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The Incidental Positive Internal Mammary Lymph Node during Delayed Microsurgical Breast Reconstruction: A Case Report and Review of the Literature

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Abstract

Opportunistic biopsy of internal mammary lymph nodes (IMLNs) during free-flap breast reconstruction can reveal otherwise occult nodal disease that directly alters staging and adjuvant therapy in selected breast cancer patients. This report describes a 42-year-old woman with pT1aN0, hormone receptor–positive, HER2-negative breast cancer who underwent delayed deep inferior epigastric perforator flap reconstruction two years after mastectomy and negative axillary sentinel node biopsy; an incidental IMLN harvested during internal mammary vessel preparation demonstrated isolated metastatic carcinoma, prompting tumor board–directed escalation to anthracycline- and taxane-based chemotherapy without post-mastectomy radiation to preserve flap integrity. Review of contemporary series shows that routine or opportunistic IMLN sampling during microsurgical breast reconstruction yields metastatic involvement in a minority of patients, including those with negative axillae, and frequently leads to nodal upstaging and modification of systemic therapy and regional nodal irradiation fields. These data support incorporating selective IMLN biopsy into reconstructive algorithms to refine N1b/N1c classification and individualize post-mastectomy radiation decisions.

Keywords: Breast cancer; Lymph nodes; Radiation; Mammoplasty; Mastectomy

Introduction

Breast cancer remains one of the most common malignancies in women worldwide and is a leading cause of cancer-related mortality despite improvements in screening and systemic therapy. Advances in oncoplastic and reconstructive techniques have reframed mastectomy from a purely oncologic procedure to one that simultaneously restores natural breast contour. Autologous free flap reconstruction, particularly with deep inferior epigastric perforator (DIEP) flaps, has become a modern standard for appropriately selected patients [1].

Within this paradigm, plastic and reconstructive surgeons have assumed a central and critical role on the multidisciplinary breast team, frequently operating on patients with hereditary risk, carcinoma, or prior radiation exposure who preferentially seek implant-sparing options [2-4].

Regional lymph node status remains a critical determinant of prognosis, staging, and adjuvant treatment planning in breast cancer, and axillary sentinel lymph node biopsy has long been the cornerstone technique for nodal evaluation in clinically node-negative patients [5]. Increasing recognition of the internal mammary lymph nodes (IMLNs) as a major and potential primary drainage basin for the breast has expanded the staging landscape, and the American Joint Committee on Cancer now incorporates IMLN involvement (pN1–pN3) into nodal categories that can drive decisions regarding systemic therapy and regional nodal irradiation [6] (Figure 1). Despite their prognostic significance and the potential for IMLN metastases in the absence of axillary disease, routine preoperative or surgical assessment of these nodes remains uncommon due to their deep anatomic location and the limited sensitivity and specificity of current imaging modalities for microscopic disease [7]. The plastic and reconstructive surgeon is often relied upon to obtain this information as it is often out of the scope of breast surgery training.

The widespread adoption of autologous microsurgical breast reconstruction using the internal mammary vessels as recipient vessels has unintentionally created a unique opportunity for IMLN evaluation [8,9]. During standard recipient vessel preparation, partial resection of the third costal cartilage exposes the internal mammary chain and associated lymphatic tissue, enabling low-morbidity sampling of clinically occult nodes without additional surgery. Large retrospective series have shown that opportunistic IMLN biopsy in this setting identifies metastatic involvement in approximately 3–7% of patients, with a substantial proportion harboring IMLN metastases despite negative axillary nodes; thus leading to nodal upstaging and modification of adjuvant chemotherapy and radiation fields [10-13].

Concurrent with the rise of autologous breast reconstruction, there has been an increase in the use of post-mastectomy radiation therapy (PMRT) [14]. As the need for PMRT is often uncertain prior to surgery and is influenced by pathologic findings at the time of mastectomy, autologous reconstruction is commonly performed in the delayed setting [15]. While most published cohorts focus on immediate reconstruction, delayed autologous reconstruction after completion of mastectomy and initial oncologic treatment is increasingly favored when post-mastectomy radiation therapy is anticipated, as this sequence mitigates the deleterious effects of radiation on free flap outcomes. With the increasing use of GLP-1 inhibitors, delaying autologous reconstruction has the added benefit of allowing for weight loss and improving patient candidacy for surgery. As delayed reconstructions utilizing internal mammary recipient vessels become more common, reconstructive surgeons are likely to encounter incidentally positive IMLNs months to years after the index cancer operation, raising distinct questions about surveillance, restaging, and late modification of systemic and regional therapies. This report describes a patient with a delayed free flap breast reconstruction in whom a pathologically positive internal mammary lymph node was incidentally identified at the time of recipient vessel dissection. We also performed a review of the literature on the incidence, oncologic impact, and implications of incidental IMLN metastases during microsurgical breast reconstruction, particularly in the delayed setting.

Case Presentation

The patient is a 42-year-old woman who presented with left bloody nipple discharge in November 2020. She has no significant past medical history. Her family history was notable for breast cancer, although her genetic testing was negative. The patient was found to have ductal carcinoma in situ in the upper outer quadrant. Preoperative MRI was negative for suspicious axillary or internal mammary adenopathy. The patient elected for left mastectomy with sentinel lymph node biopsy, which was performed in December 2020. She had immediate reconstruction using a pre-pectoral tissue expander and acellular dermal matrix. Her final pathology revealed a 3mm focus of invasive ductal carcinoma (ER positive; PR positive, HER2-negative), in addition to the DCIS. Her axillary sentinel lymph nodes were negative. Her final stage was pT1aN0. The patient did not require adjuvant chemotherapy or radiation therapy. Several months after the mastectomy, she sustained a burn to her back requiring skin grafts, delaying her breast reconstruction. In July 2022, the patient elected to have her left breast tissue expander removed and a deep inferior epigastric artery perforator flap performed. The internal mammary vessels were used as the recipient vessels. During the recipient vessel harvest, an incidental left internal mammary lymph node removed and sent for pathology. Results showed presence of invasive ductal carcinoma; 6mm with no extranodal extension (ER positive; PR negative; HER2-negative) (Figure 2). This case was discussed at a multidisciplinary tumor board review, and the patient was recommended for chemotherapy. Radiation was not recommended. The patient received systemic therapy with Adriamycin/Cytoxan and Taxol. She subsequently underwent a right mastopexy, left mound revision, and left nipple reconstruction in 9/2023 (Figure 3). Her PET scan in 8/2024 showed no evidence of disease. She continues on Lupron and Tamoxifen.

Subcategories of N1	Characteristics
N1a	1-3 Axillary lymph nodes
N1b	Internal mammary nodes (sentinel node bx)
N1c	1-3 Axillary nodes AND Internal mammary node (sentinel node bx)
Subcategories of N2	**Characteristics**
N2a	4-9 Axillary lymph nodes
N2b	Internal mammary lymph nodes enlarged and clinically detectable; Detectable on imaging (MRI, PET/CT, Ultrasound); but Axillary lymph nodes are negative
Subcategories of N3	**Characteristics**
N3b	1-9 axillary lymph nodes AND positive internal mammary nodes on imaging OR 4-9 axillary lymph nodes AND internal mammary nodes (sentinel node bx)

Figure 1

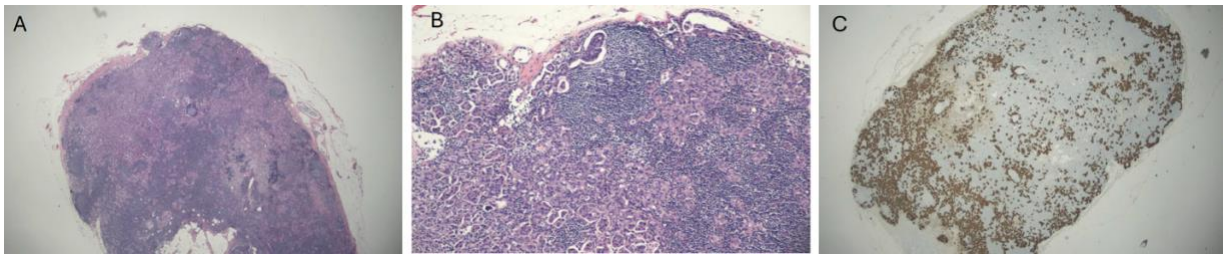

Figure 2: Left internal mammary lymph node. A) Low power showing section of IM node with metastatic carcinoma. B) On higher magnification, the metastatic carcinoma is arranged in small nests and occasional glands consistent with ductal carcinoma. C) Pan-cytokeratin immunostaining has high sensitivity for epithelial tumors. The stain highlights the metastatic ductal carcinoma within the internal mammary lymph node.

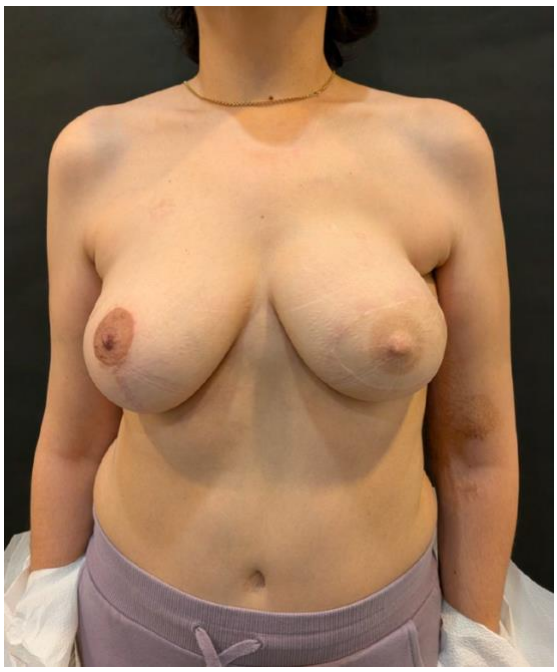

Figure 3: Patient status post left delayed DIEP flap, left nipple reconstruction, left nipple/areola tattooing, and right mastopexy for symmetry, Post-op 5 years from her mastectomy and 3 years after flap reconstruction.

Discussion

In the last decade, there has been significant change in the treatment of "intermediate risk" breast cancer with nodal metastasis (pT1N1, pT2N1) after mastectomy. Several studies have shown the benefit for PMRT in this clinical setting [14,16]. The current National Comprehensive Cancer Network (NCCN) guidelines advise strong consideration of PMRT to the chest wall and comprehensive regional node irradiation in patients with 1-3 positive axillary nodes after mastectomy. Recent data suggests there may be less absolute benefit of radiation given advances in contemporary adjuvant systemic therapy [17].

Kunkler et al showed that receipt of anthracycline-based chemotherapy with or without taxanes, with addition of Traztuzumab in Her2+ patients and endocrine therapy in ER+ patients post-mastectomy chest-wall radiation did not lead to improved overall survival at 10 years 'intermediate risk' patients. Advances in systemic therapy have contributed to deescalation of PMRT in this patient population. What requires further clarification is the stratification of pN1 designation (N1a, N1b, N1c), with particular attention to N1b and N1c which include pathologically involved IMNs. The internal mammary lymph node (IMLN) chain is an important component of the regional nodal basin in breast cancer and its involvement carries prognostic significance; however, it remains one of the most challenging regions to stage accurately and to treat safely. Whereas clinical nodal staging is easily done with preoperative imaging such as MRI, pathologic staging of IM nodes proves surgically demanding.

Jochelson et al. found that 14-16% of patients with Stage IIA and IIIA disease had identifiable internal mammary adenopathy on preoperative MRI and/or PET CT [18]. Preoperative imaging of the IMLNs with ultrasound, CT, MRI, and PET/CT has limited sensitivity and specificity, in part due to small size and deep retrosternal location of these nodes, and pathologic involvement is likely underestimated. Veronesi et al. identified the incidence of internal mammary nodal involvement to be 10.3% and showed significant improvement in survival with radiation to this lymph node basin [19]. Surgical access to the internal mammary chain through standard breast oncologic approaches is technically demanding and associated with added morbidity; thus, surgical biopsy is reserved for highly selected cases with suspicious or enlarged nodes. When IMLNs are clearly enlarged and hypermetabolic on PET imaging, most patients receive PMRT that includes the internal mammary chain as part of regional nodal irradiation. Current NCCN- guidelines support PMRT for patients with one to three positive nodes, and specify that involved internal mammary nodes should be covered when pathologically or radiographically documented. In the absence of convincing radiologic evidence or pathologic confirmation of IMLN disease, many radiation oncologists avoid elective IMLN coverage to minimize cardiopulmonary toxicity. While PMRT and regional nodal irradiation, including IMLN coverage in select high risk cases, consistently reduce locoregional recurrence, some modern series and protocol analyses suggest that the incremental survival benefit of adding elective internal mammary irradiation remains uncertain, leading to practice variation in how aggressively the internal mammary chain is targeted.

Due to the difficulty in diagnosing involvement of internal mammary lymph nodes, we believe that if the NCNN guidelines are universally followed, many IMN basins will be over-radiated. Amongst radiation oncologists, there is still some controversy of including the internal mammary chain in the radiation field of PMRT without clinical evidence and/or biopsy proven disease due to the potential negative consequences on the heart/lungs and negative impact on any potential reconstruction [20]. If we only, use N1a criteria for IM node PMRT, there may be over radiation of the IM node basin. Given the potential for positive IM nodes on incidental biopsy with negative axillary nodes, many patients who would benefit from PMRT may be excluded. There have been many studies that have evaluated the incidental biopsy of internal mammary lymph nodes in the setting of microvascular breast reconstruction using the IMV.

In this context, the reconstructive surgeon's exposure of the IMV during autologous microvascular free flap breast reconstruction has created a unique opportunity for incidental IMLN biopsy, definitively diagnosing metastatic disease to this lymph node basin. Multiple series have reported that routine sampling of the internal mammary nodes encountered during recipient vessel preparation identifies a small, but clinically meaningful number of occult metastases, including cases with otherwise negative axillary staging and normal preoperative imaging.

A systematic review of literature by To et al. showed identification of 166 positive internal mammary nodes in 3732 patients who underwent internal mammary lymph node sampling, resulting in positive detection rate of 4.4% [21]. Of the positive nodes identified, 99 were sampled at the time of mastectomy during immediate reconstruction, and 59 were sampled during delayed reconstruction. Thirty-six (21.7%) of the patients with positive IMLNs had negative axillary lymph nodes. Knowledge of IMLN involvement changed post-operative treatment in approximately 65% of IMN positive patients. Similarly, Karanetz et al. reported a series of 230 patients with 16 cases of positive IMN (7%) during lymph node sampling [13]. Five of these patients (31.3%) had negative axillary sentinel lymph node biopsies. Oscar Ochoa et al. published their review of 2057 consecutive cases where IMN biopsies were performed [22]. They found a total of 28 cases of positive IM nodes (1.3%). In 17 cases (63%) there was a change in the adjuvant therapy. The majority of patients with positive IM nodes in the delayed setting received IM node radiation. Stefan O. P. Hofer et al. presented 3 cases of IMN involvement in the delayed setting [23]. Patient 1 was 24 months after initial mastectomy (axillary LN negative) who had not received any adjuvant therapy. After the IMN positivity, the patient received chemotherapy and radiotherapy. She had no evidence of disease 3 years and 5 months after the delayed flap. Patient 2 was 21 months after initial mastectomy (axillary LN negative) who had received chemotherapy and radiotherapy after initial mastectomy. After the IMN positivity, the patient received Arimidex. She had no evidence of disease 2 years and 4 months after the delayed flap. Patient 3 was 18 months after initial mastectomy (Axillary LN positive) who had received chemotherapy and hormonal therapy. After the IMN positivity, the patient received radiotherapy and hormone therapy. She had bony metastasis.

A review of 573 flaps performed from 2008-2020 at our institution identified 18 cases of positive internal mammary lymph nodes [24]. In 16% of the cases, the IMN was positive in the absence of axillary disease, leading to upstaging and recommendation for radiation therapy. In cases of IMN positivity in presence of axillary disease, the radiation protocol required alteration to include the internal mammary nodal basin. These cases would not have been candidates for PMRT. All these cases were upstaged and further adjuvant therapies were recommended. It is important to note that when positive IMN were discovered in the setting of ALN positivity, the radiation protocols were all modified to include the IMN chain in the radiation field. Our current case represents the case of an incidentally positive IMN discovered at the time of delayed reconstruction 2 years after treatment of a breast carcinoma without axillary disease.

It is imperative to critically select patients for PMRT to help balance local control with the adverse effects of therapy. Post-mastectomy radiation can cause both cardiac and pulmonary complications, with risks increasing proportional to radiation dose. These effects can manifest from months to decades after. There is an increased risk of coronary artery disease, heart failure, pericardial disease, and conduction abnormalities [25]. Radiological pulmonary fibrosis is detected in 89-91% of patients by 12 months, though most cases are grade 1 and asymptomatic. Clinical fibrosis requiring intervention occurs in approximately 16% of patients [26-28].

Radiation therapy significantly increases complications and reduces aesthetic outcomes in autologous breast reconstruction, with the most common negative effects being fat necrosis, flap fibrosis/contracture, volume loss and decreased patient satisfaction [29]. Fat necrosis is increased to 39.5% in the irradiated vs 8.5% in the irradiated group [30]. Flap fibrosis occurred in 9.3% of cases vs 0% in the non-irradiated group. Overall complications were 46.5 % vs 23.7% in the radiated vs non-irradiated groups.

Heller et al. showed that when internal mammary node radiation is administered less than 3 months after reconstruction, the complication rate was 46.8% and reoperation was 48.9% compared to radiation administrated after 3 months 29.3% and 36.6 % respectfully [31]. Ly et al. showed that irradiated flaps had a higher rate of fibrosis (17.0% vs 0%) and multiple complications (9.6% vs 0%) [32]. Looking at the irradiated free-flaps, IMN irradiation was the only factor predictive of complications.

We have included an algorithm of our approach to the management of non-suspicious IMNs encountered during FFBR in the immediate (Figure 4) and delayed settings (Figure 5) In our practice we routinely biopsy any IMN encountered during FFBR with frozen section analysis. If the axilla is negative, we send the IMN for frozen section evaluation. If the IMN frozen section is also negative, then no modifications are made to our free flap. In the patients with known axillary disease, or a positive IMN on frozen section, our flaps are modified in preparation for PMRT. Alterations to the flap may include maintaining a larger volume, including additional perforators, and/or in-setting a larger skin paddle. In cases where PMRT is indicated, we recommend case presentation at a multidisciplinary tumor board to discuss whether radiation can be delayed by 3 months to decrease flap related complications [31].

The value of identifying a negative IMN is of equal importance to identifying metastatic disease to this nodal basin. Knowledge of pathologic IMN negativity can better stratify patients with N1 disease and allow Radiation Oncologists to determine whether de-escalation by omission of IMN radiation is appropriate, minimizing morbidity to the heart and lungs.

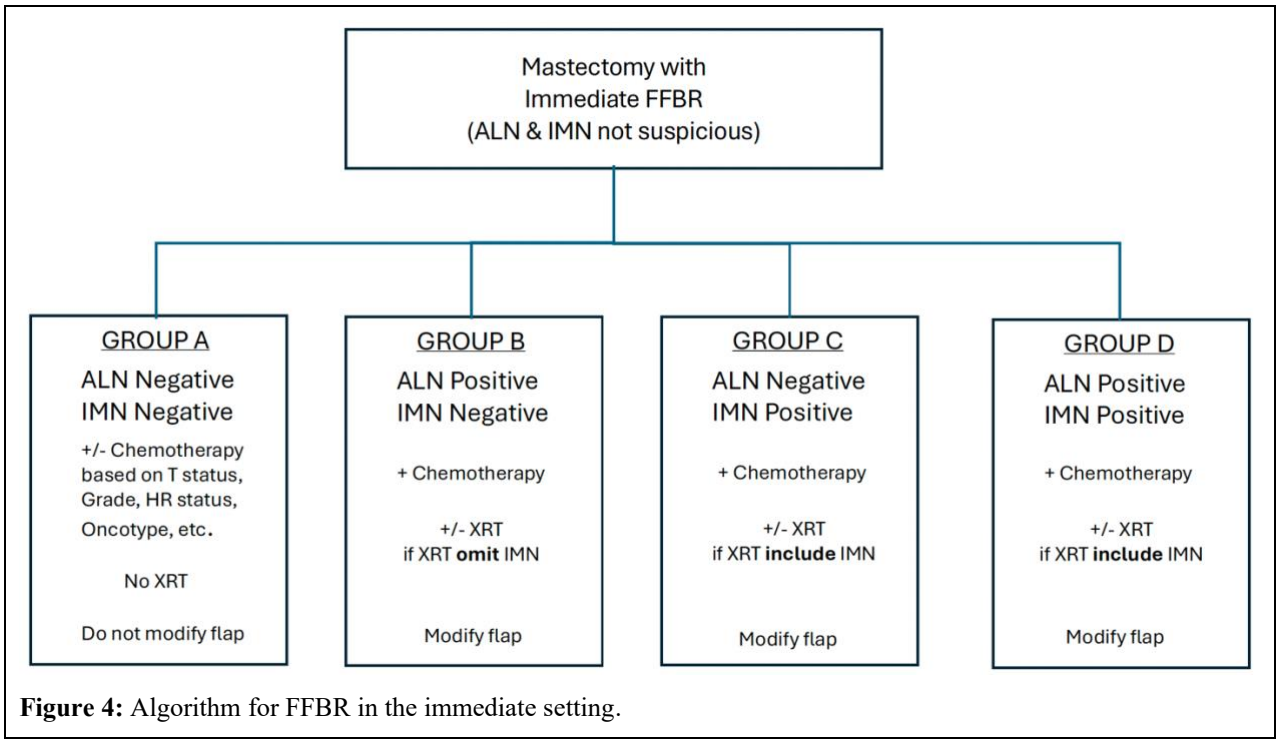

Figure 4: Algorithm for FFBR in the immediate setting.

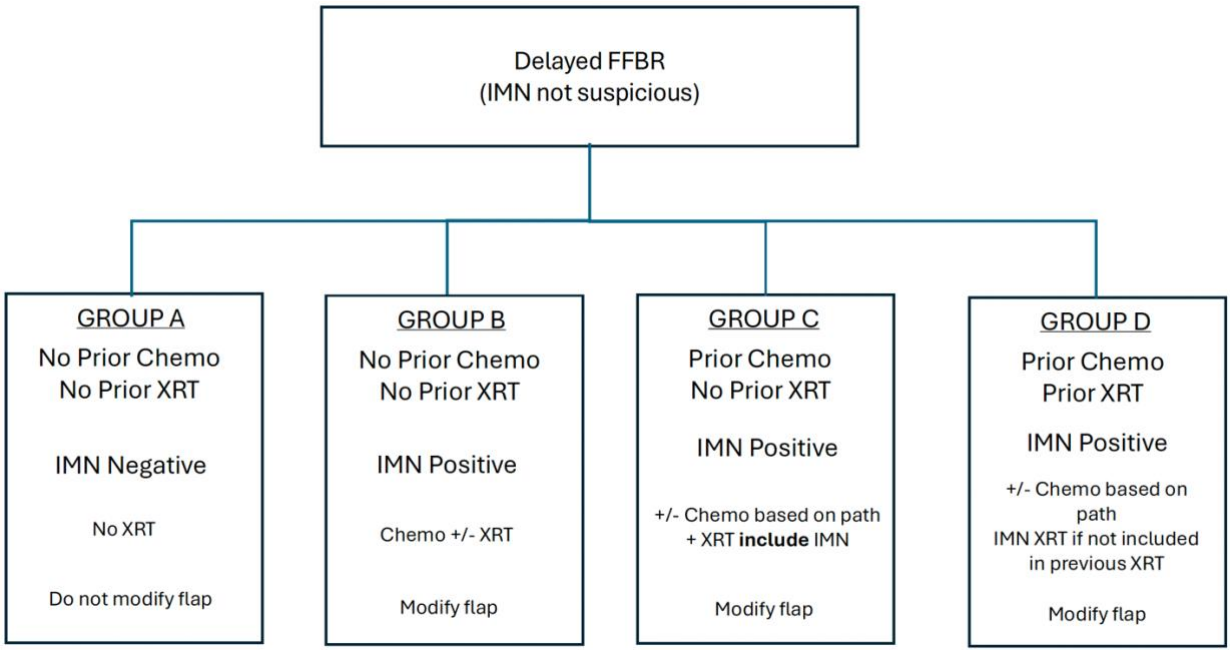

Figure 5: Algorithm for FFBR in the delayed setting.

Conclusion

Opportunistic biopsy of internal mammary lymph nodes during free flap breast reconstruction can uncover otherwise occult regional disease that meaningfully alters staging and adjuvant therapy planning. In this case, incidental internal mammary nodal involvement identified at delayed reconstruction prompted escalation of systemic treatment while allowing thoughtful de-escalation of radiation to protect the autologous flap. These findings support incorporating routine sampling of accessible internal mammary nodes into reconstructive practice to refine nodal classification and individualize post mastectomy radiation decisions. This approach will help identify N1b and N1c nodal disease and guide future trials to determine if PMRT in this setting will improve locoregional control.

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