

Guidelines concerning sentinel node biopsy : a critical review

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Guidelines : the aims

- To assist practitioners in making appropriate clinical decisions for patients
- To minimize inappropriate practice variations
- To provide indicators and criteria for external quality review
- Formulated by professionals (medical associations, expert panels...)
- Based on clinical efficacy without cost considerations

Attributes of good guidelines

- Should be based on high quality evidence
 - Should be continuously reviewed and updated
 - Should be reproducible and applicable in daily clinical practice
 - Easy and free access (websites)
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Guidelines for SLNB

- NCCN january 2011
- ASCO september 2005
- ESMO may 2010

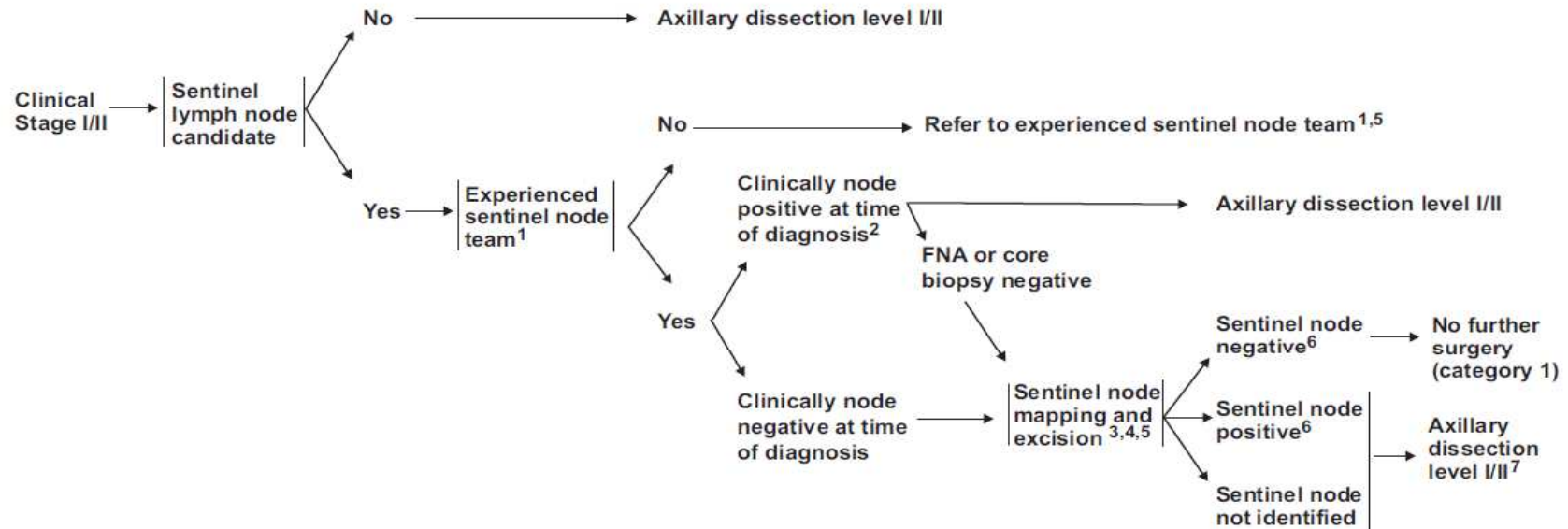
NCCN GUIDELINES

- The most comprehensive and widely used in the world
- Fullfill all criterias of accessibility and updating
- Critics : insufficient level of evidence*
 - 10% based on level I EC for initial treatment
 - 83% based on level IIA EC

*Poonacha et al JClin Oncol 2011



SURGICAL AXILLARY STAGING - STAGE I, IIA, AND IIB



¹Sentinel node team must have documented experience with sentinel node biopsy in breast cancer. Team includes surgeon, radiologists, nuclear medicine physician, pathologist, and prior discussion with medical and radiation oncologists on use of sentinel node for treatment decisions.

²Consider pathologic confirmation of malignancy in clinically positive nodes using ultrasound guided FNA or core biopsy in determining if patient needs axillary lymph node dissection.

³Axillary sentinel node biopsy in all cases; internal mammary sentinel node biopsy optional if drainage maps to internal mammary nodes (category 3).

⁴Sentinel lymph node mapping injections may be peritumoral, subareolar or subdermal. However, only peritumoral injections map to the internal mammary lymph node(s).

⁵Results of randomized clinical trials indicate that there is a lower risk of morbidity associated with sentinel node mapping and excision than with level I/II axillary dissection.

⁶Sentinel node involvement is defined by multilevel node sectioning with hematoxylin and eosin (H&E) staining. Cytokeratin Immunohistochemistry (IHC) may be used for equivocal cases on H&E. Routine cytokeratin IHC to define node involvement is not recommended in clinical decision making.

⁷Data from a single, randomized trial suggests that complete axillary lymph node dissection in women with clinically node negative T1-T2 tumors, fewer than 3 involved sentinel lymph nodes, and undergoing breast-conserving surgery and whole breast radiation results in more morbidity, no improvement in locoregional recurrence rates, and no difference in overall survival compared with sentinel lymph node procedure alone.

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

[Return to Locoregional Treatment \(BINV-2\)](#)

AXILLARY LYMPH NODE STAGING

In the absence of definitive data demonstrating superior survival from the performance of axillary lymph node dissection, patients who have particularly favorable tumors, patients for whom the selection of adjuvant systemic therapy is unlikely to be affected, for the elderly, or those with serious comorbid conditions, the performance of axillary lymph node dissection may be considered optional. The axillary dissection should be extended to include level III nodes only if there is gross disease apparent in the level II nodes.

Sentinel lymph node biopsy is the preferred method of axillary lymph node staging if there is an experienced sentinel node team and the patient is an appropriate sentinel lymph node biopsy candidate ([See BINV-D](#)).

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ASCO recommendations (1)

- Published in J Clin Oncol 2005
- Free access on ASCO website
- Answer to five specific questions
- Panel of experts conducting review of littérature
- 1 prospective control trial comparing SLNB with ALND
- 4 limited meta-analyses
- 69 non randomized trials

American Society of Clinical Oncology Guideline Recommendations for Sentinel Lymph Node Biopsy in Early-Stage Breast Cancer

False Negative Rates in Trials in Which Sentinel Lymph Node Biopsy Is Compared With Axillary Lymph Node Dissection

- False-Negative Rate (%) *P*All trials 8.4 (0-29)
- Trials with ≥ 100 patients *v* trials with < 100 patients 6.7 *v* 9.0
- Successful mapping in $\geq 90\%$ *v* $< 90\%$ 6.3 *v* 11.1 .003 Patient characteristics (given *v* not given) 7.8 *v* 11.6 .009 Measures of test performance (given *v* not given) 7.0 *v* 10.3 .009 Measures of variability (given *v* not given) 6.2 *v* 9.0 .
- 01 Use of both dye and radiolabeled colloid *v* use of only one 7.0 *v* 9.9 .07

- Table 2. 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; and Insufficient, no studies of SNB test performance based on findings on completion ALND and few if any studies of mapping success.

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ESMO guidelines

- Methodology unclear
- Free access on web site
- Annually reviewed
- Low level of evidence for SLNB

ESMO 2009

- Invasive breast cancer is operated by using BCS or mastectomy, both combined with sentinel node biopsy (SNB) alone, SNB followed by axillary dissection or axillary dissection without SNB, depending on clinical situation.
- SNB should not be performed in cases of palpable axillary node(s), **in large (>3 cm)** T2–T4 tumors, multicentric tumors, prior axillary surgery or large biopsies, after breast reconstruction or implantation of a prosthesis, during pregnancy or lactation, and after neoadjuvant systemic treatment outside clinical trials.

ESMO 2010

- **advances in axillary staging**
- Regional lymph node status remains the strongest predictor of long-term prognosis in primary breast cancer. Sentinel lymph node biopsy (SLNB) rather than full nodal clearance is now accepted as the standard of care for axillary staging in early breast cancer [II, A], unless axillary node involvement is suspected clinically or on ultrasound.
- SLNB delivers less morbidity in terms of shoulder stiffness and arm swelling and allows for reduced hospital stay [I, A]. Training and quality assurance in SLNB have been rolled out to breast units across Europe in the last 10 years.
- The presence of macrometastatic spread in the sentinel node mandates conventional axillary lymph node clearance. The optimal management of micrometastatic spread and isolated tumour cells is the subject of ongoing research.

Compliance: surveys

- Wasif and Giuliano Ann Surg Oncol 2009
 - Survey concerns management of sentinel node micro metastasis (SNMM)
 - ASCO guidelines recommend ALND for SNMM
 - 612 questionnaires completed by specialised ASCO members
 - Recommendation was followed by 23 % of surgeons, 23 % of medical oncologists, 15% of radiation oncologists

Compliance : surveys

- Mansfield Int Sem Surg Oncol 2007
- Management of the axilla in clinically ne negative breast cancer
- 271/403 UK qualified breast surgeons answered
- 52 % performed SLNB as recommended
- 33.6% of them used combination of blue dye and radioisotope(Gold Standard)

Compliance : surveys

- Glynn R AnnR Coll Surg Engl 2010
- Surgical management of the axilla in UK
- 177/350 members of the British Association of Surgical Oncology
- 10% performed ALND for all patients
- 69% performed SLND with dual localisation

Compliance

- Reasons objected for noncompliance*
- medical
 - Patient's choice
 - Patient's medical status, age, comorbidities
 - Practice of new knowledges not yet incorporated in the guidelines
 - Insufficient training (lack of time or facilities, shortage of surgeons)
- Non medical
 - Limited hospital ressources
 - Lack of nuclear medecine facilities ++

*Poonacha J Clin Oncol 2011

Critical analysis

- Heterogeneity regarding tumor size
- Often based on low level of evidence
- Lack of compliance not only due to medical reasons
- Based on clinical efficacy without cost consideration

Guidelines and breast cancer units

- Should have a complete team to perform SLND
- Should use and control guidelines compliance
- However
 - Knew knowledges should be quickly integrated in daily practice
 - Tratements should be tailored to patients conditions and personnal choices