

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

Clinical Condition:

Stage I Breast Carcinoma

Variant 1:

Rule out metastases — asymptomatic woman.

Radiologic Procedure	Rating	Comments	<u>RRL*</u>
Rule Out Bone Metastases			
Tc-99m bone scan whole body	2		Med
X-ray radiographic survey whole body	2		Med
FDG-PET whole body	2		High
Rule Out Thoracic Metastases			
X-ray chest	2		Min
CT chest with or without contrast	2		Med
X-ray tomography chest	2		Low
FDG-PET whole body	2		High
Rule Out Liver Metastases			
CT abdomen with or without contrast	2		Med
Tc-99m sulfur colloid scan liver	2		Med
US abdomen	2		None
MRI abdomen with or without contrast	2		None
FDG-PET whole body	2		High
Rule Out Brain Metastases			
MRI head with contrast	2		None
CT head with or without contrast	2		Med
FDG-PET whole body	2		High
<u>Rating Scale:</u> 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

STAGE I BREAST CARCINOMA

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Summary of Literature Review

Staging parameters for breast cancer according to the TMN classification of the American Joint Committee on Cancer include T, the local extent of disease; N, the presence of regional lymph node metastases; and M, the presence of distant metastases [1]. A diagnosis of stage I breast cancer indicates surgical removal of an invasive breast carcinoma that is 2 cm or smaller in diameter (T1), with no regional (axillary) lymph node metastases (N0) and no distant metastases (M0).

The most common sites for distant metastases from breast carcinoma are the skeleton, lung, liver, and brain [2,3]. Several imaging examinations are available that can potentially identify metastases to these organs. Surveys of patients with breast cancer indicate that most of them prefer an intensive follow-up to detect asymptomatic disease, including metastases [4]. Surveys of physicians who take care of patients with breast cancer indicate that most of these physicians also favor intensive surveillance programs in patients with breast cancer who are asymptomatic [5]. However, because of cost constraints, there should be a reasonable anticipated yield and an expected effect on patient management and outcome when imaging examinations are ordered on asymptomatic patients with breast cancer. In a Cochrane Collaboration Review of four randomized, controlled clinical trials that included 3,055 women, Rojas et al [6] found no difference in overall or disease-free survival for women who underwent intensive radiologic and laboratory testing compared with those managed with clinical visits and

mammography. This appropriateness guideline segment addresses the imaging workup of women with stage I breast carcinoma — specifically, which imaging tests should be done to rule out unexpected metastatic disease.

Skeletal Metastases

Radionuclide scanning is more effective than conventional radiography for detecting skeletal metastases because radionuclide scans have higher sensitivity and can survey the entire skeleton in one examination [7]. However, several investigations that are discussed below have revealed that bone scanning is not useful in stage I breast carcinoma because its low yield and lack of proven effect on management or survival.

A multicenter study in Italy randomized 1,320 women into a study group that would undergo “intensive surveillance” and a control group having only tests that were ordered as a result of subsequent clinical findings uncovered at routine medical visits [8]. The intensive surveillance included radionuclide bone scanning, chest radiography, and liver ultrasonography (US). The study, which included 739 node-negative women, found that metastases of all kinds were found only an average of one month earlier in the intensive surveillance group. The earlier detection of these metastases had no significant effect on overall survival.

A second large clinical trial in Italy randomized 1,243 women into “intensive” and “clinical” follow-up protocols to determine whether early detection of bone and intrathoracic metastases was effective in reducing mortality in the intensive follow-up group [9]. Fifty-two percent of the women in the latter study were node-negative. Although more bone and lung metastases were found in the intensive follow-up group, there was no significant difference in the overall 5-year survival rates between the two groups.

Another large clinical study (nonrandomized) in Italy confirmed the lack of value of regular preoperative radiography and radionuclide bone scanning performed on consecutive stage I asymptomatic breast cancer patients [10]. Only one of 633 patients with stage I disease had metastatic bone disease detected. Several other nonrandomized clinical studies with many subjects have also documented the low yield and lack of utility of radionuclide bone scanning for patients with stage I breast carcinoma [11-14].

Despite the low yield of bone scans, many clinicians have continued to recommend baseline bone scans on the basis that they could be useful for comparison with subsequent scans performed when patients develop symptoms or convert to an abnormal routine scan. In fact, routine baseline bone scans are unlikely to be useful in stage I disease because few patients will later convert to positive scans, and also because studies in the literature show that earlier detection of metastases does not reduce overall mortality [9,12,15]. Furthermore, several studies have

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reported false-positive scans as a problem encountered when screening for metastases in asymptomatic patients [15]. No information is available regarding whether positron emission tomography combined with computed tomography (PET/CT) offers an advantage over current methods for detecting skeletal metastases.

Lung Metastases

Methods for detecting lung metastases include conventional chest radiography and CT. Because of its relatively low cost when compared with the other imaging modalities, conventional chest radiography is considered the most reasonable approach for detecting unsuspected disease, as a baseline for monitoring, and for routine follow-up [16]. CT is more sensitive than conventional whole-lung tomography and is the method of choice to evaluate equivocal findings on chest radiography and to identify additional nodules in positive cases [17]. No information is available regarding whether PET/CT offers an advantage over current methods for detecting lung metastases.

Despite its relatively low cost, investigators have even questioned the use of routine chest radiography to detect intrathoracic metastases in patients with breast cancer, especially those with stage I disease. One problem is its low yield in stage I disease, reported to be less than 0.5% in asymptomatic women who had routine chest radiographs after the diagnosis of stage I breast carcinoma [10,18,19]. In a study of 412 women with newly diagnosed breast cancer, chest radiograph only showed metastasis in women previously classified as having stage III disease [20]. Furthermore, false-positive chest radiographs can lead to expensive diagnostic workups [21]. Two large Italian randomized control studies failed to show a significant outcome benefit when routine chest radiography was used to detect metastases earlier [8,9].

Liver Metastases

Both radionuclide scanning and US have been used to detect liver metastases. Although liver metastases are not as common as lung or bone metastases, the appearance of liver metastases is associated with the worst prognosis [3]. To be detected reliably by Tc-99m sulfur colloid liver scans, metastases generally must be larger than 2 cm [21]. US can also identify liver metastases 2 cm or larger, and it is often used to localize these lesions for biopsy or fine-needle aspiration cytology [22,23]. No information is available regarding whether PET/CT offers an advantage over current methods for detecting liver metastases.

As with screening for bone and lung metastases, the yield of screening with radionuclide scans or US to detect asymptomatic liver metastases is low. In one retrospective study of 234 asymptomatic patients with breast carcinoma at various stages, preoperative radionuclide liver scanning identified metastases in only 1% of the cases [24]. Furthermore, in that study eight of 11 positive scans were eventually determined to be false-positives. Another study showed the yield for detecting metastases using radionuclide scans or US to be less than 0.5% [10]. A review of four studies evaluating a total of 423 women

with stage I breast carcinoma showed no metastatic lesions on liver US [25]. In a study of 412 women with newly diagnosed breast cancer, liver US only showed metastasis in women previously classified as having stage III disease [20]. Large randomized control studies have failed to show a benefit from screening for liver metastases with US [8,9].

Although CT and magnetic resonance imaging (MRI) may show more lesions than radionuclide scanning or US [26], there is no evidence in the literature that routine imaging of the liver with either of the more sensitive modalities has clinical utility in asymptomatic patients with breast carcinoma.

Brain Metastases

Breast cancer is second only to lung carcinoma as a cause of intracerebral and orbital metastases, but few patients have brain metastases at the time of breast cancer diagnosis, particularly when the tumor is detected at stage I [27,28]. In CT examinations, brain metastases may be nodular or ring-shaped, single or multiple; are usually associated with extensive edema; and show varying amounts of enhancement with intravenous contrast agents [29]. One review of patients with breast cancer at all stages having radionuclide brain scanning and CT found that imaging studies failed to identify brain metastases in the absence of neurologic symptoms [30]. Because of its greater sensitivity, MRI has largely replaced CT for detecting and evaluating brain lesions [31]. Gadolinium-enhanced MRI increases the number of suspected cerebral metastases that can be detected [27]. Contrast-enhanced MRI has also been shown to be superior to double-dose delayed CT for detecting brain metastases [32]. However, no studies suggest any usefulness to routine imaging with any modality for detecting cerebral metastases in asymptomatic women with breast cancer. No information is available regarding whether PET/CT offers an advantage over current methods for detecting brain metastases.

Quality of Life Issues

A large randomized control study in Italy investigated quality-of-life issues, in addition to detection sensitivities and mortality rates, related to surveillance for metastatic disease in patients with breast cancer [8]. The results suggested that type of follow-up — ie, intensive surveillance vs routine clinical management — does not affect various dimensions of health-related quality-of-life. These dimensions include overall health and quality-of-life perception, emotional well-being, body image, social functioning, symptoms, and satisfaction with care. These parameters were almost identical between intensive and clinical-only surveillance groups. No differences in any quality-of-life issues were statistically significant between the two groups with different surveillance protocols. Nonetheless, more than 70% of the breast cancer subjects said they wanted to be seen frequently by a physician and undergo diagnostic tests even if they were free of symptoms. This preference for intensive surveillance was

not affected by whether the patient had been assigned to the intensive or minimalist follow-up regimen.

Summary

- There are no survival differences between women who obtain intensive screening and surveillance with imaging and laboratory studies compared with women who only undergo testing due to the development of symptoms or findings on clinical examinations.
- Women and health care professionals generally prefer intensive screening and follow-up after a diagnosis of breast cancer. However, quality-of-life is not different for women who undergo intensive screening and surveillance compared with those who do not.
- Given the lack of difference in survival or quality-of-life, there is little justification for imaging to detect or rule out metastasis in asymptomatic women with newly diagnosed stage I breast cancer.

Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations	
Relative Radiation Level	Effective Dose Estimate Range
None	0
Minimal	< 0.1 mSv
Low	0.1-1 mSv
Medium	1-10 mSv
High	10-100 mSv

Supporting Document(s)

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

References

1. American Joint Committee on Cancer. Manual for staging of cancer. 6th ed. New York: Springer; 2002:257-281.
2. Jain S, Fisher C, Smith P, Millis RR, Rubens RD. Patterns of metastatic breast cancer in relation to histological type. *Eur J Cancer* 1993; 29A(15):2155-2157.
3. Patanaphan V, Salazar OM, Risco R. Breast cancer: metastatic patterns and their prognosis. *South Med J* 1988; 81(9):1109-1112.
4. Muss HB, Tell GS, Case LD, Robertson P, Atwell BM. Perceptions of follow-up care in women with breast cancer. *Am J Clin Oncol* 1991; 14(1):55-59.
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. *Cancer* 1991; 67(1):55-60.
6. Rojas MP, Telaro E, Russo A, et al. Follow-up strategies for women treated for early breast cancer. *Cochrane Database Syst Rev* 2005; (1):CD001768.
7. O'Mara RE. Bone scanning in osseous metastatic disease. *JAMA* 1974; 229(14):1915-1917.
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. *JAMA* 1994; 271(20):1587-1592.
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. *JAMA* 1994; 271(20):1593-1597.
10. Ciatto S, Pacini P, Azzini V, et al. Preoperative staging of primary breast cancer. A multicentric study. *Cancer* 1988; 61(5):1038-1040.
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. *Am J Surg* 1993; 165(2):221-223; discussion 224.
12. Coleman RE, Rubens RD, Fogelman I. Reappraisal of the baseline bone scan in breast cancer. *J Nucl Med* 1988; 29(6):1045-1049.
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. *Am J Clin Oncol* 1987; 10(2):167-170.
14. Kunkler IH, Merrick MV, Rodger A. Bone scintigraphy in breast cancer: a nine-year follow-up. *Clin Radiol* 1985; 36(3):279-282.
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. *Surg Gynecol Obstet* 1978; 147(5):745-748.
16. Loprinzi CL. It is now the age to define the appropriate follow-up of primary breast cancer patients. *J Clin Oncol* 1994; 12(5):881-883.
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. *AJR Am J Roentgenol* 1978; 131(1):51-54.
18. Ravaioli A, Pasini G, Polselli A, et al. Staging of breast cancer: new recommended standard procedure. *Breast Cancer Res Treat* 2002; 72(1):53-60.
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. *Eur J Cancer Clin Oncol* 1989; 25(4):687-689.
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. *Ann Oncol* 2005; 16(2):263-266.
21. Bernardino ME, Thomas JL, Barnes PA, Lewis E. Diagnostic approaches to liver and spleen metastases. *Radiol Clin North Am* 1982; 20(3):469-485.
22. Friedman ML, Esposito FS. Comparison of CT scanning and radionuclide imaging in liver disease. *Crit Rev Diagn Imaging* 1980; 14(2):143-189.
23. Yeh HC, Rabinowitz JG. Ultrasonography and computed tomography of the liver. *Radiol Clin North Am* 1980; 18(2):321-338.
24. Wiener SN, Sachs SH. An assessment of routine liver scanning in patients with breast cancer. *Arch Surg* 1978; 113(2):126-127.
25. Myers RE, Johnston M, Pritchard K, Levine M, Oliver T. Baseline staging tests in primary breast cancer: a practice guideline. *CMAJ* 2001; 164(10):1439-1444.
26. Ferrucci JT, Leo J. Rigler lecture. MR imaging of the liver. *AJR* 1986; 147(6):1103-1116.
27. Russell EJ, Geremia GK, Johnson CE, et al. Multiple cerebral metastases: detectability with Gd-DTPA-enhanced MR imaging. *Radiology* 1987; 165(3):609-617.
28. Weisberg LA. The computed tomographic findings in intracranial metastases due to breast carcinoma. *Comput Radiol* 1986; 10(6):297-306.
29. Bentson JR, Steckel RJ, Kagan AR. Diagnostic imaging in clinical cancer management: brain metastases. *Invest Radiol* 1988; 23(5):335-341.

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. *Am J Surg* 1988; 155(2):232-234.
31. Brant-Zawadzki M. MR imaging of the brain. *Radiology* 1988; 166(1 Pt 1):1-10.
32. Davis PC, Hudgins PA, Peterman SB, Hoffman JC, Jr. Diagnosis of cerebral metastases: double-dose delayed CT vs contrast-enhanced MR imaging. *AJNR* 1991; 12(2):293-300.

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