Editorial

Can targeted axillary dissection reliably advise de-escalation of completion axillary lymph node dissection?

Nicci Owusu-Brackett, Bridget A. Oppong

Division of Surgical Oncology, Department of Surgery, The Ohio State University Wexner Medical Center and James Cancer Hospital, Columbus, OH, USA

Correspondence to: Nicci Owusu-Brackett, MD. Division of Surgical Oncology, Department of Surgery, The Ohio State University Wexner Medical Center and James Cancer Hospital, N924 Doan Hall, 410 West 10th Avenue, Columbus, OH 43210, USA. Email: nicci.owusu-brackett@osumc.edu.

Comment on: Vernet-Tomás M, Argudo N, Jimenez M, *et al*. Accuracy of sentinel node mapping in patients with biopsy-proven metastatic axillary lymph nodes and upfront surgery: preliminary results of the Multimodal Targeted Axillary Surgery (MUTAS) trial. Gland Surg 2023;12:140-51.

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In the manuscript of *Gland Surgery*, Vernet-Tomás *et al.* report their experience evaluating the utility and reliability of targeted axillary dissection (TAD) to predict the remaining axillary tumor load in clinically node positive patients undergoing upfront surgery (1). This prospective study included 25 patients with biopsy-proven metastatic axillary lymph nodes who underwent upfront surgery from September 2019 to March 2022. The authors report routine axillary ultrasound for all patients with a first diagnosis followed by biopsy of all suspicious nodes and routine axillary lymph node dissection for all with positive cytology or biopsy justified by the low accuracy of palpation. Patients subsequently underwent sentinel mapping with intratumoral injection of 111 MBq of 99mTc-nanocolloid, followed by excision of the biopsy-proven metastatic lymph node and sentinel lymph nodes and levels I and II axillary lymph node dissection (ALND). The mean age of the patients was 55.6 years, and the median tumor size in the pathology report was 22.55 mm. All participants were hormone-receptor-positive and human epidermal growth factor receptor 2 (HER2) negative. The false-negative rate of the sentinel lymph node biopsy overall was 28% and 28.75% for patients with 2 or fewer suspicious nodes on axillary ultrasound.

These data evaluate the reliability of TAD to predict axillary nodal status. Sentinel lymph node mapping for patients who are biopsy confirmed positive is controversial in patient undergoing upfront surgery. Current National Comprehensive Cancer Network (NCCN) guidelines recommend "sentinel lymph node mapping for patients who are clinically node negative at the time of diagnosis and who have 2 or fewer suspicious lymph nodes found on imaging" (2). These guidelines are based on the ACOSOG Z0011 data. Vernet-Tomás *et al.* compare their study results to those of the Z0011 trial; however, there are some key differences between the two studies including the high proportion of patients in this study with clinically palpable axillary metastases (14/25) and a larger median tumor size of 22.55 mm (1). Both factors are associated with an increased the tumor burden within the axilla. Despite these factors, this study revealed that 7 of 11 patients with clinically node negative disease and positive preoperative axillary needle biopsy had fewer than 3 total positive nodes at the time of surgery. Furthermore, 5 of 9 patients with clinically node-negative disease, 1–2 suspicious nodes on axillary ultrasound and positive preoperative axillary needle biopsy had less than 3 metastatic lymph nodes.

The results of this study demonstrate that in the setting of omission of physical examination status and strict reliance upon axillary ultrasound imaging that 43% of patients with 1–2 suspicious nodes on axillary imaging underwent an unnecessary ALND. These findings support previous studies demonstrating a high proportion of clinically node-negative patients with abnormal axillary imaging and

positive fine needle aspiration/core needle biopsy have 1–2 positive sentinel nodes and have the option to avoid ALND (3). While this supports TAD, it is difficult to draw significant conclusions. The small sample size of 25 patients makes comparison of these results with those of Z0011 difficult. Furthermore, given that an improved outcome with ALND was only seen in women with greater than 2 positive sentinel lymph nodes, perhaps defining a positive sentinel lymph node biopsy (SLNB) as the presence of greater than 2 positive nodes would provide more insight into the predictive value of SLNB (4). In addition, the study had an expected false negative rate of 28%. Using standard protocols of dual isotope and dye tracer mapping and identification of 1–3 sentinel lymph nodes (median of 2), sentinel lymph nodes are falsely negative in 5–10% of node-positive (5). The use of radiotracer only in this trial may have a role in the high reported false negative rates. Furthermore, studies evaluating the efficacy of SLNB following neoadjuvant chemotherapy have demonstrated the ability to lower false negative rate with removal of at least 3 nodes (6-8). While not statistically significant (likely due to the small sample size), the higher number of mean sentinel nodes excised in patients with false-negative sentinel nodes of 0.85 compared to 1.55 in those with true-negative sentinel nodes suggests that the number of sentinel lymph nodes excised may be a confounder of the false negative rate. Ultimately, the debate on the reliability of sentinel node mapping and its utility in the decision to omit ALND continues. The authors plan to further evaluate the optimal technique to identify metastatic axillary nodes in the future, to which we look forward.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated or resolved.

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