

**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		☼ ☼ ☼
X-ray radiographic survey whole body	2		☼ ☼ ☼
FDG-PET/CT whole body	2		☼ ☼ ☼ ☼
Rule Out Thoracic Metastases			
X-ray chest	2		☼
CT chest without contrast	2		☼ ☼ ☼
CT chest with contrast	2		☼ ☼ ☼
CT chest without and with contrast	2		☼ ☼ ☼
X-ray tomography chest	2		☼ ☼
FDG-PET/CT whole body	2		☼ ☼ ☼ ☼
Rule Out Liver Metastases			
CT abdomen without contrast	2		☼ ☼ ☼
CT abdomen with contrast	2		☼ ☼ ☼
CT abdomen without and with contrast	2		☼ ☼ ☼ ☼
US abdomen	2		O
MRI abdomen without contrast	2		O
MRI abdomen without and with contrast	2		O
FDG-PET/CT whole body	2		☼ ☼ ☼ ☼
Rule Out Brain Metastases			
MRI head without contrast	2		O
MRI head without and with contrast	2		O
CT head without contrast	2		☼ ☼ ☼
CT head with contrast	2		☼ ☼ ☼
CT head without and with contrast	2		☼ ☼ ☼
FDG-PET/CT whole body	2		☼ ☼ ☼ ☼
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

STAGE I BREAST CARCINOMA

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Summary of Literature Review

Introduction/Background

Staging parameters for breast cancer according to the TNM 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 rates 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 of 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 detected 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

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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 reported false-positive scans as a problem encountered when screening for metastases in asymptomatic patients [15].

The use of positron emission tomography combined with computed tomography (PET/CT) in the initial staging of early-stage primary breast cancer is not well defined. PET/CT in addition to conventional imaging modalities may offer improved diagnostic accuracy compared to current standard practice. It is uncertain whether PET/CT will serve as a replacement for current imaging technologies [16-18].

A retrospective study of 163 women with suspected metastatic breast cancer showed high concordance between PET/CT and bone scan in detecting bony metastases [19].

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 [20]. 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 [21]. 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 [10,22-23]. In a study of 412 women with newly diagnosed breast cancer, chest radiographs only showed metastasis in women previously classified as having stage III disease [24]. Furthermore, false-positive chest radiographs can lead to expensive diagnostic workups. 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]. US can also identify liver metastases ≥ 2 cm, and it is

often used to localize these lesions for biopsy or fine-needle aspiration cytology [25-26]. 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. A 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 [27]. 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 [24]. 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 [28], 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 [29-30]. 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 [31]. 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 [32]. Because of its greater sensitivity, MRI has largely replaced CT for detecting and evaluating brain lesions [33]. Gadolinium-enhanced MRI increases the number of suspected cerebral metastases that can be detected [29]. Contrast-enhanced MRI has also been shown to be superior to double-dose delayed CT for detecting brain metastases [34]. However, no studies suggest any usefulness of 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. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® [Radiation Dose Assessment Introduction](#) document.

Relative Radiation Level Designations		
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
☼	<0.1 mSv	<0.03 mSv
☼☼	0.1-1 mSv	0.03-0.3 mSv
☼☼☼	1-10 mSv	0.3-3 mSv
☼☼☼☼	10-30 mSv	3-10 mSv
☼☼☼☼☼	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as “Varies”.		

Supporting Document(s)

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

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