

## Reduced Morbidity Using Sentinel Node Biopsy in Breast Cancer Patients

Mansel RE, Fallowfield L, Kissin M, et al. Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC Trial. *J Natl Cancer Inst* 2006;98:599–609.

### Study Overview

**Objective.** To compare quality of life outcomes of sentinel lymph node biopsy (SNB) and standard axillary surgery in patients with clinically node-negative breast cancer.

**Design.** Multicenter, randomized trial.

**Setting and participants.** Patients with clinically node-negative breast cancer were randomized (1:1) to undergo SNB or standard axillary surgery (level I–III axillary lymph node dissection or 4-node axillary sampling). Patients with sentinel node involvement by cancer underwent delayed axillary surgery or axillary radiotherapy depending on physician practice. Nodes were examined by hematoxylin-eosin staining. Patients were evaluated 1, 3, 6, 12, and 18 months after surgery. Lymphedema (self-assessed by the patient and by clinical examination), arm volume (ratios of presurgery to postsurgery volume), and shoulder function (ie, flexion, abduction, rotation on both sides) were measured at baseline and at follow-up appointments. The contralateral arm was used as a control for lymphedema and shoulder function evaluations. Sensory deficits in the ipsilateral upper arm and axilla were assessed. Infection rate was determined by chart review and by observation of wounds. Quality of life was assessed using the Functional Assessment of Cancer Therapy–Breast +4 questionnaire. Baseline and follow-up questionnaires were completed by patients.

**Main outcome measures.** Arm and shoulder morbidity and quality of life.

**Main results.** 1031 patients from 11 centers in the United Kingdom were enrolled. The median number of sentinel lymph nodes removed per patient was 2 (range, 1–11). The absolute rate of moderate or severe lymphedema at 1 year for the SNB group was 5% compared with 13% in the axillary group; the relative risk of any lymphedema at 1 year was 0.37 (95% confidence interval, 0.23–0.60). Drain use, length of hospital stay, and time to return to usual activities were lower in the SNB group ( $P < 0.001$  for all comparisons). The operative time was less for the SNB group than for the axillary group (median duration, 23.3 min for SNB versus

23.4 min for axillary;  $P = 0.055$ ). Finally, quality of life and arm functioning indices were improved in the SNB group ( $P \leq 0.003$  for all comparisons).

**Conclusion.** SNB is associated with less arm morbidity and an improved quality of life compared with standard axillary surgery in patients with early-stage breast cancer and clinically negative nodes.

### Commentary

Nodal status in breast cancer patients significantly impacts prognosis and treatment planning. Historically, patients would undergo full axillary nodal dissection to discern nodal status. Unfortunately, this procedure is associated with arm lymphedema, shoulder discomfort and impaired mobility, and negative effects on quality of life [1]. SNB is a technique of identifying a limited number of lymph nodes that have the highest probability of harboring metastases. SNB is intended to limit the extent of surgery and its attendant risks, while maximizing pathologic yield. In the United States, SNB has become a standard component in the evaluation of newly diagnosed breast cancer; however, randomized studies evaluating its use are sparse.

Randomized studies are necessary to confirm the benefit of SNB. One randomized trial confirmed a sensitivity and specificity for SNB of 91% and 100%, respectively [2]. The SNB group had less arm pain and arm morbidity if subsequent axillary surgery was not performed. However, the trial was small and long-term survival between groups could not be compared due to trial design.

In the current study, Mansel et al sought to compare SNB and axillary surgery in terms of arm morbidity and quality of life. Interestingly, the trial had to be closed early because it became apparent that women in the axillary surgery group were experiencing negative effects with axillary surgery compared with the SNB group, and randomization could not be recommended by investigators. Despite this limitation in analysis, SNB proved to be better than axillary surgery in terms of the main outcome measures. The fact that differences in the study arms were first observed in the clinic underscores the impact of the differences subsequently proven in the analyses.

It is worth noting that 25% of patients in the axillary surgery group underwent relatively less extensive axillary surgery with 4-node sampling. Hence, the true morbidity of full axillary surgery may be higher than these data suggest. As well, a small portion of patients who underwent SNB went on to undergo axillary surgery, and these patients were included in the SNB group in an intent-to-treat analysis. This trial's randomized design and large sample size and the uniform training required of participating surgeons strengthens the findings. We await results to confirm local recurrence rates and long-term survival with SNB, but preliminary data from other investigators suggest equivalence [3].

### Applications for Clinical Practice

SNB is a highly accurate method of assessing lymph node

status in clinically node-negative breast cancer patients. However, it should be performed only by surgeons skilled in this technique.

—Review by David R. Spigel, MD

### References

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3. Naik AM, Fey J, Gemignani M, et al. The risk of axillary relapse after sentinel lymph node biopsy for breast cancer is comparable with that of axillary lymph node dissection: a follow-up study of 4008 procedures. *Ann Surg* 2004;240:462–8.

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