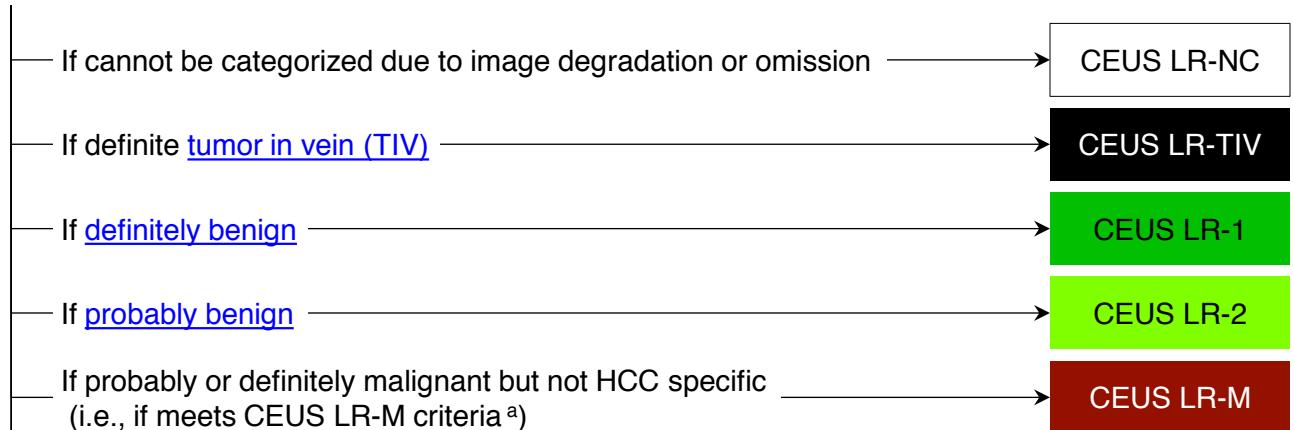




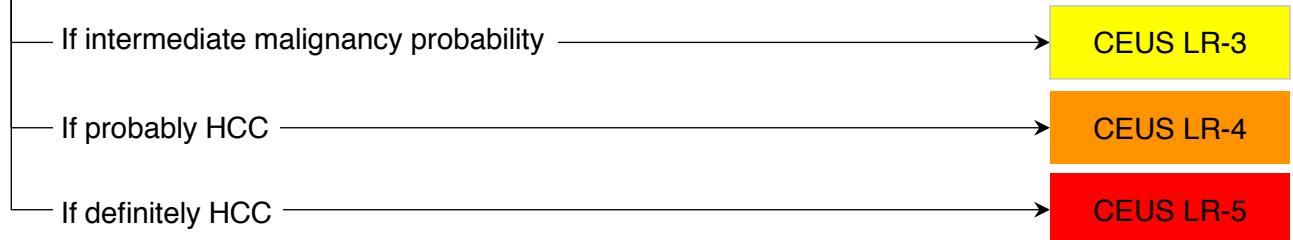
CEUS LI-RADS® v2017 CORE

(For CEUS with Pure Blood Pool Agents)

Untreated observation visible on precontrast US and without pathologic proof
in [patient at high risk for HCC](#)



Otherwise, use CEUS diagnostic table below



CEUS Diagnostic Table

Arterial phase hyperenhancement (APHE)	No APHE		APHE (not rim ^b , not peripheral discontinuous globular ^c)	
Nodule size (mm)	< 20	≥ 20	< 10	≥ 10
No washout of any type	CEUS LR-3	CEUS LR-3	CEUS LR-3	CEUS LR-4
Late and mild washout	CEUS LR-3	CEUS LR-4	CEUS LR-4	CEUS LR-5

- a. CEUS LR-M criteria – any of following:
- rim APHE **OR**
 - early (< 60 s) washout **OR**
 - marked washout
- b. rim APHE indicates CEUS LR-M
- c. peripheral discontinuous globular indicates hemangioma (CEUS LR-1)

If unsure about the presence of any major feature: characterize that feature as absent



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Other LI-RADS Documents: US LI-RADS, [CT/MRI LI-RADS](#), LI-RADS Downloads



What is CEUS?

Contrast-Enhanced Ultrasound (CEUS):

- Advanced form of ultrasound (US) in which images are acquired:
 - using intravenously injected microbubble contrast agents.
 - with technology optimized for visualizing those agents.
- Similar to CT and MRI, permits dynamic characterization of lesion and liver blood flow.
- Allows characterization with high temporal resolution of limited number of observations.
- Most suitable for problem solving.
- Not optimal for staging entire liver.
- Although it may be used with caution by expert practitioners in these contexts or for these purposes, it is not currently recommended by CEUS LI-RADS to:
 - characterize nodules occult on precontrast gray-scale images.
 - assess treatment response.

CEUS LI-RADS is being developed for precontrast occult nodules and for treatment response.

Key differences compared to CT and MRI are that CEUS:

- Permits real-time imaging, which:
 - Virtually eliminates possibility of arterial phase mistiming.
 - May allow detection of APHE missed on CT or MRI.
- Uses purely intravascular microbubble contrast agents, which affects washout and “capsule” characterization.
 - CEUS washout is true washout. Hence, CEUS uses the term washout, not the terms “washout” or washout appearance.
 - CEUS characterization of washout requires assessment of its onset (late vs. early) and degree (mild vs. marked), not just its presence. See [page 14](#) & [page 17](#).
 - CEUS does not depict “capsule” (see [page 24](#)); “capsule” is not a CEUS major feature.
- Is safer; microbubble agents have virtually no known adverse reactions.
- Allows multiple injections of microbubble contrast agents in same examination, permitting more complete characterization of the same observation and/or assessment of additional observations.
- Does not depict vascular pseudolesions such as arterioportal shunts, a frequent cause of diagnostic confusion on CT and MRI.
 - Any CEUS enhancing observation is a true lesion.
- Has fewer ancillary features (AFs). See [page 16](#).
- Permits characterization of limited number of targeted observations per examination; hence, not usually suitable for staging.
- Requires higher level of expertise for optimal performance.
- Is new in the United States, hence, not yet fully adopted or widely available.

Indications for CEUS in patients at risk for HCC:

- Assess nodules ≥ 10 mm detected on surveillance US.
- Assess LR-3, LR-4, and LR-M observations detected on prior CT or MRI.
- Detect APHE when mistiming is suspected as the reason for its absence on prior CT or MRI.
- Assess biopsied observations with inconclusive histology.
- Guide biopsy or treatment of observations difficult to visualize with precontrast US.
- Help select appropriate observation(s) or observation component(s) for biopsy.
- Monitor changes in enhancement pattern over time for selected CEUS LR-3 or CEUS LR-4 observations.
- Differentiate tumor in vein (“tumor thrombus”) from bland thrombus.



CEUS LI-RADS® 2017

Apply in patients at high risk for HCC, namely those with:



- Cirrhosis **OR**
- Chronic hepatitis B viral infection **OR**
- Current or prior HCC

Including adult liver transplant candidates and recipients posttransplant



Do not apply in patients:

- Without the above risk factors
- < 18 years old
- With cirrhosis due to congenital hepatic fibrosis
- With cirrhosis due to a vascular disorder such as hereditary hemorrhagic telangiectasia, Budd-Chiari syndrome, chronic portal vein occlusion, cardiac congestion, or diffuse nodular regenerative hyperplasia



Apply to observations:

- Visible at precontrast ultrasound



Do not assign CEUS LI-RADS categories for observations:

- That are path-proven malignancies **OR**
- That are path-proven benign lesions of non-hepatocellular origin such as hemangiomas

See [page 23](#) for guidance on reporting path-proven lesions.



Apply for CEUS exams performed with:

- Pure blood-pool agents such as Lumason® (in USA)/SonoVue® (outside USA) and Definity® (in USA, Canada)/ Luminyte® (outside USA, Canada)

See [page 8](#) for more information on CEUS agents.



Do not apply for CEUS exams performed with:

- Combined blood-pool and Kupffer-cell agents such as Sonazoid®
The current version of CEUS LI-RADS does not address use of Sonazoid®. Use of Sonazoid® will be addressed in the next version of CEUS LI-RADS.

See [page 8](#) for more information on CEUS agents.



CEUS LI-RADS® 2017 Categories

Diagnostic Categories

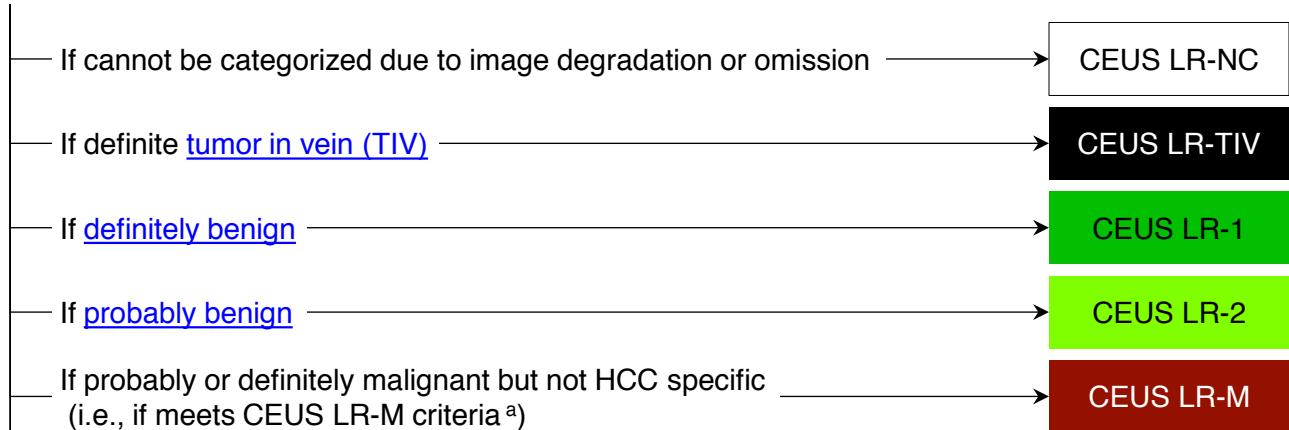
	CEUS LR-NC	Not categorizable (due to image degradation or omission)
	CEUS LR-1	Definitely benign
	CEUS LR-2	Probably benign
	CEUS LR-3	Intermediate probability of malignancy
Probably or definitely malignant, not necessarily HCC	CEUS LR-M	Probably HCC
	CEUS LR-4	
	CEUS LR-5	Definitely HCC
	CEUS LR-TIV	Tumor in vein

(Treatment response categories in development)

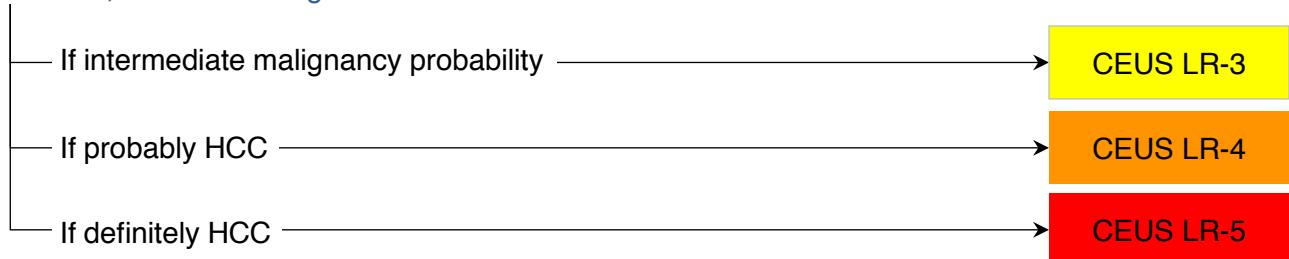


Step 1. Apply CEUS LI-RADS® Diagnostic Algorithm

Untreated observation visible on precontrast US and without pathologic proof in patient at high risk for HCC



Otherwise, use CEUS diagnostic table below



CEUS Diagnostic Table

Arterial phase hyperenhancement (APHE)	No APHE		APHE (not rim ^b , not peripheral discontinuous globular ^c)	
Nodule size (mm)	< 20	≥ 20	< 10	≥ 10
No washout of any type	CEUS LR-3	CEUS LR-3	CEUS LR-3	CEUS LR-4
Late and mild washout	CEUS LR-3	CEUS LR-4	CEUS LR-4	CEUS LR-5

- rim APHE **OR**

a. CEUS LR-M criteria – any of following:

- early (< 60 s) washout **OR**
- marked washout

b. Rim APHE indicates CEUS LR-M

c. Peripheral discontinuous globular indicates hemangioma (CEUS LR-1)

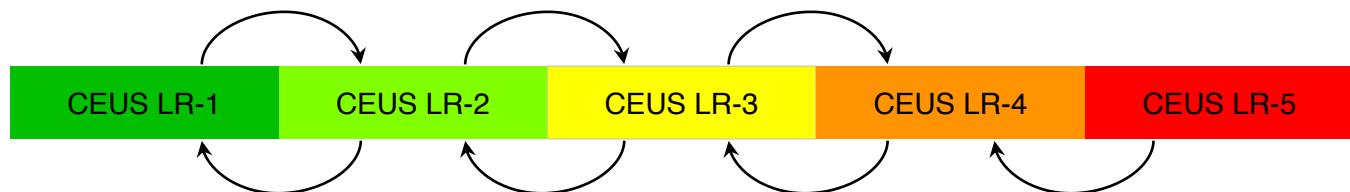
If unsure about the presence of any major feature: characterize that feature as absent

Step 2. Optional: Apply CEUS Ancillary Features (AFs)

CEUS ancillary features may be used at interpreter's discretion for:
Increased confidence or category adjustment

For category adjustment (upgrade or downgrade), apply CEUS ancillary features as follows:

One or more ancillary features favoring malignancy: upgrade by 1 category up to CEUS LR-4
(Absence of these ancillary features should not be used to downgrade)



One or more ancillary features favoring benignity: downgrade by 1 category
(Absence of these ancillary features should not be used to upgrade)

If there are conflicting AFs (i.e., one or more favoring malignancy and one or more favoring benignity):
Do not adjust category

Ancillary features cannot be used to upgrade to CEUS LR-5

CEUS AFs favoring malignancy

Favoring malignancy in general, not HCC in particular

- Definite growth

Favoring HCC in particular

- Nodule-in-nodule architecture
- Mosaic architecture

CEUS AFs favoring benignity

- Size stability ≥ 2 years
- Size reduction

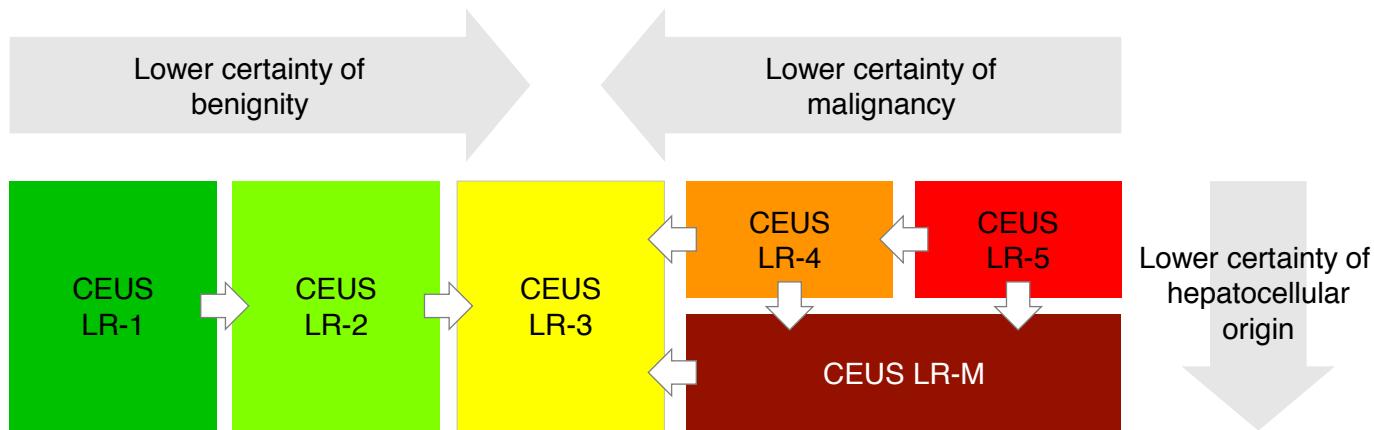
If unsure about presence of any ancillary feature: characterize that feature as absent

Step 3. Apply Tie-breaking Rules if Needed

If unsure about presence of TIV, do not categorize as CEUS LR-TIV



If unsure between two categories, choose the one reflecting lower certainty



Step 4. Final Check

After Steps 1, 2, and 3 –

Ask yourself if the assigned category seems reasonable and appropriate

If YES: You are done, move on the next observation (if any).

If NO: Assigned LI-RADS category may not be appropriate, so reevaluate.



CEUS LI-RADS® Technique: Considerations Before Performing a CEUS Exam

Obtain proper training

- Please see established guidelines from European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) Minimum Training Requirements for the Practice of Medical Ultrasound in Europe. [Appendix 14: Contrast enhanced ultrasound \(CEUS\).](#)

Become acquainted with CEUS technical terminology and concepts

Vascular phases and their typical timing

- Arterial phase (AP): usually occurs from about 10-20 s to 30-45 s after contrast injection.
- Portal venous phase (PVP): lasts from about 30-45 s to 2 min after contrast injection.
- Late phase (LP): lasts from end of PVP until there is unequivocal clearance of microbubbles from the circulation at about 4-6 min.

Continuous imaging – acquisition of images in real time, typically 10-20 frames/second. Provides real-time assessment of AP enhancement.

Intermittent imaging – a series of brief image acquisitions, each lasting a few seconds and spaced about 30 seconds apart without any imaging in between. Helps reduce bubble destruction during assessment of washout.

Recording – Saving cinematic loops and/or representative static images.

Reinjection – Microbubbles may be reinjected in the same exam to permit more complete characterization of the same observation and/or assessment of additional observations.

Become acquainted with CEUS dual-screen display and timing

Use dual-screen display to demonstrate B-mode and contrast-mode images side by side. Place electronic calipers on observation on B-mode screen, using scanner software to automatically place calipers at same position on contrast-mode screen. Simultaneous display of calipers on both screens facilitates characterization of APHE and washout. Also, use scanner timer to record time after contrast injection on all images (required for characterizing washout).

Become acquainted with US contrast agents available in your region

Agent	Generic name	Manufacturer	Distribution	Approved for liver use in
Lumason or SonoVue ^a	Sulfur hexafluoride lipid-type A microspheres	Bracco	Blood pool	Brazil, Canada, China, EU, Hong-Kong, Iceland, India, Japan, Norway, Russia, Singapore, South Korea, Switzerland, UK, USA.
Definity or Luminity ^b	Perflutren Lipid Microsphere	Lantheus	Blood pool	Australia, Brazil, Canada, India, Israel, Mexico, New Zealand.
Optison ^c	Perflutren protein-type A microspheres	GE	Blood pool	Only approved for cardiac application in EU, USA, Brazil.
Sonazoid ^d	Perflubutane	Daiichi-Sankyo/GE	Blood pool Kupffer cells	Japan, Denmark, Norway, South Korea.

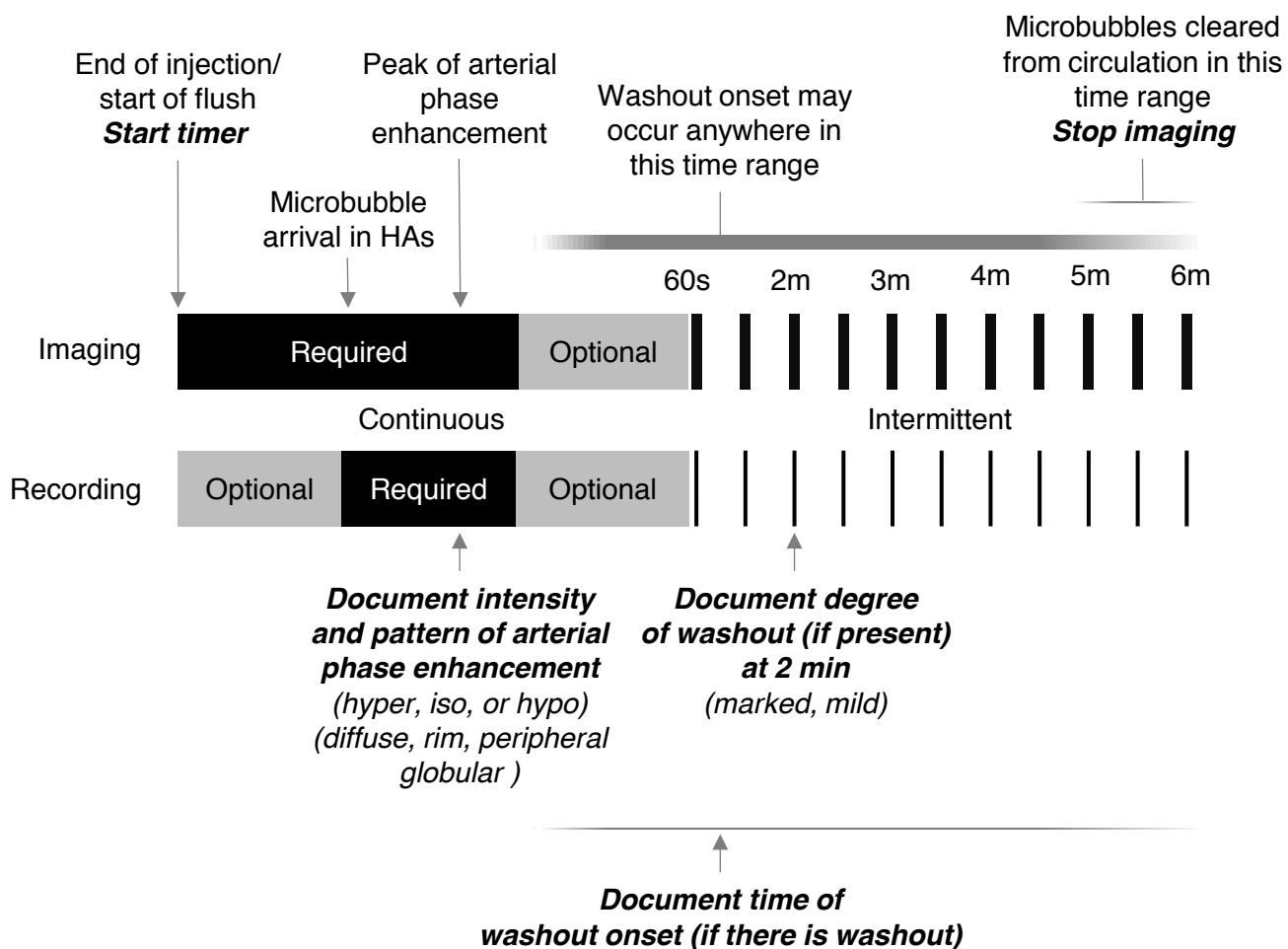
a. Lumason in USA, SonoVue outside USA; b. Definity in USA/Canada, Luminity outside USA/Canada; c. Evidence for using Optison in liver imaging is limited; d. Not addressed in current CEUS LI-RADS, to be addressed in next version.



CEUS LI-RADS® Technique: CEUS LI-RADS® Technical Recommendations

Required systems and modes	<ul style="list-style-type: none">• Ultrasound scanner with contrast-specific imaging capability, including dual-screen and timer display.• Refer to contrast-specific instructions provided by scanner manufacturer.
Contrast agents	<ul style="list-style-type: none">• Current version of CEUS LI-RADS applies to pure blood-pool agents but not to combined blood-pool/Kupffer cell agents such as Sonazoid®.• See page 8 for pure blood-pool agents available in your region.
Imaging – Recommended	<ul style="list-style-type: none">• Precontrast – identify the following:<ul style="list-style-type: none">• Target nodule(s).• Optimal patient position: supine, oblique, or left lateral decubitus.• Optimal scan plane: usually longitudinal (reduces out-of-plane resp. motion).• Optimal patient breathing: quiet or suspended (neutral, inspiration, expiration).• Arterial phase (AP):<ul style="list-style-type: none">• Image continuously from contrast injection until peak AP enhancement to capture peak AP enhancement, characterize APHE, and determine presence of early washout.• Portal venous phase (PVP) to late phase (LP):<ul style="list-style-type: none">• Image intermittently (every 30 s) to minimize microbubble destruction until microbubbles have cleared completely from the circulation (4-6 min) to detect late washout and assess its degree.
Imaging – Suggested	<ul style="list-style-type: none">• Sweep liver in PVP or LP to identify additional nodules. These may manifest as focal hypoenhancing observations in liver.
Recording – Recommended and optional	<ul style="list-style-type: none">• Record continuous cine loop from bubble arrival through peak APHE as a minimum requirement. Optionally the cine loop can be continued beyond the APHE peak until 60 seconds after injection.• Record static images at 60 seconds and with every intermittent (every ~30s) acquisition thereafter.
Imaging parameters	<ul style="list-style-type: none">• Use low (< 0.3) mechanical index (MI) to avoid microbubble destruction.• Use default machine settings.
Dual-screen imaging	<ul style="list-style-type: none">• Using B-mode image for guidance, place calipers on observation on both screens simultaneously to facilitate enhancement characterization.
Timing	<ul style="list-style-type: none">• Begin timer after end of contrast injection, at beginning of saline flush (i.e, time 0 coincides with beginning of flush).• Record time in seconds at which washout is first detected.
Injection technique	<ul style="list-style-type: none">• Use ≥ 20 G catheter.• Central venous lines and infusion ports are acceptable if safety and aseptic requirements are met.• Hand inject contrast over 2-3 seconds, maintaining constant syringe pressure.• Flush with 5-10 mL normal saline at about 2 ml/s.• Repeat injection as needed, per contrast manufacturer guidelines.• Do not exceed maximum total contrast dose listed in package insert.
Diameter measurement	<ul style="list-style-type: none">• Use B-mode (precontrast).• Use same imaging mode and plane as prior exam to assess growth.

CEUS LI-RADS® Technique: Schematic Illustration



Phases	Pre	Arterial	Portal Venous	Late
Start		10-20 s	30-45 s	120 s
End		30-45 s	120 s	4-6 min

Additional Injections (if needed)

- Use your judgment in determining whether additional injections are needed, based on the features (e.g., presence of APHE, onset of washout, degree of washout) that require additional characterization.
- Wait until near-complete clearance of the contrast agent (about 10 minutes) before next injection.
- Please refer to manufacturer's package insert for dose information.



CEUS LI-RADS®-Based Management: Suggested Imaging Workup Options & Time Intervals

Below are suggestions.

Interpreters are encouraged to use their judgment and tailor the recommendations to each patient.

CEUS LI-RADS category for untreated observations	Imaging Workup Options for Untreated Observations		
	Return to routine surveillance	Alternative diagnostic imaging (i.e., CT or MRI)	Repeat CEUS
CEUS LR-NC	—	* ≤ 3 mo	** ≤ 3 mo
CEUS LR-1	** 6 mo	—	—
CEUS LR-2	** 6 mo	—	* ≤ 6 mo
	—	** ≤ 6 mo	* ≤ 6 mo
CEUS LR-3	MDD may be needed for consensus management in selected cases. See page 22 for more information.		
CEUS LR-4	MDD may be needed for consensus management. If neither biopsy nor treatment is planned: repeat or alternative diagnostic imaging in ≤ 3 mo.		
CEUS LR-5	Diagnosis of HCC. MDD for consensus management.		
CEUS LR-M	MDD for consensus management. May include alternative or repeat imaging, biopsy, or treatment.		
CEUS LR-TIV	MDD for consensus management. May include biopsy or biomarker correlation to determine etiology of TIV: HCC, ICC, other.		
No observation detected on precontrast US	<p>Management depends on context:</p> <ul style="list-style-type: none">• CEUS is attempted because of positive screening or surveillance US exam: recommend return to routine surveillance.• CEUS is attempted to further characterize a CT/MRI LR-3, LR-4, or LR-M observation: recommend alternative imaging with CT or MRI.		

** Preferred option in most cases. * Reasonable alternative option. — Not recommended.

Multidisciplinary discussion (MDD) can be a formal meeting or an informal communication between the radiologist and other specialist(s). It may be pursued in parallel with any imaging workup option above, based on clinical context or at interpreter's discretion.



CEUS LI-RADS® v2017 Reporting: Considerations Before Issuing a CEUS LI-RADS® Report

Use your judgment and common sense

Tailor your recommendations to your patient.

- [Page 11](#) provides general guidance for imaging workup options, but note that optimal management may vary depending on the observation or patient.

Is any observation path-proven to your knowledge?

If an observation has been biopsied and there is no uncertainty about the path diagnosis (i.e., the path diagnosis is a malignant entity such as HCC or non-hepatocellular malignancy, or the path diagnosis is a non-hepatocellular benign entity such as hemangioma), then it is preferable to report the path diagnosis rather than the CEUS LI-RADS category.

If an observation has been biopsied but there is either uncertainty about the path diagnosis or the path diagnosis is a potential HCC precursor (i.e., regenerative or dysplastic nodule), it is preferable to report the CEUS LI-RADS category and the path diagnosis together. Rationale: reporting both may alert the referrer to possible false-negative biopsy results and/or to the need for close follow-up to detect progression to frank malignancy.

Is there tumor in vein?

If yes, report the likely etiology. Most CEUS LR-TIV observations are HCC but some may be ICC, H-ChC, or other non-HCC malignancies. See [page 15](#) for guidance on reporting CEUS LR-TIV.

Is your patient a liver transplant candidate?

Currently, OPTN does not recognize CEUS for HCC diagnosis. In the United States, liver transplant candidates with CEUS LR-5 observations need to undergo multiphasic CT or MRI to verify the LR-5 categorization and for staging. If CT or MRI does not verify LR-5 categorization for any CEUS LR-5 observation, consider discussion with and possible appeal to the regional review board.

Avoid language that compels biopsy or other invasive procedure

If consideration for liver biopsy is appropriate, the following phrases might be used:

- “Options for diagnostic workup include ____ and possibly biopsy.”
- “The distinction between HCC and ____ in this patient cannot be determined with imaging alone. If distinction would be helpful for patient management, biopsy may be considered.”
- “Biopsy may be necessary to distinguish between HCC and ____.”
- “...probably HCC. To establish a definite diagnosis, biopsy may be considered.”



CEUS LI-RADS® v2017 Reporting

Untreated observation	Reporting requirement	Recommended report content
CEUS LR-NC	Must be reported in Findings and Impression.	Provide causative technical limitations or artifacts, and work-up suggestions.
CEUS LR-1		
CEUS LR-2		
CEUS LR-3	Must be reported in Findings and Impression.	Provide major features, growth, and contributory ancillary features. Indicate relevant change since prior.
CEUS LR-4		
CEUS LR-5		
CEUS LR-M		
CEUS LR-TIV	Must be reported in Findings and Impression.	Indicate likely etiology (HCC, non-HCC, unsure); describe vessel(s) involved.
No observation on precontrast US	Should be reported in Impression.	"No observation on precontrast US. Therefore, CEUS not performed."

All reported observations should include

- **Identifier:** sequential number or other unique identifier, keep fixed on all exams.
- **AP enhancement features:** qualitative description as not rim (diffuse or partial), rim, or peripheral discontinuous globular.
- **Onset of washout if present:** time in seconds at which washout is first detected.
- **Degree of washout if present:** qualitatively characterized as mild or marked.

See [page 17](#) & [page 24](#) for more information on washout characterization.

Note: if observation is a path-proven malignancy or is a benign lesion of non-hepatocellular origin, report pathology diagnosis rather than the LI-RADS category. See [page 23](#).

Treated observations

- CEUS LI-RADS® v2017 does not address treatment response assessment.
- Treatment response assessment will be addressed in the next version of CEUS LI-RADS®.



CEUS LI-RADS® Major Imaging Features

APHE
(not rim or 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.
Generally diffuse, although may be partial. Contrast with **rim APHE** (CEUS LR-M criteria).



See diagnostic table, [page 5](#).

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. Can apply to any enhancing observation even in absence of APHE.



- Early (< 60 s) and/or marked washout: Major feature for LR-M; see below
- Late (≥ 60 s) and mild washout: Major feature for HCC

See diagnostic table, [page 5](#).

See [page 17](#) for more information on characterizing washout.

CEUS LI-RADS® LR-M Criteria

Rim APHE



Spatially defined subtype of APHE in which arterial phase enhancement is most pronounced in observation periphery.

Early (< 60 s)
washout



Temporally defined subtype of washout in which onset is within 60 seconds from contrast injection. Usually marked in degree (see below).

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.

See [page 17](#) for more information on characterizing washout.

CEUS LI-RADS® Tumor in Vein

Tumor in vein



Unequivocal enhancing soft tissue in vein, regardless of visualization of a parenchymal mass

Differentiation from bland thrombus

The arrival time of microbubble contrast agent to the vein helps to differentiate tumor in vein vs. partially occlusive/recanalized bland thrombus:

- Early arrival (~ same time as hepatic artery opacification): favors tumor in vein.
- Arrival several (~10) seconds after hepatic artery opacification: favors portal flow in patent portion of non-occlusive/recanalized bland thrombus.

Categorization:

Categorize as CEUS LR-TIV.

Reporting:

Indicate in report most likely etiology.

See below for guidance:

CEUS LR-TIV

- If contiguous with CEUS LR-5 → “Definitely due to HCC”
- If contiguous with CEUS LR-4 → “Probably due to HCC”
- If associated with infiltrative mass → “Probably due to HCC”
- If contiguous with CEUS LR-M → “May be due to non-HCC malignancy”
- Otherwise → “Etiology uncertain”

CEUS LI-RADS® Ancillary Imaging Features

Favoring malignancy in general, not HCC in particular



Definite growth

Unequivocal spontaneous increase in observation size.

Note: CEUS does not include “threshold growth” as a major feature. Instead, “definite growth” is an ancillary feature favoring malignancy.

Favoring HCC in particular



Nodule-in-nodule architecture

Presence of smaller inner nodule within and having different imaging features than larger outer nodule. In cirrhosis, suggests HCC.



Mosaic architecture

Presence of randomly distributed internal nodules or compartments, usually with different imaging features.

Favoring benignity

Size stability \geq 2 years

No significant change in observation size measured on exams \geq 2 years apart in absence of treatment.

Size reduction

Unequivocal spontaneous decrease in size over time, not attributable to artifact, measurement error, technique differences, or blood product resorption.



CEUS LI-RADS® – Characterizing Washout

At CEUS, all malignant nodules typically show washout, including intrahepatic cholangiocarcinoma (ICC) and other fibrotic tumors that have delayed central enhancement on CT or MRI.

Explanation: When using pure blood pool contrast agents (e.g., microbubbles), washout reflects the blood volume of lesion relative to liver. Since all malignant lesions have lower blood volume than liver, all appear to wash out. In fact, although the exact mechanism is not yet understood, ICCs and other non-HCC malignancies typically wash out earlier and more completely than HCCs.

Implication: To maintain specificity for HCC, CEUS characterization of washout requires assessment of its “onset” and “degree”, not just its presence.

		Washout Onset ^a	
		Early (< 60 s)	Late (≥ 60 s)
Washout Degree ^b	Marked	Typical of ICC and metastases	Suggests malignancy in general, not specific for any particular type
	Mild	Suggests malignancy in general, not specific for any particular type	Typical of HCC and HCC precursor nodules

a. Onset: time after injection (in seconds) at which WO is first detected relative to liver:

- Early: onset detected < 60 s after contrast injection.
- Late: onset detected ≥ 60 s after contrast injection.

b. Degree: degree of WO, assessed by comparing nodule to liver enhancement in PVP and LP:

- Marked: nodule virtually devoid of enhancement (“punched-out”) by 2 min after contrast injection.
- Mild: nodule less enhanced than liver, but not devoid of enhancement (i.e., some enhancement persists). If this persistent enhancement disappears after 2 minutes, the degree of WO is still considered mild, even if the nodule eventually becomes “punched-out”. See FAQ [page 24](#).

Effect on categorization: Nodules with late and mild washout may be categorized as CEUS LR-3, LR-4, or LR-5. Nodules with early or marked washout should be categorized LR-M.

		No APHE		APHE (not rim, not peripheral discontinuous globular)	
Nodule size (mm)		< 20	≥ 20	< 10	≥ 10
No washout of any type		CEUS LR-3	CEUS LR-3	CEUS LR-3	CEUS LR-4
Late and mild WO		CEUS LR-3	CEUS LR-4	CEUS LR-4	CEUS LR-5
Early and/or marked WO		CEUS LR-M	CEUS LR-M	CEUS LR-M	CEUS LR-M



Examples of CEUS LR-1 and criteria for LR-2 Entities

Examples and criteria:

- Cyst
 - Anechoic lesion with increased posterior acoustic through transmission showing no contrast enhancement in any phase.
- Hemangioma
 - Variable echogenicity lesion with peripheral discontinuous globular enhancement in arterial phase followed by progressive centripetal contrast filling and iso- or hyperenhancement in portal venous and late phase.
 - The filling may be complete or partial depending on lesion size.
- Hepatic fat deposition/sparing
 - Nonmasslike, nonspherical, hyper/hypoechoic area of parenchyma in a characteristic location for fat deposition/sparing and with isoenhancement in all phases.
 - Characteristic areas include around the gallbladder fossa and anterior to the right portal vein in segment 4.
 - If the hyper/hypoechoic area is not in a characteristic location for fat deposition/sparing, categorize as CEUS LR-2 (see below).
 - See CEUS LI-RADS manual (pending) for more information.

CEUS LR-1

Criteria:

- Distinct isoenhancing solid nodule < 10 mm
 - If isoenhancing nodule is ≥ 10 mm, categorize as CEUS LR-3. See CEUS LI-RADS diagnostic algorithm ([page 5](#)).
- Nonmasslike isoenhancing observation of any size, not typical hepatic fat deposition/sparing.
 - If the observation represents focal deposition/sparing, categorize as CEUS LR-1 (see above).
- CEUS LR-3 nodules with interval size stability for ≥ 2 years

CEUS LR-2

Explanation: nodules meeting these criteria are probably regenerative or low-grade dysplastic nodules.



Caution: The CEUS enhancement features for HCC, FNH, and HCA overlap. Therefore, in patients at risk for HCC in whom application of CEUS LI-RADS is appropriate, nodules with CEUS features suggestive of FNH or HCA should be categorized conservatively. In general, they should NOT be categorized CEUS LR-1 or CEUS LR-2.



Getting Started

What is a CEUS LI-RADS observation? How does it differ from a CT/MRI observation?

An observation is a distinctive area compared to background liver at imaging. In CT and MRI, it may be a lesion or pseudolesion such as an arterioportal shunt. Unlike in CT or MRI, vascular pseudolesions are rare in CEUS. Thus, almost all CEUS observations are true lesions.

I am not sure if my patient has cirrhosis. Can I apply CEUS LI-RADS?

You can apply CEUS LI-RADS and provide a conditional category. For example: "25 mm mass with APHE and washout. If the patient has cirrhosis or chronic hepatitis B, this meets criteria for CEUS LR-5 (definitely HCC)." If available, you can add elastography to the ultrasound exam to evaluate liver stiffness (or shear wave speed). If the elastographic measurement exceeds a validated threshold for cirrhosis using your scanner, you may provide a provisional CEUS LI-RADS category, making sure to comment that this assumes a diagnosis of cirrhosis as suggested by "ultrasound elastography stiffness of [XX] kPa (or shear wave speed of [XX] m/s)".

I do not see a lesion on precontrast US, can I do CEUS?

CEUS LI-RADS v2017 applies only to observations visible on precontrast US. Although CEUS LI-RADS does not yet address CEUS of nodules occult on precontrast US, expert CEUS practitioners may use anatomic landmarks to co-localize and assess CT- or MRI-detected observations.

Can CEUS LI-RADS be used in transplant candidates?

CEUS LI-RADS can be used in transplant candidates if indicated clinically. Since UNOS does not officially recognize CEUS, however, a patient with a CEUS LR-5 observation needs multiphasic CT/MRI for diagnosis verification and staging prior to receiving HCC exception points.

I have seen other systems called CEUS LI-RADS. Which is the official version?

ACR CEUS LI-RADS® is the official CEUS system endorsed by the ACR. It was developed by an international working group of experts, received critical feedback from and was approved by the ACR LI-RADS Steering Committee, and is included in the ACR LI-RADS Manual along with companion US and CT/MRI systems. Other schemes called "CEUS LI-RADS" are not ACR endorsed, Steering Committee approved, or included in the ACR LI-RADS Manual.

Why does LI-RADS not apply to patients without risk factors, to patients < 18 years old, or to patients with cirrhosis due to congenital hepatic fibrosis?

Why does LI-RADS not apply to patients with cirrhosis due to a vascular disorder such as hereditary hemorrhagic telangiectasia, Budd-Chiari syndrome, chronic portal vein occlusion, cardiac congestion, or diffuse nodular regenerative hyperplasia?

Why shouldn't I assign a LI-RADS category for path-proven malignancies and for path-proven benign lesions of non-hepatocellular origin?

Should I assign a LI-RADS category to path-proven benign lesions of hepatocellular origin (e.g., regenerative or dysplastic nodules)?

See
[CT/MRI LI-RADS Core](#)



Diagnosis

How does CEUS LI-RADS differ from CT/MR LI-RADS?

Key differences between CEUS and CT/MRI LI-RADS are summarized below:

	CEUS LI-RADS v2017	CT/MRI LI-RADS v2017
Operator expertise	High expertise required	High expertise not required
Observation visibility	Precontrast visibility required	Precontrast visibility not required
Number of observations	One to few	One to many
Context	Diagnosis	Diagnosis, staging, Rx response
Type of contrast agent	Blood pool	ECA or HBA
Permitted contrast injections	One to multiple (if needed)	Usually one
Size thresholds for APHE	< 10 mm, ≥ 10 mm	< 10 mm, 10-19 mm, ≥ 20 mm
APHE	High temporal resolution	Single or few time points
Washout phenomenon	Washout is true washout	Washout may be apparent, not true
Washout characterization	Onset and degree are critical	Onset and degree not critical
“Capsule”: type of feature	Not a CEUS feature	Major feature
Growth: type of feature	Ancillary feature	Major feature (if exceeds threshold)
Number of ancillary features	Few	Many

Why does intrahepatic cholangiocarcinoma (ICC) show early marked washout on CEUS but delayed central enhancement on CT/MRI?

CEUS microbubbles are too large to pass through vascular endothelial fenestrations. Instead, they remain confined to the blood space or blood pool (hence, “blood space agents” or “blood pool agents”) and their postarterial phase distribution reflects regional blood volume. Since ICCs have low blood volume, they show early and marked postarterial phase washout after administration of these agents – earlier and more marked, in fact, than most HCCs. By comparison, the low-molecular-weight (LMW) agents used in CT and MRI pass through endothelial fenestrations easily, extravasate into the interstitium, and accumulate progressively in the centrally located fibrous stroma of these tumors. This produces the characteristic delayed central enhancement of ICCs at CT or MRI.

Why do HCCs typically show washout on CEUS and on CT/MRI?

Washout is a poorly understood phenomenon. See Manual (pending). A partial explanation: since most HCCs have lower blood volume and lower extracellular volume than liver, they generally exhibit washout with blood-pool agents and with LMW extracellular space agents.

Why is LR-M termed “probably or definitely malignant”?

Since rare benign entities (e.g., inflammatory pseudotumor, sclerosed hemangioma, abscess) may show LR-M features (e.g., rim APHE) on all dynamic imaging modalities (CEUS, CT, MR), “probably or definitely malignant” is more appropriate than “definitely malignant.”

Is there a size threshold for CEUS LR-M?

No. Although CEUS is usually performed to assess nodules ≥ 10 mm detected on surveillance US, smaller nodules with CEUS LR-M features may be identified during CEUS and should be categorized LR-M.

Why are arterioportal shunts (APS) not visible on CEUS?

One plausible explanation is that the microscopic shunts are too small to be depicted by CEUS, whereas CT and MRI detect the extravasation of contrast material into the regional interstitium. Regardless of the mechanism, the insensitivity of CEUS to perfusion alterations is an advantage because these can cause diagnostic confusion.

Why do the tie-breaking rules choose lower certainty?

See [CT/MRI LI-RADS Core](#)



Technique

I have not started using CEUS, how can I get started?

Please see the CEUS Manual for details.

Also, please check the following websites, which have excellent educational materials and/or links to educational programs and activities:

- EFSUMB website: <http://www.efsumb.org/guidelines/guidelines-ceus.asp>
- EFSUMB guideline: <https://www.thieme-connect.de/products/ejournals/pdf/10.1055/s-0032-1325499.pdf>
- ICUS website: <http://www.icus-society.org>
- SonoWorld: <https://sonoworld.com/LectureDetails/Contrast-Enhanced Ultrasound The Nuts and Bolts.aspx?Id=2243&Sequence=1>
- Contact [CEUS LI-RADS WG](#) if you have further questions after reading the Manual and reviewing the suggested websites.

What syringe size should I use for injection?

For Definity: use a 1mL syringe.

For Lumason/SonoVue: use the supplied 5mL syringe.

How should I inject contrast?

Contrast should be injected manually over 2-3 seconds, maintaining steady hand pressure to prevent excess bubble destruction during delivery. The contrast bolus should be followed immediately by a 5-10 mL normal saline flush delivered at approximately 2 mL/sec.

How should I measure observation size?

Step 1 Acquire images in the appropriate plane – i.e., along the observation's longest axis. If CEUS is performed for follow up of a previously detected observation, replicate the prior imaging plane using anatomic landmarks (e.g., portal and hepatic veins, gallbladder, falciform ligament) for orientation.

Step 2 Measure the observation's outer-to-outer edge dimension along its longest axis, using precontrast B-mode images if possible. 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. To evaluate size change between exams, select images on each exam acquired in the same plane and temporal phase.

EFSUMB = European Federation of Societies for Ultrasound in Medicine and Biology

ICUS = International Contrast Ultrasound Society



Management

CEUS LI-RADS suggests alternative diagnostic imaging (i.e., CT or MRI) in ≤ 6 months if there is no observation on precontrast US. Can you explain the rationale?

One indication for CEUS is to assess LR-3, LR-4, and LR-M observations detected on prior CT or MRI. If CEUS is requested for this purpose but there is no observation on precontrast US, then LI-RADS recommends multiphase CT or MRI, rather than attempting CEUS. As mentioned on [page 2](#), expert practitioners may attempt CEUS if there is no observation on precontrast US, but this is not currently recommended by CEUS LI-RADS. We anticipate that CEUS LI-RADS will be expanded to include assessment of precontrast occult nodules. If alternative imaging is pursued, interpreters should use their judgment in recommending the appropriate modality (CT or MRI), contrast agent (extracellular or hepatobiliary), and time interval.

The suggested management differs for CT/MRI LR-3 and CEUS LR-3. Why the difference?

As explained in the CT/MRI manual, the suggested management for CT/MRI LR-3 is alternative or repeat diagnostic imaging in 3-6 months. By comparison, the suggested management for CEUS LR-3 is alternative or repeat diagnostic imaging in ≤ 6 months, with consideration for multidisciplinary discussion (MDD). See [page 11](#). The reason for emphasizing MDD for CEUS LR-3 is that the probability of HCC is thought to be greater for CEUS LR-3 than for CT/MRI LR-3:

- Two recent studies^{1,2} showed that most LR-3 observations detected at CT or MRI are benign or indolent lesions that can be followed safely without requiring MDD in all cases.
- Less is known about the natural history of CEUS LR-3 observations, but preliminary evidence suggests that such observations warrant closer scrutiny. By definition, all CEUS observations are distinctive nodules in a cirrhotic liver visible on precontrast B-mode images, and thus have high probability of being HCC, unless contrast enhancement features are diagnostic of a benign entity such as a hemangioma. A recent retrospective study³ found that 60% (45/75) of CEUS LR-3 observations were HCC (see below). Therefore, MDD should be considered for all CEUS LR-3 observations with deliberation of reasonable diagnostic options, which may include alternative imaging in less than 3 months or biopsy.

What is the probability of HCC for each CEUS category?

In a retrospective study³, Terzi et al. retrospectively reviewed a total of 350 consecutive CEUS-detected nodules in cirrhotic patients. Using CT/MRI (if appropriate) and/or nodule biopsy with histopathology evaluation as the reference, these authors reported the following probabilities associated with each CEUS category:

- CEUS LR-M: 6/15 (40%) HCC, 2/15 (13%) H-ChC, 7/15 (47%) ICC
- CEUS LR-5: 149/152 (98%) HCC, 1/152 (1%) H-ChC
- CEUS LR-4: 90/102 (88%) HCC
- CEUS LR-3: 45/75 (60%) HCC

References

1. J-Y Choi et al. Indeterminate observations (Liver Imaging Reporting and Data System Category 3) on MRI in the cirrhotic liver: fate and clinical implications. AJR 2013. PMID 24147469
2. M Tanabe et al. Imaging outcomes of Liver Imaging Reporting and Data System Version 2014 Category 2, 3, and 4 observations detected at CT and MR Imaging. Radiology 2016. PMID 27115054
3. E Terzi, L. De Bonis, S. Leoni, et al. Dig Liv Dis, 2017; 49, Suppl 1, e22



Reporting

Why does CEUS LI-RADS require reporting of each observation individually while CT/MRI LI-RADS allows aggregate reporting in some circumstances?

A primary goal of LI-RADS is to facilitate clear and simple communication between radiologists, other specialists, and patients. CT and MRI sometimes detect so many observations and with such a broad range of clinical relevance that reporting all observations individually may clutter the report with unnecessary detail and obscure the main message. To communicate simply and clearly, radiologists are given the discretion to report CT and MRI observations in aggregate. By comparison, CEUS is a focused exam that evaluates a limited number of specifically targeted observations. Since only a limited number of specifically targeted observations are evaluated, each observation should be reported individually.

How do I categorize and report a treated lesion?

If you encounter a treated lesion during CEUS, describe any suspicious areas of enhancement or washout in or along the treatment area, including their size(s), as well their change since prior. If appropriate, include your confidence level and suggestions for further management. For example,

- “12 mm nodular area along the treatment margin with arterial phase hyperenhancement and washout, highly suggestive of viable tumor.” **OR**
- “Thick rim of slowly progressive enhancement along the treatment margin without washout. This may represent benign posttreatment change or ischemic tumor. In my opinion, this is equivocal for viability. Consider MDD for individualized workup and management.”

Since CEUS LI-RADS treatment response criteria are not yet available, do not assign a formal CEUS LI-RADS treatment response category and consider further evaluation with CT or MRI when a treated lesion is encountered.

What should I report if an observation is biopsied and has a path-proven diagnosis?

This depends on the pathology diagnosis:

- If malignant or if benign of non-hepatocellular origin (e.g., hemangioma): report observation’s pathology diagnosis, clinically relevant imaging features, and change since prior.
- If benign of hepatocellular origin (e.g., regenerative or dysplastic nodule): report observation’s CEUS LI-RADS category and path diagnosis, imaging features, and change since prior. Also specify the date of pathology acquisition as the lesion may have changed over time, especially if the biopsy-imaging time interval is long.

What should I do if the path diagnosis of a biopsied observation is discordant with the CEUS LI-RADS category?

Indicate in your report there is discordance, providing the CEUS LI-RADS category and the path diagnosis. Specify the date of pathology acquisition as the lesion may have changed over time. Explain briefly why you believe this represents a discordance. Consider multidisciplinary discussion with consensus review of the histology, imaging, and other clinical data to adjudicate the discordance.

Where do I find report templates to use in my practice and examples of CEUS LI-RADS reports?

These can be downloaded (pending).

Imaging Features

Is washout on CEUS true washout?

Quantitative time-intensity curve measurements show that the appearance of washout on CEUS reflects true washout^{1,2}. On CT/MRI, the appearance of washout may reflect increased enhancement of surrounding parenchyma, rather than true decline in tumor enhancement, hence “washout”.

The lesion shows mild washout initially and then washes out completely to look black. Is it mild or marked?

This depends on the time after contrast injection at which the washout becomes marked. If the washout becomes marked at or before 2 minutes, characterize as marked. If the washout becomes marked only after 2 minutes, characterize as mild. If unsure, characterize as marked (to prevent false CEUS LR-5 categorization for non-HCC malignancies with borderline marked washout).

How much growth is “unequivocal growth”?

There is no “threshold” for determining unequivocal growth on CEUS. This is up to the interpreter. As a general rule, more than 5 mm is unequivocal.

Does washout apply only to observations with APHE?

No. Washout applies to isoenhancing observations in addition to observations with APHE. For example, both of the following nodules should be characterized as having washout:

- Arterial phase isoenhancement followed by late-phase hypoenhancement.
- Arterial phase hypoenhancement followed by isoenhancement followed by hypoenhancement

Washout does NOT apply to nodules that remain hypoenhancing in all phases.

See Manual/time-intensity curves (pending).

Is there peripheral washout on CEUS?

No. A CT/MRI feature of intrahepatic mass-forming cholangiocarcinomas and other non-HCC malignancies, peripheral washout is characterized by a concentric tumoral architecture (i.e., an arterialized, cellular rim and a fibrotic, watery center). The extracellular and hepatobiliary agents used in CT and MRI drain rapidly from the arterialized, cellular rim, manifesting as peripheral washout appearance. As they drain from the tumor periphery, the agents gradually accumulate in the expanded interstitial spaces of the tumor center, causing progressive/delayed central enhancement, which accentuates the conspicuity of the peripheral washout.

CEUS agents are purely intravascular contrast agents (i.e., they do not enter the interstitial compartment). They drain rapidly from all tumor components with low blood volume, including the arterialized cellular rim and the fibrotic, watery center. Hence, they yield an early-onset, marked washout throughout the tumor, not a pattern of central retention and peripheral washout.

Why is enhancing “capsule” not a CEUS major feature of HCC?

As pure intravascular agents, CEUS microbubbles do not leak into the large interstitial spaces of the tumor “capsule” and the tumor “capsule” tends to be isoechoic to surrounding liver on late-phase CEUS images. By comparison, the low-molecular-weight agents used in CT and MRI leak readily into the “capsule” interstitium, causing the characteristic enhancing capsule appearance of many progressed HCCs in the postarterial phases.

References

1. Pei XQ et al. Contrast-enhanced ultrasonography of hepatocellular carcinoma: correlation between quantitative parameters and histological grading. BJR 2012. PMCID: PMC3608056
2. Pei XQ et al. Quantitative analysis of contrast-enhanced ultrasonography: differentiating focal nodular hyperplasia from hepatocellular carcinoma. BJR 2013. PMCID: PMC3487094



Abbreviations

ACR	American College of Radiology
AF	Ancillary features
AP	Arterial phase
APHE	Arterial phase hyperenhancement
APS	Arterioportal shunt
CEUS	Contrast-enhanced ultrasound
CT	Computed Tomography
ECA	Extracellular agent
EFSUMB	European Federation of Societies for Ultrasound in Medicine and Biology
FNH	Focal nodular hyperplasia
HBA	Hepatobiliary agent
HCA	Hepatocellular adenoma
H-ChC	Hepatocholangiocarcinoma
ICC	Intrahepatic cholangiocarcinoma
HCC	Hepatocellular carcinoma
ICUS	International Contrast Ultrasound Society
LI-RADS	Liver Imaging Reporting And Data System
LMW	Low molecular weight
LP	Late Phase
MDD	Multidisciplinary discussion
MI	Mechanical index
MRI	Magnetic Resonance Imaging
PVP	Portal venous phase
TIV	Tumor in vein
UNOS	United Network for Organ Sharing
US	Ultrasound

In Memoriam
David Cosgrove
1938-2017

