American College of Radiology
ACR Appropriateness Criteria®
Suspected Liver Metastases

Variant 1: **Suspected liver metastases. Initial imaging test following detection of primary tumor.**

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen with IV contrast	9		☢ ☢ ☢
MRI abdomen without and with IV contrast	8		O
CT abdomen without and with IV contrast	5		☢ ☢ ☢ ☢
MRI abdomen without IV contrast	5		O
FDG-PET/CT skull base to mid-thigh	5		☢ ☢ ☢ ☢
In-111 somatostatin receptor scintigraphy	5		☢ ☢ ☢ ☢
US abdomen	4		O
CT abdomen without IV contrast	4		☢ ☢ ☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Variant 2: **Suspected liver metastases. Surveillance following treatment of primary tumor.**

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen with IV contrast	8		☢ ☢ ☢
MRI abdomen without and with IV contrast	6		O
CT abdomen without and with IV contrast	5		☢ ☢ ☢ ☢
MRI abdomen without IV contrast	5		O
FDG-PET/CT skull base to mid-thigh	5		☢ ☢ ☢ ☢
In-111 somatostatin receptor scintigraphy	5		☢ ☢ ☢ ☢
CT abdomen without IV contrast	4		☢ ☢ ☢
US abdomen	4		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			***Relative Radiation Level**

Variant 3: **Presurgical assessment of liver metastases.**

Radiologic Procedure	Rating	Comments	RRL*
MRI abdomen without and with IV contrast	9		O
CT abdomen with IV contrast	8		☢ ☢ ☢
US abdomen intraoperative	8	This procedure is complementary to MRI or CT.	O
MRI abdomen without IV contrast	6		O
FDG-PET/CT skull base to mid-thigh	6		☢ ☢ ☢ ☢
CT abdomen without and with IV contrast	5		☢ ☢ ☢ ☢
CT abdomen without IV contrast	3		☢ ☢ ☢
US abdomen	3		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

SUSPECTED LIVER METASTASES

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Summary of Literature Review

Introduction/Background

Liver metastases are the most common liver tumors and one of the most common indications for liver imaging. In most series, about 25% to 50% of patients who die with a malignancy have liver involvement [1]. However, the incidence of benign liver lesions, even in patients with a known malignancy, exceeds that of metastases. Two studies have shown that 51% to 80% of <1- to 1.5-cm lesions in patients with an underlying malignancy are benign [2,3]. Consequently, it is important that any imaging evaluation of the liver in a patient with a malignancy should be able to both accurately detect and characterize liver lesions.

In selected patients surgical resection is the most effective treatment for liver metastasis. This is particularly true in colorectal cancer, where improved chemotherapy and surgical techniques have widened the population eligible for surgical resection [4,5]. In addition, surgical resection has improved survival in breast and neuroendocrine metastasis [6]. Imaging has a critical role in these patients in determining tumor burden and segmental distribution to enable an accurate assessment of surgical resectability. In unresectable patients, imaging has an important role in providing a consistently reproducible assessment of treatment response to chemotherapeutic regimens.

The incidence of liver metastases at the time of initial presentation of a malignancy correlates with tumor type, location, degree of differentiation, and the T and N stage of the primary tumor. Some tumors, such as colon, pancreatic cancer, lung, gastric cancer, and neuroendocrine tumors, are more predisposed to develop liver metastasis. The pathways of spread to the liver are through the portal vein, the hepatic artery, and lymphatic spread.

Liver metastasis can be broadly classified as hypoenhancing and hyperenhancing relative to the liver parenchyma; however, these definitions require some explanation and refinement and are discussed in subsequent sections. The enhancement of liver lesions and the evolution of this enhancement over multiple imaging phases are important in their characterization. The patterns of enhancement of liver lesions observed with either iodinated computed tomography (CT) contrast or extracellular gadolinium-chelate magnetic resonance imaging (MRI) contrast are comparable as these agents have a similar pattern of distribution from the vascular to the interstitial compartment. This is in contrast to a newer hepatocyte-specific contrast agent, gadoxetic acid disodium, that is associated with a distinct pattern of distribution and consequently of enhancement on the equilibrium and delayed phase.

Numerous imaging methods are available for detecting intrahepatic metastatic disease before, during, and after definitive therapy for the primary lesion. The choice of imaging tests can vary significantly across institutions because of local radiological expertise, availability of equipment or personnel, and the wishes and biases of treating physicians and radiologists. Patient-related factors such as renal failure, cardiac pacemakers, contrast allergy, etc, also impact the choice of imaging modalities.

This document reviews multiple available imaging tests for detecting liver metastases. Unfortunately, there are no current studies comparing all known modalities. A more significant issue is that most studies do not evaluate imaging with current state-of-the-art equipment and/or contrast agents or with optimization of the compared imaging techniques, generally related to local expertise and bias for 1 modality over the other [7,8].

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Overview of Modalities

Ultrasound

Ultrasound (US) is the most widely available technique for liver imaging worldwide, and in many countries it is the major imaging test used to search for liver metastases. In the United States, the widespread availability of CT and MRI, the relatively higher dependence of US on operator skill, and the limited availability of US contrast agents contribute to a lesser role for US diagnosis.

In Europe and Canada, where contrast-enhanced US (CEUS) is widely used, studies have demonstrated a high accuracy in characterizing and detecting liver lesions, in the range of 87% to 91% [9-16]. In the evaluation of liver lesions, arterial-phase imaging on CEUS provides incremental value in lesion characterization, whereas the portal venous phase (PVP) and delayed phase improve lesion detection as almost all metastases show washout, unlike with CT and MRI, where shift of contrast into the interstitial space may conceal washout [17]. However, as with most imaging modalities, evolution of contrast enhancement over time is key to liver lesion characterization. A limitation of these studies is that the majority of articles on CEUS do not have a histopathologic standard of reference but instead are based against comparison to CT, MRI, intraoperative US (IOUS), and follow-up examinations [9,15,16].

CEUS also has a complementary role to CT or MRI for lesions that are indeterminate with these modalities. Guidelines from the European Federation of Societies for Ultrasound in Medicine and Biology updated in 2012 recommend the use of CEUS for 1) characterization of indeterminate lesions detected on MRI or CT and 2) treatment planning in selected cases to assess the number and location of liver metastases complementarily with CT and/or MRI [18].

US guidance is also useful as a guide for percutaneous biopsy of liver lesions that are suspicious for malignancy. Most centers with equivalent expertise in US and CT guidance prefer US as the primary mode of guiding biopsies if the lesion is easily visible/accessible on US.

Intraoperative ultrasound

IOUS is the most accurate imaging technique for detecting liver metastases at the time of primary tumor resection or resection of previously identified hepatic metastases. It is complementary to cross-sectional imaging, surgical inspection, and palpation. Additionally, IOUS can be important for localization of tumors for ablative techniques or to guide intraoperative biopsy or surgical resection [7,8,19-22].

Computed tomography

Multidetector helical CT (MDCT) is the preferred examination in the United States for initial assessment and subsequent surveillance for metastatic disease after diagnosis of a primary neoplasm because of its ability to image the liver and potential sites of extrahepatic disease (ie, nodes, peritoneum, chest) during the same examination.

However, the efficacy of CT is heavily dependent on technique. An expert consensus under the aegis of the Organ Procurement and Transplantation Network has recommended minimal hardware and image acquisition protocol requirements for the CT and MRI assessment of liver lesions in the pretransplant liver [23]. Although these parameters were recommended in the context of liver transplant evaluation, they are equally applicable to the assessment of all focal liver lesions, including metastasis. Some important parameters include kilovolt (peak) (kV[p]), milliamperes (mA), contrast delivery, and slice thickness. For example, the use of thinner reconstructed images (ie, 2.5 mm) over thicker images improves lesion detection and characterization [24]. The majority of papers describing a high sensitivity and specificity for liver lesion characterization with MDCT use arterial-phase and PVP imaging, 3- to 5-mL/s injection rate, 2.5- to 5-mm slice thickness, and 120 to 150 kV(p)/80 to 300 mA [25,26]. Although for most liver lesions the PVP is the most sensitive for lesion detection, the addition of arterial- and delayed-phase (3- to 5-minute) images significantly improves lesion characterization [27-30].

Liver metastases have been categorized based on enhancement relative to the adjacent liver as hyperenhancing or hypoenhancing. However, a careful review of the literature reveals that this may be somewhat confusing, as the majority (72%) of hypoenhancing metastases show peripheral ring enhancement on the arterial phase of MR and CT, a finding that has a high positive predictive value (98%) for malignancy and reflects enhancement in the compact tumor cells located in the periphery of most metastases [31,32]. Peripheral ring enhancement must be distinguished from perilesional enhancement that is due to inflammatory cells and vascular proliferation in the compressed liver and may be seen in benign lesions such as hemangiomas as well as metastases [31,33].

In general, imaging during the PVP of hepatic enhancement is adequate to detect most hypoenhancing hepatic metastases. Using histopathological gold standards, CT has a sensitivity of 85% to 91.5% in detection of metastases on the PVP [26,34]. The lesions that are missed are generally <10 mm [30]. Although PVP imaging enables superior lesion detection, the typical enhancement patterns seen during arterial-phase imaging improve diagnostic confidence [32]. However, achieving these results requires attention to the CT technique, particularly contrast dose and injection rate, which should preferably be 4 to 5 mL/s for best arterial-phase imaging [25,32].

Hyperenhancing metastases are less common and can arise from breast tumors, renal cell carcinoma, thyroid carcinoma, melanoma, and neuroendocrine tumors. Typically precontrast, arterial-phase, and PVP imaging are recommended for imaging this subgroup of patients [35]. This is because although termed hyperenhancing, these metastases behave variably; up to 59% of these metastases are isodense or hypodense to liver parenchyma on either the arterial phase or PVP. Consequently, multiphase imaging is required for the most accurate detection of such metastases. For instance, in melanoma 14% of metastases would have been missed if scans were obtained only during the PVP [35,36]. The percentage of metastases that are hyperenhancing on the arterial phase is related to tumor type. For instance, only 10% to 26% of breast metastases are hyperenhancing, with 4% to 17% showing mixed vascularity [37]. Consequently, arterial-phase imaging has limited value in the detection of breast cancer metastasis. In contrast, there is a significant benefit to arterial-phase CT in neuroendocrine tumors and renal cell carcinoma, where the majority of lesions are hyperenhancing [38].

Noncontrast images or virtual noncontrast images if dual-energy CT is used are occasionally helpful for lesions with hemorrhage or calcification (eg, melanoma, mucinous metastases). In addition, nonenhanced images can depict metastases that are isodense on the arterial phase and PVP [35]. Noncontrast images may also be helpful in metastases that have been treated with liver-directed therapy such as chemoembolization, in which high-attenuation material has been injected during the procedure, or radioembolization or radiofrequency ablation, in which it can be difficult to determine if a lesion is a viable tumor. However, in younger patients with curable disease, the radiation exposure must be balanced against the potentially increased yield obtained by doing multiphasic CT.

Magnetic resonance imaging

MRI has multiple advantages over MDCT, including superior contrast resolution compared to CT, multiphase imaging acquired with every contrast-enhanced MRI protocol, the ability to obtain diffusion-weighted imaging (DWI), and the availability of both extracellular and hepatocyte-specific contrast agents for lesion characterization.

The disadvantages of MRI include the susceptibility to motion artifact related to the length of individual MRI sequences and the length of the liver MRI examination (15 to 20 minutes). A well-performed CT of the chest, abdomen, and pelvis with contrast requires <5 minutes. Additional limitations of contrast-enhanced MRI include concerns about gadolinium administration in patients with chronic kidney disease, claustrophobia, and implanted foreign bodies that may preclude a safe MR examination.

As with CT, the most effective use of MRI requires attention to technique. Ideally MR scans should be performed with a magnet strength of 1.5T or greater, using a torso phased-array coil. Recommended sequences for liver lesion detection and characterization on MRI include the following: a fat-suppressed T2-weighted fast spin echo, gradient T1 in and out of phase, and precontrast and dynamic postcontrast T1-weighted fat-saturated images in the arterial, portal venous, equilibrium, and delayed phases. It can also be argued that DWIs should be considered a minimum requirement for liver MRI [39,40]. Slice thickness should be 5 mm or less preferably for all sequences, with 3-mm or less slice thickness preferred for the T1 precontrast and postcontrast sequences.

Although T2-weighted, in- and out-of-phase imaging, DWI, etc, are important for lesion detection and provide diagnostic value, patterns of enhancement observed on contrast-enhanced MRI remain essential for characterization of hepatic lesions. Since the distribution of both traditional extracellular MR contrast agents and iodinated CT contrast are similar, the patterns of enhancement of hypoenhancing and hyperenhancing metastasis discussed under the CT section are equally applicable to MRI.

In addition to traditional extracellular MRI contrast medium, there has been development of dual-phase MR contrast agents such as gadoxetic acid and gadobenate dimeglumine, which combine arterial and PVP imaging with a hepatobiliary phase. This theoretically enables lesion characterization based on traditional patterns of enhancement, in addition to the ability to distinguish hepatocytes from non–hepatocyte-containing lesions.

Gadoxetic acid has significant uptake into normally functioning liver hepatocytes, which provides high tumor-to-lesion contrast during the hepatobiliary phase. This has been demonstrated to improve sensitivity in the detection of focal liver lesions, particularly of lesions <1 cm. In a rigorous study comparing imaging findings with histopathologic and intraoperative findings on a lesion-by-lesion basis, the hepatocyte phase of gadoxetic acid correctly identified 69% to 87% of the lesions and correctly characterized 70% of the lesions [41]. Studies comparing arterial-phase and PVP CT and gadoxetic acid–enhanced MRI found improved lesion characterization and diagnostic confidence (89%) compared with CT (80%), and these findings have been reproduced in other multicenter trials [42-44]. Additionally, a multicenter study using an optimized triphasic CT protocol (arterial, portal venous, and delayed phase) replicated the superior sensitivity of gadoxetic acid MRI in detection of lesions <2 cm but particularly in lesions <1 cm, but it found that the 2 techniques were comparable for lesion characterization [30].

In addition to specialized liver contrast agents, DWI along with generated apparent diffusion coefficient maps is now widely used in liver imaging. This approach offers improved sensitivity, particularly for small lesions that are occult on other modalities, and in some circumstances assists in characterization of liver lesions [39,45,46].

DWI is most accurate in distinguishing solid lesions from cysts and hemangiomas but is unreliable in distinguishing solid benign lesions such as focal nodular hyperplasia (FNH) and adenomas from malignant processes and should therefore be interpreted only in conjunction with dynamic contrast-enhanced MRI sequences [45-47].

FDG-PET/CT

Fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG)–positron emission tomography (PET)/CT (with either a low-dose, attenuation-correction, noncontrast CT or contrast-enhanced CT) is widely used in detecting metastatic disease. Two meta-analyses comparing CT, MRI, and FDG-PET in patients with cancers of the gastrointestinal tract concluded that FDG-PET is the most sensitive imaging test for identifying hepatic metastases from colorectal cancer [48,49]. However, more recent articles have challenged this assumption [50-52]. FDG-PET may fail to demonstrate small (<1 cm) liver metastases and mucinous metastases [53-56]. In addition, the sensitivity of FDG-PET for demonstrating hepatic metastases from colorectal cancer is reduced in patients who have undergone recent chemotherapy [57-59].

Somatostatin receptor scintigraphy

Although MRI and CT have a significantly higher accuracy for the detection of liver metastasis, in the case of metastasis from neuroendocrine tumors, somatostatin receptor scintigraphy with indium In 111 octreotide is a useful adjunct technique, particularly when fused with single-photon emission CT and CT imaging. The strength of somatostatin receptor scintigraphy is the excellent specificity of the technique and the ability to survey the whole body for metastases. It is included in the European Consensus guidelines for imaging of neuroendocrine tumors [60,61]. Gallium 68 dotatate has recently been approved by the Food and Drug Administration (FDA). This agent is particularly useful in the detection of well-differentiated neuroendocrine tumors and in patients with equivocal findings on In 111 octreotide scans [62].

Variant 1: Suspected liver metastases. Initial imaging test following detection of primary tumor.

The incidence of liver metastasis is related to the type and stage of the primary tumor, and this information should direct the use of imaging, as a diagnostic test usually has the greatest utility when the pretest probability of disease is in the intermediate range of 20% to 50% [63]. The most frequent secondary neoplasms of the liver are carcinomas followed by melanomas, whereas lymphomas and sarcomas rarely spread to the liver. Breast, lung, colorectal, gastric, and pancreaticobiliary malignancies are the most common carcinomas to develop liver metastasis [64].

Ultrasound

US enables a rapid and noninvasive assessment of the liver. However, its utility is compromised by obesity and in the settings of chronic liver disease and fatty liver. Conventional US also has a limited sensitivity for liver metastasis, in the range of 53% to 77%, which may be as low as 20% for lesions <1 cm [65,66]. These factors limit its utility as a staging modality for liver metastasis. This has improved with the development of CEUS, which has a significantly higher sensitivity of 87% and a specificity of 88% in the detection of liver metastasis [9].

Computed tomography

CT is frequently the preferred initial imaging test for a newly diagnosed malignancy as it permits an excellent overview of the primary tumor, anticipated pathways of nodal spread, the peritoneal cavity, liver, and lungs. This enables the liver and potential extrahepatic sites of tumor spread to be evaluated during the same examination [67]. Noncontrast CT has limited sensitivity for metastasis, so a negative CT finding may not be useful.

In addition to establishing the presence or absence of metastasis, the initial imaging evaluation gives an estimation of the burden of disease and provides a baseline for neoadjuvant chemotherapy and an assessment for possible surgical resection. The examination should be optimized in terms of technical parameters and tailored according to whether hyperenhancing or hypoenhancing metastases are most likely, based on the type of tumor.

Although a comparative meta-analysis incorporating studies with variable imaging techniques reports a per-lesion sensitivity of CT for hypovascular metastasis of 74% [52], the results are significantly better when the CT imaging technique is optimized in terms of contrast quantity, injection rate, technical parameters, and spatial resolution [25,26,34,68].

Magnetic resonance imaging

Multiparametric MRI incorporating DWI, multiphase dynamic imaging, and now hepatobiliary-phase imaging is the preeminent imaging modality for the characterization and detection of liver metastases, particularly for metastases <1 cm [69]. However, its utilization remains limited by issues of scan time, susceptibility to motion artifact, complexity of interpretation, expense, and availability. It is also limited in the evaluation of extrahepatic disease, particularly the lungs, peritoneum, and bowel. Consequently, its use at time of initial staging of a primary tumor is limited.

FDG-PET/CT

FDG uptake seen on PET/CT reflects the metabolic activity of tumor cells. It is a measure of the biologic behavior of tumors and has a role in prognostication based on metabolic activity. The limitations of PET/CT are related to poor spatial resolution, false positives from inflammatory and benign conditions with FDG uptake, and false negatives seen in subcentimeter lesions or tumors with low metabolic activity or FDG avidity. The role of FDG-PET/CT in the initial staging of newly detected primary tumors is related to the type of tumor. For instance, current National Comprehensive Cancer Network (NCCN) guidelines recommend its use in the initial staging of lung cancer, esophageal cancer, head and neck cancers, lymphoma, cervical cancer, etc. However, except for lung cancer, these are tumors that do not commonly spread to the liver and the utility of PET/CT is largely related to the detection of nodal metastasis or extrahepatic metastasis. In breast, pancreatic, gastric, and colorectal cancer, tumors that commonly spread to the liver, the use of PET/CT is suggested only when there are equivocal findings on CT, MRI, or bone scan or in the preoperative setting [70]. Its role in the initial assessment of tumors that commonly spread to the liver, such as colorectal cancer, is not yet established [71].

Variant 2: Suspected liver metastases. Surveillance following treatment of primary tumor.

The role of surveillance is the early detection of a curable recurrence. Consequently, the intensity of surveillance should be guided by risk factors and the possibility of major surgical resection or chemotherapy in an individual patient. The ideal surveillance protocol should incorporate an approach that is widely available, has a high sensitivity and specificity, and is cost effective.

Ultrasound

US provides a cost-effective approach to screening of the liver but is plagued by low sensitivity and specificity, which limit its utility as a surveillance modality [49]. The advent of CEUS, however, has significantly altered the landscape, enabling detection and characterization with high accuracy [16,72]. US contrast has recently been approved for use in the liver by the FDA. Its acceptance and widespread use in the United States, however, remain to be established.

Computed tomography

CT, although inferior to MRI in detection of liver lesions, provides reasonable sensitivity and specificity in the surveillance setting. Consequently, in many tumors it is recommended as part of the standardized screening after resection of the primary tumor. For instance, in colorectal cancer most societies recommend CT imaging as a component of a standardized surveillance protocol. The guidelines suggest CT scans every 6 to 12 months, depending upon risk, for 3 to 5 years [73]. Cross-sectional imaging results in earlier and increased detection of localized recurrences, with more curative surgeries [74].

Magnetic resonance imaging
MRI has a high sensitivity and specificity in the diagnosis of liver lesions. However, surveillance is rarely performed for liver metastasis alone. It is generally a comprehensive assessment for all sites of potential recurrence, hence the current preference for CT over MRI. This may change with the more widespread use of whole-body MRI. Many patients and referring physicians, however, prefer the use of MRI in surveillance, given the lack of radiation and fears about radiation-associated cancers.

FDG-PET/CT
A meta-analysis of the most sensitive imaging modality for the diagnosis of hepatic metastasis from colorectal, gastric, and esophageal cancers concluded that the accuracy of FDG-PET exceeded that of both CT and MRI. However, most of the studies cited either did not indicate the technical parameters or reported suboptimal parameters for CT and MRI [49]. Subsequent prospective randomized trials have also countered these observations [75]. Current NCCN guidelines also suggest a more limited utility for PET/CT in oncologic surveillance. In colorectal cancer, PET/CT is not suggested for routine surveillance; however, it does have a role in the setting of rising carcinoembryonic antigen if CT fails to identify the site of disease. In other tumors that frequently spread to the liver, such as esophageal cancer and gastric cancer, there was little evidence to suggest a benefit in routine surveillance with PET/CT. However, there is a role for PET/CT in the follow-up of lung and head and neck cancers. In the assessment of metastatic spread of breast cancer, PET/CT is beneficial but should be used to complement CT [70].

Variant 3: Presurgical assessment of liver metastasis.

Surgical resection plays an important role in the treatment of liver metastasis, particularly in colorectal cancer, where metastatic disease is localized to the liver in up to 30% of cases, but also increasingly in neuroendocrine and breast cancer. Complete negative-margin hepatic resection is associated with 5-year survival of up to 58% in colorectal cancer [76]. The goal of imaging is to determine the extent and segmental distribution of liver metastases, which requires accurate detection and characterization of all liver lesions in addition to delineation of the hepatic vascular anatomy.

Since the aim is to avoid unnecessary laparotomies, an optimal and cost-effective result is generally achieved by use of a hybrid imaging model of initial CT followed by multidisciplinary review and then liver MRI and, if required, FDG-PET/CT.

Ultrasound
The role of abdominal US is limited in the presurgical setting. However, IOUS combined with surgical exploration is excellent for the definition of liver metastasis, detecting additional lesions in 20% to 27% of patients in comparison with preoperative CT [77,78]. In these studies, the majority of lesions detected by IOUS and missed on CT were <1 cm in size. It is anticipated that with improved CT and MRI technology and the increasing use of hepatobiliary contrast agents, the incremental value of IOUS will decline. However, some recent studies using optimized imaging protocols, a 64-slice CT scanner, and/or multiparametric MRI have found the added benefit of IOUS to be negligible [79]. There are still reports, particularly in the surgical literature, where IOUS impacted surgical management either by the detection of additional lesions (11.2%) or reassessment of the relationship of metastasis to hepatic vasculature (5.3%) [80]. In addition, in the setting of neoadjuvant therapy, when a metastasis appears to have resolved on preoperative CT or MRI, IOUS frequently assists in the detection and resection of these lesions.

Computed tomography
Multiphase MDCT is widely used in the preoperative assessment of liver metastasis. The majority of papers addressing this issue deal with colorectal metastasis, as this is the most common indication for resection of hepatic metastasis, and support its use in this setting [25,34,81]. The limitation of CT remains exposure to ionizing radiation; it is also limited for detection and characterization of liver lesions in the setting of fatty liver and for subcentimeter and subcapsular lesions.

Magnetic resonance imaging
Successful outcomes after hepatic metastasectomy require removal of all macroscopic disease. This requires accurate preoperative staging, which is most effectively achieved by multiparametric MRI that incorporates the use of both gadoxetic acid and DWI. This approach has a sensitivity of 97% and is superior to the sensitivity obtained with either gadoxetic acid (87%–90%) or DWI alone (91.6%) [43,82]. The benefit of MRI in the presurgical patient population is particularly significant as the increasing use of neoadjuvant chemotherapy

frequently results in fatty liver, which significantly limits detection of hypovascular metastasis on MDCT [83]. In addition, obtaining liver imaging prior to institution of chemotherapy is an important part of a successful imaging strategy and is associated with fewer intrahepatic recurrences than in patients who do not receive pretreatment scans [84]. This is partly related to the apparent resolution of metastasis on post-treatment scans, a significant portion of which harbor residual tumor cells and can be correctly identified on the pretreatment scans. The evolution of liver lesions between pre- and post-treatment scans is a reliable means of tumor characterization.

A limitation of gadoxetic acid, however, is the absence of a true equilibrium phase, which limits lesion characterization, and although there are consistent reports of the superior sensitivity of the hepatobiliary phase over CT and conventional MR contrast agents, the positive predictive value and proportion of correctly characterized lesions is frequently comparable [30,43,85]. A combined approach incorporating the strengths of MDCT and gadoxetic acid MRI frequently yields the most accurate results [85].

FDG-PET/CT

Several studies have demonstrated that the addition of FDG-PET to a conventional staging evaluation in colorectal cancer patients with potentially resectable liver metastases results in a change in management of 20% to 32% [86,87].

These results have been challenged by a prospective double-blinded trial, supported by histological confirmation, that found CT and PET of comparable accuracy, with PET-related changes in surgical management in only 9% of patients, which was partially offset by false-positive findings in 6% of patients [88]. A larger and more recent randomized control trial has confirmed these findings, with PET/CT resulting in a change in management in only 8% of presurgical patients [75]. In both these studies the impact of PET was related to the detection of unexpected sites of extrahepatic disease (ie, peritoneal metastasis, locoregional recurrence, and lymph node involvement). At this time the role of PET/CT in presurgical patients is uncertain and may be primarily as a problem-solving modality for patients at high risk for extrahepatic disease.

Special Considerations

Abnormal surveillance US, CT, or MRI in PVP

The role of imaging when a new abnormality is detected during routine surveillance is primarily characterization of the newly detected abnormality.

It is to be noted that all new liver lesions detected on surveillance scans are not always malignant. The development of FNH, regenerative nodules, and perfusion abnormalities (some related to small segmental portal thrombi) have all been reported subsequent to chemotherapy. Smith et al [89] have reported that in the pediatric population, new liver lesions were found in 16.8% of patients, in which the majority of lesions (30.4%) were FNH. Other lesions such as perfusion abnormalities, post-therapy effects, and hepatic cysts made up most of the remaining new lesions. Vascular injury in the form of sinusoidal obstructive syndrome is responsible for causing some focal lesions, such as nodular regenerative hyperplasia and peliosis. This is most commonly seen after myeloablative chemotherapy prior to bone marrow transplant or with oxaliplatin-based chemotherapy regimens [90].

It is also not uncommon to develop fatty liver after the use of chemotherapy, particularly after fluorouracil- and irinotecan-based treatment. Occasionally this may be in the form of focal fatty infiltration, generally in areas of nonportal venous supply to the liver, or rarely focal fatty infiltration may be distributed throughout the liver, mimicking liver metastases [91]. In addition, it is important to recognize that with the use of antiangiogenic agents such as bevacizumab, liver metastases may undergo cystic change and mimic benign hepatic cysts [92].

The characterization of liver lesions should be performed according to American College of Radiology (ACR) guidelines for liver characterization (see the ACR Appropriateness Criteria® "Liver Lesion—Initial Characterization" [93], variant tables 4, 5, and 6).

Summary of Recommendations

- Variant 1: Suspected liver metastases. Initial imaging test following detection of primary tumor.
  - In the setting of initial diagnosis of a malignancy, CT or MRI is appropriate. It is important to optimize the imaging techniques for accurate staging.

- Variant 2: Suspected liver metastases. Surveillance following treatment of primary tumor.
  - CT is the preferred imaging modality in the setting of surveillance. The technique should be optimized for improved accuracy.
- Variant 3: Presurgical assessment of liver metastasis.
  - MRI is the preferred imaging modality in the presurgical setting. However, CT (particularly optimized multiphase CT) is also recommended. Cross-sectional imaging can be supplemented with intraoperative US.

Summary of Evidence

Of the 93 references cited in the *ACR Appropriateness Criteria® Suspected Liver Metastases* document, 7 are categorized as therapeutic references including 1 well-designed study and 2 good-quality studies. Additionally, 79 references are categorized as diagnostic references including 3 well-designed studies, 31 good-quality studies, and 24 quality studies that may have design limitations. There are 25 references that may not be useful as primary evidence. There are 7 references that are meta-analysis studies.

The 93 references cited in the *ACR Appropriateness Criteria® Suspected Liver Metastases* document were published from 1986 through 2015.

Although there are references that report on studies with design limitations, 37 well-designed or good-quality studies provide good evidence.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document.

Relative Radiation Level Designations		
Relative Radiation Level*	**Adult Effective Dose Estimate Range**	**Pediatric Effective Dose Estimate Range**
O	0 mSv	0 mSv
☢	<0.1 mSv	<0.03 mSv
☢ ☢	0.1-1 mSv	0.03-0.3 mSv
☢ ☢ ☢	1-10 mSv	0.3-3 mSv
☢ ☢ ☢ ☢	10-30 mSv	3-10 mSv
☢ ☢ ☢ ☢ ☢	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies".		

Supporting Documents

For additional information on the Appropriateness Criteria methodology and other supporting documents go to www.acr.org/ac.

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