American College of Radiology
ACR Appropriateness Criteria®

Clinical Condition: **Stage 1 Breast Carcinoma**

Variant 1: **Rule out metastases–asymptomatic woman.**

Radiologic Procedure	Rating	Comments	RRL*
Rule Out Bone Metastases			
NUC bone scan whole body	2		Med
MRI whole body	2		None
X-ray radiographic survey whole body	2		Low
FDG-PET/CT whole body	2		High
Rule Out Thoracic Metastases			
X-ray chest	2		Min
CT chest	2		Med
X-ray tomography chest	2		Min
FDG-PET/CT whole body	2		High
Rule Out Liver Metastases			
CT liver	2		Med
NUC liver scan	2		IP
US liver	2		None
MRI liver	2		None
FDG-PET/CT whole body	2		High
Rule Out Brain Metastases			
MRI head	2		None
FDG-PET/CT whole body	2		High
CT head	2		Low
NUC brain scan	2		Med
Rating Scale: 1=Least appropriate, 9=Most appropriate			*Relative Radiation Level

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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) which has 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. This appropriateness guideline segment addresses the imaging work up 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 [6]. However, several investigations that are discussed below have revealed that bone scanning is not useful in stage I breast carcinoma because of the low yield of the examination as well as a 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 [7]. The intensive surveillance included radionuclide bone scanning, chest radiography, and liver ultrasonography. 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 [8]. 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 [9]. 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 stage I breast carcinoma [10-13].

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 because studies in the literature show that earlier detection of metastases does not reduce overall mortality [8,11,14]. Furthermore, several studies have reported false-positive scans as a problem encountered when screening for metastases in asymptomatic patients [14]. No information is available regarding whether PET/CT offers and advantage over current methods for detecting skeletal metastases.

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Lung Metastases

Methods for detecting lung metastases include conventional chest radiography and computed tomography (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 [15]. 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 [16]. 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 the low yield in stage I disease, reported at less than 0.5% in asymptomatic women who had routine chest x-rays after the diagnosis of stage I breast carcinoma [9,17,18]. Furthermore, false-positive chest radiographs can lead to expensive diagnostic work ups [19]. Two large Italian randomized control studies failed to show a significant outcome benefit when routine chest radiography was used to detect metastases earlier [7,8].

Liver Metastases

Both radionuclide scanning and ultrasonography 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 [19]. Ultrasonography can also identify liver metastases 2 cm or larger, and is often used to localize these lesions for biopsy or fine-needle aspiration cytology [20,21]. 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 ultrasonography for detecting 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 [22]. Furthermore, in that study 8 of 11 positive scans were eventually determined to be false-positives. Another study showed the yield for detecting metastases using radionuclide scans or ultrasonography to be less than 0.5% [9]. A review of four studies evaluating a total of 423 women with stage I breast carcinoma showed no metastatic lesions on liver ultrasound [23]. Large randomized control studies have failed to show a benefit from screening for liver metastases with ultrasonography [7,8].

Although CT and magnetic resonance imaging (MRI) may show more lesions than radionuclide scanning or ultrasonography [24], 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 [25,26]. 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 [27]. 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 [28]. Because of its greater sensitivity, MRI has largely replaced CT for detecting and evaluating brain lesions [29]. Gadolinium-enhanced MRI increases the number of suspected cerebral metastases that can be detected [25]. Contrast-enhanced MRI has also been shown to be superior to double-dose delayed CT for detecting brain metastases [30]. 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

One large, Italian, randomized control study investigated quality of life issues, in addition to detection sensitivities and mortality rates, related to surveillance for metastatic disease in patients with breast cancer [7]. 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 of the dimensions of 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.

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