

**Screening for Pulmonary Metastases
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Davis SD. CT evaluation for pulmonary metastases in patients with extrathoracic malignancy. <i>Radiology</i> 1991; 180(1):1-12.	Review/Other-Dx	N/A	To review the role of CT in screening patients for metastases. Compared CT with CXR and conventional linear tomography.	CT is more sensitive than CXR and should only be performed when a high propensity for metastases exists.	4
2. Snyder BJ, Pugatch RD. Imaging characteristics of metastatic disease to the chest. <i>Chest Surg Clin N Am</i> 1998; 8(1):29-48.	Review/Other-Dx	N/A	To review imaging characteristics of intrathoracic metastases.	Patients with known extrathoracic malignancy should have standard CXR. Chest CT should be performed if this malignancy frequently metastasizes to the lung. Lack of specificity may necessitate tissue evaluation through biopsy.	4
3. Herold CJ, Bankier AA, Fleischmann D. Lung metastases. <i>Eur Radiol</i> 1996; 6(5):596-606.	Review/Other-Dx	N/A	To review the pathways and radiologic appearance of pulmonary metastases.	Spiral CT is the most sensitive technique for detection of pulmonary nodules and should be used when detection of nodules may have an impact on patient management.	4
4. Puglisi F, Follador A, Minisini AM, et al. Baseline staging tests after a new diagnosis of breast cancer: further evidence of their limited indications. <i>Ann Oncol</i> 2005; 16(2):263-266.	Observational-Dx	516 patients	To determine value of bone scanning, liver US and CXR in patients with newly diagnosed breast cancer as part of baseline staging.	Bone scanning was done in 412 patients, liver US in 412 and CXR in 428. 33 patients were correctly diagnosed by the initial staging investigations as having metastatic disease (true positive cases). Bone scanning detected skeletal metastases in 6.31% of patients. Liver US detected liver metastases in 0.72% of patients. CXR detected lung metastases in 0.93% of patients. The detection rate in stage III patients was 14%, 5.6% and 7.2%, respectively for bone scanning, liver US and CXR.	3

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5. Brown RE, Stromberg AJ, Hagendoorn LJ, et al. Surveillance after surgical treatment of melanoma: futility of routine chest radiography. <i>Surgery</i> 2010; 148(4):711-716; discussion 716-717.	Experimental-Dx	1,235 patients	To determine the clinical efficacy of routine CXR for recurrence surveillance in melanoma.	Overall, 210 patients (17.0%) had a recurrence, most commonly local or in-transit. Review of CXR results showed that 4,218 CXR were obtained in 1,235 patients either before, or in the absence of, initial recurrence. To date, 88% (n=3,722) CXR are associated with no evidence of recurrence. Of CXR associated with recurrence, only 7.7% (n=38) of surveillance CXR were read as "abnormal." Overall, 99% (n=4,180) of CXR were read as either "normal" or found to be falsely positive (read as "abnormal," but without evidence of recurrence on investigation). Only 0.9% (n=38) of all CXR obtained were true positives ("abnormal" CXR, with confirmed first known recurrence). Among these 38 patients with true positive CXR, 35 revealed widely disseminated disease (multiorgan or bilateral pulmonary metastases); only 3 (0.2%) had isolated pulmonary metastases amenable to resection. Sensitivity and specificity for surveillance CXR in detecting initial recurrence were 7.7% and 96.5%, respectively.	3
6. Terhune MH, Swanson N, Johnson TM. Use of chest radiography in the initial evaluation of patients with localized melanoma. <i>Arch Dermatol</i> 1998; 134(5):569-572.	Review/Other-Dx	876 patients	Retrospective review to evaluate use of initial staging CXR in asymptomatic patients with localized melanoma.	130 (15%) of 876 patients had suspicious findings on the initial CXR, but only one (0.1%) had a true positive study for pulmonary metastases.	4
7. Mooney MM, Mettlin C, Michalek AM, Petrelli NJ, Kraybill WG. Life-long screening of patients with intermediate-thickness cutaneous melanoma for asymptomatic pulmonary recurrences: a cost-effectiveness analysis. <i>Cancer</i> 1997; 80(6):1052-1064.	Review/Other-Dx	N/A	Cost effectiveness analysis for life-long CXR screening, using a model based on a hypothetical cohort of patients with intermediate thickness, local cutaneous melanoma.	Significant cost savings are possible by decreasing the frequency of screening in the first 2 years (savings of \$2.3 million) and limiting screening to the first 5-10 years after diagnosis if the patient remains disease-free (savings of \$7.8 million).	4

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8. Gourin CG, Watts TL, Williams HT, Patel VS, Bilodeau PA, Coleman TA. Identification of distant metastases with positron-emission tomography-computed tomography in patients with previously untreated head and neck cancer. <i>Laryngoscope</i> 2008; 118(4):671-675.	Observational-Dx	27 patients	To investigate the utility of PET/CT in identifying distant metastatic disease in patients with previously untreated HNSCC prior to definitive treatment.	PET/CT had sensitivity 100%, specificity 96%, PPV 75%, NPV 100%. CXR had sensitivity 67%, specificity 100%, PPV 100%, NPV 96%. PET/CT improves detection of metastatic disease in the high-risk patient and should be performed as part of the routine pretreatment evaluation of patients with advanced stage HNSCC.	3
9. Morton RL, Craig JC, Thompson JF. The role of surveillance chest X-rays in the follow-up of high-risk melanoma patients. <i>Ann Surg Oncol</i> 2009; 16(3):571-577.	Observational-Dx	108 patients	To evaluate the accuracy of detecting asymptomatic pulmonary metastases by surveillance CXRs in melanoma patients with a positive sentinel node biopsy.	21% (23/108) developed pulmonary metastases, which were detected in 48% (11/23) by surveillance CXR (sensitivity, 48%; 95% CI, .27-.68), leading to resection in 13% (3/23). CXRs were abnormal in 19 additional patients but not due to recurrence (specificity, 78%; 95% CI, .77-.79). Additional metastatic disease was apparent in 18% of CXR-detected vs 76% of non-CXR-detected patients (P<.05), but median time to diagnosis of pulmonary metastases was 24 months (95% CI, 12-41) vs 16 months (95% CI, 10-30, P=.30 log rank) and median survival of 42 months (95% CI, 24-84) vs 36 months (95% CI, 18-46, P=.53 log rank) were not significantly different. The 6 to 12 monthly surveillance CXRs detected only half of pulmonary metastases, infrequently identified patients for potentially curative surgery, and did not lead to earlier detection of pulmonary metastases. Further, they may cause unnecessary patient anxiety, given the high rate of false-positive findings.	3
10. Casiraghi M, De Pas T, Maisonneuve P, et al. A 10-year single-center experience on 708 lung metastasectomies: the evidence of the "international registry of lung metastases". <i>J Thorac Oncol</i> 2011; 6(8):1373-1378.	Observational-Tx	575 patients	To confirm the validity of the International Registry of Lung Metastases classification system in patients who underwent curative lung metastasectomy in a single center.	After a mean follow-up of 34 months, 247 patients (43%) had died. Multivariate analysis disclosed that completeness of resection (P<0.0001), patients with germ cell tumors (P=0.04), and DFI ≥36 months (P=0.01) were also associated with a better prognosis. The actuarial survival after complete metastasectomy was 74% at 2 years and 46% at 5 years.	2

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11. Remy-Jardin M, Remy J, Giraud F, Marquette CH. Pulmonary nodules: detection with thick-section spiral CT versus conventional CT. <i>Radiology</i> 1993; 187(2):513-520.	Observational-Dx	39 patients	Prospective study to determine the sensitivity of spiral CT for detection of pulmonary nodules as compared with conventional CT.	The mean number of nodules per patient was significantly higher with spiral vs conventional CT (18 ± 4.5 vs 12.6 ± 3.2 , $P=.01$), as was the number of nodules <5 mm (12.7 ± 3.7 vs 8.4 ± 2.3 , $P<.05$) and 5-10 mm in diameter (2.9 ± 0.9 vs 2.4 ± 0.8 , $P<.05$).	2
12. McCormack PM, Ginsberg KB, Bains MS, et al. Accuracy of lung imaging in metastases with implications for the role of thoracoscopy. <i>Ann Thorac Surg</i> 1993; 56(4):863-865; discussion 865-866.	Observational-Dx	144 patients	Retrospective review to determine whether CXR or CT is accurate enough to detect pulmonary nodules prior to thoracoscopy.	CXR showed more nodules than CT in 3/17 patients and differed from pathologic findings at surgery in 57/144 patients (39%). 26/57 patients (46%) had more lesions than CXR detected and 31 had fewer. CT differed from pathologic findings in 30 of 72 patients (42%). Palpation of the lung at thoracotomy preferable to thoracoscopy.	3
13. Peldschus K, Herzog P, Wood SA, Cheema JJ, Costello P, Schoepf UJ. Computer-aided diagnosis as a second reader: spectrum of findings in CT studies of the chest interpreted as normal. <i>Chest</i> 2005; 128(3):1517-1523.	Review/Other-Dx	100 patients	To assess the performance of an automated CAD system as a second reader on chest CT studies interpreted as normal at routine clinical interpretation.	In 33% of the patients, CAD detected significant lung lesions that were not previously reported. 53 lesions were detected (mean, 1.6 lesions per case), of which 5 lesions (9.4%) were of high significance, 21 lesions (39.6%) were of intermediate significance, and 27 lesions (50.9%) were of low significance.	4
14. Rubin GD, Lyo JK, Paik DS, et al. Pulmonary nodules on multi-detector row CT scans: performance comparison of radiologists and computer-aided detection. <i>Radiology</i> 2005; 234(1):274-283.	Observational-Dx	20 patients	To compare the performance of radiologists and of a CAD algorithm for pulmonary nodule detection on thin-section thoracic CT scans.	Mean sensitivity for individual readings was 50% (range, 41%-60%); double reading resulted in increase to 63% (range, 56%-67%). Mean sensitivity was increased to 76% (range, 73%-78%) with CAD used at a threshold allowing only three false-positive detections per CT scan.	3
15. Munden RF, Pugatch RD, Liptay MJ, Sugarbaker DJ, Le LU. Small pulmonary lesions detected at CT: clinical importance. <i>Radiology</i> 1997; 202(1):105-110.	Observational-Dx	64 patients	Retrospective evaluation of histopathologic findings of pulmonary nodules ≤ 1 cm detected at CT that were removed at video-assisted thoracoscopic surgery.	In 64 patients, 65 lesions were resected, 38 (58%) of which were malignant. In 37 (58%) patients without previous malignancy, 14 (38%) had lung carcinoma (10 [27%], primary bronchogenic carcinoma; four [11%], carcinoid). Benign lesions were diagnosed in 59% (22 of 37). In 27 patients with previous malignancy, 22 (81%) lesions were malignant; this included seven (26%) patients with bronchogenic carcinoma as a second primary carcinoma. There were five (18%) benign nodules.	3

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16. Parsons AM, Detterbeck FC, Parker LA. Accuracy of helical CT in the detection of pulmonary metastases: is intraoperative palpation still necessary? <i>Ann Thorac Surg</i> 2004; 78(6):1910-1916; discussion 1916-1918.	Observational-Dx	34 patients	Retrospective review to determine whether malignant nodules (palpated, resected, and proven histologically) is reliably detected preoperatively by helical CT.	In 22% (9/41), more malignant nodules were found intraoperatively than were detected by helical CT. Of 88 malignant intraparenchymal nodules, 69 were detected by helical CT (sensitivity 78%). Palpation of the lung is recommended if the goal is to resect all detectable disease.	3
17. Lee KW, Kim M, Gierada DS, Bae KT. Performance of a computer-aided program for automated matching of metastatic pulmonary nodules detected on follow-up chest CT. <i>AJR</i> 2007; 189(5):1077-1081.	Observational-Dx	30 patients	To evaluate the performance of a computer-aided program that allows automated matching of metastatic pulmonary nodules imaged with two serial clinical chest CT studies.	Rate of automated matching of metastatic pulmonary nodules on clinical serial CT scans was high (82.4%) when the lung findings and lung expansion between the serial scans were relatively unchanged. However, the rate decreased significantly with substantial interval changes in the lung and a larger number of nodules.	4
18. Ting PT, Burrowes PW, Gray RR. Intravascular pulmonary metastases from sarcoma: appearance on computed tomography in 3 cases. <i>Can Assoc Radiol J</i> 2005; 56(4):214-218.	Review/Other-Dx	3 cases	Report three cases associated with intravascular metastases to the pulmonary vasculature and its appearance on CT.	Chest CT is a useful diagnostic tool. It demonstrated a striking pattern of multifocal tubular branching beaded opacities along the pulmonary vasculature in a multi-lobular distribution in all patients.	4
19. Shepard JA, Moore EH, Templeton PA, McLoud TC. Pulmonary intravascular tumor emboli: dilated and beaded peripheral pulmonary arteries at CT. <i>Radiology</i> 1993; 187(3):797-801.	Review/Other-Dx	4 cases	Retrospective study of four cases of pulmonary intravascular metastases shown on CT scans.	Finding of dilated and beaded peripheral pulmonary arteries at CT is highly suggestive of metastatic intravascular tumor emboli.	4
20. Jung DC, Choi HJ, Kim HY, Lee KH. Pulmonary metastasis from renal cell carcinoma: characterization using contrast-enhanced CT attenuation value measurements. <i>J Comput Assist Tomogr</i> 2009; 33(1):54-57.	Observational-Dx	39 pulmonary nodules in 36 patients with pulmonary metastasis from renal cell carcinoma	To retrospectively assess the usefulness of contrast-enhanced CT attenuation measurements for differentiating renal cell carcinoma pulmonary metastasis from primary lung cancer.	The mean attenuation value of metastatic pulmonary nodules from renal cell carcinoma (mean +/- SD, 73.6 +/- 40.6 Hounsfield units) was greater than that of primary lung cancer nodules (mean +/- SD, 47.8 +/- 17.9 Hounsfield units) (P<0.001). Pulmonary nodule attenuation measurements obtained by contrast-enhanced CT are useful for differentiating pulmonary metastasis from renal cell carcinoma and primary lung cancer.	3

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21. Cho HS, Park IH, Jeong WJ, Han I, Kim HS. Prognostic value of computed tomography for monitoring pulmonary metastases in soft tissue sarcoma patients after surgical management: a retrospective cohort study. <i>Ann Surg Oncol</i> 2011; 18(12):3392-3398.	Observational-Dx	176 patients	To evaluate the prognostic value of CT of the chest in soft tissue sarcoma patients after surgery.	The overall 5- and 10-year survival rates of 176 patients were 75.6% and 70.3%, respectively. The 5-year survival estimates of 96 patients who were included in the plain radiograph cohort and 80 patients in the chest CT cohort were 74.2% and 76.6%, respectively (P=0.70). 54 patients (30.7%) had pulmonary metastasis. Of the 54 patients, 26 belonged to the plain radiograph cohort and 28 patients belonged to the chest CT cohort. Pulmonary metastasis of chest CT cohort had the tendencies of unilaterality, a smaller number of patients, and management with metastasectomy other than palliative management. The 2- and 4-year survival rates after detection of pulmonary metastasis were 20.1% and 0% in the plain radiograph cohort and 47.4% and 31.6% in the chest CT cohort (P<0.05).	3
22. Marten K, Auer F, Schmidt S, Rummeny EJ, Engelke C. Automated CT volumetry of pulmonary metastases: the effect of a reduced growth threshold and target lesion number on the reliability of therapy response assessment using RECIST criteria. <i>Eur Radiol</i> 2007; 17(10):2561-2571.	Observational-Dx	50 patients (202 metastases)	To evaluate the reproducibility of CT-volumetric tumor response assessment of pulmonary metastasis using variable VCT and target lesions with response evaluation criteria in solid tumors.	General agreement on treatment response was very high (kappa (e) =0.93-1), but was reduced with VCT <35% (kappa (e) <0.95). Kappa correlation with VCT values was strong (r=0.94-0.96; P≤0.0002). Average confidence decreased significantly at VCT <45% (P<0.01) and agreement on stable disease at VCT <35% (kappa (e) <0.95; P<0.01). Reduction of target lesions (n<3; VCT=35%) resulted in decreased reader confidence (for n=1: kappa=0.49; P<0.05). Agreement for evaluation of treatment response was robust using VCT ≥35% and ≥3 metastases. This may translate into shortening of follow-up intervals or enable for response assessment with tumors displaying minimal volume change.	3

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23. Rasalkar DD, Chu WC, Lee V, Paunipagar BK, Cheng FW, Li CK. Pulmonary metastases in children with osteosarcoma: characteristics and impact on patient survival. <i>Pediatr Radiol</i> 2011; 41(2):227-236.	Observational-Dx	77 patients	To determine the incidence and characteristic features of pulmonary metastases in a group of osteosarcoma patients and correlate the findings with the prognostic outcome/survival.	17 patients had synchronous and 11 had metachronous lung metastases. 16 (57%) underwent pulmonary metastasectomy. 9/16 (56%) patients with metastasectomy and 10/12 (83%) patients without metastasectomy died. Poor chemonecrosis was associated with a worse outcome. Number, distribution and timing of lung metastases, but not the size of lung metastases, were of prognostic value for survival.	4
24. La Quaglia MP. Osteosarcoma. Specific tumor management and results. <i>Chest Surg Clin N Am</i> 1998; 8(1):77-95.	Review/Other-Dx	N/A	To review the biology, epidemiology, imaging, and current surgical approach to pulmonary metastases from osteogenic sarcoma.	Chest CT is the preferred study in screening for synchronous or metachronous pulmonary metastases. However, more nodules are usually identified at the time of thoracotomy than at CT examination.	4
25. Absalon MJ, McCarville MB, Liu T, Santana VM, Daw NC, Navid F. Pulmonary nodules discovered during the initial evaluation of pediatric patients with bone and soft-tissue sarcoma. <i>Pediatr Blood Cancer</i> 2008; 50(6):1147-1153.	Observational-Dx	210 patients	Retrospective review of medical records and CT scans to determine detection of small pulmonary nodules in children with bone and soft-tissue sarcoma.	Pulmonary nodules were commonly detected during the initial evaluation of pediatric cases of sarcoma. Number and distribution of nodules were significantly associated with metastatic disease and outcome.	3
26. Rissing S, Rougraff BT, Davis K. Indeterminate pulmonary nodules in patients with sarcoma affect survival. <i>Clin Orthop Relat Res</i> 2007; 459:118-121.	Observational-Dx	331 patients	Prospectively study sarcoma patients to see if small, indeterminate pulmonary nodules are of prognostic significance.	71 (21%) had indeterminate pulmonary nodules on initial spiral CT. 20/71 (28%) progressed with metastatic disease. Metastatic disease developed in 18/20 (90%) in the area of the original indeterminate nodule. The presence of tiny (<5 mm) indeterminate nodules was not a prognostic variable, however, the presence of nodules ≥5 mm was associated with worse 3 year disease-free survival compared to those with no nodules or tiny nodules (81% vs 49%) but better than those with definite metastatic disease at presentation (49% vs 5%).	3
27. Casson AG, Putnam JB, Natarajan G, et al. Five-year survival after pulmonary metastasectomy for adult soft tissue sarcoma. <i>Cancer</i> 1992; 69(3):662-668.	Observational-Tx	58 patients	To evaluate which factors are associated with improved long-term (>5 years) survival in patients undergoing pulmonary metastasectomy for soft tissue sarcomas.	Improved survival is associated with doubling times ≥40 days, unilateral disease, three or fewer nodules on CT, two or fewer nodules resected, and histology of malignant fibrous histiocytoma.	2

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28. Robinson MH, Sheppard M, Moskovic E, Fischer C. Lung metastasectomy in patients with soft tissue sarcoma. <i>Br J Radiol</i> 1994; 67(794):129-135.	Observational-Tx	189 patients	To compare the survival of a selected group of patients with soft tissue sarcoma selected for pulmonary metastasectomy with that of a cohort of patients not undergoing metastasectomy.	Overall 5-year survival (70%) and subsequent survival from the time lung metastases developed (52%) was better in the 44 patients undergoing pulmonary metastasectomy than in the 145 patients not undergoing surgery (19% and 7.5%, respectively).	3
29. Cerfolio RJ, Allen MS, Deschamps C, et al. Pulmonary resection of metastatic renal cell carcinoma. <i>Ann Thorac Surg</i> 1994; 57(2):339-344.	Observational-Tx	96 patients	To identify factors associated with prolonged survival in a series of patients undergoing complete resection of pulmonary metastases from renal cell carcinoma.	Overall 5- year survival was 35.9%. 5-year survival was better in patients with solitary lesions (45.6%), compared with those patients having multiple metastases (27.0%). 5-year survival was not significantly different for patients who underwent repeat thoracotomy or who had complete resection of extra pulmonary disease.	2
30. Lim DJ, Carter MF. Computerized tomography in the preoperative staging for pulmonary metastases in patients with renal cell carcinoma. <i>J Urol</i> 1993; 150(4):1112-1114.	Review/Other-Dx	120 patients	To evaluate the role of chest CT in staging patients with renal cell carcinoma. Patients had CXR and chest CT.	Agreement was found between the 2 modalities in 105 patients. The results of CXR and chest CT were normal in 82 and abnormal in 23 patients. 13/15 (disagreement between the 2 studies) had normal CXR with abnormal chest CT and 2 had abnormal CXR with normal chest CT. Normal CXR is sufficient for pulmonary staging in patients with relatively small tumor (stage T1). Additional chest CT should be obtained in patients with a solitary nodule on the CXR prior to metastasectomy, chest symptoms suggestive of intrabronchial metastasis, or extensive regional disease.	4

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31. See WA, Hoxie L. Chest staging in testis cancer patients: imaging modality selection based upon risk assessment as determined by abdominal computerized tomography scan results. <i>J Urol</i> 1993; 150(3):874-878.	Review/Other-Dx	74 patients	To compare chest CT with CXR as staging modalities in patients with testicular cancer, on the basis of abdominal CT findings.	In the series of patients undergoing CXR and chest CT concurrently, staging abdominal CT scans were negative in 42 patients and positive in 32 patients. Among the 42 patients with negative abdominal CT scans, chest imaging findings were discordant in 4 patients, including 3 with lesions seen only on chest CT (false positive rate of 2.3%). Among the 32 patients with positive abdominal CT, chest CT allowed detection of pulmonary metastases not seen on the CXR in 4 (12.5%) cases. CXR may be the preferred initial chest staging study in patients with negative abdominal CT, whereas chest CT is indicated in patients with a positive abdominal CT examination.	4
32. Buzaid AC, Tinoco L, Ross MI, Legha SS, Benjamin RS. Role of computed tomography in the staging of patients with local-regional metastases of melanoma. <i>J Clin Oncol</i> 1995; 13(8):2104-2108.	Observational-Dx	89 patients	Retrospective evaluation of the value of CT in the staging of asymptomatic melanoma patients who presented with or developed local-regional disease, and who had both a normal CXR and a normal serum lactate dehydrogenase level.	Among 6 patients with true positive findings, chest CT identified disease not visible on the CXR in one case. True positive findings are observed in approximately 7% of patients with local-regional disease. CT or MRI of the brain is not necessary in asymptomatic patients. CT of the chest adds little to a CXR.	3
33. Kuvshinoff BW, Kurtz C, Coit DG. Computed tomography in evaluation of patients with stage III melanoma. <i>Ann Surg Oncol</i> 1997; 4(3):252-258.	Observational-Dx	347 patients	To determine the diagnostic yield of CT in identifying metastatic melanoma in clinical stage III disease.	Chest CT had highest yield in patients with cervical adenopathy (7/35, 20%), and lowest yield in patients with groin adenopathy (1/50, 2%). Selective use of chest CT is recommended in patients with cervical adenopathy.	3
34. Ollila DW, Morton DL. Surgical resection as the treatment of choice for melanoma metastatic to the lung. <i>Chest Surg Clin N Am</i> 1998; 8(1):183-196.	Review/Other-Dx	N/A	To review the role of surgical resection in the treatment of melanoma metastatic to the lung.	Patients with limited number of pulmonary metastases may benefit from complete surgical resection if they have favorable prognostic features.	4

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35. Huang YT, Ravi Kumar AS. Potential for truncating the scan length of restaging FDG-PET/CT after chemoradiotherapy in head and neck squamous cell carcinoma. <i>Nucl Med Commun</i> 2012; 33(5):503-508.	Observational-Dx	240 patients	To explore the potential of a limited scan range from the skull vertex to lung bases, viz. an 'above diaphragm' scan, as an adequate examination for assessment of disease following chemoradiotherapy.	A total of 196 (81.7%) patients had nodal disease at PET/CT staging. Unrelated findings were present in 50 (20.8%) patients, including five colonic neoplasms and two second malignancies. After an average of 6.4 months after staging, 13 patients (5.4%) demonstrated progression to distant metastases on the post-therapy PET/CT. All patients demonstrated intrapulmonary metastases. Two patients had additional liver metastases, which would not have impacted on the overall management. No patient demonstrated isolated disease below the diaphragm.	3
36. Mercader VP, Gatenby RA, Mohr RM, Fisher MS, Caroline DF. CT surveillance of the thorax in patients with squamous cell carcinoma of the head and neck: a preliminary experience. <i>J Comput Assist Tomogr</i> 1997; 21(3):412-417.	Review/Other-Dx	93 patients	Retrospective examination of thorax CT scans to determine the number of malignancies detected by chest CT in patients with HNC at various stages of disease.	CT detected malignancy in 9/57 patients examined during diagnosis of the neck tumor, in 9/43 patients during follow-up, and in 6/18 patients evaluated at the time of local/regional neck recurrence. Chest CT showed a high number of additional malignancies in patients with advanced (stage III and IV) HNSCC.	4
37. Nilssen EL, Murthy P, McClymont L, Denholm S. Radiological staging of the chest and abdomen in head and neck squamous cell carcinoma--are computed tomography and ultrasound necessary? <i>J Laryngol Otol</i> 1999; 113(2):152-154.	Review/Other-Dx	103 patients: 57 had CT scans; 70 had US	To retrospectively review findings of routine radiologic staging of the chest and abdomen, by CT and US, in patients with HNSCC.	Among 57 patients undergoing routine CT scanning of the chest, only 2 had synchronous tumors identified. In both of these cases, disease was also evident on CXR. Routine CT of the chest and US of the abdomen have been discontinued.	4
38. Andrie J, Scharfetter VH, Schwentner I, Deibl M, Sprinzl GM. Initial staging examinations for head and neck squamous cell carcinoma: are they appropriate? <i>J Laryngol Otol</i> 2009; 123(8):885-888.	Review/Other-Dx	163 patients with HNSCC	To retrospectively evaluate the necessity to undertake bone scanning, chest CT and abdominal US in patients presenting with primary advanced HNSCC.	Distant metastases were detected in 5.52 % of the 163 patients. All of these patients had locoregional advanced (stage IV) tumors. CT scanning of the lungs revealed metastases in 6 patients. Bone metastases were found in 3 patients. Only one patient with primary liver metastases was detected by abdominal US; this patient also had pulmonary metastases. CT of the thorax is the most important technique for screening patients with HNSCC.	4
39. Kersjes W, Mayer E, Buchenroth M, Schunk K, Fouda N, Cagil H. Diagnosis of pulmonary metastases with turbo-SE MR imaging. <i>Eur Radiol</i> 1997; 7(8):1190-1194.	Observational-Dx	23 patients	To determine the diagnostic value of T2-weighted turbo-spin echo MRI sequences in patients with pulmonary metastasis. Spiral volumetric CT was the radiological standard.	286 (84%) of 340 metastases were identified at MRI. Sensitivity of MRI was 36% for nodules <5 mm, 83% for nodules 5-10 mm, 92% for nodules 10-15 mm, and 100% for nodules >15 mm. MRI does not appear to have a role in screening for pulmonary metastases.	3

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40. Bruegel M, Gaa J, Woertler K, et al. MRI of the lung: value of different turbo spin-echo, single-shot turbo spin-echo, and 3D gradient-echo pulse sequences for the detection of pulmonary metastases. <i>J Magn Reson Imaging</i> 2007; 25(1):73-81.	Observational-Dx	28 patients (225 metastases)	To compare the value of different MRI sequences (turbo spin-echo, single-shot turbo spin-echo, and 3D gradient-echo pulse sequences) for the detection of pulmonary metastases. Multi-detector CT was standard of reference.	Contrast-to-noise ratios were highest on turbo spin-echo images ($P < 0.001$). Mean sensitivity with triggered short-tau inversion recovery was 72%, turbo spin-echo 69%, and short-tau inversion recovery 63.4%. Conventional turbo spin-echo and short-tau inversion recovery sequences are more sensitive in depicting pulmonary metastases than single-shot turbo spin-echo or 3D gradient-echo sequences.	2
41. Dalrymple-Hay MJ, Rome PD, Kennedy C, Fulham M, McCaughan BC. Pulmonary metastatic melanoma -- the survival benefit associated with positron emission tomography scanning. <i>Eur J Cardiothorac Surg</i> 2002; 21(4):611-614; discussion 614-615.	Observational-Dx	121 patients: 68 had PET scan; 53 had nuclear imaging	To determine if PET scanning to detect occult extra pulmonary disease prior to thoracotomy and metastectomy is associated with improved survival compared to patients staged by conventional radiography.	Survival (\pm SE) at 1, 3, 5 and 7 years for all patients is 68%, 36.6%, 22.1% and 13.5%, respectively. Survival was significantly better at 3 and 5 years in patients who had a preoperative PET scan. No significant difference in survival by 7 years.	3
42. Paquet P, Hustinx R, Rigo P, Pierard GE. Malignant melanoma staging using whole-body positron emission tomography. <i>Melanoma Res</i> 1998; 8(1):59-62.	Review/Other-Dx	2 cases	To report two cases in which staging of malignant melanoma was performed using whole body PET as well as conventional imaging by CT and MRI.	In case one, numerous pulmonary nodules were revealed at chest CT but no uptake on whole body FDG-PET was demonstrated. Histologic examination revealed no evidence of neoplasm. Whole-body PET appears to have high specificity and sensitivity for clinical melanoma staging.	4
43. Roh JL, Ryu CH, Kim JS, et al. Clinical significance of intrathoracic lesions detected by 18F-fluorodeoxyglucose positron emission tomography in the management of patients with head and neck cancer. <i>Oral Oncol</i> 2007; 43(8):757-763.	Observational-Dx	86 patients	To retrospectively examine the role of FDG-PET in detecting thoracic malignancies in patients with previously untreated HNC.	FDG-PET had sensitivity of 80%, specificity of 85%, and accuracy of 84%. The likelihood of thoracic malignancy in the HNC patients was associated with high FDG uptake of thoracic lesions.	3

**Screening for Pulmonary Metastases
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Franzius C, Daldrup-Link HE, Sciuk J, et al. FDG-PET for detection of pulmonary metastases from malignant primary bone tumors: comparison with spiral CT. <i>Ann Oncol</i> 2001; 12(4):479-486.	Observational-Dx	71 patients	Compare FDG-PET and spiral CT to detect pulmonary metastases from malignant primary osseous tumors.	FDG-PET had a sensitivity of 0.50, specificity of 0.98, and accuracy of 0.87. Spiral CT had a sensitivity of 0.75, specificity of 1.00, and accuracy of 0.94. No patient with a true positive FDG-PET had a false negative CT scan. Pulmonary metastases were not detected earlier by FDG-PET than by spiral CT. CT is superior to FDG-PET in the detection of pulmonary metastases from malignant primary bone tumors. Therefore, a negative FDG-PET cannot be recommended to exclude lung metastases. However, as specificity of FDG-PET is high, a positive FDG-PET result can be used to confirm abnormalities seen on thoracic CT scans as metastatic.	2
45. De Wever W, Meylaerts L, De Ceuninck L, Stroobants S, Verschakelen JA. Additional value of integrated PET-CT in the detection and characterization of lung metastases: correlation with CT alone and PET alone. <i>Eur Radiol</i> 2007; 17(2):467-473.	Observational-Dx	24 patients (56 nodules – 3 groups)	Evaluate retrospectively the additional value of integrated PET and CT in the detection of pulmonary metastases in comparison with CT and PET alone.	CT had a sensitivity of 100%, accuracy of 57%. PET had a sensitivity of 90% and accuracy of 55%. PET/CT had a sensitivity of 100% and accuracy of 55%. No significant difference in the characterization of pulmonary nodules between integrated PET/CT and CT alone (P=1.000) and PET alone (P=0.1306). An accurate evaluation is only possible for lesions >1 cm.	3
46. Krug B, Crott R, Roch I, et al. Cost-effectiveness analysis of FDG PET-CT in the management of pulmonary metastases from malignant melanoma. <i>Acta Oncol</i> 2010; 49(2):192-200.	Review/Other-Dx	Complications and care costs from databases from 19 hospitals	A cost-effectiveness analysis, using a Markov model over a 10-year period, was performed to compare two different surveillance programs, either PET/CT or whole-body CT, in patients with suspected pulmonary metastasized melanoma.	The PET/CT strategy provided 86.29 LMG (95% CI: 81.50-90.88 LMG) at a discounted cost of Euros 3,974 (95% CI: Euros 339-12,303), while the conventional strategy provided 86.08 LMG (95% CI: 81.37-90.68 LMG) at a discounted cost of Euros 5,022 (95% CI: Euros 378-16,018). This PET/CT strategy resulted in a net saving of Euros 1,048 with a gain of 0.2 LMG. Based on PET/CT findings, 20% of futile surgeries could be avoided. Integrating PET/CT in the management of patients with high-risk malignant melanoma appears to be less costly and more accurate by avoiding futile thoracotomies in one of five patients as well as by providing a small survival benefit at 10 years.	4

**Screening for Pulmonary Metastases
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
47. Kochhar R, Liong S, Manoharan P. The role of FDG PET/CT in patients with colorectal cancer metastases. <i>Cancer Biomark</i> 2010; 7(4):235-248.	Observational-Dx	341 patients	To assess the role of FDG-PET/CT in metastatic colorectal cancer metastases.	On a lesion to lesion basis, PET/CT when compared with pre-PET/CT conventional imaging in patients with metastatic liver and lung lesions had a Spearman correlation coefficient of 0.8 and $P < 0.0001$ in both subgroups. PET/CT upstaged disease in 33.1% (52/157), down staged disease in 24.9% (39/157) and was in agreement with pre-PET/CT conventional imaging in the remaining 42% of patients (66/157). Based on PET/CT results surgery was averted in 33.8% patients (53/157). PET/CT had a sensitivity of 87.1%, specificity of 88.0%, PPV of 97.4%, NPV of 56.4% and an overall accuracy of 87.3% in assessing metastatic disease.	3
48. Smyth EC, Hsu M, Panageas KS, Chapman PB. Histology and outcomes of newly detected lung lesions in melanoma patients. <i>Ann Oncol</i> 2012; 23(3):577-582.	Observational-Dx	229 patients	To examine factors predictive of a positive biopsy of melanoma.	229 patients were identified; median age was 63 years; 48% were never smokers; 27% had a prior nonmelanoma cancer; 88% of lung nodules were malignant: 69% melanoma, 19% other cancers. Among 113 patients undergoing PET, proportions of benign, melanoma, and nonmelanoma FDG nodules did not differ ($P = 0.53$). On multivariable analysis, >stage I melanoma, negative smoking history, multiple lung nodules, and no prior nonmelanoma cancer were significantly associated with a melanoma biopsy result rather than other cancer.	3
49. Alonso O, Martinez M, Mut F, et al. Detection of recurrent malignant melanoma with 99mTc-MIBI scintigraphy. <i>Melanoma Res</i> 1998; 8(4):355-360.	Observational-Dx	81 patients	Prospective blinded investigation in patients with histologically confirmed malignant melanoma for assessment of the value of 99mTc-methoxyisobutylisonitrile scanning in detection of recurrent disease.	Whole body 99mTc-methoxyisobutylisonitrile scanning correctly detected 68 (92%) of 74 metastatic lesions. This included regional lymph nodes ($n = 23$), non-regional lymph nodes ($n = 10$), skin ($n = 16$), brain/cerebellum ($n = 6$), lung ($n = 8$), bone ($n = 4$) and breast ($n = 1$). Results suggest that 99mTc-methoxyisobutylisonitrile is an effective imaging modality for whole-body screening of metastatic disease in malignant melanoma patients with the potential to influence treatment planning.	2

**Screening for Pulmonary Metastases
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
50. Abdel-Nabi HH, Levine G, Lamki LM, et al. Colorectal carcinoma metastases: detection with In-111-labeled monoclonal antibody CCR 086. <i>Radiology</i> 1990; 176(1):117-122.	Observational-Dx	17 patients	To determine the effectiveness of In-111-antimucin murine monoclonal antibody in detecting colorectal metastases.	17/25 lesions were detected (sensitivity 68%); smallest lung lesion was 1 cm, smallest liver lesion was 1.5 cm. Further investigations needed.	3
51. Pevarski DJ, Drane WE, Scarborough MT. The usefulness of bone scintigraphy with SPECT images for detection of pulmonary metastases from osteosarcoma. <i>AJR</i> 1998; 170(2):319-322.	Observational-Dx	27 patients	To prospectively compare bone scintigraphy with SPECT images of the chest and CT of the chest in revealing possible osteosarcoma pulmonary metastases.	8/27 (30%) had pulmonary metastases. 4/8 had positive results on both chest CT and bone SPECT imaging, with bone SPECT demonstrating additional lesions in 2 of these 4 patients. In the other 4 patients, chest CT was positive for pulmonary metastases whereas bone SPECT studies were negative. Among 19 patients without pulmonary metastases, both CT and bone SPECT were negative in 12; in 7 (37%) patients, chest CT demonstrated abnormalities while SPECT images were negative, but these were eventually shown to represent benign lesions. Negative results on a bone SPECT study does not exclude the possibility of lung metastases, but a positive bone SPECT study is useful in confirming abnormality seen on chest CT and may also reveal additional lesions missed on CT.	3

**Screening for Pulmonary Metastases
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Ren G, Miao Z, Liu H, et al. Melanin-targeted preclinical PET imaging of melanoma metastasis. <i>J Nucl Med</i> 2009; 50(10):1692-1699.	Review/Other-Dx	In vivo distribution and small-animal PET studies conducted on mice; U87MG tumors and comparative studies performed with FDG-PET in melanoma models	To determine the value of N-[2-(diethylamino)ethyl]-4-(18)F-fluorobenzamide in imaging melanoma metastasis.	In vitro, uptake of (18)F-fluorobenzamide was significantly higher in B16F10 cells treated with l-tyrosine (P<0.001). In vivo, (18)F-fluorobenzamide displayed significant tumor uptake; at 2 h, 5.94 +/- 1.83 percentage injected dose per gram was observed in B16F10 tumors and only 0.75 +/- 0.09 percentage injected dose/g and 0.56 +/- 0.13 percentage injected dose/g was observed in amelanotic A375M and U87MG tumors, respectively. Lung uptake was significantly higher in murine lungs bearing melanotic B16F10 pulmonary metastases than in normal murine lungs (P<0.01). Small-animal PET clearly identified melanotic lesions in both primary and pulmonary metastasis B16F10 tumor models. Coregistered micro-CT with small-animal PET along with biopsies further confirmed the presence of tumor lesions in the mouse lungs. (18)F-fluorobenzamide specifically targets primary and metastatic melanotic melanoma lesions with high tumor uptake and may have translational potential.	4
53. American College of Radiology. <i>Manual on Contrast Media</i> . Available at: http://www.acr.org/~link.aspx?id=29C40D1FE0EC4E5EAB6861BD213793E5&amp;z=z .	Review/Other-Dx	N/A	Guidance document on contrast media to assist radiologists in recognizing and managing risks associated with the use of contrast media.	N/A	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.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

- CAD = Computer-aided detection
- CI = Confidence interval
- CT = Computed tomography
- CXR = Chest radiography
- FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography
- HNC = Head and neck cancer
- HNSCC = Head and neck squamous cell cancer
- LMG = Life-months gained
- MRI = Magnetic resonance imaging
- NPV = Negative predictive value
- PET = Positron emission tomography
- PPV = Positive predictive value
- SD = Standard deviation
- SPECT = Single photon emission computed tomography
- US = Ultrasound
- VCT = Volume change thresholds