Diagnostic Imaging Pathways - Focal Liver Lesion (Investigation)

Population Covered By The Guidance

This pathway provides guidance on imaging in patients with focal liver lesions, dependent on whether the patient has risk factors for primary cancer or metastases or whether the lesion is ‘incidental’.

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Date of next review: 2017/2018

Published: February 2016

Quick User Guide

Move the mouse cursor over the PINK text boxes inside the flow chart to bring up a pop up box with salient points.
Clicking on the PINK text box will bring up the full text.
The relative radiation level (RRL) of each imaging investigation is displayed in the pop up box.

SYMBOL	RRL	EFFECTIVE DOSE RANGE
	None	0
	Minimal	< 1 millisieverts
	Low	1-5 mSv
	Medium	5-10 mSv
	High	>10 mSv

Pathway Diagram

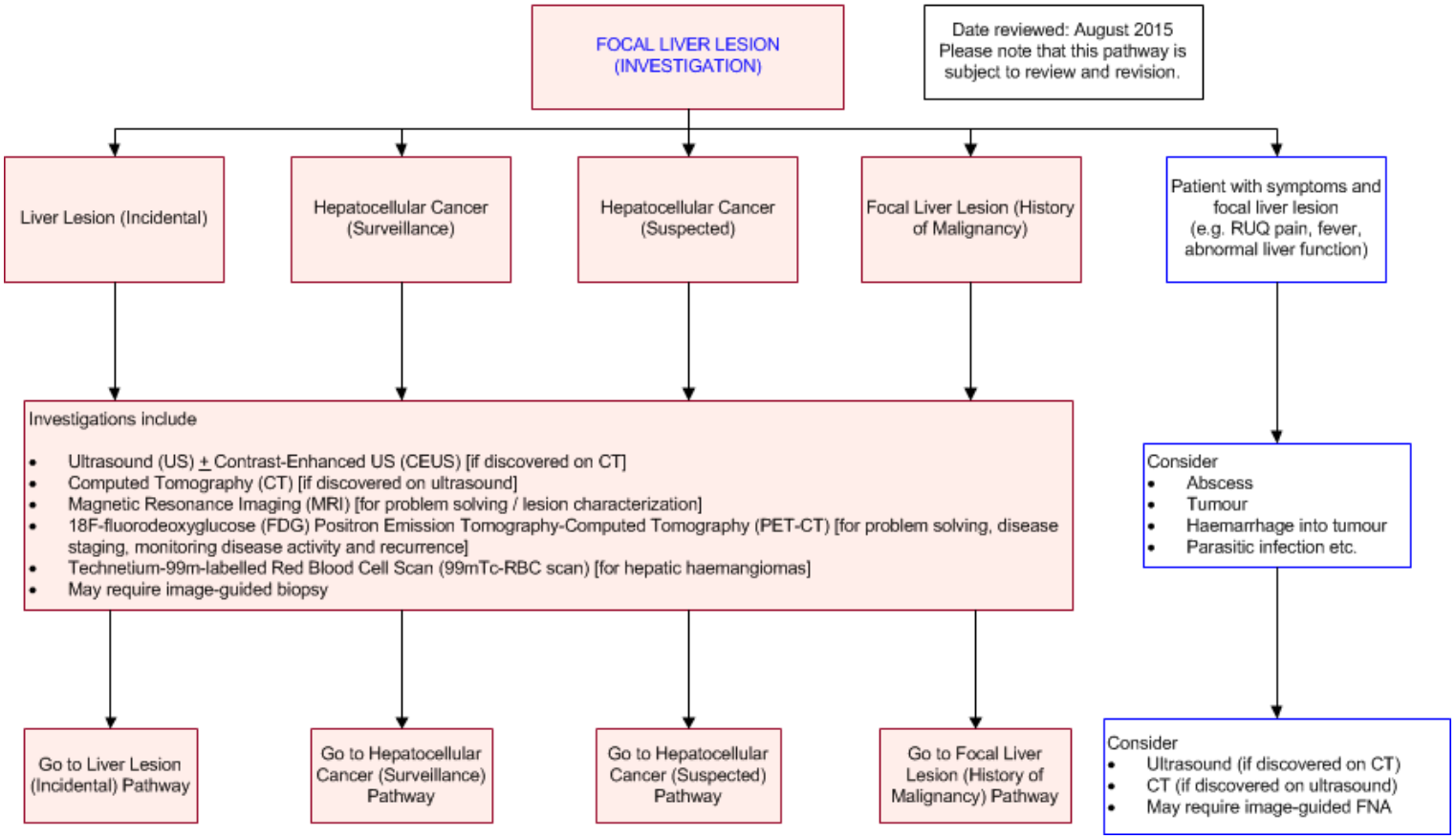
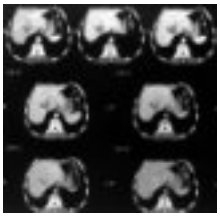


Image Gallery

Note: These images open in a new page

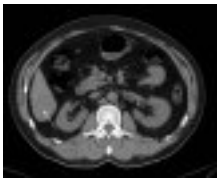
1



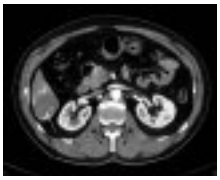
Hepatic Haemangioma

Image 1 (Computed Tomography): Post-contrast images demonstrating initial peripheral enhancement, followed by delayed filling of the lesion with contrast. These features are typical of a haemangioma.

2a



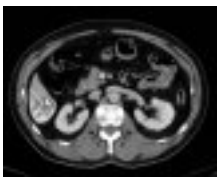
2b



Hepatic Haemangioma

Image 2a, 2b and 2c (Triphasic Computed Tomography): Non-contrast scan (Image 2a) demonstrates a subtle low attenuation lesion in segment 6 of the liver (arrow). There is globular peripheral enhancement of the lesion in the post contrast arterial phase scan (Image 2b) with delayed filling in of the lesion in the portal venous phase (Image 2c).

2c



2d

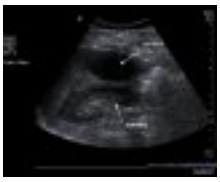
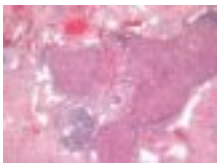


Image 2d (Ultrasound): Ultrasound scan demonstrating the liver lesion in same patient.

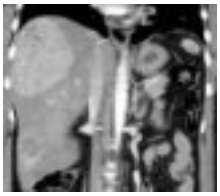
3a



Hepatic Haemangioma

Image 3a (H&E, x2.5): Histological section of a hepatic haemangioma showing variously sized, dilated and congested blood vessels set in a fibrous stroma with residual islands of liver parenchyma.

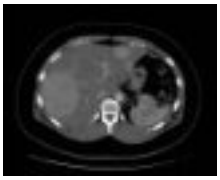
4a



Hepatic Adenoma

Image 4a and 4b (Computed Tomography): Coronal and axial views demonstrating several enhancing liver lesions.

4b



4c

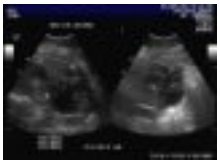
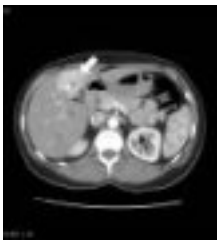


Image 4c (Ultrasound): Ultrasound scan demonstrating the liver lesions in same patient.

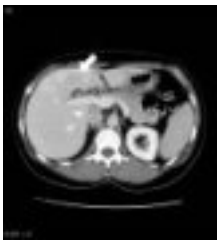
5a



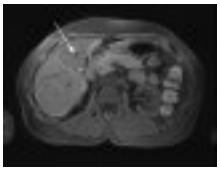
Hepatic Focal Nodular Hyperplasia

Image 5a and 5b (Triphasic Computed Tomography): The arterial phase scan (Image 5a) shows a hyperattenuating nodular lesion (narrow arrow) with the typical central scar (broad arrow) in segment 4 of the liver. On the delayed portal venous phase (Image 5b), the lesion becomes isoattenuating (arrow).

5b



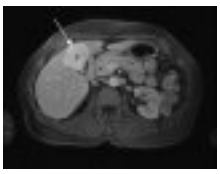
6a



Hepatic Focal Nodular Hyperplasia

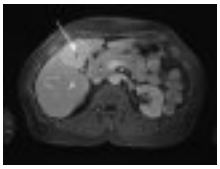
Image 6a, 6b, 6c and 6d (Magnetic Resonance Imaging): Gadolinium-enhanced T1-weighted MRI (Image 6a) demonstrates an ill-defined low-signal intensity mass in segment 4 of the liver with intense enhancement in the arterial phase (Image 6b). Minor enhancement persists in the portal

6b

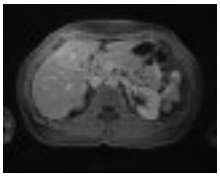


venous phase (Image 6c) and the lesion becomes isointense with enhancement of the central scar (arrow) on the delayed image (Image 6d).

6c



6d



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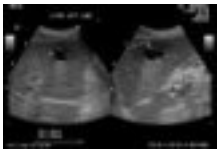
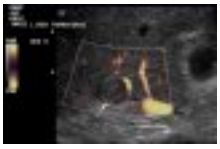


Simple Hepatic Cyst

Image 7 (Ultrasound): Simple-appearing cyst in the left lobe of liver.

8a



Hepatocellular Carcinoma

8b

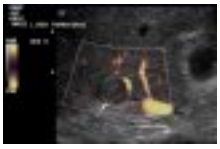


Image 8a and 8b (Ultrasound): Within segment 6 of the liver, there is an approximately 2cm subcapsular hypoechoic lesion (arrow) which does not demonstrate any increased vascularity.

8c

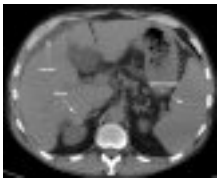
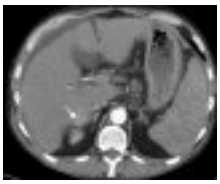


Image 8c, 8d, 8e and 8f (Triphasic Computed Tomography): CT of the same patient shows a cirrhotic liver with patent hepatic and portal veins as well as ascites. Within segment 6, there is a nodular area which demonstrates slight enhancement corresponding to the lesion identified on ultrasound (arrow). This lesion could represent either a dysplastic cirrhotic nodule or an early hepatocellular carcinoma.

8d



Focal Liver Lesion (Investigation)

Risk factors for non-cystic focal liver lesions

- For hepatocellular carcinoma
  - Positive hepatitis B or C serology
  - Cirrhosis / chronic hepatitis / primary biliary cirrhosis / autoimmune hepatitis
  - Ethnicity (South East Asians: males >40; females >50; Africans >20)
  - Family history of hepatocellular carcinoma
  - Genetic haemochromatosis

    - Non-alcoholic steatohepatitis
    - Excess alcohol consumption
- For metastatic disease
    - Current or previous extra-hepatic malignancy
- For adenomas
    - Females on oral contraceptive agents or hormonal replacement therapy
    - Males on androgenic steroids
    - Glycogen storage disease (rare)

Liver Lesion (Incidental)

- The great majority of incidentally-detected liver nodules are benign
- Even in patients with known extrahepatic primary malignancy, small liver lesions, if single or very few in number, are more likely to be benign than malignant
- The problem of incidental lesions, in the liver and elsewhere, is an important component of the burgeoning issue of over diagnosis and the potential harming of healthy people
- It is important to distinguish hepatic adenomas (HA) from focal nodular hyperplasia (FNH) as the former can present acutely due to rupture and consequent haemoperitoneum in addition to the risk of malignant transformation up to 10% of these tumours

Hepatocellular Cancer (Surveillance)

- In patients with cirrhosis, the risk of developing hepatocellular carcinoma (HCC) is highest with HCV, in Asians and in more advanced stages of cirrhosis
- Ultrasonography (US) 6 monthly is recommended as the primary surveillance modality
- Survival was significantly better in patients who underwent surveillance
- The earliest identifiable HCCs often show atypical radiological features and these are the very lesions that need to be diagnosed to enable a higher likelihood of cure
- Sensitivity for detecting hepatocellular carcinoma on US varies with the size of the lesion
- The use of serum alpha-fetoprotein (AFP) alone as a surveillance tool is not recommended
- The use of AFP to complement US surveillance is controversial

Hepatocellular Cancer (Suspected)

- In patients at risk of HCC
    - Liver lesions 1cm should undergo further imaging, preferably with MRI with a liver-specific contrast agent
    - Lesions in patients at high risk for HCC showing typical features of HCC on imaging (arterial enhancement and then wash-out) can be treated as HCC without biopsy
    - Biopsy should be reserved for lesions with non-diagnostic appearances on imaging

Focal Liver Lesion (History of Malignancy)

- Even in patients with known extra-hepatic primary malignancy, small liver lesions, if single or very few in number, are more likely to be benign than malignant
- In patients with known or suspected extra-hepatic primary malignancy, imaging is usually a

combination of ultrasound and CT, dependent on which modality the lesion was initially discovered
- Simple cysts can be confidently diagnosed on US. May detect or characterize other lesions. If US were the patient's primary imaging modality, contrast-enhanced US (CEUS) is a valuable adjunct performed at the same attendance, if available. Otherwise the next step is usually CT scan

Ultrasound (US) ± Contrast-Enhanced Ultrasound (CEUS)

- Ultrasound (US) contrast agents ('microbubbles') comprise an albumen or phospholipid shell containing a stable perfluorocarbon or sulfur hexafluoride gas. They are predominantly blood-pool agents, the encapsulated microbubbles being small enough to pass through pulmonary and systemic circulations after intravenous injection and durable enough to re-circulate for several minutes
- Examination with US contrast is based on the dynamic assessment of macro- and microvasculature of organs and their pathologies. They are, in principle, comparable to the use of contrast agents for CT and MRI with the added advantage of the capability for imaging continuously during the passage of the contrast agent, thereby obtaining what is effectively a dynamic real-time ultrasound angiogram with greater temporal resolution than contrast-enhanced CT or MRI. In addition, quantitative assessment of contrast uptake can be measured by generating Time-Intensity Curves
- CEUS improves diagnostic performance in differentiating HCCs from non-neoplastic nodules in cirrhotic patients compared with baseline ultrasound (16) and, if available, can be recommended as the first diagnostic step when liver lesions are detected on ultrasound surveillance, especially as the procedure can be performed immediately without the need for further attendance or preparation and may therefore avoid further and more expensive examinations
- Advantages of CEUS
    - Ability to assess the contrast enhancement patterns in real time
    - Higher temporal resolution when compared with other imaging modalities
    - Enhancement dynamics of the lesions can be studied quantitatively and qualitatively
    - No predefined scan time points or need to perform bolus tracking
    - Excellent tolerance and safety profiles of ultrasound contrast agents allow for their repeated administrations in the same session when needed
    - Can be given in the presence of renal impairment
    - The imaging can be performed at the same attendance as the ultrasound at which the lesion was discovered, with resultant early reassurance of the patient and his / her doctors in the majority of cases
- Disadvantages of CEUS
    - Operator and body habitus dependent
    - Specificity and sensitivity are reduced in moderately or markedly fatty livers and with deeply positioned lesions
    - Very small focal liver lesions (

Magnetic Resonance Imaging (MRI)

- MRI is more likely to provide a definitive diagnosis than CT and has an important role in characterizing benign lesions
- Usually breath hold T1 and fast spin-echo T2 weighted images are used for the evaluation of a liver nodule
- Gadolinium-enhanced dynamic MRI imaging improves the characterisation of liver lesions

- Images are commonly taken during the
    - Arterial phase (20-30 seconds after administration of contrast) – useful for identifying hyper-vascular lesions
    - Portal venous phase (70-80 seconds after administration of contrast)
- The patterns of enhancement with gadolinium at MRI of various types of liver lesion are similar to those seen with iodinated contrast at CT
- Hepatobiliary (liver-specific) gadolinium contrast agents (gadoxetic acid) are increasingly used, which are taken up by normal liver and by lesions containing hepatocytes (such as focal nodular hyperplasia) on delayed phase imaging. The use of the delayed phase of these agents has been shown to increase sensitivity compared to dynamic phases alone. Thus, MRI with these agents is useful for differentiation of FNH and HA
- These agents also have excellent sensitivities for metastases, show a better performance than triple-phase MDCT for the detection of hepatic metastasis, especially for small (?1 cm) lesions
- In the context of suspected metastatic disease MRI is usually reserved for: problem solving / lesion characterization; further liver imaging to detect additional hepatic metastases if surgical intervention is contemplated
- On a per lesion and per patient basis, MRI is the most accurate modality for evaluating colorectal liver metastases, being more sensitive than CT and having a slightly higher sensitivity to PET / CT
- Diffusion-weighted imaging (DWI) at MRI is particularly sensitive for the detection of metastases on a per-lesion basis. However, on its own, without other MRI sequences, it is controversial whether DWI is reliable in distinguishing benign from malignant lesions. In general, DWI should be combined with other MRI sequences for lesion characterization

18F-fluorodeoxyglucose (FDG) Positron Emission Tomography-Computed Tomography (PET-CT)

- Malignant cells characteristically have increased metabolism compared to normal cells, and may be reflected by areas of increased activity on PET-CT scanning
- However, the 18F-PET-avidity of metastatic disease tends to parallel the avidity of the primary tumour, which in turns varies among cancer-type and even within the same cancer type
- The roles of PET-CT in hepatic metastases are as follows
    - Occasional problem solving when diagnosis on other modalities remains uncertain
    - To determine the presence of extra-hepatic metastases in order to avoid hepatic resection in those patients in whom it is otherwise contemplated
    - To monitor disease activity and disease recurrence following treatment
- In recent years it has become possible to perform PET-CT with Somatostatin Receptors labeled with 68-gallium for the detection of neuroendocrine tumours, including carcinoid tumours. This has been shown to be highly accurate
- A further study in patients with neuroendocrine primary tumours also found PET-CT and MRI to be highly accurate

Technetium-99m-labelled Red Blood Cell Scan (99mTc-RBC

scan)

- Technetium-99m-labelled red blood cell scan has a high specificity and positive predictive value for hepatic haemangiomas but a negative test result does not indicate a diagnosis and therefore further imaging investigation is then required
- Hepatic haemangiomas occur in up to 7% of the population and are the most common benign tumour of the liver
- Some of these do not demonstrate the characteristic CT and ultrasound appearance and can be difficult to distinguish from other causes of a focal liver lesion
- An increase in delayed blood pool activity is typical of a haemangioma and this appearance is rarely seen with other causes of liver nodules
- The test has a limited sensitivity for the detection of small lesions and those located adjacent to the heart or major vessels
- The use of the test is decreasing as a negative scan excludes haemangioma but does not otherwise aid diagnosis

Image-guided Biopsy

- In the absence of risk factors, the role for biopsy in the diagnosis of hepatic incidentalomas is limited as the advances in dynamic imaging techniques are sensitive for diagnosing hepatocellular carcinoma (HCC) in most liver nodules
- The accuracy of percutaneous needle biopsy is around 90% but the risk of needle track tumour implantation following a biopsy of a hepatocellular carcinoma is 2.7% overall
- Thus needle tract seeding of tumour is a justifiable concern especially if such seeding could impact patient survival and also management options. There has been a more liberal approach for liver lesion biopsies in recent years unless transplantation is considered
- Other complications include intraperitoneal haemorrhage, haemobilia, pneumothorax, infection, bile leak, parenchymal bleeding and pericardial tamponade
- This underlines the importance of performing percutaneous needle biopsy only when absolutely necessary or when the information gained is likely to alter the management
- However, in individuals with risk factors for hepatocellular carcinoma
    - Lesions 2 cm) or,
    - Two imaging modalities (for lesions 1-2 cm) and / or,
    - Alpha-fetoprotein is raised, otherwise biopsy is recommended

◦ Image-guided fine needle aspiration (FNA) is able to distinguish benign from malignant lesion with high accuracy , but less accurate in providing a specific malignant diagnosis

References

Date of literature search: September 2015

The search methodology is available on request. Email

References are graded from Level I to V according to the Oxford Centre for Evidence-Based Medicine, Levels of Evidence. Download the document

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