LI-RADS Version 2018 Ancillary Features at MRI

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The Liver Imaging Reporting and Data System (LI-RADS) standardizes performance of liver imaging in patients at risk for hepatocellular carcinoma (HCC) as well as interpretation and reporting of the results. Developed by experts in liver imaging and supported by the American College of Radiology, LI-RADS assigns to observations categories that reflect the relative probability of benignity, HCC, or other malignancy. While category assignment is based mainly on major imaging features, ancillary features may be applied to improve detection and characterization, increase confidence, or adjust LI-RADS categories. Ancillary features are classified as favoring malignancy in general, HCC in particular, or benignity. Those favoring malignancy in general or HCC in particular may be used to upgrade by a maximum of one category up to LR-4; those favoring benignity may be used to downgrade by a maximum of one category. If there are conflicting ancillary features (ie, one or more favoring malignancy and one or more favoring benignity), the category should not be adjusted. Ancillary features may be seen at diagnostic CT, MRI performed with extracellular agents, or MRI performed with hepatobiliary agents, with the exception of one ancillary feature assessed at US. This article focuses on LI-RADS version 2018 ancillary features seen at MRI. Specific topics include rules for ancillary feature application; definitions, rationale, and illustrations with clinical MRI examples; summary of evidence and diagnostic performance; pitfalls; and future directions.

Abbreviations: ADC = apparent diffusion coefficient, APHE = arterial phase hyperenhancement, DWI = diffusion-weighted imaging, HBP = hepatobiliary phase, HCC = hepatocellular carcinoma, LI-RADS = Liver Imaging Reporting and Data System, OATP = organic anion-transporting polypeptide, PVP = portal venous phase, TE = echo time, TVDT = tumor volume doubling time

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SA-CME LEARNING OBJECTIVES

After completing this journal-based SA-CME activity, participants will be able to:

- Apply the rules for ancillary features to modify the final LI-RADS category of a liver observation.
- Recognize and describe ancillary features at MRI that favor malignancy in general, HCC in particular, and benign observations.
- Explain the rationale supporting ancillary features and their limitations.

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Introduction

Hepatocellular carcinoma (HCC) is the sixth most frequent cancer and second most common cause of mortality attributable to cancer worldwide (1). The majority of HCCs occur in cirrhosis (2,3), most often due to chronic viral hepatitis (4), nonalcoholic fatty liver disease (5,6), and excess alcohol consumption.

Unlike most other cancers, HCC can be diagnosed noninvasively with imaging without mandatory pathology confirmation (7–10). Many diagnostic systems provide algorithms and criteria for imaging-based diagnosis of HCC (11). Among these, the Liver Imaging Reporting and Data System (LI-RADS) has been developed for

TEACHING POINTS

- Ancillary features may be used to improve detection and characterization, increase confidence, or adjust observation category.
- Ancillary features favoring malignancy in general or HCC in particular may be used to upgrade by a maximum of one category up to LR-4.
- To preserve high specificity for the LR-5 category, ancillary features may not be used to upgrade observations to LR-5.
- Ancillary features favoring benignity may be used to downgrade an observation by a maximum of one category.
- If there are conflicting ancillary features (ie, one or more favoring malignancy and one or more favoring benignity), the category should not be adjusted.

standardized reporting of imaging results and data collection in patients at risk for HCC. The aims of LI-RADS are to assist radiologists in categorization of liver imaging findings in at-risk patients, diminish imaging interpretation variability, and facilitate communication between radiologists and referring clinicians by using a common terminology. With the support of the American College of Radiology, a committee of radiologists, hepatologists, hepatopathologists, surgeons, and lexicon experts has developed LI-RADS (12) on the basis of scientific evidence, expert opinion, and iterative refinements in response to user feedback (12,13).

The at-risk population targeted by LI-RADS comprises patients with cirrhosis, chronic hepatitis B virus infection without cirrhosis, or current or prior HCC, including adult liver transplant candidates and recipients. LI-RADS does not apply to children or to patients with vascular liver disorders or cirrhosis due to congenital hepatic fibrosis. CT and MRI are widely used for diagnosis of HCC. MRI is ideal for characterizing observations using LI-RADS because this modality has numerous contrast enhancement mechanisms and is the only modality that allows assessment of all major as well as ancillary imaging features.

This article focuses on LI-RADS version 2018 ancillary features visible at MRI. It reviews the rules for applying ancillary features; provides definitions and clinical illustrations; summarizes the rationale, evidence, and diagnostic performance supporting the use of ancillary features; and discusses potential pitfalls and future directions.

Categories and Major Features

In LI-RADS, observations are defined as areas with imaging features that differ from those of adjacent liver parenchyma. LI-RADS assigns to imaging-detected liver observations categories that reflect the relative probability of benignity, HCC, or other malignancy. Categories include LR-1 (definitely benign), LR-2 (probably benign), LR-3 (intermediate probability for malignancy), LR-4 (probably HCC), LR-5 (definitely HCC), LR-TIV (definite tumor in vein), and LR-M (probably or definitely malignant, not specific for HCC) (Fig 1) (12).

In LI-RADS, major features refer to five imaging features included in the diagnostic table for categorizing LR-3, LR-4, and LR-5 observations: nonrim arterial phase hyperenhancement (APHE), nonperipheral washout appearance ("washout"), enhancing capsule appearance ("capsule"), size, and threshold growth (13). Major features have previously been discussed (13,14) and are not covered in this article.

Ancillary Features

In contrast to major features, ancillary features are optional imaging features applied at the radiologist's discretion. Ancillary features may be used to improve detection and characterization, increase confidence, or adjust observation category. These ancillary features may favor malignancy in general, HCC in particular, or benignity (Table 1) (12).

Ancillary features favoring malignancy in general or HCC in particular may be used to upgrade by a maximum of one category up to LR-4. Ancillary features that favor malignancy in general can be seen not only in HCC but also in other non-HCC neoplasms such as cholangiocarcinoma, combined hepatocholangiocarcinoma, or metastases. Ancillary features that favor HCC in particular are more specific for malignancies of hepatocellular origin.

Unlike combinations of major features that can be used to establish a definite diagnosis of HCC (ie, LR-5), ancillary features alone cannot be used to definitely diagnose HCC because they lack the required specificity (15–17).

Studies assessing the clinical application of ancillary features have shown that they modify the final category in 15%–35% of observations (18–20), with about 63% of LR-4 observations being upgraded from LR-3. Use of ancillary features favoring malignancy (including ancillary features favoring HCC in particular) to upgrade LR-3 observations to LR-4 increases sensitivity for HCC (from 87% to 97%) but lowers specificity (from 69% to 51%) at MRI (21). In a separate study, using ancillary features to upgrade LR-3 observations to probable or definite HCC (LR-4, LR-5, or LR-5V [equivalent to LR-TIV in version 2018]) increased sensitivity (from 76% to 88%) while preserving high specificity (from 88% to 86%) (18).

Ancillary features that favor benignity include size stability for 2 years or longer, size reduction, and features indicative of benign entities. Hence, features that favor benignity reduce the probability of malignancy or HCC. When present, these features are highly specific for benignity (18).

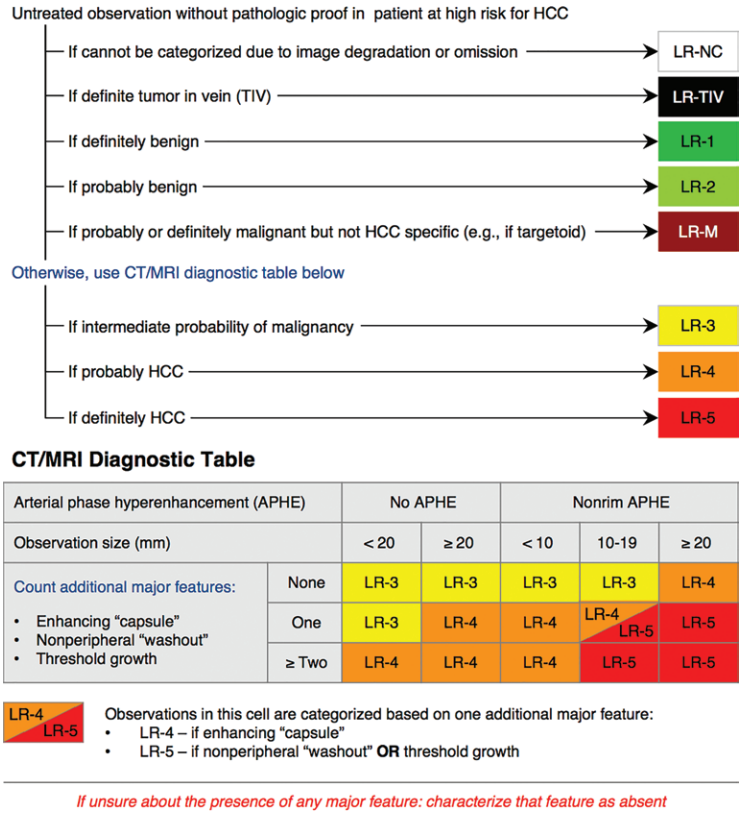


Figure 1. LI-RADS diagnostic algorithm and table. *APHE* = arterial phase hyperenhancement.

Table 1: Ancillary Features in LI-RADS Version 2018

Ancillary features favoring malignancy in general
US visibility as discrete nodule
Subthreshold growth
Corona enhancement
Fat sparing in solid mass
Restricted diffusion
Mild-moderate T2 hyperintensity
Iron sparing in solid mass
Transitional phase hypointensity
Hepatobiliary phase (HBP) hypointensity
Ancillary features favoring HCC in particular
Nonenhancing "capsule"
Mosaic architecture
Nodule-in-nodule architecture
Fat in mass, more than in adjacent liver
Blood products in mass
Ancillary features favoring benignity
Size stability for ≥2 y
Size reduction
Parallels blood pool enhancement
Undistorted vessels
Iron in mass, more than in liver
Marked T2 hyperintensity
HBP isointensity

Rules for Application of Ancillary Features

The rules for application of ancillary features are illustrated in Figure 2 and described in this section.

Optional Use of Ancillary Features in LI-RADS Version 2018

Ancillary features are optional, and the decision to use them to adjust observation category is left to the discretion of the radiologist. The optional use of ancillary features allows simplification of the LI-RADS algorithm, resulting in ease of use and wide adoption by new users (16). Nevertheless, radiologists are encouraged to use ancillary features, as these leverage complementary tissue contrast enhancement mechanisms and tumor properties to modulate the final observation category.

Category Upgrade

Ancillary features favoring malignancy in general or HCC in particular may be used to upgrade by one category only and may not be used to upgrade from LR-4 to LR-5. For example, an observation categorized LR-3 may be upgraded to LR-4 in the presence of one or more ancillary features favoring malignancy and in the absence of ancillary features favoring benignity. To preserve high specificity for the LR-5 category, ancillary features may not be used to upgrade observations to LR-5 (12).

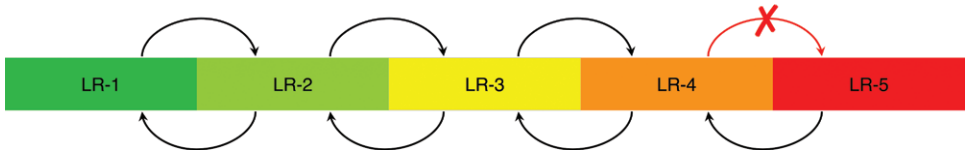


Figure 2. Rules for application of ancillary features. Use of ancillary features is optional. Ancillary features that favor malignancy in general or HCC in particular may be used to upgrade by one category only and may not be used to upgrade from LR-4 to LR-5. Ancillary features that favor benignity may be used to downgrade by one category.

Category Downgrade

Ancillary features favoring benignity may be used to downgrade an observation by a maximum of one category. For example, an observation categorized LR-4 may be downgraded to LR-3 in the presence of one or more ancillary features favoring benignity.

Absence of Ancillary Features

The absence of ancillary features should not be used to upgrade or downgrade a category. For example, absence of ancillary features favoring malignancy does not suggest benignity and should not be used to downgrade the category.

Uncertainty

When a radiologist is uncertain about the presence of an ancillary feature, it should be considered absent.

Conflicting Ancillary Features

If there are conflicting ancillary features (ie, one or more favoring malignancy and one or more favoring benignity), the category should not be adjusted. For example, if an LR-3 observation has ancillary features of both malignancy and benignity, the category should remain LR-3.

Ancillary Features Favoring Malignancy in General

Ancillary features favoring malignancy in general can be seen not only in HCC but also in other neoplasms. The ancillary features favoring malignancy in general and their definitions are given in Table 2. The diagnostic performance of ancillary features favoring malignancy in general is summarized in Table 3.

US Visibility as Discrete Nodule

Definition.—US visibility as a discrete nodule refers to visibility at nonenhanced US as a discrete nodule or mass corresponding to a CT- or MRI-detected observation (Fig 3).

Rationale.—The most common benign lesions in the cirrhotic liver (eg, regenerative or low-grade dysplastic nodules) and all benign vascular pseudolesions are typically indistinguishable from the background liver at B-mode US. Hence, lesions visible as discrete nodules are unlikely to be benign. A study revealed that nodules detected at screening US and subsequently seen at CT or MRI were HCCs in a substantial proportion of cases: 69% of LR-3, 96% of LR-4, 98% of LR-5, and 50% of LR-M (40). Because the proportions of HCCs in these LI-RADS categories are higher than for observations discovered with screening US (20), US visibility increases the pretest probability of HCC before characterization with MRI, justifying the use of this ancillary feature to increase confidence and upgrade observation category.

Diagnostic Performance.—The diagnostic performance of US visibility as a discrete nodule, in combination with major features, is unknown. However, the reported per-patient sensitivity and specificity of nonenhanced US in a surveillance setting are 78% and 89%, respectively, according to a meta-analysis by Chou et al (41). The high but imperfect specificity of nonenhanced US alone provides additional justification for US visibility as an ancillary feature.

Subthreshold Growth

Definition.—Subthreshold growth refers to unequivocal growth of a mass, but less than threshold growth. In LI-RADS version 2018, threshold growth is defined as a 50% or greater size increase in 6 months or less. Therefore, subthreshold growth may manifest as a size increase less than 50% in a time interval of 6 months or less, any size increase in a time interval of 6 months or more, or a new observation of any size (Fig 4).

As with threshold growth, subthreshold growth should not be attributable to measurement error or imprecision, differences in technique, or interval hemorrhage. Measurements should be made with the sequence, phase, and plane with which the observation is most clearly visible, using the largest dimension of the observation from outer edge to outer edge, including the "capsule" (when present) and excluding perfusion alterations. The same sequence, phase, and plane of the comparative examination should be used to

Table 2: Ancillary Features Favoring Malignancy in General

Feature	Definition	ECA MRI*	HBA MRI†
US visibility as discrete nodule	Unenhanced US visibility as discrete nodule or mass corresponding to MRI-detected observation	+	+
Subthreshold growth	Unequivocal growth of a mass, less than threshold growth	+	+
Corona enhancement	Periobservation enhancement in late arterial phase or early PVP attributable to venous drainage from tumor	+	+
Fat sparing in solid mass	Paucity of fat in solid mass relative to steatotic liver or in inner nodule relative to steatotic outer nodule	+	+
Restricted diffusion	Signal intensity at DWI, not attributable solely to T2WI shine-through, unequivocally higher than in liver and/or ADC unequivocally lower than in liver	+	+
Mild-moderate T2 hyperintensity	Signal intensity at T2WI mildly or moderately higher than in liver and similar to or less than in non–iron-overloaded spleen	+	+
Iron sparing in solid mass	Paucity of iron in solid mass relative to iron-overloaded liver or in inner nodule relative to siderotic outer nodule	+	+
Transitional phase hypointensity	Signal intensity in transitional phase unequivocally less, in whole or in part, than in liver	−	+
HBP hypointensity	Signal intensity in HBP unequivocally less, in whole or in part, than in liver	−	+

Note.—ADC = apparent diffusion coefficient, DWI = diffusion-weighted imaging, HBP = hepatobiliary phase, PVP = portal venous phase, T2WI = T2-weighted imaging.
*MRI performed with an extracellular contrast agent (ECA) can be used to characterize most ancillary features favoring malignancy.
†MRI performed with a hepatobiliary contrast agent (HBA) can be used to characterize all ancillary features favoring malignancy.

assess interval growth. Measurements in the arterial phase and with diffusion-weighted imaging (DWI) should be avoided because of potential periobservation enhancement and image distortion between two sequences, respectively, which may cause measurement error.

Rationale.—Growth rate is usually an indicator of malignancy. Unlike benign observations, which tend to remain stable, grow slowly, or disappear, malignant observations grow more rapidly. The growth rate of tumors has typically been reported in terms of tumor volume doubling time (TVDT). The median TVDT is 178 days (about 6 months) for untreated HCC and 82 days (about 3 months) for recurrent HCC after local-regional treatment (13,42). Aggressive and poorly differentiated HCCs tend to grow faster than well-differentiated HCCs.

Growth is not specific to HCC and is observed in other types of tumors as well. Hence, subthreshold growth is suggestive of malignancy in general, without being specific for HCC. The definition of subthreshold growth is adapted from the definition of threshold growth (a major feature), itself based on a combination of expert opinion and desire to maintain congruency with the OPTN/UNOS (Organ Procurement and Transplantation Network/United Network for Organ Sharing) definition of growth for prioritization of liver transplantation in HCC patients. As described earlier, threshold growth is defined in LI-RADS version 2018 as 50% or greater size increase of a mass in 6 months or less. Size should be measured with the same sequence, phase, and plane in serial examinations.

Diagnostic Performance.—According to one study (18), subthreshold growth as a stand-alone feature has sensitivity of 48% and specificity of 91% for diagnosis of HCC. The incremental effect on diagnostic performance of subthreshold growth in combination with major features is unknown. Although retrospective and prospective studies are lacking, indirect evidence and biologic plausibility suggest that subthreshold growth favors malignancy (13).

Corona Enhancement

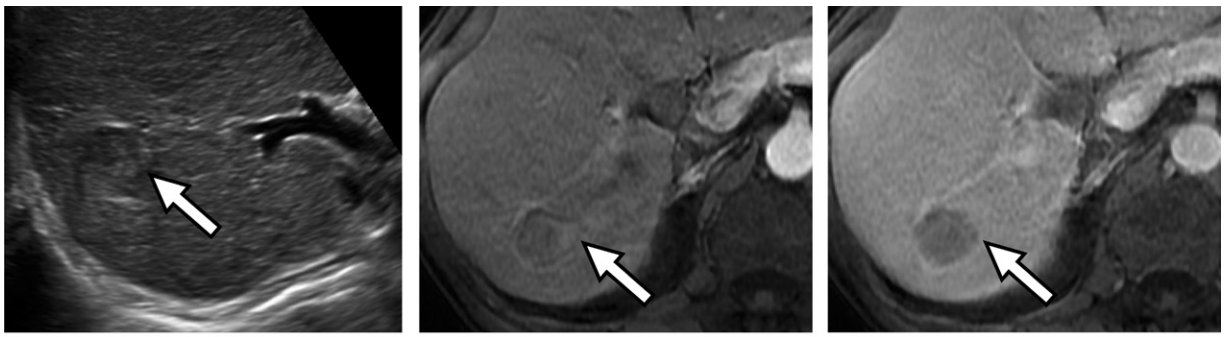
Definition.—Corona enhancement refers to periobservation enhancement in the late arterial or early portal venous phase (PVP) attributable to venous drainage from the tumor (Fig 5).

Rationale.—Also called peritumoral enhancement or corona stain, corona enhancement is

Table 3: Diagnostic Performance of Ancillary Features Favoring Malignancy in General at MRI

Ancillary Feature*	References	No. of HCCs (No. of Nodules)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Restricted diffusion	Kwon et al 2015 (22)	222 (283)	87	87	85	94
	Hwang et al 2015 (23)	25 (56)	92	84	…	…
	Xu et al 2010 (24)	40 (59)	98	…	…	…
	Inchingolo et al 2015 (25)	29 (53)	97	71	80	94
	Granata et al 2017 (26)	127 (173)	84	100	100	55
	Le Moigne et al 2012 (27)	66 (82)	88	75	…	…
Mild-moderate T2 hyperintensity	Hecht et al 2006 (28)	19 (57)	68	63	…	…
	Hwang et al 2015 (23)	25 (56)	76	87	…	…
	Kim et al 2011 (29)	108 (141)	91	79	…	…
	Granata et al 2017 (26)	127 (173)	100	55	…	…
	Ouedraogo et al 2011 (30)	54 (61)	78	73	…	…
Transitional phase hypointensity	Joo et al 2015 (31)	128 (152)	83–91	33–58	88–91	39–42
HBP hypointensity	Di Martino et al 2016 (32)	71 (118)	75–83	92–96	93–97	71–79
	Ahn et al 2010 (33)	84 (113)	87–92	90–93	…	…
	Golfieri et al 2011 (34)	20 (62)	99	95	99	98
	Sano et al 2011 (35)	96 (108)	94–97	94–96	90–94	97–98
	Haradome et al 2011 (36)	60 (86)	87	90–92	…	…
	Orlacchio et al 2016 (37)	37 (46)	95	90	…	…
	Lee et al 2011 (38)	46 (70)	85	42	…	…
	Sun et al 2010 (39)	44 (97)	93–96	96	95–96	94–96
	Joo et al 2015 (31)	292 (387)	94	48	85	72

Note.—HBP = hepatobiliary phase, NPV = negative predictive value, PPV = positive predictive value.
*Estimates of diagnostic performance are not available for the following ancillary features: US visibility as discrete nodule, subthreshold growth, corona enhancement, fat sparing in solid mass, and iron sparing in solid mass.

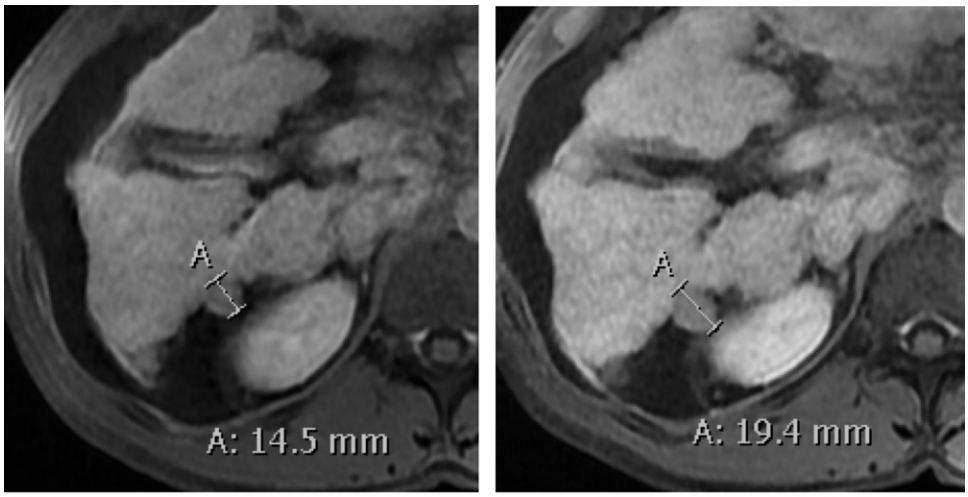


a. **b.** **c.**

Figure 3. US visibility of HCC as a discrete nodule or mass in a 67-year-old man with chronic hepatitis B infection. **(a)** On a nonenhanced screening US image, an MRI-detected observation is visible as a discrete nodule or mass (arrow). **(b, c)** Axial T1-weighted fat-saturated images in the late arterial **(b)** and portal venous **(c)** phases show the corresponding MRI-detected observation (arrow). Pathologic analysis of the hepatectomy specimen demonstrated HCC.

reported in 60%–81% of HCCs at MRI (21,43). Corona enhancement is not a feature of early and small HCC and is more often seen in hypervascular progressed HCC. This transient imaging feature is caused by venous drainage of contrast material from the tumor into the peritumoral parenchymal sinusoids and portal venules. This aberrant and disorganized venous drainage develops during hepatocarcinogenesis owing to occlusion of intranodular hepatic veins (44–48).

This ancillary feature has diagnostic value, as it can help differentiate tumors such as HCC from benign vascular pseudolesions, which do not manifest a corona. The feature is associated with microvascular invasion (49) and so has prognostic value for predicting the presence of such invasion. Additionally, since many intrahepatic metastases (ie, seeding of daughter or satellite nodules) form in the peritumoral venous drainage area (47,50), the corona enhancement



a. b.

Figure 4. Subthreshold growth of a distinctive nodule in a 37-year-old man with autoimmune cirrhosis. Baseline delayed phase image **(a)** and follow-up image 6 months later **(b)** show subthreshold growth (see measurements). Pathologic analysis of the liver specimen demonstrated HCC.

territory should be included within the surgical margin and in the ablation zone to reduce the risk of local recurrence after hepatectomy and local-regional treatment, respectively (50).

Corona enhancement can also be seen in liver metastases with peritumoral neovascularization and inflammatory changes (51). Therefore, this ancillary feature favors malignancy in general and is not specific for HCC. Corona enhancement around HCCs and other malignant lesions may overlap in appearance with arterioportal shunting, which can occur with both benign and malignant lesions. Distinguishing features are that corona enhancement tends to be confined to the immediate peritumoral parenchyma, appears in the late arterial phase, and then fades to isoenhancement, whereas arterioportal shunting tends to encompass a broader area and peaks in intensity in the early arterial phase (48,52). Corona enhancement should also be distinguished from an enhancing "capsule," which is seen as a smooth, uniformly thick, and progressively enhancing rim of tissue that appears during the portal venous, delayed, or transitional phase.

Diagnostic Performance.—The incremental effect on diagnostic performance of corona enhancement in combination with major features is unknown.

Fat Sparing in Solid Mass

Definition.—Fat sparing in a solid mass refers to relative paucity of lipid in a solid mass compared with steatotic liver or in an inner nodule relative to a steatotic outer nodule (Figs 6, 7). This feature applies only to patients with steatotic tissue—either a steatotic liver or steatotic nodules. Steatotic tissue can be recognized at gradient-echo imaging when there is signal drop on out-of-phase images in comparison with in-phase images. Fat sparing in a solid mass is seen as absence of or lesser signal drop in an observation relative to its surroundings.

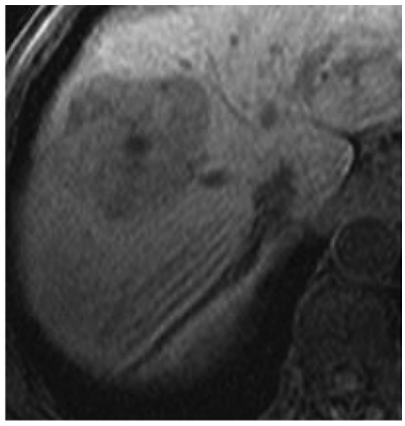
Rationale.—Evidence supporting this feature is indirect. Pathology studies have shown that progressed HCCs are rarely steatotic (the exception is steatohepatic variant), whereas early HCCs and dysplastic nodules are frequently steatotic. Additionally, fat accumulation does not occur in cholangiocarcinoma and other non-HCC malignancies (53). Therefore, the evidence that supports using fat sparing in a solid mass as a feature in favor of malignancy remains indirect (16).

Perfusional alteration and diffuse heterogeneous fatty infiltration of the liver may be associated with areas of fat sparing, which must not be mistaken for lesional fat sparing. Typical focal fat sparing occurs around the gallbladder and hepatic hilum, resulting from direct splanchnic venous supply reduced in lipid compared with portal flow, at the posterior edge of segment II/III from an aberrant left gastric vein or at the posterior edge of segment IV caused by aberrant right gastric vein drainage (54).

Diagnostic Performance.—The incremental effect on diagnostic performance of fat sparing in a solid mass in combination with major features is unknown.

Restricted Diffusion

Definition.—Restricted diffusion refers to increased signal intensity at DWI, not attributable solely to T2-weighted imaging shine-through,



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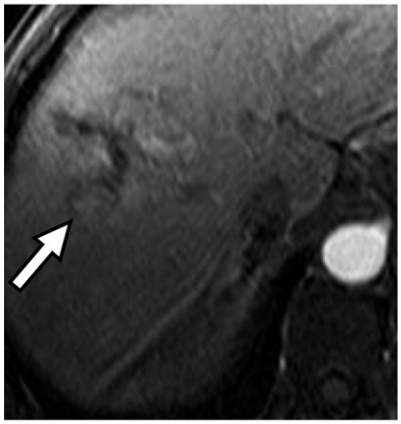

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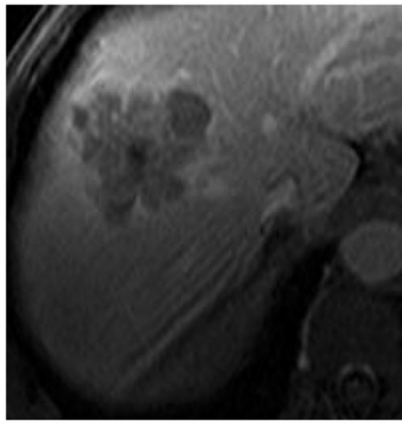
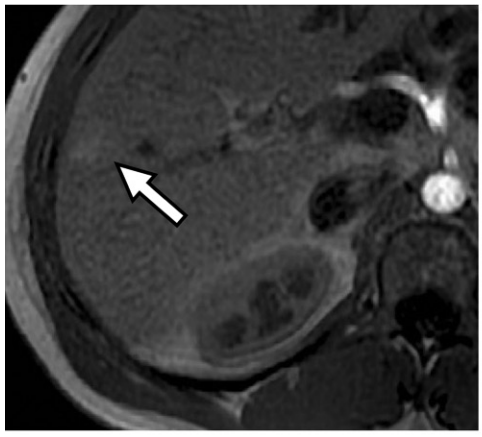


d.

Figure 5. Corona enhancement of HCC in a 61-year-old man with hepatitis C infection. Axial T1-weighted fat-saturated images obtained before contrast material administration **(a)** and in the late arterial **(b)**, portal venous **(c)**, and delayed **(d)** phases show corona enhancement (arrow in **b** and **c**).



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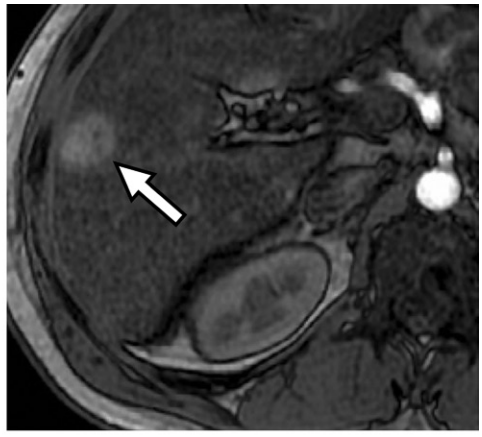
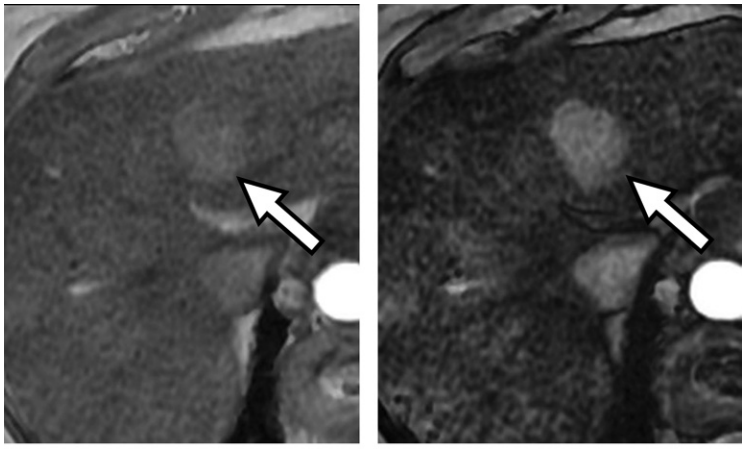


b.

Figure 6. Fat sparing in a solid mass (a dysplastic nodule) in a 41-year-old man under surveillance for cryptogenic cirrhosis. Axial in-phase **(a)** and out-of-phase **(b)** T1-weighted images show fat sparing in a solid mass (arrow), in contrast to the signal drop of the background liver seen on the out-of-phase image. Biopsy of the mass demonstrated high-grade dysplasia.

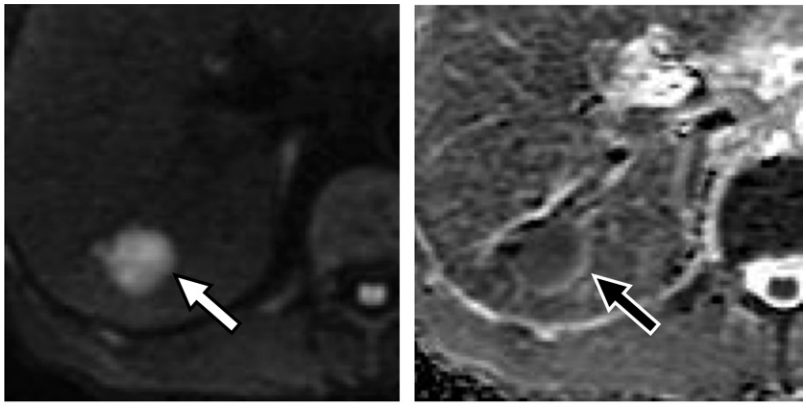
unequivocally higher than in liver and/or apparent diffusion coefficient (ADC) unequivocally lower than in liver parenchyma (Fig 8). DWI is optional in LI-RADS technical recommendations. Although there is no consensus on the optimal *b* values for diagnosing HCC in cirrhosis (55), DWI should include low *b* values (≤50 sec/mm^2) and high *b* values (≥400 sec/mm^2) (12,56).

Rationale.—Malignant tumors have higher cellular density and nucleus-to-cytoplasm ratio, leading to reduction in extracellular and intracellular space, respectively. This high cellularity restricts the motion of water molecules. DWI, a form of phase-contrast imaging to encode the diffusion of water molecules, can leverage this physical concept to provide information on tissue cellularity: diffusion is relatively unrestricted in normal tissue and restricted in tumors. However, unlike normal liver, cirrhotic liver has excess collagen in the extracellular matrix, which is thought to impede the diffusion of water. Hence, cirrhotic liver may have



a. b.

Figure 7. Fat sparing in a solid mass (HCC) in a 75-year-old woman with hepatitis C infection. Axial in-phase (echo time [TE] = 4.6 msec) **(a)** and out-of-phase (TE = 2.3 msec) **(b)** T1-weighted images show fat sparing in a solid mass (arrow), in contrast to the signal drop in the background liver on the out-of-phase image.



a. b.

Figure 8. Restricted diffusion in HCC in a 67-year-old man under surveillance for chronic hepatitis B with human immunodeficiency virus (HIV) coinfection. Axial diffusion-weighted image (b = 800 sec/mm^2) **(a)** and ADC map **(b)** show restricted diffusion (arrow), appearing as high signal intensity in **a** and low signal intensity in **b**. Restricted diffusion favors malignancy in general. Pathologic analysis of the hepatectomy specimen demonstrated HCC.

higher than normal signal intensity at DWI, potentially limiting the visibility of focal lesions (57,58).

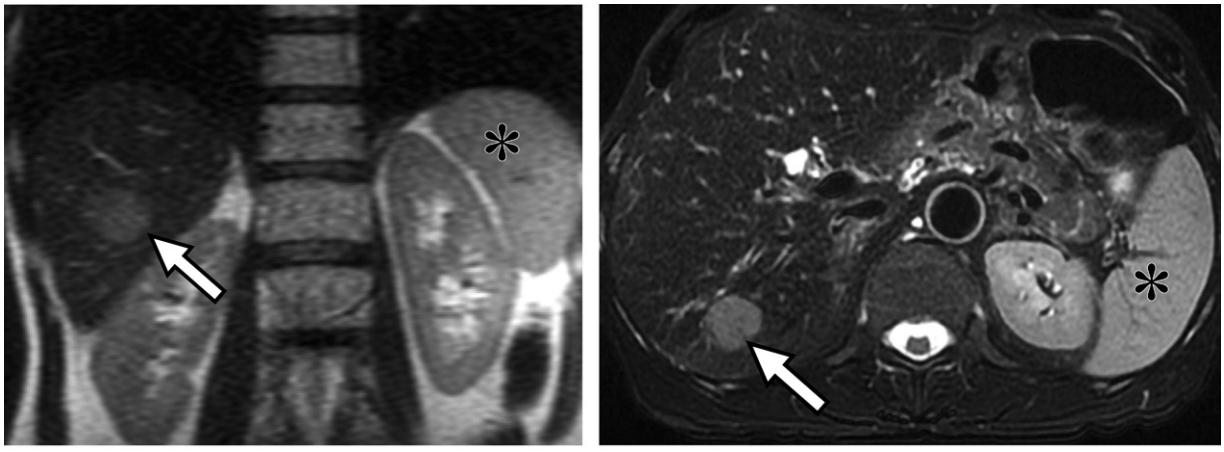
Hypovascular nodules that become hyperintense at follow-up DWI have higher risk of transformation to hypervascular HCCs (59). DWI may help differentiate chronic bland thrombus from tumor in vein (60), but this technique does not allow reliable differentiation of acute bland thrombus, which also may manifest with impeded diffusion. Some studies have found that the ADC correlates to the degree of differentiation of HCCs (61,62). However, there is overlap between the ADC of benign and malignant solid tumors, which leads to variations in diagnostic thresholds reported for characterization of lesions. Further, a major barrier to application of ADC thresholds is lack of standardization of DWI protocols and measurement techniques (63).

Diagnostic Performance.—Hyperintensity at DWI ($b \geq 500$ sec/mm^2) combined with contrast-enhanced MRI increases sensitivity for HCC versus dysplastic nodule from 68% to 98% and accuracy from 76% to 93% (24). Hyperintensity at DWI ($b \geq 500$ sec/mm^2) as an incremental feature to major features (APHE and washout) increases sensitivity for diagnosis of histologically proved HCC from 60%–62% to 70%–80% (64).

Mild-Moderate T2 Hyperintensity

Definition.—Mild-moderate T2 hyperintensity refers to signal intensity at T2-weighted imaging that is mildly or moderately higher than that of the liver and similar to or less than that of non–iron-overloaded spleen parenchyma (Fig 9). This increased signal intensity is less than that of fluid (ie, less than that of cerebrospinal fluid if taken as a comparative background).

Rationale.—T2 hyperintensity may reflect intratumoral dilated sinusoids (65), edema, or watery fibrosis (66). Regenerative nodules and dysplastic nodules are rarely hyperintense to surrounding liver parenchyma at T2-weighted imaging (35,67–69) unless infarcted (70) or in patients with Budd-Chiari syndrome (71). However, T2 hyperintensity is seen in 42%–47% of HCCs (28,72). Hence, T2 hyperintensity of an observation, compared with background liver, in addition to dynamic imaging, may help differentiate small (≤2 cm) HCCs from benign nodules



a. b.

Figure 9. Mild-moderate T2 hyperintensity of HCC in a 67-year-old man with chronic hepatitis B infection. Coronal **(a)** and axial **(b)** T2-weighted fat-saturated images show mild-moderate T2 hyperintensity (arrow), which is isointense to the spleen parenchyma (*). Pathologic analysis of the hepatectomy specimen demonstrated HCC.

(22) and hypervascular pseudolesions (73), as well as hypovascular HCCs from dysplastic nodules (23). However, T2 hyperintensity is not specific for HCC, as it may be seen in other malignancies (53).

The level of T2 hyperintensity is correlated with HCC size (74), degree of hypervascularity (75), growth rate (76), and progression from early to well-differentiated HCC (77–79). T2 hyperintensity also constitutes a risk factor for growth and development of APHE in a nodule that is initially hypovascular (80).

Diagnostic Performance.—Mild-moderate T2 hyperintensity, when used in combination with DWI, has sensitivity of 72% and specificity of 100% for distinguishing hypovascular HCC from a dysplastic nodule. Mild-moderate T2 hyperintensity has a weak incremental effect on diagnostic performance because it is more often seen in progressed HCCs and therefore in association with other major or ancillary features (28,53,72).

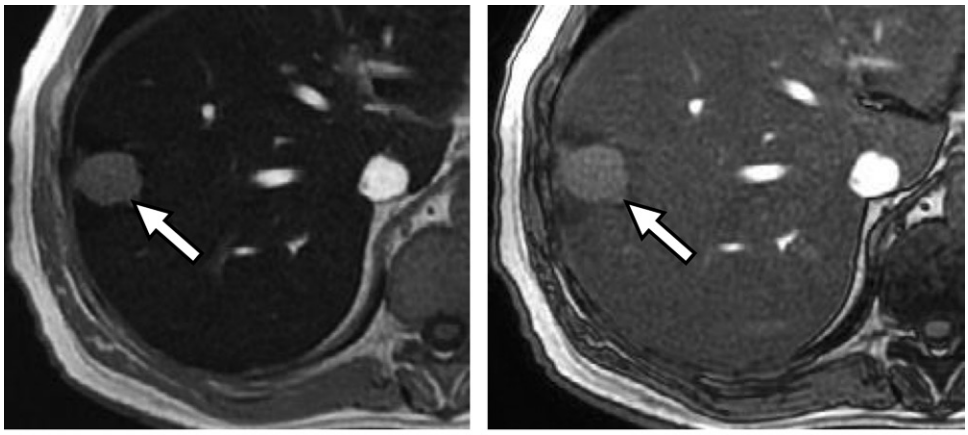
Iron Sparing in Solid Mass

Definition.—Iron sparing in a solid mass refers to a paucity of iron in an inner nodule compared with a siderotic outer nodule or to a solid mass containing less iron relative to iron-overloaded background liver (Fig 10). Iron overload in the liver can be primary (genetic) or secondary (due to exogenous iron administration) (81). At gradient-echo imaging, iron-overloaded tissue shows decreased signal intensity on images with longer echo time (TE) (typically the in-phase images compared with the out-of-phase images when using a dual-echo gradient-echo sequence). This is because the superparamagnetic effect of iron particles (ferritin and hemosiderin) shortens the transverse relaxation constants, resulting in a decrease in signal intensity of the iron-containing tissue. Solid masses with iron sparing show less signal loss than the siderotic outer nodule or the iron-overloaded background liver on the second echo of a dual-echo sequence.

Rationale.—Low-grade dysplastic nodules in cirrhotic liver tend to accumulate iron and appear T2 or T2* hypointense compared with the remaining parenchyma, presumably reflecting iron avidity by the dysplastic but nonmalignant cells. By comparison, malignant hepatocytes lose their ability to accumulate iron and become "iron-resistant" (82–84). Studies have described development of HCC foci in dysplastic nodules as a nodule-in-nodule appearance recognizable as a T2-isointense spot in a low-signal-intensity nodule, representing an iron-free HCC focus within a larger siderotic nodule (82,83,85). In patients with hemochromatosis, iron-free nodules have been shown to be premalignant (86,87).

Iron sparing in a solid mass favors malignancy but is not specific for HCC, as it may also be observed in intrahepatic cholangiocarcinoma or other non-HCC malignancies (53). Confluent fibrosis is also iron-free; however, it should not be mistaken for iron sparing in a solid mass because areas of fibrosis have an elongated, linear, branching, or wedgelike configuration, with associated capsular retraction (16,53).

Diagnostic Performance.—The incremental effect on diagnostic performance of iron sparing in a solid mass in combination with major features is unknown. Although retrospective and prospective studies are lacking, indirect evidence



a. b.

Figure 10. Iron sparing in a solid mass (cholangiocarcinoma) in a 62-year-old man with hemochromatosis. Axial in-phase (TE = 4.6 msec) **(a)** and out-of-phase (TE = 2.3 msec) **(b)** T1-weighted images show iron sparing in a solid mass (arrow), in contrast to the signal drop in the background liver on the in-phase image, obtained with a longer TE. Pathologic analysis of the biopsy specimen demonstrated cholangiocarcinoma.

and biologic plausibility suggest that iron sparing in a solid mass favors malignancy.

Transitional Phase Hypointensity

Definition.—Transitional phase hypointensity of an observation refers to signal intensity in the transitional phase unequivocally less, in whole or in part, than in the liver (Figs 11, 12). The transitional phase is the postcontrast phase performed 3–5 minutes after injection of gadoxetate disodium. It occurs after the extracellular phase (ie, after the PVP) and before the hepatobiliary phase (HBP); hence, the transitional phase may begin as early as 2 minutes after injection.

As a pure equilibrium phase does not exist with hepatobiliary agents, the transitional phase represents the period of transition in which parenchymal enhancement may be attributable to the presence of contrast agent in both the extracellular and intracellular compartments (88). During the transitional phase, liver vessels and hepatic parenchyma are of similar signal intensity. Interpretation of signal intensity during the transitional phase can be challenging, as hyperenhancement of liver parenchyma may give the impression of de-enhancement of the mass (53).

Rationale.—Transitional phase hypointensity is reported in 47%–65% of HCCs (31,35) and is thought to reflect a combination of mechanisms including "washout" and underexpression of organic anion-transporting polypeptide (OATP), the membrane transporter responsible for uptake by hepatocytes of these agents. Transitional phase hypointensity is sensitive but not specific for HCC and may be seen in any mass devoid of the molecular transporters, including cholangiocarcinoma, metastases, and hemangioma (76). Therefore, transitional phase hypointensity alone cannot be used to diagnose HCC.

Diagnostic Performance.—When used in combination with PVP "washout," transitional phase hypointensity has sensitivity of 83%–91% and specificity of 33%–58% for histopathologically confirmed HCC (31).

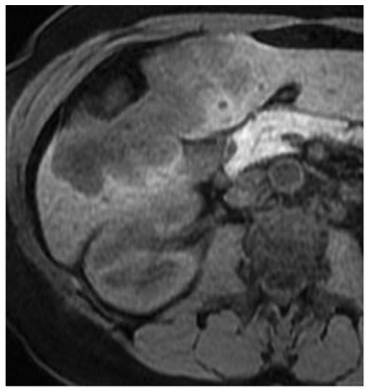
HBP Hypointensity

Definition.—HBP hypointensity refers to signal intensity in the HBP unequivocally less, in whole or in part, than in the liver (Fig 13). The HBP is the postcontrast phase performed with a hepatobiliary agent in which the liver parenchyma is hyperintense to hepatic blood vessels and there is excretion of contrast material into the biliary system. The HBP is typically performed 20 minutes after injection with gadoxetate disodium (89) and 1–3 hours after injection with gadobenate dimeglumine. The HBP is suboptimal if the liver is not more intense than the hepatic blood vessels. The presence of biliary excretion is not an indicator of an adequate HBP.

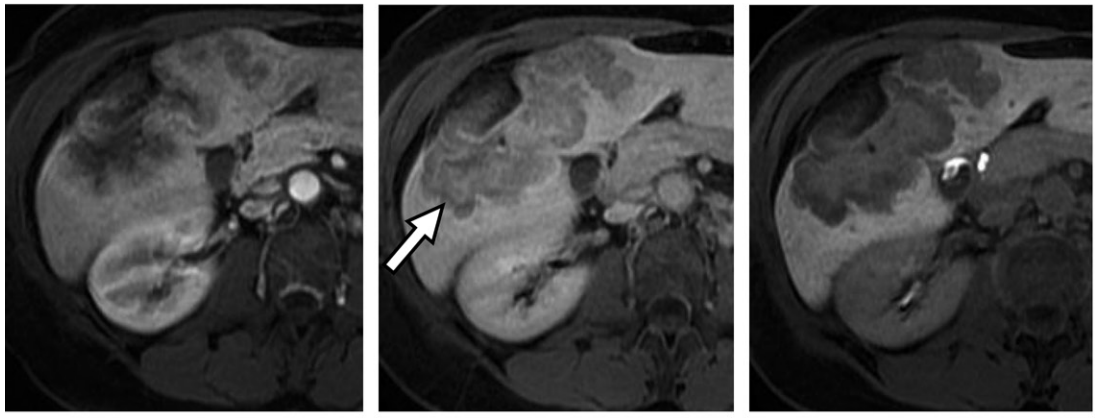
Rationale.—Hepatobiliary contrast agents provide an additional tissue contrast mechanism to characterize liver observations. OATP expression decreases during hepatocarcinogenesis, resulting in HBP hypointensity of both early and progressed HCCs (90). HBP hypointensity is reported in 79%–99% of HCCs (39,91,92).

Addition of the HBP when using a hepatobiliary contrast agent increases sensitivity by 5%–19% for diagnosis of HCC (33,34,37,93,94) because HBP hypointensity occurs before the onset of arterialization in hepatocarcinogenesis

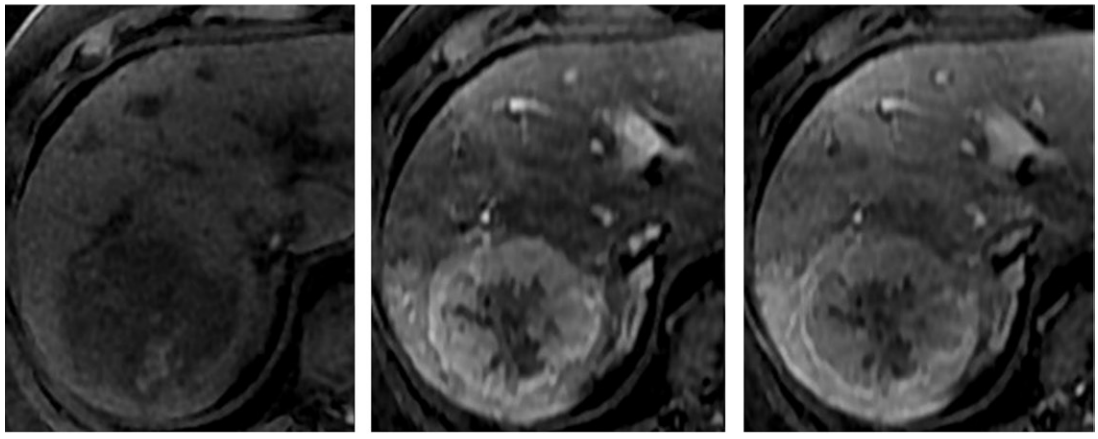
Figures 11, 12. **(11)** Transitional phase hypointensity of cholangiocarcinoma in a 58-year-old woman. Axial T1-weighted fat-saturated images before **(a)** and after **(b–d)** administration of gadoxetate disodium in the late arterial **(b)**, transitional **(c)**, and hepatobiliary **(d)** phases show transitional phase hypointensity (arrow in **c**). **(12)** Transitional phase hypointensity of HCC in a 75-year-old woman with hepatitis C infection. Axial T1-weighted fat-saturated images before **(a)** and after **(b–f)** administration of gadoxetate disodium in the early arterial **(b, c)**, portal venous **(d)**, transitional **(e)**, and hepatobiliary **(f)** phases show transitional phase hypointensity (arrow in **e**).



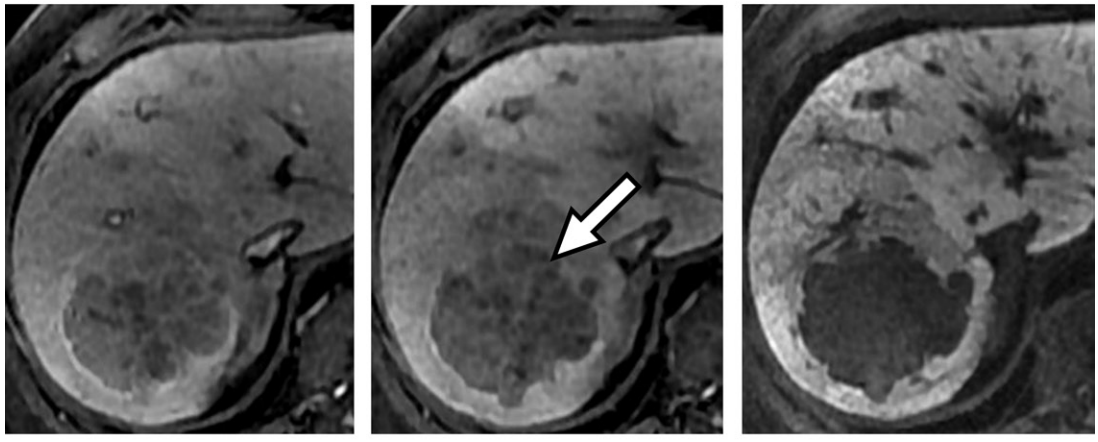
11a.



11b. 11c. 11d.



12a. 12b. 12c.



12d. 12e. 12f.

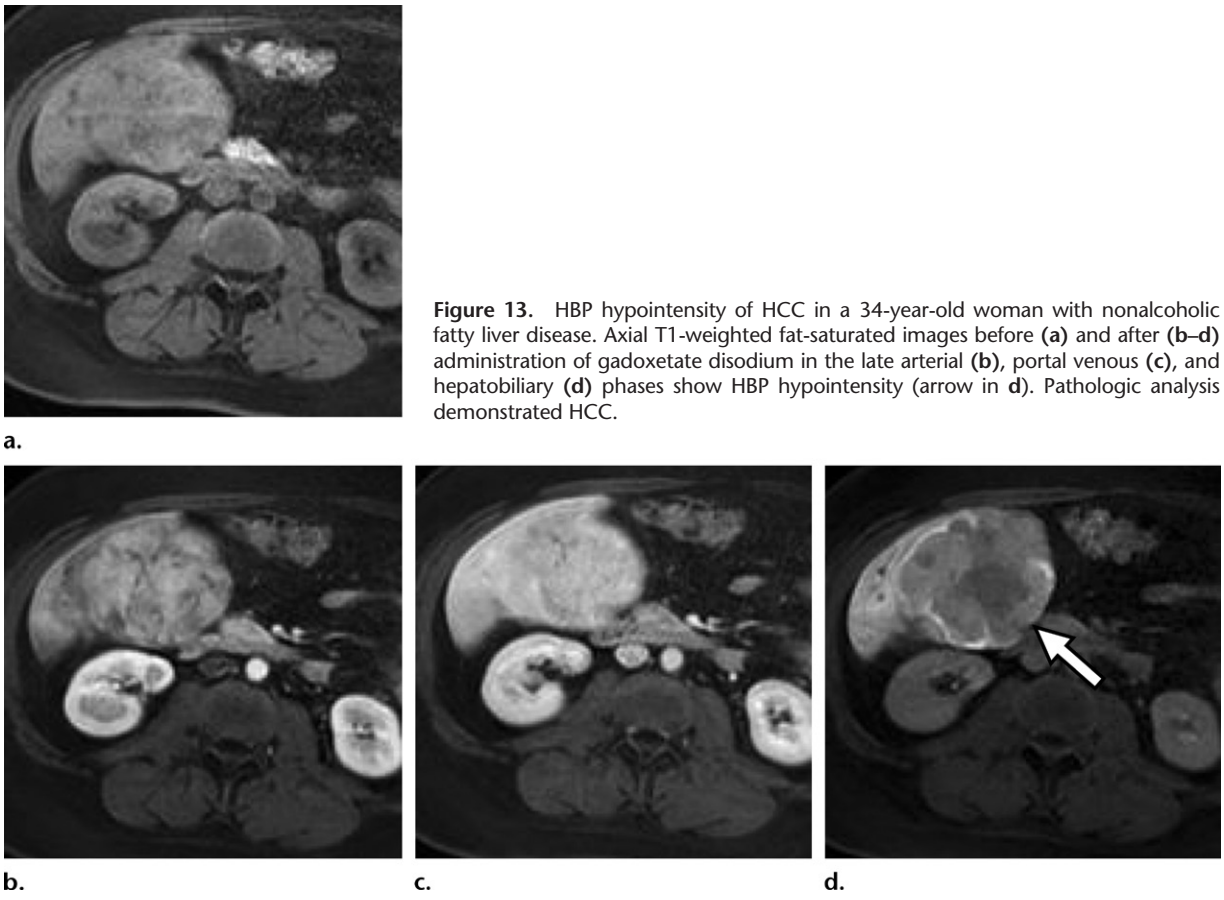


Figure 13. HBP hypointensity of HCC in a 34-year-old woman with nonalcoholic fatty liver disease. Axial T1-weighted fat-saturated images before **(a)** and after **(b–d)** administration of gadoxetate disodium in the late arterial **(b)**, portal venous **(c)**, and hepatobiliary **(d)** phases show HBP hypointensity (arrow in **d**). Pathologic analysis demonstrated HCC.

(95). Hence, HBP hypointensity can reveal early HCCs that are hypovascular (35) or indeterminate in dynamic phases alone because of their atypical features (34). HBP hypointensity may help differentiate early HCCs and high-grade dysplastic nodules from low-grade dysplastic nodules (35,38). HBP hypointensity is sensitive but not specific for diagnosis of HCC because non-HCC malignancies and benign entities such as hemangioma are devoid of OATP and typically appear hypointense in the HBP.

Diagnostic Performance.—HBP hypointensity used in combination with major features has sensitivity of 75%–99% (32,34) and specificity of 42%–96% (32,35,38,39).

Ancillary Features Favoring HCC in Particular

Ancillary features favoring HCC in particular and their definitions are given in Table 4. Estimates of diagnostic performance are not available for these ancillary features.

Nonenhancing "Capsule"

Definition.—Nonenhancing "capsule" refers to a capsule appearance that is not visible as an enhancing rim (Fig 14). This feature can appear as a hypointense rim on T2-weighted, nonenhanced T1-weighted, or HBP images. Nonenhancing "capsule" should be unequivocally thicker or more conspicuous than fibrotic tissue around background nodules.

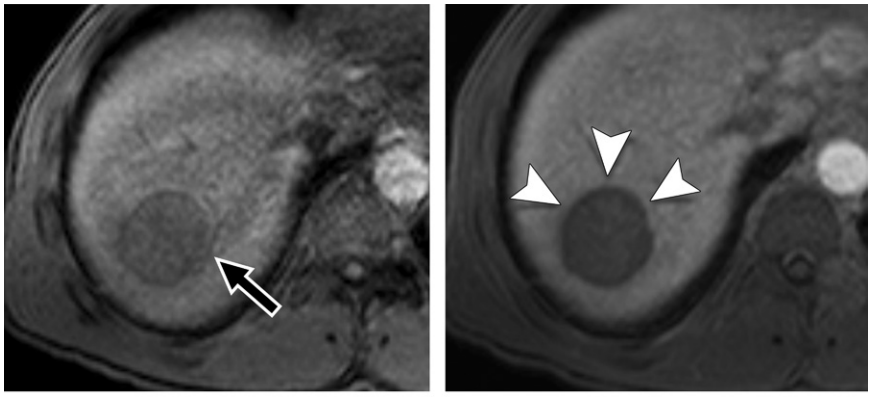
Distinction should be made from targetoid appearance and peripheral "washout," which are both features of non-HCC malignancies (LR-M). Targetoid appearance in the PVP or HBP is a concentric pattern characterized by moderate to marked hypointensity in the periphery of the observation with milder hypointensity in the center. Peripheral "washout" is a spatially defined subtype of "washout" in which apparent washout is most pronounced in the periphery of the observation (12). In both cases, the pitfall can be avoided by assessing the entire dynamic phases.

Rationale.—A radiologically identified "capsule" may represent a pseudocapsule comprising perilesion sinusoids, fibrous tissue, and compressed liver parenchyma. The distinction between a true tumor capsule and pseudocapsule can be made only at pathologic analysis, but this distinction does not appear important for diagnosing HCC or evaluating its biologic behavior. Unlike enhancing "capsule," nonenhancing "capsule" does not appear as

Table 4: Ancillary Features Favoring HCC in Particular

Feature	Definition	ECA MRI*	HBA MRI†
Nonenhancing "capsule"	Capsule appearance not detected as enhancing rim	+	+
Mosaic architecture	Presence of randomly distributed internal nodules or compartments, usually with different imaging features	+	+
Nodule-in-nodule architecture	Presence of smaller inner nodule within and having different imaging features than larger outer nodule	+	+
Fat in mass, more than in adjacent liver	Excess fat within mass, in whole or in part, relative to background liver	+	+
Blood products in mass	Intralesion or perilesion hemorrhage in absence of biopsy, trauma, or intervention	+	+

*MRI performed with an extracellular contrast agent (ECA) can be used to characterize all ancillary features favoring HCC.
†MRI performed with a hepatobiliary contrast agent (HBA) can be used to characterize all ancillary features favoring HCC.



a. **b.**

Figure 14. Nonenhancing "capsule" of HCC in a 47-year-old man with chronic hepatitis B infection. Axial T1-weighted fat-saturated images before contrast material administration **(a)** and in the HBP **(b)** show a mass (arrow in **a**) with a hypointense rim in the HBP (arrowheads in **b**), which represents a subtype of nonenhancing "capsule."

an enhancing rim. The presence of a hypointense rim in the HBP, a subtype of nonenhancing "capsule," may be due to peritumor hypoperfusion from obstructed intrahepatic portal flow and insufficient hepatic arterial supply, leading to liver parenchyma injury and subsequent decreased uptake of gadoxetate disodium (96).

Diagnostic Performance.—The incremental effect on diagnostic performance of nonenhancing "capsule" in combination with major features is unknown.

Mosaic Architecture

Definition.—Mosaic architecture refers to the presence of randomly distributed internal nodules or compartments, usually with different imaging features (Fig 15). Internal compartments may differ because of the presence of fat, fibrosis, blood products, and vascular dynamics. Heterogeneity of compartments in mosaic appearance is better depicted on T2-weighted images than on T1-weighted images (65).

Rationale.—Mosaic pattern is seen in 28%–63% of cases (17), more commonly in HCCs than in non-HCCs (97) and more frequently in large HCCs (>3 cm) (98). Mosaic appearance at imaging corresponds to the appearance at histopathologic examination (99). Multiple nodules or masses within a larger mass correspond to different foci of clonal expansion at different stages of hepatocarcinogenesis (16,17,100), some of which may contain fat metamorphosis, separated by areas of necrosis, blood products, cystic degeneration, and fibrous septa. Nodular areas that demonstrate APHE typically have higher histologic grade than hypovascular areas, which are supplied by portal venous flow. Mosaic appearance is unusual in non-HCC malignancy (53) and therefore favors HCC in particular.

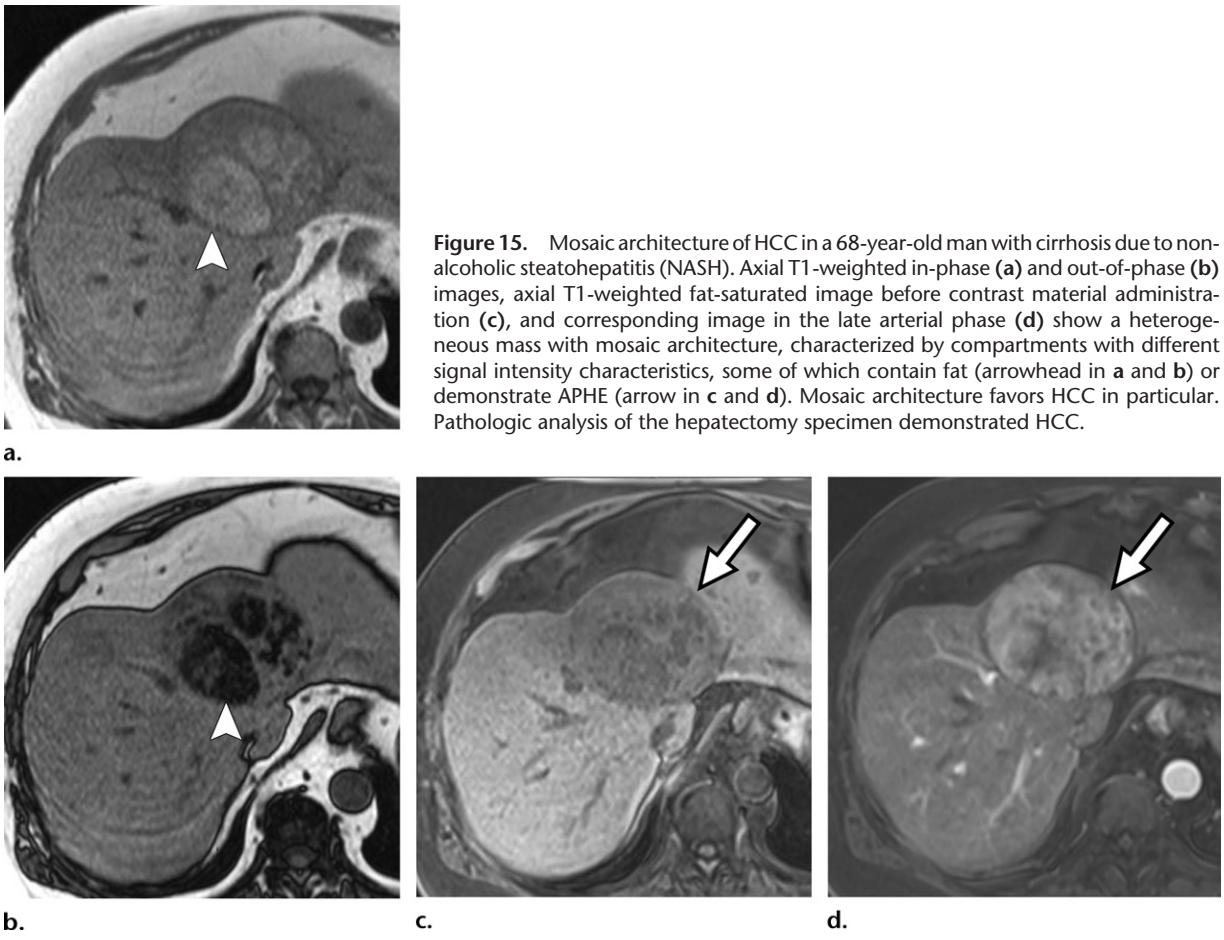


Figure 15. Mosaic architecture of HCC in a 68-year-old man with cirrhosis due to nonalcoholic steatohepatitis (NASH). Axial T1-weighted in-phase **(a)** and out-of-phase **(b)** images, axial T1-weighted fat-saturated image before contrast material administration **(c)**, and corresponding image in the late arterial phase **(d)** show a heterogeneous mass with mosaic architecture, characterized by compartments with different signal intensity characteristics, some of which contain fat (arrowhead in **a** and **b**) or demonstrate APHE (arrow in **c** and **d**). Mosaic architecture favors HCC in particular. Pathologic analysis of the hepatectomy specimen demonstrated HCC.

Diagnostic Performance.—The incremental effect on diagnostic performance of mosaic architecture in combination with major features is unknown.

Nodule-in-Nodule Architecture

Definition.—Nodule-in-nodule architecture refers to the presence of a smaller inner nodule within and having different imaging features than the larger outer aspect of the entire nodule (Fig 16). Imaging features can differ in terms of signal intensity and/or enhancement.

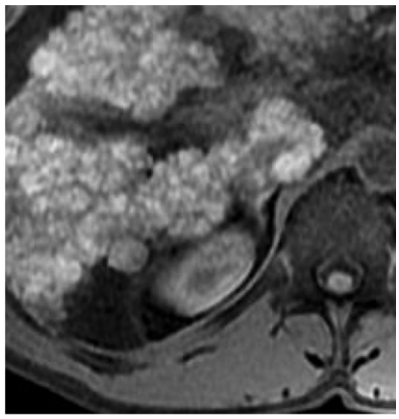
Rationale.—Nodule-in-nodule architecture appears at MRI as a central focus of HCC within a large dysplastic nodule (85). This imaging feature corresponds to the characteristic histologic growth pattern of hepatocarcinogenesis: morphologic dedifferentiation and clonal multiplication of less-differentiated cells in the inner nodule replacing the well-differentiated or dysplastic outer nodule (101,102). During hepatocarcinogenesis, inner foci of HCC may become iron-resistant (82,83), accumulate fat (35), or become hyperarterialized (103,104). The inner nodule may thus appear T2 isointense or hyperintense (68,85), show signal drop on out-of-phase images, or demonstrate APHE (35,105). Necrotic HCCs with inner nodules of viable tumor may also demonstrate nodule-in-nodule architecture (105).

The inner HCC focus demonstrates marked TVDT of 9.5 weeks and potential for rapid growth (106). Measurement of observation size should be made on the entire observation, including the larger outer nodule and smaller inner nodule. As it is characteristic of hepatocarcinogenesis but does not occur with other malignant tumors such as cholangiocarcinoma, nodule-in-nodule appearance favors HCC in particular.

Diagnostic Performance.—The diagnostic performance of nodule-in-nodule architecture, as a stand-alone feature or in combination with major features, is unknown.

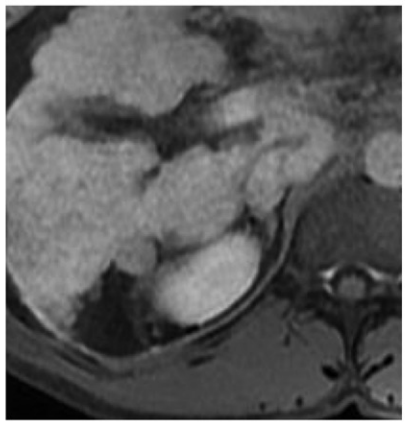
Fat in Mass, More than in Adjacent Liver

Definition.—Fat in a mass, more than in adjacent liver, refers to excess fat within a mass, in whole or in part, relative to adjacent liver (Fig 17). Intracellular fat in HCCs can be diagnosed at MRI as a drop in signal intensity of a mass on opposed-phase gradient-echo images compared with in-phase images.



a.

b.



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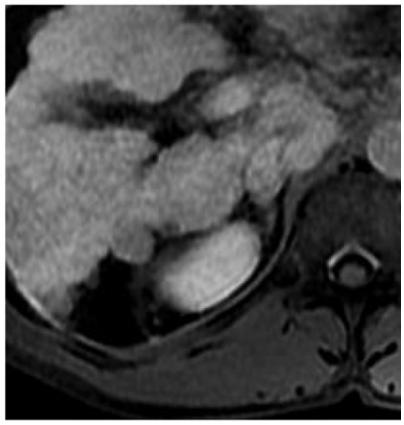


d.

Figure 16. Nodule-in-nodule architecture of HCC in a 37-year-old man with autoimmune cirrhosis. Axial T1-weighted fat-saturated images before **(a)** and after **(b–d)** contrast material administration in the late arterial **(b)**, portal venous **(c)**, and delayed **(d)** phases show a mass with APHE of a smaller inner nodule (arow in **b**) within a larger nodule with washout. Pathologic analysis of the liver specimen demonstrated HCC.

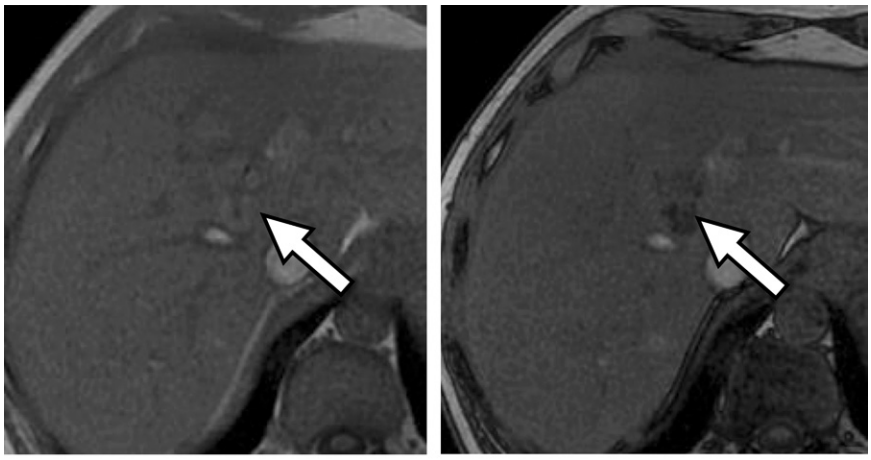
Rationale.—Fatty metamorphosis in HCCs is not fully understood. Some authors have speculated that it arises in high-grade dysplastic nodules and early HCCs in response to tumor hypoxia caused by destruction of intranodule portal tracts and incomplete neoarterialization. Once unpaired arteries develop in progressed HCCs, the hypoxia resolves and the steatosis regresses, explaining why fat deposition is infrequent in progressed and large HCCs (107). The mechanism by which hypoxia would induce fat accumulation is unclear. Another hypothesis for intralesion fatty metaplasia is clonal proliferation of hepatocytes with dysregulated lipogenesis (108).

Although fat in a mass can be found in premalignant hepatocellular lesions such as high-grade dysplastic nodules (109), it is rarely found in non-HCC malignancies such as cholangiocarcinoma (110) and therefore is considered a feature favoring HCC. However, the presence of fat in a mass should not modify the observation category if other imaging features (ie, targetoid appearance) indicate LR-M, since hepatocholangiocarcinomas may contain fat within their hepatocellular component. Other liver masses such as adenoma, angiomyolipoma, teratoma, or metastases from liposarcoma or renal cell carcinoma may also contain fat (17) but are exceptionally rare in cirrhotic livers (111). Intralesion fat should not be confused with focal liver steatosis or fat drops after transarterial chemoembolization with an oil-containing agent (Lipiodol [ethiodized oil]; Guerbet, Villepinte, France).

Diagnostic Performance.—Fat in a mass, more than in adjacent liver, is observed in 16%–18% of HCCs (112,113). However, the incremental contribution of this ancillary feature to overall diagnostic performance may be limited because fat in a mass, more than in background liver, does not allow reliable distinction of early HCCs from high-grade and even low-grade dysplastic nodules and often coexists in progressed HCCs with the hallmark enhancement pattern of APHE and "washout" (113).

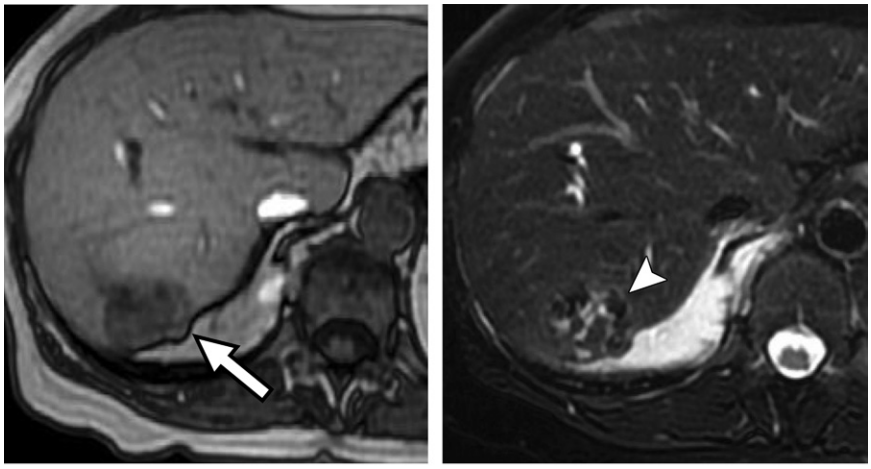
Blood Products in Mass

Definition.—Blood products in a mass refers to intralesion or perilesion hemorrhage in the absence of biopsy, trauma, or intervention (Fig 18). Acute or subacute blood products appear hyperintense on T1-weighted images (owing to intracellular or extracellular methemoglobin) and hyperintense and heterogeneous on T2-weighted images (owing to extracellular methemoglobin), while chronic blood products appear hypointense with both



a. b.

Figure 17. Fat in a mass (HCC), more than in adjacent liver, in a 58-year-old man with hepatitis C infection. Axial in-phase **(a)** and out-of-phase **(b)** T1-weighted images show a mass (arrow) with signal drop on the out-of-phase image, indicating the presence of intralesion fat. Biopsy of the mass demonstrated HCC.



a. b.

Figure 18. Blood products in a mass in a 54-year-old man without cirrhosis documented in clinical and imaging records. **(a)** Axial out-of-phase T1-weighted image shows an isointense right liver lobe mass (arrow). **(b)** Axial T2-weighted fat-saturated image shows heterogeneous blood products in the mass (arrowhead). In a high-risk patient, blood products in a mass favor the diagnosis of HCC.

sequences (owing to hemosiderin). The scavenging of methemoglobin into hemosiderin by macrophages occurs at the periphery of the hematoma, hence there is a peripheral hypointense rim on T2*-weighted images. Blood products that are hyperintense on T1-weighted images may obscure assessment of APHE (or enhancement in any phase). In such cases, a vascular subtraction series may be helpful.

Rationale.—HCCs are hypervascular tumors prone to hemorrhage. Spontaneous intralesion bleeding is reported in up to 19% of HCCs (114). Postulated mechanisms include repetitive minor blunt trauma to superficial lesions, rapid elevation in intratumor pressure caused by thrombosis of draining veins, and rupture of fragile neoarteries in the tumor (115).

Bleeding in HCC can be minor and contained within the tumor or may rupture through the tumor into the surrounding liver or the subcapsular space of the liver or even through the liver capsule into the peritoneum. Although hepatocellular adenomas and some hepatic metastases may manifest with bleeding, these tumors are exceptionally rare in cirrhotic patients (115). Other tumors such as cholangiocarcinoma are not prone to hemorrhage.

Diagnostic Performance.—The incremental effect on diagnostic performance of blood products in a mass in combination with major features is unknown. Indirect evidence and biologic plausibility suggest that blood products in an observation strongly favor HCC in particular.

Ancillary Features Favoring Benignity

Ancillary features favoring benignity are given in Table 5. The diagnostic performance of ancillary features favoring benignity is summarized in Table 6.

Size Stability for 2 Years or Longer

Definition.—Size stability for 2 years or longer is defined as absence of significant change in an observation's size when measured at examinations

Table 5: Ancillary Features Favoring Benignity

Feature	Definition	ECA MRI*	HBA MRI†
Size stability for ≥2 y	No significant change in observation size measured at examinations ≥2 y apart in absence of treatment	+	+
Size reduction	Unequivocal spontaneous decrease in size over time, not attributable to artifact, measurement error, technique differences, or resorption of blood products	+	+
Parallels blood pool enhancement	Temporal pattern in which enhancement eventually reaches and then matches that of blood pool	+	+
Undistorted vessels	Vessels traversing observation without displacement, deformation, or other alteration	+	+
Iron in mass, more than in liver	Excess iron in mass relative to that in background liver	+	+
Marked T2 hyperintensity	Signal intensity on T2-weighted images markedly higher than in liver and similar to that in bile ducts and other fluid-filled structures	+	+
HBP isointensity	Signal intensity in HBP nearly identical to that in liver	−	+

*MRI performed with an extracellular contrast agent (ECA) can be used to characterize most ancillary features favoring benignity.
†MRI performed with a hepatobiliary contrast agent (HBA) can be used to characterize all ancillary features favoring benignity.

Table 6: Diagnostic Performance of Ancillary Features Favoring Benignity at MRI

Ancillary Feature*	References	No. of Benign Entities (No. of Nodules)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Parallels blood pool enhancement	Whitney et al 1993 (116)	12 (47)	84	100	…	…
Marked T2 hyperintensity	Whitney et al 1993 (116)	12 (47)	80	100	…	…
	Motosugi et al 2011 (117)	47 (105)	75–91	89–100	…	…
HBP isointensity	Sun et al 2010 (39)	53 (97)	91–94	93	94	89–93

Note.—NPV = negative predictive value, PPV = positive predictive value.
*Estimates of diagnostic performance are not available for the following ancillary features: size stability for ≥2 years, size reduction, undistorted vessels, and iron in mass, more than in liver.

2 years or longer apart and in the absence of treatment (Fig 19). Size stability should be assessed between two examinations with measurements using the same sequence, phase, and plane.

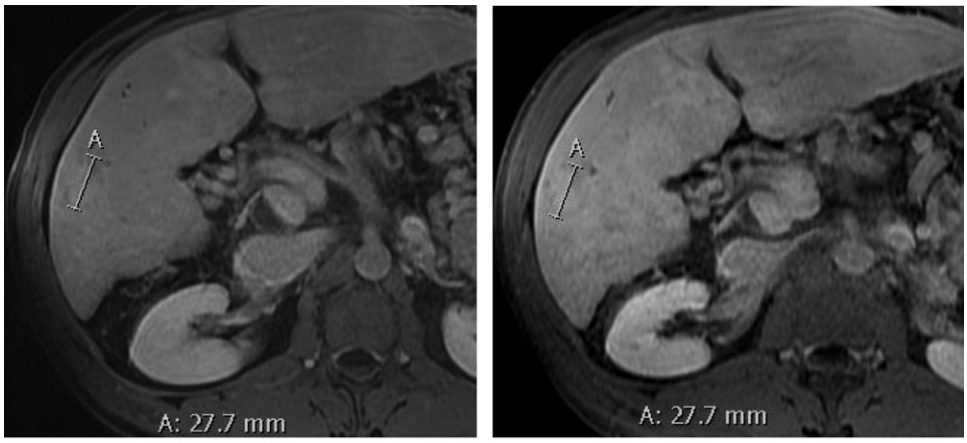
Rationale.—The reported TVDT of HCC varies from 12 to 851 days (2.3 years) (49,118) depending on the degree of dedifferentiation. The TVDT of cholangiocarcinoma in cirrhotic liver is unknown, but a median TVDT of 70 days has been reported in a noncirrhotic patient (119). Precursor nodules evolving into HCCs have a reported average TVDT of 5.3 months (76). Therefore, absence of growth for 2 years or longer would be unusual for HCC or another malignant entity in cirrhotic patients and hence size stability favors benignity.

Diagnostic Performance.—The incremental effect on diagnostic performance of size stability for 2 years or longer in combination with major features is unknown. Indirect evidence and biologic plausibility suggest that size stability for 2 years or longer favors benignity.

Size Reduction

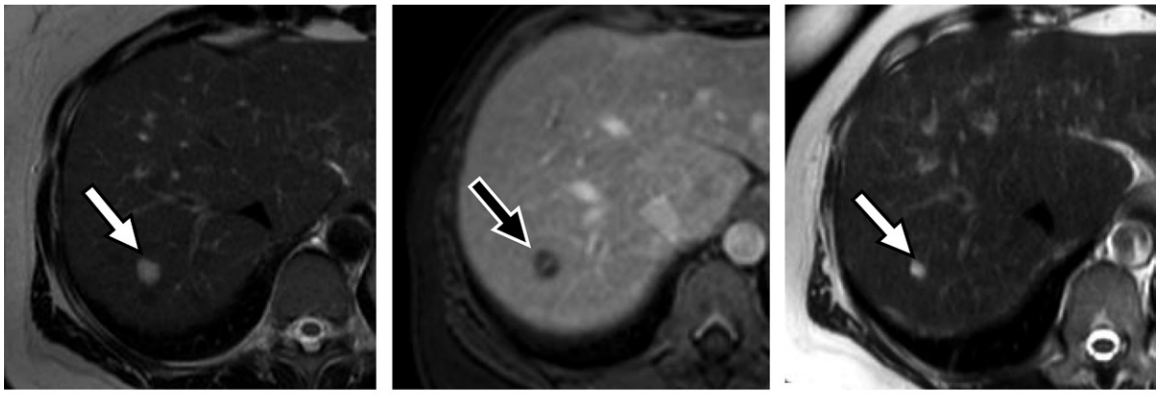
Definition.—Size reduction refers to unequivocal spontaneous decrease in size of an observation over time unattributable to artifact, measurement error, technique differences, or resorption of hemorrhage (Fig 20).

Rationale.—Malignant tumors are the result of cellular clonal multiplication and therefore grow over time. Spontaneous regression of HCC is rare: only 75 cases of spontaneous regression of HCC have been reported as of 2012 (120,121). Postulated mechanisms include tumor ischemia and necrosis

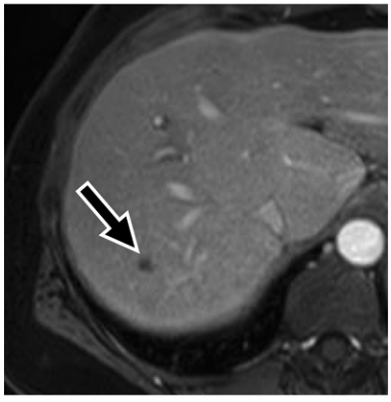


a. b.

Figure 19. Size stability for 2 years or longer of a dysplastic nodule in a 31-year-old woman undergoing surveillance for primary sclerosing cholangitis. **(a)** Baseline delayed phase image shows mild delayed phase hyperenhancement without washout appearance. **(b)** Corresponding image 3 years later shows size stability of the mass (see measurements). Biopsy of the mass demonstrated a hypervascular dysplastic nodule.



a. b. c.



d.

Figure 20. Size reduction of an involuting hemangioma in a 57-year-old woman with cirrhosis due to hepatitis C. **(a)** Baseline axial T2-weighted fat-saturated image shows a mass with marked hyperintensity measuring 11 mm (arrow). **(b)** Axial T1-weighted fat-saturated image in the PVP shows a hypoenhancing mass (arrow). **(c, d)** Corresponding images 8 years later show size reduction of the mass (arrow), which now measures 6 mm. Size reduction favors benignity.

induced by rapid growth and immune response against tumor cells triggered by an otherwise unrelated bacterial infection, although the cause of regression is unknown in one-half of cases (120). By comparison, hemangiomas in the cirrhotic liver tend to involute and eventually disappear as a result of progressive intralesion fibrosis (122).

Because spontaneous regression of HCC or other malignant entities is rare and because size reduction can be observed in benign entities such as hemangiomas, this ancillary feature favors a benign entity. However, size reduction due to resorption of blood products from a hemorrhagic HCC (Fig 21) constitutes a pitfall and should not be interpreted as favoring benignity.

Diagnostic Performance.—The incremental effect on diagnostic performance of size reduction in combination with major features is unknown. Indirect evidence and biologic plausibility suggest that size reduction favors benignity.

Parallels Blood Pool Enhancement

Definition.—Parallels blood pool enhancement refers to a temporal pattern in which enhancement

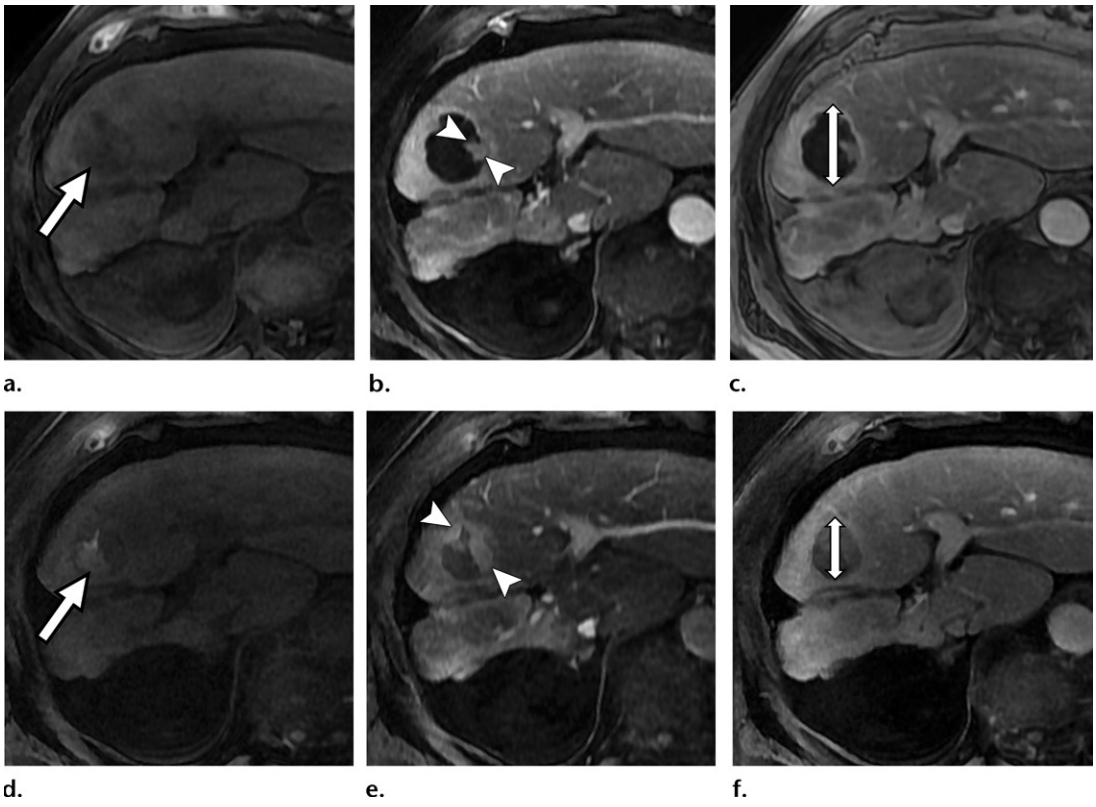


Figure 21. Pitfall of size reduction in a hemorrhagic HCC that shrank owing to resorption of blood products (ie, not owing to benignity). **(a–c)** Baseline axial T1-weighted fat-saturated images before contrast material administration **(a)** and in the late arterial **(b)** and portal venous **(c)** phases show a large hemorrhagic spontaneously hyperintense mass (arrow in **a**) with solid enhancing portions (arrowheads in **b**) within a larger mass (double-headed arrow in **c**). **(d–f)** Corresponding images obtained later show blood clot formation (arrow in **d**) and growth of enhancing nodules (arrowheads in **e**) despite overall size reduction of the mass (double-headed arrow in **f**). Size reduction due to resorption of blood products is a pitfall and does not constitute a feature favoring benignity.

eventually reaches and then matches that of the blood pool (ie, enhancement similar to that of arterial structures in the arterial phase and the portal vein or inferior vena cava in the PVP, delayed phase, transitional phase, and HBP) (Fig 22).

Rationale.—Enhancement that parallels the blood pool is a typical feature of hemangioma (123) and has been attributed to puddling of contrast material within the large endothelium-lined vascular channels. The level of enhancement of hemangiomas approximates that of the blood pool vein in all vascular phases. However, the blood pool becomes dark relative to the liver after the transitional phase using hepatobiliary agents, which may cause diagnostic confusion (123,124). In addition to hemangiomas, this temporal enhancement pattern may also be seen in observations that have direct communication with vascular structures, such as pseudoaneurysms and arteriovenous fistulas.

In contrast, HCCs typically demonstrate APHE and/or "washout" at dynamic imaging and metastases demonstrate targetoid enhancement (117). One pitfall is peliotic HCC, a rare HCC variant with dilated intratumor sinusoids. Enhancement in this type of HCC may also parallel the blood pool owing to puddling of contrast material within the dilated sinusoids (125).

Diagnostic Performance.—The diagnostic performance of blood pool parallelism, in the absence of the characteristic morphologic pattern, is unknown.

Undistorted Vessels

Definition.—Undistorted vessels refers to vessels traversing an observation without displacement, deformation, or other alteration (Fig 23).

Rationale.—Vessels traversing an observation without any alteration of their path exclude the presence of mass effect. Perfusion alterations, areas of fat deposition, and hypertrophic pseudomasses do not exert mass effect and therefore do not distort traversing vessels. In contrast, tumors are space-occupying lesions displacing or distorting vessels and surrounding parenchyma. Therefore, undistorted vessels indicate absence of an underlying mass and are a feature favoring benignity.

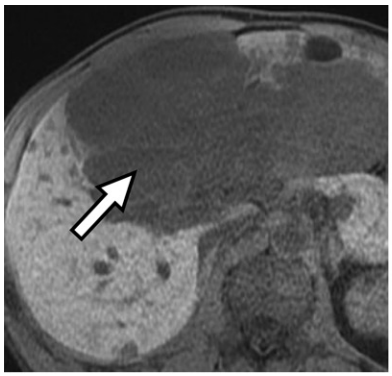
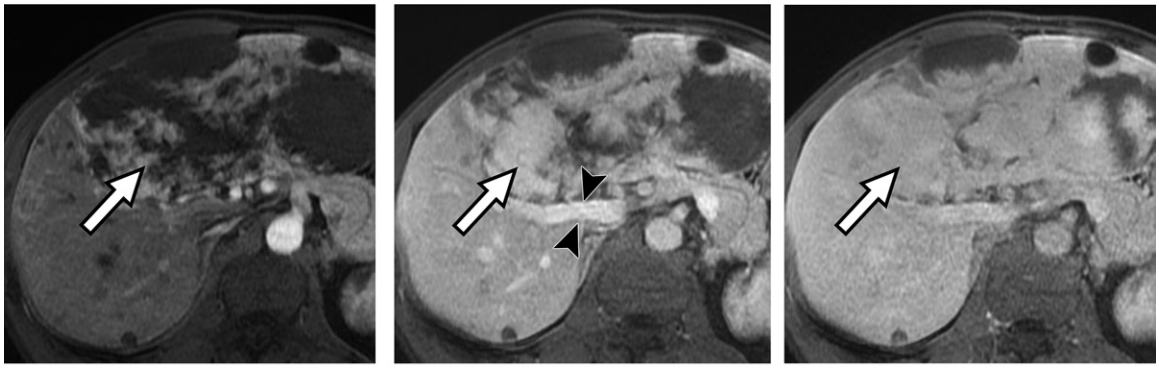


Figure 22. Hemangioma that parallels blood pool enhancement in a 45-year-old man with chronic hepatitis B infection. Axial T1-weighted fat-saturated images before contrast material administration **(a)** and in the late arterial **(b)**, portal venous **(c)**, and delayed **(d)** phases show a large mass (arrow) with areas of progressive flame-shaped and nodular enhancement that parallels blood pool enhancement. Arrowheads in **c** = right portal vein.

a.



b. **c.** **d.**

Diagnostic Performance.—The incremental effect on diagnostic performance of undistorted vessels in combination with major features is unknown. Indirect evidence and biologic plausibility suggest that undistorted vessels favor benignity.

Iron in Mass, More than in Liver

Definition.—Iron in a mass, more than in the liver, refers to excess iron in a mass relative to that in background liver. At gradient-echo imaging, iron-rich nodules show decreased signal intensity on images with longer echo time (ie, on the in-phase images) owing to shortening of transverse relaxation constants by the superparamagnetic effect of iron.

Rationale.—Iron-rich nodules, also known as siderotic nodules, are frequent in the cirrhotic liver. These lesions are usually benign low-grade dysplastic nodules; they are rarely high-grade or malignant lesions. An increased prevalence of HCC in siderotic nodules has not been demonstrated (126). For these reasons, the presence of iron favors benignity. However, the presence of blood degradation products and accumulation of hemosiderin that may be seen in hemorrhagic HCCs (Fig 24) constitutes a pitfall and should not be interpreted as a feature favoring benignity.

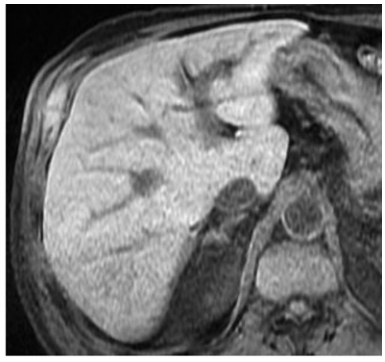
Diagnostic Performance.—The incremental effect on diagnostic performance of iron in a mass in combination with major features is unknown. Indirect evidence and biologic plausibility suggest that iron in a mass favors benignity.

Marked T2 Hyperintensity

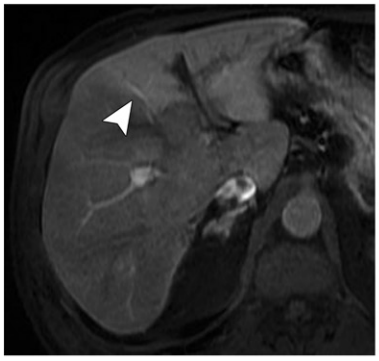
Definition.—Marked T2 hyperintensity refers to signal intensity of an observation on T2-weighted images markedly higher than that of the liver and similar to that of the bile ducts and other fluid-filled structures (Fig 25).

Rationale.—Marked T2 hyperintensity corresponds to the signal intensity of liquid and is more accentuated on heavily T2-weighted images with longer TEs. This ancillary feature is observed in benign fluid-filled structures such as liver cysts, hamartomas, biliary structures, and abscesses (127) or with slow-flowing blood in hemangiomas (123). Hepatic cystic neoplasms, such as cystadenoma or cystadenocarcinoma, or necrotic metastases may exhibit marked T2 hyperintensity in association with multiple septa or a rim of peripheral solid tissue, but these neoplasms are rare in cirrhosis. Except in areas of necrosis, HCCs seldom manifest with marked T2 hyperintensity.

Diagnostic Performance.—Marked T2 hyperintensity on heavily T2-weighted images allows distinction of hemangiomas from HCCs and other

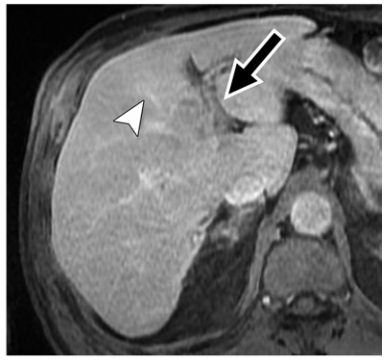


a.



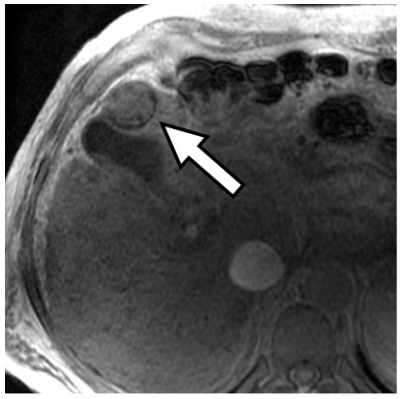
b.

c.

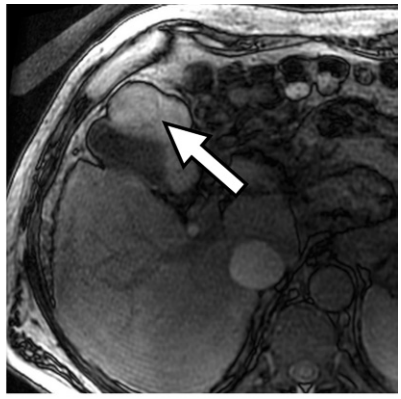


d.

Figure 23. Undistorted vessels in a 64-year-old woman with a bland left portal vein thrombus. Axial T1-weighted fat-saturated images before contrast material administration **(a)** and in the late arterial **(b)**, portal venous **(c)**, and delayed **(d)** phases show an undistorted vessel (arrow in **d**) at the junction of segments IVa and IVb in an area of perfusion alteration visible in the arterial phase (arrowhead in **b–d**) and caused by left portal vein thrombosis. Undistorted vessels favor benignity.



a.



b.

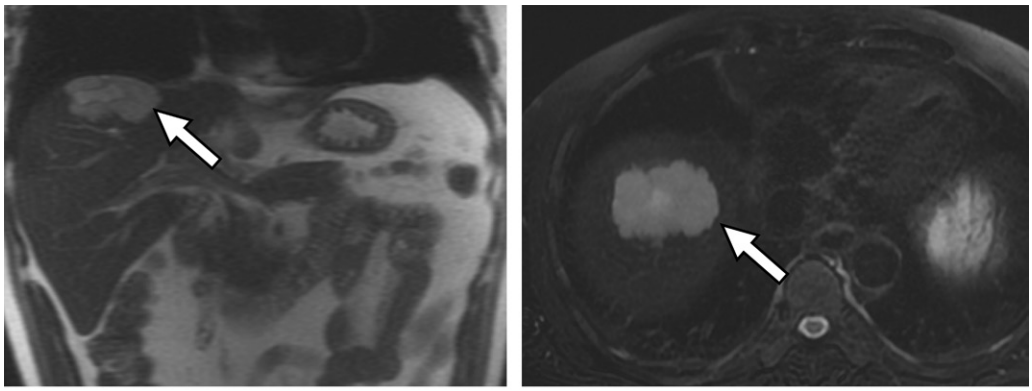
Figure 24. Pitfall of more iron in a mass (HCC) than in the liver in a 50-year-old man with alcoholic cirrhosis. Axial in-phase (TE = 4.6 msec) **(a)** and out-of-phase (TE = 2.3 msec) **(b)** T1-weighted images show iron in a solid mass (arrow) with signal drop observed on the in-phase image, which was obtained with a longer TE. The lesion was categorized LR-5. More iron in a mass than in the liver owing to resorption of blood products is a pitfall and does not constitute a feature favoring benignity.

malignant solid lesions with sensitivity of 75%–80% and specificity of 85%–100% (116,128).

HBP Isointensity

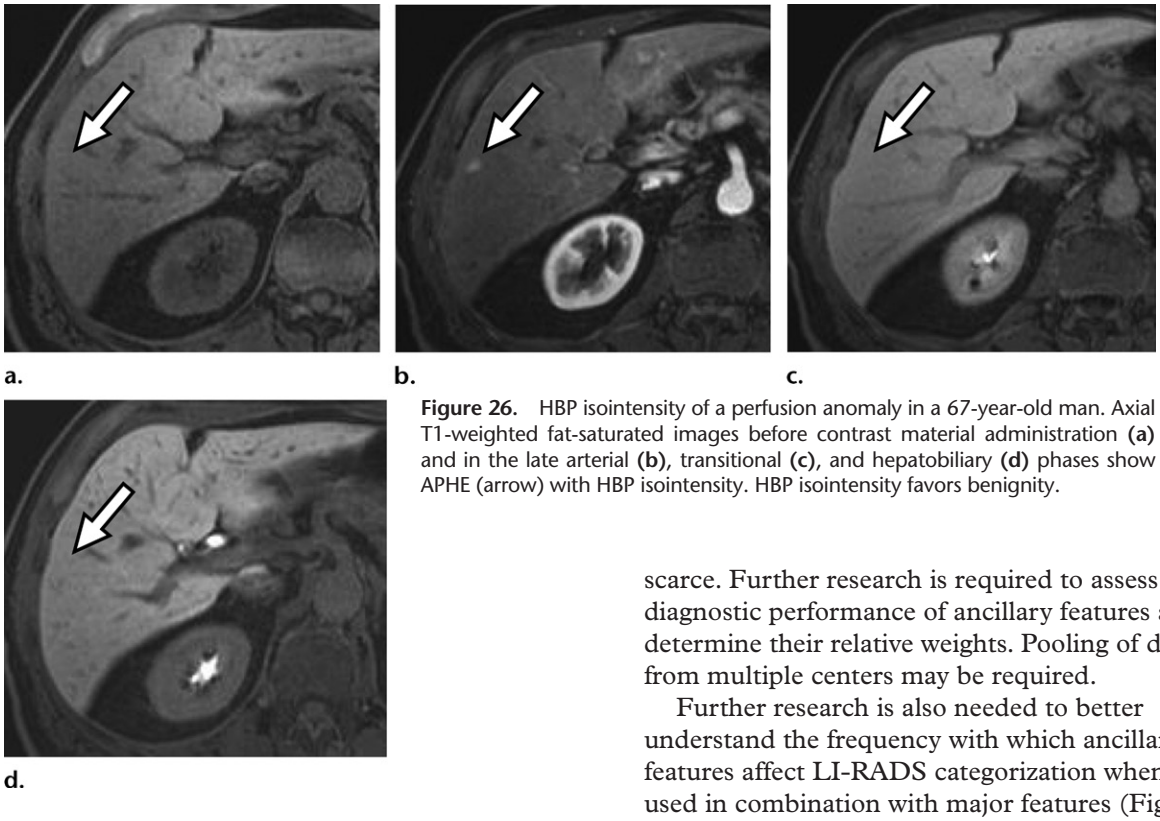
Definition.—HBP isointensity refers to signal intensity of an observation in the HBP nearly identical to that of the background liver (Fig 26).

Rationale.—As mentioned earlier, most HCCs and virtually all other malignancies have reduced or absent expression of OATP and therefore tend to appear hypointense in the HBP. Isointensity relative to the liver in the HBP indicates the presence of functional hepatocytes with preserved OATP expression, typically seen in regenerative nodules, low-grade dysplastic nodules (129,130), and benign arterioportal shunts (39,131). However, HBP isointensity does not completely exclude malignancy, as 2.5%–8.5% of HCCs may appear iso- or hyperintense relative to the surrounding parenchyma in the HBP (129). HCCs that are iso- or



a. b.

Figure 25. Marked T2 hyperintensity of a hemangioma in a 73-year-old man undergoing surveillance for chronic hepatitis B infection. Coronal **(a)** and axial **(b)** T2-weighted fat-saturated images show marked T2 hyperintensity of a mass (arrow). This imaging feature is diagnostic of hemangioma.



a. b. c. d.

Figure 26. HBP isointensity of a perfusion anomaly in a 67-year-old man. Axial T1-weighted fat-saturated images before contrast material administration **(a)** and in the late arterial **(b)**, transitional **(c)**, and hepatobiliary **(d)** phases show APHE (arrow) with HBP isointensity. HBP isointensity favors benignity.

hyperintense in the HBP tend to be more indolent and have a more favorable prognosis (53,132).

Diagnostic Performance.—HBP isointensity in combination with major features has sensitivity of 91%–94% and specificity of 93% for differentiating arterioportal shunt from HCC (39).

Future Directions

Ancillary features have been defined on the basis of imaging features described in the radiology literature. Evidence of the diagnostic accuracy and reproducibility of ancillary features—alone and in combination with other features—remains scarce. Further research is required to assess the diagnostic performance of ancillary features and determine their relative weights. Pooling of data from multiple centers may be required.

Further research is also needed to better understand the frequency with which ancillary features affect LI-RADS categorization when used in combination with major features (Figs 27, 28) as well as their effect on improving lesion detection.

Conclusion

MRI is frequently used for definitive and noninvasive diagnosis of HCC without mandatory histopathologic confirmation. Ancillary features are based on biologic and physical concepts described in the radiology literature. Although optional, use of ancillary features may improve confidence in the LI-RADS category, modify the observation category, or increase sensitivity for diagnosis of HCC. In this article, we provide the definitions for, review the rationale behind, and summarize the diagnostic performance of

Figure 27. Effect of ancillary features on LI-RADS categorization of a 25-mm mass in a 50-year-old man. **(a–d)** Axial T1-weighted fat-saturated images before contrast material administration **(a)** and in the late arterial **(b)**, portal venous **(c)**, and delayed **(d)** phases show lack of APHE, washout appearance, or capsule appearance (arrow). According to the diagnostic algorithm and table, this observation should be categorized LR-3. **(e, f)** Axial in-phase **(e)** and out-of-phase **(f)** T1-weighted images show signal drop (arrowhead) indicative of intralesion fat. **(g, h)** Axial diffusion-weighted image (b = 800 sec/mm^2) **(g)** and ADC map **(h)** show respective hyperintensity (* in **g**) and hypointensity (* in **h**) indicative of restricted diffusion. The intralesion fat and restricted diffusion led to a category upgrade to LR-4. Pathologic analysis after hepatectomy demonstrated HCC.

ancillary features favoring malignancy in general, favoring HCC in particular, or favoring benignity. Further research is needed to validate their application and inform their refinement.

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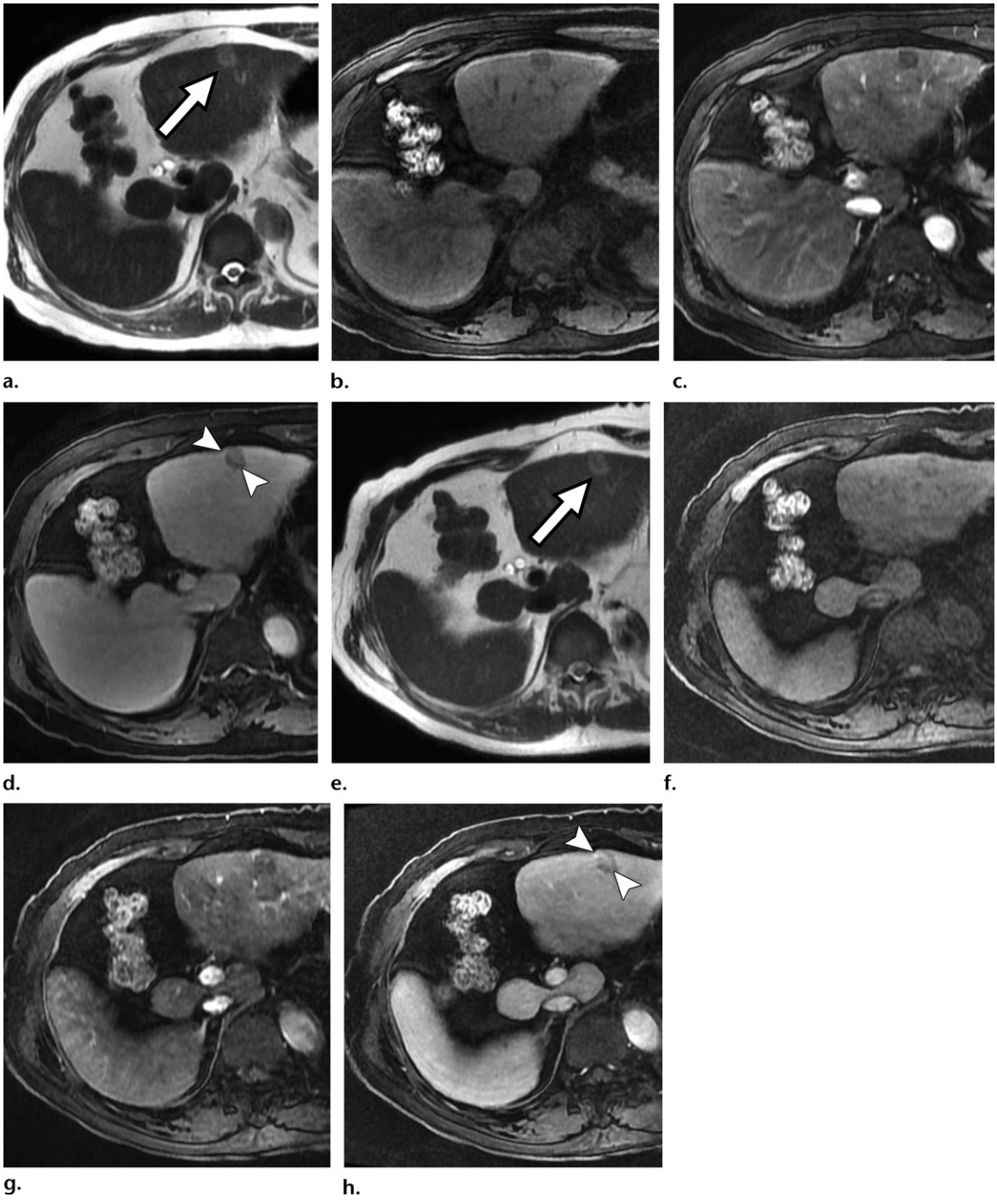
Figure 28. Effect of ancillary features on LI-RADS categorization of a 16-mm mass in a 47-year-old man. **(a–d)** Baseline axial T2-weighted fat-saturated image **(a)** and T1-weighted fat-saturated images before contrast material administration **(b)** and in the late arterial **(c)** and portal venous **(d)** phases show the mass (arrow in **a**, arrowheads in **d**). **(e–h)** Corresponding follow-up images 4 years later show the mass (arrow in **e**, arrowheads in **h**). According to the diagnostic algorithm and table, the observation would be categorized LR-3 because of its size smaller than 20 mm and absence of APHE. Although the observation shows mild-moderate T2 hyperintensity (arrow in **a** and **e**), an ancillary feature favoring malignancy, it also shows stability in size for more than 2 years (arrowheads in **d** and **h**), an ancillary feature favoring benignity. Because of conflicting ancillary features (ie, one or more favoring malignancy and one or more favoring benignity), the category remained unchanged.



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