# Complete Summary

## GUIDELINE TITLE

Stage 1 breast carcinoma.

## BIBLIOGRAPHIC SOURCE(S)

Harvey JA, Bassett L, Birdwell RL, Brenner RJ, Comstock CE, D'Orsi C, Jong RA, Mahoney MC, Morris EA, Edge SB, Expert Panel on Women's Imaging - Breast Work Group. Stage 1 breast carcinoma. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 4 p. [30 references]

## GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: American College of Radiology (ACR), Expert Panel on Women's Imaging-Breast Work Group. Imaging work-up for stage I breast carcinoma. Reston (VA): American College of Radiology (ACR); 2002. 4 p. (ACR appropriateness criteria).

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

## ** REGULATORY ALERT **

## FDA WARNING/REGULATORY ALERT

**Note from the National Guideline Clearinghouse**: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 23, 2007, Gadolinium-based Contrast Agents: The addition of a boxed warning and new warnings about the risk of nephrogenic systemic fibrosis (NSF) to the full prescribing information for all gadolinium-based contrast agents (GBCAs).

## COMPLETE SUMMARY CONTENT

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## SCOPE

### DISEASE/CONDITION(S)

Stage I breast carcinoma

### GUIDELINE CATEGORY

Evaluation
Screening

### CLINICAL SPECIALTY

Internal Medicine
Oncology
Radiology

### INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

### GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of initial radiologic examinations for the imaging work-up of patients with stage I breast carcinoma

### TARGET POPULATION

Patients with stage I breast carcinoma

### INTERVENTIONS AND PRACTICES CONSIDERED

1. X-ray
    - Bone survey
    - Chest
2. Nuclear medicine (NM)
    - Bone scan
    - Liver scan
    - Brain scan

3. Computed tomography (CT)
    - Chest
    - Liver
    - Head
4. Magnetic resonance imaging (MRI)
    - Liver
    - Brain
5. Positron emission tomography (PET)/CT
6. Ultrasonography (US), liver

### MAJOR OUTCOMES CONSIDERED

Utility of radiologic examinations in differential diagnosis

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals and the major applicable articles were identified and collected.

### NUMBER OF SOURCE DOCUMENTS

The total number of source documents identified as the result of the literature search is not known.

### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

### METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed to reach agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed by the participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1-9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by the Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

Internal Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

**ACR Appropriateness Criteria®**

**Clinical Condition: Stage I Breast Carcinoma**

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

| Radiologic Procedure | Appropriateness Rating | Comments |
|---|---|---|
| **Rule Out Bone Metastases** | | |
| X-ray, bone survey | 2 | |
| NM, bone scan | 2 | |
| MRI | 2 | |
| PET/CT | 2 | |
| **Rule Out Thoracic Metastases** | | |
| X-ray, chest | 2 | |
| Tomography, chest | 2 | |
| CT, chest | 2 | |
| PET/CT | 2 | |
| **Rule Out Liver Metastases** | | |
| NM, liver scan | 2 | |
| US, liver | 2 | |
| MRI, liver | 2 | |
| CT, liver | 2 | |
| PET/CT | 2 | |
| **Rule Out Brain Metastases** | | |
| NM, brain scan | 2 | |
| CT, head | 2 | |
| MRI, brain | 2 | |
| PET/CT | 2 | |

| Radiologic Procedure | Appropriateness Rating | Comments |
|---|---|---|
| ***Appropriateness Criteria Scale*** **1 2 3 4 5 6 7 8 9** **1 = Least appropriate 9 = Most appropriate** | | |

**Abbreviations**

- CT, computed tomography
- MRI, magnetic resonance imaging
- NM, nuclear medicine
- PET, positron emission tomography
- US, ultrasound

**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. 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. 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. Surveys of physicians who take care of patients with breast cancer indicate that most of these physicians also favor intensive surveillance programs of patients with breast cancer who are asymptomatic. 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 the detection of skeletal metastases because radionuclide scans have higher sensitivity and can survey the entire skeleton in one examination. However, several investigations 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. 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. 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. 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.

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. Furthermore, several studies have reported false-positive scans as a problem encountered when screening for metastases in asymptomatic patients. No information is available regarding whether positron emission tomography (PET)/CT offers advantage over current methods for detecting skeletal metastases.

**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 detection of unsuspected disease, as a baseline for monitoring, and for routine follow-up. 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. No information is available regarding whether PET/CT offers 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. Furthermore, false-positive chest radiographs can lead to expensive diagnostic work-ups. Two large Italian randomized control studies failed to show a significant outcome benefit when routine chest radiography was used to detect metastases earlier.

### 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. To be detected reliably by Tc-99m sulfur colloid liver scans, metastases generally must be greater than 2 cm. 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. No information is available regarding whether PET/CT offers 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 detection of 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. 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%.

Although CT and magnetic resonance imaging (MRI) may show more lesions than radionuclide scanning or ultrasonography, 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. 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. 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. Because of its greater sensitivity, MRI has largely replaced CT for the detection and evaluation of brain lesions. Gadolinium-enhanced MRI increases the number of suspected cerebral metastases that can be detected. Contrast-enhanced MRI has also been shown to be superior to double-dose delayed CT for detection of brain metastases. However, no studies suggest any usefulness to routine imaging with any modality for the detection of cerebral metastases in asymptomatic women with breast cancer. No information is available regarding whether PET/CT offers advantage over current methods for detecting brain metastases.

Refer to the original guideline document for a discussion of quality of life issues.

## CLINICAL ALGORITHM(S)

Algorithms were not developed from criteria guidelines.

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

Selection of appropriate radiologic imaging procedures for screening of metastases in stage I breast carcinoma patients

### POTENTIAL HARMS

Several studies have reported false-positive scans as a problem encountered when screening for metastases.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

An American College of Radiology (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 exams 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 U.S. Food and Drug Administration (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.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

### IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Harvey JA, Bassett L, Birdwell RL, Brenner RJ, Comstock CE, D'Orsi C, Jong RA, Mahoney MC, Morris EA, Edge SB, Expert Panel on Women's Imaging - Breast Work Group. Stage 1 breast carcinoma. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 4 p. [30 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

1996 (revised 2006)

### GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

### SOURCE(S) OF FUNDING

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

### GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Women's Imaging—Breast Work Group

### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

*Panel Members*: Jennifer A. Harvey, MD; Lawrence Bassett, MD; Robyn L. Birdwell, MD; R. James Brenner, MD; Christopher E. Comstock, MD; Carl D'Orsi, MD; Roberta A. Jong, MD; Mary C. Mahoney, MD; Elizabeth A. Morris, MD; Stephen B. Edge, MD

## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

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The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

## GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

ACR Appropriateness Criteria® *Anytime*, *Anywhere*™ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

## AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

## PATIENT RESOURCES

None available

## NGC STATUS

This summary was completed by ECRI on January 30, 2001. The information was verified by the guideline developer as of February 20, 2001. This summary was

updated by ECRI on March 31, 2003. The updated information was verified by the guideline developer on April 21, 2003. This NGC summary was updated by ECRI Institute on May 17, 2007. This summary was updated by ECRI Institute on June 20, 2007 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents.

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