

Is Sentinel Node Biopsy of the Internal Mammary Lymph Nodes Relevant in the Management of Breast Cancer?

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■ **Abstract:** The aim of this study was to review the outcomes of a series of breast cancer patients who underwent sentinel node biopsy inclusive of lymphoscintigraphy, and to assess the incidence of internal mammary node (IMN) metastatic positivity at exploration and whether these findings influenced treatment. Between April 2001 and December 2012, 581 breast cancer patients at Princess Alexandra Hospital underwent preoperative lymphoscintigraphy in the course of the performance of sentinel node biopsy. Analysis was performed of those patients who demonstrated radio-isotope uptake to the IMN chain, and who had sentinel node biopsy of the IMN's and were found to have metastatic involvement. Assessment was made to determine whether the finding of IMN metastases changed the adjuvant systemic management of these patients, and to review complication rates. 95 of 581 (16.4%) patients with preoperative breast lymphoscintigraphy had lymphatic mapping to the IMN chain. 51 (54%) of these patients had IMN chain surgically explored and IMN nodes were found in 35 of these patients (success rate of 69%). Of these, three patients (3/35 = 8.6%) had metastatic involvement of the IMN sentinel node group. All three IMN positive patients received adjuvant breast radiotherapy, chemotherapy, and hormonal therapy. In four patients (7.8%) IMN surgical exploration was complicated by pneumothorax. Only a small proportion of breast cancer patients were found to have metastatic involvement of the IMN chain and which did not significantly change their adjuvant therapy management. These findings suggest that the benefits of exploration of the IMN chain in breast cancer patients are limited and may be outweighed by the risk of complications. ■

Key Words: breast cancer, internal mammary nodes, lymphoscintigraphy, sentinel node

The surgical management of breast cancer has changed considerably over the past century. However, controversy has remained over the significance of the internal mammary node (IMN) in the management of breast cancer and debate still continues as to whether this chain of lymphatics should be the subject of surgical intervention. Indeed pursuant to the original Halsted radical mastectomy (1), Jerry Urban devised the extended radical mastectomy (2) which involving en bloc resection of the internal mammary chain. However, several randomized trials (3,4) have failed to demonstrate a survival benefit from surgical IMN dissection and evidence suggests that IMN's are rarely the first site of recurrence.

However, a shift in the perception of the natural history of breast cancer which considered the disease to be systemic from its early development, saw a shift in emphasis away from aggressive local therapies to an emphasis on drug treatments (5–7). This change in perspective also saw the adoption of sentinel node biopsy by the early 2000s which moved the regional management of the axilla to a more minimalistic approach (8,9). Paradoxically the use of lymphoscintigraphy as part of this technique has seen a renewed interest in the internal mammary chain, and in the context of nodes showing intense radioisotope uptake (hot) being identified on scintiscans there has been a renewed practice of undertaking biopsies of such IMN (10). However, particularly in the context of the recent ACOSOG Z0011 trial results (11), showing that patients who had a sentinel node biopsy of the axilla only with no other lymph node surgery performed did not sustain a survival disadvantage, questions have arisen as

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to the appropriateness of IMN biopsy in patient management.

The aim of this study was to conduct a retrospective review of breast cancer patients treated at Princess Alexandra Hospital who underwent sentinel node biopsy as part of their surgical management and in whom preoperative lymphoscintigraphy was performed with identification of sentinel nodes in the internal mammary chain. Outcomes of the study included assessment of the proportion of patients who had metastatic involvement of the IMN and whether the knowledge of this information impacted on subsequent adjuvant systemic or other treatments. Secondary goals of the study were to assess the success rates of exploration of the internal mammary chain to retrieve a sentinel node and assessment of the complication rates for this procedure.

METHODS

This was a single institution retrospective study conducted on breast cancer patients presenting at the Princess Alexandra Hospital, Queensland, Australia between April 2001 and December 2012. As part of standard breast cancer treatment, all patients with invasive breast cancer have the axilla surgically staged for disease. Standard practice is that invasive breast cancer patients with clinically and radiologically negative axillary lymph nodes will undergo sentinel node biopsy utilizing either blue dye, radio-isotope, or both. In this series we identified all patients who had preoperative lymphoscintigraphy at that time of surgery for primary breast cancer. Patients managed with radio-isotope underwent lymphoscintigraphy on the day before or the day of surgery. Preoperative

lymphoscintigraphy was performed by means of a radio-colloid injection of technetium 99—sulfur colloid which was injected into the breast peritumourly. Serial scintiscan imaging of the thorax and axillary area was usually then undertaken over the ensuing 2–3 hours, and “hot” nodes containing significant concentrations of radio-isotope subsequently identified were marked by the radiologist either in the axilla or in the region of the internal mammary chain over the edge of the sternum (Fig. 1). Depending on the significance of the drainage to the internal mammary nodal chain, the treating surgeon made the final decision as to whether or not it was deemed appropriate to pursue biopsy of the internal mammary chain, and this decision was usually undertaken in consultation with the radiologist. As a routine in our institution, patent blue V dye was also injected peritumourly as to provide a dual method technique for identifying sentinel lymph nodes (SLN). In the majority of cases, IMN biopsy was able to be performed via the incision placed for the performance of the lumpectomy, particularly when this was sighted in the medial aspect of the breast. In instances where the lumpectomy occurred in the lateral aspect of the breast, a separate incision was made over the appropriate intercostal space toward the medial edge of the breast, but preferably not crossing the midline for cosmetic reasons. Blunt dissection was then performed through the pectoralis major muscle, and the external and internal intercostal muscles were either divided or split along the line of their fibers until the extrapleural space was identified, taking care not to puncture the parietal pleura. The IMN was usually retrieved by careful dissection with fine Halstead forceps teasing the node away in among fatty tissue sited adjacent to the

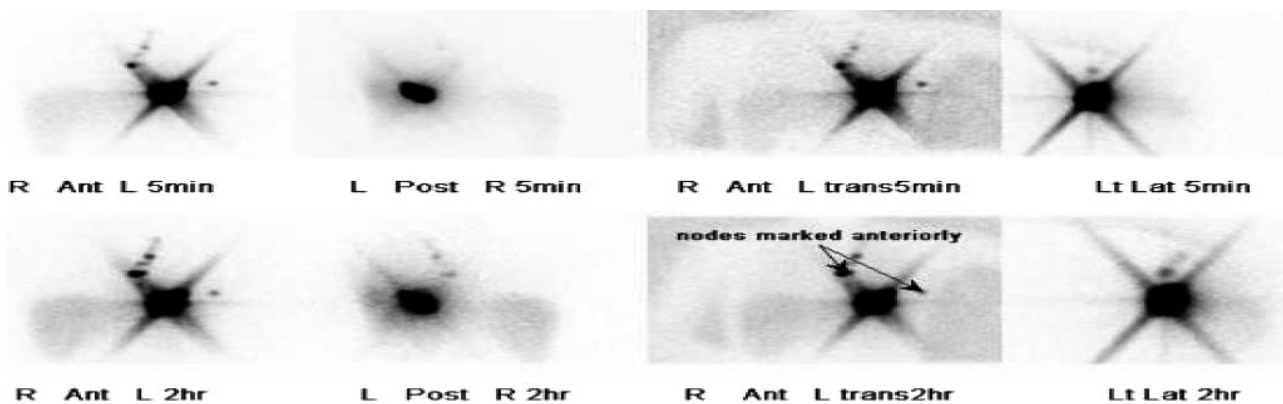


Figure 1. Scintiscan showing internal mammary node localization.

internal mammary artery and vein. The technique used was similar to that described by Sacchini et al. (10).

Further analysis was conducted of patients who had preoperative lymphoscintigraphy drainage to their internal mammary chain, including assessments of the proportion of patients who proceeded to have a sentinel node biopsy of the IMN, the rate of successful identification of the sentinel node in this region, and the percentage of patients found to have malignant involvement of the sentinel IMN node. Complication rates for the performance of this procedure were also noted and an important endpoint of the study was to determine whether the finding of an IMN metastasis altered adjuvant systemic management.

RESULTS

In the period of this study from 2001 to 2012 there were 581 breast cancer patients who underwent preoperative lymphoscintigraphy. Ninety-five patients (16.35%) had lymphatic mapping to the IMN chain. Of these 95 patients, 55 patients (57.89%) had both IMN and axillary nodes (AN) mapped on lymphoscintigraphy and 40 patients (42.11%) had only IMN identified. Thirty-nine of the 40 patients with IMN mapping only also had concurrent patent blue V dye injected into the breast as part of the localization methodology, and in 37 of these patients a blue sentinel node was identified in the axilla. The three failed axillary sentinel node biopsy patients all had successful internal mammary lymph node sentinel biopsies undertaken.

Attempted Sentinel Node Biopsy of Internal Mammary Node and Success Rate

Of the 95 patients who had lymphatic mapping to the IMN chain, attempted surgical exploration was performed in 51 (53.68%) of these patients. In 35 of

the 51 patients, the sentinel node in the internal mammary chain was successfully located (retrieval rate 68.6%). In three of these 35 patients (8.58%) the internal mammary lymph node chain was the only node found and sampled.

Oncological Outcomes

Only three of the 35 patients (8.65%) in whom a sentinel node was retrieved from the internal mammary chain demonstrated metastatic disease, representing 0.52% of all patients in the series. All three of these patients also had axillary sentinel node biopsies. Two of these patients were AN negative (IMN+, AN-) and one of these patients was AN positive (IMN+, AN+). All three of these patients were hormone receptor positive and HER 2 positive. The systemic treatment for these three patients would not have changed even if the internal mammary lymph node status was not known, as all three would have been offered adjuvant chemotherapy on the basis of their with initial histopathology (Table 1). The demographics of these three patients were female sex and their ages ranged from 29 to 54 years old. The two patients who were IMN positive and AN negative had no further surgery, however, the patient who was IMN positive and AN positive also went on to have a standard level 1–2 axillary clearance. All three patients who had positive IMN were treated in the fashion of standard breast conserving therapy (as well as all of the patients in this whole series) and which included whole breast irradiation with a boost to the lumpectomy site but no additional radiotherapy boost was administered to the IMN chain.

Complications

In four of the 51 patients (7.84%) who underwent IMN biopsy the procedure was complicated by the development of pneumothorax. None of these patients had malignant disease in their internal mammary

Table 1. Histopathology of Patients with Positive IMN

Age (years)	Pathology of primary breast cancer	Hormonal receptor status	Her2 receptor status	Size of IMN metastases	No. axillary nodes involved
54	12 mm grade 2 ductal carcinoma	Positive	Positive	Macrometastasis 3 mm	0/3
29	10 mm grade 2 ductal carcinoma	Positive	Positive	Macrometastasis 3 mm	0/2
40	16 mm, 15 mm grade 3 ductal carcinoma	Positive	Positive	Micrometastasis <1 mm	2/2

nodal chains. Two of these cases required the placement of a chest drain the other two were able to have their small pneumothoraces managed conservatively.

DISCUSSION

As a result of a number of large randomized, control trials, sentinel node biopsy has become the standard of care in the management of patients with invasive breast cancer, with this technique enabling effective staging of the axilla and the potential to avoid the need for an axillary clearance (12,13). The majority of studies reviewing the success of sentinel node biopsy have found that the best chance of localizing a sentinel node is by means of a combination of blue dye and radio-isotope, with radio-isotope uptake being ascertained by means of both preoperative lymphoscintigraphy and the utilization of an intraoperative gamma probe (14). Consistent with this approach, in Australia the National Breast and Ovarian Cancer Centre (NBOCC) has recommended the combined use of blue dye and radio-isotope with preoperative lymphoscintigraphy and an intraoperative gamma probe (15). At the Princess Alexandra Hospital the use of preoperative lymphoscintigraphy and the performance of scintiscan have become routine practice in combination with the use of patent blue V dye in the conduct of sentinel node biopsies for node negative invasive breast cancers.

Reports in the literature suggest that with the use of radioactive tracer injections, on average drainage to the IM SLN is observed in 13–37% of patients, among whom only 8–24% have metastases (16). In our report, 16.35% of patients had mapping to the internal mammary chain and only 8.65% of patients whose IMN were sampled showed evidence of metastatic disease. In our series, even if the status of these IM nodes were unknown, none of these patients would have had a change in adjuvant systemic treatment. Postma et al. (17) arrived at similar conclusions, as 16.28% of their IMN biopsies showed metastatic nodal disease but this did not affect a change in adjuvant systemic treatment in any patients. Maraz et al. (18) in their series of breast cancer patients demonstrated an 18% incidence of IMN chain metastasis but which effected a change in chemotherapy in only 1 (1.3%) of these patients. Thus, the true staging benefit of this procedure is not evident if it does not effect a change in subsequent systemic treatment. Maraz concluded that based on their findings and a review of the literature that sentinel

node biopsy of the IMN had limited value and its routine use should not be recommended.

In oncological terms, the purpose of sentinel node biopsy of the internal mammary chain would theoretically need to fulfill two goals: firstly, for staging purposes which might be anticipated to influence systemic treatment; and secondly to influence local control measures. In terms of local control, it is currently not routine to proceed to a more extensive radical surgical clearance of this nodal compartment as the morbidity is extremely high and radiotherapy to this area is of limited benefit and also associated with significant morbidity. In the context of the increasing acceptance of the ACOSOG Z0011 trial results, it would also seem that there would be little benefit of further local treatment or compartment clearance in patients with such low volume nodal disease. The other benefit of any staging information which might be gained would be in relation to independent prognostic information. Madsen et al. (19) in a multicenter cohort study demonstrated that in a multivariate analysis, IMN metastasis did not have a significant effect on overall survival, but in a subset of patients without axillary metastases, the presence of IMN malignancy was associated with worse survival (HR1.27). However, it is interesting that historically there seems to have been a transitional shift in the prognostic significance of IMN metastases over time. Recently reported survival statistics are dramatically improved upon those reported in the early 1980s when Veronesi (3) described 10-year survival rates of 50–60% with IMN only involvement, and 37.3% when both IMN and ANs were affected. The most likely explanation for the lessening clinical and prognostic relevance of IMN metastasis is two-fold. Firstly, IMN metastases detected by sentinel node biopsy are likely to reflect a different selection group compared to nodes harvested in earlier times, and are therefore more likely to represent earlier stages of the disease (lower volume of disease in the affected nodes) with an associated better prognosis. Secondly, the more liberal and widespread application of systemic therapies in the modern era has provided a greater probability of dampening the clinical significance of small and microscopic tumor deposits in IMN's.

Our study is a retrospective single institution teaching hospital experience evaluating the outcomes of the discovery of positive internal mammary chain nodes on scintiscans in the context of undertaking sentinel node biopsy in breast cancer patients. This study is

therefore subject to the usual limitations and biases associated with this type of retrospective study, however, the results of our study are comparable with other relevant similar studies in the literature and provides further knowledge specifically in relation to the operative outcomes within an Australian hospital setting.

Lastly, the potential benefits of undertaking a sentinel node biopsy of the IMN need to be balanced against the potential procedural risks. In our study, 7.85% of attempted biopsies were complicated by pneumothorax. This needs to be seen in the context of only 8.65% of patients being shown to have IMN metastases but with none of these individuals potentially having their systemic therapy altered in any case. As such, the benefits of IMN sentinel node biopsy are limited and the risks of this procedure are relatively significant.

CONCLUSION

In this series of clinically node negative breast cancer patients undergoing sentinel node biopsy, only a small proportion of our patients were found to have metastatic involvement of the internal mammary chain. For patients who were found to have metastatic nodal disease in the internal mammary chain, there was no change in subsequent adjuvant systemic therapy. These findings suggest little benefit in exploring the internal mammary chain and its routine use is not recommended.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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