

## Considerations for the use of Preoperative Axillary Ultrasound in the Setting of a Suspicious Breast Mass in Light of the ACOSOG Z0011 Trial

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### Abstract

Staging of the axilla is essential in breast cancer management as it has direct implications in prognosis and treatment. The ability to preoperatively diagnose metastatic axillary disease via ultrasound once had major clinical implications, as it allowed patients to proceed directly to axillary lymph node dissection, negating the need for a sentinel lymph node biopsy. However, this practice is evolving following the results of the American College of Surgeons Oncology Group Z0011 trial, which demonstrated some cases of limited metastatic axillary disease are eligible for a sentinel lymph node biopsy/targeted axillary dissection in lieu of the more invasive axillary lymph node dissection. These results call into question the benefit of utilizing axillary ultrasound for preoperative staging purposes.

**Keywords:** Axillary ultrasound; Sentinel lymph node biopsy; Breast cancer

### Introduction

Staging of the axilla is essential in breast cancer management as it has direct implications in prognosis and treatment. The sentinel lymph node biopsy (SLNB) has largely replaced axillary lymph node dissection (ALND) as the initial management of surgical axillary staging in early-stage breast cancers with clinically negative nodes. Historically, any metastatic disease revealed on SLNB would result in an ALND, however, the results of the American College of Surgeons Oncology Group (ACOSOG) Z0011 trial significantly changed surgical axillary management. The Z0011 trial was a prospective, randomized, multicenter trial including patients with T1 and T2N0M0 disease and two or less positive nodes on SLNB [1]. The patients were randomized to undergo either ALND or no additional axillary surgery, and the results showed no statistical difference between the groups. This study suggested that limited metastatic axillary disease did not require a complete removal of all axillary lymph nodes, preventing the need for a separate, invasive surgery. Exclusion criteria included plans for mastectomy or neoadjuvant chemotherapy (NAC), palpable axillary lymphadenopathy, three or more positive sentinel lymph nodes, and matted lymphadenopathy. These results not only called into question the necessity for ALND in all metastatic disease, but also the benefit of utilizing axillary ultrasound (US) for preoperative staging purposes. Previously, if preoperative

axillary US with percutaneous biopsy demonstrated even a single metastatic lymph node in a clinically node negative patient, this could allow a patient to directly proceed to ALND and avoid sentinel lymph node surgery. However, results of the Z0011 trial challenge the necessity of US biopsy, as surgeons may omit ALND for limited nodal disease. The practice of utilizing axillary US with possible axillary tissue sampling preoperatively is evolving in light of the Z0011 trial results. Understanding the potential benefits and drawbacks of its use is important in this transitional state of axillary imaging.

### Discussion

The de-escalation of axillary surgical management has had meaningful clinical implications as risks of ALND, including lymphedema and paraesthesia's, can significantly impact patients' quality of life. These risks speak to the importance of the ACOSOG Z0011 trial results and the potential for SLNB in clinically node negative patients with limited metastatic disease. The results of this trial have ignited a discussion regarding the utility of preoperative axillary imaging in patients with early-stage breast cancer. US is the imaging modality of choice when evaluating the axilla, however, it has a variable sensitivity and specificity for nonpalpable lymph nodes. Differentiating between benign reactive lymph nodes and malignant enlargement can often be difficult. For example, a study by Liu Q, et al. (2018)

showed the sensitivity and specificity of US at detecting axillary metastasis to be 90.4 and 68.2%, respectively [2]. Another study by Valente S, et al. (2012) showed the sensitivity and specificity to be 43.5% and 96.2%, respectively [3]. Given the Z0011 trial showed patients with two or less metastatic lymph nodes could potentially be spared ALND, the utility of preoperative US in this setting is in its ability to accurately recognize patients with two or fewer metastatic lymph nodes. Conversely, if axillary US could accurately depict metastatic involvement in three or more lymph nodes or demonstrate matted lymphadenopathy, this could declare Z0011 ineligibility preoperatively, potentially sparing them an unnecessary SLNB. The literature, however, is not consistent when it comes to the reliability of preoperative axillary US in either regard. A study from Pilewskie M, et al. (2016) showed 68-73% of clinically node negative patients with abnormal axillary imaging did not meet Z0011 criteria for ALND [4]. Results of this study infer that if abnormal imaging was used as criteria for ALND, this would have led to significant overtreatment of the axilla. A companion study by the same group showed that patients with more than one abnormal lymph node on US were more likely to have three or more positive lymph nodes on surgical pathology [5]. A study by Verheuel NC, et al. (2015) showed patients with abnormal axillary US were more likely to have higher number of positive lymph nodes, macro-metastatic disease, extra-nodal extension, and involvement of level III lymph nodes [6,7]. Although some of these studies suggest preoperative axillary US can reasonably identify patients meeting Z0011 criteria, is the literature consistent enough to justify its routine use for this purpose? The opportunity cost of reflexively performing axillary US in suspected breast cancer cases is the inevitable performance of some unnecessary US-guided core needle lymph node biopsies. This is not only a potential unnecessary cost and discomfort to the patient, but can also lead to a false positive physical exam from post-biopsy reactive nodes/hematoma. At our institution, axillary US is usually deferred in the setting of suspected breast cancer unless lymph nodes are clinically palpable or suspicious lymph nodes are seen on mammography.

## Conclusion

Axillary lymph node staging remains an important component in the workup of newly diagnosed breast cancer. The utilization of preoperative axillary lymph node staging via US was questioned in light of the results of the ACOSOG Z0011 trial. The potential benefit of axillary US relies on its ability to accurately differentiate those patients who are eligible/ineligible for Z0011 management. The literature is inconsistent in this regard, and therefore, the utilization of axillary US varies across institutions and practices.

## Conflict of Interest

No potential conflict of interest relevant to this article was reported.

## References

1. Giuliano AE, Ballman KV, McCall L, Beitsch PD, Brennan MB, Kelemen PR, Ollila DW, Hansen NM, Whitworth PW, Blumencranz PW, Leitch AM. Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: the ACOSOG Z0011 (Alliance) randomized clinical trial. *Jama*. 2017 Sep 12;318(10):918-26. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5672806/>
2. Liu Q, Xing P, Dong H, Zhao T, Jin F. Preoperative assessment of axillary lymph node status in breast cancer patients by ultrasonography combined with mammography: A STROBE compliant article. *Medicine*. 2018 Jul;97(30):e22441. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6078763/>
3. Valente SA, Levine GM, Silverstein MJ, Rayhanabad JA, Weng-Grumley JG, Ji L, Holmes DR, Sposto R, Sener SF. Accuracy of predicting axillary lymph node positivity by physical examination, mammography, ultrasonography, and magnetic resonance imaging. *Annals of surgical oncology*. 2012 Jun;19(6):1825-30. <https://pubmed.ncbi.nlm.nih.gov/22227922/>
4. Pilewskie M, Jochelson M, Gooch JC, Patil S, Stempel M, Morrow M. Is preoperative axillary imaging beneficial in identifying clinically node-negative patients requiring axillary lymph node dissection?. *Journal of the American College of Surgeons*. 2016 Feb 1;222(2):138-45. <https://pubmed.ncbi.nlm.nih.gov/26711795/>
5. Pilewskie M, Mautner SK, Stempel M, Eaton A, Morrow M. Does a positive axillary lymph node needle biopsy result predict the need for an axillary lymph node dissection in clinically node-negative breast cancer patients in the ACOSOG Z0011 era?. *Annals of surgical oncology*. 2016 Apr;23(4):1123-8. <https://pubmed.ncbi.nlm.nih.gov/26553439/>
6. Pilewskie M, Mautner SK, Stempel M, Eaton A, Morrow M. Does a positive axillary lymph node needle biopsy result predict the need for an axillary lymph node dissection in clinically node-negative breast cancer patients in the ACOSOG Z0011 era?. *Annals of surgical oncology*. 2016 Apr;23(4):1123-8. <https://www.ajronline.org/doi/10.2214/AJR.19.22022>
7. Verheuel NC, Van Den Hoven I, Ooms HW, Voogd AC, Roumen RM. The role of ultrasound-guided lymph node biopsy in axillary staging of invasive breast cancer in the post-ACOSOG Z0011 trial era. *Annals of surgical oncology*. 2015 Feb;22(2):409-15. <https://pubmed.ncbi.nlm.nih.gov/25205303>