Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Schwartz SI. Liver. In: Schwartz SI, Shires TG, Spencer FC, et al, eds. *Principles of surgery*. 7th ed. New York: McGraw-Hill, Health Professions Division; 1999:1411.	Review/Other-Tx	NA	Book discussing general surgery.	N/A	4
2. Jones EC, Chezmar JL, Nelson RC, Bernardino ME. The frequency and significance of small (less than or equal to 15 mm) hepatic lesions detected by CT. *AJR Am J Roentgenol.* 1992;158(3):535-539.	Review/Other-Dx	1454 patients	To determine the frequency of detection of small hepatic lesions (≤15 mm) in outpatients who had abdominal CT and to assess the significance of these lesions in the presence or absence of known malignant tumors.	In 254 patients (17%), hepatic lesions ≤15 mm were detected. In 51% of these patients, lesions were judged benign on the basis of other imaging studies, biopsy results, or stability for at least 6 months as shown by CT. Lesions were judged malignant on the basis of progression seen on radiologic studies or biopsy in 22%. The other 27% of the patients had lesions that could not be classified. The majority of patients with small hepatic lesions (82%) were known to have a malignant tumor; in 51% of these patients, lesions were diagnosed as benign. No patient without a known malignant tumor had a small hepatic lesion that was determined to be malignant. Multiple small lesions were more likely to represent malignant disease than were single small lesions.	4
3. Schwartz LH, Gandras EJ, Colangelo SM, Ercolani MC, Panicek DM. Prevalence and importance of small hepatic lesions found at CT in patients with cancer. *Radiology.* 1999;210(1):71-74.	Review/Other-Dx	378 patients	Retrospective follow-up CT study of patients with known malignancy to assess the frequency that 1 cm or smaller hepatic lesions were metastasis.	Small hepatic lesions demonstrated interval growth in 11.6% patients (6+ months follow-up) and were considered metastatic. In 80.2% of patients there was no interval growth (mean follow-up 25.6 months; range, 6–56 months). These were presumed benign. 8.2% of patients had <6 months follow-up and were considered indeterminate.	4
4. Khatri VP, Petrelli NJ, Belghiti J. Extending the frontiers of surgical therapy for hepatic colorectal metastases: is there a limit? *J Clin Oncol.* 2005;23(33):8490-8499.	Review/Other-Tx	N/A	To review development of innovative multidisciplinary modalities and the aggressive surgical approach that has been adopted to extend the frontiers of surgical therapy for colorectal hepatic metastases.	No results stated in abstract.	4

Suspected Liver Metastases
EVIDENCE TABLE

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5. Kopetz S, Chang GJ, Overman MJ, et al. Improved survival in metastatic colorectal cancer is associated with adoption of hepatic resection and improved chemotherapy. *J Clin Oncol.* 2009;27(22):3677-3683.	Observational-Tx	2,470 patients from 2 facilities and 49,459 from SEER registry	To evaluate the changes in survival of patients with metastatic colorectal cancer using both multi-institutional and population-based databases and to associate these changes to hepatic resection utilization and temporal trends in improvements in chemotherapy.	2470 patients with metastatic colorectal cancer at diagnosis received their primary treatment at the 2 institutions during this time period. Median overall survival for those patients diagnosed from 1990 to 1997 was 14.2 months, which increased to 18.0, 18.6, and 29.3 months for patients diagnosed in 1998 to 2000, 2001 to 2003, and 2004 to 2006, respectively. Likewise, 5-year overall survival increased from 9.1% in the earliest time period to 19.2% in 2001 to 2003. Improved outcomes from 1998 to 2004 were a result of an increase in hepatic resection, which was performed in 20% of the patients. Improvements from 2004 to 2006 were temporally associated with increased utilization of new chemotherapeutics. In the SEER registry, overall survival for the 49,459 identified patients also increased in the most recent time period.	2
6. Page AJ, Weiss MJ, Pawlik TM. Surgical management of noncolorectal cancer liver metastases. *Cancer.* 2014;120(20):3111-3121.	Review/Other-Tx	N/A	To we review the current data on the surgical management of non-neuroendocrine and neuroendocrine tumors metastatic to the liver.	No results stated in abstract.	4
7. Kruskal JB, Kane RA. Imaging of primary and metastatic liver tumors. *Surg Oncol Clin N Am.* 1996;5(2):231-260.	Review/Other-Dx	N/A	To review imaging of primary and metastatic liver tumors.	To best evaluate liver malignancies, a sensible combination of imaging modalities, depending on the patient population, radiologic strengths, and imaging equipment available, is recommended to provide the best overall assessment of the number and location of liver neoplasms.	4
8. Mahfouz AE, Hamm B, Mathieu D. Imaging of metastases to the liver. *Eur Radiol.* 1996;6(5):607-614.	Review/Other-Dx	N/A	To review the problems which face the different imaging modalities in diagnosis of liver metastases in view of the pathological background of the disease. Article also discusses the indications, strong points, and shortcomings of each of the imaging modalities in diagnosis of metastases, and surveys the recent efforts done to improve their performance through the optimization of quality control and in the innovations in the field of contrast agents.	No results stated in abstract.	4

Suspected Liver Metastases
EVIDENCE TABLE

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9. Albrecht T, Blomley MJ, Burns PN, et al. Improved detection of hepatic metastases with pulse-inversion US during the liver-specific phase of SHU 508A: multicenter study. *Radiology.* 2003;227(2):361-370.	Experimental-Dx	80 patients	To compare conventional B-mode US alone with the combination of conventional B-mode US and contrast material-enhanced (SHU 508A) late-phase pulse-inversion US for the detection of hepatic metastases by using dual-phase spiral CT as the standard of reference.	In 45/80 (56%) patients with metastases, more metastases were seen at CEUS than at conventional US. In 3 of these patients, conventional US images appeared normal. The addition of CEUS improved sensitivity for the detection of individual metastases from 71% to 87% (P<.001). On a patient basis, sensitivity improved from 94% to 98% (P=.44), and specificity improved from 60% to 88% (P<.01). Contrast enhancement improved the subjective conspicuity of metastases in 66/75 (88%) patients and the objective contrast by a mean of 10.8 dB (P<.001). CEUS showed more metastases than did CT in 7 patients, and CT showed more than did CEUS in 1 of 22 patients in whom an independent reference (MRI, IOUS, or pathologic findings) was available.	2
10. Bartolotta TV, Midiri M, Quaia E, et al. Liver haemangiomas undetermined at grey-scale ultrasound: contrast-enhancement patterns with SonoVue and pulse-inversion US. *Eur Radiol.* 2005;15(4):685-693.	Observational-Dx	20 patients 35 hemangiomas; 2 observers	Prospective blinded study to describe contrast-enhancement patterns of hepatic hemangiomas undetermined at grey-scale US on SonoVue-enhanced pulse-inversion US.	After administration of SonoVue, 31/35 (88%) hemangiomas showed peripheral hyperechoic nodules in the arterial phase. Pulse-inversion after the administration of SonoVue enabled the depiction of typical contrast-enhancement patterns in hemangiomas undetermined at baseline US.	2
11. Celli N, Gaiani S, Piscaglia F, et al. Characterization of liver lesions by real-time contrast-enhanced ultrasonography. *Eur J Gastroenterol Hepatol.* 2007;19(1):3-14.	Observational-Dx	Group 1: 125 noncirrhotic patients, 171 lesions: Group 2: 67 cirrhotic patients, 75 lesions	To examine the role of real-time CEUS in the characterization of liver lesions.	In noncirrhotic patients, the hypoechoic pattern in portal and sinusoidal phase (rapid washout) or the markedly hypoechoic or anechoic pattern in sinusoidal phase (marked late washout) showed a sensitivity, specificity and accuracy of 96.8%, 100% and 98.2% for the diagnosis of malignancy. In cirrhotic patients, early arterial enhancement showed a sensitivity of 93.9% for diagnosis of malignancy and specificity of 55.5%. Real-time CEUS provides sensitive and specific criteria for characterization of liver lesions.	2

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
12. Dietrich CF, Kratzer W, Strobe D, et al. Assessment of metastatic liver disease in patients with primary extrahepatic tumors by contrast-enhanced sonography versus CT and MRI. *World J Gastroenterol.* 2006;12(11):1699-1705.	Experimental-Dx	125 patients	To evaluate CEUS using SonoVue in the detection of liver metastases in patients with known extrahepatic primary tumors vs the combined gold standard comprising CT, MRI and clinical/histological data.	CEUS with SonoVue increased significantly the number of FLLS detected vs unenhanced US. In 31.4% of the patients, more lesions were found after contrast enhancement. The total numbers of lesions detected were comparable with CEUS (55), triple-phase spiral CT (61) and MRI with a liver-specific contrast agent (53). Accuracy of detection of metastatic disease (ie, at least 1 metastatic lesion) was significantly higher for CEUS (91.2%) than for unenhanced US (81.4%) and was similar to that of triple-phase spiral CT (89.2%). In 53 patients whose CEUS examination was negative, a follow-up examination 3-6 months later confirmed the absence of metastatic lesions in 50 patients (94.4%).	3
13. Dietrich CF, Mertens JC, Braden B, Schuessler G, Ott M, Ignee A. Contrast-enhanced ultrasound of histologically proven liver hemangiomas. *Hepatology.* 2007;45(5):1139-1145.	Observational-Dx	58 patients	Prospective study to assess the role of CEUS in patients with histological proven liver hemangiomas.	In 43 patients (74%), peripheral nodular arterial enhancement was detected. Strong homogenous arterial enhancement was found in 9/58 (16%) patients. CEUS shows typical hemangioma imaging characteristics.	3
14. Lanka B, Jang HJ, Kim TK, Burns PN, Wilson SR. Impact of contrast-enhanced ultrasonography in a tertiary clinical practice. *J Ultrasound Med.* 2007;26(12):1703-1714.	Observational-Dx	1,040 patients	To evaluate the impact of CEUS of the liver in a tertiary clinical practice.	CEUS was accurate in 233 (89.2%) of 261 with histologic proof, including 208 malignant lesions. CEUS is recommended for clinical management.	3
15. Luo W, Numata K, Morimoto M, et al. Focal liver tumors: characterization with 3D perflubutane microbubble contrast agent-enhanced US versus 3D contrast-enhanced multidetector CT. *Radiology.* 2009;251(1):287-295.	Observational-Dx	139 patients	Retrospective blinded review to examine the potential application of contrast material-enhanced 3D US, as compared with contrast-enhanced 3D CT, for characterization of focal liver tumors. Two blinded reviewers.	Readers 1 and 2 had concordant US and CT findings for 115 (83%) and 116 (83%) of the 139 lesions, respectively. No significant differences between the 2 modalities: sensitivity was 83% or greater with both modalities, specificity was 87% or greater with CEUS and 92% or greater with contrast-enhanced CT, the PPV was 71% or greater with both modalities, and the A(z) was at least 0.89 with US and at least 0.92 with CT. Contrast-enhanced 3D US potentially can be used to characterize focal liver tumors.	2

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
16. Trillaud H, Bruel JM, Valette PJ, et al. Characterization of focal liver lesions with SonoVue-enhanced sonography: international multicenter-study in comparison to CT and MRI. *World J Gastroenterol.* 2009;15(30):3748-3756.	Experimental-Dx	127 patients	Phase IIIb, controlled, multicenter, multinational study to determine whether the sonographic characterization of FLLs can be improved using SonoVue-enhancement; and to compare this method with CT and MRI.	Compared to CT and/or dynamic MRI, SonoVue-enhanced sonography was 30.2% more sensitive in the recognition of malignancy and 16.1% more specific in the exclusion of malignancy and overall 22.9% more accurate. In the subgroup with confirmative histology available (n=30), sensitivity was 95.5% (CEUS), 72.2% (CT) and 81.8% (MRI), and specificity was 75.0% (CEUS), 37.5% (CT) and 42.9% (MRI). Sensitivity and specificity of CEUS for the identification of FNH and hemangiomas was 100% and 87%, accuracy 94.5%. SonoVue-enhanced sonography is the most sensitive, most specific and thus most accurate imaging modality for the characterization of FLLs.	3
17. Wilson SR, Kim TK, Jang HJ, Burns PN. Enhancement patterns of focal liver masses: discordance between contrast-enhanced sonography and contrast-enhanced CT and MRI. *AJR Am J Roentgenol.* 2007;189(1):W7-W12.	Review/Other-Dx	44 cases	To investigate the origin of the infrequent discordance between the contrast enhancement patterns of liver lesions on US and those on CT and MRI.	4 categories of discordance were identified, 1 of which is unexplained. Contrast agent diffusion caused PVP discordance in malignant tumors (n = 6) whereby CT and MRI contrast material diffused through the vascular endothelium into the tumor interstitium, concealing washout. Sonographic microbubbles were purely intravascular and showed washout. Arterial phase timing discordance occurred in metastatic lesions (n = 10) with hypervascularity and rapid washout on CEUS. CT arterial imaging performed later showed hypovascularity. Rapidly enhancing hemangiomas (n = 7) exhibited hypervascularity on CT when CEUS also showed peripheral nodules and fast centripetal progression. Discordance caused by fat in lesions (n = 4) or liver (n = 10) reflected the inherent echogenicity of fat on US compared with its low attenuation on CT and low signal intensity on MRI.	4

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
18. Claudon M, Dietrich CF, Choi BI, et al. Guidelines and good clinical practice recommendations for contrast enhanced ultrasound (CEUS) in the liver--update 2012: a WFUMB-EFSUMB initiative in cooperation with representatives of AFSUMB, AIUM, ASUM, FLAUS and ICUS. *Ultraschall Med.* 2013;34(1):11-29.	Review/Other-Dx	N/A	Guidelines and good clinical practice recommendations for the hepatic use of CEUS using contrast specific imaging techniques.	N/A	4
19. Mazzoni G, Napoli A, Mandetta S, et al. Intra-operative ultrasound for detection of liver metastases from colorectal cancer. *Liver Int.* 2008;28(1):88-94.	Observational-Dx	167 patients	To evaluate the accuracy of IOUS imaging in detecting liver secondaries at the time of primary colorectal surgery and to evaluate the impact of IOUS on patient management.	IOUS supplied additional information in the case of 31 patients. In 28 of these patients, this information had a major impact on the intraoperative strategy, in that the procedure was altered.	2
20. Rydzewski B, Dehdashti F, Gordon BA, Teefey SA, Strasberg SM, Siegel BA. Usefulness of intraoperative sonography for revealing hepatic metastases from colorectal cancer in patients selected for surgery after undergoing FDG PET. *AJR Am J Roentgenol.* 2002;178(2):353-358.	Observational-Dx	47 patients	To compare the diagnostic performance of preoperative PET with FDG and IOUS with the standard of histologic examination of resected liver specimens in evaluating patients for curative resection of liver metastases from colorectal cancer.	87 malignant hepatic lesions were identified by histopathologic analysis of liver specimens, and 23 benign hepatic abnormalities were documented histopathologically or by uroradiologic imaging. For hepatic sections characterized as containing metastases by radiologic imaging, the PPV for FDG-PET was 93% (54/58); for IOUS, 87% (52/60); and for conventional imaging, 83% (43/52). For individual lesions characterized as probably malignant, the PPV for FDG-PET was 93% (62/68); for IOUS, 89% (63/71); and for conventional imaging, 78% (46/59). The findings at IOUS led to a change in the clinical treatment of only 1 patient (2%).	3
21. Ward J, Naik KS, Guthrie JA, Wilson D, Robinson PJ. Hepatic lesion detection: comparison of MR imaging after the administration of superparamagnetic iron oxide with dual-phase CT by using alternative-free response receiver operating characteristic analysis. *Radiology.* 1999;210(2):459-466.	Experimental-Dx	51 hepatic resection candidates	To compare the performance of MRI after the administration of SPIO and dual-phase CT in the depiction of liver metastases.	The mean sensitivity of MRI was significantly higher than that of CT ($P<.02$): 79.8% for MRI and 75.3% for CT for all lesions, and 80.6% for MRI and 73.5% for CT for malignant lesions. The mean areas under the alternative-free response ROC were 0.83 for MRI and 0.78 for CT (difference not significant). SPIO-enhanced MRI was more sensitive than dual-phase CT in the depiction of colorectal metastases.	2

Suspected Liver Metastases
EVIDENCE TABLE

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22. Wildi SM, Gubler C, Hany T, et al. Intraoperative sonography in patients with colorectal cancer and resectable liver metastases on preoperative FDG-PET-CT. *J Clin Ultrasound.* 2008;36(1):20-26.	Observational-Dx	31 patients	To compare the diagnostic performance of preoperative PET/CT alone and PET/CT combined with IOUS in the evaluation of patients who are considered for curative resection of hepatic metastases from colorectal carcinoma.	31 patients (mean age, 63.5 years [range, 53–82 years]) were analyzed. 15 patients had received preoperative chemotherapy. The mean interval between PET/CT and IOUS was 22.6 days (range, 1–56 days). In 4 cases, neither PET/CT nor IOUS correctly diagnosed the liver metastases. In all 31 patients, the sensitivity of PET/CT alone and PET/CT combined with IOUS was 63% (95% CI, 44%–80%) and 93% (95% CI, 78%–98%), respectively; the PPV was 81% and 89%, respectively. In patients without preoperative chemotherapy (n = 16), the sensitivity of PET/CT alone and PET/CT combined with IOUS was 77% (95% CI, 49%–94%) and 100% (95% CI, 79%–100%), respectively. In 11 cases (35%), IOUS altered the surgical strategy.	3
23. Pomfret EA, Washburn K, Wald C, et al. Report of a national conference on liver allocation in patients with hepatocellular carcinoma in the United States. *Liver Transpl.* 2010;16(3):262-278.	Review/Other-Dx	N/A	A national conference was held to better characterize the long-term outcomes of liver transplantation for patients with HCC and to assess whether it is justified to continue the policy of assigning increased priority for candidates with early-stage HCC on the transplant waiting list in the United States.	At the completion of the meeting, there was agreement that the allocation policy should result in similar risks of removal from the waiting list and similar transplant rates for HCC and non-HCC candidates. In addition, the allocation policy should select HCC candidates so that there are similar post-transplant outcomes for HCC and non-HCC recipients. There was a general consensus for the development of a calculated continuous HCC priority score for ranking HCC candidates on the list that would incorporate the calculated MELD score, alpha-fetoprotein, tumor size, and rate of tumor growth. Only candidates with at least stage T2 tumors would receive additional HCC priority points.	4

Suspected Liver Metastases
EVIDENCE TABLE

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24. Weg N, Scheer MR, Gabor MP. Liver lesions: improved detection with dual-detector-array CT and routine 2.5-mm thin collimation. *Radiology.* 1998;209(2):417-426.	Observational-Dx	20 patients including 167 total lesions.	To determine the feasibility and clinical benefit of routine performance of helical CT with 2.5-mm collimation for the detection of liver lesions.	Use of 2.5-mm-thick sections resulted in a 46% increase in detection rate vs use of 10.0-mm-thick sections (167 lesions vs 90 lesions), a 33% increase vs use of 7.5-mm-thick sections (167 vs 112), and an 18% increase vs use of 5-mm-thick sections (167 vs 137). Lesion conspicuity and radiologist confidence in lesion detection and characterization of lesion margins increased as section thickness decreased.	3
25. Numminen K, Isoniemi H, Halavaara J, et al. Preoperative assessment of focal liver lesions: multidetector computed tomography challenges magnetic resonance imaging. *Acta Radiol.* 2005;46(1):9-15.	Observational-Dx	31 patients	To investigate prospectively MDCT and MRI in the preoperative assessment of FLLS.	At surgery, IOUS and palpation revealed 45 solid liver lesions. From these, preoperative MDCT detected 43 (96%) and MRI 35 (78%) deposits. MDCT performed statistically better than MRI in lesion detection (P=0.008). Assessment of lesion vascular proximity was correctly determined by MDCT in 98% of patients and by MRI in 87%. Statistical difference was found (P=0.002). IOUS and palpation changed the preoperative surgical plan as a result of extrahepatic disease in 8/31 (26%) cases. In MDCT as well in MRI extrahepatic involvement was suspected in 2 cases.	3
26. Soyer P, Poccard M, Boudiaf M, et al. Detection of hypovascular hepatic metastases at triple-phase helical CT: sensitivity of phases and comparison with surgical and histopathologic findings. *Radiology.* 2004;231(2):413-420.	Experimental-Dx	32 patients with 59 hepatic metastases	To compare the respective sensitivities of unenhanced, arterial-dominant, and portal-dominant phase helical CT in the preoperative depiction of hypovascular hepatic metastases by using IOUS and histopathologic findings as the standard of reference.	Among 59 hepatic metastases, unenhanced, arterial-dominant, and portal-dominant phase helical CT imaging depicted 39 (66.1%; 95% CI: 53.3%, 76.8%), 44 (74.5%; 95% CI: 62.2%, 83.9%), and 54 (91.5%; 95% CI: 81.6%, 96.3%) metastases, respectively. Portal-dominant phase imaging depicted significantly more hypovascular hepatic metastases than did unenhanced (P<.001) or arterial-dominant (P<.01) phase imaging (Wilcoxon test).	2

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27. Kim T, Federle MP, Baron RL, Peterson MS, Kawamori Y. Discrimination of small hepatic hemangiomas from hypervascular malignant tumors smaller than 3 cm with three-phase helical CT. *Radiology.* 2001;219(3):699-706.	Observational-Dx	86 patients	To compare the appearance of small hepatic hemangiomas at nonenhanced and contrast material-enhanced helical CT with that of small (<3 cm) hypervascular malignant liver tumors and to evaluate the accuracy of multiphase helical CT for differentiating small hemangiomas from small hypervascular malignant tumors.	At arterial phase CT, enhancement similar to aortic enhancement was observed in 19%–32% of hemangiomas and 0%–2% of malignant tumors; globular enhancement, in 62%–68% and 4%–12%, respectively. At PVP CT, enhancement similar to blood pool enhancement was observed in 43%–54% of hemangiomas and 4%–14% of malignant tumors; globular enhancement, in 46%–49% and 0%–2%, respectively. For all readers and all phases of enhancement, the area under the ROC curves was 0.81–0.87, indicating that inherent accuracy of CT is high and that there was no significant difference (*P*>.28) in overall accuracy. Readers diagnosed hemangiomas with 47%–53% mean sensitivity with all enhancement phases and diagnosed malignant lesions with 95% mean specificity.	2
28. Muramatsu Y, Takayasu K, Moriyama N, et al. Peripheral low-density area of hepatic tumors: CT-pathologic correlation. *Radiology.* 1986;160(1):49-52.	Review/Other-Dx	70 patients	To aid in the distinction between colorectal cancer metastasis to the liver and HCC, findings on CT scans taken more than 5 minutes after contrast material administration ("late-enhanced CT scans") and pathologic findings were compared.	Late-enhanced CT scans of metastatic adenocarcinoma showed a peripheral low-density area that corresponded to viable tumor and a central high-density area that represented fibrous connective tissue. This phenomenon was recognized in 15/20 (75%) patients with metastatic adenocarcinoma and in 1 of 50 (2%) patients with HCC. Late-enhanced CT scans may be useful in distinguishing between metastatic nonmucinous colorectal cancer and HCC.	4
29. van Leeuwen MS, Noordzij J, Feldberg MA, Hennipman AH, Doornewaard H. Focal liver lesions: characterization with triphasic spiral CT. *Radiology.* 1996;201(2):327-336.	Review/Other-Dx	105 patients	To assess whether triphasic spiral CT enables characterization of a wide range of FLLS.	In 94 patients, 375 liver lesions were detected. The nature of the lesion was confirmed in 326 lesions (87%). 6/11 enhancement patterns were always due to benign disease and caused by areas with hyper- or hypoperfusion, hemangiomas, cysts, FNHs, or benign but nonspecified lesions. 2/11 patterns were always due to malignant disease, and 1 pattern was due to malignant disease in 38 (97%) of 39 patients with known malignancy elsewhere or with chronic liver disease. The other 2 patterns were seen in metastases and partly fibrosed hemangiomas.	4

Suspected Liver Metastases
EVIDENCE TABLE

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30. Ichikawa T, Saito K, Yoshioka N, et al. Detection and characterization of focal liver lesions: a Japanese phase III, multicenter comparison between gadoxetic acid disodium-enhanced magnetic resonance imaging and contrast-enhanced computed tomography predominantly in patients with hepatocellular carcinoma and chronic liver disease. *Invest Radiol.* 2010;45(3):133-141.	Experimental-Dx	178 patients	To prospectively evaluate the safety and efficacy of combined unenhanced and gadoxetic acid disodium-enhanced MRI compared with unenhanced MRI and triphasic contrast-enhanced spiral CT for the detection and characterization of FLLs.	Overall, 9.6% of patients who received Gd-gadoxetic acid disodium reported 21 drug-related adverse events. A total of 151 patients were included in the efficacy analysis. Combined MRI showed statistically higher sensitivity in lesion detection (67.5%–79.5%) than unenhanced MRI (46.5%–59.1%; $P<0.05$ for all). Combined MRI also showed higher sensitivity in lesion detection than CT (61.1%–73.0%), with the results being statistically significant ($P<0.05$) for on-site readers and 2 of 3 blinded readers. Higher sensitivity in lesion detection with combined MRI compared with CT was also clearly demonstrated in the following subgroups: lesions with a diameter ≤20 mm (lesions ≤10 mm: 38.0%–55.4% vs 26.1%–47.3%, respectively; lesions 10–20 mm: 71.1%–87.3% vs 65.7%–78.4%, respectively); in cirrhotic patients (64.5%–75.4% vs 54.5%–70.3%, respectively); and in patients with HCC (66.6%–78.6% vs 59.1%–71.6%, respectively). Combined MRI demonstrated a higher proportion of correctly characterized lesions (50.5%–72.1%) than unenhanced MRI (30.2%–50.0%; $P<0.05$ for all), whereas there were no significant differences compared with CT (49.0%–68.1%), except for 1 blinded reader ($P<0.05$).	2

Suspected Liver Metastases
EVIDENCE TABLE

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31. Danet IM, Semelka RC, Leonardou P, et al. Spectrum of MRI appearances of untreated metastases of the liver. *AJR Am J Roentgenol.* 2003;181(3):809-817.	Review/Other-Dx	165 consecutive patients	To identify the spectrum of MRI appearances of untreated liver metastases from different primary origins.	A total of 516 metastases (size range, 5–120 mm; mean, 28 mm) were assessed. 59 patients had hypervascular lesions, and 106 patients had hypovascular lesions. A significant difference in proportion of tumor vascularity was observed between the primary tumors described as classically hypervascular and those described as classically hypovascular (chi-square test for proportions of 70.8, $P<0.0001$). The most common pattern was peripheral ring (72% of patients) seen on the arterial dominant phase images, with incomplete central progression (63%) seen on the delayed phase images. A hypointense ring seen in the periphery of the tumor during the delayed phase was the most common appearance in hypervascular metastases (27% patients) and was particularly conspicuous in patients with neuroendocrine and carcinoid tumors. Perilesional enhancement was common (47%), mostly seen in hypovascular metastases (92%). Generally, large lesions tended to show a peripheral ring or heterogeneous enhancement, and small lesions showed homogeneous enhancement.	4
32. Nino-Murcia M, Olcott EW, Jeffrey RB, Jr., Lamm RL, Beaulieu CF, Jain KA. Focal liver lesions: pattern-based classification scheme for enhancement at arterial phase CT. *Radiology.* 2000;215(3):746-751.	Observational-Dx	100 consecutive patients	The authors present their experience with a classification scheme for categorizing FLLS on the basis of the enhancement patterns that they exhibit in the arterial phase of CT and determine whether particular enhancement patterns suggest particular diagnoses.	92% of the 100 lesions demonstrated arterial phase enhancement. Patterns associated with PPVs of 82% or greater and specificity of 80% or greater included abnormal internal vessels or variegated (HCC), peripheral puddles (hemangioma), and complete ring (metastasis).	3

Suspected Liver Metastases
EVIDENCE TABLE

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33. Semelka RC, Hussain SM, Marcos HB, Woosley JT. Perilesional enhancement of hepatic metastases: correlation between MR imaging and histopathologic findings-initial observations. *Radiology.* 2000;215(1):89-94.	Review/Other-Dx	7 patients	To correlate perilesional enhancement on gadolinium-enhanced MRI with histopathologic findings in patients with hepatic metastases.	In 3 patients, early gadolinium-enhanced images showed prominent perilesional enhancement, which correlated with a thick tumor border containing peritumoral desmoplastic reaction, peritumoral inflammation, and vascular proliferation at histopathologic examination. In 1 patient, mild perilesional enhancement was shown. At histopathologic examination, the lesion periphery showed moderate peritumoral changes. In the remaining 3 patients, no perilesional enhancement was observed, and at histopathologic examination there was a thin tumor border that contained minimal to mild perilesional changes. The thickness of hepatic parenchyma with intense perilesional enhancement on early gadolinium-enhanced images showed a strong positive correlation with tumor border thickness at histopathologic examination (r = 0.99).	4
34. Valls C, Andia E, Sanchez A, et al. Hepatic metastases from colorectal cancer: preoperative detection and assessment of resectability with helical CT. *Radiology.* 2001;218(1):55-60.	Experimental-Dx	157 patients	To prospectively evaluate helical CT in the preoperative detection of hepatic metastases and assessment of resectability with surgical, IOUS, and histopathologic correlation.	IOUS, palpation, and histopathologic examination revealed 290 liver metastases; helical CT correctly depicted 247. Helical CT results were the following: overall detection rate, 85.1% (95% CI: 80.8%, 89.3%); PPV, 96.1% (95% CI: 92.9%, 98.1%); and false-positive rate, 3.9% (10/257 findings; 95% CI: 1.9%, 7.1%). False-positive findings were related to hemangioendothelioma, hemangioma, hepatic peliosis, biliary adenoma, centrilobar hemorrhage, biliary hamartoma, periportal fibrosis, and normal liver parenchyma. Curative resection was performed in 112 instances with a resectability rate of 94.1%. 4-year patient survival rate was 58.6%.	2

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Oliver JH, 3rd, Baron RL, Federle MP, Jones BC, Sheng R. Hypervascular liver metastases: do unenhanced and hepatic arterial phase CT images affect tumor detection? *Radiology.* 1997;205(3):709-715.	Observational-Dx	84 patients	To evaluate the relative roles of unenhanced and HAP CT imaging in the detection of hypervascular liver metastases.	The 3 readers detected 381–402 lesions on the PVP images and 397–416 lesions on the unenhanced images. Unenhanced images allowed detection of 72%–80% of the lesions seen on PVP images. They detected 94–137 additional lesions on unenhanced but not PVP images. On the HAP images, 375–395 lesions were identified. HAP images allowed detection of 81%–90% of the lesions seen on PVP images. 45 to 78 additional lesions were detected on HAP but not on PVP images. In the 69-patient subset, maximal detection of tumor foci occurred in 94% of patients with unenhanced plus PVP images and in 78% with HAP plus PVP images. Unenhanced plus PVP images allowed detection of 96% of the 322 tumors in the subset population.	2
36. Blake SP, Weisinger K, Atkins MB, Raptopoulos V. Liver metastases from melanoma: detection with multiphasic contrast-enhanced CT. *Radiology.* 1999;213(1):92-96.	Experimental-Dx	CT studies in 20 patients and 13 patients had liver lesions	To assess the clinical utility of multiphasic CT of the liver in patients with metastatic melanoma.	A total of 57 liver lesions were seen on CT studies: 48 on HAP images, 49 on PVP images, and 30 on delayed phase images. Of 8 lesions overlooked on PVP images, 6 were seen on nonenhanced images, and 6 were seen on arterial phase images. 28 lesions were graded as more conspicuous on PVP images; 10 were graded as more conspicuous on arterial phase images.	3

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Sheafor DH, Frederick MG, Paulson EK, Keogan MT, DeLong DM, Nelson RC. Comparison of unenhanced, hepatic arterial-dominant, and portal venous-dominant phase helical CT for the detection of liver metastases in women with breast carcinoma. *AJR Am J Roentgenol.* 1999;172(4):961-968.	Experimental-Dx	300 patients	To evaluate triple-phase helical CT for detection of hepatic metastases from breast carcinoma.	Hepatic metastases were identified in 79 (26%) of 300 cases. Lesions detected on portal venous-dominant, hepatic arterial-dominant, and unenhanced images were as follows: observer 1, n = 198, 164, and 171; observer 2, n = 254, 233, and 233; and observer 3, n = 291, 270, and 276 (P>.05). The mean total lesion count was 387, with more lesions detected on portal venous-dominant phase than on either hepatic arterial-dominant phase or unenhanced images (P<.001 and P<.0001, respectively). For individual observers, 10%–26% of lesions were hypervascular on hepatic arterial-dominant phase images. 2% to 4% of lesions were identified only on hepatic arterial-dominant phase or unenhanced images. However, in these few cases, the lesions either were false-positives or were seen in conjunction with additional metastases on portal venous-dominant images.	2
38. Raptopoulos VD, Blake SP, Weisinger K, Atkins MB, Keogan MT, Kruskal JB. Multiphase contrast-enhanced helical CT of liver metastases from renal cell carcinoma. *Eur Radiol.* 2001;11(12):2504-2509.	Observational-Dx	45 patients	To evaluate whether in patients with metastatic renal cell carcinoma multiphase liver studies would improve detection of metastatic liver disease.	72 liver metastases were detected in 16 patients. Of these, 54 were seen on unenhanced scans; 47 in the HAP, at 25 s; 65 in the PVP, at 60 s; and 49 in delayed images, at 90 s. Scanning only during the PVP would have missed 7 lesions (10%), 6 of which were seen on unenhanced images and 6 were seen in HAP. All patients with metastatic liver disease would have been identified by combination of unenhanced and PVP or by HAP and PVP scanning. 42 lesions were graded more conspicuous on the PVP, whereas 18 (25%) were more conspicuous on the HAP.	3

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. Taouli B, Vilgrain V, Dumont E, Daire JL, Fan B, Menu Y. Evaluation of liver diffusion isotropy and characterization of focal hepatic lesions with two single-shot echo-planar MR imaging sequences: prospective study in 66 patients. *Radiology.* 2003;226(1):71-78.	Experimental-Dx	66 patients	To (a) evaluate liver diffusion isotropy, (b) compare 2 DWI-MRI sequences for the characterization of focal hepatic lesions by using 2 or 4 b values, and (c) determine an ADC threshold value to differentiate benign from malignant lesions. The images were taken before contrast administration.	Diffusion in the liver parenchyma was isotropic. ADCs of focal hepatic lesions were significantly different between sequences (P<.01). The mean (+/- standard deviation) ADCs in the first sequence were 0.94 x 10(-3) mm(2)/sec +/- 0.60 for metastases, 1.33 x 10(-3) mm(2)/sec +/- 0.13 for HCCs, 1.75 x 10(-3) mm(2)/sec +/- 0.46 for benign hepatocellular lesions, 2.95 x 10(-3) mm(2)/sec +/- 0.67 for hemangiomas, and 3.63 x 10(-3) mm(2)/sec +/- 0.56 for cysts. There was a significant difference between benign (2.45 x 10(-3) mm(2)/sec +/- 0.96, isotropic value) and malignant (1.08 x 10(-3) mm(2)/sec +/- 0.50) lesions (P<.01 for both sequences).	2
40. Lowenthal D, Zeile M, Lim WY, et al. Detection and characterisation of focal liver lesions in colorectal carcinoma patients: comparison of diffusion-weighted and Gd-EOB-DTPA enhanced MR imaging. *Eur Radiol.* 2011;21(4):832-840.	Observational-Dx	73 patients	To compare DWI and Gd-EOB-DTPA-enhanced MRI for the detection and characterization of FLLs in patients with colorectal carcinoma.	A total of 332 FLLs were evaluated. Detection rates were significantly higher for MR-Late images (94.4% for benign and 100% for malignant lesions) compared with MR-DWI (78.3% and 97.5%) and MR-Dynamic images (81.5% and 89.9%). Accuracy was 0.82, 0.76 and 0.89 for MR-DWI, MR-Dynamic and MR-Late images while sensitivity was 0.98, 0.87 and 0.95, respectively. For characterization of subcentimeter lesions sensitivity was highest for MR-DWI (0.92). Combined reading of unenhanced and contrast-enhanced images had an identical high accuracy of 0.98.	2

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
41. Huppertz A, Balzer T, Blakeborough A, et al. Improved detection of focal liver lesions at MR imaging: multicenter comparison of gadoxetic acid-enhanced MR images with intraoperative findings. *Radiology*. 2004;230(1):266-275.	Experimental-Dx	131 patients	To evaluate the safety and efficacy of gadoxetic acid disodium-enhanced MRI for the detection of FLLS, with results of histopathologic examination and/or IOUS used as a standard of reference.	Gadoxetic acid was well tolerated. In the on-site review, the number of patients in whom all lesions were correctly matched increased from 89/129 patients at precontrast MRI to 103/129 patients at postcontrast MRI. In the off-site evaluation, the number of patients in whom all lesions were correctly matched and the corresponding sensitivity values increased from 72 (55.8%), 68 (52.7%), and 66 (51.2%) with the precontrast images to 88 (68.2%), 69 (53.5%), and 76 (58.9%) with the postcontrast images for readers 1, 2, and 3, respectively. Two of the 3 blinded readers showed a statistically significant difference in lesion detection between precontrast and postcontrast MRI ($P<.001$ and $P=.008$). A large number of additionally correctly detected and localized lesions were <1 cm.	2
42. Halavaara J, Breuer J, Ayuso C, et al. Liver tumor characterization: comparison between liver-specific gadoxetic acid disodium-enhanced MRI and biphasic CT--a multicenter trial. *J Comput Assist Tomogr*. 2006;30(3):345-354.	Experimental-Dx	176 patients	To compare the potentials of biphasic contrast-enhanced CT)and a novel tissue-specific MRI contrast agent gadoxetic acid disodium in liver lesion characterization.	Both on-site and off-site evaluations demonstrated increases in the lesion classification accuracy with gadoxetic acid disodium-enhanced MRI when compared with spiral CT. This improvement was also shown for characterization. Gadoxetic acid disodium was well tolerated.	2

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
43. Hammerstingl R, Huppertz A, Breuer J, et al. Diagnostic efficacy of gadoxetic acid (Primovist)-enhanced MRI and spiral CT for a therapeutic strategy: comparison with intraoperative and histopathologic findings in focal liver lesions. *Eur Radiol.* 2008;18(3):457-467.	Experimental-Dx	169 patients	To evaluate the diagnostic efficacy of MRI using the new liver-specific contrast agent Gd-EOB-DTPA, as opposed to contrast-enhanced biphasic spiral CT, in the diagnosis of FLLS, compared with a standard of reference.	Data sets were evaluated on-site (14 investigators) and off-site (3 independent blinded readers). Gd-EOB-DTPA was well tolerated. 302 lesions were detected in 131 patients valid for analysis by standard of reference. The frequency of correctly detected lesions was significantly higher on Gd-EOB-DTPA-enhanced MRI compared with CT in the clinical evaluation [10.44%; 95% CI: 4.88, 16.0]. In the blinded reading there was a trend towards Gd-EOB-DTPA-enhanced MRI, not reaching statistical significance (2.14%; 95% CI: -4.32, 8.6). However, the highest rate of correctly detected lesions with a diameter below 1 cm was achieved by Gd-EOB-DTPA-enhanced MRI. Differential diagnosis was superior for Gd-EOB-DTPA-enhanced MRI (82.1%) vs CT (71.0%). A change in surgical therapy was documented in 19/131 patients (14.5%) post Gd-EOB-DTPA-enhanced MRI. Gd-EOB-DTPA-enhanced MRI was superior in the diagnosis and therapeutic management of FLLS compared with CT.	1
44. Raman SS, Leary C, Bluemke DA, et al. Improved characterization of focal liver lesions with liver-specific gadoxetic acid disodium-enhanced magnetic resonance imaging: a multicenter phase 3 clinical trial. *J Comput Assist Tomogr.* 2010;34(2):163-172.	Experimental-Dx	177 patients	To evaluate the safety of Gd-EOB-DTPA MRI and its efficacy in characterizing liver lesions. MRI imaging was done both without and with intravenous contrast.	Gd-EOB-DTPA was well tolerated in this study. For the clinical evaluation, more lesions were correctly characterized using combined (unenhanced and Gd-EOB-DTPA-enhanced) MRI than using unenhanced MRI and spiral CT (96% vs 84% and 85%, respectively; $P \leq 0.0008$). For the blinded evaluation, more lesions were correctly characterized using combined MRI compared with using unenhanced MRI (61%–76% vs 48%–65%, respectively; $P \leq 0.0012$ for 2/3 readers); when compared with spiral CT, a similar proportion of lesions were correctly characterized.	2

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. Parikh T, Drew SJ, Lee VS, et al. Focal liver lesion detection and characterization with diffusion-weighted MR imaging: comparison with standard breath-hold T2-weighted imaging. *Radiology.* 2008;246(3):812-822.	Observational-Dx	53 patients	To retrospectively compare DWI-MRI with standard breath-hold T2-weighted MRI for FLL detection and characterization, by using consensus evaluation and other findings as the reference standard. Contrast enhanced dynamic T1-weighted MRIs used as part of reference standard.	211 FLLs (136 malignant, 75 benign) were detected at consensus review. Overall detection rate (averaged for 2 observers) was significantly higher for DWI (87.7%) vs T2-weighted (70.1%) imaging (*P*<.001). FLL characterization was not significantly different between DWI (89.1%) and T2-weighted (86.8%) imaging (*P*=.51). ADCs of malignant FLLs were significantly lower than those of benign FLLs (*P*<.001). The area under the curve for diagnosis of malignancy was 0.839, with sensitivity of 74.2%, specificity of 77.3%, PPV of 85.5%, NPV of 62.3%, and accuracy of 75.3%, by using a threshold ADC of less than 1.60 x 10(-3) mm(2)/sec.	2
46. Zhu L, Cheng Q, Luo W, Bao L, Guo G. A comparative study of apparent diffusion coefficient and intravoxel incoherent motion-derived parameters for the characterization of common solid hepatic tumors. *Acta Radiol.* 2015;56(12):1411-1418.	Experimental-Dx	12 healthy volunteers and 43 patients	To compare the performances of ADC and intravoxel incoherent motion-derived parameters, including the pure diffusion coefficient (D), perfusion coefficient (D*), and perfusion fraction (f), in the characterization of common solid hepatic tumors.	ADC(0,500), ADCtotal, and diffusion coefficient were significantly lower in the malignant group ([1.48 +/- 0.35] x 10-3 mm2/s; [1.35 +/- 0.30] x 10-3 mm2/s; [1.18 +/- 0.33] x 10-3 mm2/s) compared to the hemangioma group ([2.74 +/- 1.03] x 10-3 mm2/s; [2.61 +/- 0.81] x 10-3 mm2/s; [1.97 +/- 0.79] x 10-3 mm2/s]. Perfusion coefficient did not differ among multiple comparisons. For the area under the ROC curve, the maximum value was attained with ADCtotal (0.983) and was closely followed by ADC(0,500) (0.967), with lower values obtained for diffusion coefficient (0.837), f (0.649), and perfusion coefficient (0.599). Statistically significant differences were found between the area under the ROC curve of both ADCs (ADCtotal and ADC(0,500)) and diffusion coefficient. There was no statistically significant difference between the area under the ROC curve of ADCtotal and ADC(0,500).	2

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
47. Agnello F, Ronot M, Valla DC, Sinkus R, Van Beers BE, Vilgrain V. High-b-value diffusion-weighted MR imaging of benign hepatocellular lesions: quantitative and qualitative analysis. *Radiology.* 2012;262(2):511-519.	Observational-Dx	67 patients	To analyze the signal intensity of benign hepatocellular lesions in high-b-value DWI-MRIs and to compare the ADC values of FNHs with those of HCCs. All MRIs and DWI sequences were with and without contrast.	The mean ADC value of all FNHs and HCCs was significantly lower than that of the liver (P=.004). An ADC ratio below 15% was observed in 50/54 (93%) FNHs and in 29/36 (81%) HCCs. The mean ADC value of FNHs was significantly higher than that of HCCs (P<.001). The area under the ROC curve was 0.760. With a cutoff value of 1.37x10(-3) mm2/sec, the sensitivity and specificity for differentiating HCC from FNH were 70% and 76%, respectively. There was no significant difference in ADC values between HCC subtypes. The signal intensity of most FNHs and HCCs (78/90, 87%) increased with increasing b values, whereas none showed a decrease in signal intensity with increasing b values. When the DWI-MRI criteria for benign and malignant liver tumors were applied, 44/90 (49%) lesions would have been considered malignant lesions, whereas the other lesions (46/90, 51%) would have been considered indeterminate.	3
48. Bipat S, van Leeuwen MS, Comans EF, et al. Colorectal liver metastases: CT, MR imaging, and PET for diagnosis--meta-analysis. *Radiology.* 2005;237(1):123-131.	Meta-analysis	61 studies; 3,187 patients	To perform a meta-analysis to obtain sensitivity estimates of CT, MRI, and FDG-PET for detection of colorectal liver metastases on per-patient and per-lesion bases.	Of 165 identified relevant articles, 61 fulfilled all inclusion criteria. Sensitivity estimates on a per-patient basis for nonhelical CT, helical CT, 1.5-T MRI, and FDG-PET were 60.2%, 64.7%, 75.8%, and 94.6%, respectively; FDG-PET was the most accurate modality. On a per-lesion basis, sensitivity estimates for nonhelical CT, helical CT, 1.0-T MRI, 1.5-T MRI, and FDG-PET were 52.3%, 63.8%, 66.1%, 64.4%, and 75.9%, respectively; nonhelical CT had lowest sensitivity. Estimates of gadolinium-enhanced MRI and SPIO-enhanced MRI were significantly better, compared with nonenhanced MRI (P=.019 and P<.001, respectively) and with helical CT with 45 g of iodine or less (P=.02 and P<.001, respectively). For lesions of 1 cm or larger, SPIO-enhanced MRI was the most accurate modality (P<.001).	M

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Kinkel K, Lu Y, Both M, Warren RS, Thoeni RF. Detection of hepatic metastases from cancers of the gastrointestinal tract by using noninvasive imaging methods (US, CT, MR imaging, PET): a meta-analysis. *Radiology.* 2002;224(3):748-756.	Meta-analysis	54 studies; 3,080 patients	To perform a meta-analysis to compare current noninvasive imaging methods (US, CT, MRI, and FDG-PET) in the detection of hepatic metastases from colorectal, gastric, and esophageal cancers.	Among 111 data sets, 9 US (509 patients), 25 CT (1,747 patients), 11 MRI (401 patients), and 9 PET (423 patients) data sets met the inclusion criteria. In studies with a specificity higher than 85%, the mean weighted sensitivity was 55% (95% CI: 41, 68) for US, 72% (95% CI: 63, 80) for CT, 76% (95% CI: 57, 91) for MRI, and 90% (95% CI: 80, 97) for FDG-PET. Results of pairwise comparison between imaging modalities demonstrated a greater sensitivity of FDG-PET than US (P=.001), CT (P=.017), and MRI (P=.055).	M
50. Albrecht MH, Wichmann JL, Muller C, et al. Assessment of colorectal liver metastases using MRI and CT: impact of observer experience on diagnostic performance and inter-observer reproducibility with histopathological correlation. *Eur J Radiol.* 2014;83(10):1752-1758.	Observational-Dx	51 CT and 54 MRI examinations of 105 patients	To compare the diagnostic performance and inter-observer reproducibility of CT and MRI in detecting colorectal liver metastases of observers with different levels of experience. MRIs were with and without contract; CT was with contrast.	CT sensitivity and specificity was for reviewer A 89.71%/94.41%, B 78.50%/88.37%, C 63.55%/85.58%, D 84.11%/78.60% and regarding MRI A 90.40%/95.43%, B 74.40%/90.04%, C 60.00%/85.89% and D 65.60%/75.90%. The overall inter-observer agreement was higher for CT (kappa=0.43, P<0.001; ICC=0.75, P<0.001) than MRI (kappa=0.38, P<0.001; ICC=0.65, P<0.001). The experienced reviewers A and B achieved better agreement for MRI (kappa=0.54, P<0.001; ICC=0.77, P<0.001) than CT (kappa=0.52, P<0.00; ICC=0.76, P<0.001) unlike the less experienced C and D (MRI kappa=0.38, ICC=0.63 and CT kappa=0.41, ICC=0.74, respectively, P<0.001).	2
51. Maegerlein C, Fingerle AA, Souvatzoglou M, Rummeny EJ, Holzapfel K. Detection of liver metastases in patients with adenocarcinomas of the gastrointestinal tract: comparison of (18)F-FDG PET/CT and MR imaging. *Abdom Imaging.* 2015;40(5):1213-1222.	Observational-Dx	49 patients	To compare the diagnostic performance of FDG-PET/CT and MRI in the detection of liver metastases in patients with adenocarcinomas of the gastrointestinal tract. MRIs were with and without contrast.	A total of 151 metastases were confirmed. For lesion detection, MRI was significantly superior to FDG-PET/CT. Sensitivity of MRI in detecting metastases was 86.8% for Reader 1 (R1) and 87.4% for Reader 2 (R2), of PET/CT 66.2% for R1 and 68.2% for R2. Regarding only metastases with diameters of 10 mm or less, sensitivities of MRI were 66.7% for R1 and 75.0% for R2, and were significantly higher than those of PET/CT (17.9% for R1 and 20.5% for R2). ROC analysis showed superiority for lesion classification of MRI as compared to FDG-PET/CT.	3

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Niekel MC, Bipat S, Stoker J. Diagnostic imaging of colorectal liver metastases with CT, MR imaging, FDG PET, and/or FDG PET/CT: a meta-analysis of prospective studies including patients who have not previously undergone treatment. *Radiology.* 2010;257(3):674-684.	Meta-analysis	39 studies; 3,391 patients	To obtain diagnostic performance values of CT, MRI, FDG-PET, and FDG-PET/CT in the detection of colorectal liver metastases in patients who have not previously undergone therapy.	39 articles (3391 patients) were included. Variation existed in study design characteristics, patient descriptions, imaging features, and reference tests. The sensitivity estimates of CT, MRI, and FDG-PET on a per-lesion basis were 74.4%, 80.3%, and 81.4%, respectively. On a per-patient basis, the sensitivities of CT, MRI, and FDG-PET were 83.6%, 88.2%, and 94.1%, respectively. The per-patient sensitivity of CT was lower than that of FDG-PET (P=.025). Specificity estimates were comparable. For lesions <10 mm, the sensitivity estimates for MRI were higher than those for CT. No differences were seen for lesions measuring at least 10 mm. The sensitivity of MRI increased significantly after January 2004. The use of liver-specific contrast material and multisection CT scanners did not provide improved results. Data about FDG-PET/CT were too limited for comparisons with other modalities.	M
53. Fong Y, Saldinger PF, Akhurst T, et al. Utility of 18F-FDG positron emission tomography scanning on selection of patients for resection of hepatic colorectal metastases. *Am J Surg.* 1999;178(4):282-287.	Observational-Dx	40 patients	To examine the utility of FDG-PET scanning in patients with metastatic colorectal cancer being evaluated for liver resection.	Findings on FDG-PET scanning influenced the clinical management in 16 patients (40%) and directly altered management in 9 cases (23%). 6 patients were spared laparotomy, and 3 others had PET-directed surgery that found extrahepatic tumor and spared the patient unwarranted liver resection. In 3 cases PET missed peritoneal metastases found on laparotomy. In these cases all missed tumors were <1 cm in size. Out of 52 resected hepatic lesions, FDG-PET detected 37. Within the liver, sensitivity of detection was also related to size. Only 25% of hepatic lesions <1 cm were detected by PET, while 85% of lesions >1 cm were detected.	3

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
54. Rohren EM, Paulson EK, Hagge R, et al. The role of F-18 FDG positron emission tomography in preoperative assessment of the liver in patients being considered for curative resection of hepatic metastases from colorectal cancer. *Clin Nucl Med.* 2002;27(8):550-555.	Observational-Dx	23 patients	To determine the sensitivity and specificity of FDG-PET for identifying patients with hepatic metastases from colorectal cancer and the accuracy of PET for determining the number and distribution of lesions within the liver.	The FDG-PET results were positive in 21 of the 22 patients ultimately found to have metastatic disease to the liver, and they were negative in the single patient without metastases. Therefore, for identification of patients with hepatic metastatic disease, PET has a sensitivity of 95% and a specificity of 100%. In all, 48 metastatic lesions were identified in these patients, of which 38 (79%) were identified on PET images. The probability of lesion detection by PET was directly correlated with lesion size ($P<0.01$). The assessment of lobar disease distribution in the liver was discordant between PET and surgery in 3 of 23 (13%) patients.	2
55. Ruers TJ, Langenhoff BS, Neeleman N, et al. Value of positron emission tomography with [F-18]fluorodeoxyglucose in patients with colorectal liver metastases: a prospective study. *J Clin Oncol.* 2002;20(2):388-395.	Experimental-Dx	51 patients	To assess prospectively the value of FDG-PET, in addition to conventional diagnostic methods, as a staging modality in candidates for resection of colorectal liver metastases. CT scans were both with and without contrast.	In 10 (20%) out of 51 patients, clinical management decisions based on conventional diagnostic methods were changed after FDG-PET findings were known. FDG-PET detected unresectable pulmonary (n = 5) and hepatic metastases (n = 1) and ruled out extrahepatic (n = 2) and hepatic disease (n = 2). Due to FDG-PET, 8 patients were spared unwarranted liver resection or laparotomy and 2 other patients were identified as candidates for liver resection. When the results of FDG-PET were regarded as decisive in a retrospective analysis, potential change of management was 29% (15 patients). FDG-PET and conventional diagnostic methods showed discordant extrahepatic results in 11 patients (22%) and discordant hepatic results in 8 patients (16%). Compared with conventional diagnostic methods, FDG-PET resulted in true upstaging (n = 11), true downstaging (n = 5), false upstaging (n = 1), and false downstaging (n = 2). The detection rate of liver metastases on a lesion basis was generally better for CT than for FDG-PET (80% vs 65%); this was related to tumor size.	3

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
56. Sahani DV, Kalva SP, Fischman AJ, et al. Detection of liver metastases from adenocarcinoma of the colon and pancreas: comparison of mangafodipir trisodium-enhanced liver MRI and whole-body FDG PET. *AJR Am J Roentgenol.* 2005;185(1):239-246.	Observational-Dx	34 patients	To assess the relative performance of mangafodipir trisodium-enhanced liver MRI and whole-body FDG-PET for the detection of liver metastases from adenocarcinoma of the colon and pancreas. MRI was with and without contrast.	30 patients had hepatic metastases and 4 had no hepatic metastases according to the standard of reference. The total number of metastases was 79, including 33 that measured <1 cm. Based on a per-patient analysis, MRI and FDG-PET showed sensitivities of 96.6% and 93.3%, PPVs of 100% and 90.3%, and accuracies of 97.1% and 85.3%, respectively. According to a per-lesion analysis, MRI and FDG-PET showed sensitivities of 81.4% and 67.0%, PPVs of 89.8% and 81.3%, and accuracies of 75.5% and 64.1%, respectively. MRI detected more hepatic metastases than FDG-PET (P=0.016). Of the 33 subcentimeter lesions confirmed on the standard of reference, all were identified on MRI, whereas only 12 were detected on FDG-PET (P=0.0001).	3
57. Akhurst T, Kates TJ, Mazumdar M, et al. Recent chemotherapy reduces the sensitivity of [18F]fluorodeoxyglucose positron emission tomography in the detection of colorectal metastases. *J Clin Oncol.* 2005;23(34):8713-8716.	Experimental-Dx	42 patients	To assess the effects of chemotherapy on PET imaging.	There was significantly decreased tumor FDG uptake (as measured by the maximal standardized uptake value) in patients treated preoperatively with chemotherapy, resulting in less efficient detection of cancerous lesions. One biologic basis of this change in accuracy of PET was a significant decrease in the activity of the key glycolytic enzyme hexokinase in tumors from patients treated with chemotherapy.	2
58. Adie S, Yip C, Chu F, Morris DL. Resection of liver metastases from colorectal cancer: does preoperative chemotherapy affect the accuracy of PET in preoperative planning? *ANZ J Surg.* 2009;79(5):358-361.	Observational-Dx	74 patients	To investigate FDG-PET/CT as a preoperative planning tool for detecting liver lesions in patients with and without preoperative chemotherapy.	A total of 21 patients had preoperative FDG-PET/CT scans with preoperative chemotherapy and 53 without. Accurate tests were 6 (29%) for the chemotherapy group vs 28 (53%) for the non-chemotherapy group (P=0.06). Notably, there were 11 (52%) underestimations in the chemotherapy group vs 18 (34%) in the non-chemotherapy group. A total of 1.7 lesions were missed per patient in the chemotherapy group vs 0.7 in those who did not receive chemotherapy.	3

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
59. Lubezky N, Metser U, Geva R, et al. The role and limitations of 18-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) scan and computerized tomography (CT) in restaging patients with hepatic colorectal metastases following neoadjuvant chemotherapy: comparison with operative and pathological findings. *J Gastrointest Surg.* 2007;11(4):472-478.	Observational-Dx	75 patients with 155 suspected metastatic lesions	To examine the effect of neoadjuvant chemotherapy for hepatic colorectal metastases on CT and FDG-PET/CT findings and to define the role of these imaging techniques in this setting. CT scans were with contrast.	27 patients (33 lesions) underwent immediate hepatic resection (group 1), and 48 patients (122 lesions) received preoperative neoadjuvant chemotherapy (group 2). Sensitivity of FDG-PET and CT in detecting colorectal metastases was significantly higher in group 1 than in group 2 (FDG-PET: 93.3% vs 49%, $P<0.0001$; CT: 87.5% vs 65.3%, $P=0.038$). CT had a higher sensitivity than FDG-PET in detecting colorectal metastases following neoadjuvant therapy (65.3% vs 49%, $P<0.0001$). Sensitivity of FDG-PET, but not of CT, was lower in group 2 patients whose chemotherapy included bevacizumab compared to patients who did not receive bevacizumab (39% vs 59%, $P=0.068$).	3
60. Dromain C, de Baere T, Lumbroso J, et al. Detection of liver metastases from endocrine tumors: a prospective comparison of somatostatin receptor scintigraphy, computed tomography, and magnetic resonance imaging. *J Clin Oncol.* 2005;23(1):70-78.	Experimental-Dx	64 patients 2 observers	Prospective blinded study to compare the sensitivity of somatostatin receptor scintigraphy, CT and MRI in the detection of liver metastases from endocrine tumors.	Hepatic metastases present in 40/64 patients. Somatostatin receptor scintigraphy, CT and MRI detected a total of 204, 325 and 394 metastases, respectively. MRI superior to CT and somatostatin receptor scintigraphy for detection of liver metastases from endocrine tumors.	1
61. Sundin A, Vullierme MP, Kaltsas G, Plockinger U. ENETS Consensus Guidelines for the Standards of Care in Neuroendocrine Tumors: radiological examinations. *Neuroendocrinology.* 2009;90(2):167-183.	Review/Other-Dx	N/A	No abstract available.	No abstract available.	4

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
62. Srirajaskanthan R, Kayani I, Quigley AM, Soh J, Caplin ME, Bomanji J. The role of 68Ga-DOTATATE PET in patients with neuroendocrine tumors and negative or equivocal findings on 111In-DTPA-octreotide scintigraphy. *J Nucl Med.* 2010;51(6):875-882.	Observational-Dx	51 patients	To evaluate the role of 68Ga-DOTATATE PET in a selected group of patients with negative or weakly positive findings on 111In-DTPA-octreotide scintigraphy to determine whether 68Ga-DOTATATE PET is able to detect additional disease and, if so, whether patient management is altered.	Of the 51 patients, 47 had evidence of disease on cross-sectional imaging or biochemically. 68Ga-DOTATATE PET was positive in 41 of these 47 patients (87.2%). No false-positive lesions were identified. 68Ga-DOTATATE PET detected 168 of the 226 lesions (74.3%) that were identified with cross-sectional imaging. 68Ga-DOTATATE PET identified significantly more lesions than 111In-DTPA-octreotide scintigraphy ($P<0.001$). There was no correlation between 68Ga-DOTATATE uptake and histologic grade of neuroendocrine tumors. 68Ga-DOTATATE imaging changed management in 36 patients (70.6%), who were subsequently deemed suitable for peptide receptor-targeted therapy.	2
63. Lind SE, Singer DE. Diagnosing liver metastases: a Bayesian analysis. *J Clin Oncol.* 1986;4(3):379-388.	Meta-analysis	20 studies	To review a set of recent studies of noninvasive tests for liver metastases that used invasive tests to establish the true disease state of the patient.	No results stated in abstract.	M
64. Disibio G, French SW. Metastatic patterns of cancers: results from a large autopsy study. *Arch Pathol Lab Med.* 2008;132(6):931-939.	Review/Other-Dx	Review of data from 3827 autopsies	To provide a quantitative description of metastatic patterns among different primary cancers based on data obtained from a large focused autopsy study.	Testicular cancers were most likely to metastasize (5.8 metastases per primary cancer), whereas duodenal cancers were least likely to do so (0.6 metastases per primary cancer). Preferred metastatic sites varied among the primary cancers analyzed. Overall, regional lymph nodes were the most common metastatic target (20.6% of total), whereas testes were the least common (0.1% of total).	4
65. Ohlsson B, Tranberg KG, Lundstedt C, Ekberg H, Hederstrom E. Detection of hepatic metastases in colorectal cancer: a prospective study of laboratory and imaging methods. *Eur J Surg.* 1993;159(5):275-281.	Observational-Dx	71 patients	To assess and compare the accuracy of imaging methods (US, CT, angiography, arterially enhanced CT with CT arterial portography), biochemical analyses, and surgical assessment during the operation, in detecting the presence of absence of hepatic metastases in patients with colorectal cancer.	Accuracy of surgical assessment, angiography, US, CT and CT arterial portography was 90%, 77%, 80%, 82%, and 83%, respectively, and corresponding predictive values of a negative test were 87%, 75%, 77%, 80%, and 84%. Measurement of bilirubin concentration and hepatic enzyme activities were not helpful, and that of carcinoembryonic antigen had an accuracy of only 70%. Accuracy and predictive values were not improved by combining tests.	2

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
66. Wernecke K, Rummeny E, Bongartz G, et al. Detection of hepatic masses in patients with carcinoma: comparative sensitivities of sonography, CT, and MR imaging. *AJR Am J Roentgenol.* 1991;157(4):731-739.	Observational-Dx	75 patients	To evaluate the sensitivity of US, CT, and MRI in the detection of hepatic masses in carcinoma patients.	65 (68%) of 95 focal hepatic masses were detected by CT, 60 lesions (63%) by MR, and 50 lesions (53%) by US. Although lesions 1–2 cm were shown almost equally well by CT and MR (74% and 77%, respectively), the detection rate of smaller lesions (<1.0 cm) decreased more drastically with MR (31%) than with CT (49%). US had a sensitivity of only 20% with the smaller lesions. All imaging techniques had a sensitivity of 100% for focal hepatic masses >2.0 cm. Our results show that CT has a higher overall sensitivity (68%) than MR and US for the detection of focal hepatic masses. When the results of the three procedures are combined, the overall sensitivity is 77%.	2
67. Bipat S, Niekel MC, Comans EF, et al. Imaging modalities for the staging of patients with colorectal cancer. *Neth J Med.* 2012;70(1):26-34.	Review/Other-Dx	N/A	To summarize the use of imaging modalities and the variation in techniques.	For liver metastases, the first modality of choice was CT in 52 (78.8%) and US in 12 hospitals (18.2%). Lung metastases were evaluated by either chest X-ray or chest CT and extrahepatic metastases mainly by CT (n=55). In the radiological and nuclear medicine surveys, some variations in techniques of US, CT, MRI, FDG-PET and FDG-PET/CT were seen. CT is primarily used for liver and extrahepatic metastases and both chest CT and chest X-ray for lung metastases. There are discrepancies between the survey of daily practice and the present guidelines.	4
68. Scott DJ, Young WN, Watumull LM, et al. Accuracy and effectiveness of laparoscopic vs open hepatic radiofrequency ablation. *Surg Endosc.* 2001;15(2):135-140.	Observational-Tx	10 pigs	To compare the accuracy (in terms of US-guided probe placement) and the effectiveness (in terms of pathologic tumor-free margin) of laparoscopic vs open radiofrequency ablation.	Off-center distance (3.5 +/- 1.6 vs 4.2 +/- 1.4 mm), size (24.7 +/- 3.1 vs 25.6 +/- 3.8 mm), symmetry (40% vs 73%), margin positivity (33% vs 9%), and margin distance (1.1 +/- 1.2 vs 2.2 +/- 1.6 mm) were not significantly different between laparoscopic (n = 15) and open (n = 11) ablations, respectively. The proportion of round/ovoid lesions (20% vs 64%) was lower (P=0.043), and warm-up time (20.2 +/- 14.0 vs 10.7 +/- 7.5) was longer (P=0.049) for the laparoscopic than for the open groups, respectively.	1

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
69. Eiber M, Fingerle AA, Brugel M, Gaa J, Rummeny EJ, Holzapfel K. Detection and classification of focal liver lesions in patients with colorectal cancer: retrospective comparison of diffusion-weighted MR imaging and multi-slice CT. *Eur J Radiol.* 2012;81(4):683-691.	Observational-Dx	68 patients	To compare the diagnostic performance of DWI-MRI with multi-slice CT in the detection and classification of FLLs in patients with colorectal cancer.	For lesion detection, DWI was significantly superior to multi-slice CT both on a per-lesion (difference in sensitivities for reader 1 and 2 22.65% and 19.06%, $P<0.0001$) and a per-segment basis (16.86% and 11.76%, $P<0.0001$). Especially lesions <10 mm were better detected with DWI compared to multi-slice CT (difference 41.10% and 29.45%, $P<0.0001$). ROC-analysis showed superiority for lesions classification ($P<0.0001$) of DWI (AUC: 0.949 and 0.951) as compared to multi-slice CT (AUC: 0.879 and 0.892, $P<0.0001$ and $P=0.005$). DWI was able to filter out metastatic segments with a higher sensitivity (88.2% and 86.5%) compared to multi-slice CT (68.0% and 67.4%, $P<0.0001$ and $P=0.005$, respectively).	3
70. Fletcher JW, Djulbegovic B, Soares HP, et al. Recommendations on the use of 18F-FDG PET in oncology. *J Nucl Med.* 2008;49(3):480-508.	Review/Other-Dx	N/A	To develop recommendations on the use of FDG-PET in breast, colorectal, esophageal, head and neck, lung, pancreatic, and thyroid cancer; lymphoma, melanoma, and sarcoma; and unknown primary tumor.	FDG-PET should be used as an imaging tool additional to conventional radiologic methods such as CT or MRI; any positive finding that could lead to a clinically significant change in patient management should be confirmed by subsequent histopathologic examination because of the risk of false-positive results. FDG-PET should be used in the appropriate clinical setting for the diagnosis of head and neck, lung, or pancreatic cancer and for unknown primary tumor. PET is also indicated for staging of breast, colon, esophageal, head and neck, and lung cancer and of lymphoma and melanoma. In addition, FDG-PET should be used to detect recurrence of breast, colorectal, head and neck, or thyroid cancer and of lymphoma.	4

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Brush J, Boyd K, Chappell F, et al. The value of FDG positron emission tomography/computerised tomography (PET/CT) in pre-operative staging of colorectal cancer: a systematic review and economic evaluation. *Health Technol Assess.* 2011;15(35):1-192, iii-iv.	Meta-analysis	30 studies	To evaluate the diagnostic accuracy and therapeutic impact of FDG-PET/CT for the preoperative staging of primary, recurrent and metastatic cancer using systematic review methods; undertake probabilistic decision-analytic modelling (using Monte Carlo simulation); and conduct a value of information analysis to help inform whether or not there is potential worth in undertaking further research.	The review found 30 studies that met the eligibility criteria. Only 2 small studies evaluated the use of FDG-PET/CT in primary colorectal cancer, and there is insufficient evidence to support its routine use at this time. The use of FDG-PET/CT for the detection of recurrent disease identified data from 5 retrospective studies from which a pooled sensitivity of 91% (95% CI, 0.87% to 0.95%) and specificity of 91% (95% CI, 0.85% to 0.95%) were observed. Pooled accuracy data from patients undergoing staging for suspected metastatic disease showed FDG-PET/CT to have a pooled sensitivity of 91% (95% CI, 87% to 94%) and a specificity of 76% (95% CI, 58% to 88%), but the poor quality of the studies means the validity of the data may be compromised by several biases. The separate hand search study did not yield any additional unique studies relevant to FDG-PET/CT. Models for recurrent disease demonstrated an incremental cost-effectiveness ratio of pound 21,409 per quality-adjusted life-year for rectal cancer, pound 6189 per quality-adjusted life-year for colon cancer and pound 21,434 per quality-adjusted life-year for metastatic disease. The value of hand searching to identify studies of less clearly defined or reported diagnostic tests is still to be investigated.	M
72. Larsen LP, Rosenkilde M, Christensen H, et al. The value of contrast enhanced ultrasonography in detection of liver metastases from colorectal cancer: a prospective double-blinded study. *Eur J Radiol.* 2007;62(2):302-307.	Experimental-Dx	461 patients	To compare sensitivity and specificity of CEUS with conventional US in detection of liver metastases in patients with colorectal adenocarcinoma in a patient-by-patient analysis.	Standard of reference found liver metastases in 54 patients (14.8%). CEUS improved the sensitivity significantly in detection of liver metastases from 0.69 by US to 0.80 (P=0.031). In 24 patients, CEUS found a higher number of metastases than US (P<0.001). The specificity (0.98) and the PPV (0.86) was the same.	2

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
73. Meyerhardt JA, Mangu PB, Flynn PJ, et al. Follow-up care, surveillance protocol, and secondary prevention measures for survivors of colorectal cancer: American Society of Clinical Oncology clinical practice guideline endorsement. *J Clin Oncol.* 2013;31(35):4465-4470.	Review/Other-Dx	N/A	To review Cancer Care Ontario's (CCO) Guideline on Follow-up Care, Surveillance Protocol, and Secondary Prevention Measures for Survivors of Colorectal Cancer.	No results stated in abstract.	4
74. Jeffery M, Hickey BE, Hider PN. Follow-up strategies for patients treated for non-metastatic colorectal cancer. *Cochrane Database Syst Rev.* 2007(1):CD002200.	Meta-analysis	8 studies	To review the available evidence concerning the benefits of intensive follow-up of colorectal cancer patients with respect to survival. Secondary endpoints include time to diagnosis of recurrence, quality of life and the harms and costs of surveillance and investigations.	8 studies were included in this update of the review. There was evidence that an overall survival benefit at 5 years exists for patients undergoing more intensive follow-up OR was 0.73 (95% CI, 0.59 to 0.91); and RD -0.06 (95% CI, -0.11 to -0.02). The absolute number of recurrences was similar; OR was 0.91 (95% CI, 0.75 to 1.10); and RD -0.02 (95% CI, -0.06 to 0.02) and although the weighted mean difference for the time to recurrence was significantly reduced by -6.75 (95% CI, -11.06 to -2.44) there was significant heterogeneity between the studies. Analyses demonstrated a mortality benefit for performing more tests vs fewer tests OR was 0.64 (95% CI, 0.49 to 0.85), and RD -0.09 (95% CI, -0.14 to -0.03) and liver imaging vs no liver imaging OR was 0.64 (95% CI, 0.49 to 0.85), and RD -0.09 (95%CI, -0.14 to -0.03). There were significantly more curative surgical procedures attempted in the intensively followed arm: OR 2.41(95% CI, 1.63 to 3.54), RD 0.06 (95% CI, 0.04 to 0.09). No useful data on quality of life, harms or cost-effectiveness were available for further analysis.	M

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
75. Moulton CA, Gu CS, Law CH, et al. Effect of PET before liver resection on surgical management for colorectal adenocarcinoma metastases: a randomized clinical trial. *JAMA*. 2014;311(18):1863-1869.	Experimental-Dx	270 patients in the PET/CT group and 134 patients in the control group	To determine the effect of preoperative PET/CT vs no PET/CT (control) on the surgical management of patients with resectable metastases and to investigate the effect of PET/CT on survival and the association between the standardized uptake value (ratio of tissue radioactivity to injected radioactivity adjusted by weight) and survival.	Of the 263 patients who underwent PET/CT, 21 had a change in surgical management (8.0%; 95% CI, 5.0%–11.9%). Specifically, 7 patients (2.7%) did not undergo laparotomy, 4 (1.5%) had more extensive hepatic surgery, 9 (3.4%) had additional organ surgery (8 of whom had hepatic resection), and the abdominal cavity was opened in 1 patient but hepatic surgery was not performed and the cavity was closed. Liver resection was performed in 91% of patients in the PET/CT group and 92% of the control group. After a median follow-up of 36 months, the estimated mortality rate was 11.13 (95% CI, 8.95–13.68) events/1000 person-months for the PET/CT group and 12.71 (95% CI, 9.40–16.80) events/1000 person-months for the control group. Survival did not differ between the 2 groups (hazard ratio, 0.86 [95% CI, 0.60–1.21]; P=.38). The standardized uptake value was associated with survival (hazard ratio, 1.11 [90% CI, 1.07–1.15] per unit increase; P<.001). The C statistic for the model including the standardized uptake value was 0.62 (95% CI, 0.56–0.68) and without it was 0.50 (95% CI, 0.44–0.56). The difference in C statistics is 0.12 (95% CI, 0.04–0.21). The low C statistic suggests that the standard uptake value is not a strong predictor of overall survival.	1

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
76. Abdalla EK, Vauthey JN, Ellis LM, et al. Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases. *Ann Surg.* 2004;239(6):818-825; discussion 825-817.	Observational-Tx	418 patients	To examine recurrence and survival rates for patients treated with hepatic resection only, radiofrequency ablation plus resection or radiofrequency ablation only for colorectal liver metastases.	Of 418 patients treated, 190 (45%) underwent resection only, 101 radiofrequency ablation + resection (24%), 57 radiofrequency ablation only (14%), and 70 laparotomy with biopsy only or arterial infusion pump placement ("chemotherapy only," 17%). Radiofrequency ablation was used in operative candidates who could not undergo complete resection of disease. Overall recurrence was most common after radiofrequency ablation (84% vs 64% radiofrequency ablation + resection vs 52% resection only, $P<0.001$). Liver-only recurrence after radiofrequency ablation was four-fold the rate after resection (44% vs 11% of patients, $P<0.001$), and true local recurrence was most common after radiofrequency ablation (9% of patients vs 5% radiofrequency ablation + resection vs 2% resection only, $P=0.02$). Overall survival rate was highest after resection (58% at 5 years); 4-year survival after resection, radiofrequency ablation + resection and radiofrequency ablation only were 65%, 36%, and 22%, respectively ($P<0.0001$). Survival for "unresectable" patients treated with radiofrequency ablation + resection or radiofrequency ablation only was greater than chemotherapy only ($P=0.0017$).	2
77. Foroutani A, Garland AM, Berber E, et al. Laparoscopic ultrasound vs triphasic computed tomography for detecting liver tumors. *Arch Surg.* 2000;135(8):933-938.	Experimental-Dx	55 patients	The findings of the preoperative CT scan for each patient were compared with the findings on LUS to evaluate the usefulness of LUS in this patient population for intraoperative staging.	The LUS detected all 201 tumors seen on preoperative CT and detected 21 additional tumors (9.5%) in 11 patients (20.0%). These tumors missed by CT ranged in size from 0.3 to 2.7 cm. Smaller tumors tended to be missed by CT scan (28.6% of the lesions <1 cm, 15.8% of those 1–2 cm, 4% of those 2–3 cm, and 0% of those >3 cm), as did those in segments III and IV. There was good correlation between the size of lesions imaged by the 2 modalities (Pearson r = 0.86; $P<.001$).	3

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
78. Scaife CL, Ng CS, Ellis LM, Vauthey JN, Charnsangavej C, Curley SA. Accuracy of preoperative imaging of hepatic tumors with helical computed tomography. *Ann Surg Oncol.* 2006;13(4):542-546.	Observational-Dx	250 patients	To review the data from our departmental prospective database with the hypothesis that IOUS still detects more hepatic tumors than are evident on preoperative helical CT scans.	In this time period, 250 patients underwent surgical resection and/or radiofrequency ablation of hepatic tumors. In 67 (27%) of these patients, IOUS identified more hepatic tumors than were seen on preoperative helical CT scan. In 8 patients (3%), CT underestimated local extension of the disease into the diaphragm. The incidence of inaccurate preoperative prediction of the extent of disease increased significantly with a greater number of hepatic tumors.	3
79. Wagnetz U, Atri M, Massey C, Wei AC, Metser U. Intraoperative ultrasound of the liver in primary and secondary hepatic malignancies: comparison with preoperative 1.5-T MRI and 64-MDCT. *AJR Am J Roentgenol.* 2011;196(3):562-568.	Observational-Dx	292 patients	To compare IOUS and preoperative contrast-enhanced MRI or 64-MDCT for the depiction of malignant lesions and for prediction of hepatic segments positive and negative for malignancy in patients undergoing partial hepatic resection.	The sensitivity and NPV of IOUS and preoperative cross-sectional imaging were calculated. The mean (+/- SD) time intervals to surgery were 37.6 +/- 26 days for 64-MDCT and 48.1 +/- 34 days for MRI. Surgical histopathologic examination was the reference standard. Changes in surgical management were recorded. Logistic regression models were used to estimate and compare proportions. For all 561 malignant lesions, the sensitivity of IOUS was 95.1%, compared with 96.8% for 64-MDCT (P=0.025) and 94.4% for MRI (P=0.960); 64-MDCT was also more sensitive than IOUS in identifying positive liver segments (P=0.013). After controlling for patient group and time interval between imaging and surgery, the NPV of 64-MDCT and MRI was higher than that of IOUS (P<0.001 and P=0.040, respectively). In only 8 cases (2.7%) was surgical management changed after IOUS.	3

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
80. D'Hondt M, Vandenbroucke-Menu F, Preville-Ratelle S, et al. Is intra-operative ultrasound still useful for the detection of a hepatic tumour in the era of modern pre-operative imaging? *HPB (Oxford).* 2011;13(9):665-669.	Observational-Dx	418 patients	To determine the accuracy of IOUS in the detection of a hepatic tumor compared with a preoperative MDCT scan and MRI.	Correlation rates for the number of detected lesions compared with pathology results were 0.627 for SCAN8, 0.785 for SCAN64, 0.657 for MRI and 0.913 for IOUS. Compared with pathology, the rate of concordance was significantly higher with IOUS (0.871) than with SCAN8 (0.736; *P*=0.011), SCAN64 (0.792; *P*<0.001) and MRI (0.742; *P*<0.001). IOUS was responsible for a change in operative strategy in 16.5% of patients. Surgery was extended in 12.4%, limited in 1.7% and abandoned in 2.4%.	3
81. Adams RB, Aloia TA, Loyer E, Pawlik TM, Taouli B, Vauthey JN. Selection for hepatic resection of colorectal liver metastases: expert consensus statement. *HPB (Oxford).* 2013;15(2):91-103.	Review/Other-Dx	N/A	To achieve adequate patient selection and curative surgery, (i) precise assessment of the extent of disease, (ii) sensitive criteria for chemotherapy effect, (iii) adequate decision making in surgical indication and (iv) an optimal surgical approach for pre-treated tumors are required.	No results stated in abstract.	4
82. Kim YK, Lee MW, Lee WJ, et al. Diagnostic accuracy and sensitivity of diffusion-weighted and of gadoxetic acid-enhanced 3-T MR imaging alone or in combination in the detection of small liver metastasis (</= 1.5 cm in diameter). *Invest Radiol.* 2012;47(3):159-166.	Observational-Dx	86 patients	To compare the diagnostic accuracy and sensitivity of combined gadoxetic acid-enhanced MRI and DWI with each imaging approach alone for detecting small hepatic metastases (≤1.5 cm).	There was a tendency toward an increased diagnostic accuracy for the combined set (mean, 0.965) compared with that for each image set alone (mean, 0.911 for gadoxetic acid set; 0.926 for DWI set). The combined set showed better sensitivity (mean, 97.47%/95.0%: values on per-lesion/per-patient basis) than each imaging set alone (mean, 90.7%/83.7% for gadoxetic acid set; 91.6%/83.0% for DWI set) (*P*<0.05) on both per-lesion basis and per-patient basis. All image sets showed similar PPVs.	2

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
83. Kulemann V, Schima W, Tamandl D, et al. Preoperative detection of colorectal liver metastases in fatty liver: MDCT or MRI? *Eur J Radiol.* 2011;79(2):e1-6.	Observational-Dx	20 patients	To compare the diagnostic value of MDCT and MRI in the preoperative detection of colorectal liver metastases in diffuse fatty infiltration of the liver, associated with neoadjuvant chemotherapy.	Overall, 51 metastases were found by histopathology of the resected liver segments/lobes. The size of the metastases ranged from 0.4 to 13 cm, with 18 (35%) being up to 1cm in diameter. In the overall rating, MDCT detected 33/51 lesions (65%), and MRI 45/51 (88%). For lesions up to 1cm, MDCT detected only 2/18 (11%) and MRI 12/18 (66%). One false positive lesion was detected by MDCT. Statistical analysis showed that MRI is markedly superior to MDCT, with a statistically significant difference (P<.001), particularly for the detection of small lesions (≤1 cm; P<.004). There was no significant difference between the 2 modalities in the detection of lesions >1cm.	2
84. Knowles B, Welsh FK, Chandrakumaran K, John TG, Rees M. Detailed liver-specific imaging prior to pre-operative chemotherapy for colorectal liver metastases reduces intra-hepatic recurrence and the need for a repeat hepatectomy. *HPB (Oxford).* 2012;14(5):298-309.	Review/Other-Dx	242 patients	Retrospective review of a prospective database to determine whether liver-specific MRI prior to preoperative chemotherapy affects intra-hepatic recurrence and long-term outcome after hepatectomy.	A liver-specific MRI pre-chemotherapy changed the staging in 56% of patients. At a median (range) follow-up of 55 (6–94) months, there was a higher incidence of intra-hepatic recurrence at a new site in the non-PCI group (65% vs 48% in the PCI group, P=0.041) and an increased rate of recurrence in patients with the same number of lesions pre- and post-chemotherapy [hazard ratio 2.02, 1:10-3.37, P=0.024]. The non-PCI group underwent more repeat hepatectomies than the PCI group (24.7% vs 13%, P=0.034), achieving similar long-term survival.	4
85. Sofue K, Tsurusaki M, Murakami T, et al. Does Gadoxetic acid-enhanced 3.0T MRI in addition to 64-detector-row contrast-enhanced CT provide better diagnostic performance and change the therapeutic strategy for the preoperative evaluation of colorectal liver metastases? *Eur Radiol.* 2014;24(10):2532-2539.	Observational-Dx	39 patients	To compare diagnostic performance in the detection of colorectal liver metastases between 64-detector-row contrast-enhanced CT alone and the combination of contrast-enhanced CT and EOB-MRI at 3.0T, and to assess whether EOB-MRI in addition to contrast-enhanced CT results in a change to initially planned operative strategy.	Sensitivity and area under the alternative free-response ROC curve with the combination of contrast-enhanced CT and EOB-MRI were significantly superior to those with contrast-enhanced CT alone. Changes in surgical therapy were documented in 13/39 patients.	2

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
86. Briggs RH, Chowdhury FU, Lodge JP, Scarsbrook AF. Clinical impact of FDG PET-CT in patients with potentially operable metastatic colorectal cancer. *Clin Radiol.* 2011;66(12):1167-1174.	Observational-Dx	102 patients	To assess the clinical impact of FDG-PET/CT in patients with potentially resectable metastatic colorectal cancer.	Of 102 patients (mean age 67 years, range 27-85 years), 94 had liver, 5 had isolated lung, and 3 had limited peritoneal metastases. In 31 patients (30%) PET/CT had a major impact on subsequent management, by correctly clarifying indeterminate lesions on conventional imaging as inoperable metastatic disease in 16 patients, detecting previously unsuspected metastatic disease in 9 patients, identifying occult second primary tumors in 3 patients, and correctly down-staging 3 patients. PET/CT had a minor impact in 12 patients (12%), no impact in 49 cases (48%), and a potentially negative impact in 10 cases (10%). Following PET/CT, 36 (35%) patients were no longer considered for surgery. Of those remaining operative 45 of 66 (68%) underwent potentially curative metastatic surgery. In this cohort PET/CT saved 16 futile laparotomies.	3

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
87. Wiering B, Krabbe PF, Jager GJ, Oyen WJ, Ruers TJ. The impact of fluor-18-deoxyglucose-positron emission tomography in the management of colorectal liver metastases. *Cancer.* 2005;104(12):2658-2670.	Meta-analysis	32 studies	To assess the usefulness of FDG-PET for the selection of patients to undergo resection for colorectal liver metastases.	For FDG-PET, the pooled sensitivity and specificity results were 88.0% and 96.1%, respectively, for hepatic disease and 91.5% and 95.4%, respectively, for extrahepatic disease. For the 6 articles that reported the highest scores on the index, the sensitivity and specificity of FDG-PET for hepatic metastatic disease were 79.9% and 92.3%, respectively, and 91.2% and 98.4%, respectively, for extrahepatic disease, respectively. CT, the pooled sensitivity and specificity results were 82.7% and 84.1%, respectively, for hepatic lesions and 60.9% and 91.1%, respectively, for extrahepatic lesions. The percentage change in clinical management due to FDG-PET was 31.6% (range, 20.0%–58.0%) in the articles that scored above the mean and reported this item. For the 6 highest scoring studies, the percentage change in clinical management was 25.0% (range, 20.0%–32.0%). Despite apparent omissions in the literature, the combined sensitivity and specificity of FDG-PET clearly indicated that FDG-PET has added value in the diagnostic workup of patients with colorectal liver metastases. FDG-PET can be considered a useful tool in preoperative staging and produced superior results compared with conventional diagnostic modalities, especially for excluding or detecting extrahepatic disease.	M

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
88. Truant S, Huglo D, Hebbar M, Ernst O, Steinling M, Pruvot FR. Prospective evaluation of the impact of [18F]fluoro-2-deoxy-D-glucose positron emission tomography of resectable colorectal liver metastases. *Br J Surg.* 2005;92(3):362-369.	Observational-Dx	53 patients	To assess the additional value of information provided FD-PET over that provided by CT in patients with resectable liver metastases from colorectal cancer.	Histological examination confirmed the presence of malignant or benign lesions detected by PET and/or CT in 95% of instances. Overall sensitivity (78%) and accuracy (88%) of PET were equivalent to those of CT (76% and 86%, respectively). The sensitivity of PET was equivalent to that of CT for hepatic sites (both 79%), but was superior for extrahepatic abdominal sites (63% and 25%, respectively). PET provided additional information in 5 patients, mainly by revealing abdominal extrahepatic metastases, but falsely upstaged three patients.	2
89. Smith EA, Salisbury S, Martin R, Towbin AJ. Incidence and etiology of new liver lesions in pediatric patients previously treated for malignancy. *AJR Am J Roentgenol.* 2012;199(1):186-191.	Review/Other-Dx	273 patients	To retrospectively evaluate the time course, cause, and imaging characteristics of all new liver lesions in pediatric patients with a previously treated malignancy.	Of 967 patients who met the initial inclusion criteria, 273 had adequate follow-up to be included in the study. 46 patients (16.8%) developed new liver lesions during the study period, and 14 of those 46 were classified into the FNH group (30.4%) and 7 were classified into the metastasis group (15.2%). A significant difference was found in the median time to the development of FNH vs metastasis and other lesions (FNH, 92.9 months; metastasis, 43.2 months; other lesions, 18.5 months; $P<0.0001$). A significant difference was also seen in the median length of follow-up between the groups (FNH, 115.6 months; metastasis, 57 months; other lesions, 50.8 months; $P=0.002$). The imaging features of the groups also differed.	4

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
90. Zorzi D, Laurent A, Pawlik TM, Lauwers GY, Vauthey JN, Abdalla EK. Chemotherapy-associated hepatotoxicity and surgery for colorectal liver metastases. *Br J Surg.* 2007;94(3):274-286.	Review/Other-Tx	N/A	To synthesize data from a systematic review of the existing literature to clarify which drugs are implicated in liver injury following preoperative chemotherapy for colorectal liver metastases.	Hepatic steatosis, a mild manifestation of non-alcoholic fatty liver disease, may occur after treatment with 5-fluorouracil and is associated with increased postoperative morbidity. Non-alcoholic steatohepatitis, a serious complication of non-alcoholic fatty liver disease that includes inflammation and hepatocyte damage, can occur after treatment with irinotecan, especially in obese patients. Irinotecan-associated steatohepatitis can affect hepatic reserve and increase morbidity and mortality after hepatectomy. Hepatic sinusoidal obstruction syndrome can occur in patients treated with oxaliplatin, but does not appear to be associated with an increased risk of perioperative death.	4
91. Marin D, Iannaccone R, Catalano C, Passariello R. Multinodular focal fatty infiltration of the liver: atypical imaging findings on delayed T1-weighted Gd-BOPTA-enhanced liver-specific MR images. *J Magn Reson Imaging.* 2006;24(3):690-694.	Review/Other-Dx	1 patient	To present a case with multiple rounded areas of fatty infiltration simulating liver malignancy, in which MRI was performed after administration of Gd-BOPTA, a liver-specific paramagnetic gadolinium-based MR contrast agent that has been proposed for imaging of focal liver disease.	In the present case, multiple rounded areas of fatty infiltration, although confidently diagnosed using chemical shift sequences due to a significant signal intensity reduction on out-of-phase images, were unexpectedly hypointense during the delayed liver-specific phase of Gd-BOPTA. Reduced Gd-BOPTA concentration during the liver-specific phase is generally correlated with liver malignancy. Since such lesions can be prospectively mistaken for metastatic disease, we performed a hepatic biopsy to establish a definitive diagnosis. Our empirical observations suggest that Gd-BOPTA uptake may be impaired in fatty infiltrated liver tissue.	4

Suspected Liver Metastases
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
92. Chun YS, Vauthey JN, Boonsirikamchai P, et al. Association of computed tomography morphologic criteria with pathologic response and survival in patients treated with bevacizumab for colorectal liver metastases. *JAMA.* 2009;302(21):2338-2344.	Observational-Dx	234 colorectal liver metastases were analyzed from 50 patients; 82 patients in validation cohort	To validate novel tumor response criteria based on morphologic changes observed on CT in patients with colorectal liver metastases treated with bevacizumab-containing chemotherapy regimens.	Interobserver agreement for scoring morphologic changes was good among 3 radiologists (kappa, 0.68-0.78; 95% CI, 0.51-0.93). In resected tumor specimens, the median (interquartile range) percentages of residual tumor cells for optimal morphologic response was 20% (10%–30%); for incomplete response, 50% (30%–60%); and no response, 70% (60%–70%; $P<.001$). With RECIST, the median (interquartile range) percentages of residual tumor cells were for partial response 30% (10%–60%); for stable disease, 50% (20%–70%); and for progressive disease, 70% (65%–70%; $P=.04$). Among patients who underwent hepatic resection, median overall survival was not yet reached with optimal morphologic response and 25 months (95% CI, 20.2-29.8 months) with incomplete or no morphologic response ($P=.03$). In the validation cohort, patients with optimal morphologic response had median overall survival of 31 months (95% CI, 26.8–35.2 months) compared with 19 months (95% CI, 14.6–23.4 months) with incomplete or no morphologic response ($P=.009$). RECIST did not correlate with survival in either the surgical or validation cohort.	2
93. American College of Radiology. ACR Appropriateness Criteria®: Liver Lesion—Initial Characterization. Available at: https://acsearch.acr.org/docs/69472/Narrative/.	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for a specific clinical condition.	No results stated in abstract.	4

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.
- M = Meta-analysis

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

ADC = Apparent diffusion coefficient

CEUS = Contrast-enhanced ultrasound

CI = Confidence interval

CT = Computed tomography

DWI = Diffusion-weighted imaging

FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography

FLLS = Focal liver lesion(s)

FNH = Focal nodular hyperplasia

Gd-BOPTA = Gadobenate dimeglumine

Gd-EOB-DTPA = Gadolinium-ethoxybenzyl-diethylenetriamine pentaacetic acid

HAP = Hepatic arterial phase

HCC = Hepatocellular carcinoma

HU = Hounsfield units

ICC = Intra-class correlation coefficients

IOUS = Intraoperative ultrasound

LUS = Laparoscopic ultrasound

MDCT = Multidetector computed tomography

MRI = Magnetic resonance imaging

NPV = Negative predictive value

PET = Positron emission tomography

PPV = Positive predictive value

PVP = Portal venous phase

ROC = Receiver-operator characteristic

SPIO = Superparamagnetic iron oxide

US = Ultrasound