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The Role of Radiology in Advancing Detection and Characterization of Liver Diseases: Insights from Ultrasonography and MR Imaging

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Abstract

Ultrasonography and magnetic resonance (MR) imaging play crucial roles in detecting, characterizing, and monitoring liver diseases. Dynamic contrast-enhanced ultrasonography enhances focal liver lesion detection and characterization, while dynamic ultrasound elastography assesses liver fibrosis and portal hypertension. Transient elastography is the most validated elastography method for liver fibrosis evaluation. Acoustic radiation force impulse and shear wave elastography offer diagnostic accuracy comparable to transient elastography with additional advantages. Diffusion-weighted MR imaging improves solid liver tumor detection and characterization, with malignant tumors generally exhibiting lower apparent diffusion coefficients than benign lesions. It is valuable for monitoring treatment response, as early diffusion changes correlate with necrosis. Dynamic contrast-enhanced MR imaging, particularly with gadoxetate, improves focal liver lesion detection and characterization. Perfusion alterations detected by dynamic contrast-enhanced MR imaging occur in liver fibrosis and cirrhosis, correlating with disease severity. Quantitative perfusion MR imaging evaluates tumor response to antiangiogenic or local therapies. MR elastography is a reliable, reproducible, and accurate method for detecting and staging liver fibrosis, outperforming transient ultrasound elastography. It may detect early non-alcoholic steatohepatitis and contribute to liver tumor characterization and treatment response assessment. Advances in ultrasonography and MR imaging have significantly enhanced our ability to diagnose and manage liver diseases non-invasively.

Keywords: Radiology, Ultrasonography, Magnetic resonance imaging, Perfusion and diffusion imaging, Liver diseases, Liver tumors

Introduction

Liver ultrasonography and magnetic resonance (MR) imaging are increasingly employed for the detection, characterization, and treatment monitoring of both focal and diffuse liver diseases (Galea et al., 2013). Ultrasonography remains a first-line diagnostic tool; however, its capabilities have expanded significantly with the integration of dynamic contrast-enhanced (DCE) studies and elastography.

The quality and efficiency of MR imaging have greatly advanced due to the development of higher clinical field strengths, improved gradient systems, enhanced surface coils, and parallel imaging techniques. Additionally, the introduction of hepatobiliary contrast agents, such as gadoxetate, has enhanced DCE MR imaging (Van Beers et al., 2012). Compared to computed tomography (CT), MR imaging offers several advantages, including the absence of ionizing radiation, superior contrast-to-noise ratios, and multiparametric imaging capabilities. The versatility of MR imaging is further highlighted by its adjustable pulse sequences, which allow for the evaluation of various tissue characteristics, such as diffusion, perfusion, and viscoelasticity. These functional properties can be assessed not only qualitatively but also quantitatively, providing valuable imaging biomarkers.

Ultrasonography

Dynamic Contrast-Enhanced Ultrasonography

Method

Dynamic contrast-enhanced ultrasonography involves intravenous administration of ultrasound contrast agents. These agents consist of gas-filled microbubbles stabilized by a lipid, protein, or polymer shell. Due to the non-linear oscillation of microbubbles at low to mid-high mechanical index, harmonic or non-linear imaging techniques are employed, which enhance the contrast-to-tissue ratio compared to fundamental B-mode imaging (Kiessling et al., 2014).

LiverTumors

Dynamic contrast-enhanced ultrasonography enhances the detection and characterization of focal liver lesions. Technical and diagnostic guidelines for liver lesion detection, characterization, and treatment monitoring using contrast-enhanced ultrasonography have been established by organizations such as the World Federation for Ultrasound in Medicine and Biology (WFUMB) and the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB).

Despite its utility, the diagnostic role of DCE ultrasonography compared to DCE-CT and MR imaging remains a topic of debate. DCE ultrasonography was initially included in the diagnostic algorithm for suspected hepatocellular carcinoma (HCC) in liver cirrhosis, as recommended by the American Association for the Study of Liver Diseases (AASLD) in 2005 and the Japan Society of Hepatology. However, more recent updates to the AASLD and European Association for the Study of the Liver (EASL) guidelines have excluded DCE ultrasonography from their recommendations. This exclusion is based on observations that the typical hypervascularity and washout patterns of HCC identified by DCE ultrasonography can also be seen in some intrahepatic cholangiocarcinomas, whereas these patterns may not be present on DCE MR imaging (Vilana et al., 2010). Differences in imaging patterns between ultrasonography and MR imaging or CT are attributed to variations in the distribution volumes of contrast agents. Ultrasound microbubbles remain intravascular, while the small-molecular-weight contrast materials used in CT and MR imaging distribute within both vascular and extravascular-extracellular compartments.

Other challenges affecting the widespread use of DCE ultrasonography include limited standardization, operator dependency, variability in results due to patient-specific physical characteristics, and the absence of three-dimensional dynamic imaging capabilities. Nevertheless, the real-time imaging capability of DCE ultrasonography provides an advantage over CT and MR imaging for capturing transient signal intensity enhancements in hypervascular liver tumors such as HCCs.

A meta-analysis of sulphur hexafluoride microbubble-enhanced ultrasonography demonstrated improved cost-effectiveness and diagnostic performance comparable to DCE-CT and MR imaging for assessing focal liver lesions. However, the authors highlighted several limitations in the reporting of included studies and emphasized the need for high-quality research adhering to the Standards for Reporting of Diagnostic Accuracy (STARD) criteria. These studies should compare the performance of DCE ultrasonography, CT, and MR imaging in the same patients while employing standardized definitions of a positive imaging test for each target condition. Additionally, the effectiveness of DCE ultrasonography in evaluating multiple liver lesions requires further investigation.

Future developments in DCE ultrasonography include quantitative perfusion imaging and molecular imaging. Studies have demonstrated the feasibility of determining absolute tumor perfusion parameters in vivo by deconvolving the tumor enhancement curve using the arterial input function. In animal models, molecular imaging of angiogenesis and inflammation has been achieved using targeted ultrasound contrast agents designed to bind surface receptor molecules expressed on the luminal side of activated endothelium in response to inflammatory or angiogenic stimuli. However, the non-specific accumulation of microbubbles in Kupffer cells poses challenges for targeted imaging approaches in liver diseases.

Dynamic Ultrasound Elastography

Method

Dynamic elastography involves evaluating the propagation of shear waves within tissues to determine their viscoelastic properties. Displacement is measured using either ultrasonography or MR imaging, while stress can be applied externally or internally. External stress is typically delivered via an actuator directly contacting the skin, whereas internal stress methods often employ focused ultrasound pulses to generate acoustic radiation force (ARF). These pulses induce tissue displacement and simultaneously capture the resulting tissue motion (DeWall, 2013).

External mechanical excitation may be either continuous or transient. With ultrasonography, transient pulses are generally preferred to minimize issues related to wave reflections caused by continuous vibrations. Transient elastography (Fibroscan©, Echosens, Paris, France) represents a first-generation dynamic ultrasound elastography technique that applies a brief external shear wave pulse tracked via one-dimensional ultrasound imaging. Second-generation ultrasound elastography techniques based on ARF include acoustic radiation force imaging (ARFI) (Siemens Healthcare, Erlangen, Germany), supersonic shear imaging, also referred to as shear wave elastography (Supersonic Imagine, Aix-en-Provence, France), and shear wave dispersion ultrasound vibrometry (Philips Healthcare, Best, The Netherlands) (Chen et al., 2013).

ARFI-based methods quantitatively estimate shear wave speed by tracking the propagation of the wave laterally from its point of origin, while supersonic shear imaging utilizes ultrafast imaging, achieving frame rates of up to 4000 frames per second to measure the displacements induced by shear wave propagation.

With ultrasound elastography, transient waves typically allow for the calculation of wave speed, which correlates with tissue stiffness or elasticity under the assumption that tissues are purely elastic. However, biological tissues exhibit viscoelasticity, behaving as both solid and liquid. Ultrasound elastography can evaluate viscoelastic properties using Voigt model fitting to analyze frequency-dependent wave speed dispersion. Nonetheless, the application of the Voigt model to human tissues remains a subject of debate.

In first-generation transient elastography, shear wave speed is measured within a cylindrical volume approximately 10 mm in diameter and 40 mm in length, located 25–65 mm below the skin's surface. Fibroscan is dedicated to liver fibrosis assessment but does not provide conventional B-mode ultrasound imaging. Consequently, the accurate positioning of the elastography region within the liver cannot be verified, nor can transient elastography be applied to focal liver lesions.

Second-generation ARF-based elastography methods offer several advantages over transient elastography. First, elasticity measurement regions are overlaid onto conventional B-mode images. Second, ARF-based methods can be used in patients with ascites, unlike transient elastography, as focused ultrasound beams can penetrate through liquids, unlike shear waves. Third, ARF methods allow for the assessment of deeper liver regions. However, evaluating the deepest areas of the liver remains challenging, with depth limits for ARFI and shear wave elastography reported to be approximately 8 cm. ARFI provides a single stiffness estimate within a small tissue region (10 × 5 mm), while shear wave elastography generates an entire elasticity map within the region of interest (Guibal et al., 2013).

Diffuse Liver Diseases

The validation of dynamic elastography for liver disease assessment is ongoing. Transient elastography is currently the most validated method for liver fibrosis evaluation, particularly in viral hepatitis. Its diagnostic accuracy is superior for cirrhosis compared to significant fibrosis, with mean areas under the receiver operating characteristic curves (AUROCs) of 0.94 and 0.84, respectively, in patients with interpretable results. However, the diagnostic performance of transient elastography for significant fibrosis is insufficient to recommend it as a standalone examination in clinical practice. Additionally, its applicability is limited, with examination failures or uninterpretable results occurring in approximately 20% of patients, predominantly due to obesity, ascites, or operator inexperience.

ARFI exhibits diagnostic accuracy for liver fibrosis comparable to transient elastography, while one single-center study suggests that shear wave elastography may surpass transient elastography in diagnosing significant fibrosis in hepatitis C virus (HCV) patients. Beyond fibrosis staging, ultrasound elastography is emerging as a reliable method for staging portal hypertension and detecting esophageal varices (Takuma et al., 2013).

Liver Tumors

Several studies have explored the role of second-generation ultrasound elastography in liver tumor characterization. Although significant stiffness overlap exists between benign and malignant lesions, elastography may assist in addressing specific clinical questions, such as distinguishing adenomas from focal nodular hyperplasia or differentiating hepatocellular carcinoma from cholangiocellular carcinoma. For instance, focal nodular hyperplasia lesions tend to be stiffer than adenomas, while cholangiocellular carcinomas exhibit greater stiffness than hepatocellular carcinomas. Moreover, higher stiffness values are observed in inflammatory adenomas compared to steatotic adenomas (Ronot et al., 2015).

Preliminary evidence indicates that combining dynamic contrast-enhanced (DCE) ultrasonography with ultrasound elastography may enhance the characterization of liver tumors compared to each method used independently. Biomechanical tissue parameters could complement biomarkers derived from Doppler and DCE ultrasonography, potentially adding significant diagnostic value. However, further validation and standardization of ultrasound elastography are required before its full clinical utility can be realized. It is important to note that various factors, such as hepatic fibrosis, inflammation, cholestasis, congestion, steatosis, and portal hypertension, can result in the overestimation of liver stiffness (Berzigotti & Castera, 2013).

MR Imaging

The role of MR imaging in evaluating both focal and diffuse liver diseases has been strengthened in recent years by the introduction of quantitative imaging techniques. These methods provide functional data and new imaging biomarkers. Among these techniques are diffusion-weighted (DW) MR imaging, DCE MR imaging, and MR elastography.

Diffusion-Weighted MR Imaging

Method

Diffusion-weighted (DW) MR imaging examines the movement of water molecules within intracellular and extracellular spaces by integrating two diffusion gradients into an echo-planar MR imaging sequence. These gradients reduce signal intensity based on tissue diffusibility and the strength of the gradient (b-value). On high b-value MR images, lesions with high diffusibility, such as cysts or hemangiomas, will exhibit minimal signal intensity, whereas lesions with restricted diffusion, like highly cellular malignant tumors, will retain high signal intensity.

The decline in tissue signal intensity with increasing b-values is exponential, with the slope of this decline on a semi-logarithmic graph representing the apparent diffusion coefficient (ADC). Additional diffusion parameters can be derived by analyzing signal intensity across multiple b-values. Using the intravoxel incoherent motion (IVIM) model, signal intensity reduction at low b-values (<100 s/mm^2) is primarily attributed to perfusion, which occurs at a much higher speed than extravascular diffusion. At low b-values, perfusion-related diffusion coefficient ($D*$) and the fraction of diffusion associated with microcirculation (f) can be calculated, while at high b-values, pure molecular diffusion coefficient (D) is measurable.

Reproducibility and Motion Compensation

The precision and reproducibility of diffusion parameter measurements in the liver are often limited by macroscopic motion, including respiratory and cardiac motion. Strategies to compensate for motion include signal averaging, respiratory triggering, breath-holding, and cardiac triggering. However, the effectiveness of these techniques remains debated due to associated drawbacks, such as increased scan time or reduced signal-to-noise ratio (Dyvorne et al., 2013).

Reproducibility varies among diffusion parameters. ADC and D, which represent the apparent and true diffusion coefficients, show high reproducibility, while f (the microcirculation-related diffusion fraction) and $D*$ (the perfusion-related diffusion coefficient) exhibit lower reproducibility. Reported repeatability coefficients for ADC and D are approximately 10–15% in the liver and 25–30% in malignant liver tumors. The reliability of diffusion parameter measurements can be improved by acquiring MR images during breath-holding, increasing the number of b-values, and applying Bayesian analysis (Orton et al., 2014).

Liver Tumors

Diffusion-Weighted MR Imaging for Focal Liver Diseases

Diffusion-weighted (DW) MR imaging is now a standard practice for patients with focal liver diseases, offering improvements in the detection, characterization, and treatment assessment of liver tumors. Compared to T2-weighted fast spin-echo imaging, DW MR imaging significantly enhances the detection of solid liver tumors, with accuracy that is either slightly lower or comparable to that of dynamic contrast-enhanced (DCE) MR imaging. Combining DW MR imaging with DCE MR imaging enhances diagnostic accuracy beyond what is achieved by analyzing either sequence independently.

DW MR imaging is also instrumental in characterizing tumors. Malignant liver tumors generally exhibit lower apparent diffusion coefficients (ADC) than benign lesions, primarily due to their higher cellularity. Clinical criteria for distinguishing benign from malignant liver lesions based on DW MR imaging include tumor-to-liver contrast. A lesion is typically considered benign if it is hyperintense on DW images at a b-value of 0 s/mm², demonstrates a strong signal decrease at a b-value of 500 s/mm² or higher, and remains hyperintense relative to the liver on the ADC map. Conversely, a lesion is likely malignant if it is mildly too moderately hyperintense on DW images at a b-value of 0 s/mm², retains hyperintensity at a b-value of 500 s/mm² or higher, and appears hypointense on the ADC map.

However, ADC-based characterization of liver tumors often reveals substantial overlap between benign and malignant lesions. Benign lesions with high fluid content, such as liver cysts and hemangiomas, exhibit significantly higher ADC values than solid malignant lesions. Still, solid benign hepatocellular lesions, like focal nodular hyperplasia and adenomas, show ADC values that are not markedly different from solid malignant tumors. Consequently, DW MR imaging criteria for tumor characterization are less effective in distinguishing benign hepatocellular from malignant liver lesions in a normal liver.

One application of DW MR imaging is in characterizing nodules in cirrhotic livers. Hepatocellular carcinomas (HCC) are often hyperintense on DW MR images, while dysplastic nodules rarely display this feature. Hyperintensity on DW MR images has been found to be a more reliable indicator of HCC than delayed hypointensity on DCE MR images obtained with non-specific or hepatobiliary contrast agents. The utility of IVIM-derived diffusion parameters in tumor characterization has also been evaluated. In a study involving 86 solid liver tumors, Doblas et al. found that IVIM diffusion parameters did not enhance the ability to differentiate malignancy or identify tumor type compared to ADC. Similarly, Woo et al. observed a stronger negative correlation between tumor grade and the pure diffusion coefficient (D) than with ADC in 42 surgically confirmed HCC cases, although D's ability to distinguish high-grade from low-grade HCC remained modest due to significant overlap (AUROC: 0.84) (Woo et al., 2014).

Assessment of Tumor Response to Treatment

DW MR imaging is valuable for monitoring tumor response to treatment, as it can detect early changes in diffusion parameters linked to necrosis. Volumetric ADC changes measured one month after intra-arterial treatment of HCC have been shown to correlate more strongly with tumor response than size changes evaluated using response criteria such as RECIST, mRECIST, and EASL criteria. These findings are attributed to the use of functional imaging biomarkers like ADC, as opposed to structural criteria, and the application of three-dimensional tumor volume analysis for diffusivity measurements. Tumor heterogeneity analysis using semi-automatic three-dimensional assessments has demonstrated better interobserver agreement compared to manual two-dimensional region-of-interest measurements (Bonekamp et al., 2014).

ADC measurements may also predict treatment response to radioembolization. An increase in tumor ADC was observed one month after treating HCC with yttrium-90-labeled microspheres, despite no significant change in tumor size.

Some studies have reported on the role of DW MR imaging after antivascular therapies. Following sunitinib treatment of HCC, perfusion parameters assessed via perfusion MR imaging were found to be more sensitive biomarkers for early response prediction than ADC. In another study, changes in the perfusion fraction (f) were reported to help differentiate between responders and non-responders to sorafenib treatment.

Limited research exists on the value of DW MR imaging for evaluating colorectal cancer metastases' response to chemotherapy. Post-treatment increases in ADC have been documented. However, diffusion parameter changes following therapy are expected to be less pronounced in colorectal metastases than in HCC because colorectal metastases are less vascularized and characterized by fibrotic overgrowth rather than necrosis after successful chemotherapy. DW MR imaging can differentiate fibrotic from viable tumor zones by measuring the pure diffusion coefficient (D), although differences in diffusion parameters between fibrotic and viable zones are less marked than between necrotic and viable zones (Wagner et al., 2012).

Diffuse Liver Diseases

DW MR imaging shows a progressive reduction in ADC with advancing liver fibrosis. However, significant overlaps in ADC values between fibrosis stages limit its utility. At present, DW MR imaging alone is not recommended for liver fibrosis staging, as its diagnostic accuracy does not surpass that of plasma biomarkers or transient ultrasound elastography, which are more accessible. Furthermore, studies in animals and humans indicate that ADC reductions in liver fibrosis may be influenced by factors other than fibrosis, such as inflammation, steatosis, and reduced perfusion. MR elastography has been shown to be more accurate than DW MR imaging in staging liver fibrosis (Wang et al., 2011).

Dynamic Contrast-Enhanced MR Imaging

Method

Dynamic contrast-enhanced (DCE) MR imaging is a core component of liver MR imaging, particularly for detecting and characterizing liver tumors. This technique involves acquiring whole-liver images during the arterial, portal venous, and delayed phases (3–5 minutes post-injection) following the administration of an extracellular gadolinium-based contrast agent.

When a hepatocyte-specific contrast agent such as gadoxetate (Primovist©, Bayer, Berlin, Germany) is used, an additional hepatobiliary phase (20 minutes post-injection) is included in the dynamic imaging protocol. This phase evaluates the intracellular retention of the contrast agent. In humans, gadoxetate is taken up by hepatocytes via organic anion-transporting polypeptides OATP1B1 and OATP1B3 and excreted into bile through multidrug resistance protein MRP2 transporters. Backflow to the sinusoids occurs via MRP3 and bidirectional OATP1B1/B3 transporters. In chronic liver diseases and hepatocellular carcinoma (HCC), altered expression and function of these hepatocyte transporters affect gadoxetate enhancement during the hepatobiliary phase. These changes predominantly involve decreased expression of OATP1B1/B3 and MRP2 and increased expression of MRP3 resulting in reduced signal intensity of lesions during this phase. However, some HCC lesions appear hyperintense during the hepatobiliary phase due to an observed increase in OATP1B3 expression in these tumors.

Quantitative perfusion MR imaging requires high temporal resolution, typically with a time resolution of less than 3 seconds, and acquisition of three-dimensional MR images of the entire liver. Simple enhancement-time curve parameters, such as peak enhancement, time to peak, steepest slope, or area under the enhancement curve, are only semi-quantitative since the shape of the enhancement curve is influenced by the arterial input function. To obtain physiological parameters like perfusion or extravascular space volume, pharmacokinetic modeling must be performed, necessitating measurements of both the arterial input function and tissue enhancement curve.

For liver perfusion analysis, dynamic enhancement curves should be modeled using a dual-input approach to account for the liver's dual blood supply via the hepatic artery and portal vein. A widely used method is the dual-input compartmental model validated by Materne et al. This model enables calculation of arterial (K_{1a}), portal venous (K_{1p}), and total liver plasma transfer constants (K_{1t}, in mL/min/100 mL), along with distribution volume (v_d, %) and mean transit time (MTT, in seconds). The transfer constant K1K1K1 is a combined representation of perfusion and permeability, where $K_1=F\times EK_1$ = F \times $EK_1=F\times E$, with FFF as plasma perfusion and EEE as the extravascular extraction fraction. In normal liver tissue, where permeability is high due to fenestrated sinusoids (~100 nm), the extraction fraction equals one, and K_1 reflects perfusion. When permeability is low, K_1 approximates the permeability-surface area product. Hepatic perfusion imaging is best performed on fasting patients to enhance reproducibility.

Unlike liver parenchyma, primary and secondary liver tumors (except early-stage HCC) typically lack portal venous input, relying solely on arterial input. Thus, hepatic tumor perfusion, aside from early HCC, can be analyzed using single-input models. The most commonly employed single-input models are the Kety and extended Kety models. The Kety model, also known as the Tofts model, is a straightforward dual-compartmental model that calculates K^{trans} equal to K_1 and the extravascular extracellular volume v_e equivalent to v_d. The extended Kety model adds v_p the plasma volume, to these calculations. While distributed-parameter models have been proposed for more complex analyses, they are less precise than compartmental models due to interdependencies among multiple free parameters and their sensitivity to initial conditions.

Perfusion measurements require assessment of both the transfer constant K^{trans} and the extravascular extracellular volume v_e (Leach et al., 2012). Reported coefficients of repeatability for K^{trans} in liver tumors range from 20% to 40%. Notably, v_e has demonstrated better reproducibility than K^{trans}, and v_e measurements can assess vascular permeability by evaluating the volume accessible to contrast agents of varying molecular weights. Since the reproducibility of perfusion measurements depends on the organ, imaging protocols, and analysis techniques, it is recommended to validate reproducibility before initiating clinical trials aimed at evaluating treatment responses using DCE MR imaging (Leach et al., 2012).

A significant challenge in perfusion analysis is the lack of standardized post-processing protocols among commercially available software, leading to substantial variability in measured perfusion parameters (coefficients of repeatability >130%). This variability primarily stems from the use of population-based arterial input functions rather than patient-specific input functions. To mitigate this, standardization of perfusion measurements and a shift toward patient-specific arterial input functions are crucial. Additionally, semi-automatic registration and histogram analysis can improve interobserver reproducibility (Heye et al., 2013).

By applying pharmacokinetic modeling to dynamic gadoxetate-enhanced MR images, liver perfusion and hepatocyte transport function can be independently assessed using deconvolution or compartmental analysis methods.

Diffuse Liver Diseases

Dynamic contrast-enhanced MR imaging is a valuable tool for evaluating microcirculatory changes associated with liver fibrosis and cirrhosis. These changes include a reduction in portal and total hepatic perfusion, along with an increase in arterial perfusion and mean transit time, while the distribution volume remains preserved or increases. Such perfusion alterations occur even at intermediate stages of liver fibrosis but are more pronounced in cirrhosis, where they correlate with the severity of liver dysfunction and portal hypertension. Additionally, the reduced hepatobiliary excretion of organic anions via the OATP/MRP pathway observed in conditions such as liver fibrosis, cirrhosis, and non-alcoholic steatohepatitis (NASH) can be detected using gadoxetate-enhanced MR imaging. Furthermore, gadoxetate-enhanced MR imaging shows potential for predicting the risk of liver failure following major liver resection (Wibmer et al., 2013).

Liver Tumors

Dynamic contrast-enhanced MR imaging is routinely utilized during the arterial, portal venous, and delayed phases for detecting, characterizing, and evaluating the treatment response of liver tumors. Gadoxetate is increasingly preferred over extracellular contrast agents for these purposes. Studies have demonstrated improved detection and characterization of focal liver lesions, such as hepatocellular carcinoma (HCC), adenomas, focal nodular hyperplasias, and liver metastases, during the hepatobiliary phase of gadoxetate-enhanced MR imaging. Importantly, some early hypovascular HCC lesions may only appear as hypointense nodules during the hepatobiliary phase, without visibility during dynamic imaging. However, lesions that lack arterial phase enhancement and show hypointensity during the hepatobiliary phase are diagnostically challenging, as not all such lesions correspond to HCC or progress to HCC. In this context, hyperintensity on diffusion-weighted MR images increases the likelihood of early HCC or progression to hypervascular HCC (Ronot & Vilgrain, 2014).

Although qualitative assessments of liver tumors with DCE MR imaging are common, quantitative perfusion MR imaging is less frequently applied in clinical practice. The primary indication for perfusion MR imaging is to evaluate tumor response to antiangiogenic or local therapies.

In patients with HCC treated with sorafenib combined with metronomic tegafur/uracil therapy, K^{trans} values obtained from DCE-MR imaging correlated significantly with tumor response and survival outcomes. Similarly, in HCC patients treated with sunitinib, perfusion parameters demonstrated greater sensitivity as biomarkers for predicting early response and progression-free survival compared to RECIST and mRECIST criteria. Another study involving sunitinib-treated HCC patients revealed a significantly greater reduction in K^{trans} among patients with partial response or stable disease, as defined by RECIST, compared to those with progressive disease or early mortality during the initial treatment cycles. Comparable findings were observed in patients with potentially resectable metastatic colorectal cancer treated with chemotherapy and bevacizumab, where a >40% reduction in K^{trans} was associated with improved progression-free survival (De Bruyne et al., 2012).

Dynamic contrast-enhanced MR imaging, when combined with diffusion-weighted MR imaging, can provide complementary predictive insights. In a study by Bonekamp et al., volumetric DCE MR imaging and diffusion-weighted MR imaging were performed one month after intra-arterial therapy in HCC patients. The study reported significant differences in overall survival among dual-parameter responders (patients with >65% decrease in venous enhancement and >25% increase in apparent diffusion coefficient), single-parameter responders, and patients with stable disease. These findings highlight the potential of multiparametric functional MR imaging for evaluating treatment responses.

MR Elastography

Method

MR elastography employs external vibrators to generate shear or compression waves. In cases where compression waves are used, shear waves necessary for calculating viscoelastic parameters are produced through mode conversion at tissue interfaces. Compression waves offer the advantage of deeper tissue penetration compared to shear waves. Three-dimensional MR elastography enables comprehensive evaluation of tissue viscoelastic properties by measuring shear wave propagation and attenuation. These properties include the complex shear modulus (G*), the storage modulus (G_d), which reflects elasticity, and the loss modulus (G_l), indicative of viscosity. Multifrequency MR elastography further provides the wave scattering coefficient, representing the slope of the viscoelasticity-frequency curve (Garteiser et al., 2013).

Breath-hold MR elastography has shown repeatability coefficients of 22% for elasticity and 26% for viscosity in the liver. Moreover, its reproducibility in assessing liver fibrosis surpasses that of FibroScan©.

Diffuse Liver Diseases

Single-center studies have demonstrated that MR elastography is a reliable, reproducible, and accurate method for detecting and staging liver fibrosis. It outperforms transient ultrasound elastography and the aspartate aminotransferase-to-platelet ratio index (APRI) for staging hepatic fibrosis. Animal studies have established correlations between liver viscoelastic properties and the percentage of hepatic fibrosis determined via morphometry.

Additionally, other conditions, such as inflammation, cholestasis, congestion, and portal hypertension, may also alter liver mechanical properties. Multifrequency MR elastography parameters can aid in characterizing these conditions. For instance, liver fibrosis stage primarily correlates with tissue elasticity, inflammation grade with the wave scattering coefficient and portal hypertension degree with liver and spleen viscosity (Ronot et al., 2014). Studies in animals and humans suggest that MR elastography may detect early non-alcoholic steatohepatitis (NASH) by revealing early increases in elasticity associated with inflammation and stellate cell activation.

If multicenter trials confirm the high diagnostic performance of MR elastography, it could complement ultrasound elastography and reduce the need for liver biopsy in intermediate fibrosis stages, facilitate portal hypertension staging, and evaluate responses to antifibrotic treatments.

LiverTumors

MR elastography may contribute to liver tumor characterization and treatment response assessment. Preliminary research indicates that malignant liver tumors exhibit higher stiffness compared to benign lesions. A subsequent study suggested that malignant liver tumors are mainly characterized by increased viscosity.

In small animal studies, MR elastography has proven useful for evaluating early tumor responses to vascular-disrupting agents and chemotherapy (Li et al., 2014). Further clinical trials are required to elucidate the role of multifrequency MR elastography in characterizing liver tumors and monitoring their treatment responses.

Conclusion

Radiology plays an indispensable role in the diagnosis, characterization, and monitoring of liver diseases, leveraging advancements in ultrasonography and MR imaging. Dynamic contrast-enhanced and functional imaging techniques have significantly enhanced the detection and characterization of liver tumors and the staging of diffuse liver diseases, such as fibrosis and cirrhosis. Multiparametric approaches combining MR imaging with ultrasonography or elastography offer complementary diagnostic and predictive information, improving the evaluation of treatment responses and therapeutic outcomes. Despite the promising advancements, challenges such as standardization of imaging protocols, variability in quantitative measures, and operator dependency highlight the need for continued research and validation. The integration of functional imaging biomarkers with existing techniques underscores the transformative potential of radiology in personalized medicine for liver diseases.

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