MR Elastography and Functional MRI of the Liver

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Ioana G. Lupescu, Mugur Cristian Grasu, and Radu Lucian Dumitru

Key Concepts

- Magnetic Resonance Elastography (MRE) is a noninvasive MRI technique for quantitatively assessing the mechanical properties of the tissues in vivo in our case the liver parenchyma.
- There is a strong correlation between MRE-measured hepatic stiffness and the stage of fibrosis at histology demonstrated by multiple studies.
- MRE is a safer, less expensive, and accurate alternative to invasive liver biopsy which is currently considered the gold standard for diagnosis and staging of liver fibrosis.
- Multiparametric MRI of the liver, combining morphologic and functional informations, represent an essential tool for radiologists and include in the functional part of the MR protocol diffusion weighted imaging, multiphase dynamic 3D T1 weighted GRE (Gradient Echo) imaging evaluation with hepato-specific contrast agents, and qualitative and quantitative analysis of the liver parenchyma particularly in the hepatobiliary phase.

46.1 Magnetic Resonance Elastography

46.1.1 Introduction

Hepatic fibrosis and cirrhosis represent an important health public problem worldwide. Liver biopsy is necessary for the diagnosis and staging of liver fibrosis. However, it is an invasive method with risk and potential complications [1]. MR elastography (MRE) techniques and automated analysis, permits a more accurate assessment of liver fibrosis especially in cases in which fibrosis is not uniform [1–3]. Even if MRE cannot differentiate fibrosis distribution as histopathologic examination does, it may distinguish the various degrees of tissue stiffness by drawing a ROI (region of interest) on each of four liver axial images acquired, and by measuring the mean stiffness [1]. The degree of fibrosis quantified by MRE are classified into: F1: mild fibrosis, F2: moderate fibrosis, F3: severe fibrosis and F4: cirrhosis [1, 4].

Definitions

MR elastography is a noninvasive medical imaging technique by means of which it can be appreciated the mechanical properties of a soft tissue such as elasticity, corresponding to the deformation resistance of a tissue on which was applied a stress [1–7].

46.1.2 Principles

MRE uses a modified phase-contrast method to image the propagation characteristics of the shear wave in the liver [1–7]. Elasticity is quantified by MRE (expressed in kPa-KiloPascal) using a formula that determines the shear modulus [7]. The normal liver stiffness range is between 1.54 and 2.87 kPa [4]. The theoretical advantages of MRE include its ability to analyze almost the entire liver and its good applicability in patients with obesity or ascites [1–6]. Liver stiffness measurement using MRE is reproducible, operator independent and has a good consistency across vendor platforms [7, 8].

46.1.3 Technical Aspects

Elastography techniques may be classified according to the source (static, quasistatic, or dynamic) and duration (transient or continuous) of tissue deformation and the modality

I. G. Lupescu (✉) · M. C. Grasu · R. L. Dumitru
Radiology, Medical Imaging and Interventional Radiology Department, Fundeni Clinical Institute, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania

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used for tracking (ultrasound or MRI). Techniques also may be classified according to the device type (stand alone or adjunct to an imaging scanner), wave generation method (external vibrator or internally focused acoustic radiation force), inversion algorithm (1D, 2D, or 3D), reported parameters (shear-wave speed, magnitude of complex shear modulus, and the Young modulus), or output display (purely numeric, M-mode image, or parametric imaging map) [2, 8]. MRE techniques use continuous waves and requires five components: a driver system to generate oscillatory mechanical waves continuously at a fixed frequency, a phase-contrast multiphase pulse sequence with motion-encoding gradients that are synchronized to the mechanical waves, processing of phase-sensitive MR images to depict wave amplitudes (shear-wave displacement images or, simply, wave images), further postprocessing (using an inversion algorithm) to generate elastograms and analysis of the elastograms [2–7]. In MRE, images are acquired with a modified phase-contrast technique that generates both magnitude and phase images. The total acquisition time in liver MRE is about 1 min, typically divided into four separate approximately 15-s breath-holds (one for each slice liver location), acquired in end expiration if possible. Images at each phase offset are acquired through color maps and are typically applied to these wave images, in which red and blue hues indicate opposite wave polarity and color saturation indicates wave amplitude. The color elastograms represent the shear modulus with scales of 0–8 kPa [1–6].

In clinical practice, the patient is placed in supine position with a pneumatic driver placed over the liver on the anterior abdominal wall. The pneumatic driver generates mechanical waves by vibrating at low frequencies. The waves propagating into the liver are measured using a 2D gradient-echo sequences and cyclic motion-encoding gradients (MEG). Specialized computer-based algorithms analyse these mechanical waves [7].

Fibrosis leads to increased liver stiffness (Fig. 46.1). As shear waves travel through a tissue, the speed of the wave depends on the tissue stiffness [1–6]. In stiffer tissues, the shear-wave speed is greater, enabling estimation of the degree of liver fibrosis from measuring the speed of a shear wave [2]. In MRE, increased wavelength is evident in stiffer tissues. An obstacle to direct comparison between techniques is the frequency dependence of biologic tissue. Higher frequency shear waves produce higher stress and strain rates, resulting in higher stiffness measurements [2–4, 6, 9].

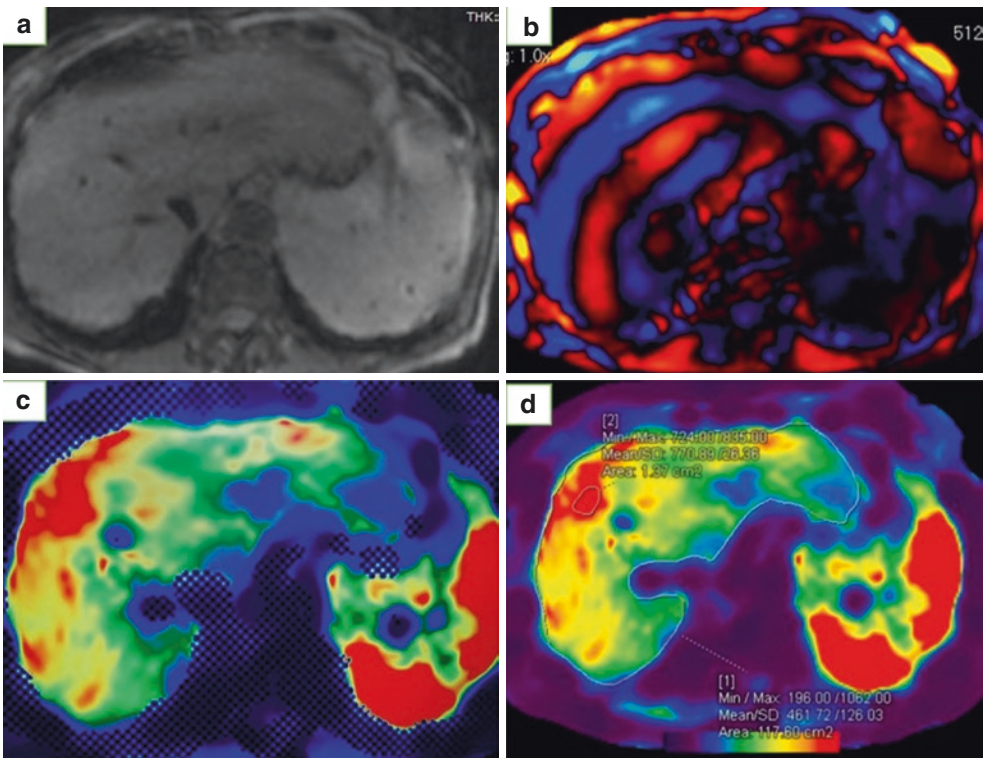

Fig. 46.1 MRE. (**a**) *Magnitude image*—image quality is lower compared to standard imaging due to the acquisition technique, but is sufficient to visualize the anatomy; (**b**) *wave image*—the unwrapped and corrected wave displacements are displayed in this series; (**c**) *relative stiffness 95% Map*—stiffness map with checkered areas for low confidence areas standard; (**d**) *elastogram* or *relative stiffness map*—contains the magnitude of the complex shear modulus, providing reliable data about liver stiffness. By applying a ROI that includes the hepatic contour it is possible to calculate the mean value of the hepatic elasticity, and at the level of the area corresponding to the color map with an increased fibrosis, by overlapping an ROI circumscribing the respective area, the value corresponding to the degree of maximal fibrosis

46.2 Clinical Applications of MRE

46.2.1 MRE in Staging of Liver Fibrosis

Chronic HBV and HCV infections. Knowledge of liver fibrosis stage in chronic HBV and HCV infections is beneficial for prognosis, follow-up, and treatment decisions [3, 8–14]. From the published studies in chronic HCV or HBV infections, 2D GRE MRE has shown excellent accuracy in diagnosing liver fibrosis or cirrhosis, with AUC (area under the curve) for the diagnosis of fibrosis stages F2–F4, F3–F4, and F4 of 0.95–0.99, 0.94–1, and 0.92–1, respectively [3, 9, 14]. Several studies also showed that necroinflammation may increase liver stiffness [9, 15–19].

46.2.2 Nonalcoholic Steatohepatitis (NASH) and Nonalcoholic Fatty Liver Disease (NAFLD)

Liver fibrosis has been shown to be the strongest predictor of complications in NAFLD patients, which motivates the need for reliable noninvasive techniques for detection of liver fibrosis and will be of major interest for clinicians and in terms of public health perspective. A meta-analysis of nine studies with 232 patients [15] reported AUCs of 0.90 or greater for the diagnosis of fibrosis stages F3–F4 and F4, with associated cutoffs of 3.77 kPa and 4.09 kPa, respectively [15]. In patients with NAFLD MRE is highly accurate, for liver fibrosis staging, and is not significantly influenced by age, sex, obesity or by the degree of inflammation [15].

There is also evidence that MRE may be able to differentiate NASH and simple steatosis in NAFLD patients with a reported AUC of 0.93, but this needs further confirmation [9]. In steatohepatitis or NASH, liver stiffness (LS) measured by MRE increase, even before the onset of fibrosis [4]. MRE is more accurate than acoustic radiation force impulse (ARFI) for diagnosing any fibrosis in all NAFLD patients and obese NAFLD patients [16–18]. Both 2D and 3D-MRE at the standard shear-wave frequency, are highly accurate in diagnosing NAFLD advanced fibrosis [18]. Patients with steatosis had lower liver inflammation and fibrosis compared to patients with non-alcoholic steatohepatitis [19].

46.2.3 Primary Sclerosing Cholangitis

MRE may be useful in detection of early fibrosis in primary sclerosing cholangitis (PSC) especially when there are no other morphological signs of disease; in these cases, stiffness measurement at baseline and longitudinal changes has been shown to be a useful biomarker for monitoring and prognostication [20].

46.2.4 MRE Potential Role in Liver Tumors

Other potential clinical application of MRE is to add more information to the classical appearance of a liver nodule on T2, diffusion weighted images, and on unenhanced and dynamic enhancement T1 features of the nodule after bolus injection of a gadolinium-based contrast agent. Malignant liver tumors had significantly greater mean shear stiffness (10.1 kPa); than benign tumors (2.7 kPa), also significantly greater shear stiffness than normal liver parenchyma. Cholangiocarcinoma and HCC had greater stiffness than fibrotic liver, benign tumors, and normal liver parenchyma. MRE can stratify the risk for development of HCC during follow-up in patients with chronic liver disease [21, 22]. The LS value can be used as a predictive factor for occurrence of hepatocellular carcinoma [22].

Obese patients can be reliably examined by MRE and no observer variability exists [23]. *MR elastography is preferable to US elastography* because an acoustic window is not needed and the entire liver can be assessed compared with US elastography in which only small regions of interest can be explored [16, 17, 24].

46.2.5 Limitations and Pitfalls of MRE

The most common technical limitation of MRE is liver hemochromatosis [1, 3]. In patients with moderate to severe hepatic iron overload (the short $T2^*$ time of the affected liver) the signal intensity of the liver is so low that the shear waves cannot be visualized on the phase-contrast 2D gradient-echo (GRE) image. There is conflicting evidence on the effect of body mass index on MRE measurements. A recent study found that body mass index was not a contributing factor in failure but found waist circumference to be a significant factor of failure. In contrast, a recent large retrospective study investigating the cause of MRE failure using a 2D GRE sequence found that body mass index, iron deposition, massive ascites, and use of 3 T were significantly associated with MRE failure. This limitation can be suppressed using Short echo time (TE) 2D spin echo echoplanar imaging (SE-EPI)-based MRE which may allow measurement of stiffness in the iron loaded liver [25]. In context of biliary system dilatation, the elevated liver stiffness is nonspecific and does not indicate fibrosis (this is a false positive MRE). Sarcoidosis, amyloidosis or sinusoidal obstruction syndrome (SOS) are other examples of false positive MRE [9, 12].

The actual trend, is to combine MRE with lipid and iron quantification sequences, which allows a so called multiparametric MR approach to diffuse liver disorders [1, 5, 8, 19, 26].

46.3 Functional MRI of the Liver

46.3.1 Introduction

In the last decade, the MRI evaluation of the liver, include outside the conventional morphological MRI sequences, *functional techniques* such as diffusion weighted imaging (DWI), perfusion weighted imaging (PWI) and dynamic 3D GRE T1 multiphase acquisition with hepato-specific Gadolinium based contrast agents allowing both vascular and interstitial distribution, but also a specific hepatocyte uptake during the "hepatobiliary" phase (HBP), which improves detection and characterization of nodular liver lesions. DWI sequences are important to characterize nodular lesions developed into a cirrhotic liver, but also in oncological patients which are suspected to have secondary hepatic nodules and take an important place in the evaluation of tumor functional response [26–32].

46.3.2 DWI Definition

DWI gives information's about the movement of water molecules at the microscopic scale. In water, the diffusion of the water molecules is free compared with the tissues DWI in which is restricted, because restriction of diffusion in biological tissues is correlated with tissue cellularity, cell membrane integrity, and tissue vascularization [26, 31, 32].

46.3.3 Principles and Applications of DWI

The factor b called "diffusion constant" is expressed in s/mm^2 and corresponds to the combination of the amplitude, the duration and the time separating the two gradient pulses. The optimal values of b for the evaluation of liver focal lesions ranged from 100 to 800 s/mm^2. For interpretation, it is important to calculate the apparent diffusion coefficient (ADC) value in addition to the qualitative approach. In current practice, DWI sequence is performed with multiple b values: 0, 50, 500 and 800 s/mm^2 allowing the calculation of the ADC. Small values of b are particularly interesting for the detection of liver lesions but not for characterization, being superior to a T2 fast-spin echo (FSE) sequence for tumor detection due to a best contrast-to-noise ratio of the DWI and the absence of the endovascular signal [31]. The persistence of the hypersignal at high b values reflects a restriction of the diffusion while a drop of the signal reflects a freer diffusion. A tumor signal intensity that is higher than that of the surrounding liver on high b DW value, and correspond to low ADC values on quantitative maps, has a "diffusion restriction" [32]. Simplifying, in clinical practice, protonic movements into a cyst are free without "restriction of diffusion" and the intracystic signal decreases as the b factor value increases (cysts have a high ADC). Conversely, in hepatic malignant lesions (primary and secondary lesions), protonic movements are constrained due to increased intratumoral cellularity, and the ADC is low [30]. But, the characterization of liver focal lesions only on the basis of DWI is impossible. The current data published in the literature shows an overlap of the ADC values, for example between hepatocellular carcinoma (HCC) and benign solid liver tumors such adenoma or focal nodular hyperplasia [30]. Several studies have shown statistically higher ADC values in benign lesions than in malignant lesions [31–33]. In the cirrhotic liver compared with the normal liver it has been known for several years that there is a restriction of diffusion; the decrease of ADC values in cirrhotic patients is found in all studies and the assumption is increased of the collagenous weft associated with a fall in hepatic perfusion [34]. The ADC values of patients with moderate to severe fibrosis (F2–F4) were lower than those measured in cases of minimal or no fibrosis (F0–F1). DWI may be superior to Fibroscan and serum tests for patient identification of F3–F4 stage [34].

DWI is a simple aid for the liver MRI interpretation and is integrated into the classification and characterization algorithms for nodular liver lesions. Li-RADS (Liver Imaging Reporting and Data System) developed by the American College of Radiology (ACR), integrates DWI as an ancillary criterion of liver lesion malignancy appeared into a cirrhotic liver.

Moreover, DWI is very sensitive to show the appearance of necrosis into a tumor (passage from restricted diffusion to free diffusion due to necrosis), allowing to appreciate the tumoral response under treatment [30]. Numerous articles have evaluated the value of diffusion imaging for measuring the therapeutic response (chemotherapy, radiotherapy or local ablation) in experimental studies. Pre-treatment ADC may be a predictor of successful chemotherapy for hepatic metastases [32–34].

46.4 Liver-Specific Gadolinium (Gd) Based Contrast Agents

46.4.1 Introduction

Liver-specific Gadolinium (Gd) based contrast agents or hepato-biliary (HB) contrast agents include Gd-EOB-DTPA, Gadoxetic Acid (Primovist®, Bayer Schering Pharma, Berlin, Germany) 0.25 mol/l and Gd-BOPTA (Multihance®, Bracco, Italy) 0.5 mol/l, both being positive T1 weighted image (wi) contrast agents, with a higher T1 relaxivity compared to the conventional extracellular agents [35].

46.4.2 Definition and Mechanism

These two specific liver contrast agents are capable to provide vascular and interstitial enhancement images identical to extracellular Gadolinium chelates, but have an additional property represented by the hepatocyte uptake via OATP receptors expressed on the hepatocyte surface before being partially excreted into the bile through MRP2 canalicular ducts. The hepatobiliary phase, which reflects at the cellular level the concentration balance between input OATP receptors and MRP2 output, is observed 20 min after the intra venous (i.v.) injection of Gd-EOB-DTPA, and 1 h after i.v. injection of Gd-BOPTA. Approximately 3–5% of the intravenous injected dose of Gd-BOPTA (0.05–0.1 mmol/kg bodyweight (bw) or 0.1–0.2 ml/kg; flow rate: 2 ml/s) is taken up by functioning hepatocytes and excreted via the biliary system, the hepatocytic uptake given at the normal liver parenchyma a strong enhancement on delayed T1-weighted images that is maximal between 1 and 2 h after i.v. administration. Gd-EOB-DTPA is injected manually or using a power injector through an intravenous route in a dose of 0.025 mmol/kg bw or 0.1 ml/kg, flow rate—1 ml/s, it is taken up by hepatocytes and has a double excretion: hepatobiliary (50%) and renal (50%). In patients with severe hepatic impairment (>3 mg/dl serum bilirubin levels) the elimination half-life of Primovist increase, the hepatobiliary excretion substantially decrease, and the hepatic signal enhancement is reduced [28–30, 35–39].

46.4.3 Contrast MR Acquisitions

Two type of MR acquisitions after i.v. injection of HB contrast agents can be performed*: "classical"* ***dynamic multiphase 3DT1*** *wi sequence* and ***dynamic contrast-enhanced (DCE) MR perfusion (MRP)***. DCEMRP is a particular MRI sequence also known as permeability MRI, which calculates perfusion parameters by evaluating T1 shortening induced by a gadolinium-based contrast bolus passing through tissue. Liver perfusion MRI gives information about microcirculation and microenvironment of liver tumors and the underlying hepatic parenchyma [35, 37–39].

In cases of HCC evaluate by DCEMRP there is an increased of the: arterial flow, of the total blood flow as well as early contrast arrival time. The early contrast arrival is related to angiogenesis of the tumor caused by branches with direct supply from the hepatic artery. Tumor vascularity (fractional intravascular volume) is in general higher and portal venous flow is decreased [30, 31].

DCEMRP is indicated also to improve detection of liver metastases; to assess the efficacy of anti-angiogenic therapy and the viable HCC after intraarterial chemotherapy or postablation; to evaluate cirrhosis and its severity. Gd-EOB-DTPA-enhanced MRI associated with DW-MRI is the best combination for detection and follow-up of liver metastasis [33].

46.4.4 Indications

These two hepato-specific contrast agents are particularly interesting for the following indications [30, 32–39]:

- Characterization of certain liver lesions, in particular to delineate between lesions with increased expression of OATPs (such as focal nodular hyperplasia-HNF) and lesions free of overexpression of OATP (such as moderately or poorly differentiated HCC or hepatocellular adenomas);
- Non-invasive assessment of hepatic function, with a lack of hepatocyte uptake correlating with loss of hepatic function observed in metabolic/toxic steatohepatitis, in chronic liver disease, or after chemotherapy especially Oxaliplatin-based treatments [40–43].

46.4.5 Advantage

The main advantage of the selective uptake by functioning hepatocytes is that the normal liver enhances (normal hepatic parenchyma exhibit T1 shortening in the longitudinal relaxation time), while tumors of non-hepatocytic origin (e.g. metastases and cholangiocarcinoma as well as non-functioning hepatocytic tumors) are unable to take up HB contrast agents, remaining unenhanced, getting an optimal liver-lesion contrast-to-noise ratio (CNR) and increasing the ability to detect supplementary liver lesions [30, 32]. Also, the use of hepato-specific Gd based agents allow to optimize the liver fibrosis assessment using a qualitative approach (Fig. 46.2). In oncological patients who received Oxaliplatin-based chemotherapy or in a context of hematopoietic stem-cell transplantation, it is possible to observe in the HBP using Gd-EOB-DTPA, a patchy or diffuse reticular T1 wi hypointensity associated with hepatocyte dysfunction related to sinusoidal obstruction syndrome (SOS) or heterogenous liver enhancement, FHN-like lesions (which appears because of vascular injury induced by chemotherapy and represent benign hyperplasia of hepatic parenchyma due to increased arterial perfusion in area with reduced portal blood flow), marked periportal hyperintensity (due to increased liver function) and fat spare liver areas mimicking metastasis (Fig. 46.3). Liver function recovery following interruption of chemotherapy may be monitored with by Gd-EOB-DTPA MRI. The literature reported that Gd-EOB-DTPA-enhanced liver MRI could identify SOS with high specificity and good interobserver agreement [40–43].

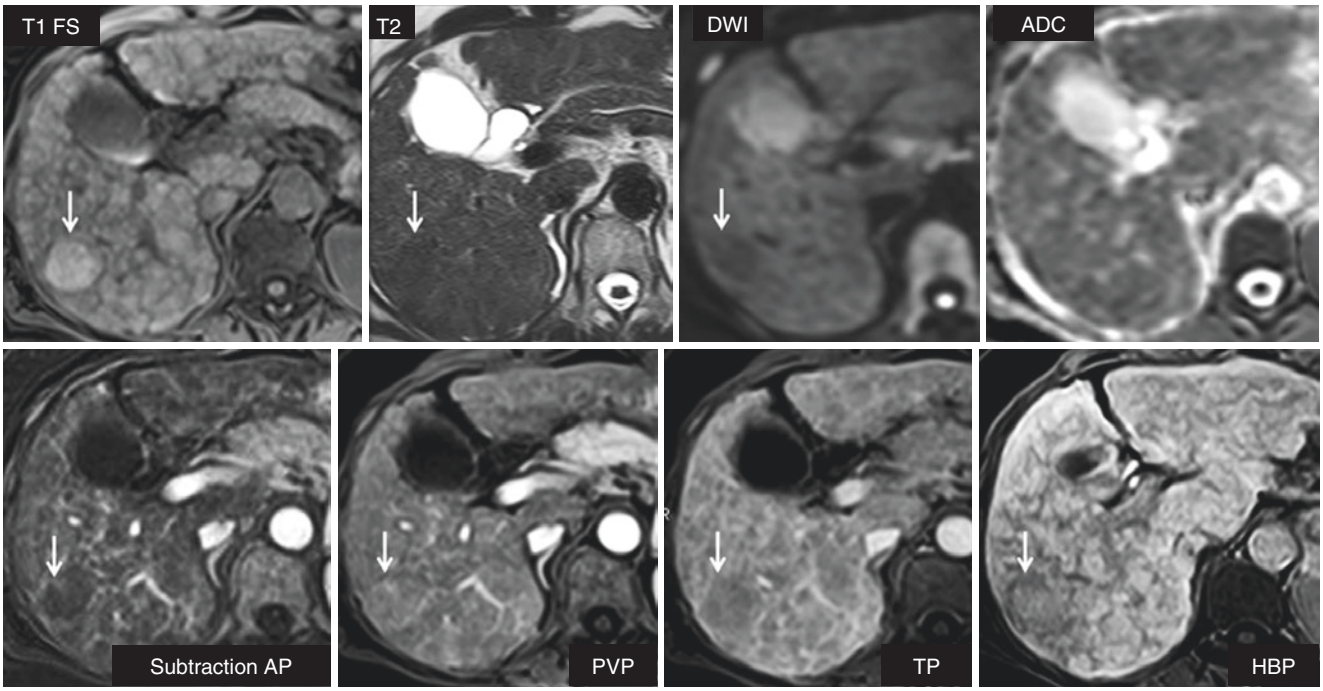

Fig. 46.2 Multiparametric MRI evaluation of the liver in a cirrhotic patient—T1 Fat Sat, T2 wi, DWI and ADC, dynamic 3D T1 FatSat acquisition with Gd-EOB-DTPA in arterial phase (subtraction), portal venous phase, transitional phase and hepato-biliary phase: important liver fibrosis in association with multiple regenerative nodules and a dysplastic nodule (white arrow)

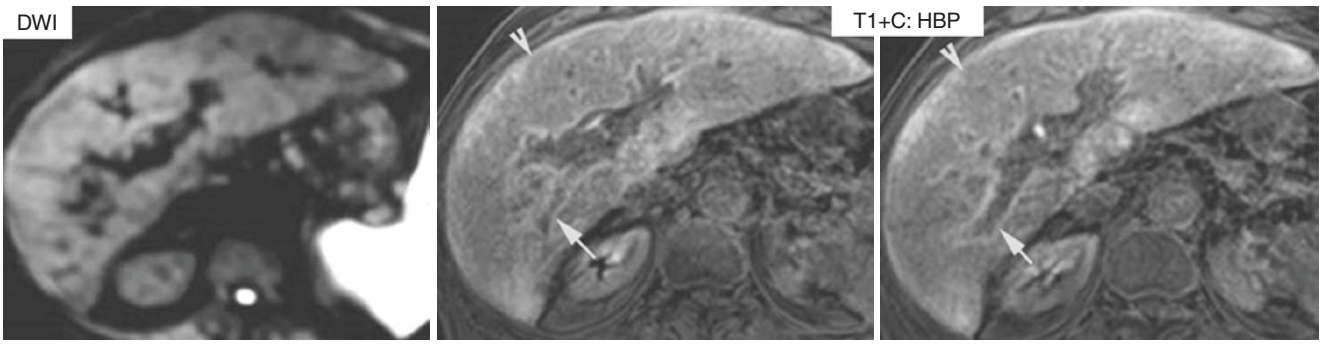

Fig. 46.3 Liver MP MRI evaluation in a patient with hepatocyte dysfunction related to SOS after chemotherapy: comparison between DWI and hepato-biliary phase after Gd-EOB-DTPA i.v. injection: periportal T1 hyperintensity (arrow) associated with large and confluent hypointense T1 liver areas (arrowhead) visible in HBP

Based on T1 shortening effects of hepatocellular Gd-EOB-DTPA uptake, the quantitative evaluation allows for the direct measurement of liver function, with the possibility to correlate the liver function evaluated by Gd-EOB-MRI with MELD (Model for End Stage Liver Disease)/or Child-Pugh score [30, 44]. Measurement of T_1 relaxation time on Gd-EOB-DTPA-enhanced MR imaging is accurate in evaluating liver function in patients with HBV-related HCC and can be used as a biomarker for estimating the remnant liver functional reserve [32, 37, 45]. Histogram analyses of the HBP after gadoxetic acid-enhanced MRI may be used as a biomarker for liver function assessment, liver fibrosis, and necro-inflammation.

Primovist MRI protocol: multiphased array coil, locator 3 plans, T1 dual GRE (TE-Echo Time in/out of phase), MRCP (Magnetic Resonance Cholangiopancreatography) ssFSE (single shot Fast Spin Echo) long TE; 3D T1 FAME/VIBE unenhanced and enhanced dynamic multiphase acquisition with Gd-EOB-DTPA (late arterial phase, portal venous phase and transitional phase); ssFSE with short TE; DWI and ADC (b: 50, 500, 800); T2 FSE (+/−FatSat); T2 GR (T2*); 3D T1 axial/coronal in hepatobiliary (HBP) phase 20 min after contrast material (CM) i.v. injection; 3D T1—MRCP (Magnetic Resonance Cholangio-Pancreatography) T1 wi in the HBP permit an optimal evaluation of the biliary tree. *Optimal window for Primovist®* in patients without cholestasis using T1 wi acquisition is 20 min after CM i.v. injection

and in patients with cholestasis 40–60 min after CM i.v. injection.

46.4.6 Pitfalls Using Primovist

Lesions such as hemangiomas and hepatic fibrosis, and also areas of altered liver perfusion, may be mistaken for malignancy due to their hypointense T1 wi signal on the HBP.

The principles and recommendations for the use of HB contrast agents were the subject of expert recommendations in 2015 [29]. An expert position of the European Society of Abdominal and Digestive Radiology (ESGAR) recalled four major applications [28]:

- Optimizing the characterization of benign hepatocellular (HC) nodules [30, 32]. HB contrast agents allow a significant improvement in diagnostic performance of focal nodular hyperplasia (FNH) and propose to perform an MRI with HB contrast agents for the characterization of indeterminate atypical hepatocyte lesions on conventional MRI sequences with a reduction of the number of biopsies or monitoring of these benign lesions.
- Optimization of the detection of secondary liver lesions [33]. The combination of HB imaging after injection of Gd-EOB-DTPA and DWI represents the best MR modality for evaluating oncological patients, the HBP making possible to optimize the identification of infracentimetric metastatic liver lesions.
- Optimization of the characterization of primary HC lesions [29–34]. The presence of hypersignal lesions in T2 wi and DWI (with low ADC) correlated with hyposignal in the HBP would be in favor of high-grade dysplastic lesions or beginning HCC whatever their vascular profile [30]. In some recommendations, HB contrast agents are recommended as first-line tool to evaluate patients with chronic hepatopathy [37].
- Optimization of the biliary imaging; because HB contrast agents are excreted by the bile ducts after their hepatocyte capture, they allow positive enhancement of the biliary tree; this allows a positive contrast imaging of the bile ducts, but also allows the detection of biliary leakage by showing the presence of contrast agent outside the bile ducts [30].

46.4.7 Limitations

Even if Gd-EOB-DTPA is now integrated in the algorithms for characterization of nodules developed into a chronic liver disease, its use poses some difficulties because there exists a rapid competition between the interstitial enhancement of the lesion and the specific capture: the tumors enhancement beyond 90 s after injection is no longer the same as that seen with extracellular gadolinium chelates. The "wash-out" observed conventionally in the portal or late phase after injection of extracellular gadolinium chelates is then no longer specific for HCC after injection of Gd-EOB-DTPA and it can also be observed in case of cholangiocarcinoma [30]. So, the use of HB contrast agents tends to increase the sensitivity of HC nodules detection at the expense of limiting specificity regarding characterization [32]. In addition, the interpretation of the HBP signal intensity may require quantitative measurements, especially when the liver contrast is modified (e.g. in liver steatosis).

In summary, DW imaging is validated as a cellularity-/architecture biomarker; hepatospecific MR contrast agents represents biomarkers of the hepatocellular functions, and molecular imaging of tumors biology.

46.5 Conclusions: Future Perspectives

Liver MR-elastography represents a field of research in continuous evolving and refining. Beyond liver fibrosis assessment, liver MR-elastography has been proposed for liver stiffness monitoring, assessment of liver cirrhosis, detection of inflammation, to obtain additional information's concerning portal hypertension, liver tumors, and for the hepatic complications' prognosis [14–25].

Concerning liver functional MRI, there are several important issues [26–40]:

- DWI sequences are now systematically performed in the exploration of nodular liver lesions, adding also information's regarding liver fibrosis.
- DWI sequences are essential to explore patients with suspicion of secondary liver lesions and for monitoring the effectiveness of oncology therapies.
- DCEMRP together with DWI, contribute to a multiparametric functional assessment of the liver pathology improving the diagnosis.
- MRI with liver-specific contrast agents allows optimization for characterization of hepatocellular lesions and to detect supplementary liver nodules. They are useful for the evaluation of benign hepatocellular nodules particularly for small FNH and for the characterization of HCC.
- Hepatobiliary contrast agents appear to be useful to evaluate liver diffuse pathology such as fibrosis and steatohepatitis, and to give information about liver function considering that functioning areas of the hepatic parenchyma exhibit shortening of the T1 relaxation time, with the possibility to make a qualitative and quantitative analysis.
- In oncological patients treated by chemotherapy, after liver transplantation, in biliary cirrhosis, in primary sclerosing cholangitis, or in other biliary tree malformations or tumors, Gd-EOB MRI add more information's allowing also to have a mapping of hepatocytes function, correlated with specific lab data and MELD/or Child-Pugh score.

Self Study

Questions

1. Which are the incorrect answers concerning the use of Gd-EOB-DTPA (Primovist) in liver evaluation?
   (a) Primovist is an extracellular contrast agent
   (b) In liver cirrhosis with a multinodular pattern the MRI protocol include obligatory DWI and multiphase dynamic 3DT1 wi acquisition with Gd-EOB-DTPA
   (c) Around 3–5% of the i.v. injected dose is uptake by functioning hepatocytes and excreted via the biliary tree
   (d) The 3D T1 acquisition for the hepatobiliary phase is made in a nonicteric patient after 20 min
   (e) Liver fibrosis is better delineated in HBP compared to the nonenhanced 3D T1 MRI acquisition
2. Which answers are incorrect?
   (a) MR-elastography (MRE) is optimal to detect liver hemochromatosis
   (b) In liver fibrosis there is a decrease of stiffness
   (c) DWI correlated with ADC values can be used as biomarkers in monitoring the effectiveness of oncology therapies
   (d) ADC values doesn't allow to evaluate patients with moderate or severe liver fibrosis
   (e) MRE stiffness is different in liver solid tumors compared with the normal liver parenchyma

Answers

1. Which are the incorrect answers concerning the use of Gd-EOB-DTPA (Primovist) in liver evaluation?
   Incorrect answers: a, c because:
   (a) Primovist is a hepato-specific contrast agent
   (c) About 50% of the i.v. injected dose is uptake by functioning hepatocytes and excreted via the biliary tree
2. Which answers are incorrect?
   Incorrect answers: a, b, d because:
   (a) MRE is not indicate in liver hemochromatosis. In patients with moderate to severe hepatic iron overload (the short $T2^*$ time of the affected liver) the signal intensity of the liver is so low that the shear waves cannot be visualized on the phase-contrast 2D GRE acquisition
   (b) In liver fibrosis there is an increase of stiffness
   (d) ADC values of patients with moderate to severe fibrosis are lower than those measured in cases of minimal or no fibrosis.

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