

# Management of the Regional Lymph Nodes in Early-Stage Breast Cancer



Julia S. Wong, MD,\* Laura E.G. Warren, MD,† and Jennifer R. Bellon, MD\*

**The management of regional nodes in early-stage invasive breast cancer continues to evolve. Improved systemic therapy has contributed to better local regional control, and at the same time it has drawn more attention to its importance. Axillary dissections have decreased, in part because of the increased efficacy of systemic therapy, and also because adjuvant therapy decisions are increasingly driven by biologic characterization of the tumor rather than pathologic nodal information. The trend toward less axillary surgery and a shift toward increased reliance on systemic and radiation therapy to address nodal disease has created interesting questions that were subsequently addressed in recent trials. We review the controversies in regional nodal management, the benefits of current treatment paradigms, the balance between less surgery and more radiation, and the potential tradeoffs vs toxicity. Semin Radiat Oncol 26:37-44 © 2016 Elsevier Inc. All rights reserved.**

Breast-conserving surgery with radiation therapy (RT) as an alternative to mastectomy for early-stage invasive cancer represents one of the greatest advances in contemporary breast cancer management, offering patients comparable local recurrence and survival. Outcomes have only improved in the setting of modern mammographic and pathologic evaluation coupled with increasingly effective systemic therapy. The management of regional nodes, however, remains a source of ongoing controversy. Historically, axillary lymph node dissection (ALND) was performed as a therapeutic and prognostic tool. In addition, pathologic nodal information was relied upon heavily to guide adjuvant systemic therapy and RT. In recent years, however, the importance of tumor biology as a driver of tumor recurrence and response to therapy has supplanted anatomical considerations as the sole determinant of clinical outcomes.

The advent of sentinel lymph node biopsy (SNB) for patients with clinically negative axillary nodes enabled surgeons to accurately stage the axilla with less morbidity and no decrement in oncologic outcomes. A randomized study of clinical T1N0 breast cancer and a negative SNB that assigned patients

to completion ALND or SNB alone found no difference in breast cancer events or overall survival (OS).<sup>1</sup> Similar results were seen from the National Surgical Adjuvant Breast and Bowel Project (NSABP).<sup>2</sup>

Once SNB alone was established as sufficient for node-negative patients, another key question was whether selected patients in the current era with positive sentinel nodes (SNs) might be appropriately treated with SNB alone, in the absence of completion ALND. The American College of Surgeons Oncology Group Z0011 trial assessed the need for completion dissection in patients with early-stage breast cancer with positive SNs.<sup>3,4</sup> Patient eligibility included clinical T1-2 N0 tumors with 1 or 2 positive SNs on hematoxylin and eosin staining, managed with breast-conserving surgery and whole breast RT. A specific nodal radiation field was prohibited. Patients were randomized to SNB alone or with completion ALND. Extensive axillary disease, including matted nodes and gross extra nodal extension, was excluded. The median age was 55 years. Overall, 83% had estrogen receptor (ER)-positive tumors, 69% had T1 cancers, and 72% had grade 1 or 2 disease. Nodal positivity was micrometastatic in 45% of the SLNB-only group and 38% in the ALND group. In the ALND group, 27% had additional positive axillary nodes. Overall, 97% of the patient population received systemic therapy. At a median follow-up of 6.3 years, the regional nodal failure rate was less than 1% in both groups (0.9% for SNB alone and 0.5% for ALND). OS and disease-free survival (DFS) were not different between the 2 arms.

\*Department of Radiation Oncology, Dana-Farber Cancer Institute and Brigham and Women's Hospital, Boston, MA.

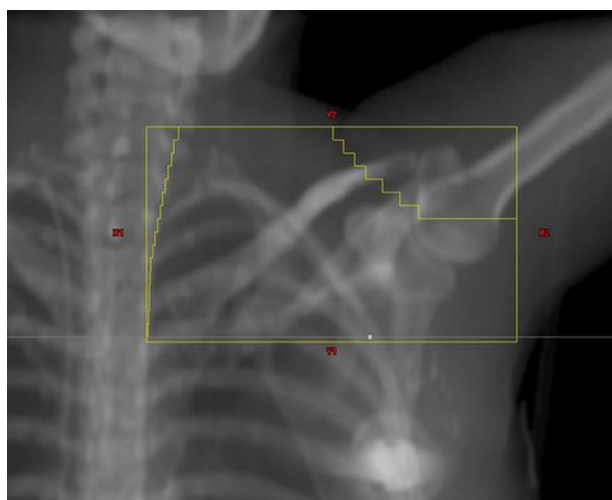
†Harvard Radiation Oncology Program, Boston, MA.

The authors declare no conflicts of interest.

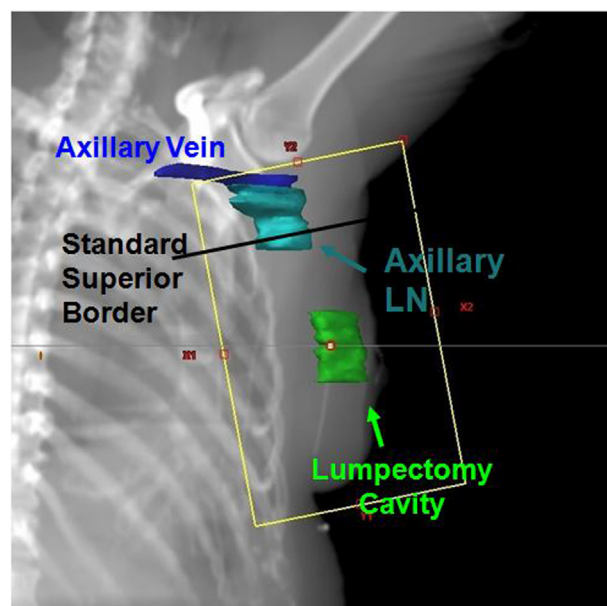
Address reprint requests to Jennifer R. Bellon, MD, Dana-Farber Cancer Institute, 450 Brookline Ave, Yawkey 1472, Boston, MA 02215. E-mail: jbellon@lroc.harvard.edu

Clinicians have been eager to apply these results to clinical practice and omit ALND, but there are key details that limit broad adoption of this approach. The study closed early owing to slow accrual and a low number of events and therefore was underpowered to demonstrate a difference between the 2 arms. Patients in this study had favorable disease characteristics, and were at low risk for additional nodal involvement, as evidenced by the low percentage of additional positive nodes found on ALND. They were likely not representative of the average patient with breast cancer who was nonetheless eligible for the trial.

In addition, the technical aspects of the radiation fields were not specified in advance. An assumption is that the low axillary failure rate in the SNB-only group was due to inclusion of the lower axillary nodes in the tangential whole breast radiation fields. A subsequent retrospective review of a subset of patients from the study reveals considerable inconsistency in the way the radiation fields were designed.<sup>5</sup> Detailed information on the radiation fields was available in 228 patients (27%). A review of a larger cohort of 605 patients with less detailed RT data found that 89% received whole breast RT and 15% also received supraclavicular radiation (Fig. 1). A review of the 228 patients with more details showed that 18.9% received specific nodal RT. Use of a prohibited nodal field did not differ between the 2 arms of the study. Those receiving directed nodal radiation had greater nodal involvement ( $P < 0.001$ ) than those who did not. Among those who received a nodal field, there was a trend suggesting that use of a posterior axillary boost field, to increase the dose to the axilla, was more common in the SNB-only group compared with the ALND group (57% vs 27%,  $P = 0.066$ ). High tangential radiation fields (defined here as a superior field border within 2 cm of the humeral head) were used in 52.6% of patients in the SNB-only group and 50.0% of the ALND group (Fig. 2). It is noted that some patients received no RT at all. The inconsistency in the fields used makes it impossible to draw definitive conclusions regarding the appropriate extent of nodal



**Figure 1** Radiation field demonstrating inclusion of the axillary and supraclavicular lymph nodes. (Color version of figure is available online.)



**Figure 2** Tangential radiation field showing standard tangents, as well as “high” tangents. (Color version of figure is available online.)

irradiation. Nevertheless, there is reassurance in the very low regional nodal failure rates in both arms.

In a similar vein, the European Organization for Research and Treatment (EORTC) After Mapping of the Axilla: Radiotherapy or Surgery (AMAROS) 10981/22023 trial also addressed the need for completion ALND in patients with clinically node-negative breast cancer and a positive sentinel node biopsy. Patients were randomized to SNB only followed by axillary RT, vs completion ALND.<sup>6</sup> The primary end point was noninferiority in 5-year axillary recurrence rates. Median follow-up was 6.1 years. Overall, 82% underwent breast-conserving surgery and 18% underwent mastectomy. Tumors were between 0.5 and 3 cm. Median age was 56 years, median tumor size was 1.7 cm, and 72.5% were grade 1 or 2. In all, 90% of patients in both arms received systemic therapy. In contrast to the American College of Surgeons Oncology Group (ACOSOG) Z0011 study, the radiation fields specifically included the supraclavicular and levels I-III axillary nodes. Across the study population as a whole, approximately 40% of the lymph nodes had micrometastases or isolated tumor cells. Of the patients who underwent completion ALND, 33% of the additional nodes found were positive. The 5-year axillary recurrence rate was 0.43% in the completion ALND group and 1.19% in the nodal radiation group; OS and DFS were comparable. Of note, there was a higher rate of clinical lymphedema in the ALND group vs the axillary RT group (23% vs 11% at 5 years,  $P < 0.0001$ ). Even though the study was underpowered due to the low number of events, it is reassuring that axillary recurrence rates were low in this generally favorable patient population. Furthermore, unlike the Z0011 trial, the AMAROS trial did not solely include breast conservation patients, allowing for extrapolation to patients of similar characteristics who have undergone mastectomy.

Despite the imperfections of the Z0011 and AMAROS trials, their importance lies in showing consistently low axillary

Download English Version:

<https://daneshyari.com/en/article/2726570>

Download Persian Version:

<https://daneshyari.com/article/2726570>

[Daneshyari.com](https://daneshyari.com)