



Complete Summary

GUIDELINE TITLE

Diagnostic imaging in breast cancer.

BIBLIOGRAPHIC SOURCE(S)

Myers R, Minuk T, Johnston M, Diagnostic Imaging Guidelines Panel. Diagnostic imaging in breast cancer: recommendations report. Toronto (ON): Cancer Care Ontario (CCO); 2006 Apr 12. 19 p. [18 references]

GUIDELINE STATUS

This is the current release of the guideline.

Please visit the [Cancer Care Ontario Web site](#) for details on any new evidence that has emerged and implications to the guidelines.

COMPLETE SUMMARY CONTENT

SCOPE
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SCOPE

DISEASE/CONDITION(S)

Breast cancer

GUIDELINE CATEGORY

Diagnosis
Evaluation

CLINICAL SPECIALTY

Oncology
Radiology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

- To evaluate when ultrasonography (US), computed tomography (CT) scan, or magnetic resonance imaging (MRI) should be used in patients with breast cancer:
 - For the initial staging of patients with newly diagnosed breast cancer
 - To assess tumour response in patients with breast cancer undergoing chemotherapy
 - To detect disease recurrence in patients who have completed primary treatment for breast cancer
- To evaluate how often imaging should be repeated during treatment and follow-up

TARGET POPULATION

Women with breast cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Ultrasound
2. Magnetic resonance imaging (MRI)
3. Computed tomography (CT)

MAJOR OUTCOMES CONSIDERED

- Disease recurrence
- Quality of life
- Survival
- Frequency of true- and false-positive tests
- Sensitivity and specificity of diagnostic tests
- Positive predictive and negative predictive value

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature Search Strategy

An inventory of diagnostic imaging guidelines published in English after 1998 was completed by the Program in Evidence-based Care (PEBC) in October 2003 and used to identify existing evidence-based guidelines. MEDLINE (Ovid-1980 to 23 September 2004), EMBASE (Ovid-1980 to 23 September 2004), and the Cochrane Databases of Systematic Reviews and Abstracts of Reviews of Effects (2nd Quarter 2004) were searched for meta-analyses, primary studies, and additional guidelines.

Search strategies were modified for each database and disease site. Searches of MEDLINE and EMBASE relied primarily on subject headings, with appropriate terms chosen for each database from the list in Appendix A in the original guideline document. MEDLINE and EMBASE searches were conducted for breast neoplasms and breast cancer. Supplementary searches were conducted across disease sites for randomized trials and for studies reporting sensitivity/specificity; those searches used broader (i.e., less specific) search strategies in order to ensure that no relevant studies were missed. Titles, abstracts, full text, and keywords in the Cochrane databases of reviews were searched using text works such as ultrasound, computed tomography, magnetic resonance, cancer, and :carcinoma.

Study Selection/Eligibility Criteria

The Research Coordinator working with the guideline panel applied the eligibility criteria below to the titles and abstracts of the citations listed in output from the literature searches. Where titles and abstracts provided insufficient information to determine a study's eligibility for inclusion in the systematic review, the full report was examined online or in paper form.

Inclusion Criteria

Studies were included if they:

1. Included patients with confirmed cancer of the breast
2. Evaluated computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound (US)
3. Reported data for disease recurrence, quality of life, survival, frequency of true- and false-positive tests for extent of disease, or sensitivity, specificity, positive predictive value, or negative predictive value to detect distant metastases
4. Were randomized trials, comparative cohort studies, case series (prospective or retrospective) with more than 12 consecutive patients, meta-analyses (published in English after 1998) of data from randomized trials, comparative cohort studies, or case series

Literature searches for primary studies were not restricted by language, but, because resources for translation were limited, evidence was abstracted only from English-language papers. Evidence-based guidelines from the Program in Evidence-Based Care or other guideline developers were reviewed. Those guidelines provide descriptive and interpretive summaries of the evidence, as well as recommendations based on evidence, values, and expert opinion. Clinical practice guidelines were eligible if they stated objectives or guideline questions, described the literature searched, and cited references for the evidence described.

Exclusion Criteria

Letters, editorials, and meeting abstracts were not included.

NUMBER OF SOURCE DOCUMENTS

Four practice guidelines, one randomized trial, and 12 case series were eligible for review

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The Research Coordinator extracted the following information from the published reports eligible for inclusion in the systematic review:

- Recommendations and qualifying statements for evidence-based practice guidelines
- Survival, recurrence, surgery, and quality-of-life data for randomized trials
- The percent of cases categorized as true positive and false positive, sensitivity, specificity, positive predictive, negative predictive value, and proportion of patients with disease from case series

Where necessary, true positive, false positive, sensitivity, specificity, positive predictive value, and negative predictive value rates were calculated from data provided in primary reports, using the Predictive Value Calculator available on the Web at <http://www.azzopardi.freeserve.co.uk/easycalc/Additions/predict.htm>.

Sets of tables summarizing the available evidence were distributed for review to individual panel members according to their area of practice, along with copies of guidelines and primary study reports. The guideline authors did not pool data from individual studies, but published meta-analysis were considered with the other evidence.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

This guideline is one of a set developed by the Program in Evidence-Based Care's (PEBC) Diagnostic Imaging Guidelines Panel, using methods adapted from the Practice Guidelines Development Cycle. These guidelines are intended to:

- Promote evidence-based practice
- Provide guidance to clinicians about which imaging techniques are the most appropriate to use in the workup and management of their patients
- Provide information that is useful to those charged with planning for the number of imaging machines needed for patients with cancer in Ontario
- Assist in monitoring the use of imaging modalities in patients with cancer

Panel members included medical, radiation, and surgical oncologists; diagnostic radiologists; and methodologists. Prior to embarking on the guideline development, members were asked to disclose information on any potential conflicts of interest, but there were none. The PEBC is editorially independent of Cancer Care Ontario and the Ontario Ministry of Health and Long-term Care.

The Diagnostic Imaging Guideline panel:

1. Formulated a set of guideline questions relevant to cancer care in Ontario
2. Systematically reviewed existing evidence-based guidelines and evidence from primary studies

The Breast Working panel:

1. Considered the quantity, quality, consistency, completeness and relevance of the available evidence
2. Drafted recommendations
3. Consulted members of relevant PEBC Disease Site Groups and external reviewers for feedback

Evidence and expert opinion were considered in determining whether imaging should be conducted (e.g., How often would diagnostic imaging with computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound (US) revise staging in patients with cancer?) and then which imaging test would be most appropriate (e.g., Should CT, MRI, or US be used to detect liver metastases?). An informal consensus process was used to reach agreement on recommendations.

A focused external review process was planned for each document, utilizing the expertise of a small panel of experts. That was obtained through a mailed survey consisting of items that addressed the quality of the draft report and recommendations and whether the recommendations should serve as a practice guideline.

How often would diagnostic imaging with computed tomography (CT), magnetic resonance imaging (MRI), or ultrasound revise staging in patients with newly diagnosed cancer?

Imaging to detect metastatic disease

The guideline panel considered the role of staging in breast cancer at diagnosis to be effectively dealt with by the PEBC guideline. However, two issues were not directly assessed in that original guideline. First, there is no evidence to help determine what blood work is needed preoperatively in patients undergoing breast cancer surgery. Generally, that would be decided by each local hospital in accordance with the anesthesia requirements and general health of the patient. The second issue involves patients found to have clinical stage III cancers preoperatively, a group not commonly seen now because of more aggressive screening and increasing breast cancer awareness. They can be assessed in the same way as other patients with earlier stage disease. If they are clinically operable, surgery is still usually the best initial approach unless there are features in their physical exam that would suggest inoperability. If surgery is not felt to be initially possible then referral to a multidisciplinary clinic consisting of a general surgeon, radiation oncologist, and medical oncologist is advised to determine their optimal management. At that clinic, they would be staged through a bone scan, abdominal ultrasound, and a chest radiograph. Although diagnostic imaging tests continue to evolve rapidly, there is, unfortunately, no conclusive evidence to support changing the approach discussed above.

Imaging to determine extent of disease in the breast

Limited evidence was identified on the use of imaging to determine the extent of disease in the breast, and some of the evidence was contradictory. In general, ultrasound was found to have a relatively low sensitivity and high specificity, with the exception of one study. Mammography was similar to ultrasound in performance. MRI was generally found to have high sensitivity and good specificity. The weight of the identified evidence is in favour of MRI for the detection of multifocal or diffuse disease.

In what circumstances and with what frequency would diagnostic imaging with CT, MRI, or ultrasound be useful in determining tumour response in patients undergoing chemotherapy or radiotherapy?

Only evidence that evaluated chemotherapy in the neoadjuvant setting with regard to detecting tumour response was available. No studies were identified addressing chemotherapy in the adjuvant or metastatic setting or radiotherapy. In the neoadjuvant studies, both the clinical examination and MRI had generally high specificity. Clinical examination had a generally low sensitivity (11% to 39%), while MRI had widely varying sensitivity (0% to 100%, median 74%). That wide variation in sensitivity for MRI was not immediately explained through this review of the studies.

What is the role of CT, MRI, and ultrasound in the detection of recurrent disease during the follow-up of patients who have completed primary treatment for cancer, and what should be the frequency of use of those tests during follow-up?

No evidence beyond existing systematic reviews and guidelines was obtained for this review. The Diagnostic Imaging Guidelines Panel endorses the recently

updated Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer guideline.

What is the role of CT, MRI, or ultrasound in assessing patients who develop symptoms of disease recurrence or elevated biochemical markers after primary treatment for cancer?

Only one study was identified that looked at imaging modalities in assessing patients who developed symptoms of disease recurrence. The randomized controlled trial (RCT) did not detect a significant difference between CT and MRI.

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

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

External Review

The draft report, with recommendations developed by a small panel of experts in oncology and radiology, was distributed with a 4-item survey in February and March 2006 for review as part of an external consultation process to a broader group of Ontario radiologists and oncologists. The external consultation included the 24 members of the provincial Breast Cancer Disease Site Group and 20 other Ontario health care providers. Among the 15 respondents (34%), which included four radiologists, one pathologist, three radiation oncologists, and seven medical oncologists, fourteen filled in the questionnaire and eleven provided written comments. Fourteen agreed that the methods used in the report development were appropriate. Thirteen agreed with the draft recommendations as stated, and would follow the recommendations of the report whereas one would neither agree nor disagree to those statements. Twelve respondents agreed that the recommendations should be approved as guidelines for practice, one neither agreed nor disagreed and one disagreed.

Report Approval Panel

The Program in Evidence-based Care (PEBC) Report Approval Panel felt that the guideline was well written, the recommendations were clear and that the authors appropriately balanced the input coming from the limited published literature, other guidelines, and a consensus process.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note: A summary of the recommendations can be found in Table 5 in the original guideline document.

Staging

Before Surgery

Until further information becomes available, magnetic resonance imaging (MRI) and mammography are both useful tools to determine the extent of disease in women with operable breast cancer. The choice between those modalities should be made based on the particular conditions of each patient and the equipment availability to handle the increased workload that would entail. However, MRI should not be used as a substitute for detailed mammographic or sonographic work-up of any abnormalities detected at a routine screening or as a substitute for the clinical or image-guided core biopsy of mammographic, sonographic, or clinical abnormalities. Pathology is the gold standard. Subsets of patients that may benefit from MRI include:

- Women with clinically palpable and mammographically occult breast cancer.
- Women with metastatic adenocarcinoma to axillary lymph nodes, with an unknown primary (normal mammogram and ultrasound)—75% to 85% of breast malignancies will be detected by MRI in these cases, and most will be <2 cm.
- Women with lobular carcinoma. That histology is associated with a higher risk of multifocal and multicentric spread, and the extent is frequently underestimated mammographically and sonographically. MRI is not perfect in this area and may also underestimate the extent of disease; however, it is more sensitive than standard imaging.
- Patients who require re-excision because of positive surgical margins may benefit from the increased sensitivity of MRI. The group of patients with >50% dense fibroglandular tissue (Breast Imaging Reporting and Data System [BIRADS] densities 3 or 4), may benefit the most.
- Patients with a high risk of multifocal disease may warrant an MRI. The youngest patients (24 to 39 years) have significant multifocality not detected on routine imaging. Their surgical treatment is frequently dramatically altered by MRI.

After Surgery

The practice guideline issued by Cancer Care Ontario's Program in Evidence-Based Care (PEBC) should be followed. That guideline applies to women with newly diagnosed breast cancer who have undergone surgical resection, and who have no symptoms, physical signs, or hematological or biochemical evidence of metastases.

- In women with intraductal and pathological stage I tumours, routine bone scanning, liver ultrasonography, and chest radiography are not indicated as part of baseline staging.
- In women who have pathological stage II tumours, a postoperative bone scan is recommended as part of baseline staging. Routine liver ultrasonography and chest radiography are not indicated for that group.
- In women with pathological stage III tumours, bone scanning, liver ultrasonography, and chest radiography are recommended postoperatively as part of baseline staging.
- In women for whom treatment options are restricted to tamoxifen or hormone therapy, or for whom no further treatment is indicated because of age or other factors, routine bone scanning, liver ultrasonography, and chest radiography are not indicated as part of baseline staging.

Response

Locally Advanced Breast Cancer

In the follow-up of locally advanced breast cancer patients receiving adjuvant chemotherapy, mammography and ultrasound are not accurate at assessing tumour response. Clinical assessment is subjective and lacks accuracy as well. MRI will determine whether the tumour is responding to chemotherapy, which does have long-term prognostic implications. As well, it will determine which tumours do not respond to chemotherapy, in which case the therapeutic regime could be altered.

Metastatic Breast Cancer

In order to determine if a treatment is successfully causing tumour regression or stability and inform decisions about continuing, changing, or stopping therapy, imaging tests that are abnormal at baseline could be repeated every three or four months. The one exception to this process would be bone scanning, which can be misleading in follow-up, as healing can look very similar to new disease in bone. If a patient is diagnosed with metastatic breast cancer, staging is required to identify the full extent and patterns of spread to determine if the patient should be treated with hormonal therapy instead of chemotherapy.

Follow-up

The Canadian practice guideline issued by the Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer should be followed. In patients who have been treated curatively, routine imaging tests to detect distant metastases should not be carried out.

Diagnosing Recurrence

Patients who develop symptoms or signs suggestive of recurrence require individualized testing to determine if recurrence has occurred. Recurrent breast cancer may be difficult to fully assess on mammography due to scarring and inflammation from previous surgery or radiation. If the patient is a candidate for repeat lumpectomy, MRI should be considered.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are supported by practice guidelines, one randomized trial, and case series.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of diagnostic imaging in breast cancer

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- In general, the evidence base available to evaluate the relative merits of computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound is limited. Several well-written clinical practice guidelines are available that address some of the questions in this report, but, where existing guidelines are not available, the evidence on which to base a guideline is poor. There is a great need for further comparative studies, preferably randomized studies that are designed and powered to provide definitive evidence regarding the utility of the different modalities.
- Because of this lack of evidence, the Diagnostic Imaging Guidelines Panel has developed the recommendations through a consensus process, using the existing evidence, professional experience, and clinical judgement to arrive at recommendations that the panel believes will improve patient care and outcome.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

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)

Myers R, Minuk T, Johnston M, Diagnostic Imaging Guidelines Panel. Diagnostic imaging in breast cancer: recommendations report. Toronto (ON): Cancer Care Ontario (CCO); 2006 Apr 12. 19 p. [18 references]

ADAPTATION

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

DATE RELEASED

2006 Apr 12

GUIDELINE DEVELOPER(S)

Program in Evidence-based Care - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Program in Evidence-based Care (PEBC) is a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Diagnostic Imaging Guidelines Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Authors: R. Myers; T. Minuk; M. Johnston

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Prior to embarking on the guideline development, members were asked to disclose information on any potential conflicts of interest, but there were none.

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GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Cancer Care Ontario Web site](#).

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on October 28, 2006. The information was verified by the guideline developer on November 24, 2006.

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