

Lymph Node Staging in Newly Diagnosed Breast Cancer: Point—Preoperative Staging Axillary Ultrasound Is Valuable in the Contemporary Evaluation of Newly Diagnosed Breast Cancer

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Please see the corresponding Counterpoint by Bhole and Friedewald in this issue:

Lymph Node Staging in Newly Diagnosed Breast Cancer: Counterpoint—Sentinel Biopsy Surpasses Axillary Imaging in Early-Stage Cancers, but Is the Sun Setting on This Controversy? doi.org/10.2214/AJR.21.26767

The management of newly diagnosed breast cancer includes axillary staging, as the axilla is the primary site of lymphatic drainage for most breast cancers. Axillary ultrasound (US) plays an important role in the initial imaging evaluation of women with both early-stage and locally advanced breast cancer. Identification of axillary metastases guides treatment decisions including recommendation for neoadjuvant chemotherapy (NAC), the choice of axillary surgery, and the decision of whether to proceed with adjuvant radiation therapy. As axillary surgery continues to evolve toward minimally invasive techniques with less morbidity, the value of axillary US in the patient with newly diagnosed breast cancer continues to grow.

Axillary US with high-frequency transducers provides detailed assessment of nodal morphology and detects subtle changes of metastatic disease. Pretreatment axillary US provides a rapid, inexpensive, and accurate assessment of potential metastatic lymph nodes and offers the added benefit of allowing US-guided fine-needle aspiration (FNA) or core needle biopsy for definitive diagnosis. The sensitivity and specificity of axillary US increase when combined with US-guided biopsy, which is well tolerated with minimal risk and complications. For example, a meta-analysis found that axillary US with US-guided biopsy has sensitivity of 79.6% and specificity of 98.3% for nodal metastases [1].

Surgical management of the axilla has deescalated in recent years. Based on results of the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial, sentinel lymph node biopsy (SLNB), rather than axillary lymph node dissection (ALND), is becoming the standard of care for T1–T2 tumors in patients with one or two positive lymph nodes [2]. The benefits of SLNB include lower complication rates than ALND, maintained high accuracy, disease-free survival comparable to that of ALND, and regional control [2].

Axillary US was not included in the Z0011 trial, and its utility in the preoperative evaluation of breast cancer has been questioned after publication of the trial's results. Nonetheless, preoperative axillary staging must remain a critical component of the initial imaging evaluation after the Z0011 trial. Physical examination is not sufficiently sensitive or specific to assess metastatic disease in the axilla, and determining whether a patient meets the Z0011 criteria at presentation can be difficult. Preoperative axillary US detects patients with a higher burden of nodal metastases, allowing appropriate preoperative triage and informed discussion with patients. In a study by Caudle et al. [3], patients with axillary metastasis detected by axillary US versus those with axillary metastasis detected by SLNB had a higher number of positive nodes (4.1 vs 2.2 nodes), larger metastasis (13.8 vs 5.3 mm), and higher rate of extranodal extension (53% vs 24%). In addition,

the likelihood of finding additional positive nodes at pathology (defined as ≥ 3 positive nodes) is greater when axillary US is positive [3]. Patients with a high metastatic burden by imaging may proceed directly to ALND without SLNB, decreasing surgical time and cost. These findings support axillary US as an important aspect of the preoperative evaluation of newly diagnosed breast cancer, especially for the initial identification of nodal disease burden, that helps optimize surgical care.

Reluctance to perform presurgical axillary US may be based on the assumption that axillary US is overly sensitive and could commit patients to full ALND who otherwise would have met Z0011 criteria and been spared ALND. This argument is refuted by studies showing only small subsets of patients who received unnecessary ALND. For example, a study by Boland et al. [4] showed that only 27 (6%) patients over a 6-year period would have avoided ALND after positive axillary US and FNA based on Z0011 criteria. Thus, axillary US appears to perform well as a triage test mainly because of its adequate, but not overly high, sensitivity along with its high specificity and high PPV. The utility of axillary US in correctly triaging patients to axillary clearance will be even greater in settings with increased prevalence of nodal metastasis (e.g., large tumors, clinically detected tumors, and high-grade tumors).

SLNB is also increasingly used for management of patients with positive nodes who receive NAC. The ACOSOG Z1071 trial enrolled 756 patients with clinically node-positive disease based on US-guided biopsy, including 525 patients who had clinically N1 disease and who were eligible for SLNB [5]. The false-negative rate of SLNB with radioactive colloid and blue dye was 10.8% overall and 6.8% when a clipped node was removed. Therefore, axillary US and biopsy of abnormal nodes, including clip placement in the metastatic node to guide post-NAC localization, are critical to enhance clinical staging of the axilla before initiation of NAC and to reduce the false-negative rate of post-NAC SLNB. Breast cancer therapy emphasizes treatment based on tumor biology, particularly for triple-negative and human epidermal growth factor receptor 2–positive malignancies. Some patients with T1–T2 tumors that appear to meet Z0011 criteria on initial imaging presentation may show biology on pathology that could benefit from NAC. Therefore, axillary US is an important aspect of the initial imaging evaluation of patients being considered for NAC.

To date, the NPV of axillary US is insufficient to preclude surgical staging of the axilla. However, the paradigm of surgical evaluation of the axilla for invasive breast cancer is being challenged through three current clinical trials (Sentinel Node Versus Observation After Axillary Ultrasound [SOUND], Intergroup-Sentinel-Mamma [INSEMA], and Clinically Node Negative Breast Cancer Patients Undergoing Breast Conserving Therapy: Sentinel

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Lymph Node Procedure Versus Follow-Up [BOOG 2013-08]) investigating staging axillary US in patients with early-stage breast cancer who receive breast conservation therapy and who have a clinically negative axilla. These trials are evaluating whether patients with negative axillary US require additional axillary surgery and may further deescalate axillary surgical management for breast cancer when axillary US is negative.

Axillary US provides a useful alternative in certain scenarios in which SLNB is not indicated—for example, locally advanced inflammatory breast cancer. As an adjunct to SLNB, axillary US may mitigate false-negative SLNB due to lymphatic mapping failures and may decrease surgical costs and time. Failure to localize the sentinel lymph node may result from significant axillary tumor burden, large bulky breast tumors, extranodal extension of malignancy, and surgeon experience [6].

In conclusion, axillary staging with US is critical in the initial imaging evaluation of breast cancer. Axillary US can guide surgical treatment by identification of patients with high nodal disease burden, determine nodal disease burden before NAC, document metastases, allow clipping of a malignant node to decrease the false-negative rate of SLNB, guide decisions for adjuvant radiation therapy, and inform discussions with patients.

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