Liver Imaging Reporting and Data System (LI-RADS) Version 2018: Imaging of Hepatocellular Carcinoma in At-Risk Patients

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Conflicts of interest are listed at the end of this article.

The Liver Imaging Reporting and Data System (LI-RADS) is composed of four individual algorithms intended to standardize the lexicon, as well as reporting and care, in patients with or at risk for hepatocellular carcinoma in the context of surveillance with US; diagnosis with CT, MRI, or contrast material–enhanced US; and assessment of treatment response with CT or MRI. This report provides a broad overview of LI-RADS, including its historic development, relationship to other imaging guidelines, composition, aims, and future directions. In addition, readers will understand the motivation for and key components of the 2018 update.

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The Liver Imaging Reporting and Data System (LI-RADS), supported by the American College of Radiology (ACR), provides standardization for hepatocellular carcinoma (HCC) imaging in the contexts of screening and surveillance, diagnosis, and treatment response assessment. LI-RADS was developed by a multinational consortium of radiologists and other specialists with expertise in liver cancer imaging, and it was integrated into the most recent HCC clinical practice guidance by the American Association for the Study of Liver Diseases (AASLD) (1). This adoption of LI-RADS by the AASLD was motivated by emerging evidence that LI-RADS categories accurately stratify the probability of HCC and overall malignancy (2). While the AASLD is an American institution, it exerts strong influence globally, and its guidance documents aid clinicians worldwide in understanding and applying available evidence in practice. The integration of LI-RADS into the AASLD guidance therefore represents a major milestone toward establishing a universal approach to the imaging diagnosis of HCC and acknowledges the vital role of LI-RADS and radiologists in this process. This report provides an overview of LI-RADS and its application in practice, including changes introduced in the most recent update (version 2018) required for harmonization with the AASLD. For more detailed information on LI-RADS, the interested reader is directed to the ACR website and selected references (3–16).

History of LI-RADS

The first version of LI-RADS was released in 2011 by the ACR after approximately 3 years of arbitration and eventual consensus by a committee of radiologists. Major LI-RADS updates followed in 2013, 2014, and 2017, each of which was informed by user feedback, accrued experience, emerging evidence, and harmonization efforts with clinical organizations, such as the AASLD, United Network for Organ Sharing, European Association for the Study of the Liver, and other international groups. With the changes introduced in the most recent update in 2018 (Fig 1), LI-RADS was integrated into AASLD clinical practice guidance.

In parallel with these developments, LI-RADS expanded from one committee of 12 North American radiologists in 2008 to an international multidisciplinary consortium that is presently composed of more than 250 members from more than 100 institutions and more than 30 countries and that is organized into a writing group and 15 working groups overseen by a steering committee. In addition to geographic diversity, the members and contributors come from community and academic settings and include experts in radiology, interventional radiology, hepatology, surgery, and pathology.

LI-RADS is a dynamic system that will continually be refined and updated by these active working groups. Future updates are anticipated to occur in 3–4-year cycles, with the next release scheduled for 2021 (the 10-year anniversary of LI-RADS).

LI-RADS Scope

Terminology

Synthesis of the historic imaging literature on HCC has been challenged by ambiguous and inconsistent

Abbreviations

AASLD = American Association for the Study of Liver Diseases, ACR = American College of Radiology, APHE = arterial phase hyperenhancement, HCC = hepatocellular carcinoma, iCCA = intrahepatic cholangiocarcinoma, LI-RADS = Liver Imaging Reporting and Data System, mRECIST = modified Response Evaluation Criteria in Solid Tumors

Summary

By updating the criteria for small (size range, 10–19 mm) LR-5 observations and simplifying the definition for threshold growth, Liver Imaging Reporting and Data System v2018 achieved consistency with and integration into the American Association for the Study of Liver Diseases 2018 hepatocellular carcinoma (HCC) clinical practice guidance, a major milestone toward establishing a universal approach to the imaging diagnosis of HCC.

Implications for Patient Care

- The Liver Imaging Reporting and Data System (LI-RADS) provides algorithms for use in diagnosis, surveillance, and treatment response assessment of hepatocellular carcinoma (HCC).

- All LI-RADS algorithms are built on the foundation of standardized lexicon, technique, management, and reporting guidelines.

- LI-RADS version 2018 updated the criteria for small (size range, 10–19 mm) LR-5 lesions and simplified the definition for threshold growth, thereby achieving consistency with and integration into the American Association for the Study of Liver Diseases 2018 HCC clinical practice guidance.

terminology. To facilitate progress and construction of an evidence-based diagnostic algorithm, LI-RADS first established a comprehensive lexicon of precisely defined radiologic terms aimed to standardize terminology and enable clear communication for clinical care, education, and research.

International Considerations

Regional HCC Imaging Systems

For nearly 2 decades, numerous scientific organizations and societies have proposed imaging-based criteria and guidelines that can be used to diagnose HCC (14). Three systems originate from Europe; six, from Asia; and four, from North America. One system was produced by a global organization. While these guidelines and imaging-based criteria have advanced the field, incongruities between the systems have introduced regional differences and have prevented global adoption of one guideline for use around the world.

Global Unification of Systems

A long-term goal of LI-RADS is to unify HCC imaging and diagnosis worldwide. The adoption of a unified system would improve clinical care, promote creation of registries, enable multicentric and international studies with common reporting criteria, and facilitate meta-analyses of the published literature. Congruency of LI-RADS with United Network for Organ Sharing/Organ Procurement and Transplantation Network technical and reporting requirements for liver transplantation candidates and the 2018 integration of LI-RADS with AASLD clinical guidance recommendations are important steps toward unification in North America (1). Global unification will require additional effort, and future versions of LI-RADS must account for regional variation in the epidemiology and biology of HCC, as well as financial and technical resource availability (14,17). Importantly, geographic differences in treatment practice affect the desired balance of sensitivity and specificity for diagnosis: While high specificity for HCC is favored for transplantation eligibility in the United States, high sensitivity is favored to maximize early HCC detection for primary resection or local-regional therapy in Asia. For this reason, Western imaging criteria tend to be more stringent, requiring both arterial phase hyperenhancement (APHE) and a size of at least 10 mm in combination with other features (5,6). In comparison, Asian criteria for HCC are more expansive and do not require arterial phase hyperenhancement (14,18–20). Future versions of LI-RADS will need to address and balance these different priorities.

International Membership of LI-RADS and Translation

The LI-RADS international working group was created in 2016 to promote international collaboration; global adoption of LI-RADS for research, education, and clinical care; and worldwide validation of LI-RADS in different patient populations. A key step toward global unification and a major initiative of the international working group is the translation of LI-RADS from English to other languages. Accordingly, LI-RADS is now translated in eight national and supraregional languages (Chinese [both simplified and traditional], French, German, Italian, Japanese, Korean, Portuguese, and Spanish) with other translations (eg, Russian and Arabic) planned (16).

Education

Although standardized interpretation and reporting of liver imaging has many benefits, it represents a new paradigm in many radiology practices, and it requires education. To address this need, the ACR website provides free educational LI-RADS reference materials (16). Additionally, the 40-member LI-RADS Outreach & Education working group develops educational materials and organizes lectures and workshops for radiologists, clinicians, and surgeons involved in the care of patients at risk for or with HCC.

Imaging Contexts and Population

LI-RADS offers four individual imaging algorithms designed for different clinical contexts: (a) US LI-RADS for surveillance, (b) CT/MRI LI-RADS for diagnosis and staging, (c) contrast material–enhanced US LI-RADS for diagnosis, and (d) treatment response LI-RADS to assess response to local-regional therapies (Fig 2). Each LI-RADS core document includes a graphic algorithmic display, a lexicon of relevant terminology, instructions, and supplementary information.

Essential for proper application of an imaging algorithm is a well-defined target population. A sufficiently high pretest probability is required for the algorithm to achieve the desired accuracy. Figure 2 summarizes the target population in each imaging context. Exclusion criteria are provided for
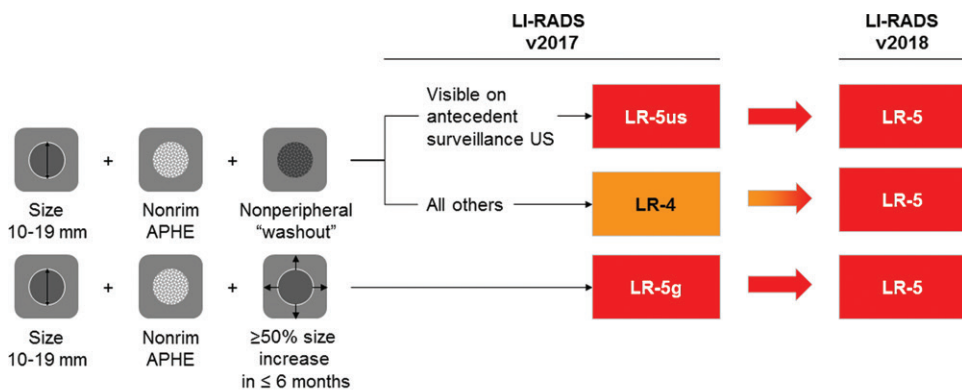
a.
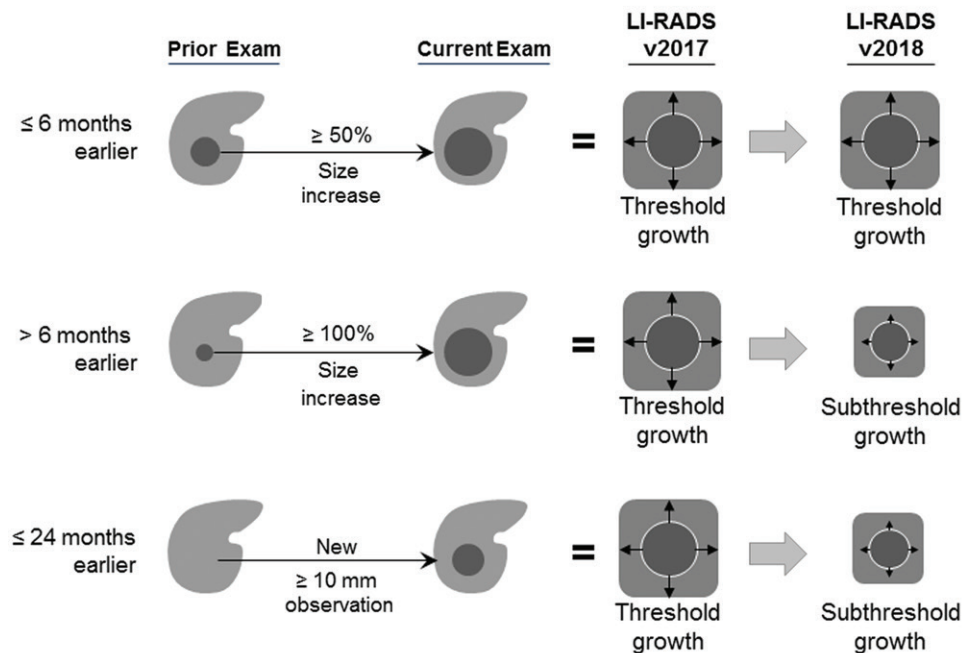
b.

Figure 1: Diagram shows changes introduced in Liver Imaging Reporting and Data System (LI-RADS) version 2018. **(a)** Changes in categorization. Observations 10–19 mm with arterial phase hyperenhancement (APHE) and nonperipheral "washout" are categorized as LR-5 (definite hepatocellular carcinoma), regardless of appearance on antecedent surveillance US images. Qualifiers "-us" and "-g" have been removed. **(b)** Change in threshold growth definition. Only 50% size increase in 6 months or less qualifies as threshold growth; all other size increases qualify as subthreshold growth.

nancies, including intrahepatic cholangiocarcinoma (iCCA) and combined HCC-iCCA, also may occur. All three types may invade major vessels, manifesting as tumor in vein, or metastasize to extrahepatic locations. Rarely, metastatic disease, sarcomas, or lymphomas may be encountered.

US for Surveillance

Surveillance refers to the repeated application of a diagnostic test at a defined interval in a population at risk for developing a disease (21). All clinical practice guidelines currently recommend US, typically performed every 6 months, as the primary surveillance method for HCC. The goal is to identify HCC at an early stage when it is potentially curable (20–23).

US Technique

As explained in the in US LI-RADS v2017 Core available online (24), US imaging of the liver should be performed with gray-scale and color Doppler US in transverse and longitudinal views, taking care to depict the entire liver.

US Image Interpretation

Unlike CT/MRI LI-RADS or contrast-enhanced US LI-RADS, both of which assign categories for each individual observation, US LI-RADS provides scores for the entire examination. Two scores are assigned (Fig 3): *(a)* the US LI-RADS category, which is used to determine management, and *(b)* the US LI-RADS visualization score, which is analogous to the breast density score in Breast Imaging Reporting and Data System mammography and conveys the expected level of sensitivity (25,26). Because the effect of visualization scores on outcomes has yet to be studied, the scores are not currently linked directly to management recommendations.

CT/MRI for Diagnosis

The CT/MRI algorithm permits definitive diagnosis of HCC without pathologic confirmation when applied in patients at high risk (Fig 2) who are undergoing diagnostic CT or MRI.

the diagnostic, staging, and treatment response algorithms to avoid false-positive diagnosis when the pretest probability is insufficiently high or when there is a propensity for benign nodules that may resemble or be mistaken for HCC.

The LI-RADS Observation

LI-RADS uses the term *observation* to generically refer to an area with an imaging appearance that is distinctive from the rest of the liver. Such an area may be a true lesion or a pseudolesion; the former has a corresponding pathologic abnormality, and the latter does not. Observations span the spectrum from benign to neoplastic and from to premalignant to malignant, and lesions may be of hepatocellular or nonhepatocellular origin. While HCC is the most common primary hepatic malignancy in LI-RADS target populations, other primary malig-

CT/MRI Technique

The minimal required and optional images for CT and MRI are listed in Figure 4. Multiphase contrast-enhanced imaging is necessary to capture the features essential to make a diagnosis and assess treatment response. Intravenous extracellular contrast agents are used for CT, while those used for MRI may be extracellular or hepatobiliary; the latter enable both extracellular and hepatobiliary phase imaging. Both gadoxetate disodium and gadobenate dimeglumine may be used in hepatobiliary phase imaging, though gadobenate requires longer delays (1–3 hours for gadobenate vs about 20 minutes for gadoxetate). For treatment-naive patients undergoing CT, unenhanced imaging is optional; however, it is required in the posttreatment setting for CT and all MRI examinations. Late arterial phase imaging is strongly preferred over early arterial phase imaging to maximize the likelihood of depicting APHE, which is a major feature of HCC, as will be discussed later in this article. Guidance on how to achieve optimal arterial phase timing and a more detailed discussion of imaging parameters is provided in the review article by Kambadakone et al (11).

When compared with CT or MRI with extracellular contrast agents, MRI with gadoxetate permits detection of not only arterialized cancers in the dynamic phases but also detection of small nonarterialized cancers in the hepatobiliary phase, which increases sensitivity for diagnosis of small HCC (<2 cm) (27). Because of its higher sensitivity, MRI with gadoxetate may be preferable in clinical practice paradigms (such as those in Asia) that emphasize aggressive local-regional treatment or resection for small HCCs. By comparison, MRI with extracellular contrast agents and CT are more specific in the diagnosis of small HCC; thus, they may be preferred in clinical practice paradigms (such as in the United States) that emphasize liver transplantation without biopsy confirmation in the treatment of early stage HCC (27). Recent meta-analyses based on studies at academic centers have suggested that MRI is more sensitive than CT, with a similar specificity; however, the differences are small, and the comparative performance of CT and MRI has not been studied in community settings (27,28). In recognition of the fact that the choice of modality (CT or MRI) and MRI contrast agent (extracelllar or hepatobiliary) depends on patient, institutional, and regional factors, LI-RADS does not endorse any particular imaging method. Rather, it provides guidance on technique, terminology, interpretation, and reporting.

LI-RADS Algorithm	Context	Target population
Ultrasound LI-RADS	Surveillance[a]	**Apply in patients undergoing ultrasound for HCC surveillance. According to AASLD 2018 guidance, surveillance is beneficial in adults with[b]:** **Cirrhosis of any etiology** • Child-Pugh A • Child-Pugh B • Child-Pugh C if on the transplant list **Noncirrhotic chronic HBV** • Asian male > 40 years • Asian female > 50 years • African or North American black • Family history of HCC
CEUS LI-RADS	Diagnosis	**Apply in patients at high risk for HCC. This includes adults[c] with:** • Cirrhosis • Chronic HBV even in absence of cirrhosis • Current or prior HCC **Do not apply in patients:** • Without the above risk factors • < 18 years • With chronic liver disease due to vascular disorders[d] or cirrhosis due to congenital hepatic fibrosis
CT/MRI Diagnostic LI-RADS	Diagnosis and/or Staging	
CT/MRI Treatment Response LI-RADS	Treatment response	

[a] Some centers may elect to perform contrast-enhanced CT or MR imaging instead of US for surveillance in select patients such as those on the transplant list or those in whom ultrasound visualization is severely limited. LI-RADS recommends neither for nor against the use of these modalities for this purpose.

[b] Listed are the groups recommended by 2018 AASLD guidance for surveillance. Other regional clinical practice guidelines may expand the groups to potentially include:
• Adults with cirrhosis of any cause, regardless of Child-Pugh score.
• Some adults with chronic hepatitis C virus infection even in the absence of cirrhosis.

[c] Includes liver transplant candidates and recipients with any of the listed risk factors.

[d] Vascular disorders of the liver have a propensity to form benign nodules that may resemble and be mistaken for HCC. Therefore, LI-RADS should not be applied in patients in whom chronic liver disease is due to any of the following:
• Chronic vascular outflow obstructions (cardiac congestion, pulmonary hypertension, Budd-Chiari).
• Chronic sinusoidal obstructions (diffuse nodular regenerative hyperplasia).
• Chronic inflow obstructions (occlusion or absence of portal vein).
• Hereditary hemorrhagic telangiectasia.

Figure 2: Chart summarizes Liver Imaging Reporting and Data System (LI-RADS) algorithms and target populations for surveillance, diagnosis, staging, and treatment response. AASLD = American Association for the Study of Liver Diseases, CEUS = contrast-enhanced US, HBV = hepatitis B virus, HCC = hepatocellular carcinoma.
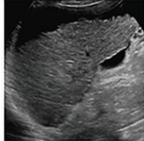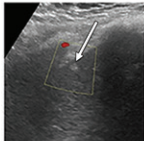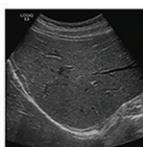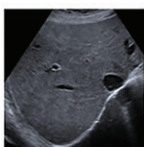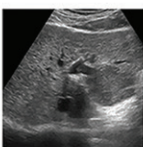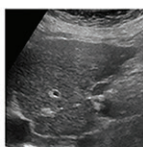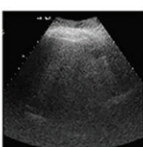
US Categories	Definition	Examples	
US-1: Negative	No observation **OR** Only definitely benign observation(s)		Advanced cirrhosis with ascites but no focal liver observation
US-2: Subthreshold	Observation(s) < 10 mm in diameter, not definitely benign		A subcentimeter hyperechoic observation (arrow) is identified that warrants short-interval follow-up in 3-6 months to ensure stability
US-3: Positive	Observation(s) ≥ 10 mm in diameter, not definitely benign **OR** New thrombus in vein. Observation may be a solid nodule of any echogenicity or area of parenchymal distortion ≥10 mm with one or more of the following manifestations: • Ill-defined area of heterogeneity • Refractive edge shadows • Loss of normal hepatic architecture	Solid hypoechoic observation ≥ 10 mm in size (arrow), not definitely benign is present in the left lobe of the liver / New thrombus in main portal vein (arrow) / Parenchymal distortion resulting in loss of normal portal triads (arrow)	

Visualization Score	Definition	Examples	
A: No or minimal limitations	Limitations if any are unlikely to meaningfully affect sensitivity. **Comment:** Visualization A is assigned even when mild heterogeneity of the liver is present due to underlying cirrhosis, as long as the liver is well-visualized in near entirety.	Homogeneous liver / Minimal beam attenuation / Liver visualized in near entirety	
B: Moderate limitations	Limitations may obscure small masses. **Comment:** Visualization B is assigned when there is moderate parenchymal heterogeneity, ultrasound beam attenuation, or shadowing obscuring portions of the liver.	Moderately heterogeneous liver / Moderate beam attenuation / Some portions of liver not visualized	
C: Severe limitations	Limitations significantly lower sensitivity for focal liver lesions. **Comment:** Visualization C is assigned when there is severe parenchymal heterogeneity, ultrasound beam attenuation, or shadowing obscuring majority (>50%) of liver.	Severely heterogeneous liver / Severe beam attenuation (> 50% of diaphragm not visualized) / Majority (>50%) of liver not visualized	

Figure 3: Summary of US Liver Imaging Reporting and Data System categories and visualization scores.

CT/MR Image Interpretation

LI-RADS defines eight unique diagnostic categories (Fig 5) based on imaging appearance that reflect the probability of HCC or malignancy with or without tumor in vein (6). The category LR-NC (not categorizable) is applied when image omission or degradation precludes categorization. The categories LR-1 (definitely benign) and LR-2 (probably benign) range from simple cysts to LR-2 distinctive nodules. An LR-2 distinctive nodule is defined by its size (<20 mm) and the absence of any major features of HCC, any features of LR-M, or any ancillary features of malignancy. Examples include otherwise unremarkable T1 hyperintense nodules, T2 hypointense nodules, and hepatobiliary phase hyperintense nodules. LR-3 (intermediate probability of HCC) includes some perfusion alterations that have a nodular

shape and true nodules with one or two malignant features. The malignant categories range from probable to definite malignancy and include LR-4 (probably HCC), LR-5 (definitely HCC), LR-M (probably or definitely malignant, not specific for HCC), and LR-TIV (malignancy with tumor in vein). While tumor in vein is often associated with HCC, it can occur in the setting of non-HCC malignancy. Malignant lesions previously confirmed with biopsy (eg, HCC, iCCA) or benign lesions of nonhepatocellular origin (eg, hemangioma) do not require LI-RADS categorization unless there is discordance between imaging and pathology findings or unless there is some other doubt about the diagnosis.

The LI-RADS algorithm is a decision tree designed to provide specificity for the diagnosis of HCC through stepwise consideration of other diagnostic categories first (LR-1 or LR-2, LR-TIV, LR-M, or LR-NC) and followed by a diagnostic table to differentiate between LR-3, LR-4, and LR-5 (5,16). A key category in ensuring specificity for HCC is LR-M, which is intended to capture all malignant lesions with a substantial possibility of being something other than HCC. The differential diagnosis of observations categorized as LR-M includes iCCA, combined HCC-CCA, and HCC with atypical or nonspecific imaging features (3,6).

For observations that land in the diagnostic table, the combination of major features is used to determine whether a lesion is categorized as LR-3, LR-4, or LR-5 (5). Importantly, no one feature by itself is enough to categorize a lesion as LR-5 (6). In LI-RADS version 2018, a change in LR-5 criteria was introduced: lesions 10–19 mm in size with APHE and washout are categorized as LR-5 (Fig 1). In prior LI-RADS versions, such observations were categorized as LR-4 or, if visible on antecedent US images, as LR-5us (5). This important change allowed for AASLD integration and consensus in practice guidance (1). In concordance with this change, LI-RADS version 2018 eliminated the "-g" and "-us" qualifiers used previously for subsets of LR-5 observations.

The LI-RADS lexicon divides imaging features into major features, LR-M features, and ancillary features. Only major

CT	Recommended equipment	• Multidetector CT with ≥ 8 detector rows
	Required images	• Arterial phase (late arterial phase strongly preferred) • Portal venous phase • Delayed phase (2 to 5 minutes after injection)
	Suggested images	• Precontrast, if patient has had local-regional treatment • Multiplanar reformations
MRI	Recommended equipment	• 1.5T or 3T • Torso phased-array coil

	Required images	• Unenhanced T1-weighted OP and IP imaging
		• T2-weighted imaging (fat suppression per institutional preference)
		• All contrast agents: Multiphase T1-weighted imaging, preferably using a 3D sequence with ≤ 5 mm slice thickness
		  • Precontrast imaging
		  • Arterial phase (late arterial phase strongly preferred)
		  • Portal venous phase
		• MR imaging with extracellular contrast agents or gadobenate dimeglumine
		  • Delayed phase (2 to 5 minutes after injection)
		• MR imaging with gadoxetate disodium
		  • Transitional phase (2 to 5 minutes after injection)
		  • Hepatobiliary phase (about 20 minutes after injection); use the same sequence type as for earlier phases, may use higher flip angle to increase T1 contrast

	Suggested or optional images	• Diffusion-weighted imaging • Subtraction imaging • Multiplanar acquisition • 1-to 3-hr hepatobiliary phase with gadobenate dimeglumine (same sequence type as for multiphase, may use higher flip angle to increase T1 contrast)

Figure 4: Chart summarizes Liver Imaging Reporting and Data System version 2018 technical requirements for CT and MRI. IP = in phase, OP = opposed phase, 3D = three dimensional.

features contribute to LR-5 categorization (6,7). These features (Fig 6) include nonrim APHE, nonperipheral "washout" appearance, enhancing "capsule" appearance, size, and threshold growth (7). Quotation marks are placed around these terms to signify that these features may be imaging phenomena without definitive pathophysiologic correlates. To ensure specificity, major features should be applied only when their presence is unequivocal. Size should be measured from outer border to outer border (including the "capsule," if seen) in the phase in which the border is best defined and preferably not on arterial phase images to avoid inclusion of perilesional enhancement. For LR-5 categorization, both APHE and lesion size of at least 10 mm are required. Importantly, LI-RADS version 2018 simplified the threshold growth definition to a size increase of at least 50% in 6 months or less (Fig 1). "Washout" can apply to any enhancing observation, even if there is no APHE. "Washout" assessment is restricted to the portal venous phase with gadoxetate disodium; however, it can be assessed in either the portal venous phase or the delayed phase with extracellular contrast agents or gadobenate dimeglumine (7).

LR-M features (Fig 7) include a targetoid or nontargetoid mass with one or more of the following findings: infiltrative appearance, marked diffusion restriction, necrosis, or other features suggestive of non-HCC malignancy. LR-M features

are highly suggestive of malignancy but are not specific for HCC, and the presence of even one such feature prompts categorization as LR-M. There is no requirement that lesions be 10 mm or larger to be categorized as LR-M. Rim APHE is perhaps the most frequently encountered LR-M feature, and differentiation of rim APHE from nonrim APHE is essential for accurate LI-RADS categorization (3,7).

Ancillary features, tie-breaking rules, and the final diagnostic check are intended to improve the accuracy of categorization while preserving specificity for HCC and sensitivity for malignancy in general (5,8). Ancillary features are divided into those favoring benignity, those favoring malignancy, and those favoring HCC (8). Their use is optional, and they may be used to up- or downgrade a category by one, but they cannot be used to upgrade to LR-5. Ancillary features also can be used to improve lesion detection or diagnostic confidence. Detailed discussion of ancillary features and tie-breaking rules can be found on the ACR website and in review articles (5,8,29).

Contrast-enhanced US for Diagnosis

Contrast-enhanced US is performed with intravenous injection of a microbubble contrast agent. Contrast-enhanced US is most suitable for problem solving, categorizing individual observations, and differentiating tumor in vein from bland thrombus rather than for staging the entire liver. Contrast-enhanced US requires expertise and specialized equipment designed to maximize sensitivity to microbubbles. Real-time imaging is performed continuously for the 1st minute to capture the arterial phase. This is followed by intermittent scanning every 30–60 seconds for up to about 5 minutes to evaluate washout.

Diagnostic Category	Conceptual Definition	CT/MR Criteria
LR-NC: Noncategorizable	Observation that cannot be meaningfully categorized because image omission or degradation prevents assessment of one or more major features	<u>Both</u> of the following: • One or more major features cannot be assessed because of image omission or degradation **AND** • As a direct result, possible categories range from those in which cancer is unlikely (LR-1 or LR-2) to those in which cancer is likely (LR-4, LR-5, LR-M)
LR-1: Definitely Benign	100% certainty that observation is nonmalignant	LI-RADS does not provide criteria for most entities that may be categorized LR-1, but instead provides examples (Reference15)
LR-2: Probably Benign	High probability but not 100% certainty observation is non-malignant	LI-RADS does not provide criteria for most entities that may be categorized LR-2, but instead provides examples (Reference15) **Criteria for LR-2 distinctive nodule:** • Size <20 mm • **NO** major features, LR-M features or ancillary features favoring malignancy
LR-3: Intermediate probability of malignancy	Nonmalignant & malignant entities each have moderate probability	**Nonrim arterial phase hyperenhancement AND:** • < 20 mm with no additional major features **Arterial phase hypo- or isoenhancement AND:** • < 20 mm with ≤ 1 additional major feature **OR** • ≥ 20 mm with no additional major features
LR-4: Probably HCC	High probability but not 100% certainty observation is HCC	**Nonrim arterial phase hyperenhancement AND:** • < 10 mm with ≥ 1 additional major feature OR • 10-19 mm with "capsule" and no other major features OR • ≥ 20 mm with no additional major feature **Arterial phase hypo- or isoenhancement AND:** • < 20mm with ≥ 2 additional major features OR • ≥ 20 mm with ≥ 1 additional major feature
LR-5: Definitely HCC	100% certainty observation is HCC	**Nonrim arterial phase hyperenhancement AND:** • 10-19 mm with nonperipheral "washout" and no other major features OR • 10-19 mm with ≥ 50% size increase in ≤ 6 months and no other major features OR • ≥ 20 mm with ≥ 1 additional major feature
LR-TIV: Malignancy with tumor in vein	100% certainty there is malignancy with tumor in vein	Presence of definite enhancing soft tissue in vein, regardless of visualization of parenchymal mass
LR-M: Probably or definitely malignant, not HCC specific	High probability or 100% certainty observation is malignant but features are not HCC specific **Comment**: LR-M does not exclude HCC. Rather, it indicates a substantial probability of a malignant neoplasm other than HCC.	**Targetoid mass:** • Rim APHE • Peripheral washout appearance • Delayed central enhancement • Targetoid diffusion restriction • Targetoid TP or HBP signal intensity **Nontargetoid mass not meeting LR-5 criteria and without TIV, with ≥ 1 of the following:** • Infiltrative appearance • Marked diffusion restriction • Necrosis or severe ischemia • Other feature suggesting non-HCC malignancy

Figure 5: Summary of CT and MRI diagnostic Liver Imaging Reporting and Data System (LI-RADS) categories. APHE = arterial phase hyperenhancement, HBP = hepatobiliary phase, HCC = hepatocellular carcinoma, TIV = tumor in vein, TP = transitional phase.
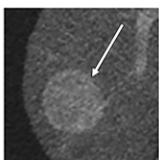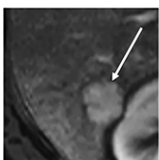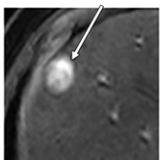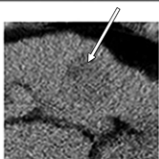
Scanning should be kept brief to minimize the destruction of microbubbles by US energy.
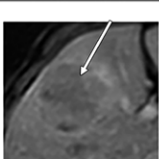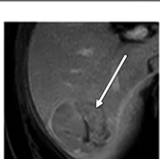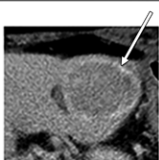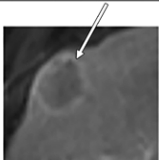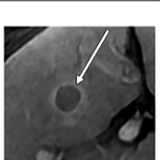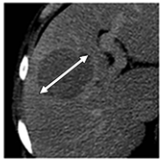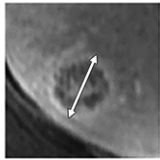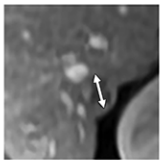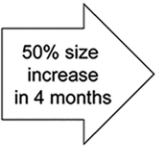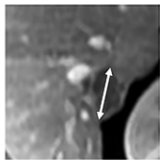
Major Feature	Definition	Examples		
		CT	MRI-ECA	MRI-Gadoxetate
Nonrim arterial phase hyperenhancement (APHE)	Nonrim-like enhancement in arterial phase unequivocally greater in whole or in part than liver. Enhancing part must be higher in attenuation or intensity than liver in arterial phase. **Comment:** Nonrim APHE is **required** for LR-5 categorization.	 Arterial phase	 Arterial phase	 Arterial phase
Nonperipheral washout appearance ("washout")	Nonperipheral visually assessed temporal reduction in enhancement in whole or in part relative to composite liver tissue from earlier to later phase resulting in hypoenhancement in the extracellular phase: • portal venous or delayed phase with ECA or gadobenate • portal venous phase with gadoxetate	 Portal or delayed phase	 Portal or delayed phase	 Portal phase **only**
Enhancing capsule appearance ("capsule")	Smooth, uniform, sharp border around most or all of an observation, unequivocally thicker or more conspicuous than fibrotic tissue around background nodules, and visible as as enhancing rim in portal venous phase, delayed phase, or transitional phase.	 Portal or delayed phase	 Portal or delayed phase	 Portal or transitional
		Examples		
Size	Largest outer-edge-to-outer-edge dimension of an observation **Comment:** Do not measure in arterial phase or DWI if margins are clearly visible on different phase or sequence (size may be overestimated in arterial phase due to summation with periobservation enhancement and is not measured reliably on DWI due to anatomic distortion).	 Pick phase, sequence, plane in which margins are clearest	 Include "capsule" in measurement	
Threshold growth	Size increase of a mass by ≥ 50% in ≤ 6 months **Comments:** • Measure on same phase, sequence, and plane if possible. • Apply threshold growth **only** if there is a prior CT or MRI exam. Do not assess threshold growth by comparing to prior US or CEUS exams.	50% size increase in 4 months		

Figure 6: Summary of CT and MRI diagnostic Liver Imaging Reporting and Data System major features. APHE = arterial phase hyperenhancement, CEUS = contrast-enhanced US, DWI = diffusion-weighted imaging, ECA = extracellular contrast agent.

The contrast-enhanced US LI-RADS algorithm is similar in concept and application to the CT/MRI LI-RADS algorithm, albeit with some modifications (13). Chief among them is the characterization of washout, which at contrast-enhanced US is considered true washout and therefore requires no quotation marks. Unlike CT and MRI contrast agents, microbubbles are pure blood pool agents that are about the size of red blood cells. They are confined within the blood space and do not leak through endothelial fenestrations into the tumor or parenchymal interstitium. As a result, their distribution on postarterial phase images reflects the relative blood volume. Accordingly, tumors such as HCC, which tend to have only slightly lower blood volume than the liver, typically exhibit mild and late-onset washout. In comparison, iCCAs and other non-HCC malignancies have much lower blood volume than liver, and their washout is early and marked. For these reasons, contrast-enhanced US LI-RADS requires assessment not only for the presence of washout but also for its time of onset after injection and its degree (Fig 8).

Another unique feature is that arterioportal shunts, which are a frequent cause of diagnostic confusion at CT and MRI, are not visible on US or contrast-enhanced US images. Since vascular pseudolesions do not occur, any contrast-enhanced US observation that enhances during the arterial phase is a true arterialized nodule. In the setting of cirrhosis, in which benign
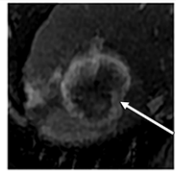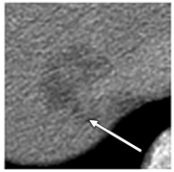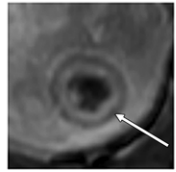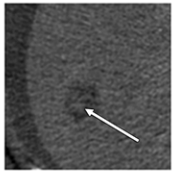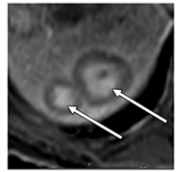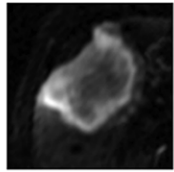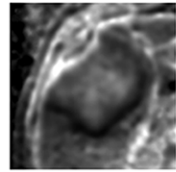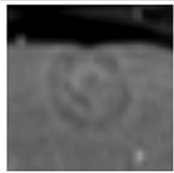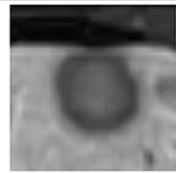
LR-M Imaging Feature	Definition	Examples	
		CT	MRI
Targetoid dynamic enhancement			
Rim arterial phase hyperenhancement (APHE)	Spatially defined subtype of APHE in which arterial phase enhancement is most pronounced in observation periphery		
Peripheral washout appearance	Spatially defined subtype of "washout" in which apparent washout is most prounced in observation periphery		
Delayed central enhancement	Central area of progressive postarterial phase enhancement		
Targetoid appearance on diffusion-weighted imaging (DWI) or transitional phase (TP)/ hepatobiliary phase (HBP)			
Targetoid restriction	Concentric pattern on DWI characterized by restricted diffusion in observation periphery with less restricted diffusion in observation center	DWI B=800	ADC
Targetoid TP or HBP appearance	Concentric pattern in TP or HBP characterized by moderate-to-marked hypointensity in observation periphery with milder hypointensity in center	TP	HBP

Figure 7: Summary of CT and MRI LR-M (probably or definitely malignant, not hepatocellular carcinoma specific) features. ADC = apparent diffusion coefficient, APHE = arterial phase hyperenhancement, DWI = diffusion-weighted imaging, HBP = hepatobiliary phase, TP = transitional phase.

arterialized lesions such as focal nodular hyperplasias and hepatocellular adenomas are rare, the majority of such nodules are premalignant or malignant and warrant categorization as LR-4 or higher (13). Additionally, threshold growth and enhancing capsule are not major features for contrast-enhanced US, the former because it is not reliably measured on contrast-enhanced US images and the latter because it is not detectable on US images. For similar reasons, the list of ancillary features is shorter for contrast-enhanced US LI-RADS than for CT/MRI LI-RADS.

Treatment Response

The LI-RADS treatment response algorithm applies to multiphase CT or MRI used to assess response after local-regional therapy (15), which includes percutaneous therapy (eg, ethanol and radiofrequency or microwave ablation), transcatheter therapy (eg, transarterial chemoembolization or radioembolization), and external beam radiation therapy. The algorithm also applies to observations at the surgical margin after resection of
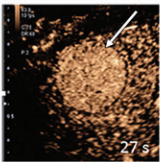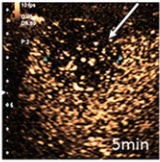
HCC; observations elsewhere in the liver remnant should be assessed with a diagnostic algorithm. The LI-RADS treatment response algorithm does not apply to systemic chemo-, targeted, or immunologic therapies, nor does it apply to treatment response using contrast-enhanced US. In patients who underwent both systemic therapy and local-regional treatment, the LI-RADS treatment response algorithm can be applied at the discretion of the interpreting radiologist.

Analogous in concept to the diagnostic algorithms, LI-RADS treatment response category codes reflect the relative probability of tumor viability after local-regional therapy to guide management decisions. Similar to the modified Response Evaluation Criteria in Solid Tumors (mRECIST) (30), the LI-RADS algorithm is based on unidimensional measurements of the largest enhancing component of a treated tumor, excluding areas of nonenhancement (Fig 9), an approach that shows high reproducibility in response categories and better prognostication when compared with traditional Response Evaluation Criteria in Solid Tumo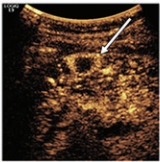rs, version 1.1, after local-regional therapy (31–35). The LI-RADS algorithm expands on the mRECIST approach not only by defining viable disease but also by providing nonevaluable, equivocal, and nonviable treatment response categories. Unlike mRECIST, the LI-RADS treatment response categories are assigned on a lesion-by-lesion basis and are not assigned to the whole liver or patient. The imaging features used in LI-RADS treatment response categorization are summarized in Figure 9. Unlike diagnostic LI-RADS, where APHE and size of at least 10 mm are required for categorization as LR-5, presence of either APHE or washout or enhancement similar to the pretreatment condition, regardless of size, is sufficient to categorize a treated lesion as viable.

Reporting

The radiology report should guide management decisions through clear and concise communication of hepatic observations and other findings that may affect treatment decisions. Surveillance reports should include LI-RADS US category and

Major Feature	Definition	Example
Arterial phase hyperenhancement (APHE) – nonrim and not peripheral discontinuous	Enhancement in arterial phase that is neither rimlike nor peripheral discontinuous globular. Enhancing part must be higher in echogenicity than liver in arterial phase, unequivocally greater in whole or in part than liver. APHE is required for CEUS LR-5 categorization	
Late washout	Visually assessed temporal reduction in enhancement in whole or in part relative to liver beginning in or after arterial phase and resulting in hypoenhancement. Late (≥ 60 s) and mild washout is required for CEUS LR-5 categorization.	
Size	Largest outer-edge-to-outer-edge dimension of a nodule using precontrast B-mode images if possible. **Comments:** • Size ≥ 10 mm is required for CEUS LR-5 categorization. • If the margins are not clear on precontrast B-mode images, choose the CEUS image on which the margins are most clearly defined, avoiding the peak of arterial phase enhancement if possible.	

a.

LR-M Imaging Feature	Definition	Example
Rim arterial phase hyperenhancement (APHE)	Spatially defined subtype of APHE in which arterial phase enhancement is most pronounced in observation periphery.	
Early washout	Temporally defined subtype of washout in which onset is within 60 seconds from contrast injection.	
Marked washout	Degree-defined subtype of washout in which the degree of washout is marked within 2 minutes after contrast injection. Observation appears black or punched out.	

b.

Figure 8: Summary of contrast-enhanced US Liver Imaging Reporting and Data System **(a)** major and **(b)** LR-M (probably or definitely malignant, not hepatocellular carcinoma specific) features. APHE = arterial phase hyperenhancement, CEUS = contrast-enhanced US,

visualization scores. Diagnostic and staging reports should describe individual observations, including their size, major features (and ancillary features if used for category adjustment), and final diagnostic category. Treatment response reports should assign a LI-RADS treatment response category, include the pretreatment LI-RADS category (or histologic diagnosis, if known), and provide a measure of viable or equivocally viable tumor. When the number of untreated or treated observations exceeds five, radiologists may report lesions in aggregate rather than individually to maintain clarity and brevity. Through the ACR website, LI-RADS provides templates, sample reports, and guidance for radiologists in creating comprehensive yet concise reports with relevant acquisition details and features (16).

LI-RADS soon will be integrated into commercial reporting systems to assist the radiologist in applying LI-RADS properly. The dissemination and adoption of these reporting tools will facilitate the use of LI-RADS for clinical care and help ensure that radiology reports are complete and accurate. In addition to imaging features and categorization, reports should also include management recommendations, as will be discussed later in this article.

Management

Management is determined on the patient level, but it is typically strongly influenced by the imaging observation with the highest risk of malignancy (eg, if a patient has multiple LR-3 lesions and an LR-5 lesion, management would be driven by the LR-5 lesion). Figure 10 provides a general management approach for CT- and MRI-based LI-RADS diagnostic categories, which is consistent with the newest AASLD guidance (1). Management for contrast-enhanced US-assigned categories is similar for all categories except contrast-enhanced US LR-3, which is thought to convey slightly higher likelihood of HCC than CT or MRI LR-3 and therefore warrants closer scrutiny (9,13). Figure 10 also provides general management guidance for treatment response categories.

Imaging findings are one of several elements that may be used to determine diagnosis and management. Although radiologists provide an initial estimate of the relative likelihood of HCC or viable tumor after local-regional treatment by assigning a LI-RADS diagnostic or treatment response category, respectively, this estimate may be refined by clinical history, biomarker levels, and other factors. Similarly, decisions between management options (ie, return to surveillance, repeat diagnostic imaging, alternative diagnostic imaging, biopsy, or treatment as HCC without biopsy) do not follow solely from the estimated probability of HCC but incorporate additional information, including patient comorbidities, preferences, and eligibility for organ transplantation. For these reasons, management decisions are best determined with a multidisciplinary approach, in which physicians consider all potential work-up or treatment options to tailor care to the individual patient. Evidence suggests that such an approach improves accuracy and timeliness of diagnosis, appropriate treatment allocation, and overall survival of patients with or at risk for HCC (36).

Biopsy Considerations

Judicious use of biopsy in select patients with LR-3, LR-4, or LR-M observations may help tailor management decisions. General indications for biopsy are listed in Fig 11. In general, LR-5 observations do not require pathologic proof of diagnosis, although biopsy may allow for molecular characterization or be needed for a clinical trial.

Biopsy of LR-3, LR-4, or LR-M observations should be based on a multidisciplinary discussion. A radiology report should not compel a clinician to perform biopsy, as factors outside of the radiologist's knowledge may affect these decisions.

LI-RADS: Emerging Evidence

By necessity, the creation of LI-RADS preceded clinical validation, and the supporting evidence is just now emerging (8,37–54). Evidence supporting each LI-RADS major feature of HCC is reported in a systematic review and is summarized in this article (39). In patients at risk for disease, nonrim APHE is a sensitive imaging feature for progressed HCC (55–58). The combination of nonrim APHE and nonperipheral washout appearance provides high specificity (39,58–60). Larger observation size increases sensitivity (61–67), specificity (68,69), and probability of HCC (56,61,70,71). Capsule appearance yields high specificity (42,64); however, its incremental value has been questioned (58). Threshold growth helps differentiate HCC from benign entities (72).

The application of ancillary features modifies the LI-RADS category in about 10%–20% of observations (42,73), with upgrades being slightly more common than downgrades (42). Recent data suggest that use of ancillary features increases sensitivity while preserving the specificity of LR-4 or LR-5 for HCC (42).
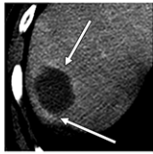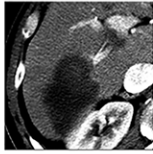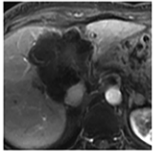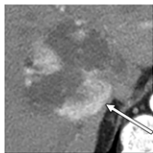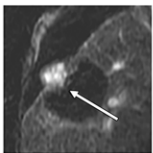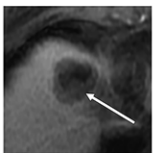
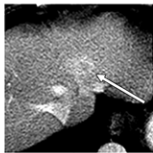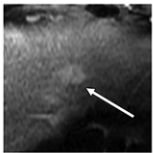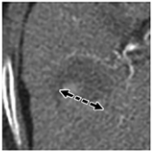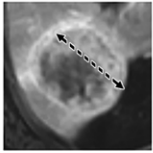| LR-Treatment Response Assessment Feature	Definition	Examples	
		CT	MRI
Treatment-specific expected enhancement	Expected temporal and spatial pattern of posttreatment enhancement attributable to treatment-related changes in parenchymal perfusion.		
No lesional enhancement	Absence of enhancement within or along the margin of a treated lesion. **Comment**: Complete disappearance after locoregional treatment is considered equivalent to absence of enhancement.		
Posttreatment Arterial phase hyperenhancement (APHE)	Nodular, masslike, or thick and irregular APHE contained within or along the margin of a treated lesion suggests posttreatment tumor viability. **Comment**: Subtraction imaging on MRI can help assess APHE posttreatment, if there are hyperintense areas on precontrast T1-W sequences.		
Posttreatment "washout"	Nodular, masslike, or thick and irregular washout appearance contained within or along the margin of a treated lesion suggests posttreatment tumor viability.		
Posttreatment enhancement similar to pretreatment	Nodular, masslike, or thick and irregular enhancement similar to pretreatment enhancement in all postcontrast phases contained within or along the margin of a treated lesion suggests posttreatment tumor viability, even in the absence of APHE or washout appearance.		
Size of equivocally, probably, or definitely viable tumor	Longest dimension through enhancing area of treated lesion, not traversing nonenhancing area		

Figure 9: Summary of CT and MRI treatment response Liver Imaging Reporting and Data System imaging features. APHE = arterial phase hyperenhancement T1-W = T1 weighted.

Interreader agreement on LI-RADS categories has been assessed in several studies (73–79). In a large international multireader study, interreader agreement was excellent (range, 0.84–0.87) for APHE and "washout" (73), and it was unaffected by modality or by readers' liver imaging expertise, prior familiarity with LI-RADS, or number of years of postresidency practice (73). Interreader agreement for "capsule" was excellent in one study (73) but not in the others (74–79). In studies focused on agreement for LI-RADS categories, interreader agreement was fair for contrast-enhanced US (κ = 0.3–0.39) (80,81), fair to substantial for MRI (κ = 0.35–0.61 [54,74,76,81,82], intraclass correlation coefficient = 0.73 [73]), and substantial for CT (κ = 0.79 [54], intraclass correlation coefficient = 0.67 [73]).

Recent studies show that the likelihood of an observation being an HCC in particular or a malignant neoplasm in general increases with higher ranked LI-RADS categories (Table) (2,40–42,44–53), enabling confirmation that LI-RADS can be used to stratify the probability of HCC and overall malignancy, as intended.

A detailed discussion on the advantages and disadvantages of contrast-enhanced US, CT, and MRI in the diagnosis of HCC is beyond the scope of this report. However, inherent differences in sensitivity and specificity of each modality in the detection of the major features exist, and these result in discordances between the final LI-RADS categories assigned with different modalities (46,54,75–77,81,83–85). Emerging literature indicates that intermodality agreement for LI-RADS category is fair (κ = 0.33–0.39) between CT and MRI and slight to fair between MRI and contrast-enhanced US (κ = 0.22) (54,81). CT has a tendency to result in undercategorization as compared with MRI (84,85).

Gaps and Future Directions

Although each version of LI-RADS has been informed by the best available evidence, there are insufficient high-quality data
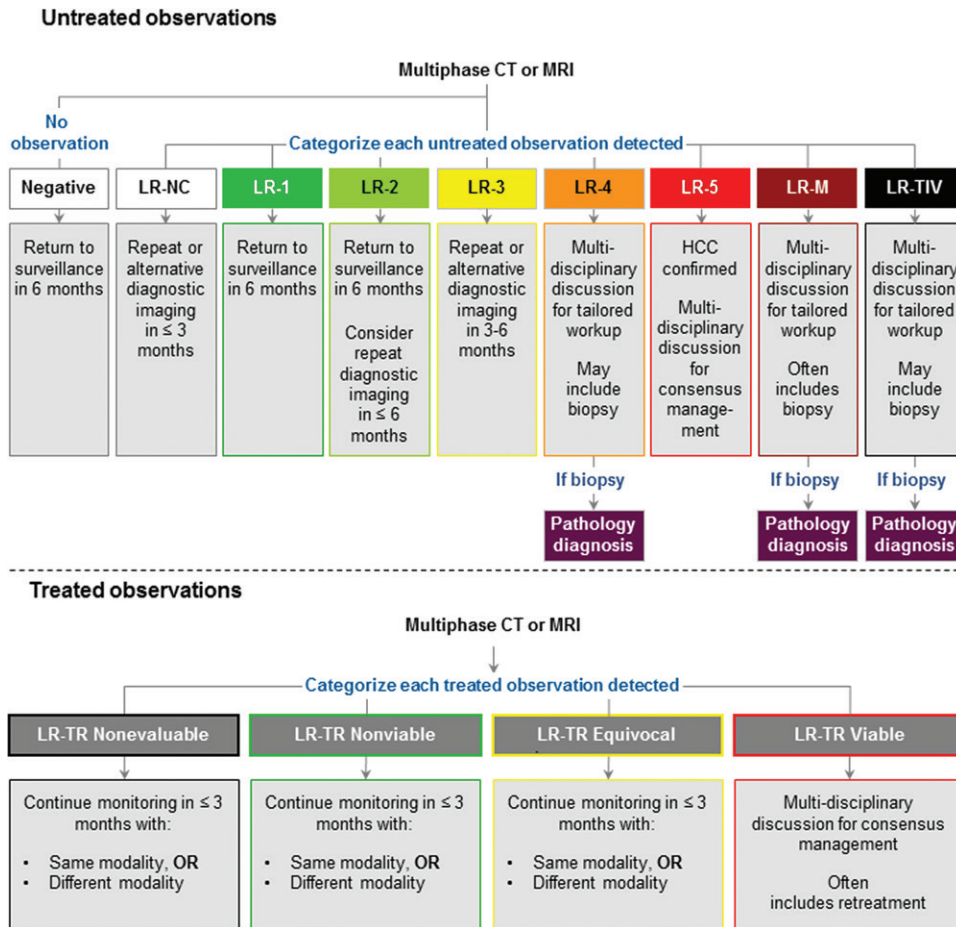

Figure 10: Summary of management recommendations for CT and MRI diagnostic and treatment response Liver Imaging Reporting and Data System categories.

Initial biopsy	• Lesion is suspicious for malignancy but not LR-5 (eg, LR-4 or LR-M) • Lesion meets imaging criteria for LR-5 but: ◦ Patient is not considered at high risk for HCC development (ie, not appropriate for using LI-RADS) ◦ Patient has elevated CA 19–9 or CEA or has another primary malignancy that can metastasize to liver ◦ Confirmation of HCC metastasis that could change clinical decision-making ◦ Histologic grading or molecular characterization is desired ◦ Clinical trial requirement
Repeat biopsy	• Prior nondiagnostic biopsy • Prior biopsy discordant with imaging, biomarkers, or other factors

Figure 11: Chart summarizes indicators for biopsy considerations. CEA = carcinoembryonic antigen, HCC = hepatocellular carcinoma, LI-RADS = Liver Imaging Reporting and Data System.

for many questions in HCC imaging. For example, the interrater reliability is controversial for "capsule" and poorly understood for ancillary features, causing the incremental benefit of these features for LI-RADS categorization to be debated among experts (74–79). Additionally, newer components of LI-RADS, including LI-RADS treatment response and LR-M diagnostic criteria, still require validation. Similarly, the US LI-RADS visualization

Hepatocellular Carcinoma and Overall Malignancy per LI-RADS Category

LI-RADS Category	HCC (%)	Overall Malignancy (%)
LR-1	0	0
LR-2	13 (8, 22)	14 (9, 21)
LR-3	38 (31, 45)	40 (31, 50)
LR-4	74 (67, 80)	80 (75, 85)
LR-5	94 (92, 96)	97 (95, 99)
LR-M	36 (26, 48)	93 (87, 97)

Note.—Adapted from reference 2. Data are based on meta-analysis of 15 published articles and two scientific abstracts using Liver Imaging Reporting and Data System (LI-RADS) version 2014 or LI-RADS version 2017. Data in parentheses are confidence intervals. There are no confidence intervals for the LR-1 estimates, since all studies reported 0% rates of hepatocellular carcinoma (HCC) and overall malignancy. Data from LI-RADS version 2018 are not yet available.

score was proposed based on expert opinion instead of on data demonstrating an association with surveillance failure. LI-RADS was developed for widespread use; therefore, it purposely avoids the requirements of state-of-the-art imaging technology, such as multiarterial phase MRI and spectral CT. As these cutting-edge technologies become mainstream, research will be needed to determine their effect on LI-RADS categorization and accuracy. Finally, and perhaps most importantly, studies are needed to define the optimal work-up strategy of indeterminate (LR-3) and suspicious (LR-4) observations. Although these lesions carry the risk of being or progressing to HCC, it is unclear how long they require monitoring with diagnostic imaging, if they should undergo biopsy, and whether patients can ever return to the original surveillance schedule. The LI-RADS Research and Development Working Group was formed to help identity, prioritize, and address these gaps to inform future improvements in LI-RADS. Additionally, by linking structured data elements with de-identified databases, the commercial reporting systems for LI-RADS now in development are expected to enable the creation of large multinational observational tumor registries, facilitate big data analytics, and thereby advance understanding of the natural history and outcomes of LI-RADS observations as detected and reported in real-world clinical practice.

Conclusion

By updating the criteria for small (10–19 mm) LR-5 observations and simplifying the definition for threshold growth, LI-RADS version 2018 achieved consistency with and integration into the AASLD 2018 HCC clinical practice guidance, a major milestone toward establishing a universal approach to the imaging diagnosis of HCC. Beyond diagnostic criteria, LI-RADS also provides algorithms for surveillance, treatment response, and contrast-enhanced US–based diagnosis. All LI-RADS algorithms are built on the foundation of standardized lexicon, technique, management, and reporting guidelines. Through education, international collaboration, and continual evaluation of existing and missing evidence, LI-RADS aims to unite and eventually achieve consensus among liver experts around the world on the best practices for caring for patients with or at risk for HCC.

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