Focal liver lesions in the cirrhotic liver - not always HCC

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Focal liver lesions in the cirrhotic liver

- **Not** every focal liver lesion in the cirrhotic liver is **malignant**

- **Not** every malignant FLL in the cirrhotic liver is **HCC**

How many solid lesions in the cirrhotic liver are HCC?

- 76% of all solid lesions (CT/MRI) (1)

- In a CEUS study 81% of solid liver lesions corresponded to HCC (2)

(1)- Seitz K, Greis C, Schuler A, Bernatik T, Blank W, Dietrich CF, et al. Frequency of tumor entities among liver tumors of unclear etiology initially detected by sonography in the noncirrhotic or cirrhotic livers of 1349 patients. Results of the DEGUM multicenter study. Ultraschall Med 2011;32:598–603.
(2)- Terzi E, Iavarone M, Pompili M, Veronese L, Cabibbo G, Fraquelli M, et al. Contrast ultrasound LI-RADS LR-5 identifies hepatocellular carcinoma in cirrhosis in a multicenter restropective study of 1,006 nodules. J Hepatol 2018;68:485–92.

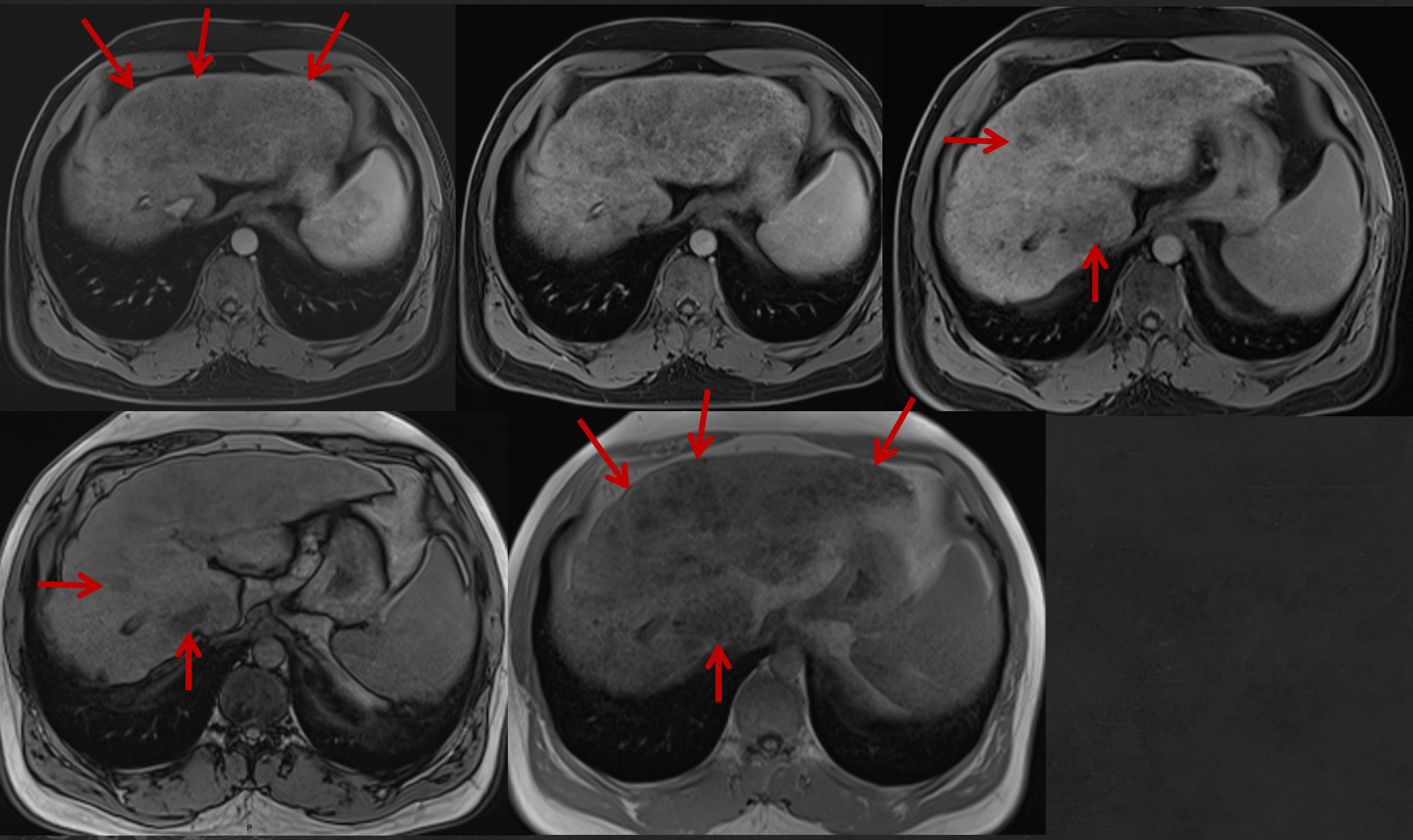
Focal liver lesions in the cirrhotic liver (other than HCC)

Benign lesions:

- Hemangioma, biliary cyst
- Regenerative nodules
- Dysplastic nodules

Malignant lesions:

- Cholangiocarcinoma
- Hepatocholangiocarcinoma
- Metastases



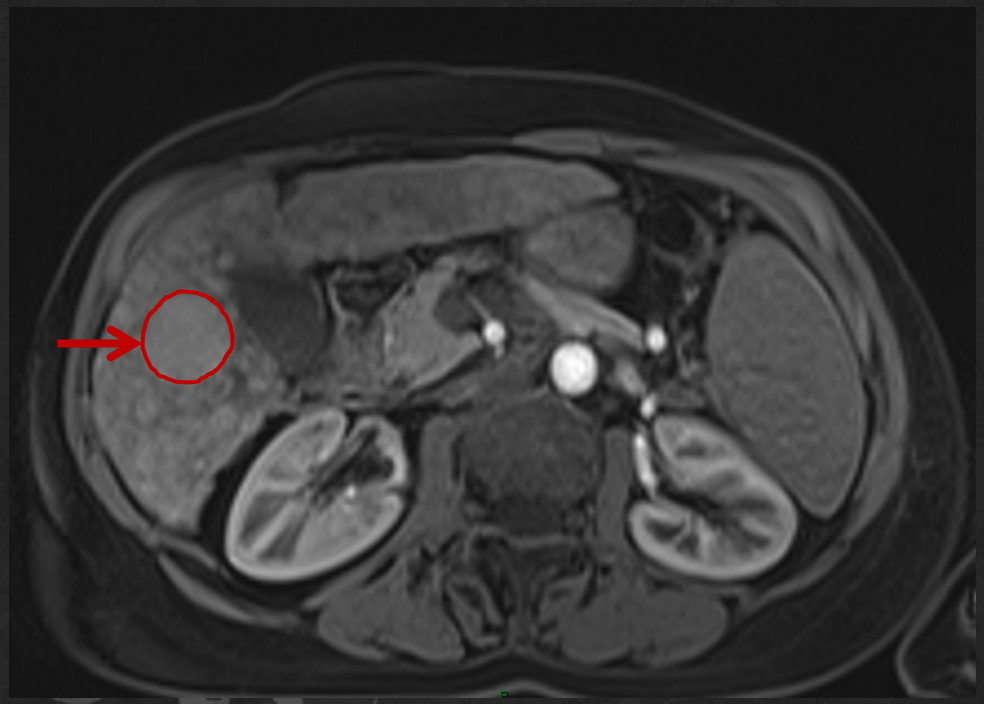
M, 43 years, liver cirrhosis. **Diffuse HCC?**

What makes a lesion less probable to be a HCC?

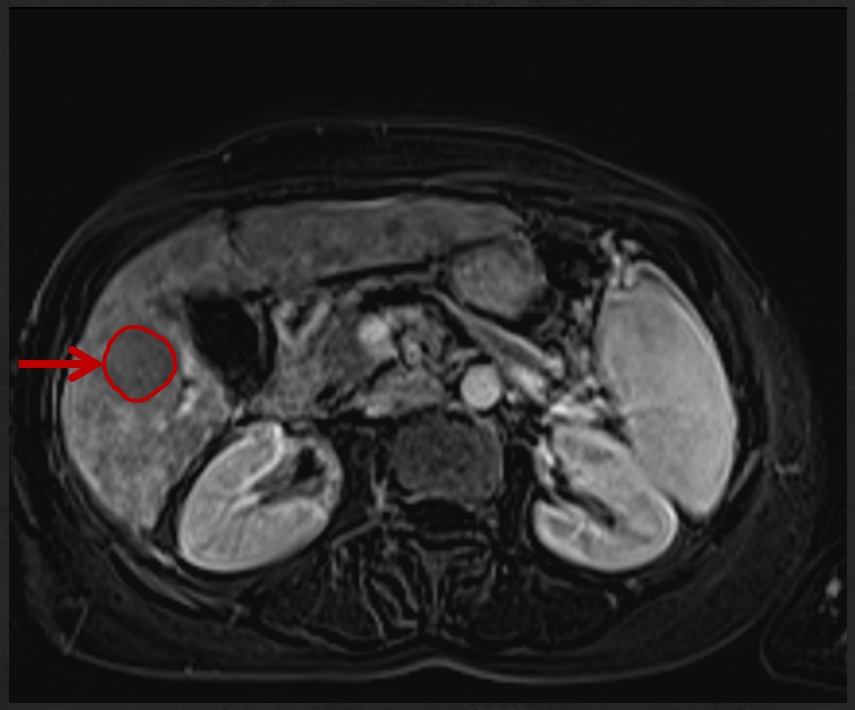
- ***Absence*** of arterial phase hyperenhancement (**APHE**)
- **APHE** is defined as **non-rim enhancement** of the entire lesion or of part of the observation, unequivocally more than the surrounding liver
- APHE has good sensitivity for the diagnosis of **advanced HCC** but may be **absent** in **well-differentiated HCC**
- Always look at the **T1 unenhanced images** (!)

Tang, A.; Bashir, M.R.; Corwin, M.T.; Cruite, I.; Dietrich, C.F.; Do, R.K.G.; Ehman, E.C.; Fowler, K.J.; Hussain, H.K.; Jha, R.C.; et al. Evidence Supporting LI-RADS Major Features for CT- and MR Imaging-based Diagnosis of Hepatocellular Carcinoma: A Systematic Review. Radiology **2018**, 286, 29–48.

HCC/ LI-RADS 5 lesion? – APHE and wash-out in the late phase?



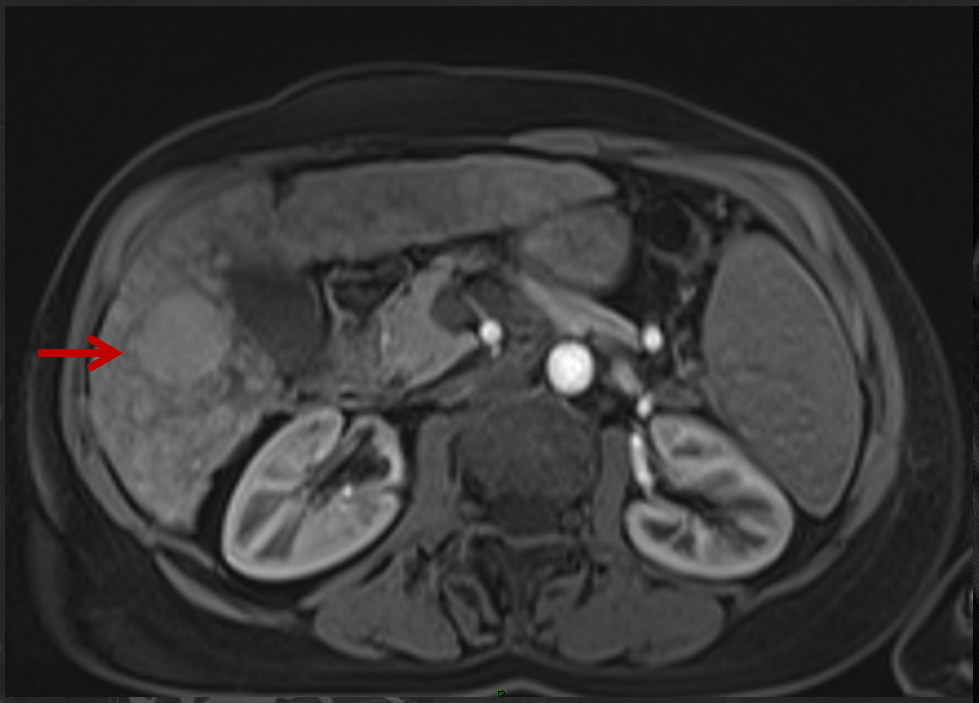
Arterial phase



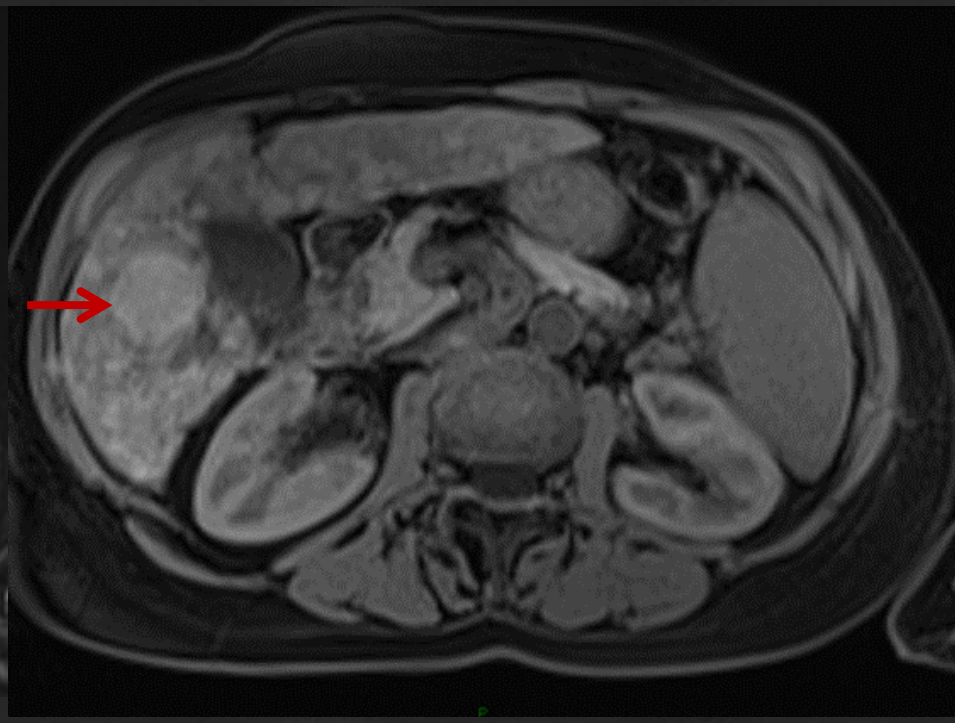
Late phase

But…

- There was **no** **arterial phase hyperenhancement**



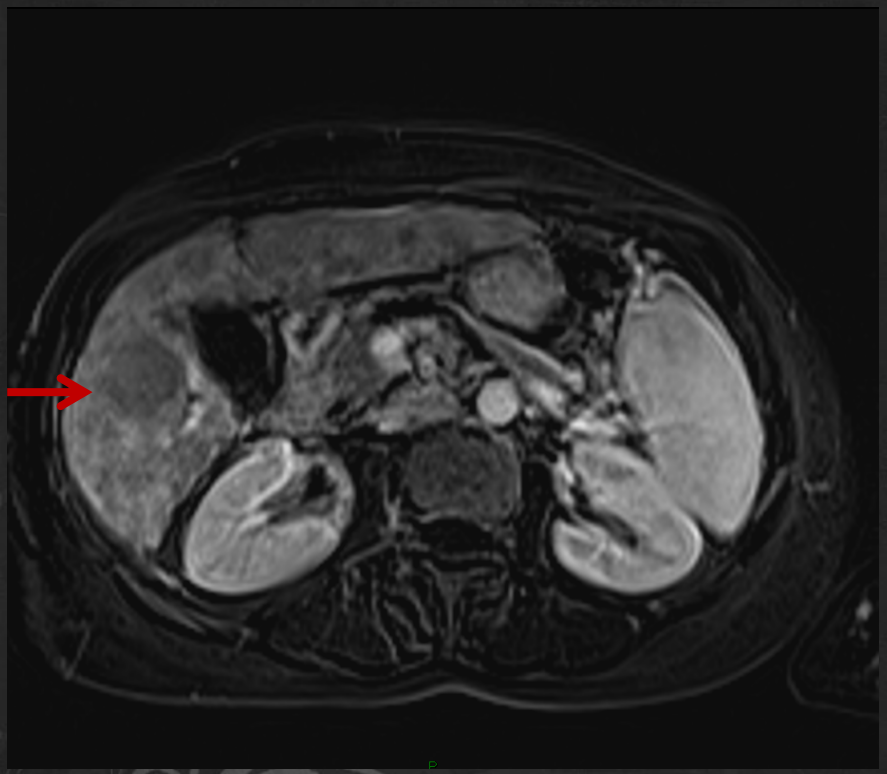
Arterial phase



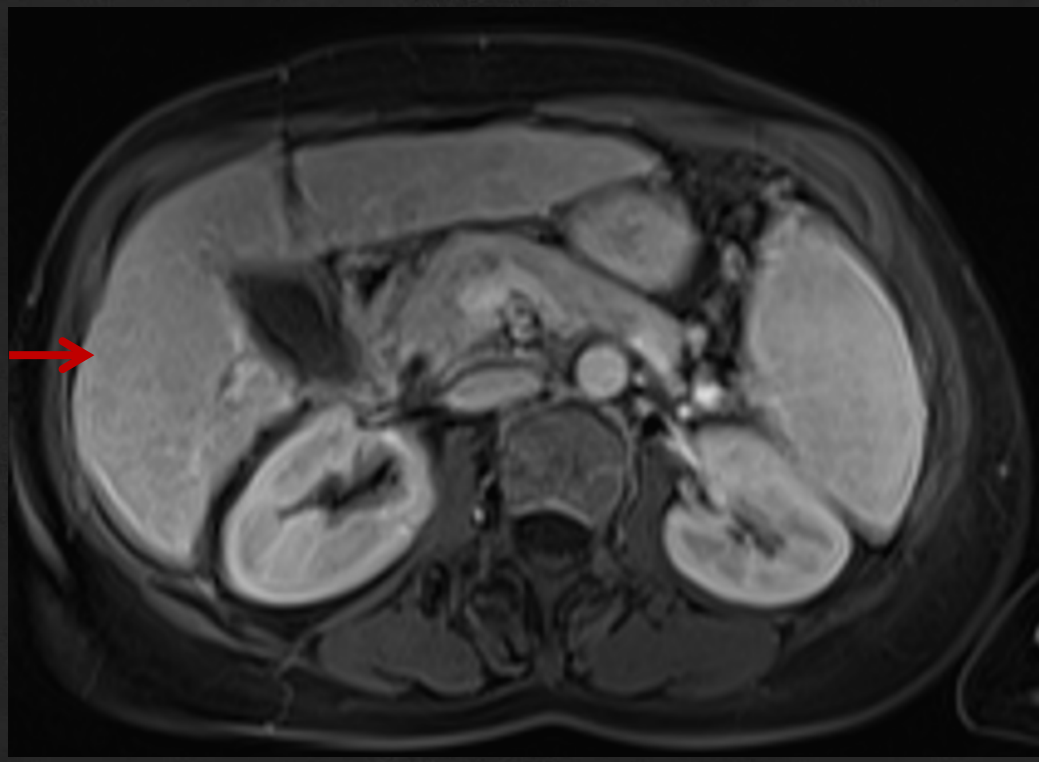
Unenhanced T1

And…

- There was **no** **wash-out** either

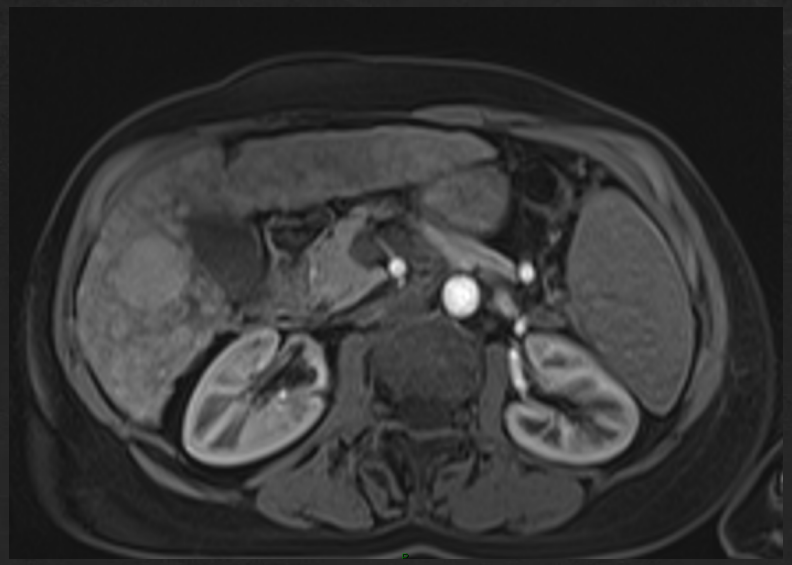


Subtracted image, late phase

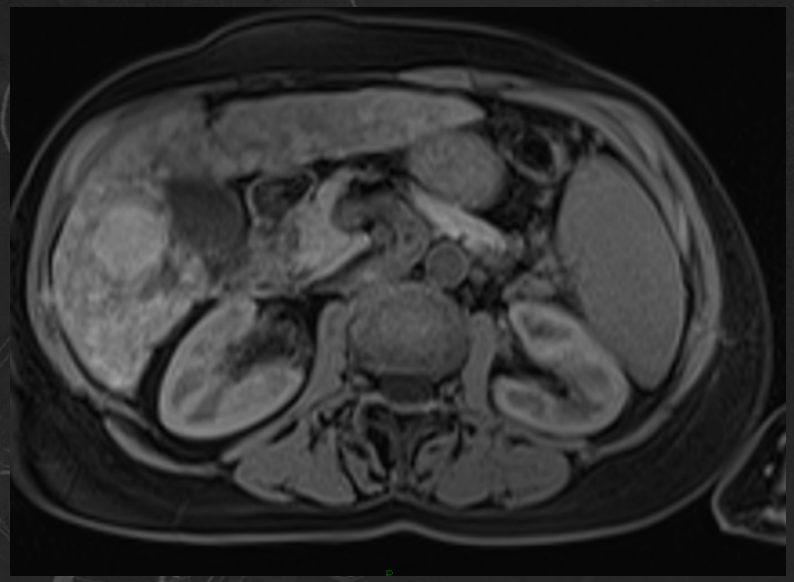


Late phase

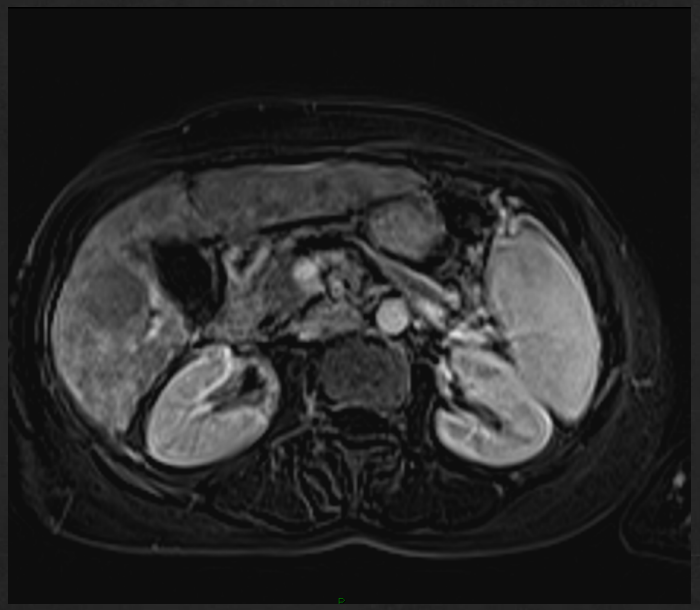
Li-RADS 5 observation – HCC?



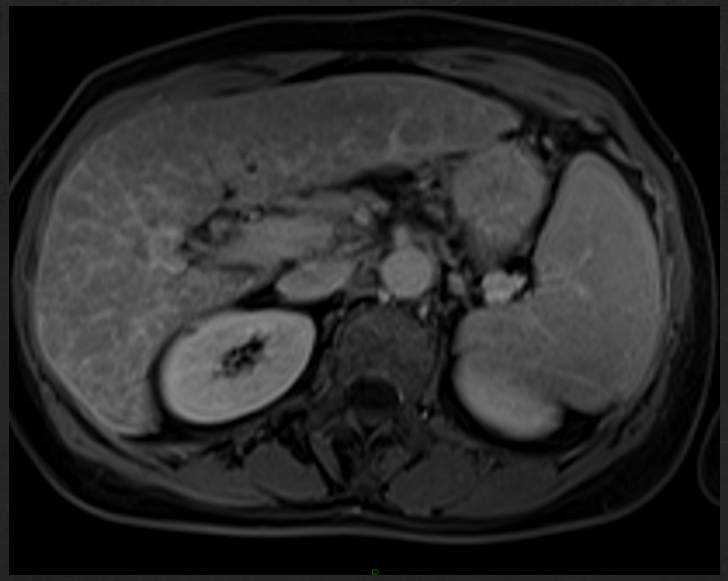
Arterial phase

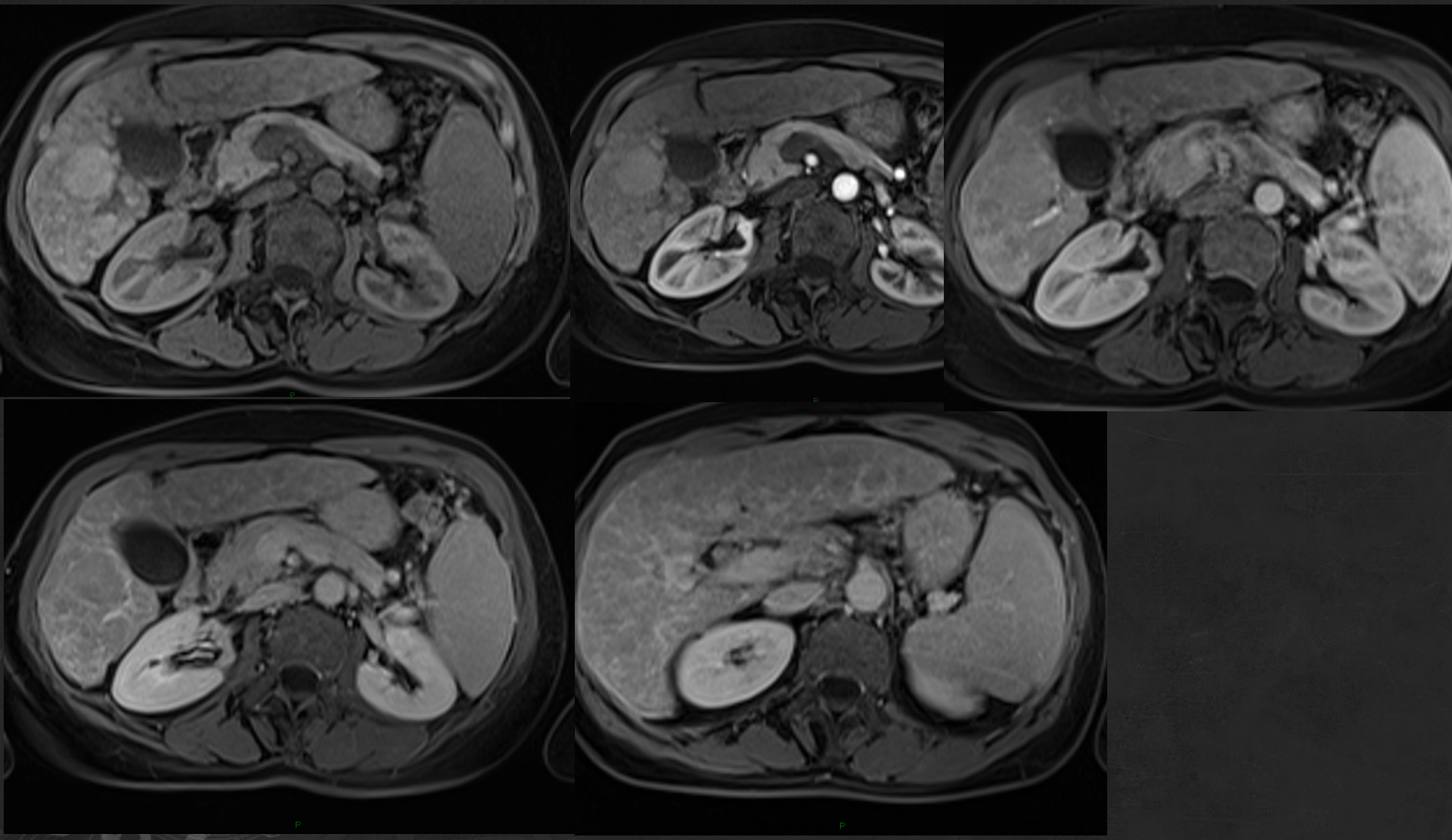


Biopsy: **regenerative nodule**



Late phase





W, 63 years, liver cirrhosis, **regenerative nodule**

Focal liver lesions in the cirrhotic liver

- Before reporting that a FLL has APHE always look at the **T1 unenhanced images**
- Liver fibrosis can enhance in the **late phases** more than the surrounding liver
- Always be cautious when interpreting **subtracted images**

Delayed Phase Pitfalls

In the early stages of hepatocarcinogenesis, the portal venous blood supply to the nodule decreases before the arterial neovascularization is sufficient to result in arterial phase hyperenhancement [12]. As a result, 10–20% of HCCs do not show arterial phase hyperenhancement and are visible only in the portal venous or delayed phase [13, 14]. Therefore, it is imperative to recognize that early HCC may be best seen in the portal venous and delayed phases and that review of portal venous and delayed phase images may reveal an early HCC [15]. Most portal venous and delayed phase hypoenhancing nodules are not HCCs, however; the differential diagnosis includes regenerative and dysplastic nodules. Another delayed phase pitfall is that delayed enhancing fibrosis around regenerative or dysplastic nodules may be mistaken for a capsule appearance, potentially causing false-positive interpretation of these benign lesions as HCC. Similarly, enhancing fibrosis can create the perception of washout in a nodule when this imaging feature is absent, potentially causing misdiagnosis.

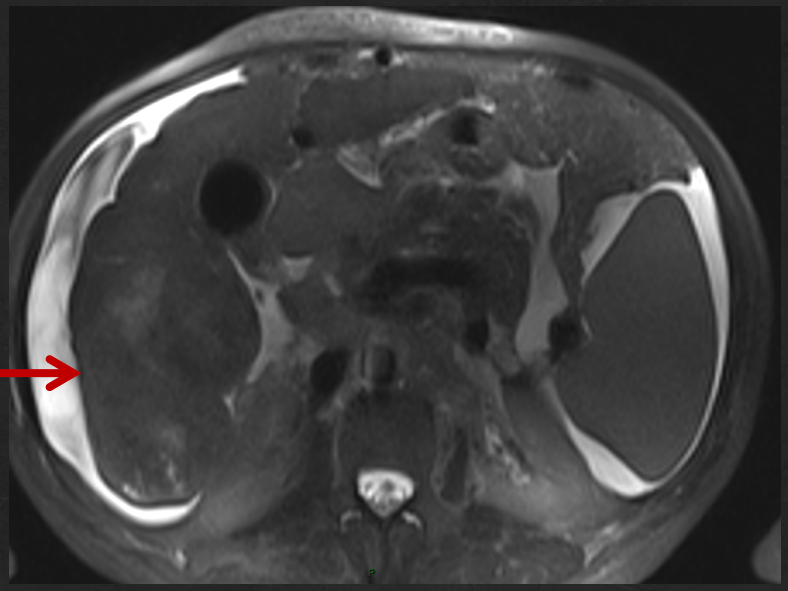
Heavily T2-Weighted Imaging Pitfalls

Some benign hepatic lesions, such as hemangiomas and cysts, typically appear markedly hyperintense compared with background liver on T2-weighted images, and this relative hyperintensity is accentuated on heavily T2-weighted images with longer TE. A sequence may be considered heavily T2-weighted when the TE is at least 140 ms [16]. Malignant hepatic lesions appear slightly hyperintense on T2-weighted images, and the degree of relative hyperintensity often decreases with the prolonged TE, to the point at which lesions may appear nearly isointense on heavily T2-weighted images [17] (Fig. 2). Therefore, heavily T2-weighted images may not depict malignant solid lesions that would otherwise be discernible on routine T2-weighted images [18]. Thus, to improve detection of malignant hepatic lesions, heavily T2-weighted sequences should not be used as the sole T2-weighted sequence for screening of patients with chronic liver disease.

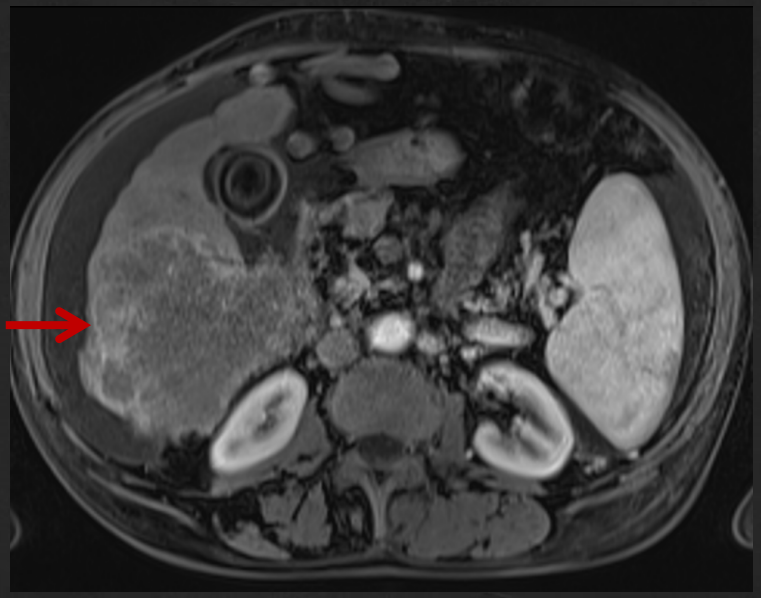
Elsayes KM, Chernyak V, Morshid AI, et al. Spectrum of pitfalls, pseudolesions, and potential misdiagnoses in cirrhosis. *AJR* 2018; 211:87–96

What makes a lesion less probable to be a HCC?

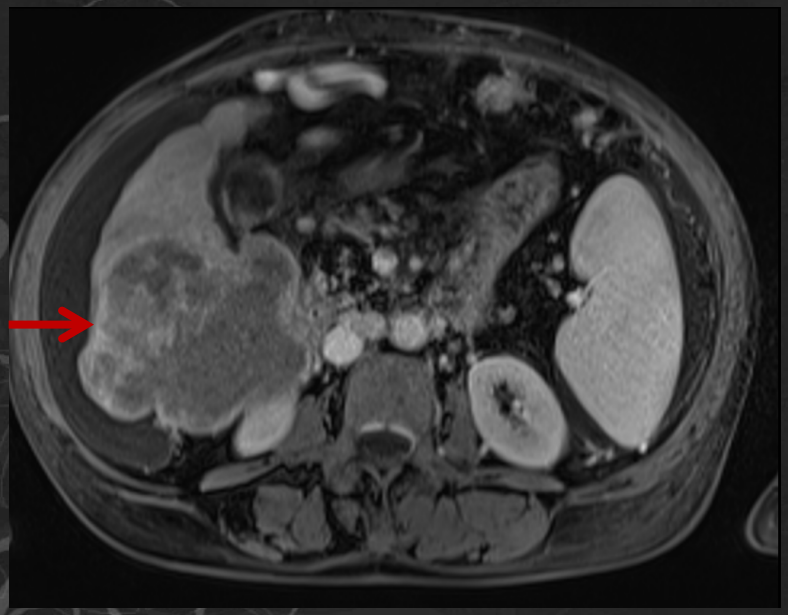
- **Rim enhancement** of the lesion
- Rim enhancement and +/- **rim wash-out**, only involving the **periphery** of the lesion, suggests a **non-HCC malignancy**
- Rim enhancement can be present in **cholangiocellular carcinoma**, **metastases** or **mixed** hepatocellular-cholangiocellular **carcinomas**
- But still, many of the observations which present rim enhancement are **HCC nodules**.
- ↑ **AFP** vs ↑ **CA 19-9**



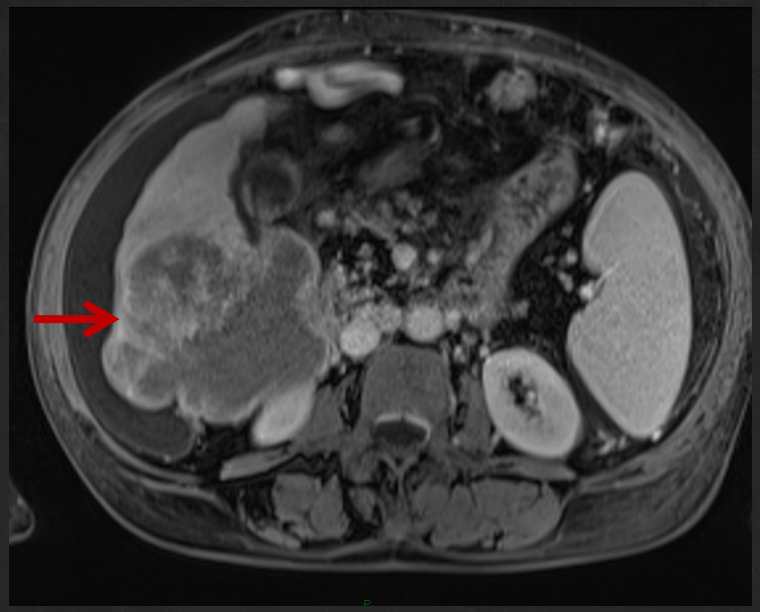
T2



Arterial phase



Portal phase

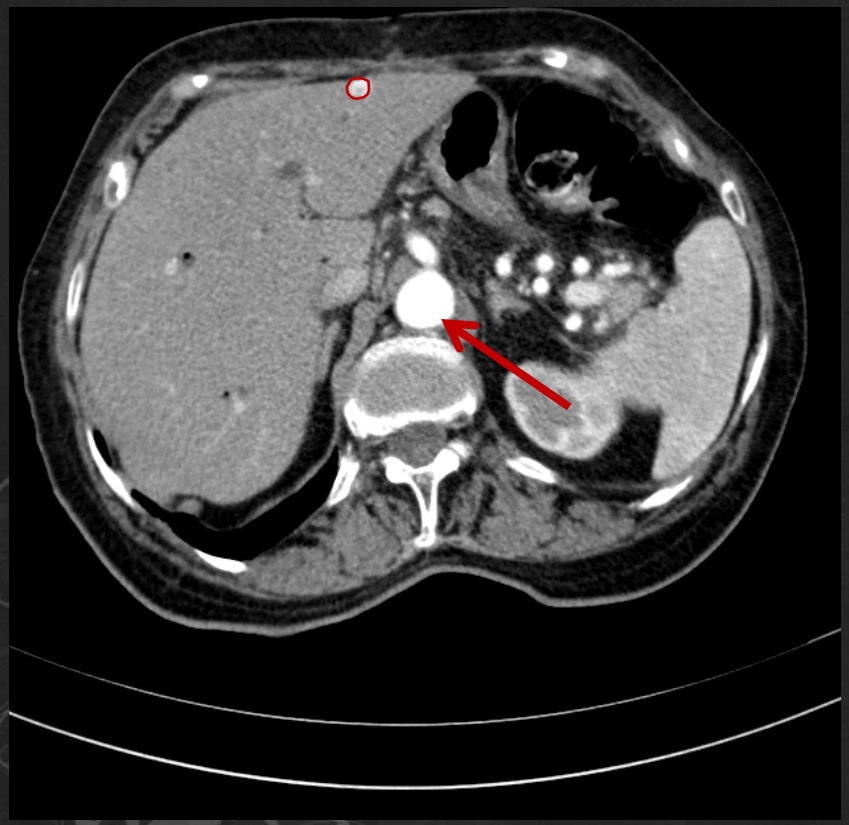


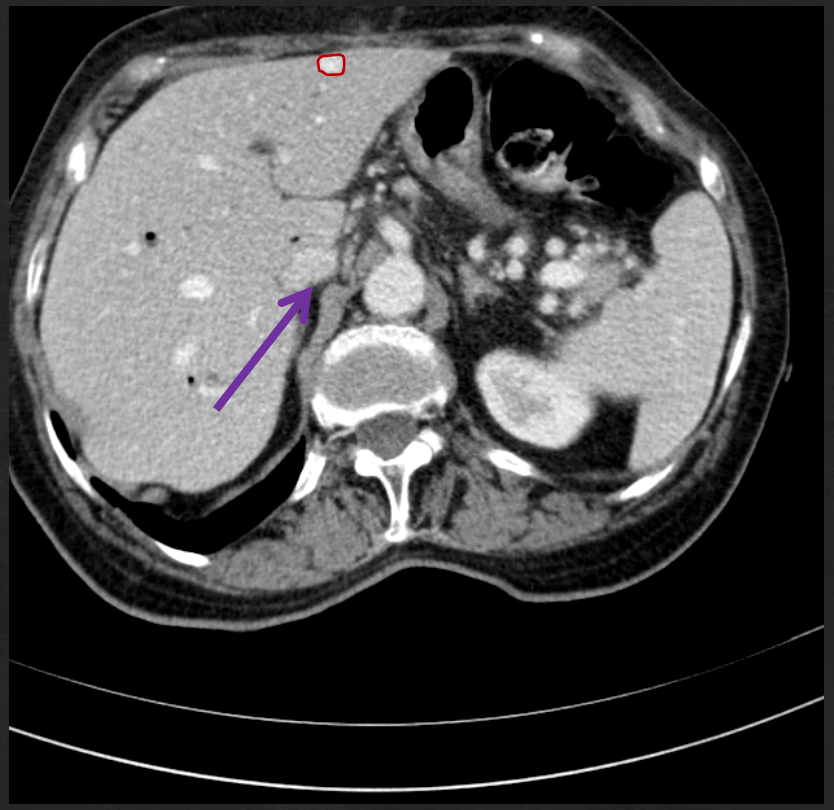
Late phase

What makes a lesion less probable to be a HCC?

- The enhancement of the lesion **parallels** the enhancement of the **blood vessels**
- **"Blood-pool sign"**
- Small, rapidly enhancing **hemangiomas**
- ***No*** true washout is present
- **Pseudo washout** in the **transitional phase**
- ***Absence*** of enhancement in the **hepatobiliary phase**

Capillary hemangioma - small liver lesion which has an enhancement parallel to the blood flow

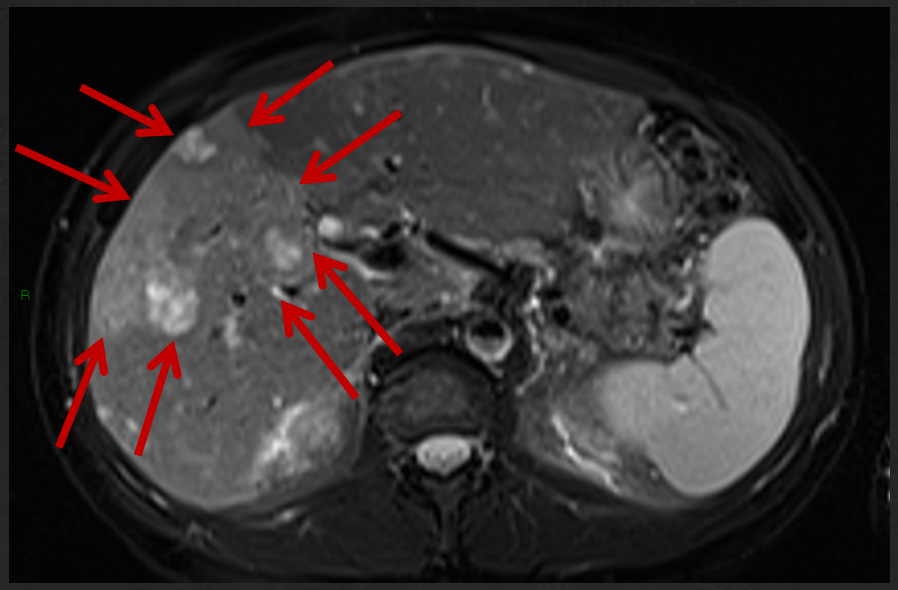




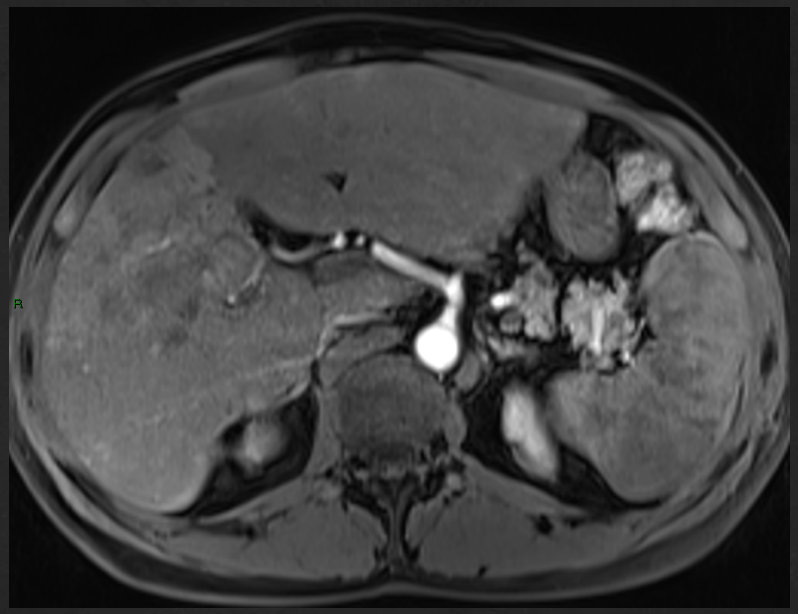
What makes a lesion less probable to be a HCC?

- Marked **T2 hyperintensity**
- A lesion which shows marked T2 hyperintensity is more likely to contain **fluid** (**biliary cyst** or **hemangioma**)
- The **whole lesion** has to be T2 hyperintense, not only its central part (differential diagnosis: **necrosis** inside a HCC)
- **Hemangiomas** decrease in size and become fibrotic in the cirrhotic liver. They can **loose their typical** enhancement pattern

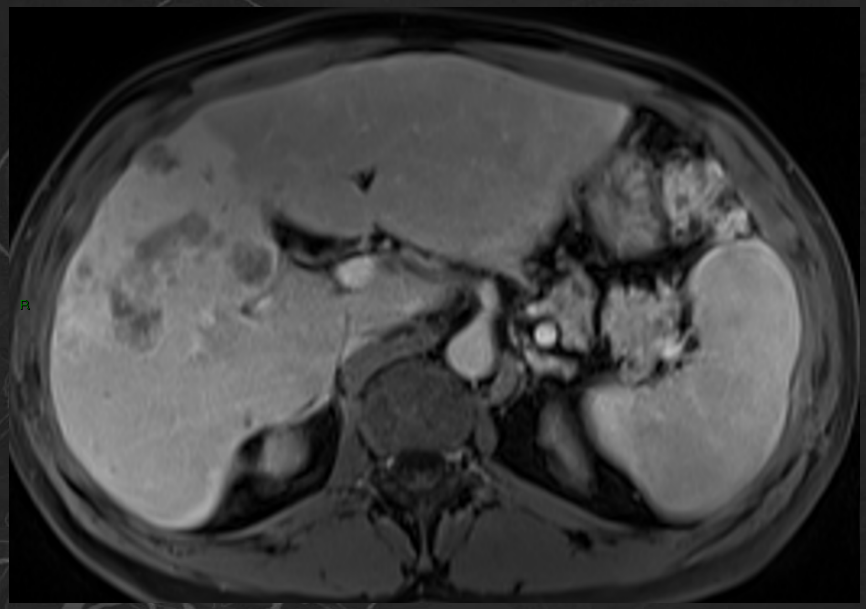
Brancatelli G, Federle MP, Blachar A, Grazioli L. Hemangioma in the cirrhotic liver: diagnosis and natural history. Radiology 2001;219:69–74.



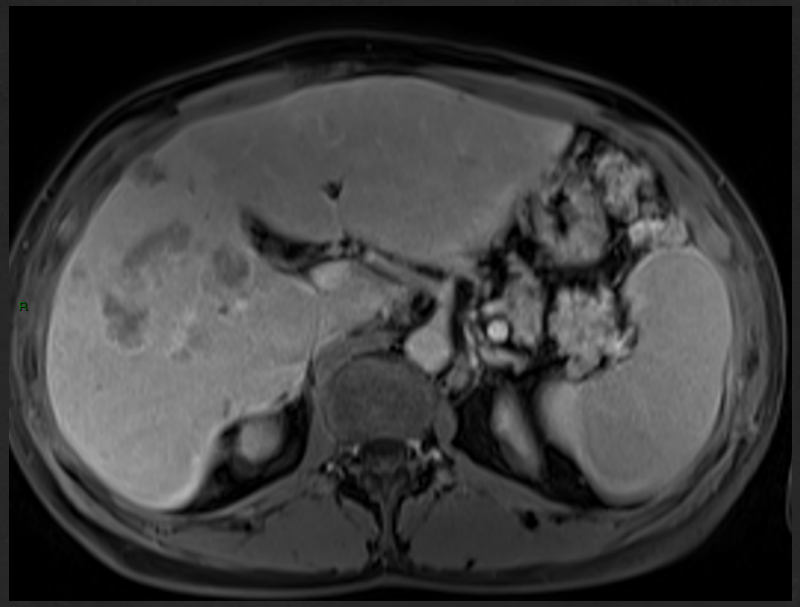
T2



T1 arterial phase



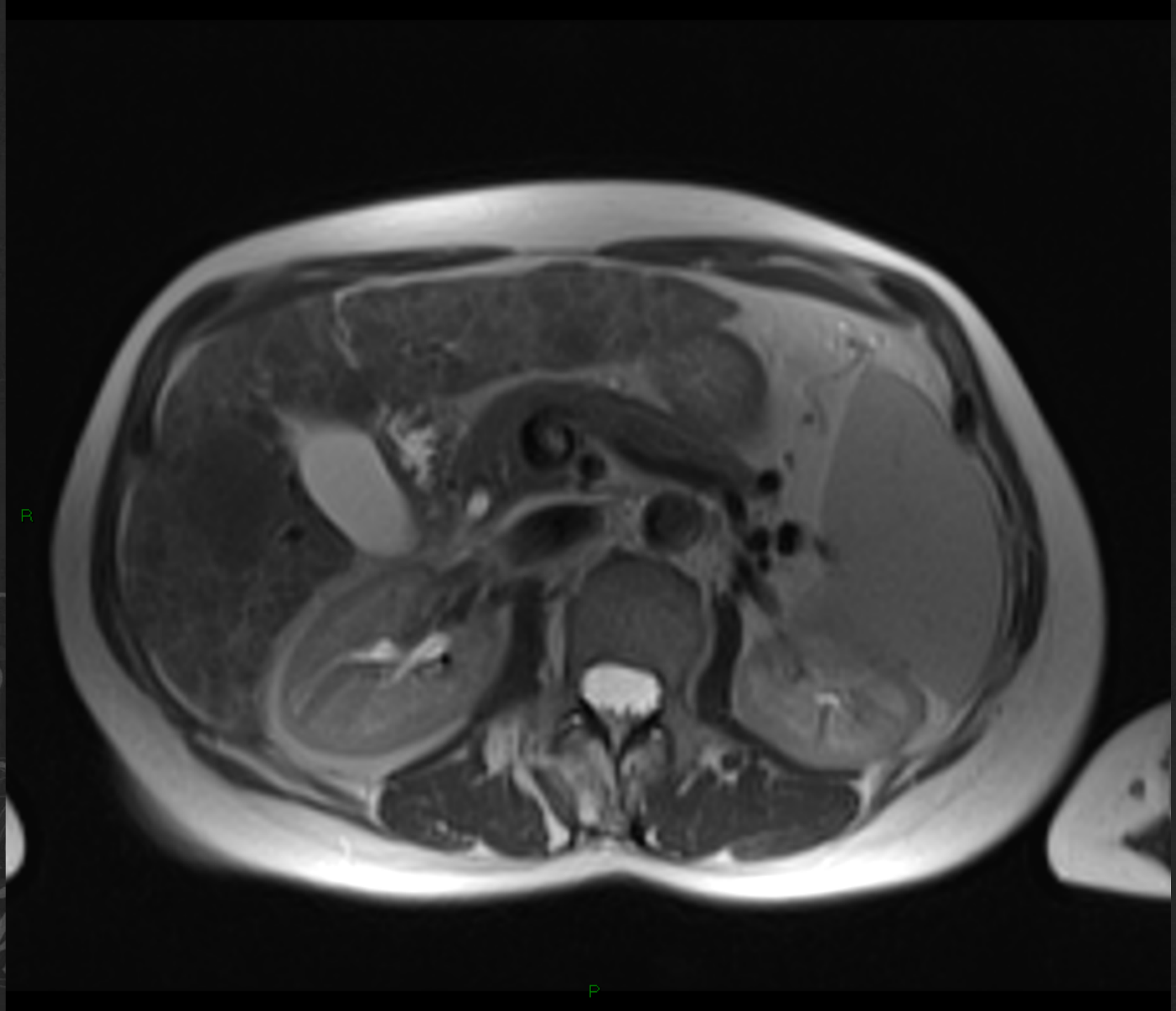
T1 portal phase



T1 late phase

What makes a lesion less probable to be a HCC?

- Presence of **iron** **in the lesion** more than in the surrounding liver
- **Low signal** on the **T2/T2* weighted** images
- The presence of iron is indicative of a **regenerative nodule** more than a HCC
- Siderotic regenerative nodules are a marker for **severe** alcoholic or viral cirrhosis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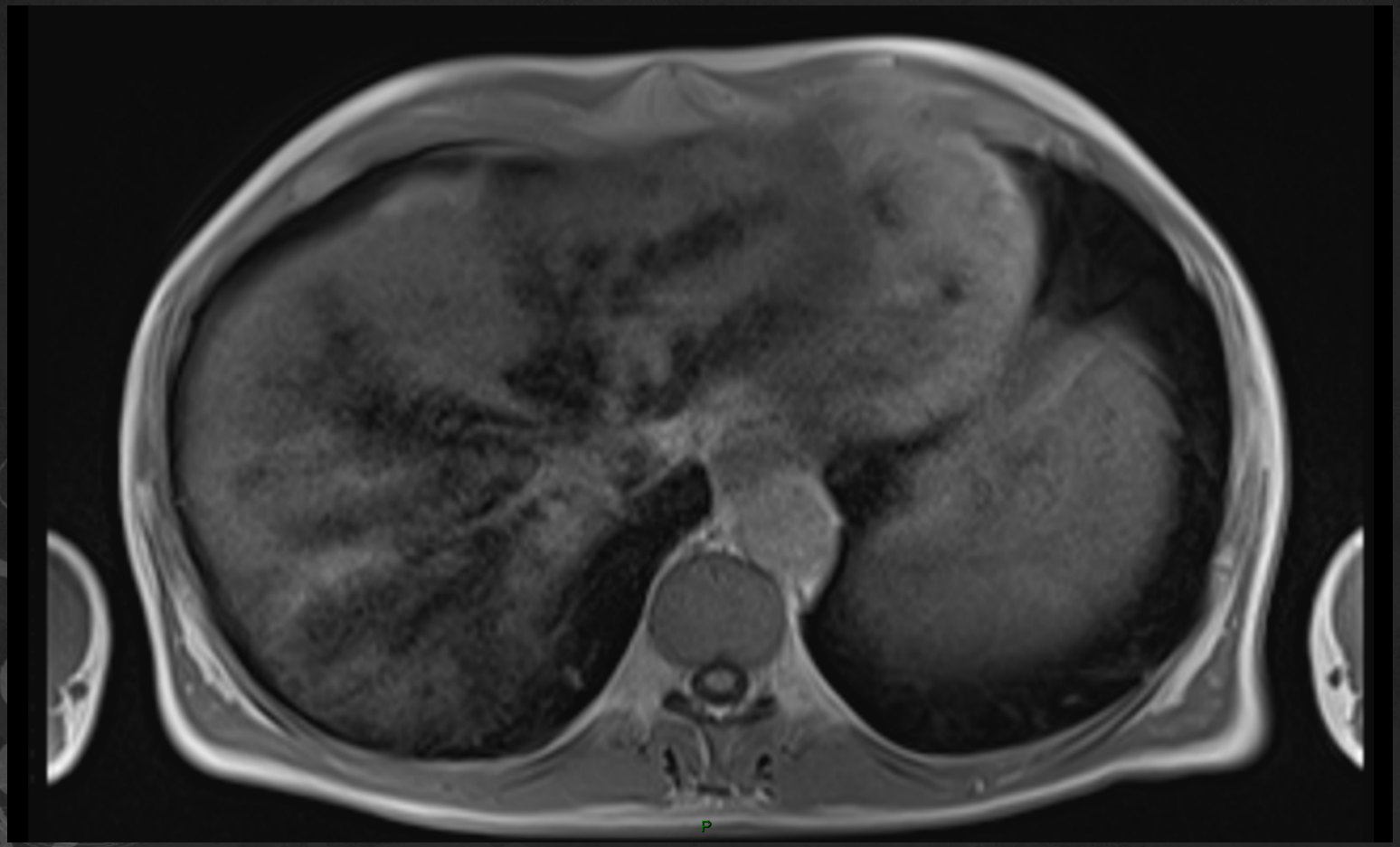
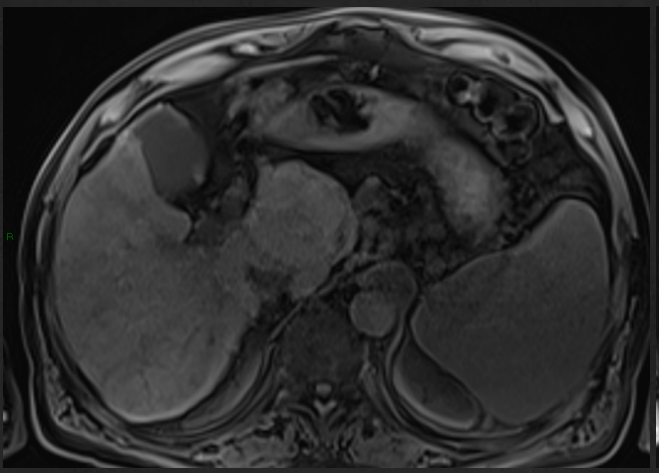


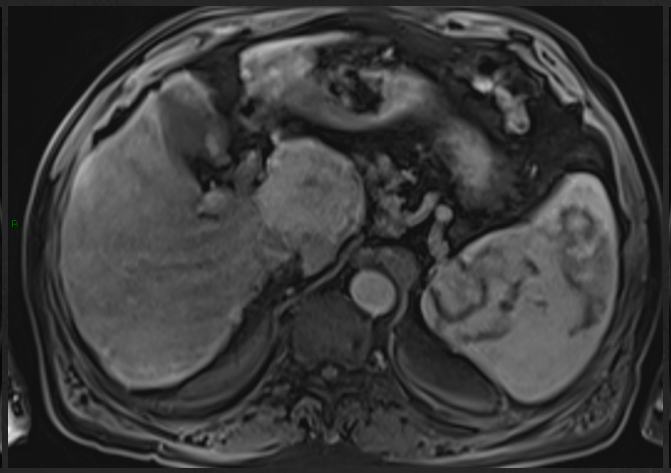
T1 in phase

What makes a lesion less probable to be a HCC?

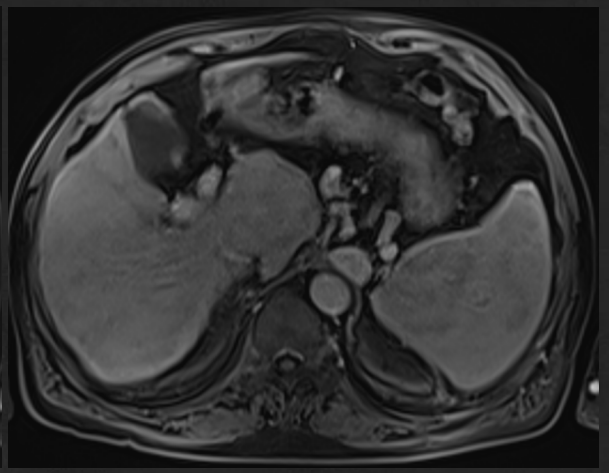
- **Isointensity** to the liver parenchyma in the **late, hepatobiliary** phase
- Most **regenerative and dysplastic nodules** are **isointense** to the liver parenchyma in the hepatobiliary phase
- Most **HCC's are hypointense** to the surrounding liver parenchyma in the hepatobiliary phase
- But **12%** of HCC nodules are **hyperintense** in the hepatobiliary phase
- Most of those HCC nodules have a **capsule**, which is seen **hypointense** in the hepatobiliary phase.
- In **LI-RADS**, isointensity to the liver parenchyma is a ancillary feature which **favors benignity**



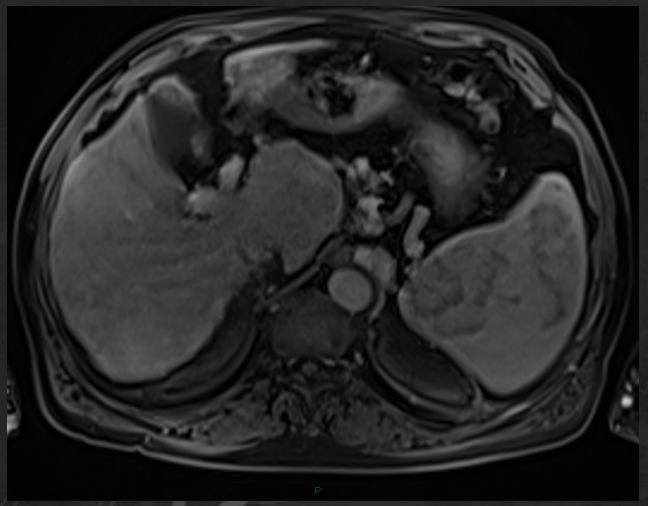
T1



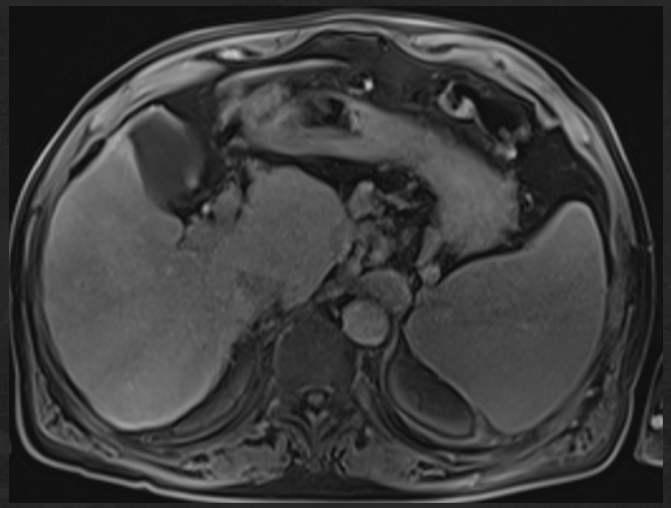
Arterial phase



Venous phase



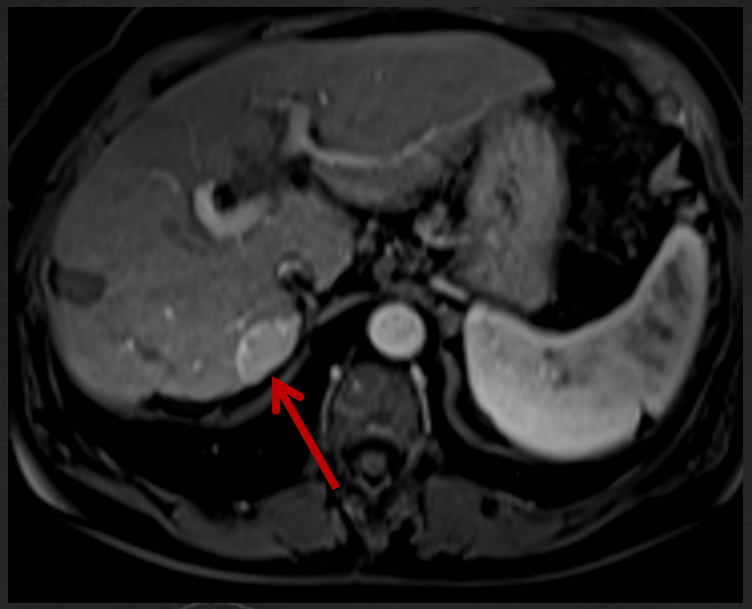
Late phase



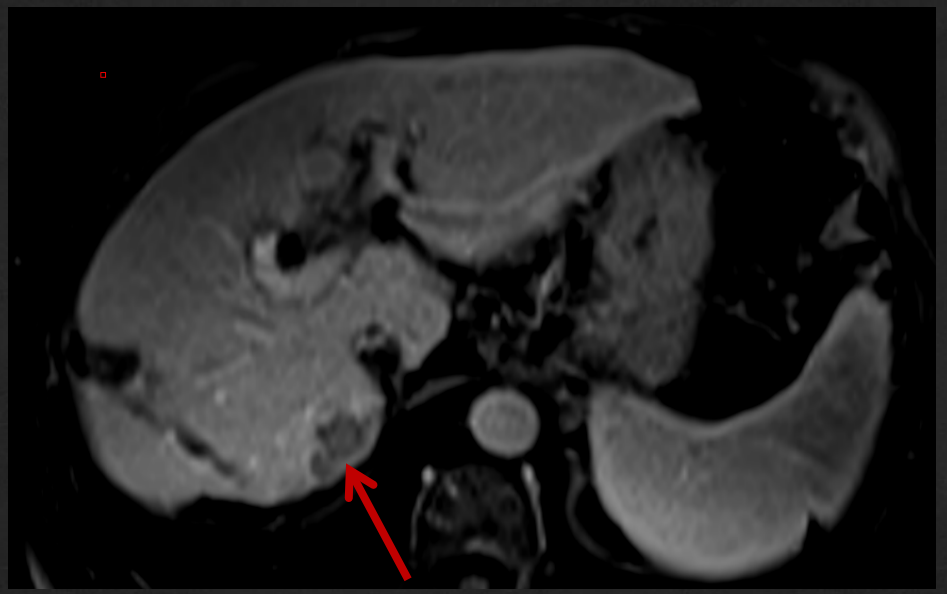
Hepatobiliary phase

APHE		Absent		Present		
Observation size		< 20 mm	≥ 20 mm	< 10 mm	10-19 mm	≥ 20 mm
Additional major features:	None	LR-3	LR-3	LR-3	LR-3	LR-4
Enhancing capsule Washout	One	LR-3	LR-4	LR-4	LR-4* LR-5*	LR-5
Threshold growth	≥ Two	LR-4	LR-4	LR-4	LR-5	LR-5

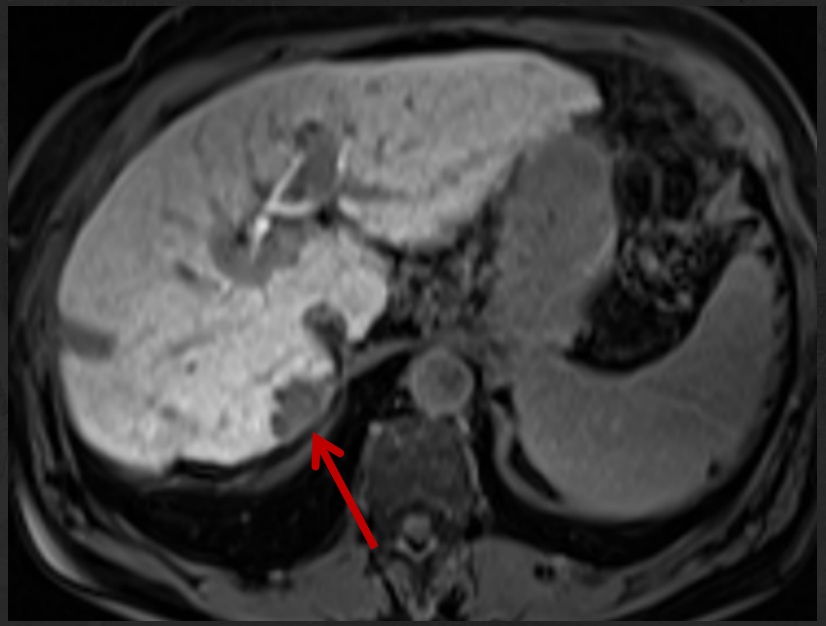
W, 56 years, cirrhosis, **HCC**



T1 arterial phase

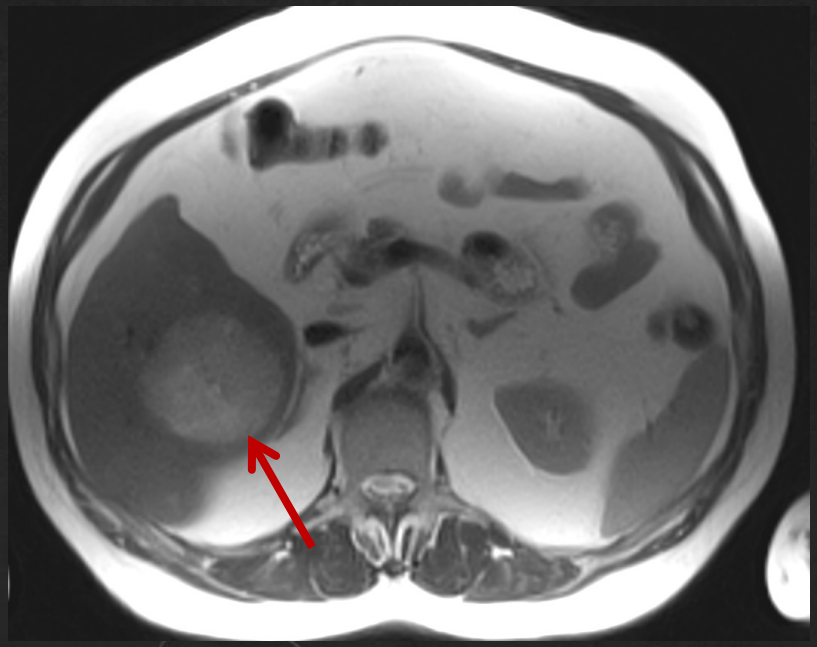


T1 venous phase

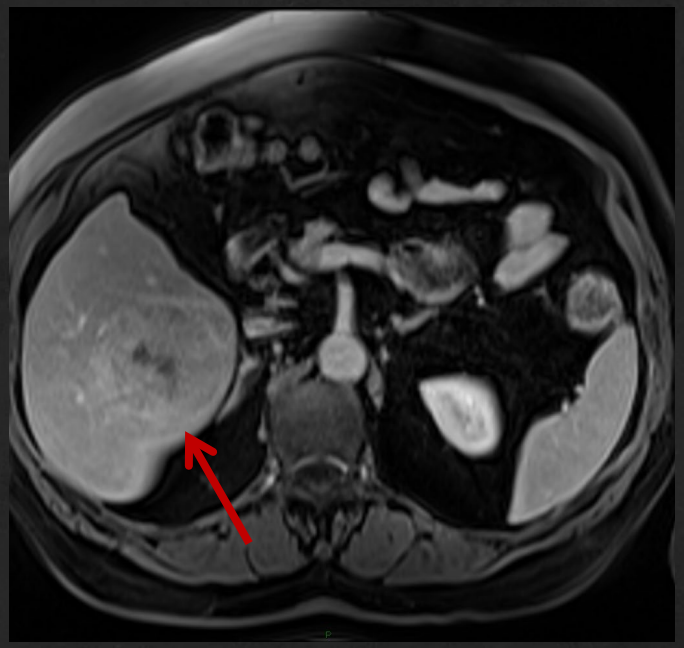


T1 hepatobiliary phase

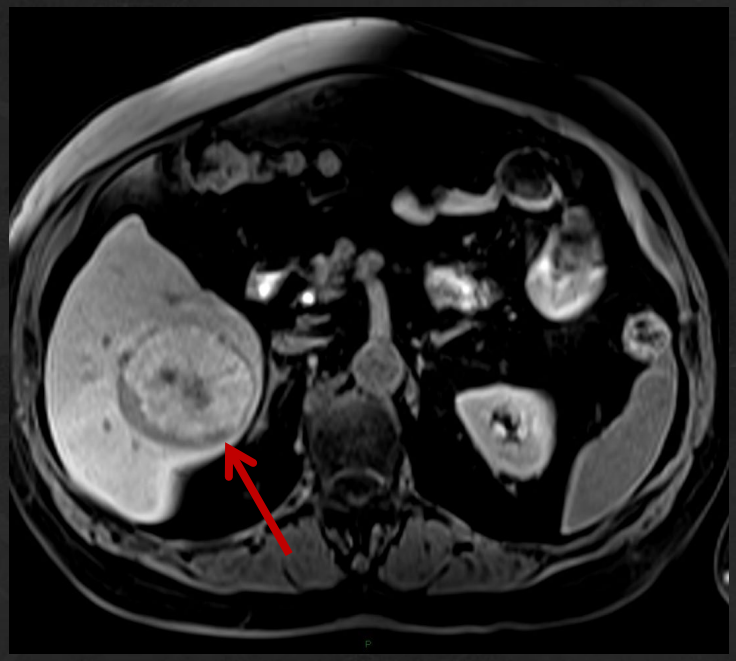
M, 65 y, HCV related cirrhosis, **HCC**



T2



T1 portal phase



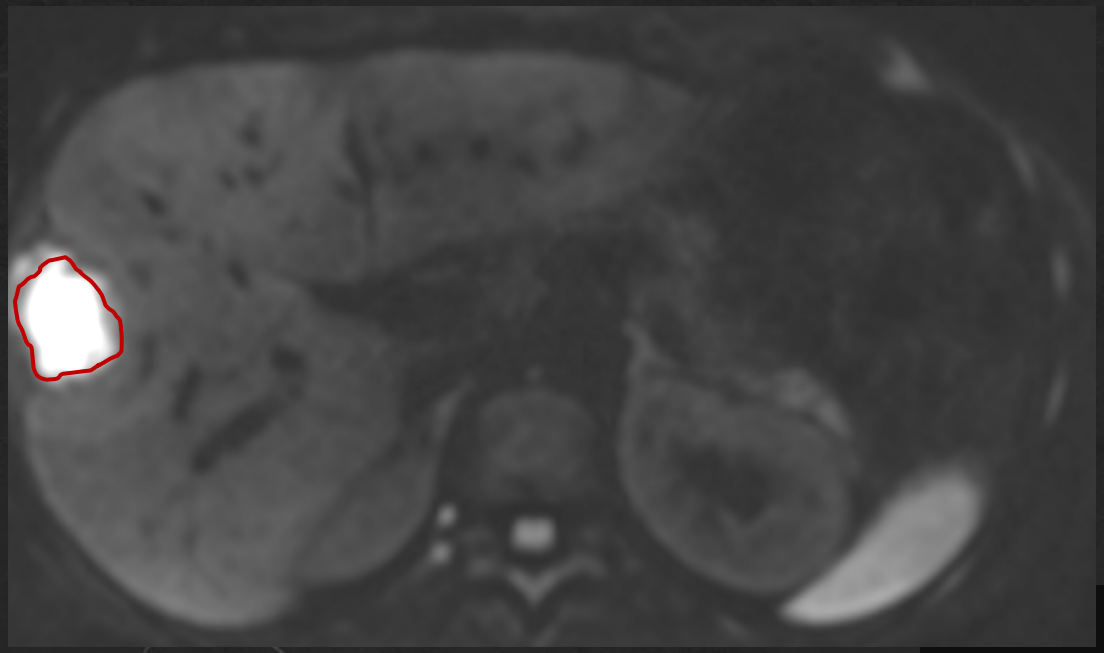
T1 hepatobiliary phase

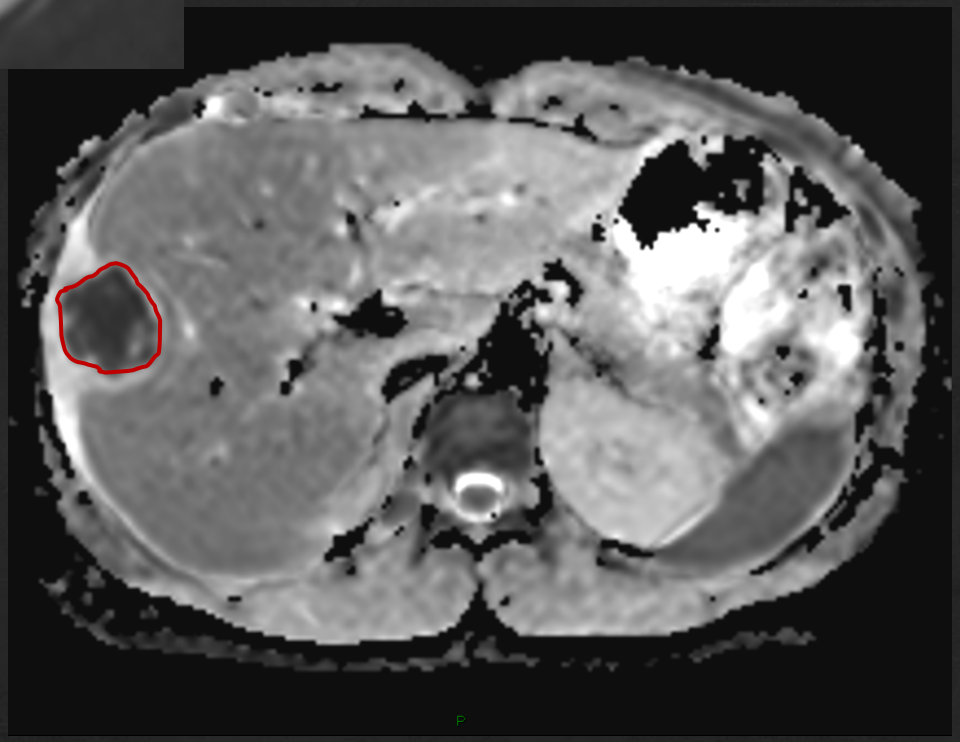
Is restricted diffusion always a sign of malignancy?

- DWI is **restricted** in focal liver lesions with **high cellularity**
- DWI, at **low b-values**, performs **better** than **T2 weighted** images in detecting focal liver lesions, particularly in detecting **malignant** lesions
- Some **well differentiated** HCC will ***not*** exhibit restricted diffusion
- Benign lesions, such as **hemangiomas** and **liver cysts** will have **T2 shine through**

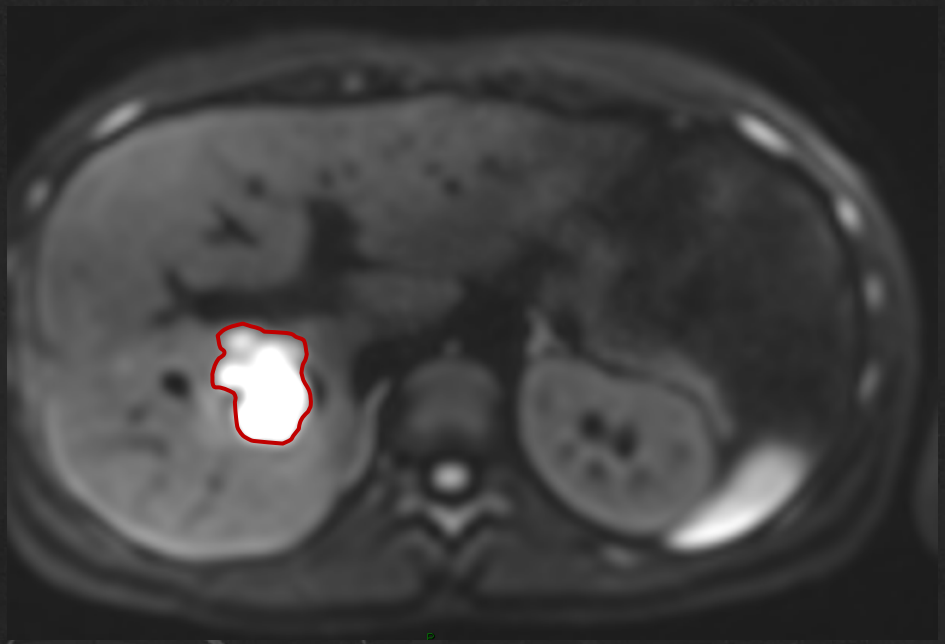
Okada Y, Ohtomo K, Kiryu S, Sasaki Y. Breath-hold T2-weighted MRI of hepatic tumors: value of echo planar imaging with diffusion-sensitizing gradient. J Comput Assist Tomogr. 1998;22:364–371.

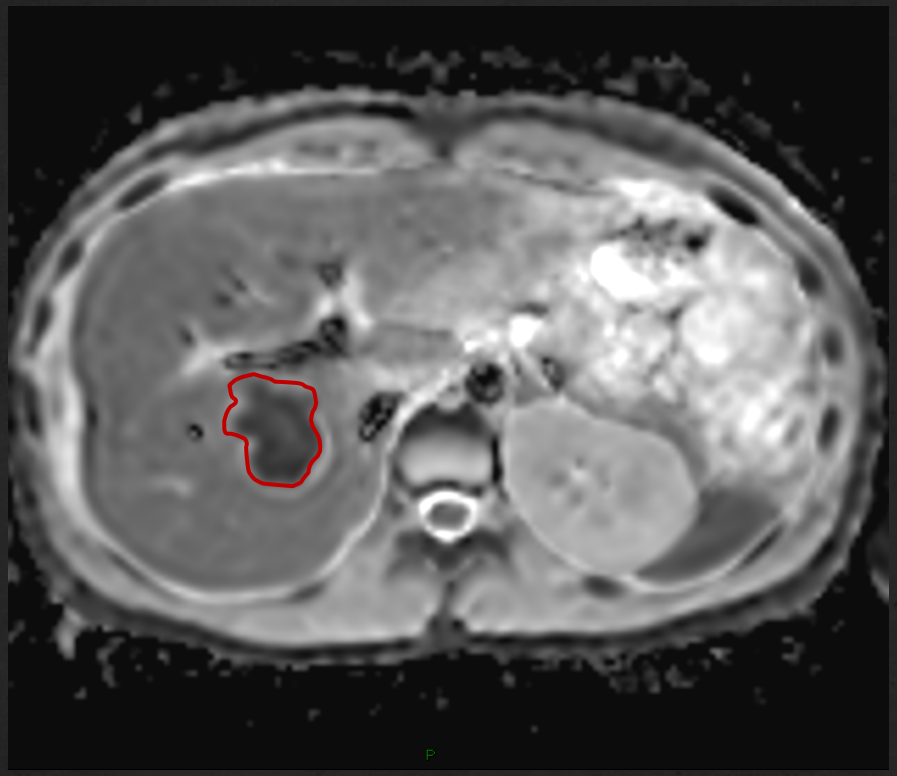
W, 30 years old, MR Enterography for Crohn’s disease



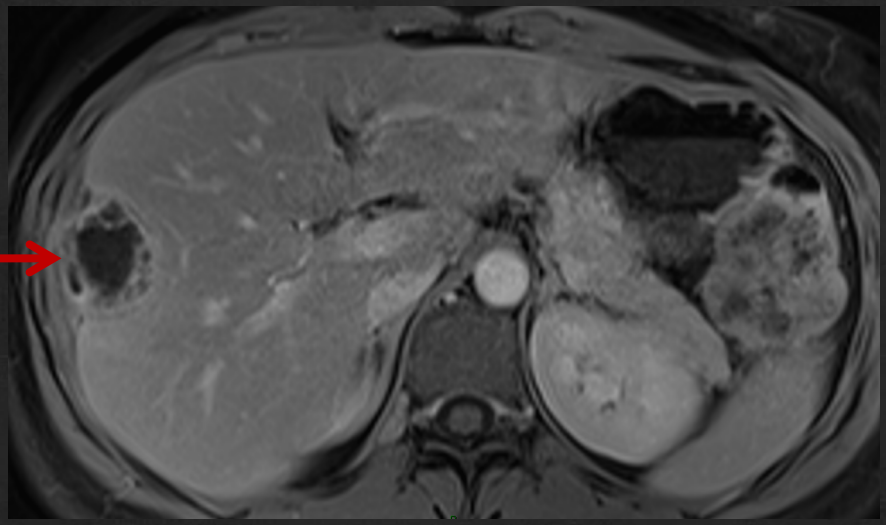


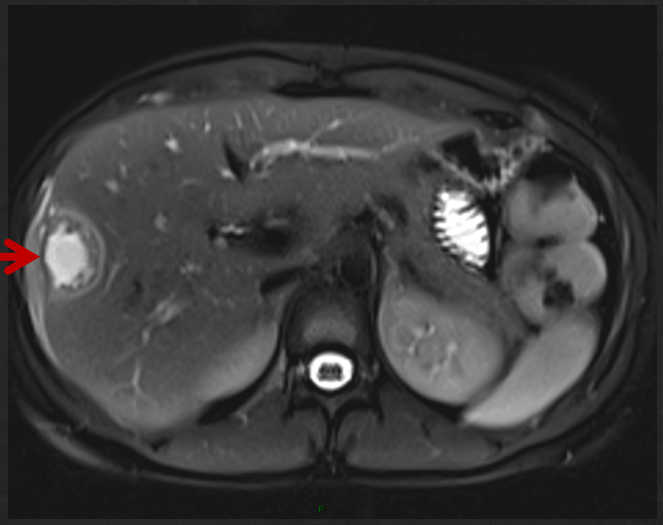
W, 30 years old, MR Enterography for Crohn’s disease, 3 months later - follow up MRI

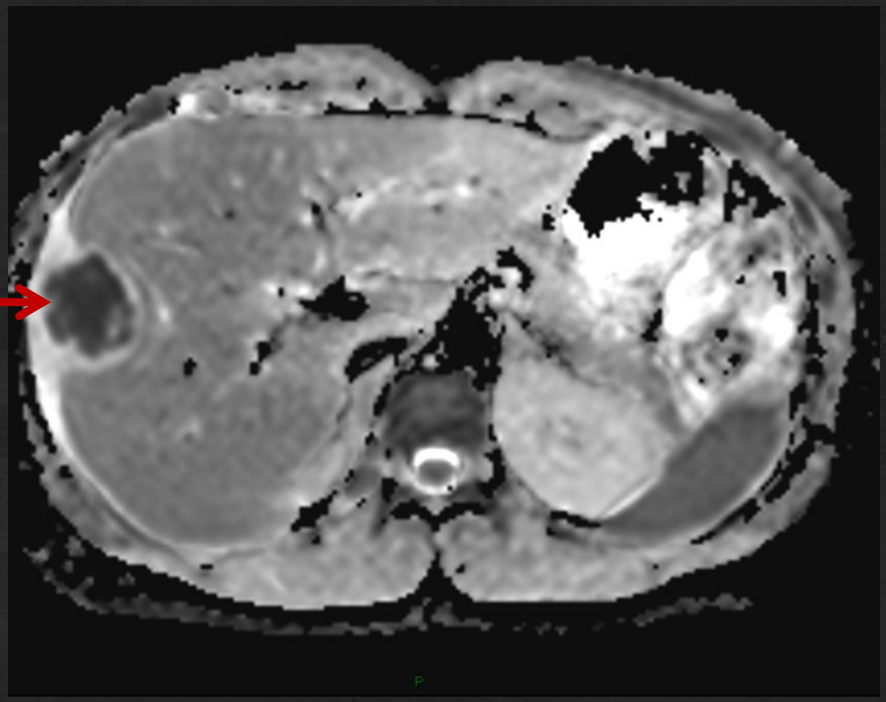




W, 30 years old, MR Enterography for Crohn’s disease







Is restricted diffusion always a sign of malignancy?

- DWI is **restricted** in the **solid component** of **malignant** lesions
- DWI is **restricted** in the **fluid component** of **infectious** lesions
- In lesions containing **both** a solid and a fluid component, DWI will be **restricted** in the **periphery** **of malignant** lesions and in the **center** of **infectious** lesions
- **Regenerative nodules** may, in some cases, exhibit ***slightly*** restricted diffusion

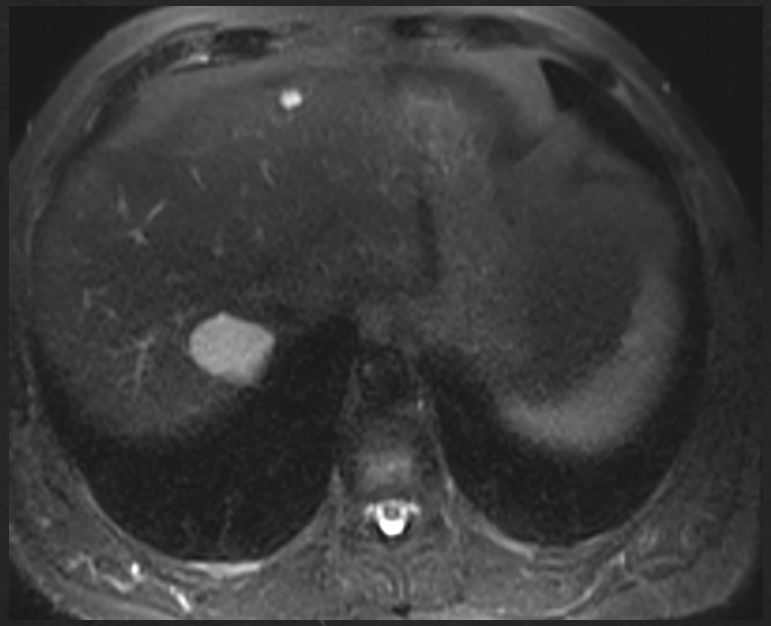
Is restricted diffusion always a sign of malignancy?

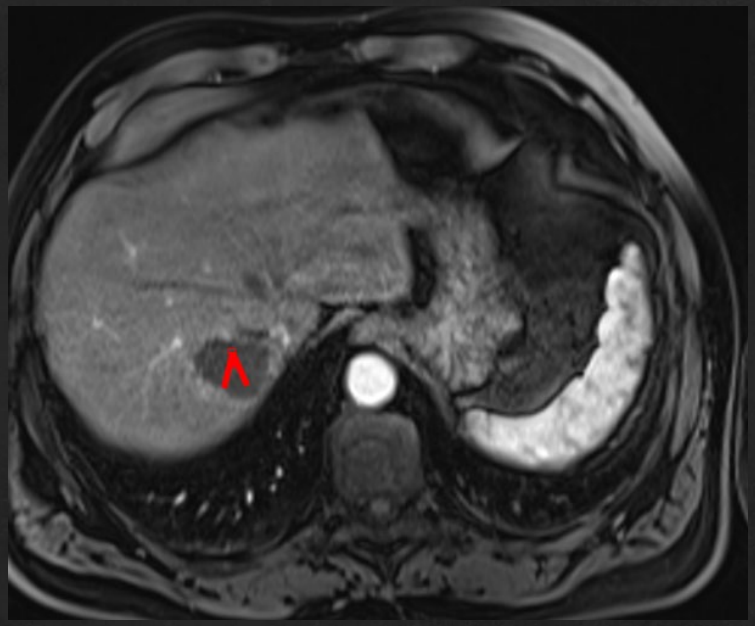
- **Not** every FLL which shows restricted diffusion is **malignant**
- **Not** every malignant lesion will exhibit **restricted diffusion**

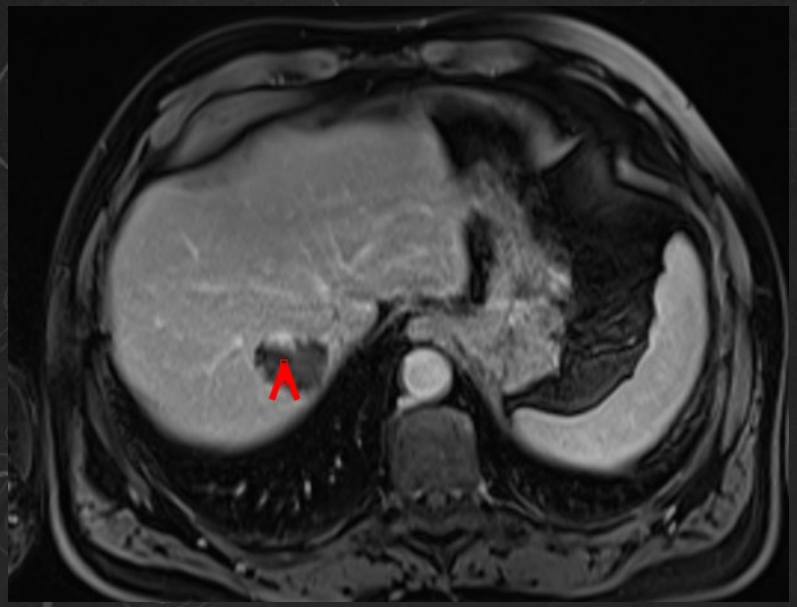
What did my parents expect me to do as a doctor?

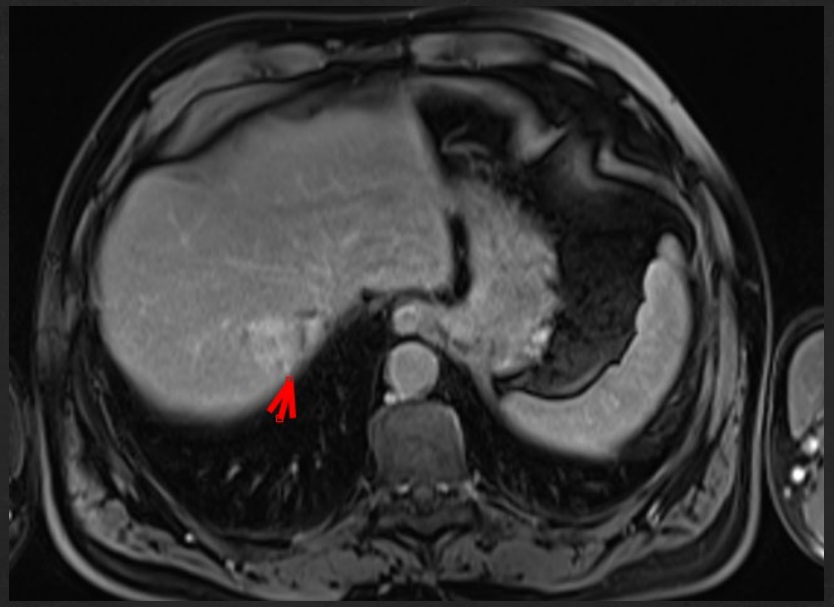
What am I actually doing as a doctor?

How do we expect a liver hemangioma to look like?

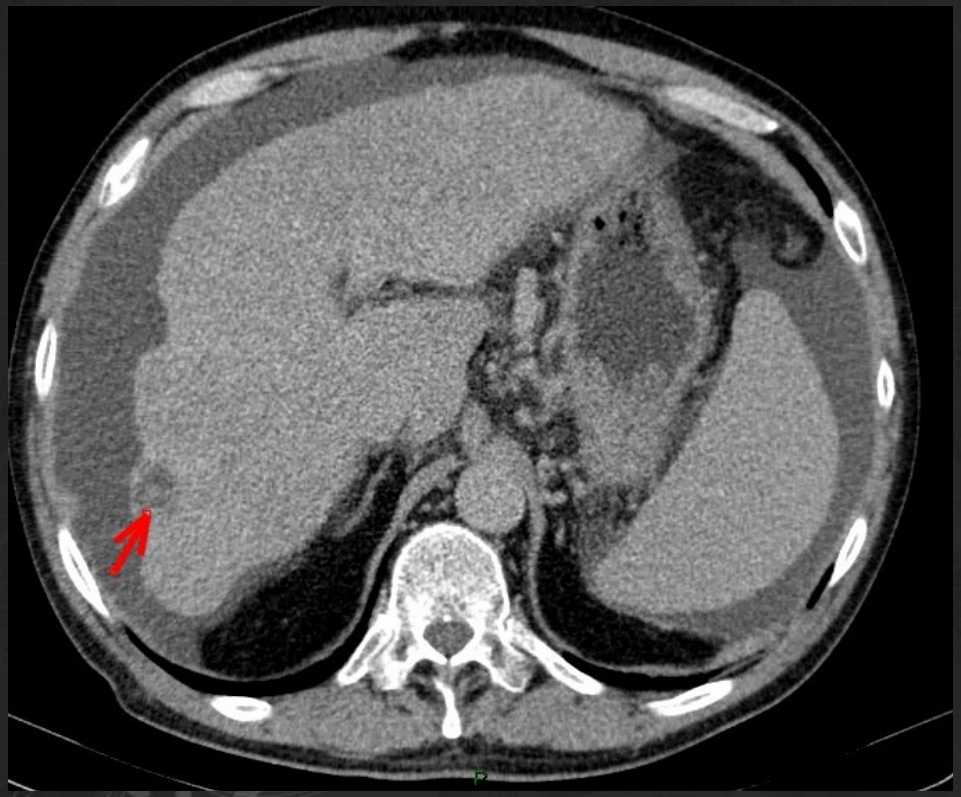


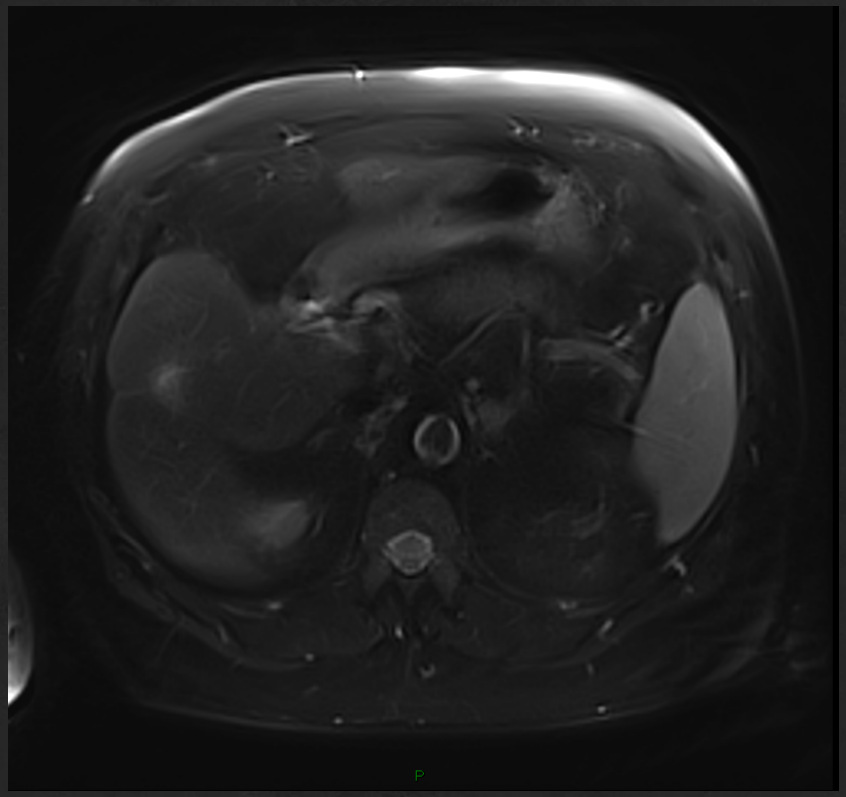




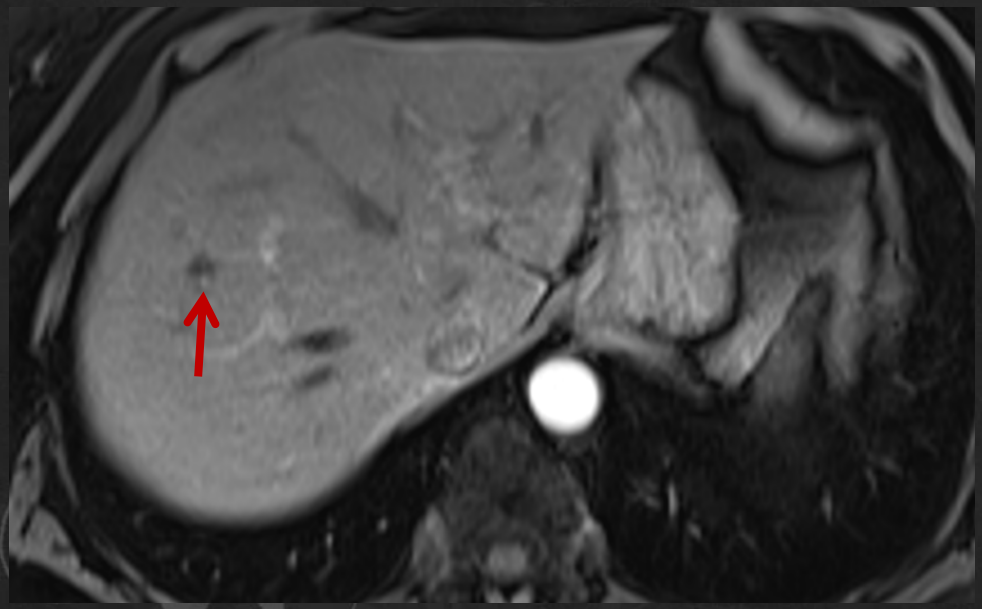


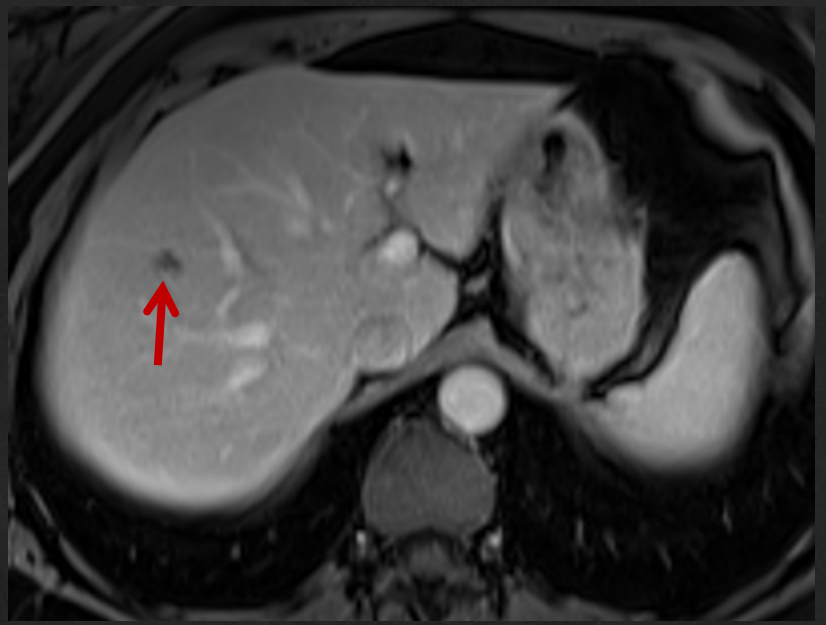
How does a hemangioma look like in a cirrhotic liver?





Bright dot sign



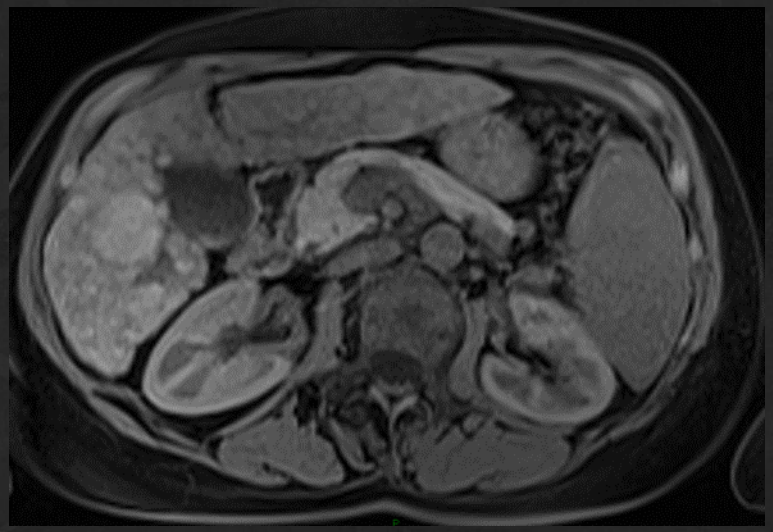


Hemangioma in the cirrhotic liver

- May be affected by **fibrosis/sclerosis**
- They may **loose** **their T2 hyperintensity**
- They may **loose** **their centripetal fill-in** pattern
- **Bright dot sign**: Small enhancing area inside the hemangioma in the arterial phase which remains enhancing and does not change size or shape in the subsequent phases of enhancement
- Due to fibrosis they may be **retraction of the liver capsule** in relation to the hemangioma

Regenerative nodule

- May be **hyperintense** to the surrounding liver on **T1 weighted** images
- Unlike HCC nodules, they may be **hypointense** to the surrounding liver on **T2 weighted** images
- In most cases their enhancement is ***similar*** to the liver parenchyma enhancement in the **early phases**
- They enhance ***similar*** to the liver parenchyma in the **late, HBP phase**



Dysplastic nodule

- **Low grade** and **high grade** dysplastic nodules
- **Hyper- to isointense** on **T1** and **hypo- to isointense** on **T2**
- **Iso- or hypointense** on the **arterial phase** (but **hyperintensity** in the arterial phase can be present in HGDN)
- ***No*** wash-out
- They can be **hypointense** in the **HBP**
- Use **LI-RADS** rather than trying to correlate the imaging aspect with the histopathology of the nodule

Non-HCC malignancies

- **Peripheral**, **rim like**, **corona** enhancement
- **Restricted diffusion**
- **Hypointense** to the liver parenchyma in the **HBP**
- **LI-RADS** M and **biopsy** is needed

Think of something other than a HCC (but not completely exclude) when…

- The lesion has ***no*** **APHE**
- There is ***rim enhancement***
- The enhancement of the lesion ***follows the blood pool***
- The lesion is either ***strongly*** **hyperintense or hypointense** on **T2**
- The lesion is ***isointense*** to the liver parenchyma on the **HBP** (not when it is hypointense or hyperintense with an hypointense rim)


Thank
you!