity and flow were significantly lower in cirrhosis for both sequences ($p < 0.001$ and $p < 0.04$ respectively). PV velocity correlated negatively with Child-Pugh class ($r = -0.50$, $p < 0.001$), while ART measured with PC-SPARSE was higher in Child-Pugh B/C patients compared to Child Pugh A, with trend towards significance ($p = 0.055$).

Conclusion—A highly accelerated/high spatial resolution compressed sensing technique allows for total hepatic blood flow measurement in a breath hold with improved delineation of hepatic vessels compared to a standard PC MRI sequence, and can potentially be used for noninvasive assessment of liver cirrhosis.

Keywords

phase-contrast MRI; portal vein flow; hepatic artery flow; cirrhosis; portal hypertension

INTRODUCTION

Portal hypertension (PH) is an important cause of morbidity and mortality in patients with liver cirrhosis. Manifestations of PH include ascites, splenomegaly, and varices which carry a high risk of bleeding [1]. The definitive diagnosis of PH is the invasive measurement of

hepatic venous pressure gradient (HVPG) [2–4]. There is a strong need for non-invasive markers of PH in patients with chronic liver disease to provide screening for PH and to monitor changes after medical therapy and/or TIPS (transjugular intrahepatic portosystemic shunt) placement. PH is associated with changes in hepatic blood flow, including a decrease in portal venous (PV) flow and velocity due to a higher parenchymal resistance to flow, and an increase in hepatic arterial (HA) flow and velocity secondary to an arterial buffer response [5]. The effects of PH on liver hemodynamics have been investigated using Doppler ultrasound [6–9] and phase-contrast (PC) MRI [10, 11]. With Doppler ultrasound, variable correlations ranging from -0.2 [6] to -0.69 [8] were observed when comparing PV blood flow and mean velocity with HVPG measurement, although no correlation was found in one study [9]. The variability of these findings may be due to the high inter-observer variability of the technique. Phase contrast (PC) MRI is a viable option to measure blood flow with lower variability than Doppler ultrasound [12–14], while offering slice [15] or volume [16–18] depiction of the main hepatic vessels. Using 2D PC MRI, Nanashima et al [11] found a significant negative correlation ($r = -0.722$) between PV velocity and portal pressure measured during hepatectomy. HA circulation was investigated by Wilson et al [19], who reported higher HA flow in 8 patients with PH compared to 9 patients with no PH. Of note, while the measurement of total hepatic blood flow has been studied in healthy volunteers [14, 15], fewer studies have reported concomitant HA and PV flow in subjects with liver cirrhosis using 2D PC MRI [17, 20].

Although PC MRI is a valid technique for hemodynamic assessment of liver cirrhosis, it can be hampered by long acquisition times, because of the need to acquire multiple velocity-encoded datasets. In the abdomen where breathing motion imposes short breath-held acquisitions, only moderate spatial and temporal resolutions may be achieved with conventional techniques. Higher resolution may be reached using navigator or respiratory-gated acquisitions, although the scan time of such techniques is significantly longer. Faster imaging, with acceleration techniques such as parallel imaging [21–23] or compressed sensing [24, 25], should provide better vessel depiction, by improving the spatial and temporal resolution.

The main objective of this study was to evaluate a highly accelerated compressed sensing 2D PC MRI sequence for HA and PV hemodynamic measurements in comparison with a standard PC MRI sequence. A secondary objective of the study was to investigate the performance of both PC MRI sequences for the diagnosis and assessment of severity of liver cirrhosis.

We hypothesized that a compressed sensing PC MRI technique would allow a better depiction of hepatic vessels than a technique using parallel imaging acceleration, thus improving precision for HA flow measurement.

PATIENTS AND METHODS

Patients

This was a HIPAA compliant prospective study approved by an exemption from our institutional review board, and funded by ----. From May 2012 to July 2012, 99 patients

underwent routine liver MRI exam including PC sequences to assess hepatic blood flow. A total of 23 subjects were excluded from the study for the following reasons: TIPS (n=3), post-liver transplant (n=15), or difficulty breath-holding (n=5). 76 patients were assessed (M/F 48/28, mean age 54 ± 13 y), including 39 non-cirrhotic patients (M/F 21/18, mean age 46 ± 14 y) and 37 with cirrhosis (M/F 27/10, mean age 61 ± 9 y). The diagnosis for liver cirrhosis was established in the presence of hepatic contour nodularity and the presence of signs of portal hypertension (including varices, splenomegaly or ascites). The diagnosis was confirmed with histopathology when available (n=8). In cirrhotic subjects, the etiology of liver disease included: chronic hepatitis C (n=21), chronic hepatitis B (n=5), alcohol abuse (n=5), nonalcoholic steatohepatitis (n=4), genetic hemochromatosis (n=1) and primary biliary cirrhosis (n=1). Child-Pugh class was determined in 36 cirrhotic subjects (blood tests were not available in one subject), with the following distribution: A (n=20), B (n=14) and C (n=2). In non-cirrhotic subjects, indications for MRI were hepatic steatosis (n=6), chronic hepatitis B (n=5), chronic hepatitis C (n=4), genetic hemochromatosis (n=1), sarcoidosis (n=1), nonalcoholic steatohepatitis (n=1), Wilson's disease (n=1), benign hepatic lesions (n=8), liver metastases (n=3), acute pancreatitis (n=1), acute cholecystitis (n=1), biliary distension (n=1), primary sclerosing cholangitis (n=1) and potential liver donors (n=5). Liver biopsy was available in 9 subjects in the non-cirrhotic group (n=2/3/4 with METAVIR stages F1/F2/F3) and 8 subjects in the cirrhotic group (METAVIR stage F4).

Phase-contrast MRI

All examinations were performed on a 1.5T scanner (Avanto, Siemens Healthcare) equipped with body and spine coil arrays (12 channels) by experienced technologists. Cine 2D PC MRI was performed after routine sequences [including a 3-axis balanced SSFP (Steady State Free Precession) localizer, axial and coronal HASTE] and before contrast injection. Two gradient echo-based PC acquisitions were performed (Table 1), first using parallel imaging acceleration [21] (Generalized Autocalibrating Partially Parallel Acquisitions, labeled PC-GRAPPA) then followed by an acquisition combined with compressed sensing acceleration [25, 26] (labeled PC-SPARSE), for which patients were asked to hold their breath at end expiration (15–20 s per acquisition). After the PC measurements, gadolinium contrast was injected as part of the routine exam, and the arterial, venous and liver enhancement phases were obtained using an axial 3D gradient echo T1-weighted VIBE (Volume Interpolated Breath Hold). Patients were not asked to fast before the study. The slice for PC imaging was selected perpendicular to the main PV, 1–2 cm below the bifurcation, using a balanced SSFP sequence to locate the PV. The same plane was measured by PC-SPARSE and PC-GRAPPA, and both sequences had similar breath hold duration.

Interpolation was performed for PC-GRAPPA to yield similar voxel size as PC-SPARSE. For each sequence, the acquisition consisted of dummy excitation for the first cardiac cycle in order to reach steady state, followed by 17 heartbeats. A retrospective pulse triggering approach was chosen in order to preserve steady state.

PC-SPARSE sampling and reconstruction

The PC-SPARSE sequence with compressed sensing implementation was locally developed and has been previously published [27]. Incoherent artifacts are crucial for successful

compressed sensing reconstruction. These artifacts were generated using a variable density random Cartesian sampling in the phase encoding direction, with a 8th degree polynomial weighting function featuring higher sampling density near the center of k-space (Fig. 1). To achieve incoherence in the dynamic direction, a different random sampling pattern was generated for each cardiac phase and each velocity encoded or reference measurement (for example, an acquisition of 20 cardiac phases would result in 40 different sampling patterns). The sampling pattern was generated at runtime depending on sequence parameters and was different for each subject. For image reconstruction a conjugate gradient approach was selected, using temporal principal component analysis as a sparsifying transform, similar to an algorithm used previously [27, 28]. 30 iterations were used for convergence and we selected a weight of 0.01 that trades off sparsity vs. data consistency [25]. In addition, the algorithm included multiple receiver information in the compressed sensing framework, as described previously [26]. Reconstruction was performed on a Mac Pro workstation (Intel Xeon, 16GB RAM), and took 60–120 min per scan. Once the images were reconstructed, magnitude and phase difference images were derived and background phase correction was performed on the phase difference image, using a 2nd order polynomial fit performed on static tissue.

Flow phantom validation

PC-GRAPPA and PC-SPARSE techniques were validated in a flow phantom experiment against a high resolution reference phase contrast sequence labeled PC-REF with the following parameters: Venc 50 cm/s, temporal resolution 40.7 ms, spatial resolution 1.04×1.04 mm², TR/TE 6.7/4.0 ms, flip angle 15, no parallel imaging acceleration, acquisition time 1:48 min. All phantom experiments were performed on a 1.5T scanner (Magnetom Aera, Siemens). The in-vitro setup consisted of a controllable gear pump (MP Chemflo unit, Quackenbush Co., Inc., Illinois, USA) generating steady flow in a module consisting of 5 MRI compatible tubes (diameters of 5, 7, 13, 19 and 26 mm) placed on the scanner table. The circuit was set to atmospheric pressure.

Image analysis

Image quality—Two independent observers [observer 1 and observer 2, radiologists with 3 and 1 year(s) of abdominal MRI experience, respectively] assessed PC image quality using Osirix DICOM viewer. Readers were blinded to the sequence type and series were randomized. Image quality was assessed on magnitude images as follows: HA and PV delineation (1: blurred, 2: mildly blurred: 3: sharp), vessel-to-background contrast (1: minimal, 2: moderate, 3: excellent) and background artifacts (1: severe, 2: moderate, 3: minimal/none). Quality ratings were added to yield an overall quality score (maximum 15 per sequence and patient).

PC MRI quantification—The phase contrast plane selection as well as presence and anatomy of HA branches on PC imaging were confirmed by observers 1 and 2 in consensus using contrast-enhanced imaging (axial VIBE performed during the arterial phase after contrast injection). The HA was assessed only when the main HA was parallel to the PV. In the case of multiple HA branches/early bifurcation, total HA flow was computed as the sum of all branches when present on PC imaging. Subjects with no visible HA on PC MRI, or

with in-plane HA component were excluded from the HA flow evaluation. Quantitative analysis was performed by observer 3, a post-doctoral fellow with 3 years of experience in image processing. Regions of interest (ROIs) were drawn on the vessel contour in the HA and PV using local software developed on Matlab (2012b, Matworks, Natick, Mass). The magnitude image was used to select brighter vessels and discard low intensity regions. ROIs were propagated across the cardiac cycle and pixel velocity was extracted from the phase difference image at each phase of the cardiac cycle (Fig. 2). The choice of $V_{enc} = 50$ cm/s, although higher than the range of PV velocities, was found to induce phase aliasing in the HA at systole in some subjects. Therefore an anti-aliasing technique was implemented that corrected the aliased pixels with velocity between 50 and 100 cm/s in the HA. After ROI processing, mean vessel velocity (cm/s), total flow (mL/s) and vessel area (mm²) were averaged over the cardiac cycle for the PV and HA. In addition, arterial fraction (ART in % = $100 \times \text{HA flow} / \text{HA flow} + \text{PV flow}$) was computed from the PV and HA flow parameters for both sequences.

Flow phantom—Observer 3 performed flow quantification for in vitro experiments, using in house software designed on Matlab. The magnitude image was used to segment the inflowing fluids, using the same threshold value for all 3 sequences (PC-GRAPPA, PC-SPARSE and PC-REF). Velocity was extracted in each pixel, in order to compute mean velocity and flow. Area was estimated as (pixel count) $\times$ (spatial resolution).

Statistical analysis

Statistical analysis was performed using Matlab statistics toolbox (2012b). Wilcoxon rank-sum test was used to compare PC-GRAPPA and PC-SPARSE in terms of image quality and flow parameters. Bland-Altman analysis was performed to compare flow parameters between both in vivo sequences. Comparisons between subjects with and without liver cirrhosis and between cirrhotic subjects with Child Pugh A vs. Child Pugh B and C were assessed using Mann Whitney nonparametric test. Dependence of flow parameters with Child-Pugh class was assessed using Spearman rank correlation coefficient.

RESULTS

Flow phantom experiment

Two tubes of 13 mm and 5 mm diameters were selected to emulate the PV and the HA, respectively (Fig. 3). Flow parameters derived from the phantom experiment are summarized in Table 2. The largest deviations from the reference acquisition PC-REF were observed for PC-GRAPPA when measuring the 5 mm-diameter tube. Poor definition can be observed for PC-GRAPPA in the 5 mm-diameter tube (Fig. 3).

Image quality and HA selection (Table 3)

Among the 76 patients, all subjects had successful flow measurement in the PV, while 31 had successful flow measurement in the HA. In the 31 cases with HA measurement, the HA was clearly identified with both sequences. PC-SPARSE had better overall quality than PC-GRAPPA ($p < 0.02$), especially for edge delineation ($p < 0.034$ for PV, $p < 0.001$ for HA). PC-SPARSE had however more artifacts than PC-GRAPPA ($p < 0.013$ for both observers).

Comparison of in vivo flow measurements between sequences

Bland-Altman limits of agreement between the two sequences were larger for the HA than for the PV (SD range 40–50% and 15–20 % respectively) (Table 4, Fig. 4). Flow and vessel area were significantly lower for PC-SPARSE ($p = 0.003$) in both vessels.

Flow parameters in cirrhosis (Table 5)

One subject (classified Child-Pugh B) had hepatofugal PV flow, resulting in negative PV velocity and ART >100%. In all other subjects, PV flow was hepatopetal. Subjects with cirrhosis had significantly lower PV velocity using PC-GRAPPA and PC-SPARSE ($p < 0.001$ for both) (Table 5). PV flow was also significantly lower in these subjects using PC-GRAPPA ($p = 0.006$) and PC-SPARSE ($p = 0.042$), and the observed ART was higher, although without significance. Correlation with Child-Pugh class was moderate for PV velocity ($r = -0.50$, $p < 0.001$ for PC-GRAPPA and $r = -0.50$, $p < 0.001$ for PC-SPARSE), and weak for PV flow ($r = -0.32$, $p = 0.006$ for PC-GRAPPA, $r = -0.24$, $p = 0.038$ for PC-SPARSE), while no significant correlation was observed for ART ($p > 0.09$).

No significant difference was observed between patients with compensated cirrhosis (Child-Pugh A) vs. those with Child-Pugh B and C. In Child-Pugh B and C patients, PV velocity was lower and ART was higher, with a trend towards significance for PC-SPARSE ($p = 0.050$ and $p = 0.055$ for PV and ART respectively) (Table 5).

DISCUSSION

We evaluated fast breath-held PC MRI acquisitions for hepatic blood flow quantification and their potential for assessment of cirrhosis. A high resolution compressed sensing technique (PC-SPARSE) was developed in order to improve hepatic vessel detection, and was compared to a lower spatial resolution parallel imaging technique (PC-GRAPPA) for the measurement of PV and HA flow and velocity. We found that PC-SPARSE presented better delineation of hepatic vessels, and provided lower estimated flow and area, as also shown by in vitro validation experiments. PV flow and velocity were significantly lower in cirrhotic patients, and moderate correlation was observed between PV velocity and Child-Pugh class, with similar performance for PC-SPARSE and PC-GRAPPA. HA flow parameters and arterial fraction (ART) did not reflect significant change in cirrhosis, although higher ART was observed in advanced cirrhosis subjects (Child-Pugh B and C), with a trend toward significance using PC-SPARSE.

Compressed sensing is a recent theory that may provide increased acceleration to the MR acquisition, and is under active development [24–26]. To the best of our knowledge, this is the first study reporting hepatic blood flow measurement in cirrhotic patients, using the high acceleration factors offered by compressed sensing. Such high acceleration factors enable faster and higher resolution measurements in a breath hold, allowing fast phase contrast exams to be performed routinely. As faster imaging can be obtained from higher acceleration factors, we decided to leverage the power of compressed sensing to achieve higher spatial resolution, in order to improve the precision of flow measurement in small hepatic vessels such as the HA. Our phantom experiment showed that PC-GRAPPA

overestimated vessel area and flow in smaller vessels, likely due to partial volume effect, while PC-SPARSE had higher concordance with a fully sampled, high resolution acquisition.

In the PV, PC-SPARSE was in good agreement with PC-GRAPPA, with limits of agreement similar to a previous report comparing parallel imaging to compressed sensing (mean PV velocity 13.3 cm/s, limits of agreement $-3.79 / 3.02$ cm/s in [27]). In the HA, lower agreement was observed between the two sequences. Furthermore, PC-GRAPPA was found to overestimate in vitro flow in small caliber vessel (5 mm diameter) by more than 50%, which may be due to the limited spatial resolution achieved by PC-GRAPPA.

In vivo PV and HA velocity and flow values were similar to previous reports. In 29 subjects, Sugano et al. [29] measured PV flow of 25.0 and 18.3 mL/s and PV velocity of 14.3 and 10.1 cm/s for non-cirrhotic and cirrhotic subjects respectively, while Nanashima et al [11] measured PV velocity of 12.8 cm/s in 58 subjects with liver disease. In 9 healthy subjects measured at two time points, Yzet et al [14] reported PV and HA flow of 15.8/17.1 and 3.2/4.0 mL/s respectively, and corresponding ART of 16.8/19.0%. Recent work reported ART of 16.4 ± 15.8 % in 17 patients with liver cirrhosis using 4D flow imaging [17]. Using dynamic contrast-enhanced (DCE) MRI, Annet et al [30] reported significantly higher portal fraction (100 - ART) in cirrhotic patients (43.81 ± 31.97 vs. 82.58 ± 14.88 for non-cirrhotic liver) and substantial correlation with HVPG ($r = -0.769$, $p < 0.001$). In our experience, ART was lower than these findings in PH subjects. One possible reason is the low number of Child Pugh C patients in our study, which would otherwise tend to bias the distribution towards higher ART. Another reason may be the conceptual nature of DCE-MRI, which estimates parenchymal flow, while PC MRI measures vessel flow, some of which might be diverted from the parenchyma via collaterals.

HVPG measurement remains the reference technique to diagnose portal hypertension. However, prognosis is routinely evaluated using Child Pugh score [31] and by assessing risk factors such as the presence and size of varices [32]. We found moderate correlations between PV velocity and Child-Pugh score. Similarly, decreased PV velocity with increasing Child-Pugh scores was previously observed using Doppler technique [33–35]. The large size of the portal vein does not require high-spatial resolution, hence the performance of both sequences for diagnosis of cirrhosis were similar using PV velocity. For the measurement of the PV alone, the 6 fold acceleration provided by compressed sensing could be used to decrease the breath-hold time compared to the PC-GRAPPA sequence at similar spatial resolution, thereby improving the success rate of the technique in patients having difficulty breath holding.

None of the PV and HA flow parameters reflected significant changes in advanced and decompensated cirrhosis (Child-Pugh B and C). This may be due to the low number of decompensated cirrhosis in our cohort ($n=2$). Our preliminary data suggest that ART may have potential for detecting advanced cirrhosis. PC-SPARSE demonstrated higher ART in patients Child Pugh B and C (with trend towards significance).

A high resolution compressed sensing acquisition resulted in better vessel depiction, higher precision of the flow measurement in small vessels (as demonstrated by flow phantom experiments), and lower partial volume effect (as evidenced by significantly lower measured vessel area). However a higher level of artifact was also observed with PC-SPARSE, which may be reduced further by using a higher magnetic field (3.0 T) to improve SNR, or by exploiting spatial sparsity in addition to temporal sparsity of cine PC, as well as sparse properties of the phase contrast angiography technique [36].

Measuring a small pulsatile vessel such as the HA can be challenging. First, localizing the HA vascular tree is not trivial because of anatomical variants [37]. Our HA flow analysis was performed only on 31 subjects for which the HA and PV were parallel to each other. Total HA flow estimation would benefit from a 4D flow technique [17, 18, 38], which would theoretically increase the precision and success rate of HA flow measurement. Recent work proposed accelerated 4D flow [39, 40], making this technique potentially usable clinically.

There are several limitations to this study. First, the prandial state of the subjects was not controlled. Increased PV flow may occur after a meal [41], and these effects should be addressed in a prospective study. Second, flow parameters were compared to the Child-Pugh class. Future work should address the comparison of hepatic flow PC MRI with quantitative metric such as the HVPG. Finally, comparisons with fibrosis stage was not performed since histopathology was available only in a limited number of cases (n=17).

In conclusion, high-resolution phase contrast MRI can be performed in a single breath hold acquisition using compressed sensing acceleration and provides improved hepatic vessel delineation while reflecting changes in hepatic flow in liver cirrhosis.

REFERENCES

1. Escorsell A, Bosch J. Pathogenesis of bleeding in portal hypertension. *Digestion*. 1998; 59(Suppl 2): 2–5. [PubMed: 9718409]
2. Garcia-Tsao G, Groszmann RJ, Fisher RL, Conn HO, Atterbury CE, Glickman M. Portal pressure, presence of gastroesophageal varices and variceal bleeding. *Hepatology* (Baltimore, Md). 1985; 5:419–424.
3. Ripoll C, Groszmann R, Garcia-Tsao G, et al. Hepatic venous pressure gradient predicts clinical decompensation in patients with compensated cirrhosis. *Gastroenterology*. 2007; 133:481–488. [PubMed: 17681169]
4. Wadhawan M, Dubey S, Sharma BC, Sarin SK, Sarin SK. Hepatic venous pressure gradient in cirrhosis: correlation with the size of varices, bleeding, ascites, and child's status. *Dig Dis Sci*. 2006; 51:2264–2269. [PubMed: 17080245]
5. Gulberg V, Haag K, Rossle M, Gerbes AL. Hepatic arterial buffer response in patients with advanced cirrhosis. *Hepatology*. 2002; 35:630–634. [PubMed: 11870377]
6. Haag K, Rossle M, Ochs A, et al. Correlation of duplex sonography findings and portal pressure in 375 patients with portal hypertension. *AJR Am J Roentgenol*. 1999; 172:631–635. [PubMed: 10063849]
7. Merkel C, Sacerdoti D, Bolognesi M, Bombonato G, Gatta A. Doppler sonography and hepatic vein catheterization in portal hypertension: assessment of agreement in evaluating severity and response to treatment. *J Hepatol*. 1998; 28:622–630. [PubMed: 9566831]

8. Taourel P, Blanc P, Dauzat M, et al. Doppler study of mesenteric, hepatic, and portal circulation in alcoholic cirrhosis: relationship between quantitative Doppler measurements and the severity of portal hypertension and hepatic failure. *Hepatology* (Baltimore, Md). 1998; 28:932–936.
9. Choi YJ, Baik SK, Park DH, et al. Comparison of Doppler ultrasonography and the hepatic venous pressure gradient in assessing portal hypertension in liver cirrhosis. *J Gastroenterol Hepatol*. 2003; 18:424–429. [PubMed: 12653891]
10. Burkart DJ, Johnson CD, Ehman RL, Weaver AL, Ilstrup DM. Evaluation of portal venous hypertension with cine phase-contrast MR flow measurements: high association of hyperdynamic portal flow with variceal hemorrhage. *Radiology*. 1993; 188:643–648. [PubMed: 8351326]
11. Nanashima A, Shibasaki S, Sakamoto I, et al. Clinical evaluation of magnetic resonance imaging flowmetry of portal and hepatic veins in patients following hepatectomy. *Liver Int*. 2006; 26:587–594. [PubMed: 16762004]
12. Hara AK, Burkart DJ, Johnson CD, et al. Variability of consecutive in vivo MR flow measurements in the main portal vein. *AJR Am J Roentgenol*. 1996; 166:1311–1315. [PubMed: 8633438]
13. Paulson EK, Kliewer MA, Frederick MG, Keogan MT, DeLong DM, Nelson RC. Doppler US measurement of portal venous flow: variability in healthy fasting volunteers. *Radiology*. 1997; 202:721–724. [PubMed: 9051024]
14. Yzet T, Bouzerar R, Allart JD, et al. Hepatic vascular flow measurements by phase contrast MRI and doppler echography: a comparative and reproducibility study. *J Magn Reson Imaging*. 2010; 31:579–588. [PubMed: 20187200]
15. Yzet T, Bouzerar R, Baledent O, et al. Dynamic measurements of total hepatic blood flow with Phase Contrast MRI. *Eur J Radiol*. 2010; 73:119–124. [PubMed: 19008062]
16. Frydrychowicz A, Francois CJ, Turski PA. Four-dimensional phase contrast magnetic resonance angiography: potential clinical applications. *Eur J Radiol*. 2011; 80:24–35. [PubMed: 21333479]
17. 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*. 2012
18. Stankovic Z, Csatai Z, Deibert P, et al. Normal and altered three-dimensional portal venous hemodynamics in patients with liver cirrhosis. *Radiology*. 2012; 262:862–873. [PubMed: 22357888]
19. Wilson DJ, Ridgway JP, Evans JA, Robinson P. Measurement of hepatic arterial flow using phase contrast magnetic resonance imaging. *Physics in medicine and biology*. 2009; 54:N439–N449. [PubMed: 19729714]
20. Stankovic Z, Csatai Z, Deibert P, et al. Normal and altered three-dimensional portal venous hemodynamics in patients with liver cirrhosis. *Radiology*. 2012; 262:862–873. [PubMed: 22357888]
21. Griswold MA, Jakob PM, Heidemann RM, et al. Generalized autocalibrating partially parallel acquisitions (GRAPPA). *Magn Reson Med*. 2002; 47:1202–1210. [PubMed: 12111967]
22. Pruessmann KP, Weiger M, Scheidegger MB, Boesiger P. SENSE: sensitivity encoding for fast MRI. *Magn Reson Med*. 1999; 42:952–962. [PubMed: 10542355]
23. Sodickson DK, Manning WJ. Simultaneous acquisition of spatial harmonics (SMASH): fast imaging with radiofrequency coil arrays. *Magn Reson Med*. 1997; 38:591–603. [PubMed: 9324327]
24. Donoho DL. Compressed sensing. *Ieee T Inform Theory*. 2006; 52:1289–1306.
25. Lustig M, Donoho D, Pauly JM. Sparse MRI: The application of compressed sensing for rapid MR imaging. *Magn Reson Med*. 2007; 58:1182–1195. [PubMed: 17969013]
26. Otazo R, Kim D, Axel L, Sodickson DK. Combination of compressed sensing and parallel imaging for highly accelerated first-pass cardiac perfusion MRI. *Magn Reson Med*. 2010; 64:767–776. [PubMed: 20535813]
27. Blinded Reference.
28. Feng L, Otazo R, Jung H, et al. Accelerated cardiac T2 mapping using breath-hold multiecho fast spin-echo pulse sequence with k-t FOCUSS. *Magn Reson Med*. 2011; 65:1661–1669. [PubMed: 21360737]

29. Sugano S, Yamamoto K, Takamura N, Momiyama K, Watanabe M, Ishii K. Azygos venous blood flow while fasting, postprandially, and after endoscopic variceal ligation, measured by magnetic resonance imaging. *J Gastroenterol.* 1999; 34:310–314. [PubMed: 10433004]
30. Annet L, Materne R, Danse E, Jamart J, Horsmans Y, Van Beers BE. Hepatic flow parameters measured with MR imaging and Doppler US: correlations with degree of cirrhosis and portal hypertension. *Radiology.* 2003; 229:409–414. [PubMed: 12970464]
31. Angermayr B, Cejna M, Karel F, et al. Child-Pugh versus MELD score in predicting survival in patients undergoing transjugular intrahepatic portosystemic shunt. *Gut.* 2003; 52:879–885. [PubMed: 12740346]
32. Bari K, Garcia-Tsao G. Treatment of portal hypertension. *World J Gastroenterol.* 2012; 18:1166–1175. [PubMed: 22468079]
33. Taourel P, Blanc P, Dauzat M, et al. Doppler study of mesenteric, hepatic, and portal circulation in alcoholic cirrhosis: relationship between quantitative Doppler measurements and the severity of portal hypertension and hepatic failure. *Hepatology.* 1998; 28:932–936. [PubMed: 9755228]
34. Zironi G, Gaiani S, Fenyves D, Rigamonti A, Bolondi L, Barbara L. Value of measurement of mean portal flow velocity by Doppler flowmetry in the diagnosis of portal hypertension. *J Hepatol.* 1992; 16:298–303. [PubMed: 1487606]
35. Ljubicic N, Duvnjak M, Rotkvic I, Kopjar B. Influence of the degree of liver failure on portal blood flow in patients with liver cirrhosis. *Scand J Gastroenterol.* 1990; 25:395–400. [PubMed: 2186474]
36. Kwak Y, Nam S, Akcakaya M, et al. Accelerated aortic flow assessment with compressed sensing with and without use of the sparsity of the complex difference image. *Magn Reson Med.* 2012
37. Hiatt JR, Gabbay J, Busuttil RW. Surgical anatomy of the hepatic arteries in 1000 cases. *Ann Surg.* 1994; 220:50–52. [PubMed: 8024358]
38. Markl M, Harloff A, Bley TA, et al. Time-resolved 3D MR velocity mapping at 3T: improved navigator-gated assessment of vascular anatomy and blood flow. *Journal of magnetic resonance imaging : JMRI.* 2007; 25:824–831. [PubMed: 17345635]
39. Hsiao A, Lustig M, Alley MT, et al. Rapid pediatric cardiac assessment of flow and ventricular volume with compressed sensing parallel imaging volumetric cine phase-contrast MRI. *AJR Am J Roentgenol.* 2012; 198:W250–259. [PubMed: 22358022]
40. Sigfridsson A, Petersson S, Carlhall CJ, Ebbens T. Four-dimensional flow MRI using spiral acquisition. *Magn Reson Med.* 2012; 68:1065–1073. [PubMed: 22161650]
41. Lycklama a Nijeholt GJ, Burggraaf K, Wasser MN, et al. Variability of splanchnic blood flow measurements using MR velocity mapping under fasting and post-prandial conditions--comparison with echo-Doppler. *J Hepatol.* 1997; 26:298–304. [PubMed: 9059950]

Fig. 1.

Example of PC-SPARSE random sampling and reconstruction using dynamic compressed sensing in a 54-year old female patient with non cirrhotic liver. A: measured k-space with random variable density sampling applied in the phase encoding direction (Ky) and the dynamic direction (cardiac phase and velocity encoding). B: image before reconstruction (zero filled Fourier transform). C: reconstructed image, after 30 iterations, shows excellent conspicuity of the portal vein (PV) and hepatic artery (HA) (arrows).

Fig. 2. PC-GRAPPA (A, B and C) and PC-SPARSE (D, E and F) magnitude (A, D) and phase difference images (B, E) in the same subject as Fig. 1. Mean vessel velocity curves (C, F) are displayed for the PV (solid blue line) and HA (dashed red line). Compared with PC-GRAPPA acquisition, PC-SPARSE has well delineated vessels (PV and HA, blue and red arrows). Stronger noise appears on PC-SPARSE, visible as speckle on the phase image background tissue and as fluctuations on the velocity curves.

Fig. 3.

Experimental flow phantom setup to measure steady flow in tubes of various diameters. A: picture of the setup, including 5 tubes of diameter 5 to 26 mm. B: magnitude image derived from high resolution phase contrast MRI acquisition (PC-REF). C: from left to right, zoomed magnitude images for PC-GRAPPA (low resolution, parallel imaging acceleration), PC-SPARSE (high resolution, compressed sensing acceleration) and PC-REF (high resolution, no acceleration), for tubes of diameter 13 mm (top) and 5 mm (bottom, magnified). PC-GRAPPA suffers from increased blurring and partial volume effect, especially visible in the smaller vessel.

Fig. 4.

Bland-Altman plots depicting the comparison of PC-SPARSE with PC-GRAPPA for portal venous flow (PVF), velocity (PVV) and area (PVA), and hepatic arterial flow (HAF), velocity (HAV) and area (HAA). Difference between the two techniques is given as a percentage of the corresponding average parameter value. Lines indicate bias, lower and higher limits of agreement. Better agreement is observed in PV.

Table 1

Imaging parameters for the two accelerated phase contrast MRI sequences. For similar temporal resolution, PC-SPARSE has about 5x smaller acquired voxel size than PC-GRAPPA (5.57 mm² for PC-GRAPPA and 1.04 mm² for PC-SPARSE).

	PC-GRAPPA	PC-SPARSE
Time resolution (ms)	39.25	41.60
TR (ms)	6.54	6.93
TE (ms)	3.48	4.16
Flip angle	30	25
Field of view (mm ²)	320 × 270	350 × 280
Acquisition matrix	192 × 162	384 × 307
Acquired voxel size (mm ²)	1.67 × 3.34	0.91 × 1.14
Slice thickness (mm)	7	7
Phase resolution	50 %	80 %
Segments per cardiac phase	3	3
Velocity encoding (cm/s)	50	50
Number of cardiac phases	20	14–26
Acceleration	GRAPPA R=2	SPARSE R=6
Acquisition time	15–20 s (18 R-R)	15–20 s (18 R-R)

Table 2

Quantitative flow parameters derived from the flow phantom experiment in the 13 and 5 mm – diameter tubes. Coefficients of variation (CV, in %), given in parenthesis, were calculated with respect to PC-REF (high resolution PC sequence used as reference) parameters. The largest deviations from the reference acquisition (PC-REF) were observed for PC-GRAPPA when measuring the 5 mm-diameter tube.

Tube diameter	Parameter	PC-REF	PC-GRAPPA	PC-SPARSE
13 mm	Flow	4.95	5.23 (5.5%)	5.58 (12.0%)
	Velocity	3.81	3.75 (1.9%)	3.99 (4.8%)
	Area	119.9	129.1 (7.4%)	128.8 (7.2%)
5 mm	Flow	2.03	3.51 (53.4%)	2.17 (6.7%)
	Velocity	7.13	9.35 (27.0%)	8.29 (13.1%)
	Area	26.3	34.6 (27.3%)	24.2 (8.3%)

Units: flow (mL/s), velocity (cm/s), area (mm²)

Image quality scores for PC-GRAPPA and PC-SPARSE sequences.

	Observer 1			Observer 2		
	PC-GRAPPA	PC-SPARSE	p*	PC-GRAPPA	PC-SPARSE	p*
PV edge	1.8 ± 0.7	2.3 ± 0.7	< 0.001	2.6 ± 0.6	2.7 ± 0.5	0.034
PV contrast	2.8 ± 0.5	2.8 ± 0.4	0.637	2.9 ± 0.3	2.9 ± 0.3	0.739
HA edge	0.9 ± 0.7	1.3 ± 1.0	0.001	1.4 ± 0.8	2.1 ± 0.9	< 0.001
HA contrast	1.4 ± 1.1	1.6 ± 1.1	0.159	1.7 ± 1.0	2.2 ± 1.0	0.001
Artifacts	2.8 ± 0.3	2.7 ± 0.4	0.008	2.9 ± 0.2	2.7 ± 0.5	0.013
Total score	9.8 ± 2.2	10.9 ± 2.6	0.006	11.5 ± 2.0	12.7 ± 2.3	< 0.001

PV: portal vein, HA: hepatic artery

Table 4

Comparison of flow parameters obtained with PC-GRAPPA and PC-SPARSE using Bland-Altman analysis and paired Wilcoxon test. Estimated flow and area were higher for PC-GRAPPA than for PC-SPARSE.

	PC-GRAPPA	PC-SPARSE	p *	Bland-Altman LA **
PV flow	20.9 ± 8.8	18.0 ± 7.5	<0.001	-50.4 – 22.5
HA flow	5.9 ± 5.8	3.6 ± 2.9	<0.001	-138.2 – 60.2
PV velocity	10.1 ± 3.6	10.6 ± 3.4	<0.001	-26.5 – 38.2
HA velocity	13.7 ± 9.5	11.6 ± 6.5	0.13	-108.6 – 86.5
PV area	199.8 ± 72.3	168.6 ± 53.1	<0.001	-53.0 – 22.0
HA area	35.5 ± 16.6	30.7 ± 20.2	0.003	-108.3 – 56.0

PV: portal vein, HA: hepatic artery, ART: arterial fraction

Units: flow (mL/s), velocity (cm/s), area (mm²)

* Wilcoxon test, values are bolded when significant (p < 0.05).

** Limits of agreement (in % of the population averaged parameter value)

Table 5

Discrimination between subjects without and with liver cirrhosis and between subjects with Child-Pugh A vs. Child-Pugh B and C. Flow parameters are given as mean $\pm$ standard deviation.

		No Cirrhosis*	Cirrhosis	p**	Child-Pugh A	Child-Pugh B & C	p
PC GRAPPA	PV velocity*	11.8 $\pm$ 3.1	8.4 $\pm$ 3.3	<0.001	9.5 $\pm$ 2.2	7.1 $\pm$ 4.0	0.072
	HA velocity	14.3 $\pm$ 12.5	13.3 $\pm$ 7.0	0.562	13.9 $\pm$ 8.4	13.3 $\pm$ 5.0	0.669
	PV flow	23.0 $\pm$ 6.7	18.6 $\pm$ 10.1	0.005	19.8 $\pm$ 8.6	17.3 $\pm$ 12.1	0.381
	HA flow	5.8 $\pm$ 6.4	5.9 $\pm$ 5.5	0.347	4.6 $\pm$ 1.5	8.3 $\pm$ 8.4	0.364
	ART	17.2 $\pm$ 14.4	28.2 $\pm$ 31.6	0.180	18.7 $\pm$ 6.5	43.9 $\pm$ 47.8	0.417
PC SPARSE	PV velocity	12.2 $\pm$ 2.9	9.0 $\pm$ 3.2	<0.001	10.0 $\pm$ 2.1	7.7 $\pm$ 3.9	0.050
	HA velocity	13.1 $\pm$ 7.7	10.6 $\pm$ 5.6	0.435	11.2 $\pm$ 5.5	10.6 $\pm$ 6.0	0.887
	PV flow	19.7 $\pm$ 7.0	16.3 $\pm$ 7.7	0.042	17.7 $\pm$ 6.5	14.8 $\pm$ 9.1	0.364
	HA flow	3.5 $\pm$ 3.1	3.7 $\pm$ 2.9	0.484	2.8 $\pm$ 1.4	5.2 $\pm$ 4.0	0.133
	ART	14.6 $\pm$ 10.5	24.3 $\pm$ 34.8	0.307	12.7 $\pm$ 5.4	42.6 $\pm$ 52.5	0.055

PV: portal vein, HA: hepatic artery, ART: arterial fraction

Units: flow (mL/s), velocity (cm/s), area (mm²)

* PV assessed in 76 subjects (39 with cirrhosis, 37 without), HA and ART in 31 subjects (18 with cirrhosis, 13 without).

** Mann Whitney test, bolded when significant (p < 0.05).