

**Stage I Breast Carcinoma  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
1. American Joint Committee on Cancer. Manual for staging of cancer. 6th ed. New York: Springer; 2002:257-281.	15	N/A	Book chapter.	N/A	N/A
2. Jain S, Fisher C, Smith P, Millis RR, Rubens RD. Patterns of metastatic breast cancer in relation to histological type. <i>Eur J Cancer</i> 1993; 29A(15):2155-2157.	13	1,238	Examine clinical records of patients with operable breast cancer to identify patterns of metastatic breast cancer in relation to histological type.	<ul style="list-style-type: none"> <li>• Infiltrating ductal carcinoma (IDC) recurred more in lung (P&lt;0.05), pleura (P&lt;0.05) and brain (P&lt;0.05).</li> <li>• Infiltrating lobular carcinoma (ILC) recurred more in metastasized to the bone marrow (P&lt;0.01) and peritoneum (P&lt;0.01).</li> <li>• Bone involvement as the initial presentation of distant metastatic disease occurred in over 50% of women with ILC, significantly more commonly than in those with IDC (34%, P&lt;0.01).</li> </ul>	2
3. Patanaphan V, Salazar OM, Risco R. Breast cancer: metastatic patterns and their prognosis. <i>South Med J</i> 1988; 81(9):1109-1112.	15	145	To examine metastatic patterns and prognosis of breast cancer.	Most common first site of distant spread was bone (51%), lung (17%), brain (16%), and liver (6%). The remaining 10% of patients had multiple metastatic sites. No correlation between time until relapse and survival after metastasis. Patients in whom distant metastases developed relatively soon after the initial diagnosis had the same post-metastatic prognosis as patients whose disease metastasized later. No correlation was found between age at initial diagnosis and metastasis-free interval or survival after metastasis.	3
4. Muss HB, Tell GS, Case LD, Robertson P, Atwell BM. Perceptions of follow-up care in women with breast cancer. <i>Am J Clin Oncol</i> 1991; 14(1):55-59.	13	101 with breast cancer (48-localized 53- metastatic)	To examine the perceptions of patients regarding follow-up examinations in women with breast cancer.	Only a third of the patients recognized the value of history in detecting recurrence, and two-thirds felt the physical examination was helpful. Study recommends greater emphasis on history and physical examination.	3
5. Loomer L, Brockschmidt JK, Muss HB, Saylor G. Postoperative follow-up of patients with early breast cancer. Patterns of care among clinical oncologists and a review of the literature. <i>Cancer</i> 1991; 67(1):55-60.	13	80 oncologists	Review literature and conduct a survey among oncologists to determine strategies for follow-up care after primary treatment of early-stage breast cancer.	Yearly mammograms were recommended by more than 95% of respondents. History and physical examination are cost-effective in detecting recurrence during follow-up.	2

**Stage I Breast Carcinoma  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
6. Rojas MP, Telaro E, Russo A, et al. Follow-up strategies for women treated for early breast cancer. <i>Cochrane Database Syst Rev</i> 2005; (1):CD001768.	11	3,055 patients (4 RCT) 2 observers	Collate randomized controlled trials (RCT) to determine the effectiveness of different policies for follow-up for distant metastasis on mortality, morbidity, and quality of life for women with stage I, II, and III breast cancer.	No difference in survival for women with intensive screening compared with those who had only clinical examination and mammography. Patient satisfaction was higher for women with follow-up by general practitioner.	1
7. O'Mara RE. Bone scanning in osseous metastatic disease. <i>JAMA</i> 1974; 229(14):1915-1917.	12	N/A	Review comparing bone scan to roentgenogram in the detection of osseous metastatic disease.	In patients with abnormal roentgenogram, the scan will usually show greater tumor involvement. The scan may also be helpful in areas like the sternum and scapula. Scan has small percentage of false-negatives (3%-8%). Since scan is highly sensitive but nonspecific, both procedures are recommended for accurate detection.	3
8. Impact of follow-up testing on survival and health-related quality of life in breast cancer patients. A multicenter randomized controlled trial. The GIVIO Investigators. <i>JAMA</i> 1994; 271(20):1587-1592.	8	1,320	To determine effectiveness of intensive follow-up testing for breast cancer metastases. Multicenter study at 26 hospitals randomized women to "intensive surveillance" (annual bone scan, annual liver echography, biannual chest radiograph and lab tests) at predetermined intervals and "control regimen" (patients seen by physicians at same frequency but only clinically indicated tests performed). Also evaluated quality of life issues.	Of the women in this study, 739 (56%) were node negative, equally randomized to the two groups. No significant differences were found in distant metastasis-free survival between the two groups; early detection group started treatment only 1-month earlier on the average. No evidence of benefit from intensive surveillance emerged within subsets of patients grouped by nodal status. Concluded no benefit from frequent diagnostic tests added to routine medical surveillance. Results of quality of life assessment indicate that type of follow-up does not affect various dimensions of quality of life: perception, emotional well-being, body image, social functioning, symptoms or satisfaction with care. On the other hand, this study did not show that frequent testing increased stress.	1
9. Rosselli Del Turco M, Palli D, Cariddi A, Ciatto S, Pacini P, Distante V. Intensive diagnostic follow-up after treatment of primary breast cancer. A randomized trial. National Research Council Project on Breast Cancer follow-up. <i>JAMA</i> 1994; 271(20):1593-1597.	8	1,243 stage I=56%	To determine whether early detection of intrathoracic and bone metastases were effective in reducing breast cancer mortality. Clinical follow-up group (included physical examination and mammography) was compared with intensive follow-up group (added chest radiography and bone scan every 6 months).	640 (52%) node negative. In total, 393 recurrences (104 local and 289 distant) occurred. Increased detection of intrathoracic and bone metastases was evident in intensive follow-up group. However, there was no difference in overall 5-year survival rates. Periodic intensive follow-up with chest radiography and bone scan not recommended as routine policy.	1

**Stage I Breast Carcinoma  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
10. Ciatto S, Pacini P, Azzini V, et al. Preoperative staging of primary breast cancer. A multicentric study. <i>Cancer</i> 1988; 61(5):1038-1040.	9	3,627 patients stage I=1,038	To assess the cost-effectiveness of pre-operative imaging to detect distant metastases in breast cancer with chest radiographs (all 3,627), bone scans (2,450), bone radiographs (1,708), liver sonography (836), and liver scintigraphy (435).	The detection rate of preclinical asymptomatic distant metastases depended on the T and N category (TNM classification system), and was very low (chest radiograph: 0.30%, bone radiograph: 0.64%, bone scintigraphy: 0.90%, liver ecography: 0.24%, liver scintigraphy: 0.23%). The sensitivity, determined after a 6-month follow-up, was below 0.50% for all tests. The highest value (0.48%) was recorded for bone scintigraphy, which also had the lowest specificity (0.95%). Study does not recommend preoperative staging, especially for stage I cases.	1
11. Brar HS, Sisley JF, Johnson RH, Jr. Value of preoperative bone and liver scans and alkaline phosphatase in the evaluation of breast cancer patients. <i>Am J Surg</i> 1993; 165(2):221-223; discussion 224.	9	133 bone scans 63 liver scans stage I=21	Review results of 133 bone scans, 63 liver scans (CT, liver spleen radionuclide scan, or US) for preoperative staging of breast cancer (TNM classification). Went through medical records at Medical College of Georgia, 1984-1990.	Only 4/133 patients (3%) had positive bone scan that correlated with results of radiographs. <u>Stage I=0 positive</u> . Only 1/63 patients had liver scan suggestive of possible metastases. In 103 with normal bone scans the majority (54%) had elevated alkaline phosphate levels; 9/30 patients (30%) with abnormal scans had normal alkaline phosphatase levels. 51/63 with elevated alkaline phoshatase levels had normal liver scans. Cost of scans=\$74,000.	2
12. Coleman RE, Rubens RD, Fogelman I. Reappraisal of the baseline bone scan in breast cancer. <i>J Nucl Med</i> 1988; 29(6):1045-1049.	10	1,267 patients stage I=271	To assess the utility of bone scintigraphy in the staging of patients with breast carcinoma. (Tc-99m MDP).	Positive scans for T1=0.3%; but zero were due to metastases. Only 18 (7%) of stage I cases eventually converted to positive scan. While 47 (17%) of stage I cases did develop distant metastases, the skeleton was the site of first metastases in only 9 (3%). Baseline scans recommended only for stage II or greater cases.	2
13. Khansur T, Haick A, Patel B, Balducci L, Vance R, Thigpen T. Evaluation of bone scan as a screening work-up in primary and local-regional recurrence of breast cancer. <i>Am J Clin Oncol</i> 1987; 10(2):167-170.	10	265 patients with primary and 39 patients with local regional recurrence; stage I=92	Review scans to determine usefulness of bone scans in staging patients with primary (265) and local-regional recurrence (39) of breast cancer.	Zero of 92 stage I cases had positive bone scans. Suggests limiting scans to the highest risk groups (positive nodes).	2

**Stage I Breast Carcinoma  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
14. Kunkler IH, Merrick MV, Rodger A. Bone scintigraphy in breast cancer: a nine-year follow-up. <i>Clin Radiol</i> 1985; 36(3):279-282.	10	465 patients stage I=57	To determine value of bone scintigraphy in women with histologically confirmed breast carcinoma by stage in patients followed at least 2 years and up to 9 years.	Overall incidence of positive scans was 9%; but only 1 of 57 stage I cases had positive bone scan (1.5%); 8 had benign or equivocal (12.1%). Concluded that there is no justification for the routine use of scintigraphy in patients with early breast carcinoma.	2
15. McNeil BJ, Pace PD, Gray EB, Adelstein SJ, Wilson RE. Preoperative and follow-up bone scans in patients with primary carcinoma of the breast. <i>Surg Gynecol Obstet</i> 1978; 147(5):745-748.	10	153 patients stage I=37	To evaluate the role of preoperative and postoperative bone scans in patients with localized carcinoma of the breast.	Median follow-up of patients was 18 months. No abnormal scans found in the patients with stage I disease (lesions <2 cm with negative nodes). Greater yield for higher stages. 7% with stage I disease converted to positive scans over time (compared to 25% for stage II and 58% for stage III). False positives are also a significant problem in these patients.	2
16. Loprinzi CL. It is now the age to define the appropriate follow-up of primary breast cancer patients. <i>J Clin Oncol</i> 1994; 12(5):881-883.	12	N/A	Editorial. To define the appropriate follow-up for patients with primary breast cancer.	Recommends follow-up guidelines for stage I and II breast cancer patients. History and physical examination should be basis of follow-up.	4
17. Schaner EG, Chang AE, Doppman JL, Conkle DM, Flye MW, Rosenberg SA. Comparison of computed and conventional whole lung tomography in detecting pulmonary nodules: a prospective radiologic-pathologic study. <i>AJR</i> 1978; 131(1):51-54.	9	25	Prospective radiologic-pathologic correlative study to compare computed and conventional whole lung tomography in detecting pulmonary nodules.	CT defined more nodules than conventional tomography in 48% of cases. CT identified 78% of all resected nodules >3 mm in diameter, compared to 59% using conventional tomography. CT was also of value in detecting bilateral nodules earlier than conventional tomography and in documenting small nodule growth on successive examination. However, 60% of the additional nodules defined by CT and resected proved to be benign granulomas and pleural-based nodes.	2
18. Ravaioli A, Pasini G, Polselli A, et al. Staging of breast cancer: new recommended standard procedure. <i>Breast Cancer Res Treat</i> 2002; 72(1):53-60.	9	1,218 patients stage I=497	Review data from cases of breast cancer to determine value of preoperative bone scan, chest radiograph, liver US.	True positive, false positive, and false negative for bone scan 4 (0.8%), 13 (2.6%), 0; for chest radiograph 0, 3 (0.6%), 0; for liver US 0, 2 (0.4%), 1 (0.2%). Conclude that only laboratory analysis indicated for initial staging.	2
19. Vestergaard A, Herrstedt J, Thomsen HS, Dombernowsky P, Zedeler K. The value of yearly chest X-ray in patients with stage I breast cancer. <i>Eur J Cancer Clin Oncol</i> 1989; 25(4):687-689.	10	263 patients	To determine the value of yearly chest radiograph in patients with stage I breast cancer.	For 1,599 examinations performed, unsuspected malignant changes were observed in only 0.25% (4 patients). Study concludes that repeated chest radiographs in patients with stage I breast cancer are not necessary.	2

**Stage I Breast Carcinoma  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
20. 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.	9	516 patients stage I =236 of 412 bone scan; stage I=232 of 412 liver US; stage I=234 of 428 chest radiograph	To determine the usefulness of bone scan, liver US, and chest radiograph in the staging of asymptomatic women with newly diagnosed breast cancer. Reviewed results for 516 consecutive patients.	For women with stage I disease, 12/236 (5.1%) had unsuspected bone metastases on bone scan. For liver US and chest radiograph, only women with stage III disease had metastatic disease found using these modalities.	2
21. Bernardino ME, Thomas JL, Barnes PA, Lewis E. Diagnostic approaches to liver and spleen metastases. <i>Radiol Clin North Am</i> 1982; 20(3):469-485.	12	N/A	Review comparing different diagnostic approaches to liver and spleen metastases.	Radionuclide imaging is sensitive, but nonspecific. It has significant false negative and false positive rate. US has accuracy of 80%-85%, but limited in the size of lesions it can detect. CT is very accurate (>90%). Angiography is an accurate procedure. Authors suggest US should be first modality of choice and if inadequate, CT be used.	3
22. Friedman ML, Esposito FS. Comparison of CT scanning and radionuclide imaging in liver disease. <i>Crit Rev Diagn Imaging</i> 1980; 14(2):143-189.	12	N/A	Review comparing CT scanning with radionuclide imaging in liver disease.	For jaundiced patient, CT provides more specific information about the liver than radionuclide liver scan. For mass lesions of the liver, radionuclide scan is more sensitive than CT but less specific.	3
23. Yeh HC, Rabinowitz JG. Ultrasonography and computed tomography of the liver. <i>Radiol Clin North Am</i> 1980; 18(2):321-338.	9	N/A	To compare US and CT in the evaluation of the liver.	CT and US are recommended for the evaluation of the liver. CT and US have different physical principles, and therefore differences in techniques used and information provided.	3
24. Wiener SN, Sachs SH. An assessment of routine liver scanning in patients with breast cancer. <i>Arch Surg</i> 1978; 113(2):126-127.	10	234	Retrospective review to assess the value of routine preoperative liver scanning in patients with breast cancer.	Liver was considered normal in 231/234 patients. The hepatoscan uncovered only one patient with unsuspected metastases. 8 false positives were noted. Routine hepatoscanning is not recommended unless there is evidence of abnormal liver function.	2

**Stage I Breast Carcinoma  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
25. Myers RE, Johnston M, Pritchard K, Levine M, Oliver T. Baseline staging tests in primary breast cancer: a practice guideline. <i>CMAJ</i> 2001; 164(10):1439-1444.	11	5,407 patients bone scan; 1,625 patients liver US; 3,884 patient's chest radiograph.	Review studies using bone scan, liver US, and chest radiograph for baseline staging in women with newly diagnosed breast cancer.	9 studies performed between 1985 and 1995 of 5,407 women undergoing bone scan detected skeletal metastasis in 7/1,419 women with stage I disease (0.5%). Liver US and chest radiograph detected metastatic disease in 0% and 0.1% of women respectively. Study does not recommend routine use of bone scan, liver US, or chest radiograph as part of baseline staging.	1
26. Ferrucci JT, Leo J. Rigler lecture. MR imaging of the liver. <i>AJR</i> 1986; 147(6):1103-1116.	9	142 3 observers	Review technical and clinical advances of MRI of the liver. Also, performed a blinded retrospective study to compare MRI with CT in 42 patients.	MRI discovered 14% more individual metastases and 3% more patients with liver cancer than CT. MRI also showed greater specificity (98%) than CT (91%) in distinguishing patients without liver metastases. Study suggest MRI can be appropriate as a primary screening method for detecting liver neoplasms if optimal pulse sequences are used.	2
27. Russell EJ, Geremia GK, Johnson CE, et al. Multiple cerebral metastases: detectability with Gd-DTPA-enhanced MR imaging. <i>Radiology</i> 1987; 165(3):609-617.	10	16 2 observers	To determine if Gd-DTPA-enhanced MRI improves detection of multiple cerebral metastases.	6/7 (86%) patients with multiple metastases, had at least one tumor nodule depicted by post-infusion MRI that was missed by one or both observers on review of pre-infusion images alone. Authors believe contrast enhancement improves detection of metastatic foci with MRI and that the findings indicate broader implications for the detection of multiple lesions from other causes.	2
28. Weisberg LA. The computed tomographic findings in intracranial metastases due to breast carcinoma. <i>Comput Radiol</i> 1986; 10(6):297-306.	13	17	To review CT findings in intracranial metastases due to breast carcinoma.	16 patients showed neurological abnormalities on examination; 1 patient had no abnormalities. CT showed evidence of basal parasellar lesions (3 cases), orbital lesions (2 cases), or cerebral hemispheric (intracerebral or subdural) lesions (11 cases). CT showed evidence of bone lesions in 8 cases and there were accompanying parasellar (3 cases), orbital (2 cases), and subdural lesions (3 cases).	3

**Stage I Breast Carcinoma  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Strength of Evidence
29. Bentson JR, Steckel RJ, Kagan AR. Diagnostic imaging in clinical cancer management: brain metastases. <i>Invest Radiol</i> 1988; 23(5):335-341.	12	N/A	To review roles of imaging in the management of brain metastases.	CT scans easily detect brain metastases because of the extensive brain edema caused by metastases. Use of a contrast medium improves detection rate. MRI is becoming a popular modality for detecting brain metastases, but specificity is lower than CT in detecting intracranial metastases.	4
30. Khansur T, Haick A, Patel B, Balducci L, Vance R, Thigpen JT. Preoperative evaluation with radionuclide brain scanning and computerized axial tomography of the brain in patients with breast cancer. <i>Am J Surg</i> 1988; 155(2):232-234.	9	226 patients with breast cancer 34 patients with loco regional recurrence 131 scans; stage I=52 patients	Review clinical and radiological findings to determine value of radionuclide brain scanning and CT of brain in the pretreatment evaluation of patients with primary and loco regional recurrence of breast cancer.	<ul style="list-style-type: none"> <li>• For primary breast cancer, 4/131 radionuclide scans suggested calvarial metastasis, and the findings were confirmed with bone scans and skull radiographs. One of 95 CT scans of brain showed brain metastasis.</li> <li>• For locoregional recurrence, the results of 2/23 radionuclide scans and 1/11 CT scans were positive.</li> <li>• CT brain scans only useful in the presence of neurological signs. Not one case of brain metastases was found in the absence of neurological signs and symptoms.</li> </ul>	2
31. Brant-Zawadzki M. MR imaging of the brain. <i>Radiology</i> 1988; 166(1 Pt 1):1-10.	12	N/A	To review clinical applications of MRI in the diagnosis of brain disorders.	The greater sensitivity of MRI to pathologic alteration of cerebral tissues assures its replacement of CT as the first-line diagnostic imaging study for most patients with neurologic manifestations.	4
32. Davis PC, Hudgins PA, Peterman SB, Hoffman JC, Jr. Diagnosis of cerebral metastases: double-dose delayed CT vs contrast-enhanced MR imaging. <i>AJNR</i> 1991; 12(2):293-300.	9	23	To compare double-dose delayed CT with contrast-enhanced MRI in the diagnosis of cerebral metastases.	Contrast-enhanced MRI was better than double-dose delayed CT for lesion detection, anatomic localization of lesions, and differentiation of solitary vs multiple lesions.	3

## Evidence Table Key

### Study Type Key

*Numbers 1-7 are for studies of therapies while numbers 8-15 are used to describe studies of diagnostics.*

1. Randomized Controlled Trial — Treatment
2. Controlled Trial
3. Observation Study
  - a. Cohort
  - b. Cross-sectional
  - c. Case-control
4. Clinical Series
5. Case reviews
6. Anecdotes
7. Reviews
  
8. Randomized Controlled Trial — Diagnostic
9. Comparative Assessment
10. Clinical Assessment
11. Quantitative Review
12. Qualitative Review
13. Descriptive Study
14. Case Report
15. Other (Described in text)

### Strength of Evidence Key

- Category 1 - The conclusions of the study are valid and strongly supported by study design, analysis and results.
- Category 2 - The conclusions of the study are likely valid, but study design does not permit certainty.
- Category 3 - The conclusions of the study may be valid but the evidence supporting the conclusions is inconclusive or equivocal.
- Category 4 - The conclusions of the study may not be valid because the evidence may not be reliable given the study design or analysis.