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KEYNOTE LECTURE

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Critical questions in the imaging of colorectal hepatic metastases

Dow-Mu Koh[a] and Jonathan Berry[b]

[a]*Department of Radiology, Royal Marsden NHS Foundation Trust, UK;*
[b]*Department of Radiology, North Cumbria Acute Hospital NHS Trust, UK*

Corresponding address: Dr D.M. Koh, Department of Radiology, Royal Marsden Hospital, Downs Road, Sutton, SM2 5PT, UK.
Email: dowmukoh@icr.ac.uk

Abstract

Aggressive treatment of patients with colorectal liver metastases can improve treatment outcome. In this paper, we review current management of patients with colorectal liver metastases and discuss the critical questions that the radiologist should consider when reviewing the imaging of these patients, so as to provide information that is important for formulating treatment strategies by the multidisciplinary management team.

Keywords: *Colorectal cancer; liver; metastases; CT; MR; PET.*

Introduction

Up to 70% of patients with colorectal cancer will develop liver metastases[1] and of those who have metastatic disease, about one-third will be confined to the liver[2]. Despite the presence of metastatic disease, patients with liver disease that can be surgically managed have a better long term survival compared with those with irresectable disease[3]. Effective treatment of colorectal hepatic metastases is therefore integral to improving outcomes and reducing mortality.

With no treatment, the prognosis for patients with liver metatases is poor with studies[4] indicating median survival of 6–9 months. In the past, patients with hepatic metastases received only palliative treatment. However, developments in chemotherapy, surgery and minimally invasive therapies have led to more aggressive treatment options. Increasingly, neoadjuvant chemotherapy is used to downsize the number and size of hepatic metastases, which can result in sufficient tumour regression that up to one-third of patients with irresectable liver disease at the outset are rendered resectable[5,6]. Whilst surgical treatment of liver metastases is expensive, analysis of cost per life-year gained demonstrates it to be a cost effective option long term[7].

Current management of colorectal liver metastases

Whilst medical history, clinical examination and laboratory tests all play a part, it is the imaging modalities of ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET)-CT, either alone or in combination, that are used to diagnose and evaluate liver metastases. Liver metastases can present at the time of diagnosis of the primary tumour (synchronous metastases, which carry a worst prognosis) or during follow-up after treatment of the primary tumour (metachronous metastases). Suspicion of metachronous disease may be prompted by abnormal liver function tests or elevated carcinoembryonic antigen (CEA).

Chemotherapy

Once a metastasis is diagnosed, the disease extent is defined using imaging and chemotherapy (either neoadjuvant or palliative) is usually offered in the absence of contraindications. Standard combination chemotherapy regimes for metastatic colorectal cancer include FOLFOX (folinic acid, fluorouracil and oxaliplatin)

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and FOLFIRI (folinic acid, fluorouracil and irinotecan) to which an anti-angiogenic monoclonal anti-body Bevacizumab (Avastin®) is often added.

Surgical management

The criteria for eligibility for resection of hepatic metastases have evolved over time and although there continues to be variation between centres, there is now consensus in opinion, if not in detail but in the broad principles, which guide surgical resection[8]. In the past, criteria for resectability have varied between centres and included, for example, having at least a 1 cm margin of normal hepatic parenchyma around each lesion[9]. It is now widely regarded that the absolute number, size and location of metastases are less important for the success of surgery than the volume of functional residual liver.

Previously, the presence of metastatic disease outside of the liver was an absolute contra-indication to liver resection. This is no longer the case with many specialist centres now willing to resect or ablate, for example, lung metastasis[10]. The surgical decision may be influenced by the characteristics of the primary tumour and local lymph node status, since these also have a bearing on long term disease free survival. When all factors are considered, only a relatively small percentage of patients with liver metastases are suitable for liver resection[11]. Even so, a significant number of patients who meet the criteria for liver resection do not undergo surgery.

Patients whose burden of hepatic metastases is considered resectable are now offered neo-adjuvant chemotherapy prior to surgery. Recent data from the European Organisation for Research and Treatment of Cancer (EORTC) study has demonstrated that the progression free survival following liver metastases resection is improved by using such a regime[12]. Following neoadjuvant chemotherapy, it is usual to re-image the liver to assess for improvement in disease status prior to surgery.

Local therapy

The role of local therapy in the management of colorectal hepatic metastases continues to evolve. At present, patients considered for local therapy include those with co-morbidity preventing hepatic resection, those who decline surgery and patients whose metastases have been downsized by chemotherapy but remain unsuitable for resection[13]. Local therapies such as radio-frequency thermal ablation (RFA) and chemoembolization may also be combined with liver resection. There is some evidence that combining treatment modalities can be more effective for disease control[14]. Using such a paradigm, suitable lesions are resected and the remaining lesions are subject to local therapy.

Detecting disease relapse

Despite advances in the treatment of colorectal liver metastases, the recurrence rate remains high (60%). When disease recurs, only a minority will be confined to the liver, and as such suitable for repeat resection[15]. In patients who develop recurrent disease, approximately 90% will do so within the first 2 years after resection[16]. Following surgery, there is data to support the continuation of adjuvant chemotherapy with a demonstrable improvement in 5-year survival[17].

Given the high rate of disease recurrence after resection of liver metastases and the potential to offer further treatment should recurrence occur, a careful follow-up program is required. A variety of follow-up schedules have been investigated and current evidence suggests optimal follow up should include both measurement of tumour markers (e.g. carcinoembryonic antigen and carbohydrate antigen 19.9) and contrast-enhanced CT of the thorax, abdomen and pelvis, with the combination able to detect significantly more recurrence than either modality alone[18]. The length of time after surgery for colorectal cancer during which follow up should be continued and the optimal interval between follow up appointments is still being investigated. This is the subject of the Follow-up After Colorectal Surgery Trial (FACS Trial) recruitment into which is due to end in December 2008.

Critical questions in the imaging of colorectal liver metastases

Contrast-enhanced CT is the most widely used imaging technique for colorectal cancer staging. Contrast-enhanced MRI, especially with the use of liver specific contrast medium, and PET imaging are increasing employed in the management of the patient with colorectal liver metastases. Thorough management of colorectal cancer requires a multi-disciplinary approach, with joint decision making by surgeons, oncologists, radiotherapists, pathologist and radiologists. The radiologist plays a central role in this management model, and aims to provide critical information for treatment decisions. In a patient presenting with suspected or confirmed liver metastasis from colorectal cancer, there are a number of questions that are frequently asked by members of this multi-disciplinary team:

Is the liver lesion a metastasis?

Focal liver lesions are not uncommon in the patient with colorectal cancer, and are usually demonstrated at staging or follow-up CT. In the absence of a known malignancy, incidental hepatic lesions are rarely malignant[19]. In the patient with colorectal cancer, when a lesion is large and appropriate contrast-enhanced CT is utilised, there is rarely difficulty in characterising a lesion as, for example, a haemangioma or simple hepatic cyst. On dual phase contrast-enhanced CT, metastases typically show peripheral enhancement in the arterial phase and are centrally hypo-enhancing in the venous phase. The enhancing rim of colorectal metastasis has been

shown pathologically to be related to desmoplasia, angiogenesis and inflammation, while the hypo-enhancing centre is related to central necrosis, a feature which occurs frequently.

Small lesions (less than 10 mm) can be problematic on a staging CT, but only in 10% of cases will these actually be metastases[20]. Small lesions may be too small to confidently characterise on CT, and knowledge of the pre-test probability of developing liver metastases can influence the decision to seek immediate clarification with further imaging versus a watch-and-wait approach. If the local staging has demonstrated the primary tumour to be locally advanced (T3/T4), have associated extramural venous invasion or multiple involved local lymph nodes, then the probability of liver metastasis is increased and further imaging should be actively pursued for lesion characterisation. By comparison, a significant increase in lesion size or the emergence of new lesions on interval CT examinations in patients on a follow-up policy may be taken as evidence of metastatic disease.

On greyscale trans-abdominal ultrasound, colorectal hepatic metastases show irregular borders and are hypo-echoic to the liver. However, some metastases may have similar echotexture to the liver and therefore may be undetectable. The characterisation of focal liver lesions can be improved through the use of micro-bubble ultrasound contrast agents[21,22]. However, contrast-enhanced US is not widely performed and is utilised as a problem solving tool where available. Typically, following the injection of micro-bubble contrast, liver metastases show rim enhancement or are iso-enhancing in arterial phase and are hypo-enhancing in both venous and delayed phases of imaging. However, even using micro-bubble contrast, some lesions such as von Meyenberg complexes, can still be difficult to differentiate from metastases[23].

MRI is an effective method for further characterising indeterminate liver lesions detected on CT or US imaging. Colorectal hepatic metastases are typically of low T1 and intermediate to high T2 signal intensity. The longer echo-time (TE $\geq$ 180 ms) T2-weighted sequences are particularly useful for distinguishing between cystic and solid lesions. However, metastases of a mucinous nature may appear cystic and be erroneously classified as benign. In and out of phase T1 weighted imaging may increase lesion conspicuity because of fatty sparing around metastases. Three broad classes of MR contrast agent are used for lesion characterisation in the liver: non-specific extra-cellular space gadolinium chelates (ECS-Gd), hepatocyte selective gadolinium chelates and non-gadolinium liver-specific contrast agents. Each contrast agent has its own merits and pitfalls and the choice of contrast agent used is in part influenced by institutional and personal experience (Table 1, Fig. 1).

PET-CT studies can be used to demonstrate foci of liver metastases by their increased metabolic activity

Table 1 Three broad classes of MR contrast agent are used for lesion characterisation in the liver: non-specific extracellular space gadolinium chelates (ECS-Gd), hepatocyte selective gadolinium chelates (HS-Gd) and non-gadolinium liver-specific contrast agents

	Type of contrast medium Non-specific gadolinium chelates (ECS-Gd)	Hepatocyte selective gadolinium chelates (HS-Gd)	Non-gadolinium liver specific contrast agents	
Subtypes			Hepatocyte selective	Kupffer cells selective
Examples	Magnevist® (Gd-DTPA, Bayer-Schering); Omniscan® (Gd-DTPA-BMA, Amersham); Dotarem® (Gd-DOTA, Guerbet); Prohance® (Gd-HP-DO3A, Bracco); Gadovist® (gd-DO3A-butriol, Bayer-Schering)	Multihance® (Gd-BOPTA, Bracco); Primovist® (Gd-EOB-DTPA, Schering)	Teslascan (MnDPDP, Amersham)	Endorem (SPIO, Guerbet); Resovist (SPIO, Bayer-Schering)
Imaging	Dynamic contrast-enhanced T1-weighted imaging in arterial, portovenous and interstitial phase	Dynamic contrast-enhanced T1-weighted imaging in arterial, portovenous and interstitial phase Delayed imaging in hepatocellular phase (e.g. 20 min to 2 h)	Dynamic scan not performed as contrast is infused T1-weighted imaging at 20 min post contrast ± imaging at 24 h	T2 or T2*-weighted imaging 15–30 min after contrast administration ± T1-weighted imaging during contrast administration
Appearance of colorectal metastases	Arterial phase: rim enhancement	Arterial phase: rim enhancement	20 min: T1 hypointensity	High signal intensity lesions on T2/T2*-weighted imaging
	Portovenous and interstitial phase: T1 hypointensity	Portovenous and interstitial phase: T1 hypointensity Hepatocellular phase: T1 hypointensity	24 h: rim and segmental enhancement	
Potential pitfalls	Breathing and motion artefacts may confound interpretation of dynamic scans	Small metastases adjacent to blood vessels may be missed	Small metastases adjacent to blood vessels may be missed	Small metastases may be mistaken for blood vessels

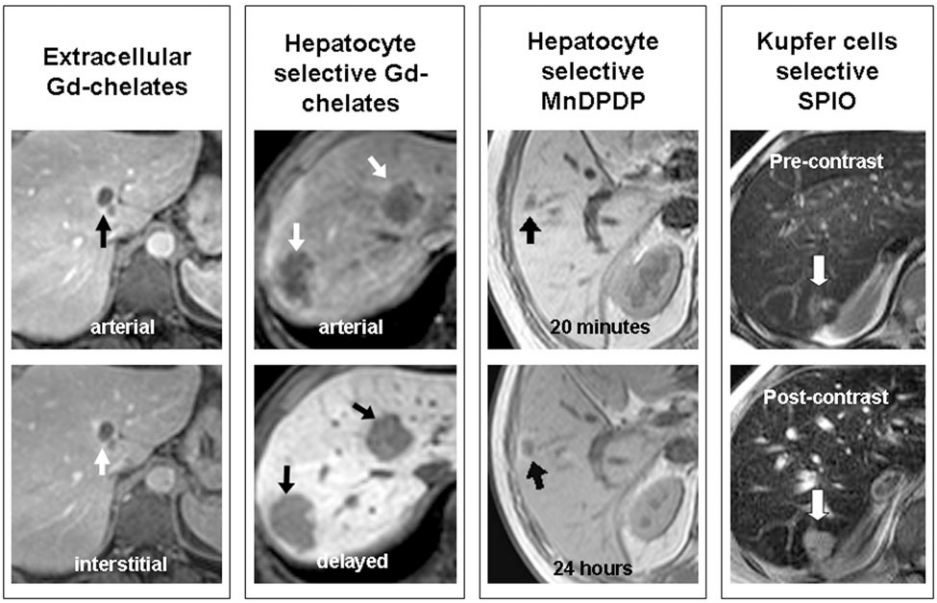

Figure 1 **Illustrative examples of the appearances of colorectal liver metastases (arrows) after the administration of different contrast media. Left to right: using extracellular gadolinium chelates, metastases show rim enhancement in the arterial phase and appear hypointense to the liver in the portovenous phase on T1-weighted imaging. When a hepatocyte selective gadolinium contrast is used (e.g. Gd-EOB-DTPA), metastases show rim T1 enhancement in the arterial phase, but are most conspicuous as hypointense lesions in the delayed hepatocellular phase. Note the striking liver parenchymal enhancement with contrast washout from the intrahepatic vasculature in the delayed phase. Following MnDPDP contrast infusion, metastases typically appear as hypointense lesions against the enhancing liver parenchyma on T1-weighted imaging at 20 min. Rim enhancement is frequently observed around metastases at 24 h. The administration of SPIO contrast results in signal loss from the normal liver on T2* gradient echo imaging, facilitating the detection of the higher signal intensity metastases.**

through the accumulation of the radioisotope [^{18}F]fluorodeoxyglucose ([^{18}F]FDG). Although PET-CT is a powerful imaging tool, it has a number of potential pitfalls, including poorer sensitivity for mucinous tumours and for the detection and characterisation of smaller lesions (<1 cm). In many countries, access to PET-CT is a limiting factor to its widespread use. In difficult cases, combining the diagnostic information from CT, MRI and PET-CT usually allows the best assessment to be made.

Is the hepatic metastatic disease potentially resectable?

The aim of liver resection must be to remove all macroscopic disease and leave clear resection margins. Liver resection may be achieved either by anatomical resection in which one or more whole segments of the liver are removed, or alternatively, a wedge resection in which a portion of a segment is removed. Segmental resection is advocated by some as the ultimate oncological procedure with data to suggest that it results in the best chance of tumour clearance and long term survival[24]. Some advocate that most lesions can be successfully removed using wedge resection, particularly if they are small and peripheral[25].

Whilst in the past, various guidelines involving the number, size and position of metastases have dictated whether disease is resectable or not, current thinking is that the key factors are whether all disease can be removed with clear margins whilst leaving sufficient liver parenchyma to maintain life. However, for the optimal planning of the nature and extent of surgery; the number, location and segmental distribution of metastases still need to be accurately mapped. Predicating whether there will be life threatening hepatic dysfunction after liver resection is difficult but an estimate of whether sufficient parenchyma will remain can be made using CT volumetry[26]. Experience from hepatic transplant surgery suggests one-third of the original liver volume or approximately two disease-free liver segments are needed to prevent morbidity.

Burden of metastases

There is heavy reliance on imaging to detect and define the burden of metastatic liver disease. Ultrasound is generally not useful in mapping disease burden. Using CT, imaging in the arterial phase can increase lesion conspicuity, but no significant improvement in lesion detection has been shown compared to venous phase

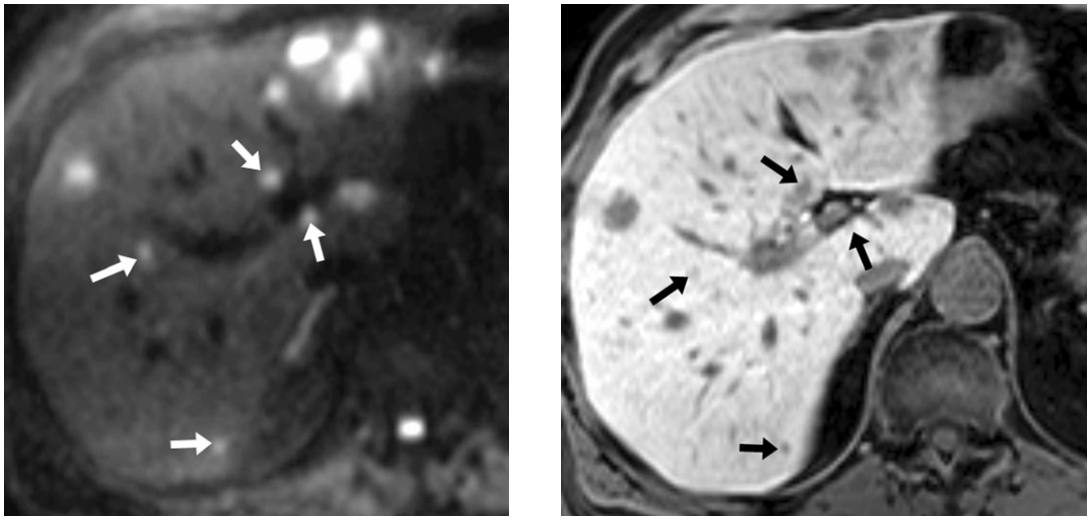

Figure 2 **Diffusion-weighted MRI (DW-MRI) improves the detection of colorectal liver metastases. Left: delayed T1-weighted imaging after the administration of Gd-EOB-DTPA shows a number of hypointense metastases in the liver. Note, however, that the smaller metastases less than 1 cm in size (arrows) are easy to overlook, especially when they are located adjacent to intrahepatic vasculature, as they can mimic blood vessels. Right: DW-MRI performed using a *b*-value of 750 s/mm^2 reveals both the larger and smaller (arrows) metastases as conspicuous high signal intensity lesions.**

imaging alone[27,28]. The sensitivity of CT is diminished by hepatic steatosis.

Dynamic ECS-Gd enhanced MRI is widely used to define disease burden. Sub-centimetre metastases may be best appreciated in the arterial phase when they are hypo-enhancing on T1-weighted imaging, after which time they become increasingly less distinct[29]. However, dynamically acquired images can be degraded by motion/breathing artefacts which can limit their usefulness.

Using hepatocyte selective gadolinium chelates (HS-Gd) such as gadobenate (Multihance®, Gd-BOPTA, Bracco) and gadoxetic acid (Primovist®, Gd-EOB-DTPA, Schering), metastases appear hypointense against the avidly enhancing liver parenchyma on T1-weighted imaging in the delayed hepatocellular phase of contrast enhancement, and is particularly effective for detecting small metastases[30]. Similarly, mangafodipir trisodium (Mn-DPDP, Teslascan®, Nycomed Amersham) has also been shown to be useful for defining sub-centimetre lesions[31,32]. Metastases are non-enhancing at 20 min after injection although some are best appreciated at 24 h post-injection when they may be conspicuous because of lesional rim or segmental liver enhancement. Superparamagnetic iron oxide (SPIO) enhanced MRI can reveal small metastases as high signal intensity lesions against the darkened liver on T2 or T2*-weighted MRI. However, small metastases may sometimes be mistaken for blood vessels, as both appear high signal intensity after contrast administration. The liver specific contrast agents result in prolonged liver parenchymal enhancement, and allow for repeat imaging should respiratory or other image artefacts cause difficulties in interpretation.

An evolving technique that has great potential for the detection of colorectal liver metastasis is diffusion-weighted MRI (DW-MRI). Recent data suggest that the addition of DWI to contrast-enhanced imaging can further improve lesion detection by identifying small (<1 cm) metastases lying at the periphery of the liver or adjacent to vessels[33,35] (Fig. 2).

[^{18}F]FDG-PET imaging has been shown to be highly sensitive on a per patient basis for the detection for colorectal liver metastases but the sensitivity for the detection of disease on a per lesion basis within the liver[34] may be limited by the metabolic activity in small metastases[1,35]. It would appear that at present, MRI, particularly when combined with liver specific contrast agents, is the most useful in defining the disease burden in the liver on a lesion by lesion basis.

Location of liver metastases

Undoubtedly the location of certain metastases, for example at the confluence of the hepatic veins or adjacent to the inferior vena cava, makes them unfavourable for resection, but even these patients should not be entirely discounted. Disease involving or in close proximity to the inferior vena cava (IVC) is increasingly being resected and the IVC either reconstructed or an interposition graft is used. Even in those patients in whom initial imaging assessment deems their liver disease inoperable, there are new aggressive management strategies which may render the liver disease suitable for surgery. These include the use of neo-adjuvant chemotherapy to down

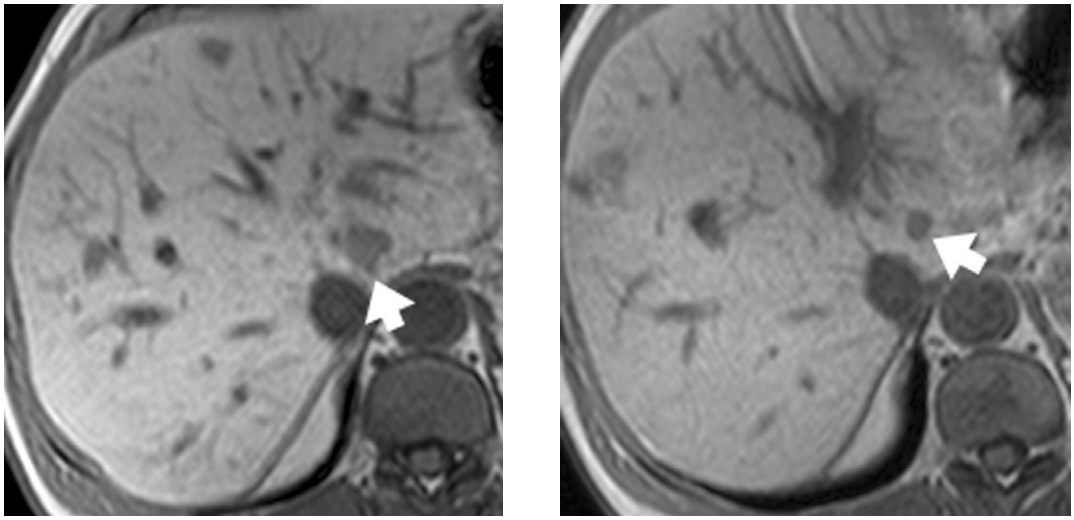

Figure 3 **Neo-adjuvant chemotherapy with tumour regression. Pre-chemotherapy (left) and post-chemotherapy (right) T1-weighted MRI obtained at 20 min after the administration of MnDPDP contrast medium. Prior to neoadjuvant treatment, note the 2 cm hypointense metastasis (arrow) lying in close proximity to the intrahepatic inferior vena cava. Treatment with neoadjuvant chemotherapy resulted in downsizing of the metastasis to 1 cm in size with regression of tumour away from the inferior vena cava, thus facilitating surgical clearance.**

stage hepatic disease (Fig. 3), pre-operative portal vein embolisation to hypertrophy remaining liver segments prior to resection of diseased segments, two stage resections to ensure sufficient liver parenchyma remains after all the metastases are removed and radiofrequency ablation of tumours not suitable for resection[36–40].

Distribution of liver metastases

The segmental distribution of liver metastases is described using Couinard segmental anatomy of the liver (segments I–VIII), which is defined according to the anatomical planes of the portal and hepatic veins. A line drawn 1 cm to the right of the middle vein is often used to define the surgical right lobe from the left lobe of the liver. When performing contrast-enhanced CT of the liver, 3D and multi-planar reformats allows the hepatic vascular anatomy to be clearly demonstrated. An appreciation of the normal variants in venous anatomy, and meticulous tracing of the paths of intra-hepatic veins are important for accurate localisation of disease in the hepatic segments.

Others

The presence and degree of hepatic steatosis on US, CT or MRI should be noted as this has a bearing on the risk of peri-operative morbidity.

Is there extra-hepatic metastatic disease?

The presence of extra-hepatic disease is no longer an absolute contraindication for resection of liver metastases. Data suggest that patients may achieve long term survival if lung metastases are also resected and therefore such an approach should be encouraged[41].

The advent of PET or more recently PET-CT has improved the sensitivity of extra-hepatic disease detection. Studies indicate that PET will identify occult disease, such as in the bones, peritoneum, stoma site, lymph nodes and anastomotic sites; in approximately one in six patients who have completed the standard CT imaging regime[42]. Not uncommonly PET can also offer re-assurance when an anatomical abnormality, for example an adrenal nodule, is discovered on CT and is found to be metabolically inactive on PET. Overall PET-CT has been shown to significantly alter patient management in around 16% of cases[43] (Fig. 4). As with any diagnostic test, PET-CT does have limitations. Of particular note with regard to the assessment of extra-hepatic disease is the detection of pulmonary metastases. Subcentimetre pulmonary nodules may appear metabolically inactive due to respiratory volume averaging or image misregistration, and therefore benign due to their apparent lack of FDG tracer uptake. It is therefore essential to correlate PET and CT findings to ensure small pulmonary metastases are not overlooked.

Has there been a response to chemotherapy and what is the burden of residual disease?

Since its publication in 2000, the Response Evaluation Criteria in Solid Tumours (RECIST) is widely used to assess response to therapy[44]. Using standard chemotherapy, a response rate of approximately 30% is usual, with a small percentage of patients achieving complete response (i.e. no visible tumour seen on conventional imaging).

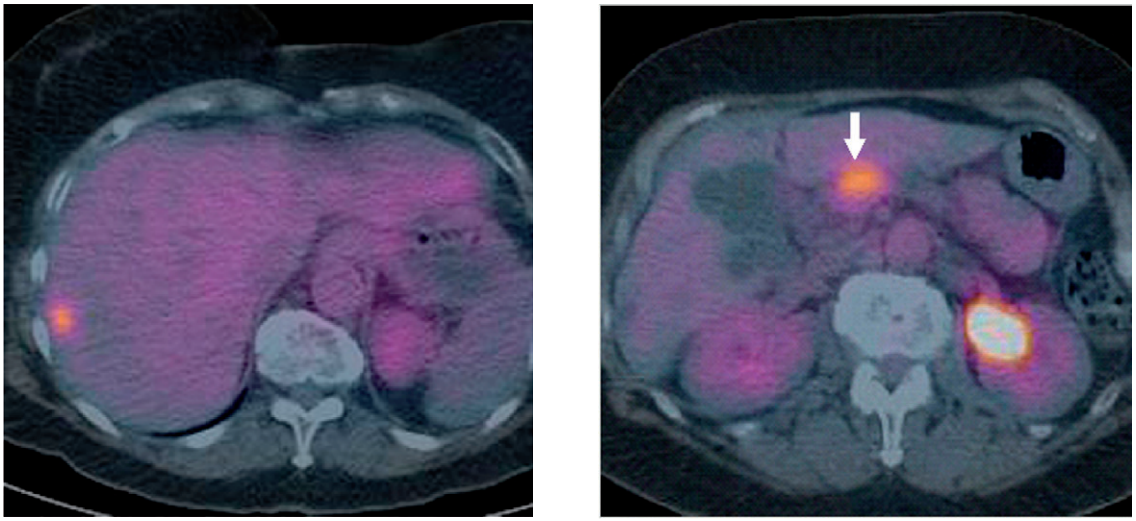

Figure 4 **FDG-PET detects unsuspected extra-hepatic disease. Left: FDG-PET/CT of the liver demonstrated a solitary hypermetabolic liver metastasis in the right lobe of the liver. Right: FDG-PET/CT more inferiorly in the abdomen also showed increased tracer uptake in the neck of the pancreas which was confirmed to be an unsuspected pancreatic carcinoma, thus contraindicating curative surgical resection. Note that the low-density cysts in the liver showed no appreciable tracer uptake.**

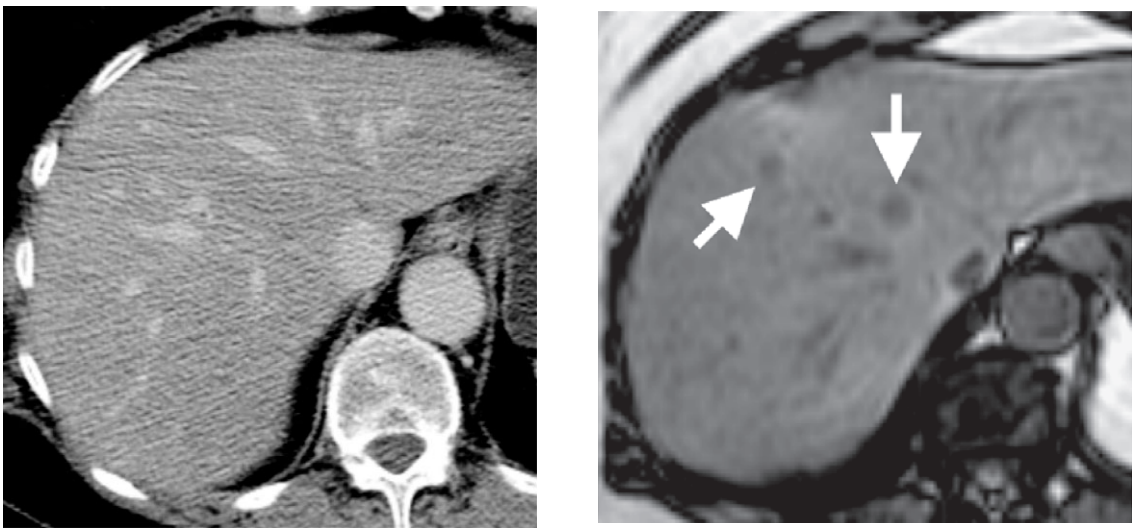

Figure 5 **Diffuse liver steatosis can obscure liver metastases. Left: contrast-enhanced CT in the portovenous phase in a 45-year-old man shows diffuse low-density changes in the liver consistent with hepatic steatosis. Right: T1-weighted out-of-phase MR image shows signal loss in the liver parenchyma confirming fatty infiltration. However, two liver metastases (arrows) are also visible which are not seen at CT scanning.**

Although CT imaging is widely used to assess treatment response, neoadjuvant chemotherapy (especially with the use of irinotecan) can result in significant hepatic steatosis, making it difficult to identify small foci of residual disease (Fig. 5). Similarly, chemotherapy may render metastases relatively inactive, making them difficult to detect on FDG PET-CT. Recent studies comparing PET-CT and MRI have shown that MRI is more accurate in defining residual disease after chemotherapy. The role of US in the assessment of response to treatment is limited due to its operator dependence and measurement reproducibility[45].

What is currently controversial is the significance of a radiological 'complete response' to treatment. Data suggest that up to 83% of those thought to have a 'complete response' in liver metastases were subsequently found to have microscopic or macroscopic residual disease or early disease recurrence[46]. Hence, it is still a matter

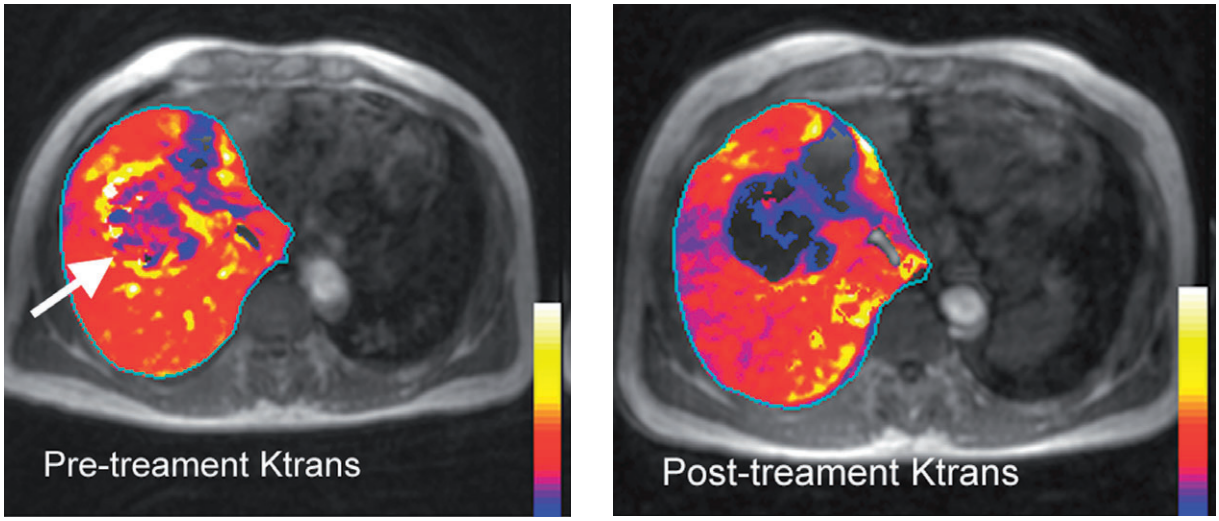

Figure 6 **Maps of vascular parameter *Ktrans* obtained using DCE-MRI before and after vascular targeted therapy. These maps were created by overlaying the quantitative vascular parameter *Ktrans* (in colour) on the morphological T1-weighted images. Left: prior to treatment, the liver metastasis (arrow) showed an increase in *Ktrans*, particular at the tumour rim. Right: the *Ktrans* was substantially reduced at 14 days after the initiation of vascular targeted treatment.**

of debate as to whether surgery should be performed to remove liver segments that contained liver metastases even though no focus of tumour may be seen after neoadjuvant treatment.

Are the lesions suitable for radio-frequency ablation and how do I assess response to treatment?

Radiofrequency thermal ablation (RFA) is an attractive therapeutic option since surgical excision is not always possible in patients with advance age, co-morbidities, unfavourable extra-hepatic disease or compromised liver function. Radiofrequency thermal ablation results in coagulative necrosis of the metastases. Studies have shown that using RFA alone is associated with a low complication rate (2.4–12%) with good 1-year survival of >90% and a 5-year survival rate of about 25%[47,48]. Even patients with potentially resectable small solitary metastasis <4 cm in size could be treated with excellent results and 5-year survival in excess of 50%[49,50]. Of course, RFA can be and is increasingly combined with liver resection to maximise tumour ablation; and may be the only viable option when the disease relapses in the remnant liver after surgery. Local recurrence following RFA is higher in lesions found adjacent to vascular structures and for those measuring >3 cm in size.

The suitability of lesions for RFA is in part dependent on the operator expertise. However, in general, numerous metastases (>4), large lesions (>4 cm)[47], lesions in sub-diaphragmatic or sub-capsular locations, and those abutting major vascular structures are less desirable.

Imaging assessment post-RFA treatment is optimum on CT or MRI. Triphasic contrast-enhanced CT imaging performed immediately or within a month of RFA, is commonly used to evaluate the success of treatment. After RFA, it is usual to see low attenuation at the site of previous disease, but there should also be a wider ablative zone that extends beyond ($\geq$0.5 cm) the footprint of the metastasis. Within the first month after treatment, there may be an enhancing ablative margin due to tissue hyperaemia, but this usually resolves with time. The centre of the treated tumour may also appear high in CT density due to severe cellular disruption[51]. Eccentric nodular enhancement at the edge of ablation raises the suspicion for residual or recurrent disease.

How can I assess the effectiveness of novel therapeutics?

Novel targeted therapies (e.g. anti-angiogenic treatment) are increasingly forming part of the treatment regimes for the treatment of advanced metastatic disease. Conventional size measurement criteria are inadequate for assessing response to such treatment since these drugs may arrest tumour growth without decreasing tumour size.

Imaging techniques which inform on the patho-physiological changes within tumours, such as dynamic-contrast-enhanced MRI (DCE-MRI) (Fig. 6), diffusion-weighted MRI (DW-MRI) and positron emission tomography (PET) are increasingly employed. There is some evidence that these techniques can detect and quantify changes within tumours, prior to a measurable change in tumour size. Treatment response or tumour characteristics as determined by these techniques may also predict for treatment outcome[52].

How do I monitor for disease relapse?

Current follow-up imaging practice varies considerably. Whilst some advocate clinical assessment, tumour marker estimates and CT at 3–4-month intervals for the first year post surgery and then annually thereafter for the next 4 years, others suggest that in the absence of symptoms, a single CT at 1 year post surgery is adequate. Clearly, there are significant cost implications depending on which path is followed. This has prompted suggestions that money may be wasted on imaging follow up that is of uncertain benefit to the patient[53]. Clearly, a defined follow-up strategy needs to be established. Answers regarding how best to monitor patients may in part be provided by the FACS trial.

Can I predict the likelihood of developing liver metastases?

The published literature suggests that the hepatic perfusion index (HPI) is increased in the liver prior to the appearance of macroscopic liver metastases. However, the clinical utility of this test is not fully established The hepatic perfusion index (HPI) can be estimated using ultrasound, CT or MRI, by calculating the hepatic arterial perfusion as a fraction of the total hepatic perfusion (arterial and portal perfusion). It is believed that because liver metastases derive their blood supply predominantly from the hepatic artery, the presence of micro-metastases in the liver could result in an elevated HPI. However, an elevated HPI is non-specific, which can also be encountered in conditions that result in decreased portal flow, such as in liver fibrosis or cirrhosis. Furthermore, the HPI in the liver parenchyma may not be elevated even in the presence of metastases. Nevertheless, the HPI remains a unique vascular parameter due to the dual blood supply of the liver, and can provide insight into altered haemodynamics in the liver as a consequence of metastatic disease. More recently, the HPI has been shown to be another potentially reproducible method of assessing response of metastases to treatment[54].

Conclusions

The prognosis of patients with colorectal liver metastases is not invariably dismal. The use of neoadjuvant chemotherapy, together with active surgical and interventional treatment can improve treatment outcome. Imaging needs to be responsive to current management strategies. Once liver metastases are diagnosed, imaging has a central role to play in defining the extent and distribution of the intra-hepatic and extra-hepatic disease, so that the treatment option with potentially the best outcome can be planned by the multidisciplinary management team. Functional imaging techniques are likely to have an increasing role to play in assessing the treatment effects of novel therapeutics and can also provide unique prognostic information.

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