INTRODUCTION

The liver is the largest organ in the abdomen, weighing about 1800 g in men and slightly less in women. Classically, the liver is divided into right and left lobes by the falciform ligament. The liver lies in the right upper quadrant of the abdomen, suspended from the right hemidiaphragm. Functionally, it can be divided into three lobes—right, left, and caudate lobes.

A space occupying lesion by definition is a discrete abnormality arising within the liver. Space occupying lesions of the liver can be classified into developmental, neoplastic, inflammatory and miscellaneous. Although in some cases, it is difficult to distinguish these entities with imaging criteria alone, certain focal liver lesions have classic ultrasonic, computed tomographic (CT) and magnetic resonance (MR) imaging features.

GOALS OF IMAGING

The main goals of imaging are to assess:
1. The number and size of the liver abnormalities
2. The location of abnormalities relative to the liver vessels
3. The nature of the lesions (benign versus malignant)
4. The origin (primary versus secondary) of abnormalities
5. The liver parenchyma surrounding the lesions.

It is important to emphasize that primary objective in imaging the liver is to distinguish benign from metastatic and primary malignant lesion.

Currently, there is no consensus concerning the optimal strategy for imaging the liver for focal liver disease.

Imaging modalities are often used based on the requests of referring physicians and the availability of equipment and experience of the radiologists. Most centers use ultrasound (US), computed tomography (CT), and US-guided biopsy. MR imaging is often used as a problem-solving modality. In addition, other modalities, such as CT arteriopertography (CTAP), CT hepatic arteriography (CTHA), PET, and laparoscopy with or without intraoperative US, are also used depending on the availability and experience of the clinicians and radiologists.

US is widely available, and many clinicians request US as the initial imaging modality for the assessment of the upper abdomen including the liver to narrow down the differential diagnosis in a relatively quick and cost-effective manner. The initial US, may be followed by an US-guided biopsy, CT or MR imaging.

IMAGING TECHNIQUE

The practice for liver imaging has undergone a significant change over the past two decades. The primary radiological evaluation of the liver using nuclear scintigraphy and angiography has given way to multidetector computed tomography (CT), ultrasonography, and magnetic resonance imaging (MRI).

Ultrasonography

Ultrasonography is a relatively inexpensive and noninvasive method of evaluating the upper abdomen. It is especially useful in evaluating for the presence of bile duct obstruction and the presence or absence of gallstones. Ultrasonography
Technique:
Abdominal ultrasound (US) is mainly performed with phased array transducers operating between 3-5 MHz. Doppler capability, both spectral and colour, is an integral part of the examination of the liver, allowing demonstration of hepatic blood flow and unequivocal identification of the bile ducts.

Computed Tomography
The development of multidetector row CT (MDCT) technology has helped CT to continue to excel in its already established indication i.e., hepatic lesion detection and characterization and to add new clinical indication i.e., CT angiography for preprocedure mapping and liver perfusion. With MDCT there is faster scanning. In liver imaging faster scanning decreases respiration artifacts and improves multiphase imaging.

Multiphasic CT Liver protocol on 128 slice CT Scanner:
For multiphasic hepatic imaging in our hospital, nonionic contrast material is administered at a rate of 4 mL/sec for 20 seconds. The scans are acquired prior to contrast administration (Non-Contrast scans), one each during the early arterial phase (15 seconds after injection of contrast medium), Late arterial phase (25 seconds after the initiation of injection), and hepatic venous phase (60 seconds after the start of injection). In some cases delayed scanning is also done after 3 to 5 minutes of contrast administration.

Perfusion Imaging
Perfusion is the process of nutritive delivery of arterial blood to a capillary bed in the biological tissue. Perfusion imaging provides the ability to detect regional and global alterations in organ blood flow. Perfusion imaging helps in non-invasive assessment of tumor grade depending upon its vascularity. It helps in biopsy planning and in evaluation of response to treatment. It also helps to differentiate between post treatment changes and residual tumor. Primary goal of perfusion imaging is resolution of arterial and portal venous components of hepatic blood flow on a global and regional basis. As normal liver receives majority of blood supply from portal vein, in primary and metastatic hepatic malignancies and cirrhosis, there is relative increase in hepatic arterial blood flow which can be demonstrated by perfusion imaging. This new field of liver imaging may have profound implications for the diagnosis and surveillance of liver diseases in the future.

CT protocol of perfusion imaging:
Perfusing imaging of liver in our hospital is performed by acquiring a non contrast scan of upper abdomen to localize the area of interest. Hepatic perfusion CT for the entire liver volume (maximum span 14.2cm) is then performed using a dedicated perfusion protocol combining a multiphasic CT acquisition with simultaneous intravenous injection of contrast. Fifty ml of low osmolar nonionic contrast is injected at the rate of 5ml/s followed by 30 ml of saline chase using a dual head pressure injector. Nineteen phase dynamic CT acquisition of the entire liver volume is done at same time at 80 mAS, collimation 128x.6 mm; rotation time .3 s lasting for approximately 40 sec, during quite respiration.

For the quantification of hepatic perfusion and for the generation of blood-flow maps, the 19 phase perfusion CT images were loaded on to separate workstation with dedicated hepatic CT perfusion software. The parameters evaluated are blood flow (ml/100ml/min), blood volume (ml/100ml), time to peak (sec), permeability (ml/100ml/min), arterial liver perfusion (ml/100ml/min), portal venous perfusion (ml/100ml/min) and hepatic perfusion index (%). These parameters are used to assess and characterize the space occupying lesions of liver.

MR Imaging
MRI has a wider range of contrast mechanisms than other imaging techniques. Although primarily used for lesion detection and characterization, the biliary system anatomy and hepatic vascular patency can also be assessed during the same examination. A wide range of protocols is available due to the numerous combinations of field strength, pulse sequence implementation and interdependent sequence parameters, all of which can influence image quality. Comprehensive liver imaging using MRI now includes breath-hold T2- and T1-weighted (T2w and T1w) imaging, including in- and out-of-phase sequences for fat detection. Higher quality T2W imaging is obtained with respiratory-triggered multi-shot RARE sequences and pre- and post-gadolinium multiphase imaging similar to CT using rapid breath-hold T1w volume imaging.11

Intravenous MR Contrast agents:
The major classes of contrast agents currently used for magnetic resonance (MR) imaging of the liver include extracellular agents (eg, low molecular-weight gadolinium chelates), reticuloendothelial agents (eg, ferumoxides, SPIO), hepatobiliary agents (eg, mangafodipir), blood pool
agents (ultrasmal SPIO), and combined agents (Gadobenate dimeglumine). Mechanisms of action, dosage, elimination, toxic effects, indications for use, and MR imaging technical considerations vary according to class. Gadolinium chelates are the most widely used. Ferumoxides are a useful adjunct for detection of hepatocellular carcinoma, particularly when used in combination with gadolinium to achieve improved lesion-to-liver contrast over that achievable with gadolinium alone. Magnevist is a prototype hepatobiliary agent that is taken up by lesions with functioning hepatocytes. It may be used for MR cholangiography as well as liver imaging. Blood pool agents such as ultrasmall SPIO particles are currently undergoing investigation for potential use in angiography. Gadobenate dimeglumine, a combined MR contrast agent exhibits a spectrum of characteristics with potential applications in angiographic and tumor imaging.

IMAGING CHARACTERS OF VARIOUS SPACE OCCUPYING LESIONS

Benign Lesions

**Hepatic cyst:**

Hepatic cysts are amongst the most common space occupying lesion of the liver. Hepatic cysts are developmental benign lesions in the liver that do not communicate with the biliary tree. On USG simple cysts appear as defined echo-free lesions with almost imperceptible walls and enhanced through transmission. Thin septations can be present. The presence of internal echoes, debris, thick septations, mural calcification or nodules suggests an alternative diagnosis or a complicated cyst. On CT it appears as a well defined intrahepatic lesion having water attenuation (0-15 HU). It is round or oval in shape with smooth thin walls and homogeneous appearance. (Fig.1)

There are no internal structures and no enhancement after contrast administration. MRI shows hepatic cysts as homogeneous, sharply margined masses hypointense on T1 and markedly hyperintense on T2-images. No enhancement is seen after administration of gadolinium chelates. An increase in signal intensity is seen on heavily T2-weighted images. This allows differentiation of these lesions from metastatic disease. When more than 10 cysts are present, a polycystic disease should be considered.

**Hemangioma:**

Hemangiomas are small, asymptomatic lesions seen in all age groups that are most often discovered incidentally on routine cross-sectional imaging studies. On USG hemangiomas appear as well defined homogenously hyperechoic lesion mostly in the peripheral location or close to the hepatic veins. The larger lesions (>2 cm) have more heterogenous echopattern. (Fig.2)

On multiphasic CT imaging they shows characteristic nodular peripheral enhancement on arterial phase images with gradual centripetal filling and enhancement on delayed phase images. On MRI they are typically hypointense on T1W images and significantly hyperintense on T2W images. The diagnosis of haemangioma by MR imaging rests not only in the signal characteristics but also in morphological features such as sharp and geographic margins, lack of peripheral halo on T2W images, lack of deformity of the liver surface in the majority of cases, superficial location, and lack of displacement of the hepatic vessels surrounding the lesion.

**Hepatocellular Adenoma (HA):**

Hepatocellular adenoma (HA) is an uncommon solid primary
liver tumor. These are usually solitary greater than 10 cm in size. HA is usually seen as a heterogeneous but primarily echogenic hepatic mass, the echogenicity being due to the intratumoral fat and glycogen. On non-contrast scans, adenomas are predominantly isodense with liver but may appear hypodense due to excessive steatosis. On contrast administration, adenomas demonstrate rapid, early and transient enhancement owing to hepatic artery hypervascularity of these tumors. There is rapid wash in and washout of the contrast agent that renders the tumors isodense to liver during the portal venous phase when normal liver tissue is maximally enhanced. The high fat or glycogen content or both render these tumors isointense or even hyperintense on T1 images. When present, a hypointense capsule can be identified on T1 images. Blood degradation products can be seen as hyperintense regions on T1 and hypointense on T2 images. Immediate enhancement is seen on the arterial phase images after IV gadolinium chetate but rapidly fades to near isointensity on all subsequent images.

**Focal Nodular Hyperplasia (FNH):**
FNH is well-circumscribed, non-encapsulated and usually solitary (95%) mass that is characterized by a centrally located scar surrounded by nodules of hyperplastic hepatocytes. FNHs appear homogeneous and isoechoic to normal liver and may be visible only because of the mass effect they exert on adjacent hepatic vessels. FNHs are hypervascular tumors. Numerous scattered arterial and venous Doppler signals may be seen throughout the tumor exhibiting a ‘comet tail’ appearance. There is rapid enhancement of FNH appearing hyperdense relative to liver in the arterial phase (approx first 30 seconds) with a steady decrease in attenuation during the portal phase during which it appears relatively isodense to hypodense to the normal liver tissue and the central scar remains of low density. On delayed images there is accumulation of contrast within the scar which appears hyperdense. On MRI FNH is mostly slightly hypointense on T1-weighted images and hyperintense on T2-weighted images. FNH often contains a central scar which is hyperintense on T2 due to presence of oedema and hypointense on T1 weighted images. Dynamic post-gadolinium images frequently depict the central scar not seen on unenhanced images. The scar shows a delayed and persistent enhancement after administration of Gd. Contrast agents with hepato-specific properties have been shown to increase the sensitivity of MR imaging for the detection of focal hepatic lesions. Gadobenate dimeglumine (Gd-BOPTA) is a gadolinium based contrast agent in common with other gadolinium agents, has a vascular interstitial distribution in the first few minutes after injection. Thereafter, some 2 to 4% of the administered dose is taken up by functioning hepatocytes and contrast is excreted in the bile, while the remaining dose undergoes renal excretion. In FNH, there is prolonged and excessive accumulation of this contrast agent because FNH lacks a well-formed canalicular system to permit normal excretion. There is much less
enhancement of the hepatocellular adenoma on dynamic phase MR images and a markedly hypointense appearance on delayed images as compared to FNH. Although adenomas have functioning hepatocytes they lack bile ducts. SPIO is a contrast agent that undergoes phagocytosis by the reticuloendothelial system (Kupffer cells). The use of SPIO results in shortening of T2-relaxation time of lesions containing Kupffer cells causing decreased signal intensity on T2-weighted images. On T2W SPIO enhanced MRI, FNH shows a dramatic decrease in signal intensity (60 to 70%). SPIO uptake is expected in FNH as the lesion contains Kupffer cells and has an excellent vascular supply. The uptake of SPIO in hepatic adenomas is poor compared to FNH.

**Amoebic liver abscess:**
Amoebic liver abscess is the most common extraintestinal manifestation of amoebiasis. Sonographic features include a round or oval lesion, absence of a prominent abscess wall, hypochochogenicity compared to normal liver, fine low level internal echoes, distal sonic enhancement and continuity with the diaphragm. On CT scans, amoebic abscesses of the liver appear as low attenuation lesions, with the density of the lesion dependent on its stage of development and internal contents. Lesions that are early in development may have an appearance similar to that of solid tumors. Older abscesses are more cystic in appearance. On T1 images, the central cavity is usually of decreased signal intensity relative to liver and has increased signal intensity on T2-weighted images; the central cavity is often surrounded by a ring of higher signal intensity that corresponds to the reactive zone. After Gd-DTPA the hyperemic reactive zone demonstrates enhancement.

**Pyogenic liver Abscess:**
The ultrasound features of pyogenic liver abscesses are varied. Frankly purulent abscesses appear cystic with fluid ranging from echo free to highly echogenic. CT has greater than 90% sensitivity for the detection of hepatic abscesses which appear as low attenuation rounded masses on both non-contrast and contrast-enhanced scans. On administration of IV contrast, most abscesses have an enhancing peripheral rim.

**Fungal Hepatic Abscesses:**
Fungal abscess of liver, in general being uncommon, are seen in immunocompromised hosts, those receiving intensive chemotherapy and in patients with AIDS, lymphoma or acute leukemia. Sonographically, four major patterns of hepatic candidiasis are seen: (i) “Wheel within a wheel”, in which a peripheral zone surrounds an inner echogenic wheel, which, in turn surrounds a central hypoechoic nidus, (ii) “Bull’s eye”, a lesion with a hyperechoic centre surrounded by hypoechoic rim, (iii) “Uniformly hypoechoic”, the most common appearance, and (iv) “Echogenic”, caused by scar formation. On CT scan, the most common pattern is multiple small, rounded areas of decreased attenuation. Areas of scattered increased attenuation representing calcification can be seen on NCCT. Periportal areas of increased attenuation, correlating with fibrosis, may also be seen.

**Hydatid Cyst:**
Hydatid disease is prevalent throughout the world and the two main forms that affect humans are echinococcus granulosus and echinococcus multilocularis. Five sonographic patterns were described by Gharbi on the basis of morphology and structure of the hydatid cyst of the liver. Type I: Pure Fluid Collection, Type II: Fluid Collection with a Split Wall, Type III: Fluid Collection with Septa, Type IV: Heterogeneous Echo Patterns & Type V: Reflecting Thick Walls. (Fig.4 & 5)
Echinococcal cyst of the liver appears on CT scans as a well-defined, round or oval cystic mass of the liver having a density near that of water where they appear hyperdense compared to normal hepatic parenchyma. Daughter cysts, indicating viability, give the lesions a multilocular appearance. The daughter cysts usually contain fluid with a lower attenuation than that of the fluid in the mother cyst. Daughter cysts can also float free in the lumen of the mother cyst, so altering the patient’s position may change the position of these cysts, confirming the diagnosis of echinococcal disease. Detachment of the laminated membrane from the pericyst can be visualized as linear areas of increased attenuation within the cyst. Postcontrast scan shows enhancement of internal septation. Calcification of the cyst wall or internal septae are easily detected at CT. Hepatic hydatid cysts appear hypointense on T1 and

**Fig. 4:** Diagram illustrating the types of cystic echinococcosis according to classification of WHO Informal Working Group based on sonographic findings relating to the viability of parasite. CE cystic echinococcosis

**Fig. 5(a):** US scan showing membranes as serpentine linear structures floating within a hydatid cyst US scan showing a characteristic appearance of cysts enclosed within a cyst giving rise to honeycomb pattern seen in a hydatid cyst. CECT of the same patient shows similar finding.

**Fig. 5(b):** Axial (A) and Coronal (B) MR images showing hepatic hydatids with multiple daughter cysts within appearing hyperintense on the T2-weighted images.
hyperintense on T2-weighted images. The pericyst usually has low signal on T1 and T2-weighted images because it is rich in collagen.

**Malignant Lesions**

**Hepatocellular carcinoma:**
HCC represents 6% of all cancers and is the most common primary hepatic malignancy worldwide. HCC may present as a solitary mass, multifocal nodules, or diffuse disease throughout the liver. Pathologic features that may affect the imaging findings include the presence of a capsule, necrosis, calcifications, hemorrhage, fibrosis, or fat. Imaging plays an essential role in the clinical management of HCC with MDCT and MR imaging as the most commonly used imaging modality in the diagnosis, staging, and surveillance of the disease. Grey scale ultrasound shows non-specific echopattern varying from hyperechoic to heteroechoic pattern usually in a background of cirrhotic liver. On Doppler internal vascularity can be seen. Other supportive evidence include portal vein thrombosis, invasion of adjacent structures. The typical CT appearance of HCC during a multiphasic scan is an early enhancing mass with rapid washout. A capsule, if present, demonstrates late enhancement. MDCT is also highly accurate in staging HCC. MDCT can detect the number of lesions, segments involved, regional adenopathy, vascular tumor invasion, and metastases. MDCT also plays a major role in posttreatment evaluation including surveillance following surgical intervention, local therapy, or systemic therapy. Portal and hepatic vein invasion by HCC may be present. The distinction between tumor thrombus and bland thrombus is aided by the detection of early enhancement of the thrombus during the early or late arterial phase. On perfusion imaging BF, BV, ALP, PMB would be elevated with reduced TTP. (Fig.6)

Fibrolamellar hepatocellular carcinoma is a rare variety of hepatocellular carcinoma more commonly seen in younger patients with a roughly equal sex distribution. There is a tendency for intralesion calcification and central scar formation. There is a better prognosis with lesions being more amenable to surgical resection. On MR, the T1 appearance of HCC ranges from hypointense to slightly hyperintense, depending on fat content, copper deposition within the tumor, and the degree of differentiation. On T2 images, most HCC demonstrate increased signal compared to the surrounding liver, although the tumors tend to be inhomogeneous. Contrast-enhanced MR imaging may play a role in characterizing and detecting small HCC in patients (fig.7 & 8) with underlying cirrhosis. In these cases, the T1 and T2 of the tumors may not be substantially different from that of the surrounding liver, or the underlying liver heterogeneity may make the tumor difficult to detect. Additionally, in patients with cirrhosis and ascites, significant motion artifacts obscure the underlying liver parenchyma. In these cases, imaging following rapid IV injection of gadolinium may increase lesion conspicuity.

Early imaging at 30 to 40 seconds after contrast injection results primarily in a hepatic arterial phase image of the liver, and some tumors-particularly small, well-differentiated tumors—are better visualized during this phase of hepatic enhancement. Fibrolamellar HCC is typically a well-circumscribed lesion that is hypointense on T1 images and hyperintense on T2 images. A central scar may be present. Central calcifications are present in one third of lesions. The differential diagnosis includes adenoma or FNH.

**Cholangiocarcinoma:**
Cholangiocarcinoma is the second most common primary hepatobiliary malignancy, after HCC. These tumors can be divided into intrahepatic and extrahepatic locations. Tumors at the periphery of the biliary tree are intrahepatic.

![Fig.6 (A) and (B): USG reveals a large heterogeneously hyperechoic lesion with intense central and peripheral vascularity in right hepatic lobe](image-url)
Fig. 7: Triphasic study reveals a large iso to hypodense lesion in right hepatic lobe showing intense enhancement in arterial phase (F), with relative washout in portal venous phase.

Fig. 8: Colour maps show increased ALP as indicated by red colour, increased BF, BV as indicated by patchy areas of green colour and decreased TTP shown by areas of yellow within the lesion in a case of hepatocellular carcinoma.
Peripheral cholangiocarcinomas are usually large because they are rarely symptomatic early in their course. The most common CT appearance of cholangiocarcinoma is that of a low-attenuation mass with irregular margins with mild peripheral enhancement on the delayed phase of imaging. This delayed enhancement is a result of slow diffusion of contrast into the interstitial space and results in prolonged enhancement. Satellite nodules, regional lymph nodes, and capsule retraction may be present. Rimlike contrast enhancement is one of the most frequent patterns observed in either arterial- or portal-phase imaging. In contrast to HCC, these tumors usually do not invade adjacent vessels but encase them. Invasion of the bile ducts, perineural spaces, and lymphatic vessels is seen, however, resulting in lymph node metastasis and intrahepatic metastasis. The most prominent feature with central cholangiocarcinoma on MR is usually intrahepatic biliary duct dilatation. Morphologic changes may occur late in the disease process, with atrophy of the left lobe of the liver compared with the right lobe. The left-sided hepatic ducts may be more dilated than are those in the right lobe. Central tumors tend to show high signal intensity on T2 images near the porta hepatis, but because of associated bile duct dilatation, it is difficult to distinguish tumor from bile duct and vessels. For this reason, contrast-enhanced MR is recommended using a T1-weighted GRE sequence. On T1 images, the bile ducts are dark (fluid). The tumor demonstrates late enhancement following gadolinium that differentiation between tumor and bile ducts is readily recognized. Ferumoxides have also been proven to be valuable in imaging patients with intrahepatic cholangiocarcinoma. Vascular invasion and portal nodes should be carefully searched for because these findings preclude resection of the tumor. Solitary peripheral masses appear similar to HCC or hepatic metastases.

**Metastasis:**
Metastatic spread of tumor to the liver is much more common than the occurrence of primary liver malignancy. The most common tumors to metastasize to the liver are colon, lung, pancreatic, melanoma, and sarcoma. Except for infiltrative tumors, such as lymphoma, most metastatic disease to the liver manifests on CT as multiple masses, usually with ill-defined margins and an irregular rim. Those lesions that enhance rapidly, such as metastatic disease from breast cancer, renal cell carcinoma, thyroid cancer, and neuroendocrine or carcinoid tumors, appear hyperdense compared with normal liver parenchyma particularly on arterial phases of imaging and may appear isodense, or hypodense, to the normal liver parenchyma on the portal-venous phase of imaging. In contrast, most metastatic liver disease arising from gastrointestinal tract tumors, such as colon cancer, typically is best identified as hypodense lesions on the portal-venous phase of imaging. Perfusion imaging will show elevated BF, BV, ALP, PMB, however values will be lower than HCC’s. The most common appearance of metastatic disease in the liver by MR is rounded or focal lesions with decreased signal on T1 images and moderately increased signal on T2 images. (Fig. 9)

Malignant tumors tend to have margins that are not sharply

![Fig.9: USG demonstrates multiple target lesions. Triphasic CT reveals hypodense lesions in noncontrast scans(E), showing complete ring enhancement in arterial phase(F). Lesions appear hypodense on portal venous phase](image-url)
defined, and the signal intensity on T2 images is usually not as bright as CSF. Tumors may be single or multiple. Hypervascular metastases may have hyperintense signal on T2 images, and so potentially could be mistaken for hemangioma or cyst. In addition, most of these tumors have an increased tendency to have intratumoral hemorrhage. This results in increased signal on T1 images as well as T2 images. Melanoma, due to the T1 shortening effect of melanin, shows increased signal on T1 image even if hemorrhage is not present25,10,12,17.

Proposed strategy for imaging of space occupying lesion

The large number of studies suggests that the state-of-the-art MR imaging of the liver should play a pivotal role as a comprehensive approach for the work-up of patients with suspected or known liver abnormalities. USG with Doppler may be used as an initial screening modality. However, characterization of lesion is not very well possible. Multiphasic CT along with perfusion imaging is the most comparable modality to MR imaging in its overall diagnostic accuracy, but a use of MR imaging will further increase owing to the increasing concern of the risks of cancer induction by excessive use of CT.

REFERENCES