Surveillance and diagnosis of HCC

The imaging techniques for hepatocellular carcinoma: indications and limits

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Il sottoscritto dichiara di non aver avuto negli ultimi 12 mesi conflitto d’interesse in relazione a questa presentazione

e

che la presentazione non contiene discussione di farmaci in studio o ad uso off-label
Late Phase

Wash-in…
In cirrhosis…

Wash-out

…HCC diagnosis!!

>95% Specificity and PPV
In patients with cirrhosis with a 1-2 cm nodule detected during surveillance, a single imaging technique showing a typical contrast pattern confidently permits the diagnosis of HCC, thereby reducing the need for FNB examinations.

Sangiovanni A et al, Gut 2010
*One imaging technique only recommended in centers of excellence with high-end radiological equipment
“Since MRI or CT would be anyhow recommended for HCC staging, after the detection of a nodule by US, the cheapest approach is to prescribe in first line MRI or CT and to resort to CEUS in case of inconclusive diagnosis”
Microwave ablation

1 month follow-up
Typical vascular pattern
CT vs MR

**Table 4** Rates of sensitivity and specificity of arterial hypervascularisation, portal vein washout in the late venous phase and typical vascular pattern for the diagnosis of 34 HCCs detected in 55 patients with 1–2 cm nodules

<table>
<thead>
<tr>
<th>Arterial hypervascularisation</th>
<th>Portal/vein washout</th>
<th>Typical vascular pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CE-US CT MRI</td>
<td>CE-US CT MRI</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>68 55 66</td>
<td>38 53 59</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>76 81 62</td>
<td>95 100 95</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>82 95 72</td>
<td>93 100 95</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>59 59 54</td>
<td>49 57 51</td>
</tr>
<tr>
<td>LR+</td>
<td>2.8 3.4 1.7</td>
<td>8.0 ∞</td>
</tr>
<tr>
<td>LR−</td>
<td>0.42 0.44 0.56</td>
<td>0.6 0.47 0.43</td>
</tr>
<tr>
<td>Accuracy (%)</td>
<td>71 71 64</td>
<td>65 71 74</td>
</tr>
</tbody>
</table>

CE-US, contrast-enhanced ultrasound; HCC, hepatocellular carcinoma; LR, likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

**Sangiovanni A et al, Gut 2010**

**Table 4. Correlation Between Tumor Size and Rates of Typical Vascular Pattern (Wash-In Followed by Wash-Out) for HCC in Contrast Imaging Techniques**

<table>
<thead>
<tr>
<th>Tumor Size</th>
<th>No. Of Nodules</th>
<th>Wash-In + Wash-Out Positives</th>
<th>Radiological Diagnosis of HCC</th>
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<tr>
<td></td>
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<td>CE-US CT MRI</td>
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</tr>
<tr>
<td>0.5-1 cm</td>
<td>3</td>
<td>0 1 1</td>
<td>–</td>
</tr>
<tr>
<td>1-2 cm</td>
<td>47</td>
<td>15 21 19*</td>
<td>19</td>
</tr>
<tr>
<td>&gt;2 cm</td>
<td>12</td>
<td>6 10 9</td>
<td>10</td>
</tr>
</tbody>
</table>

*Two patients with HCC not investigated with MRI owing to claustrophobia and a bone metallic plaque, respectively.

**Iavarone M et al, Hepatology 2010**
Typical vascular pattern

CT vs MR

- 75 small (10-30mm) HCCs
- Gad-MR was the most sensitive technique for detecting the typical vascular pattern

Leoni S et al, Am J Gastroenterol 2010
Typical vascular pattern

CT vs MR

CT

MR

HB phase
Typical vascular pattern

CT vs MR

Dual source CT Spectral imaging

Virtual non-enhanced

Arterial 70KeV

Iodine only
Dual-Source CT
Detection of typical vascular pattern

Easy work!
The best has yet to come....

- Characterization of nodules with atypical vascular pattern
- Staging
- Vascular mapping for treatment planning
Typical vascular pattern

An “atypical” finding in HCC

- Using the EASL noninvasive criteria, the false-negative rate was approximately **20%**.

  *Iavarone M et al, Hepatology 2010*

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False negatives: **30/59 (50.8%)**

*Iavarone M et al, Hepatology 2010*
“Equivocal nodules”

arteriosa tardiva
<table>
<thead>
<tr>
<th>Features</th>
<th>HCC Diagnosed (n = 29)</th>
<th>HCC Undiagnosed (n = 33)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>23 (79)</td>
<td>20 (61)</td>
<td>0.11</td>
</tr>
<tr>
<td>Age &gt;66 years</td>
<td>11 (41)</td>
<td>18 (55)</td>
<td>0.19</td>
</tr>
<tr>
<td>HCV-positive</td>
<td>21 (72)</td>
<td>24 (72)</td>
<td>0.97</td>
</tr>
<tr>
<td>Child-Pugh class A</td>
<td>28 (97)</td>
<td>31 (94)</td>
<td>0.63</td>
</tr>
<tr>
<td>AFP &gt;100 ng/mL</td>
<td>4 (14)</td>
<td>3 (9)</td>
<td>0.56</td>
</tr>
<tr>
<td>Tumor size 1-2 cm</td>
<td>18 (62)</td>
<td>29 (88)</td>
<td>0.035</td>
</tr>
<tr>
<td>Tumor grade 1</td>
<td>2 (7)</td>
<td>16 (48)</td>
<td>0.0003</td>
</tr>
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Data are presented as n (%).

Abbreviations: AASLD, American Association for the Study of Liver Diseases; HCV, hepatitis C virus.
Exploring the grey area
The added value of MRI

- Large RN
- Low-grade DN
- High-grade DN
  - Premalignant!!
  - Early HCC
  - Equivocal nodules
    - (No wash-in/wash-out)
- Overt HCC
  - Wash-in/wash-out
HEPATOCARCINOGENESIS: Pathological Features

- **Cell changes**
  - Cellular content

- **Architectural changes**
  - Cell density
  - Cords number

- **Biliary impairment**

- **Vascular supply**
Hepatobiliary function

CEA immunostaining

Regenerative nodule

High grade DN

Well diff HCC

Bilirubin
Biliary acids
Fatty acids

Hepatocyte-targeted Contrast agent

Sinusoidal pole

Biliary canaliculus
Table 5. Nodules’ patterns in the dynamic study and hepatobiliary phase

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<td>B</td>
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<td>HCC</td>
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<td>0</td>
<td>11</td>
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<td>HGDN</td>
<td>30</td>
<td>10</td>
<td>20</td>
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<tr>
<td>LGDN</td>
<td>32</td>
<td>32</td>
<td>0</td>
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HCC, hepatocellular carcinoma; HGDN, high grade dysplastic nodule; LGDN, low grade dysplastic nodule

A: iso or hyperintensity in both arterial and late phases
B: iso or hypointensity in the arterial phase and hypointensity in the late phase
C: hyperintensity in the arterial phase and hypointensity in the late phase

Typical vascular pattern
100% Spec
72.5% Sens

Bartolozzi C et al. Abdom Imaging 2012
# Hepatobiliary contrast agents

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Hypo HB phase
97.5% Sens

*Bartolozzi C et al. Abdom Imaging 2012*
“The HB phase is 11% more sensitive in the classification of HGDN/early HCC than dynamic MRI, with an added value of 32.5% in the NPV.

The high incidence (33%) of atypical nodules and their frequent malignancy (32%) suggest the widespread employment of Gd-EOB-DTPA-MRI in the follow-up of small nodules (≤ 2 cm) in cirrhosis.”

Golfieri R et al. Eur Radiol 2011
Equivocal nodule?
Small hepatocellular carcinomas: improved sensitivity by combining gadoxetic acid-enhanced and diffusion-weighted MR imaging patterns

- 130 patients, 179 surgically confirmed small HCCs (≤2.0 cm)
- 130 patients with cirrhosis without HCC

“The combination of gadoxetic acid-enhanced MR imaging and DW imaging yielded better diagnostic accuracy and sensitivity in the detection of small HCCs than each MR imaging technique alone.”

Park MJ et al. Radiology 2012
March, 2012

- T1w. i
- Fat sat T2w. i
- DWI, b 800
- Arterial
- Late
- HB
Hypovascular hypointense nodules on hepatobiliary phase gadoxetic acid-enhanced MR images in patients with cirrhosis: potential of DW imaging in predicting progression to hypervascular HCC

“Hyperintensity on DW images in hypovascular hypointense nodules on hepatobiliary phase gadoxetic acid-enhanced MR images in patients with cirrhosis is strongly associated with progression to hypervascular HCC”

Kim YK et al. Radiology 2012
The best has yet to come....

- Characterization of nodules with atypical vascular pattern
- Staging
- Vascular mapping for treatment planning
The best has yet to come....

- Characterization of nodules with atypical vascular pattern
- Staging
- Vascular mapping for treatment planning
Staging

Intra-hepatic

Arterial

Hepatobiliary
Staging

Extra-hepatic

CT pros
✓ Volume coverage
✓ Speed
✓ Availability
✓ Costs...
Vascular mapping

Pre-LT

Pre-TACE
The best has yet to come....

- Characterization of nodules with atypical vascular pattern
  - MRI

- Staging
  - MRI / CT

- Vascular mapping for treatment planning
  - CT
CT vs MRI

- Local availability
- Costs
- Indications
- Specific anatomic conditions…
Guidelines - Clinical practice - Technology

Diffusion WI, b 800

Perfusion

HB contrast agents

Spectral Imaging

11C-choline PET  FDG PET