

## EDITORIAL

# Detecting and characterising small liver tumours

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### Abstract

The successful treatment of liver tumours is more likely if they are found early. The use of high-resolution CT and MRI with contrast enhancement allows more sub-centimetre liver lesions to be detected, but some small tumours remain occult even at surgery with intra-operative sonography. An indication of the accuracy of imaging in detecting liver metastases may be given by the proportion of lesions found which are under 1–2 cm in size. The characterisation of small lesions remains problematic on CT, with benign and malignant tumours showing overlapping imaging features. However, with appropriate use of chemical shift, heavy T2 weighting, gadolinium enhancement, and liver-specific contrast agents, a carefully tailored MRI examination will usually produce diagnostic appearances.

**Keywords:** *Liver; metastasis; diagnosis; MRI.*

### Introduction

All tumours start out small, and treatment is more effective if the disease is detected early; thus the current focus of imaging is to improve our ability to recognise small lesions. With colorectal liver metastases, careful MRI or CT will detect 95% or more of lesions larger than about 15 mm, and it is now uncommon for our surgeons to discover lesions at the time of operation that were not already detected by earlier imaging. The real issue now is the accuracy of detection for lesions smaller than this. The addition of intra-operative ultrasound (IOUS) has improved our ability to find small tumours, but in a current study in my own department, 20% of patients undergoing liver resection assisted by IOUS were found to have 'new' metastases on follow-up within 6 months. Surgical findings at laparotomy, even with IOUS, no longer represent an adequate suitable standard of reference for measuring the accuracy of imaging. One possible approach would be to look at the distribution of sizes amongst the lesions detected. A recent study<sup>[1]</sup> found that almost 60% of colorectal liver metastases were smaller than 20 mm at the time of detection, and 30% were smaller than

10 mm. If we can detect more lesions in this size range we can be confident that our imaging techniques are improving.

Once we have found a small lesion, we need to determine whether it is benign or malignant. Small (<15 mm) lesions discovered incidentally in patients with no known primary malignancy are virtually always benign<sup>[2,3]</sup>, but in patients with known malignant disease there are some metastases with CT appearances which overlap with those of benign lesions<sup>[4]</sup>. Larger benign lesions are less problematic on CT, but at all sizes the MR appearances are more characteristic<sup>[5]</sup>.

### Liver cysts

Simple cysts are round unless deformed by more rigid adjacent structures. Their contents are anechoic on US, show water attenuation on CT, low signal on T1 MRI and high signal on T2 which is maintained on heavily T2-weighted sequences. They are unchanged after gadolinium—an enhancing rim suggests necrotic metastasis, or in the appropriate clinical context, abscess.

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## Haemangiomas

Characteristically, haemangiomas are hyper-echoic on sonography, show geographic shape with low attenuation on unenhanced CT and on T1-weighted MRI. Their high signal on conventional T2-weighted MRI is maintained with more heavy T2 weighting (TE = 180 ms, or HASTE). With contrast-enhanced CT or gadolinium-enhanced MRI, the lesions show nodular enhancement at the periphery, followed by centripetal infilling over the next 5–10 min. The discontinuity of the peripheral nodular enhancement is a specific feature, and peripheral wash-out does not occur. In contrast, metastases with necrotic centres are usually round in shape and although they may show peripheral enhancement, the ring is more uniform. Whilst delayed enhancement of the necrotic centre of metastases is not uncommon, the brightly enhancing peripheral ring fades fairly rapidly. Some small haemangiomas show uniform and rapid enhancement starting in the arterial phase, similar to small hepatocellular lesions, but they usually show intensely bright signal on T2-weighted MRI, in contrast to the iso-intense or mildly hyper-intense appearance of small benign hepatocellular lesions. Other atypical haemangiomas include small lesions with centrifugal enhancement from a single vascular nodule (central dot sign) and in other cases the lesion may be predominantly fibrous, so enhancement is patchy and delayed, with little of the typical peripheral nodular vascularity.

## Fatty change

Fatty infiltration is often heterogeneous, sometimes focal, and in other cases small focal areas of liver parenchyma may be spared from fatty change. On sonography, either focal fatty change or focal sparing can produce lesions which are difficult to distinguish from metastases. One helpful feature with focal fatty change or sparing is that there is usually no mass effect—vessels run normally through the apparently abnormal areas. Focal fat may be recognisable on CT by its geographic distribution, normal contrast enhancement, and the lack of a mass effect, but a more reliable diagnosis can be made on MRI. In patients with diffuse fatty change, metastases may be obscured on CT because their low attenuation is matched by the low attenuation of the surrounding liver. Occasionally, a ring of liver tissue immediately surrounding the lesion may be spared from fatty change, producing an irregular halo of denser tissue within an otherwise homogeneous liver. This appearance can be seen with haemangiomas in a fatty liver, as well as with metastases. Using in-phase and opposed-phase T1 sequences, MRI offers a rapid and reliable approach for the recognition of focal fat, and reveals metastatic lesions in the diffusely fatty liver. Where any diagnostic doubt remains, liver specific contrast agents may be given.

## Focal nodular hyperplasia (FNH)

With the widespread use of dual-phase CT, multi-phase contrast-enhanced MR, and the recent introduction of vascular contrast agents in sonography, has come a realisation that FNH is not rare. Larger lesions typically show a rounded or lobulated shape with clear-cut margin, a mass effect displacing adjacent vessels, and a central scar sometimes with radiating spokes towards the periphery. Their echogenicity, attenuation and signal characteristics are little different to those of normal liver tissue. The lesions show marked arterial phase contrast enhancement which usually fades rapidly to become iso-intense in the portal phase, although occasionally increased enhancement lasts for several minutes. Delayed enhancement of the central scar is characteristic. Lesions smaller than about 2 cm are often homogeneous with no central scar, but show the same enhancement characteristics. It is not rare for these small lesions to be multiple, and they may co-exist with other benign lesions. When found in patients with known malignancy, a confident diagnosis of FNH requires the demonstration of intact liver function within the lesion. The most effective method is to use superparamagnetic iron oxide (SPIO) enhancement. Some FNH lesions will take up as much SPIO as normal liver, so the lesion appears black on the post-contrast T2-weighted images. In other cases the lesion may take up some SPIO, but less than the surrounding liver, so that the lesion becomes more apparent after contrast. In these cases it is important to use the same T2-weighted sequence before and after SPIO, and measure the change in signal intensity in both liver and lesion. If the lesion shows substantial SPIO uptake (more than 40–50% reduction in signal), it may be regarded as benign. Metastases do not take up SPIO, but well differentiated hepatocellular cancers may take up a little. Another approach is to use one of the hepatocellular MR contrast agents (mangafodipir, gadobenate, or gadoxetic acid). All of these agents are taken up by the functioning hepatocytes present in FNH lesions (and also in well differentiated HCC), but because there is no biliary excretory pathway, the lesions retain the contrast for much longer than the normal liver, so becoming brighter than liver on delayed T1-weighted images.

## Focal perfusion artefacts

Peripheral wedge-shaped areas of abnormal perfusion, usually seen only in the arterial dominant phases of enhanced CT and MRI, are probably caused by segmental portal vein occlusion which in some cases is associated with parenchymal tumour deposits, but in other cases no cause can be found. Such transient hepatic attenuation defects (THADs) may also be associated with parenchymal oedema within the liver which appears hyper-intense on

T2-weighted MRI. Around the periphery of segment 4, particularly just to the right of the falciform ligament anteriorly, and also anterior to the bifurcation of the portal vein, small areas of liver parenchyma may receive non-portal venous supply from the parabiliary venous plexus and from anomalous drainage of gastric, duodenal and pancreatic veins. This can produce small nodules of focal fatty change in these areas, or more commonly may result in small areas of altered enhancement after contrast.

### Other benign malformations

Biliary microhamartomas (von Meyenburg complexes) show imaging characteristics which overlap between cysts and haemangiomas. These biliary malformations are often irregular or even angular in shape, and usually only a few millimetres in diameter.

### Conclusions and key points

Incidental small benign lesions are relatively common in patients with malignant disease, and must be distinguished from metastatic disease in order to avoid erroneous management.

Focal fat, focal sparing and haemangiomas may be diagnosed on sonography or CT if they are typical, but in other cases MRI is usually decisive. FNH can be diagnosed with confidence using liver-specific MR contrast agents. Discriminating small cysts and haemangiomas from metastases is best done with MRI using a heavily T2-weighted sequence followed by dynamic gadolinium-enhanced T1. Tiny lesions which appear on CT to have an angular shape and low attenuation will usually be biliary microhamartomas.

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