

**American College of Radiology
ACR Appropriateness Criteria®**

Clinical Condition: Suspected Liver Metastases

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

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen with contrast	8	Images are acquired during portal venous phase (PVP). Hepatic arterial phase (HAP) imaging is useful for patients with a hypervascular primary tumor such as (but not limited to) renal cell, pancreatic islet cell, and thyroid carcinoma; carcinoid and other neuroendocrine tumors; and melanoma.	☼☼☼
MRI abdomen without and with contrast	8	Dynamic gadolinium-chelate-enhanced imaging is used most commonly. Delayed imaging after iron oxide or gadolinium-based hepatobiliary contrast agents (eg, BOPTA or gadoteric acid) can be useful for staging patients with liver metastases. See statement regarding contrast in text under "Anticipated Exceptions."	O
FDG-PET skull base to mid-thigh and CT abdomen with contrast	8	When the primary tumor is known to be FDG-PET avid. May be particularly valuable if liver-directed therapy is planned. A diagnostic-quality CT examination is performed.	☼☼☼☼
FDG-PET skull base to mid-thigh and CT abdomen without contrast	6	When the primary tumor is known to be FDG-PET avid. May be particularly valuable if liver-directed therapy is planned. A diagnostic-quality CT examination is performed.	☼☼☼☼
FDG-PET skull base to mid thigh	5	Whole-body PET can be done for primaries like melanoma or sarcoma. Attenuation correction by radionuclide methods or, more commonly, with CT is considered part of the examination.	☼☼☼☼
MRI abdomen without contrast	5		O
CT abdomen without contrast	4	CT of the abdomen without contrast is potentially indicated if patients cannot receive iodinated contrast and/or gadolinium, and/or cannot undergo MRI.	☼☼☼
US abdomen	4	Doppler may be useful, particularly in vascular lesions.	O
CTA abdomen with contrast	2	Only for operative planning – not for diagnosis of metastases.	☼☼☼
In-111 somatostatin receptor scintigraphy	2	May be useful in patients with neuroendocrine tumors.	☼☼☼☼
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Clinical Condition:**Suspected Liver Metastases****Variant 2:****Surveillance following treatment of primary tumor.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
CT abdomen with contrast	8	Images are acquired during PVP. HAP imaging is useful for patients with a hypervascular primary tumor such as (but not limited to) renal cell, pancreatic islet cell, and thyroid carcinoma; carcinoid and other neuroendocrine tumors; and melanoma.	☼ ☼ ☼
MRI abdomen without and with contrast	8	Dynamic gadolinium-chelate-enhanced imaging is used most commonly. Delayed imaging after-iron oxide or gadolinium-based hepatobiliary contrast agents (eg, BOPTA or gadoxetic acid) can be useful for staging patients with liver metastases. See statement regarding contrast in text under “Anticipated Exceptions.”	O
FDG-PET skull base to mid-thigh and CT abdomen with contrast	8	When the primary tumor is known to be FDG-PET avid. May be particularly valuable if liver-directed therapy is planned. A diagnostic-quality CT examination is performed.	☼ ☼ ☼ ☼
FDG-PET skull base to mid-thigh and CT abdomen without contrast	6	When the primary tumor is known to be FDG-PET avid. May be particularly valuable if liver-directed therapy is planned. A diagnostic-quality CT examination is performed.	☼ ☼ ☼ ☼
FDG-PET skull base to mid thigh	5	Whole-body PET can be done for primaries like melanoma or sarcoma. Attenuation correction by radionuclide methods or, more commonly, with CT is considered part of the examination.	☼ ☼ ☼ ☼
MRI abdomen without contrast	5		O
CT abdomen without contrast	4	CT of the abdomen without contrast is potentially indicated if patients cannot receive iodinated contrast and/or gadolinium, and/or cannot undergo MRI.	☼ ☼ ☼
US abdomen	4	Doppler may be useful, particularly in vascular lesions.	O
In-111 somatostatin receptor scintigraphy	4	May be useful in patients with neuroendocrine tumors.	☼ ☼ ☼ ☼
CTA abdomen with contrast	2	Only for operative planning – not for diagnosis of metastases.	☼ ☼ ☼
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Clinical Condition:**Suspected Liver Metastases****Variant 3:****Abnormal surveillance US, CT, or MRI, in PVP: high suspicion of malignancy.**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI abdomen without and with contrast	9	Dynamic gadolinium-chelate-enhanced imaging is used most commonly. Delayed imaging after iron oxide or gadolinium-based hepatobiliary contrast agents (eg, BOPTA or gadoxetic acid) can be useful for staging patients with liver metastases. See statement regarding contrast in text under "Anticipated Exceptions."	O
Percutaneous biopsy liver	8		NS
CT abdomen with contrast	8	Images are acquired during PVP. HAP imaging is useful for patients with a hypervascular primary tumor such as (but not limited to) renal cell, pancreatic islet cell, and thyroid carcinoma; carcinoid and other neuroendocrine tumors; and melanoma.	☼ ☼ ☼
FDG-PET skull base to mid-thigh and CT abdomen with contrast	8	When the primary tumor is known to be FDG-PET avid. May be particularly valuable if liver-directed therapy is planned. A diagnostic-quality CT examination is performed.	☼ ☼ ☼ ☼
FDG-PET skull base to mid-thigh and CT abdomen without contrast	6	When the primary tumor is known to be FDG-PET avid. May be particularly valuable if liver-directed therapy is planned. A diagnostic-quality CT examination is performed.	☼ ☼ ☼ ☼
FDG-PET skull base to mid thigh	6	Whole-body PET can be done for primaries like melanoma or sarcoma. Attenuation correction by radionuclide methods or, more commonly, with CT is considered part of the examination.	☼ ☼ ☼ ☼
MRI abdomen without contrast	5		O
US abdomen	4	Doppler may be useful, particularly in vascular lesions.	O
US abdomen intraoperative/laparoscopic	4		O
In-111 somatostatin receptor scintigraphy	3	May be useful in patients with neuroendocrine tumors.	☼ ☼ ☼ ☼
CTA abdomen with contrast	3	Only for operative planning – not for diagnosis of metastases.	☼ ☼ ☼
CT abdomen without contrast	3	CT of the abdomen without contrast is potentially indicated if patients cannot receive iodinated contrast and/or gadolinium, and/or cannot undergo MRI.	☼ ☼ ☼
<u>Rating Scale:</u> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Clinical Condition:**Suspected Liver Metastases****Variant 4:****Abnormal surveillance US, CT, or MRI in PVP suggests but is not definitive for benign lesion(s).**

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
MRI abdomen without and with contrast	9	Dynamic gadolinium-chelate-enhanced imaging is used most commonly. Delayed imaging after iron oxide or gadolinium-based hepatobiliary contrast agents (eg BOPTA or gadoxetic acid) can be useful for staging patients with liver metastases. See statement regarding contrast in text under “Anticipated Exceptions.”	O
CT abdomen with contrast	8	Images are acquired during PVP. HAP imaging is useful for patients with a hypervascular primary tumor such as (but not limited to) renal cell, pancreatic islet cell, and thyroid carcinoma; carcinoid and other neuroendocrine tumors; and melanoma.	☼ ☼ ☼
MRI abdomen without contrast	5		O
Percutaneous biopsy liver	4		NS
US abdomen	4	Doppler may be useful, particularly in vascular lesions.	O
FDG-PET skull base to mid-thigh and CT abdomen with contrast	4	When the primary tumor is known to be FDG-PET avid. Depends on the lesion and what prior imaging has shown. See the ACR Appropriateness Criteria topic on “Liver Lesion — Initial Characterization.” A diagnostic-quality CT examination is performed.	☼ ☼ ☼ ☼
In-111 somatostatin receptor scintigraphy	3	May be useful in patients with neuroendocrine tumors.	☼ ☼ ☼ ☼
CTA abdomen with contrast	3	Only for operative planning – not for diagnosis of metastases.	☼ ☼ ☼
US abdomen intraoperative/laparoscopic	3		O
CT abdomen without contrast	3	CT abdomen without contrast is potentially indicated if patients cannot receive iodinated contrast and/or gadolinium, and/or cannot undergo MRI.	☼ ☼ ☼
FDG-PET skull base to mid-thigh and CT abdomen without contrast	3	When the primary tumor is known to be FDG-PET avid. A diagnostic-quality CT examination is performed.	☼ ☼ ☼ ☼
FDG-PET skull base to mid thigh	2	Whole body PET can be done for primaries like melanoma or sarcoma. Attenuation correction by radionuclide methods or, more commonly, with CT is considered part of the examination.	☼ ☼ ☼ ☼
<u>Rating Scale:</u> 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

In the United States, metastatic disease is the most common cause of malignancy in the liver and is 20 to 50 times more common than primary liver cancer. The colon, stomach, pancreas, and breast are the most common primary sites. The appearance of a new lesion in the liver in a patient with a history of cancer strongly suggests hepatic metastasis. On the other hand, most small (≤ 1 -1.5 cm) liver lesions, even in patients with known malignancy, are not malignant, especially if there are fewer than five lesions [1-2]. The ACR has recently published a white paper on the management of incidental findings on abdominal CT [3]. In most series, about one-third of patients who die with a malignancy have liver involvement.

The liver is susceptible to metastatic disease, primarily due to the nature of the endothelial lining. The dual blood supply to the liver has an effect on the vascularity of liver metastases, with those supplied by the hepatic arterial system being more vascular than those supplied by the portal venous system. Most gastrointestinal cancer is spread through the portal venous system, whereas other tumors are spread through the hepatic arterial system [4].

Numerous imaging methods are available for detecting intrahepatic metastatic disease before, during, and after definitive therapy for the primary lesion. The usefulness

of various 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.

This document reviews the broad variety of available imaging tests so that each can be rated by the expert panel, realizing that many published scientific studies do not compare all imaging tests at the current state of the art [5-6].

Ultrasound

Ultrasound (US) is the most available technique for liver imaging worldwide, and in many countries is the major imaging test used to search for liver metastases. In the United States, the widespread availability of computed tomography (CT) and magnetic resonance imaging (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 the United States pretreatment and post-treatment screening for metastases is performed infrequently with US. Comparative studies demonstrate that unenhanced gray-scale US has high specificity but lower sensitivity than CT and MRI [5-7]. With US, metastases can be hypoechoic, hyperechoic, cystic, or diffuse. Doppler may be useful, particularly in vascular lesions such as neuroendocrine tumors and sarcomas.

Research on current US contrast agents has demonstrated high accuracy in characterizing liver lesions [8-13]. The second-generation agents generally consist of either stable perfluorocarbon or sulphur hexafluoride-containing microbubbles which are injected intravenously and insonated with low acoustic pressure. The particle then emits a harmonic signal and can be detected with pulse inversion recovery to show the vascular architecture of a lesion and temporal course of enhancement and thereby help characterize the lesion. These second-generation agents, however, have not yet been approved for hepatic imaging in the United States.

In patients with lesions which are suspicious for malignancy, percutaneous biopsy, under either US or CT guidance, may be appropriate as clinically indicated.

Intraoperative/Laparoscopic Ultrasound

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 surgical inspection and palpation. Additionally, IOUS can be important for localization of tumors for ablative techniques or to guide intraoperative biopsy or surgical resection [5-6,14-17].

Laparoscopic US (LUS), an alternative to open IOUS, has shown promising results. In one study of 55 patients with primary and secondary liver neoplasms who underwent LUS as part of a tumor ablation procedure, LUS

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demonstrated all 201 liver tumors shown by triphasic CT and an additional 21 lesions not shown by CT [18].

Endoscopic US (EUS) has emerged as an alternative tool for imaging the liver. In one study the diagnostic accuracies of EUS with or without fine-needle aspiration (FNA) and CT were 98% and 92%, respectively [19]. However, in this study the CT collimation was suboptimal at 10 mm, and the study authors acknowledged that EUS/EUS-FNA has some limitations in examining the right hepatic lobe.

Computed Tomography

CT is particularly suited for evaluating metastatic disease, because the liver and potential extrahepatic sites of tumor spread can be evaluated during the same examination. Multidetector helical CT (MDCT) is the preferred examination in the United States for surveillance for metastatic disease after treatment of the primary neoplasm. Because most hepatic metastases are relatively hypovascular compared with normal liver parenchyma, the lesions are hypoattenuating when imaged during the peak of hepatic parenchymal enhancement (portal venous phase [PVP]). In general, therefore, imaging during the PVP of hepatic enhancement is adequate to detect most hepatic lesions in most patients [20-22].

Hypervascular lesions are less common, and tumors in this group include metastases from renal cell carcinoma, carcinoid tumor, islet cell carcinoma, thyroid carcinoma, melanoma, and neuroendocrine tumors. In a large series of patients, small (<2 cm) hypervascular lesions were seen better in the arterial phase than in the PVP [20]. With the widespread use of multidetector scanners, arterial phase scanning can be routine. Although metastases from breast carcinoma are sometimes hypervascular, two studies showed that arterial phase imaging was not necessary in this group [20,22]. Hypervascular lesions may be isoattenuating to liver during the PVP of hepatic enhancement. With helical CT, both arterial and PVP imaging are recommended for patients with hypervascular primary tumors [23]. 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). However, in younger patients with curable disease, the radiation exposure must be balanced against the potentially increased yield obtained by doing multiphasic CT.

CT arterial portography is almost never used at present, as it is an invasive angiographic technique that often yields artifacts that decrease accuracy [5-7,23]. CT angiography (CTA) is no longer used for diagnostic purposes and is rarely used for preoperative planning.

Magnetic Resonance Imaging

With MRI, most hepatic metastases are hypointense to normal liver on T1-weighted images and hyperintense to liver on T2-weighted images. Morphologic, signal intensity, and contrast enhancement features have been shown to be useful in distinguishing metastatic lesions

from common benign lesions such as hemangiomas and cysts.

Contrast-enhanced imaging is an important part of the hepatic MRI examination for detecting metastases and is particularly useful in characterizing hepatic lesions that are identified. Gadolinium chelates, which are the most widely used MR contrast agents, are most useful when used with dynamic T1-weighted gradient echo sequences. Comparative studies have shown gadolinium-enhanced MRI to be more sensitive in the detection of liver metastases than positron emission tomography (PET) and PET/CT [24-25]. Gadolinium ethoxybenzyl diethylenetriaminepentaacetic acid (gadoteric acid disodium or Gd-EOB-DTPA) is a more recently developed liver-specific contrast agent with combined perfusion and hepatocyte-selective properties. A comparative study demonstrated a superior detection rate and higher confidence in characterization of liver metastases for Gd-EOB-DTPA-enhanced MRI than for PET/CT [26]. MRI using superparamagnetic iron oxide (SPIO) contrast agents, which are taken up selectively by the reticuloendothelial system, has been shown to be more sensitive than unenhanced MRI and equal to or more sensitive than gadolinium-enhanced MRI [27-28]. In one study iron-oxide-enhanced MRI also was more sensitive than 16-row MDCT for detecting liver metastases [29]. Another study demonstrated that iron-oxide-enhanced MRI was more sensitive but less specific than PET in detecting liver metastases [30]. In one study, gadoteric acid showed comparable diagnostic performance to iron-oxide-enhanced MRI for detecting liver metastases [31]. Delayed-phase imaging during gadobenate dimeglumine (GD-BOPTA)-enhanced MRI [27] and mangafodipir trisodium (Mn-DPDP)-enhanced MRI [32-33] have been shown to be equivalent to iron-oxide-enhanced MRI for detecting liver metastases, but mangafodipir and SPIO are currently not available in the United States. In another study Mn-DPDP MRI proved to be superior to PET/CT in detecting small liver metastases [34].

Nuclear Imaging

PET has become more widely used in detecting metastatic disease. Two meta-analyses comparing CT, MRI, and fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) PET in patients with cancers of the gastrointestinal tract concluded that FDG-PET is the most sensitive imaging test for distinguishing hepatic metastases from colorectal cancer [35-36]. In addition, 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%-32%, mainly due to detection of unknown extrahepatic disease. PET also has been shown to be accurate in distinguishing benign from malignant liver tumors. A limitation of FDG-PET, however, is that it may fail to demonstrate small (<1 cm) liver metastases [37-40]. In addition, the sensitivity of FDG-PET for demonstrating hepatic metastases from colorectal cancer is reduced in patients who have undergone recent chemotherapy [41-44]. One study

demonstrated that acquisition of delayed images improved the hepatic detection of pathological FDG uptake [45]. For staging and restaging patients with colorectal liver metastases, integration of CT and FDG-PET data, either by fusion or by integrated PET/CT imaging, enables better management guidance than with either technique alone. PET/CT has been shown to have high sensitivity and specificity for the presence of liver metastases, and this capability has been well documented in patients with colorectal cancer [34,46].

Traditional reticulo-endothelial radionuclide imaging is no longer used for detecting liver metastases. Somatostatin receptor scintigraphy is capable of demonstrating hepatic metastases from endocrine tumors but is not as sensitive as CT and MRI [47].

Summary

- Many radiologic techniques are available for preoperative detection of liver metastases and postoperative surveillance.
- Some of the less widely used screening techniques can be useful when there is a need for specific problem solving.
- Rapid technological and clinical advances in equipment, contrast agents, and radioisotopes make direct comparison of the various techniques difficult.
- In addition, local custom and equipment availability within communities or medical centers can be expected to lead to a variety of indications and applications in detecting hepatic metastatic disease.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF) is a disorder with a scleroderma-like presentation and a spectrum of manifestations that can range from limited clinical sequelae to fatality. It appears to be related to both underlying severe renal dysfunction and the administration of gadolinium-based contrast agents. It has occurred primarily in patients on dialysis, rarely in patients with very limited glomerular filtration rate (GFR) (ie, <30 mL/min/1.73m²), and almost never in other patients. There is growing literature regarding NSF. Although some controversy and lack of clarity remain, there is a consensus that it is advisable to avoid all gadolinium-based contrast agents in dialysis-dependent patients unless the possible benefits clearly outweigh the risk, and to limit the type and amount in patients with estimated GFR rates <30 mL/min/1.73m². For more information, please see the [ACR Manual on Contrast Media](#) [48].

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 NS (not specified).		

Supporting Document(s)

- [ACR Appropriateness Criteria® Overview](#)
- [Procedure Information](#)
- [Evidence Table](#)

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.