Incidental Internal Mammary Nodes during Recipient Vessel Dissection in Breast Reconstruction: Are They Significant?

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Assessment of nodal basins can provide important information on staging, local-regional management, and adjuvant therapy in women with breast cancer. Although up to 25% of lymphatic drainage of the breast is to the internal mammary (IM) nodes, there is controversy over the benefit of IM node biopsy, as some studies suggest IM dissection does not improve survival. The recent American Joint Committee on Cancer staging guidelines, however, stratify patients by IM nodal positivity in addition to axillary node status.

Plastic surgeons can encounter IM nodes at the time of free-flap breast reconstruction using IM vessels (Fig. 1). The purpose of this study was to systematically review the incidence of IM nodes encountered incidentally during recipient site preparation in free-flap breast reconstruction and to determine if biopsy affected treatment.

METHODS

Search Methodology

A systematic review was performed using electronic searches completed by 2 reviewers. Databases included PubMed, Ovid MEDLINE, Embase, and the Cochrane Registry. Microsurgical society Web

Summary: Internal mammary (IM) lymph nodes may be exposed during recipient vessel preparation in free-flap breast reconstruction, and in rare cases, positivity of these nodes may affect treatment in patients with breast cancer. This systematic review examines the incidence and significance of IM nodes identified by plastic surgeons. Eligibility criteria included free-flap breast reconstruction with concurrent IM node biopsy. Data were analyzed for incidence of IM node biopsy and nodal positivity. Ten studies met inclusion criteria, with a total of 2055 patients and 717 nodes submitted to pathology. Incidence of IM positivity ranged approximately from 1% to 11%, for a calculated gross overall incidence of 2.9%. Of 59 patients with a positive IM node, 50 patients received additional adjuvant therapy, with insufficient data to determine the effect of treatment on survival. (Plast Reconstr Surg Glob Open 2014;2:e276; doi: 10.1097/GOX.0000000000000245; Published online 23 December 2014)
sites were also searched for relevant abstracts. Preset search terms included combinations of “breast reconstruction,” “microsurgery,” “internal mammary lymph node,” “internal thoracic lymph node,” “lymphatic drainage,” “metastasis,” “biopsy,” “free flap,” “DIEP,” “GAP,” “SIEA,” and “TRAM/msTRAM.” Search dates included all years up to June 2014.

Selection Criteria
Eligibility criteria included free-flap breast reconstruction using IM recipient vessels and concurrent IM node biopsy. Exclusion criteria included nonmicrosurgical breast reconstruction and thoracodorsal recipient vessel use.

Data Collection and Analysis
All relevant data were collected including demographics, type of breast reconstruction, number of nodes biopsied, number of nodes positive for metastasis, any additional adjuvant therapy, and survival. The data were pooled, and simple statistical analysis was completed. A combined statistic of \([x] \text{nodes positive}/[y] \text{patients}\) provided gross overall incidence of nodal positivity.

RESULTS
Search methods identified 24 potentially appropriate articles. Fourteen met exclusion criteria, leaving 10 articles to be included in the analysis (Fig. 2). The 2 reviewers agreed on all selected articles.

Sample size ranged from 32 to 519 for a total of 2055 patients. Two of the included studies sampled 100% of the nodes encountered. The remaining 8 studies described sampling only those nodes that incited clinical suspicion. A total of 717 nodes were sampled and examined histologically (Table 1).

Of the biopsied nodes, 59 had evidence of metastasis on examination for a gross overall incidence of 2.9%. The incidence of nodal positivity by total number of patients ranged from 1.2% to 10.7%. The incidence of nodal positivity by number of nodes sampled ranged from 3.1% to 23.1% (Table 1).

We calculated a gross comparison between articles that sampled all nodes versus those that sampled only clinically suspicious nodes as an estimate of concordance between clinical suspicion and actual positivity \([x] \text{nodes positive}/[y] \text{nodes sampled}\). When all nodes encountered were sampled, 4.0% were found to be positive. When only suspicious nodes were sampled, 10.4% had evidence of metastasis (Table 1).

There were insufficient data on tumor type, stage, or biology for patients with IM nodal metastasis. Tumor location was also underreported. Axillary node status was reported for the majority of these patients, with 71% having axillary nodal metastasis (Table 2).

Following the diagnosis of IM nodal metastasis, adjuvant therapy was given to the majority of these patients (50 of 59). Most received combinations of chemotherapy and radiotherapy, with or without hormonal therapy (Table 2). In most cases, there was concurrent axillary node positivity and only 0.6% had treatment based solely on IM node positivity.

Figure 1. Internal mammary vessel exposure with IM nodal biopsy in the second intercostal space.
Of those patients with IM nodal metastasis in whom survival was reported, 32 patients were alive at the time of publication of the corresponding articles. Nine patients had succumbed to disease, and the range of survival in this group was 23–55 months (Table 2).

No complications were reported as a consequence of sampling the IM nodes.

**DISCUSSION**

Accurate staging plays an important role in treatment planning and has significant prognostic value in patients with breast cancer.\(^5\,19\) Although an isolated IM metastasis is rare, it carries a similar prognostic importance to a positive axillary node, and when both basins are positive, there is a worse prognosis.\(^20\,21\)

Recent studies have shown an IM nodal metastasis rate of 1.8%.\(^22\) This seems to be in concordance with our review which revealed a crude incidence of 2.9%.

This review found that 1 positive node was identified for every 10 nodes sampled due to clinical suspicion. When all nodes encountered were submitted to pathology, 1 metastasis was identified for every 25 nodes harvested.

| Articles that biopsied clinically suspicious nodes |
|--------------------------------------------------|
| **Year of Publication** | **Sample Size (No. Patients)** | **Delayed or Combined\(^\text{a}\) Reconstruction** | **Patients with IM Node Biopsy** | **Patients with Positive IM Node** | **Percent of Positive Nodes of Those Sampled** | **Total Nodes Positive of Those Sampled** |
|-------------------------|---------------------------------|---------------------------------|-------------------------------|---------------------------------|---------------------------------|---------------------------------|
| 2005\(^9\)             | 54                              | Combined                        | 11/54 (20.4%)                | 1/54 (1.9%)                    | 1/11 (9.1%)                     | 49/469 (10.4%)                  |
| 2005\(^10\)            | 81                              | Delayed                         | 13/81 (16.0%)                | 3/81 (3.7%)                    | 3/13 (23.1%)                    | 15/81 (18.6%)                  |
| 2008\(^11\)            | 232                             | Combined                        | 26/232 (11.2%)               | 5/232 (2.2%)                  | 5/26 (19.2%)                    | 31/232 (13.4%)                |
| 2011\(^12\)            | 293                             | Combined                        | 43/293 (14.7%)               | 6/293 (2.0%)                  | 6/43 (14.0%)                    | 52/293 (17.6%)                |
| 2012\(^13\)            | 519                             | Combined                        | 195/519 (37.6%)              | 6/519 (1.2%)                  | 6/195 (3.1%)                    | 215/519 (41.6%)               |
| 2013\(^14\)            | 122                             | Combined                        | 63/122 (51.6%)               | 13/122 (10.7%)                | 13/63 (20.6%)                   | 76/122 (61.0%)                |
| 2013\(^15\)            | 474                             | Combined                        | 86/474 (18.1%)               | 11/474 (2.3%)                 | 11/86 (12.8%)                   | 97/474 (20.6%)                |
| 2014\(^16\)            | NA                              | Combined                        | 32/NA                        | 4/NA                           | 4/32 (12.5%)                    | 36/NA                         |

| Articles that biopsied all nodes encountered |
|---------------------------------------------|
| **Year of Publication** | **Sample Size (No. Patients)** | **Delayed or Combined\(^\text{a}\) Reconstruction** | **Patients with IM Node Biopsy** | **Patients with Positive IM Node** | **Percent of Positive Nodes of Those Sampled** | **Total Nodes Positive of Those Sampled** |
|-------------------------|---------------------------------|---------------------------------|-------------------------------|---------------------------------|---------------------------------|---------------------------------|
| 2009\(^17\)            | 44                              | Combined                        | 44/44 (100%)                 | 4/44 (9.1%)                    | 4/44 (9.1%)                     | 10/248 (4.0%)                  |
| 2014\(^18\)            | 204                             | Combined                        | 204/204 (100%)               | 6/204 (2.9%)                  | 6/204 (2.9%)                    | 210/204 (10.4%)               |

\(^a\)Studies including immediate and delayed reconstructions.

NA, not available.
Potential indications for IM node biopsy in the immediate reconstruction setting include evidence of a “hot” IM node on lymphoscintigraphy or a blue node encountered on dissection. 23,24 In such cases, management may be discussed with the mastectomy surgeon.

In this review, adjuvant therapy after breast reconstruction was reported in 50 of the 59 patients with a positive IM node. The majority of patients had systemic chemotherapy and/or radiotherapy (including to the IM nodal basin), with or without hormonal therapy. There are multiple factors that affect the choice of therapy, and the upstaging of a patient based on IM metastasis may or may not affect treatment should there be concomitant axillary nodal involvement. 25 In our review, 13 patients were axillary node negative (0.6%), and nodal status was based solely on IM nodes. Some guidelines suggest that IM nodal involvement alone warrants additional adjuvant chemotherapeutic treatment and IM chain irradiation. 26 These complex patients require discussion at multidisciplinary breast tumor board rounds as the management is not clearly defined.

Recent studies have provided evidence that local-regional tumor control is associated with improvement in long-term survival. 21,27,28 Although these studies included treatment to the IM nodal basin, it is unclear how this additional therapy contributes to survival. 29 In the current review, roughly 80% of the breast reconstruction patients with positive IM nodes were alive at
the time of publication. Of those that succumbed to disease, survival ranged from 23 to 55 months.

IM node metastasis without concurrent positive axillary nodes is rare. With an unknown effect on treatment or survival, routine biopsy of the internal mammary nodes may not be beneficial. A prospective study looking at the impact of IM node biopsy on treatment would be beneficial.

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REFERENCES
1. Estourgie SH, Nieweg OE, Olmos RA, et al. Lymphatic drainage patterns from the breast. *Ann Surg* 2004;239:232–237.
2. Kong AL, Tereffe W, Hunt KK, et al. Impact of internal mammary lymph node drainage identified by preoperative lymphoscintigraphy on outcomes in patients with stage I to III breast cancer. *Cancer* 2012;118:6287–6296.
3. Veronesi U, Marubini E, Mariani L, et al. The dissection of internal mammary nodes does not improve the survival of breast cancer patients. 30-year results of a randomised trial. *Eur J Cancer* 1999;35:1320–1325.
4. van der Ent FW, Kengen RA, van der Pol HA, et al. Halsted revisited: internal mammary sentinel lymph node biopsy in breast cancer. *Ann Surg* 2001;234:79–84.
5. Edge S, Byrd D, Compton C, et al., eds. *AJCC Cancer Staging Manual*. 7th ed. New York, N.Y.: Springer; 2010.
6. American Society for Reconstructive Microsurgery. ASRM Website. Available at: http://www.micorsurg.org/. Accessed June 1, 2014.
7. World Society for Reconstructive Microsurgery. WSRM Website. Available at: http://www.wsrm2013.org/. Accessed June 1, 2014.
8. European Society of Federations for Microsurgery. ESFM Website. Available at: http://www.esfm.eu/. Accessed June 1, 2014.
9. Arnez ZM, Snoj M. Sampling of internal mammary chain lymph nodes during breast reconstruction by free flaps from the abdomen. *Tumori* 2005;91:415–417.
10. Hofer SO, Rakhorst HA, Mureau MA, et al. Pathological internal mammary lymph nodes in secondary and tertiary deep inferior epigastric perforator flap breast reconstructions. *Ann Plast Surg* 2005;55:583–586.
11. Knight MA, Nguyen DT, Kobayashi MR, et al. Incidental positive internal mammary lymph nodes: a multiple international institutional investigation. *J Reconstr Microsurg*. 2008;24:197–202.
12. Yu JT, Provenzano E, Forouhi P, et al. An evaluation of incidental metastases to internal mammary lymph nodes detected during microvascular abdominal free flap breast reconstruction. *J Plast Reconstr Aesthet Surg* 2011;64:716–721.
13. Andree C, Schmidt VJ, Munder Bj, et al. Detection of breast cancer metastasis by means of regional lymph node sampling during autologous breast reconstruction—a screening of 519 consecutive patients. *Med Sci Monit*. 2012;18:605–610.
14. Schaverien MV, Purdie CA, Munnnoch DA. Clinical value of internal mammary lymph node metastases found incidentally during free flap recipient vessel exposure. *Eur J Surg Oncol*. 2013;39:608–612.
15. Wong KY, Yu JT, Mahler-Araujo B, et al. Opportunistic internal mammary lymph node biopsy during microvascular free flap breast reconstruction: a useful technique? *Int J Surg*. 2013;11:1027–1028.
16. Hellman JB, Shore AM, Park JE. Biopsy of internal mammary chain lymph nodes found incidentally during autologous breast reconstruction. *Plast Reconstr Surg*. 2014;133:896e–897e.
17. Eldor L, Baker TP, Spiegel AJ. The routine sampling of internal mammary lymph nodes during free flap based breast reconstruction. *Plast Reconstr Surg* 2009;124:51.
18. Wright E, Momeni A, Lee GK. Internal mammary lymph node biopsy during microsurgical breast reconstruction: should this be routine? Paper presented at: 2014 meeting of the American Society for Reconstructive Microsurgery. Kauai, Hawaii, January 2014.
19. Veronesi U, Cascinelli N, Bufalino R, et al. Risk of internal mammary lymph node metastases and its relevance on prognosis of breast cancer patients. *Ann Surg*. 1983;198:681–684.
20. van Rijk MC, Tanis PJ, Nieweg OE, et al. Clinical implications of sentinel nodes outside the axilla and internal mammary chain in patients with breast cancer. *J Surg Oncol*. 2006;94:281–286.
21. Chen RC, Lin NU, Golshan M, et al. Internal mammary nodes in breast cancer: diagnosis and implications for patient management—a systematic review. *J Clin Oncol*. 2008;26:4981–4989.
22. Leidenius MH, Krogerus LA, Toivonen TS, et al. The clinical value of parasternal sentinel node biopsy in breast cancer. *Ann Surg Oncol*. 2006;13:321–326.
23. Borgstein PJ, Meijer S, Pijpers R, et al. Functional lymphatic anatomy for sentinel node biopsy in breast cancer: echoes from the past and the periareolar blue method. *Ann Surg* 2000;232:81–89.
24. Klümborg VS, Rubio IT, Henry R, et al. Subareolar versus peritumoral injection for location of the sentinel lymph node. *Ann Surg Oncol* 1999;22:860–864.
25. Galimberti V, Veronesi P, Armone P, et al. Stage migration after biopsy of internal mammary chain lymph nodes in breast cancer patients. *Ann Surg Oncol*. 2002;9:924–928.
26. Nationaal Borstkanker Overleg Nederland. Breast Cancer Dutch Guideline, Version 2.0. Available at: http://www.oncoline.nl/mammacarcinoom. Accessed February 22, 2014.
27. Overgaard M, Jensen MB, Overgaard J, et al. Postoperative radiotherapy in high-risk postmenopausal breast-cancer patients given adjuvant tamoxifen: Danish Breast Cancer Cooperative Group DBCG 82c randomised trial. *Lancet* 1999;353:1641–1648.
28. Hylton KC, Olivo AA, Spinelli JJ, et al. Loco-regional radiotherapy in patients with high-risk breast cancer receiving adjuvant chemotherapy: 20-year results of the British Columbia randomized trial. *J Natl Cancer Inst*. 2005;97:116–126.