# Primary Benign Liver Lesions

Reza Javadrashid
Professor of radiology
Tabriz university of medical sciences

- Most benign tumors are incidental findings during abdominal ultrasonography
- Each of the cellular components of the liver - hepatocytes, biliary epithelium and mesenchyme - can give rise to benign tumors. It is possible to classify these tumors based on their cellular origin:

The most commo entities are simple cysts, cavernous hemangiomas and focal nodular hyperplasia.

- **Hepatocellular Origin**
  Hepatocellular adenoma
  Hepatocellular hyperplasia
  Focal nodular hyperplasia (FNH)
  Nodular regenerative hyperplasia
- **Cholangiocellular Origin**
  Hepatic cyst
  Simple hepatic cyst
  Congenital hepatic fibrosis or polycystic liver disease
- **Mesenchymal Origin**
  Mesenchymal hamartoma
  Hemangioma
  Lipoma,Angiomyolipoma,Myelolipoma
  Leiomyoma

# Hemangioma

- Hepatic hemangioma is the most common primary liver tumor; the incidence of this lesion in the general population varies in published reports from 0.4% to 20%.

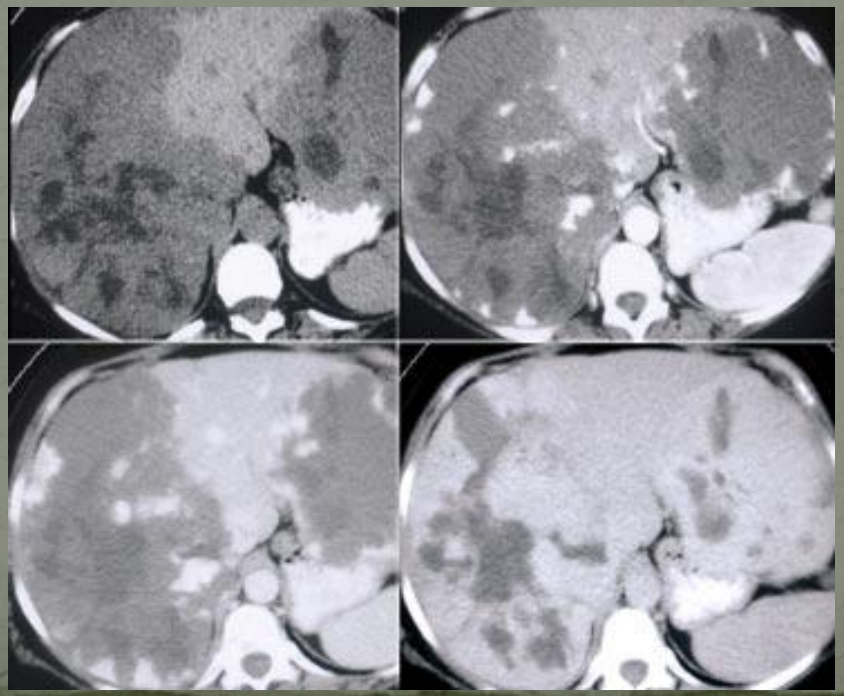
- Hemangiomas may be multiple in up to 50% of cases, but may also be found in conjunction with other neoplasms. An association with focal nodular hyperplasia occurs in 10-20% of cases

- There are two forms of this neoplasm: those that occur in childhood and those that occur in adults. Infantile hepatic hemangioma frequently resolves spontaneously. However, it may also become life-threatening due to arterio-venous shunting and resulting cardiac failure. In such cases, the lesion requires aggressive surgical intervention.

- Hemangiomas in adults occur most frequently in the fourth and fifth decades of life and there is a much higher incidence in women (about 80%). Estrogen replacement therapy may play a role in the pathogenesis of this type of tumor .Hemorrhage is the most common reason for prophylactic resection, although this occurs relatively infrequently

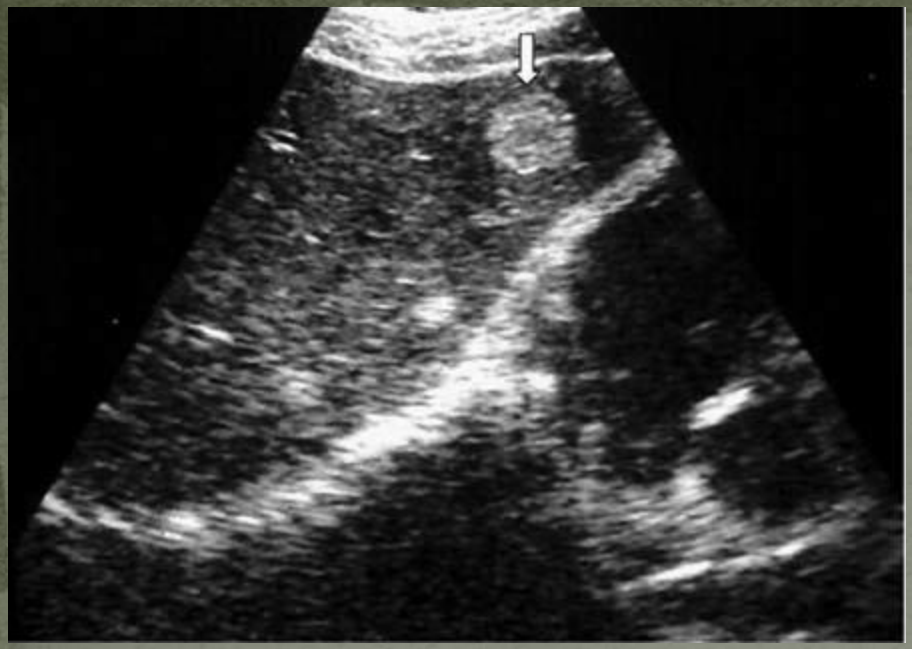
- Hemangioma,whether solitary or multiple, is a well-defined lesion that ranges in size from a few mm to more than 20 cm. Hemangiomas largerthan 10 cm are considered “giant” hemangiomas. Microscopically, they are tumors composed of multiple vascular channels lined by a single layer of endothelial cells supported by a thin, fibrous stroma.
- Large lesions almost always have a heterogeneous composition with areas of fibrosis, necrosis, cystic changes and intratumoral coarse calcifications.
- In some cases, abundant fibrous tissue completely replaces the lesion

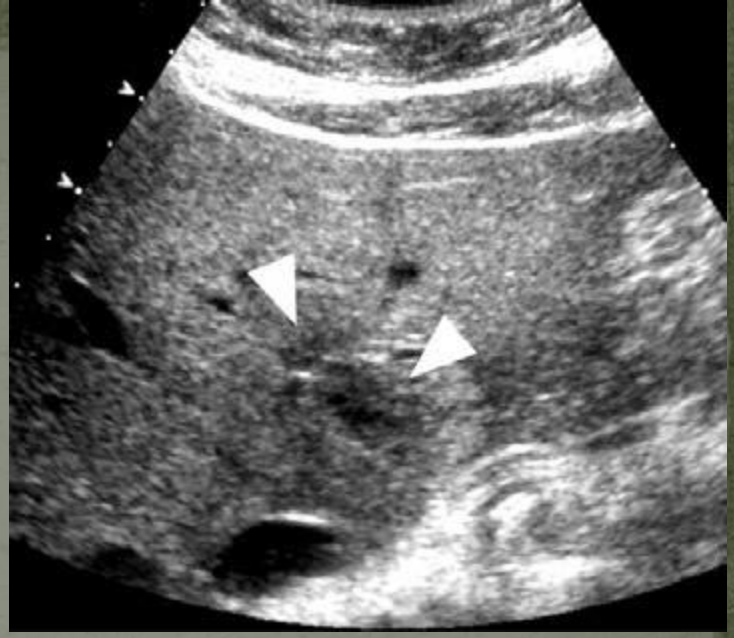
- Rarely, patients present with abdominal pain, and in exceptional cases, with fever, leukocytosis, thrombocytopenia, consumptive coagulopathy (Kasabach-Merritt Syndrome) or cholestasis. Occasionally, very large hemangiomas may cause symptoms by compressing adjacent organs

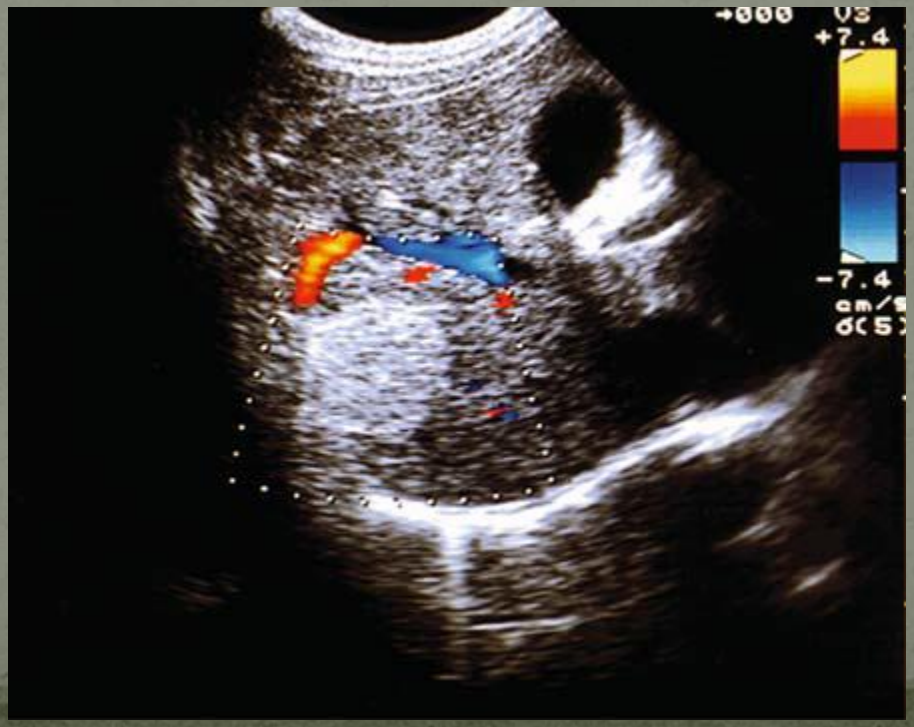


- On ultrasound (US) examination, hemangiomas are typically homogeneously hyperechoic with well-defined margins, and may exhibit faint acoustic enhancement. The echogenicity may vary because these tumors may contain cystic and fibrotic regions; this is especially true in large hemangiomas

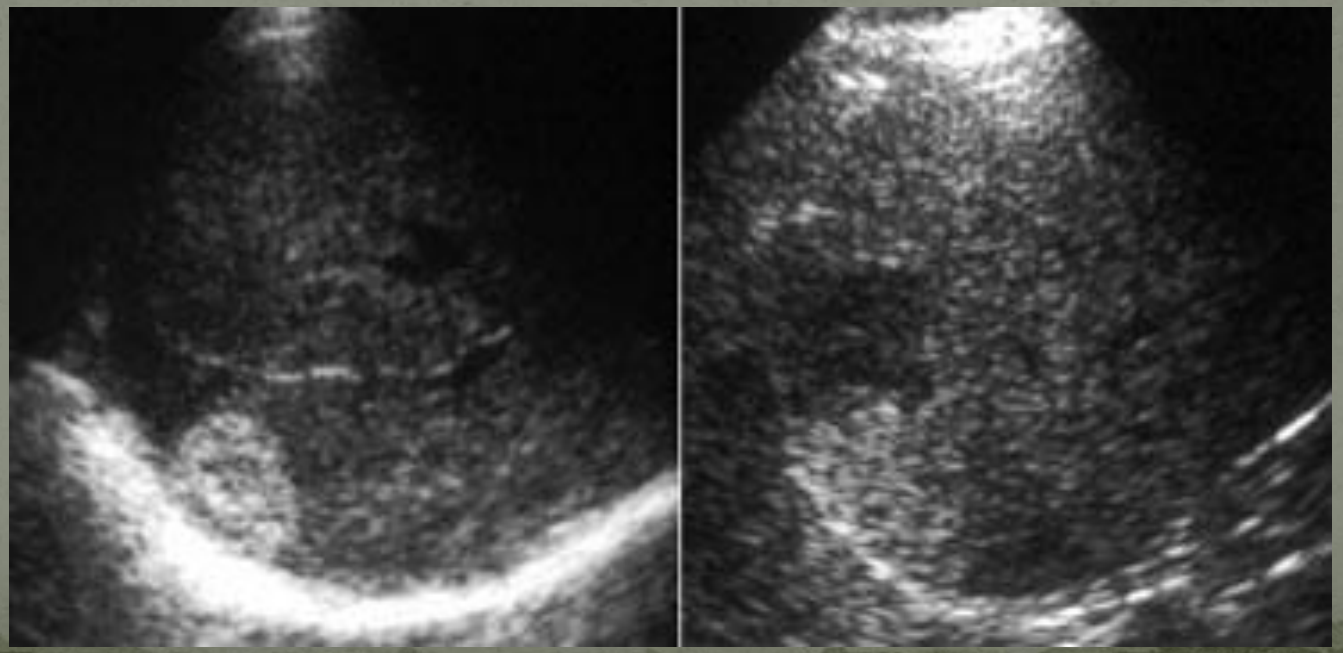
- Color Doppler US demonstrates filling vessels in the periphery of the tumor but no significant Color Doppler flow deep within the hemangioma itself



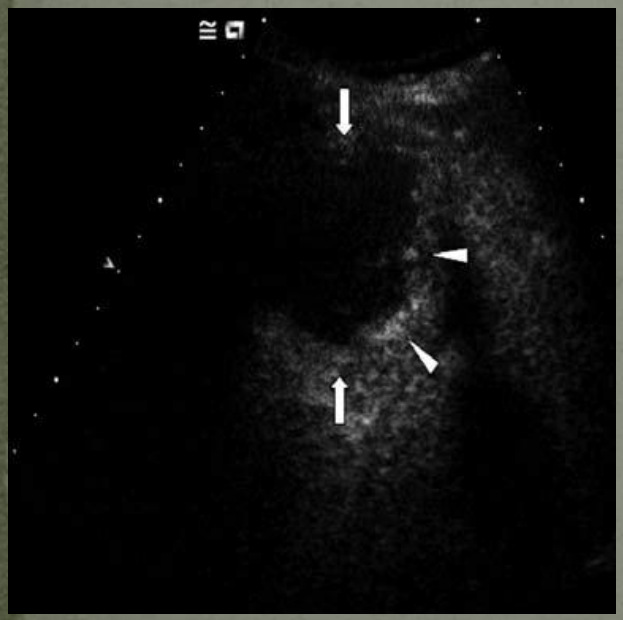
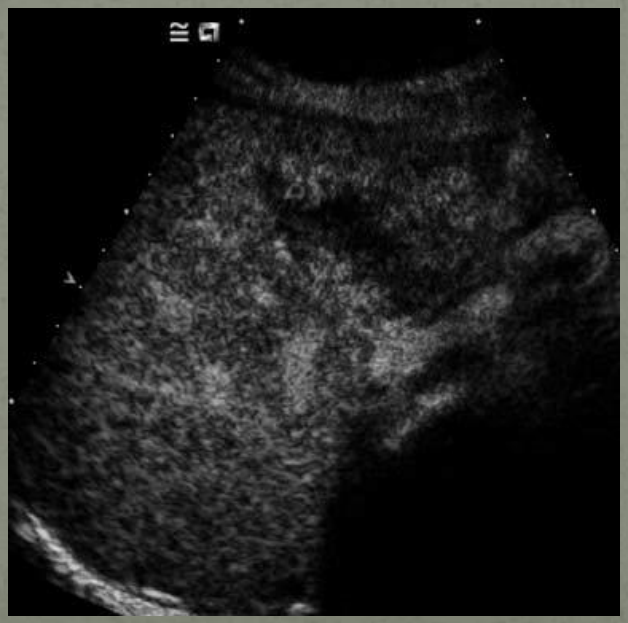
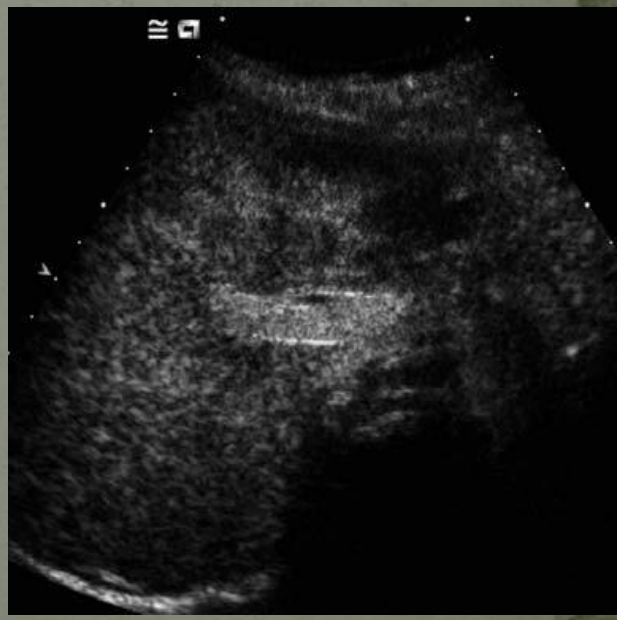



+7.4
-7.4

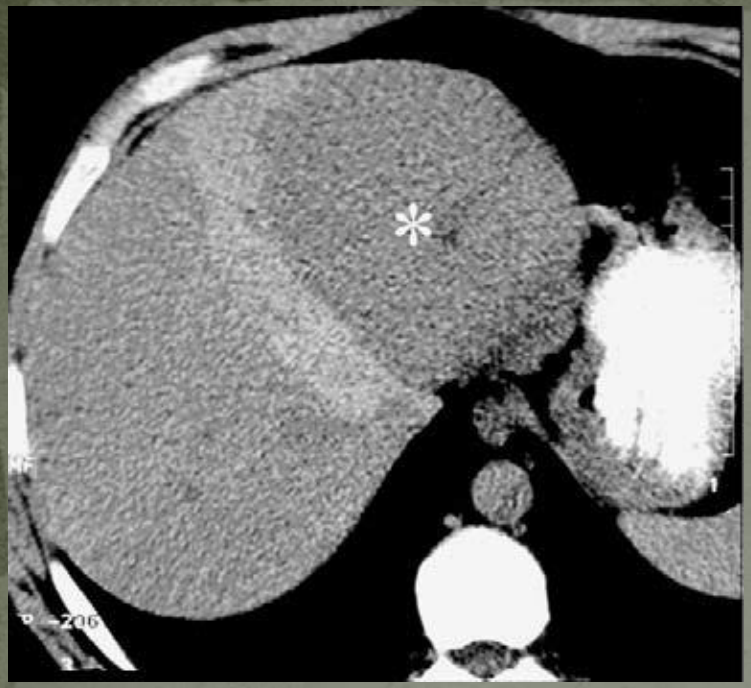
- If the liver is hyperechoic due to steatosis, the hemangioma can appear hypoechoic
- Another important feature of hemangiomas is the increased sound transmission.

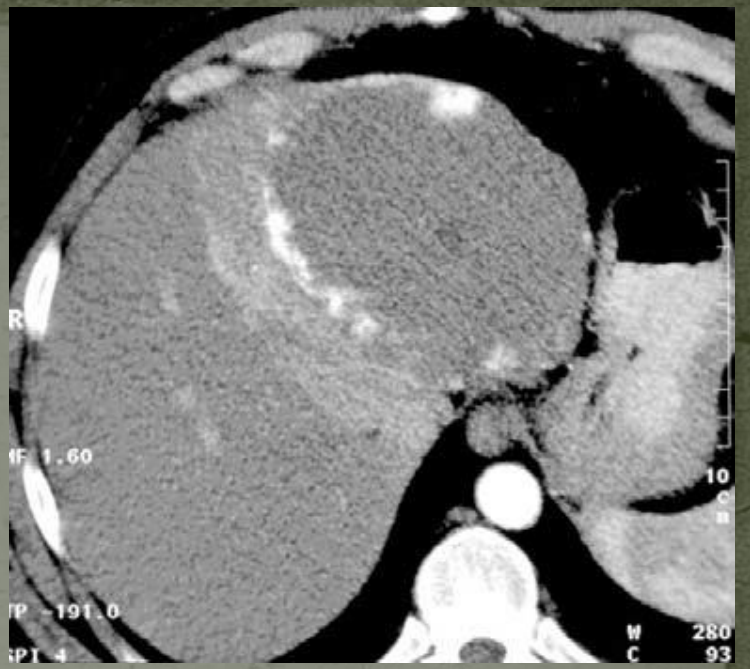


- Contrast-enhanced US allows monitoring of the dynamic enhancement behavior of hemangioma.

- Hemangiomas typically appear as low density masses on computed tomography (CT) imaging, with well-defined lobulated margins on unenhanced scans. During the arterial phase, hemangiomas demonstrate an initial peripheral nodular enhancement on spiral CT; this enhancement is isodense with the the aorta and progresses central with time. On delayed scans, the lesion becomes hyperdense or isodense compared with normal liver parenchyma

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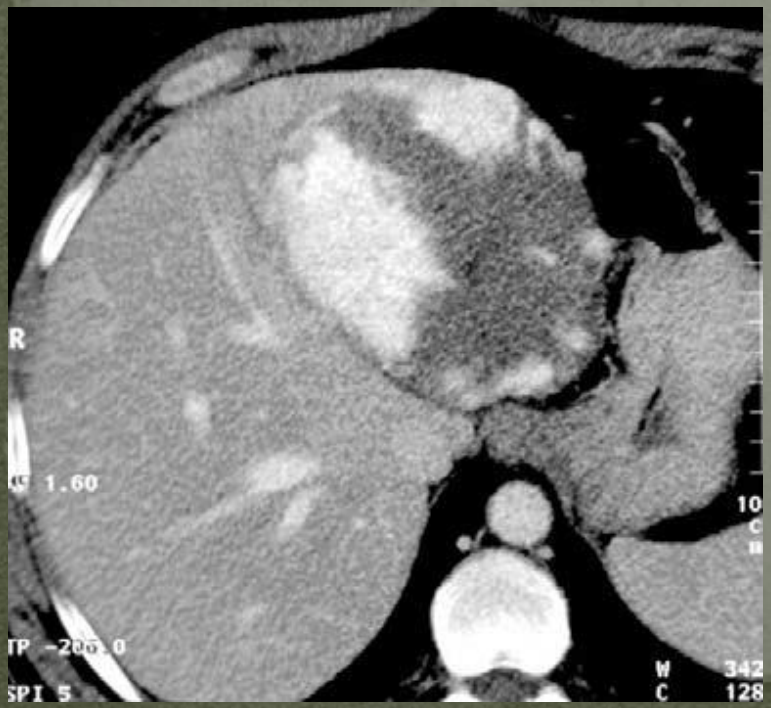
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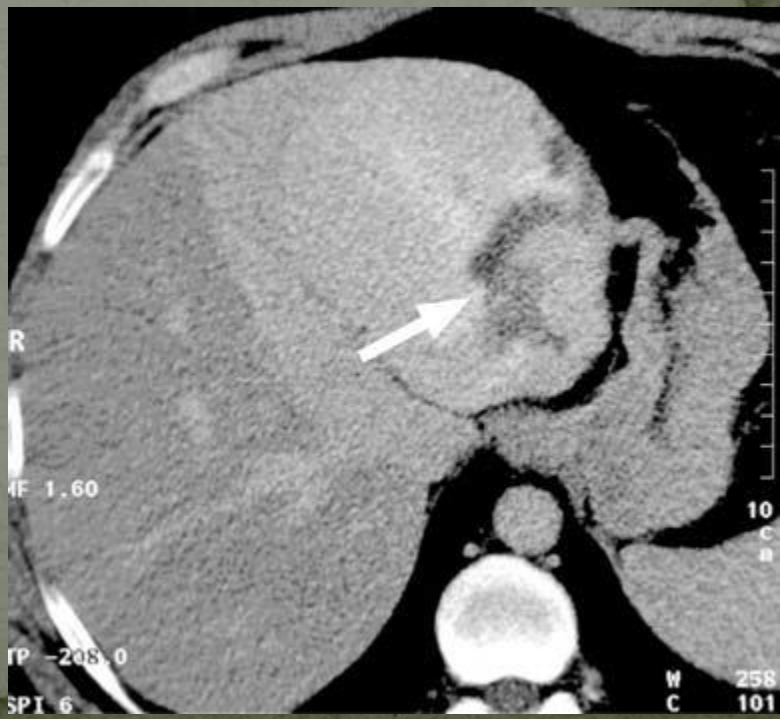
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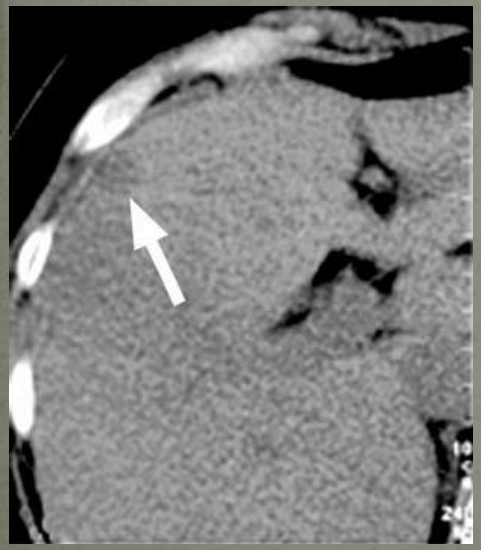
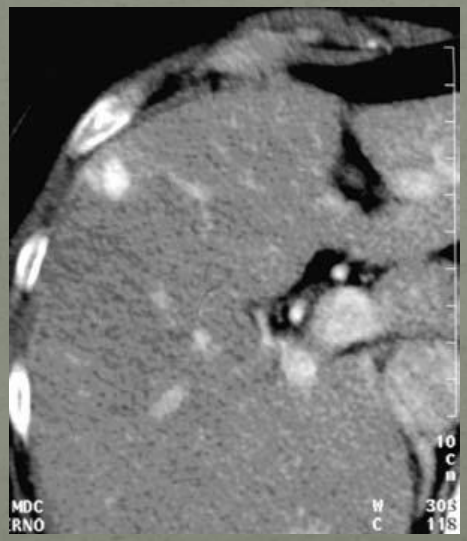
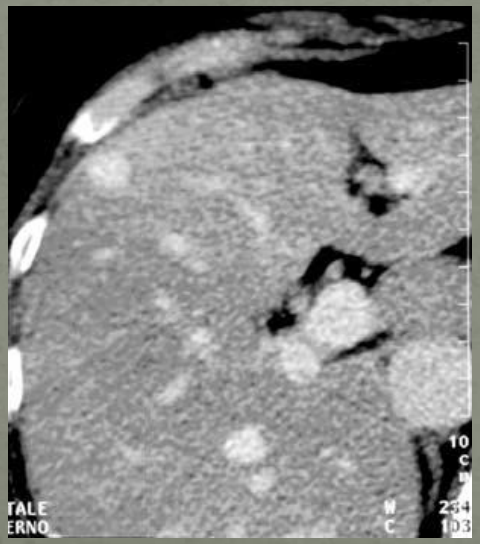
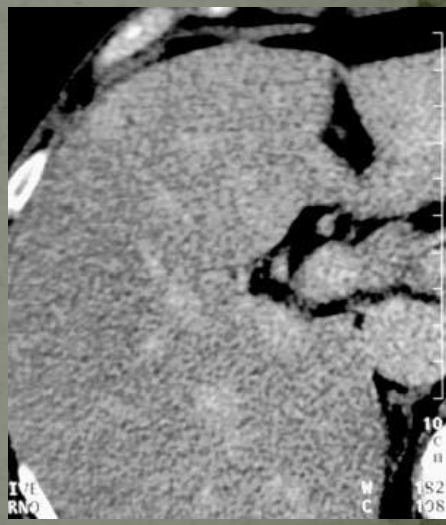
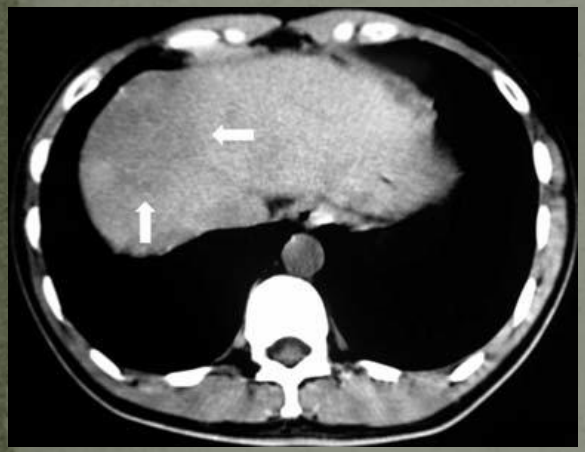
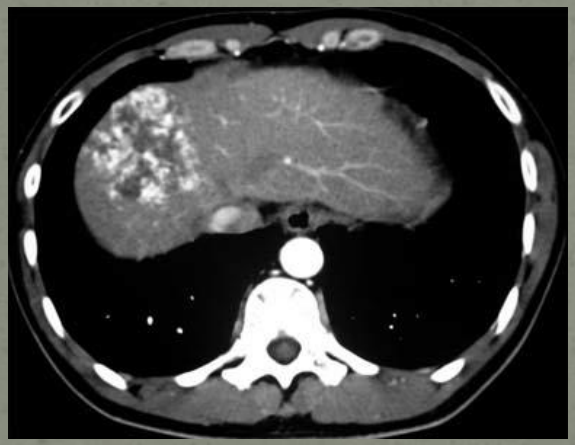
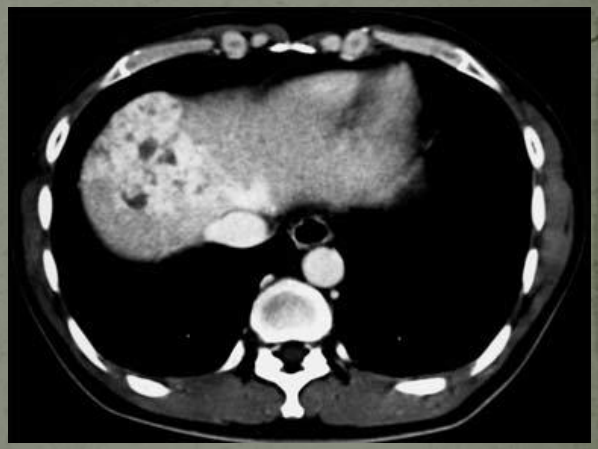
- Although small lesions often fill-in rapidly and completely .large tumors may show central non-enhanced areas corresponding to scar tissue, myxoid changes or cystic cavities

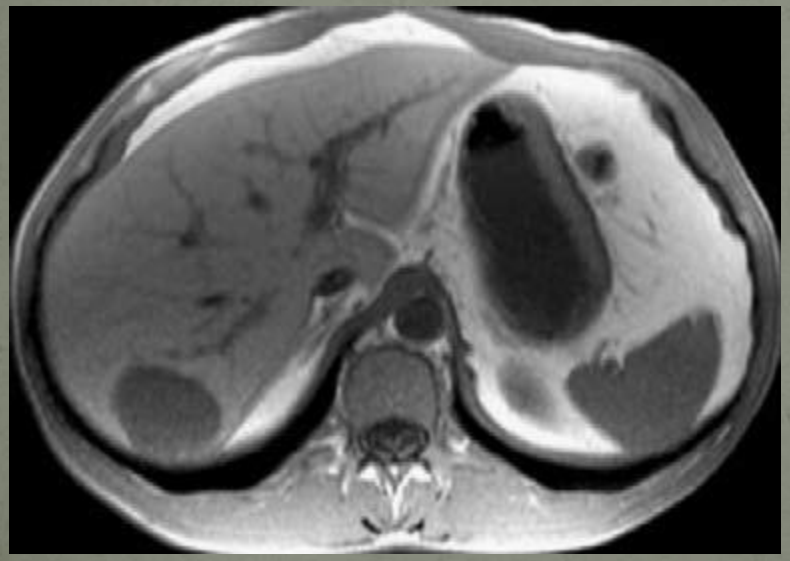
- Evaluation of hemangiomas of the liver is one of the major applications of magnetic resonance (MR) imaging, particularly in oncology patients with atypical hemangiomas detected on CT or US examinations

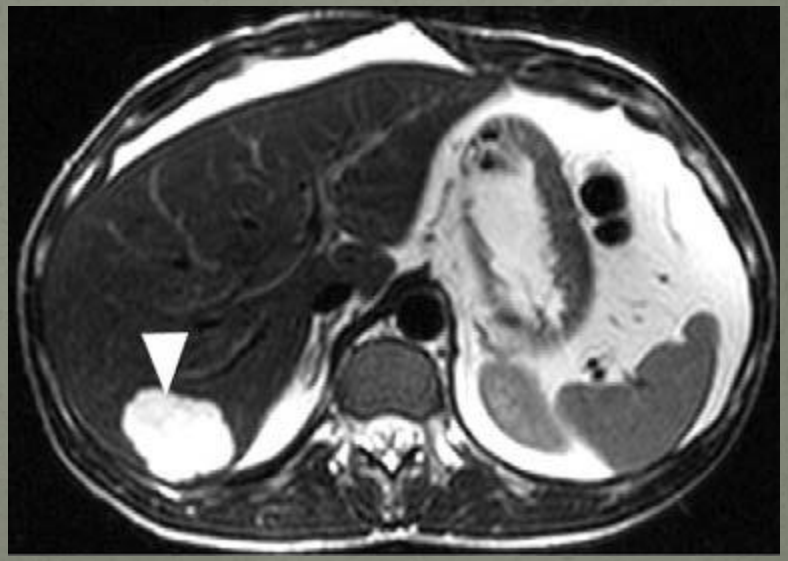




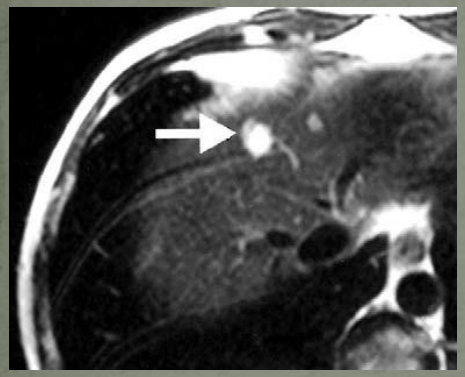


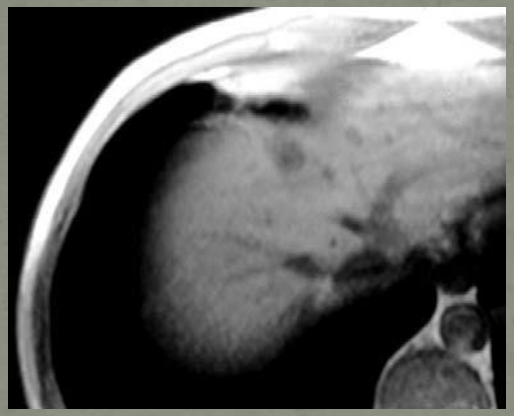
- On unenhanced T1-weighted MR images, hemangiomas are most commonly visualized as welldefined, typically homogeneous, hypointense masses with lobulated borders. On T2-weighted images they characteristically show marked homogeneous hyperintensity with occasional low signal intensity areas corresponding to areas of fibrosis

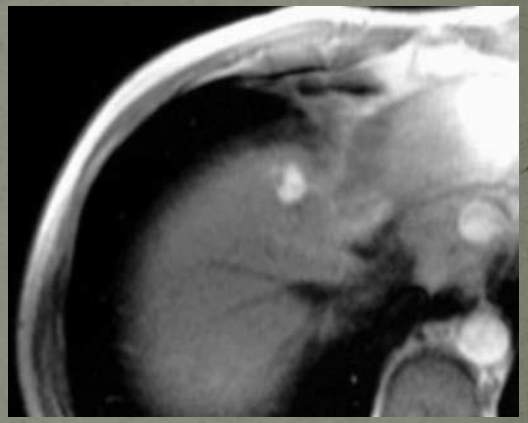


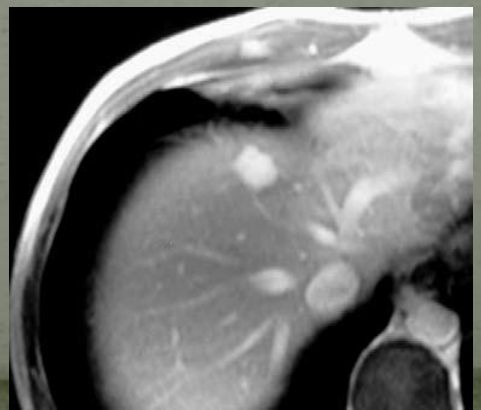


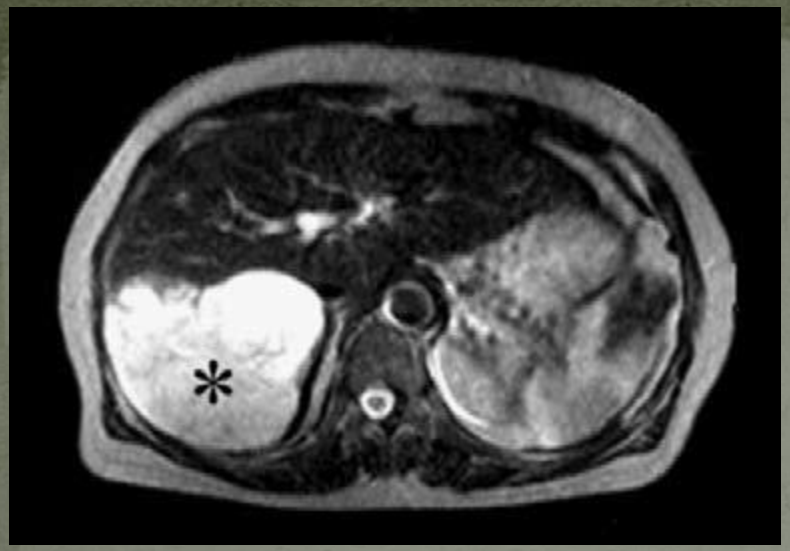
- These lesions typically show a peripheral nodular enhancement that progresses centripetally to a uniform enhancement in the equilibrium phase at 3-5 min post-contrast. In particular, large hemangiomas may show peripheral nodular enhancement with persistent central hypointensity corresponding to fibrosis and or cystic areas

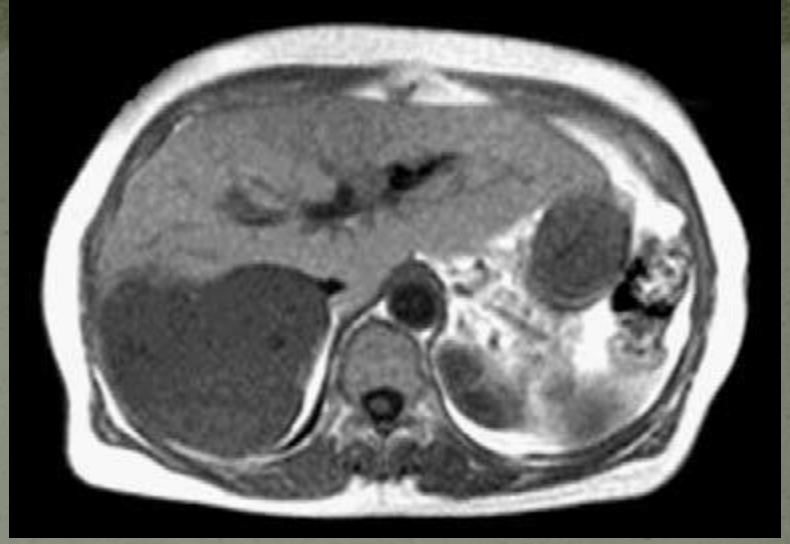


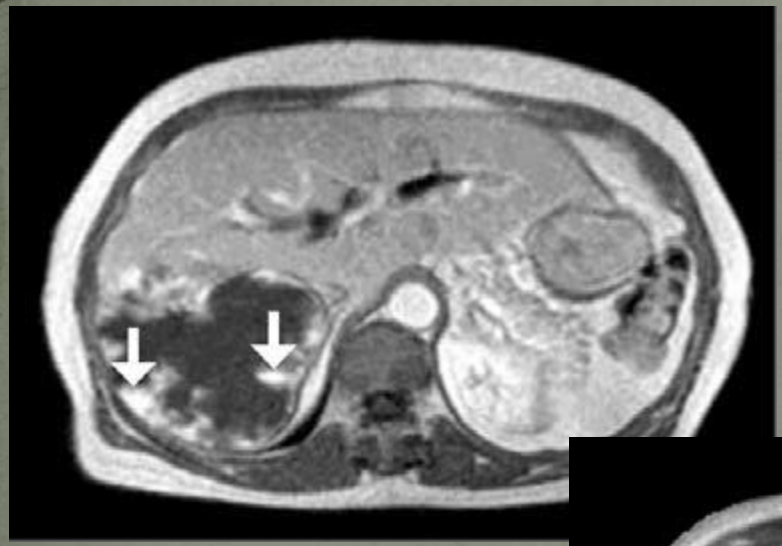


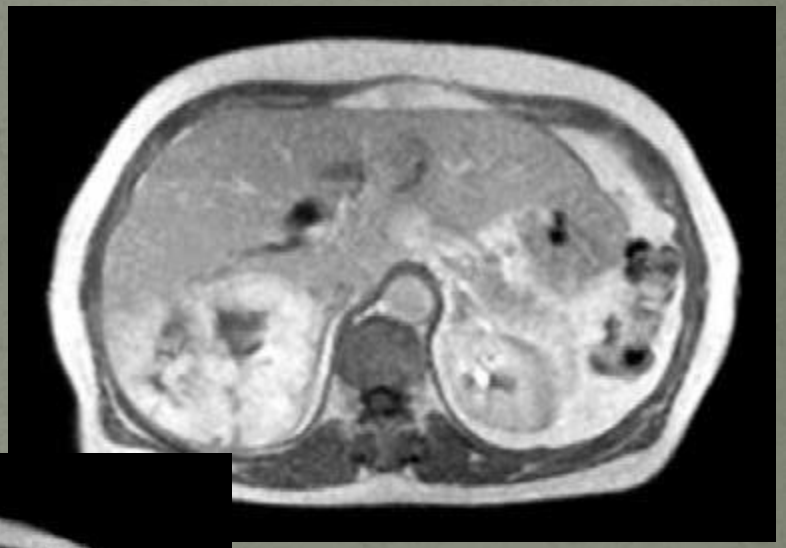


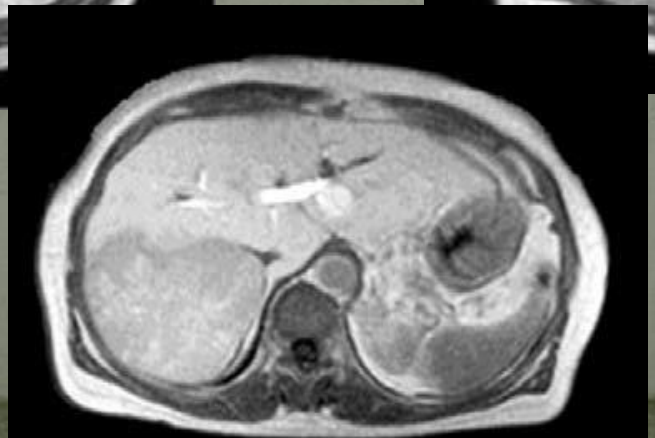




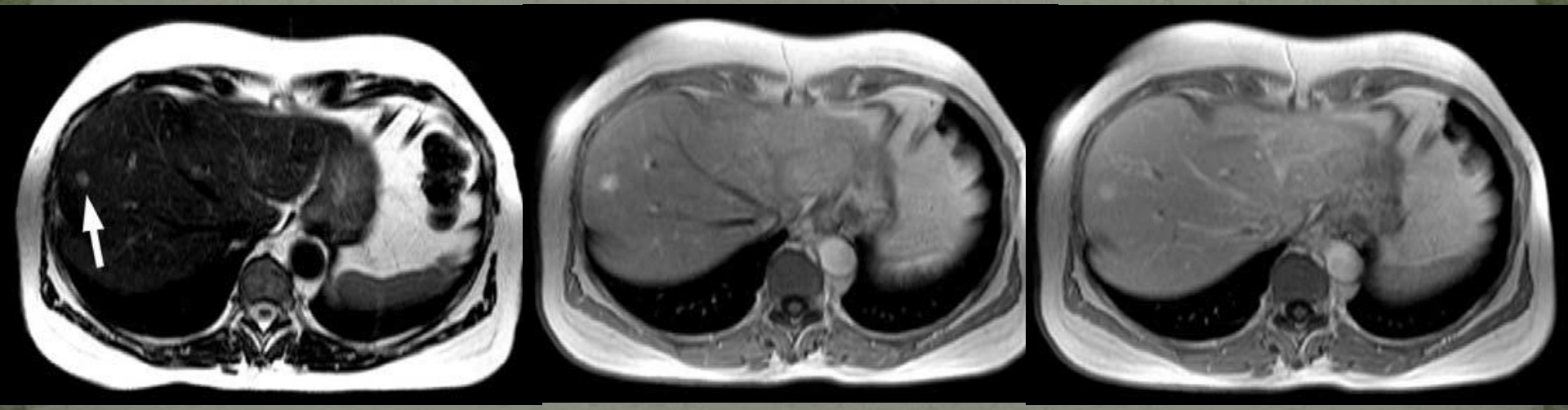





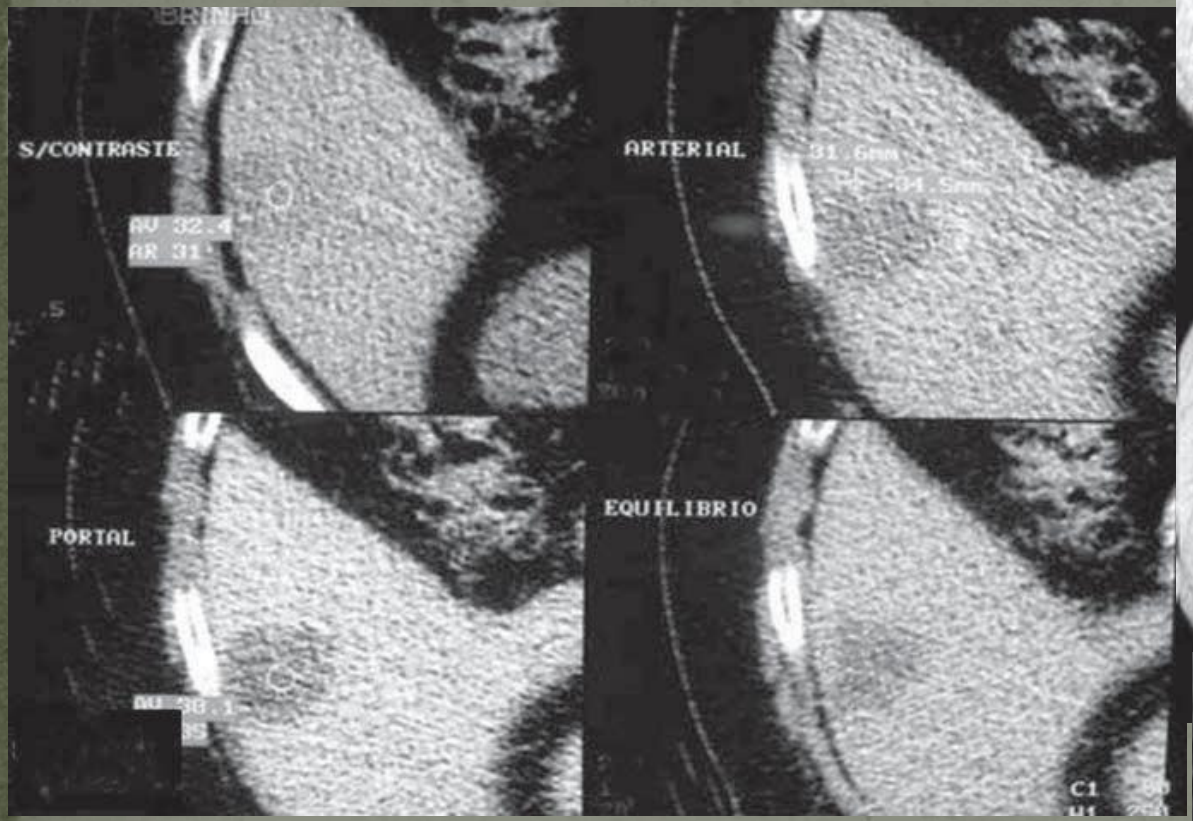


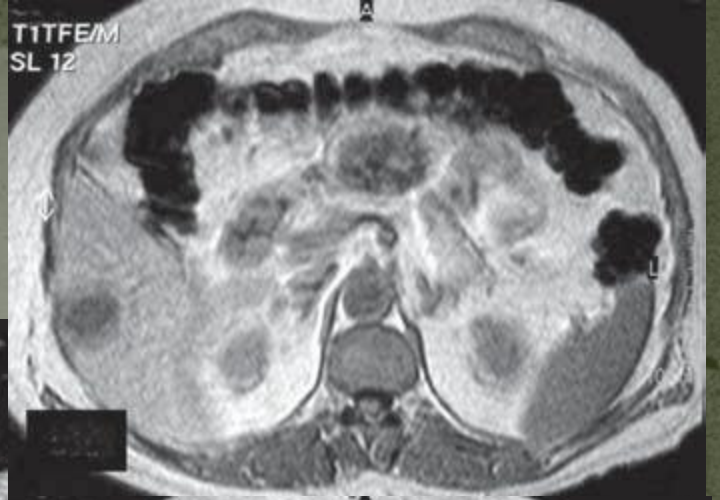


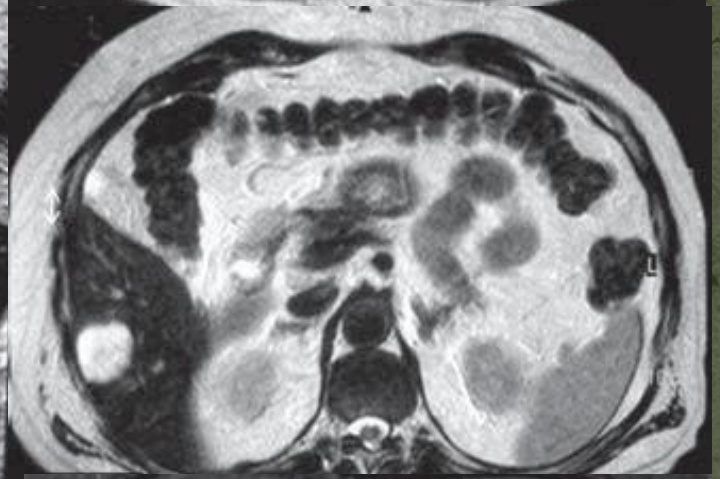
- The third pattern of enhancement includes lesions that enhance homogeneously and thus may be difficult to differentiate from hypervascular metastases, which may demonstrate similar enhancement behavior. For these lesions, the combination of T2-weighted and serial dynamic post-contrast T1-weighted images facilitates a confident diagnosis of hemangioma

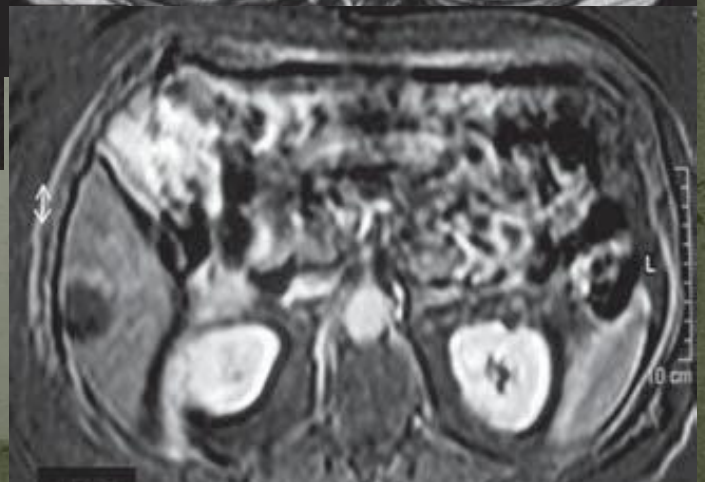


# sclerosing hemangioma



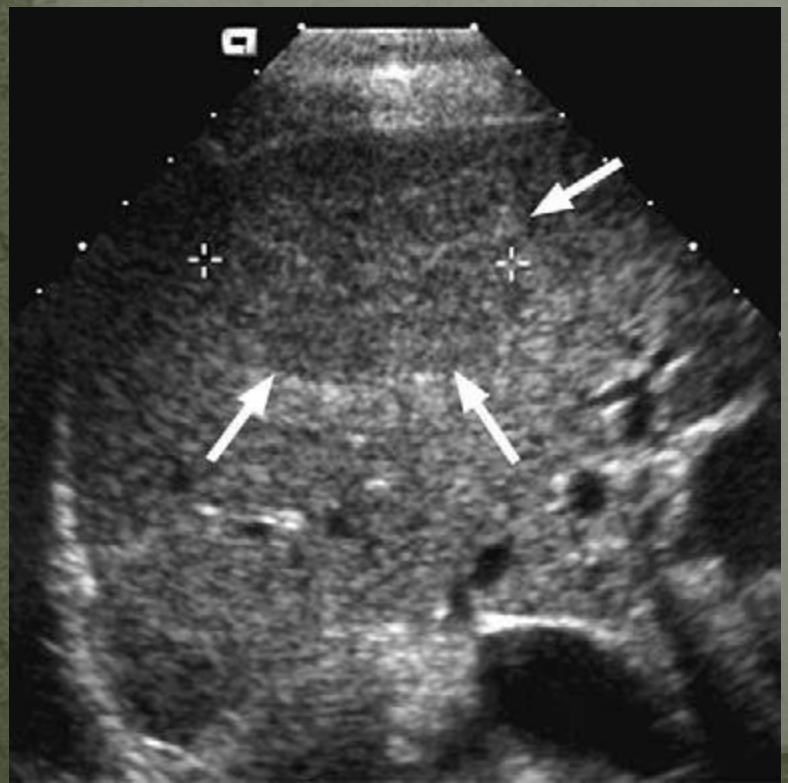


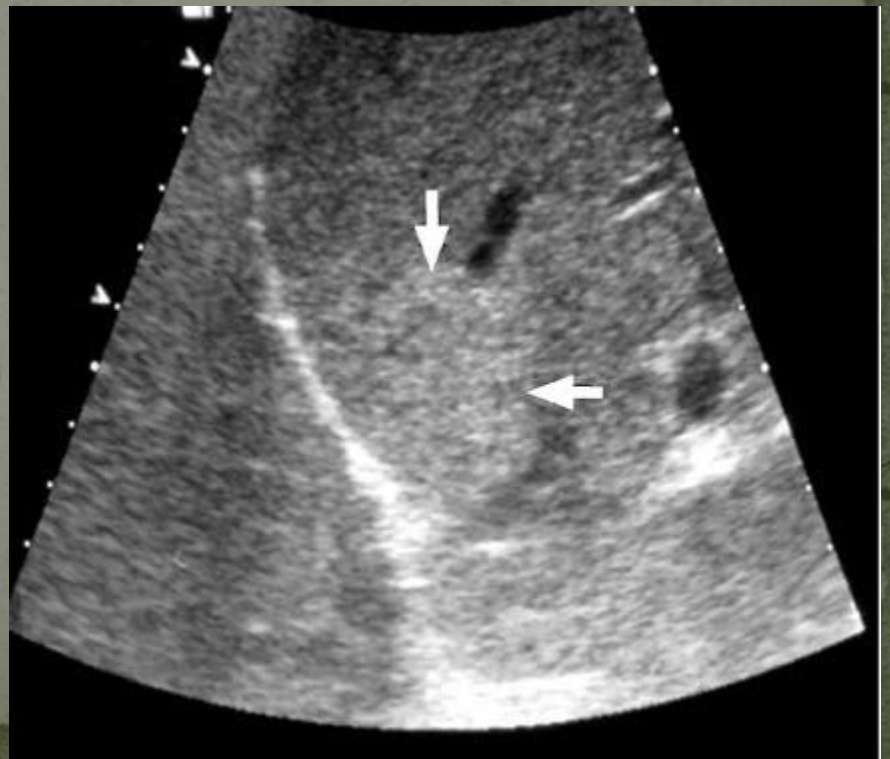
# Focal Nodular Hyperplasia

- FNH is a benign tumor-like lesion of the liver which is considered to be the result of a hyperplastic response of the hepatocytes to the presence of a pre-existing vascular malformation.
- In frequency, FNH is the second most common benign hepatic tumor after hemangioma and has been shown to constitute about 8% of primary hepatic tumors at autopsy.
- It usually occurs in women of childbearing- and middle-age, but cases have been reported in men and children as well. Most investigators agree that oral contraceptives are not the causal agents of FNH. However estrogens could have a trophic effect on FNH

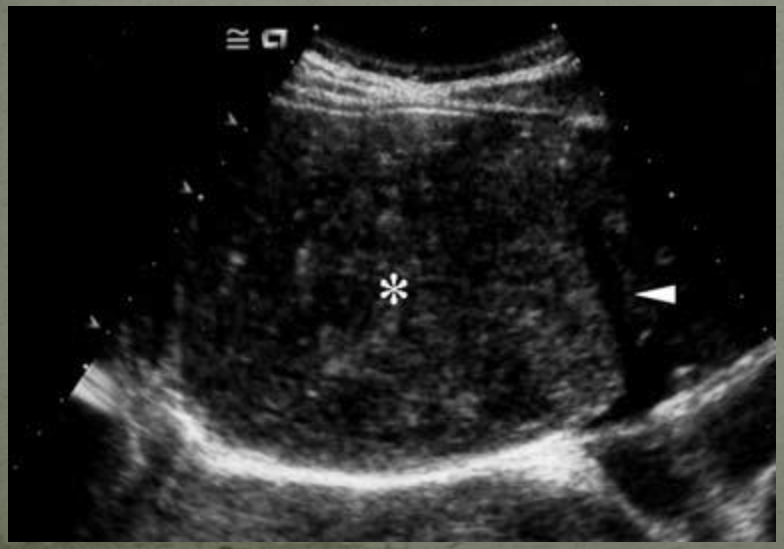
- FNH is usually a solitary, subcapsular nodular mass, but cases with several nodules have been described
- On cut section the majority of these tumors have a central fibrous scar and although the margin is sharp, generally there is no capsule
- When multiple, FNH lesions tend to be associated with other lesions, such as hepatic hemangioma, meningioma, astrocytoma, teleangiectasia of the brain, and systemic arterial dysplasia.
- FNH has also been described in association with hepatocellular adenoma and liver adenomatosis.

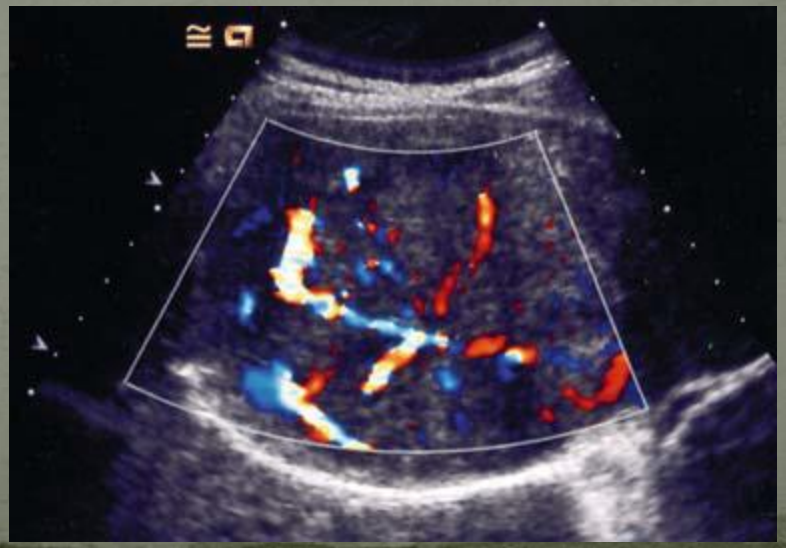
- On US images, classic FNH appears as a homogeneous well-demarcated nodule which may be hypoechoic, isoechoic or slightly hyperechoic relative to the normal liver parenchyma
- Displacement of contiguous hepatic vessels may be the only detectable abnormality. Some lesions may show a hypoechoic halo surrounding the lesion;



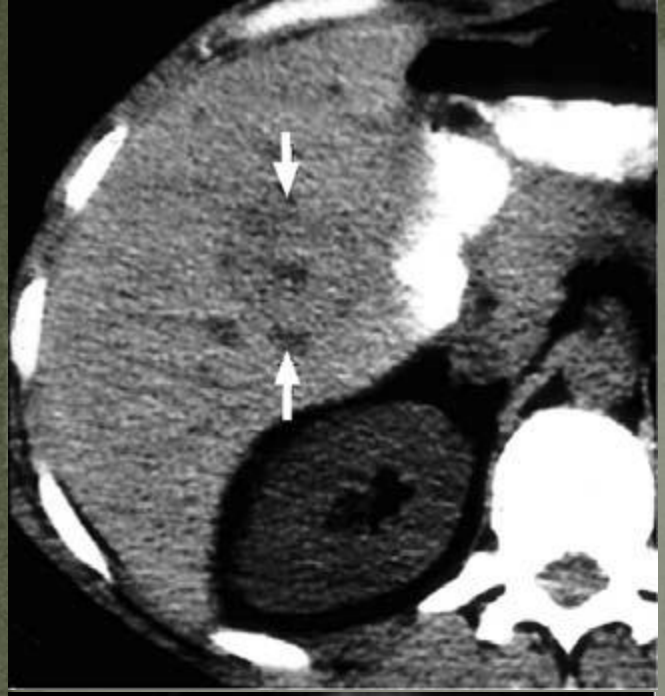


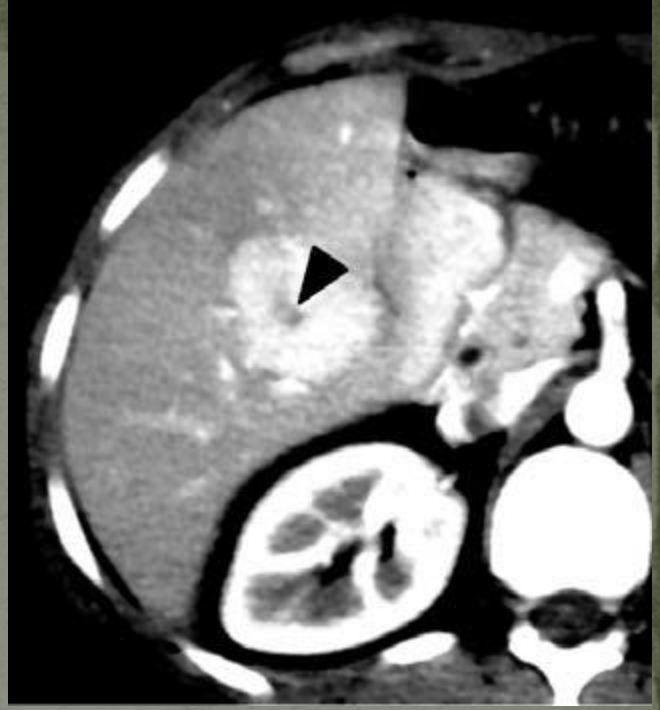
- Characteristic findings at color Doppler US include the presence of a central feeding artery with a stellate or spokewheel pattern, which corresponds to vessels running into the radiating fibrous septa from the central scar

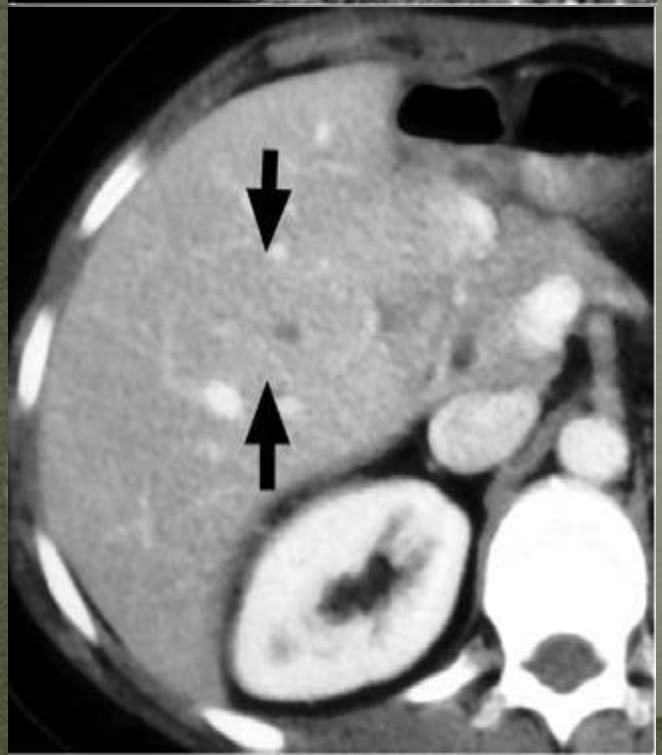


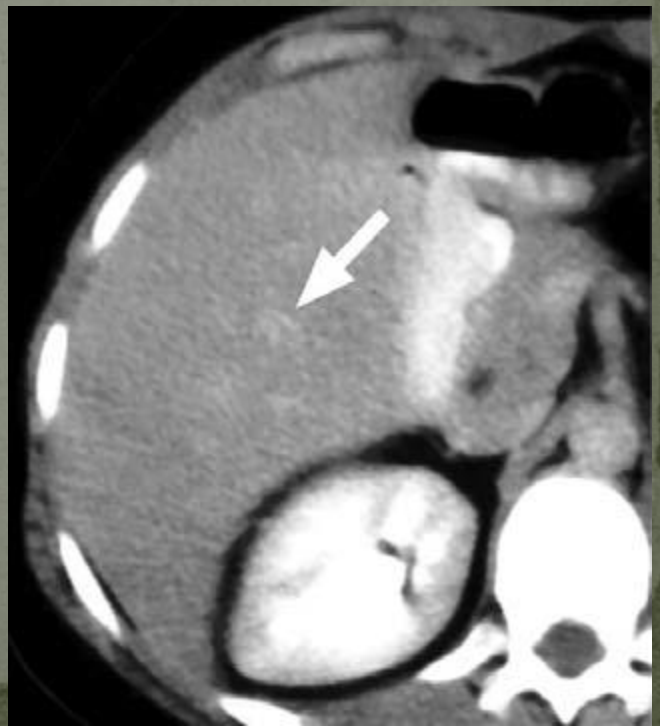


- On unenhanced CT FNH is usually isoattenuating or slightly hypoattenuating
- During the arterial phase of contrast-enhanced CT, FNH enhances rapidly and becomes hyperdense compared to normal liver. The low-attenuation scar appears conspicuous against the hyperdense tissue, and foci of enhancement representing feeding arteries may be seen within the scar
- In the portal-venous phase of enhancement, the difference in attenuation between FNH and normal liver decreases and FNH may become isodense with normal liver parenchyma
- On delayed scans, however, there is retention of contrast material within the fibrous scar, giving it an isoattenuating or,more frequently, a hyperattenuating appearance

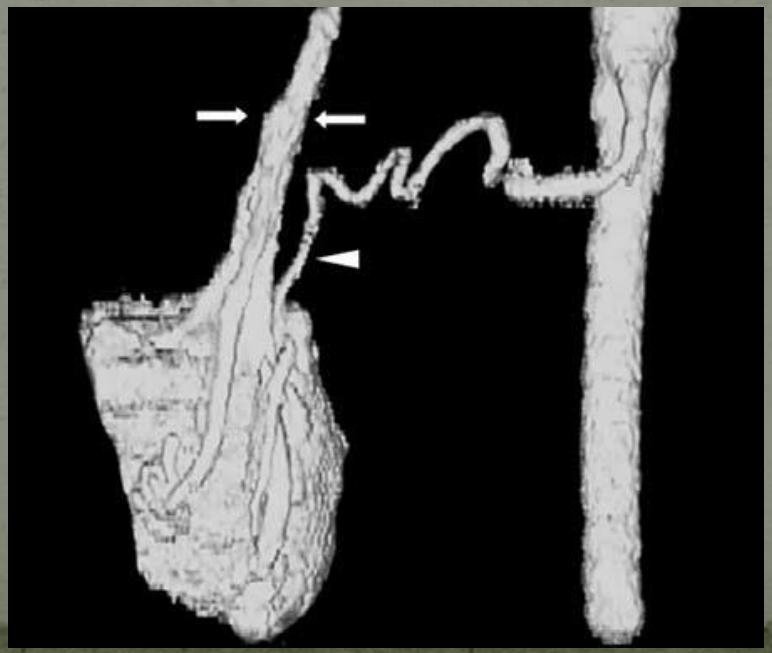








- Detection of the central scar is related to the size of the lesion; while a central scar may be identified in as many as 65% of larger FNH, it may be seen in only about 35% of lesions smaller than 3 cm in diameter
- 3D multidetector CT angiography is very useful in demonstrating the intratumoral vascularization of FNH which is characterized by hepatic venous drainage and by the absence of portal-venous supply



- On MR, FNH are considered classic when they appear as homogeneously isointense or slightly hyperintense on T2-weighted images, and isointense or slightly hypointense on T1-weighted images before contrast agent administration.
- Typical behavior during the dynamic phase of contrast enhancement is marked and homogeneous signal intensity enhancement during the arterial phase, rapid and homogeneous signal intensity wash-out during the portal-venous phase, and signal isointensity (with the exception of the scar) during the equilibrium phase .
- A typical scar appears as a hyperintense central stellate area on T2-weighted images and as a hypointense area on T1-weighted images.
- During the dynamic phase of contrast enhancement a typical scar is hypointense during the arterial and portal-venous phases and slightly hyperintense in the equilibrium phase

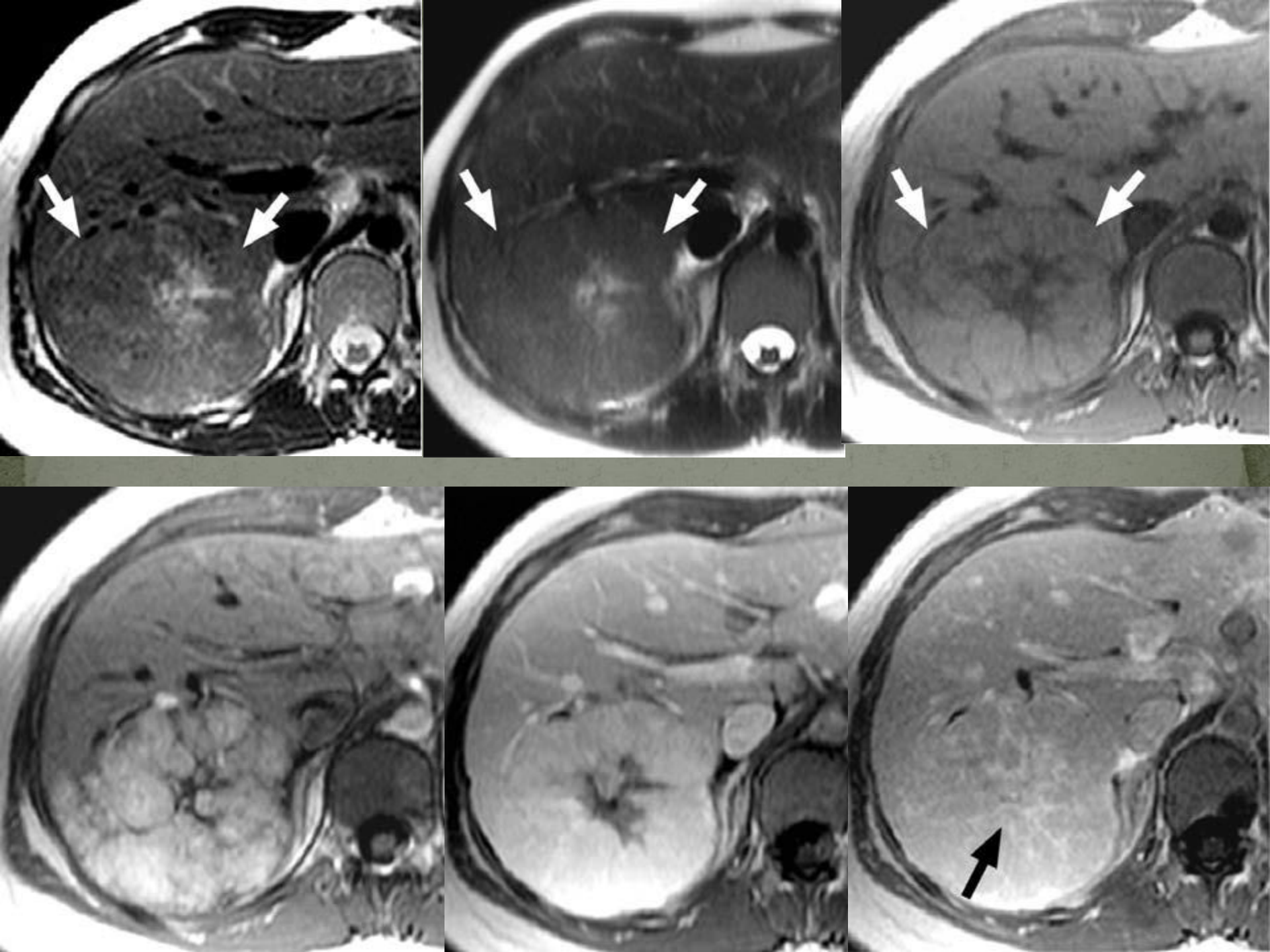
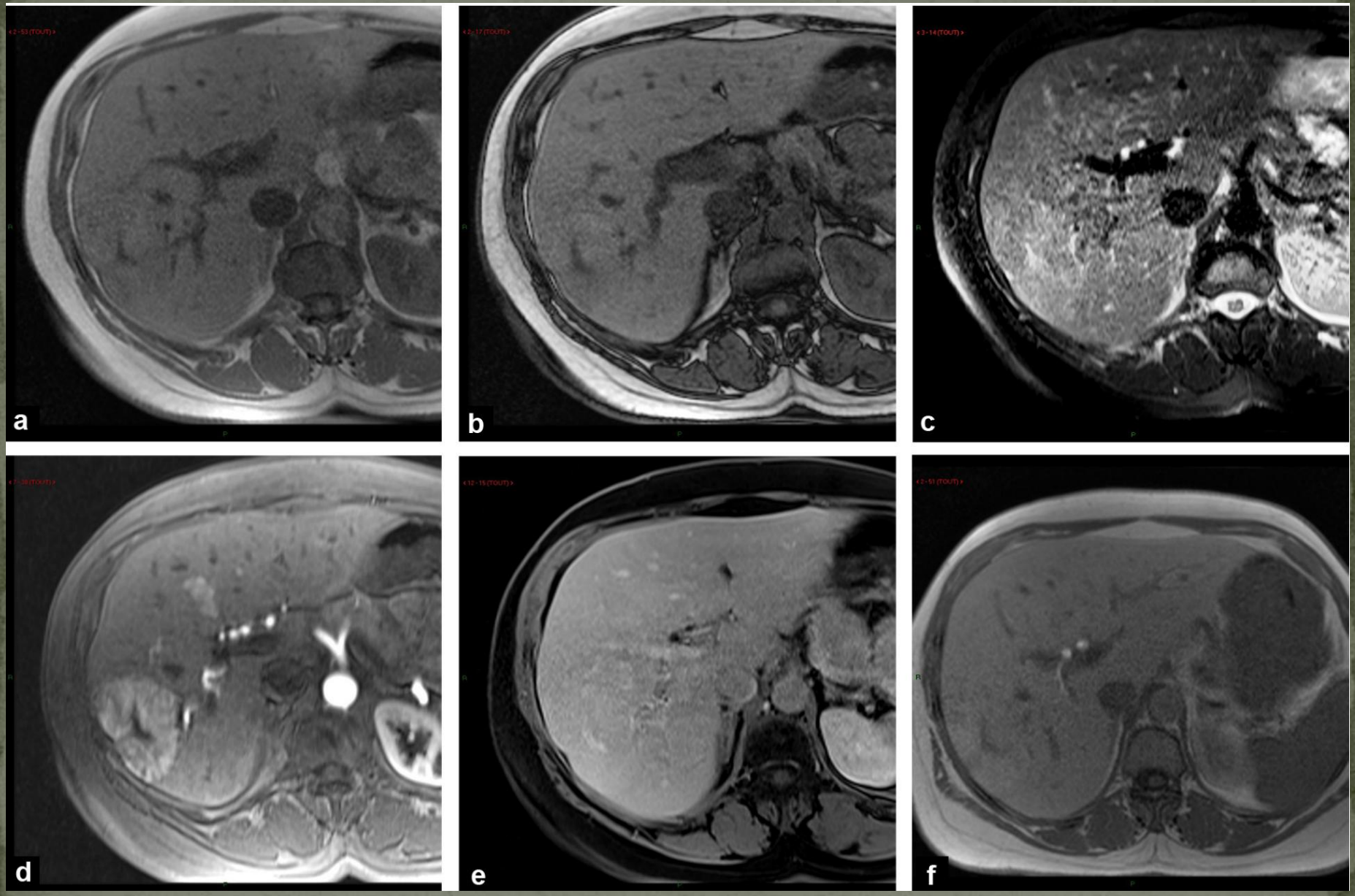


**Table 1** Criteria of typical focal nodular hyperplasia (FNH) (Figs. 1 and 2).

| MRI | | Contrast enhanced ultrasound |
|---|---|---|
| Without injection | T1-weighted isointensity or discreet hypointensity<br>T2-weighted isointensity or discreet hyperintensity<br>Homogeneity outside of the central stellate scar<br>Central stellate scar with T2-weighted hyperintensity | Early, arterial, centrifugal, spoke-wheel contrast uptake<br>Nodule hyperechoic at the end of the arterial phase<br>Nodule iso- or discreetly hyperechoic in the portal and late phases |
| Injection of gadolinium chelates | Intense uniform arterial contrast uptake<br>Nodule isointense with the liver in the portal and late phases<br>Late contrast uptake by the central stellate scar | |
| Analysis in the hepatocyte phase (only for liver-specific gadolinium contrast agents) | Nodule is iso- or hyperintense relative to the adjacent liver | |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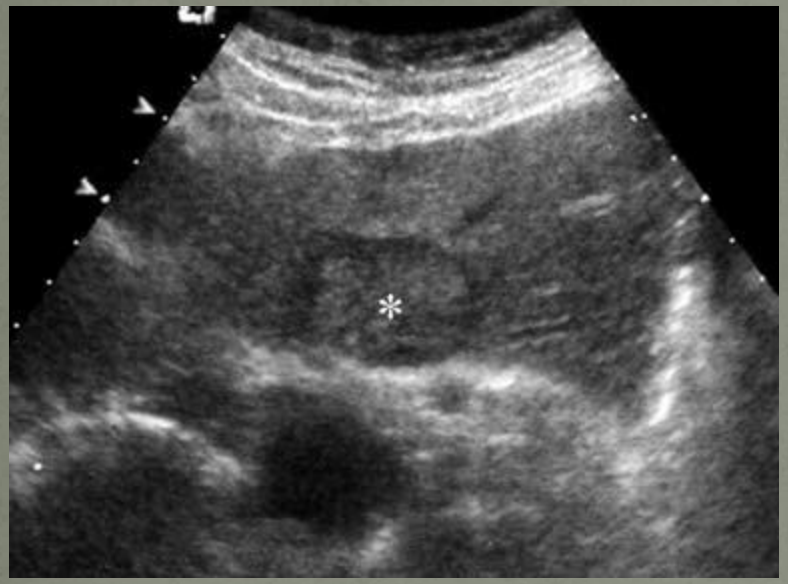
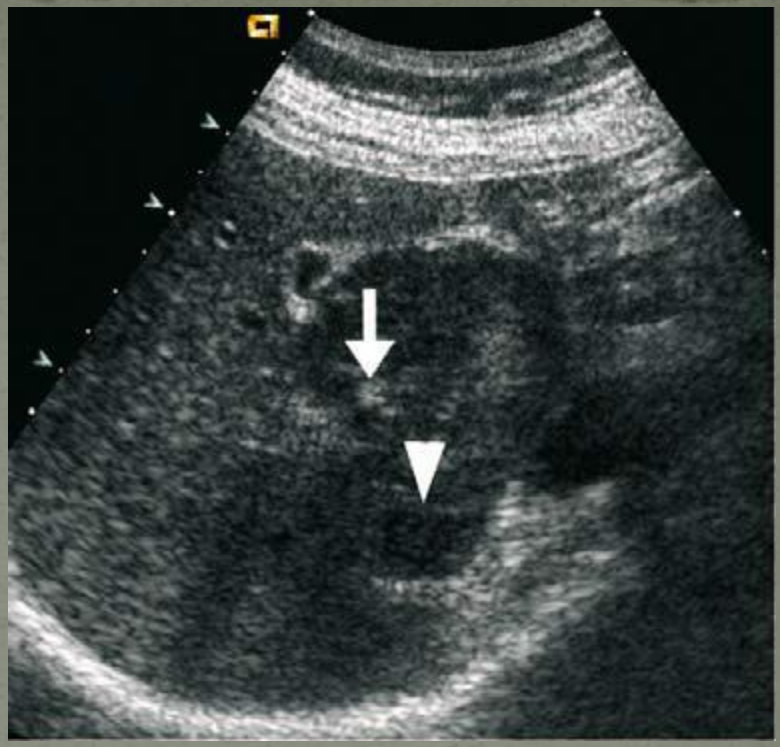
# Hepatocellular Adenoma

- Hepatocellular adenoma (HA) is a rare benign tumor of hepatocellular origin which is most common in middle-aged women.
- Typical HA is defined as a tumor composed of hepatocytes arranged in cords, that only occasionally produces bile. The tumor lacks portal tracts and terminal hepatic veins
- Although the precise pathogenic mechanism of HA is unknown, the use of estrogen-containing [110] or androgen-containing steroid medications clearly increases their prevalence, number and size within the affected population
- Another risk group for HA are patients affected by glycogenosis, in particular, type I glycogen storage disease.
- An association with pregnancy has also been described

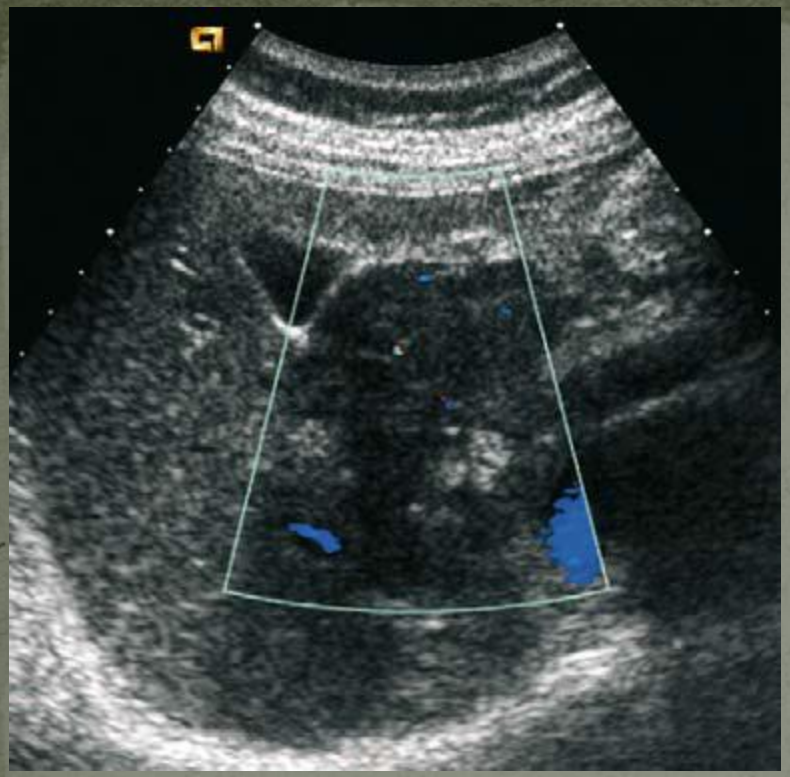
- Most patients with only one or few HA are asymptomatic and almost invariably have normal liver function
- However, the classic clinical manifestation of HA is spontaneous rupture or hemorrhage,leading to acute abdominal pain and possibly progressing to hypotension and even death
- HA is solitary in 70-80% of cases, but it is not unusual to encounter two or three HA in one patient,
- Patients with glycogen storage disease or LA may have dozens of adenomas

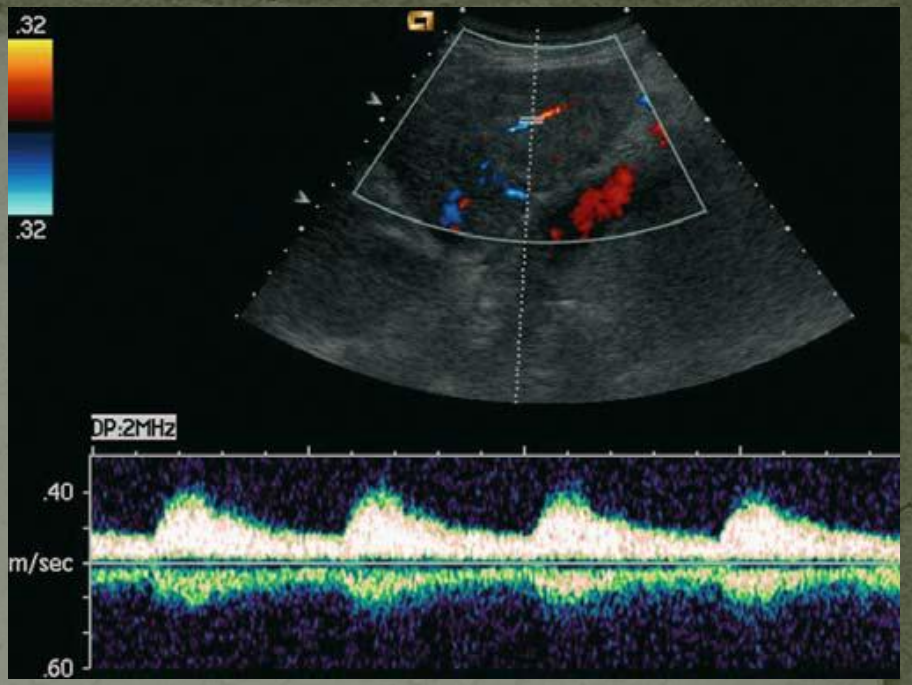
- In many cases HA is seen as a large, predominantl hypoechoic lesion on US with central anechoic areas corresponding to areas of internal hemorrhage
- Non-complicated HA may appear as an iso- or hypoechoic mass with a relatively homogeneous aspect However, fatty components within the lesion may result in focal hyperechogenicity.
- A peripheral pseudocapsule,which is present in about one third of HA lesions, is seen as a hypoechoic peripheral rim on US.





Larger adenomas are often heterogeneous in echogenicity (b), with both hyperechoic (arrow)
and hypoechoic areas (arrowhead), which correspond to areas of hemorrhage, necrosis and fatty infiltration

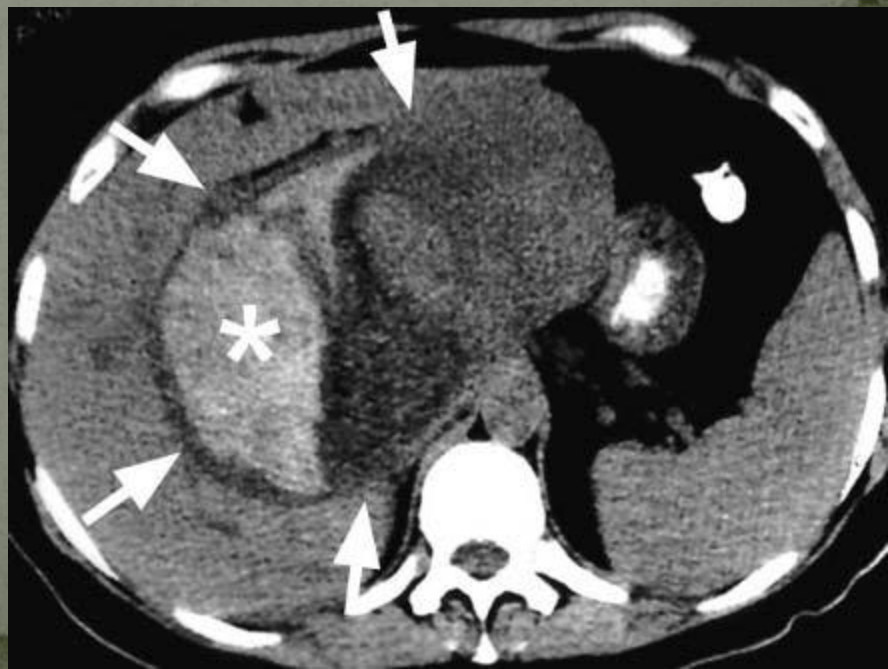




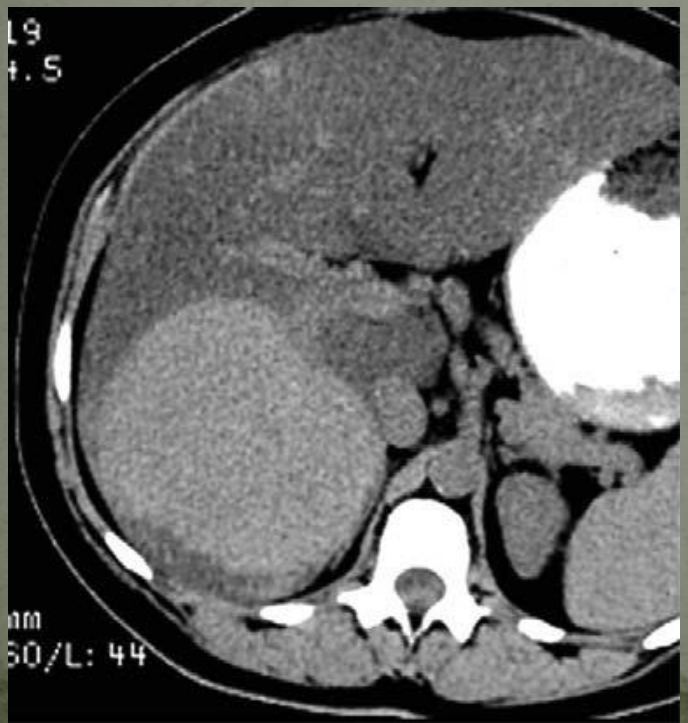

Color Doppler US reveals peripheral arteries and veins

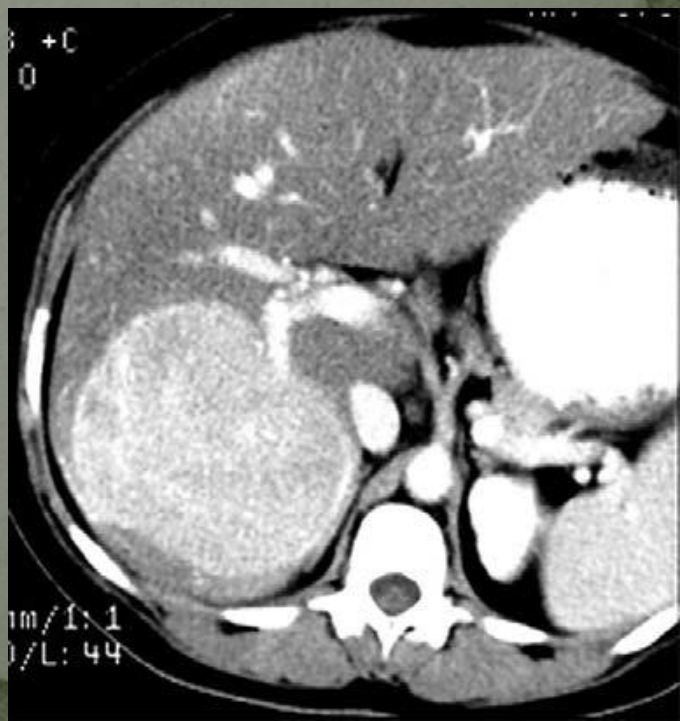
In addition, Color Dopple may identify intratumoral arteries. This finding is absent in FNH and may be a useful discriminating feature for HA

- On unenhanced CT, HA may appear as a hypodense mass due to the presence of fat and glycoge within the tumor. However, hyperdense areas corresponding to acute or subacute hemorrhage can be noted frequently in large, complicated lesions

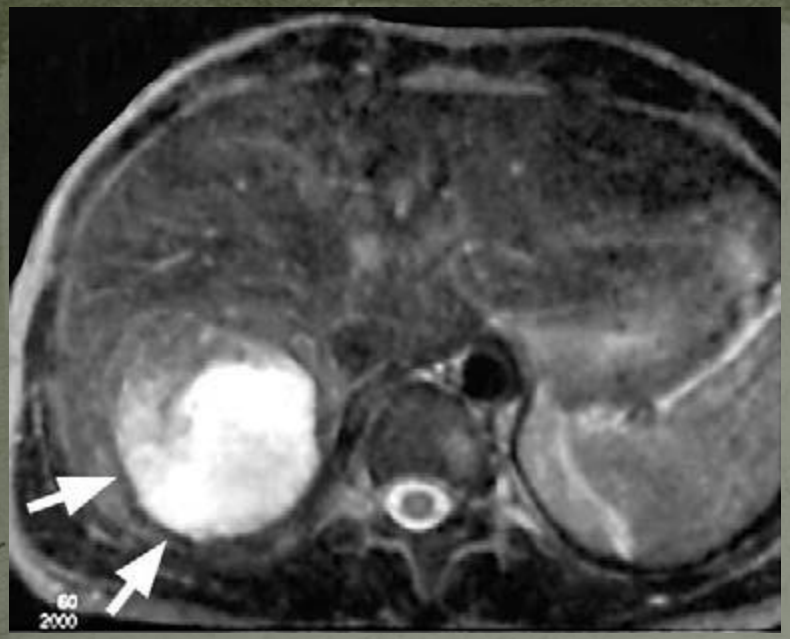


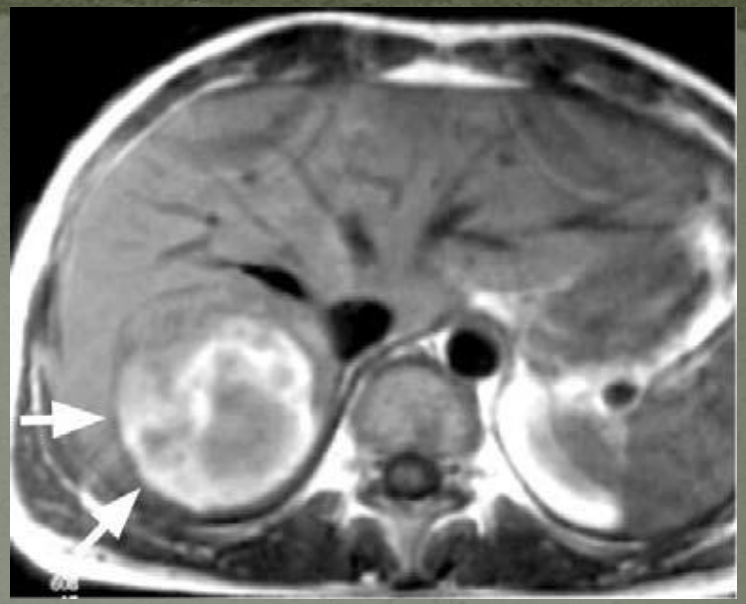
- On contrast-enhanced dynamic CT scanning, non-complicated HA generally enhances rapidly and homogeneously and have increased attenuation relative to the liver. A pseudocapsule is frequently seen in larger lesions as a hypodense and hyperdense rim on non-contrast and equilibrium phase CT images, respectively . The enhancement in adenomas typically does not persist because of arteriovenous shunting

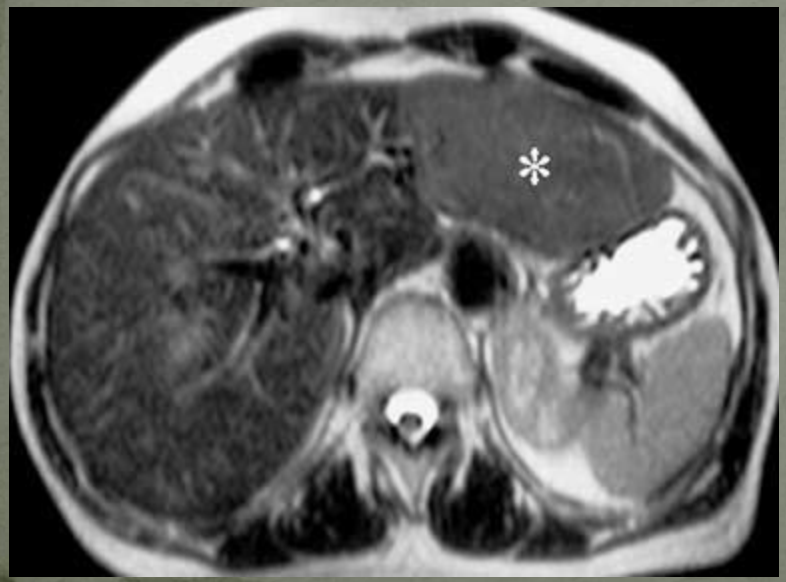


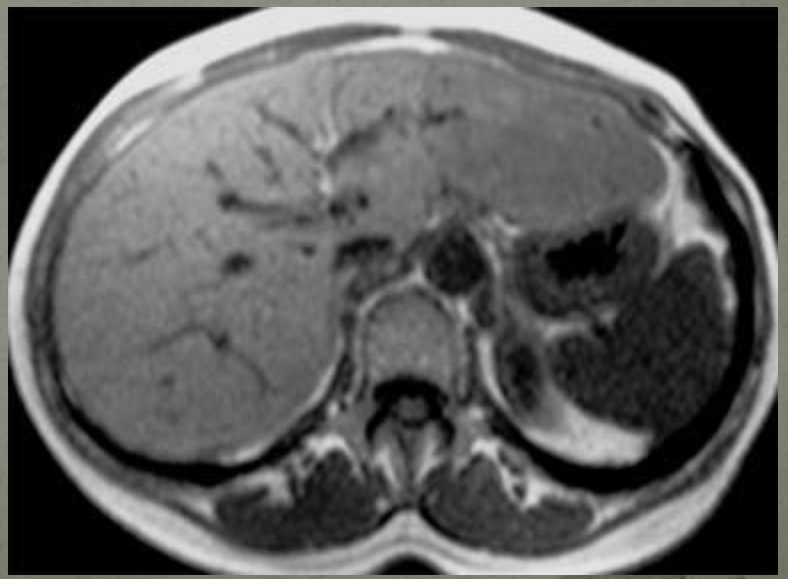


- On MR images, HA frequently show heteroge neous hyperintensity on unenhanced T2-weighted images and heterogeneous hypointensity on unenhanced T1-weighted images. Areas of increase signal intensity on T1-weighted images indicate the presence of fat and hemorrhage,while areas of reduced signal intensity indicate necrosis
- Because non-complicated HA frequently have a homogeneous iso- or slightly hyperintense signal on T2-weighted images and an iso- or hypointense signal on T1-weighted images they may be hard to distinguish from surrounding normal liver parenchyma









- Dynamic MR imaging is able to demonstrate the early arterial enhancement that results from the presence of large subcapsular feeding vessels.
- On portal-venous and equilibrium phase images HA generally appear isointense or slightly hypointense,with focal heterogeneous hypointense areas of necrosis, calcification or fibrosis.
- On delayed liver-specific phase images after Gd-BOPTA administration, the common appearance is hypointensity of the solid, non-hemorrhagic components of the lesion

# Characterization of HCAs Subtypes with MRI

# Inflammatory HCAs

- Inflammatory HCA is the most common subtype and accounts for about 30%–50% of all hepatocellular adenomas.
- These tumors are mainly seen in women, in association with obesity, hepatic steatosis, diabetes mellitus, glycogenesis (in particular, type I glycogen storage diseases), and alcohol abuse.
- More than 90% of women have a history of contraceptive use.
- Patients with inflammatory HCA may present with signs of chronic anemia and/or "systemic inflammatory syndrome," characterized by fever, leukocytosis, and elevated serum levels of C-reactive protein
- Inflammatory HCAs are associated with a definitive increased risk of bleeding (>30%) and a risk of malignant transformation(5–10%)

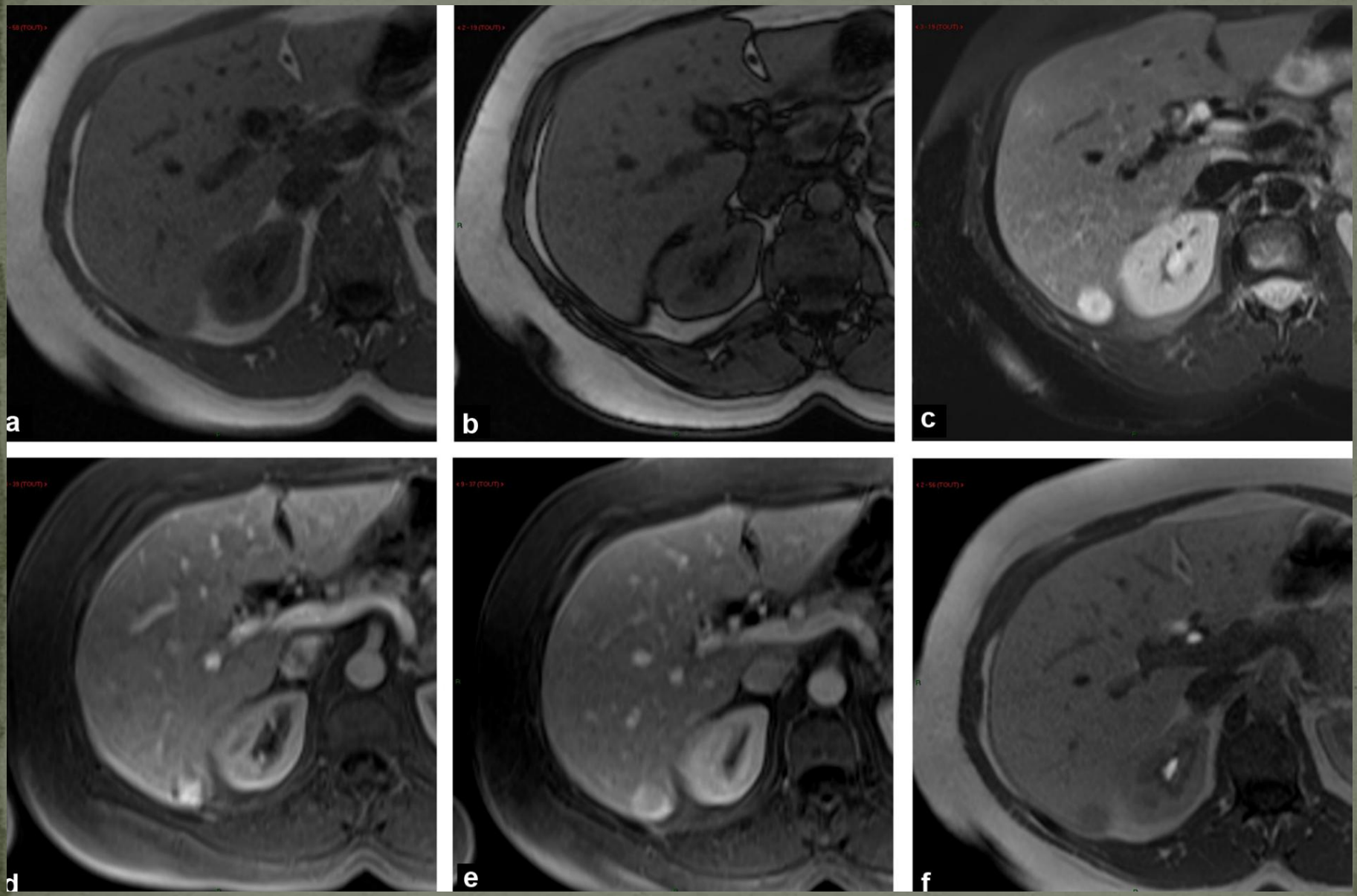
- On plain MR imaging inflammatory HCA is often hyperintense on T2w images and hypointense on T1w sequence, frequently with heterogeneous signal intensity.

- Hyper- and hypointensity on T2w and T1w images, respectively, correspond mainly to areas of sinusoidal dilatation and inflammatory infiltrates.

- Focal areas of fat may be seen as hypointense areas on T1 out-phased images due to signal drop.

- Inflammatory HCA may appear as a hypervascular mass with persistent enhancement during dynamic evaluation and may show a variable uptake in the hepatobiliary phase specially at the periphery.

- Sometimes because of sinusoidal dilatation, inflammatory component and ductal reaction, in the hepato-biliary phase image areas of hypointensity in adenomas, mainly in the periphery, may be seen .
- Marked T2 hyperintensity associated with delayed persistent enhancement has a sensitivity of as much as 85% and a specificity of 87% for the diagnosis of inflammatory HCA.
- Peripheral hyper-intensity (atoll sign) reflects the abnormal ductal reaction with altered biliary excretion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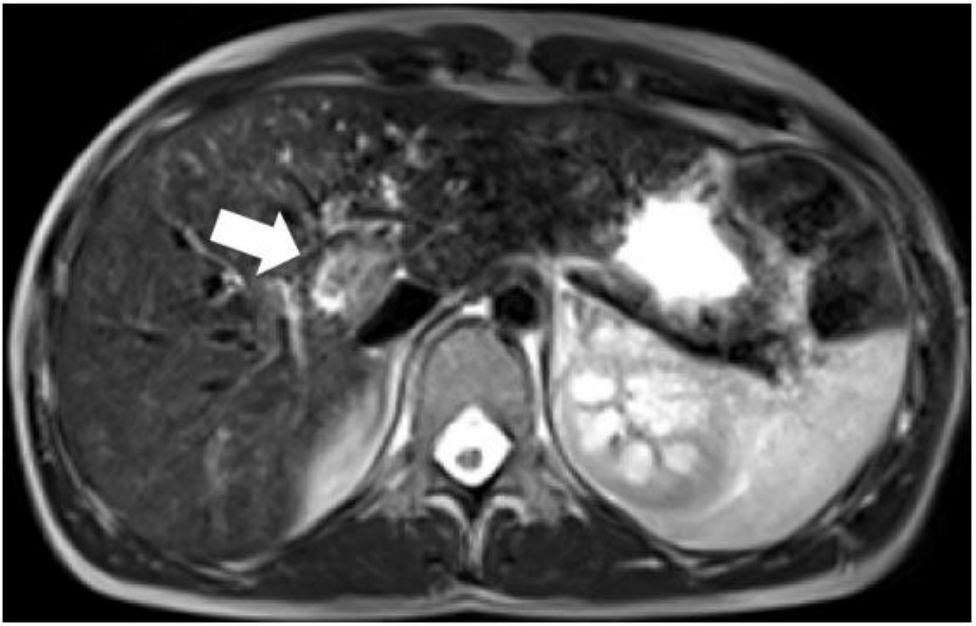
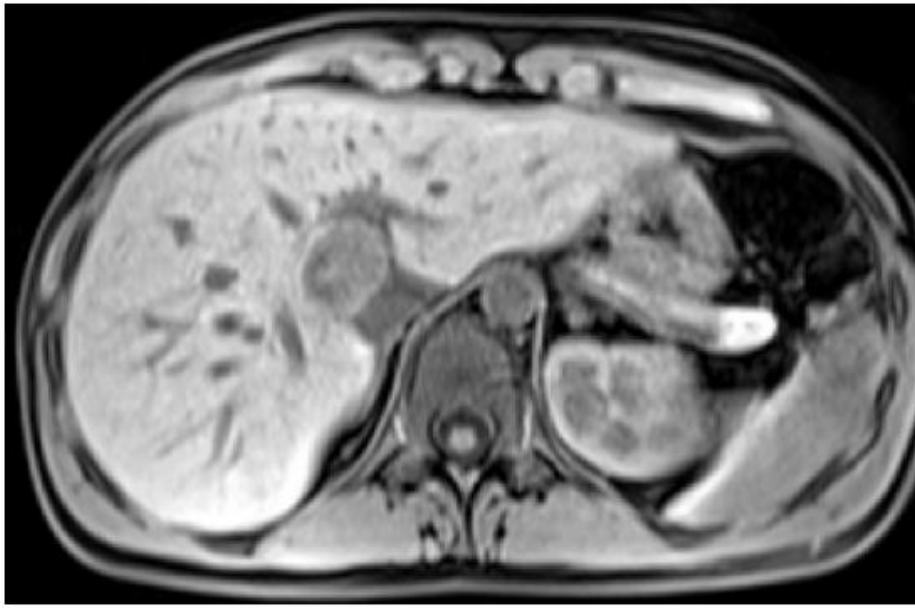
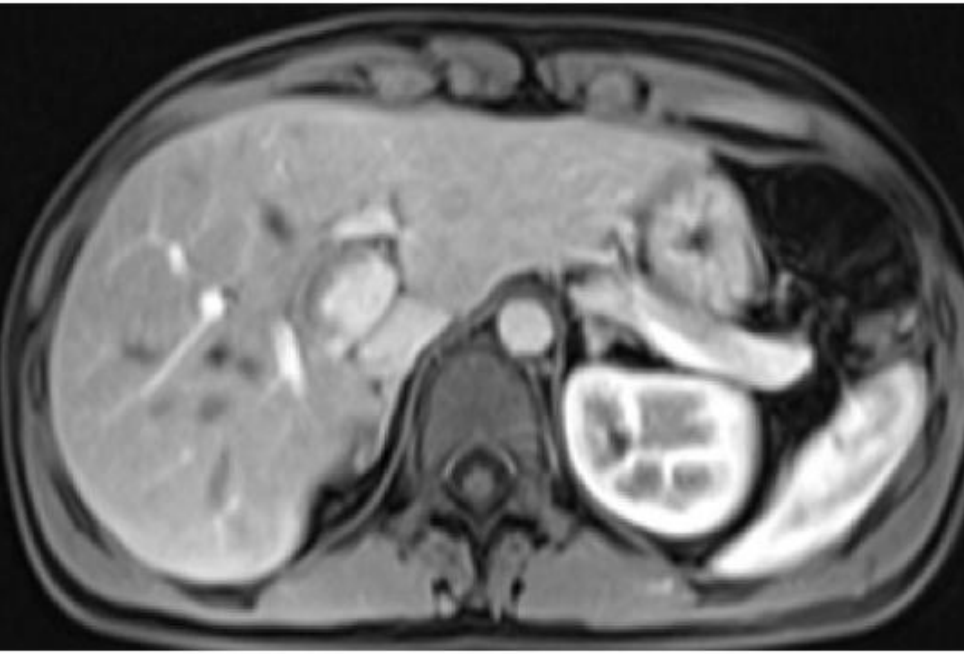
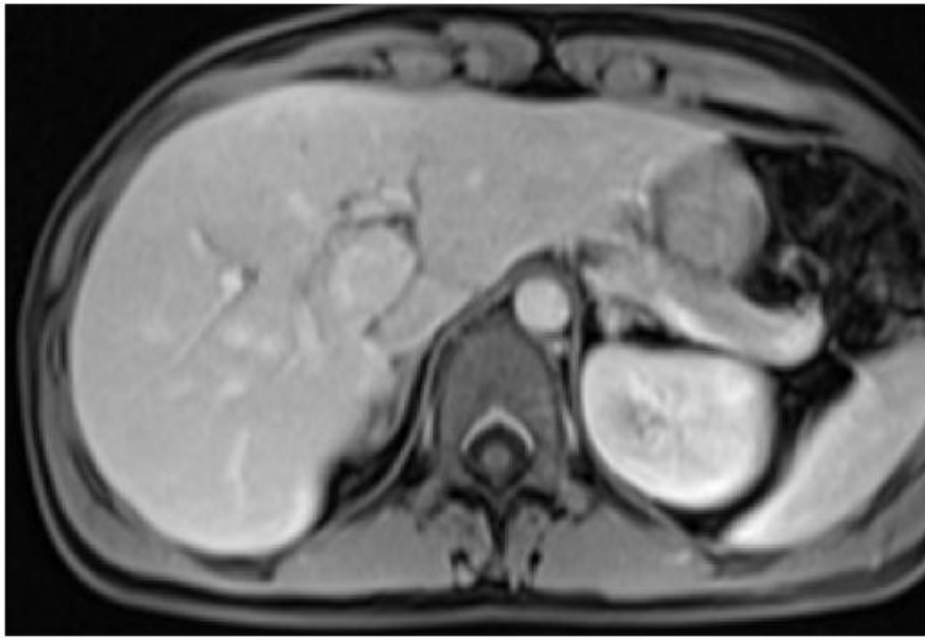
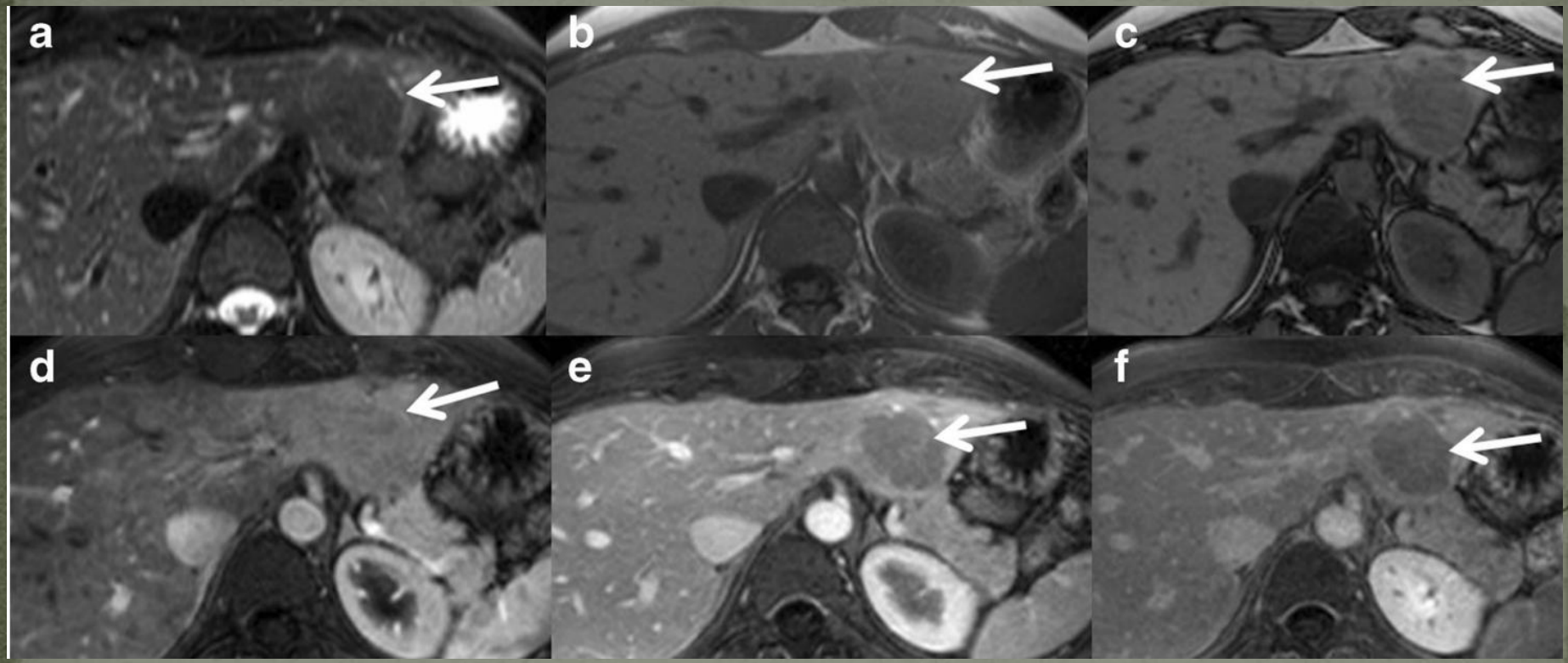





# HNF-1α-Mutated HCAs

- HNF-1α-mutated HCA is the second most common type; it constitutes about 30–35% of all HCAs and arises because of biallelic inactivation of transcription factor 1 gene located in chromosome twelve.
- This kind of adenoma is nearly exclusively seen in women, except for rare HCA with germline HFN-1α mutations which can be also observed in men.
- HNF-1α-mutated HCA is characterized by diffuse intralesional steatosis. HNF-1α mutation may be the primary inciting event that results in the accumulation of estrogen metabolites that unconditionally stimulate hepatocyte proliferation

- On MR examination, HNF-1α-mutated HCA often shows heterogeneous hypointensity areas on T1 out-phased sequences with significant signal drops on out-phased in comparison with in-phased sequences, corresponding to fatty deposition. Hyperintensity on T1 in-phased and out-phased images signal drop may correspond to glycogen component or less commonly haemorrhage.
- On T2w images the lesion tends to appear as iso- or hypointense nodule without significant restriction on DWI.

- On dynamic evaluation after Gd-BOPTA and Gd-EOB-DTPA, HNF-1α-mutated HCA appears hypervascular with variable degrees, but usually less evident than inflammatory adenoma. On portal venous and equilibrium phases the lesion tends to be hypointense; on hepatobiliary phase the mass appears hypointense in almost all cases with homogeneous appearance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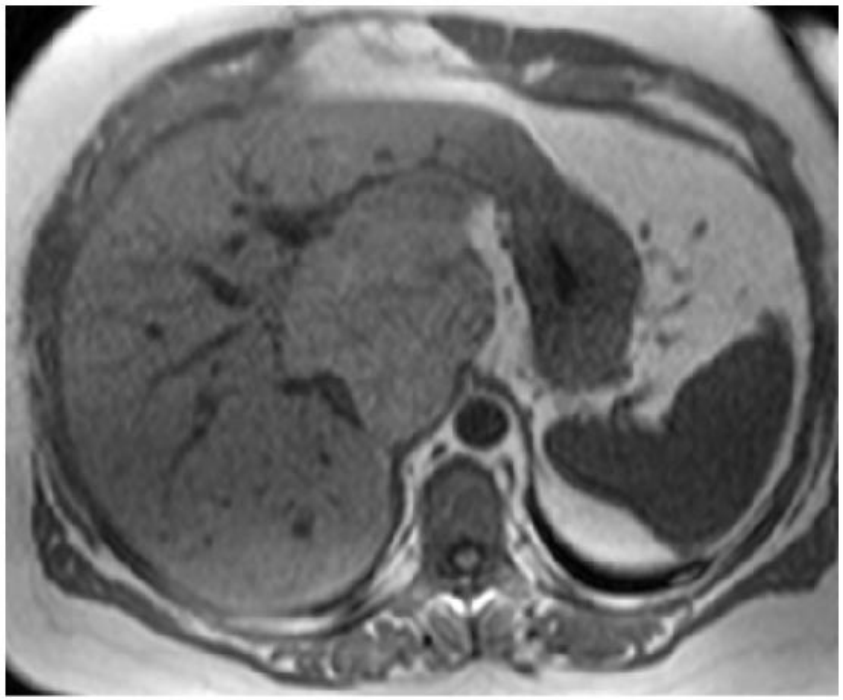
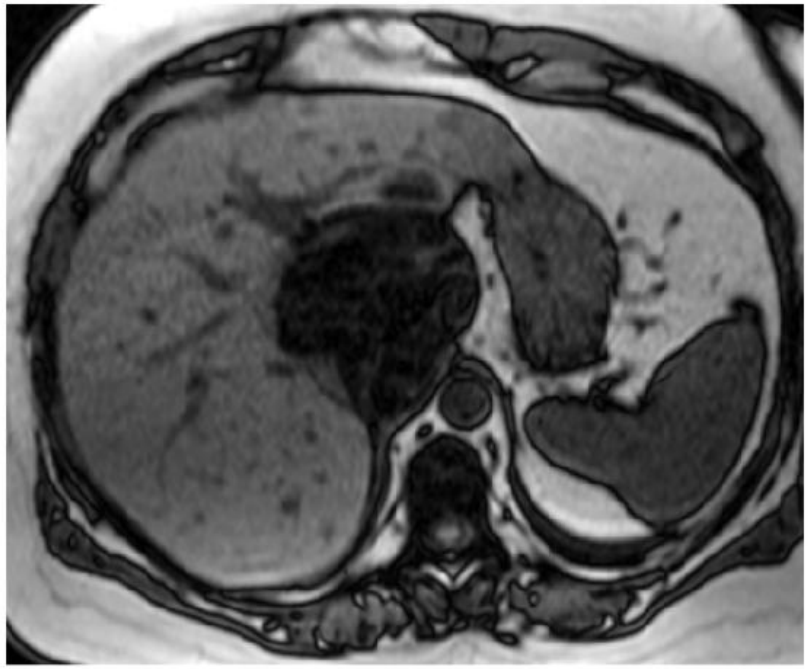
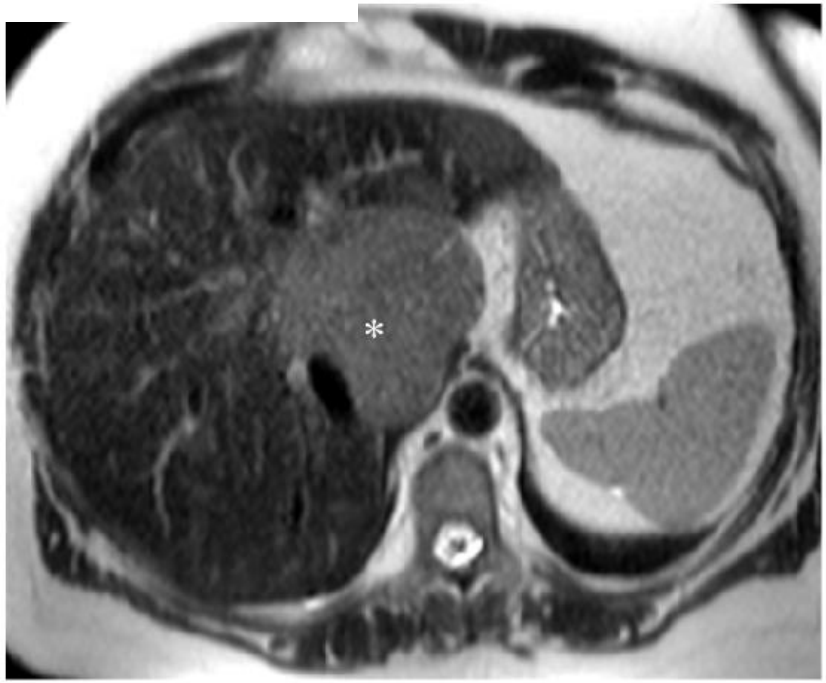




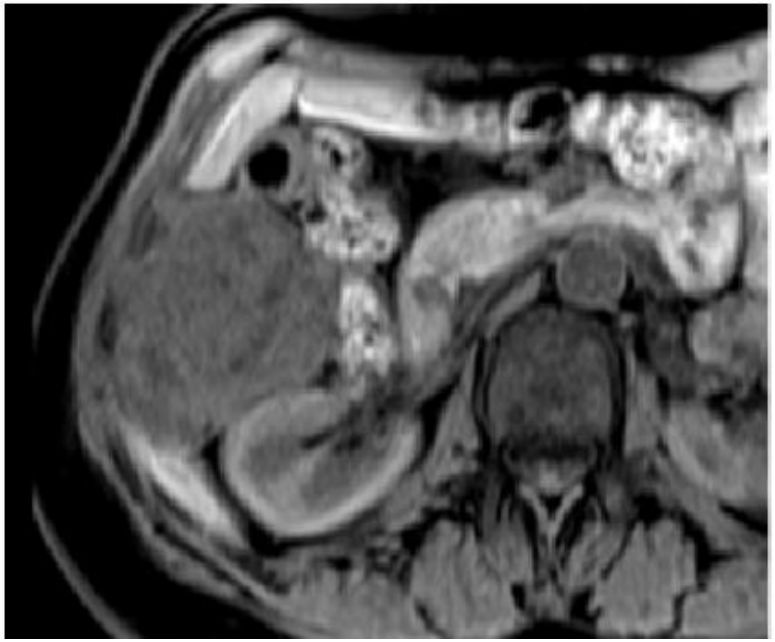


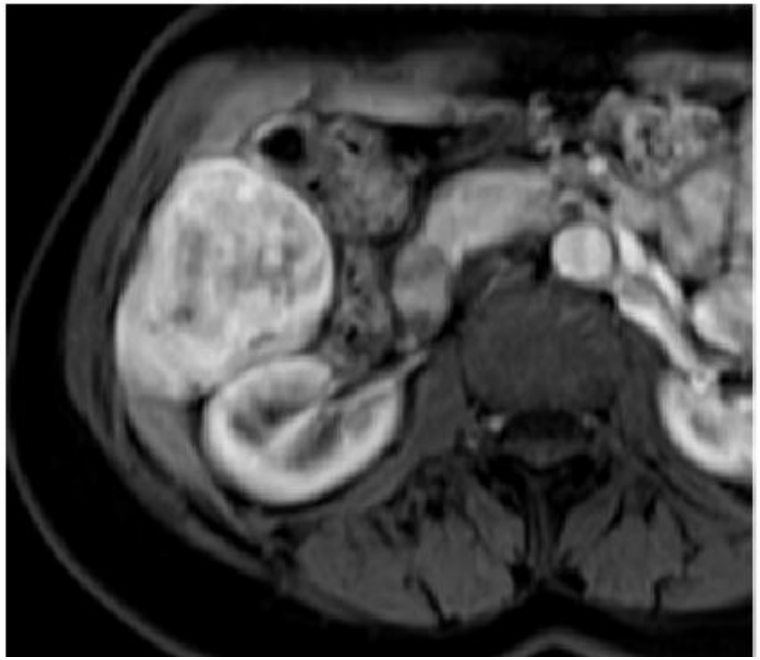
# β-Catenin-Mutated HCAs

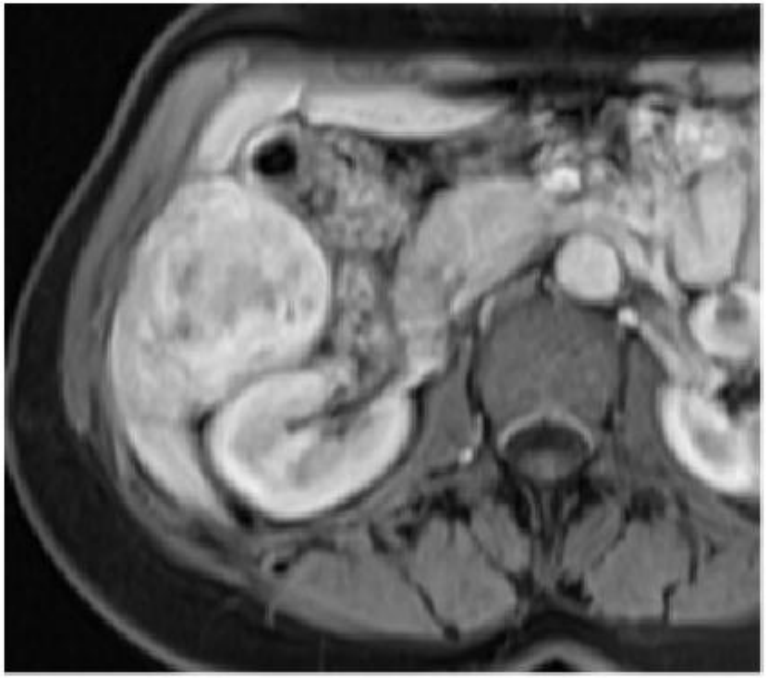
- β-Catenin-mutated HCAs constitute about 10–15% of all HCAs; they originate from sustained activation of β-catenin because of mutations involving the CTNNB1 gene (catenin β1). These tumors primarily involve patients with glycogen storage disease and on androgen treatment and have a greater propensity to undergo malignant transformation to HCCs. β-Catenin plays a major role in hepatocyte development, differentiation, proliferation, and regeneration.

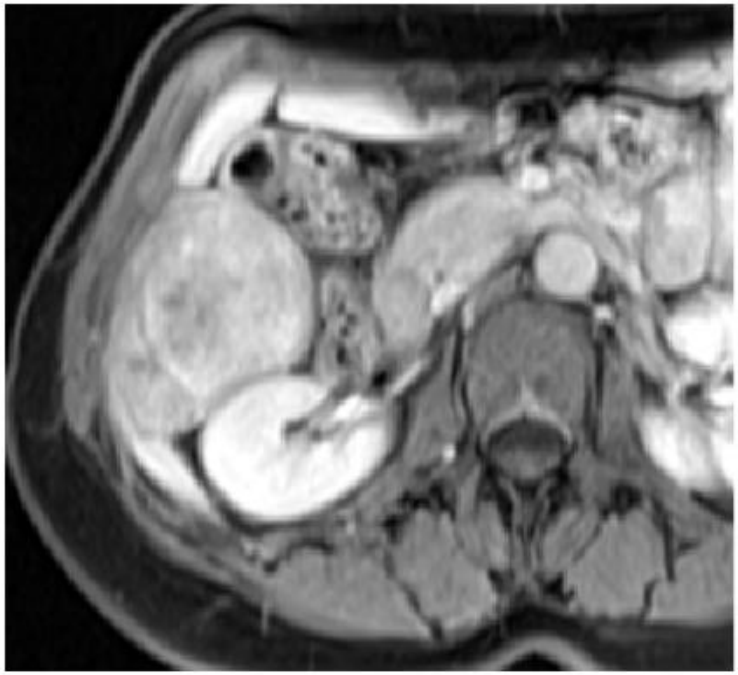
- On MR imaging β-catenin-mutated HCA appears as homogeneous or heterogeneous hypervascular mass with persistent or nonpersistent enhancement during the delayed-phase images. Signal intensity on T2 and on T1 precontrast sequences is variable but mainly heterogeneously hyper-and hypointense, respectively. Malignant transformation simulates HCC on imaging and does not show peculiar findings

- A recent study correlates the presence of a vaguely demarcated scar and poorly delimited high-signal-intensity areas on T2- weighted images to β-catenin positivity



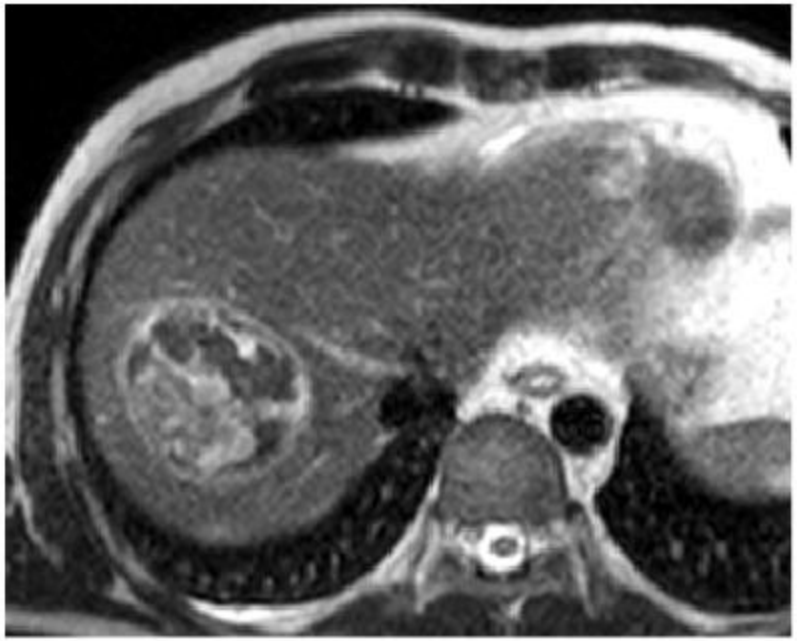


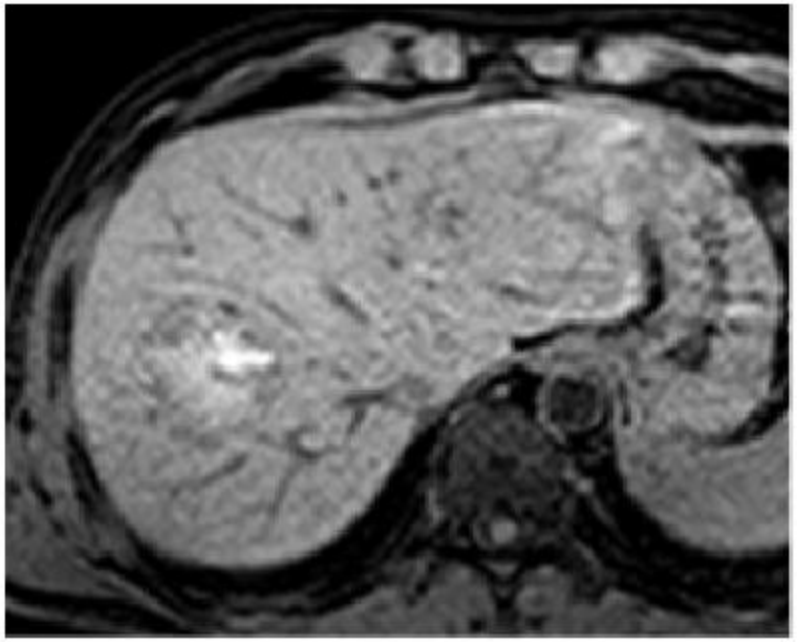


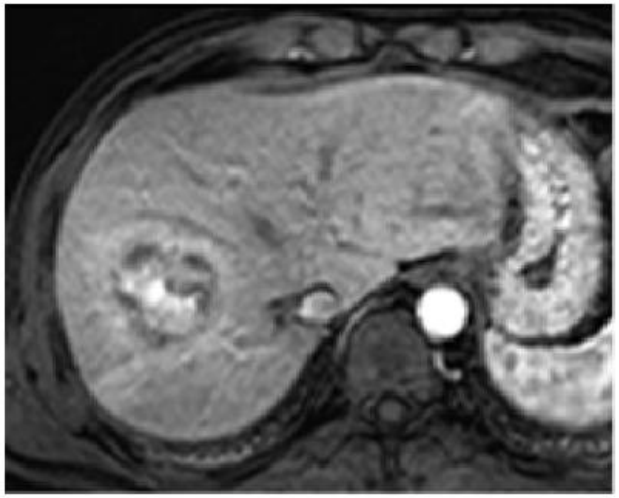


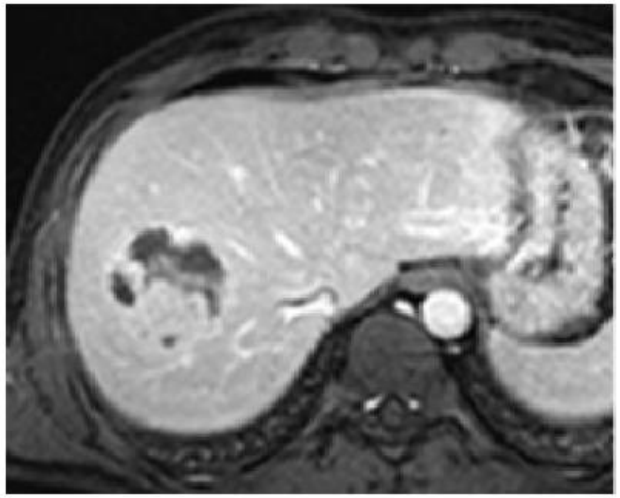
# Unclassified HCAs

- Approximately 10% of all HCAs are without specific genetic and/or pathologic abnormalities. Frequently, the presence of haemorrhage may be one of the reasons that justify the unclassified categorization of the lesion . No specific MR imaging patterns have yet been proposed to identity unclassified HCAs also because imaging experience is very limited









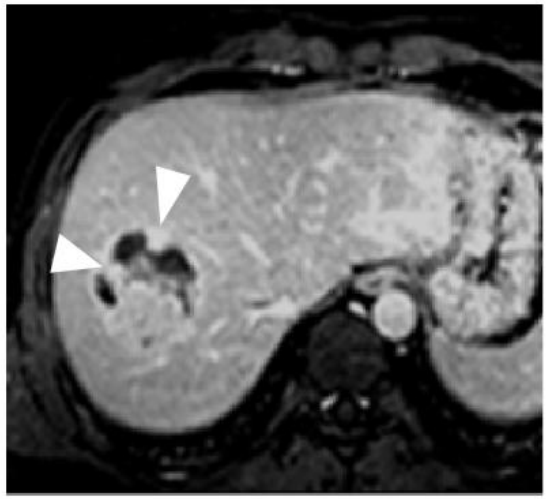
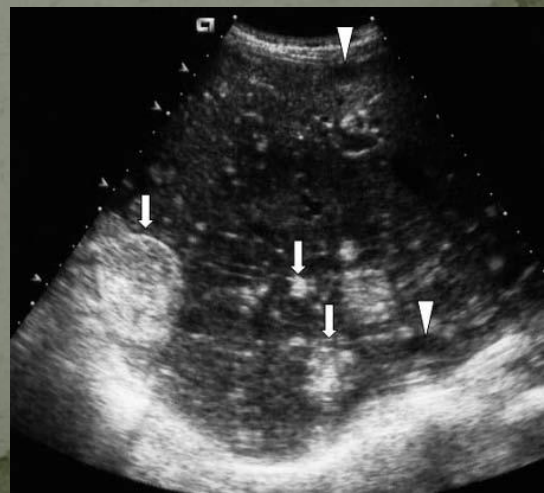


**Table 2** Summary of MRI features of major subtypes of hepatocellular adenoma (HCA) and focal nodular hyperplasia (FNH)

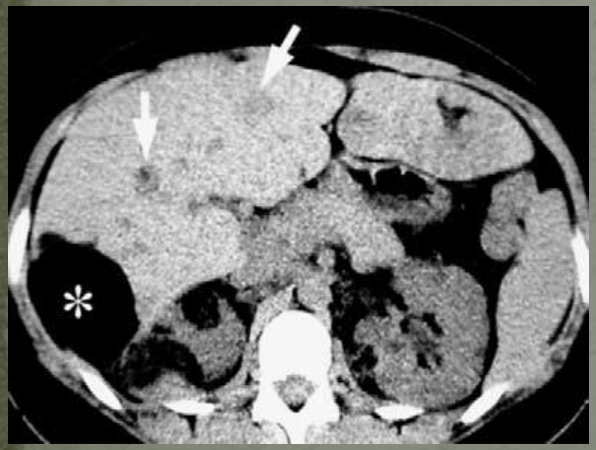
| | Subtype | T1W | T2W | In and out of phase | Arterial | Portal venous/delayed | Remarks |
|---|---|---|---|---|---|---|---|
| Focal nodular hyperplasia | Classic | Iso- to mildly hypointense | Iso- to mildly hyperintense | No signal drop | Intense enhancement | Persistent enhancement | T2 hyperintense scar showing delayed enhancement |
| | Non-classic | Heterogeneous hypo- or iso- or hyperintense | Heterogeneous iso- or hyperintense | Focal signal drop rarely | Intense heterogeneous enhancement | Heterogeneous persistent enhancement with pseudocapsule | Absent or atypical scar |
| Hepatocellular adenoma | Inflammatory HCA | Iso- to mildly hyperintense | Diffusely hyperintense | No diffuse signal drop | Intense enhancement | Persistent enhancement | Atoll sign-T2 hyperintense rim. 10 % can have focal intratumoral fat |
| | HNF1a-mutated HCA | Iso- to hyperintense | Iso- to mildly hyperintense | Diffuse signal drop | Moderate enhancement | No persistent enhancement | |
| | ß-catenin-mutated HCA | Isointense | Iso-, hypo- or hyperintense | No diffuse signal drop | Intense | Variable. May show portal venous washout | Faint scar and ill-defined T2 hyperintense foci |
| | Unclassified | – | – | – | – | – | |

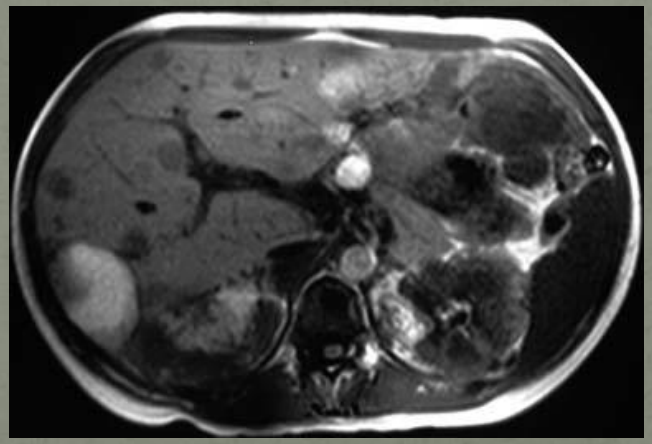
# Lipomatous Tumors

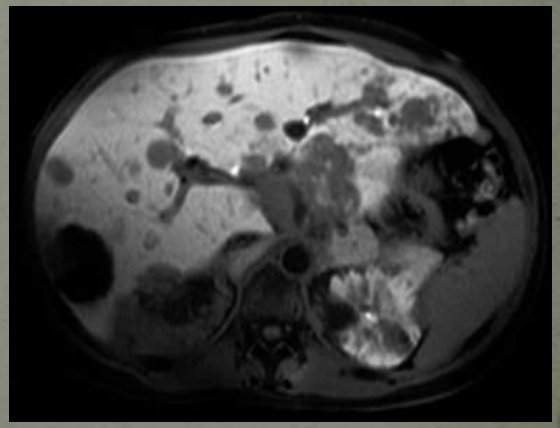
- Benign hepatic tumors composed of fat cells include lipoma, and combined tumors such as angiomyolipoma (fat and blood vessels), myelolipoma (fat and hematopoietic tissue) and angiomyelolipoma
- Angiomyolipomas are often highly echogenic on US and are essentially indistinguishable from hemangiomas, although they may also present a mixed hyper-hypoechoic pattern



Density measurements on unenhanced CT are characteristic of fat (–20 to –115 HU). Pure lipomas do not enhance, but variable enhancement occurs in lesions containing angiomatous elements



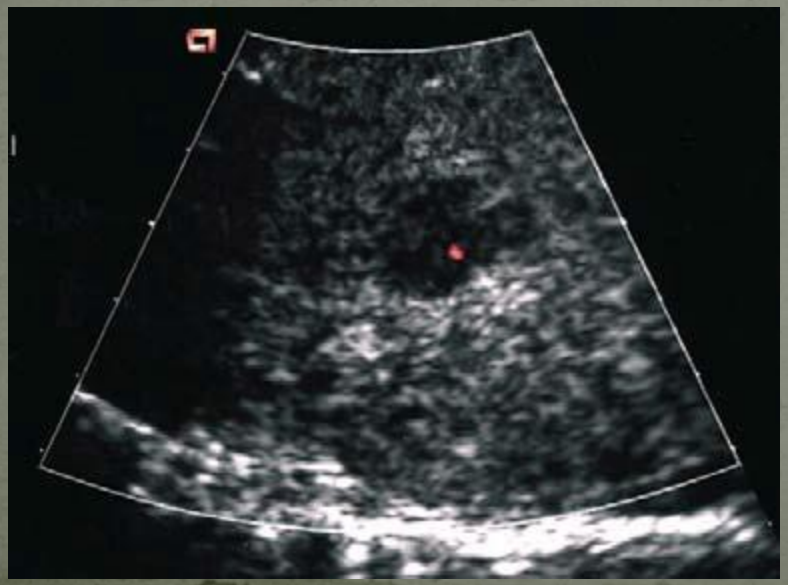


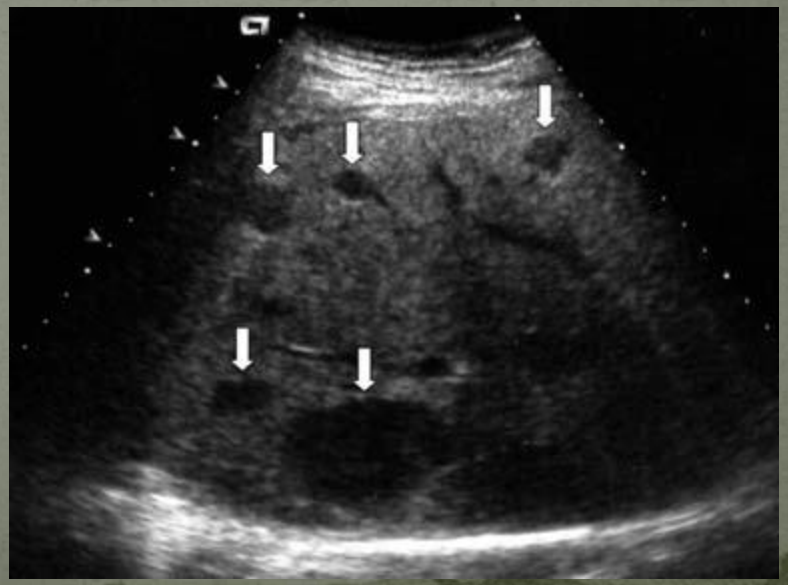


# Nodular Regenerative Hyperplasia

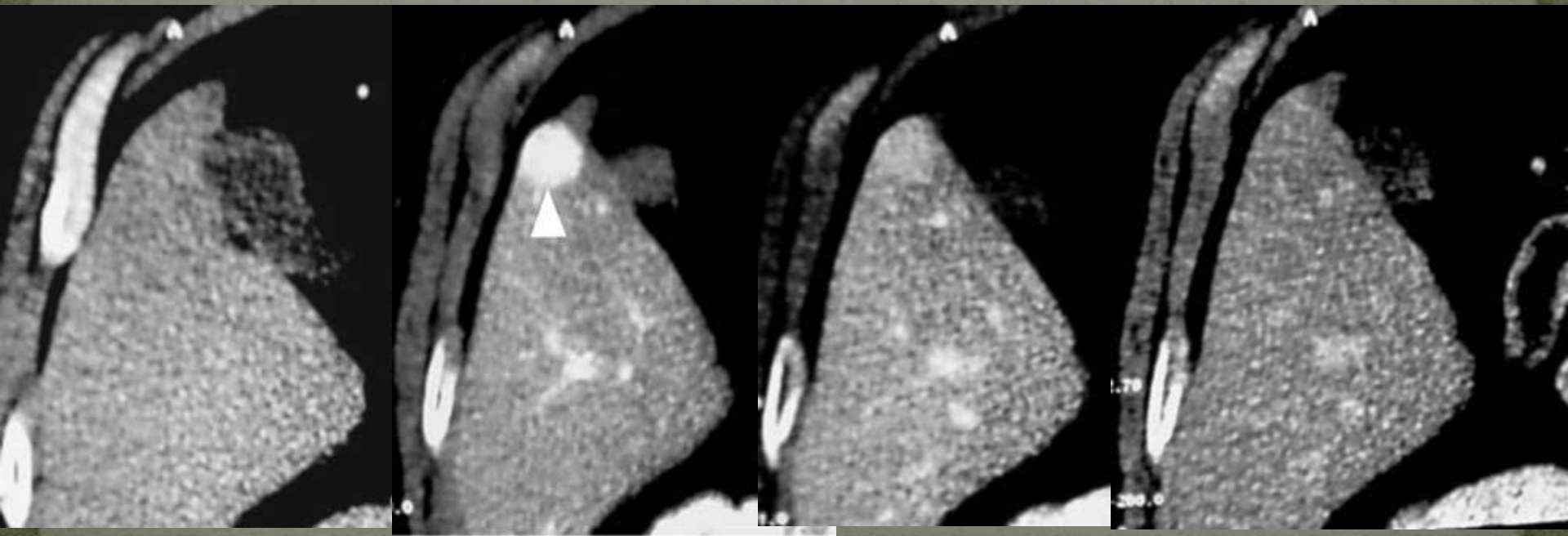
- Nodular regenerative hyperplasia (NRH) of the liver is a condition characterized by diffuse micronodular transformation of the hepatic parenchyma without the formation of fibrous septa between the nodules
- The nodules vary in size (0.1 to 3 cm) but are usually smaller than 1 cm.
- Various systemic diseases and drugs are often associated with NRH: myeloproliferative syndromes); lymphoproliferative syndromes chronic vascular disorders (polyarteritis nodosa); rheumatologic disorders, lupus erythematosus; steroids and anti-neoplastic medication

- Disturbance in the hepatic microcirculation isbelieved to be the primary cause of NRH
- NRH occurs in all ages with a mean age of 50 years, with no gender predilection.
- In most cases NRH is not visible on US due to the same echogenecity as the surrounding parenchyma. In other cases, well-delineated hypoechoic or isoechoic nodules can be seen

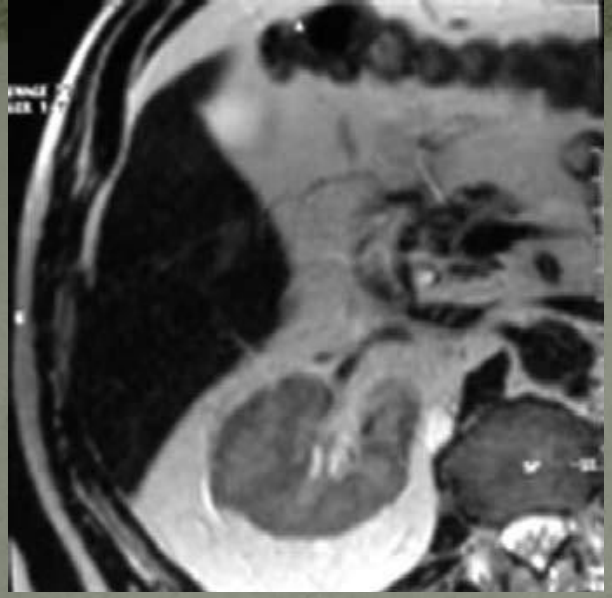


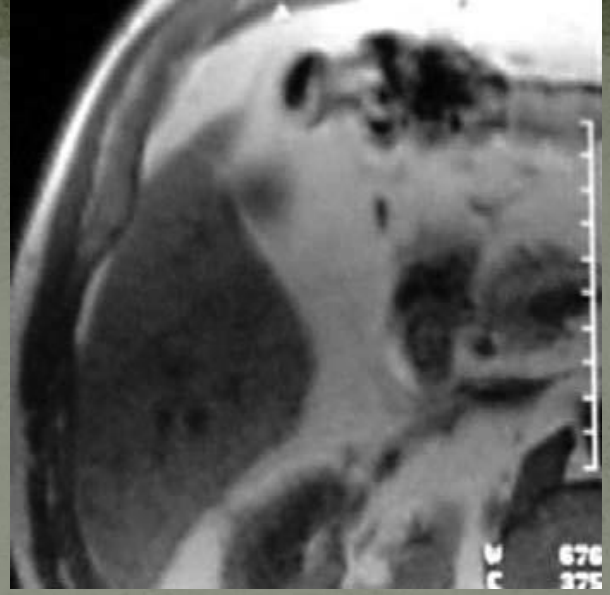


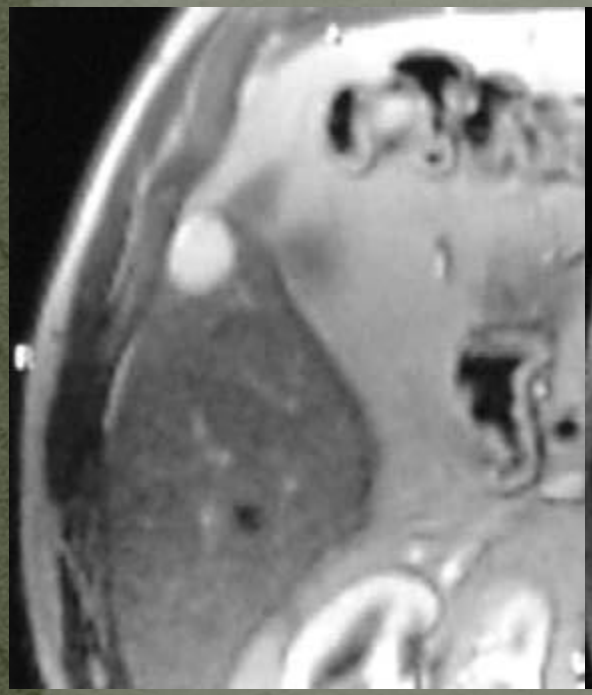
- On CT imaging, approximately half of the cases appear normal,while the nodules in the remaining cases are typically hypoattenuating relative to the adjacent normal hepatic parenchyma .
- Usually the nodules enhance homogeneously to different degrees after the intravenous administration of contrast media

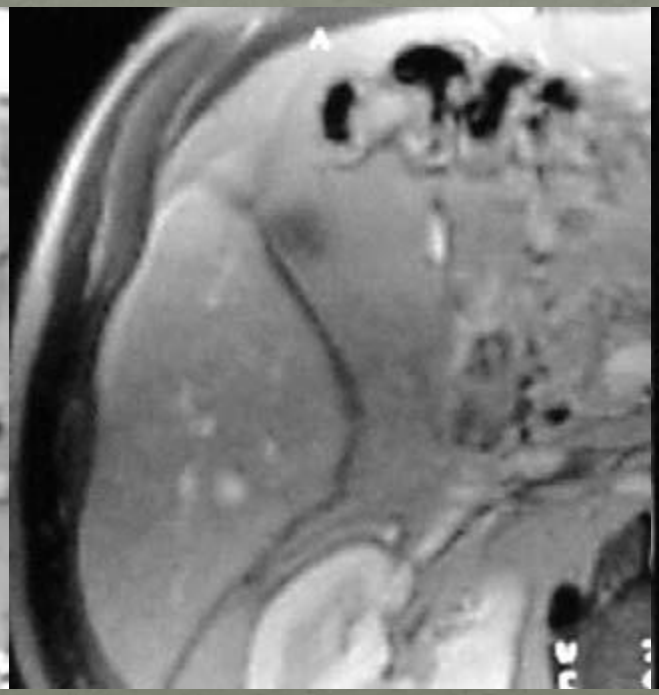


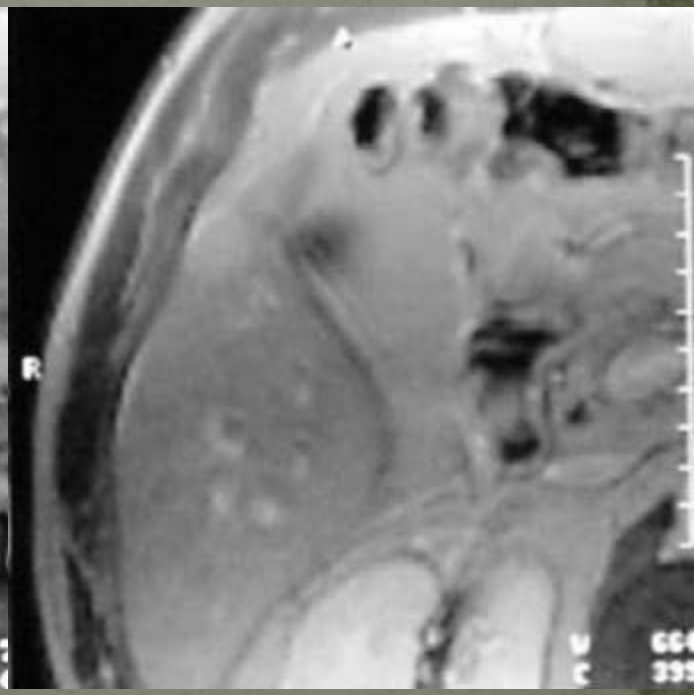
- On unenhanced T1-weighted MR images the lesions are generally almost isointense or slightly hyperintense compared to the surrounding liver parenchyma, while on unenhanced T2-weighted images the nodules appear iso- or slightly hypointense.
- On dynamic MR imaging, the nodules are usually hyperintense in the arterial phase, and iso- or slightly hyperintense in the portal-venous and equilibrium phases. In the delayed, liver-specific phase after Gd-BOPTA administration, the lesions may appear isointense or hyperintense since they consist of benign hepatocytes with abnormal biliary system drainage

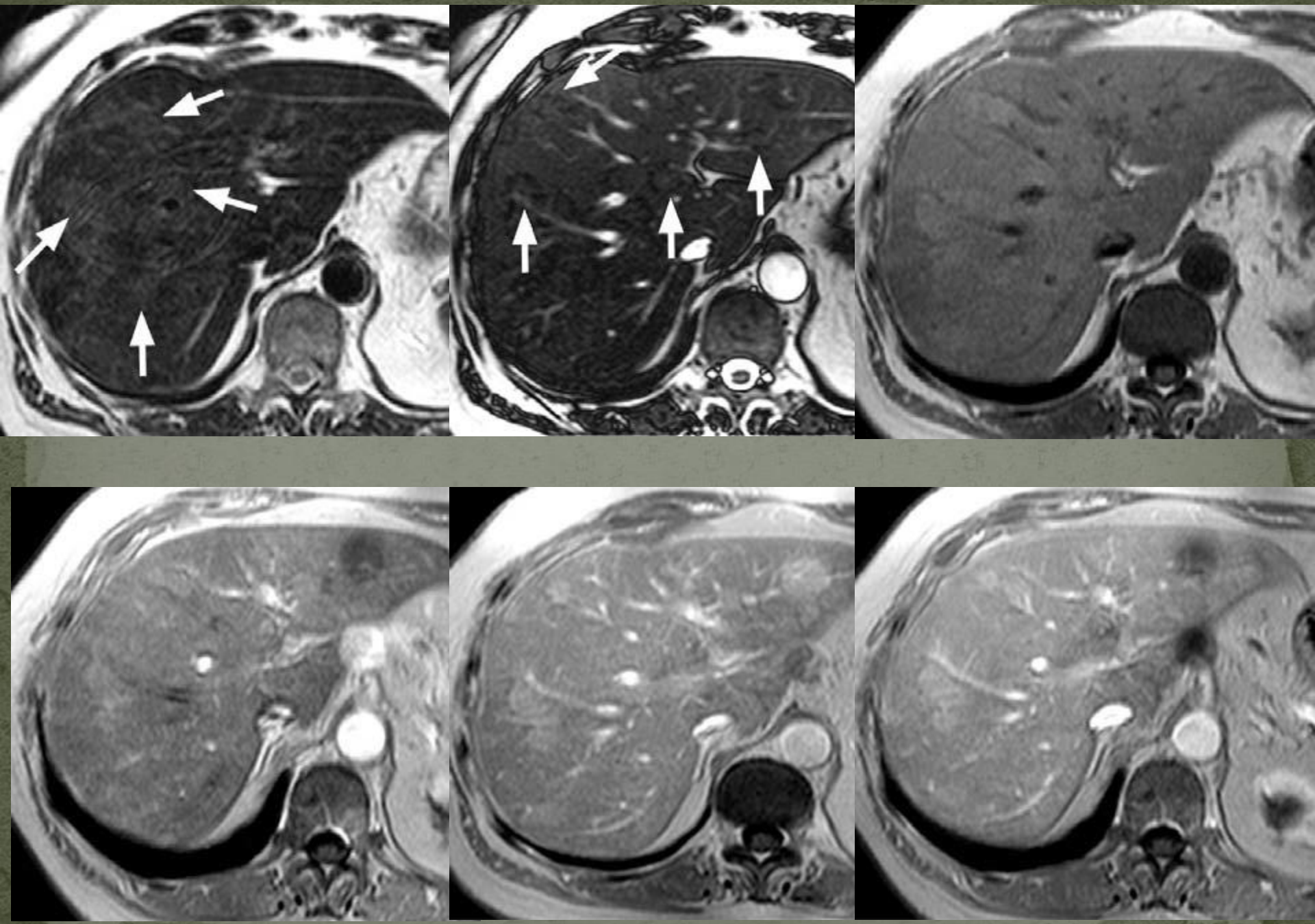












# Hepatic mesenchymal hamartoma

- Hepatic mesenchymal hamartoma (HMH) is a rare, benign tumor that occurs in pediatric patients
- often affecting children younger than 2 years
- HMH may present as a large, benign, cystic mass, as a solid mass, or as a mass with mixed cystic and solid components