

Evaluation of internal mammary lymph node biopsy during microsurgical breast reconstruction: An analysis of 230 consecutive patients

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Abstract

Introduction: Clinical significance of internal mammary (IM) lymph node biopsy during microvascular free flap breast reconstruction remains controversial. Some microsurgeons may choose to biopsy an IM lymph node during routine IM vessel dissection. The authors reviewed the results of IM lymph node biopsy during autologous breast reconstruction.

Methods: A retrospective chart review of patients who underwent autologous breast reconstruction during a seven-year period (January 2010 to January 2017) was performed. Patient demographic data, disease staging, flap details, pathology reports, and adjuvant treatment were evaluated.

Results: A total of 230 patients with a mean age of 52.1 (SD 9.3) underwent IM lymph node biopsy (n = 297). Single IM lymph node was removed in 169 patients, 2 nodes were removed in 56 patients, 3 nodes in 4 patients, and 4 nodes in a single patient. Histopathologic analysis demonstrated presence of IM lymph node metastasis in 16 patients (7.0%). Thirteen patients were found to have metastatic IM lymph nodes in the setting of immediate reconstruction. Three patients were found to have metastatic IM lymph nodes in the setting of delayed. Five out of 16 patients (31.3%) had negative axillary sentinel lymph node biopsy and IM lymph nodes were the only site of nodal metastases. All five of these patients were upstaged accordingly and received adjuvant therapy based on the discussion at the multidisciplinary breast tumor conference.

Conclusions: Opportunistic internal mammary lymph node sampling during autologous breast reconstruction can be performed with minimal morbidity and has significant impact on the disease staging and adjuvant treatment.

KEYWORDS

breast cancer, breast cancer reconstruction, internal mammary lymph, internal mammary lymph node, microsurgical breast, node biopsy, reconstruction

1 | INTRODUCTION

Breast cancer affects approximately 1 in 8 American women with an estimated 276 480 new cases to be diagnosed in 2020. Despite the rising incidence, mortality rates are steadily declining secondary to diagnostic and therapeutic advancements.¹ Accurate assessment of regional lymph node basin remains an essential component in the management and staging of patients with primary breast cancer. Axillary lymph node chain is the primary drainage site of the breast and prognostic significance of axillary lymph node involvement is well established.² The current standard of care is to perform axillary sentinel lymph node biopsy (SLNB) by injecting blue dye or radioactive colloid around the tumor in clinically node-negative patients, thus potentially avoiding a more morbid axillary lymph node dissection.^{3,4}

Even though internal mammary (IM) lymph node chain is the second most important drainage site outside of axilla, the role of internal mammary lymph node biopsy remains controversial.⁵⁻⁷ Long-term outcome studies have demonstrated that routine IM lymph sampling is not indicated because it does not offer survival benefit.⁸⁻¹⁰ In addition, elective IM lymph node dissection may require a separate skin incision and can be complicated by IM vessel bleeding and iatrogenic pulmonary injury.^{11,12} The introduction of preoperative lymphoscintigraphy has rekindled interest in the IM lymph node sampling. However, SLNB has failed to reliably identify involved IM lymph nodes secondary to interference from radioactivity at the primary tumor site.^{13,14} Additional noninvasive methods for IM node assessment may be helpful, including magnetic resonance imaging (MRI) or positron emission tomography (PET) scanning, although these imaging modalities are unable to definitively identify positive nodes.¹⁵

Nevertheless, IM lymph node status is included in the current breast cancer staging and metastatic IM lymph nodes carry unfavorable prognosis, regardless of the axillary node status.^{2,16} The diagnosis of positive IM lymph nodes may affect patient's disease stage and need for adjuvant therapy, especially since up to 10% of patients with pathologically node-negative axillary disease, may harbor regional metastases to the IM lymph nodes.¹⁷

With the advent of axillary SLNB and evolution of microsurgical free flap breast reconstruction, IM vessels are often used as recipient vessels.¹⁸ IM artery and vein are commonly exposed by excising a portion of third costal cartilage, which allows easy exposure and identification of IM lymphatic system. Though some surgeons may use an intercostal vessel or limit dissection between the rib spaces which may make identification of the IM lymphatic system more difficult. In addition, preoperative use of lymphoscintigraphy has demonstrated that IM nodal metastases are most frequently located in the second and third intercostal space, which are routinely exposed during recipient vessels dissection.¹⁹

The objectives of this study were to determine the results of IM lymph node biopsy during free flap breast reconstruction and to evaluate the impact of metastatic IM lymph nodes on the adjuvant treatment and disease staging.

2 | METHODS

After receiving approval from the Internal Review Board, a retrospective chart review was performed that included all consecutive patients who underwent immediate or delayed autologous free flap breast reconstruction at three Northwell Health System institutions: Lenox Hill Hospital, Northshore University Hospital and Long Island Jewish Medical Center. The study period was 7 years (January 2011 to January 2017). A total of 18 different plastic surgeons and a number of Physician Assistants and Plastic Surgery Residents participated in dissection of the recipient internal mammary vessels. IM lymph nodes were biopsied by the surgeon who was dissecting out the IM vessels at their discretion. No additional preoperative internal mammary SLNB techniques or diagnostic imaging were employed.

Patient demographic data, disease staging, axillary node status, timing of the reconstruction, pathology reports and adjuvant treatment were evaluated. Patients with incomplete medical records, inadequate follow-up and the use of thoracodorsal recipient vessels were excluded. Patients with metastatic IM lymph nodes were reviewed with the breast cancer multidisciplinary team for changes in therapy.

3 | RESULTS

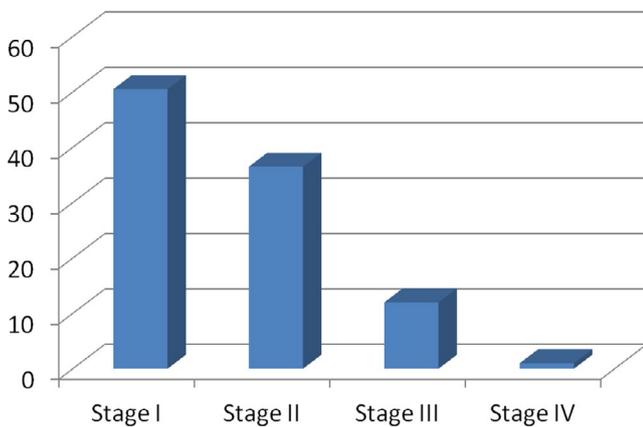
During the study period, a total of 230 patients having autologous breast reconstructions underwent IM lymph node biopsy ($n = 297$). It was up to the surgeons discretion as to whether a IM lymph node biopsy was taken. Over 18 surgeons, and several Physicians assistants and Residents dissected the IM vessels. Though some surgeons had a higher biopsy rate than others, no surgeon or group performed a majority of the biopsies. Though most obvious lymph nodes were sent for biopsy, there was no standardized way that a decision was made for submission of lymph node specimens as this was a retrospective review. The mean age of patients who had IM lymph node biopsy was 52.1 (SD 9.3). One hundred ninety-four patients (84.3%) underwent reconstruction in the immediate setting and 36 patients (15.7%) in the delayed fashion (Table 1). The majority of patients had stage I and stage II breast cancer (Figure 1).

A total of 297 IM lymph nodes were harvested in 230 patients without additional surgical morbidity. Specifically, there were no cases of IM vessel bleeding or iatrogenic pulmonary injury. Single IM lymph node was removed in 169 patients, 2 nodes were removed in 56 patients, 3 nodes removed in 4 patients and 4 nodes in a single patient. Among the patients biopsied with unilateral malignancy, 75.5% of patients had IM lymph node sampling on the side ipsilateral to breast cancer ($P < .0001$).

Histopathologic analysis demonstrated presence of internal mammary lymph node metastasis in 16 (7.0%) patients (Table 2). Average tumor focus was 6 mm (range 3-11 mm). Thirteen of 194 patients (6.7%) who had immediate reconstruction were found to have metastatic IM lymph nodes. Three of thirty six patients (8.3%) who had delayed reconstruction following previous mastectomy and

TABLE 1 Patient demographics and flap characteristics

No. patients	230
Total no. flaps	373
Age (y)	
Mean	52.1
Range	29-80
Timing of reconstruction	
No. patients	
Immediate	194
Delayed	36
Type of reconstruction	
Unilateral	76
Bilateral	154
Length of follow-up (y)	
Median	2.2

**FIGURE 1** Breast cancer stage distribution in patients who underwent IM lymph node biopsy [Color figure can be viewed at wileyonlinelibrary.com]

axillary lymph node dissection were found to have positive IM lymph nodes. Within IM node-positive group, majority of patients had histologic diagnosis of invasive ductal carcinoma, and stage II or stage III breast cancer. Five out of 16 patients (31.3%) with metastatic IM lymph nodes had negative axillary SLNB and IM nodes were the only site of nodal metastases. All five of these patients were upstaged accordingly and the recommendations for adjuvant treatment were based on the discussion at the multidisciplinary breast tumor conference. The remaining eleven patients had positive IM lymph nodes in the setting of axillary node-positive breast cancer. Adjuvant therapy included chemotherapy and radiation to the internal mammary chain and chest wall. One patient with advanced stage III breast cancer refused adjuvant therapy and succumbed to the disease 9 months after the initial diagnosis.

In patients with metastatic IM lymph nodes, initial tumor localization was nearly evenly distributed among all the breast quadrants. (Figure 2) In 8 patients, the information regarding initial tumor localization was not available because the initial biopsy was performed

at the outside institution and/or because of the delayed nature of reconstruction. Given the small number of patients, no correlation was seen between tumor location and presence of metastatic IM lymph nodes ($P = .25$).

4 | DISCUSSION

Accurate assessment of regional lymph node basin plays an important role in staging and local-regional management of breast cancer patients. While most breast cancers drain to the axillary nodal basin, up to 50% of patients can also have IM drainage.^{19,20} The development of axillary sentinel lymph node dissection and preoperative lymphoscintigraphy has become the current standard of treatment, and avoids a more morbid axillary lymph node dissection.²¹⁻²³ The role of IM lymph node biopsy, however, remains controversial.

Prior studies have demonstrated that routine sentinel biopsy of the IM lymph nodes is not indicated because it does not offer survival advantage.^{9,10,24} In addition, the accessibility of IM lymphatic chain poses another challenge to the elective lymph node sampling.²⁵ Nevertheless, metastatic IM nodes are included in the current AJCC staging system, and have significant impact on prognosis and treatment of patients with breast cancer.^{26,27} While IM nodal metastases are rare, they can occur in the absence of axillary metastases, and can result in a change in management in up to 30% of IM node-positive patients.^{11,19,28,29} A study by Sugg et al, showed that in patients with axillary node-negative breast cancer, positive IM lymph nodes convey a 2-fold increase in recurrence or death at 10 years when compared to negative IM lymph nodes.³⁰ In addition, Veronesi et al, demonstrated that patients with metastatic IM lymph nodes who received appropriate adjuvant therapy had improved survival, further highlighting the prognostic value of IM lymph node involvement.²⁴

The internal mammary lymphatic system receives drainage from all breast quadrants with a preference for medial tumors.^{19,20} Interestingly, up to 65% of patients with metastatic IM lymph nodes demonstrate no axillary involvement.²⁵ Recent data demonstrated that patients with medially located tumors had worse prognosis, presumably because of unidentified involvement of IM lymph nodes, and potentially under-staging and under-treating those patients.^{14,17} This can potentially result in withholding adjuvant treatment in a substantial number of patients secondary to solely relying on axillary staging alone.

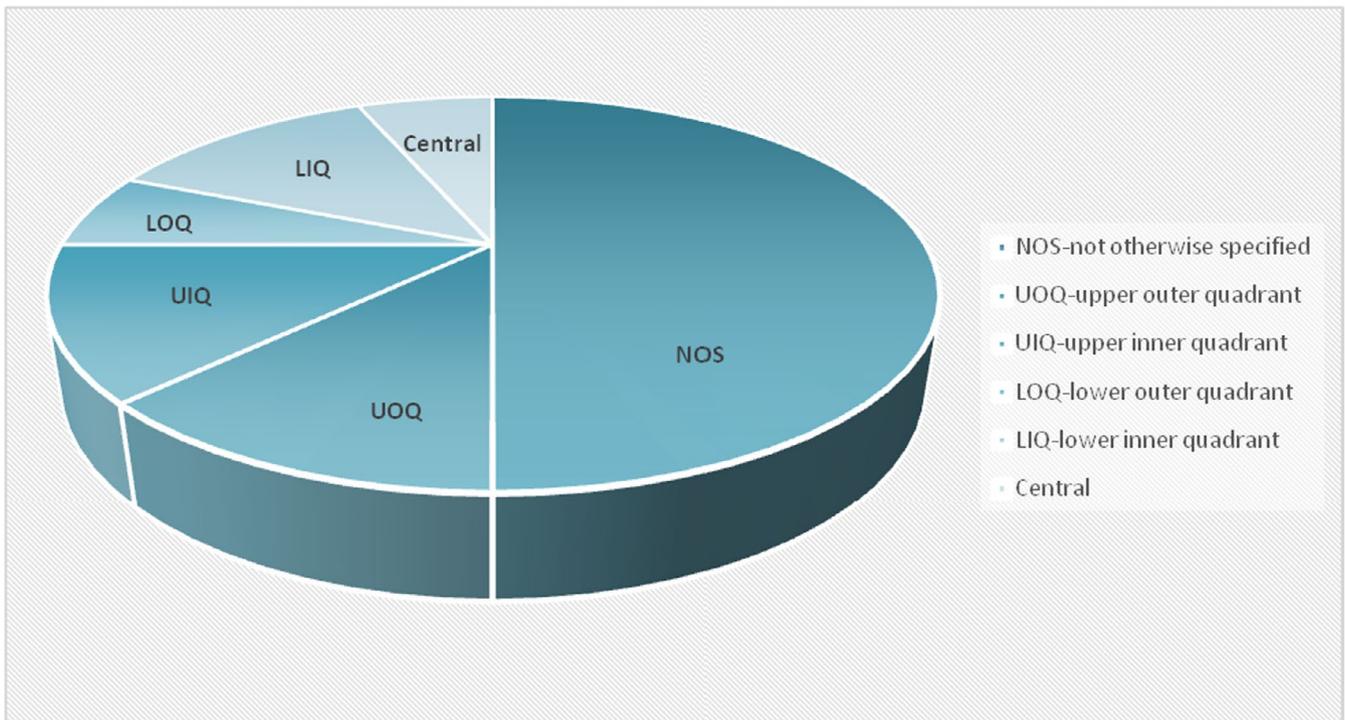
Autologous breast reconstruction has had an increased use of internal mammary vessels as recipient vessels. This has led to decreased patient morbidity and improved esthetic outcomes secondary to more favorable flap positioning compared to use of the thoracodorsal vessels.¹⁸ The internal mammary vessels are often exposed by removing a portion of third rib which allows easy exposure of second and third intercostal space where the majority of metastatic IM lymph nodes are usually found. Alternatively, the surgeon may choose to expose the vessels within the interspace, thereby

TABLE 2 Patients with metastatic IM lymph nodes

Case	Histology	Cancer stage	Delayed Reconstruction	Axillary SLNB	ALND	IM node status	Adjuvant treatment
1	IDC	III	No	Neg	No	1/1	Chemo
2	IDC	II	No	Neg	No	1/1	Chemo/XRT
3	IDC	II	No	N/A	Yes	1/2	Chemo
4	IDC	N/A	Yes	Pos	Yes	1/1	Chemo
5	IDC	II	No	Pos	Yes	2/2	XRT
6	IDC	II	No	Neg	No	1/4	chemo
7	IDC	III	No	N/A	Yes	2/2	Chemo/XRT
8	ILC	N/A	Yes	Neg	No	1/1	Chemo
9	IDC	IV	Yes	N/A	N/A	2/2	Chemo
10	ILC	III	No	Neg	No	1/1	Chemo/XRT
11	IDC	III	No	Pos	Yes	1/1	Chemo
12	IDC	III	No	Pos	Yes	1/1	Refused treatment
13	IDC	II	No	N/A	Yes	1/1	Chemo
14	IDC	III	No	Pos	Yes	1/1	Chemo/XRT
15	IDC	III	No	N/A	Yes	1/1	Chemo
16	ILC	III	No	N/A	Yes	2/2	Chemo/XRT

Abbreviations: ALND, axillary lymph node dissection; ILC, infiltrating lobular carcinoma; N/A, not applicable; SLNB, sentinel lymph node biopsy; XRT, radiation therapy.

*IDC-infiltrating ductal carcinoma.

**FIGURE 2** Initial tumor localization in patients with metastatic IM lymph nodes [Color figure can be viewed at wileyonlinelibrary.com]

preserving the rib, which may make exposure of the IM lymph nodes more difficult, but still possible.

The data presented herewith demonstrate that 230 patients undergoing IM vessel dissection for free flap breast reconstruction had

IM lymph node biopsies. No preoperative imaging or lymphoscintigraphy is employed to evaluate IM lymph node chain. In our review, 16 patients (7.0%) of those that had a biopsy were identified with IM lymph node metastases. In the recent comparable studies by Wright

et al and Andree et al, the incidence of metastatic IM lymph nodes was lower (2.9 and 3.1%, respectively) which can be explained by a smaller sample size and potential selection bias due to sampling of enlarged or suspicious IM lymph nodes only.^{31,32} Recent systematic review of 10 studies by Grant et al, revealed a crude incidence of IM nodal metastases on 2.9%, ranging approximately from 1% to 11%, which is similar to our findings.³³ The majority of patients with metastatic IM nodes in these studies received additional adjuvant therapy, however, the data was insufficient to determine the overall treatment effect on survival.³¹⁻³⁶

In this review, the presence of positive IM nodes in the setting on negative axillary SLNB, resulted in stage migration and alteration of adjuvant treatment in 6 out of 230 patients (2.6%). In addition, three patients who had already undergone treatment for breast cancer were found to have positive IM lymph nodes during delayed reconstruction. In these patients, IM lymph node sampling during autologous free flap reconstruction provided invaluable prognostic information to accurately stage and treat patients, who would have received potentially insufficient oncologic treatment based on the axillary nodal assessment alone. In addition, the finding of metastatic IM lymph nodes during 2 delayed reconstructions after completion of treatment, significantly altered the management of these patients, with one of the patients receiving radiation therapy alone, and the other concurrent chemotherapy and radiation. Given the small number of patients with metastatic IM lymph nodes, no statistically significant correlation was seen between initial tumor localization and involvement of IM lymph nodes.

Limitations of the study include retrospective study design and small number of patients with positive IM nodes, which precluded a more meaningful statistical analysis. In addition, data of the IM lymph nodes status of patients who did not have IM lymph node biopsies is not available. Patients may not have had IM lymph node biopsy due to a number of reasons. These patients may not have had significant visible nodes, these patients may have had limited IM vessel dissection, or the surgeon may not have paid attention to lymph nodes during the dissection of the vessels. In addition, the follow-up is too short to identify disease recurrence and overall survival. Future prospective trials should be undertaken to further evaluate the impact of IM node biopsy on treatment and disease-free survival.

5 | CONCLUSIONS

Opportunistic IM lymph node sampling can be easily performed in the setting of autologous breast reconstruction and results in the identification of a notable rate metastases (7.0%). In this review, the presence of positive IM nodes in the setting of a negative axillary SLNB, resulted in stage migration and alteration of adjuvant treatment in 5 out of 16 patients with metastatic IM lymph nodes (31.3%). In these patients, IM lymph node sampling during autologous free flap reconstruction provided invaluable prognostic information to

accurately stage and treat patients, who would have received potentially insufficient oncologic treatment based on axillary nodal assessment alone. The data herewith suggest, that it should be considered routine practice in microsurgical breast reconstruction. As such, some surgeons at our hospitals have modified their practice so that they routinely send all lymphatic tissue dissected during IM vessel dissection to pathology for evaluation.

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