American College of Radiology
ACR Appropriateness Criteria®
Chronic Liver Disease

Variant 1: **Chronic liver disease. Diagnosing liver fibrosis.**

Procedure	Appropriateness Category	Relative Radiation Level
MR elastography abdomen	Usually Appropriate	O
US elastography ARFI abdomen	Usually Appropriate	O
1D transient elastography abdomen	Usually Appropriate	O
MRI abdomen without IV contrast	May Be Appropriate	O
MRI abdomen without and with IV contrast	May Be Appropriate	O
MRI abdomen without and with hepatobiliary contrast	May Be Appropriate	O
US abdomen	May Be Appropriate	O
CT abdomen with IV contrast multiphase	May Be Appropriate	☢☢☢☢
CT abdomen without IV contrast	May Be Appropriate	☢☢☢
CT abdomen without and with IV contrast	Usually Not Appropriate	☢☢☢☢

Variant 2: **Chronic liver disease. Screening and surveillance for hepatocellular carcinoma (HCC). No prior diagnosis of HCC.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen without and with IV contrast	Usually Appropriate	O
MRI abdomen without and with hepatobiliary contrast	Usually Appropriate	O
US abdomen	Usually Appropriate	O
CT abdomen with IV contrast multiphase	Usually Appropriate	☢☢☢☢
MRI abdomen without IV contrast	May Be Appropriate	O
MR elastography abdomen	May Be Appropriate	O
US elastography ARFI abdomen	May Be Appropriate	O
CT abdomen without IV contrast	Usually Not Appropriate	☢☢☢
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢
1D transient elastography abdomen	Usually Not Appropriate	O
CT abdomen without and with IV contrast	Usually Not Appropriate	☢☢☢☢

Variant 3: **Chronic liver disease. Surveillance for hepatocellular carcinoma (HCC). Previous diagnosis of HCC.**

Procedure	Appropriateness Category	Relative Radiation Level
MRI abdomen without and with IV contrast	Usually Appropriate	O
CT abdomen with IV contrast multiphase	Usually Appropriate	☢☢☢☢
MRI abdomen without and with hepatobiliary contrast	Usually Appropriate	O
MRI abdomen without IV contrast	May Be Appropriate	O
CT abdomen without and with IV contrast	May Be Appropriate	☢☢☢☢
US abdomen	May Be Appropriate	O
MR elastography abdomen	Usually Not Appropriate	O
CT abdomen without IV contrast	Usually Not Appropriate	☢☢☢
US elastography ARFI abdomen	Usually Not Appropriate	O
1D transient elastography abdomen	Usually Not Appropriate	O
FDG-PET/CT skull base to mid-thigh	Usually Not Appropriate	☢☢☢☢

CHRONIC LIVER DISEASE

Expert Panel on Gastrointestinal Imaging: Jeanne M. Horowitz, MD[a]; Ihab R. Kamel, MD, PhD[b]; Hina Arif-Tiwari, MD[c]; Sumeet K. Asrani, MD, MSc[d]; Nicole M. Hindman, MD[e]; Harmeet Kaur, MD[f]; Michelle M. McNamara, MD[g]; Richard B. Noto, MD[h]; Aliya Qayyum, MD[i]; Tasneem Lalani, MD.[j]

Summary of Literature Review

Introduction/Background

Chronic liver disease is an important cause of morbidity and mortality both worldwide and in the United States. Patients with hepatitis C, hepatitis B, alcoholism, nonalcoholic fatty liver disease (NAFLD), autoimmune hepatitis, and others are at risk for developing hepatic fibrosis. In the United States, nearly two million deaths annually are attributable to chronic liver disease, and liver-related mortality has been underestimated during the past two decades in the United States [1,2], particularly in nonwhite and Hispanic patients. In the United States, 1.3% of the population is chronically infected with hepatitis C, and hepatitis C morbidity and mortality are increasing because of the aging of persons who were infected in past decades [3-5]. In a study examining ultrasound (US) in a national health survey in the United States from 1988 to 1994, the prevalence rates of hepatic steatosis and NAFLD were 21.4% and 19.0%, respectively, corresponding to estimates of 32.5 million adults with hepatic steatosis and 28.8 million adults with NAFLD nationwide [6].

Hepatic fibrosis slowly progresses to cirrhosis, typically over a period of decades. Once thought to be irreversible, hepatic fibrosis is now known to be a dynamic process that, if diagnosed in an early stage, can be treated and potentially reversed. The gold standard for diagnosing liver fibrosis and cirrhosis is liver biopsy [7]. However, liver biopsy is not an ideal method for diagnosis because it is disliked by patients, has complications, and is plagued by sampling errors [8,9]. More importantly, it is not practical to use repeatedly as a method to monitor patients' response to treatment of liver fibrosis.

Noninvasive assessment of liver fibrosis can be done with serologic tests or imaging [10]. Serologic tests include the serum aspartate aminotransferase–to–platelet ratio index, FibroTest (Biopredictive, Paris, France)/FibroSure (LabCorp, Burlington, NC, USA), and others. However, these serum tests are not reliable because several factors not related to fibrosis (eg, active hepatitis or Gilbert syndrome) can contribute to false-positive test results; in addition, serum tests cannot distinguish between different levels of fibrosis [11].

Traditional imaging options to diagnose cirrhosis include assessment for morphologic features on cross-sectional imaging, including US, computed tomography (CT), and magnetic resonance imaging (MRI). Imaging techniques currently being used to diagnose liver fibrosis and cirrhosis include US elastography and MR elastography. Novel imaging techniques being investigated to diagnose liver fibrosis but that are not yet validated include MRI using diffusion, perfusion, and hepatobiliary contrast agents and CT using dual-energy and perfusion.

Patients at risk of developing cirrhosis require screening for hepatocellular carcinoma (HCC) [12]. HCC is the fifth most common cancer in men, the seventh most common cancer in women, and the third leading cause of cancer mortality globally [13,14]. In the United States, HCC related to hepatitis C has recently become the fastest-rising cause of cancer-related death, and during the past two decades, the incidence of HCC has tripled while the 5-year survival rate has remained below 12% [15]. Worldwide, most cases of HCC (approximately 80%) are associated with chronic hepatitis B or hepatitis C infections [13]. However, NAFLD is becoming a common cause of cirrhosis in the United States. There is epidemiologic evidence to support an association between NAFLD and an increased risk of HCC in individuals with cirrhosis [16].

[a]Principal Author, Northwestern University, Chicago, Illinois. [b]Co-Author and Panel Chair, Johns Hopkins University School of Medicine, Baltimore, Maryland. [c]University of Arizona, Banner University Medical Center, Tucson, Arizona. [d]Baylor University Medical Center, Dallas, Texas; American Association for the Study of Liver Diseases. [e]New York University Medical Center, New York, New York. [f]University of Texas, MD Anderson Cancer Center, Houston, Texas. [g]University of Alabama Medical Center, Birmingham, Alabama. [h]Brown University Rhode Island Hospital, Providence, Rhode Island. [i]University of Texas, MD Anderson Cancer Center, Houston, Texas. [j]Specialty Chair, Inland Imaging Associates and University of Washington, Seattle, Washington.

Reprint requests to: publications@acr.org.

Discussion of Procedures by Variant

Variant 1: Chronic liver disease. Diagnosing liver fibrosis.

Certain morphologic features of cirrhosis can be assessed on US, CT, or MRI. These include liver surface nodularity, particularly of the anterior left lobe [17,18]; an atrophic right lobe and hypertrophied caudate lobe and lateral segment left lobe [19]; an atrophied medial segment left lobe [20]; a right hepatic posterior "notch" [21,22]; an expanded gallbladder fossa [23,24]; narrow hepatic veins (right hepatic vein <5 mm) [25]; an enlarged caudate–to–right lobe ratio (modified ratio >0.90) [26,27]; and enlargement of the hilar periportal space (>10-mm thickness) [28,29]. Although these morphologic features are fairly good at diagnosing cirrhosis, they are subjective and are present only in later stages of fibrosis.

US

Conventional grayscale and Doppler US are safe and can be used to diagnose cirrhosis. In addition to the morphologic signs described above, a coarsened or heterogeneous hepatic echotexture has been associated with cirrhosis [30,31]. However, this is subjective and the appearance of coarsening is often US-dependent. Furthermore, the sonographic appearance of hepatic steatosis and cirrhosis often overlap, with a "fatty-fibrotic" pattern [31,32]. Evaluation of the liver with conventional US is also limited in obese patients because of poor penetration of the US beam. This limits assessment for cirrhosis and liver lesions. US can also assess for splenomegaly and other signs of portal hypertension.

Color Doppler US can be helpful in diagnosing signs of portal hypertension in the main portal vein, including slow velocity or hepatofugal (reversed) direction of flow [33]. However, these findings will be seen only in advanced cirrhosis and not in the early stages of fibrosis. Decreased phasicity of the hepatic venous waveforms in spectral Doppler US correlates with hepatic fibrosis as well as steatosis [34,35]. Doppler US measurements for diagnosis of hepatic fibrosis have not been shown to be helpful in all studies [36].

US elastography includes shear-wave elastography and strain elastography. Shear-wave elastography can quantify elasticity, whereas strain elastography is semiquantitative and determines elasticity relative to other structures. Types of shear-wave elastography used to diagnose liver fibrosis include 1-D transient elastography (TE) and acoustic radiation force impulse (ARFI) elastography.

US elastography attempts to predict the histologic stage of hepatic fibrosis, typically the METAVIR score (F0-F4, where F2 or greater is clinically significant fibrosis and F4 is cirrhosis). This score helps predict the response to treatment because F3 and F4 patients are less likely to respond, and determines if the patient has cirrhosis and requires screening for HCC. Noninvasive monitoring of hepatic fibrosis is also helpful for patients taking hepatotoxic drugs.

The most commonly used types of US elastography for assessment of liver fibrosis are TE and ARFI. TE is predominantly performed with FibroScan (Echosens, Paris, France) and can be performed at point of care during a patient's clinic visit without any additional equipment. TE was developed before ARFI and has been heavily studied and validated more than other elastography methods as a method of diagnosing liver fibrosis. TE has a sensitivity and specificity of 70% and 84%, respectively, for diagnosing significant fibrosis (F2 or greater) and 87% and 91%, respectively, for diagnosing cirrhosis (F4) [37]. TE is not reliable in patients with obesity or ascites and cannot distinguish between intermediate stages of fibrosis [38]. An extra-large probe for TE is now available for obese patients, which tries to overcome some limitations of TE [39].

Unlike TE, ARFI can be combined with conventional US and can be used in patients with obesity, ascites, and NAFLD [40-42]. Because ARFI is 2-D or B-mode US, specific larger areas of the liver can be chosen for study compared with TE, which has a single-element US transducer. In a meta-analysis comparing TE and ARFI, rates of unreliable examinations were three times higher with TE as compared with ARFI (6.6% versus 2.1%, $P < .001$) [43]. One limitation of ARFI is that it is operator dependent. In this document, it is assumed all studies are performed by an expert.

It should be noted that liver stiffness measurements on elastography can be influenced not only by fibrosis but also by edema, inflammation [44], extrahepatic cholestasis [45], and passive congestion [46]. Patients undergoing US elastography should be fasting [47,48]. The studies performed to validate US elastography have used liver biopsies as the reference standard. Thus, this imaging technique may be subject to the same sampling error that plagues liver biopsies.

Contrast-enhanced US (CEUS) has also been used to diagnose fibrosis and cirrhosis. A US contrast agent has recently been approved in the United States, and some institutions use US contrast off-label. Discussion of the role of CEUS is beyond the scope of this document, but CEUS can exclude cirrhosis using contrast agent transit or disappearance times but cannot be used for staging fibrosis [31].

CT

Multiphase CT is predominantly performed in patients with chronic liver disease for diagnosis of HCC, as discussed in Variant 2. However, cirrhosis can be assessed for using the morphologic features described above either on noncontrast CT, contrast-enhanced single-phase CT, or multiphase CT. Similar to MRI, bands of fibrosis will appear as linear areas of enhancement in portal venous or delayed phases. CT performs better than US for assessment of cirrhosis in obese patients.

CT perfusion and dual-energy CT have recently been used to assess for fibrosis and cirrhosis with some promising results [49-52]. CT perfusion has been able to distinguish between stages of fibrosis [49]. Because CT perfusion requires significant postprocessing, it is not used clinically.

MRI

MRI is more accurate than US for the evaluation of cirrhosis in obese patients and patients with NAFLD. MRI can assess for morphologic features of cirrhosis, and fibrosis can be evaluated on dynamic contrast-enhanced (DCE) sequences with extracellular gadolinium contrast agents. Bands of fibrosis will be seen as linear areas of high T2 signal and enhancement on delayed-phase sequences [53]. Although visible fibrosis can be seen in later stages of fibrosis and cirrhosis, earlier stages of fibrosis will not be visible on conventional MRI with contrast.

MR elastography has also been used to noninvasively diagnose hepatic fibrosis and cirrhosis with good reliability. Although the other imaging techniques and modalities, including US elastography, can often distinguish well between cirrhosis or severe fibrosis and normal liver, MR elastography is the most accurate technique for diagnosing intermediate stages of fibrosis [31].

Compared with US elastography, MR elastography performs better for diagnosing fibrosis in obese patients and patients with ascites, has the fewest unreliable examinations, is able to assess fibrosis throughout the largest amount of liver parenchyma, and can evaluate for HCC at the same time [54]. The diagnostic capability of MR elastography is unaffected by obesity, whereas with US elastography, unreliable measurements were found in 35.4% of TE examinations in obese patients [55] and 17.6% of ARFI examinations in obese patients [56]. In a recent meta-analysis, MR elastography could also distinguish between levels of hepatic fibrosis, with good sensitivity (73%-91%) and specificity (79%-85%) [54]. The main limitation in MR elastography is that it is not accurate in patients with hepatic iron deposition [57], contributing to a failure rate of 4.3% [54].

Diffusion-weighted imaging (DWI) in MRI can be used to diagnose fibrosis and cirrhosis as well, either with qualitative subjective evaluation or quantitatively measuring of the apparent diffusion coefficient (ADC) value; at this time, it is mostly of research interest. DWI is better at distinguishing between cirrhotic and normal livers than distinguishing between stages of fibrosis [58,59]. One study showed a positive predictive value, negative predictive value, and overall accuracy of 100%, 99.9%, and 96.4%, respectively, for diagnosing cirrhosis compared with controls with DWI [60]. However, a meta-analysis showed that DWI distinguished F0-F1 from F2-F4 with a sensitivity of 77%, specificity of 78%, and summary receiver operating characteristic of 0.83 [58]. DWI image quality can suffer particularly in patients with cirrhosis, ascites, and those who have difficulty breath holding. ADC values are also dependent on the MRI scanner used, so published ADC results are not generalizable to all scanners.

Hepatobiliary MRI contrast agents such as gadoxetate disodium (Eovist; Bayer Healthcare, Wayne, NJ, USA) and gadobenate dimeglumine (MultiHance; Bracco Diagnostics, Princeton, NJ, USA) are not as widely used as extracellular agents, but research is ongoing regarding their use in diagnosing fibrosis [61]. MR elastography has been shown to be superior to MRI with gadoxetate disodium for staging hepatic fibrosis [62].

Assessing liver fibrosis with MR perfusion has also been studied in recent years. Arterial blood flow, arterial fraction, portal venous fraction, distribution volume, and mean transit time in one study were significantly different between patients with and without severe fibrosis [63]. Another study showed that DCE-MRI with gadoxetate disodium can be used to stage liver fibrosis [64]. The combination of DCE-MRI and DWI was able to accurately diagnose cirrhosis in one study [65]. However, perfusion analysis is laborious, so this is mostly a research interest and not clinically utilized at this time.

As with US elastography, studies of these MR techniques use liver biopsies as the reference standard.

Variant 2: Chronic liver disease. Screening and surveillance for hepatocellular carcinoma (HCC). No prior diagnosis of HCC.

Patients with cirrhosis and selected chronic liver disease patients without cirrhosis, such as chronic hepatitis B patients at high risk, need to be screened for HCC. More intense surveillance for HCC may be required for patients on the transplant waiting list regardless of etiology of cirrhosis. Cirrhotic patients whose liver contains small nodules are at increased risk for HCC as well [66]. The American Association for the Study of Liver Diseases (AASLD) reports that surveillance is cost effective if the expected HCC risk exceeds 1.5% per year in patients with cirrhosis and 0.2% per year in patients with hepatitis B [12]. Studies have shown that patients who have been screened for HCC have improved detection of HCC, improved receipt of curative therapy, improved survival, and lower mortality [67-71].

The accurate diagnosis of HCC with imaging is important because a liver lesion that meets strict diagnostic imaging criteria for HCC does not need to be biopsied. Using the Milan criteria, patients with one 2- to 5-cm HCC or two to three HCCs measuring up to 3 cm may be assigned priority for transplantation according to the Organ Procurement and Transplantation Network (OPTN) and the United Network of Organ Sharing (UNOS) [72,73]. HCCs invading portal veins and extrahepatic metastases are not eligible for transplantation, according to OPTN and UNOS. Although HCC can be diagnosed on imaging without a confirmatory biopsy before initiating treatment, including transplantation, the diagnosis of HCC cannot be made on US alone. Multiphase CT or MRI is necessary. Biopsy is reserved for indeterminate nodules on CT or MRI, particularly nodules 1 to 2 cm in size [74]. Biopsy results can be falsely negative in small HCCs and carry the risk of potential complications, including needle tract seeding and bleeding [75-77].

The American College of Radiology (ACR) Liver Imaging Reporting and Data System (LI-RADS) was created in part to standardize the reporting of CT and MRI for HCC to encourage consistent terminology and reduce image interpretation errors [78]. LI-RADS uses diagnostic algorithms to characterize liver lesions and diagnose HCC. It should be noted that the ACR Appropriateness Criteria® "Liver Lesion—Initial Characterization" [79] also discusses various scenarios about how to characterize incidentally found liver lesions. Detailed descriptions of imaging characteristics of HCC are beyond the scope of this document but will be briefly described below. OPTN and UNOS also encourage structured reporting regarding CT or MRI imaging diagnostic of HCC, representing "class 5" lesions [72]. It is also important to provide information on conventional versus variant vascular anatomy when reporting CT and MRI for HCC because this impacts the approach for local–regional therapy and surgery.

Potential noninvasive diagnostic modalities used for screening and diagnosing HCC include US, CT, MRI, and serum biomarkers. It should be noted that screening with α-fetoprotein (AFP) alone is not recommended because of the inadequate sensitivity of AFP, and the addition of AFP to US screening does not show a statistically significant improvement in HCC detection [80-82]. One review showed AFP >20 ng/mL to have a sensitivity of 41% to 65% and specificity of 80% to 94% for HCC screening [82].

US

Although most international groups recommend US screening and surveillance for HCC, the evidence to support this practice is weak. The recommendation for screening with US every 6 months by the AASLD [12] is based on a prospective Chinese study of hepatitis B patients that showed that patients who had an US survived longer [83]. However, there is no good evidence to show that these results apply to the population in the United States, which has a much higher percentage of obese patients, fewer patients with chronic hepatitis B, and many more patients with alcoholic cirrhosis, often with hepatitis C and NAFLD. US is insensitive for detection of HCC in patients with hepatic steatosis as well as nodular cirrhotic livers who are undergoing surveillance [84]. The regenerative nodules in cirrhotic livers alter the background hepatic echotexture, making HCC difficult to detect. Another inherent limitation of US is its operator dependence [85]. In this document, it is assumed that all studies are performed by an expert.

Some international guidelines permit surveillance by CT or MRI when US is limited by obesity or other factors [86-88] or if the patient is at very high risk of HCC [87,89]. Patients may present with HCC, including advanced HCC (T stages T1–T4), even if US findings are negative within 1 year before diagnosis [90].

US can be unreliable in detection of HCC, and studies have shown sensitivity ranging from 21% to 94% [81,91-93]. At the low end, Yu et al [91] in 2011 calculated the sensitivity of US to detect HCC <2 cm to be 21% but for all sizes to be 46%, whereas sensitivity for detection of HCC of all sizes at CT and MR was 65% and 72%, respectively. Another study showed that pooled sensitivity of US, CT, and MRI for facilitating the diagnosis of HCC was 60%, 68%, and 81%, respectively, and concluded that US is highly specific but insufficiently sensitive to detect HCC in many cirrhotic patients or to support an effective surveillance program [93]. At the high end, one meta-analysis showed a 94% sensitivity for US detection of HCC of all sizes but a sensitivity of 63% for early HCC [81].

CEUS can be used for liver lesion characterization and diagnosis of HCC with high specificity in a few studies, 92% to 100% [94-96], although another more recent, larger study had concerns regarding the sensitivity and accuracy of CEUS for HCCs <2 cm [97]. CEUS may be helpful to diagnose HCC in patients who cannot receive intravenous iodinated contrast for CT and cannot receive gadolinium for MRI. However, CEUS is not practical for screening because it is difficult or impossible to examine the entire liver during the arterial phase to look for hyperenhancing nodules [98].

CT and MRI

Multiple international groups recognize the limitations of US; once a liver lesion >1 cm is found on US in a patient at risk for HCC, all international guideline groups recommend multiphase CT or MRI for diagnosis and staging [12,86-88,99,100]. Additionally, many institutions in the United States provide multiphase CT or MRI to screen cirrhotic patients for HCC when ordered by their physicians, as long as the practice can accommodate a large volume of patients for imaging.

The diagnosis of HCC on multiphase CT and MRI is made on postcontrast imaging when there is late hepatic arterial-phase hyperenhancement, venous- or delayed-phase washout appearance, and venous- or delayed-phase capsule appearance. The specificity and positive predictive value of this appearance on CT or MRI for HCC is nearly 100% [75,76,101,102]. For HCC of all sizes, the sensitivity of MRI is 59% to 95% [76,103-107] and the sensitivity of multiphase CT is 43% to 63% [103,104,108]. For HCCs greater than 2 cm, sensitivity of MRI is 100% [106] and multiphase CT is 98% [108]. For HCCs less than 2 cm, sensitivity of MRI is 58% to 100% [99,101,102,105,106,109-113] and sensitivity of CT is 53% to 68% [99,112,113]. These studies show a diagnostic advantage of MRI over multiphase CT. Studies also show improved sensitivity by using a delayed phase rather than the venous phase [114,115].

Advantages of multiphase CT compared with MRI include the fact that it is a rapid test and easier to interpret. Dual-energy CT has an advantage in being able to make virtual unenhanced images that are adequate to replace separately acquired noncontrast images [116]. Disadvantages of CT include repeated exposure of patients to ionizing radiation and lower soft-tissue contrast [75], as well as risk of contrast nephropathy in patients with renal insufficiency.

Advantages of MRI include better chances for lesion detection and characterization, and higher soft-tissue contrast [117]. Disadvantages of MRI include increased sensitivity for hypervascular lesions that are not HCC (often transient shunts that are usually subcapsular), it takes more time than CT, and it is more frequently affected by artifacts (especially when there is moderate to severe ascites) [75].

Multiphase CT

To accurately diagnose HCC on multiphase imaging, both late hepatic arterial and portal venous postcontrast phases are absolutely necessary. The addition of a delayed phase is considered by most to be essential to increase conspicuity of the HCC's washout and capsular appearance [114] and help distinguish HCC from cholangiocarcinoma [118]. This delayed phase is recommended by the UNOS [72]. A noncontrast phase is unnecessary if the patient has not received previous liver treatment [119-121]. Multiphase CT has been advocated in the past for screening cirrhotic patients on the transplant waiting list [122-124]. However, this does increase overall radiation exposure with repeated surveillance scans and is less preferable than MRI. Exposure to ionizing radiation is a concern with multiphase CT, particularly in patients with chronic liver disease who are undergoing multiple CT scans for screening, diagnosis, and/or staging.

MRI

MRI has become more accessible in recent years, and more radiologists are comfortable with interpreting MRI than in the past, particularly with the efforts of ACR's LI-RADS [78]. Liver MRI for the diagnosis of HCC should include pre- and postcontrast T1-weighted and T2-weighted sequences, and DWI is helpful as well [125].

Gadolinium is needed to distinguish dysplastic nodules, early HCC, and small-progressed HCC [89], and distinguishes between these diagnoses better than CT [126,127]. If gadolinium cannot be administered because of renal function or gadolinium allergy, T2-weighted sequences and DWI can be helpful in identifying liver lesions. DWI in MRI can be used for problem solving or increasing confidence when other MR sequences are equivocal. Increased conspicuity of lesions on DWI increases sensitivity and justifies its routine use in MRI in detection of HCC [125,128-130].

Although extracellular gadolinium agents are most commonly used in liver MRI to diagnose HCC, hepatobiliary contrast agents such as gadoxetate disodium (also called gadoxetic acid, Gd-EOB-DTPA) and gadobenate dimeglumine (also called Gd-BOPTA) have also been used in recent years. An advantage of hepatobiliary agents compared with traditional extracellular agents is their decreased dose of contrast in patients with impaired renal function. Gadobenate dimeglumine can be given at a half-dose in patients with impaired renal function. The dose of gadoxetate disodium is one-quarter of the dose of extracellular agents.

An advantage of hepatobiliary contrast agents is that they can detect early HCC that shows relative hypoenhancement on the hepatobiliary phase when there is not yet arterial enhancement or venous-phase washout, enhancing the sensitivity and accuracy for HCC diagnosis [110,131]. Hepatobiliary phase hypointensity favors a malignant or premalignant lesion rather than a low-grade dysplastic or cirrhotic nodule in studies with both hepatitis B and C patients [89,113,132-134]. MRI with hepatobiliary contrast may be the most sensitive imaging method to detect small HCCs and premalignant lesions that could progress to HCC; adding the hepatobiliary phase improves sensitivity of HCC detection by 5% to 16% compared with MRI using the other DCE sequences [109,135-137]. One recent meta-analysis regarding diagnosis of HCC using hepatobiliary contrast showed sensitivity of 91% and specificity of 95% [138], and another meta-analysis showed higher sensitivity for HCC diagnosis with hepatobiliary contrast (93%) compared with contrast-enhanced CT (78%) [139]. Most hypoenhancing lesions on the hepatobiliary phase will progress to an arterial-enhancing HCC within 12 months [75,140] or during the follow-up period [141], which has important treatment implications.

A limitation of hepatobiliary contrast agents is that in patients with severe cirrhosis, where there is decreased liver function, the hepatocytes do not take up the hepatobiliary contrast agent well, and lesions may not be as conspicuous [142-144]. A disadvantage of decreasing the volume of contrast injected with gadoxetate disodium is that the arterial and portal venous enhancement can be suboptimal. Additionally, the findings gleaned from hepatobiliary contrast agent use in MR have not been integrated into the UNOS criteria for the diagnosis of HCC. Distinguishing HCC from cholangiocarcinoma can be challenging with hepatobiliary contrast as well because intrahepatic cholangiocarcinomas are often arterial enhancing in cirrhotic compared with normal livers [145].

The combination of hepatobiliary MRI and DWI was more accurate and sensitive in detecting small HCCs than each MRI technique alone in one study [128], and in another study the combination of hyperintensity on DWI and hypointensity on the hepatobiliary phase predicted progression to HCC [130].

MR elastography is primarily used for diagnosis of liver fibrosis and cirrhosis rather than diagnosis of HCC, although attempts have been made to characterize liver lesions and HCC with elastography. No association was found between MR elastography stiffness and HCC presence in at least one study [146]. Emerging data indicate that elevation of stiffness is associated with future development of liver-related decompensation, HCC, and death [147].

FDG-PET/CT

Positron emission tomography/CT (PET/CT) is not an appropriate screening test for HCC. PET/CT is also of limited utility in the diagnosis of HCC, because HCC uptake of fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)-PET is variable [148-150]. One study, however, showed that PET/CT in HCC may be useful for predicting prognosis and treatment responses and for planning treatment in patients with locally advanced HCC [151]. Another study showed that combining choline 11 and FDG-PET/CT detected HCC with high sensitivity compared with FDG-PET/CT alone because of the variability of FDG-PET/CT uptake in HCC [152].

Variant 3: Chronic liver disease. Surveillance for hepatocellular carcinoma (HCC). Previous diagnosis of HCC.

Treatment options for HCC include surgical resection, liver transplant, liver-directed therapy, and systemic therapy [12]. Liver-directed therapy can include treatments such as chemoembolization, radioembolization with yttrium 90, thermal ablation, or percutaneous ethanol ablation, amongst others. These various treatment options

are thoroughly discussed in the ACR Appropriateness Criteria® "Radiologic Management of Hepatic Malignancy" [153] and are beyond the scope of this document.

Surveillance for HCC is required for patients who have received liver-directed therapy, surgical resection, medical treatment, or a transplant for HCC. Potential noninvasive diagnostic modalities used for HCC surveillance and diagnosis are the same as for HCC screening and include US, CT, MRI, and serum biomarkers. These modalities have the same strengths and weaknesses for surveillance as for HCC screening and surveillance before treatment, as discussed in Variant 2. However, because of the higher risk of tumor recurrence, US is not typically used for surveillance for HCC in the first 2 years after treatment because of the low sensitivity of US. Similarly, US has low sensitivity in patients who are obese, have NAFLD, or have very nodular cirrhotic livers, as discussed above.

CT and MRI play an important role in surveillance for recurrence of HCC and are necessary for further HCC treatment planning in the case of tumor progression, notably when planning liver-directed therapy. In HCC patients who have already received liver-directed therapy, recurrence is 6.5 times more likely in the first year after treatment than in the second year.

There is currently a lack of evidence regarding the optimal follow-up strategy for patients treated with liver-directed therapy for HCC. There is variability in the interventional radiology community with regards to the type of and frequency of imaging follow-up after treatment for HCC [154,155].

Results of a survey of Society of Interventional Radiology members showed that CT or MRI was typically performed for follow-up after HCC treatment [155]. Most commonly, the first follow-up imaging was 1 month post-treatment, followed by 3 months post-treatment. This was followed by imaging every 3 months with CT or MRI. This strategy of imaging for HCC surveillance every 3 months after treatment is also supported by other society guidelines, including the European Association for the Study of the Liver (EASL) and the National Comprehensive Cancer Network (NCCN) [86,156]. NCCN guidelines recommend at least three-phase high-quality CT or MRI every 3 to 6 months for 2 years and then every 6 to 12 months after HCC resection, based on the consensus that earlier identification of disease may facilitate treatment [156]. EASL recommends multiphase CT or MRI to assess response 1 month after resection or locoregional or systemic therapies, followed by one imaging technique every 3 months to complete at least 2 years, and then regular US every 6 months [86]. A separate publication recommended the optimal schedule for follow-up after HCC treatment at 2, 4, 6, 8, 11, 14, 18, and 24 months with either CT or MRI, reporting that this reduces diagnostic delay and is cost-effective [157]. However, this schedule is more frequent than some of the other society recommendations and the most common practice among interventional radiologists (every 3 months) [155].

Regarding multiphase CT after treatment for HCC, a noncontrast phase is strongly recommended, particularly if the patient has received liver-directed therapy [119,120,158]. This can result in a patient having 4-phase CT examinations, including noncontrast, arterial, portal venous, and delayed phases. Dual-energy CT has the advantage of making virtual unenhanced images and/or iodine maps, which decrease the amount of radiation per multiphase CT and are adequate to replace standard unenhanced images, particularly for those patients who have previously undergone treatment for HCC [89,116]. Perfusion CT can calculate hepatic blood flow and portal blood flow using a color-coded display and can thus analyze tumor angiogenesis and assess tumor response to treatment [159]. However, this is currently predominantly used in research and not in surveillance for HCC.

Many centers treating HCC prefer MRI over multiphase CT in post-treatment surveillance of HCC because the ethiodized oil used in transarterial chemoembolization can make assessment for tumor recurrence difficult on CT, whereas the presence of ethiodized oil will not confound the assessment for tumor recurrence on MRI. Subtraction images on MRI can help diagnose new HCC or tumor recurrence in patients with previous liver-directed therapy or T1 hyperintense dysplastic nodules [160].

CEUS can be used to assess for local tumor progression and treatment planning after focal ablation of HCC lesions [161,162], but is not practical for surveillance of the whole liver [98]. Also, the sensitivity of CEUS in detecting local tumor recurrence and new intrahepatic recurrence after percutaneous ablation therapy is relatively low in comparison with multiphase CT [163]. After radiofrequency ablation and percutaneous ethanol ablation, tumor response can be evaluated with CEUS immediately after the procedure, after 1 day, after 1 month, or later [162]. Interestingly, the pattern of HCC on CEUS after cryoablation seems different compared with after radiofrequency ablation because the margins of the lesions are less well defined and shrink significantly faster than radiofrequency ablation lesions [164].

Summary of Recommendations

- Because liver fibrosis can now be treated, it is more important than ever to be able to diagnose liver fibrosis noninvasively and monitor its response to treatment. Liver biopsy is plagued by sampling error and complications, and serology tests have significant limitations. Although US (grayscale and Doppler) can diagnose cirrhosis, it does so unreliably using morphologic and sonographic features, and it cannot diagnose earlier stages of fibrosis. TE can more reliably diagnose cirrhosis compared with grayscale and Doppler US but is unreliable in patients with obesity and ascites, which is a significant portion of cirrhotic patients living in the United States. ARFI elastography can reliably diagnose cirrhosis and can stage hepatic fibrosis as well, and ARFI is added to grayscale and Doppler US. MR elastography is the most accurate method for diagnosing liver fibrosis noninvasively because it assesses the whole liver and can stage liver fibrosis.
- All international organizations recommend US to screen for HCC. However, US is particularly limited for identifying HCC in patients with obesity, NAFLD, and nodular cirrhotic livers, which is a large portion of the United States' cirrhotic population receiving screening. In these patient groups as well as patients who are on the liver transplant wait list, US is so limited that consideration should be made for screening for HCC with either MRI or multiphase CT. If a suspicious liver lesion >1 cm is identified on a screening US, the diagnosis of HCC cannot be made on US alone and the HCC diagnosis needs to be confirmed on MRI or multiphase CT. Although MRI is preferable because of its slightly increased accuracy compared with CT and its ability to detect premalignant nodules, multiphase CT can accurately diagnose HCC as well. Many MRI centers now include techniques that further increase accuracy of HCC diagnoses, including DWI and hepatobiliary contrast.
- Patients who have been previously diagnosed with and treated for HCC require continued surveillance for recurrent HCC. Given the high rate of recurrence (particularly within the first year after treatment) and insensitivity of US, multiphase CT or MRI is suggested to assess response 1 month after resection or therapy, followed by imaging every 3 months for at least 2 years. Many centers treating HCC prefer MRI over multiphase CT in post-treatment surveillance of HCC because the ethiodized oilused in transarterial chemoembolization can make assessment for tumor recurrence difficult on CT.

Summary of Evidence

Of the 165 references cited in the *ACR Appropriateness Criteria® Chronic Liver Disease* document, 146 are categorized as diagnostic references including 4 well-designed studies, 51 good-quality studies, and 50 quality studies that may have design limitations. Additionally, 5 references are categorized as therapeutic references. There are 45 references that may not be useful as primary evidence. There are 14 references that are meta-analysis studies.

The 165 references cited in the *ACR Appropriateness Criteria® Chronic Liver Disease* document were published from 1986 through 2017.

Although there are references that report on studies with design limitations, 55 well designed or good quality studies provide good evidence.

Appropriateness Category Names and Definitions

Appropriateness Category Name	Appropriateness Rating	Appropriateness Category Definition
Usually Appropriate	7, 8, or 9	The imaging procedure or treatment is indicated in the specified clinical scenarios at a favorable risk-benefit ratio for patients.
May Be Appropriate	4, 5, or 6	The imaging procedure or treatment may be indicated in the specified clinical scenarios as an alternative to imaging procedures or treatments with a more favorable risk-benefit ratio, or the risk-benefit ratio for patients is equivocal.
May Be Appropriate (Disagreement)	5	The individual ratings are too dispersed from the panel median. The different label provides transparency regarding the panel's recommendation. "May be appropriate" is the rating category and a rating of 5 is assigned.
Usually Not Appropriate	1, 2, or 3	The imaging procedure or treatment is unlikely to be indicated in the specified clinical scenarios, or the risk-benefit ratio for patients is likely to be unfavorable.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document [165].

Relative Radiation Level Designations		
Relative Radiation Level*	**Adult Effective Dose Estimate Range**	**Pediatric Effective Dose Estimate Range**
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢☢	0.1-1 mSv	0.03-0.3 mSv
☢☢☢	1-10 mSv	0.3-3 mSv
☢☢☢☢	10-30 mSv	3-10 mSv
☢☢☢☢☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies".		

Supporting Documents

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

References

1. Asrani SK, Larson JJ, Yawn B, Therneau TM, Kim WR. Underestimation of liver-related mortality in the United States. *Gastroenterology.* 2013;145(2):375-382 e371-372.
2. Udompap P, Kim D, Kim WR. Current and Future Burden of Chronic Nonmalignant Liver Disease. *Clin Gastroenterol Hepatol.* 2015;13(12):2031-2041.
3. Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med.* 2006;144(10):705-714.
4. Davis GL, Alter MJ, El-Serag H, Poynard T, Jennings LW. Aging of hepatitis C virus (HCV)-infected persons in the United States: a multiple cohort model of HCV prevalence and disease progression. *Gastroenterology.* 2010;138(2):513-521, 521 e511-516.
5. Morgan RL, Baack B, Smith BD, Yartel A, Pitasi M, Falck-Ytter Y. Eradication of hepatitis C virus infection and the development of hepatocellular carcinoma: a meta-analysis of observational studies. *Ann Intern Med.* 2013;158(5 Pt 1):329-337.
6. Lazo M, Hernaez R, Eberhardt MS, et al. Prevalence of nonalcoholic fatty liver disease in the United States: the Third National Health and Nutrition Examination Survey, 1988-1994. *Am J Epidemiol.* 2013;178(1):38-45.
7. Rockey DC, Caldwell SH, Goodman ZD, Nelson RC, Smith AD. Liver biopsy. *Hepatology.* 2009;49(3):1017-1044.
8. Ratziu V, Charlotte F, Heurtier A, et al. Sampling variability of liver biopsy in nonalcoholic fatty liver disease. *Gastroenterology.* 2005;128(7):1898-1906.
9. Regev A, Berho M, Jeffers LJ, et al. Sampling error and intraobserver variation in liver biopsy in patients with chronic HCV infection. *Am J Gastroenterol.* 2002;97(10):2614-2618.
10. Asrani SK. Incorporation of Noninvasive Measures of Liver Fibrosis Into Clinical Practice: Diagnosis and Prognosis. *Clin Gastroenterol Hepatol.* 2015;13(12):2190-2204.
11. Parkes J, Guha IN, Roderick P, Rosenberg W. Performance of serum marker panels for liver fibrosis in chronic hepatitis C. *J Hepatol.* 2006;44(3):462-474.
12. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update. *Hepatology.* 2011;53(3):1020-1022.
13. El-Serag HB. Epidemiology of viral hepatitis and hepatocellular carcinoma. *Gastroenterology.* 2012;142(6):1264-1273 e1261.
14. Altekruse SF, McGlynn KA, Reichman ME. Hepatocellular carcinoma incidence, mortality, and survival trends in the United States from 1975 to 2005. *J Clin Oncol.* 2009;27(9):1485-1491.
15. El-Serag HB. Hepatocellular carcinoma. *N Engl J Med.* 2011;365(12):1118-1127.
16. White DL, Kanwal F, El-Serag HB. Association between nonalcoholic fatty liver disease and risk for hepatocellular cancer, based on systematic review. *Clin Gastroenterol Hepatol.* 2012;10(12):1342-1359 e1342.
17. Di Lelio A, Cestari C, Lomazzi A, Beretta L. Cirrhosis: diagnosis with sonographic study of the liver surface. *Radiology.* 1989;172(2):389-392.
18. Simonovsky V. The diagnosis of cirrhosis by high resolution ultrasound of the liver surface. *Br J Radiol.* 1999;72(853):29-34.
19. Torres WE, Whitmire LF, Gedgaudas-McClees K, Bernardino ME. Computed tomography of hepatic morphologic changes in cirrhosis of the liver. *J Comput Assist Tomogr.* 1986;10(1):47-50.
20. Lafortune M, Matricardi L, Denys A, Favret M, Dery R, Pomier-Layrargues G. Segment 4 (the quadrate lobe): a barometer of cirrhotic liver disease at US. *Radiology.* 1998;206(1):157-160.
21. Ito K, Mitchell DG, Kim MJ, Awaya H, Koike S, Matsunaga N. Right posterior hepatic notch sign: a simple diagnostic MR finding of cirrhosis. *J Magn Reson Imaging.* 2003;18(5):561-566.
22. Tan KC. The right posterior hepatic notch sign. *Radiology.* 2008;248(1):317-318.
23. Ito K, Mitchell DG, Gabata T, Hussain SM. Expanded gallbladder fossa: simple MR imaging sign of cirrhosis. *Radiology.* 1999;211(3):723-726.
24. Yu JS, Shim JH, Chung JJ, Kim JH, Kim KW. Double contrast-enhanced MRI of viral hepatitis-induced cirrhosis: correlation of gross morphological signs with hepatic fibrosis. *Br J Radiol.* 2010;83(987):212-217.

25. Zhang Y, Zhang XM, Prowda JC, et al. Changes in hepatic venous morphology with cirrhosis on MRI. *J Magn Reson Imaging.* 2009;29(5):1085-1092.
26. Awaya H, Mitchell DG, Kamishima T, Holland G, Ito K, Matsumoto T. Cirrhosis: modified caudate-right lobe ratio. *Radiology.* 2002;224(3):769-774.
27. Giorgio A, Amoroso P, Lettieri G, et al. Cirrhosis: value of caudate to right lobe ratio in diagnosis with US. *Radiology.* 1986;161(2):443-445.
28. Tan KC. Enlargement of the hilar periportal space. *Radiology.* 2008;248(2):699-700.
29. Ito K, Mitchell DG, Gabata T. Enlargement of hilar periportal space: a sign of early cirrhosis at MR imaging. *J Magn Reson Imaging.* 2000;11(2):136-140.
30. Colli A, Colucci A, Paggi S, et al. Accuracy of a predictive model for severe hepatic fibrosis or cirrhosis in chronic hepatitis C. *World J Gastroenterol.* 2005;11(46):7318-7322.
31. Bonekamp S, Kamel I, Solga S, Clark J. Can imaging modalities diagnose and stage hepatic fibrosis and cirrhosis accurately? *J Hepatol.* 2009;50(1):17-35.
32. Tchelepi H, Ralls PW, Radin R, Grant E. Sonography of diffuse liver disease. *J Ultrasound Med.* 2002;21(9):1023-1032; quiz 1033-1024.
33. Haktanir A, Cihan BS, Celenk C, Cihan S. Value of Doppler sonography in assessing the progression of chronic viral hepatitis and in the diagnosis and grading of cirrhosis. *J Ultrasound Med.* 2005;24(3):311-321.
34. Kawanaka H, Kinjo N, Anegawa G, et al. Abnormality of the hepatic vein waveforms in cirrhotic patients with portal hypertension and its prognostic implications. *J Gastroenterol Hepatol.* 2008;23(7 Pt 2):e129-136.
35. Oguzkurt L, Yildirim T, Torun D, Tercan F, Kizilkilic O, Niron EA. Hepatic vein Doppler waveform in patients with diffuse fatty infiltration of the liver. *Eur J Radiol.* 2005;54(2):253-257.
36. Bernatik T, Strobel D, Hahn EG, Becker D. Doppler measurements: a surrogate marker of liver fibrosis? *Eur J Gastroenterol Hepatol.* 2002;14(4):383-387.
37. Talwalkar JA, Kurtz DM, Schoenleber SJ, West CP, Montori VM. Ultrasound-based transient elastography for the detection of hepatic fibrosis: systematic review and meta-analysis. *Clin Gastroenterol Hepatol.* 2007;5(10):1214-1220.
38. Degos F, Perez P, Roche B, et al. Diagnostic accuracy of FibroScan and comparison to liver fibrosis biomarkers in chronic viral hepatitis: a multicenter prospective study (the FIBROSTIC study). *J Hepatol.* 2010;53(6):1013-1021.
39. Myers RP, Pomier-Layrargues G, Kirsch R, et al. Discordance in fibrosis staging between liver biopsy and transient elastography using the FibroScan XL probe. *J Hepatol.* 2012;56(3):564-570.
40. Yoneda M, Suzuki K, Kato S, et al. Nonalcoholic fatty liver disease: US-based acoustic radiation force impulse elastography. *Radiology.* 2010;256(2):640-647.
41. Palmeri ML, Wang MH, Rouze NC, et al. Noninvasive evaluation of hepatic fibrosis using acoustic radiation force-based shear stiffness in patients with nonalcoholic fatty liver disease. *J Hepatol.* 2011;55(3):666-672.
42. Ochi H, Hirooka M, Koizumi Y, et al. Real-time tissue elastography for evaluation of hepatic fibrosis and portal hypertension in nonalcoholic fatty liver diseases. *Hepatology.* 2012;56(4):1271-1278.
43. Bota S, Herkner H, Sporea I, et al. Meta-analysis: ARFI elastography versus transient elastography for the evaluation of liver fibrosis. *Liver Int.* 2013;33(8):1138-1147.
44. Arena U, Vizzutti F, Corti G, et al. Acute viral hepatitis increases liver stiffness values measured by transient elastography. *Hepatology.* 2008;47(2):380-384.
45. Millonig G, Reimann FM, Friedrich S, et al. Extrahepatic cholestasis increases liver stiffness (FibroScan) irrespective of fibrosis. *Hepatology.* 2008;48(5):1718-1723.
46. Millonig G, Friedrich S, Adolf S, et al. Liver stiffness is directly influenced by central venous pressure. *J Hepatol.* 2010;52(2):206-210.
47. Mederacke I, Wursthorn K, Kirschner J, et al. Food intake increases liver stiffness in patients with chronic or resolved hepatitis C virus infection. *Liver Int.* 2009;29(10):1500-1506.
48. Popescu A, Bota S, Sporea I, et al. The influence of food intake on liver stiffness values assessed by acoustic radiation force impulse elastography-preliminary results. *Ultrasound Med Biol.* 2013;39(4):579-584.

49. Bonekamp D, Bonekamp S, Geiger B, Kamel IR. An elevated arterial enhancement fraction is associated with clinical and imaging indices of liver fibrosis and cirrhosis. *J Comput Assist Tomogr.* 2012;36(6):681-689.
50. Lv P, Lin X, Gao J, Chen K. Spectral CT: preliminary studies in the liver cirrhosis. *Korean J Radiol.* 2012;13(4):434-442.
51. Ronot M, Asselah T, Paradis V, et al. Liver fibrosis in chronic hepatitis C virus infection: differentiating minimal from intermediate fibrosis with perfusion CT. *Radiology.* 2010;256(1):135-142.
52. Zhao LQ, He W, Yan B, Wang HY, Wang J. The evaluation of haemodynamics in cirrhotic patients with spectral CT. *Br J Radiol.* 2013;86(1028):20130228.
53. Martin DR, Lauenstein T, Kalb B, et al. Liver MRI and histological correlates in chronic liver disease on multiphase gadolinium-enhanced 3D gradient echo imaging. *J Magn Reson Imaging.* 2012;36(2):422-429.
54. Singh S, Venkatesh SK, Wang Z, et al. Diagnostic performance of magnetic resonance elastography in staging liver fibrosis: a systematic review and meta-analysis of individual participant data. *Clin Gastroenterol Hepatol.* 2015;13(3):440-451 e446.
55. Castera L, Foucher J, Bernard PH, et al. Pitfalls of liver stiffness measurement: a 5-year prospective study of 13,369 examinations. *Hepatology.* 2010;51(3):828-835.
56. Bota S, Sporea I, Sirli R, et al. Factors associated with the impossibility to obtain reliable liver stiffness measurements by means of Acoustic Radiation Force Impulse (ARFI) elastography--analysis of a cohort of 1,031 subjects. *Eur J Radiol.* 2014;83(2):268-272.
57. Huwart L, Sempoux C, Vicaut E, et al. Magnetic resonance elastography for the noninvasive staging of liver fibrosis. *Gastroenterology.* 2008;135(1):32-40.
58. Wang QB, Zhu H, Liu HL, Zhang B. Performance of magnetic resonance elastography and diffusion-weighted imaging for the staging of hepatic fibrosis: A meta-analysis. *Hepatology.* 2012;56(1):239-247.
59. Taouli B, Tolia AJ, Losada M, et al. Diffusion-weighted MRI for quantification of liver fibrosis: preliminary experience. *AJR Am J Roentgenol.* 2007;189(4):799-806.
60. Girometti R, Furlan A, Bazzocchi M, et al. Diffusion-weighted MRI in evaluating liver fibrosis: a feasibility study in cirrhotic patients. *Radiol Med.* 2007;112(3):394-408.
61. Watanabe H, Kanematsu M, Goshima S, et al. Staging hepatic fibrosis: comparison of gadoxetate disodium-enhanced and diffusion-weighted MR imaging--preliminary observations. *Radiology.* 2011;259(1):142-150.
62. Choi YR, Lee JM, Yoon JH, Han JK, Choi BI. Comparison of magnetic resonance elastography and gadoxetate disodium-enhanced magnetic resonance imaging for the evaluation of hepatic fibrosis. *Invest Radiol.* 2013;48(8):607-613.
63. Hagiwara M, Rusinek H, Lee VS, et al. Advanced liver fibrosis: diagnosis with 3D whole-liver perfusion MR imaging--initial experience. *Radiology.* 2008;246(3):926-934.
64. Chen BB, Hsu CY, Yu CW, et al. Dynamic contrast-enhanced magnetic resonance imaging with Gd-EOB-DTPA for the evaluation of liver fibrosis in chronic hepatitis patients. *Eur Radiol.* 2012;22(1):171-180.
65. Patel J, Sigmund EE, Rusinek H, Oei M, Babb JS, Taouli B. Diagnosis of cirrhosis with intravoxel incoherent motion diffusion MRI and dynamic contrast-enhanced MRI alone and in combination: preliminary experience. *J Magn Reson Imaging.* 2010;31(3):589-600.
66. Shah TU, Semelka RC, Pamuklar E, et al. The risk of hepatocellular carcinoma in cirrhotic patients with small liver nodules on MRI. *Am J Gastroenterol.* 2006;101(3):533-540.
67. Singal AG, Pillai A, Tiro J. Early detection, curative treatment, and survival rates for hepatocellular carcinoma surveillance in patients with cirrhosis: a meta-analysis. *PLoS Med.* 2014;11(4):e1001624.
68. Gaba RC, Kallwitz ER, Parvinian A, et al. Imaging surveillance and multidisciplinary review improves curative therapy access and survival in HCC patients. *Ann Hepatol.* 2013;12(5):766-773.
69. El-Serag HB, Kramer JR, Chen GJ, Duan Z, Richardson PA, Davila JA. Effectiveness of AFP and ultrasound tests on hepatocellular carcinoma mortality in HCV-infected patients in the USA. *Gut.* 2011;60(7):992-997.
70. Wong GL, Wong VW, Tan GM, et al. Surveillance programme for hepatocellular carcinoma improves the survival of patients with chronic viral hepatitis. *Liver Int.* 2008;28(1):79-87.
71. Stravitz RT, Heuman DM, Chand N, et al. Surveillance for hepatocellular carcinoma in patients with cirrhosis improves outcome. *Am J Med.* 2008;121(2):119-126.

72. Wald C, Russo MW, Heimbach JK, Hussain HK, Pomfret EA, Bruix J. New OPTN/UNOS policy for liver transplant allocation: standardization of liver imaging, diagnosis, classification, and reporting of hepatocellular carcinoma. *Radiology.* 2013;266(2):376-382.
73. U.S. Department of Health & Human Services. Organ Procurement and Transplantation Network. Policy 9. Available at: https://optn.transplant.hrsa.gov/media/1200/optn_policies.pdf#nameddest=Policy_09. Accessed September 1, 2017.
74. Bolondi L, Gaiani S, Celli N, et al. Characterization of small nodules in cirrhosis by assessment of vascularity: the problem of hypovascular hepatocellular carcinoma. *Hepatology.* 2005;42(1):27-34.
75. Choi JY, Lee JM, Sirlin CB. CT and MR imaging diagnosis and staging of hepatocellular carcinoma: part II. Extracellular agents, hepatobiliary agents, and ancillary imaging features. *Radiology.* 2014;273(1):30-50.
76. Forner A, Vilana R, Ayuso C, et al. Diagnosis of hepatic nodules 20 mm or smaller in cirrhosis: Prospective validation of the noninvasive diagnostic criteria for hepatocellular carcinoma. *Hepatology.* 2008;47(1):97-104.
77. Perkins JD. Seeding risk following percutaneous approach to hepatocellular carcinoma. *Liver Transpl.* 2007;13(11):1603.
78. American College of Radiology. Liver Imaging Reporting and Data System (LI-RADS). http://www.acr.org/quality-safety/resources/LIRADS. Accessed September 1, 2017.
79. American College of Radiology. ACR Appropriateness Criteria®: Liver Lesion — Initial Characterization. Available at: https://acsearch.acr.org/docs/69472/Narrative/. Accessed September 1, 2017.
80. Forner A, Reig M, Bruix J. Alpha-fetoprotein for hepatocellular carcinoma diagnosis: the demise of a brilliant star. *Gastroenterology.* 2009;137(1):26-29.
81. Singal A, Volk ML, Waljee A, et al. Meta-analysis: surveillance with ultrasound for early-stage hepatocellular carcinoma in patients with cirrhosis. *Aliment Pharmacol Ther.* 2009;30(1):37-47.
82. Gonzalez SA, Keeffe EB. Diagnosis of hepatocellular carcinoma: role of tumor markers and liver biopsy. *Clin Liver Dis.* 2011;15(2):297-306, vii-x.
83. Zhang BH, Yang BH, Tang ZY. Randomized controlled trial of screening for hepatocellular carcinoma. *J Cancer Res Clin Oncol.* 2004;130(7):417-422.
84. Taouli B, Krinsky GA. Diagnostic imaging of hepatocellular carcinoma in patients with cirrhosis before liver transplantation. *Liver Transpl.* 2006;12(11 Suppl 2):S1-7.
85. Finberg HJ. Whither (wither?) the ultrasound specialist? *J Ultrasound Med.* 2004;23(12):1543-1547.
86. EASL-EORTC clinical practice guidelines: management of hepatocellular carcinoma. *J Hepatol.* 2012;56(4):908-943.
87. Kudo M. Real practice of hepatocellular carcinoma in Japan: conclusions of the Japan Society of Hepatology 2009 Kobe Congress. *Oncology.* 2010;78 Suppl 1:180-188.
88. Omata M, Lesmana LA, Tateishi R, et al. Asian Pacific Association for the Study of the Liver consensus recommendations on hepatocellular carcinoma. *Hepatol Int.* 2010;4(2):439-474.
89. Choi JY, Lee JM, Sirlin CB. CT and MR imaging diagnosis and staging of hepatocellular carcinoma: part I. Development, growth, and spread: key pathologic and imaging aspects. *Radiology.* 2014;272(3):635-654.
90. Kim KA, Kim MJ, Choi JY, Chung YE. Development of hepatocellular carcinomas in patients with absence of tumors on a prior ultrasound examination. *Eur J Radiol.* 2012;81(7):1450-1454.
91. Yu NC, Chaudhari V, Raman SS, et al. CT and MRI improve detection of hepatocellular carcinoma, compared with ultrasound alone, in patients with cirrhosis. *Clin Gastroenterol Hepatol.* 2011;9(2):161-167.
92. Singal AG, Conjeevaram HS, Volk ML, et al. Effectiveness of hepatocellular carcinoma surveillance in patients with cirrhosis. *Cancer Epidemiol Biomarkers Prev.* 2012;21(5):793-799.
93. Colli A, Fraquelli M, Casazza G, et al. Accuracy of ultrasonography, spiral CT, magnetic resonance, and alpha-fetoprotein in diagnosing hepatocellular carcinoma: a systematic review. *Am J Gastroenterol.* 2006;101(3):513-523.
94. Jang HJ, Kim TK, Wilson SR. Small nodules (1-2 cm) in liver cirrhosis: characterization with contrast-enhanced ultrasound. *Eur J Radiol.* 2009;72(3):418-424.

95. D'Onofrio M, Faccioli N, Zamboni G, et al. Focal liver lesions in cirrhosis: value of contrast-enhanced ultrasonography compared with Doppler ultrasound and alpha-fetoprotein levels. *Radiol Med.* 2008;113(7):978-991.
96. Wang JH, Lu SN, Hung CH, et al. Small hepatic nodules (< or =2 cm) in cirrhosis patients: characterization with contrast-enhanced ultrasonography. *Liver Int.* 2006;26(8):928-934.
97. Xu HX, Lu MD, Liu LN, et al. Discrimination between neoplastic and non-neoplastic lesions in cirrhotic liver using contrast-enhanced ultrasound. *Br J Radiol.* 2012;85(1018):1376-1384.
98. Claudon M, Dietrich CF, Choi BI, et al. Guidelines and good clinical practice recommendations for Contrast Enhanced Ultrasound (CEUS) in the liver - update 2012: A WFUMB-EFSUMB initiative in cooperation with representatives of AFSUMB, AIUM, ASUM, FLAUS and ICUS. *Ultrasound Med Biol.* 2013;39(2):187-210.
99. Khalili K, Kim TK, Jang HJ, et al. Optimization of imaging diagnosis of 1-2 cm hepatocellular carcinoma: an analysis of diagnostic performance and resource utilization. *J Hepatol.* 2011;54(4):723-728.
100. Sangiovanni A, Manini MA, Iavarone M, et al. The diagnostic and economic impact of contrast imaging techniques in the diagnosis of small hepatocellular carcinoma in cirrhosis. *Gut.* 2010;59(5):638-644.
101. Kim TK, Lee KH, Jang HJ, et al. Analysis of gadobenate dimeglumine-enhanced MR findings for characterizing small (1-2-cm) hepatic nodules in patients at high risk for hepatocellular carcinoma. *Radiology.* 2011;259(3):730-738.
102. Rimola J, Forner A, Tremosini S, et al. Non-invasive diagnosis of hepatocellular carcinoma </= 2 cm in cirrhosis. Diagnostic accuracy assessing fat, capsule and signal intensity at dynamic MRI. *J Hepatol.* 2012;56(6):1317-1323.
103. Akai H, Kiryu S, Matsuda I, et al. Detection of hepatocellular carcinoma by Gd-EOB-DTPA-enhanced liver MRI: comparison with triple phase 64 detector row helical CT. *Eur J Radiol.* 2011;80(2):310-315.
104. Inoue T, Kudo M, Komuta M, et al. Assessment of Gd-EOB-DTPA-enhanced MRI for HCC and dysplastic nodules and comparison of detection sensitivity versus MDCT. *J Gastroenterol.* 2012;47(9):1036-1047.
105. Marrero JA, Hussain HK, Nghiem HV, Umar R, Fontana RJ, Lok AS. Improving the prediction of hepatocellular carcinoma in cirrhotic patients with an arterially-enhancing liver mass. *Liver Transpl.* 2005;11(3):281-289.
106. Ooka Y, Kanai F, Okabe S, et al. Gadoxetic acid-enhanced MRI compared with CT during angiography in the diagnosis of hepatocellular carcinoma. *Magn Reson Imaging.* 2013;31(5):748-754.
107. Rhee H, Kim MJ, Park MS, Kim KA. Differentiation of early hepatocellular carcinoma from benign hepatocellular nodules on gadoxetic acid-enhanced MRI. *Br J Radiol.* 2012;85(1018):e837-844.
108. Luca A, Caruso S, Milazzo M, et al. Multidetector-row computed tomography (MDCT) for the diagnosis of hepatocellular carcinoma in cirrhotic candidates for liver transplantation: prevalence of radiological vascular patterns and histological correlation with liver explants. *Eur Radiol.* 2010;20(4):898-907.
109. Golfieri R, Renzulli M, Lucidi V, Corcioni B, Trevisani F, Bolondi L. Contribution of the hepatobiliary phase of Gd-EOB-DTPA-enhanced MRI to Dynamic MRI in the detection of hypovascular small (</= 2 cm) HCC in cirrhosis. *Eur Radiol.* 2011;21(6):1233-1242.
110. Granito A, Galassi M, Piscaglia F, et al. Impact of gadoxetic acid (Gd-EOB-DTPA)-enhanced magnetic resonance on the non-invasive diagnosis of small hepatocellular carcinoma: a prospective study. *Aliment Pharmacol Ther.* 2013;37(3):355-363.
111. Piana G, Trinquart L, Meskine N, Barrau V, Beers BV, Vilgrain V. New MR imaging criteria with a diffusion-weighted sequence for the diagnosis of hepatocellular carcinoma in chronic liver diseases. *J Hepatol.* 2011;55(1):126-132.
112. Sano K, Ichikawa T, Motosugi U, et al. Imaging study of early hepatocellular carcinoma: usefulness of gadoxetic acid-enhanced MR imaging. *Radiology.* 2011;261(3):834-844.
113. Sun HY, Lee JM, Shin CI, et al. Gadoxetic acid-enhanced magnetic resonance imaging for differentiating small hepatocellular carcinomas (< or =2 cm in diameter) from arterial enhancing pseudolesions: special emphasis on hepatobiliary phase imaging. *Invest Radiol.* 2010;45(2):96-103.
114. Furlan A, Marin D, Vanzulli A, et al. Hepatocellular carcinoma in cirrhotic patients at multidetector CT: hepatic venous phase versus delayed phase for the detection of tumour washout. *Br J Radiol.* 2011;84(1001):403-412.

115. Cereser L, Furlan A, Bagatto D, et al. Comparison of portal venous and delayed phases of gadolinium-enhanced magnetic resonance imaging study of cirrhotic liver for the detection of contrast washout of hypervascular hepatocellular carcinoma. *J Comput Assist Tomogr.* 2010;34(5):706-711.
116. Anzidei M, Di Martino M, Sacconi B, et al. Evaluation of image quality, radiation dose and diagnostic performance of dual-energy CT datasets in patients with hepatocellular carcinoma. *Clin Radiol.* 2015;70(9):966-973.
117. Hanna RF, Aguirre DA, Kased N, Emery SC, Peterson MR, Sirlin CB. Cirrhosis-associated hepatocellular nodules: correlation of histopathologic and MR imaging features. *Radiographics.* 2008;28(3):747-769.
118. Loyer EM, Chin H, DuBrow RA, David CL, Eftekhari F, Charnsangavej C. Hepatocellular carcinoma and intrahepatic peripheral cholangiocarcinoma: enhancement patterns with quadruple phase helical CT--a comparative study. *Radiology.* 1999;212(3):866-875.
119. Doyle DJ, O'Malley ME, Jang HJ, Jhaveri K. Value of the unenhanced phase for detection of hepatocellular carcinomas 3 cm or less when performing multiphase computed tomography in patients with cirrhosis. *J Comput Assist Tomogr.* 2007;31(1):86-92.
120. Iannaccone R, Laghi A, Catalano C, et al. Hepatocellular carcinoma: role of unenhanced and delayed phase multi-detector row helical CT in patients with cirrhosis. *Radiology.* 2005;234(2):460-467.
121. Luke FE, Allen BC, Moshiri ST, et al. Multiphase multi-detector row computed tomography in the setting of chronic liver disease and orthotopic liver transplantation: can a series be eliminated in order to reduce radiation dose? *J Comput Assist Tomogr.* 2013;37(3):408-414.
122. Van Thiel DH, Yong S, Li SD, Kennedy M, Brems J. The development of de novo hepatocellular carcinoma in patients on a liver transplant list: frequency, size, and assessment of current screening methods. *Liver Transpl.* 2004;10(5):631-637.
123. Valls C, Cos M, Figueras J, et al. Pretransplantation diagnosis and staging of hepatocellular carcinoma in patients with cirrhosis: value of dual-phase helical CT. *AJR Am J Roentgenol.* 2004;182(4):1011-1017.
124. Ronzoni A, Artioli D, Scardina R, et al. Role of MDCT in the diagnosis of hepatocellular carcinoma in patients with cirrhosis undergoing orthotopic liver transplantation. *AJR Am J Roentgenol.* 2007;189(4):792-798.
125. Lim KS. Diffusion-weighted MRI of hepatocellular carcinoma in cirrhosis. *Clin Radiol.* 2014;69(1):1-10.
126. Lencioni R, Mascalchi M, Caramella D, Bartolozzi C. Small hepatocellular carcinoma: differentiation from adenomatous hyperplasia with color Doppler US and dynamic Gd-DTPA-enhanced MR imaging. *Abdom Imaging.* 1996;21(1):41-48.
127. Libbrecht L, Bielen D, Verslype C, et al. Focal lesions in cirrhotic explant livers: pathological evaluation and accuracy of pretransplantation imaging examinations. *Liver Transpl.* 2002;8(9):749-761.
128. Park MJ, Kim YK, Lee MW, et al. Small hepatocellular carcinomas: improved sensitivity by combining gadoxetic acid-enhanced and diffusion-weighted MR imaging patterns. *Radiology.* 2012;264(3):761-770.
129. Le Moigne F, Durieux M, Bancel B, et al. Impact of diffusion-weighted MR imaging on the characterization of small hepatocellular carcinoma in the cirrhotic liver. *Magn Reson Imaging.* 2012;30(5):656-665.
130. Kim YK, Lee WJ, Park MJ, Kim SH, Rhim H, Choi D. Hypovascular hypointense nodules on hepatobiliary phase gadoxetic acid-enhanced MR images in patients with cirrhosis: potential of DW imaging in predicting progression to hypervascular HCC. *Radiology.* 2012;265(1):104-114.
131. Hyodo T, Murakami T, Imai Y, et al. Hypovascular nodules in patients with chronic liver disease: risk factors for development of hypervascular hepatocellular carcinoma. *Radiology.* 2013;266(2):480-490.
132. Bartolozzi C, Battaglia V, Bargellini I, et al. Contrast-enhanced magnetic resonance imaging of 102 nodules in cirrhosis: correlation with histological findings on explanted livers. *Abdom Imaging.* 2013;38(2):290-296.
133. Gatto A, De Gaetano AM, Giuga M, et al. Differentiating hepatocellular carcinoma from dysplastic nodules at gadobenate dimeglumine-enhanced hepatobiliary-phase magnetic resonance imaging. *Abdom Imaging.* 2013;38(4):736-744.
134. Golfieri R, Grazioli L, Orlando E, et al. Which is the best MRI marker of malignancy for atypical cirrhotic nodules: hypointensity in hepatobiliary phase alone or combined with other features? Classification after Gd-EOB-DTPA administration. *J Magn Reson Imaging.* 2012;36(3):648-657.

135. Ahn SS, Kim MJ, Lim JS, Hong HS, Chung YE, Choi JY. Added value of gadoxetic acid-enhanced hepatobiliary phase MR imaging in the diagnosis of hepatocellular carcinoma. *Radiology.* 2010;255(2):459-466.
136. Di Martino M, De Filippis G, De Santis A, et al. Hepatocellular carcinoma in cirrhotic patients: prospective comparison of US, CT and MR imaging. *Eur Radiol.* 2013;23(4):887-896.
137. Onishi H, Kim T, Imai Y, et al. Hypervascular hepatocellular carcinomas: detection with gadoxetate disodium-enhanced MR imaging and multiphasic multidetector CT. *Eur Radiol.* 2012;22(4):845-854.
138. Liu X, Zou L, Liu F, Zhou Y, Song B. Gadoxetic acid disodium-enhanced magnetic resonance imaging for the detection of hepatocellular carcinoma: a meta-analysis. *PLoS One.* 2013;8(8):e70896.
139. Wu LM, Xu JR, Gu HY, et al. Is liver-specific gadoxetic acid-enhanced magnetic resonance imaging a reliable tool for detection of hepatocellular carcinoma in patients with chronic liver disease? *Dig Dis Sci.* 2013;58(11):3313-3325.
140. Kumada T, Toyoda H, Tada T, et al. Evolution of hypointense hepatocellular nodules observed only in the hepatobiliary phase of gadoxetate disodium-enhanced MRI. *AJR Am J Roentgenol.* 2011;197(1):58-63.
141. Higaki A, Ito K, Tamada T, et al. High-risk nodules detected in the hepatobiliary phase of Gd-EOB-DTPA-enhanced MR imaging in cirrhosis or chronic hepatitis: incidence and predictive factors for hypervascular transformation, preliminary results. *J Magn Reson Imaging.* 2013;37(6):1377-1383.
142. Tamada T, Ito K, Higaki A, et al. Gd-EOB-DTPA-enhanced MR imaging: evaluation of hepatic enhancement effects in normal and cirrhotic livers. *Eur J Radiol.* 2011;80(3):e311-316.
143. Kim HY, Choi JY, Park CH, et al. Clinical factors predictive of insufficient liver enhancement on the hepatocyte-phase of Gd-EOB-DTPA-enhanced magnetic resonance imaging in patients with liver cirrhosis. *J Gastroenterol.* 2013;48(10):1180-1187.
144. Verloh N, Haimerl M, Rennert J, et al. Impact of liver cirrhosis on liver enhancement at Gd-EOB-DTPA enhanced MRI at 3 Tesla. *Eur J Radiol.* 2013;82(10):1710-1715.
145. Xu J, Igarashi S, Sasaki M, et al. Intrahepatic cholangiocarcinomas in cirrhosis are hypervascular in comparison with those in normal livers. *Liver Int.* 2012;32(7):1156-1164.
146. Anaparthy R, Talwalkar JA, Yin M, Roberts LR, Fidler JL, Ehman RL. Liver stiffness measurement by magnetic resonance elastography is not associated with developing hepatocellular carcinoma in subjects with compensated cirrhosis. *Aliment Pharmacol Ther.* 2011;34(1):83-91.
147. Singh S, Fujii LL, Murad MH, et al. Liver stiffness is associated with risk of decompensation, liver cancer, and death in patients with chronic liver diseases: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol.* 2013;11(12):1573-1584 e1571-1572; quiz e1588-1579.
148. Delbeke D, Martin WH, Sandler MP, Chapman WC, Wright JK, Jr., Pinson CW. Evaluation of benign vs malignant hepatic lesions with positron emission tomography. *Arch Surg.* 1998;133(5):510-515; discussion 515-516.
149. Khan MA, Combs CS, Brunt EM, et al. Positron emission tomography scanning in the evaluation of hepatocellular carcinoma. *J Hepatol.* 2000;32(5):792-797.
150. Trojan J, Schroeder O, Raedle J, et al. Fluorine-18 FDG positron emission tomography for imaging of hepatocellular carcinoma. *Am J Gastroenterol.* 1999;94(11):3314-3319.
151. Kim BK, Kang WJ, Kim JK, et al. 18F-fluorodeoxyglucose uptake on positron emission tomography as a prognostic predictor in locally advanced hepatocellular carcinoma. *Cancer.* 2011;117(20):4779-4787.
152. Castilla-Lievre MA, Franco D, Gervais P, et al. Diagnostic value of combining (11)C-choline and (18)F-FDG PET/CT in hepatocellular carcinoma. *Eur J Nucl Med Mol Imaging.* 2016;43(5):852-859.
153. American College of Radiology. ACR Appropriateness Criteria®: Radiologic Management of Hepatic Malignancy. Available at: https://acsearch.acr.org/docs/69379/Narrative/. Accessed September 1, 2017.
154. Gaba RC. Chemoembolization practice patterns and technical methods among interventional radiologists: results of an online survey. *AJR Am J Roentgenol.* 2012;198(3):692-699.
155. Gaba RC, Baerlocher MO, Nikolic B, Venkatesan AM, Lewandowski RJ. Clinical and Imaging Follow-up Practices after Transarterial Therapy for Primary and Secondary Hepatic Malignancies: Results of an Online Survey. *Acad Radiol.* 2015;22(12):1510-1515.
156. NCCN Clinical Practice Guidelines in Oncology. Hepatobiliary Cancers. Version 2.2017. 2017; Available at: https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary.pdf. Accessed September 1, 2017.
157. Boas FE, Do B, Louie JD, et al. Optimal imaging surveillance schedules after liver-directed therapy for hepatocellular carcinoma. *J Vasc Interv Radiol.* 2015;26(1):69-73.

158. Chiu RY, Yap WW, Patel R, Liu D, Klass D, Harris AC. Hepatocellular Carcinoma Post Embolotherapy: Imaging Appearances and Pitfalls on Computed Tomography and Magnetic Resonance Imaging. *Can Assoc Radiol J.* 2016;67(2):158-172.
159. Okada M, Kim T, Murakami T. Hepatocellular nodules in liver cirrhosis: state of the art CT evaluation (perfusion CT/volume helical shuttle scan/dual-energy CT, etc.). *Abdom Imaging.* 2011;36(3):273-281.
160. Yu JS, Kim YH, Rofsky NM. Dynamic subtraction magnetic resonance imaging of cirrhotic liver: assessment of high signal intensity lesions on nonenhanced T1-weighted images. *J Comput Assist Tomogr.* 2005;29(1):51-58.
161. Liu LN, Xu HX, Zhang YF, Xu JM. Hepatocellular carcinoma after ablation: the imaging follow-up scheme. *World J Gastroenterol.* 2013;19(6):797-801.
162. Roccarina D, Garcovich M, Ainora ME, et al. Usefulness of contrast enhanced ultrasound in monitoring therapeutic response after hepatocellular carcinoma treatment. *World J Hepatol.* 2015;7(14):1866-1874.
163. Zheng SG, Xu HX, Lu MD, et al. Role of contrast-enhanced ultrasound in follow-up assessment after ablation for hepatocellular carcinoma. *World J Gastroenterol.* 2013;19(6):855-865.
164. Guibal A, Bertin C, Egels S, Savier E, Grenier PA, Lucidarme O. Contrast-enhanced ultrasound (CEUS) follow-up after radiofrequency ablation or cryoablation of focal liver lesions: treated-area patterns and their changes over time. *Eur Radiol.* 2013;23(5):1392-1400.
165. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: http://www.acr.org/~/media/ACR/Documents/AppCriteria/RadiationDoseAssessmentIntro.pdf. Accessed September 1, 2017.