Primovist MRI Evaluation of FNH vs. Hepatocellular Adenoma

BODY DIVISION GRAND ROUNDS – JANUARY 14, 2018

DR. SAMUEL XU – PGY3
DR. AASHISH GOELA

Conflicts of Interest

None to declare

Agenda

- Introduction to Primovist
- Evaluation of Focal Nodular Hyperplasia
- Evaluation of Hepatocellular Adenoma
- Comparison of the Two Lesions
- Quality Improvement Case
- Questions and QA

What is Primovist?

Primovist

- Gadoxetate Disodium OR Gadoxetic Acid OR Gadoxetate Ethoxybenzyl Dimeglumine
  - Hepatobiliary Specific Contrast Agent approved in Canada in 2010
  - Highest uptake by hepatocytes out of all the agents of 50% in the normal liver

Table 2
Hepatobiliary-specific Contrast Agents Used for Liver MR Imaging

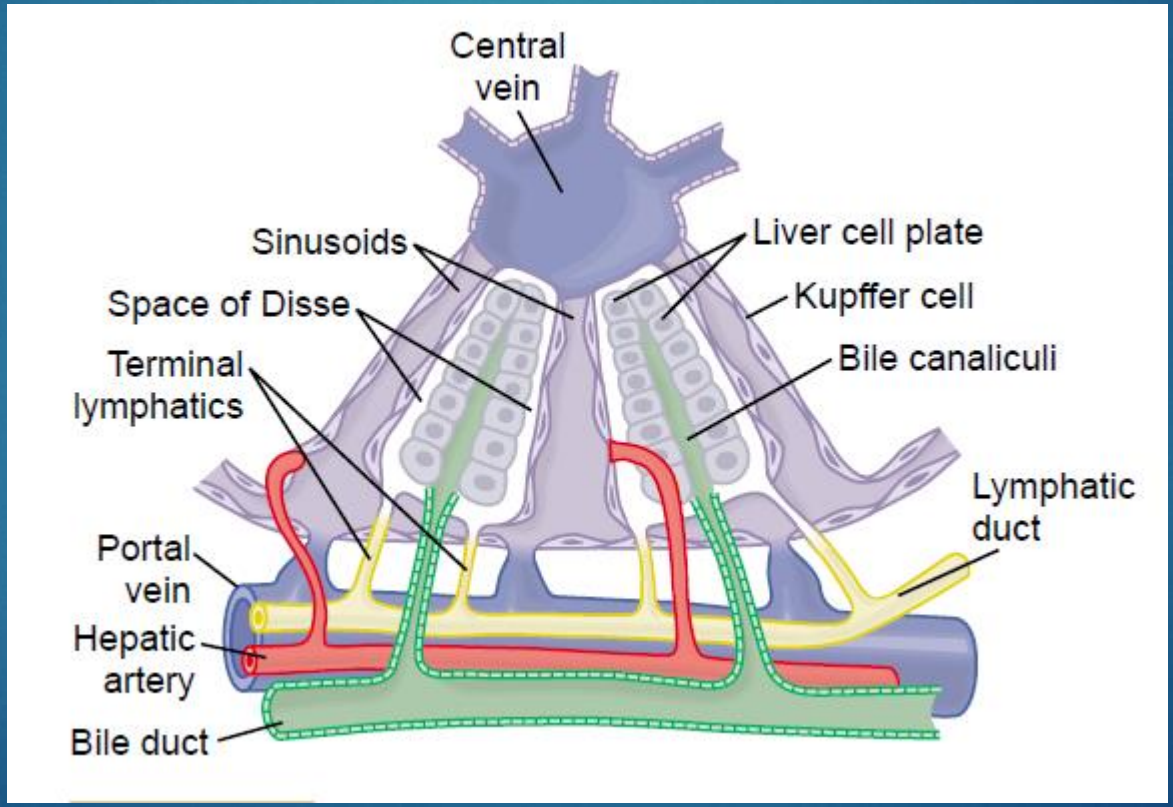
Generic Name	Abbreviated Name	Trade Name	Manufacturer
Mangafodipir trisodium	Mn-DPDP	Teslascan	GE Healthcare
Gadobenate dimeglumine	Gd-BOPTA	MultiHance	Bracco
Gadoxetic acid (or gadoxetate disodium)	Gd-EOB-DTPA	Eovist (United States), Primovist (EU, Australia)	Bayer

Note.—EU = European Union.

Seale et al, 2009

Primovist

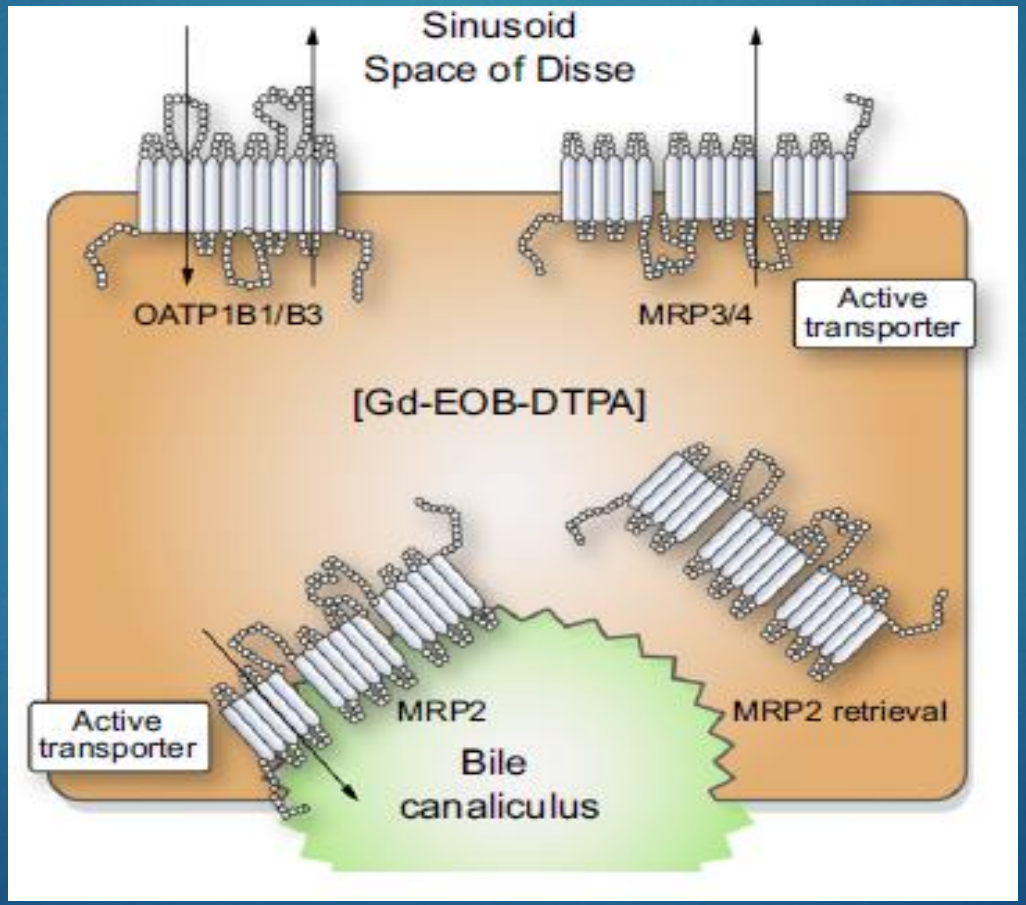
- Review of Microscopic Hepatic Anatomy



Guyton & Hall, 2006

Primovist

- Biochemical level of function



Van Beers et al, 2012

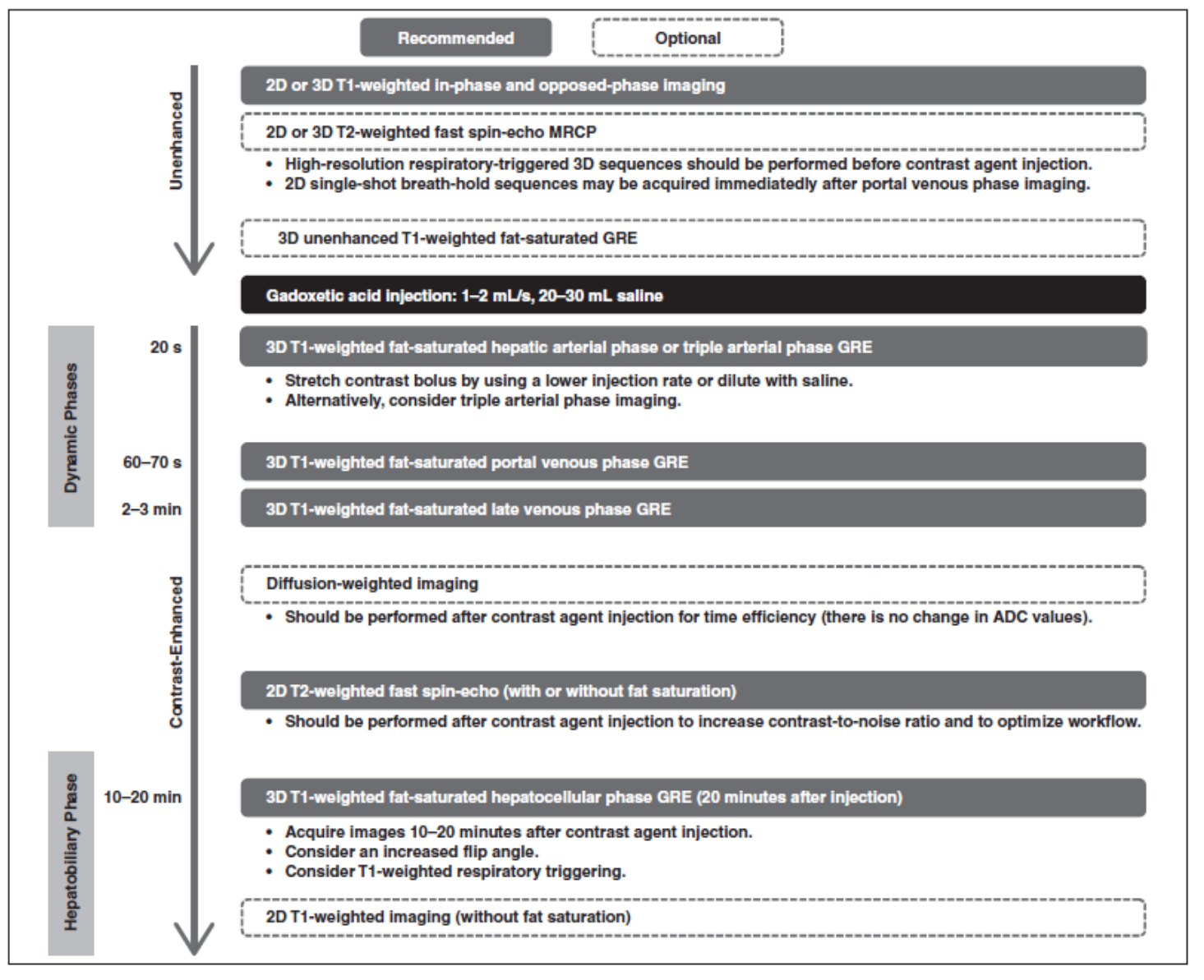
Primovist

- Due to the absence of normal hepatocytes in many pathologic lesions, there is no uptake of the lesion in the delayed phases
- This allows for much higher sensitivity in detection of liver lesions such as HCC or metastatic deposits
- The cost of Primovist is higher than non-specific agents
  - Initial cost analysis though showed overall cost savings with the use of Primovist

Primovist

- Dosage of Primovist is comparably lower compared to non-specific agents – 0.025 mmol/kg vs 0.1 mmol/kg
- Leads to some timing challenges, with solutions including
  - Dilution of the contrast into normal saline rather than a saline flush immediately following injection
  - Doubling the dose to 0.05mmol/kg which can also used in patients with poor liver function
- Adverse events similar to non-specific Gadolinium chelates

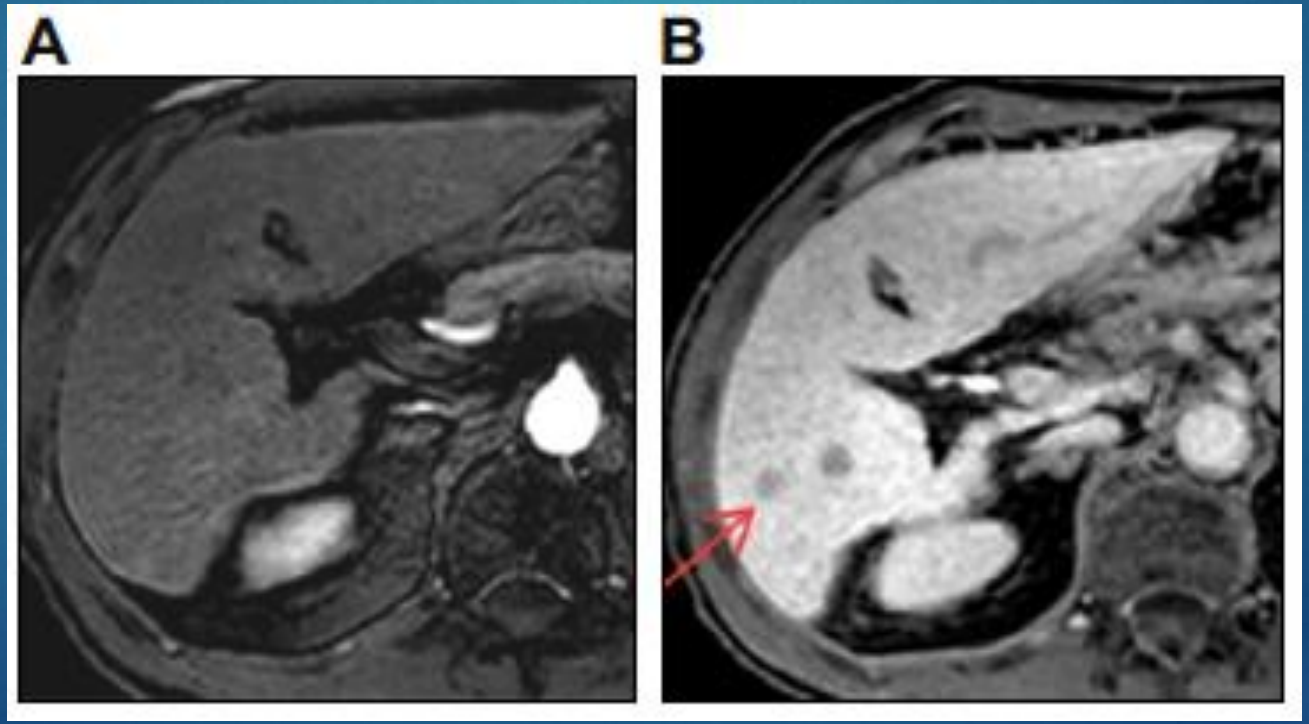
Primovist



Jhaveri et al, 2015

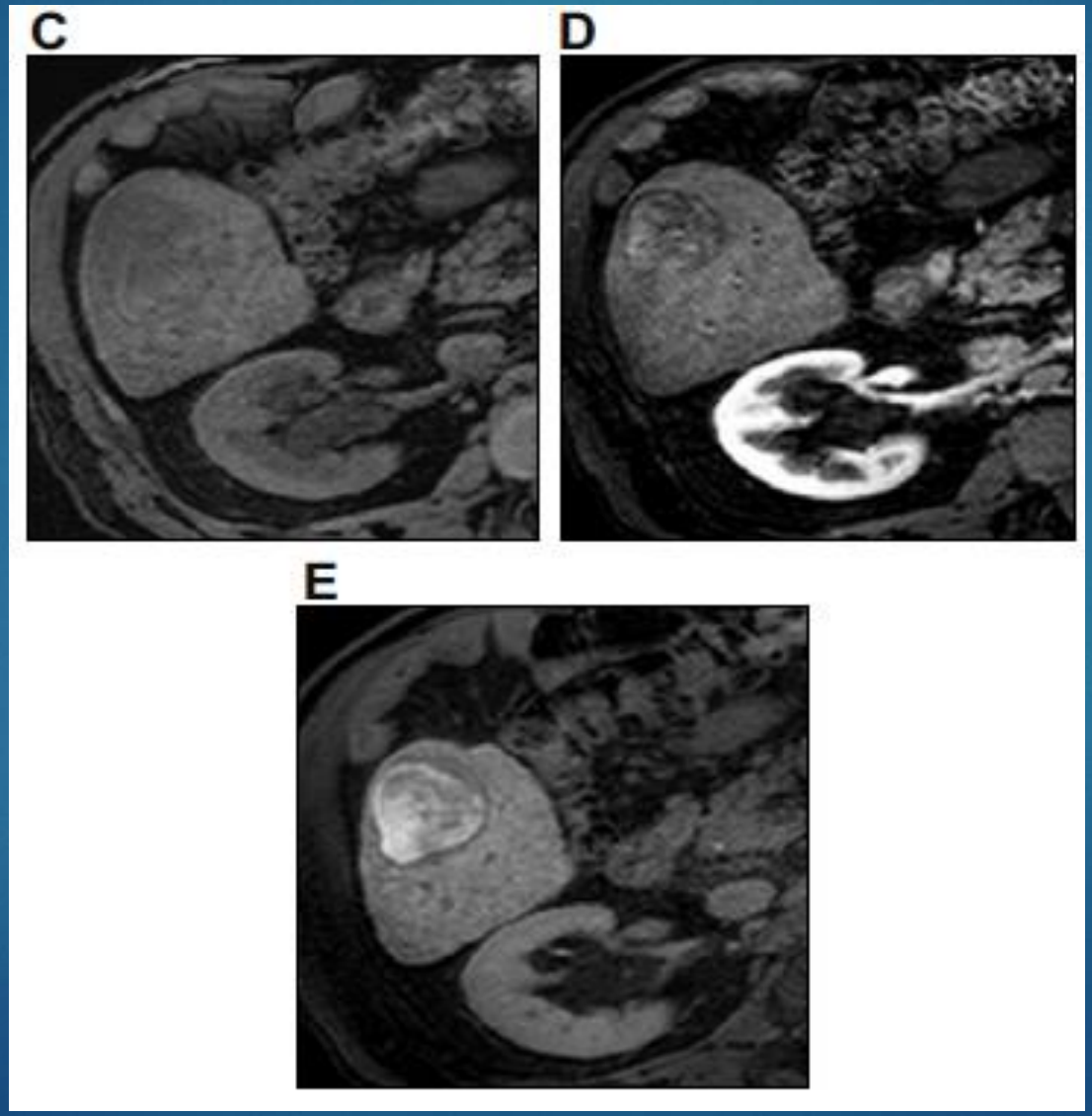
Primovist

- Characterization of lesions with Primovist adds the benefit of the hepatobiliary phase
  - Allows for the detection of smaller, less vascular lesions



Van Beers et al, 2012

Primovist



Van Beers et al, 2012

Primovist

- Utility Chart Summary

Table 1. Enhancement characteristics of the most frequent liver tumors.

	Arterial phase	Portal venous phase	Equilibrium phase	Hepatobiliary phase
Hemangioma	Iso-hypo (peripheral nodular enhancement)	Iso-hypo (peripheral nodular enhancement)	Iso-hypo	Hypo
FNH	Hyper	Iso	Iso	Iso-hyper
Adenoma	Variable	Variable	Variable	Hypo or hyper
Metastasis	Hypo (ring enhancement) or hyper	Hypo (ring enhancement)	Hypo	Hypo
HCC	Hyper or iso, hypo	Hypo	Hypo	Hypo or hyper
CCC	Hypo or hyper	Variable, mostly hypo	Variable, mostly hypo	Hypo

Van Beers et al, 2012

Focal Nodular Hyperplasia

Focal Nodular Hyperplasia

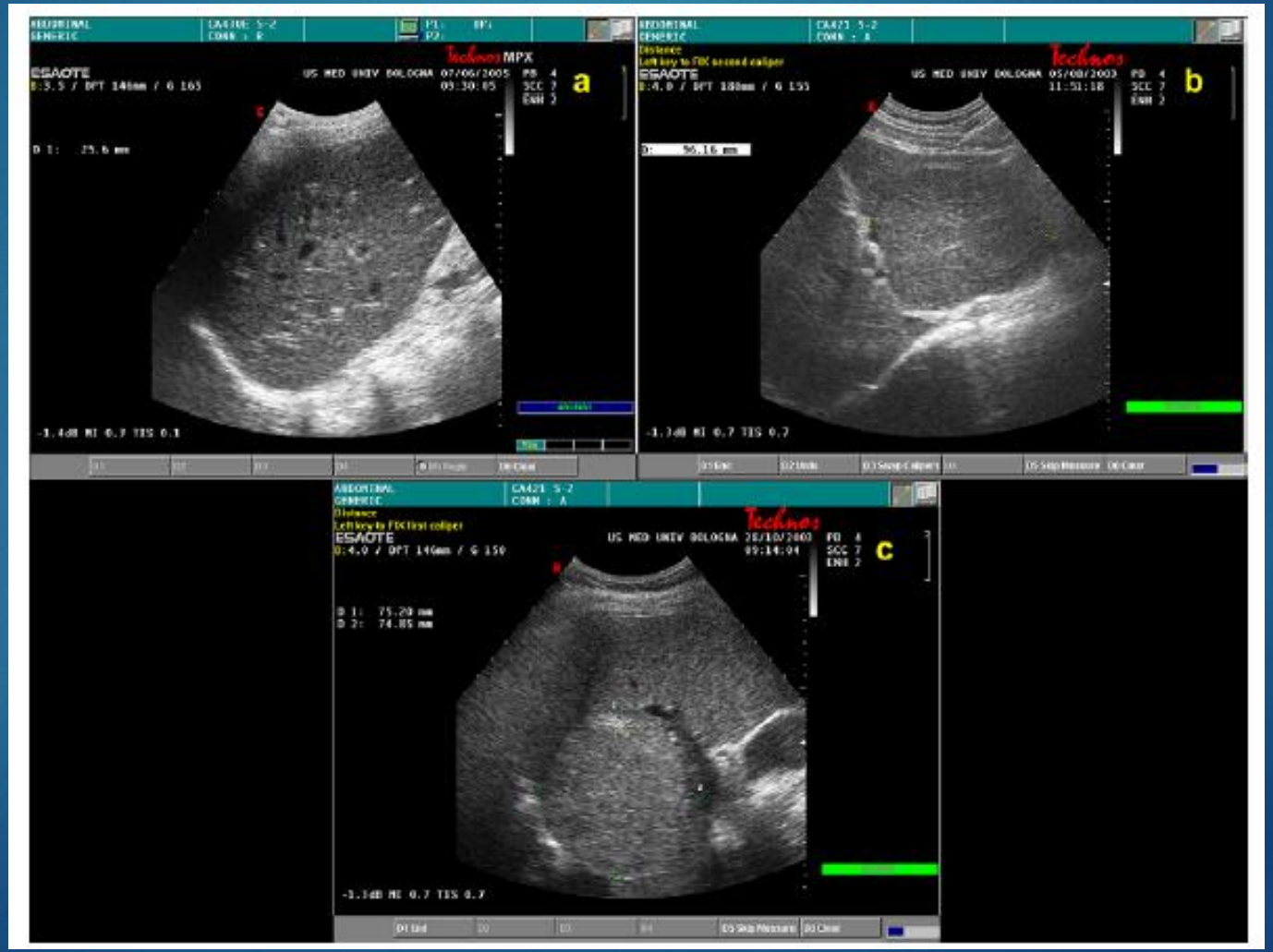
- Most common hepatocellular "tumor"
  - Although not a true tumor
  - Localized liver response to small arterial malformations
- Typically found incidentally for other RUQ symptoms
  - Population usually young females taking OCPs
  - Prevalence of 3%

Focal Nodular Hyperplasia

- Diagnosis
  - Through imaging, rarely requires biopsy
- Treatment
  - Follow up, no surgical resection unless causing symptomatic mass effect

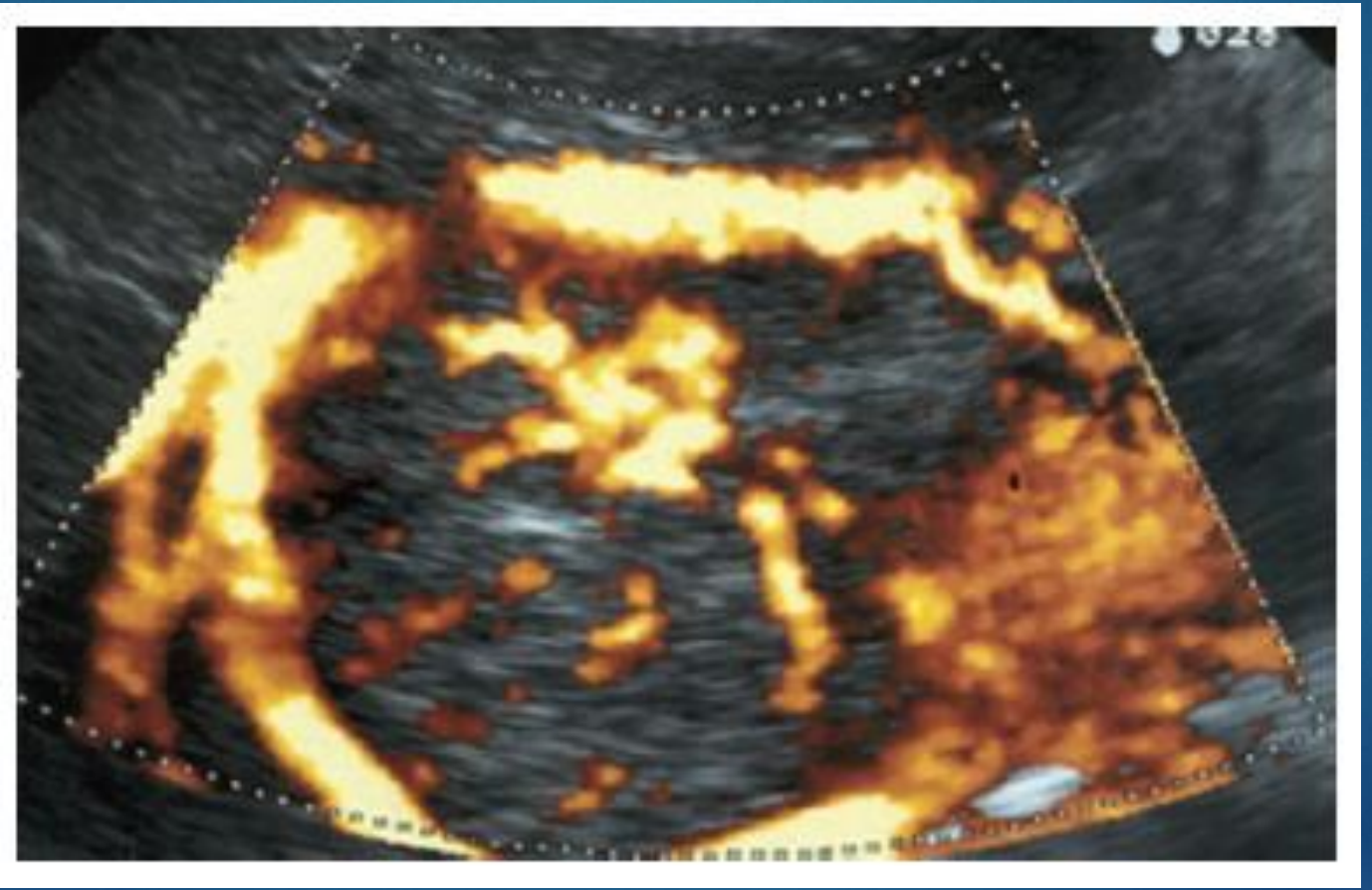
Focal Nodular Hyperplasia

- Appearance on US



Venturi et al, 2007

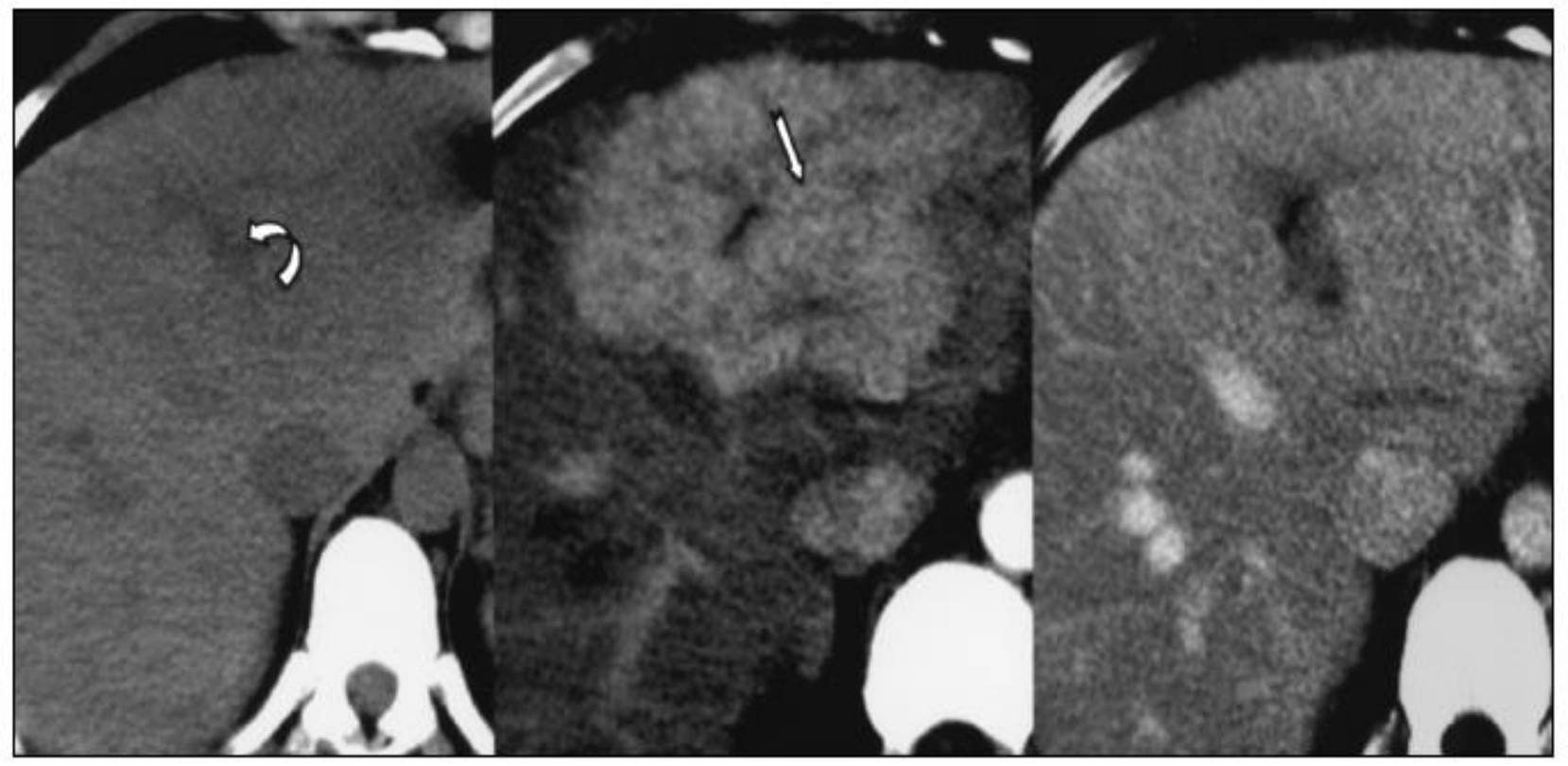
Focal Nodular Hyperplasia



Venturi et al, 2007

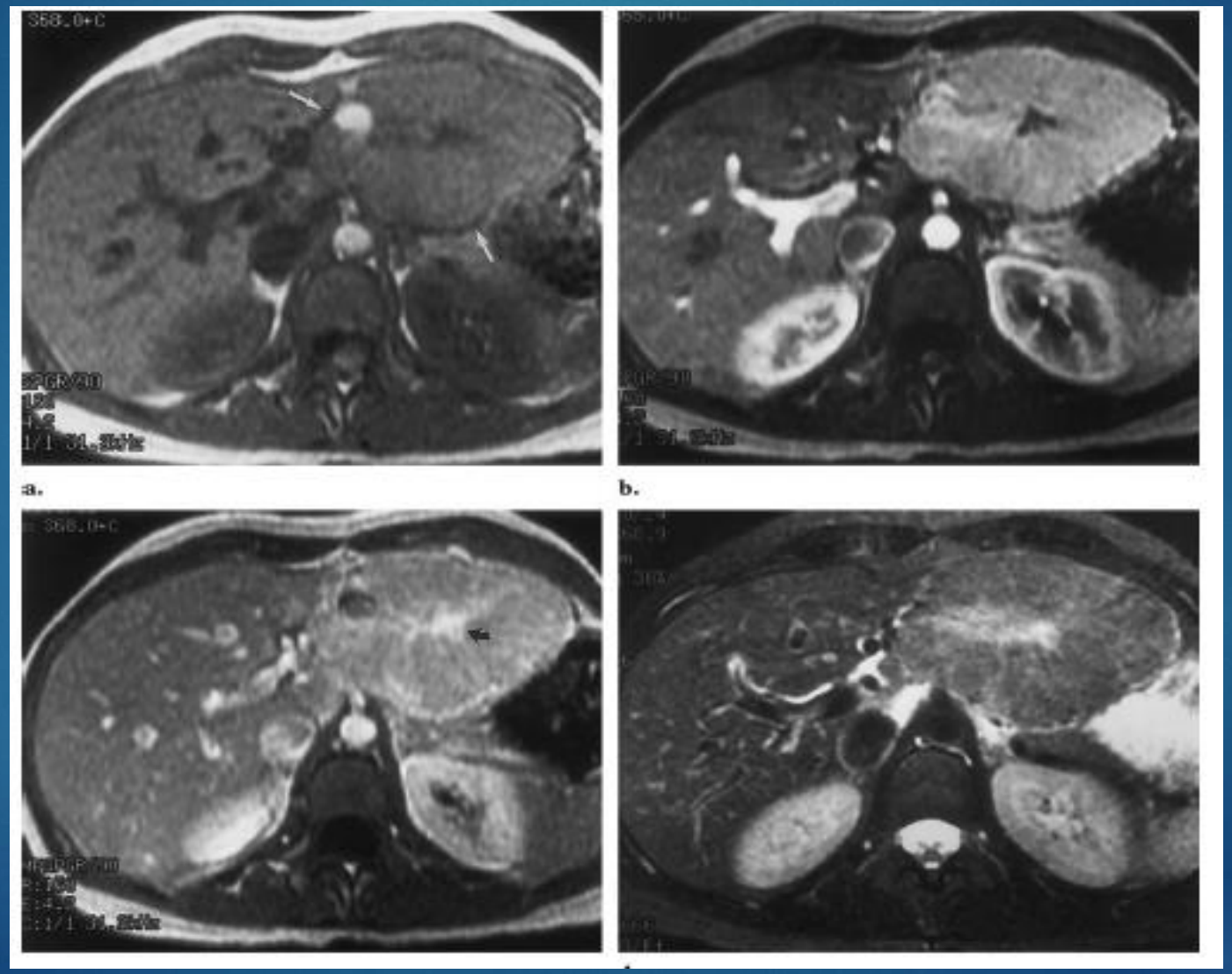
Focal Nodular Hyperplasia

- Appearance on CT



Horton et al, 1999

Focal Nodular Hyperplasia



Horton et al, 1999

Focal Nodular Hyperplasia

- Can also be characterized with Nuclear Medicine
  - Tc-99m SC study uptakes in Kupffer cells, which are present in FNH and thus will have strong uptake in the lesions
  - Tc-99m HIDA uptake theoretically similar in hepatocytes as Primovist so will show persistent retention of the radionucleotide with increased uptake in the lesion
    - However, HIDA scans also has high uptake in other lesions such as adenomas

Hepatocellular Adenoma

Hepatocellular Adenoma

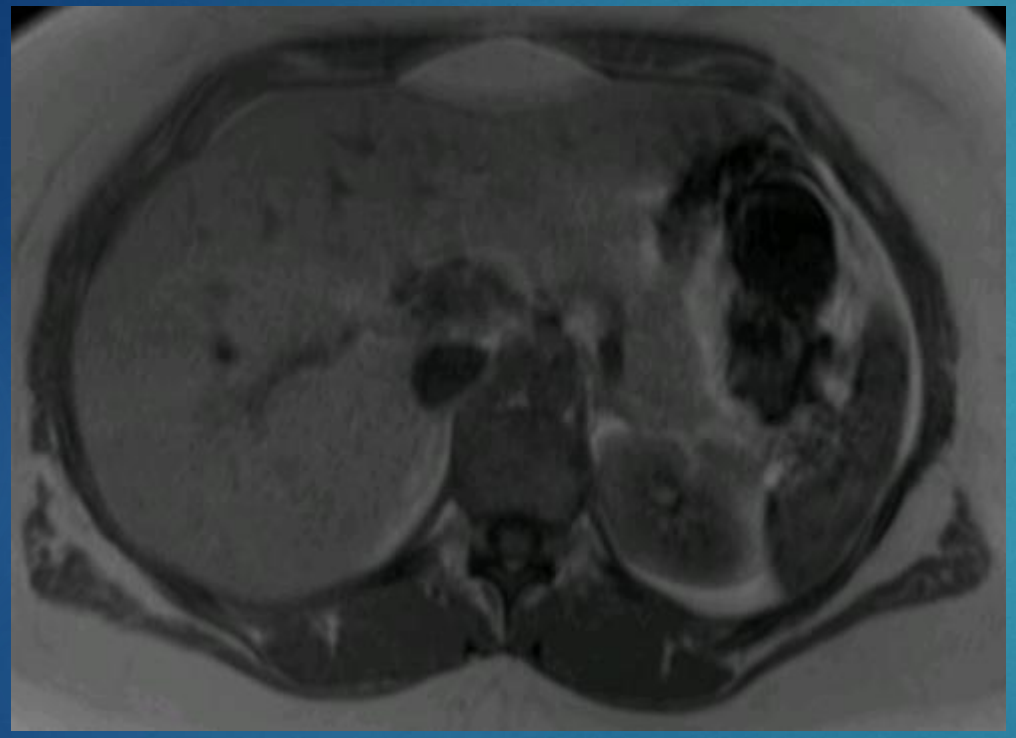
- Second most common benign hepatocellular tumor
  - Estimated incidence of 0.004%
  - Commonly found in younger female patients with use of OCPs, but other patient populations also present
  - Usually asymptomatic

- Subtypes include
  - **Inflammatory**
  - **HFNF1a**
  - ß-catenin activated
  - Nonspecified/Noninflammatory

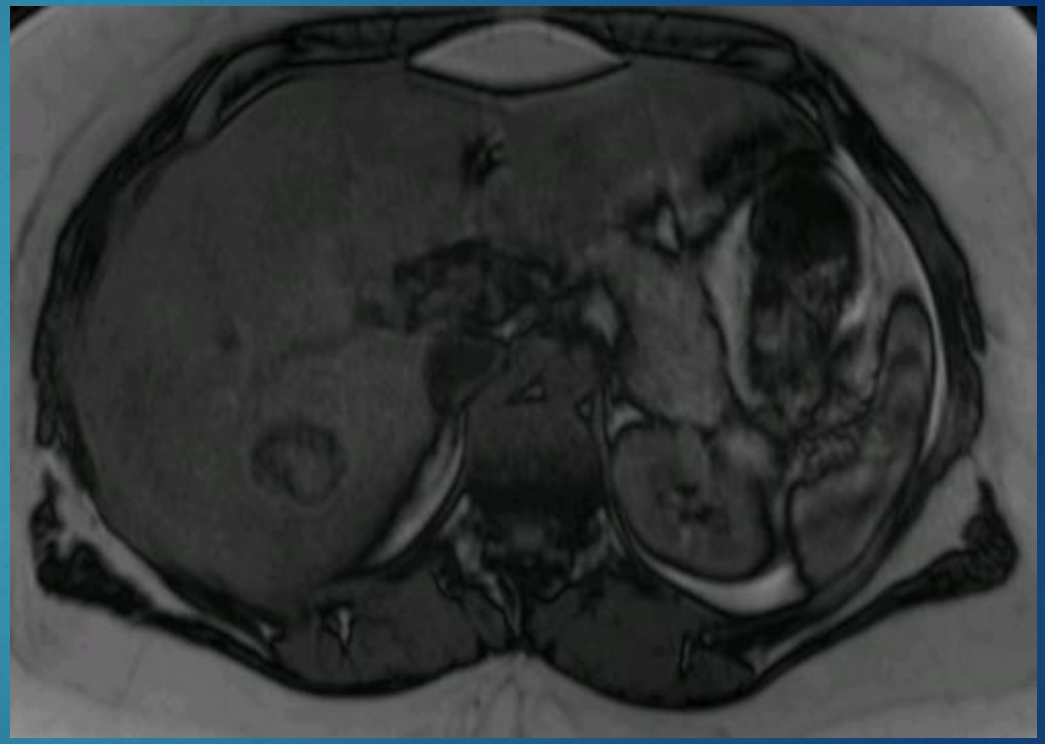
Hepatocellular Adenoma

- HFNF1a Subtype
  - Represents approximately 30-40% of all HCAs
  - Usually the more fat containing HCAs
  - Imaging features of diffuse and homogenous signal dropout on opposed phase T1

Hepatocellular Adenoma



Ax T1 in phase

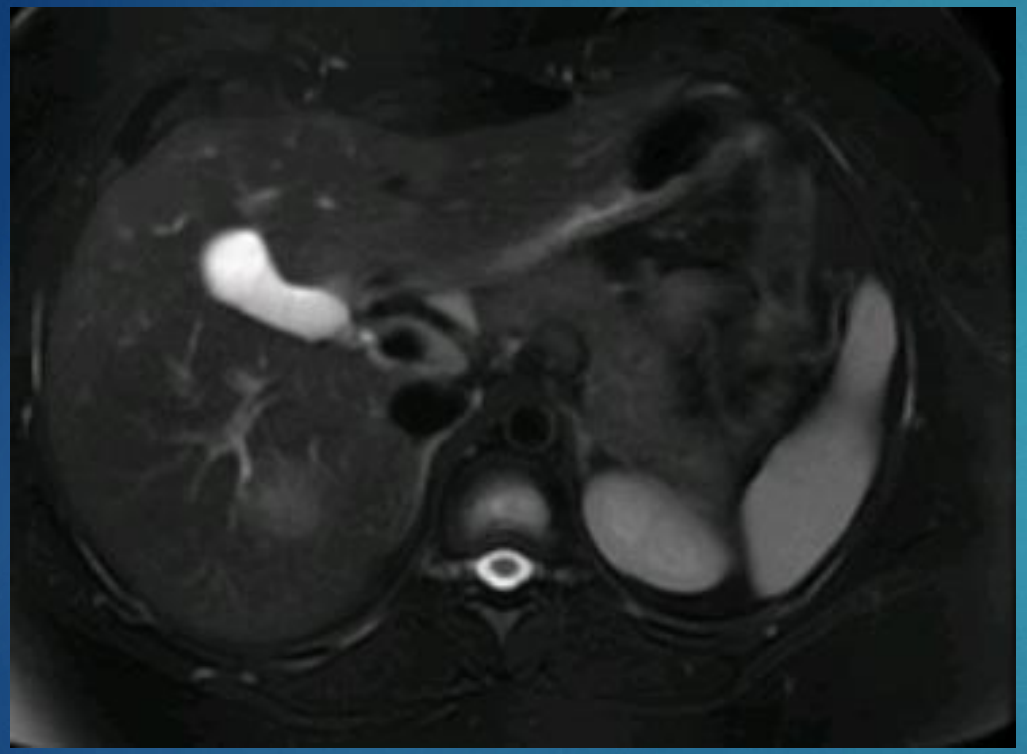


Ax T1 out-of-phase

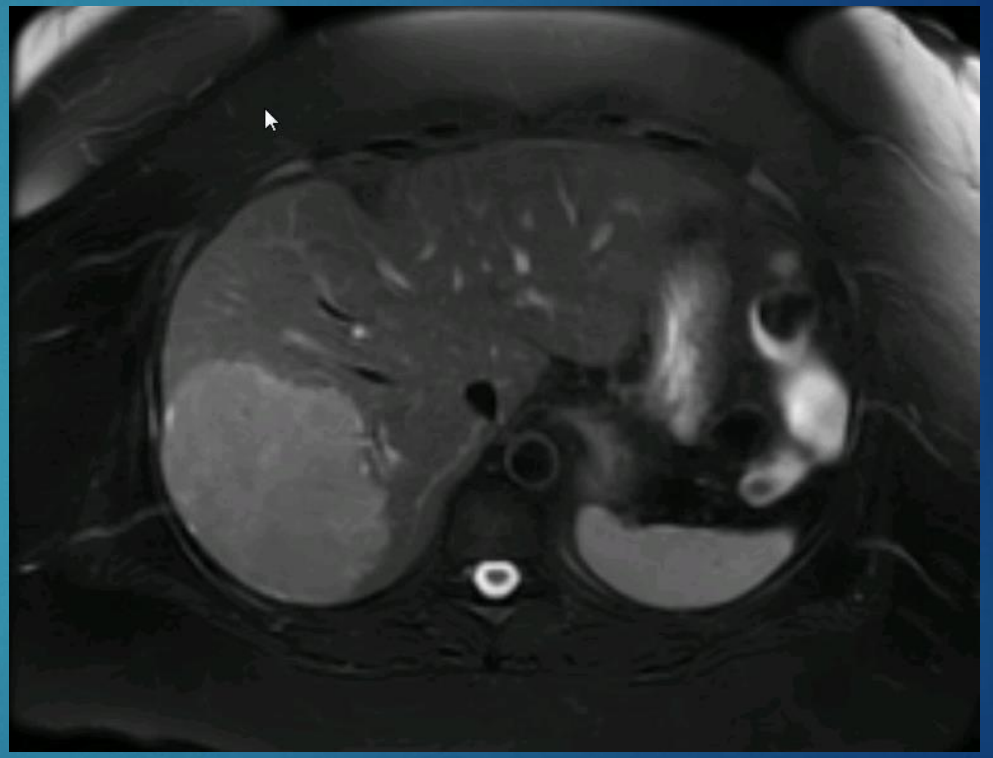
Hepatocellular Adenoma

- Inflammatory Subtype
  - Previously identified as telangiectatic FNH, but has been re-classified
  - Accounts for roughly 40-55% of HCAs
  - Imaging features of strong hyperintense on T2 compared to other HCAs, with persistent enhancement on delayed phase with extracellular agents
    - However, there have been reports of I-HCA mimicking FNH because it can retain contrast on the hepatobiliary phase and remain hyperintense

Hepatocellular Adenoma



Ax T2
Non I-HCA



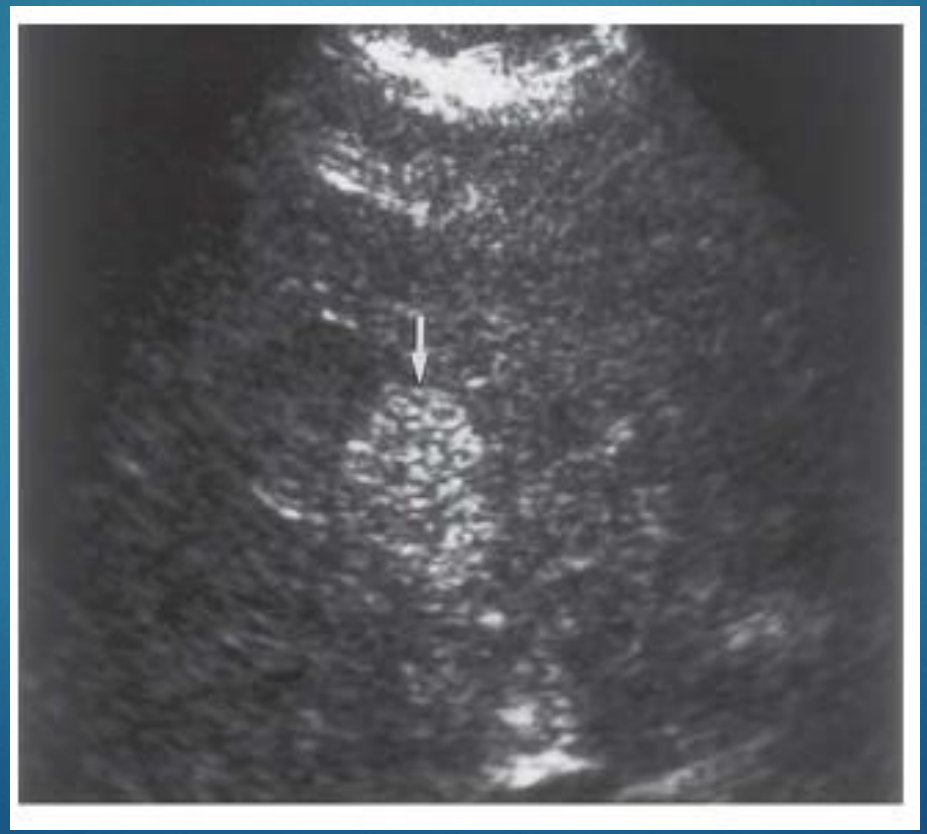
Ax T2
Presumed I-HCA

Hepatocellular Adenoma

- Diagnosis
  - Heavily reliant on imaging
  - Definitive diagnosis is through biopsy
- Treatment
  - Surgical resection due to the associated complications of hemorrhage/rupture and malignant transformation

Hepatocellular Adenoma

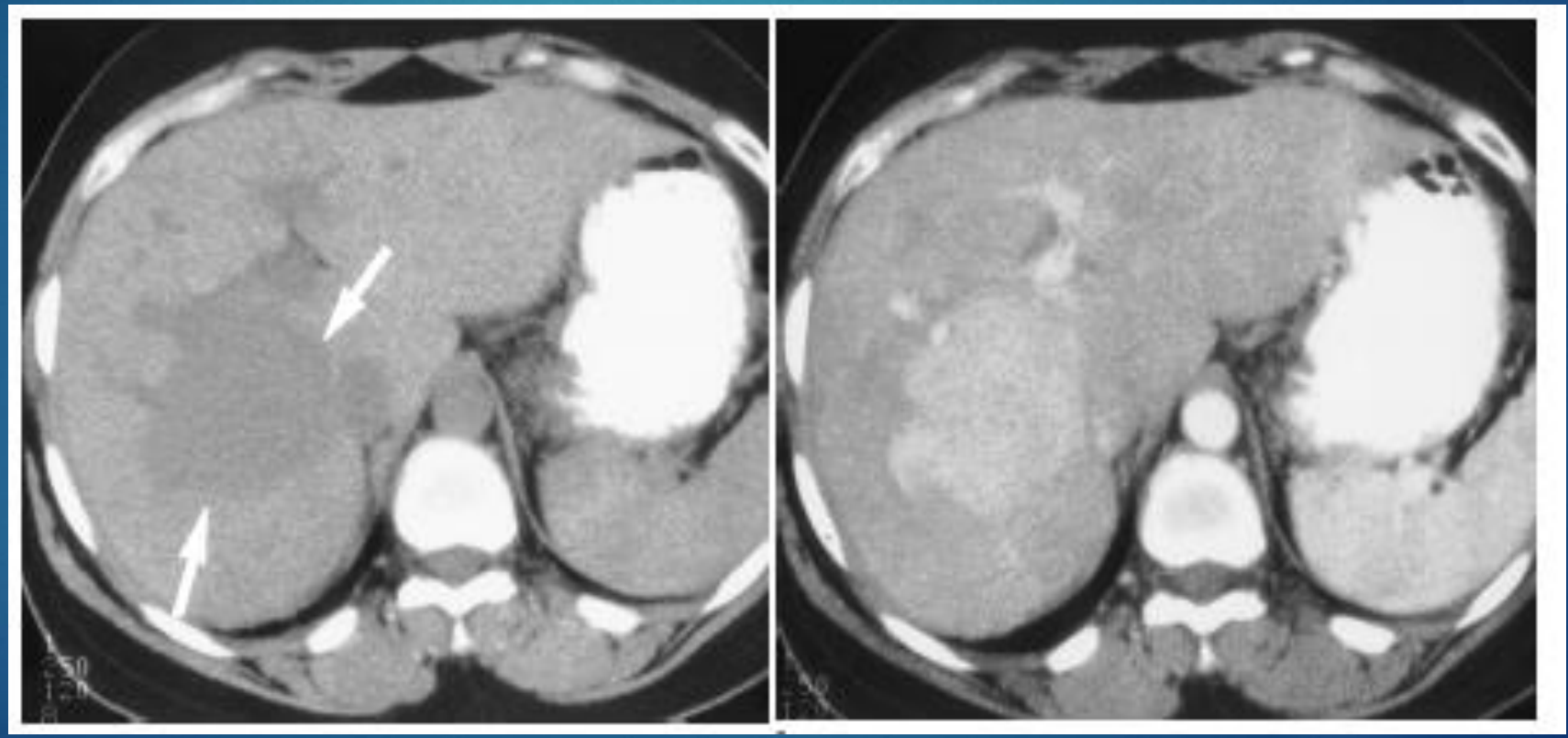
- Appearance on US



Grazioli et al, 2001

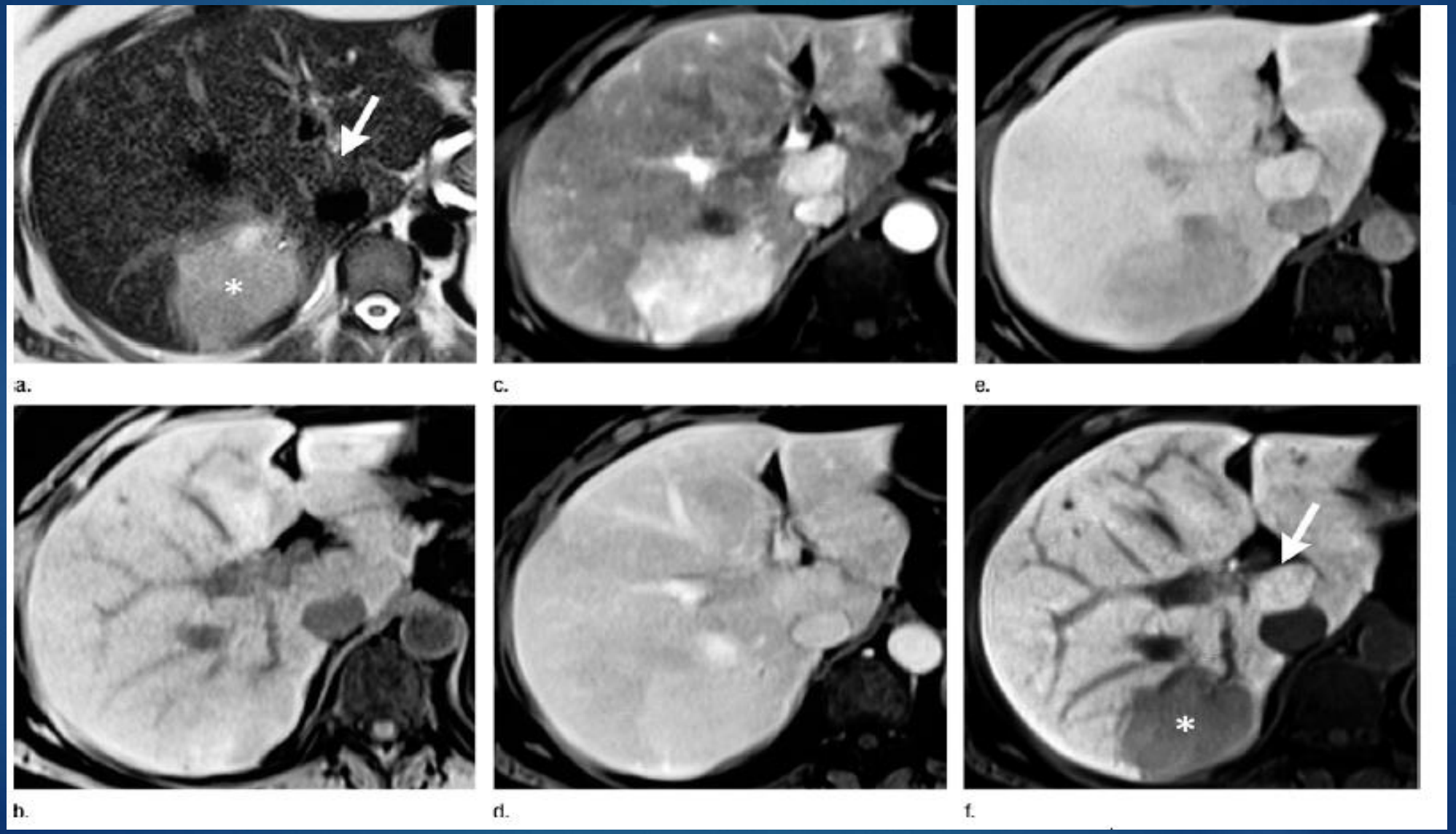
Hepatocellular Adenoma

- Appearances on CT



Ruppert-Kohlmayr et al, 2000

Hepatocellular Adenoma



Seale et al, 2009

Hepatocellular Adenoma

- Can also be evaluated with Nuclear Medicine
  - Due to absence of Kupffer cells, should be photopenic on a Tc-99 sulfur colloid study
    - However, this is not always the case

Comparing the Two

Comparing the Two

Table 1

Clinical and Pathologic Findings in Patients with HCA and Those with FNH

Parameter	Patients with HCA ($n = 24$)	Patients with FNH ($n = 58$)
Age (y)*	42.4 ± 13.6 (11–75)	41.7 ± 12.7 (14–78)
Male:female ratio	1:23	7:51
Lesion diameter (mm)*	29.5 ± 23.0 (8–110)	36.0 ± 23.7 (6–127)
No. of lesions	15 Solitary, four multiple (three patients with three nodules; one patient with four nodules), five patients with liver adenomatosis	48 Solitary, 10 multiple (10 patients with two nodules)
Clinical manifestation	Eight lesions resulted in upper quadrant pain,16 were asymptomatic	Five lesions resulted in abdominal pain, 53 were asymptomatic
Oral contraceptive use†	8 (7) [4–12]	11 (5.7) [3–8]
Background disorders	Ovarian cancer ($n = 1$), breast cancer ($n = 1$), acute lymphatic leukemia ($n = 1$)	Colon cancer ($n = 5$), pulmonary cancer ($n = 5$), breast cancer ($n = 1$), melanoma ($n = 1$), ovarian lymphoma ($n = 1$), acute lymphatic leukemia ($n = 1$)
Other associated hepatic lesions	FNH ($n = 7$)‡, hemangioma ($n = 1$)	HCA ($n = 7$)‡, hemangioma ($n = 3$), cyst ($n = 4$)
Hepatic steatosis	2	9
Diagnostic confirmation	Surgical resection ($n = 4$), fine-needle biopsy ($n = 20$)	Fine-needle biopsy (n = 24), follow-up imaging studies (n = 34)
Histologic subgroups	Steatotic type in 12 patients (23 lesions), inflammatory type in seven patients (12 lesions), and unclassified in five patients (eight lesions)	Intranodule fat component in two patients (two lesions)

Graziiolo et al, 2012

Comparing the Two

Table 3

MR Imaging Findings in HCA and FNH

Finding	HCA ($n = 43$)	FNH ($n = 68$)	*P* Value
Central scar	0	23 (33.8)	<.0001
SI dropout on out-of-phase T1-weighted images	23 (53.5)	2 (2.9)	<.0001
Arterial phase enhancement			<.0001*
Mild	30 (69.8)	0	
Moderate	9 (20.9)	7 (10.3)	
Marked	4 (9.3)	61 (89.7)	
Portal venous phase enhancement			<.0001
Hypointense	25 (58.1)	1 (1.5)	
Iso- to hyperintense	18 (41.9)	67 (98.5)	
Late dynamic phase enhancement			<.0001
Hypointense	31 (72.1)	2 (2.9)	
Iso- to hyperintense	12 (27.9)	66 (97.1)	
Hepatobiliary phase enhancement†			<.0001
Hypointense	40 (93.0)	6 (8.8)	
Iso- to hyperintense	3 (7.0)	62 (91.2)	

Note.—Data are numbers of nodules, with percentages in parentheses.

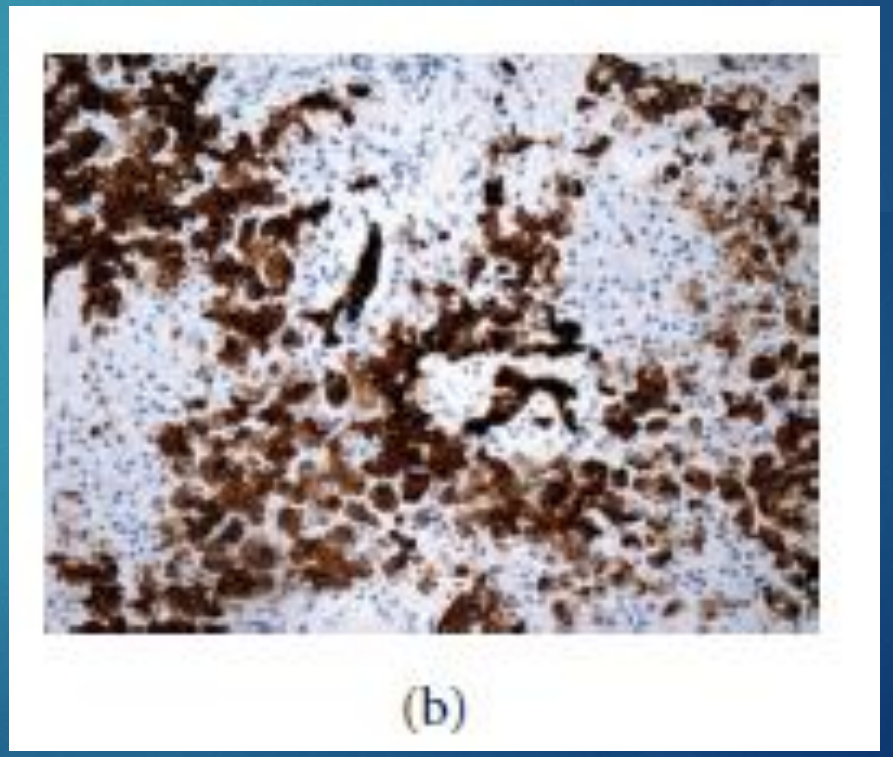
* Calculated with Fisher exact test.

† Hepatobiliary phase at 20 minutes.

Graziiolo et al, 2012

Comparing the Two

- Pathology staining appearance in the ideal situation



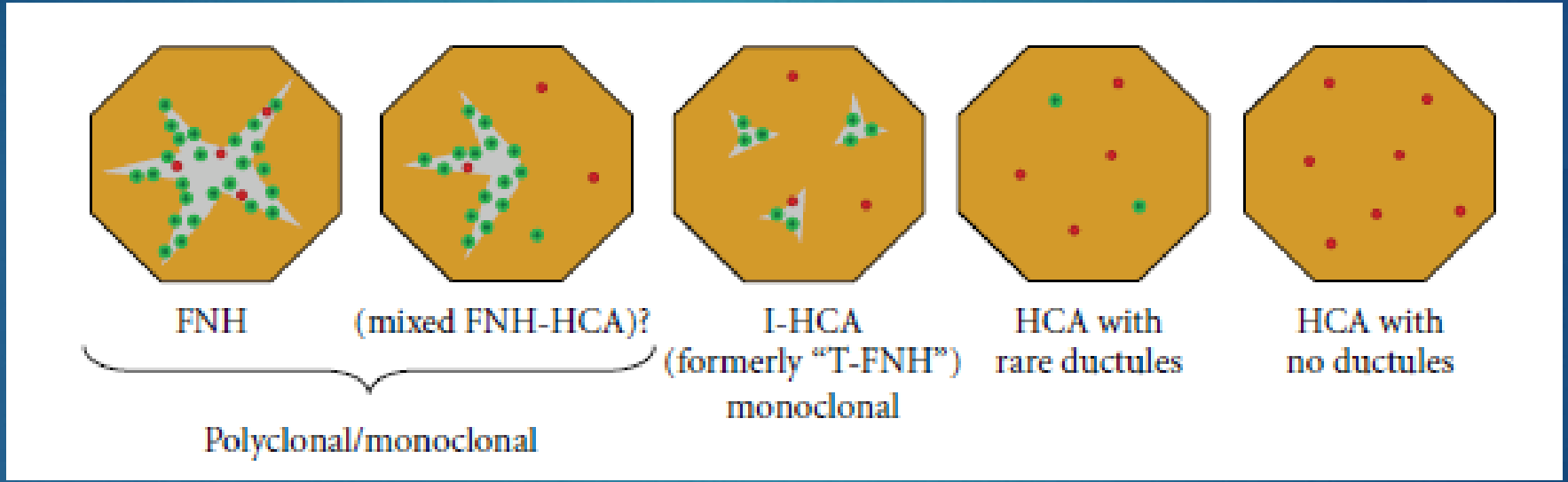
FNH

HCA

Walther & Jain, 2011

Comparing the Two

- Possibly thought of on a spectrum?



- Thus, sometimes may be hard to make a definitive distinction on imaging

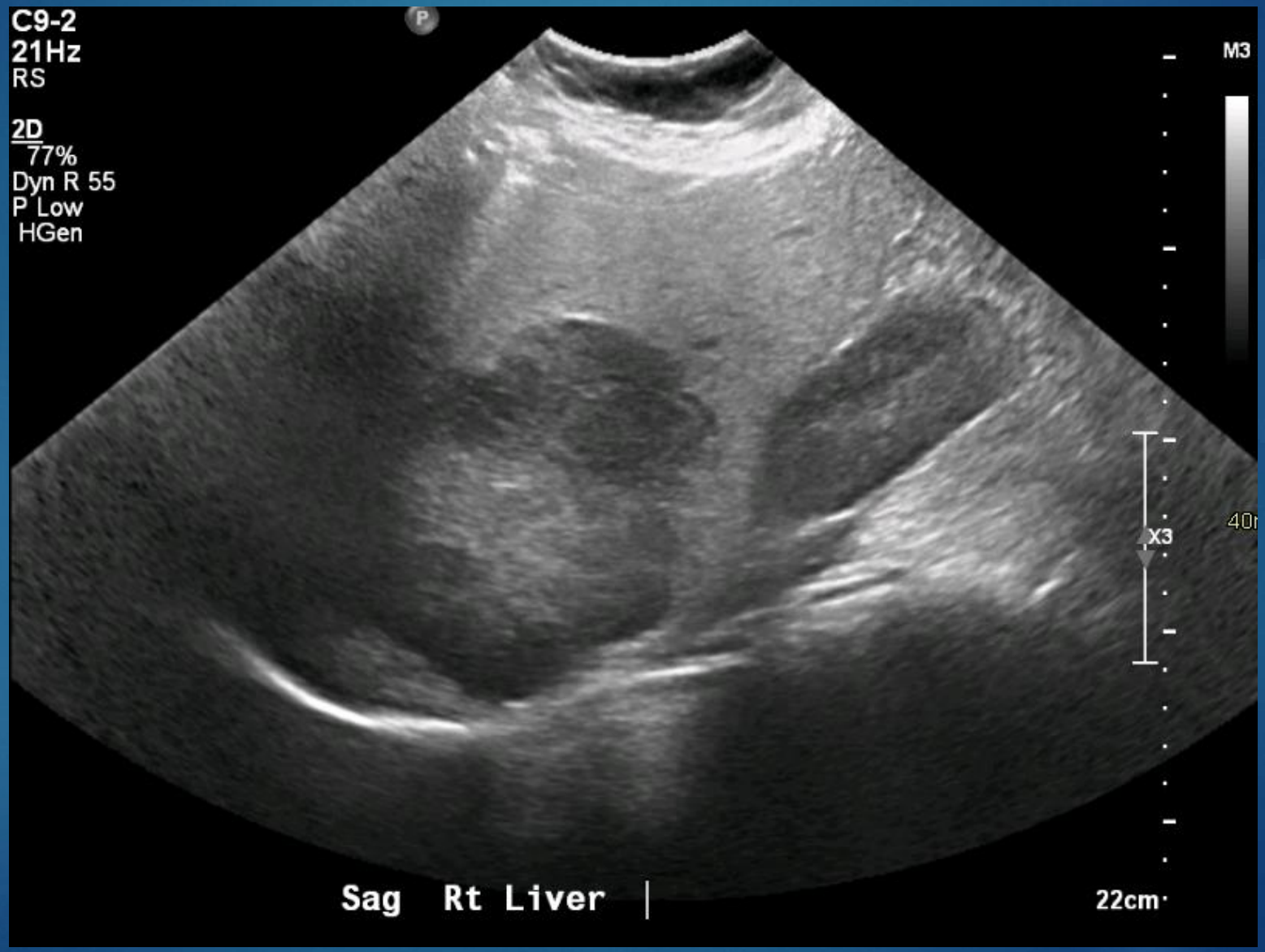
Walther & Jain, 2011

Quality Improvement Case

Case

- 38 yo female presented to emergency department with RUQ pain
- PMHx includes:
  - T2DM
  - Asthma
  - Hypothyroidism
  - Severe OCD/Anxiety Disorder
  - Hepatic Steatosis
- On OCP

Case



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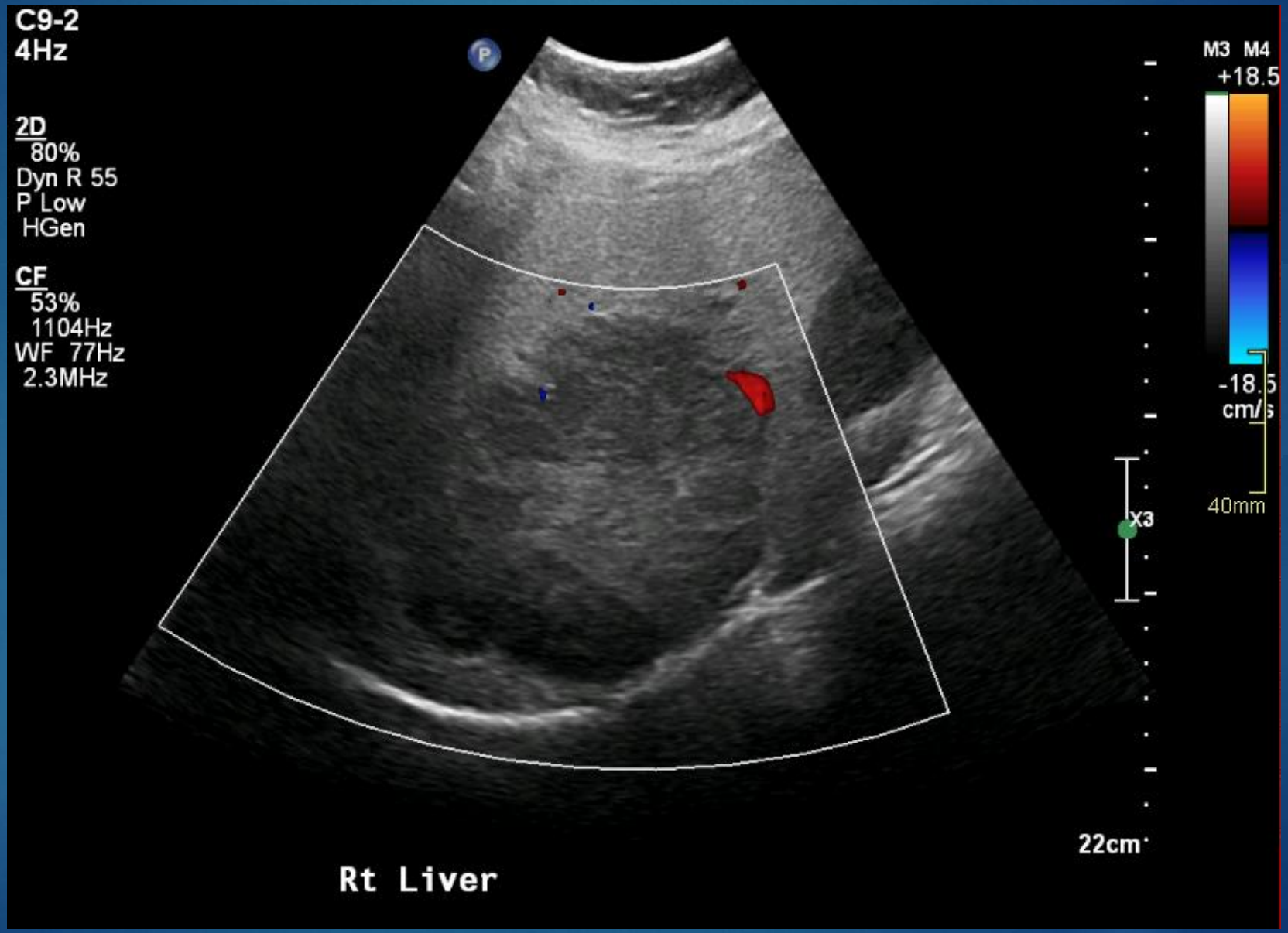
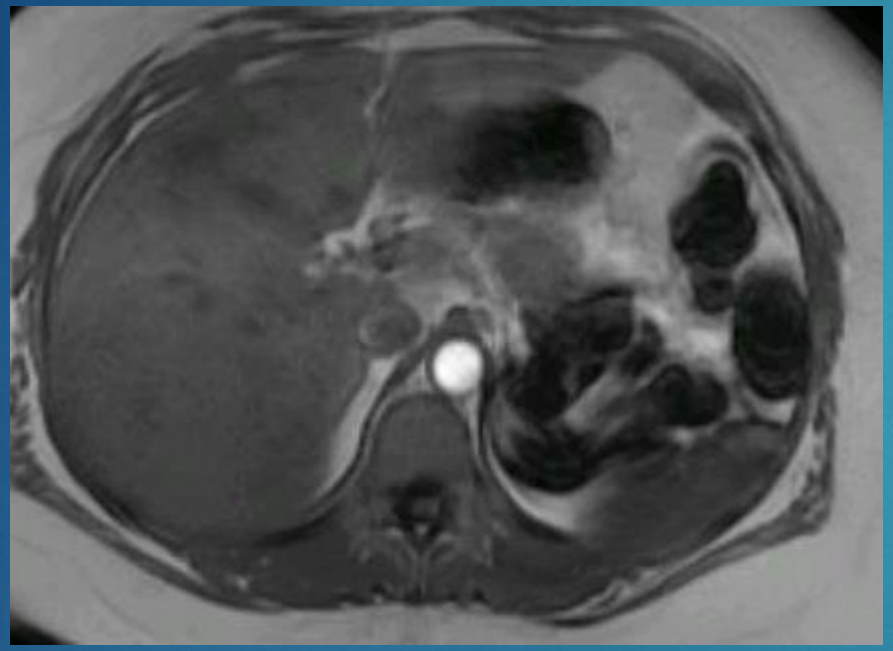
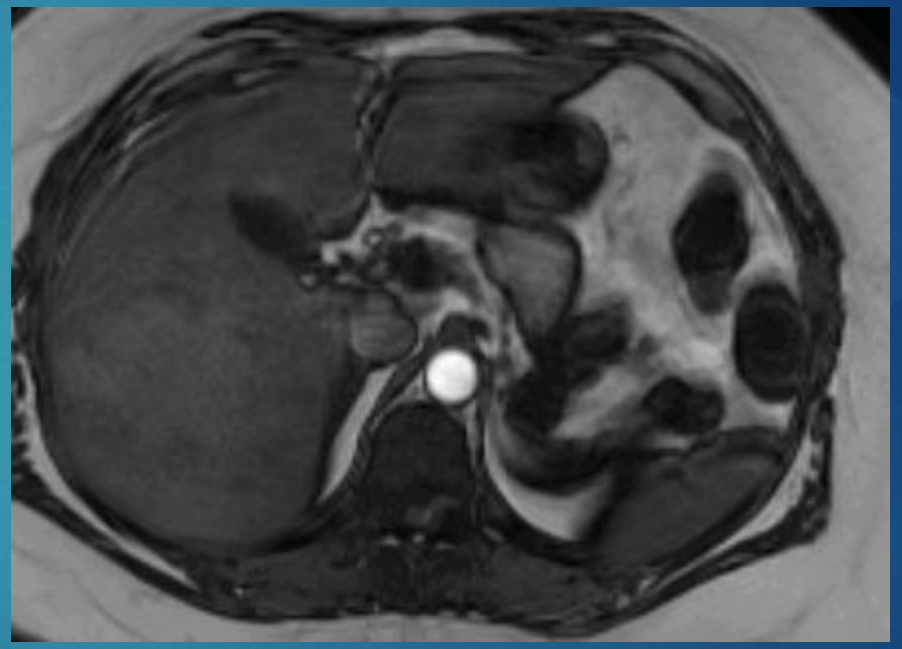

C9-2
4Hz
2D
80%
Dyn R 55
P Low
HGen
CF
53%
1104Hz
WF 77Hz
2.3MHz
M3 M4
+18.5
-18.5
cm/s
40mm
X3
22cm
Rt Liver

Case

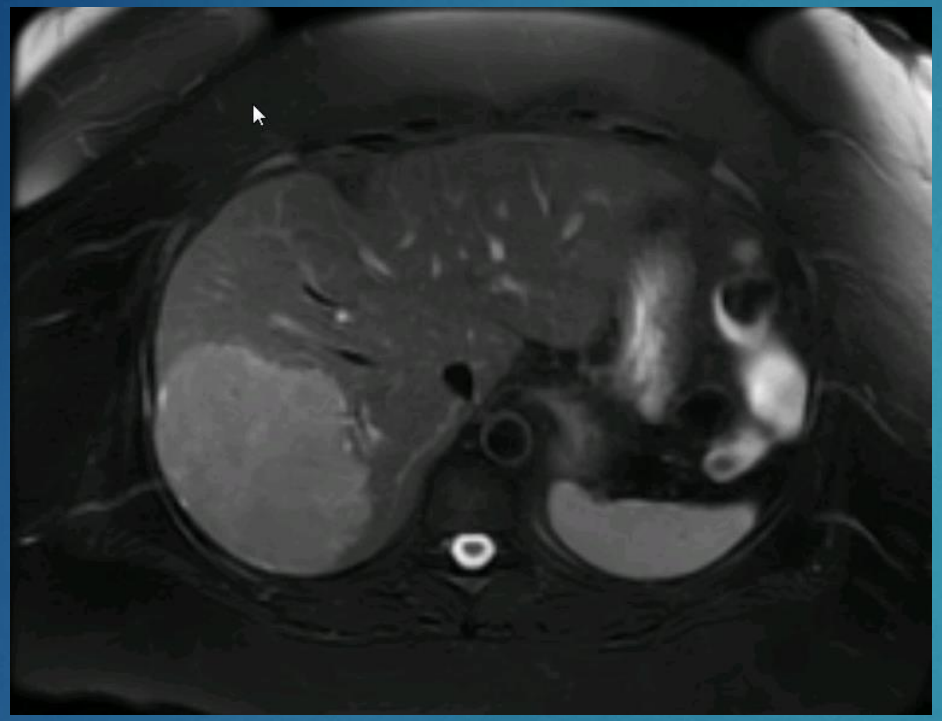


Ax fSPGR in-phase

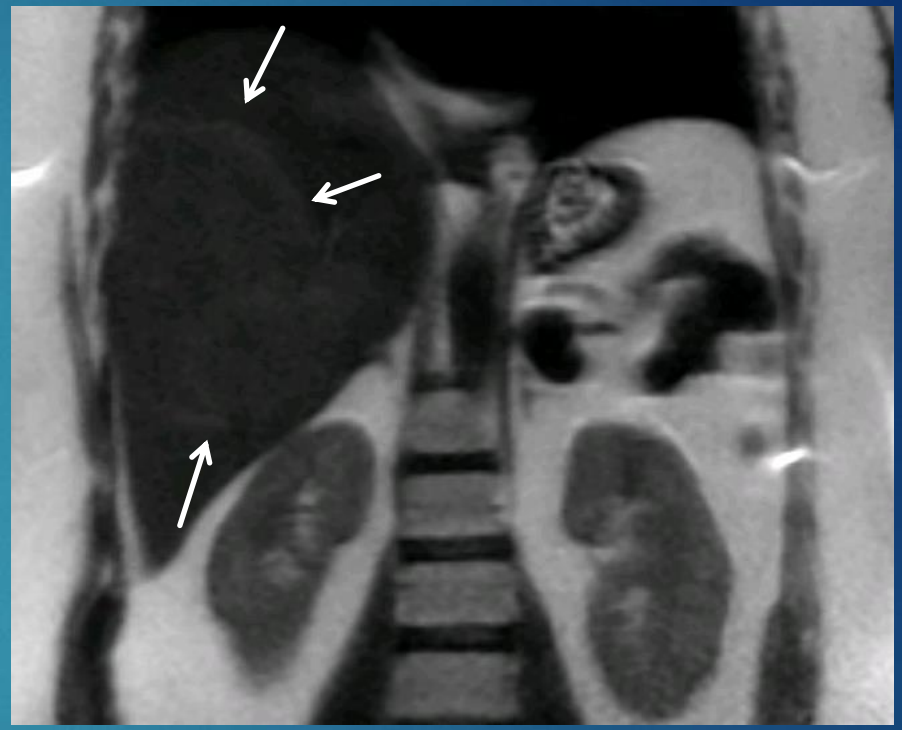


Ax fSPGR out-of-phase

Case



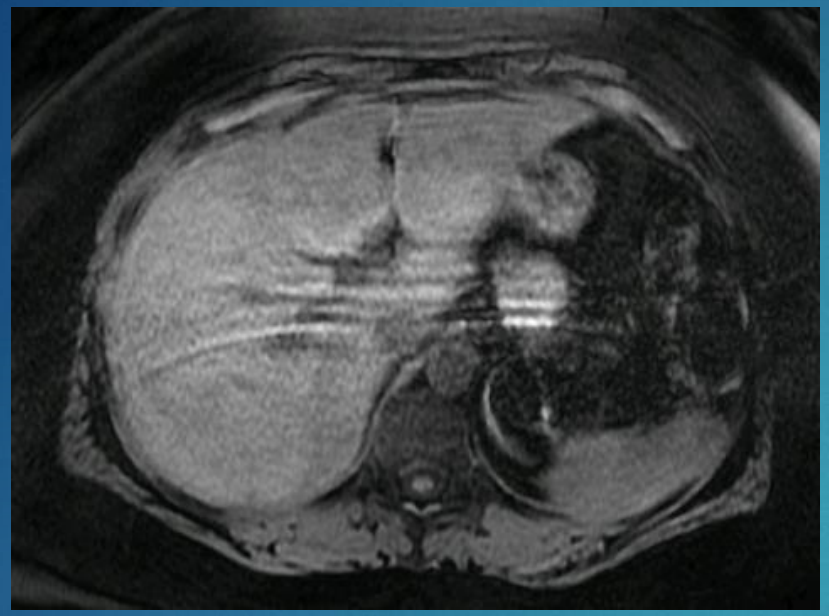
Ax FRFSE + FS

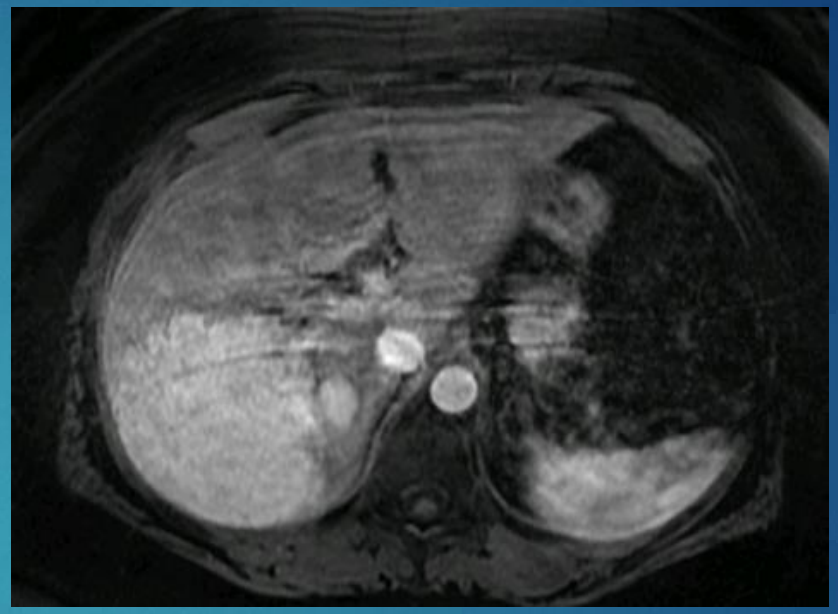


Cor SSFSE

Case

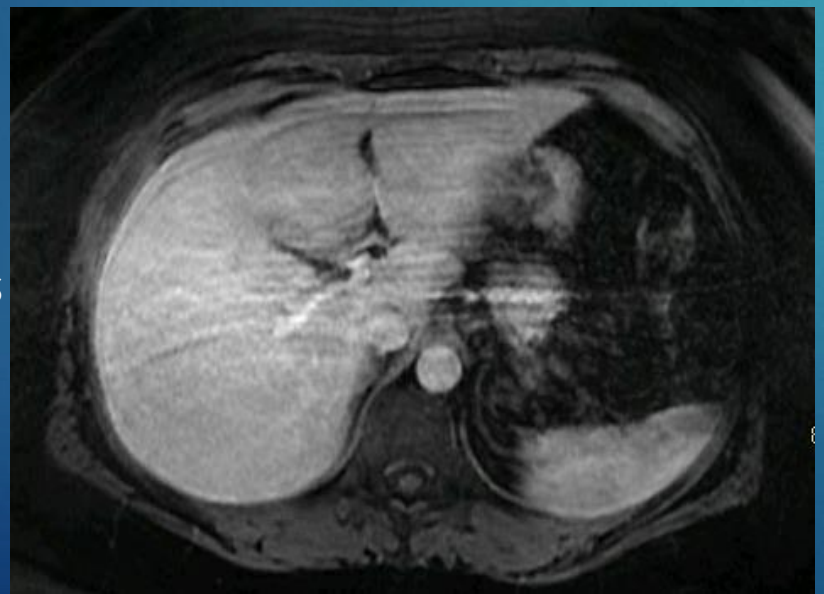
Unenhanced

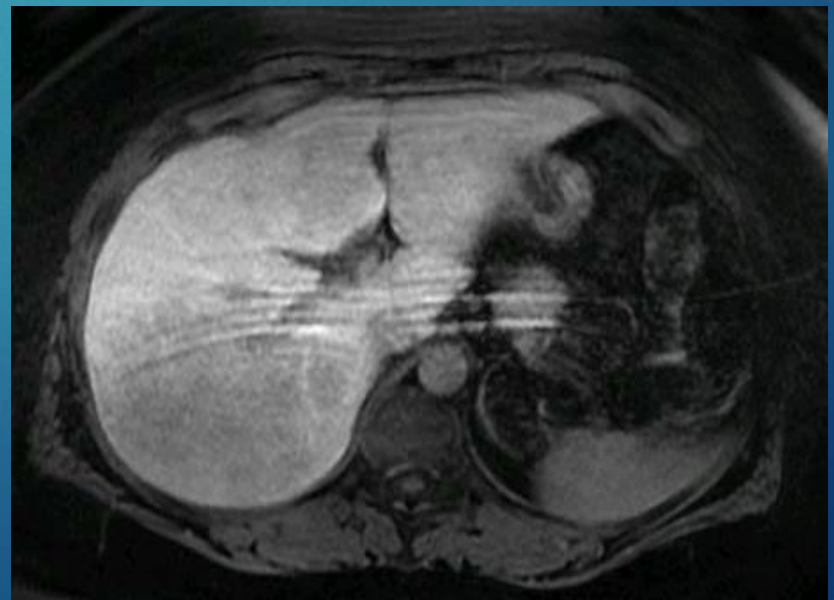




Arterial

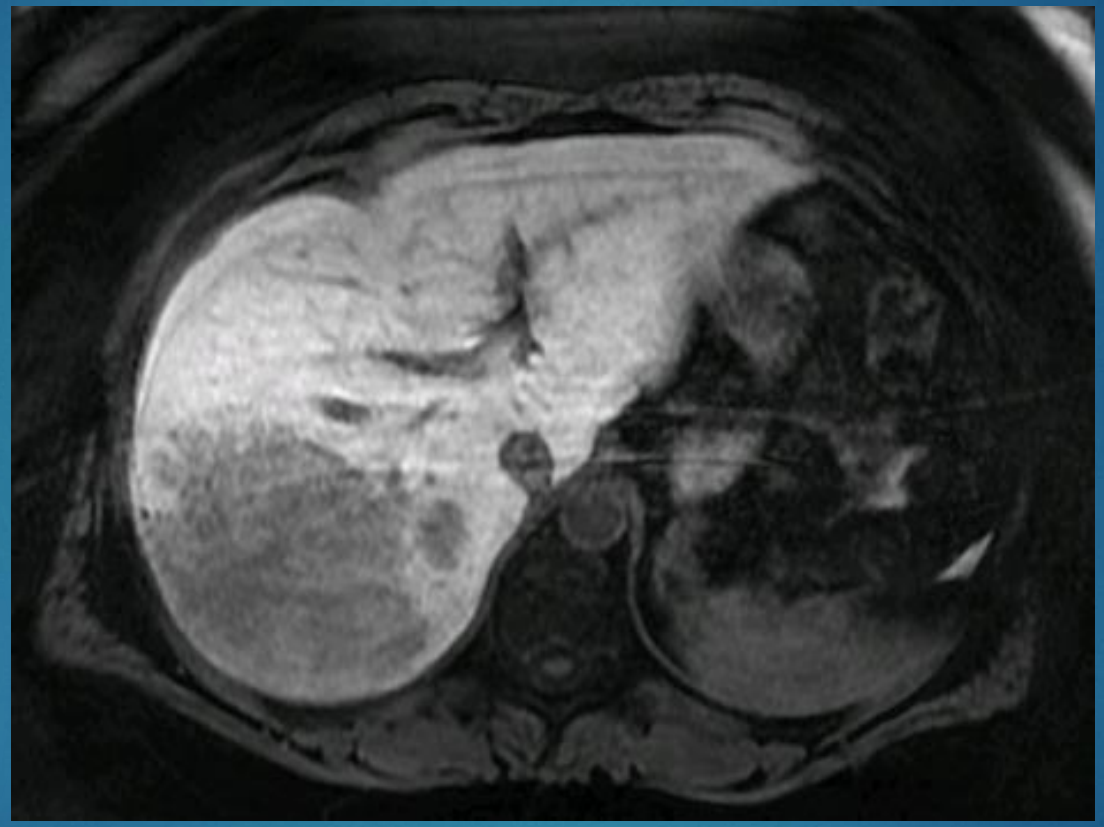
Portal Venous





Delayed

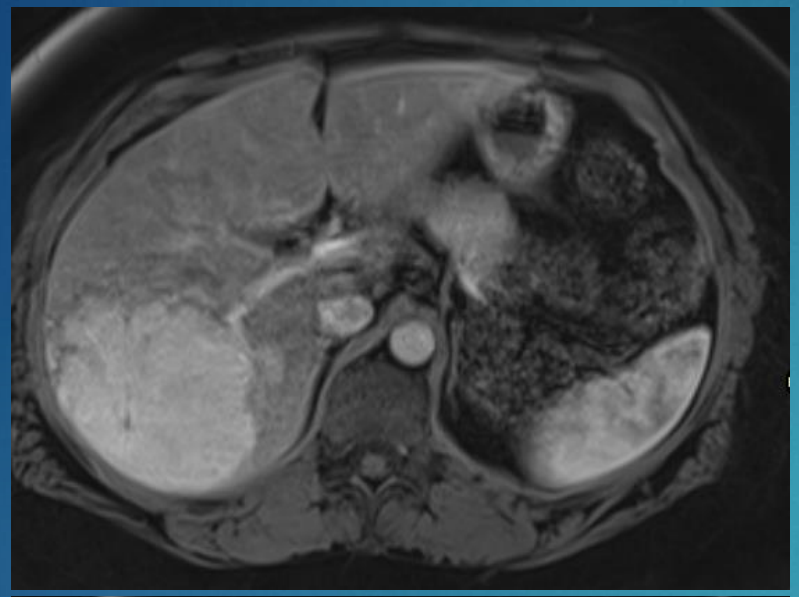
Case

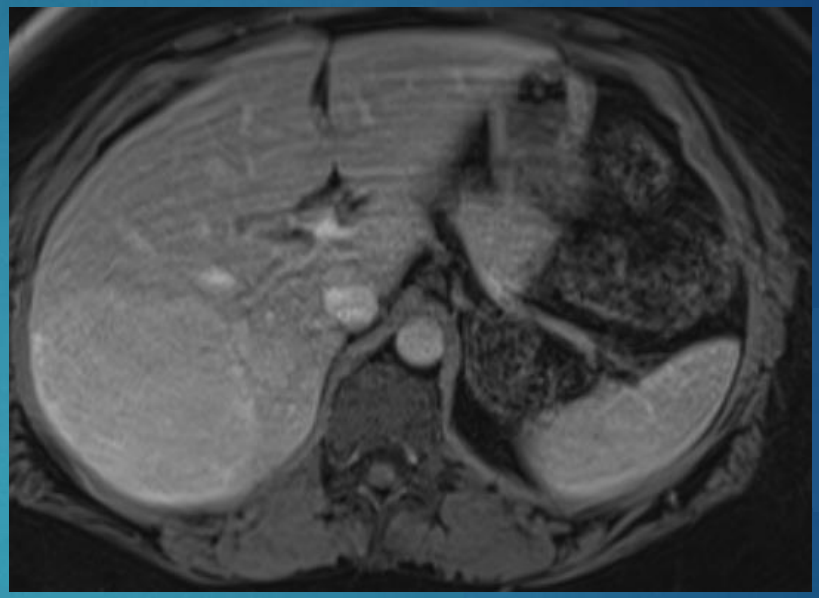


Hepatobiliary Phase

Case

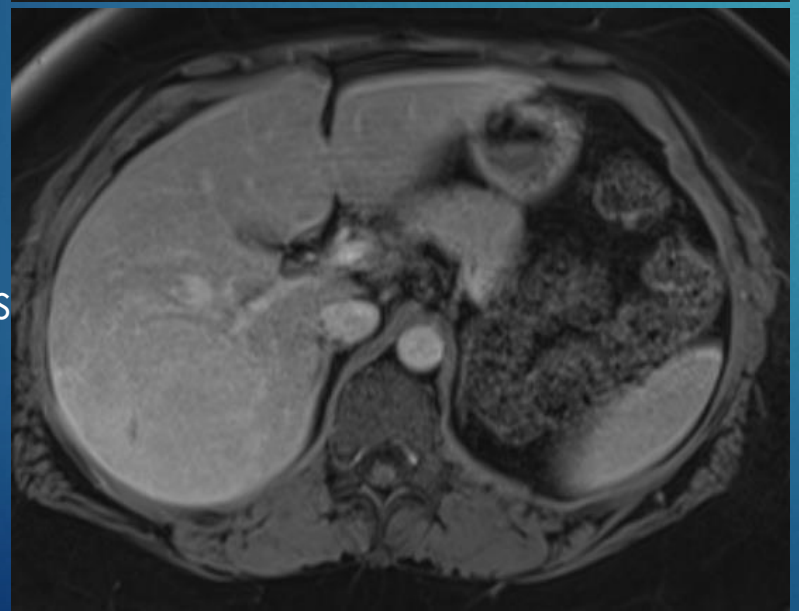
Unenhanced

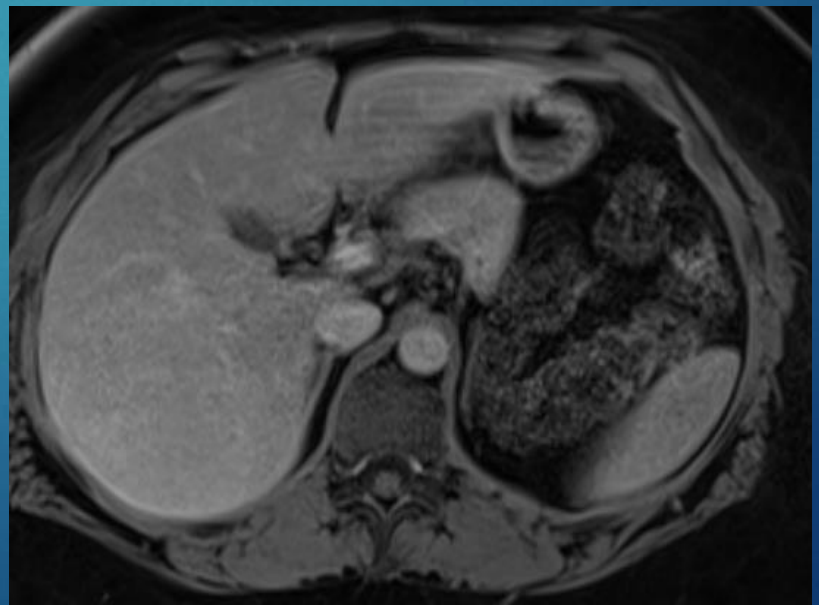




Arterial

Portal Venous



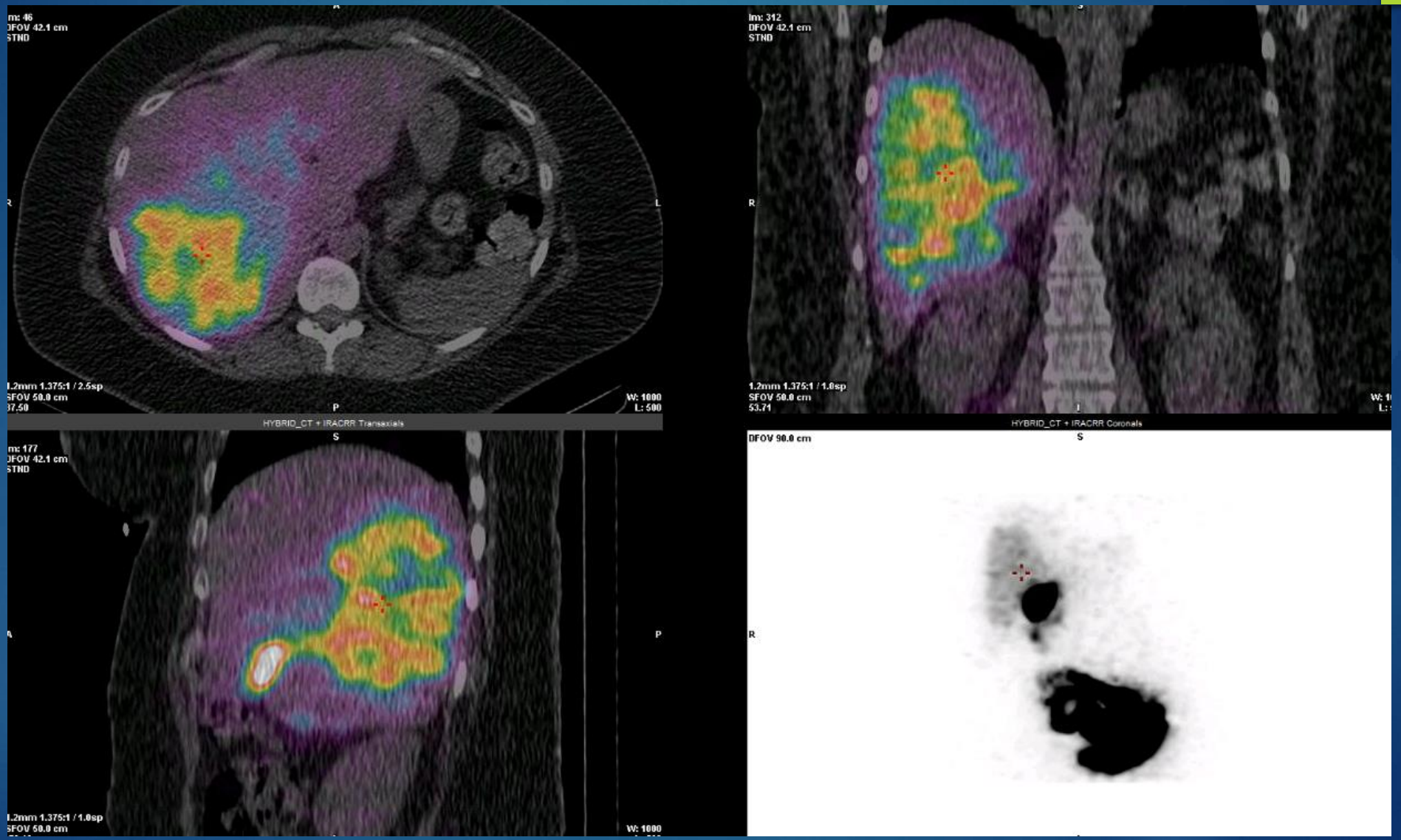


Delayed

Case

- However….
- Given the difference between the two MRI study results, patient's clinical team wanted confirmation study with Nuclear Medicine

Case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DFOV 42.1 cm
STND
1.2mm 1.375:1 / 2.5sp
SFOV 50.0 cm
W: 1000
L: 500
HYBRID_CT + IRACRR Transaxials
Im: 312
DFOV 42.1 cm
STND
1.2mm 1.375:1 / 1.0sp
SFOV 50.0 cm
HYBRID_CT + IRACRR Coronals
Im: 177
DFOV 42.1 cm
STND
1.2mm 1.375:1 / 1.0sp
SFOV 50.0 cm
W: 1000
DFOV 90.0 cm

Case

- Thoughts?
- Probably HCA, inflammatory subtype
- Further tests would be warranted

Summary

- Primovist is a hepatobiliary MRI contrast agent helpful in characterization of liver lesions, specifically differentiating FNH from other liver lesions and finding small malignancies
- FNH is a common liver lesion that is benign and does not require surgical resection, whereas HCA has a similar appearance and patient population, but treatment recommendation is surgical resection
- Clear communication with clinical team and clarify any possible misunderstandings where applicable

Questions?

- Thank you!

References

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