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Editorial

Sentinel Lymph Node Biopsy for Breast Cancer: Will Variations in Technique Influence Long-Term Outcome?

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Lymphatic mapping was introduced to the medical community as an addition to the armamentarium of breast cancer management strategies just over a decade ago.[1,2] The biological plausibility of sentinel node biopsy is based on the rationale that we can replicate the pathway that would be traversed by cancer cells from a primary breast tumor through intramammary lymphatic channels en route to implantation in the first nodal recipients of metastasis. Early studies involved sentinel lymphadenectomy performed with a concomitant axillary lymph node dissection (ALND) so that accuracy rates could be defined. Within the following 5 years, identification rates in excess of 95% and false-negative rates of $< 5\%$ were being consistently reported by numerous investigators internationally.[3–7] These promising results led to the acceptance of a cancer-free sentinel lymph node as a reliable means of identifying the node-negative patient who could be spared the morbidity of a standard ALND. In this issue of *Annals of Surgical Oncology*, two reports[8,9] serve as reminders that while we continue to search for ways that we can revise and improve sentinel node biopsy algorithms, we must remember the ultimate goals of axillary surgery in breast cancer patients: the accurate determination of nodal status for prognostic value and regional control of disease. In the studies reported herein, Degnim et al.[9] have systematically evaluated whether selected patients can avoid the allergenic risks of blue dye mapping, and Fan et al.[8] have looked at their institution's outcome experience after sentinel lymphadenectomy.

Initial mapping experiences included rigorous attention to technical and anatomical details. The blue dye and/or radioactive label was injected peritumorally, and after waiting some prespecified interval, the patient would undergo axillary exploration. Blue dyes were injected during surgery, approximately 5 minutes before sentinel node dissection. Radioactive isotopes were injected peritumorally, and the timing of the surgery was based on subsequent lymphoscintigraphy, which was frequently performed on a sequential basis until sentinel uptake was identified on a preoperative scan. These techniques were mechanistically sound; however, they became logistically burdensome as the volume of mapping cases increased. Patients with nonpalpable tumors frequently required additional image-guided localization procedures to facilitate injection of the mapping label, and surgical schedules were disrupted by the unpredictability of lymphoscintigraphy results: uptake in a nodal basin might occur within 30 minutes, or it might require several hours. It was therefore inevitable that variations in technique would be explored to improve the efficiency and ease of incorporating lymphatic mapping cases into busy operating room caseloads.

Some of the first variations in mapping technique involved alternative injection sites, such as dermal injections overlying the breast tumor[10,11] or subareo-

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lar injections.[12,13] These approaches made it easier to handle nonpalpable lesions. Other variations addressed consideration of alternative isotope strategies, such as abandoning the preoperative lymphoscintigram[14] or performing isotope injections on the day before surgery.[15,16] These strategies facilitated integration of mapping cases into the main surgical schedules. A meta-analysis of the worldwide experience with sentinel lymph node biopsy performed in conjunction with a standard ALND[17] validated the conventional routine for lymphatic mapping, but many of the studies evaluating novel mapping techniques that have been reported in the more recent literature focused on the ability to identify a sentinel lymph node; the false-negative rates associated with these alternative methods are more uncertain because the completion ALND is not performed consistently in these series. It is therefore conceivable that we are missing some finite proportion of false-negative cases with these alternative mapping strategies, although this proportion is likely to be very small.

The absolute number of sentinel lymph nodes that should be removed has also been questioned. Although the average lymphatic mapping case will identify two or three sentinel nodes, it is not uncommon for patients to have very exuberant uptake of the mapping label, resulting in five or more sentinel nodes. Because avoidance of extensive surgery, thereby minimizing the risk of lymphedema secondary to impaired lymphatic drainage, is a major goal of the sentinel node procedure, it is appropriate to question whether surgical attention can be focused on a fixed, limited number of sentinel nodes. McCarter et al.[18] addressed this question in a Memorial Sloan-Kettering review of patients with four or more sentinel lymph nodes; this subset comprised 15% of their sentinel lymph node dataset. When metastatic disease was present in this category of multiple sentinel node cases, it was identified in the first three sentinel nodes resected for the vast majority (98%); however, in a small proportion of cases, metastatic disease was detected only with aggressive resection of all sentinel nodes beyond the first three encountered.

Degnim et al.[9] have evaluated the question of whether blue dye–related morbidity can be avoided by relying on isotope mapping alone in cases in which the preoperative lymphoscintigraphy identifies axillary radioactivity. This study of University of Michigan breast cancer patients demonstrated that even when isotope mapping was successful, the metastatic disease was detected in sentinel nodes identified by their uptake of blue dye only in 2.5% of cases. This suggests that although the overwhelming majority of metastatic sentinel nodes will be identified with standard isotope mapping, a well-defined subset of cases will be understaged if blue dye is excluded from the procedure.

The results of Fan et al.[8] demonstrating an axillary relapse rate of only 3.3% in breast cancer patients whose axillary operation was limited to the resection of negative sentinel lymph nodes are modestly reassuring. However, the traditional ALND will usually keep axillary failure rates below 2%. It is therefore critical that individual breast surgical oncology programs continue to track their own outcome results over time, especially if variations in the lymphatic mapping methodology have been introduced into local practices. Small incremental increases in risk for missed metastatic sentinel lymph nodes may be cumulative over time, and the effect of these effects can be determined only with ongoing, long-term follow-up.

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