Imaging features of benign hepatic lesions at US and CT imaging: a pictorial review.

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Learning objectives

- Describe and illustrate the use of US and CT imaging in the detection and characterization of focal benign tumors of the liver.

- List the differentiating clinical, radiologic and histopathologic findings in most frequent liver lesions.

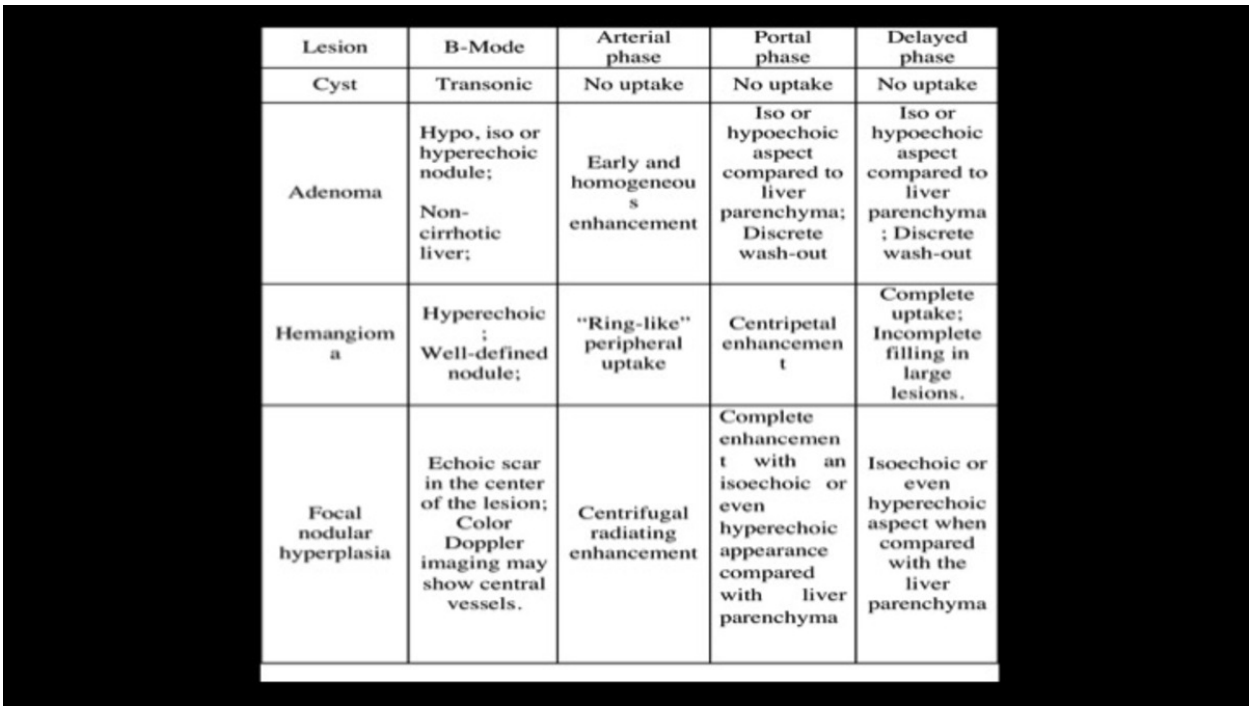
Background

Incidental focal lesions in the liver are frequently detected at routine abdominal ultrasonography (US) and their characterization continues to be a challenge because many may present with atypical imaging features. In addition, certain iatrogenically induced abnormalities of the liver may be confused with hepatic tumor or infection.

Often the sonographic findings are nonspecific and other imaging modalities such as US microbubble contrast and contrast enhanced computed tomography (CT) are helpful for characterization of these lesions. The development of US microbubble contrast has considerably improved the diagnostic accuracy and allows real-time evaluation of the microcirculation and macrocirculation of the hepatic lesions. The knowledge of the contrast-enhanced ultrasound (CEUS) enhancement patterns characterizing liver lesions (Fig. 1 on page 2) is crucial in the appropriate management of these patients.

In the majority of cases, familiarity with the most characteristic radiologic findings in combination with clinical information, provides useful information for adequate lesion characterization.

Images for this section:



Lesion	B-Mode	Arterial phase	Portal phase	Delayed phase
Cyst	Transonic	No uptake	No uptake	No uptake
Adenoma	Hypo, iso or hyperechoic nodule; Non-cirrhotic liver;	Early and homogeneous enhancement	Iso or hypoechoic aspect compared to liver parenchyma; Discrete wash-out	Iso or hypoechoic aspect compared to liver parenchyma ; Discrete wash-out
Hemangioma	Hyperechoic ; Well-defined nodule;	"Ring-like" peripheral uptake	Centripetal enhancement	Complete uptake; Incomplete filling in large lesions.
Focal nodular hyperplasia	Echoic scar in the center of the lesion; Color Doppler imaging may show central vessels.	Centrifugal radiating enhancement	Complete enhancement with an isoechoic or even hyperechoic appearance compared with liver parenchyma	Isoechoic or even hyperechoic aspect when compared with the liver parenchyma

Fig. 1: B-Mode scan and pattern of contrast enhancement at CEUS. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

Findings and procedure details

This review discusses the characteristic US, CEUS and CT imaging findings of the benign hepatic lesions, along with their most important clinical differential points and their histopathologic background.

BENIGN HEPATIC LESIONS

Adenoma

- Rare;
- The majority of adenomas are solitary (80%);
- Most common in female patients;
- May be asymptomatic or present with pain or shock in association with bleeding or tumor rupture;
- Histopathologic analysis: well-differentiated hepatocytes lacking bile ducts or portal triads. Kupffer cells are few or absent;
- They are arterialized and do not contain portal vessels.

There are four subtypes of hepatic adenoma:

- **Inflammatory hepatic adenoma:** most common, higher propensity for bleeding and rupture;
- **Beta catenin-mutated hepatic adenoma:** more common in men on anabolic steroids, glycogen storage disease, familial adenomatous polyposis.
- **HNF 1alpha mutated hepatic adenoma:** often multiple;
- **Unclassified hepatocellular adenoma.**

Predisposing factors to adenoma formation:

- Oral contraceptive use in female patients;
- Anabolic steroid use in male patients;
- Glycogen storage disease. Patients with type IA glycogen storage disease (von Gierke disease) often develop multiple hepatic adenomas beginning at a young age (Fig. 2 on page 13), and these may rarely degenerate into hepatocellular carcinoma.

The ultrasonographic (US) characteristics #of adenomas are nonspecific:

- Adenomas may#be hypo, iso or hyperechoic;

- They are typically heterogeneous with areas of fluid from intralesional hemorrhage.
- They are generally well encapsulated without lobulation of their contour and have variable degrees of hemorrhage, necrosis, fat, and rarely calcification. Calcifications may represent long term evolution of intralesional hemorrhage.

Contrast-enhanced ultrasound (CEUS):

- Early and homogeneous enhancement during the arterial phase, due to early draining feeding vessels, with centripetal or diffuse filling of the tumor, which is different from the centrifugal enhancement of FNH.
- The enhancement in the portal and delayed phases is usually isoechoic, due to the lack of a portal supply. The differential diagnosis of hepatic adenoma versus other benign lesions is mainly due to the lack of the portal supply, with mild progressive washout during the portal and delayed phase.
- The hemorrhagic regions do not show enhancement in any phase.

The CT characteristics #of adenomas are:

- At unenhanced CT, adenomas are typically hypo- to nearly isoattenuating relative to surrounding liver parenchyma, and depends on the fat content (hypoattenuating) and hemorrhage (hyperattenuating);
- On contrast administration they reveal relatively homogenous enhancement returning to near isodensity on portal venous and delayed phase.
- Absence of a peripheral rim of high attenua#tion on delayed phase images, as may be seen in hepatocellular carcinoma (HCC).

Occasionally adenomas have imaging features overlapping with those of HCC, especially in cases of well-differentiated tumors. In these doubtful cases other distinguishing characteristics of adenomas include negativity at serologic analysis, absence of an elevated fetoprotein level, and differences in the patient population, which tends to be younger and healthy in cases of hepatic adenomas.

Complications related to hepatic adenomas include the risk of spontaneous hemorrhage and progression to hepatocellular carcinoma (rare). Then, surgical resection is commonly advised.

Hepatic adenomatosis (Fig. 3 on page 14 Fig. 4 on page 15 Fig. 5 on page 16) is the presence of more than 10 hepatic adenomas, and occurs with similar frequency in male and female patients. Imaging characteristics of the individual adenomas are the same to those of a solitary lesion.

Focal nodular hyperplasia (FNH)

- Focal nodular hyperplasia (FNH) is the second most common benign tumor of the liver after hepatic hemangiomas.
- More common in young female patients;
- Usually asymptomatic;
- Typically occurs as a solitary lesion, but it can present with multiple liver lesions;
- Often lobulated and well circumscribed, although unencapsulated.
- Histopathologic analysis: FNH consists of aggregates of hepatocytes and is thought to be secondary to a proliferative response of non-neoplastic hepatocytes secondary to an underlying vascular malformation, and frequently associated with a central fibrous scar. Biliary structures proliferate without connection to the adjacent biliary tree. Kupffer cells are present in greater amounts than in the surrounding liver parenchyma.
- No malignant potential;
- FNH are usually treated conservatively.

- Approximately 20% of FNH cases are classified as nonclassic and may demonstrate atypical imaging features including lack of a central scar, intralesional fat and persistent enhancement on delayed phase images. FNH variants: **Telangiectatic FNH; FNH with cytologic atypia; Mixed hyperplastic and adenomatous FNH.**

The ultrasonographic characteristics #of FNH are nonspecific:

- FNH may range from iso to hypoechoic;
- The central scar may be identified as a linear hyperechoic structure;
- At US color Doppler imaging may show central vessels - "the spoke-wheel sign" which is pathognomonic of classical FNH.

At CEUS:

- FNH rapidly enhances during the arterial phase (Fig. 6 on page 17).
- Typical centrifugal radiating enhancement (in contrast to haemangioma and adenoma)
- FNH becomes isoechoic or even hyperechoic to the surrounding liver during the portal-venous and delayed phases.
- Unenhanced fibrous central scar is another typical feature of FNH.

At CT:

- FNH is typically hypo or isoattenuatung to surrounding normal parenchyma, but it may be hyperattenuating if the rest of the liver is fatty.

- There is typically quick homogeneous enhancement on arterial phase images, possibly with visualization of large feeding arteries and the scar remains relatively hypoattenuating. It is followed by early washout during the portal venous phase.
- FNH may be imperceptibly on delayed phase images when the central scar has filled.
- The presence of central scar is not pathognomonic of FNH and may be present in hemangiomas and fibrolamellar hepatocellular carcinoma.

Hemangioma

- Hemangiomas represent the most common primary liver tumor and consist of multiple large, blood-filled vascular channels of varying size.
- Typically, hemangiomas are solitary, although multiplicity is not uncommon.
- Hemangiomas are associated with several clinical syndromes including Klippel-Trenaunay-Weber syndrome, Osler-Rendu-Weber disease, and von Hippel-Lindau disease.

At US:

- Typical pattern: focal with distinct margins, homogeneous and echogenic lesions;
- However, this appearance is variable depending on the degree of fatty infiltration of the liver, which may result in a relatively hypoechoic appearance of the lesion. The US microbubble contrast may be useful in characterizing hepatic hemangiomas in cases with atypical features related to fatty infiltration of the liver.

At CEUS:

- Peripheral nodular enhancement in the arterial phase and complete or incomplete filling in portal-venous and late phases (Fig. 7 on page 18) This typical pattern of enhancement is more common in lesions > 2cm. In smaller lesions the filling is more rapid and appearing isoechoic in all vascular phases. This persistent isoechogenicity may also be present in other type of focal lesions, such as focal fatty infiltration.
- In larger hemangiomas often there is incomplete filling in portal and delayed phase, which has been attributed to central scarring.

At CT:

- Hemangiomas are typically hypoattenuating to liver parenchyma at unenhanced CT.
- Peripheral nodular enhancement with centripetal progression, resulting in diffuse high attenuation on delayed phase images.

- Flash filling of the entirety of a small hemangioma may be seen.
- Larger lesions may not demonstrate uniform enhancement on delayed phase images and central scars may be seen.

Hepatic Cyst

- Hepatic cysts are common and are almost always asymptomatic.
- May be single or multiple.
- Multiple hepatic cysts may be found in patients with Von Hippel-Lindau disease and polycystic liver disease, which is frequently associated with polycystic kidney disease.
- The simple hepatic cysts are thought to arise from precursor microhamartomas, lined by biliary epithelium, which enlarge over time and do not communicate with the biliary ducts;
- Histopathologic analysis: hepatic cysts are lined by a thin wall consisting of cuboidal epithelium, similar to that of bile ducts.

Ultrasonographic characteristics:

- Round or ovoid anechoic lesion, well-marginated and with posterior acoustic enhancement.
- Fine partial or complete septa are often visualized.
- Complications such as hemorrhage or infection may result in debris, thickened septa, and complex internal fluid.

At CEUS:

- Hepatic cysts (simple or hemorrhagic) have a characteristic appearance of clearly defined perfusion defects throughout all phases (Fig. 15 on page 23).

At CT:

- A hepatic cyst appears as a homogeneous and hypoattenuating (water attenuation) lesion on nonenhanced CT scans, with no enhancement of its wall or content after intravenous administration of contrast material.

Biliary Hamartomas

- Also referred as von Meyenburg complexes;
- Represent failure of involution of embryonic bile ducts.
- May occur as either isolated or multiple lesions and can mimic metastases.

Ultrasonographic characteristics:

- Biliary hamartomas are usually too small to be seen with US, however, small echogenic cystic lesions with comet-tail echoes may be seen.

CT:

- Typically reveals multiple, widely scattered, small (2-15 mm), low-attenuation lesions;
- The majority of which do not demonstrate enhancement, although mural nodular enhancement may be seen.

Peribiliary Cyst

- Peribiliary cysts represent cystic dilatation of glands in the bile duct walls and typically are more prominent within the hepatic hilum and in the larger portal tract.
- Associated with cirrhosis and portal hypertension.
- Rarey focal biliary obstruction secondary to larger cysts may occur.
- Histopathologic analysis: dilatations of extramural peribiliary gland.

Ultrasonographic characteristics:

- Rounded or tubular anechoic structures are seen along the portal tracts, findings that may be mistaken for dilated bile ducts.

At CT:

- Hypoattenuating cystic structures along the larger portal veins as a linear cluster, resembling a string of beads.

Caroli Disease

- Caroli disease is secondary to the failure of the embryologic remodeling of bile ducts and is among the ductal plate malformations.
- Rare autosomal recessive disorder;
- No gender predilection.
- Saccular dilatation of the larger intrahepatic bile ducts (Fig. 10 on page 20)
- Typically the intrahepatic ductal dilatation is segmental and more often saccular than fusiform. Commonly, alternating areas of stricture and dilatation are seen.

- If the malformation involves the entire intrahepatic biliary tree Caroli's syndrome (a combination of Caroli's disease and congenital hepatic fibrosis) develops.
- Caroli disease is associated with biliary stasis and stones, and recurrent cholangitis and hepatic abscesses.
- Patients with Caroli disease are at risk of cholangiocarcinoma.

US:

- Saccular dilatation of the intrahepatic bile ducts;
- Intraductal calculi.

CT:

- Saccular or fusiform biliary dilatation with attenuation similar to that of water.
- A well-known imaging feature at contrast-enhanced CT is the so-called "central dot sign", which represents enhancing fibrovascular bundles within the dilated bile ducts (Fig. 11 on page 20)

Focal Fatty infiltration and focal fatty sparing

- Focal fatty infiltration and focal fatty sparing may pose a diagnostic dilemma at imaging and may be mistaken for an infiltrative neoplasm or can simulate metastatic disease.
- Focal fatty infiltration is not seen to produce mass effect on adjacent structures and vessels are seen to pass through these areas freely.
- Typically distribution of the lesions:
- The medial aspect of the left lobe;
- Along the falciform ligament;
- The gallbladder fossa;
- The central aspect of segment IV, adjacent to the porta hepatis.

At US:

- Focal fatty deposit may be seen as #a focal, well-circumscribed, hyperechoic area (Fig. 12 on page 21) In other hand, focal fatty sparing appears hypoechoic relative to surrounding fatty infiltration (Fig. 13 on page 22).

At CEUS:

- These lesions show no difference in vascularity from the parenchyma.

At CT:

- Steatosis may be seen as focal areas of relative low attenuation.

- Areas of fatty sparing appear hyperattenuating relative to surrounding steatosis.

Lipoma

- Extremely uncommon;
- Asymptomatic;
- Typically range from 1-5 cm in diameter.

At US:

- Well-circumscribed, uniformly hyperechoic lesions and may be mistaken for a hemangioma.
- May or may not show acoustic shadowing.

At CT:

- Rounded lesion with low attenuation (Fig. 14 on page 22) corresponding to fat (-10 to -100 HU) and do not enhance after contrast material administration.

Inflammatory Lesions

Abscess

- Can be classified as pyogenic, amebic, or fungal.
- Pyogenic hepatic abscesses are most often caused by *Clostridium* species and gram-negative bacteria (*Escherichia coli* and *Bacteroides*). Ascending cholangitis and portal phlebitis are the most frequent causes of pyogenic hepatic abscesses.
- An amebic abscess results from infection with the Entamoeba histolytica and is the most commonly encountered hepatic abscess in the world.
- Fungal abscesses are most commonly caused by Candida albicans.

AT US:

- Poorly demarcated ranging from hypoechoic with some internal echoes to hyperechoic lesions.

At CEUS:

- Contrast enhanced ultrasound shows wall enhancement during arterial phase and progressive washout during portal and delayed phases.
- The necrotic area does not enhance.

At CT:

- Abscesses usually appear as thick-walled lesions with homogeneous low attenuation (necrosis and liquefaction).
- Occasionally they contain gas.
- Contrast-enhanced CT scan shows enhancing abscess wall and typically shows increased peripheral rim enhancement, which is secondary to increased capillary permeability in the surrounding liver parenchyma ("double target" sign) (Fig. 16 on page 24)

Intrahepatic Hydatid Cyst

- Hepatic echinococcosis - ingestion of eggs of the tapeworm *Echinococcus granulosus.*
- Liver filters most of these embryos but those that are not destroyed then become hepatic hydatid cysts.
- Typically it has a large cyst within which numerous peripheral daughter cysts are present.
- Peripheral calcifications are common in viable or nonviable cysts (Fig. 8 on page 19, Fig. 9 on page 18)

At US:

- US is the most sensitive modality for the detection of membranes, septa, and hydatid sand within the cyst.
- The cyst wall usually manifests as double echogenic lines separated by a hypoechogenic layer.
- Hydatid cysts may demonstrate multiple echogenic foci due to hydatid sand within the lesion and fall to the most dependent portion of the cavity "the snowstorm sign".
- The cyst may appear as a well-defined fluid collection with a localized split in the wall and "floating membranes" inside the cavity. Membranes may appear within the matrix as serpentine linear structures.
- Daughter cysts appear as cysts within a cyst.
- When the cyst wall is calcified US demonstrates a hyperechoic contour with a posterior acoustic shadow.

At CT:

- Well-defined hypoattenuating lesion (3-30 HU) with a distinguishable wall.
- Separation of the laminated membrane from the pericyst can be visualized as linear areas of increased attenuation within the cyst (Fig. 9 on page 18)
- Peripheral focal areas of calcification and daughter cysts are often identified.

Effects of Percutaneous Intervention

In patients who undergo radiofrequency ablation to treat malignant hepatic tumors, nonenhancing postprocedure areas of relative low attenuation are typically identified. The lack of enhancement is useful in differentiating these postprocedure areas from true hepatic mass lesions. Efficacy of the ablation is evaluated by the absence of contrast enhancement (complete necrosis)(Fig. 17 on page 24) .

At CEUS:

- Appear as dark defects whereas the enhancement persists in the normal liver parenchyma.

At CT:

- Focal, well circumscribed area of low attenuation without enhancement.
- The development of peripheral nodular enhancement is suggestive of tumor recurrence.

Images for this section:

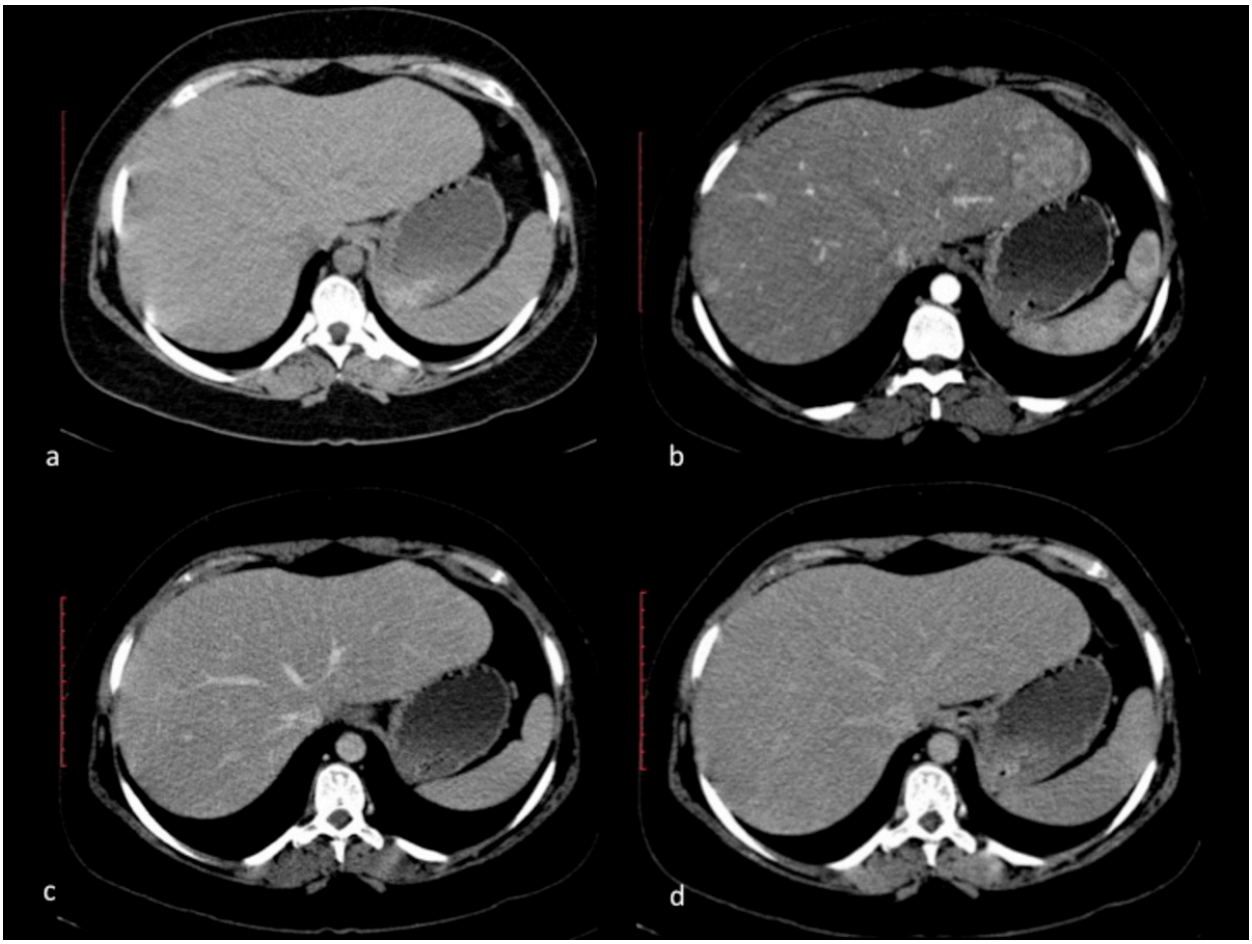


Fig. 2: Axial precontrast and contrast-enhanced CT scan of the abdomen shows hepatic adenomas in a patient with type IA glycogen storage disease (von Gierke disease). Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

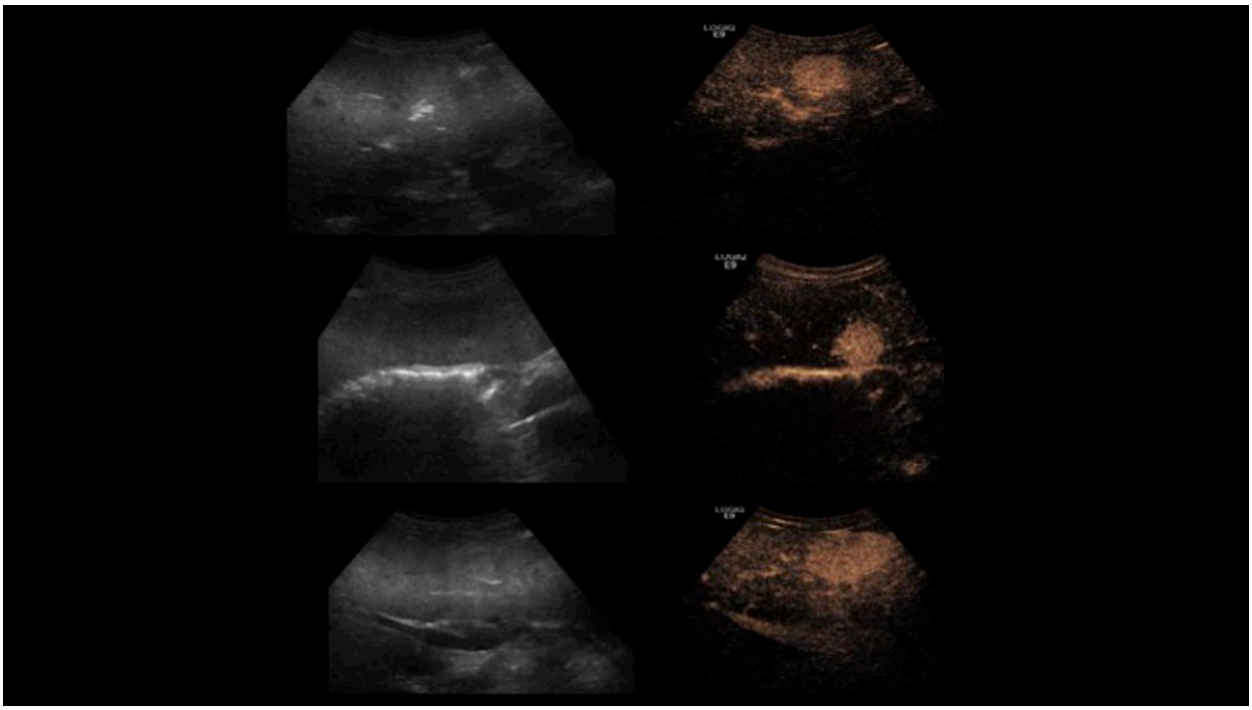


Fig. 3: Hepatic adenomatosis. Early and homogeneous enhancement during the arterial phase (both images), due to early draining feeding vessels, with centripetal or diffuse filling of the lesion. The enhancement in the portal and delayed phases is usually isoechoic, due to the lack of a portal supply. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

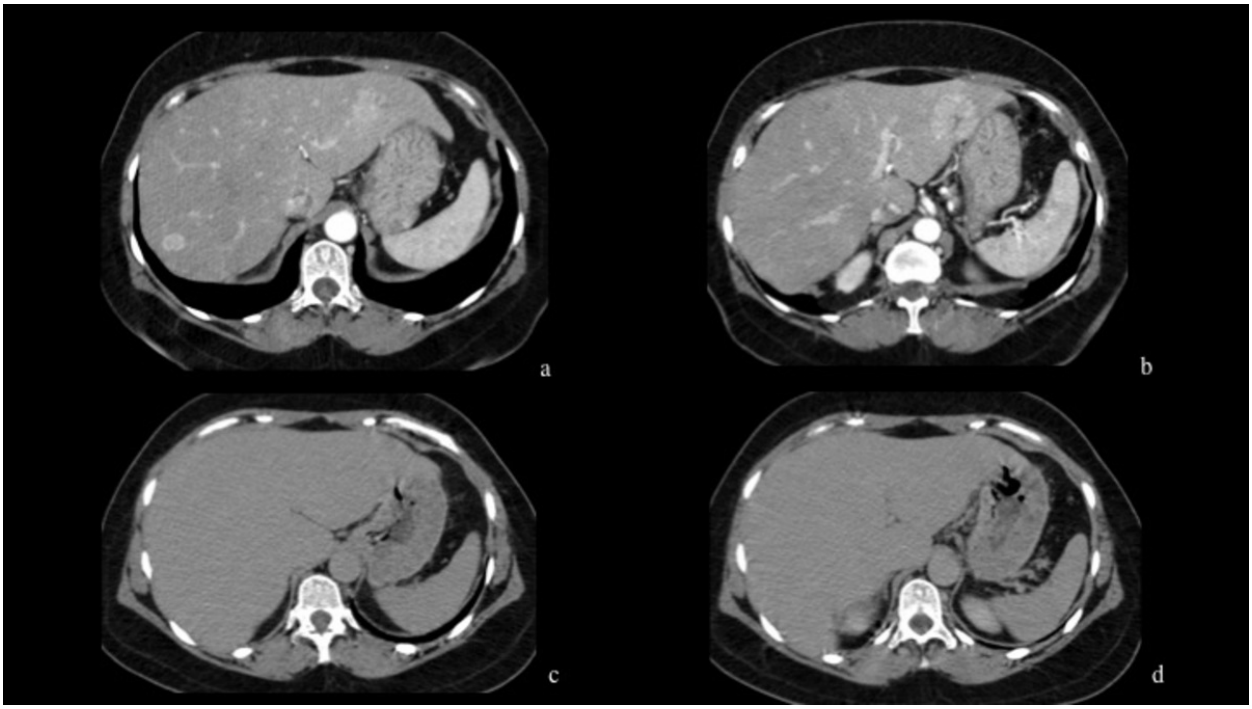


Fig. 4: Hepatic adenomatosis. CT scan shows some hepatic nodular lesions, they reveal relatively homogenous enhancement (a, b) returning to near isodensity on portal venous and delayed phase (c, d) .

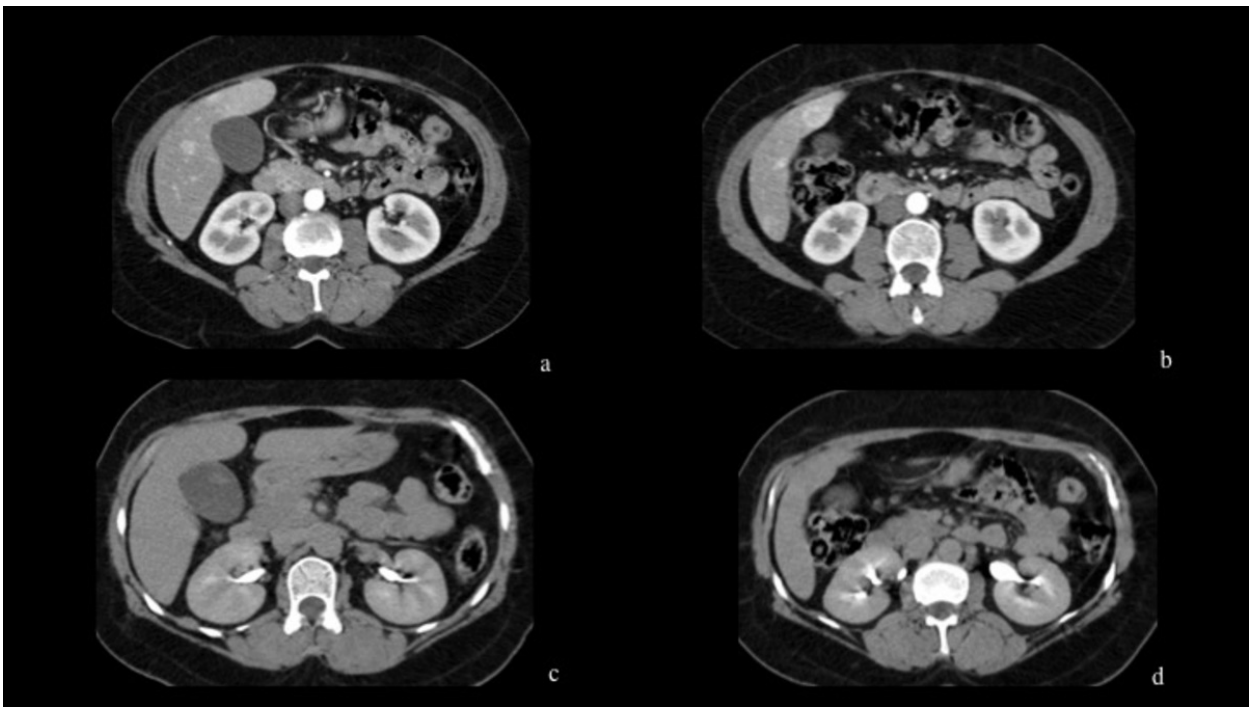


Fig. 5: Hepatic adenomatosis. CT scan shows some hepatic nodular lesions, they reveal relatively homogenous enhancement (a, b) returning to near isodensity on portal venous and delayed phase (c, d). Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

Lesion	B-Mode	Arterial phase	Portal phase	Delayed phase
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Hemangioma	Hyperechoic ; Well-defined nodule;	"Ring-like" peripheral uptake	Centripetal enhancement	Complete uptake; Incomplete filling in large lesions.
Focal nodular hyperplasia	Echoic scar in the center of the lesion; Color Doppler imaging may show central vessels.	Centrifugal radiating enhancement	Complete enhancement with an isoechoic or even hyperechoic appearance compared with liver parenchyma	Isoechoic or even hyperechoic aspect when compared with the liver parenchyma

Fig. 1: B-Mode scan and pattern of contrast enhancement at CEUS. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

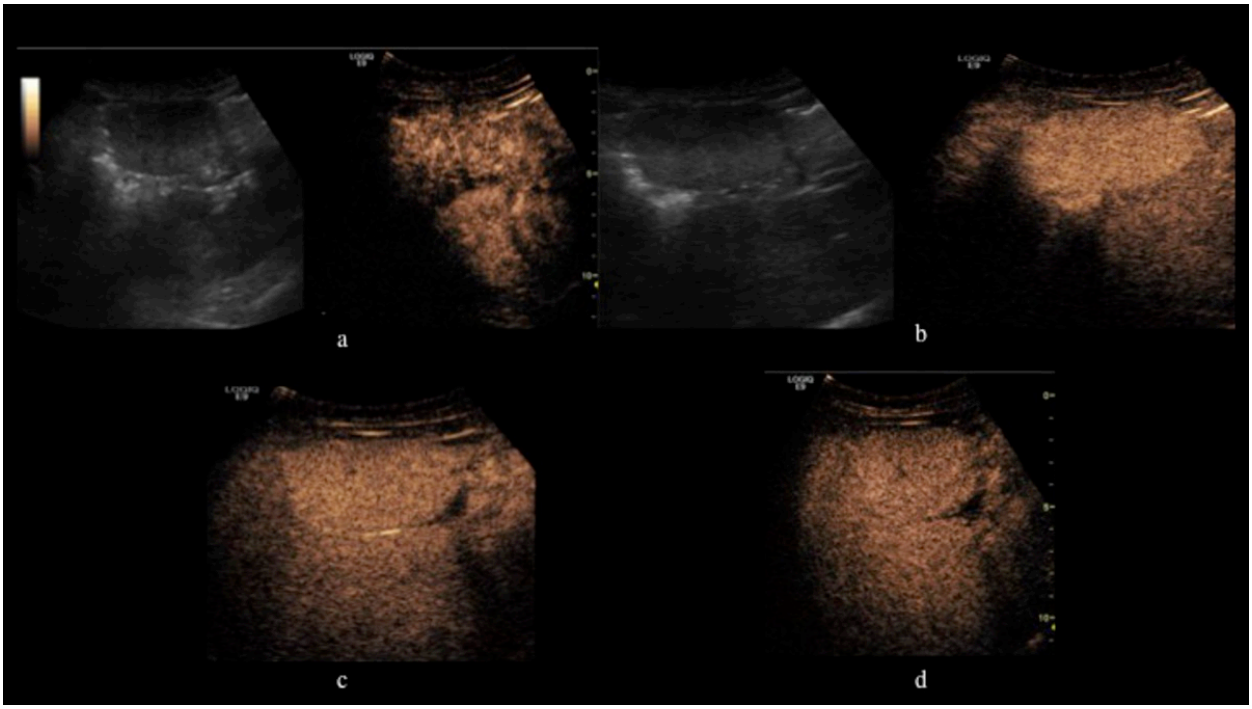

Fig. 6: Focal nodular hyperplasia. In arterial phase (a) shows a typical centrifugal radiating enhancement, complete enhancement with a hyperechoic appearance

compared with liver parenchyma in portal (b and c) and isoechoic in delayed phase (d). Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

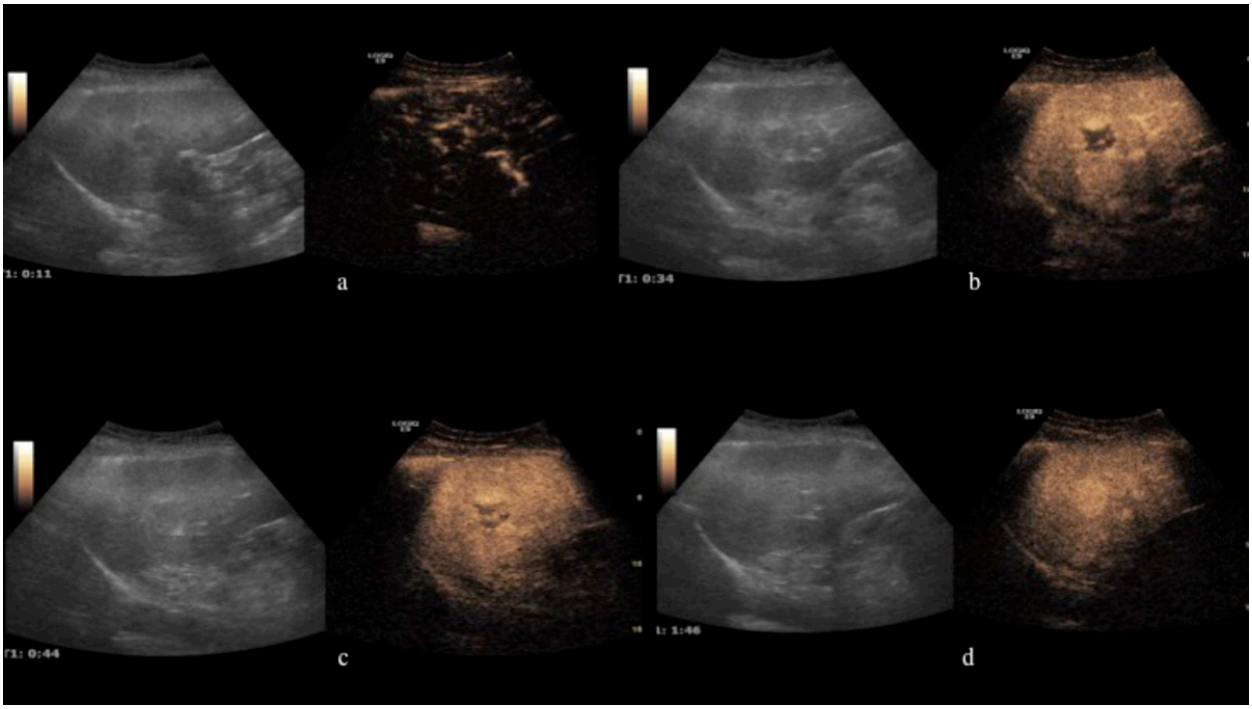

Fig. 7: Hemangioma. In arterial phase (a) shows a typical peripheral nodular enhancement, centripetal enhancement in portal phase (b, c) and complete filling in delayed phase (d). Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

Fig. 9: Intrahepatic hydatid cyst. CT scan shows a well-defined hypoattenuating lesion with a peripheral coarse area of calcification and septation. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

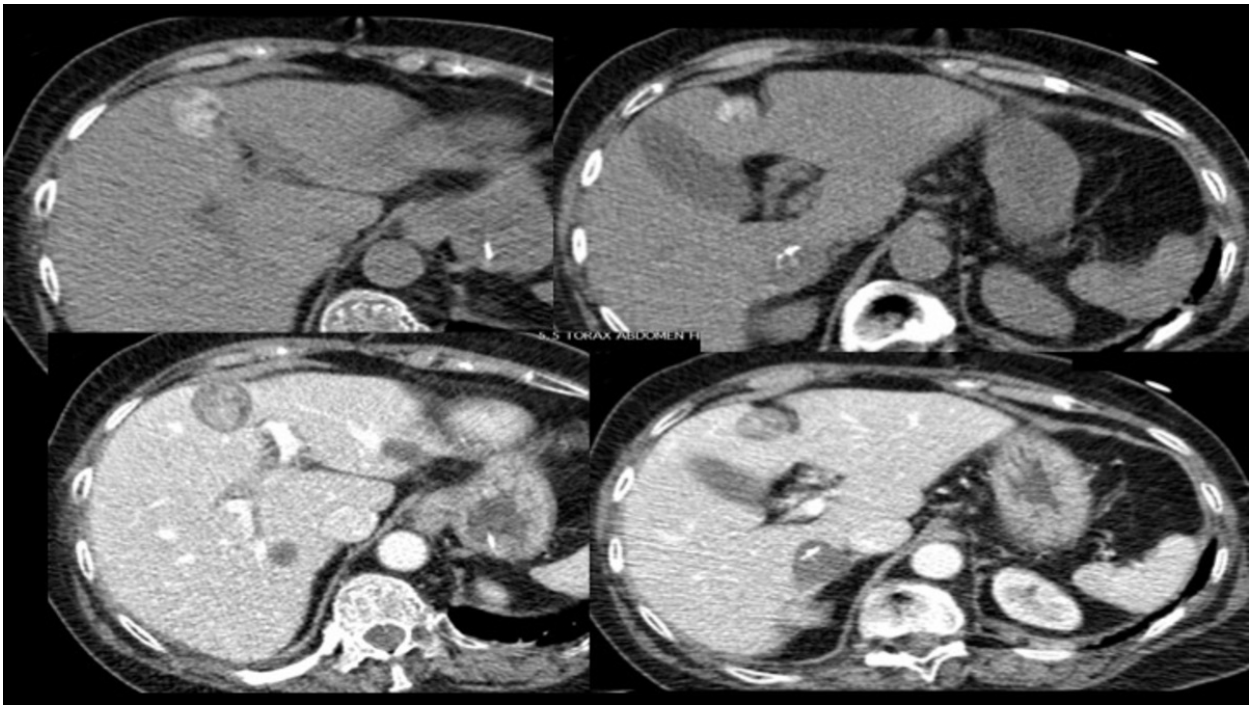

Fig. 8: Intrahepatic hydatid cyst. CT scan shows two well-defined hypoattenuating lesions, both with a coarse area of calcification. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

Fig. 10: D. Caroli. Axial contrast-enhanced CT image shows segmental saccular dilatation of intra-hepatic bile ducts. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

Fig. 11: D. Caroli. Axial contrast-enhanced CT image shows segmental saccular dilatation of intra-hepatic bile ducts. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

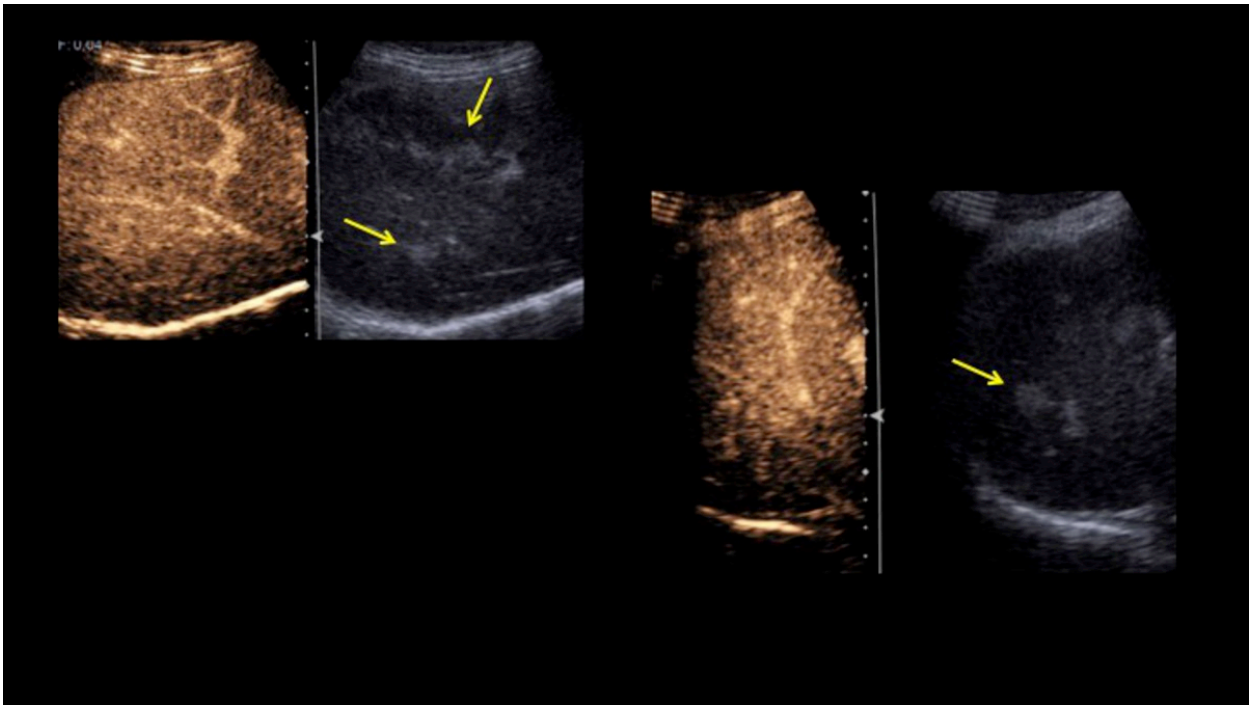

Fig. 12: Focal hepatic steatosis. US scan of the liver shows a multiple hyperechoic focus a finding consistent with focal fat. At CEUS these lesions show no difference in vascularity from the parenchyma. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

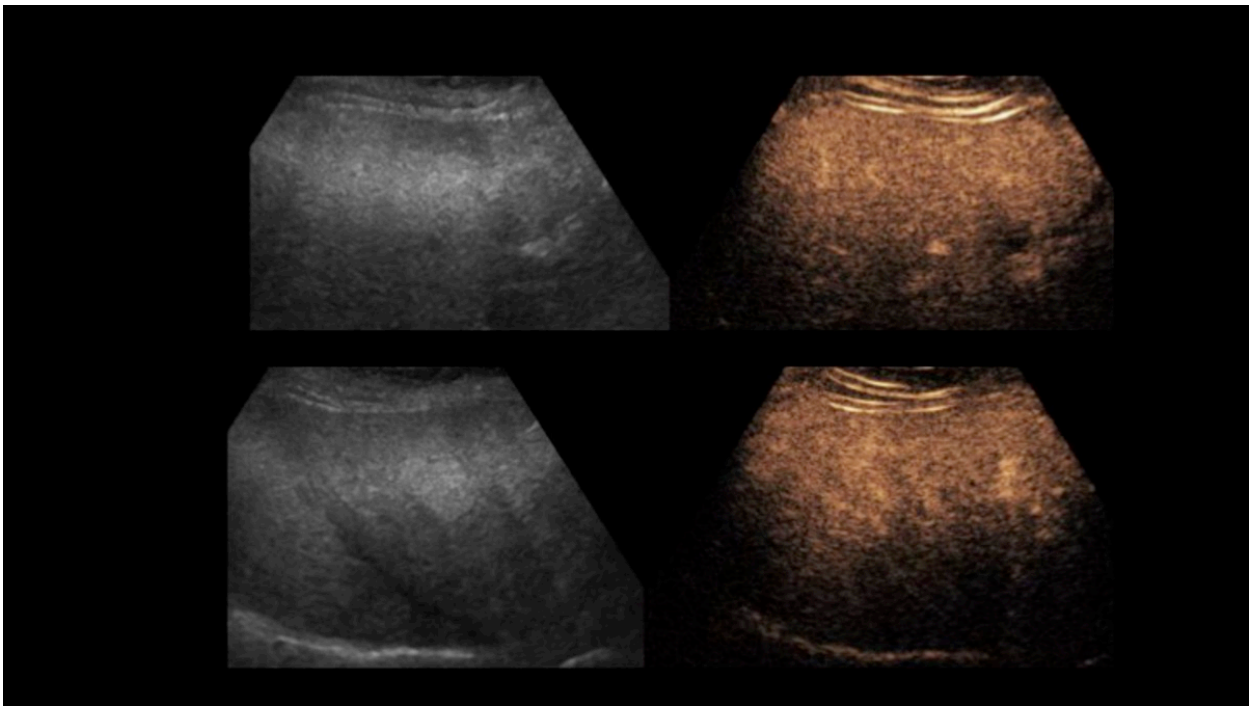

Fig. 13: Focal fatty sparing. US scan of the liver shows a hypoechoic lesion a finding consistent with focal fatty sparing. At CEUS shows no difference in vascularity from the parenchyma. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

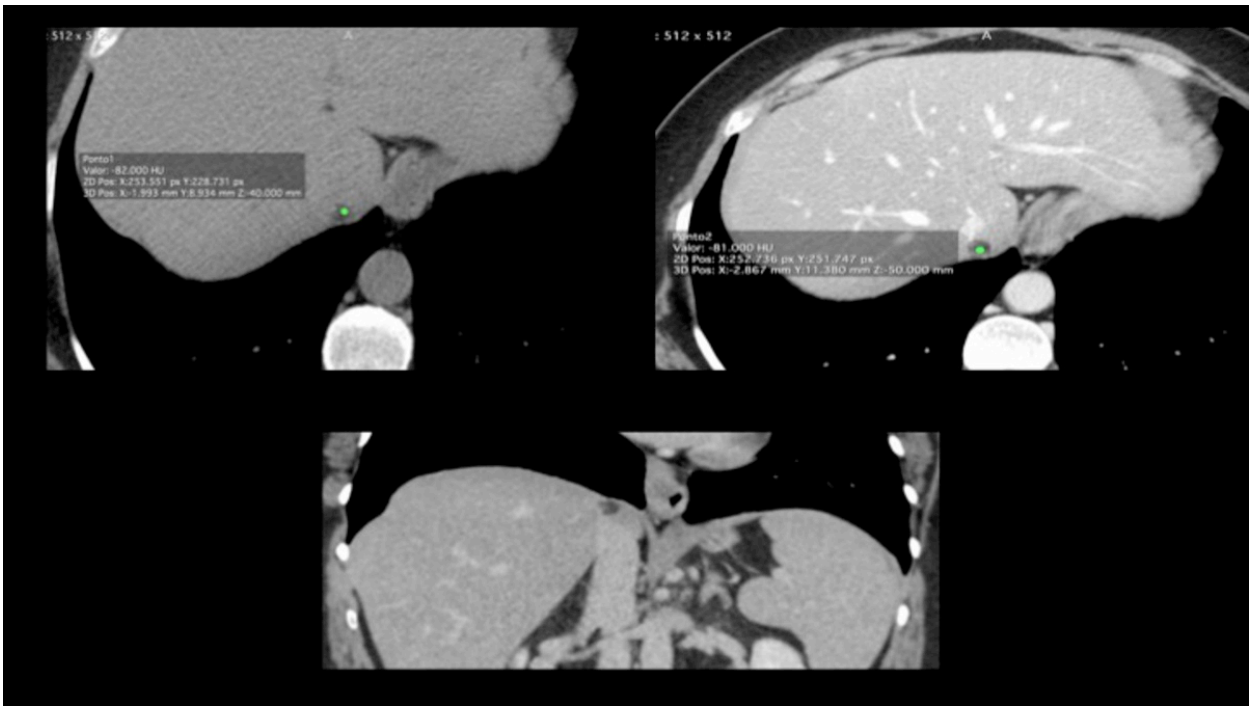

Fig. 14: Hepatic lipoma. CT scan reveals a small lesion with attenuation corresponding to fat (-82 HU) and do not enhance after contrast administration. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

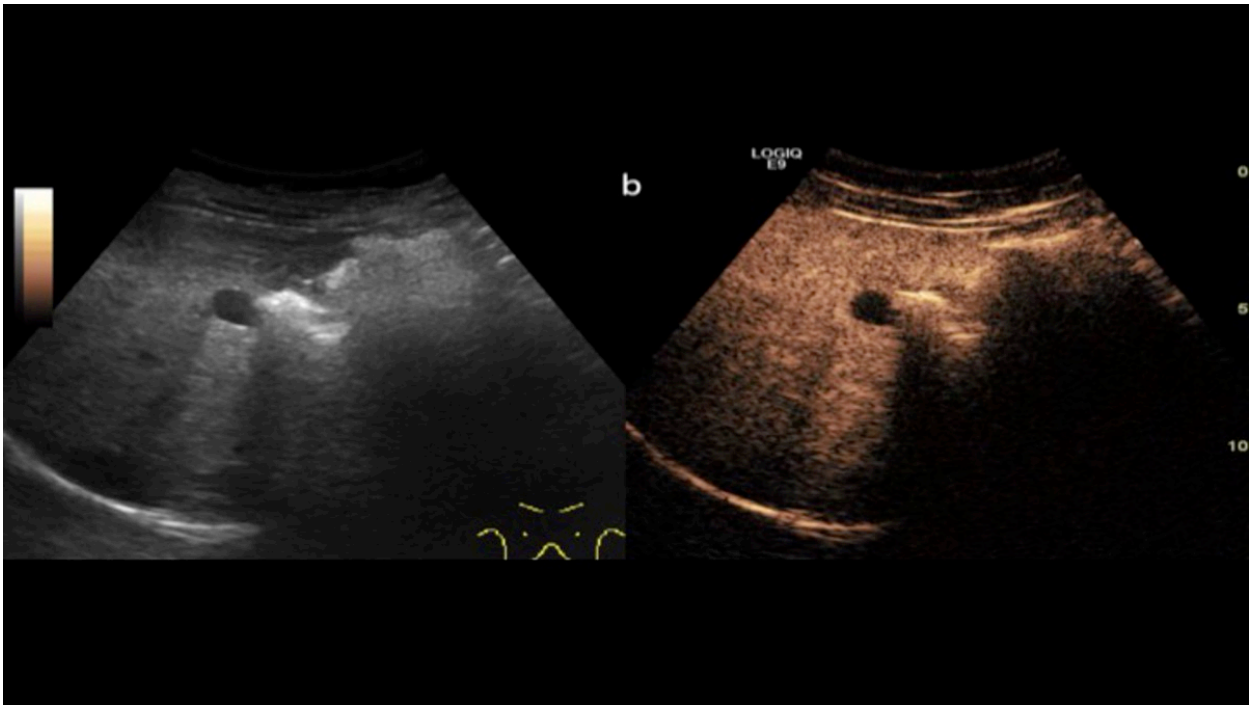

Fig. 15: B-mode US and CEUS shows simple cyst as a avascular lesion with posterior acoustic enhancement. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

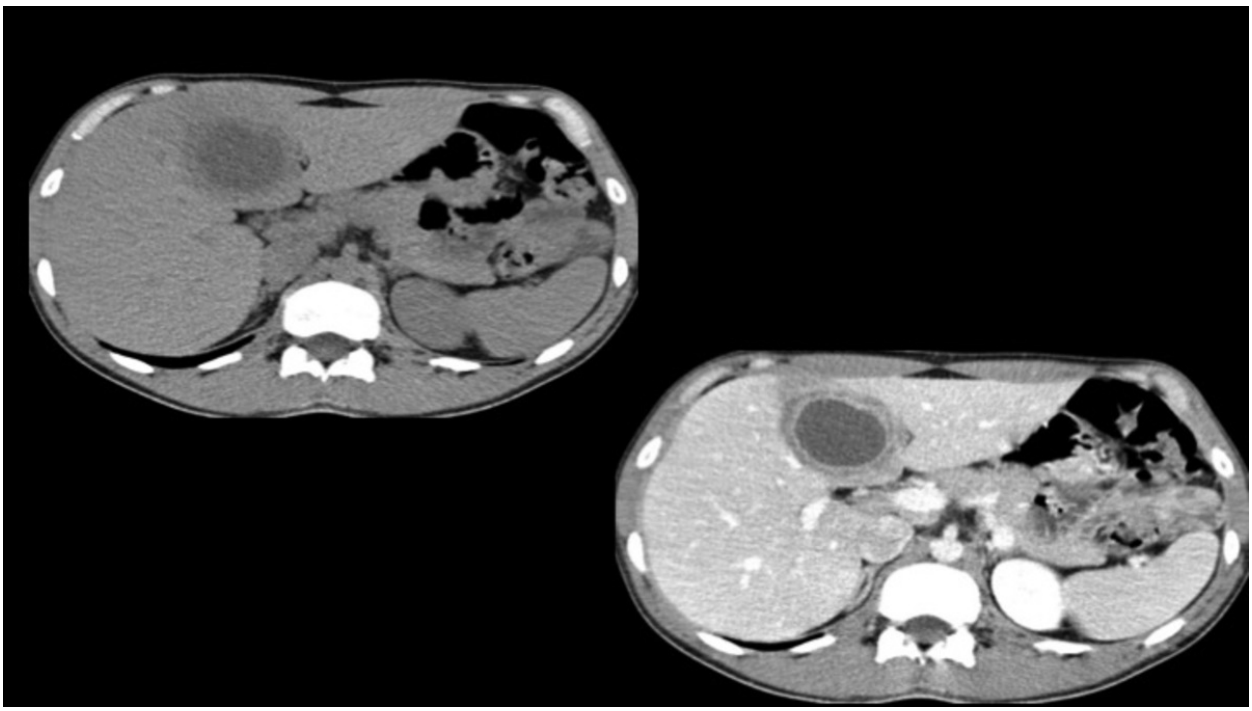

Fig. 16: Amebic abscess. Contrast-enhanced CT scan shows a thick-walled cystic lesion with low attenuation center and peripheral enhancement. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

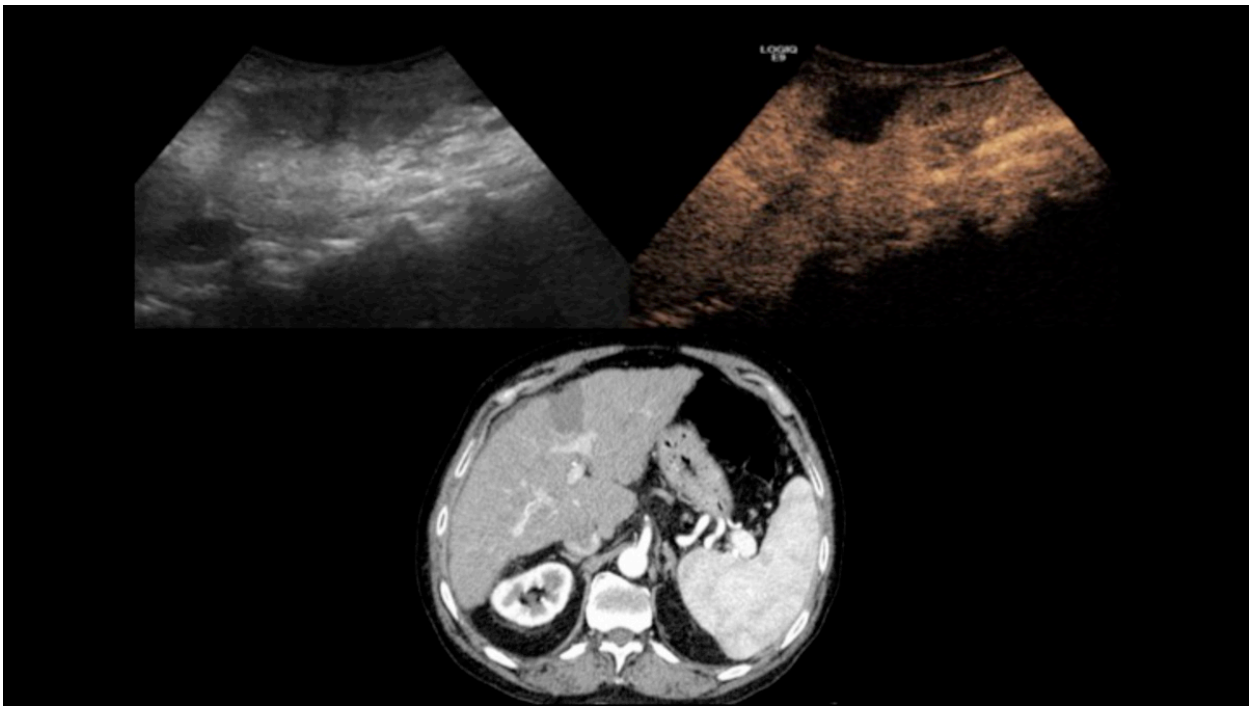

Fig. 17: Efficacy of the ablation is evaluated by the absence of contrast enhancement (complete necrosis) and appear at CEUS as dark defects whereas the enhancement persists in the normal liver parenchyma. Axial contrast-enhanced CT image shows a focal area of low attenuation. Without clinical history, this finding may be mistaken for a focal mass lesion or a hepatic collection. Serviço de Imagem Médica, Centro Hospitalar e Universitário de Coimbra, Coimbra/PT

Conclusion

There are several benign hepatic lesions, however, the majority are rarely encountered in clinical practice. The vast majority of the benign hepatic tumors can be diagnosed with ultrasound and CT imaging. Even when a specific diagnosis cannot be provided, the benign nature of the tumor can be confidently suggested, avoiding more aggressive diagnostic approaches such as biopsy or surgical excision.

Radiologists should be familiarized the classic US, CEUS and CT imaging appearances of focal liver lesions to help to ensure a presumptive diagnosis and shorten the diagnostic workup. However, atypical appearances of common liver lesions may pose a diagnostic challenge and access to clinical information, such as age, gender and symptoms remains extremely important.

Personal information

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