Update on Imaging of Focal Liver Lesions

Name: Dushyant Sahani MD
dsahani@partners.org

Objectives

1. Discuss common focal liver lesions
2. Provide the clinical perspective
3. Review the imaging of common benign and malignant lesions
4. Learn pitfalls and benefits of advanced imaging methods

Evolution of Liver Imaging

“Clinical correlation is required”

Focal Liver Lesions

Non-cirrhotic
- Hemangioma
- FNH
- Adenoma
- Biliary Hamartoma
- Metastases
- Cholangiocarcinoma
- Fibro Lamellar HCC
- Lymphoma

Cirrhotic
- RGN
- DSN
- HCC
- Cholangiocarcinoma

Clinical Perspective for Liver Lesions

- HCC: Resect/Ablate/Chemoembo/OLTx
- FL-HCC: Resect
- Mets: Resect/Chemo/IA therapy
- Adenoma: Resect/FU
- FNH: Ignore
- Hemangioma: Ignore

Liver Cancer Therapies
Liver Surgery: Considerations

- Poor prognostic factors
  - Tumor > 7 cm
  - Multiple lesions
  - Tumors involving > 2 segments
  - Requiring major hepatectomy

- Selection for liver Tx
  - Single tumor < 5 cm
  - Up to 3 lesions (< 3cm)
  - Lack of vascular invasion
  - Absence of extra-hepatic ds.

Lesion Detection and Staging

Homsi J, Garrett CR. Cancer Control 2006;13:42-47
Cohen AD, Keneny NE. Oncologist 2003;6:553-66
Marrero JA. Current opinion in Gastroenterology 2006;22:248-253

Liver Lesion Characterization

- Pijl et al (Radiology Nov '98)
  - 28 patients undergoing liver tumor surgery
  - 186 lesions: 135 malignant; 51 benign (30 hemangiomas, 19 cysts)

Case RS

- 51 yr old women who initially presented with right upper quadrant pain

Follow up

- Undergoes elective lap cholecystectomy and lap wedge resection of liver lesion in segment 4A.
- Post operative course complication by hepatic hematoma, hypotension, shock liver and acute renal failure
- Presented to ER one month after discharge with dyspnea and diaphoresis
Hepatic necrosis

- Right hepatic lobe hemorrhagic necrosis secondary to clipping of the right hepatic artery and hypotension from hematoma secondary to pseudoaneurysm.
- Pseudoaneurysm of distal branch of segment 4/middle hepatic artery

Imaging Choices For Liver Lesions

- MDCT
- MR
- US
- FDG-PET/PET-CT

Liver Cancer Therapy Clinical Desicion Making

<table>
<thead>
<tr>
<th>Tumor Burden</th>
<th>Vascular Involvement</th>
<th>Extra-hepatic Disease</th>
<th>Functional Reserve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>Arterial/portal</td>
<td>Distal metastases</td>
<td>Residual volume</td>
</tr>
<tr>
<td>Size</td>
<td>Liver resection</td>
<td>Chemotherapeutic</td>
<td>Child's weight</td>
</tr>
<tr>
<td>Location</td>
<td>Tumor involvement</td>
<td>Osteosclerotic</td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>Tumor involvement</td>
<td>Osteosclerotic</td>
<td>Residual volume</td>
</tr>
</tbody>
</table>

Why use CT for Liver Imaging?

- Assess Lesion/tumor burden
  - Number
  - Size
  - Location
  - Treatment

- Evaluate Functional Reserve
  - Future residual volume
  - Stenosis

- Evaluate Vasculature
  - Tumor involvement
  - Variations that may alter surgical resection

- Evaluate for other sites of metastases
  - May provide additional details
Benefits of MDCT for Liver Imaging

Advantages:
- Fast scan (10 sec breathhold)
- Thin section acquisitions
- Retrospective slice recon
  - Multi-phase
  - Excellent quality 3D images

CT Advantages:
Detects Aberrant Vasculature

CTA: IA Chemotherapy Pump Placement

CT Advantage: Pre-surgical planning

Monitoring Response to Chemotherapy

Conventional method of monitoring treatment response is change in tumor area

RECIST 1.0
5 Target Lesions (>1-2 cm)
5 max in all organs
Non-target lesions

RECIST 1.1
5 Target Lesions (>1 cm)
2 max in all organs
Short-axis of Lesions

WHO

Radiofrequency Ablation

CT Advantages: Treatment Response

RECIST/WHO Response Evaluation Criteria in Solid Tumors

WHO - World Health Organization
Monitoring Antiangiogenic Response: CT perfusion

Favourable Response
Drop in Blood Flow
Drop in Blood Volume


CT Disadvantage:
“Lesion Is Too Small To Characterize”

Lesions > 1.5 cm can be routinely characterized on a MDCT

Small Lesion Detection: CT vs. MR

MRI can detect lesions < 1 cm 87-92%
In fatty liver, hypovascular lesions are less conspicuous on CT

MR Advantages

- Very sensitive for liver lesion detection
- Better lesion detection if hepatic steatosis
- Advanced MR Techniques: Liver-specific (Hepatocyte) contrast agents
  - Gd-EOB-DTPA: Eovist/Primovist
  - Gd-BOPTA: Multihance

Small Lesion Detection: CT vs. MR

MRI can detect lesions < 1 cm 87-92%
In fatty liver, hypovascular lesions are less conspicuous on CT

CRC Restaging Post Chemotherapy
Liver Metastases: CT vs. MR

<table>
<thead>
<tr>
<th>Studies</th>
<th>CT</th>
<th>MR</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1 cm</td>
<td>91/128 (71%)</td>
<td>115/128 (90%)</td>
</tr>
<tr>
<td>&lt; 1 cm</td>
<td>17/47 (38%)</td>
<td>39/47 (83%)</td>
</tr>
</tbody>
</table>

Bartolozzi et al, Radiology 2004

Hemangioma: CECT

MRI & MRCP

- Evaluate the bile ducts both above and below a stricture
- Also identifying any intrahepatic mass lesions
- Sensitivity 86-100 % for defining stenosis and the level of obstruction.

Adamek HE. 1998 GUT 43:680-683

Clinical and MR Considerations

- Demographics and clinical hx
- Enhancement patterns
- Other MR features
  - Signal intensity
  - Margins
  - Central Scar
  - Lipid
  - Hemorrhage
  - Vascular invasion

Approach to focal liver lesion

Look for Characteristic Features

Common benign lesions
- Hemangioma
- FNH
- Adenoma

Malignant Lesions
- Heterogeneity
- Wash-out
- Capsule Retraction
- Vascular invasion
- Biliary obstruction
**Suspicious Features**
(non FNH/Hemangioma) or Malignant

- Heterogeneity
- Wash-out
- Hemorrhage
- Capsular Retraction
- Bilary Obstruction
- Vascular Encasement/Invasion

**Hemangioma: MRI**

- T2WI
- Arterial
- Portal
- Equilibrium

**Hemangioma - MR**

- sensitivity
- specificity

- > 95%

- heavily T2-weighted images
- Dynamic CE-MRI

**Hemangioma - Pathology**

- Capillary
- Cavernous
- Sclerosing
- Sclerosed

**Focal Nodular Hyperplasia: Gd-DTPA MRI**

- T2WI
- Arterial Phase
- Portal Venous
- Equilibrium Phase

**Focal Nodular Hyperplasia**

**MR criteria (7):**

- homogeneous lesion (except scar)
- iso/slightly hyperintense on T2-WI
- hyperintense scar on T2-WI
- high enhancement at the arterial phase (gd chelates)
- delayed enhancement of the scar on T1-WI
- absence of capsule
**Focal Nodular Hyperplasia**

- Characterization
  - Sensitivity: 74%
  - Specificity: 100%


---

**Hepatocellular Adenoma**

- Intra-Lesion Hemorrhage

---

**Hepatocellular Adenoma: MR**

- 50-60% of hepatocellular adenomas are hyperintense on T1-WI
  - Fat accumulation
  - Hemorrhage
  - Sinusoidal dilatation or peliosis


---

**Adeomatosis: Intratumoral fat**

- Young women 30-50 yrs
- OCP or men anabolic steroids
- Benign hepatocellular lesion with capsule
- Risk of bleeding for > 4 cm lesion
- Multiple: Adenomatosis

---

**FNH Vs. Adenoma: MRI Features**

**Supporting FNH**
- Scar
- Homogenous enhancement

**Supporting Adenoma**
- Lipid (OP drop in SI)
- Hemorrhage
- Capsule

When in doubt, use of hepatobiliary MR contrast agent.
Tissue Characterization: Morphologic Overlap (Central Scar)

- FLC
- FNH
- HCC
- Metastasis
- Carcinoid
- Hemangioma

Hepatobiliary Contrast Agents

<table>
<thead>
<tr>
<th>Properties</th>
<th>MnDPDP (Teslascan)</th>
<th>Gd-BOPTA (Multihance)</th>
<th>Gd-EOB-DTPA (Eovist)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dynamic</td>
<td>++</td>
<td>+++</td>
<td>++</td>
</tr>
<tr>
<td>H-B phase</td>
<td>+++ = &gt;10 min-hours</td>
<td>+++ = &gt; 60 min-2 hrs</td>
<td>+++ = &lt;10 min-hrs</td>
</tr>
<tr>
<td>Biliary Excretion</td>
<td>50%</td>
<td>6%</td>
<td>50%</td>
</tr>
<tr>
<td>FDA Approved</td>
<td>PULLED OUT</td>
<td>Approved in US and EU</td>
<td>Approved in US and EU</td>
</tr>
<tr>
<td>Examples</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Tissue Characterization: H-B MR Contrast Agents


Multiple FNH's

Gd-BOPTA- Liver Adenoma
EOB-MR: FNH and Adenoma

5 minutes

10 minutes

Fibrolamellar HCC

• Young age 30-50
• No cirrhosis
• Pathology
  • Heterogeneous lesion
  • Necrosis and hemorrhage
  • Fibrous/Calcified central scar
  • Nodes

Fibrolamellar HCC

• CT
  • Heterogeneous lesion
  • Calcified central scar

Fibrolamellar HCC

• MR
  • Heterogeneous lesion
  • Hypointense central scar on T2 WI

Fibrolamellar HCC

FNH Vs. FL-HCC: MRI Features

Supporting FNH
  • Scar-T2 Bright/delayed ++
  • Lesion homogenous +++

Supporting Adenoma
  • Scar-T2 Dark/delayed-
  • Lesion heterogeneous
  • Enlarged LN
### HB-MR and Liver Lesion

<table>
<thead>
<tr>
<th>Dynamic</th>
<th>(HB phase)</th>
<th>Other Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyst</td>
<td>No enhancement</td>
<td>—</td>
</tr>
<tr>
<td>Metastasis</td>
<td>Hypo/hyper ++</td>
<td>—</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>Usually characteristic peripheral nodular enhancement with centripetal progression</td>
<td>—</td>
</tr>
<tr>
<td>Adenoma</td>
<td>Hypervascular, but often not as vividly enhancing as FNH</td>
<td>—</td>
</tr>
<tr>
<td>FNH</td>
<td>Hypervascular to liver on PV phase</td>
<td>—</td>
</tr>
</tbody>
</table>
| FL-HCC  | Heterogeneous variable enhancement | Commonly have a T1 and T2 hypointense, non-enhancing central scar.

### MR: Diffusion Weighted Imaging (DWI)

* Uses of DWI:
  - Tissue Characterization:
    - Lesion Detection
    - Lesion characterization
    - Malignant tumors show restricted diffusion
  - Functional Evaluation
    - Biomarker of tumor treatment response

### Advanced MR Techniques: Diffusion Weighted Imaging

- **Metastases**
- **HCC**
- **Cholangiocarcinoma**

### Primary Malignant Tumors

- **HCC**
- **Fibrolamellar HCC**
- **Cholangiocarcinoma**

### Malignant Transformation In Cirrhosis

14-38% of cirrhotic liver have DNs

DN is a premalignant lesion and a target for HCC prevention

*Courtesy: Glenn Krinsky NYU*
Cirrhotic Nodules: Blood Supply

- portal vein
- hepatic artery

Cirrhosis: Nodules

Dysplastic Nodule

T1W T2W Dynamic

HCC Arising in DN

T2 HAP
Progression from DN to HCC over 6 months 2002 with NIN

HCC in Cirrhotic Liver: Spectrum

- Imaging appearance depends
  - size of the lesion
  - patterns of growth of HCC
  - tumor biology/angiogenesis

HCC screening: CT Vs. MR

Small Lesions
Detection of HCC in Cirrhosis

Explant correlation

<table>
<thead>
<tr>
<th>CT</th>
<th>CT*</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>71% (15/21)</td>
<td>37% (30/82)</td>
<td>53% (11/19)</td>
</tr>
<tr>
<td>&lt;2cm 62%</td>
<td>Detected 24 mm</td>
<td>&gt;2cm 33%</td>
</tr>
<tr>
<td>2-5 cm 52%</td>
<td>Undetected 13 mm</td>
<td>1-2 cm 50%</td>
</tr>
</tbody>
</table>

Mean size

Detects     Undetected

Detection of HCC in Cirrhosis with new Tx criteria of lesion >2cm size

Recent studies showing MR accuracy >70%.
False +ve and False-ve reduced with the new Tx criteria of lesion >2cm size.

95% HCC are hypointense in H-B phase

At risk nodule for HCC development

95% HCC are hypointense in H-B phase

At risk nodule for HCC development

Detection of HCC in Cirrhosis

Explant correlation

<table>
<thead>
<tr>
<th>CT</th>
<th>CT*</th>
<th>MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>71% (15/21)</td>
<td>37% (30/82)</td>
<td>53% (11/19)</td>
</tr>
<tr>
<td>&lt;2cm 62%</td>
<td>Detected 24 mm</td>
<td>&gt;2cm 33%</td>
</tr>
<tr>
<td>2-5 cm 52%</td>
<td>Undetected 13 mm</td>
<td>1-2 cm 50%</td>
</tr>
</tbody>
</table>

Mean size

Detection of HCC in Cirrhosis with new Tx criteria of lesion >2cm size

Recent studies showing MR accuracy >70%.
False +ve and False-ve reduced with the new Tx criteria of lesion >2cm size.

95% HCC are hypointense in H-B phase

At risk nodule for HCC development

95% HCC are hypointense in H-B phase

At risk nodule for HCC development

Hypothetical mechanism of gadoxetic acid accumulation in HCC.
Improved HCC Detection

- 59 patients with 84 HCCs
- EOB-enhanced MR imaging
  - 1.5-T in 19 and a 3.0-T system in 40 patients
- For all observers, A(z) values were higher with HB-phase MR.
- HB-phase MR improved performance of least experienced reader (2 years) A(z), from 0.895 in set 1 to 0.951 (P = .049).
- Nine HCCs (10.7%) in six patients (10.1%) were seen only on HB-phase images.

HB-MR and Cirrhotic Nodules

<table>
<thead>
<tr>
<th>Lesion</th>
<th>T1</th>
<th>T2</th>
<th>Dynamic</th>
<th>HB-Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>RM</td>
<td>Iso-Hyper</td>
<td>Non- Hypointense</td>
<td>Enhance in PV phase</td>
<td>++</td>
</tr>
<tr>
<td>RM-DNM</td>
<td>Often hyper</td>
<td>Non-Hypointense</td>
<td>Enhance in PV phase</td>
<td>++</td>
</tr>
<tr>
<td>RM-DNM</td>
<td>Variable</td>
<td>Mottly hyper</td>
<td>++</td>
<td>+/-</td>
</tr>
<tr>
<td>RM-DNM</td>
<td>Variable</td>
<td>Hypointense</td>
<td>In arterial phase</td>
<td>+/-</td>
</tr>
<tr>
<td>WD-HCC</td>
<td>Usually Hypointense</td>
<td>Diffuse</td>
<td>Hypointense in arterial phase</td>
<td>++/?</td>
</tr>
<tr>
<td>WD-HCC</td>
<td>Heterogeneous</td>
<td>Variable</td>
<td>In arterial phase</td>
<td>+/-?</td>
</tr>
<tr>
<td>WD-HCC</td>
<td>Heterogeneous</td>
<td>Variable</td>
<td>In arterial phase</td>
<td>+/-</td>
</tr>
</tbody>
</table>

Cholangio Carcinoma

Rare - 3000 deaths USA 2002 vs. 16,600 HCC

- 60%-65% at hilar bifurcation
- 20-30% at distal CBD
- 10-15% in the liver
- 5% multi-focal

CC Features

- Desmoplastic tumor
  - Cellule retraction
  - Vascular encasement
  - Delayed enhancement

CC Features

- Desmoplastic tumor
  - Few hrs post
Liver Mets: MR vs. FDG-PET

<table>
<thead>
<tr>
<th>PET Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions &gt; 2 cm: 100%</td>
</tr>
<tr>
<td>30-60% lesions &lt; 1 cm</td>
</tr>
<tr>
<td>Post-ChemoTx: 63% overall sensitivity</td>
</tr>
</tbody>
</table>

Lesions: 65 Metastases: 88
Lesions <1cm: 12 Lesions <1cm: 33

PET Sensitivity

<table>
<thead>
<tr>
<th>PET Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesions &gt; 2 cm: 100%</td>
</tr>
<tr>
<td>30-60% lesions &lt; 1 cm</td>
</tr>
<tr>
<td>Post-ChemoTx: 63% overall sensitivity</td>
</tr>
</tbody>
</table>

Lesions: 65 Metastases: 88
Lesions <1cm: 12 Lesions <1cm: 33

Image Guided Biopsy of < 3 cm
Lesions: Accuracy > 95% (MGH Data)

Ma X et al. JVIR (2010)

Summary

• CE-MRI is a highly accurate for liver lesion characterization
  • Liver specific contrast agents and DWI has further empowered MR
  • Recognition of imaging features typical of a benign lesion is most crucial
  • Role of PET/PET-CT is evolving
    • Extrahepatic disease
    • Problem Solving
  • Image guided FLL biopsy is safe and highly accurate

Approach to focal liver lesion

Look for Characteristic Features

Common benign lesions
- Hemangioma
- FNH
- Adenoma

Malignant Lesions
- Heterogeneity
- Wash-out
- Capsule Retraction
- Vascular invasion
- Biliary obstruction
Suspicious Features (non FNH/Hemangioma) or Malignant

- Heterogeneity
- Wash-out
- Hemorrhage
- Capsular Retraction
- Biliary Obstruction
- Vascular Encasement/Invasion

Summary

- Advances in CT and MR technique
  - Improved HCC detection
  - Candidate selection for optimal therapy
- Dynamic HAP imaging with CT and MR is essential for best results.
- Screening strategy and choice of imaging dependent on local expertise
  - Dynamic MR best for small lesion detection and characterization