

There is No Role (yet) for Axillary Sentinel Lymph Node Biopsy in Inflammatory Breast Cancer

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Abstract

Axillary staging has evolved from routine axillary dissection to sentinel node biopsy with selective omission of axillary staging for patients with early-stage, non-inflammatory breast cancer. For patients with inflammatory breast cancer, axillary dissection remains technically and oncologically necessary. However, studies have demonstrated a trend away from guideline concordant axillary surgery for patients with IBC without the literature to support it. Improved understanding of the biology and genetic drivers of the disease, systemic and locoregional therapies, and techniques may offer opportunities to de-escalate axillary surgery. This review summarizes the history and role of axillary surgery in patients with IBC as of January 2026.

Introduction

Breast cancer is the most common cancer among women in the United States ¹. Most subtypes of breast cancer are increasingly and durably curable. Despite this good news, rare and aggressive subtypes remain challenging to treat, not only due to tumor biology, but also the complexities of multidisciplinary care across a variety of clinical settings ². For early-stage breast cancer, recent studies and guidelines have supported the concept of de-escalation. However, for locally advanced breast cancer, such as inflammatory breast cancer (IBC), there is a limited role for de-escalation and perhaps a need to escalate care. Care must be "right sized" for both the patient and the disease. This review summarizes the history of and provides a conceptual and clinically focused synthesis of the role of axillary staging for patients with IBC.

Historical Context

The prognostic role of axillary staging for non-inflammatory breast cancer (non-IBC) was based on the findings of the landmark study NSABP B04 ³. Between 1971 and 1974, women with non-IBC were randomized to radical mastectomy vs total mastectomy with or without adjuvant radiation. It is worth pointing out that the groups who underwent total mastectomy with or without radiation did not undergo any axillary surgery. Despite this, there was no statistically significant difference in survival between the groups. Locoregional approaches that did not involve deliberate removal of lymph nodes demonstrated similar outcomes to those achieved with radical mastectomy; no therapeutic benefit was seen. In summary, NSABP04 demonstrated that axillary surgery for breast cancer provided a prognostic rather than therapeutic benefit.

Despite these findings, axillary staging provided information essential to informing adjuvant therapy decisions, and thus axillary dissection remained an integral part of the operative approach for breast cancer for many years. It was not until Dr. Armando Giuliano and Dr. Don Morton pioneered the sentinel node biopsy (SNB) procedure in the mid-1990s that this changed ⁴. Sentinel node biopsy then became the preferred technique to stage the axilla for women with node-negative breast cancer. Thereafter, the findings of NSABP B04 provided the basis for ACOSOG Z0011 and other studies and extension of the SNB concept to patients with limited axillary disease ⁵⁻¹¹. In ACOSOG Z0011, neither 10-year overall survival nor nodal recurrence differed in the SNB alone group compared to those who underwent axillary lymph node dissection (ALND) (OS: 86.3% SNB vs 83.6% ALND; nodal recurrence: 1.5% SNB vs 0.5% ALND). Further randomized controlled trials have continued to demonstrate similarly low rates of locoregional recurrence with a de-escalated approach to axillary surgery for patients with limited axillary disease. Most recently, guidelines now support the omission of axillary staging in women over 50 years of age with early-stage, clinically node-negative hormone receptor-positive breast cancer ¹²⁻¹⁴. While studies support the de-escalation of axillary surgery for non-IBC, this does not apply to IBC.

IBC has unique clinicopathologic features that make axillary surgery de-escalation technically infeasible. Dermal lymphatic invasion results in lymphatic obstruction and blockage by tumor emboli. This limits the applicability of SNB for patients with IBC. For patients with IBC, modified radical mastectomy (MRM), including Level I and II axillary dissection, rather than mastectomy with attempt at SNB, is recommended. Historically, three retrospective studies ¹⁵⁻¹⁷ and one prospective study ¹⁸ attempted to define the role and feasibility of SNB for patients with IBC (Table 1). Even with immunohistochemistry, these studies demonstrated low sentinel node identification rates and prohibitively high false-negative rates of 68-80% and 18-25%, respectively. Given these findings, axillary dissection remains the preferred staging procedure for patients with IBC.

In addition to technical non-feasibility, axillary dissection for patients with IBC is an essential component of tri-modality care, which includes neoadjuvant systemic therapy (NAST), MRM, and adjuvant radiation to the chest wall and regional lymph node basins ¹⁹. Patients with IBC

treated with a tri-modality approach have 5-year local-regional recurrence rates similar to those of non-IBC patients (IBC 30% (3-year) vs non-IBC 7% (5-year)) ²⁰. In contrast, non-adherence to a tri-modality approach is associated with inferior survival ^{19,21}. Thus, axillary dissection is necessary not only for technical reasons but also to improve outcomes.

Contemporary Therapies and Considerations

Contemporary NAST regimens have resulted in high rates of pathologic complete response (pCR). At the time of diagnosis, up to 90% of patients with IBC have nodal involvement at presentation ²². Following NAST, studies have demonstrated axillary pCR rates of 30%-50% ²³⁻²⁶. A study by Grova et al also found that patients with pathologically negative lymph nodes had a statistically significant improvement in recurrence-free survival compared to those patients with pathologically positive lymph nodes (3-year RFS: 77% vs. 38%, p<0.001) ²⁷. Conversely, patients with residual nodal disease following NAST have been found to have increased 5-year mortality compared to those who achieve axillary pCR. Identifying patients with residual nodal disease provides meaningful prognostication. This supports continued pathologic nodal assessment, which, for patients with IBC, is rendered through axillary dissection.

The prospect of high rates of axillary pCR renews interest in identifying patients who may be candidates for the de-escalation of axillary surgery. Although studies have failed to demonstrate the feasibility of the traditional sentinel node biopsy technique in patients with IBC, alternative staging methods, such as selective removal of the clipped node, may be considered. This resurrects the debate as to whether there is a role for a less extensive axillary surgery for the subset of patients with clinically node-positive IBC who achieve an axillary pCR.

Selective removal of the biopsy-proven clipped node in lieu of SNB may provide a means to determine the feasibility of de-escalating axillary surgery. Localizing the clipped lymph node either by wire or seed allows for selective removal of the biopsy proven node to evaluate the clinical response. This has the potential to bypass the need for lymphatic mapping to identify the sentinel node. To test this hypothesis, Lohani et al. evaluated whether a biopsy-proven clipped axillary lymph node could serve as a surrogate for axillary status in patients with IBC treated

Table 1. Studies on the feasibility of SNB in IBC

Type of study	Author	Date	# pts	Technique	ID Rate	Median # SN	% SN+	FNR
Retrospective	Stearns et al.	1997-2000	8 (34)	Blue dye	75%	2 (range 1-7)	38%	25%
Retrospective	Hidar et al.	2006-2009	20	Blue dye	80%	2 (range 1-3)	56%	18.2%
Prospective	DeSynder et al.	2013-2015	16	Blue dye + radioisotope + US	25%	2.5 (range 1-4)	25% (75% pCR)	-
Retrospective	Karanlik et al.	2010-2018	25	Blue dye +/- radioisotope	68%	1 (range 1-3)	-	20%

FNR: False negative rate

with NAST²⁴. Among 28 patients with retrieved clipped nodes that were pathologically node-negative, only one had an additional positive node identified in the axillary dissection, resulting in a false-negative rate of 4%. This study provides convincing evidence that removal of the clipped node can serve as a surrogate for axillary status in patients with clinically node-positive IBC treated with NAST and who achieve axillary pCR. Selective removal of the biopsy-proven clipped node may be a feasible technique to de-escalate axillary surgery for patients with IBC. However, these findings must be interpreted with caution given the study's retrospective design, limited sample size, and single institution setting, which constrain generalizability.

However, feasibility may not necessarily translate to oncologic safety. Fayanju et al performed a National Cancer Database study between 2010 and 2014 evaluating the association between axillary surgery and overall survival in patients with IBC treated with NAST²⁵. Overall, axillary pCR was associated with improved overall survival. However, when analyzed by clinical nodal status, there was a trend towards improved survival for patients with cN2-3 disease who underwent removal of 10 or more lymph nodes (HR 0.78, 95% CI 0.60-1.01, $p = 0.06$). This study suggests that patients with IBC and a significant pre-treatment nodal burden benefit from axillary dissection even in the setting of pCR. Even if selective removal of the biopsy-proven clipped node is technically feasible for staging the axilla, it may not be appropriate for patients with IBC due to oncologic concerns and potential impact on outcomes as demonstrated by Fayanju et al. Axillary dissection may be necessary for locoregional control and may impact survival.

Deviation from Guideline Concordant Care

Though there is convincing evidence regarding the technical limitations of SNB and the need for tri-modality care, studies have demonstrated reduced rates of guideline-concordant care for patients with IBC²⁸⁻³¹. Regarding axillary surgery, there has been an alarming trend towards de-escalation across breast cancer subtypes. A National Cancer Database (NCDB) study found that rates of SNB for patients with IBC treated between 2012 and 2017 doubled (11% to 22%)²⁸. Another study of the NCDB found that patients with lobular IBC underwent lower rates of axillary dissection compared to those with invasive ductal carcinoma³¹.

A 2023 survey by the American Society of Breast Surgeons identified self-reported practice strategies among members for IBC patients²⁹. Ninety percent of surveyed surgeons reported a tri-modality approach as standard practice; however, nearly one-third of respondents favored SNB or targeted axillary dissection to axillary dissection. More recently, Tadros et al evaluated the NCDB to assess receipt of tri-modality treatment in a contemporary cohort

of patients with IBC treated between 2010 and 2018³⁰. Only about half of patients (51.3%) underwent guideline-concordant surgery, and 20.6% underwent SNB or no axillary surgery. These findings indicate providers' desire to identify a less invasive axillary operative approach, although the literature does not support this. Further studies are needed to elucidate the reasons for axillary de-escalation and whether this derives from extrapolation of findings from non-IBC studies, patient preferences, or other factors.

The drive for de-escalated axillary surgery may stem in part from the desire to prevent breast cancer-related lymphedema (BCRL). BCRL has been associated with taxane-based systemic therapy³², axillary dissection³³, and regional nodal radiation^{32,33}, all of which are part of the tri-modality treatment for IBC. A recent study by Farley et al reported a BCRL rate of 51% in their cohort of IBC patients who underwent tri-modal care, with a mean time to development of 13 months following surgery³⁴. A less invasive operative approach to axillary staging would be of benefit to patients regarding lymphedema risk; however, de-escalated axillary approaches remain investigational. Axillary reverse mapping (ARM) and lymphovenous bypass are techniques developed to re-anastomose the microvasculature in the axilla and have been shown to decrease rates of lymphedema^{35,36}. Though these techniques rely on lymphatic mapping, mapping is performed via the extremity to identify transected arm lymphatic channels rather than lymphatic channels arising from the breast with the goal of preserving arm lymphatics during axillary surgery and thereby mitigating lymphedema risk. Thus, dermal lymphatic obstruction within the breast rendering sentinel node biopsy non-feasible is not an issue. A recent systemic review and meta-analysis including 17 studies found that patients who underwent immediate lymphatic reconstruction were significantly less likely to develop BCRL than those who underwent ALND alone³⁷. While promising, these studies have relatively few patients with short follow up and do not specifically identify whether patients with IBC were included. Nonetheless, a focus on decreasing BCRL rates via lymphovenous bypass or ARM rather than de-escalated axillary surgery may be worthwhile, as the oncologic safety of selective removal of the biopsy-proven clipped node or SNB is being further investigated.

Potential Future Directions

Currently, three prospective trials are evaluating the feasibility and safety of de-escalated axillary surgery for patients with IBC³⁸⁻⁴⁰ (Table 2). Sentinel Lymph Node Biopsy After Neoadjuvant Chemotherapy For Locally Advanced Breast Cancer at Memorial Sloan Kettering Cancer Center (NCT03255577) seeks to evaluate the feasibility of SNB for patients with IBC treated with NAST. Sentinel Lymph

Table 2. Contemporary prospective trials evaluating the role of SNB in IBC

Title	Website	Outcome	Institution
Sentinel Lymph Node Biopsy After Neoadjuvant Chemotherapy in IBC (SYMPHONY)	https://clinicaltrials.gov/study/NCT07080944	Feasibility, DFS, DRFS, BCSS, OS	European Institute of Oncology
Refining Local-Regional Therapy for IBC	https://clinicaltrials.gov/study/NCT04636710	Feasibility, Lymphedema rate, LRRFS, DRFS, DFS	Dana Farber Cancer Institute
Sentinel Lymph Node Biopsy After Neoadjuvant Chemotherapy For Locally Advanced Breast Cancer	https://clinicaltrials.gov/study/NCT03255577	FNR	Memorial Sloan Kettering

DFS: Disease-free survival

DRFS: Distant recurrence-free survival

BCSS: Breast cancer-specific survival

OS: Overall survival

LRRFS: Locoregional recurrence-free survival

DRFS: Distant recurrence-free survival

DFS: Disease-free survival

FNR: False negative rate

Node Biopsy After Neoadjuvant Chemotherapy in IBC (SYMPHONY) through the European Institute of Oncology (NCT07080944) and the Refining Local-Regional Therapy for IBC at Dana Farber (NCT04636710) seek to evaluate survival outcomes, in addition to feasibility, after SNB. Results of these contemporary studies will continue to define the role of axillary surgery for patients with IBC and determine if de-escalation is feasible, safe, or both.

As there is growing momentum towards de-escalation of axillary surgery for non-IBC, we must take a pause when considering this for patients with IBC. While we await the results of ongoing studies and gain further understanding into the biology and genetics of IBC, axillary dissection remains the most technically feasible and oncologically sound surgery for patients with IBC. The integration of prospective studies on axillary surgery, response to NAST, advanced imaging, and molecular profiling will allow for optimized oncologic outcomes while minimizing treatment-related morbidity.

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