Clinical Applications of 4D Flow MRI in the Portal Venous System

Thekla H. Oechtering¹,², Grant S. Roberts³, Nikolaos Panagiotopoulos¹,², Oliver Wieben¹,³, Scott B. Reeder¹,³,⁴,⁵,⁶, and Alejandro Roldán-Alzate¹,⁴,⁵

Evaluation of the hemodynamics in the portal venous system plays an essential role in many hepatic pathologies. Changes in portal flow and vessel morphology are often indicative of disease. Routinely used imaging modalities, such as CT, ultrasound, invasive angiography, and MRI, often focus on either hemodynamics or anatomical imaging. In contrast, 4D flow MRI facilitates a more comprehensive understanding of pathophysiological mechanisms by simultaneously and noninvasively acquiring time-resolved flow and anatomical information in a 3D imaging volume.

Though promising, 4D flow MRI in the portal venous system is especially challenging due to small vessel calibers, slow flow velocities, and breathing motion. In this review article, we will discuss how to account for these challenges when planning and conducting 4D flow MRI acquisitions in the upper abdomen. We will address patient preparation, sequence acquisition, postprocessing, quality control, and analysis of 4D flow data.

In the second part of this article, we will review potential clinical applications of 4D flow MRI in the portal venous system. The most promising area for clinical utilization is the diagnosis and grading of liver cirrhosis and its complications. Relevant parameters acquired by 4D flow MRI include the detection of reduced or reversed flow in the portal venous system, characterization of portosystemic collaterals, and impaired response to a meal challenge. In patients with cirrhosis, 4D flow MRI has the potential to address the major unmet need of noninvasive detection of gastroesophageal varices at high risk for bleeding. This could replace many unnecessary, purely diagnostic, and invasive esophagogastroduodenoscopy procedures, thereby improving patient compliance with follow-up. Moreover, 4D flow MRI offers unique insights and added value for surgical planning and follow-up of multiple hepatic interventions, including transjugular intrahepatic portosystemic shunts, liver transplantation, and hepatic disease in children. Lastly, we will discuss the path to clinical implementation and remaining challenges.

Keywords: cirrhosis, 4D flow magnetic resonance imaging, hemodynamics, portal hypertension, portal vein

Hemodynamic Characteristics and Clinical Relevance of the Portal Venous System

Flow in the portal vein and associated pathologies

The portal vein delivers approximately 80% of the liver’s blood supply by draining blood from the gastrointestinal tract, spleen, pancreas, and gallbladder to the liver for metabolism of nutrients and removal of potentially toxic substances. In contrast, the hepatic artery only contributes about 20% to the total blood flow to the liver. The normal flow waveform in the portal vein is constant, nonpulsatile, and hepatopetal, i.e., unidirectional blood flow toward the liver.

Changes in portal flow are characteristic for a number of pathologies: Decreased flow or even hepatofugal flow (i.e., flow reversal away from the liver) are typical features of end-stage liver disease (cirrhosis). Pulsatile flow can occur occasionally in patients with right-sided congestive heart failure.
been described in patients with advanced cirrhosis.\(^4\) The postprandial hyperemia is due to increased portal flow in response to a meal.\(^2,3\) An impaired ability of the portal venous system significantly increases hepatic congestion due to stagnation of portal blood flow.\(^2,3\) Physiologically, portal hypertension occurs in the setting of infiltrative malignancies or in cirrhosis due to heart failure, leading to portal vein pulsatility. The absence of flow associated with portal vein thrombosis can occur in the setting of infiltrative malignancies or in cirrhosis due to stagnation of portal blood flow.\(^2,3\) Physiologically, flow in the portal venous system significantly increases after a meal (postprandial hyperemia). An impaired ability to increase the portal venous flow in response to a meal has been described in patients with advanced cirrhosis.\(^4-7\)

There are a variety of surgical and interventional procedures involving the portal vein and altering its hemodynamics. They can be aimed at decreasing the flow to one liver lobe as it is the case for embolization before hemihepatectomy to induce hypertrophy of the remaining liver segment.\(^8\) Others are associated with a flow increase, e.g., in procedures aimed at treating portal hypertension by establishing portosystemic venous shunts that bypass flow around the liver.\(^9\) Portal venous complications after surgery or transplantation or congenital anomalies can include stenosis or aneurysms.\(^3\) Moreover, medical treatment can alter hemodynamics in the portal vein: Nonselective beta-blockers are used to treat portal hypertension by reducing splanchnic blood flow and thus by reducing portal pressure.\(^10\)

**Imaging of the portal venous system**

In all these examples and pathologies, noninvasive anatomical and functional imaging of the portal venous system is of great interest.\(^3\) In many imaging centers, contrast-enhanced CT angiography is the modality of choice for rapid anatomical evaluation with high resolution.\(^11,12\) However, the associated hemodynamic and functional parameters cannot be assessed with CT, and the use of iodinated contrast agents may be contraindicated in patients with renal dysfunction, which is often present in patients with liver disease. Ultrasound can provide both anatomic and functional evaluations of the large veins in the portal venous system. However, it is highly operator-dependent and can only measure velocity, but not flow volume. Furthermore, ultrasound is very limited in its ability to provide accurate depiction of variceal pathways often present in patients with advanced portal hypertension.\(^13,14\) Moreover, there is often a limited acoustic window in patients with liver disease.\(^11\)

MRI offers both anatomical and functional assessments of the portal venous system. For example, it plays an important role in the detection of portal vein thrombosis and characterizing its etiology.\(^2\) 2D phase-contrast MRI (2D flow MRI) has been well validated for both velocity and flow volume measurements in the main portal vein\(^15-17\) and showed lower variability and higher reproducibility than ultrasound.\(^18\) Moreover, results correlated better with the degree of cirrhosis and portal hypertension than Doppler ultrasound parameters.\(^19\) However, for comprehensive assessment of liver flow, numerous double-oblique 2D planes are required. This presents a prohibitively burdensome practical challenge as the prescription of such planes is complex, and variable anatomy requires a high degree of operator expertise. Fortunately, these challenges can be overcome by time-resolved 3D phase-contrast MRI with 3D flow encoding, i.e., 4D flow MRI. 4D flow MRI allows the easy prescription of a large imaging volume covering the upper abdomen and the retrospective analysis of flow and morphology within the volume of interest. Velocity measurements made using abdominal 4D flow MRI have been well validated against ultrasound measurements\(^20-22\) and 2D flow MRI.\(^23,24\) Mean velocity and flow volume at the splenomesenteric confluence of volunteers correlated moderately (\(r = 0.644\) and \(r = 0.515\), respectively) between MRI and ultrasound with an underestimation by MRI.\(^22\) They showed strong repeatability and reproducibility,\(^25\) as well as internal consistency.\(^26-29\) Two acquisitions that were at least five months apart yielded average differences of 5% for mean velocities and of 6% for flow volume for the portal venous system.\(^25\)

**4D Flow MRI in the Portal Venous System – Technical Aspects**

Imaging of the portal venous system in general and specifically with 4D flow MRI is challenging. Not only is the anatomy complex and highly variable (Fig. 1b and 1c) but also the vessels of interest are relatively small with slow flow, resulting in imprecise measurements. Moreover, it is necessary to cover a large area of the upper abdomen, which may be complicated by artifacts related to breathing motion.

4D flow MRI provides a unique and comprehensive set of information within a single acquisition by establishing volumetric 3D velocity encoding in three directions together with anatomical information, making it a powerful technique for comprehensive noninvasive portal venous imaging. It gathers anatomical and functional flow information that can be quantified and visualized (Fig. 2). All these aspects can help understand and diagnose portal venous pathologies.\(^30,31\)

**Patient preparation**

Prior to 4D flow MRI, the subject should be instructed to fast (typically 3–5 hours\(^26,27,32\)) since there is a significant increase in flow volume and velocity after a meal, which can introduce considerable variability into quantitative results,\(^27,28\) and thus may impede comparisons to reference values and long-term follow-up studies.

To examine the hemodynamic response to a meal, which can be reduced in advanced cirrhosis,\(^4-7\) the postprandial MRI examination should be scheduled during the maximum hemodynamic response to a controlled meal stimulus. Depending on energy content and composition of the meal, time of maximum blood flow increase in the superior mesenteric artery measured by ultrasound has been reported between 15 and 60 mins with an increase in blood flow...
Fat-rich meals typically induce a more intense and longer increase in blood flow and velocity compared with carbohydrate meals. Hyperemia after fat-rich meals can remain at 79% above baseline 180 mins after the meal, whereas blood flow typically returns to baseline values 150 mins after a carbohydrate-rich meal. In our experience, a delay of 20 mins after ingestion of a standardized meal (e.g., a readily available nutrition shake) is sufficient to induce a strong hyperemic response. Other authors prefer delays of up to 60 mins.

**Data acquisition**

4D flow MRI can be acquired at 1.5T or 3T. Most MRI vendors offer 4D flow MRI as a product sequence. Several sequences using either the traditional Cartesian or non-Cartesian spatial encoding techniques have been validated for abdominal flow measurements. Non-Cartesian
Table 1 Typical acquisition parameters for Cartesian, radial, and spiral spatial encoding techniques found in the literature

|                        | Cartesian                                      | Radial                                      | Spiral                                      |
|------------------------|------------------------------------------------|---------------------------------------------|---------------------------------------------|
| References             | 21, 22, 24, 29, 47                              | 26-28, 32, 44, 45                          | 36, 37                                      |
| FOV (cm³)              | 22 × 32 × 8.6 **                         | 32 × 32 × 22–32                            | 40 × 40 × 6                                 |
| Spatial resolution (mm³) | 1.3–2.8 × 1.7–3.2 × 1.3–4.0 (not specified if acquired or interpolated) | 1.25–1.4 isotropic (acquired)                | 2.5 × 2.5 × 5 (acquired); (1.3 × 1.3 × 2.5, interpolated) |
| Mean number of time frames in cardiac cycle | 9–20                                           | 14                                          | 8–15**                                      |
| Temporal resolution (ms) | 29–64                                          | 43–71 **                                   | 66–71                                       |
| Mean scan duration (min) | 7–23                                           | 10–12                                      | 0.3–0.4 (1 breath hold)                     |

*FOV mentioned only in 1 study. ** calculated for 60-100 bpm

Acquisition time is a critical factor for 4D flow sequences, which tend to be long due to the encodes needed to provide cine data over a large imaging volume and 3D velocity encoding. Therefore, novel acceleration methods, such as radial undersampling,40 k-t acceleration,41,42 and compressed sensing,36,37 have been introduced instead of the traditional parallel imaging. Acceleration factors typically start at 2 and can have clinically feasible acquisition times for the portal venous system range in the order of 10–15 mins, which can be further accelerated by advanced acceleration methods. An overview of typical acquisition parameters and acquisitions times can be found in Table 1.

The preferred orientation of the imaging slab depends on the specific task. Axial slabs are well suited for non-Cartesian acquisitions because the slab excitation effectively limits the spatial extend of the imaging volume, minimizes artifact from signal outside the imaging volume, and takes advantage of signal gains from the inflow effect. For Cartesian encoding, coronal acquisitions may be advantageous with superior robustness to respiratory motion and larger volumetric coverage of the abdomen and pelvis. Axial oblique25,43 or paracoronal44 orientations angled along the portal vein also allow the coverage of the portal vein in a smaller FOV to minimize the acquisition time for Cartesian 4D flow acquisitions.

To reduce motion artifacts, respiratory gating should be applied. Using an adaptive window, the acceptance rate is typically set to 50% during expiration.27,28,32,45,46 Using a gating navigator at the liver–lung interface, an acceptance window of 6–8 mm21,24,47 typically corresponds to 50%–60% acceptance. If needed, the navigator can be placed on the spleen–lung interface to avoid interference with the main ROI. Recently, a free-breathing self-navigated, Cartesian 4D flow sequence36 has been proposed for hepatic flow analysis that uses scan time more efficiently.

Spatial encoding techniques, such as radial20,26 or spiral36,37 undersampling, accelerate data acquisition, which can be used to increase the FOV and improve spatial or temporal resolution. Moreover, they are more robust to motion.38,39

To account for the pulsatile blood flow during the cardiac cycle, cardiac synchronization must be used, typically accomplished with electrocardiogram (ECG) triggering. Retrospective cardiac gating is superior to prospective gating as it covers the entire cardiac cycle.46 Studies using prospective gating need to adjust the quantitative flow measurements to represent the full cardiac cycle based on the percent captured and the heart rate46 – this is more important when measuring nonpulsatile flow (e.g., in the portal vein) compared with pulsatile flow (e.g., in large arteries), where late diastole contributes very little to the flow volume.

While high temporal resolution is required to resolve pulsatile flow with large velocity changes during the cardiac cycle, e.g., in the aorta, high temporal resolution is not necessary in the portal vein, which has largely steady flow. Landgraf et al.46 proposed to use time-averaged reconstructions for the portal venous system to save imaging time. They showed that time-averaged reconstructions outperform time-resolved reconstructions regarding flow quantification, average streamline length, and visualization quality. However, to date, most studies use time-resolved reconstructions, allowing not only the assessment of flow volumes and mean velocity but also the assessment of dynamic parameters such as peak velocities.

4D flow can be acquired with or without an exogeneous contrast agent used in MR angiography, such as gadolinium chelates or iron nanoparticles. The use of a contrast agent provides better image quality and velocity measurements through improved SNR and noise reduction in the velocity data.50 Many sites acquire the 4D flow sequence after contrast administration for a clinical contrast-enhanced angiography. The flip angle should be increased for contrast-enhanced acquisitions compared to exams without contrast in order to maximize SNR and optimize T1 weighting.48

To acquire flow velocities accurately, an optimal choice of the velocity encoding setting (venc) is of vital importance. The venc is set during scan prescription and adjusts the velocity encoding gradients such that the maximum velocity
that can be measured with phase-contrast MRI without velocity aliasing. If it is chosen too low, the velocities higher than the venc cannot be encoded properly, and aliasing occurs. If the venc is chosen too high, the velocity-to-noise ratio (VNR) decreases. Ideally, the venc should be chosen approximately 10% above the peak velocity.\(^{48}\) 50–60 cm/s is a typical venc used for portal venous imaging.\(^{21,24,32,46,49}\) However, this choice of venc may be too low for the arterial system,\(^{22,27,28}\) or postinterventional imaging in patients after transjugular intrahepatic portosystemic shunt (TIPS)\(^{3,2}\), where a venc of 100 cm/s (80–120 cm/s) may be helpful. In contrast to other studies, one group\(^{47}\) stated that a very high venc of 225 cm/s helped them to better evaluate TIPS performance, although further evaluation of this venc recommendation is needed. Since even a venc of 100 cm/s inevitably compromises the quality of portal venous flow measurements, contrast administration is recommended to improve SNR performance when attempting to evaluate both portal venous and hepatic arterial flows in a single acquisition.

**Postprocessing and quality assurance**

Postprocessing of 4D flow MRI should include correction for concomitant gradient field effects (Maxwell terms) and phase background effects due to eddy currents.\(^{46}\) In order to analyze flow information in vessels that may be corrupted by velocity aliasing (phase wraps), phase-unwrapping algorithms should be used. Simple phase wraps can be detected visually in the areas of high-flow velocities where the flow direction of some voxels apparently changes without any physiological explanation.\(^{51}\)

For quality assurance of 4D flow data, visual inspection of not only the magnitude data but also the velocity images in all three directions is recommended to evaluate for artifacts, such as wrap-around artifacts and velocity aliasing. Moreover, conservation of mass\(^{25–29,45}\) analysis in the portal venous system is an important component of quality assurance. For example, flow volume of superior mesenteric vein and splenic vein should add up to match that of the proximal portal vein (Fig. 2). Similarly, the distal portal vein should distribute its flow volume into its branching veins. Often, there will remain a small error since many small veins contribute to and originate from the portal vein, or from inherent imprecision in flow measurements. Typical mean errors of the conservation of mass analysis for the portal vein for radial acquisitions range from 5% to 7% (standard deviation [SD], between 3% and 5%) with excellent correlation (\(r^2 = 0.98-0.99\) and \(R^2 = 0.89\)).\(^{26,27,46}\) For Cartesian acquisitions, which frequently have a lower spatial resolution, reported errors range between 3% and 9% (SD, 5%–16%).\(^{25,49}\)

**Analysis**

There are several software tools available for analyzing 4D flow MRI data, ranging from in-house developed solutions to regulatory approved software packages for purchase. However, most focus on thoracic and arterial analyses and offer no dedicated workflow for the portal venous circulation. For this article, image preprocessing and background phase correction were performed using a customized MATLAB toolbox (Mathworks, Natick, MA, USA). Time-averaged complex difference datasets were exported to Mimics (Materialize, Leuven, Belgium) for semi-automatic vessel segmentation. Segmented angiograms and time-resolved velocity data were then exported to Ensight (ANSYS, Canonsburg, PA, USA) for blood flow visualization and cut-plane flow quantification. Depending on the complexity of the case and the number of measurement planes, an individual analysis typically takes between 20 and 50 mins.

For quantitative analysis in the portal venous system, the vessel contour should be segmented at the position of interest. There exist two main approaches that will depend on the software used. First, a 2D ROI can be placed to delineate the cross section of a vessel. Alternatively, a 3D mask of the vasculature of interest can be created. Cut planes are then placed with no need to delineate the vessel again. We recommend using the time-averaged complex difference angiogram or a contrast-enhanced angiogram for delineating 3D contours in the portal venous system. In our experience, movement of the portal vein during the cardiac cycle is negligible and can be ignored. Moreover, one does not need to account for pulsatility. This allows the delineation of vessels in the time-averaged data, which have higher SNR than the time-resolved dataset.

Most relevant quantitative parameters in the assessment of portal venous flow are the direction (hepatofugal or hepatopetal), maximum and mean velocity (m/s), as well as flow. There are two different flow measurements: “Instantaneous flow” (mL/s) quantifies the flow in a ROI, e.g., a vessel cross section, at a specific time point. If the vessel cross section is contoured not only at one time point but throughout the cardiac cycle, “flow volume” can be calculated by integrating the instantaneous flow measurements over time. Flow volume can be expressed as L/min or L/cardiac cycle – since portal venous flow is not pulsatile but constant, most often L/min is given. Published quantitative results for healthy subjects and patients with liver cirrhosis are summarized in Table 2. Vessel area can also be assessed and can be used to detect dilatation of the portal vein in portal hypertension, or in response to a meal.\(^{52}\) Advanced quantitative flow parameters, such as wall shear stress or energy loss, have not been tested in the portal venous system, and the clinical relevance of such parameters is not clear. Secondary quantitative flow parameters are often vulnerable to acquisition parameters such as spatial resolution and to low SNR. This can lead to poor reproducibility due to a large impact from anticipated small-scale changes in the venous system, particularly in the setting of steady flow.

Qualitative analysis of portal venous flow patterns is not well established. Typically, qualitative description of flow patterns includes helices and vortices. A helix is defined as a spiral, antegrade movement of blood in main flow direction. In contrast, a vortex describes recirculating blood deviating...
Table 2  Reference values for the portal vein for healthy subjects and patients with liver cirrhosis

| Publication                  | Subjects (number) | Subjects (age, y) | Fasting prior to MR exam | Maximum velocity (m/sec) | Mean velocity (m/sec) | Flow volume (L/min) |
|-----------------------------|-------------------|-------------------|--------------------------|--------------------------|-----------------------|---------------------|
| Healthy volunteers          |                   |                   |                          |                          |                       |                     |
| Brunsing et al. 2021        | 21 (14♀)          | 50.4 (26–77)      | Not specified            | –                        | –                     | 0.97 ± 0.32         |
| Roberts et al. 2021         | 20 (8♀)           | 44.4 (19–73)      | 5 hrs fasting            | –                        | –                     | 1.1 ± 0.35          |
| Roldán-Alzate et al. 2015   | 6 (2♀)            | 32±10 (20–45)     | 5 hrs fasting            | –                        | –                     | 1.13 ± 0.46         |
| Landgraf et al. 2014        | 15                | –                 | Not specified            | –                        | –                     | 0.93 ± 0.27         |
| Roldán-Alzate et al. 2013   | 7 (3♀)            | 32.2 ± 10.1       | 3 hrs fasting            | –                        | –                     | 1.1 ± 0.4 (0.9-2.1) |
| Stankovic et al. 2012       | 21 (14♀)          | 27.5 ± 3.3 (22–37)| Not specified            | 0.26 ± 0.09              | 0.11 ± 0.04           | 0.67 ± 0.54         |
| Stankovic et al. 2012       | 20 (10♀)          | 58.5 ± 5.9 (50-69)| Not specified            | 0.22 ± 0.04              | 0.10 ± 0.02           | 0.64 ± 0.19         |
| Stankovic et al. 2010       | 18 (10♀)          | 28.6 ± 3.1        | Not specified            | 0.27 ± 0.07              | 0.12 ± 0.03           | –                   |
| Patients with liver cirrhosis with and without portal hypertension (different stages of cirrhosis, no TIPS) |             |                   |                          |                          |                       |                     |
| Brunsing et al. 2021        | 19 (8♀)           | 57.3 (20–79)      | Not specified            | –                        | –                     | 0.84 ± 0.28         |
| Motosugi et al. 2019        | 23 (9♀)           | 52.3 (25–75)      | 5 hrs fasting            | –                        | –                     | High risk varices: 0.82 (0.05–1.70) |
|                            |                   |                   |                          |                          |                       | Low risk varices: 0.78 (0.65–1.06) |
|                            |                   |                   |                          |                          |                       | No varices: 0.94 (0.52–1.35) |
| Bannas et al. 2016          | 7 (1♀)            | 52 ± 10           | 3 hrs fasting            | 0.40 ± 0.16              | –                     | 0.76 ± 0.62         |
| Roldán-Alzate et al. 2015   | 12 (5♀)           | 54 ± 12 (26–73)   | 5 hrs fasting            | –                        | –                     | 1.04 ± 0.37         |
| Stankovic et al. 2015       | 11 (2♀)           | 62.5 ± 9.0        | Not specified            | 0.19 ± 0.05              | –                     | 0.56 ± 0.37         |
| Landgraf et al. 2014        | 29                | –                 | Not specified            | –                        | –                     | 1.34 ± 0.61         |
| Roldán-Alzate et al. 2013   | 17 (4♀)           | 58.6 ± 6.7        | 3 hrs fasting            | –                        | –                     | 1.09 ± 0.8 (-0.4 to 3.2) |
| Stankovic et al. 2013       | 5 (1♀)            | 66.4 ± 7.0        | Not specified            | 0.17 ± 0.06              | 0.07 ± 0.02           | 0.45 ± 0.28         |
| Stankovic et al. 2012       | 20 (8♀)           | 57.7 ± 11.6 (27–73)| Not specified            | 0.20 ± 0.06              | 0.08 ± 0.03           | 0.79 ± 0.32         |
| Stankovic et al. 2010       | 5 (3♀)            | 62.5 ± 13.7       | Not specified            | 0.17 ± 0.06              | 0.09 ± 0.03           | –                   |
| Patients with liver cirrhosis and portosystemic shunt (TIPS) |             |                   |                          |                          |                       |                     |
| Brunsing et al. 2021        | 7 (5♀)            | 59.9 (33–76)      | Not specified            | –                        | –                     | 1.51 ± 0.81         |
| Bannas et al. 2016          | 7 (1♀)            | 52 ± 10           | 3hrs fasting             | 0.60 ± 0.18              | –                     | 1.64 ± 0.98         |
| Stankovic et al. 2015       | 11 (2♀)           | 62.5 ± 9.0        | Not specified            | 0.28 ± 0.07              | –                     | 1.83 ± 0.97         |

Values are given as mean ± standard deviation and (range), where available. *Included patients with portosystemic shunt (either TIPS or large collaterals). Measurement planes were placed in the proximal portal vein near the confluence or in the middle segment of the portal vein. ♀, female; hrs, hours; SD, standard deviation; TIPS, transjugular intrahepatic portosystemic shunt; y, years of age.
from main flow direction and therefore is characterized by areas with antegrade as well as retrograde flow.\textsuperscript{53–55} Stankovic et al.\textsuperscript{24} found homogenous filling of the portal vein with laminar flow and clearly separated flow channels from splenic vein and superior mesenteric vein contributions in 17 volunteers in contrast to 1 volunteer who presented with helical mixing of both inflow streams. With increasing experience over the years, it is now known that a small helical flow structure often develops distal to the splenic–mesenteric confluence in the portal vein. In fact, Rutkowski et al.\textsuperscript{56} showed, using computational fluid dynamic (CFD) simulations and phantom studies, that vessel geometry and a meal challenge influence both the flow distribution and helical flow development.

More pronounced helical or even vortical flow was described in children after surgery (e.g., after correction of a portal shunt) or with portal hypertension.\textsuperscript{43} Abnormal flow characteristics in patients with liver cirrhosis include vortical flow in the splenic–mesenteric confluence, retrograde flow in any veins of the portal venous system, and detection of flow in portosystemic collaterals.\textsuperscript{21,24,45}

The time-averaged complex difference angiogram allows for anatomical assessment of the portal venous vasculature, mainly detection of anatomical variants and varices. However, this requires excellent image quality and high spatial resolution.

**Clinical Applications of 4D Flow MRI in the Portal Venous System**

**Liver cirrhosis and portal hypertension: Diagnosis and risk stratification**

Cirrhosis is characterized by advanced liver fibrosis, liver failure, and portal hypertension. Its incidence is expected to increase dramatically due to the rapidly rising prevalence of nonalcoholic fatty liver disease (NAFLD),\textsuperscript{57} which is emerging as a leading cause of cirrhosis.\textsuperscript{58} Sinusoidal fibrosis results in increased liver stiffness, which elevates the resistance to blood flow and therefore portal blood pressure. Decreased flow to the liver leads to circulating endogenous vasodilators that further exacerbate portal pressure by paradoxically increasing splanchic blood flow.

Direct pressure measurements in the portal vein are highly invasive and no longer conducted.\textsuperscript{59} An indirect method to assess portal pressure is the invasive measurement of the hepatic venous pressure gradient (HVPG). The HVPG is the pressure difference between the portal vein and the inferior vena cava. It is invasively determined by measuring pressure in the hepatic veins with a balloon catheter with the balloon inflated and thus occluding the hepatic veins (wedge pressure) and with the deflated balloon in the patent hepatic veins, respectively.\textsuperscript{60}

Portal hypertension is characterized by an elevated HVPG over 5 mmHg.\textsuperscript{61} When the HVPG exceeds 10 mmHg, patients can develop portosystemic collaterals that shunt blood away from the liver\textsuperscript{62} (Fig. 1a). The most clinically relevant collaterals are gastroesophageal varices (GEV) that are fragile and can rupture if the HVPG exceeds 12 mmHg.\textsuperscript{62} Rupture can lead to catastrophic exsanguination being the direct cause of death in about 30% of cirrhotic patients and frequently the precipitating factor leading to liver failure and death.\textsuperscript{63} Early detection of GEV at risk for bleeding is of paramount importance to initiate primary prophylaxis,\textsuperscript{64} which reduces mortality by 50%–70%.\textsuperscript{64–66} Currently, the American Society for the Study of Liver Diseases (AASLD) and Baveno guidelines recommend initial esophagogastroduodenoscopy (EGD) screening in patients with newly diagnosed cirrhosis.\textsuperscript{61,67,68}

Depending on the severity of cirrhosis, indefinite surveillance for GEV with EGD is recommended every 1–3 years.\textsuperscript{61,67,68} However, EGD is invasive, expensive, and requires sedation, and compliance with surveillance is very poor. For these reasons, the AASLD has identified the development of noninvasive markers that predict the presence of high-risk varices as a major unmet need in the management of cirrhosis.\textsuperscript{68}

Early studies have shown very promising results, indicating that 4D flow MRI may be a suitable approach for the noninvasive identification of high-risk GEV with a single MRI examination. Previous studies\textsuperscript{22,26,69} have confirmed feasibility and excellent internal consistency of flow measurements in patients with liver cirrhosis. Under normal conditions, the left gastric vein drains blood from the stomach into the portal vein. A flow reversal with hepatofugal flow develops in the left gastric vein in the presence of increased portal venous pressure. It becomes the main contributor to GEV by shunting blood away from the liver. GEV drain into the systemic circulation, mainly the azygos vein. To detect high-risk varices, Motosugi et al.\textsuperscript{45} focused on these two characteristic hemodynamic changes: flow reversal in the left gastric vein and increased flow in the azygos vein. Since the left gastric vein was often too small to be directly analyzed by 4D flow MRI, they developed an indirect metric of hepatofugal blood flow. They calculated the fractional flow change in the portal vein by measuring flow volume in the portal vein in the liver hilum (PV\(_{\text{dist}}\)) compared to the portal vein at the mesosplenic confluence (PV\(_{\text{prox}}\)). In order to capture the left gastric vein between both measurement planes, it is recommended to measure flow volumes from superior mesenteric vein (SMV) and splenic vein (SV) as a proxy for the most proximal part of the portal vein (Fig. 3):

\[
\text{Fractional flow change in portal vein} = \frac{\text{PV}_{\text{dist}} - \text{PV}_{\text{prox}}}{\text{PV}_{\text{prox}}} = \frac{\text{PV}_{\text{dist}} - (\text{SMV} + \text{SV})}{\text{SMV} + \text{SV}} \quad \text{(1)}
\]

If the fractional flow change in the portal vein was less than 0, i.e., less blood arrived in the portal vein in the liver hilum than initially flowed into the portal vein, the presence of hepatofugal flow in tributary vessels to the portal vein is indirectly demonstrated. Importantly, a negative fractional...
flow change in the portal vein was highly predictive of high-risk varices as seen on endoscopy. Using this new noninvasive quantitative biomarker, the authors identified at-risk varices with 4D flow MRI with high sensitivity (100%) and specificity (94%) in 7 out of 23 patients with cirrhosis. Similarly, azygos flow greater than 0.1 L/min was an independent indicator for high-risk varices with high sensitivity (100%), but lower specificity (62%).

Importantly, the calculation of the fractional flow change in the portal vein as proposed in this study did not account for anatomical variants, e.g., when the left gastric vein drains into the splenic vein (Fig. 1b) and will therefore need to be adapted to the individual’s anatomy. These promising results need to be confirmed in a larger patient cohort, along with correction methods for anatomical variants. If confirmed, 4D flow MRI could reduce unnecessary EGD procedures and increase compliance of GEV surveillance through access to a noninvasive method.

Roldán-Alzate et al. proposed another promising approach to diagnose and grade liver cirrhosis. They analyzed portal venous hemodynamics after 5 hours of fasting, as well as 20 mins after a standardized meal challenge. They did not observe significant differences in portal flow between healthy volunteers and patients with cirrhosis in the fasting state. However, they found a significant increase in azygos vein blood flow in patients with cirrhosis after a meal, indicating increased portosystemic shunting volume. After a meal challenge, flow volumes in portal vein and superior mesenteric vein increased to a lesser extent in patients as compared with volunteers (Fig. 4). The same was true for the fraction of portal vein flow volume (PV) compared to the total blood supply of the liver (flow volume in portal vein and hepatic artery, PV + HA):

$$\text{Portal vein fraction} = \frac{PV}{PV + HA}$$

Patients with liver cirrhosis showed a lower increase in portal vein fraction after the meal challenge compared with healthy volunteers. However, these differences between patients and volunteers were not statistically significant with patients presenting higher variability in their results – presumably due to a heterogenous patient cohort with mostly mild cirrhosis stage. This underlines the importance of accounting for different grades of cirrhosis when assessing the value of 4D flow MRI. Similar to a stress test in cardiac MRI, the combination of a resting state examination and a meal challenge has the potential to detect early stages of portal hypertension that might not have been detected with the analysis of fasting hemodynamics alone.

In multiple studies, the authors reported flow reversal in the portal vein, superior mesenteric vein, or splenic vein, as well as direct visualization and measurement of collateral flow, e.g., in the umbilical vein, in a small subset of examined patients with cirrhosis (Fig. 5). Both observations are highly specific to portal hypertension. However, given the relatively low percentage of cirrhotic patients that presented with these findings, they do not seem very sensitive, especially in less severe cases.
A recent case report by Hyodo et al. presents two patients with liver cirrhosis having large portosystemic collaterals, which shunt the blood from the superior mesenteric vein directly into the systemic circulation and lead to hepatic encephalopathy. With 4D flow MRI, they were able to identify the varices that were then treated interventionaly, highlighting the clinical relevance of this diagnostic method.

**Surgical planning and follow-up: TIPS**

Patients with portal hypertension that cannot be controlled by medical therapy can be treated by the creation of portosystemic venous shunts that divert flow from the portal system directly into the systemic circulation and bypassing the liver. This intervention reduces the HVPG and thus ascites, the accumulation of fluid in the peritoneal cavity, and risk for variceal hemorrhage. Historically, a variety of surgical procedures were used to create portosystemic shunts. Today, the interventional placement of a TIPS is the most commonly used approach to create portosystemic shunting without the need for laparotomy. The two major long-term complications of TIPS are a shunting volume that is either too high, leading to increased levels of circulating ammonia inducing hepatic encephalopathy, or too low, failing to decrease the pressure gradient adequately to reduce bleeding risk. Reasons for these complications are either miss-sizing of the stent, in-stent stenosis, or thrombosis.

The feasibility of TIPS flow measurements using 4D flow MRI has been demonstrated by Stankovic et al., as well as Bannas et al., who proposed 4D flow MRI for pre- and postinterventional follow-up imaging for TIPS in a pilot study with seven patients. As expected and confirmed by other studies, both groups found a significant increase in flow volume and peak velocity in the portal venous system after the procedure (Fig. 6). They also calculated the shunt fraction, defined as the ratio between flow volumes in the TIPS in relation to the portal vein, and compared peak velocity in the TIPS to the portal vein. Interestingly, in the Bannas study, a single patient with recurrent postprocedural ascites presented with an increased shunt fraction and peak velocity in the TIPS. This was explained by the presence of an arterio-portal-venous shunt from a peripheral branch of the left hepatic artery into a branch of the left portal vein, which was only detected by 4D flow MRI. This
example underscores the importance of analyzing all available data comprehensively.

Owen et al.47 performed 4D flow MRI in 16 patients after TIPS to evaluate possible shunt dysfunction, namely, stenosis or occlusion compared to Doppler ultrasound, venogram, and 6-month clinical follow-up. In three patients with venogram confirmed stenosis, they found focal turbulence and abnormal peak velocities (for ultrasound defined as > 190 cm/s or < 90 cm/s1), in contrast to seven patients without evidence of stenosis, who presented without turbulence and normal flow velocities. However, they found either turbulence or abnormal velocities in six patients without evidence of shunt dysfunction. They concluded that both parameters must be abnormal to detect stenosis with high specificity and sensitivity. Unfortunately, they did not define the term “turbulence” in this context and did not provide image examples.

Shunt fraction, peak velocity (ratio), and abnormal flow patterns are promising parameters to assess TIPS function comprehensively using 4D flow MRI. Further evaluations of these parameters in larger studies with long-term follow-up are needed to determine their diagnostic performance and clinical utility.

**Surgical planning and follow-up: Liver transplantation**

Pre-operative 4D flow MRI of the portal venous system can be used for surgical planning and prediction of postsurgical outcome. Assessment of the portal hemodynamics in living liver donors and recipients is crucial as a pre- and postoperatively constant blood volume must flow through fewer central portal venous vessels postoperatively, inevitably leading to higher resistance. Potentially, this may lead to presinusoidal portal hypertension, early graft dysfunction, and tissue damage in recipients.75

Importantly, the hemodynamic outcomes of healthy liver donors that underwent partial liver resection for living donor liver transplantation must also be considered. Rutkowski et al.52 proposed a workflow that includes pre-operative 4D flow MRI, virtual surgery, CFD simulations, and in vitro models. They were able to predict postoperative hemodynamics in three living liver donors considering the ability of the portal venous system in healthy volunteers to dilate after a meal.27 It is known that the individual’s capacity of portal venous dilation varies significantly.27 The proposed method could be optimized by performing an MRI examination in preparation for surgery. The individual capacity of a liver donor to increase portal venous flow and adapt the vascular anatomy to those flow changes could be determined by 4D flow MRI before and after a meal challenge. If the results correlate with the dilation of the portal vein after partial liver resection, this could become a valuable marker to predict the risk of postoperative portal hypertension.

Lenz et al.76 presented a patient who had received a liver transplant with renoportal anastomosis due to thrombosis of the native portal vein, superior mesenteric vein, and splenic vein. Postoperatively, she developed bleeding from GEV. After EGD-assisted hemostasis, further surgical procedures were discussed. At this point, 4D flow MRI was considered crucial as it showed hepatopetal flow in both varices and relevant veins, indicating reversal of portal hypertension after transplantation and thus substantial risk reduction in bleeding. Informed by this finding, further surgery could be avoided.
Hyodo et al.\(^7\) reported the case of a 33-year-old woman who had a portal vein stenosis after living-liver transplantation. Preprocedural 4D flow MRI offered viable information on the flow direction and the impact of the stenosis in the whole portal venous vasculature. They found a poststenotic dilatation with vortex formation in the anterior branch of the portal vein. Moreover, they were able to quantify flow volume within the segmental branches of the portal vein and proved an inhomogeneous flow distribution throughout the liver transplant. The stenosis was successfully treated interventionaly by the placement of a stent. Treatment success could be confirmed by postinterventional 4D flow MRI. It showed a reduction in vortical flow and more homogenous flow throughout the segmental branches of the portal vein.

**Surgical planning and follow-up in children**

Noninvasive, radiation-free surgical planning and follow-up is of paramount importance, particularly in children. Parekh et al.\(^4\) demonstrated the feasibility of portal flow evaluation with 4D flow MRI in children between 5 and 17 years. They included children with a non-operated portal system, as well as children with surgically palliated extrahepatic portal vein thrombosis that was bypassed either by a meso-portal or portosystemic shunt. They found flow acceleration and atypical helical and/or vortical flow patterns in patients with stenosis of the shunt or portal vein and in one patient with new onset of portal hypertension. There are several other clinical scenarios in children, who could benefit from 4D flow MRI of the portal venous system. These include follow-up of children after liver transplantation, who have an increased risk of developing portal vein thrombosis and portal hypertension.\(^7\)

**Unmet Needs for Implementation in Clinical Routine**

The clinical relevance of the method and the quantitative parameters that 4D flow MRI can measure must be established for different indications prior to its widespread implementation into clinical routine for evaluation of the portal venous system. Therefore, studies with large cohorts and long-term follow-up must be performed. The added diagnostic value of a meal challenge should also be assessed. This may be important in the setting of mild-to-moderate disease, where a meal challenge may play a helpful role to unmask more subtle hemodynamic abnormalities.

Several technical improvements could also facilitate the integration of 4D flow MRI into daily practice. Sequences that acquire two or more venc settings during one acquisition without increasing scan time could considerably improve data quality, improving the dynamic range of interrogated blood flow velocities. With such a multi-venc sequence, a comprehensive, simultaneous assessment of portal, arterial, and venous flow in the upper abdomen should be possible, and promising approaches are emerging.\(^7\)–\(^8\) However,

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**Fig. 6** Assessment of TIPS placement in a 54-year-old man with nonalcoholic steatohepatitis, portal hypertension, and resultant refractory ascites. (a and c) Colored 3D segmentation masks of the complex difference angiogram and (b and d) velocity streamlines with arrowheads depict anatomy and hemodynamics, respectively. (a and b) before and (c and d) 2 weeks after TIPS procedure. Note the increase in blood flow in the portal vasculature after the procedure and the high velocities within the shunt. Disordered flow explains the signal dropout at the proximal end of the shunt. Ascites resolved after TIPS placement. IVC, Inferior vena cava; PV, portal vein; SMV, superior mesenteric vein; SV, splenic vein; TIPS, transjugular intrahepatic portosystemic shunt.
these methods all require longer acquisition times compared to a single venc sequence. Moreover, a reduction in acquisition and postprocessing time could improve acceptance in daily routine. Deep learning-based solutions could significantly reduce the burden of postprocessing as it has been recently proposed for the thoracic aorta.83 Other potential areas of improvement for 4D flow MRI generally include test–retest repeatability, as well as reproducibility and standardization between sites, MRI system vendors, sequences, and postprocessing software.

Conclusion

4D flow MRI offers unique advantages over clinically established imaging modalities by providing temporally resolved information on both hemodynamics and morphology, in a 3D volume. These characteristics can be utilized to address clinically relevant pathologies of the portal venous system. The most relevant clinical applications are the diagnosis and risk stratification of cirrhotic liver disease. Most notably is the potential to provide noninvasive bleeding risk stratification of GEV in portal hypertension. Initial studies confirmed that 4D flow MRI meets all requirements laid out by the AASLD for a noninvasive marker to identify high-risk varices in patients with liver cirrhosis. Moreover, 4D flow MRI offers unique insights and added value for surgical planning and follow-up of multiple hepatic interventions.

On the path to clinical implementation, large multicenter and multivendor follow-up studies are needed to confirm the diagnostic value of 4D flow MRI in the portal venous system. Furthermore, improvements to the workflow, including standardized and faster acquisition and postprocessing, will facilitate its widespread clinical implementation.

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Conflicts of Interest

None of the authors have any relevant conflicts. Unrelated to this work, Dr. Reeder has ownership interests in Calimetrix, Reveal Pharmaceuticals, Cellcertar Biosciences, Elucent Medical, and HeartVista. The University of Wisconsin receives research support from GE Healthcare and Bracco Diagnostics.

References

1. McNaughton DA, Abu-Yousef MM. Doppler US of the liver made simple. Radiographics 2011; 31:161–188.
2. Jha RC, Khera SS, Kalaria AD. Portal vein thrombosis: Imaging the spectrum of disease with an emphasis on MRI features. AJR Am J Roentgenol 2018; 211:14–24.
3. Tirumani SH, Shanbhogue AK, Vikram R, et al. Imaging of the porta hepatic spectrum of disease. Radiographics 2014; 34:73–92.
4. Gaiani S, Bolondi L, Li Bassi S, et al. Effect of meal on portal hemodynamics in healthy humans and in patients with chronic liver disease. Hepatology 1989; 9:815–819.
5. Ludwig D, Schwarting K, Korbel CM, et al. The postprandial portal flow is related to the severity of portal hypertension and liver cirrhosis. J Hepatol 1998; 28:631–638.
6. Jajamovich GH, Dvorne H, Donnerhack C, et al. Quantitative liver MRI combining phase contrast imaging, elastography, and DWI: assessment of reproducibility and postprandial effect at 3.0 T. PLoS One 2014; 9:e97355.
7. Cox EF, Palaniyapppan N, Athal GP, et al. MRI assessment of altered dynamic changes in liver haemodynamics following a meal challenge in compensated cirrhosis. Eur Radiol Exp 2018; 2:26.
8. Eshmuninov D, Raptis DA, Lenecker M, et al. Meta-analysis of associating liver partition with portal vein ligation and portal vein occlusion for two-stage hepatectomy. Br J Surg 2016; 103:1768–1782.
9. Tripathi D, Stanley AJ, Hayes PC, et al. Transjugular intrahepatic portosystemic stent-shunt in the management of portal hypertension. Gut 2020; 69:1173–1192.
10. Tripathi D, Hayes PC. Beta-blockers in portal hypertension: new developments and controversies. Liver Int 2014; 34:655–667.
11. Lee WK, Chang SD, Duddalwar VA, et al. Imaging assessment of congenital and acquired abnormalities of the portal venous system. Radiographics 2011; 31:905–926.
12. Nardelli S, Riggio O, Turco L, et al. Relevance of spontaneous portosystemic shunts detected with CT in patients with cirrhosis. Radiology 2021; 299:133–140.
13. Thabut D, Moreau R, Lebrec D. Noninvasive assessment of portal hypertension in patients with cirrhosis. Hepatology 2011; 53:683–694.
14. Vizzutti F, Arena U, Rega L, et al. Performance of Doppler ultrasound in the prediction of severe portal hypertension in hepatitis C virus-related chronic liver disease. Liver Int 2007; 27:1379–1388.
15. Gouya H, Mallet V, Scatton O. Magnetic resonance imaging (MRI) flow, a new non-invasive method for the evaluation of systemic, splanchic, and azygos blood flows in patients with portal hypertension. (abstr). Hepatology 2008; 48:1049A.
16. Burkart DJ, Johnson CD, Ehman RL, et al. Evaluation of portal venous hypertension with cine phase-contrast MRI flow measurements: high association of hyperdynamic portal flow with variceal hemorrhage. Radiology 1993; 188:643–648.
17. Burkart DJ, Johnson CD, Morton MJ, et al. Volumetric flow rates in the portal venous system: measurement with cine phase-contrast MR imaging. AJR Am J Roentgenol 1993; 160:1113–1118.
18. 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.
19. Annet L, Materne R, Danse F, et al. Hepatic flow parameters measured with MR imaging and Doppler US: correlations.
with degree of cirrhosis and portal hypertension. Radiology 2003; 229:409–414.

20. Frydrychowicz A, Roldán-Alzate A, Winslow E, et al. Comparison of radial 4D Flow-MRI with perivascular ultrasound to quantify blood flow in the abdomen and introduction of a porcine model of pre-hepatic portal hypertension. Eur Radiol 2017; 27:5316–5324.

21. Stankovic Z, Csatari Z, Deibert P, et al. Normal and altered three-dimensional portal venous hemodynamics in patients with liver cirrhosis. Radiology 2012; 262:862–873.

22. Stankovic Z, Csatari Z, Deibert P, et al. A feasibility study to evaluate splanchnic arterial and venous hemodynamics by flow-sensitive 4D MRI compared with Doppler ultrasound in patients with cirrhosis and controls. Eur J Gastroenterol Hepatol 2013; 25:669–675.

23. Wentland AL, Grist TM, Wieben O. Repeatability and internal consistency of abdominal 2D and 4D phase contrast MR flow measurements. Acad Radiol 2013; 20:699–704.

24. 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; 32:466–475.

25. 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 Imaging 2014; 72:477–484.

26. Roldán-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; 37:1100–1108.

27. Roldán-Alzate A, Frydrychowicz A, Said A, et al. Impaired regulation of portal venous flow in response to a meal challenge as quantified by 4D flow MRI. J Magn Reson Imaging 2015; 42:1009–1017.

28. Roberts GS, François CJ, Starekova J, et al. Non-invasive assessment of mesenteric hemodynamics in patients with suspected chronic mesenteric ischemia using 4D flow MRI. Abdom Radiol (NY) 2021 Feb 6. doi: 10.1007/s00261-020-02900-0. [Epub ahead of print]

29. Brunsing RL, Brown D, Almahoud H, et al. Quantification of the hemodynamic changes of cirrhosis with free-breathing self-navigated MRI. J Magn Reson Imaging 2021; 53:1410–1421.

30. Roldán-Alzate A, François CJ, Wieben O, et al. Emerging applications of abdominal 4D flow MRI. AJR Am J Roentgenol 2016; 207:58–66.

31. Riedel C, Lenz A, Fischer L, et al. Abdominal applications of 4D flow MRI. Rofo 2021; 193:388–398.

32. Bannas P, Roldán-Alzate A, Johnson KM, et al. Longitudinal monitoring of hepatic blood flow before and after TIPS by Using 4D-flow MR imaging. Radiology 2016; 281:574–582.

33. Someya N, Endo MY, Fukuba Y, et al. Blood flow responses in celiac and superior mesenteric arteries in the initial phase of digestion. Am J Physiol Regul Integr Comp Physiol 2008; 294:R1790–1796.

34. Sidery MB, Macdonald IA, Blackshaw PE. Superior mesenteric artery blood flow and gastric emptying in humans and the differential effects of high fat and high carbohydrate meals. Gut 1994; 35:186–190.

35. Hall Barrientos P, Knight K, Black D, et al. A pilot study investigating the use of 4D flow MRI for the assessment of splanchnic flow in patients suspected of mesenteric ischaemia. Sci Rep 2021; 11:5914.

36. Bane O, Peti S, Wagner M, et al. Hemodynamic measurements with an abdominal 4D flow MRI sequence with spiral sampling and compressed sensing in patients with chronic liver disease. J Magn Reson Imaging 2019; 49:994–1005.

37. Dyvorne H, Knight-Greenfield A, Jajamovich G, et al. Abdominal 4D flow MR imaging in a breath hold: combination of spiral sampling and dynamic compressed sensing for highly accelerated acquisition. Radiology 2015; 275:245–254.

38. Glover GH, Pauly JM. Projection reconstruction techniques for reduction of motion effects in MRI. Magn Reson Med 1992; 28:275–289.

39. Anderson AG, Velikina J, Block W, et al. Adaptive retrospective correction of motion artifacts in cranial MRI with multi-coil three-dimensional radial acquisitions. Magn Reson Med 2013; 69:1094–1103.

40. Gu T, Korosec FR, Block WF, et al. PC VIPR: a high-speed 3D phase-contrast method for flow quantification and high-resolution angiography. AJNR Am J Neuroradiol 2005; 26:743–749.

41. Stankovic Z, Fink J, Collins JD, et al. K-t GRAPPA-accelerated 4D flow MRI of liver hemodynamics: influence of different acceleration factors on qualitative and quantitative assessment of blood flow. MAGMA 2015; 28:149–159.

42. Sekine T, Amano Y, Takagi R, et al. Feasibility of 4D flow MR imaging of the brain with either cartesian y-z radial sampling or k-t SENSE: Comparison with 4D flow MR imaging using SENSE. Magn Reson Med Sci 2014; 13:15–24.

43. Parekh K, Markl M, Rose M, et al. 4D flow MR imaging of the portal venous system: a feasibility study in children. Eur Radiol 2017; 27:832–840.

44. Hyodo R, Takehara Y, Mizuno T, et al. Time-resolved 3D cine phase-contrast magnetic resonance imaging (4D-flow MRI) can quantitatively assess portosystemic shunt severity and confirm normalization of portal flow after embolization of large portosystemic shunts. Hepatol Res 2021; 51:343–349.

45. Motosugi U, Roldán-Alzate A, Bannas P, et al. Four-dimensional flow MRI as a marker for risk stratification of gastroesophageal varices in patients with liver cirrhosis. Radiology 2019; 290:101–107.

46. Landgraf BR, Johnson KM, Roldán-Alzate A, et al. Effect of temporal resolution on 4D flow MRI in the portal circulation. J Magn Reson Imaging 2014; 39:819–826.

47. Owen JW, Saad NE, Foster G, et al. The feasibility of using volumetric phase-contrast MR imaging (4D Flow) to assess for transjugular intrahepatic portosystemic shunt dysfunction. J Vasc Interv Radiol 2018; 29:1717–1724.

48. Dyverfeldt P, Bissell M, Barker AJ, et al. 4D flow cardiovascular magnetic resonance consensus statement. J Cardiovasc Magn Reson 2015; 17:72.

49. Keller EJ, Collins JD, Rigsby C, et al. Superior abdominal 4D flow MRI data consistency with adjusted preprocessing workflow and noncontrast acquisitions. Acad Radiol 2017; 24:350–358.

50. Bock J, Frydrychowicz A, Stalder AF, et al. 4D phase contrast MRI at 3 T: effect of standard and blood-pool contrast agents on SNR, PC-MRA, and blood flow visualization. Magn Reson Med 2010; 63:330–338.
51. Loecher M, Schrauben E, Johnson KM, et al. Phase unwrapping in 4D MR flow with a 4D single-step laplacian algorithm. J Magn Reson Imaging 2016; 43:833–842.
52. Rutkowski DR, Reeder SB, Fernandez LA, et al. Surgical planning for living donor liver transplant using 4D flow MRI, computational fluid dynamics and “in vitro” experiments. Comput Methods Biomech Biomed Eng Imaging Vis 2018; 6:545–555.
53. Oechtering TH, Sieren MM, Hunold P, et al. Time-resolved 3-dimensional magnetic resonance phase contrast imaging (4D Flow MRI) reveals altered blood flow patterns in the ascending aorta of patients with valve-sparing aortic root replacement. J Thorac Cardiovasc Surg 2020; 159:798–810.e1.
54. Oyama-Manabe N, Aikawa T, Tsuneta S, et al. Clinical Applications of 4D Flow MR Imaging in Aortic Valvular and Congenital Heart Disease. Magn Reson Med Sci 2022; 21:319–326.
55. Takahashi K, Sekine T, Miyagi Y, et al. Four-dimensional flow analysis reveals mechanism and impact of turbulent flow in the dissected aorta. Eur J Cardiothorac Surg 2021 May 17. doi: 10.1093/ejcts/eza201. [Epub ahead of print]
56. Rutkowski DR, Medero R, Garcia FJ, et al. MRI-based modeling of spleno-mesenteric confluence flow. J Biomech 2019; 88:95–103.
57. Scaglione S, Kliethermes S, Cao G, et al. The Epidemiology of Cirrhosis in the United States: A Population-based Study. J Clin Gastroenterol 2015; 49:690–696.
58. Estes C, Anstee QM, Arias-Loste MT, et al. Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030. J Hepatol 2018; 69:896–904.
59. Suk KT. Hepatic venous pressure gradient: clinical use in chronic liver disease. Clin Mol Hepatol 2014; 20:6–14.
60. Lebrec D, Sogni P, Vilgrain V. Evaluation of patients with portal hypertension. Baillieres Clin Gastroenterol 1997; 11:221–241.
61. Garcia-Tsao G, Abraides JG, Berzigotti A, et al. Portal hypertensive bleeding in cirrhosis: Risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the study of liver diseases. Hepatology 2017; 65:310–335.
62. Garcia-Tsao G, Groszmann RJ, Fisher RL, et al. Portal pressure, presence of gastroesophageal varices and variceal bleeding. Hepatology 1985; 5:419–424.
63. Saunders JB, Walters JR, Davies AP, et al. A 20-year prospective study of cirrhosis. Br Med J (Clin Res Ed) 1981; 282:263–266.
64. Bernard B, Lebrec D, Mathurin P, et al. Beta-adrenergic antagonists in the prevention of gastrointestinal rebleeding in patients with cirrhosis: a meta-analysis. Hepatology 1997; 25:63–70.
65. Khuroo MS, Khuroo NS, Farahat KL, et al. Meta-analysis: endoscopic variceal ligation for primary prophylaxis of oesophageal varical bleeding. Aliment Pharmacol Ther 2005; 21:347–361.
66. Pascal JP, Cales P. Propranolol in the prevention of first upper gastrointestinal tract hemorrhage in patients with cirrhosis of the liver and esophageal varices. N Engl J Med 1987; 317:856–861.
67. de Franchis R, Baveno V Faculty. Revising consensus in portal hypertension: report of the Baveno V consensus workshop on methodology of diagnosis and therapy in portal hypertensio. J Hepatol 2010; 53:762–768.
68. Garcia-Tsao G, Sanyal AJ, Grace ND, et al. Practice Guidelines Committee of the American Association for the Study of Liver Diseases; Practice Parameters Committee of the American College of Gastroenterology, Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Hepatology 2007; 46:922–938.
69. 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; 34:577–584.
70. Boyer TD, Haskal ZJ; American Association for the Study of Liver Diseases. The Role of Transjugular Intrahepatic Portosystemic Shunt (TIPS) in the Management of Portal Hypertension: update 2009. Hepatology 2010; 51:306.
71. Allaire M, Walter A, Sutter O, et al. TIPS for management of portal-hypertension-related complications in patients with cirrhosis. Clin Res Hepatol Gastroenterol 2020; 44:249–263.
72. Wolff M, Hirner A. Current state of portosystemic shunt surgery. Langenbecks Arch Surg 2003; 388:141–149.
73. Stankovic Z, Blanke P, Markl M. Usefulness of 4D MRI flow imaging to control TIPS function. Am J Gastroenterol 2012; 107:327–328.
74. Stankovic Z, Rössele M, Euringer W, et al. Effect of TIPS placement on portal and splanchnic arterial blood flow in 4-dimensional flow MRI. Eur Radiol 2015; 25:2634–2640.
75. Vasavada BB, Chen CL, Zakaria M. Portal flow is the main predictor of early graft dysfunction regardless of the GRWR status in living donor liver transplantation - a retrospective analysis of 134 patients. Int J Surg 2014; 12:177–180.
76. Lenz A, Fischer L, Li J, et al. 4D Flow MRI for Monitoring Portal Flow in a Liver Transplant Recipient with a Renoportal Anastomosis. Rofo 2019; 191:847–848.
77. Hyodo R, Takehara Y, Mizuno T, et al. Portal Vein Stenosis Following Liver Transplantation Hemodynamically Assessed with 4D-flow MRI before and after Portal Vein Stenting. Magn Reson Med Sci 2020; 20:231–235.
78. Jensen MK, Campbell KM, Alonso MH, et al. Management and long-term consequences of portal vein thrombosis after liver transplantation in children. Liver Transpl 2013; 19:315–321.
79. Schnell S, Ansari SA, Wu C, et al. Accelerated dual-venc 4D flow MRI for neurovascular applications. J Magn Reson Imaging 2017; 46:102–114.
80. Nakaza M, Matsumoto M, Sekine T, et al. Dual-VENC 4D Flow MRI Can Detect Abnormal Blood Flow in the Left Atrium That Potentially Causes Thrombosis Formation after Left Upper Lobectomy. Magn Reson Med Sci 2021 March 31. doi.org/10.2463/mrms.mp.2020-0170. (Epub ahead of print)
81. Corrado PA, Medero R, Johnson KM, et al. A phantom study comparing radial trajectories for accelerated cardiac 4D flow MRI against a particle imaging velocimetry reference. Magn Reson Med 2021; 86:363–371.
82. Kroeger JR, Pavesio FC, Mörsdorf R, et al. Velocity quantification in 44 healthy volunteers using accelerated multi-VENC 4D flow CMR. Eur J Radiol 2021; 137:109570.
83. Berhane H, Scott M, Elbaz M, et al. Fully automated 3D aortic segmentation of 4D flow MRI for hemodynamic analysis using deep learning. Magn Reson Med 2020; 84:2204–2218.