What has been the routine use of axillary lymph node dissection? Why has there been a shift away from its use?

Axillary lymph node dissection (ALND) has been traditionally performed for 3 reasons. It has been used to maximize cure as part of the surgical treatment of breast cancer; it has been used for regional control—eradication of disease in a specific location; and it has been utilized for obtaining prognostic information and defining lymph node status, which helps aid in decision management for systemic adjuvant therapy. The downside of ALND is that it is fairly extensive and tends to have more side effects, such as edema, decreased shoulder function, and sensory deficits, compared to other treatments of breast cancer. Another limitation with ALND is that approximately two-thirds of women with newly diagnosed breast cancer have no pathologic evidence of cancer in the lymph nodes, and thus the procedure in this group of patients has no therapeutic purpose.

Sentinel node biopsy (SNB) for breast cancer gained recognition in 1993, when new methods showed that the lymph nodes most likely to first receive cancer could be identified by a radioactive tracer or a blue dye. During the mid-1990s, SNB was refined, and once it was a reasonably accepted procedure, it began being evaluated in clinical trials, which looked at the transition from total to partial lymphadenectomy, which is the sentinel node procedure. These trials were somewhat different from those evaluating a specific drug because the goal was no reduction in survival, and improvement was measured in the form of less morbidity.

What are the benefits of SNB?

The fundamental reason behind performing SNB is that we see decreased morbidity with this procedure. Furthermore, SNB allows for the identification of a minority of patients who have breast lymphatic drainage that goes into the supraclavicular or infraclavicular areas or even towards the sternum (internal mammary nodes). Identifying such patients with a more accurate technique such as SNB makes it possible to avoid the more invasive procedure of removing all the nodes in the axilla.

Can you discuss the ACOSOG Z0011 and NSABP B3-2 trials presented at the 2010 meeting of the American Society of Clinical Oncology?

The American College of Surgeons Oncology Group (ACOSOG) Z0011 is a surgical trial that randomized patients who had breast cancer with a pathologically positive sentinel node to either observation only or to ALND. The objective was to determine whether SNB would provide the same survival and regional control as full ALND. There were 446 patients randomized to...
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Study findings? The National Surgical Adjuvant Breast and Bowel Project protocol B-32 is a prospective trial that randomized clinically node-negative breast cancer patients to ALND or SNB. It is the largest surgical trial in breast cancer. One arm received SNB and ALND, and the experimental arm started with SNB; if their node was positive, they then received ALND. A total of 5,611 patients were enrolled, with 1,975 patients receiving SNB and ALND and 2,011 receiving SNB alone. Five-year overall survival was estimated at 96.4% in the control arm and 95% in the experimental arm, and the 8-year estimates were 91.8% and 90.3%, respectively. In the women receiving SNB and ALND, 54 local recurrences were observed compared to 49 in the experimental arm; 8 and 14 regional node recurrences were seen in the arms, respectively. The 2 groups were so large in order to detect a 2% survival difference between the groups, as we did not want to encounter decreased survival. We found no detectable difference in survival or regional control between the 2 groups and concluded that the decreased morbidity was much in favor of the sentinel node group.

H&O ACOSOG Z0010 evaluated sentinel node and bone marrow micrometastases. Can you discuss the study findings?

DK In this study, patients underwent lumpectomy and SNB with bilateral iliac crest bone marrow aspiration. Bone marrow and histologically negative sentinel nodes were evaluated with immunohistochemistry (IHC). The study findings showed that sentinel nodes were identified in 5,184 of 5,485 patients. Histologic sentinel node micrometastases were seen in 1,239 patients. IHC identified an extra 350 patients with sentinel node metastases and 105 of 3,491 patients with bone marrow metastases. The analysis showed that sentinel node metastases detected by IHC have minimal impact on overall survival and that IHC for examination of sentinel nodes is not advised in this patient population.

H&O What implications, if any, will these findings have on current detection techniques?

DK I do not think that the finding regarding the use of IHC will cause an overall change in how pathologists analyze nodes. I do think that there will be further analysis, and subsets of patients may be identified that will benefit from this approach. When there are thousands of patients being analyzed, as in ACOSOG Z0010, it allows for the opportunity to study such patient characteristics. SNB is a technique that allows individualized patient management. Hence, these findings probably do not warrant a complete change in practice pathologically, but hopefully we are able to identify a subset of patients in which procedures such as IHC should be done.

H&O Are there any ongoing studies evaluating ALND and SNB?

DK There is an ancillary study with the NSABP B-32 trial that has not yet been reported. This study has evaluated approximately 4,000 sentinel node–negative cancers in the B-32 trial. These nodes were re-evaluated with additional sections and IHC. This has been done in a blinded manner, and the results of identification of occult node metastases will be reported shortly.

There is also an international, multicenter, phase III study being done in Europe, AMAROS (After Mapping of the Axilla: Radiotherapy Or Surgery), which is headed up by the European Organisation for Research and Treatment of Cancer. In this trial, patients with proven axillary metastases by SNB are randomized to ALND or axillary radiation therapy. The main objective is to compare the regional control of the axilla obtained by ALND versus axillary radiotherapy. This study is in the process of accruing patients. Another ongoing study is ALMANAC (Axillary Lymphatic Mapping Against Nodal Axillary Clearance). This study performed in the United Kingdom has compared the morbidity of SNB to ALND.

H&O How do you foresee the findings regarding ALND and SNB changing current practice?

DK In regard to practice patterns, oncologists have largely moved away from ALND in the past few years. The findings from these studies, particularly the NSABP B-32 trial, will close the book on the necessity of performing an ALND in the case of pathologically nega-
tive sentinel lymph nodes. It is now proven that there is no benefit in removing additional nodes, and the National Comprehensive Cancer Network guidelines have been updated to reflect current practice, stating that in women with stage I/II breast cancer who have clinically negative axilla, SNB is now the standard of care. For those women with breast cancer who have positive nodes, there are still disagreements in terms of treatment choice; however, I think there is enough justification from the ACOSOG Z0011 trial for oncologists to move away from ALND and consider SNB for this group of patients.

**Suggested Readings**


