Innovations in HCC Imaging: MDCT/MRI

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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)

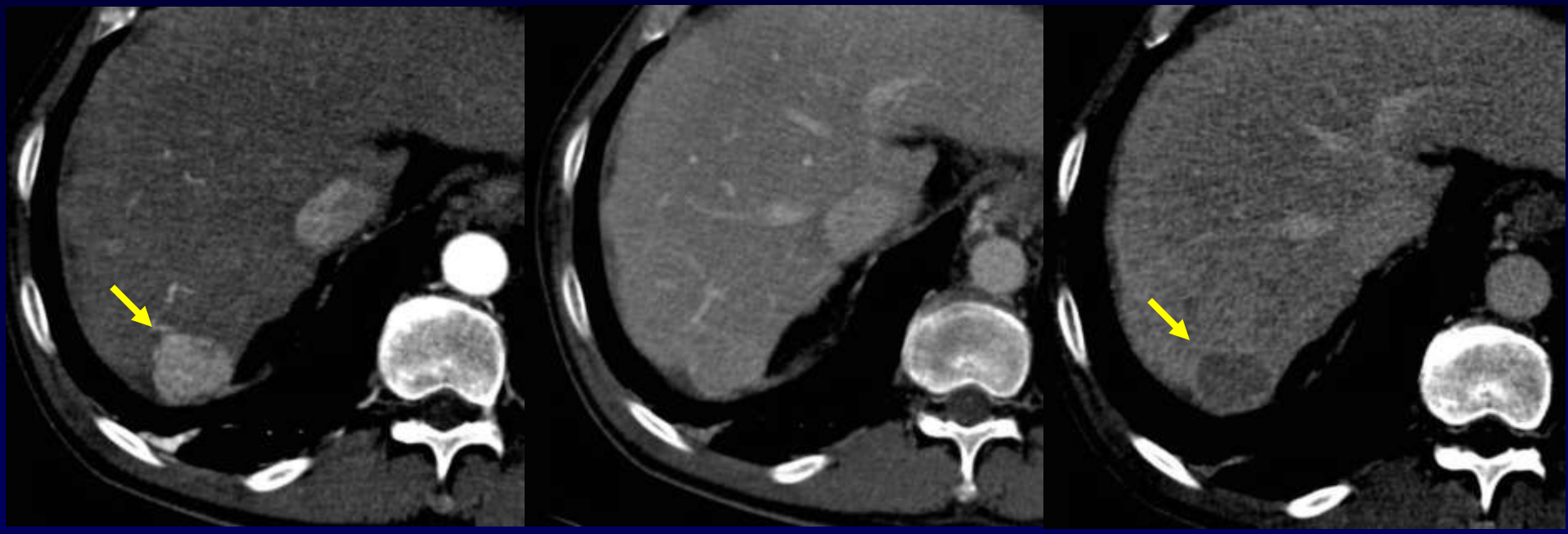
Dynamic MRI Protocol

- 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

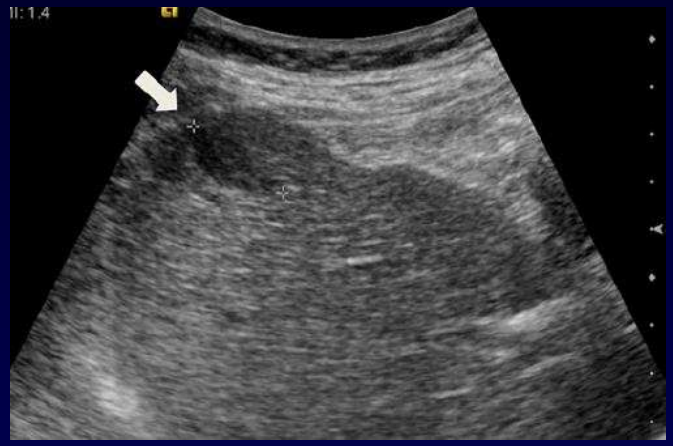
HCC – typical vascular pattern

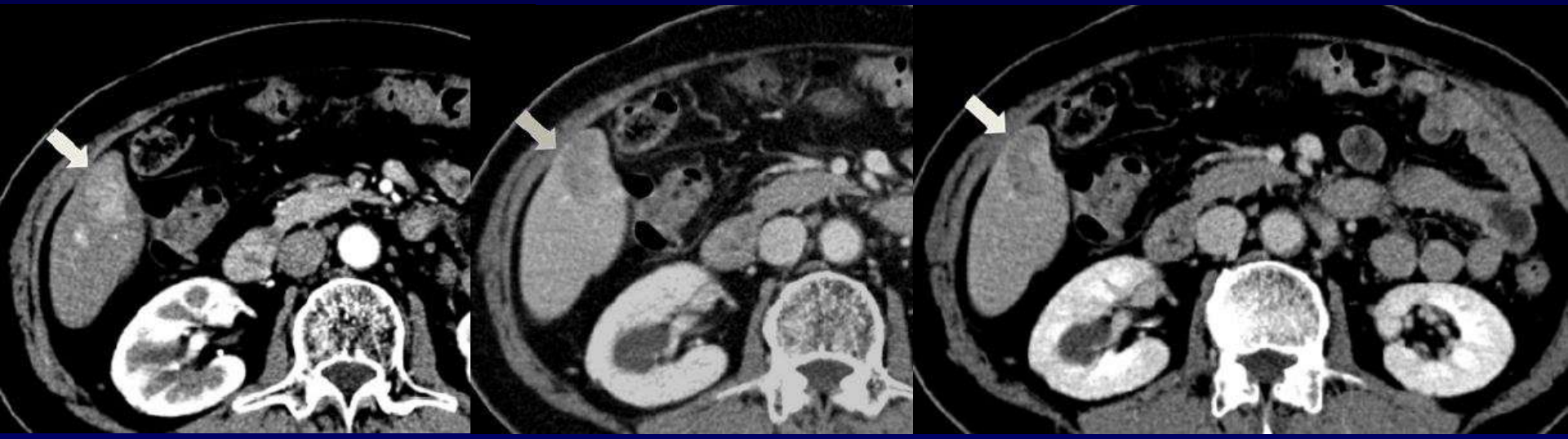
Enhancement on arterial phase

Wash-out on venous/delayed phase

(Ronzoni et al)

US – hypoechoic nodule, MDCT – HCC

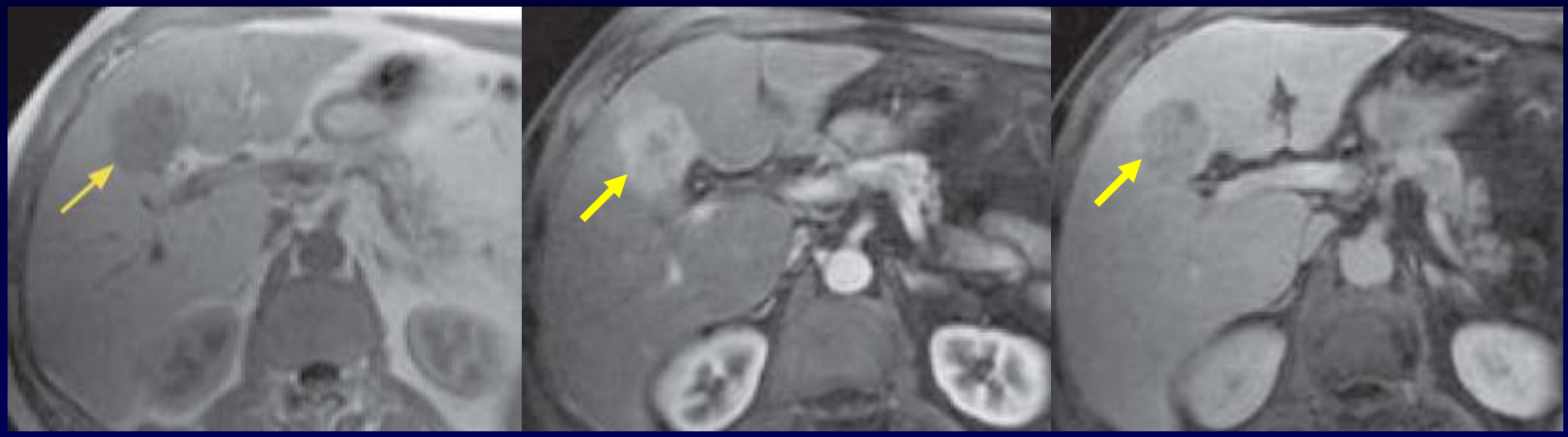




Arterial Phase Venous Phase Delayed Phase

(Lee JM et al)

MRI – HCC



Pre-contrast | Arterial Phase | Venous Phase

HCC – typical vascular pattern

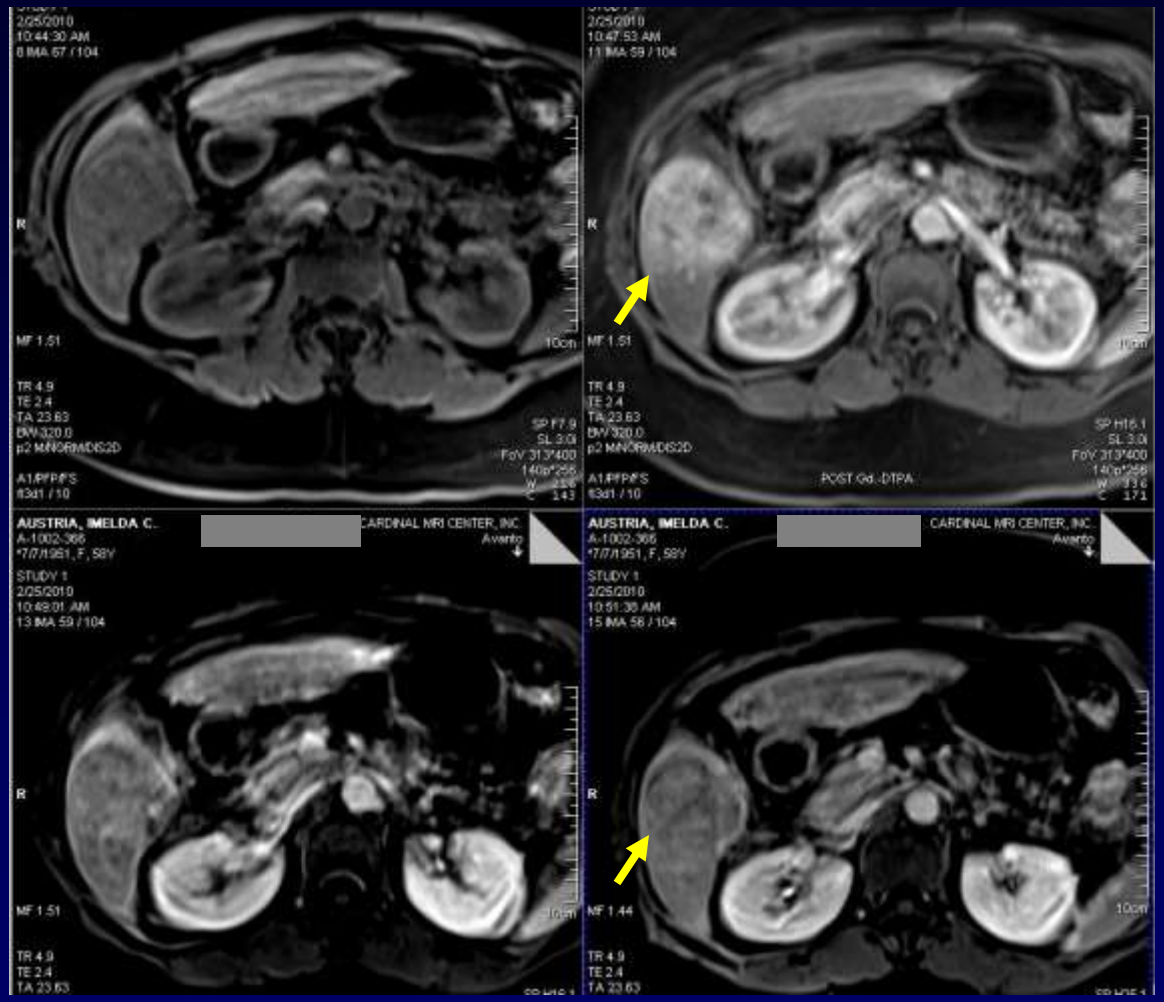
Enhancement on arterial phase

Wash-out on venous/delayed phase

MRI – HCC

Pre-contrast

Arterial Phase



Venous Phase

Delayed Phase

Enhancement on arterial phase

Wash-out on venous/delayed phase

CARDINAL MRI CENTER

Detection of HCC

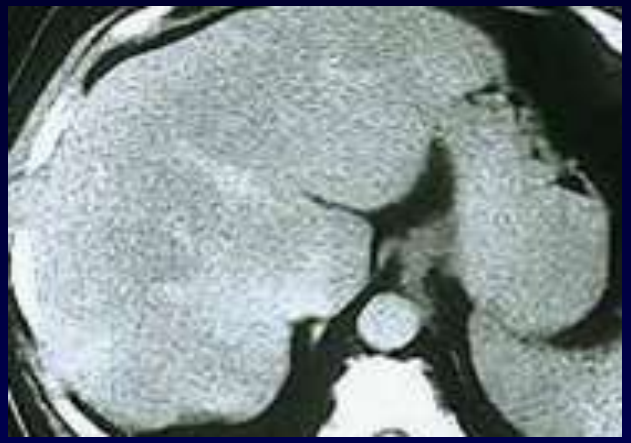
MDCT Advantages

- 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

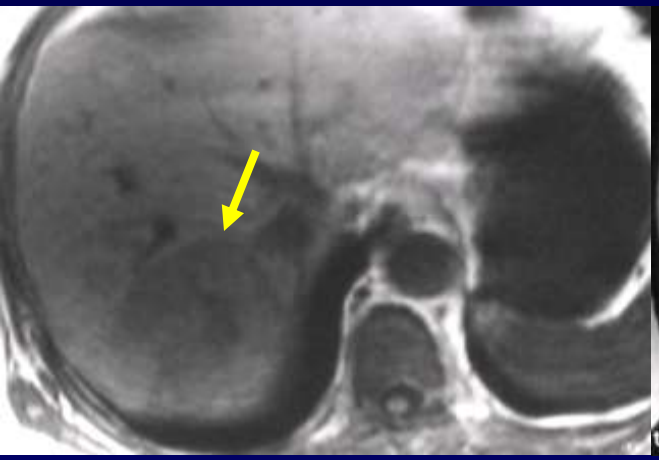
73 y.o. with progressive weight loss referred for MRI (negative CT done at outside facility)



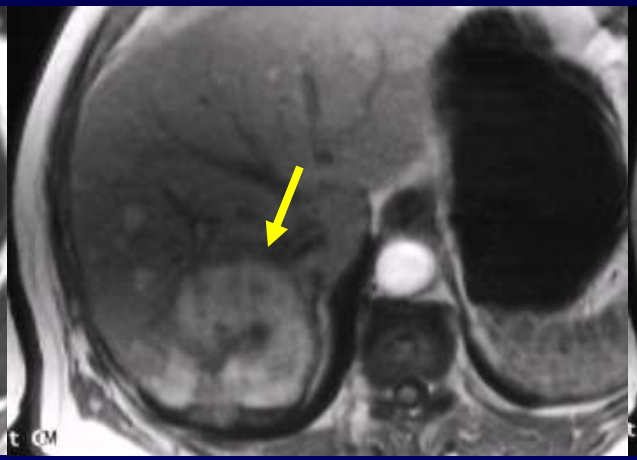
Post-contrast CT

MRI: Better soft tissue-contrast

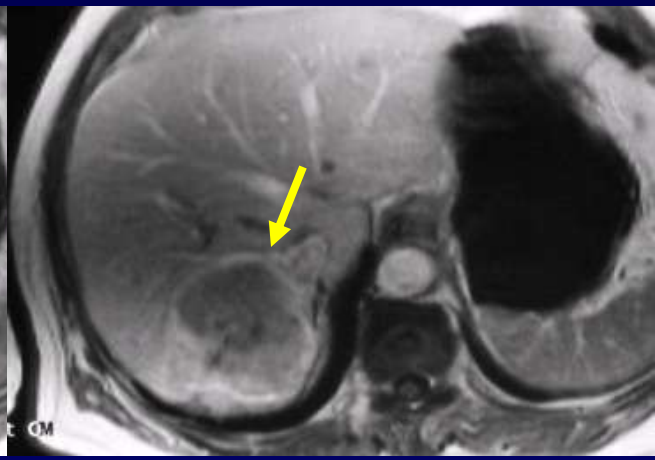
Surgically confirmed HCC



Pre-contrast T1



Arterial Phase

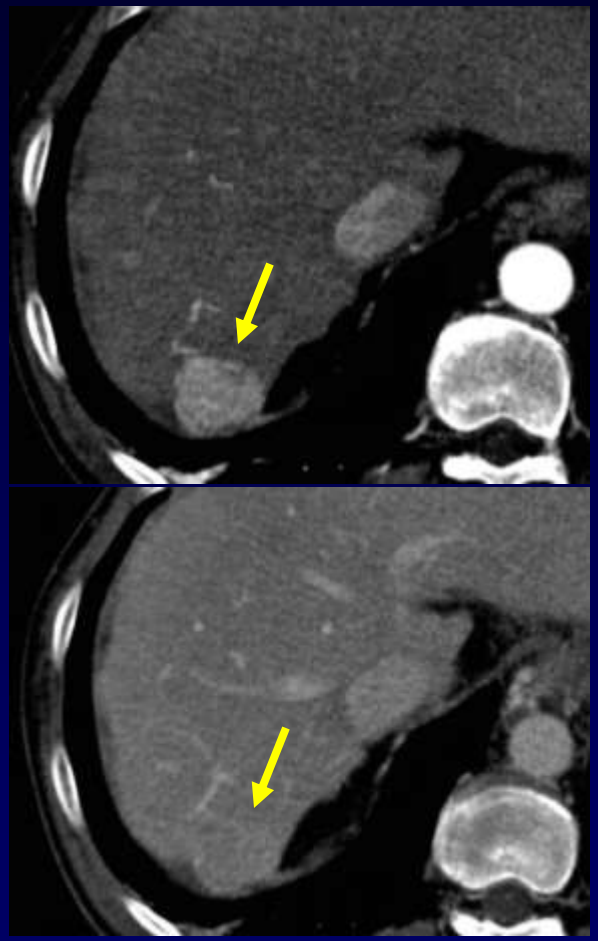


Venous Phase

CARDINAL MRI CENTER

CT and MRI

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 sytems 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

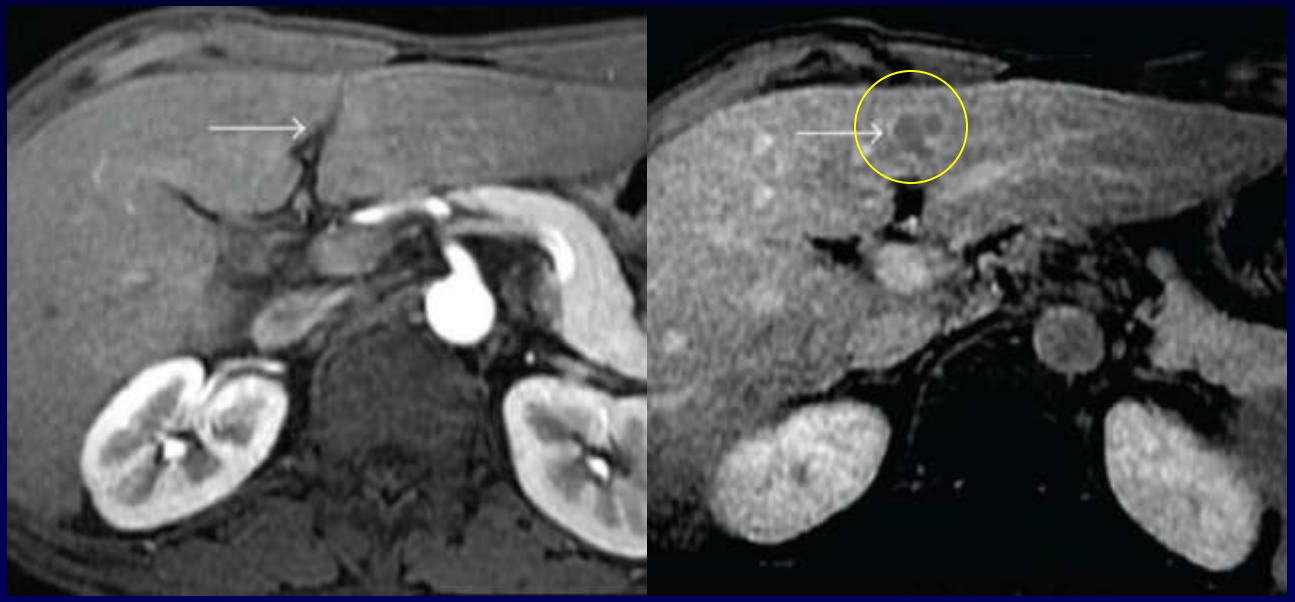
- Yu NC et al. February 2011
  - UCLA publication comparing sensitivities of conventional US, CT and MRI for HCC
  - 638 patients with cirrhosis
  - Patients received liver transplants within 6 months of diagnostic imaging
    - 35% (225) had path-proven HCC
    - Overall sensitivities – 46%(US), 65%(CT),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



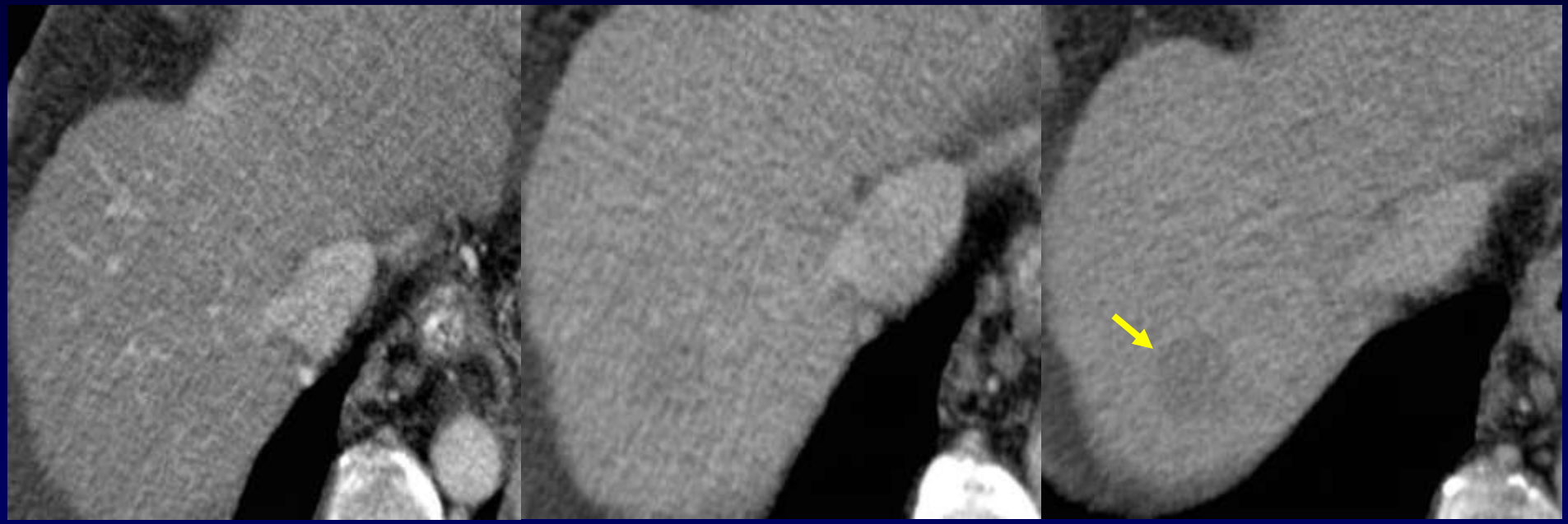
Arterial Phase

Venous Phase

No arterial hypervascularity
Wash-out on venous phase → Biopsy:
Well-differentiated HCC

(Tan CH et al)

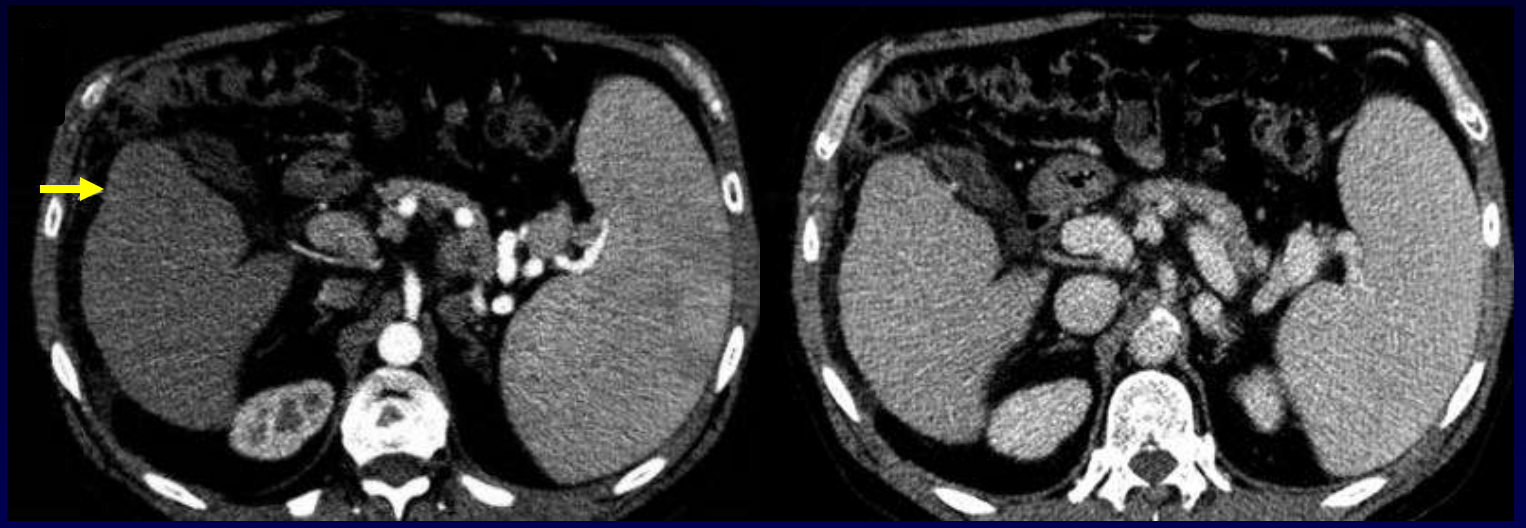
Early HCC – Hypovascular Pattern (MDCT)



Arterial Phase | Venous Phase | Delayed Phase

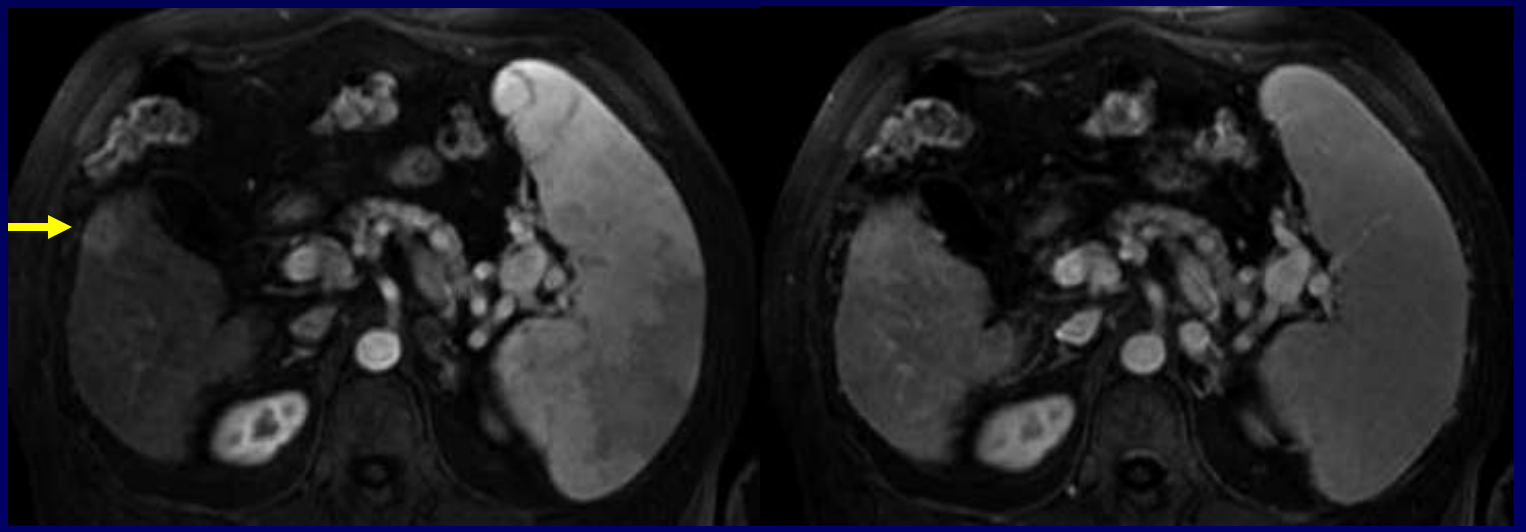
(Ronzoni et al)

Small HCC – visualized on MRI, not CT



Arterial Phase

Venous Phase

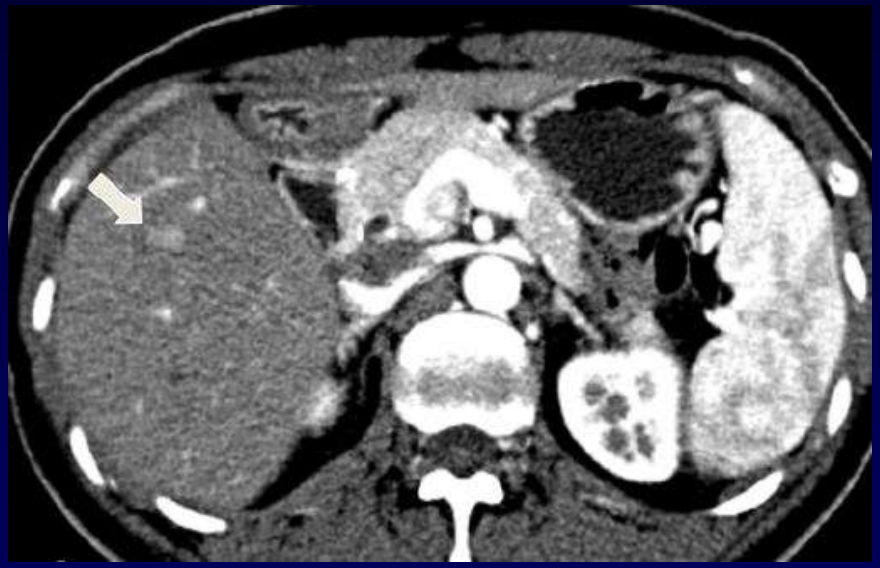


(Pitton et al)

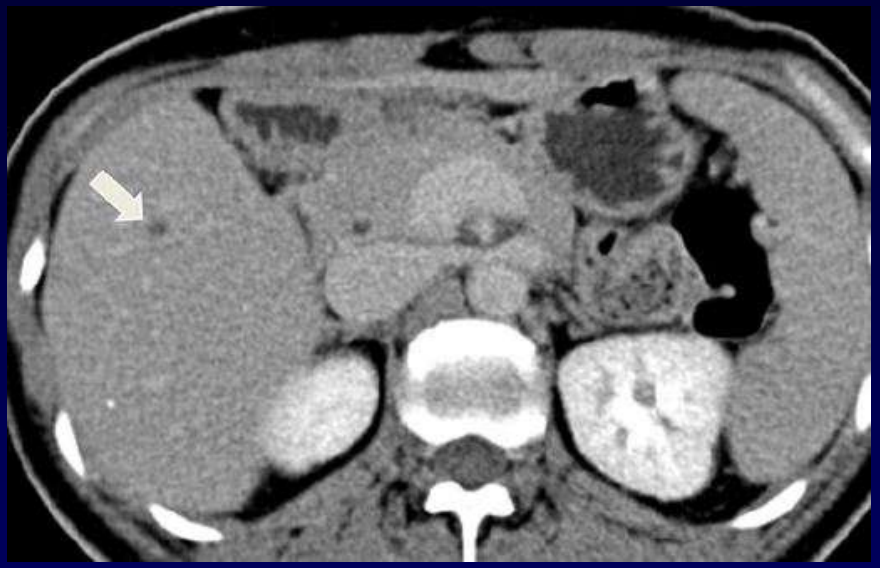
Recent Advances in MDCT and MRI

- 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)

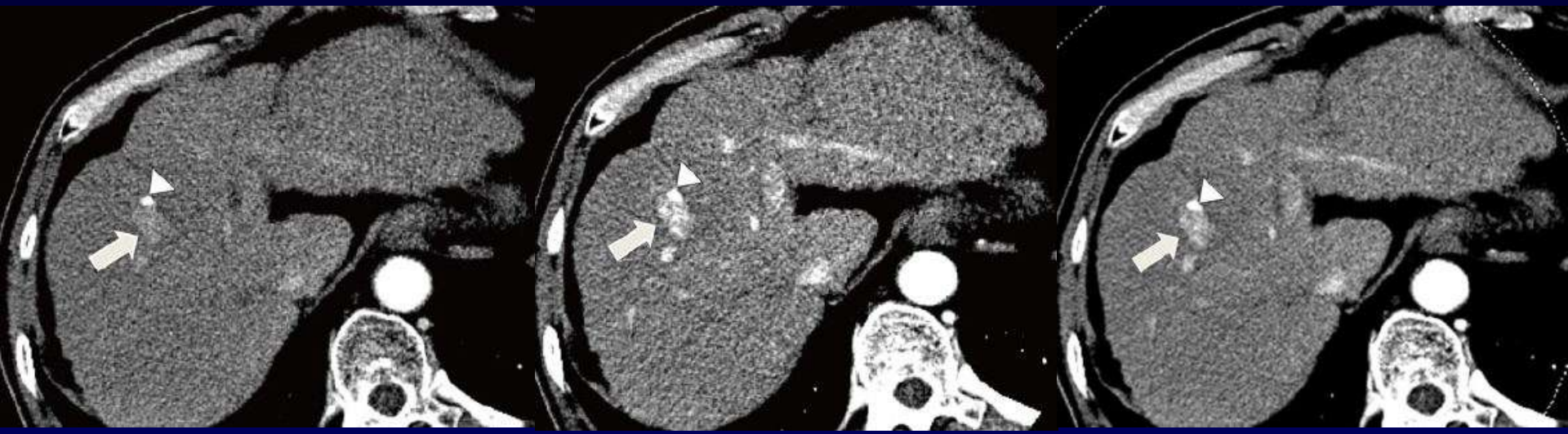
Dynamic CT: 120-kVp standard

Low-tube-voltage CT: 80-kVp

Higher sensitivity to detect iodinated contrast

(Lee JM et al)

Small HCC: dual-energy CT



140-kVp 80-kVp 120-kVp (blended image)

Dynamic CT: 120-kVp standard

Low-tube-voltage CT: 80-kVp

Higher sensitivity to detect iodinated contrast

Increased noise

(Lee JM et al)

MRI: Diffusion-Weighted Imaging (DWI)

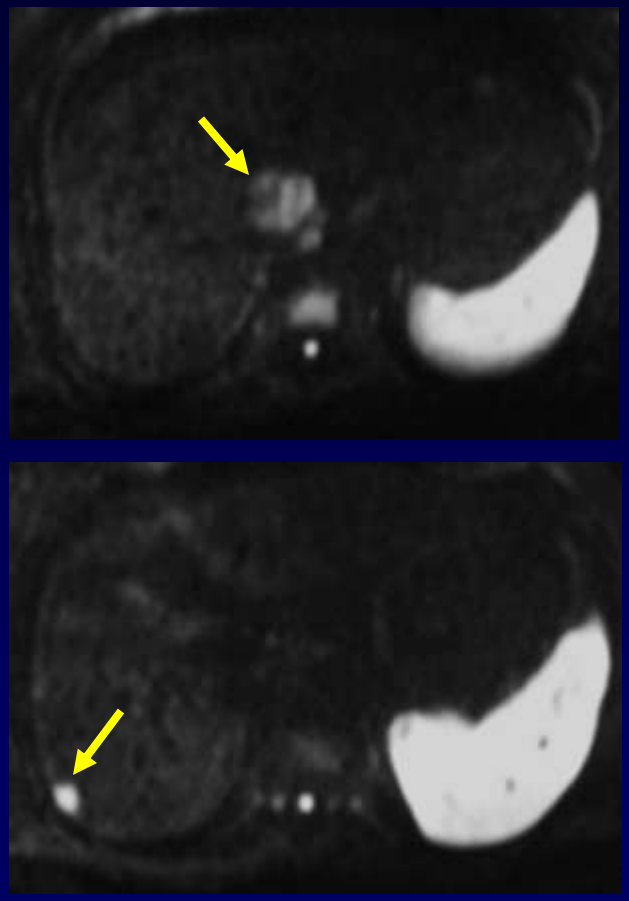
- Non-invasive way of quantifying water diffusion in tissues
  - No contrast required
- Widely used in neuroradiology
  - Acute stroke
  - Tumor grading (research centers)
    - High cellularity in malignancy restricts mobility of protons
      - Decreased ADC (apparent diffusion coefficient)
      -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

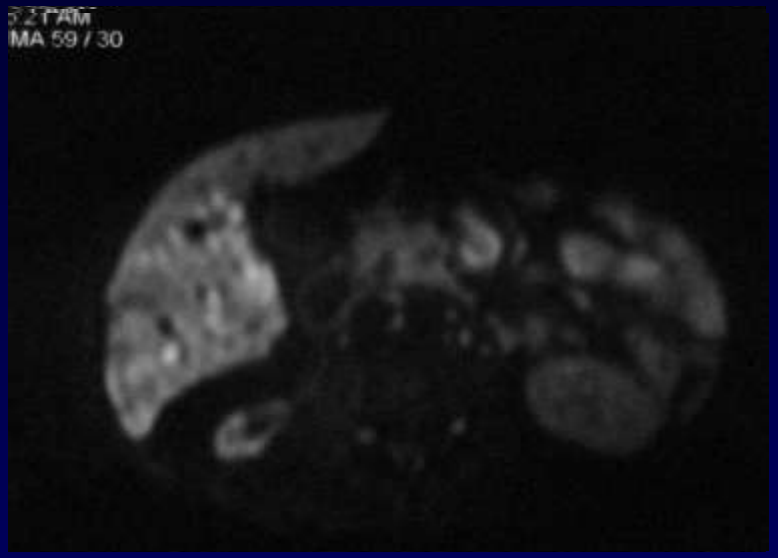
DWI: HCC's

Case 1



Two foci of HCC

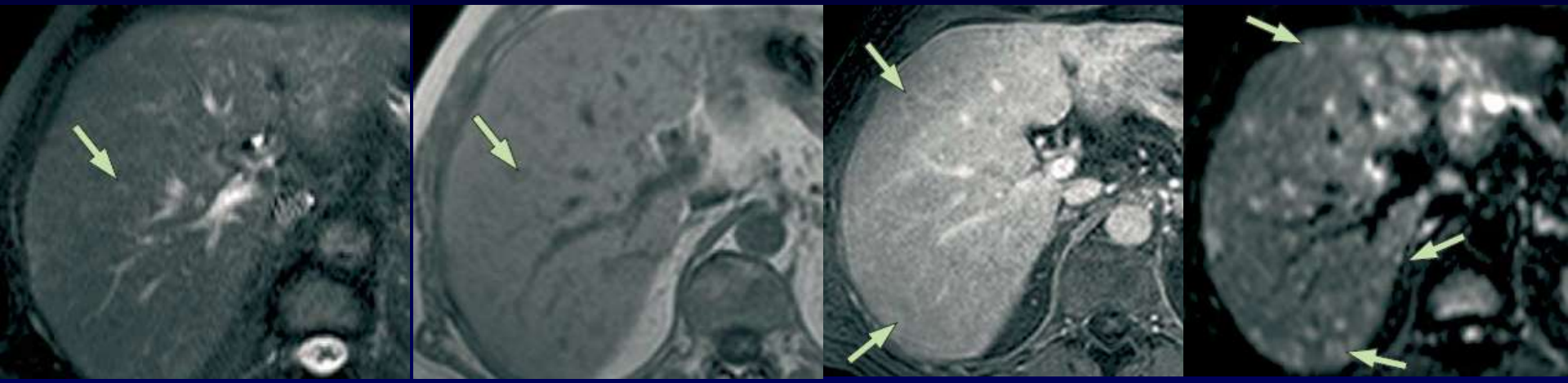
Case 2



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

Bright = restricted diffusion

DWI – Liver Metastases



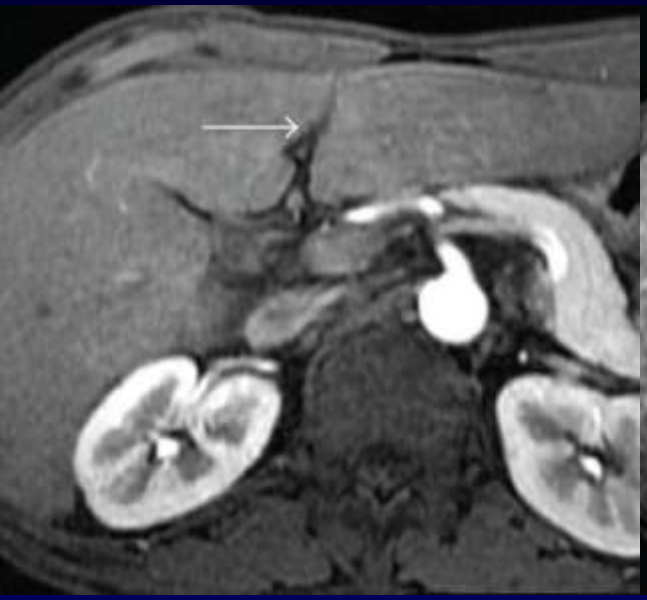
T2 T1 Venous Phase DWI

Standard MRI sequences: subtle small metastatic lesions

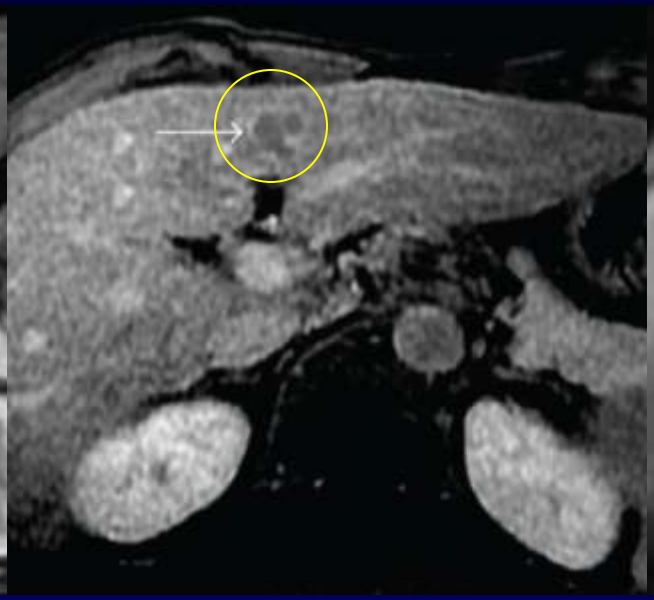
Diffusion-weighted image: many more small metastases seen

(Low RN et al)

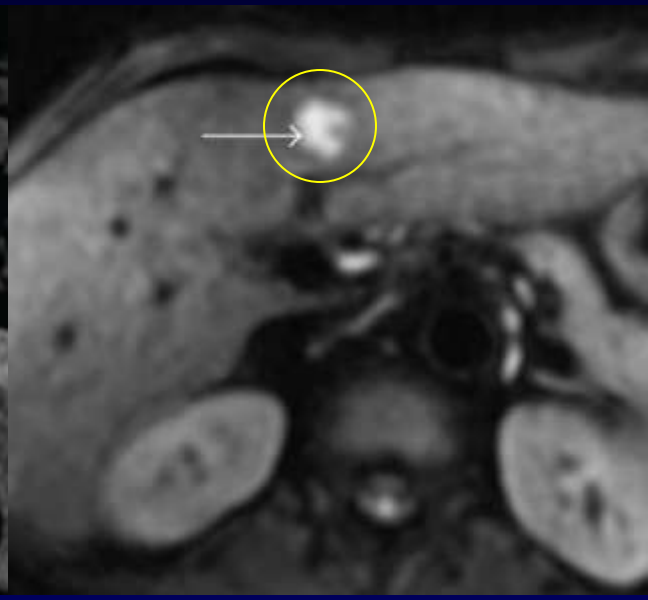
Early HCC – Atypical Enhancement on MRI



Arterial Phase



Venous Phase



Diffusion-weighted image (DWI)

No arterial hypervascularity
Wash-out on venous phase

→ Biopsy:
Well-differentiated HCC

Restricted diffusion

(Tan CH et al)

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)

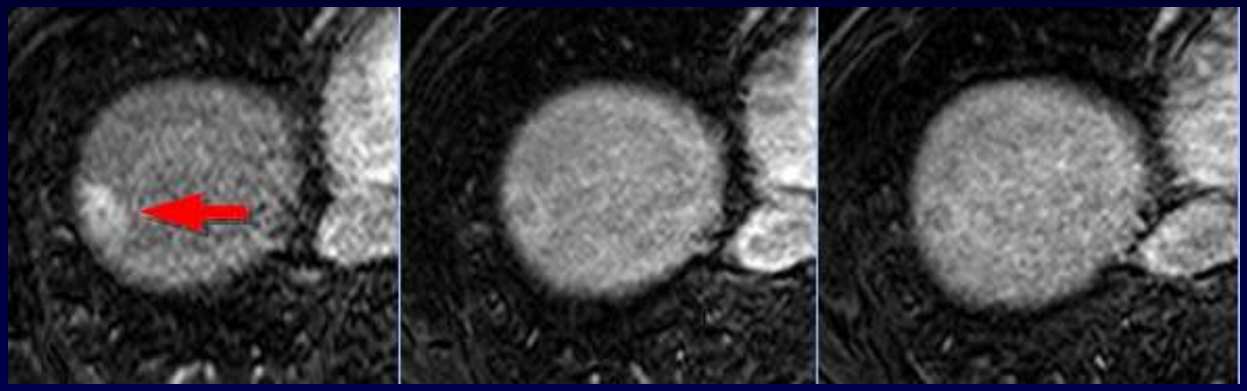
- Administered as a rapid bolus to obtain vascular information (same as extracellular contrast agents)
  - 50% taken up by functioning hepatocytes and subsequently excreted into bile
  - Uptake by hepatocytes peaks at 20 minutes
    - Acquire hepatobiliary phase images

Gadoxetic acid (Primovist/Eovist, Bayer)

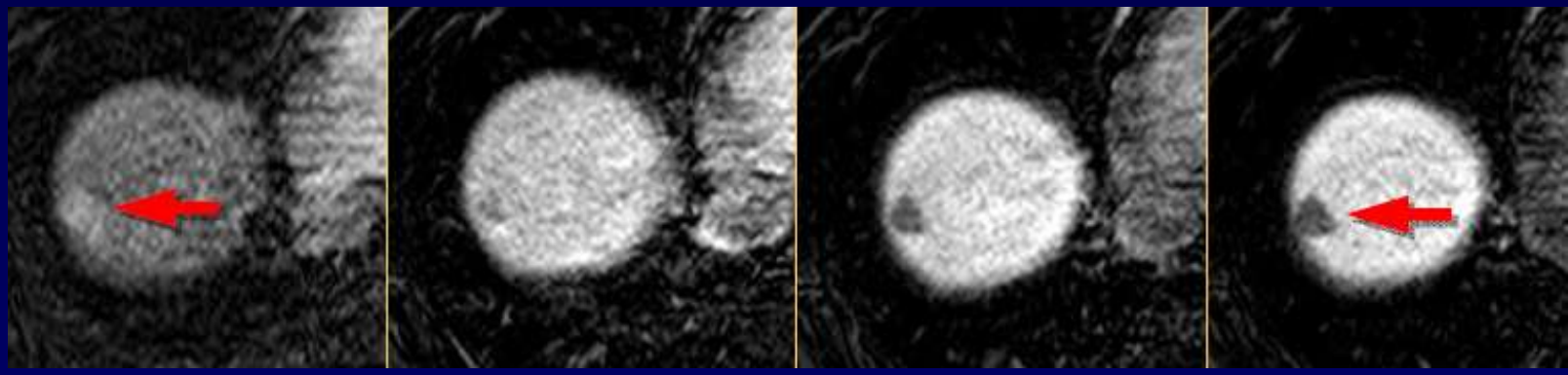
- Malignant lesions
  - No contrast uptake (no functioning hepatocytes)
  - Metastases, CholangioCA and most HCCs
- Uptake seen in focal liver lesions containing functioning hepatocytes
  - FNH
  - Adenoma
  - Regenerative/dysplatic nodules
  - *Well-differentiated HCC*

Hepatobiliary Phase Imaging (Primovist) – HCC

ECCM

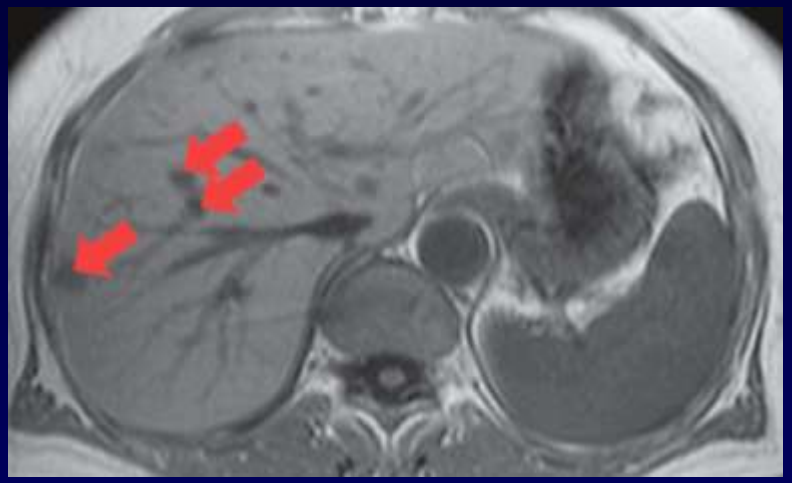


Primovist

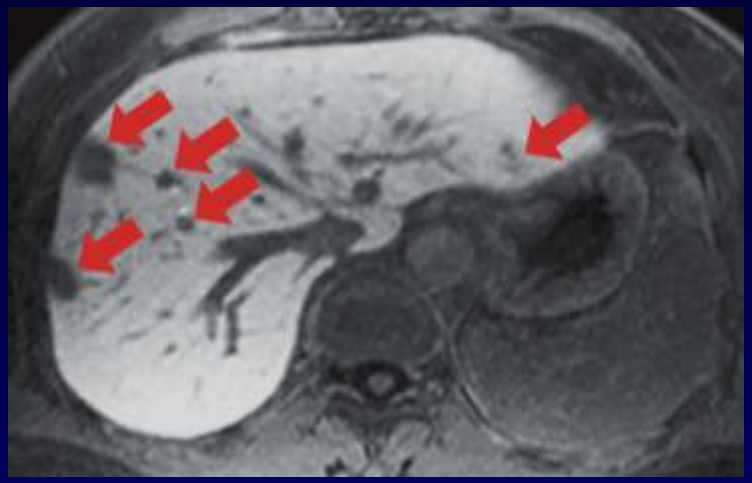


Arterial	Portal venous	Equilibrium	Hepatocyte
30-60 sec	60-90sec	2-5mins	10-20min

Primovist: Metastases



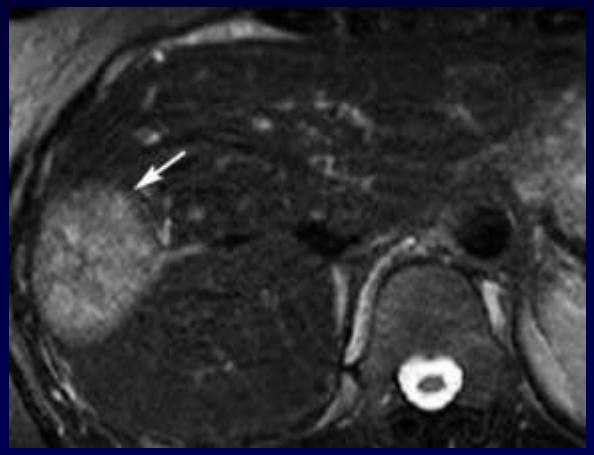
Precontrast T1



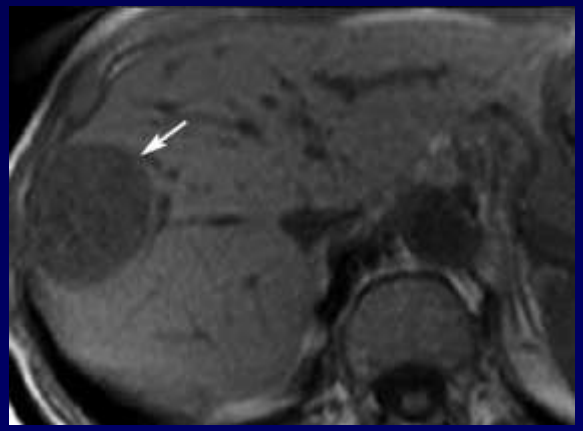
Hepatobiliary Phase
(20 mins)

Metastases – no uptake of Primovist
More metastatic lesions detected

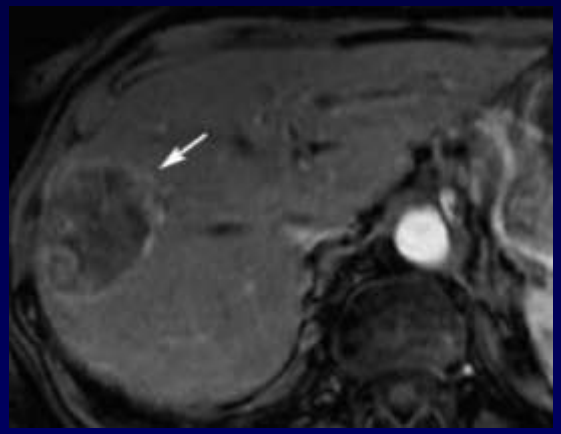
Hepatobiliary Phase Imaging (Primovist)
Poorly differentiated HCC



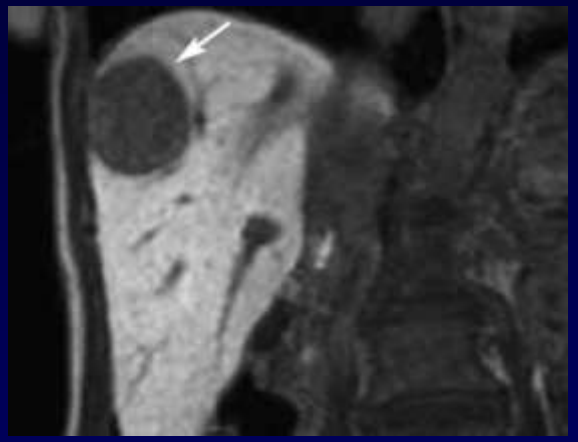
T2-W



T1-weighted



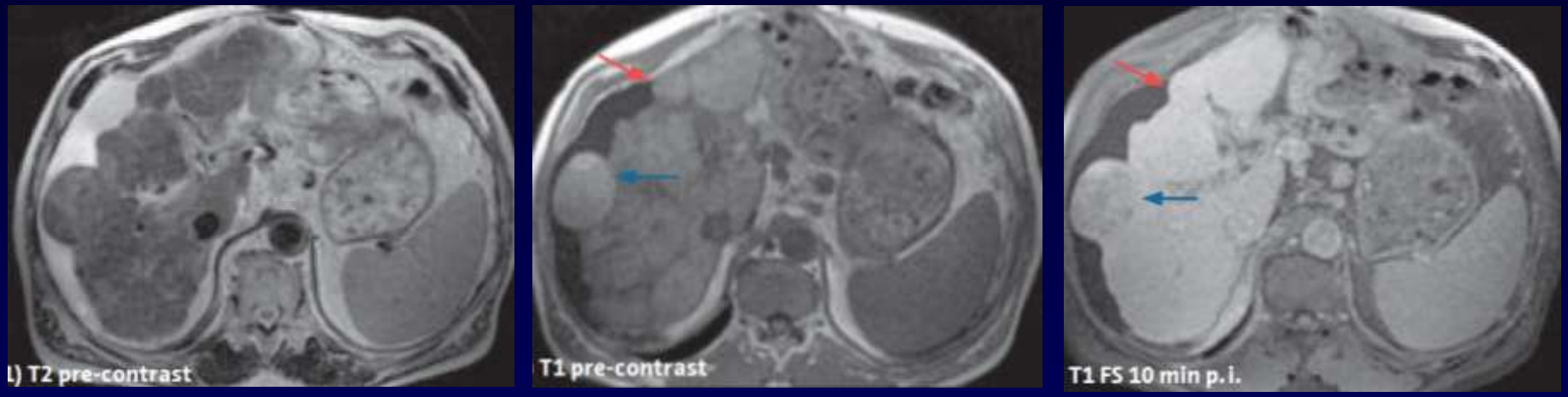
Arterial Phase



Hepatobiliary Phase

Hepatobiliary Phase Imaging (Primovist) Cirrhosis and HCC

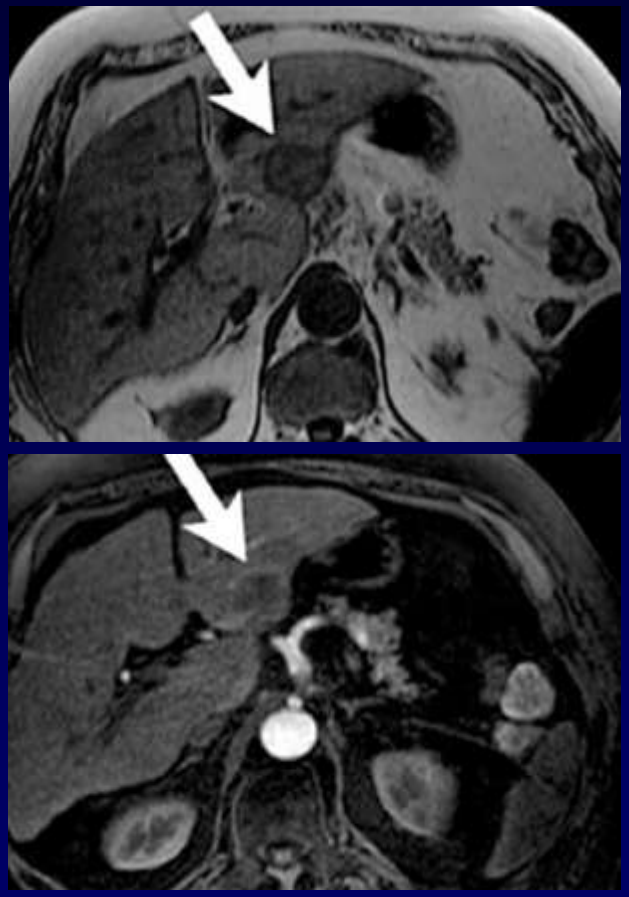
Hepatobiliary Phase



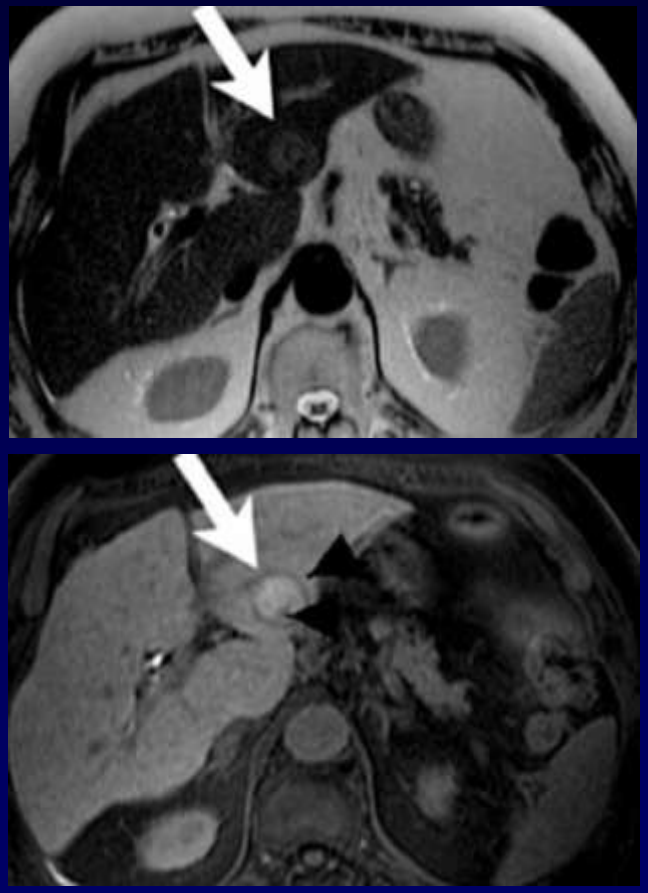
- Majority of HCCs do not contain significant hepatocytes
  - Will not take up Primovist
- Regenerative and dysplastic nodules contain hepatocytes
  - Will take up Primovist

- *Well differentiated HCC can also take up Primovist*

Not all hepatocyte containing lesions are benign! – Well-differentiated HCC



Arterial Phase



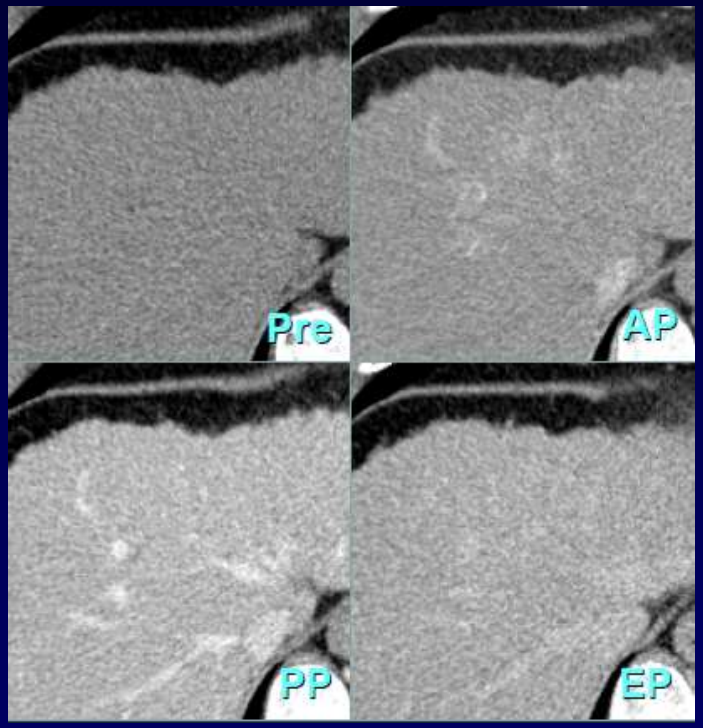
Hepatocyte phase

CARDINAL MRI CENTER

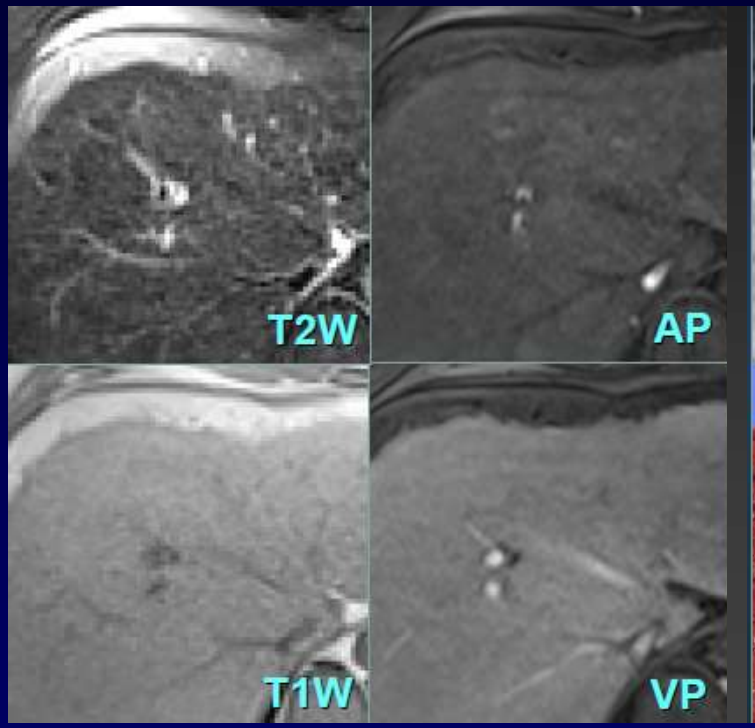
Gadoxetic acid (Primovist/Eovist, Bayer)

- 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

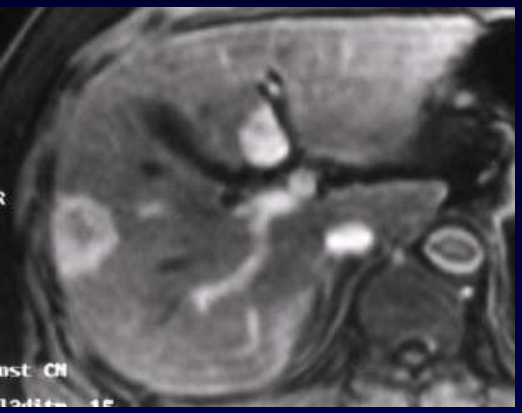
Primovist

Golfieri R et al

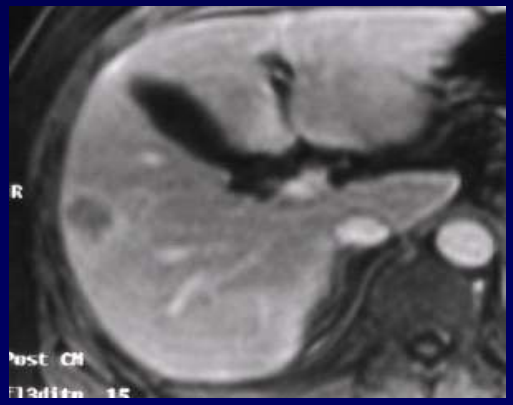
Gadoxetic-acid and DWI

- 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



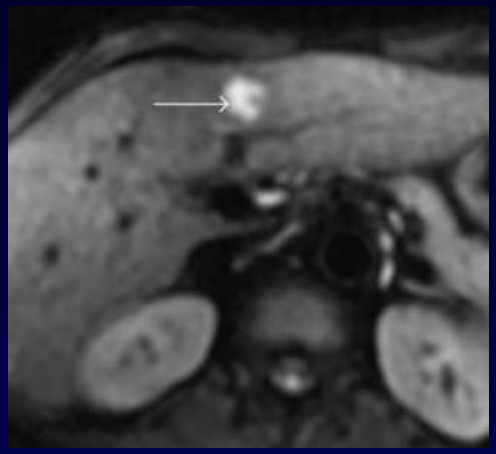
Arterial Phase



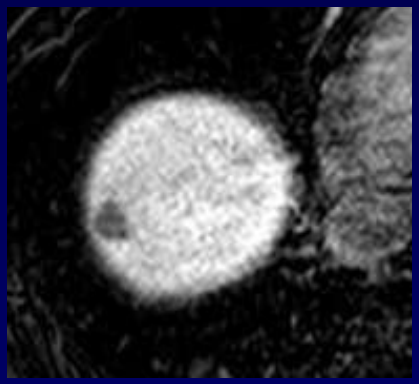
Venous Phase

- 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



DWI



Hepatobiliary Phase (Primovist)

- 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)

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Thank you

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