Contrast Enhanced Ultrasound Liver Reporting and Data Collection System (CEUS LI-RADS) v2017 in Multimodality Interpretation: Differences from CT/MR LI-RADS and Successful Resolution in Discordant Cases

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Learning Objectives

01 Learning Objectives

- Familiarize with CEUS LI-RADS v2017 algorithm
- Review advantages unique to CEUS in characterizing focal liver lesions in high risk group for hepatocellular carcinoma (HCC)
- Compare enhancement behaviors of each modality of CEUS, CT and MRI
- Clarify how to interpret and correlate appropriately when the categories are discordant between imaging modalities
- Understand when and where to integrate CEUS in the multimodality diagnostic algorithm of HCC



Background

02 CEUS LI-RADS v2017: Categories



LR-M is developed to prevent a misdiagnosis of nonhepatocellular malignancy (mostly intrahepatic cholangiocarcinoma or hepatocholangiocarcinoma) as HCC on imaging. Biopsy is usually required for LR-M nodules to exclude non-HCC malignancy.

- CEUS LI-RADS was recently developed in 2017 by American College of Radiology (ACR) to improve diagnostic algorithm of HCC by inclusion of CEUS into the standardized reporting and data collecting system.
- CEUS LI-RADS assigns category for probability of HCC for patients at risk for HCC, therefore guiding further management.

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O2 Timing and Degree of Washout is Key in CEUS LI-RADS LR-M Category

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

- On CEUS, Marked washout before 60 s following contrast suggests non-hepatocellular maglignancy. Mild washout after 60 s following contrast is typical of HCC.
- The timing and degree of washout is integrated into the CEUS LI-RADS algorithm, given their significance for differentiation of LR-M category. It is not part of CT/MR LI-RADS.

02 Diagnostic Algorithm of LI-RADS: CEUS vs CT/MR

CEUS

Arterial phase hyperenhancement (APHE)	No A	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		
Late and mild washout *Lesions with marked or early wa	CEUS LR-3	CEUS LR-4	CEUS LR-4	CEUS LR-5		

CT/MR	Arterial phase hyperenhancement (APHE)		No APHE		APHE (not rim)		
	Observation size (mm)		< 20	≥ 20	< 10	10-19	≥ 20
	Count major features:	None	LR-3	LR-3	LR-3	LR-3	LR-4
 "Washout" (not peripheral) Enhancing "capsule" Threshold growth 	 "Washout" (not peripheral) Enhancing "capsule" 	One	LR-3	LR-4	LR-4	LR-4 LR-5	LR-5
	≥Two	LR-4	LR-4	LR-4	LR-5	LR-5	

https://www.acr.org/Quality-Safety/Resources/LIRADS/LIRADS-v2017

02 Unique Advantages of CEUS over CT and MRI

Nature of CEUS	Advantage of CEUS over CT/MRI	Common Clinical Indications
Real-time imaging	Depicts enhancement pattern regardless of rapidity	 Metastasis vs benign small indeterminate lesion Hypervascular mets vs focal nodular hyperplasia (FNH) vs hemangioma
Purely intravascular contrast	No leakage of contrast out of the vasculature; better characterization of washout of malignancy	Benign vs malignancyHCC vs non-HCC malignancy
Extremely sensitive to contrast	Inherent superior sensitivity of CEUS to microbubbles compared to CT/MR to their contrast agents	 Neoplastic vs non neoplastic cysts Mass characterization & detection of recurrence
Disruption- replenishment technique	Microbubbles quickly cleared and replenished, enabling repetitive demonstration of arterial filling pattern and quantification of perfusion	 FNH vs adenoma vs HCC
No renal toxicity	Safe to use in patient with renal impairment Liu XY, Jang	 Patient with renal failure HJ, Khalili K, Atri M, Kim TK. RadioGraphics 2018 (in pres

02 Real-Time Contrast Enhancement Profiles of Common Liver Lesions



- The real-time nature of CEUS allows for more accurate assessment of arterial enhancement than CT or MR, which have set scanned time points.
- Examples of indeterminate hypo- or hyperattenuating appearance at pre-determined scanned time points (yellow box) on CT or MR.
- Each green box detailed early AP or very late vascular pattern that can be depicted on real-time CEUS with high temporal resolution, leading to a specific diagnosis.

AP: arterial phase. PVP: portal venous phase. Extended P: extended phase.

Adapted from Wilson SR & Burns PN. Radiology. 2010; 257:24-39



Key Differences Between CEUS LIRADS and CT/MR LIRADS

03 Real-time Nature of CEUS for Diagnosis of Rapidly Enhancing Hemangiomas LR-1

<u>**Real-time nature**</u> of CEUS differentiates rapidly enhancing hemangiomas as LR-1, from their classification of LR-2 or LR-3 in CT/MRI LI-RADS.



- Homogeneous APHE
- Persistent hyperenhancement at 3m
- Bright T2 hyperintensity



- Peripheral globular APHE
- Gradual central fill-in
- Homogeneous hyperenhancement in the PVP

LR-1 Hemangioma

03 Differentiating True HCC from Pseudolesion

A frequent cause of diagnostic confusion on CT/MR is pseudolesion due to arterioportal shunt. CEUS does not have this problem since it evaluates only **true liver nodules** already seen on unenhanced ultrasound.



- 12-mm lesion on MRI
- Arterial phase hyperenhancement
- No washout



Indeterminate Arterioportal shunt or HCC

- 15-mm true nodule on gray-scale ultrasound
- Hypervascularity at early arterial phase
- Subtle washout



HCC

O3 Different Categories for Lesions with APHE and Size ≥10 mm

CEUS LI-RADS Lesions ≥10 mm with APHE are highly suspicious for HCC, irrespective of washout, and are either LR-4 (without washout) or LR-5 (with washout) in category.

CT/MR LI-RADS Lesions between 10-19 mm with APHE but no washout can represent arterioportal (AP) shunt or HCC, therefore indeterminate (LR-3) in category



- 15-mm observation with APHE.
- No washout



- 12-mm hyperechoic nodule on unenhanced ultrasound (true nodule) – excluding the possibility of pseudolesion due to nontumorous arterioportal shunt
- APHE
- No washout



O3 Significant Difference for LR-M Diagnostic Criteria between CEUS and CT/MR

On CEUS, non HCC malignancy shows early and marked washout; HCC shows late and mild washout.

CEUS LR-M Criteria

Any of following:

- **Rim APHE**
- Early (<60 s) washout
- Marked washout

CT/MR LR-M Criteria

Targetoid lesion (rim APHE, peripheral washout, delayed central enhancement)

OR

Nontargetoid mass with ≥ 1 of the following:

- Infiltrative appearance
- Marked diffusion restriction
- Necrosis or severe ischemia
- Other feature by radiologist



- 15-mm nodule
- Early (30 s) and marked washout

- 25-mm mass
- Mild and late (2-4 min) washout



Discordant Cases Between CEUS and CT/MR LI-RADS Categories

04 Case 1: Discrepancy in Detection of APHE

CEUS allows for more sensitive detection of APHE than CT/MR due to its <u>real-time nature</u>. CT/MR may fail to demonstrate APHE due to arterial phase mistiming.





- CT failed to demonstrate APHE
- Mild washout

LR-3 Indeterminate



- 15 mm
- APHE
- Late washout (>60 s)

LR-5 HCC

04 Case 2: Discrepancy in Washout Pattern

Microbubbles used as CEUS contrast agent are **purely intravascular** and do not leak into tumor interstitium. The CT/MR contrast agent may leak into the interstitium, therefore fail to show washout.



- 28mm liver mass on CT and MR
- APHE
- Mild late washout

LR-5 Definitely HCC



- 28 mm with APHE on CEUS
- Early (31 s) and marked washout on CEUS

LR-M Non HCC malignancy

Biopsy: intrahepatic cholangiocarcinoma

04 Case 3: Discrepancy in Arterial Enhancement

Real-time nature of CEUS allows for demonstration of very early arterial enhancement, which can be missed by CT/MR due to the pre-determined scan time.



- 25-mm liver mass on CT
- Hypovascular lesion on both arterial and venous phase

LR-4 Indeterminate

- Dysmorphic arteries
- APHE
- Early marked washout

LR-M Non HCC malignancy

Biopsy: intrahepatic cholangiocarcinoma

O4 Case 4: Discordance Due to Severe Fatty Liver

Washout may be <u>falsely demonstrated</u> and arterial hyperenhancement may be <u>masked</u> on CEUS due to the intensely echogenic background liver from severe fatty infiltration.



Pre: Hyper

- Mild Washout in delayed phase
- Query real vs apparent washout due to extremely bright background fatty liver

- Severe fatty liver with marked hypoattenuation/ hypointensity on CT/fat-sat MR.
- No washout seen

Bx: Dysplastic nodule & 2 years stability

04 Case 5: Discordance Due to Fat in Nodule

<u>Arterial hyperenhancement may not show on CT</u> due to the low attenuation of the hepatic lesions containing fat.



- 18-mm liver mass on CT
- No APHE
- Arterial enhancement is masked due to marked hypoattenuation on non enhanced scan due to fat.

LR-3 Indeterminate



- APHE on CEUS
- Mild and late washout

LR-5 Typical HCC

Biopsy: HCC



Conclusions



- CEUS is a real-time dynamic imaging method for characterization of focal liver lesions, which provides sensitive detection of arterial phase vascularity often superior to CT or MR.
- Developed in 2017, CEUS LIRADS integrates timing and degree of CEUS washout, which allows for differentiation of HCC from non HCC malignancies.
- CEUS LIRADS improves diagnostic algorithms of HCC by inclusion of CEUS into the standardized reporting and data collecting system.
- Accurate categorization and diagnosis of focal hepatic lesion according to LI-RADS using multimodality approach relies on understanding of the cause of discordance.



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