Assessment of the tumor characteristics with imaging

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1. Diagnosis of HCC
   - Multistep hepatocarcinogenetic pathway
   - ECS agent, Kupffer cell imaging, Dual agent (Gd-EOB-DTPA)
     Diffusion-weighted imaging

2. D/Dx Cirrhosis-associated hepatocellular nodules (DN)
   Mass-forming cholangiocarcinoma
   Focal nodular hyperplasia
Liver MRI protocols

- Chemical shift information: Dual GRE, IDEAL, mDixon
- T2 information: SSFSE, FSE, STIR
- pre- & post-contrast information: LAVA/THRIVE/VIBE, Water image IDEL, Water image mDixon
- Diffusion information: DWI low b-value, DWI high b-value, ADC
Three parallel processes during carcinogenetic pathway

1. The progressive sinusoidal capillarization with an increase in number of unpaired A
   ⇒ Arterial hypervascularization of HCC : ECS agent (Gd)

2. The progressive nodular depletion of Kupffer cells
   ⇒ Hyperintensity on SPIO-enhanced T2- & T2* WI

3. The progressive loss of biliary polarization of the hepatocyte & the derangement of the microscopic secretory structure
   ⇒ Hypointensity on hepatocyte phase imaging (MN-DPDP, Gd-BOPTA, Gd-EOB-DTPA)
Hemodynamic changes during hepatocarcinogenesis

- Dr. Matsui 0
Sequential increase of expression of CD34 positive sinusoids and α-SMA positive unpaired arteries (Nakamura k, Zen Y, Matsui 0, et al. Human Pathol. 2007)

Double staining of CD34 (blue) & α-SMA (brown)

<table>
<thead>
<tr>
<th>Spotty</th>
<th>Localized</th>
<th>Diffuse</th>
<th>Diffuse, intense</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dysplastic nodule</td>
<td>early HCC</td>
<td>Classic HCC</td>
<td></td>
</tr>
</tbody>
</table>
Multi-step changes of drainage vessels during hepatocarcinogenesis

(Kitao A, Zen Y, Matsui O, Nakanuma N. Radiology 2009;252;605)
Drainage blood flow from a hypervascular encapsulated HCC (connections between tumor blood sinusoids & surrounding portal venules).

VS

Early HCC

Hypervascular HCC

Overt HCC

Efremidis SC Eur Radiol 2007; 17

Courtesy of Dr. Matsui O
Moderately differentiated HCC with fibrotic capsule
Vaguely nodular

Distinctly nodular

Early HCC

Distinctly nodular
Stepwise Hepatocarcinogenesis and Changes of Intranodular Blood Supply

- Portal venous supply
- Hepatic arterial supply
- Abnormal arterial supply

RN
Low DN
High DN
Early HCC
Well HCC
Moderately HCC

(Hayashi M, Matsui O, et al. AJR 172: 969-976, 1999)
Stepwise Hepatocarcinogenesis and Changes of Intranodular Blood Supply


- Portal venous supply
- Hepatic arterial supply
- Abnormal arterial supply

RN, Low DN, High DN, Early HCC, Well HCC, Moderately HCC
Dynamic CT in an Early HCC
Dynamic MRI in an Early HCC
Multi-step Hepatocarcinogenesis
Dynamic CT in High grade DN
## Comparison of morphologic features in dysplastic nodules & early HCC

<table>
<thead>
<tr>
<th>Morphology</th>
<th>Low-grade DN</th>
<th>High-grade DN</th>
<th>Early HCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonelike populations</td>
<td>Present</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Nuclear hyperchromasia</td>
<td>Absent</td>
<td>Present</td>
<td>Present</td>
</tr>
<tr>
<td>Irregularity of nucleus</td>
<td>Absent</td>
<td>Mild</td>
<td>Moderate</td>
</tr>
<tr>
<td>Pseudoglands</td>
<td>Absent</td>
<td>Frequent</td>
<td>Frequent</td>
</tr>
<tr>
<td>Increased cell density</td>
<td>&gt; 2 times</td>
<td>2-3 times</td>
<td>2-3 times or more</td>
</tr>
<tr>
<td>Number of cells thick</td>
<td>1-2</td>
<td>2-3</td>
<td>2-3</td>
</tr>
<tr>
<td>Reticulin framework</td>
<td>Normal</td>
<td>Normal</td>
<td>Normal or decreased</td>
</tr>
<tr>
<td>Stromal invasion</td>
<td>Absent</td>
<td>Absent</td>
<td>Present</td>
</tr>
<tr>
<td>Fatty change</td>
<td>Rare or absent</td>
<td>Occasional</td>
<td>30-40%</td>
</tr>
<tr>
<td>Unpaired artery</td>
<td>Rare or absent</td>
<td>Frequent</td>
<td>Present</td>
</tr>
</tbody>
</table>
Fat-containing Well Diff-HCC
HCC with Fatty metamorphosis

1 year F/U
Advanced HCC with Fat component
Arterial-only enhancing lesion

- **Jeong YY et al.** Small (<20 mm) enhancing hepatic nodules seen on arterial phase MR imaging of the cirrhotic liver: clinical implications. *AJR* 2002;178:1327-34.


- **Holland AE, et al.** Importance of small (< or = 20-mm) enhancing lesions seen only during the hepatic arterial phase at MR imaging of the cirrhotic liver: evaluation and comparison with whole explanted liver. *Radiology.* 2005;237:938-44.
Trans-sinusoidal route

ex) Liver cirrhosis, HV thrombosis

PV

Vasa vasorum

Peribiliary plexus

Liver cirrhosis, HV thrombosis
Added diagnostic value of T2-weighted MR imaging to gadolinium-enhanced three-dimensional dynamic MR imaging for the detection of small hepatocellular carcinomas

Kim YK EJR 2008
### MRI appearance of wd-HCC

<table>
<thead>
<tr>
<th></th>
<th>T2WI</th>
<th>Fat sat T2WI</th>
<th>In-phase T1WI</th>
<th>Opp-phase T1WI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperintense</td>
<td>12</td>
<td>8</td>
<td>15</td>
<td>11</td>
</tr>
<tr>
<td>Isointense</td>
<td>17</td>
<td>17</td>
<td>16</td>
<td>8</td>
</tr>
<tr>
<td>Hypointense</td>
<td>4</td>
<td>6</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>33</td>
<td>31</td>
<td>33</td>
<td>26</td>
</tr>
</tbody>
</table>

- **18 (54.5%)** of wd HCC: hyperintense on T2 & API
Well-differentiated HCC
T1WI –High/ T2WI-Low
Three parallel processes during carcinogenetic pathway

1. The progressive sinusoidal capillarization with an increase in number of unpaired A
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RES-targeted agents

SPIO: Ferumoxides, Ferucarbotran (Resovist®)
Uptaked by Kupffer cell & macrophage
T2 shortening & susceptibility effect
Hypovascular nodule on cirrhosis

Kim YK, et al JCAT 2007
Well differentiated HCC
1.8cm sized HCC

Arterial phase

HBP (20m)
Sonazoid-enhanced US: HCC

Arterial phase

Delayed phase

Post-vascular Kupffer phase
SPIO: limitation in wd- HCC
Dual Imaging
Dynamic & Hepatocyte imaging

Bolus injection

GD-EOB-DTPA

PreT2
AP
PP
3 min
Post T2

Hepatocyte imaging

20 min

Kim YK, et al JMRI 2009
HCC: MDCT vs Gd-EOB-DTPA

Kim YK. JCAT 2009
HCC:  Gd-DTPA vs Gd-EOB-DTPA

Kim YK. Br J Radiol 2010
Detection of Small Hepatocellular Carcinoma
Can Gadoxetic Acid-Enhanced Magnetic Resonance Imaging Replace Combining Gadopentetate Dimeglumine-Enhanced and Superparamagnetic Iron Oxide-Enhanced Magnetic Resonance Imaging?

Kim YK  Invest Radiol  2010

Gd-DTPA  3 min  SPIO T2*WI

Gd-EOB-DTPA  3 min  Wd- HCC  20min
G1 HCC + HGDN

Diagnostic discrepancy of early hepatocellular carcinoma between Japan and West

Masamichi Kojiro

Hepatology Research 2007; 37 (Suppl. 2): S121–S124
HCC, GI, Bile stasis

6-15% OATP8 overexpression, probably due to some genetic alteration

- Matsui O
FNH-Like nodule

Arterial phase

Hepatobiliary phase

courtesy of DR. Mortel KJ

Ring-like enhancement of focal nodular hyperplasia with hepatobiliary-phase Gd-EOB-DTPA-enhanced magnetic resonance imaging: radiological-pathological correlation


OATP5 expression
DWI: Stejskal and Tanner (1965)

Water diffusion is observed as signal loss.
Biological correlates of Diffusion-weighted MRI

Apparent diffusion
Reflects:
- Cell membrane integrity
- Cellular density
- Macromolecules
- Microstructural organization
- Fluid homeostasis
- Microcapillary function
Free fluids exhibit a linear relationship with increasing B-value and tissue signal attenuation.

Cellular tissues show less signal attenuation at higher B-values.

Log of signal intensity is plotted against B-value for vascular, free fluids, and solid tissue conditions.
DWI

HCC

b=0

b=100

b=800

ADC map

Hemangioma
Utility of Diffusion-Weighted MRI in Distinguishing Benign and Malignant Hepatic Lesions


Bachir Taouli, MD

Powered by tremendous advances in image quality over the past few years, diffusion-weighted (DW) liver parenchyma, as opposed to benign nonsolid lesions, such as liver cysts and hemangiomas, with ADC of malignant...
Improved Sensitivity by Combining Gadoxetic acid-enhanced MR Imaging and Diffusion-weighted Imaging for Detecting Small (≤ 2.0 cm) Hepatocellular Carcinoma

Park MJ, Kim YK. Radiology 2012 Sept
HCC: AP- iso / HBP- iso/ DWI-high
Categorization of HCC and benign hepatocellular nodules according to the findings on gadoxetic acid MRI and DWI

Park MJ, Kim YK. *Acta Radiol* 2013 in press
High grade dysplastic nodule
Predicting factor for progressing to Hypervascular HCC
Hypovascular hypointense nodules on hepatobiliary phase gadoxetic acid-enhanced MR images in patients with cirrhosis: Potential of diffusion-weighted imaging in helping predict progression to hypervascular HCC

Tumor characterization with Gd-EOB-DTPA & DWI
Mass-forming Cholangiocarcinoma

Kim YK. Eur Radiol. 2008
Intrahepatic Mass-forming Cholangiocarcinomas: Enhancement Patterns at Multiphasic CT, with Special Emphasis on Arterial Enhancement Pattern—Correlation with Cytology

Kim SA, Lee JM, Radiology 2011
Target sign on DWI: ICC

Park HJ, Kim YK, Abd imaging 2013 in press
Noncontrast MRI:
DWI & Blood Oxygen Level Dependent (BOLD) MRI
Hypovascular cholangiocarcinoma
Conclusion

- Combination of Gd-EOB-DTPA and DWI
  - Hemodynamic information, hepatocyte uptake, tissue diffusivity
  - Detection & characterization of HCC
    (differentiation from cholangiocarcinoma & FNH)
    D/Dx Early HCC vs Dysplastic nodule?

- Noncontrast MR protocol: DWI, BOLD
  - Alternative tool for patients with renal dysfunction
감사합니다