Complete Summary

GUIDELINE TITLE

American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer.

BIBLIOGRAPHIC SOURCE(S)

Lyman GH, Giuliano AE, Somerfield MR, Benson AB 3rd, Bodurka DC, Burstein HJ, Cochran AJ, Cody HS 3rd, Edge SB, Galper S, Hayman JA, Kim TY, Perkins CL, Podoloff DA, Sivasubramaniam VH, Turner RR, Wahl R, Weaver DL, Wolff AC, Winer EP. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol 2005 Oct 20;23(30):7703-20. [147 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

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SCOPE

DISEASE/CONDITION(S)

Early-stage breast cancer

GUIDELINE CATEGORY

Evaluation
Management
Risk Assessment

CLINICAL SPECIALTY

Oncology
Pathology
Radiation Oncology
Surgery

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To develop a guideline for the use of sentinel lymph node biopsy (SNB) in early stage breast cancer

TARGET POPULATION

Patients with early-stage breast cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Sentinel lymph node biopsy (SNB)
2. Axillary lymph node dissection in patients with negative findings on SNB
3. Axillary lymph node dissection in patients with positive sentinel lymph nodes
4. Performance of SNB in special circumstances in clinical practice

MAJOR OUTCOMES CONSIDERED

- False positive, false negative rate
- Negative predictive value
- Lymphatic mapping success rate
- Accuracy of sentinel lymph node biopsy (SNB)
- Side effects of procedures (including lymphedema, sensory deficits, infection and axillary web syndrome)
- Axillary tumor recurrence
- Morbidity and mortality

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

This review utilized electronic techniques (Medline, the Cochrane Library, Best Evidence [ACP Journal Club and Evidence-Based Medicine], DARE [Database of Abstract of Reviews of Effectiveness], Dissertation Abstracts) and hand-searching techniques. Only studies incorporating full lymph node dissection, regardless of

the results of sentinel lymph node biopsy (SNB), were included. Between 1994 and 2004, 69 trials that met eligibility criteria were reported.

NUMBER OF SOURCE DOCUMENTS

The literature review identified one published prospective randomized controlled trial in which sentinel node biopsy (SNB) was compared with axillary lymph node biopsy (ALNB), four limited meta-analyses, and 69 published single-institution and multicenter trials in which the test performance of SNB was evaluated with respect to the results of ALND (completion axillary dissection).

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Good: Multiple studies of sentinel lymph node biopsy (SNB) test performance based on findings on completion axillary lymph node dissection (ALND)

Limited: Few studies of SNB test performance based on findings on completion ALND or multiple studies of mapping success without test performance assessed

Insufficient: No studies of SNB test performance based on findings on completion ALND and few if any studies of mapping success

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Study quality was evaluated by two blinded observers on a 5-point modified scale with factors of description of patient characteristics, reason for study withdrawal, test performance measures, measures of variability, and a description of the sentinel node biopsy technique. The relationships of the rate of false-negative findings, predictive value, and the proportion of successful lymphatic mappings to study size, the proportion of patients with positive lymph nodes, the technique used, and study quality were evaluated.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The American Society of Clinical Oncology (ASCO) Health Services Committee (HSC) convened an Expert Panel consisting of experts in clinical medicine and research relevant to breast cancer management, including surgical oncology, pathology, radiation oncology, and medical oncology. Academic and community practitioners, an oncology fellow, and a patient representative were also part of the Panel.

Consensus Development Based on Evidence

The entire Panel met twice; additional work on the guideline was completed through teleconferences of a steering group of the Panel. The purposes of the Panel meetings were to refine the questions addressed by the guideline and to make writing assignments for the respective sections. All members of the Panel participated in the preparation of the draft guideline.

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

The draft guideline was disseminated for review by the entire Panel. Feedback from external reviewers was also solicited. The content of the guideline and the manuscript were reviewed and approved by the Health Services Committee (HSC) and by the American Society of Clinical Oncology (ASCO) Board of Directors before dissemination.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

How Should The Results Of SNB Be Utilized In Clinical Practice?

Can Full Axillary Lymph Node Dissection (ALND) be Avoided in Patients With Negative Findings on Sentinel Lymph Node Biopsy (SNB)?

The reported test performance characteristics of SNB vary widely across studies reported in the medical literature. However, when carried out by an experienced team, negative findings appear to be predictive of negative axillary nodes for most patients with breast cancer. Significant predictors of posttest probability include

the percentage of patients in the study population with positive axillary nodes and the proportion of successful lymphatic mappings. In addition, the incidence of axillary recurrence after negative findings on SNB is comparable to that following ALND. On the basis of the available evidence, the Panel supports the use of SNB for staging disease in most women with clinically negative axillary lymph nodes. The concept of SNB has been so appealing to physicians and patients that the identification and biopsy of sentinel lymph nodes (SLNs) has largely replaced ALND for patients with clinically and histologically tumor-free lymph nodes. The Panel recommends that suspicious palpable nodes should also be submitted as SLNs, and that, in this context, the surgeon should have a low threshold for default to ALND, particularly for patients whose clinical presentation suggests a high risk of axillary metastasis. SNB works well, with a comparable false-negative rate in the setting of both mastectomy and breast-conserving surgery. Nevertheless, the Panel concluded that, on the basis of the available literature, there are compelling reasons for the operating surgeon to default to ALND, including a failed or technically unsatisfactory SNB procedure, and the presence of clinically suspicious nodes in the axilla after the removal of all SLNs. About half of patients in whom the identified SLN proves to be falsely negative will have had clinically suspicious nodes palpable at surgery, because gross tumor involvement may interfere with the uptake of both radiolabeled colloid and dye and deviate lymph flow to a node other than the true SLN.

Is Full ALND Necessary for All Patients With Positive Findings on SNB?

The recently reported meta-analysis demonstrates that, among patients with a positive SLN, 48.3% (95% CI, 35 to 62) were found to have additional node disease on ALND. Thus, the Panel recommends routine ALND for patients with a positive SLN according to routine histopathologic examination. More problematic is the management of patients for whom the SLN is positive only with use of special studies, primarily immunohistochemical (IHC) analysis with antibodies to cytokeratin. IHC evaluation can upstage disease for approximately 10% of patients who have a negative SLN, but whether this conversion to a higher stage is relevant remains unknown at this time. In the new American Joint Cancer Commission (AJCC) staging system, the node classification (pN0) is not altered by clusters of isolated tumor cells of 0.2 mm or less, regardless of the staining technique used to identify them.

It remains unclear whether isolated tumor cells or micrometastases (lymph node metastases larger than 0.2 mm but not larger than 2 mm) detected with hematoxylin and eosin (H&E) staining or special stains represents an adverse prognostic indicator and whether ALND should be carried out in all such cases. Likewise, there are insufficient data to determine whether the presence of isolated tumor cells or micrometastases should be a factor in treatment decisions. However, metastasis is found in nonsentinel nodes in approximately 10% of patients with isolated tumor cells in the SLN and in 20% to 35% of patients with micrometastases in the SLN. Until further studies addressing the clinical relevance of isolated tumor cells or micrometastases in the SLN are complete, the Panel recommends routine ALND for patients with micrometastases ($>0.2 \leq 2$mm) found on SNB, regardless of the method of detection. Regarding the question of which patients with a positive SLN may be appropriately treated with breast or axillary radiation and which patients should have completion ALND, relevant studies have included short follow-up and small numbers of patients in retrospective series,

and no results from randomized controlled trials (RCTs) are available. Therefore, the Panel concluded that there are insufficient data to answer this question.

What Is the Role of SNB in Special Circumstances in Clinical Practice?

On the basis of the available literature, the Panel concluded that SNB is not recommended for large or locally advanced invasive breast cancers (T3 and T4); inflammatory breast cancer; ductal carcinoma in situ (DCIS), when breast-conserving surgery is to be done; pregnancy, in the setting of prior nononcologic breast surgery or axillary surgery; and in the presence of suspicious palpable axillary lymph nodes. Data are available to support the use of SNB for smaller tumors (T1 and T2); multicentric tumors; DCIS, when mastectomy or immediate reconstruction is planned; for older or obese patients; in male breast cancer; and prior excisional or diagnostic biopsy. The recommendations and levels of evidence are provided in the Table below.

Recommendations and Levels of Evidence

Clinical Circumstance	Recommendation for Use of Sentinel Node Biopsy	Level of Evidence*
T1 or T2 tumors	Acceptable	Good
T3 or T4 tumors	Not recommended	Insufficient
Multicentric tumors	Acceptable	Limited
Inflammatory breast cancer	Not recommended	Insufficient
DCIS with mastectomy	Acceptable	Limited
DCIS without mastectomy	Not recommended except for large DCIS (>5 cm) on core biopsy or with suspected or proven microinvasion	Insufficient
Suspicious, palpable axillary nodes	Not recommended	Good
Older age	Acceptable	Limited
Obesity	Acceptable	Limited
Male breast cancer	Acceptable	Limited
Pregnancy	Not recommended	Insufficient
Evaluation of internal mammary lymph nodes	Acceptable	Limited
Prior diagnostic or excisional breast biopsy	Acceptable	Limited
Prior axillary surgery	Not recommended	Limited
Prior non-oncologic breast surgery (reduction or augmentation mammoplasty, breast reconstruction, etc)	Not recommended	Insufficient
After preoperative systemic therapy	Not recommended	Insufficient
Before preoperative systemic therapy	Acceptable	Limited

Abbreviations: DCIS, ductal carcinoma-in-situ; SNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection.

*Levels of Evidence: Good: Multiple studies of SNB test performance based on findings on completion ALND; Limited: Few studies of SNB test performance based on findings on completion ALND or multiple studies of mapping success without test performance assessed; Insufficient: No studies of SNB test performance based on findings on completion ALND and few if any studies of mapping success.

What Factors Affect the Success of SNB (Including Low Rates of Complications and False Negative Findings)?

The ability to evaluate individual or institutional accuracy with SNB on the basis of the proportion of successful mappings and the false-negative rate has enabled the procedure to gain widespread acceptance without prospective randomized trials. As SNB continues to replace ALND for staging of breast cancer, the Panel believes that appropriate training in the procedure and issues of quality control are very important. The strongest predictor of the false-negative rate across trials appears to be the proportion of patients for whom mapping is successful. In addition, the greatest proportion of successful mappings and the lowest false-negative rates were associated with studies in which both blue dye and radiolabeled colloid were used. While the Panel does not believe that American Society of Clinical Oncology (ASCO) should present separate guidelines for surgeons or institutions about the performance of this procedure, the Panel strongly supports the Guidelines for Performance of Sentinel Lymphadenectomy for Breast Cancer developed and updated in 2003 by the American Society of Breast Surgeons (http://www.breastsurgeons.org/officialstmts/sentinel.shtml). The American Society of Breast Surgeons recommends a rate of SLN identification of 85% with a false-negative rate of 5% or less in order to abandon axillary dissection. This Society maintains that performance of a minimum of 20 SNB procedures in combination with axillary dissection or with mentoring is necessary to minimize the risk of false-negative results. The Panel also recommends that surgeons (a) take a formal course on the technique, with didactic and hands-on training components; (b) have an experienced mentor; (c) keep track of individual results, including the proportion of successful mappings, false-negative rates, and complication rates; and (d) maintain follow-up on all patients over time. The Panel believes that these issues are important quality control measures as they could meaningfully impact on false-negative rates. While awaiting further results from RCTs, the Panel believes that high false-negative rates may have a direct adverse impact on patient care including accurate staging, treatment decision making, and long-term outcomes including survival. Clearly, the potential for both local as well as systemic undertreatment of patients increases as the false-negative rate increases. Case volume and experience are clearly important determinants of success, but there are insufficient data to recommend specific volume levels to maintain proficiency. However, the systematic review indicates that the proportion successfully mapped represents the strongest predictor of false-negative rate and may serve as a reasonable quality indicator for this procedure. In addition, the review demonstrates the anticipated reduction in the predictive value of a negative SNB with an increasing lymph node–positive rate in the population studied. Therefore, caution is required when applying the SNB procedure in patients at considerably increased risk for lymph node-positive disease.

Finally, the SNB procedure is very much a team effort with active skilled involvement of multiple disciplines including surgery, pathology, radiology, nuclear medicine, nursing, and pharmacy, among others. In addition to the individual training and experience required of all team members, optimal results

with the SNB requires the integrated and highly coordinated effort that comes with experience and frequent application of the procedure. Importantly, pathologists evaluating SNB specimens should be trained and experienced in the detection of the minimal amount of disease that is characteristically found in SLNs (See Appendix 3 of original guideline document).

What Are the Potential Benefits and Harms of SNB?

The reported incidence of lymphedema following ALND varies widely and is dependent on many variables, including definition of lymphedema, the extent of surgery, use of radiation therapy, and length of follow-up, among others. SNB is thought to be associated with fewer complications such as infection (cellulitis) of the chest wall and arm, sensory changes, and lymphedema than conventional ALND. The Panel recommends that, as with any medical procedure, written informed consent be obtained from all patients before SNB. The benefits and harms of the procedure, including the potential for a false-negative result should be explained to the patient. Written patient educational materials should provide accurate information on the risk of complications, contraindications for the procedure, the need for a multidisciplinary team (surgeon, nuclear medicine technician, and pathologist), the potential costs (which may be offset by fewer complications and less follow-up care), the lack of long-term survival data, the risk of radiation exposure, and the follow-up protocols for each procedure. A comparison of the data in an understandable format will help to clarify some of the issues for patients making treatment choices.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on one published prospective randomized controlled trial in which sentinel node biopsy (SNB) was compared with axillary lymph node biopsy (ALNB), four limited meta-analyses, and 69 published single-institution and multicenter trials in which the test performance of SNB was evaluated with respect to the results of ALND (completion axillary dissection).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of sentinel lymph node biopsy (SNB) in patients with early stage breast cancer which may reduce the risk of side effects associated with axillary lymph node dissection (ALND) and improve quality of life

POTENTIAL HARMS

- Morbidity associated with sentinel lymph node biopsy (SNB) and axillary lymph node dissection (ALND)
- False positive results leading to unnecessary procedures
- False negative results leading to inappropriate patient management

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- It is important to note that guidelines cannot always account for individual variation among patients. Guidelines are not intended to supplant physician judgment with respect to particular patients or special clinical situations and cannot be considered inclusive of all proper methods of care or exclusive of other treatments reasonably directed at obtaining the same result.
- Accordingly, the American Society of Clinical Oncology (ASCO) considers adherence to these guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in light of each patient's individual circumstances. In addition, these guidelines describe the use of procedures and therapies in clinical practice; they cannot be assumed to apply to the use of these interventions performed in the context of clinical trials, given that clinical studies are designed to evaluate or validate innovative approaches in a disease for which improved staging and treatment is needed. In that guideline development involves a review and synthesis of the latest literature, a practice guideline also serves to identify important questions and settings for further research.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Patient Resources
Personal Digital Assistant (PDA) Downloads
Slide Presentation

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

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Lyman GH, Giuliano AE, Somerfield MR, Benson AB 3rd, Bodurka DC, Burstein HJ, Cochran AJ, Cody HS 3rd, Edge SB, Galper S, Hayman JA, Kim TY, Perkins CL, Podoloff DA, Sivasubramaniam VH, Turner RR, Wahl R, Weaver DL, Wolff AC, Winer EP. American Society of Clinical Oncology guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer. J Clin Oncol 2005 Oct 20;23(30):7703-20. [147 references] PubMed

ADAPTATION

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

DATE RELEASED

2005 Oct 20

GUIDELINE DEVELOPER(S)

American Society of Clinical Oncology - Medical Specialty Society

SOURCE(S) OF FUNDING

American Society of Clinical Oncology

GUIDELINE COMMITTEE

American Society of Clinical Oncology (ASCO) Expert Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Gary H. Lyman, MD, MPH (*Co-Chair*); Armando E. Giuliano, MD (*Co-Chair*); Al B. Benson III, MD; Diane C. Bodurka, MD; Harold J. Burstein, MD, PhD; Alistair J. Cochran, MD; Hiram S. Cody III, MD; Stephen B. Edge, MD; Sharon Galper, MD; James A. Hayman, MD; Theodore Y. Kim, DO; Cheryl L. Perkins, MD, RPH; Donald A. Podoloff; Visa Haran Sivasubramaniam, MD; Roderick R. Turner, MD; Richard Wahl, MD; Donald L. Weaver, MD; Eric P. Winer, MD; Antonio C. Wolff, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Although all authors completed the disclosure declaration, the following authors or their immediate family members indicated a financial interest.

Authors	Employment	Leadership	Consultant	Stock	Honoraria	Research Funds	Testimony	Other
Alistair J. Cochran						HIH/John Wayne Cancer Institute (C)		
Donald A. Podoloff		GE Healthcare (A); IDEC(A); Bexxar (A)	GE Healthcare (A); IDEC(A); Bexxar (A)		GE Healthcare (A); IDEC(A); Bexxar (A)			
Richard Wahl					Cardinal Health (A): GE Healthcare (A); Philips Medical (A)	GE Healthcare (A)		
Dollar Amount Codes: (A) < $10,000 (B) $10,000-99,999 (C) ≥ $100,000 (N/R) Not Required								

No conflict exists for drugs or devices used in a study if they are not being evaluated as part of the investigation. For a detailed description of the disclosure categories, or for more information about ASCO's conflict of interest policy, please refer to the Author Disclosure Declaration and the Disclosures of Potential Conflicts of Interest section in Information for Contributors.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American Society of Clinical Oncology (ASCO) Web site.

Print copies: Available from American Society of Clinical Oncology, Cancer Policy and Clinical Affairs, 1900 Duke Street, Suite 200, Alexandria, VA 22314; E-mail: guidelines@asco.org.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- ASCO guideline recommendations for sentinel lymph node biopsy in early-stage breast cancer: guideline summary. Alexandria (VA): American Society of Clinical Oncology; 2005. 3 p. Electronic copies: Available in Portable Document Format (PDF) from the American Society of Clinical Oncology

(ASCO) Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site.
- Sentinel lymph node biopsy in early-stage breast cancer. American Society of Clinical Oncology guidelines recommendations. Slide set. 2005 Sep 28. 29 p. Electronic copies: Available in Portable Document Format (PDF) from the ASCO Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site.

Guidelines are available for Personal Digital Assistant (PDA) download from the ASCO Web site.

PATIENT RESOURCES

The following is available:

- ASCO patient guide. Sentinel lymph node biopsy in early-stage breast cancer. 2005 Aug. Electronic copies available from the Cancer.Net Web site. See the related QualityTool summary on the Health Care Innovations Exchange Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI on November 18, 2005. The information was verified by the guideline developer on December 1, 2005.

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