Innovations in HCC Imaging: MDCT/MRI

Anthony E. Cheng, M.D.
Cardinal MRI Center
Cardinal Santos Medical Center, Wilson Street, San Juan
Innovations in HCC Imaging: MDCT/MRI

- Goals/Objectives
  - Learn the diagnostic criteria for HCC by CT and MRI
  - Discuss the accuracy of CT and MRI for diagnosing HCC
  - Review recent advances in CT and MRI that help detect HCC at the earlier stages
Hepatocellular Carcinoma (HCC)

- Incidence of HCC is rising as a result of hepatitis infections and cirrhosis
  - Patients with cirrhosis from chronic HBV/HCV
    - 5-year cumulative risk of developing HCC: 15-30%
  - Curative treatment (surgical or ablative) depends on diagnosing HCC in the early stages
  - Screening for HCC
    - Serum alpha-fetoprotein (AFP) levels and ultrasound every 6 months
    - CT and MRI are not routinely used for screening
Hepatocellular Carcinoma (HCC)

• Biopsy is no longer needed to diagnose HCC
  – American Association for the Study of Liver Diseases (AASLD) guideline for 2010
    • Any nodule larger than 1 cm that demonstrates the *typical vascular pattern* on dynamic contrast-enhanced CT or MRI, can be considered and treated as HCC without biopsy
    • In the presence of atypical findings, further assessment with the other imaging modality (CT or MRI) is recommended. If still atypical, then biopsy is advised.
Hepatocellular Carcinoma (HCC)

• Biopsy is no longer needed to diagnose HCC
  – European Association for the Study of the Liver (EASL) guideline in 2012
    • Any nodule $\geq 1$ cm that demonstrates the *typical vascular pattern* on dynamic contrast-enhanced CT or MRI, can be considered and treated as HCC without biopsy
    • In the presence of atypical findings, biopsy is advised.
Hepatocellular Carcinoma (HCC)

- Biopsy is no longer needed to diagnose HCC
  - Asia-Pacific Association for the Study of the Liver (APASL) guideline in 2010
    - A nodule regardless of size, demonstrating the typical vascular pattern on 4-phase MDCT or dynamic MRI, can be considered HCC without biopsy
    - In the presence of atypical findings, further examinations should be performed
      - SPIO MRI or contrast-enhanced US (CEUS)
Detection of HCC – requires *dynamic* study using extracellular contrast material (ECCM)

**Dynamic MDCT Protocol**
- Non-enhanced Phase
- Tri-phasic contrast study
  - Arterial Phase (20-30s)
  - Venous Phase (~60-80s)
  - Delayed Phase (120-180s)

**Dynamic MRI Protocol**
- Non-enhanced sequences
  - T1, T2, Fat-suppression, DWI
- Tri-phasic contrast study
  - Arterial Phase (20-30s)
  - Venous Phase (~60-80s)
  - Delayed Phase (120-180s)
HCC – Imaging Criteria by CT and MRI

• Diagnosis by CT and MRI is based on the vascular pattern of HCC
  – Arterial phase
    • Early enhancement (hypervascularity)
    • HCC receives vascular supply mainly from Hepatic A.
  – Venous or delayed phases
    • Contrast wash-out
    • Decreased portal flow
  – Both combined: high specificity and PPV (>90%)
HCC (16 slice MDCT, 3 mm)

Arterial Phase  Venous Phase  Delayed Phase

HCC – typical vascular pattern

*Enhancement* on arterial phase
*Wash-out* on venous/delayed phase

(Ronzoni et al)
US – hypoechoic nodule, MDCT – HCC

Arterial Phase  Venous Phase  Delayed Phase

(Lee JM et al)
MRI – HCC

HCC – typical vascular pattern

*Enhancement* on arterial phase

*Wash-out* on venous/delayed phase
MRI – HCC

Pre-contrast

Arterial Phase

Enhancement on arterial phase

Venous Phase

Delayed Phase

Wash-out on venous/delayed phase
Detection of HCC

**MDCT Advantages**
- Higher spatial resolution
- Much shorter scan time
  - Less motion
- Thin slices (3D recon.)

**MRI Advantages**
- Better soft tissue-contrast
  - Normal vs. abnormal tissue
- Able to provide functional information
  - Diffusion-weighted imaging (DWI)
  - Hepatocyte-specific contrast agents
- Higher ability to detect and characterize focal liver lesions
73 y.o. with progressive weight loss referred for MRI (negative CT done at outside facility)

**MRI:** Better soft tissue-contrast

Post-contrast CT

**Surgically confirmed HCC**

Pre-contrast T1  Arterial Phase  Venous Phase
A significant number of tumors equilibrate by the venous phase examination (60sec)

- These lesions may only be visible transiently during arterial phase imaging (20-30sec)
- Easily missed on non-dynamic CT
  - Non-arterial phase imaging is inadequate for tumor screening/detection
Accuracy of MDCT and MRI for HCC

• Wide range of sensitivities reported for both techniques, ranging from 60-90%
  – Conclusions derived from recent papers
    • Latest MDCT and MRI systems have similar overall detection rates for HCC using standard contrast agents (extracellular contrast material)
    • Size of HCC lesions is an important factor
      – For small lesions (< 20 mm), MRI is superior to CT
MDCT and MRI, vs. Ultrasound for HCC

- Yu NC et al. February 2011
  - UCLA publication comparing sensitivities of conventional US, CT and MRI for HCC
  - 638 patients with cirrhosis
  - Patients received liver transplants within 6 months of diagnostic imaging
    - 35% (225) had path-proven HCC
    - Overall sensitivities – 46%(US), 65%(CT), 72%(MRI)
    - Small (< 2 cm) HCCs – 21%(US), 40%(CT), 47%(MRI)
Small HCCs

- Small HCCs more difficult to diagnose
- Atypical enhancement pattern often seen in “early” HCCs
  - Lesions smaller than 20 mm in size
    - 41-62% show either absence of arterial hypervascularity, venous wash-out, or both
  - Well-differentiated HCC
    - Majority show either absence of arterial hypervascularity, venous wash-out, or both

(Song et al)
Early HCC – Atypical Enhancement (MRI)

No arterial hypervascularity
*Wash-out* on venous phase

Biopsy:
*Well-differentiated HCC*

(Tan CH et al)

CARDINAL MRI CENTER
Early HCC – Hypovascular Pattern (MDCT)

Arterial Phase

Venous Phase

Delayed Phase

(Ronzoni et al)
Small HCC – visualized on MRI, not CT

Arterial Phase

Venous Phase

(Pitton et al)
Recent Advances in MDCT and MRI

• New techniques have been introduced to improve the sensitivity of diagnosing small HCCs
  – MDCT: Improve the detection of small amounts of iodine
    • Low-peak-tube voltage (kVp) CT
    • Dual-energy CT
  – MRI: Obtain functional/cellular information
    • Diffusion-Weighted Imaging (DWI)
    • Liver-specific contrast agents
Small HCC: low-tube-voltage CT

Arterial Phase (80-kVp)
Venous Phase (120-kVp)

Dynamic CT: 120-kVp standard
Low-tube-voltage CT: 80-kVp
Higher sensitivity to detect iodinated contrast

(Lee JM et al)
Small HCC: dual-energy CT

140-kVp
Dynamic CT: 120-kVp standard
Low-tube-voltage CT: 80-kVp
Higher sensitivity to detect iodinated contrast
Increased noise

80-kVp

120-kVp (blended image)

(Lee JM et al)
MRI: Diffusion-Weighted Imaging (DWI)

- Non-invasive way of quantifying water diffusion in tissues
  - No contrast required
- Widely used in neuroradiology
  - Acute stroke
  - Tumor grading (research centers)
    - High cellularity in malignancy restricts mobility of protons
      - Decreased ADC (apparent diffusion coefficient)
      - High signal on DWI
Diffusion-Weighted Imaging (DWI)

- Abdominal imaging: applications
  - Improve detection rate of focal liver lesions
    - Malignant lesions (HCC, metastasis) have lower ADC values compared to benign lesions (cysts, hemangiomas)
      - Bright on DWI: restricted diffusion
  - Monitor early response to therapy of tumors
    - Cell necrosis causes increased membrane permeability
      - Less restriction of water diffusion
      - Increased ADC
DWI: HCC’s

Case 1

Case 2

Diffuse Multifocal HCC with portal vein, splenic vein and SMV thrombosis

Bright = restricted diffusion
Standard MRI sequences: subtle small metastatic lesions

Diffusion-weighted image: many more small metastases seen

(Low RN et al)
Early HCC – Atypical Enhancement on MRI

Arterial Phase
No arterial hypervascularity

Venous Phase
Wash-out on venous phase

Diffusion-weighted image (DWI)
Restricted diffusion

Biopsy:
Well-differentiated HCC

(Tan CH et al)
CARDINAL MRI CENTER
MRI: Liver-specific contrast agents

• Hepatobiliary agents target *hepatocytes*
  – Gadoxetate acid (Gd-EOB-DTPA, Primovist)
  – Gadobenate dimeglumine (Gd-BOPTA, Multihance)

• Reticuloendothelial agents target *Kupffer cells*
  – Super paramagnetic iron oxides (SPIO):
    • Ferucarbotran (Resovist) and Ferumoxide (Feridex)
    • Usage has fallen out of favor
Gadoxetic acid (Primovist/Eovist, Bayer)

- Administered as a rapid bolus to obtain vascular information (same as extracellular contrast agents)
  - 50% taken up by functioning hepatocytes and subsequently excreted into bile
  - Uptake by hepatocytes peaks at 20 minutes
    - Acquire hepatobiliary phase images
Gadoxetic acid (Primovist/Eovist, Bayer)

• Malignant lesions
  – No contrast uptake (no functioning hepatocytes)
  – Metastases, CholangiocA and most HCCs

• Uptake seen in focal liver lesions containing functioning hepatocytes
  – FNH
  – Adenoma
  – Regenerative/dysplastic nodules
  – Well-differentiated HCC
Hepatobiliary Phase Imaging (Primovist) – HCC

ECCM

Primovist

Arterial 30-60 sec
Portal venous 60-90sec
Equilibrium 2-5mins
Hepatocyte 10-20min
Primovist: Metastases

Precontrast T1  
Hepatobiliary Phase (20 mins)

Metastases – no uptake of Primovist  
More metastatic lesions detected
Hepatobiliary Phase Imaging (Primovist)
Poorly differentiated HCC

T2-W

T1-weighted

Arterial Phase

Hepatobiliary Phase

CARDINAL MRI CENTER
Hepatobiliary Phase Imaging (Primovist)  
Cirrhosis and HCC

- Majority of HCCs do not contain significant hepatocytes  
  - Will not take up Primovist
- Regenerative and dysplastic nodules contain hepatocytes  
  - Will take up Primovist

- **Well differentiated HCC can also take up Primovist**
Not all hepatocyte containing lesions are benign! – Well-differentiated HCC
Gadoxetic acid (Primovist/Eovist, Bayer)

- Incremental value of additional hepatocyte phase imaging to dynamic CE-MRI
  - Increased liver-to-lesion contrast for lesions not containing functioning hepatocytes
    - HCC
    - Metastasis
  - Studies show gadoxetic acid-enhanced MRI adds ~10-15% to the sensitivity of routine MRI
Small HCC seen only on hepatobiliary phase

Dynamic MDCT

Dynamic MRI

Primovist

Golfieri R et al

CARDINAL MRI CENTER
Gadoxetic-acid and DWI

- September 2012 – Radiology
  - *Small HCCs: Improved Sensitivity by Combining Gadoxetic Acid-enhanced MRI and DWI*
  - Park MJ et al. Samsung Medical Center
  - 179 surgically confirmed small HCCs (< 20 mm)
  - Detection rate
    - Gadoxetic-acid (Primovist) alone: 80.5-82.1%
    - Diffusion-weighted imaging alone: 77.7-79.9%
    - Combined Primovist and DWI: 91.1 to 93.3%
Summary

• Diagnostic criteria for HCC by MDCT/MRI
  – Based on the vascular pattern of HCC
    • Early arterial enhancement
    • Venous or delayed phase wash-out
    • High specificity
  – Dynamic contrast-enhanced study (4-phase) is essential
Summary

- Accuracy of dynamic MDCT and MRI for HCC detection
  - High sensitivity for lesions > 2 cm
  - Low sensitivity for detecting small (1-2 cm) HCCs
- Negative predictive value of 42-50%
  - Atypical enhancement pattern
- Recent developments improve detection rate to 78-90%
  - Diffusion-weighted imaging (DWI)
  - Liver-specific contrast agents (Primovist)
References

- Ronzoni A et al. Role of MDCT in the Diagnosis of HCC in Pts with Cirrhosis Undergoing Orthotopic Liver Transplantation. AJR (2007) 189: 792-798
Thank you

Anthony E. Cheng, M.D.
Cardinal MRI Center
Cardinal Santos Medical Center, Wilson Street, San Juan