ECOGRAFIA CON CONTRASTO NELL’HCC
Ruolo attuale e prospettive future

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Nodular lesions in liver cirrhosis

Serstè et al, Hepatology 2012;55:800-806
Ultrasound guided fine needle biopsy of early hepatocellular carcinoma complicating liver cirrhosis: a multicentre study

E Caturelli, L Solmi, M Anti, S Fusilli, P Roselli, A Andriulli, F Formari, C Del Vecchio Blasco, I de Sio


US detection of new liver nodule

- AFP+
  - HCC
- AFP-
  - FNBP

HCC or other malignancies

ND or diagnosis

2nd Imaging

294 nodules ≤20 mm

- 48 ≤10 mm (16.3%)
  - 33 HCC (68.7%)
    - 7 DN (14.6%)
    - 8 RN (16.7%)
  - 246 11–20 mm (83.7%)
    - 225 HCC (91.5%)
      - 9 DN (3.7%)
      - 7 RN (2.8%)
    - 4 NHL (1.6%)
    - 1 HA (0.4%)

ALMA MATER STUDIORUM - UNIVERSITÀ DI BOLOGNA
Nodule in cirrhosis: a whole explant analysis in patients submitted to transplantation for HCC

50 pts submitted to OLT:

127 nodules

- 76 HCC (58.9%) 29±14 mm
- 13 HGDN (10.2%)
- 31 MRN (24.4%) 11±7 mm
- 7 Hem (5.5%)

Absence of Lymphoma and Cholangiocarcinoma may follow the selection criteria for transplantation

Burrel et al, Hepatology 2003
Newly developed nodular lesions in liver cirrhosis

Prospective surveillance program (1989–1997) in 313 cirrhotics

78 nodules without malignant features at detection

61 HCC (78.2%) and 17 (21.8%) non-HCC (3 hemangioma, 6 dysplastic nodules, 4 cirrhosis, 4 HCC in follow up)

72 nodules 1–3 cm in cirrhosis first detected at US

Final diagnoses: 60 HCC (83%) and 12 (17%) benign lesions (MRN/dysplastic)

89 nodules < 2 cm at first US detection in cirrhosis

Final diagnoses: 60 HCC (67.4%), cholangiocarcinoma (n = 1), and 28 benign lesions (31.5%)
(regenerative/dysplastic nodule, hemangioma, focal nodular hyperplasia) (n = 28)

67 early nodules (55 of 1–2 cm) in 64 cirrhotics first detected at US

Final diagnoses: 44 HCC (66%), 2 CCC, and 21 (31.3%) benign FLL (RN/dysplastic)

Newly developed nodular lesions in liver cirrhosis

To summarize:

Which nature is expected to have a focal liver lesion newly detected in a cirrhotic liver?

From a likelihood approach:

- **65% HCC if 1-2 cm**
- **85% HCC if 2-3 cm**
- **>90-95% if >3 cm**

If not an HCC

1. Regenerative dysplastic nodule
2. Hemangioma
3. Cholangiocellular carcinoma
4. Lymphoma
5. Metastasis or other extremely rare entities

Vascularization of hepatocellular liver nodules during multistep carcinogenesis

LRN  LGDN  HGDN  e-HCC  wdHCC  classic HCC

Benign ------ Early HCC ------ Malignant

AASLD PRACTICE GUIDELINE

Management of Hepatocellular Carcinoma

Jordi Bruix\(^1\) and Morris Sherman\(^2\)


8. Nodules between 1-2 cm found on ultrasound screening of a cirrhotic liver should be investigated further with two dynamic studies, either CT scan, contrast ultrasound or MRI with contrast. If the appearances are typical of HCC (i.e., hypervascular with washout in the portal/venous phase) in two techniques the lesion should be treated as HCC. If the findings are not characteristic or the vascular profile is not coincidental among techniques the lesion should be biopsied (level II).
Intrahepatic Peripheral Cholangiocarcinoma in Cirrhosis Patients May Display a Vascular Pattern Similar to Hepatocellular Carcinoma on Contrast-Enhanced Ultrasound

Ramón Vilana,1,2* Alejandro Forner,2,3* Luis Bianchi,1,2 Ángeles García-Criado,1 Jordi Rimola,1,2 Carlos Rodríguez de Lope,3 María Reig,2,5 Carmen Ayuso,1,2 Concepció Brú,1,2 and Jordi Bruix2,3

Hepatology 2010;51:2020-2029

2010

10 of 21 HCC retrospectively investigated HCC showed the Hyper=>Wash-out pattern at CEUS. Only between 1-3 patients of the 10 had lesions <3 cm
At MRI: arterial phase: 90.5% rim HyperE, 5.5% homogeneous HyperE.
These were 10 patients over 6 years (1-2 pts/y) out of the many hundreds seen in Barcelona

CEUS was removed from the AASLD and EASL guidelines based on this retrospective study on 21 CCC
Updated guidelines do not include CEUS due to imperfect specificity

Fig. 2. Diagnostic algorithm and recall policy.
*One imaging technique only recommended in centers of excellence with high-end radiological equipment.
**HCC: radiological hallmark: arterial hypervascularity and venous/late phase washout.
**Contrast imaging pattern of small ICC (<5 cm) (Bologna+Milan retrospective analysis).**

<table>
<thead>
<tr>
<th>Nr of lesion</th>
<th>Tumour size (cm)</th>
<th>Arterial phase (CEUS)</th>
<th>Portal phase (CEUS)</th>
<th>Late phase (CEUS)</th>
<th>CT</th>
<th>MRI</th>
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<tbody>
<tr>
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<td>Intensely hypo</td>
<td>Hypo</td>
<td>Hypo</td>
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<tr>
<td>2</td>
<td>4.5</td>
<td>Heterogeneous hyper</td>
<td>Hypo</td>
<td>Intensely hypo</td>
<td>Hypo</td>
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<tr>
<td>3</td>
<td>5</td>
<td>Slightly hyper</td>
<td>Hypo</td>
<td>Intensely hypo</td>
<td>Heterogeneous hypo</td>
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<tr>
<td>4</td>
<td>1.6</td>
<td>Slightly hyper</td>
<td>Hypo</td>
<td>Intensely hypo</td>
<td>Heterogeneous iso (some hypo areas)</td>
<td>Centre hypo</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td>Slightly hyper</td>
<td>Hypo</td>
<td>Intensely hypo</td>
<td>Heterogeneous iso (some hypo areas)</td>
<td>Centre hypo</td>
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<td>6</td>
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<td>7</td>
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<td>Hypo</td>
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<tr>
<td>8</td>
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<td>Hyper</td>
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<tr>
<td>9</td>
<td>4.6</td>
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<td>10</td>
<td>3</td>
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<td>Not observed</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
<td>Hyper</td>
<td>Iso</td>
<td>Intensely hypo</td>
<td>Rim-like hyper (centre hypo)</td>
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<tr>
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<tr>
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</tr>
<tr>
<td>15</td>
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<td>Ring hyper (centre hypo)</td>
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<td>–</td>
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<td>Hypo</td>
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<td>21</td>
<td>2.9</td>
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<td>Iso</td>
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<td>Hypo</td>
<td>–</td>
</tr>
<tr>
<td>22</td>
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<td>Hypo</td>
<td>Hypo</td>
<td>Ring iso (centre hypo)</td>
<td>Hyper</td>
</tr>
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<td>2</td>
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<td>Hypo</td>
<td>Ring hyper (centre hypo)</td>
<td>–</td>
</tr>
<tr>
<td>25</td>
<td>1.6</td>
<td>Iso</td>
<td>Hypo</td>
<td>Hypo</td>
<td>Not observed</td>
<td>–</td>
</tr>
</tbody>
</table>

Approximately 60% of ICC similar to HCC at CEUS, not considering the intensity and timing of wash-out.
Approximately 25% non diagnostic pattern (even of malignancy)

Galassi, ..., Piscaglia F, Liver Internat 2013;33:771-9
Should this be no more held diagnostic of HCC?
CEUS and diagnosis of HCC

Hyper-E in the arterial phase

YES

Hypo-E in the portal and late phases (=wash-out)*

Malignant.
Consider as HCC

Typical for HCC?

Typical for malignancy1-3

1. Forner A et al, Hepatology, 2008;47:97-104

ALL STUDIES PROSPECTIVE WITH HISTOLOGICAL CONFIRMATION

*In cases with marked and rapid (<60s) wash-out in portal/late phase consider the possibility of Peripheral Cholangiocarcinoma, especially if the pattern with MRI or CT does not confirm late wash-out, or consider (exceptionally) metastasis or primary hepatic lymphoma

Claudon M, Dietrich CF. Ultraschall Med 2013;34:11-29

www.efsumb.org
### Additional table 1: Demographic characteristics of 29 patients with cirrhosis and the 7 patients with F3 fibrosis

<table>
<thead>
<tr>
<th>parameters</th>
<th>Rim-like enhancement (n=8)</th>
<th>Non-rim-like enhancement (n=28)</th>
<th>P value</th>
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<tr>
<td>Age (years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean</td>
<td>53.13±13.75</td>
<td>50.25±10.32</td>
<td>0.523</td>
</tr>
<tr>
<td>Median, range</td>
<td>54 , 32-74</td>
<td>51 , 35-75</td>
<td></td>
</tr>
<tr>
<td>Gender male/female</td>
<td>5/3</td>
<td>25/3</td>
<td>0.109</td>
</tr>
<tr>
<td>Child-pugh class *</td>
<td></td>
<td></td>
<td>0.515</td>
</tr>
<tr>
<td>A</td>
<td>5 (83.3%)</td>
<td>21 (91.3%)</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>1 (16.7%)</td>
<td>2 (8.7%)</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Size of ICC nodules (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>50.75±24.38</td>
<td>53.75±30.16</td>
<td>0.798</td>
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<tr>
<td>Median, range</td>
<td>45.50, 25-93</td>
<td>43.00, 17-114</td>
<td></td>
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<tr>
<td>Mean CA 19-9 (U/ml)</td>
<td>139.85±236.05</td>
<td>170.68±206.33</td>
<td>0.720</td>
</tr>
<tr>
<td>Mean alpha-fetoprotein (ng/ml)</td>
<td>84.30±138.22</td>
<td>191.54±569.23</td>
<td>0.604</td>
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<tr>
<td>Underlying liver disease</td>
<td></td>
<td></td>
<td>0.639</td>
</tr>
<tr>
<td>cirrhosis</td>
<td>6 (75.0%)</td>
<td>23 (82.1%)</td>
<td></td>
</tr>
<tr>
<td>chronic hepatitis</td>
<td>2 (25.0%)</td>
<td>5 (17.9%)</td>
<td></td>
</tr>
<tr>
<td>Portal vein thrombosis</td>
<td>1</td>
<td>1</td>
<td>0.400</td>
</tr>
</tbody>
</table>
Early wash-out (<60 seconds) after globular hyperenhancement is not typical of HCC and should raise the suspicion of alternative malignancy (mainly HCC)

Also in nodules <3 cm the onset of wash-out occurs <1 min

Onset of wash out occurs early (<60 seconds) in most CholangioCarcinoma
Reasons supporting CEUS to be accepted for the diagnosis of HCC

- Overall rate of intrahepatic cholangiocarcinoma (ICC) (or more rarely lymphoma) in new liver lesions in cirrhosis 1–2% (but only half at risk of misdiagnosis for HCC, corresponding to 0.5-1% of all lesions)¹-²

- The “Hyper => Hypo” pattern at CEUS is specific for malignancy. MRI and CT are often unable to establish a diagnosis of malignancy in case of ICC¹,³ Removing CEUS would remove the possibility to establish a diagnosis of malignancy in those small focal liver lesions (not a few) not well suitable to biopsy, either for location or clotting impairment or contraindications to CT/MRI⁴.

- CEUS has a PPV of about 98-99%!

- Discrepancy between CEUS vs MRI (or CT) in detection of wash-out (CEUS+ and MRI/CT-) should raise the strong suspicion upon ICC.

1. Vilana, Hepatology 2010;51:2020-29  
CEUS IN HCC GUIDELINES AROUND THE WORLD

CEUS ACCEPTED FOR DIAGNOSIS OF HCC?

<table>
<thead>
<tr>
<th>REGION</th>
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<th>Reference</th>
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<tr>
<td>Europe</td>
<td>NO</td>
<td>The role of CEUS is controversial</td>
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<tr>
<td>Japan</td>
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<td>Kudo M et al Dig Dis 2011;29:339-364</td>
</tr>
<tr>
<td>World/Eu</td>
<td>YES</td>
<td>Claudon M, Dietrich CF. Ultraschall Med 2013;34:11-29</td>
</tr>
<tr>
<td>Italy</td>
<td>YES</td>
<td>AISF expert panel. Dig Liver Dis 2013;45:712-723</td>
</tr>
</tbody>
</table>

Recommendations of the Asia Pacific Association for the Study of the Liver (APASL)
At least use the wash-in wash-out CEUS pattern as a marker of malignancy

CEUS SHOULD BE HELD AS AN “OTHER DIAGNOSTIC TOOL” (BESIDE MRI / CT)

Dig Liver Dis 2013;45:712-723

Progress Report
Position paper of the Italian Association for the Study of the Liver (AISF):
The multidisciplinary clinical approach to hepatocellular carcinoma
Dig Liver Dis 2013;45:712-723
LI-RADS
Liver Imaging Reporting and Data System 2013.v1

Introduction

What is LI-RADS (Liver Imaging Reporting And Data System)?
• A system of standardized terminology and criteria to interpret and report imaging examinations of the liver.
• Supported and endorsed by the American College of Radiology (ACR).
• LI-RADS is a dynamic document: it will be expanded and refined as knowledge accrues and in response to user feedback.

Who is developing LI-RADS?
• LI-RADS is being developed by an ACR-supported committee of diagnostic radiologists with expertise in liver imaging.
• The committee receives input from hepatobiliary surgeons, hepatologists, hepatopathologists, and interventionalists.

How does LI-RADS work?
• LI-RADS categorizes observations from LR1 to LR5, reflecting probability of benignity or HCC in at-risk patients.

What’s new in LI-RADS v2013.1?

http://www.acr.org/quality-safety/resources/LIRADS
The American College of Radiology released on its website in 2013 the flowchart defining liver observations in conditions at risk for HCC as assessed by CT or MRI.

The flowchart, definitions and illustrations can be found on the ACR website, while pictorial assays were published in scientific journals.

http://www.acr.org/quality-safety/resources/LIRADS
CT MRI LI-RADS scheme update v2014
Liver Imaging Reporting And Data System

LI-RADS v2014

Observation in high-risk patient

Treated observation

Untreated observation

Definitely benign

Probably benign

Neither definite nor probable benign

LR-Treated

LR-1

LR-2

Probable malignancy, not specific for HCC

LR-M

Tumor in vein

LR-5V

Arterial phase hypo- or iso-enhancement

Arterial phase hyper-enhancement

Diameter (mm):

< 20

≥ 20

< 10

10-19

≥ 20

"Washout"

None:

LR-3

LR-3

LR-3

LR-3

LR-4

"Capsule"

One:

LR-3

LR-4

LR-4

LR-5

LR-5

Threshold growth:

≥ Two:

LR-4

LR-4

LR-4

LR-5

LR-5

Apply ancillary features and then tie-breaking rules to adjust category

Observations in this cell are categorized LR-4 except as follows:

- LR-5g, if there is a 50% diameter increase in ≤ 6 months. These observations are equivalent to OPTN 5Ag.
- LR-5cs, if there is both "washout" and visibility as discrete nodules at antecedent surveillance ultrasound, per AASLD HCC criteria.
CT MRI LI-RADS scheme update 2014
Liver Imaging Reporting And Data System

LI-RADS v2014 also includes a key modification to achieve congruency between LR-5 and OPTN Class 5 and AASLD:

- 10-19mm observations with arterial phase hyper-enhancement and one major feature can sometimes be categorized as LR-5 rather than LR-4
  - Observations with washout appearance and visibility on antecedent surveillance ultrasound meet criteria for HCC using AASLD criteria. These observations can be categorized as LR-5us.
  - Observations with ≥ 50% diameter increase in ≤ 6 months meet criteria for OPTN 5A-g HCC. These observations can be categorized as LR-5g.

---

**LR-5: Definitely HCC**

**Concept:**
100% certainty that observation is HCC and, if resection/explantation were performed, would be confirmed pathologically as HCC.

**Definition:**
Observation with imaging features diagnostic of HCC.

**Criteria:**
Not definitive benign entity, not probable benign entity, not non-HCC malignancy, not tumor in vein, and as follows:

- 10-19mm mass
  - Hepatic arterial phase hyper-enhancement AND
  - ≥ 1 of following: washout, “baldness”, threshold growth

- ≥ 20mm mass
  - Hepatic arterial phase hyper-enhancement AND
  - ≥ 1 of following: washout, “baldness”, threshold growth

**If unsure about category**
- Do not characterize as LR-5
- Characterize as LR-4 or LR-M as appropriate

**Reporting:**
- LR-5 observations must be reported.
- Features seen on CT and MRI can be integrated to yield the final LI-RADS category. If this is done, it must be explicitly stated in the radiology report.
- Since LR-5 observations represent definite HCC, they may determine the patient’s eligibility for transplantation or other treatment modalities. Thus LR-5 observations must be reported.
- LR-5 observations may be reported in aggregate if there are numerous observations which share similar features. However, up to five such observations should be individually described in the Findings. If there are no LR-M or LR-5v observations.

**Management implications:**
**CT MRI LI-RADS scheme version 2014**

Liver Imaging Reporting And Data System

**LI-RADS 3 (CT):** Figure collage shows a LI-RADS 3 observation at CT. A less than 20 mm mass with arterial phase hyperenhancement and none of following: “washout”, “capsule”, threshold growth.

**LR-3: Intermediate Probability for HCC**

**Concept:**
- Both HCC and benign entity are considered moderate probability

**Definition:**
- Observation that does not meet unusual criteria for other LI-RADS categories.

**Criteria**
- Not definite benign entity, not probable benign entity, not non-HCC malignancy, not tumor in vas and one of the following:
  - Mass with hepatic arterial phase hyper- or isoenhancement
  - <20mm mass with x1 of following: “washout”, “capsule”, and threshold growth
  - <20mm mass with none of following: “washout”, “capsule”, and threshold growth
  - Mass with hepatic arterial phase hyperenhancement
  - <20mm mass with none of following: “washout”, “capsule”, and threshold growth

**If unsure about category:**
- Categorize as LR-3 if unsure between LR-3 and LR-4
- Categorize as LR-4 if unsure between LR-3 and LR-DW
- Categorize as LR-3 if unsure of LR-2 or LR-4 using lesbreaker rules

**Reporting:**
- LR-3 observations should be reported.
- Features seen on CT and MRI can be integrated to yield the final LI-RADS category. If this is done, it must be explicitly stated in the radiology report.
- LR-3 observations may be indeterminate for HCC. If other, more suspicious observations are not present, LR-3 observations should be reported. If other, more suspicious observations are present (LR-5, LR-6, LR-6.1, or LR-6.2), the LR-3 observations may be reported at the radiologist's discretion.
- LR-3 observations may be reported in aggregate.

**Acknowledgements**

Feedback? Email mcr@acr.org
**CT MRI LI-RADS scheme version 2014**
Liver Imaging Reporting And Data System

**LR-M: Probably malignant, not specific for HCC**

**Concept:**
Observation is probably malignant, but imaging features are not specific for HCC.

**Definition:**
Observation with one or more imaging features that favor non-HCC malignancy.

**Characteristic Imaging Features:**
- Features that favor other malignancy over HCC include (partial list):
  - Arterial phase rim or peripheral enhancement
  - Portal venous and delayed phase central enhancement
  - Progressive concentric enhancement
  - Peripheral washout appearance
  - Liver surface retraction
  - Biliary obstruction disproportionate to mass diameter
  - Target appearance at ENVI or hepatobiliary phase
- Features that favor HCC over other malignancy include (partial list):
  - Diffuse arterial phase hyperenhancement
  - Diffuse portal venous or delayed phase washout appearance
  - Capsule appearance
  - Diaphragmatic rim
  - Intra-tumoral fat
  - Spontaneous hemorrhage
  - Diffuse T1 hyperintensity
  - Diffuse hepatobiliary phase hyperintensity
  - Nodules in regenerating or nodular architecture
  - Tumor in vein

**LI-RADS Reporting:**

LR-M: Probably malignant, not specific for HCC. Pre and post-contrast CT images demonstrate a peripherally enhancing observation on arterial phase with progressive central enhancement on portal venous and delayed phase images. This observation is a biopsy proven poorly differentiated cholangiocarcinoma.
LI-RADS
Liver Imaging Reporting and Data System 2013.v1
The documents illustrates how to arrive to a report indicating one of 8 different types of observation categories

- LR-Treated
- OM = Other Malig
- LR-1
- LR-2
- LR-3
- LR-4
- LR-5
- LR-V tumor in vein

http://www.acr.org/quality-safety/resources/LIRADS
LI-RADS
Liver Imaging Reporting and Data System 2013.v1

Pictorial assays

LI-RADS Categorization of Benign and Likely Benign Findings in Patients at Risk of Hepatocellular Carcinoma: A Pictorial Atlas

AJR 2014: 203:W43-W69

LI-RADS (Liver Imaging Reporting and Data System): Summary, Discussion, Consensus of the LI-RADS Management Working Group and Future Directions

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Hepatology 2015
Created originally to standardize the reporting and data collection of CT and MR imaging for hepatocellular carcinoma (HCC), LI-RADS is expanded here to include contrast-enhanced ultrasound (CEUS) for the same indication. This method of categorizing liver findings for patients with cirrhosis or other risk factors for developing HCC allows the radiology community to:

- Apply consistent terminology
- Reduce imaging interpretation variability and errors
- Enhance communication with referring clinicians
- Facilitate quality assurance and research
- Facilitate integration and correlation between imaging modalities
- Enhance communication with and understanding by patients
In 2014 the working groups for the CEUS LI-RADS is established

Steering Committee:
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LI-RADS Algorithm **RULES of UTILIZATION**

1. As with CT and MRI LI-RADS categorization, the CEUS LI-RADS algorithm imposes a **categorization order**:

2. **first, CEUS LR inadequate** (due to technical or other factors), LR-treated, LR-1 (definitely benign observations or nodules) and LR-5V (If there is definite tumor within vein even if a parenchymal nodule is not identified).

3. If no nodule is seen on pre contrast ultrasound, no categories will be assigned at this point.

4. **Only observations with visible nodules on pre contrast ultrasound will be further categorized with CEUS.**

5. **LR-M will be assigned next** (features that favor non-HCC malignancy).

6. **Observations with visible nodules on pre contrast ultrasound will then be assigned categories of CEUS LR-2, -3, -4, or -5 as appropriate**
Draft proposal of CEUS LI-RADS scheme
version updated March 2016 (not yet ACR approved)
Liver Imaging Reporting And Data System

CEUS LI-RADS

Algorithm for CEUS

Observation in high-risk patient on pre-contrast US

- Inadequate assessment
- Treated observation

Untreated observation

- Definitely benign
- Probably benign
- Solid nodule, not definitely or probably benign
- Tumor in vein

LR-5V

Probable malignancy, not specific for HCC
LR-M

Arterial phase
Iso/Hypo-enhancement
< 20mm ≥ 20mm
No washout of any type LR-3 LR-3
Late and mild washout LR-3 LR-4

Arterial phase
Hyper-enhancement
< 10mm ≥ 10mm
LR-3 LR-4 LR-5

Apply ancillary features and then apply tie-breaking rules to adjust category as appropriate

Acknowledgments
<table>
<thead>
<tr>
<th>LI-RADS Category</th>
<th>Concept and Definition</th>
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<tbody>
<tr>
<td>LR-1 Definitely Benign</td>
<td><strong>Concept:</strong> 100% certainty observation is benign.</td>
</tr>
<tr>
<td></td>
<td><strong>Definition:</strong> Observation with imaging features diagnostic of a benign entity, or definite disappearance at follow up in absence of treatment.</td>
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<tr>
<td>LR-2 Probably Benign</td>
<td><strong>Concept:</strong> High probability observation is benign.</td>
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<td></td>
<td><strong>Definition:</strong> Observation with imaging features suggestive but not diagnostic of a benign entity.</td>
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<tr>
<td>LR-3 Intermediate probability for HCC</td>
<td><strong>Concept:</strong> Both HCC and benign entity have moderate probability.</td>
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<td></td>
<td><strong>Definition:</strong> Observation that does not meet criteria for other LI-RADS categories.</td>
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<tr>
<td>LR-4 Probably HCC</td>
<td><strong>Concept:</strong> High probability observation is HCC but there is not 100% certainty.</td>
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<td></td>
<td><strong>Definition:</strong> Observation with imaging features suggestive but not diagnostic of HCC.</td>
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<tr>
<td>LR-5 Definitely HCC</td>
<td><strong>Concept:</strong> 100% certainty observation is HCC.</td>
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<td></td>
<td><strong>Definition:</strong> Observation with imaging features diagnostic of HCC or proven to be HCC at histology.</td>
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<tr>
<td>LR-5V Definitely HCC with Tumor in Vein</td>
<td><strong>Concept:</strong> 100% certainty that observation is HCC invading vein.</td>
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<tr>
<td></td>
<td><strong>Definition:</strong> Observation with imaging features diagnostic of HCC invading vein.</td>
</tr>
<tr>
<td>LR-M Probable malignancy, not specific for HCC</td>
<td><strong>Concept:</strong> High probability that observation is a malignancy, but imaging features are not specific for HCC.</td>
</tr>
<tr>
<td></td>
<td><strong>Definition:</strong> Observation with one or more imaging features that favor non-HCC malignancy.</td>
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<tr>
<td>LR-Treated Treated Observation</td>
<td><strong>Concept:</strong> Loco-regionally treated observation.</td>
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<tr>
<td></td>
<td><strong>Definition:</strong> Observation that has undergone loco-regional treatment.</td>
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</table>
Draft proposal of CEUS LI-RADS scheme v2015
Draft proposal of CEUS LI-RADS scheme v2015

CEUS LR-T: Treated

PEI => 24h later
Concept: 100% certainty observation is benign

Definition:
- Liver observation with imaging features diagnostic of a definitely benign entity
- Definite spontaneous disappearance at follow up

Examples:
- Simple cyst
- Classic hemangioma
- Definite focal hepatic fat deposition
- Definite focal hepatic fat sparing

Comments:
- Observations interpreted as definite cysts or hemangiomas at CEUS should be categorized LR-1 (definitely benign). If there is uncertainty in the diagnosis, categorize as LR≥2.
- Observations interpreted as focal hepatic fat deposition or focal hepatic fat sparing can be categorized LR-1 (definitely benign) if and only if the CEUS features are unequivocal and/or if the diagnosis was previously confirmed on CT or MR. If there is uncertainty in the diagnosis, categorize as LR≥2.
- Except for simple cyst(s), classic hemangiomas, and some cases of focal hepatic fat deposition or sparing, ultrasound-detectable observations should not be categorized LR-1 (definitely benign) in at-risk patients unless the diagnosis of a benign entity was previously established by other tests (CT, MRI, or biopsy).

Management implications:
- Continued routine surveillance usually is appropriate
Draft proposal of CEUS LI-RADS scheme v2015

CEUS LR-1: Definitely Benign

Arterio-Venous large aneurismatic fistula
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CEUS LR-1: Definitely Benign

Simple Cyst
Draft proposal of CEUS LI-RADS scheme v2015

CEUS LR-1: Definitely Benign

Hemangioma
Concept:
High likelihood observation is benign

Definition:
Liver observation or nodule with imaging features suggestive but not diagnostic of a benign entity

Criteria:
- Solid nodule <10mm with iso-enhancement throughout all phases
- Not a distinct mass on pre contrast ultrasound with iso-enhancement throughout all phases
- Nodule previously LR-3, and stable in size for 2 years or more

Examples:
Probable cirrhotic regenerative nodule or low-grade dysplastic nodule

Management implications
Continued routine surveillance usually is appropriate.
Draft proposal of CEUS LI-RADS scheme v2015

CEUS LR-2: Probably Benign

Pseudonodular observation in cirrhosis
**Draft proposal of CEUS LI-RADS scheme v2015**

**CEUS LR-M: Probably Malignant, not specific for HCC**

**Concept:**
Observation is probably or definitely malignant, but imaging features are not specific for HCC.

**Definition:**
Nodule with one or more imaging features that favor non-HCC malignancy.

**Criteria:**
- Nodule with at least some enhancement in the arterial phase (regardless of morphological pattern or degree) with either or both of the following:
  - Early washout relative to liver within 60 seconds of contrast injection
  - Marked washout resulting in a “punched out” appearance
- Arterial phase rim enhancement, followed by washout (regardless of onset or degree)

**Comments:**
- Nodules with enhancement of any degree or morphology in the arterial phase followed by marked early washout should be categorized LR-M.
- Nodules with mild and late washout may be categorized LR-3, LR-4, LR-5, or LR-5V depending on other features. Such washout is slow in onset (onset after 60 seconds) and mild in degree.

**Potential pitfalls and challenges**
- Inflammatory masses, especially inflammatory pseudotumors, generally show APHE and early marked washout on CEUS.  

**Management**
- Variable, depending on type of malignancy suspected.
- Biopsy is frequently needed for a LR-M categorization as there is a lack of specificity for a diagnosis.
- Appropriate management may include follow-up, additional imaging, resection, or other treatment.
- Does not contribute to HCC radiology T staging and does not provide HCC exception points for determining priority for liver transplantation, unless tissue sampling with histology analysis establishes a diagnosis of HCC. See UNOS/OPTN policy.
- An LR-M nodule proven to be HCC at histology should be categorized LR-5 at follow up imaging.
Draft proposal of CEUS LI-RADS scheme v2015

CEUS LR-M: Probably Malignant, not specific for HCC

Cholangiocarcinoma
Draft proposal of CEUS LI-RADS scheme v2015

CEUS LR-M: Probably Malignant, not specific for HCC

Cholangiocarcinoma
Draft proposal of CEUS LI-RADS scheme v2015

CEUS LR-M: Probably Malignant, not specific for HCC

Mixed Hepato-Cholangiocarcinoma
Draft proposal of CEUS LI-RADS scheme v2015

**Concept:**
- Both HCC and benign entity are considered intermediate probability.

**Definition:**
- Nodule that does not meet unequivocal criteria for other LI-RADS categories.

**Criteria:**
- \( \geq 10 \text{mm} \) nodule with arterial phase iso-enhancement without washout of any type.
- \( \text{Any size nodule with arterial phase hypo-enhancement without washout of any type} \).
- \( < 20 \text{mm} \) nodule with arterial phase iso- or hypo-enhancement and mild/late washout.
- \( < 20 \text{mm} \) nodule with arterial phase iso-enhancement and mild/late washout.
- \( < 10 \text{mm} \) nodule with APHE (in whole or in part, excluding rim and peripheral discontinuous globular enhancement) and without washout of any type.

**Management implications:**
- Appropriate management is variable, depending mainly on nodule diameter and stability, as well as clinical considerations.
- Please see Management section for details.
Draft proposal of CEUS LI-RADS scheme v2015

CEUS LR-3: Intermediate Probability for HCC  
CEUS LR-4: Probably HCC  
CEUS LR-5: Definitely HCC

Assessment: LR-Inadequate  
Observation: LR-Treated

Definitely benign  
Probably benign  
Solid nodule, not definitely or probably benign

Tumor in vein

Probable malignancy, not specific for HCC

Arterial phase Iso/Hypo-enhancement

<table>
<thead>
<tr>
<th>Arterial phase Hyper-enhancement¹</th>
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<tbody>
<tr>
<td>&lt; 20mm</td>
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<tr>
<td>&lt; 10mm</td>
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No washout of any type

<table>
<thead>
<tr>
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<tr>
<td>LR-3</td>
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Late and mild washout²

<table>
<thead>
<tr>
<th>Arterial phase Hyper-enhancement</th>
</tr>
</thead>
<tbody>
<tr>
<td>LR-3</td>
</tr>
</tbody>
</table>

Apply ancillary features and then apply tie-breaking rules to adjust category as appropriate

¹ Arterial phase hyper-enhancement: whole or in part, excluding rim and peripheral discontinuous globular enhancement
² Late in onset (> 60 seconds) and mild in degree: in whole or in part, with no part showing early or marked washout
**Draft proposal of CEUS LI-RADS scheme v2015**

**CEUS LR-4: Probably HCC**

**Concept:**
Observation is probably HCC but there is not 100% certainty

**Definition:**
Nodule with imaging features suggestive but not diagnostic of HCC

**Criteria:**
- Á 10mm nodule with APHE (in whole or in part, excluding rim and peripheral discontinuous globular enhancement) without washout of any type
- Á 20mm nodule with arterial phase hypo- or iso-enhancement with mild and late washout
- Á < 10mm nodule with APHE (in whole or in part, excluding rim and globular peripheral enhancement) with mild and late washout

**Management implications**
Á Please see Management section for details
Concept:
100% certainty observation is HCC. LR5 is essentially equivalent to OPTN 5

Definition:
Nodule with imaging features diagnostic of HCC

Criteria:
≤10mm nodule with APHE (in whole or in part, excluding rim and peripheral discontinuous globular enhancement) with mild and late washout

Management
Proceed with treatment for HCC
OPEN RESEARCH FIELDS

1. Rates of different histological nodular lesions according to the different CEUS patterns

2. Validation of the CEUS LI-RADS scheme (particularly LR-M, LR-3, LR-4)
Thank you for your attention