

How to characterise the incidental liver lesion

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Abstract

The widespread use of imaging techniques for abdominal investigation has led to an increased detection of the so-called 'incidental liver lesion'. This article gives an overview of the major categories of hepatic nodules that may be encountered in this clinical scenario. In addition, the article describes the different imaging techniques and diagnostic strategy that can be used to identify these nodules, with an emphasis on cross-sectional techniques. The difficulty in characterising small-sized nodules using cross-sectional imaging techniques is also addressed.

Introduction

The term 'incidental liver lesion' refers to the fortuitous detection of a focal nodule in an asymptomatic patient. The widespread use of imaging modalities for liver investigation, particularly ultrasound (US), has led to an increased detection of focal liver lesions, which may prompt further assessment for malignancy and avoid unnecessary invasive procedures. Today, spiral computed tomography (CT) and magnetic resonance imaging (MRI) play a major role in these evaluations, using state-of-the-art techniques and dedicated contrast agents. By using these imaging techniques, the use of guided biopsies is limited to cases where malignancy cannot be excluded by imaging alone.

The aim of this article is to review the imaging characteristics of liver lesions detected most frequently in daily clinical practice using cross-sectional imaging techniques, and to assess the role of these imaging techniques as predictors of the benign or malignant nature of these lesions. A simplified flow chart for the study of the incidental liver lesion is given in Figure 1.

Simple biliary cysts

Simple biliary cysts are common among the general population, and are considered to be of developmental origin.¹ Ultrasound is the best imaging method for characterising these purely cystic liver lesions, and shows the following features:

- Well-defined homogeneous cystic component
- Posterior acoustic enhancement
- Absence of a Doppler signal

The demonstration of internal or mural solid components precludes the diagnosis of a simple biliary cyst and justifies further imaging investigations.^{2,3} In these cases, the differential diagnosis should include cystic malignant tumours, such as the rare cystadenocarcinoma, a cystic metastasis or a cystic hydatid lesion (type 1). When the criteria for an ultrasonographic diagnosis of a simple cyst are not fulfilled, a spiral CT should be performed.

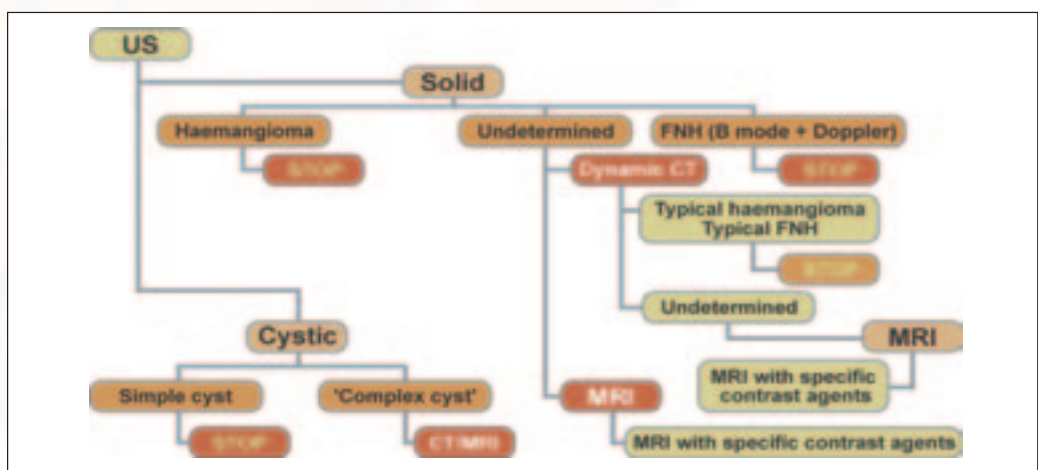
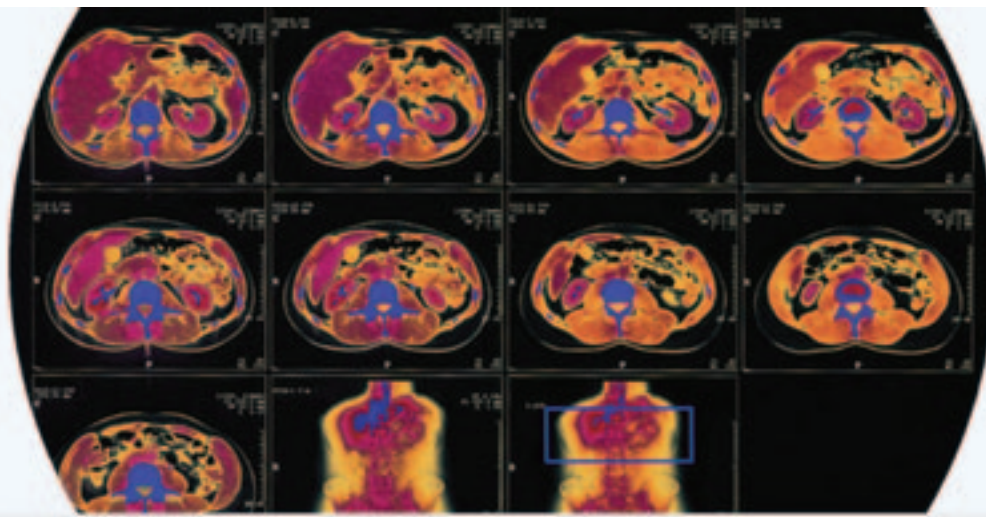


Figure 1. Simplified flow chart of imaging techniques commonly used to study the incidental liver lesion. MRI plays an increasing role in the characterisation of solid lesions encountered on US or CT images



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Detection of peripheral calcification, a thickened wall (1–2 mm) and absence of contrast enhancement favours a cystic hydatid lesion (Figure 2).⁴ A thickened, irregular, enhancing wall – as well as internal septa and heterogeneity – favours a cystic neoplasm.²⁵

Difficulties with diagnosis can arise in cases of: small-sized lesions (< 1 cm); hypervascular behaviour after contrast enhancement (the 'flash-filling haemangioma'); or in cases of absent or delayed fill-in pattern.^{8,9} There are clear advantages of MRI over CT

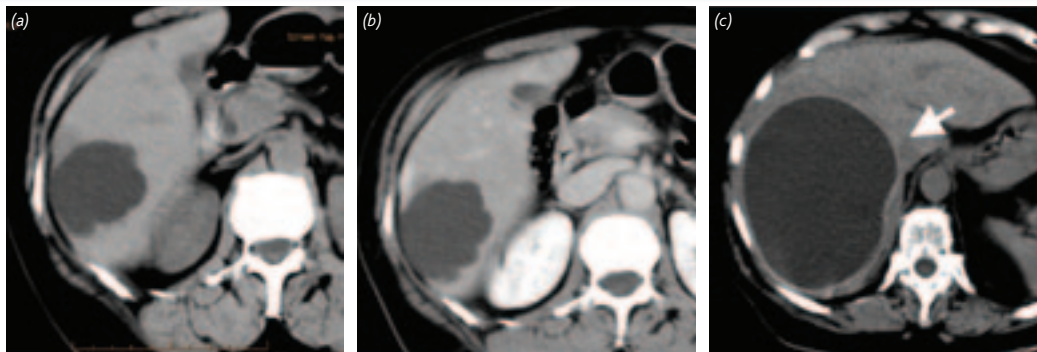


Figure 2. Differential diagnosis of cystic lesions by CT. (a) and (b) Simple biliary liver cyst with the absence of a definite wall and lack of enhancement. (c) Type I hydatid cyst showing subtle calcifications within the peripheral wall (arrow)

Haemangioma

Haemangiomas are one of the most frequently discovered benign tumours observed using cross-sectional techniques. This liver lesion is a pseudo-tumour composed of blood-filled spaces, and it displays characteristic ultrasonographic features:

- Well-defined, homogeneous, hyperechoic lesion
- Posterior acoustic enhancement
- No signal on colour-coded Doppler⁶

In cases where the US findings are not diagnostic, or where doubts persist (especially in oncological patients), CT with iodinated contrast media injection is necessary to assess tumour vascularity and provides diagnostic tumour enhancement showing:

- A lesion hypodense to the liver before the injection of iodinated contrast media (similar to that of vessels)
- Patchy globular enhancement in the early phase of contrast media administration (arterial phase) beginning at the periphery of the tumour
- Progressive centripetal fill-in
- Persistent enhancement on delayed imaging (Figure 3)⁷

since MRI combines static and dynamic imaging features. Characteristics of a haemangioma imaged by MRI include:

- A homogeneous, well-defined lesion, with lobulated contours
- Hypointensity on T1-weighted images
- Strong hyperintensity on heavily T2-weighted images
- Typical filling pattern with dynamic imaging, observed after intravenous administration of gadolinium chelates

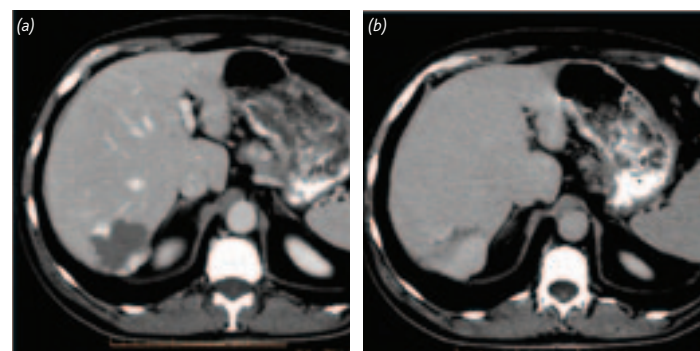


Figure 3. Haemokinetics of liver haemangioma by dynamic CT. (a) The hypodense lesion on the right liver lobe shows peripheral enhancement at the early phase of this study with (b) subsequent hyperdensity (retention) in the late phase

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It is unusual for a haemangioma to display atypical features with MRI, and this happens much less frequently than with CT or US examinations. It is only in such rare cases that image-guided, fine needle biopsy may be required. In spite of early safety concerns, the technique is considered to be safe and accurate.¹⁰

If any of these features are lacking from the ultrasound study (particularly the vascularised central scar), alternative imaging modalities are required for diagnosis. Dynamic CT or MRI can assess the haemokinetics of FNH. With CT, the major features of FNH are:

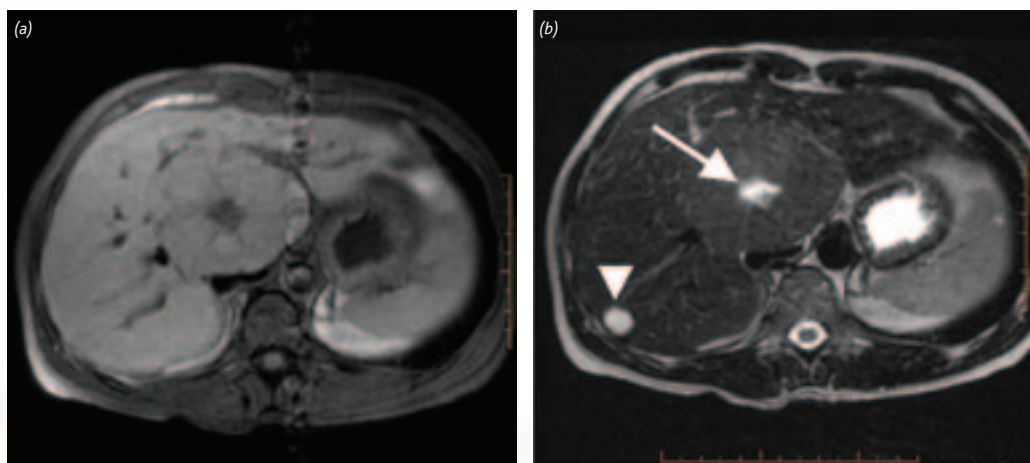


Figure 4. Focal nodular hyperplasia in a young woman. The tumour is isointense with the normal liver parenchyma except for the central scar (long arrow) which is (a) hypointense on the T1-weighted MRI image and (b) bright on the T2-weighted image. Incidentally there is a bright lesion on the right liver lobe corresponding to a small haemangioma (short arrow)

Focal nodular hyperplasia

Focal nodular hyperplasia (FNH) is a benign tumour-like lesion (containing a highly vascularised central scar), which occurs predominantly in young females.¹¹ This lesion has no malignant potential, and complications are also exceedingly rare. Therefore, adequate diagnosis by non-invasive imaging techniques avoids unjustified surgical resection. However, FNH lesions share some imaging features with other primary liver tumours including some of malignant origin (e.g. adenoma, hepatocellular carcinoma), and thus a diagnosis of FNH must be unequivocal.¹²⁻¹⁴ An accurate diagnosis of FNH can be made from an ultrasound study showing:

- A homogeneous, solid lesion of variable echogenicity
- Absence of a peripheral hypoechoic rim (capsule)
- Hyperechoic or hypoechoic central scar, displaying arterial vessels within the central scar on colour-coded Doppler^{12,15}

- Solid, generally isodense nodule on plain scans
- Vigorous and transient (seconds) enhancement on dynamic CT during the arterial phase
- Hypodense central scar on pre-contrast and early post-contrast images
- Isodense or hyperdense scar on late-phase imaging
- Absence of peripheral rim enhancement¹³

Findings with dynamic MRI are similar to those with dynamic CT, but further characterisation of the lesion can be provided by analysis of plain images.¹⁴ Since the FNH nodule is composed of normal hepatocytes, it is expected to be isointense compared with the normal liver parenchyma on both the T1- and T2-weighted images, except for the central scar that remains hypointense or hyperintense, respectively (Figure 4). These features can rapidly distinguish FNH from other focal liver lesions. Another diagnostic feature of FNH derives from the fact that it contains functional Kupffer cells (specialised hepatic macrophages).



Therefore, using MRI with large iron oxide particles as a specific contrast agent, phagocytosis can be assessed in both the tumour and normal liver parenchyma. In the past decade, a variety of specific contrast agents for labelling different physiological processes within normal hepatocytes have been developed and are available for clinical use.

If any of the features of FNH are lacking from CT or MRI images, a confident diagnosis is precluded and patients must undergo a more invasive diagnostic procedure, preferably a surgical biopsy. Image-guided percutaneous biopsies can be inconclusive since they may not represent the overall histology of the tumour. Surgical removal remains the treatment of choice in the case of an atypical diagnosis of FNH.

complications. However, differential diagnosis of a hepatic adenoma should not be performed by imaging methods alone since the tumour should always be surgically removed.¹⁸

The 'sub-centimetre' liver lesion

Current imaging technology allows increased spatial resolution of liver images, especially due to the routine use of fast imaging protocols and thinner slice collimations with CT and MRI. However, with increased resolution has come an increased detection of small nodules: 17% of patients with or without known previous malignancies may display small liver nodules – ≤ 15 mm in diameter – which are difficult or even impossible to characterise adequately.¹⁹ The majority of these small lesions are benign, such as tiny biliary cysts

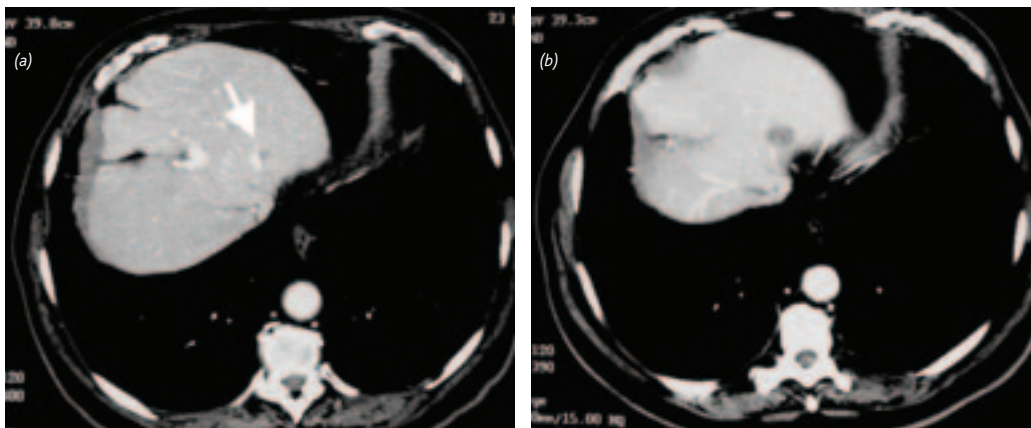
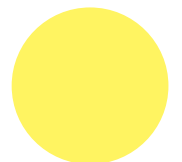


Figure 5. Sub-centimetre lesion showing interval growth. This patient was screened for metastases from a colorectal cancer. (a) A tiny hypodense nodule is indicated by the arrow. (b) Characterisation was not possible, but a control CT scan performed 4 months later showed clear enlargement. The final diagnosis was a hepatic metastasis

Hepatic adenoma

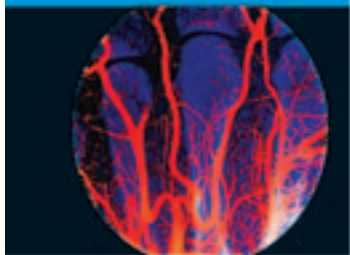
A hepatic adenoma is a benign tumour of hepatocellular origin and is exceedingly rare compared with the previously described lesions. They are generally related to long-term use of contraceptive pills or the use of sex steroids. The hepatic adenoma has a high propensity to bleed and may undergo malignant transformation.^{16,17} Imaging methods are helpful in the differentiation of hepatic adenomas from other hepatic lesions such as FNH, and for analysing its haemorrhagic

or biliary hamartomas, but they can also be malignant. High-resolution, state-of-the-art US techniques can be diagnostic for sub-centimetre cystic nodules,²⁰ but small solid nodules are generally invisible in most US examinations. The small solid nodules are being increasingly recognised in good-quality spiral CT studies. The majority of these nodules are not reliably characterised simply based on attenuation coefficient measurements, despite reduced slice thickness and reduced partial volume effects.



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Consequently, since confidence criteria for differentiation between benign and malignant lesions are not based on the visual inspection of images, it is advisable to obtain a new control examination after about 3–4 months. Any intervening growth may justify the use of another diagnostic procedure, such as an image-guided percutaneous biopsy (Figure 5).

The case for contrast media administration

As mentioned previously, most CT and MRI examinations, to characterise the focal liver lesion, are regularly performed with the intravenous administration of extracellular, non-specific contrast agents such as iodinated compounds or gadolinium chelates, respectively. However, in the past decade, new, specific contrast agents for use with MRI have emerged, to further the study of focal liver lesions. These specific agents can be classified according to their dominant effect in T1- or T2-weighted imaging:

- T1-enhancers
 - Mn-DPDP (Teslascan™)
 - Gd-BOPTA (Multihance™)
 - Gd-EOB-DTPA (Eovist™)
- T2-enhancers
 - iron oxide particles (Endorem™)
 - iron oxide particles (Resovist™)

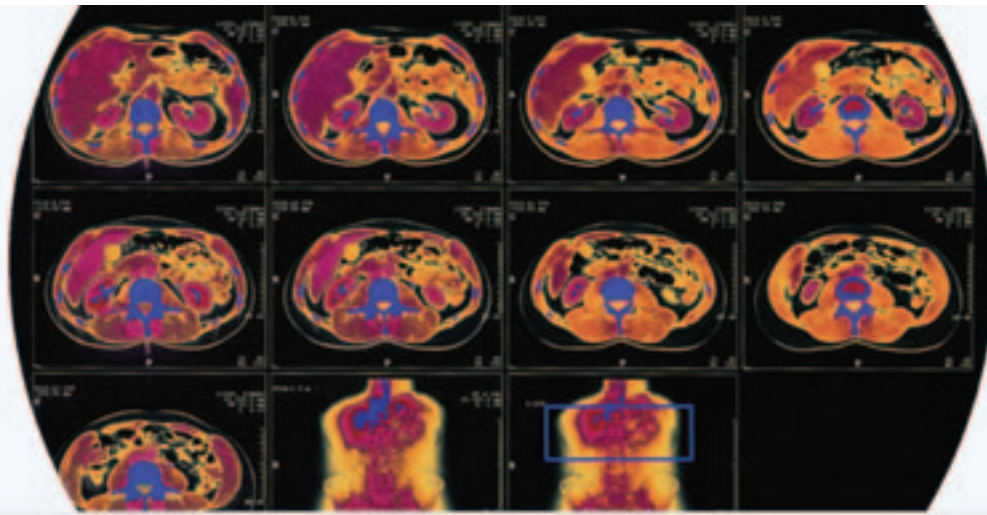
The choice of second-line, 'problem-solving', liver-specific, MRI contrast agent should be based on

the findings of clinical and plain MRI, however previous experience and expected patient cooperation may also play an important role. The broad current indications for T1 and T2 agents are to:

- Increase the sensitivity of MRI for the detection of malignant, focal liver lesions, especially metastases
- Reduce the false-positive rate for malignancy, as seen with plain MRI and other imaging techniques
- Distinguish between focal liver lesions of hepatocellular origin (enhancers) and non-hepatocellular origin (non-enhancers)

Conclusions

Current imaging techniques can accurately characterise incidental liver lesions in a non-invasive fashion. Ultrasound is used as a primary screening modality, but in several instances, CT or MRI act as the 'problem-solving' technique. Magnetic resonance imaging is superior to helical CT for focal liver lesion characterisation as a result of its high intrinsic contrast resolution and potential use of different types of contrast agents, both specific and non-specific. Sub-centimetre nodules continue to be a diagnostic dilemma demanding a close-imaging examination, which depends largely on the clinical situation of the patient.



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