

Diagnostic Imaging Pathways - Focal Liver Lesion (History of Malignancy)

Population Covered By The Guidance

This pathway provides guidance on the imaging of adult patients with a focal liver lesion and a history of previous malignancy. Is the lesion a metastasis?

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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

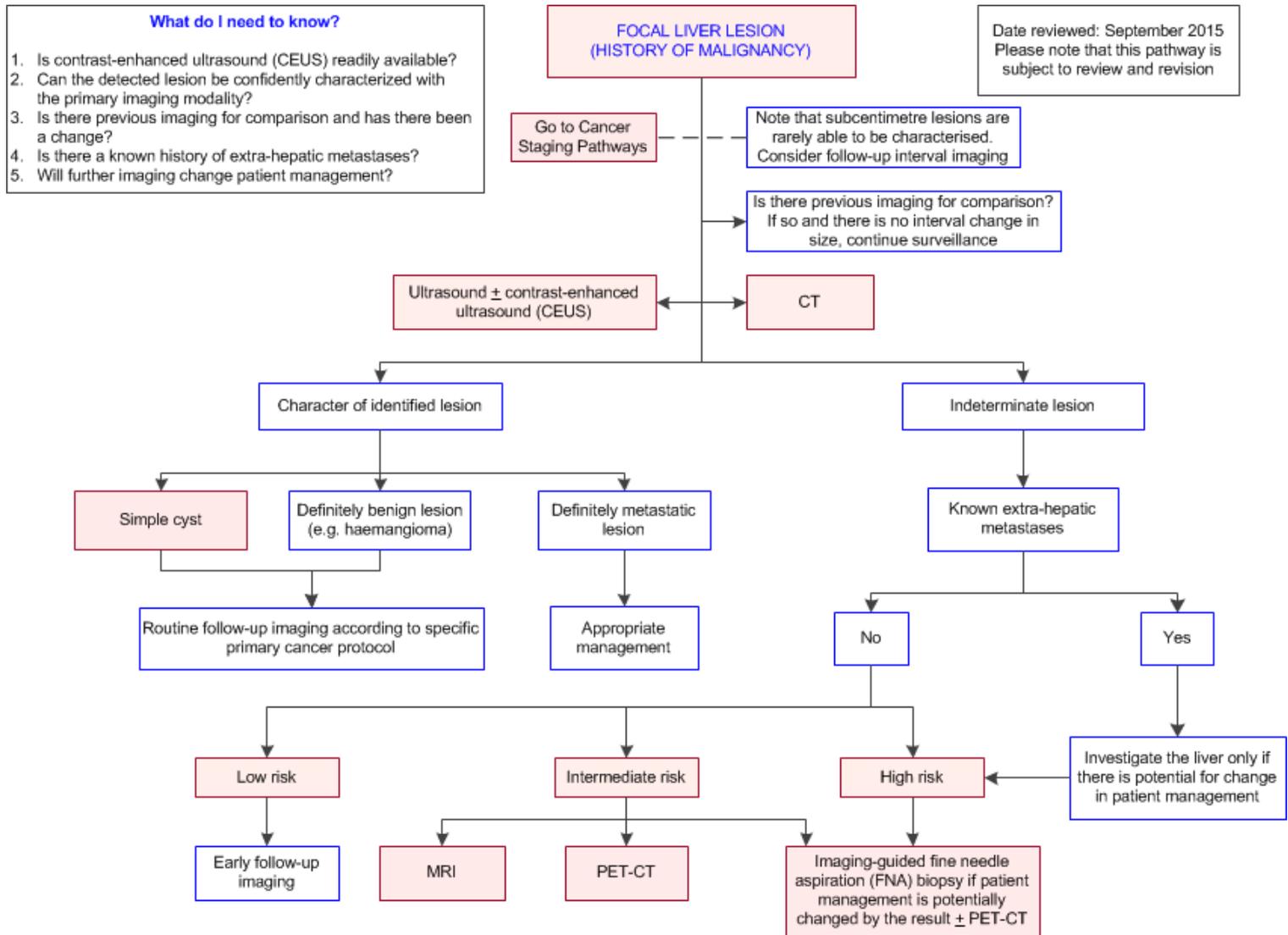
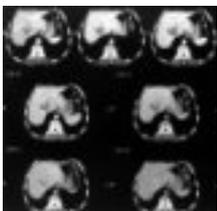


Image Gallery

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



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).

2b



2c

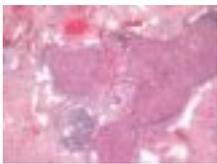


2d



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.

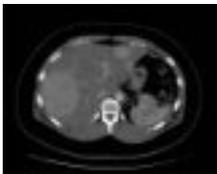
4a



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

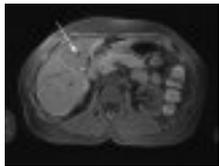
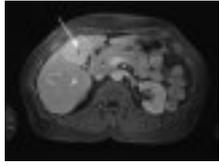


Image 6a, 6b, 6c and 6d (Magnetic Resonance Imaging): Gadolinium-enhanced T1-weighted MRI (Image 6a) demonstrates an ill-defined low-signal intensity mass in segment 4 of the liver with intense enhancement in the arterial phase (Image 6b). Minor enhancement persists in the portal venous phase (Image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

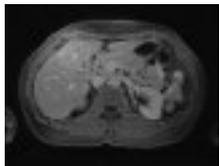
6b



6c



6d



7



Simple Hepatic Cyst

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

8a



Hepatocellular Carcinoma

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.

8b



8c

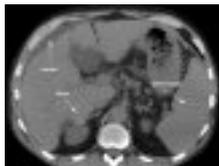
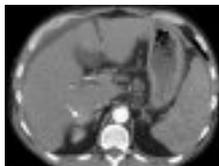
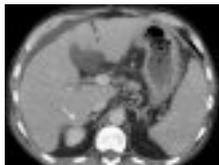


Image 8c, 8d, 8e and 8f (Triphasic Computed Tomography): CT of the same patient shows a cirrhotic liver with patent hepatic and portal veins as well as ascites. Within segment 6, there is a nodular area which demonstrates slight enhancement corresponding to the lesion identified on ultrasound (arrow).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

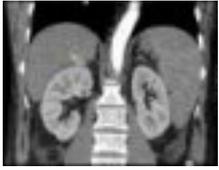
8d



8e



8f



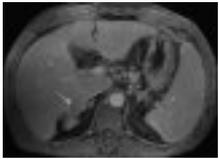
8g



8h



8i



8j

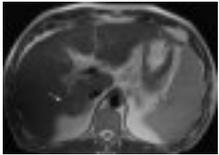


Image 8g, 8h, 8i and 8j (Magnetic Resonance Imaging): MRI of the same patient demonstrates a lesion measuring approximately 2.5 cm in diameter on the inferomedial aspect of segment 5 in a subcapsular location. This is bulging the capsule of the liver at the level of the upper pole of the right kidney. The lesion is essentially isointense to the rest of the liver on T1 weighted imaging (out of phase) but is slightly hyperintense on in-phase imaging suggesting that the rest of the liver has some fatty infiltration. The lesion is slightly hyperintense on first echo T2 but is not clearly visible on more heavily weighted T2 imaging. The lesion shows arterial enhancement but washes out in the portal venous phase, with the rim of the lesion remaining enhanced. The appearances are consistent with a hepatocellular carcinoma.

9a



Hepatocellular Carcinoma

Image 9a and 9b : Hepatectomy specimens showing a multifocal hepatocellular carcinoma with areas of necrosis and haemorrhage arising in a cirrhotic liver.

9b



9c



Image 9c (H&E, x2.5) and 9d (H&E, x10): Histological sections of a hepatocellular carcinoma arising on a background of cirrhosis. The usual lobular architecture is replaced by irregular and thickened trabeculae of malignant hepatocytes. There is mild nuclear pleomorphism.

9d



Teaching Points

- Ultrasound (US) can confidently diagnose simple cysts. 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
- CT scan is the usual first line investigation of metastatic disease, being of high sensitivity and able

- to perform widespread extra-hepatic imaging of the abdomen, pelvis and thorax
- 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
 - Gadoxetic acid-enhanced MRI is becoming the preferred contrast agent for liver MRI, having excellent sensitivity for metastases, showing a better performance than triple-phase MDCT for the detection of hepatic metastasis, especially for small (< 1 cm) lesions
 - 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
 - Image guided fine needle aspiration (FNA) biopsy is able to distinguish benign from malignant lesion with high accuracy, but less accurate in providing a specific malignant diagnosis

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
- Temporal relationship to the presentation of the primary cancer should be considered in assessing likelihood of metastasis

Computed Tomography (CT)

- CT scan is the usual first line investigation of metastatic disease, being of high sensitivity and able to perform widespread extra-hepatic imaging of the abdomen, pelvis and thorax. 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
- Depending on the primary tumour, hepatic metastases may be hypervascular (higher attenuation) or hypovascular (lower attenuation) relative to the surrounding liver. The latter are more common and are seen, for example, in colorectal cancer, most lung cancers and most breast cancers. Hypervascular metastases may be seen in malignant carcinoid, neuroendocrine cancers, melanoma, renal cell cancer, thyroid cancer and hepatocellular cancer
- CT with the administration of IV iodinated contrast is used to detect and characterize liver lesions. Images are commonly taken during the
 - Arterial phase (20-30 seconds after administration of contrast) - useful for identifying hypervascular lesions
 - Portal venous phase (70-80 seconds after administration of contrast) - often sufficient for hypovascular metastases
 - Non-contrast phase (3-10 minutes after administration of contrast) - useful for identifying hypervascular lesions
- Classical appearances of liver lesions, other than metastases, include [8](#)
 - Simple cysts (common) - homogeneously low attenuation content, avascular, smooth walls
 - Focal nodular hyperplasia (common) - usually homogeneous early enhancement becoming isoattenuating to liver on delayed phases, often with a central scar which may enhance late
 - Haemangiomas (common) - initial peripheral enhancement with subsequent delayed filling

of the lesion

- Adenomas (rare) - may contain fat, usually heterogeneous enhancement
- Hepatocellular carcinoma - usually appears as a discrete nodule that rapidly enhances (hyperattenuation) during the arterial phase, with washout (hypoattenuation) during the portal venous phase

Magnetic Resonance Imaging (MRI)

- CT scan is the usual first line investigation of metastatic disease, being of high sensitivity and able to perform widespread extra-hepatic imaging of the abdomen, pelvis and thorax. 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
- MRI is more likely to provide a definitive diagnosis than CT [9](#) and has an important role in the characterization of benign lesions [10](#)
- On a per lesion and per patient basis, MRI is the most accurate modality for evaluating colorectal liver metastases, [11](#) being more sensitive than CT [12](#) and having a slightly higher sensitivity to PET / CT [13](#)
- Usually breath-hold T1 and fast spin-echo T2 weighted images are used for the evaluation of a focal liver lesion gadolinium-enhanced dynamic MRI imaging improves the detection and 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
- However, 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 [14](#)
- A meta-analysis in 2012 showed MRI with a liver-specific gadolinium contrast agent to have high sensitivity and specificity for the detection of liver metastases, but the methodological quality of the analysed studies was only moderate [15](#)
- Gadoxetic acid-enhanced MRI is becoming the preferred contrast agent for liver MRI, having excellent sensitivity for metastases, [15](#) showing a better performance than triple-phase MDCT for the detection of hepatic metastasis, [16,17](#) especially for small (<1 cm) lesions [18](#)
- Gadoxetic acid is also useful for the differentiation of focal nodular hyperplasia (FNH) and hepatic adenoma (HA) [19,20](#)
- Classical appearances of liver lesions, other than metastases, include [8,10](#)
 - Simple cysts (common) - homogeneously low signal intensity content on T1 images and hyper-intense on T2 (increasing with the degree of T2 weighting); avascular, smooth walls
 - Focal nodular hyperplasia (common) - typically almost isointense to liver on non-enhanced T1 and T2 images, apart from hyper-intense central scar on T2; usually homogeneous early enhancement becoming isointense to liver on delayed phases, often with a central scar which may enhance late. Uptake of contrast on delayed phase with hepatobiliary contrast agents
 - Haemangiomas (common) - hypointense on T1, hyperintense on T2 (increasing with the degree of T2 weighting); initial peripheral enhancement with subsequent delayed filling of the lesion
 - Adenomas (rare) - may contain fat, usually heterogeneous enhancement

- Hepatocellular carcinoma - usually appears as a discrete nodule that rapidly enhances (hyperattenuation) during the arterial phase, with washout (hypoattenuation) during the portal venous phase
- Diffusion-weighted imaging (DWI) at MRI is particularly sensitive for the detection of metastases on a per-lesion basis. [21](#) However, on its own, without other MRI sequences, it is controversial whether DWI is reliable in distinguishing benign from malignant lesions. [10,22,23,24](#) In general, DWI should be combined with other MRI sequences for lesion characterization
- A combination of CE-MRI and DW-MRI can improve the diagnostic accuracy of magnetic resonance (MR) imaging. [25,26,27](#) Another study further confirms that DW-MRI can accurately detect hepatic metastases regardless of the lesion size. However, a further meta-analysis suggests that the capability of MRI may have been overestimated. [21,28](#) It has been suggested to perform DW-MRI by 3.0 T devices, which might have high specificity to identify liver metastases [27](#)

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
- PET-CT may be falsely negative in small lesions especially <1cm
- 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 a recent meta-analysis [13](#) of 1105 patients over 10 studies, comparing 18F-PET-CT and gadolinium-enhanced MRI, both modalities had excellent diagnostic performance for the detection of hepatic metastases (with MRI having a slightly better sensitivity). However, this meta-analysis included patients with a mixture of primary tumours
- A further meta-analysis, [29](#) focusing only on patients with colorectal cancers found that FDG PET/CT is highly accurate for the detection of liver metastases on a patient basis but less accurate on a lesion basis. Compared to MRI, PET is less sensitive but more specific and affects the management of about one-quarter of patients
- 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 [30,31](#)
- A further study in patients with neuroendocrine primary tumours also found PET-CT and MRI to be highly accurate [32](#)

Image-guided Fine Needle Aspiration (FNA) Biopsy

- Able to distinguish benign from malignant lesion with high accuracy, but less accurate in providing a specific malignant diagnosis [33](#)
- Information for consumers on [Image Guided Liver Biopsy](#)

Ultrasound (US) +/- Contrast-Enhanced Ultrasound (CEUS)

- US can confidently diagnose simple cysts. [1](#) For the detection of liver metastases unenhanced US has a high specificity but low sensitivity (mean sensitivity of 55%) [2](#), [3](#)
- 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
- 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 IV injection and durable enough to re-circulate for several minutes
- Ultrasound contrast agents are mainly based on the dynamic assessment of macro- and micro-vasculature 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
- The addition of contrast enhanced ultrasound (CEUS) has been found to improve the characterization of focal liver lesions [4,5,6](#) with enhancement patterns generally similar to CECT and CEMRI, and can be utilized in the presence of renal impairment
- CEUS 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 and the avoidance of further investigations
- For colorectal metastatic disease similar costs and effects for the detection of liver metastases were found to CT in one systematic analysis [7](#)
- However, it is acknowledged that CEUS is of limited availability in many countries

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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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