

# Implications of abnormal preoperative axillary imaging in the post Z011 era

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We read the recent paper evaluating the benefit of preoperative axillary imaging in clinically node negative patients by Pilewskie *et al.* in the February 2016 issue of the *Journal of the American College of Surgeons* with great interest (1). The authors took an interesting approach to evaluate the role of axillary imaging, more specifically the role of abnormal axillary imaging in predicting the need for axillary lymph node dissection (ALND) in T1–T2 breast cancer patients who were deemed node negative by physical exam and managed according to ACOSOG Z011 criteria.

The authors performed a retrospective review of 425 patients with cT1–2N0 breast cancer who underwent breast-conserving surgery and sentinel lymph node dissection (SLND) and were found to have nodal metastasis. Mammogram was performed in all women, 242 had axillary ultrasound (AUS) and 172 had MRI. Abnormal nodes were seen on 7%, 25%, and 30% of mammograms, US, and MRIs, respectively. In women who had any abnormal lymph nodes seen on imaging, 68% to 73% had only 1 or 2 positive sentinel lymph nodes and therefore were spared ALND. Of the 61 patients with abnormal AUS, 18 (30%) underwent ALND. Overall 27% to 32% of women with abnormal lymph nodes seen on axillary imaging underwent ALND. The authors concluded that abnormal nodes on US, MRI, or mammogram in clinically node-negative patients are not reliable indicators of the need for ALND.

Unlike several other studies that have investigated the issue of preoperative axillary imaging, the study by Pilewskie *et al.* focused on patients who underwent SLND regardless of abnormal axillary imaging findings (1). The utility of routine axillary imaging in patients with T1–T2 breast cancer who do not have enlarged nodes by physical

exam or abnormal nodes on breast imaging (mammogram or MRI) is certainly questionable. On the other hand, if abnormal nodes are seen on breast imaging, further evaluation of axilla with AUS ± needle biopsy is a widely accepted practice.

Examination of the results of the study by Pilewskie *et al.* raises some concerns. Of the 242 patients who underwent preoperative AUS, only 61 (25%) patients had any abnormal imaging findings, accounting for a false negative rate (FNR) of 75% in this cohort of T1–T2 breast cancer patients with axillary metastases (1). This, high FNR is particularly notable since a radiologist, who was aware that the study population consisted of node positive patients, reviewed the AUS. Reyna *et al.*, evaluated the role of AUS in 384 patients with T1–2 breast cancer and positive sentinel lymph node disease. In this study, the FNR of AUS ± FNA was 48% and 45% respectively (2). Recent meta-analysis by Diepstraten *et al.*, evaluated the utility of preoperative AUS ± needle biopsy for axillary staging. Thirty-one studies published between 1999 and 2012 met the inclusion criteria for the meta-analysis. A total 9,232 cases of preoperative axillary staging procedures were performed in 9,212 breast cancer patients. One in four women with negative AUS ± needle biopsy was found to have SLN metastases accounting for a pooled FNR of 25% (3).

Additionally, in the study by Pilewskie *et al.* (1), percutaneous LN needle biopsy was performed only if three or more abnormal lymph nodes or matted nodes were seen on imaging. Of the small number of patients (n=18) who underwent preoperative percutaneous needle biopsy, and had nodal metastasis, 45% required ALND. The same group of authors recently evaluated the utility of a positive

axillary lymph node needle biopsy result to predict the need for an axillary lymph node dissection in clinically node-negative breast cancer patients who met ACOSOG Z011 era (4). Clinicopathologic and axillary imaging results of 141 women with cT1–2N0 breast cancer with abnormal axillary imaging and positive needle biopsy were analyzed. Presence of >1 abnormal lymph node on axillary imaging was significantly associated with having  $\geq 3$  positive nodes on final pathology (68% vs. 43% P=0.003). Studies that have evaluated the role of preoperative ultrasound for predicting N2 disease have produced conflicting results (5–7). Abe *et al.*, investigated the utility of AUS for predicting pN2 disease. Of 559 patients with invasive breast cancer, 181 had abnormal axillary imaging and 50/181 had pN2–3 disease. Patients with two or more suspicious axillary LN were more likely to have pN2 or pN3 disease. The positive predictive value for identifying pN2 or N3 disease when two or more abnormal lymph nodes were seen on AUS was 82% (5). Schipper *et al.*, evaluated the role AUS in cT1–2 breast cancer patients treated by breast conserving surgery. Presence of 1–3 suspicious lymph nodes on AUS was associated with pN2–3 disease in 41.2% of patients (6). Recent investigation by Zhu and colleagues evaluated the optimal US criterion on US-guided fine needle aspiration cytology to identify patients with N2 or higher disease. The authors reported that cortical thickness of >3.5 mm had a sensitivity and specificity of 75.6% and 82.7% respectively to identify N2 or higher disease (8). Although, there is no uniform consensus on the utility of routine AUS to distinguish pN1 from pN2–3 disease, the presence of more than one abnormal lymph node in the axilla certainly warrants further evaluation.

Accurate preoperative staging of the axilla, especially in patients with abnormal lymph nodes on breast imaging has wider implications than the need for ALND. Several ongoing clinical trials are evaluating various neoadjuvant systemic treatments in patients with T1–4 and node positive breast cancer. Appropriate axillary staging is imperative to evaluate the eligibility of an individual patient to enroll in these trials. Additionally, axillary management in breast cancer is evolving with more and more emphasis on avoidance of ALND. Currently, two RCTs are evaluating the optimal management of axilla in patients with node positive disease who undergo neoadjuvant systemic treatment. Alliance A011202 trial is a randomized phase III trial that is comparing ALND to axillary radiation in breast cancer patients (cT1–3 N1) who have positive sentinel lymph node disease after neoadjuvant chemotherapy (9).

NSABP-B-51/RTOG 1304 is evaluating post-mastectomy chest wall and regional nodal radiation therapy (XRT) and post-lumpectomy regional nodal XRT in patients with T1–T3N1 breast cancer before neoadjuvant chemotherapy who convert to pathologically negative axillary nodes after neoadjuvant chemotherapy (10).

In the current era of breast cancer management, mere presence of abnormal lymph nodes on imaging is not an indication for ALND. However, in patients with cT1–2 breast cancer if abnormal lymph nodes are detected on preoperative breast imaging further evaluation of axilla with AUS  $\pm$  needle biopsy should be considered, to appropriately triage patients to neoadjuvant chemotherapy and assess their candidacy for ongoing clinical trials.

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### Footnote

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*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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