The Hypervascular Liver Lesion on MDCT: Approach, Differentials and Pitfalls

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Learning Objectives

To illustrate the spectrum of arterially enhancing foci in the liver and their imaging characteristics on CT. To provide a diagnostic approach to the incidental finding of a hypervascular focus in the liver, highlighting key features which allow some lesions to be confidently characterized on CT, as well as demonstrating variants and pitfalls with CT imaging.
Background

Multi phase computed tomography (MDCT) of the liver is a commonly utilized imaging technique for the evaluation of ultrasound detected lesions in the routine screening of chronic liver disease patients, as well as the characterisation of incidentally discovered focal liver lesions. Arterially enhancing lesions are also a frequent incidental finding in CT studies of the chest and abdomen. It is important to recognize the unique imaging features of benign lesions such as focal nodular hyperplasia and haemangiomas, to avoid unnecessary further investigation. Malignant lesions include hepatocellular carcinoma (HCC), fibrolamellar HCC and hypervascular metastases from primary tumours such as renal cell carcinoma, neuroendocrine tumours, carcinoid, and thyroid carcinomas. In a third category, there are also a number of vascular anomalies to be aware of, including THED's (Transient Hepatic Enhancement Differences), portohepatic shunts, as well as less common phenomena such as hepatic artery aneurysms and the 'Hot Quadrate Sign' in SVC occlusive syndromes.
Typical Multiphase CT

In our institution a multiphase hepatic CT comprises a non-contrast, arterial dominant, portal venous and equilibrium phase. A power injector through a large bore (20 gauge or larger) cannula in a proximal vein is used with typical timing post injection of approximately 30 seconds. A good quality arterial dominant phase has contrast in the hepatic artery, some enhancement in the portal vein but no contrast in the hepatic veins.

Hepatic Cavernous Haemangiomas:

The most common benign enhancing liver lesion that is encountered on CT imaging is the cavernous haemangioma. Studies report the prevalence of haemangiomas in the general population to range from 1-2% (1), up to 20% (2). Haemangiomas are more common in females, with a female to male ratio of 2-5:1 (3). It is also common to encounter more than one haemangioma within the same liver with multiple lesions seen in 15 - 20% (4). Frequently detected as an incidental, asymptomatic lesion, haemangiomas are composed of vascular lakes. The typical haemangioma demonstrates a classic appearance on the arterial phase of a CT study, with early, peripheral globular enhancement (Fig 1). The attenuation of the peripheral nodules is equal to that of the adjacent aorta (5). This is followed by centripetal fill in of the lesion with contrast on the portal venous and delayed phase, however the arterial appearance is pathognomonic of haemangiomas.

An imaging variant is the 'flash filling' haemangioma which is homogeneously hyperenhancing in the arterial phase (Fig 2). These lesions are typically small lesions, < 1 cm and may be difficult to differentiate from HCC or hypervascular metastases (4). Flash filling haemangiomas remain hyperenhancing in the portal venous and delayed phase, following the density of the portal veins, which is in contradistinction to the rapid washout of HCC and hypervascular metastases.

Although common in haemangiomas of other sites in the body, the presence of calcification (or phleboliths) is not a typical feature of hepatic haemangiomas and its presence should provoke further investigation with MRI. When seen, the calcification is usually marginal and nodular in appearance, although large areas of calcification have been documented (3). The presence of capsular retraction is also rare, is thought to relate to fibrous degeneration (3). This feature should also result in the lesion being further characterised with MRI.
Although most haemangiomas remain stable over time, they can occasionally increase in size and even appear during pregnancy. In both cases, the characteristic imaging features of haemangiomas are present, and allow for diagnostic confidence (3).

**Focal Nodular Hyperplasia:**

Focal Nodular Hyperplasia (FNH) is the second most common benign liver tumor, after haemangiomas, with a prevalence of approximately 0.9% (6). The male to female ratio is 1:8 and approximately 20% of patients have multiple foci of FNH (6). FNH is described as a nodule composed of benign appearing hepatocytes occurring in a liver that is otherwise histologically normal (7). The pathogenesis is uncertain, however they are thought to represent a hamartomatous lesion due to disorganized growth of hepatocytes and ducts forming an unencapsulated mass, with abnormally structured bile ducts and vessels (4). This is potentially a reaction to intrahepatic vascular disturbance explaining the increased incidence of FNH in Osler Weber Rendu and coexisting haemangioms. They commonly occur near the capsular surface of the liver and the characteristic feature is the formation of a central fibrovascular scar (4).

Lesions are typically hypodense on non-contrast images but may be isodense. The scar is more difficult to appreciate than on post contrast sequences, but is hypodense when seen (Fig 3). They show homogeneous hepatic arterial phase hyperenhancement that gradually fades to background liver density with increasing delay. In the arterial phase, FNH is usually less than 50% of the density of the aorta, while in the portal venous phase is most commonly slightly lower density than the inferior vena cava (8). Larger lesions may become slightly hypoenhancing in the late phase. The degree of arterial enhancement in FNH has been shown to be consistently greater than the arterial enhancement of hepatocellular adenoma, a feature that can be used for lesion differentiation (9) (Fig 4). The margins are often ill defined and more often smooth than lobulated. A central scar is seen in approximately 50% of cases, is more likely to be appreciated in large lesions, and is hypoenhancing in the hepatic arterial dominant phase with hyperenhancement appreciated in the delayed phase. Septae radiating from the scar are uncommonly appreciated, as is a pseudocapsule while calcification is only rarely encountered. FNH are benign and do not have an association with haemorrhage or malignant transformation.

**Hepatic Adenomas:**

Hepatocellular Adenomas (HCA) are rare benign lesions of epithelial origin, which demonstrate the most common association with young women and a history of oral contraceptive use. A causal relationship is shown between oestrogen containing or androgen containing medications and adenomas, with increasing prevalence with increasing dose and duration of medication use (10). The annual incidence of hepatic
adenoma increases from 1 per million to 30 - 40 per million in long-term users of the oral contraceptive pill (11). Type 1 Glycogen storage disease is also a risk group for hepatic adenoma (12). It is noted however, that these lesions can occur sporadically in individuals without risk factors. Most patients are asymptomatic, however large lesions can result in right upper quadrant fullness or discomfort (13). Although they are benign, isolated HCA are frequently excised as they can undergo malignant transformation or have catastrophic haemorrhage, particularly during periods of growth such as hormonal stimulation of pregnancy.

The imaging appearance of hepatic adenomas is dependent on their composition, with lesions comprising varying amounts of intratumoral fat as well as haemorrhage, which will be hypoenhancing. Viable tumor consists of uniform hepatocytes and a variable number of Kupffer cells (13). The typical appearance is of transient enhancement on the arterial phase, followed by variable washout of contrast on the portal venous phase, and the lesions are hypoattenuating to surrounding liver on a delay (4)(Fig 5). Adenomas are typically well circumscribed and occasionally encapsulated (approximately 30%)(13). Calcification is rare at 10% (13). Adenomas, enhance less than FNH in the arterial phase and are often more heterogenous due to fat, glycogen and blood products.

Although adenomas can mimic hepatocellular carcinoma on CT, as well as MRI, they are typically seen in a different demographic and a non-cirrhotic liver. The presence of intratumoral fat is supportive of adenoma, however is only identified in 10% of cases on CT (13).

**Hepatocellular Carcinoma and Hypervascular lesions in the cirrhotic liver:**

The primary goal of screening in patients with chronic liver disease is the early detection of hepatocellular carcinoma (HCC). Detection of a solitary small lesion allows for potentially curative treatment with alcohol or radio-frequency ablation, chemoembolization or surgical resection. Patients may also be considered for transplantation if disease has not reached an advanced stage. Patients with chronic liver disease who are candidates for screening programs undergo ultrasound evaluation at 6-12 monthly intervals. Sonographically detected lesions over 10mm in size are further characterized with MDCT, due to the ease of accessibility and lower cost in comparison to the more sensitive and specific MR examination.

Lesions are considered hypervascular if they are more dense than surrounding liver parenchyma in the arterial phase. Hepatocellular carcinoma is most commonly a hypervascular tumor as it derives its blood supply primarily from the hepatic artery (14) (Fig 6). A small proportion of HCC's are hypoenhancing and seen better on the portal venous phase (15). Some authors have correlated increased arterial enhancement with more poorly differentiated lesions, due to recruitment of arterial supply (16). Others
attribute variation in enhancement largely to size, with smaller lesions demonstrating homogeneous enhancement and larger lesions (>5cm) being more likely to show heterogeneous enhancement (17). In cirrhotic patients, a triple phase CT (non-contrast, arterial and portal venous phases), have been associated with sensitivities of 59-68% in detecting the presence of hepatocellular carcinoma (18). The optimal timing for the arterial phase of a study is debatable, with some authors recommending a delay of 20 - 30 seconds post injection, while others suggest a later arterial phase may have superior sensitivity (19). To be able to make a non-invasive diagnosis of hepatocellular carcinoma, the lesion must be arterially hyperenhancing and then washout in either the portal venous or delayed phase. Lesions that cannot be definitively diagnosed require further evaluation with MRI.

**Fibrolamellar HCC:**

A rare form of hepatocellular carcinoma to describe is the fibrolamellar HCC. This is usually a solitary, non-encapsulated liver mass with a central fibrous scar. This lesion is not associated with cirrhotic liver disease and is often found in the otherwise normal livers of young patients. Fibrolamellar HCC typically shows arterial phase enhancement on CT with a central non-enhancing scar, and the diagnostic dilemma becomes distinguishing this lesion from the more common, benign focal nodular dysplasia (Fig 7). The central scar is calcified in 35 - 50% of fibrolamellar HCC, which can help distinguish the lesion from FNH on CT (4). The scar is also typically larger than an FNH scar. The presence of metastases to nodes, bone or viscera are secondary signs the lesion is malignant. These lesions are further characterized with liver MRI, with a hepatocyte specific agent allowing accurate diagnosis and the detection of small intrahepatic metastases that may alter the surgical approach.

**Hypervascular metastases:**

The liver is a common site of metastatic lesions due to its dual blood supply (portal vein, and hepatic artery), and there are a number of recognized hypervascular metastases. The most frequently seen primary tumors with hypervascular metastases are renal cell carcinoma, neuroendocrine tumors, carcinoids, melanoma and thyroid carcinoma. The majority of lesions are hypoattenuating to the surrounding liver on a non-contrast phase, with the exception of neuroendocrine metastases which, may be hyperattenuating (4). There is typically early, homogeneous enhancement on the arterial phase, with washout on the portal venous phase (4)(Fig 8). When confronted with a hypervascular liver lesion, it is important to assess the pancreas, kidneys and mesentery for potential primary malignancies (Fig 9).

**Flow related phenomena:**
The liver is unique in its blood supply, receiving inflow from both the hepatic artery (25%) and the portal vein (75% of blood supply). These systems are not completely independent however, and there are several potential routes of communication, including transsinusoidal, transtumoral and transplexal (peribiliary) (20). Areas of transient hepatic enhancement differences (THED's) can be appreciated on dual phase CT, where there is an area of higher attenuation on the arterial phase, returning to homogeneous enhancement on the portal venous phase (Fig 10). This represents an redistribution of the hepatic arterial flow and can result from numerous causes, including portal vein obstruction, liver cirrhosis, hepatic neoplasms, hepatic trauma, hereditary haemorrhagic telangiectasia (HHT), hepatic vein obstruction, hepatic steal phenomenon from hypervascular tumors, hepatic parenchymal compression and aberrant blood supply to the liver (21). The phenomenon can be characterised as tumorous or non-tumorous, with tumorous shunts resulting from portal obstruction or stenosis, while non-tumorous shunts represent a direct communication between the arterial system and the portal venous system of the liver (22). The THED is characterized by a wedge-shaped morphology and nondisplaced internal vasculature (15). Upon discovery of a THED, the most important step is assessment of its apex, looking for a causal lesion or visible portal vein thrombosis (Fig 11,12).

The inflammatory processes involved in causes of chronic liver disease can result in changes to the normal liver architecture, with various patterns of fibrosis, scarring and nodular regeneration (15). This can result in areas of portal vein obstruction, or thrombosis as well as development of arterioportal shunts. Up to 63% of patients with large HCC's will have associated arterioportal shunts (23), however small shunts without HCC, can sometimes appear as nodular foci of enhancement and mimic small tumors (Fig 13). Vascular pseudoaneurysms, a more rare phenomenon, can also appear as a nodular focus of arterial enhancement in the liver (Fig14). The prevalence of small arteriovenous shunts and pseudoaneurysms in cirrhotic livers is thought often to relate to previous liver biopsy or transhepatic biliary catheter placement (15). These lesions may be distinguished from HCC on the later phases of imaging where they follow vascular density rather than demonstrate washout. For small shunts however, this can be difficult to characterize confidently on CT. In fact, arterioportal shunts are one of the most common mimics of HCC (pseudolesions) and frequently require close monitoring with CT, or MR imaging with a hepatocyte specific agent and diffusion weighted imaging (24).

Portal venous shunts are abnormal communications between the portal venous system and the systemic venous system (portosystemic shunts), or between the portal venous system and the hepatic artery (arterioportal shunts), as described above. Extrahepatic portosystemic shunts are frequently encountered in cirrhotic patients with portal hypertension where enlargement of pre-existing but usually insignificant portosystemic anastomoses. Congenital extrahepatic and intrahepatic portosystemic shunts can also occur, although both are rare (25). The intrahepatic portosystemic shunts are usually well delineated on the portal venous phase of a CT study.
Hot Quadrate Sign:

An odd and rare phenomenon is the intense arterial enhancement of the quadrate lobe of the liver in cases of superior vena cava obstruction. SVC obstruction most commonly occurs due to malignant extrinsic compression in cases of bronchogenic carcinoma, lymphoma or metastatic lymph node disease. Rarer causes include aortic aneurysms, fibrosing mediastinitis and iatrogenic causes such as line placement (26). The SVC syndrome manifests clinically with upper body venous dilatation and oedema, as well as CNS disturbance and respiratory distress. There are 4 main collateral pathways to return blood to the right side of the heart: The azygous/hemiazygous route, the internal thoracic veins, the lateral thoracic and superficial thoracoabdominal veins and the vertebral venous plexus. There are varying degrees and levels of SVC obstruction and if there is complete occlusion of the SVC azygous tributary, the anterolateral collaterals are recruited. These may communicate with the umbilical and paraumbilical veins through the musculophrenic and superficial epigastric veins (27,28). These branches preferentially drain into the left branch of the portal vein, resulting in a systemic-portal shunt. This in turn creates the 'focal hepatic hot spot' in the quadrate lobe, which is a functional part of the left lobe of the liver, lying between the gallbladder fossa and the fissure for the ligamentum teres (segment 4, by the Bismuth-Couinaud classification)(26) (Fig 15). The prefix of "hot" is historic as the sign was first described in nuclear medicine.

Peliosis:

Peliosis hepatitis is a rare and benign disorder which causes sinusoidal dilatation and multiple blood filled lacunae within the liver, varying from 1mm to several centimetres in diameter (23). The pathogenesis of this condition is not well understood, however it is recognized to be secondary to a number of conditions. There is an association with chronic wasting conditions such as tuberculosis and leprosy, with malignancies, such as HCC, and with drugs and toxins, such as steroids, the oral contraceptive and polyvinyl chloride. In HIV patients, Bacillary peliosis hepatitis is the result of Bartonella infection (29). There are links with renal and cardiac transplant, as well as chronic illnesses such as diabetes mellitus and coeliac disease. In 20-50% of cases however, no causal factor is identified (23). The lesions are typically hypointensuative relative to liver on a non-contrast study and on the arterial phase may demonstrate early globular or vascular like enhancement (Fig 16). On the portal venous phase, a centrifugal or occasionally a centripetal pattern of enhancement can be observed (30). Contrast can accumulate in these lesions on delayed imaging, making them hyperattenuating compared to surrounding liver parenchyma (30). Thrombosed nodules are hypoattenuating and can mimic abscesses or metastases (29). The enhancement patterns can cause these lesions to mimic haemangiomas or hypervascular metastases and the clinical history can be vital for these cases.
**Fig. 1:** Large segment 2 haemangioma demonstrating classic peripheral nodular enhancement on the arterial phase (arrow). The patient has multiple haemangiomas as well as focal nodular hyperplasia, with an adjacent pedunculated FNH (arrow head).

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**Fig. 2:** Flash filling subcapsular segment 2/3 haemangioma in a non-cirrhotic HBV patient. The lesion was further characterised with MRI.

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Fig. 3: Large enhancing FNH in the right lobe of the liver, with central hypodense scar on the arterial phase.

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**Fig. 4:** Incidentally discovered liver lesions in a 36 yr old female. Segment 7 FNH (arrow head) demonstrates stronger arterial phase enhancement than the segment 2 adenoma (arrow).

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Fig. 5: Hepatic adenoma. 2 cm hypervascular lesion in a 29 yr old female. The lesion is low attenuation on the non-contrast study suggestive of a degree of internal fat. It remains mildly hypervascular on the portal venous phase with washout by 5 minutes.

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Fig. 6: Hepatocellular carcinoma. Arterially enhancing segment 6 lesion, with capsular distortion, in a 65 yr old male with chronic hepatitis B and previously treated multifocal HCC.

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Fig. 7: Large fibrolamellar HCC in a 24 yr old female. Heterogeneous arterial enhancement with large central non-enhancing scar.

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Fig. 8: Multiple hypervascular hepatic metastases from a paraganglioma primary lesion. Mixed pattern of homogeneous and peripheral enhancing lesions on the arterial phase.

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**Fig. 9:** Same patient as Fig 8. The primary lesion is a heterogeneous arterially enhancing peri-renal mass, consistent with a paraganglioma.

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Fig. 10: Extensive THED due to spontaneous portal vein thrombosis in a 40 yr old woman. Increased arterial enhancement of the left lobe, and segments 5 and 8 of the right lobe, due to thrombosis of the left portal vein and anterior sectoral branch of the right portal vein (arrow). Homogeneous enhancement on the portal venous phase.

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Fig. 11: THED with increased arterial enhancement in segments 6 and 7 of the liver in a cirrhotic patient.

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**Fig. 12:** Same patient as figure 11. The THED is due to tumour thrombus related to a large enhancing hepatocellular carcinoma in segment 6.

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Fig. 13: Segment 5 perfusion anomaly in a patient with chronic Hepatitis B.

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Fig. 14: Mycotic aneurysm of an hepatic arterial branch in a 48 yr old male with infective endocarditis manifests as a small arterially enhancing lesion in segment 8.

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Fig. 15: 'Hot Quadrate' sign in a lymphoma patient with chronic SVC occlusion. Hyperenhancement of segment 4 of the liver on the arterial phase. Blood from the upper body drains into the liver via anterolateral collaterals recruited in the lateral chest wall.

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Fig. 16: A case of presumed Hepatic Peliosis in an elderly female. The arterial phase demonstrates vascular like enhancement.

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Conclusion

There is a diverse range of benign and malignant hypervascular liver lesions as well a number of tumor mimics which result from vascular phenomena that create areas of enhancement in the arterial phase of a CT study. Knowledge of these pathologies and their imaging features can result in confident characterization of many of these lesions with CT, as well as recognition of the limitations of CT, tailoring appropriate referral for differentiation with MRI.
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