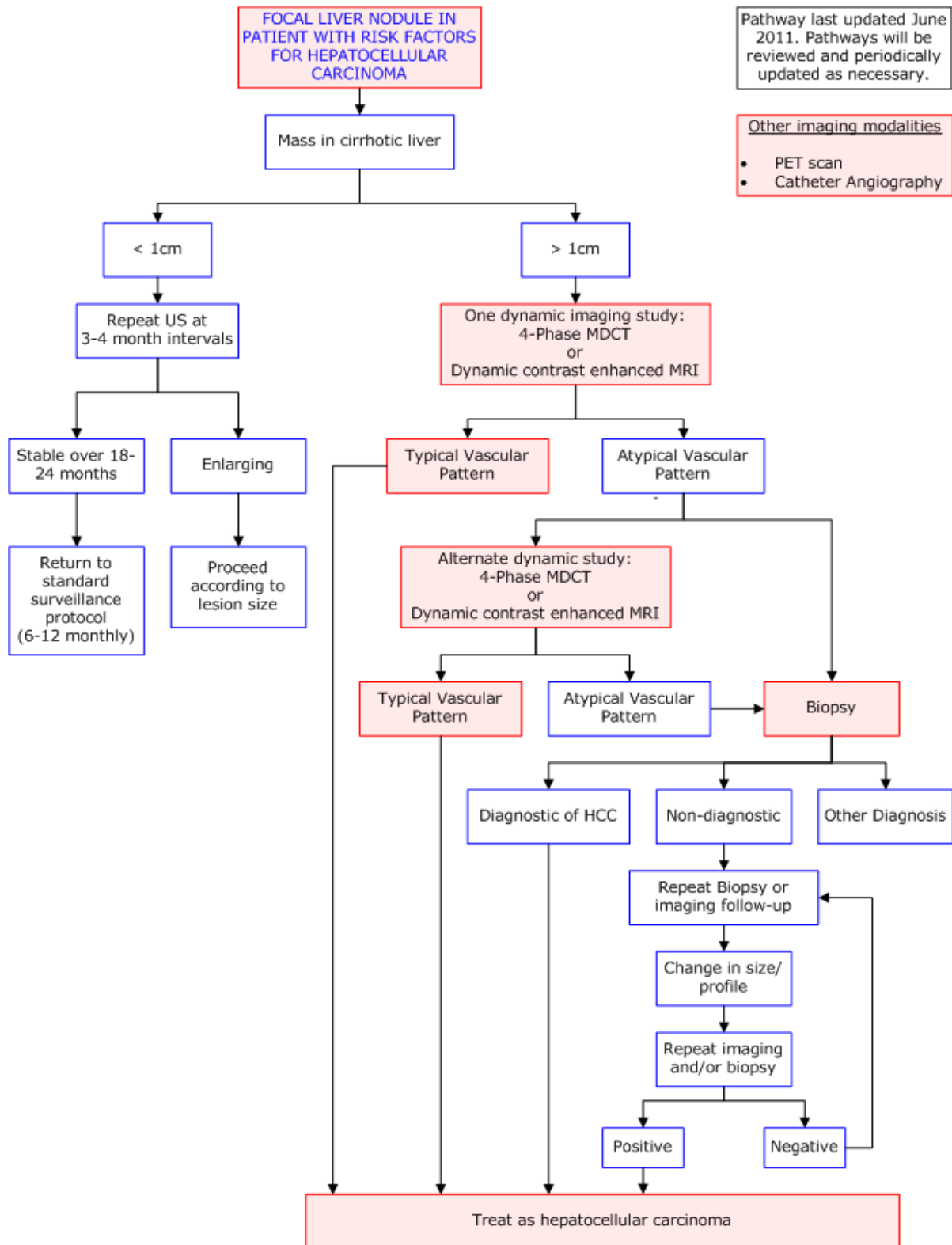




DIAGNOSTIC IMAGING PATHWAYS

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PATIENTS AT RISK FOR THE DEVELOPMENT OF HEPATOCELLULAR CARCINOMA

The following diagnostic criteria for HCC in patients with cirrhosis was developed by the American Association for the Study of Liver Diseases (AASLD). Regular surveillance using 6-12 monthly US without AFP has been recommended for the following groups as they are at significant risk for the development of hepatocellular carcinoma.¹

- Hepatitis B carriers
 - All cirrhotic hepatitis B carriers
 - Asian Males \geq 40 years
 - Asian Females \geq 50 years
 - Family History of HCC
 - Africans over the age 20
 - For non-cirrhotic hepatitis B carriers not listed above the risk of HCC varies depending on the severity of the underlying liver disease, and current and past hepatic inflammatory activity. Patients with high HBV DNA concentrations and those with ongoing hepatic inflammatory activity remain at risk for HCC.
- Non-Hepatitis B Cirrhosis
 - Hepatitis C
 - Alcoholic Cirrhosis
 - Genetic Haemochromatosis
 - Primary Biliary Cirrhosis
 - Although the following groups have an increased risk of HCC no recommendations for or against surveillance can be made because a lack of data precludes an assessment of whether surveillance would be beneficial
- The following conditions have a lower risk for the development of hepatocellular carcinoma:
 - Alpha1-antitrypsin deficiency
 - Non-alcoholic steatohepatitis
 - Autoimmune hepatitis

COMPUTED TOMOGRAPHY

- According to the recent AASLD guidelines (2010), nodules larger than 1 cm found on ultrasound screening of a cirrhotic liver should be investigated further with either 4-phase multidetector CT scan or dynamic contrast enhanced MRI. [32](#)
- 4-phase CT imaging consists of unenhanced, arterial, venous and delayed phases.
 - If the appearances are typical of HCC (described below), the lesion should be treated as HCC.
 - If the appearances are atypical, a second contrast enhanced study with the other imaging modality should be performed, or the lesion should be biopsied.
- These guidelines have been partially validated. [33,34](#)
- Classical appearances of different types of liver lesions include:
 - Haemangiomas: initial peripheral enhancement with subsequent delayed filling of the lesion. [2,3](#)
 - Metastases: Hypovascular metastases show low attenuation compared to surrounding liver during the portal venous phase.
 - Hepatocellular carcinoma: Usually appear as discrete nodules that rapidly enhance (hyperattenuation) during the arterial phase, with washout (hypoattenuation) during the portal venous phase. [4-6](#)

MAGNETIC RESONANCE IMAGING

- 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. [7,8](#)
- There is significant overlap between the MRI characteristics of various liver lesions. However, classical appearances include:
 - Haemangiomas: progressive centripetal enhancement after initial peripheral nodular hyperintense enhancement. [7](#)
 - Hepatocellular carcinoma: hyperintense on T1-weighted images, variable signal intensity on T2-weighted images, discrete capsule and rapid enhancement. [8](#)
- MRI has a better sensitivity and specificity than CT for the detection of hepatocellular carcinoma in patients with cirrhosis. [9](#)
- According to the recent AASLD guidelines (2010), nodules larger than 1 cm found on ultrasound screening of a cirrhotic liver should be investigated further with either 4-phase multidetector CT scan or dynamic contrast enhanced MRI. [32](#)
 - If the appearances are typical of HCC, the lesion should be treated as HCC.
 - If the appearances are atypical, a second contrast enhanced study with the other imaging modality should be performed (If the appearances are typical, the diagnosis is confirmed.), or the lesion should be biopsied.
 - These guidelines have been partially validated. [33,34](#)

TYPICAL VASCULAR PATTERN

- Arterial enhancement followed by washout is considered the typical vascular pattern of HCC. [32](#)
- This can be demonstrated on either 4-phase Multidetector CT or dynamic contrast enhanced MRI. During the arterial phase, HCC enhances more intensely than the surrounding liver while during the venous phase HCC enhances less than the surrounding liver (known as 'wash out'). During the delayed phase, the 'wash out' persists, sometimes the 'wash out' is only present during the delayed phase. [32](#)

BIOPSY

- Biopsy of a suspicious liver lesion can guide management where previous imaging is equivocal. Biopsy of liver lesions are usually performed percutaneously under imaging guidance (usually ultrasound) using either fine needle aspiration with cytological examination or needle core biopsy. The aim of biopsy is to acquire adequate sample tissue for accurate tissue diagnosis.
- The accuracy of ultrasound guided fine needle biopsy is around 90%, sensitivity ranges from 67-100% and specificity 80-100%. [14,36](#)
- If biopsy is negative for patients with HCC, the lesion should be followed by imaging at 3-6 monthly intervals until the nodule either disappears, enlarges, or displays diagnostic characteristics of HCC. If the lesion enlarges but remains atypical for HCC a repeat biopsy is recommended. [32](#)
- Biopsy is generally well tolerated, though there is a small risk of complications such as post-operative pain and haemorrhage. [15,36,37](#) The risk of major complications requiring surgery is 0.05%, and less than 0.01% risk of mortality.
- There is also a risk of seeding of tumour cells along the needle tract. Months to years post-biopsy, a parietal tumour can present affecting soft tissue, skin or peritoneum. The risk is small and is thought to vary depending on the size & type of needle used, the number of

passes made and the amount of normal parenchyma traversed by the needle. [15,36](#) Interestingly, several groups have reported 0% incidences of seeding. Chang et al reported no seeding in 433 patients who had ultrasound guided biopsy using a tru-cut biopsy needle. [15](#) Maturen et al. used a coaxial cutting needle technique for biopsy of suspected HCC and reported 0% seeding in 101 patients who were positive for HCC and had adequate follow up (mean 14 months). [38](#)

- A meta-analysis by Silva et al, found the incidence of needle tract seeding to be 2.7% overall or 0.9% per year (26 with seeding out of 1340 total patients). The median time to seeding was 17 months. [35](#)
- In most cases, the treatment of parietal seeding is local surgical excision, which can provide lengthy recurrence-free survival. Potential transplantation is not a contraindication for percutaneous liver biopsy. [37](#)

POSITRON EMISSION TOMOGRAPHY (PET)

- Malignant cells characteristically have increased metabolism compared to normal cells, and may be reflected by areas of increased activity on PET scanning. [10](#)
- Increased uptake is seen in around 50-70% of patients with hepatocellular carcinoma. In these patients PET imaging may help assess tumor differentiation and may be a useful test in conjunction with CT for staging. [10,11](#)
- Higher sensitivity compared to CT, MR and US for detection of hepatic metastases from cancers of the colon, rectum, stomach, and oesophagus. [12,13](#)

ANGIOGRAPHY

- Largely replaced by newer non-invasive imaging techniques, but still has a role in portal vein embolisation, therapeutic chemoembolisation, and transarterial catheter embolisation of the feeding branch from the hepatic artery. [4](#)

STAGING OF HEPATOCELLULAR CARCINOMA

- Several staging methods for hepatocellular carcinoma exist, and as yet no consensus has been reached.
- The Barcelona-Clinic Liver Cancer (BCLC) staging system was shown to most accurately reflect survival distribution and is the only method that guides treatment according to cancer stage. [30](#)
- The BCLC staging system is tabulated below: [31](#)

STAGE	DESCRIPTION
Stage A (Early HCC) · A1 · A2 · A3 · A4	Single tumours with no evidence of portal hypertension and normal bilirubin. Single tumours associated with portal hypertension and normal bilirubin. Single tumours with portal hypertension and raised bilirubin. Three tumours smaller than 3cm regardless of liver function.
Stage B (Intermediate HCC)	Includes patients with asymptomatic multinodular tumours without vascular invasion or extra-hepatic spread.
Stage C (Advanced HCC)	Includes patients with either symptomatic tumours or constitutional syndrome, or with invasive tumours (either vascular or extrahepatic spread).
Stage D (End-Stage HCC)	Includes patients with severe cancer related symptoms and a deteriorated performance status, in the setting of very advanced liver impairment.

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