Magnetic resonance imaging (MRI) examination of the liver is an important tool for the detection and characterization of focal liver lesions and for the evaluation of diffuse liver disease. The advantages of MRI over other imaging modalities include superior soft-tissue contrast, avoidance of ionizing radiation and iodinated contrast media, and the possibility of performing functional imaging sequences. However, MRI is not without disadvantages, which include limited availability, higher cost, and a longer examination time. One must also consider the recently described risk for nephrogenic systemic fibrosis (NSF), which is associated with gadolinium-based contrast media in patients with renal failure. Furthermore, it has been shown that MRI is superior to CT in the detection and characterization of focal hepatic lesions. Recent studies have also shown the ability of functional MRI techniques to non-invasively diagnose and quantify hepatic fibrosis, liver steatosis, and siderosis. These techniques have the potential to replace liver biopsy in the assessment of diffuse liver disease.

Technical Considerations

A magnet with a field strength of 1.5 Tesla (T) or higher is required to optimally perform a liver MRI examination. Over the last decade, there has been significant progress in the development of hardware such as high-performance gradients, parallel imaging techniques, and advanced coil systems; this has enabled faster scanning and improved image quality. These faster scanning techniques allow radiologists to perform breath-hold acquisitions, which reduce respiratory motion and examination times.

The standard liver MRI protocol used at our institution (see Table 1) includes the following sequences: axial T2-weighted fat-suppressed, coronal T2-weighted half-fourier acquisition single-shot turbo spin-echo (HASTE), axial T1-weighted in and out of phase, axial pre- and post-contrast 3D T1-weighted fat-suppressed, and time-of-flight gradient echo sequence at the level of the portal vein to access flow direction in the portal vein. Advanced techniques such as diffusion-weighted imaging (for lesion detection and characterization) and multiecho T2* sequence (for iron quantification) are routinely used. MR spectroscopy for fat quantification is utilized if clinically indicated.

High-field and Parallel Imaging

Recent technical advances such as high-field imaging and parallel imaging with multichannel systems have the potential to further improve image quality and decrease the acquisition time. High-field-strength imaging at 3T has several potential advantages, but also brings a new set of challenges.

The advantages include a higher signal-to-noise ratio (SNR), higher spatial resolution, and faster imaging. However, pulse sequence parameters used on lower-field-strength systems cannot be simply transferred to 3T systems. For example, the T1 relaxation times differ.
at higher field strengths and modification of the echo times is therefore required. Another challenge is the increased specific absorption rate (SAR) at 3T. Since SAR is proportional to the square of the main magnetic field, radiofrequency (RF) deposition is four times greater at 3T than at 1.5T. Strategies to limit energy deposition that have gained interest include the modification of the pulse sequence design using variable-rate selective excitation methods, variable flip angle sequences, and parallel imaging techniques.

Other challenges with less straightforward solutions include the heterogeneities in the main magnetic field and the magnetic field associated with the RF excitation pulse. To harness the potential of high-field imaging, parallel imaging with a multichannel system needs to be exploited. This offers the potential to decrease imaging times without sacrificing spatial resolution. More than one receiver coil is required, with each coil having its own receiver channel. This technique utilizes the difference in signal detected by receiver coils positioned over different parts of the body. By incorporating the differences in sensitivity of multiple coils to detect signal from the same source, information regarding spatial localization may be obtained, reducing the number of phase-encoding steps required to produce an image. Consequently, imaging times will be decreased. There are two main techniques of parallel imaging: simultaneous acquisition of spatial harmonics (SMASH) and sensitivity encoding (SENSE). There are several challenges in incorporating these techniques. First, special coils must be designed, with independent coil elements having their own receiver channels. Second, the accuracy of coil sensitivity measurements may be difficult to determine. Third, extensive computational time is required to integrate the independent data from multiple channels.

### Role of Magnetic Resonance Imaging for Detection and Characterization of Focal Liver Lesions

There has been an increase in the incidence of hepatocellular carcinoma (HCC) in the US since 1980, which can partly be attributed to the epidemic of viral hepatitis C infection. Currently, 8,000–10,000 new cases are diagnosed each year in the US alone. Diagnosing HCCs while they are small and amenable to liver transplantation is the goal of imaging as liver transplantation is the only curative therapy. Furthermore, differentiating HCC from other primary liver lesions or metastases is important because confident diagnosis of HCC obviates the need for liver biopsy.

CT and ultrasound allow the evaluation of liver lesions on the basis of a single physical parameter such as attenuation or echogenicity. In contrast, MRI provides the unique ability to interrogate multiple parameters such as T1, T2, diffusion characteristics, and enhancement patterns of focal liver lesions, enabling liver lesion detection and characterization. Most normal tissues possess short T1 and T2 values. Benign liver lesions such as cysts and hemangiomas have longer T2 relaxation times than other primary liver lesions and most metastases, and thus appear brighter on T2-weighted images. However, one must bear in mind that cystic or mucinous metastases (for example from colon cancer) can also have long T2 relaxation times and can be mistaken for benign lesions on T2-weighted sequence. Most focal hepatic lesions, including cysts, hemangiomas, HCCs, and metastases, possess longer T1 relaxation times and consequently appear hypointense relative to hepatic parenchyma on T1-weighted images. Other lesions, such as fat-containing lesions (adenomas and some HCCs), hemorrhagic lesions, melanin-containing lesions, and proteinaceous lesions, possess shorter T1 relaxation times and can be mistaken for benign lesions on T1-weighted images. Hypervascular metastases, and cavernous hemangiomas. For example, in the case of cavernous hemangioma, the arterial phase images may demonstrate the characteristic discontinuous nodular peripheral enhancement or flash filling enhancement confirming the diagnosis. Delayed phase-enhancing liver lesions include cholangiocarcinoma, the central scar of focal nodular hyperplasia (FNH), hepatic fibrosis, and peliosis hepatis. Non-enhancing lesions such as cysts can be differentiated from other lesions.

### Liver-specific Contrast Agents

Liver-specific contrast agents, including hepatobiliary agents such as gadolinium-ethoxybenzyl (Gd-EOB-DTPA, Eovist, Bayer HealthCare Pharmaceuticals) and gadobenate dimeglumine (MultiHance, Bracco Diagnostics, Inc.) and reticuloendothelial agents such as super-paramagnetic iron oxide particles (SPIO, Feridex, Bayer HealthCare Pharmaceuticals), have the potential to further improve the sensitivity and specificity of MRI in the diagnosis of focal liver lesions. Studies have shown the potential of these hepatobiliary agents in differentiating HCC from metastases and discriminating FNH from adenomas with the use of delayed phase of enhancement obtained 20 minutes to one hour after contrast administration. FNH and adenoma may have similar T1 and T2 signal characteristics and enhancement patterns. The use of a

#### Table 1: New York University Liver Magnetic Resonance Imaging Protocol

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Acquisition Plane</th>
<th>TR/TE (milliseconds)</th>
<th>Slice/Gap (mm)</th>
<th>Matrix</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 gradient echo in- and out-of-phase</td>
<td>Axial</td>
<td>180/2.2–4.4</td>
<td>8/1</td>
<td>256x118</td>
</tr>
<tr>
<td>T2 turbo spin echo fat-suppressed</td>
<td>Axial</td>
<td>5,300/93</td>
<td>8/1</td>
<td>256x80</td>
</tr>
<tr>
<td>T2 HASTE</td>
<td>Coronal</td>
<td>900/Infinity-65</td>
<td>4/1</td>
<td>256x256</td>
</tr>
<tr>
<td>Time-of-flight gradient echo</td>
<td>Axial oblique</td>
<td>26/9–10</td>
<td>5</td>
<td>138x256</td>
</tr>
<tr>
<td>Multi echo T2*</td>
<td>Axial</td>
<td>1694/8–28.7</td>
<td>10/2</td>
<td>174x256</td>
</tr>
<tr>
<td>Diffusion (b = 0, 50, 100, or 50, 50, 1,000 seconds/mm²)</td>
<td>Axial</td>
<td>2,000/61–82</td>
<td>7/1,4</td>
<td>144x192</td>
</tr>
<tr>
<td>3D T1 fat-suppressed gradient-echo VIBE pre- and post-contrast</td>
<td>Axial</td>
<td>3.5/1.6</td>
<td>2.1–2.5</td>
<td>98x256</td>
</tr>
</tbody>
</table>

**Note:** TR = routine echo time/repetition time; HASTE = half Fourier acquisition single shot turbo spin echo; VIBE = volume interpolated breath-hold examination. All sequences are breath-hold.
Liver-specific contrast agent with delayed imaging allows differentiation between these two entities due to the presence of normal hepatocytes within the FNH that are absent in the adenoma (see Figure 1). Superparamagnetic iron oxide (SPIO) particles distribute specifically in the hepatic Kupffer cells, producing magnetic susceptibility effect and darkening of the liver parenchyma on T2-weighted images. SPIO-enhanced MRI has been shown to be superior to dual-phase CT in the depiction of liver metastases.42 SPIO particles have been used sequentially with gadolinium chelates for HCC diagnosis and have shown improved sensitivity over the use of single (positive or negative) contrast examination.43,44

Nephrogenic Systemic Fibrosis
Recently, a rare and potentially life-threatening condition, NSF, has been reported in patients with advanced renal failure receiving contrast material containing gadolinium.45-47 This disease causes fibrosis of the skin and connective tissues throughout the body. Patients may develop skin thickening to such an extent that it results in decreased joint mobility. Fibrosis may also occur in other parts of the body including the diaphragm, musculature of the lower abdomen and extremities, and the pulmonary vasculature. The clinical course of NSF is progressive and may be fatal. No treatment has been identified. Consequently, extreme caution is advised in administering gadolinium-based contrast material in patients with impaired renal function. In our institution, we do not recommend the use of gadolinium-based contrast agents in patients with a glomerular filtration rate (GFR) <30 ml/minute/1.73 m².

Diffusion-weighted Imaging
Diffusion-weighted imaging (DWI) is based on thermally induced motion of water molecules in biologic tissues. Diffusion weighting by means of apparent diffusion coefficient (ADC) calculation can be used for in vivo quantification of the combined effects of capillary perfusion and diffusion. The more restricted the diffusion, the lower the ADC values. This has shown early potential in liver lesion detection and characterization without the use of an exogenous contrast agent.48-52 Diffusion images with low b-values are similar to T2-weighted black-blood images, in which the background signal of vessels in the liver parenchyma is suppressed. Studies have shown that low b-value diffusion images perform better than T2-weighted images in liver lesion detection, and equivalent to T2-weighted images for lesion characterization.48,49 DWI has shown higher accuracy in detection of hepatic metastasis compared to SPIO enhance study. 53 DWI with higher b-values gives diffusion information that can be expressed in the form of ADC and helps with lesion characterization. Malignant lesions can be discriminated from benign lesions using specific ADC cut-off values on diffusion-weighted images50-52 (see Figure 2). Cysts and hemangiomas have much higher ADC values (less restricted water diffusion) whereas metastases and HCCs have lower ADC values (more restricted water diffusion). However, primary hepatic lesions such as FNH, adenomas, and HCCs have overlapping ADC values and cannot be reliably separated from each other. Similarly, cystic, necrotic, and mucinous metastases have higher ADC values that overlap with benign lesions.

Diffuse Liver Disease
Early detection of liver fibrosis has important clinical implications. Usually, the diagnosis of fibrosis is made on biopsy, which is limited by risks, sampling errors, and a lack of repeatability. With the application of advanced MRI techniques, it is possible to diagnose liver fibrosis and to diagnose and quantify liver iron and fat deposition. This has the potential to replace core liver biopsy.
Liver Fibrosis
Diffusion, perfusion, and MR elastography (MRE) have been investigated as non-invasive tools for staging liver fibrosis in patients with chronic liver disease.

Patients with liver fibrosis and inflammation have less free water and more restriction to the motion of the water molecules, thus lower liver ADC values than subjects without fibrosis or inflammation. There are multiple studies that have attempted to quantify liver fibrosis by using specific ADC cut-off values. For example, in our experience, we found sensitivity of 89% for detecting fibrosis stage ≥1 disease with ADC cut-off values ≤2.5kPa.60 Lewin et al. have showed that DWI performs comparably to if not better than other non-invasive tests (such as ultrasound elastography and blood tests) available for the detection of moderate to severe fibrosis.57 We and others have also been using perfusion-weighted imaging to detect fibrosis and cirrhosis. We showed an increase in hepatic arterial blood flow, distribution volume, and mean transit time along with a decrease in hepatic portal venous flow in patients with advanced fibrosis. Distribution volume had the best performance, with a sensitivity of 77% and a specificity of 78.5% in the prediction of advanced liver fibrosis.12

Since the liver becomes stiffer with advanced fibrosis, this can be exploited by the MRE technique. MRE is performed by transmitting low-frequency mechanical waves into the liver with a transducer placed at the patient’s back. The MR pulse sequence is a motion-sensitized spin-echo sequence, phase-locked to the mechanical excitation. The phase maps are processed to obtain shear elasticity and viscosity maps. Studies have shown significantly higher mean elasticity/stiffness in cirrhosis and advanced fibrosis compared with patients without advanced fibrosis.13,34–47 The mean shear viscosity is also shown to be higher in cirrhosis. The study by Huwart et al. has shown a sensitivity of 98% and a specificity of 100% for the diagnosis of liver fibrosis stage ≥2 using a cut-off of ≥2.5kPa.46

Liver Iron Quantification
Stratifying patients with chronic liver disease on the basis of iron overload is important, as hepatic iron overload is thought to play an important synergistic role in the development and progression of cirrhosis and fibrosis in patients with chronic liver disease. MRI has been investigated for the detection and quantification of liver iron deposition. The detection of iron with MRI is based on local field inhomogeneity generated by the paramagnetic effect of iron particles. Spin echo and gradient echo sequences have been used over the last two decades with good results.61–64 However, some of these methods require complex mathematical modeling and cumbersome post-processing, which limits their use in clinical practice.

Multi-TE sequences that calculate liver T2* have previously been investigated for iron quantification.65 We have recently been using a multislice multiecho T2* sequence that interrogates three to five slices through the liver within one breath-hold, thus providing a more global overview than liver biopsy. In our experience, liver T2* cut-off of <24msec has a sensitivity of 91% and a specificity of 100% for liver iron detection. With liver T2* of <14msec, we can detect moderate to severe liver iron deposition with 100% sensitivity and 97% specificity (see Figure 3).

Liver Fat Quantification
Non-alcoholic fatty liver disease (NAFLD) is now considered to be a common cause of chronic liver disease and cirrhosis in the US, due to the high prevalence of obesity. In most patients, hepatic steatosis is a benign process, but some of these patients can progress to non-alcoholic steatohepatitis (NASH) and cirrhosis.66 In patients with chronic liver disease, similarly to liver iron deposition, liver steatosis is also suspected to play a synergistic role in fibrosis progression.67 Various MR techniques including fast spin echo (FSE) and opposed-phase imaging (OPI) have shown considerable promise.68 More advanced techniques such as MR spectroscopy and two- and three-point Dixon have shown promising results.69 In our experience, single-voxel MR spectroscopy is highly accurate in quantifying hepatic steatosis, and fat fraction calculated by single-voxel spectroscopy showed excellent correlation with histopathological fat fraction with coefficient correlation of 0.91.

Conclusion
Advances in MRI techniques and technology have made liver MRI an excellent imaging modality for the detection and characterization of focal liver lesions and the evaluation of diffuse liver disease, with promising results of functional MRI methods.


42. Benodit S, Yoonpall J, Non-alcoholic fatty liver disease and Hepatitis C infection, Minerva Gastroenterol Dietol, 2006;52(2):135–48.
