

ORIGINAL ARTICLE – BREAST ONCOLOGY

## Selecting Node-Positive Patients for Axillary Downstaging with Neoadjuvant Chemotherapy

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### ABSTRACT

**Background.** Axillary lymph node dissection (ALND) can be avoided in node-positive patients who receive neoadjuvant chemotherapy (NAC) if three or more negative sentinel lymph nodes (SLNs) are retrieved. We evaluate how often node-positive patients avoid ALND with NAC, and identify predictors of identification of three or more SLNs and of nodal pathological complete response (pCR).

**Methods.** From November 2013 to July 2019, all patients with cT1-3, biopsy-proven N1 tumors who converted to cN0 after NAC received SLN biopsy (SLNB) with dual mapping and were identified from a prospectively maintained database.

**Results.** 630 consecutive N1 patients were eligible for axillary downstaging with NAC; 573 (91%) converted to cN0 and had SLNB, and 531 patients (93%) had three or more SLNs identified. Lymphovascular invasion (LVI; odds ratio [OR] 0.46, 95% confidence interval [CI] 0.24–0.87;  $p = 0.02$ ) and increasing body mass index (BMI; OR 0.77, 95% CI 0.62–0.96 per 5-unit increase;  $p = 0.02$ ) were significantly associated with failure to identify three or more SLNs. 255/573 (46%) patients achieved nodal pCR; 237 (41%) had adequate mapping. Factors associated with ALND avoidance included high grade (OR 2.51, 95% CI 1.6–3.94,  $p = 0.001$ ) and receptor status (HR+/HER2- [referent]: OR 1.99, 95% CI

1.15–3.46 [ $p = 0.01$ ] for HR-/HER2-, OR 3.93, 95% CI 2.40–6.44 [ $p < 0.001$ ] for HR+/HER2+, and OR 8.24, 95% CI 4.16–16.3 [ $p < 0.001$ ] for HR-/HER2+). LVI was associated with a lower likelihood of avoiding ALND (OR 0.28, 95% CI 0.18–0.43;  $p < 0.001$ ).

**Conclusions.** ALND was avoided in 41% of cN1 patients after NAC. Increased BMI and LVI were associated with lower retrieval rates of three or more SLNs. ALND avoidance rates varied with receptor status, grade, and LVI. These factors help select patients most likely to avoid ALND.

Indications for neoadjuvant chemotherapy (NAC) have evolved over time.<sup>1</sup> Currently, in patients who are clinically node positive at presentation, NAC is administered with the aim of achieving nodal pathological complete response (pCR) and de-escalating axillary surgery.<sup>2–5</sup> The rate of nodal response depends on tumor biology, with lower rates in hormone receptor positive (HR+)/human epidermal growth factor receptor 2 negative (HER2-) tumors, and higher rates in triple negative (TN) and HER2 positive (HER2+) tumors.<sup>3,6,7</sup>

Patients who become clinically node negative (cN0) after NAC are eligible for sentinel lymph node biopsy (SLNB). Four prospective multi-institutional trials have examined the accuracy of SLNB after NAC in patients who were clinically node positive at presentation.<sup>8–11</sup> The sentinel lymph node (SLN) identification rate in these trials ranged from 79.5 to 92.7%, and the false-negative rate (FNR) ranged from 11.9 to 14.2%, exceeding the 10% threshold considered to be clinically acceptable. All trials consistently showed that the accuracy of SLNB increased with the number of SLNs retrieved, and when three or more

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SLNs were removed and dual tracer mapping was used, the FNPs were uniformly  $< 10\%$ .<sup>8–12</sup> Since the publication of these trials, the use of SLNB after NAC for node-positive patients at presentation has increased,<sup>13–16</sup> but little information is available on how often axillary lymph node dissection (ALND) is avoided with the use of NAC in patients presenting with nodal metastases. A previous report from our institution described our experience with 128 consecutive node-positive patients receiving NAC and found that 48% had identification of three or more SLNs and nodal pathologic complete response (pCR), and were able to avoid ALND.<sup>3</sup> In this study, we sought to confirm this finding in a larger cohort of node-positive patients receiving NAC, and to identify clinicopathological factors associated with finding three or more SLNs and achieving nodal pCR, the two mandatory conditions required to safely avoid ALND.

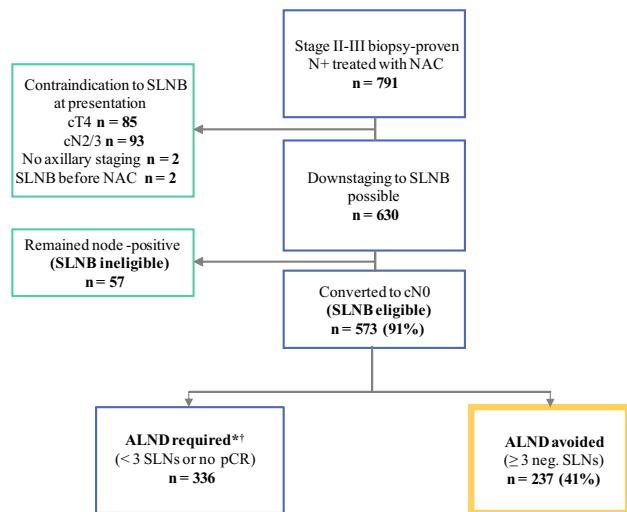
## METHODS

Beginning in 2013, clinically node-positive patients with biopsy-proven metastases treated at our institution received NAC with the intention of downstaging the axilla to avoid ALND. Those who presented with cT1–3 N1 disease, who converted to cN0 on physical exam, were eligible for SLNB. Sonographic evaluation of the axilla after NAC was not routine, and nodal clipping was not routinely employed. In patients presenting with clips placed in metastatic nodes elsewhere, retrieval of the clipped node was not required. Clinical T4 and cN2/3 patients were considered ineligible for SLNB irrespective of their response to NAC. SLNB was performed with dual tracer (technetium-99m sulfur colloid and isosulfan blue dye) in all patients. Sentinel nodes were defined as hot, blue, or palpably abnormal nodes. Based on the results of clinical trials demonstrating FNPs of  $< 10\%$  with retrieval of three or more SLNs, ALND was omitted if three or more SLNs were identified (adequate mapping) and nodal pCR in the SLNs was achieved.

Frozen section of the lymph nodes was performed intraoperatively, followed by routine histological assessment; immunohistochemistry was not routinely performed. Macrometastases, micrometastases, and isolated tumor cells in the SLN post-NAC were all considered indications for ALND.

After Institutional Review Board approval, we queried our prospectively maintained database to identify consecutive stage II–III breast cancer patients with biopsy-proven

nodal metastasis at presentation. Patients with a prior history of ipsilateral breast cancer were excluded. The majority of patients (85%) received dose-dense anthracycline and taxane-based chemotherapy regimens, 6% received concomitant platinum salts, and all HER2+ patients received trastuzumab and pertuzumab. Of patients who converted to cN0 and had SLNB, we compared those who had three or more SLNs identified (adequate mapping) with those who did not (inadequate mapping). We also compared those who had three or more SLNs and nodal pCR who avoided ALND versus all others. Demographic and clinical characteristics were compared between groups using Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. Univariate and multivariable logistic regression was used to estimate the odds of finding three or more SLNs, and the odds of finding three or more SLNs and having nodal pCR. All tests were evaluated for statistical significance at alpha level 0.05. Statistical analysis was performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).



**FIG. 1** Study flowchart. *NAC* neoadjuvant chemotherapy, *cT* clinical tumor stage, *cN* clinical nodal stage, *SLNB* sentinel lymph node biopsy, *SLNs* sentinel lymph nodes, *pCR* pathologic complete response, *ALND* axillary lymph node dissection, *NAC* neoadjuvant chemotherapy \*Thirty-three patients were randomized to axillary radiation therapy in the Alliance A011202 trial. †ALND was deferred for 27 cases with residual disease by either patient preference or clinical judgment (14 patients had isolated tumor cells, 10 had micrometastases, and 3 had macrometastases)

**TABLE 1** Clinicopathological features

	Overall (n = 573)	< 3 SLNs retrieved (n = 42)	≥ 3 SLNs retrieved (n = 531)	p value <sup>a</sup>	ALND avoided (n = 237)	ALND required (n = 336)	p value <sup>a</sup>
Age, years	49 (24–82)	53 (36–78)	49 (24–82)	0.07	49 (24–82)	50 (27–78)	0.08
BMI, kg/m <sup>2</sup>	25.8 (15.9–68.3)	28.4 (17.4–47.5)	25.7 (15.9–68.2)	<b>0.01</b>	25.6 (16.9–68.2)	26.1 (15.9–47.5)	0.24
Palpable node at presentation				0.84			0.55
No	146	10 (7)	136 (93)		55 (38)	91 (62)	
Borderline	13	0 (0)	13 (100)		6 (46)	7 (54)	
Yes	414	32 (8)	382 (92)		176 (43)	238 (57)	
Palpable tumor at presentation				0.19			0.23
No	59	6 (10)	53 (90)		26 (44)	33 (56)	
Borderline	12	2 (17)	10 (83)		2 (17)	10 (83)	
Yes	502	34 (7)	468 (93)		209 (42)	293 (58)	
Clinical T at presentation				<b>0.03</b>			0.85
1	110	6 (5)	104 (95)		42 (38)	68 (62)	
2	334	19 (6)	315 (94)		141 (42)	193 (57)	
3	125	16 (13)	109 (87)		52 (41)	73 (58)	
X	4	1 (25)	3 (75)		2 (50)	2 (50)	
Subtype				0.55			<b>&lt; 0.001</b>
HR+/HER2–	241	14 (6)	227 (94)		49 (20)	192 (80)	
HR+/HER2+	138	13 (9)	125 (91)		76 (55)	62 (45)	
HR-/HER2+	80	7 (9)	73 (91)		62 (78)	18 (23)	
HR-/HER2–	114	8 (7)	106 (93)		50 (44)	64 (56)	
Histology				0.60			<b>0.002</b>
Ductal	437	31 (7)	406 (93)		194 (44)	243 (56)	
Lobular and mixed	41	2 (5)	39 (95)		7 (17)	34 (83)	
Micropapillary and mixed	36	5 (14)	31 (86)		10 (28)	26 (72)	
Apocrine and mixed	40	3 (8)	37 (93)		20 (50)	20 (50)	
Other	19	1 (5)	18 (95)		6 (32)	13 (68)	
LVI <sup>b</sup>	213	23 (11)	190 (89)	<b>0.02</b>	46 (22)	167 (78)	<b>&lt; 0.001</b>
Grade				0.72			<b>&lt; 0.001</b>
I	7	0 (0)	7 (100)		1 (14)	6 (86)	
II	228	19 (8)	209 (92)		55 (24)	173 (76)	
III	338	23 (7)	315 (93)		181 (54)	157 (46)	

Data are expressed as frequency (row percentage) for categorical variables and median (range) for continuous variables

Statistically significant values are indicated in bold

SLNs sentinel lymph nodes, BMI body mass index, HR hormone receptor, LVI lymphovascular invasion, ALND axillary lymph node dissection, HR hormone receptor, HER2 human epidermal growth factor receptor

<sup>a</sup>Results from Fisher's exact test for categorical variables and Wilcoxon rank-sum test for continuous variables

<sup>b</sup>LVI was present on core biopsy or final biopsy

## RESULTS

Between November 2013 and July 2019, 791 biopsy-proven node-positive patients were treated with NAC; 630 patients had cN1 disease and were eligible for downstaging

to SLNB. Of these, 573 (91%) converted to cN0 and had SLNB, and comprised the primary study group (Fig. 1). Table 1 shows the clinicopathological characteristics of the entire cohort and compares patients with three or more SLNs identified versus those with fewer than three SLNs

identified, as well as patients who were spared ALND versus those who were not. Median patient age was 49 years (range 24–82 years) and median body mass index (BMI) was 25.8 kg/m<sup>2</sup> (range 15.9–68.3 kg/m<sup>2</sup>). The majority of patients (58%) had cT2 tumors. Clinically palpable axillary adenopathy at presentation was present in 72% of cases. Forty-two percent of patients had HR+/HER2– tumors, 38% had HER2+ tumors, and 20% had TN tumors. Ninety-nine percent of tumors were poorly or moderately differentiated, and lymphovascular invasion (LVI) was present on core biopsy ( $n = 101$ ) or at final pathology ( $n = 112$ ) in 213 (37%) tumors.

#### *Predictors of Retrieval of Three or More Sentinel Lymph Nodes*

Inadequate mapping, defined as identification of fewer than three SLNs, occurred in 42 (7%) patients; failed mapping was rare and occurred in only 11 (2%) cases. In the inadequate-mapping group, the median number of SLNs removed was 1 (range 0–2). Three or more SLNs were found in 531 (93%) cases, with a median of four SLNs retrieved (range 3–10). While the average number of SLNs retrieved varied by surgeon, all 16 surgeons included in the study removed, on average, more than three SLNs.

On univariate analysis, patients with inadequate mapping had higher BMI (median BMI 28.4 kg/m<sup>2</sup> vs. 25.7 kg/m<sup>2</sup>;  $p = 0.01$ ), were more likely to present with T3 tumors (38% vs. 21%;  $p = 0.03$ ), and were more likely to have LVI (55% vs. 36%;  $p = 0.02$ ). Patients with inadequate mapping were older (median age 53 vs. 49 years), but the difference did not reach statistical significance ( $p = 0.07$ ). The presence of palpable nodes at presentation did not impact the accuracy of mapping ( $p = 0.84$ ) (Table 1). On multivariable analysis, BMI and LVI remained independently associated with decreased odds of retrieving three or more SLNs (odds ratio [OR] 0.77, 95% confidence interval [CI] 0.62–0.96, and OR 0.46, 95% CI 0.24–0.87, respectively) (Table 2).

#### *Predictors of Avoiding Axillary Lymph Node Dissection*

Overall, 255/573 (46%) patients achieved nodal pCR. Of these, 18 had inadequate mapping and 237 (or 41% of the study cohort) had adequate mapping and were able to avoid ALND. Patients with ductal and apocrine tumors were more likely to avoid ALND compared with those with lobular and micropapillary histology (44% and 50% vs. 17% and 28%, respectively;  $p = 0.002$ ). Omission of ALND occurred in 20% of HR+/HER2– tumors, 44% of TN tumors, 55% of HR+/HER2+ tumors, and 78% of HR-/HER2+ tumors ( $p < 0.001$ ). LVI was more often present in patients requiring ALND than in those who did

not require ALND (78% vs. 22%;  $p < 0.001$ ), and high-grade tumors were more frequently associated with avoidance of ALND than moderate- and low-grade tumors (54% vs. 24% and 14%, respectively;  $p < 0.001$ ) (Table 1). On multivariable analysis, factors that remained independently associated with avoidance of ALND were high grade (OR 2.51, 95% CI 1.6–3.94;  $p < 0.001$ ) and receptor status (HR+/HER2– [referent]: OR 1.99, 95% CI 1.15–3.46,  $p = 0.01$  for HR-/HER2–; OR 3.93, 95% CI 2.40–6.44,  $p < 0.001$  for HR+/HER2+, and OR 8.24, 95% CI 4.16–16.3,  $p < 0.001$  for HR-/HER2+), while LVI (OR 0.28, 95% CI 0.18–0.43;  $p < 0.001$ ) was associated with a lower likelihood of avoiding ALND (Table 3).

## DISCUSSION

In this large series of biopsy-proven, stage II–III, node-positive breast cancer patients undergoing NAC, the rate of adequate SLN mapping post-NAC, defined as the identification of three or more SLNs, was 93%. This is higher than the rate reported in previous studies. In the SENTinel NeoAdjuvant (SENTINA) and American College of Surgeons Oncology Group (ACOSOG) Z1071 trials, three or more SLNs were found in only 34% and 57%<sup>8,9</sup> of cases, respectively. In a recent study from Dana-Farber Cancer Institute/Brigham and Women's Cancer Center (DFCI/BWCC) assessing the impact of residual disease burden on SLNB outcome, Laws et al.<sup>17</sup> reported a rate of adequate mapping of 67% among cN1 patients after NAC. In a previous study from our institution evaluating the effect of clinical nodal status on the number of SLNs retrieved after NAC, Baker et al.<sup>20</sup> reported that the median number of SLNs retrieved after NAC in cN1 patients was four (range 1–14), and that the rate was stable over the 3-year study period; this is in line with the number of SLNs retrieved in the upfront surgery setting (mean 2.8, range 1–25).<sup>18,19</sup> The low rates of identification of three or more SLNs in the SENTINA and ACOSOG Z1071 studies may be attributed to the use of dual mapping in only 28% and 79% of cases, respectively. Additionally, in the ACOSOG Z1071 trial, surgeons were only required to retrieve two SLNs, and in the SENTINA trial, a minimum number of SLNs was not pre-specified. In light of the protocol specifications and the requirement for ALND in all patients, surgeons may not have been inclined to continue to search for and remove higher numbers of SLNs. Considering the high frequency of retrieval of three or more SLNs at our institution and the reproducibility of this technique among surgeons, SLNB with dual tracer is our preferred approach to avoid ALND in cN1 patients after NAC.

**TABLE 2** Univariate and multivariable associations between clinicopathological factors and the odds of finding three or more SLNs

	Univariate		Multivariable	
	OR (95% CI)	p value	OR (95% CI)	p value
Age, per 5-year increase	0.88 (0.77–1.01)	0.07		
BMI, per 5-unit increase	0.77 (0.62–0.96)	<b>0.02</b>	0.77 (0.62–0.96)	<b>0.02</b>
Palpable node at presentation	0.91 (0.43–1.90)	0.80		
Palpable tumor at presentation	1.50 (0.61–3.73)	0.38		
cT at presentation; Ref: 1				
2	0.96 (0.37–2.46)	0.93		
3	0.39 (0.15–1.04)	0.06		
Subtype; Ref: HR+/HER2–				
HR+/HER2+	0.59 (0.27–1.30)	0.19		
HR-/HER2+	0.64 (0.25–1.65)	0.36		
HR-/HER2–	0.82 (0.33–2.01)	0.66		
Histology; Ref: ductal				
Lobular and mixed	0.94 (0.27–3.23)	0.92		
Micropapillary and mixed	1.49 (0.34–6.46)	0.60		
Apocrine and mixed	0.47 (0.17–1.30)	0.15		
Other	1.37 (0.18–10.6)	0.76		
LVI	0.46 (0.24–0.87)	<b>0.02</b>	0.46 (0.24–0.87)	<b>0.02</b>
Grade III; Ref: I/II	1.20 (0.64–2.27)	0.56		

Statistically significant values are indicated in bold

OR odds ratio, CI confidence interval, BMI body mass index, HR hormone receptor, HER2 human epidermal growth factor receptor 2, LVI lymphovascular invasion

**TABLE 3** Univariate and multivariable associations between clinicopathological factors and the odds of avoiding ALND (when three or more SLNs are retrieved and nodal pCR is achieved)

	Univariate		Multivariable	
	OR (95% CI)	p value	OR (95% CI)	p value
Age, per 5-year increase	0.93 (0.87–1.00)	0.07		
BMI, per 5-unit increase	0.95 (0.83–1.09)	0.46		
Palpable node at presentation	1.23 (0.84–1.81)	0.30		
Palpable tumor at presentation	0.88 (0.51–1.52)	0.66		
cT at presentation; Ref: 1				
2	1.18 (0.76–1.84)	0.46		
3	1.15 (0.68–1.95)	0.59		
Subtype; Ref: HR+/HER2–				
HR+/HER2+	4.80 (3.03–7.60)	< <b>0.001</b>	3.93 (2.40–6.44)	< <b>0.001</b>
HR-/HER2+	13.5 (7.32–24.9)	< <b>0.001</b>	8.24 (4.16–16.3)	< <b>0.001</b>
HR-/HER2–	3.06 (1.88–4.97)	< <b>0.001</b>	1.99 (1.15–3.46)	<b>0.01</b>
Histology; Ref: ductal				
Lobular and mixed	1.25 (0.66–2.39)	0.50	0.75 (0.35–1.62)	0.47
Micropapillary and mixed	0.26 (0.11–0.59)	<b>0.001</b>	0.46 (0.19–1.15)	0.10
Apocrine and mixed	0.48 (0.23–1.02)	0.06	0.63 (0.25–1.60)	0.33
Other	0.58 (0.22–1.55)	0.28	0.55 (0.19–1.63)	0.28
LVI	0.24 (0.17–0.36)	< <b>0.001</b>	0.28 (0.18–0.43)	< <b>0.001</b>
Grade III; Ref: I/II	3.69 (2.55–5.33)	< <b>0.001</b>	2.51 (1.60–3.94)	< <b>0.001</b>

Statistically significant values are indicated in bold

ALND axillary lymph node dissection, SLNs sentinel lymph nodes, pCR pathologic complete response, OR odds ratio, CI confidence interval, BMI body mass index, HR hormone receptor, HER2 human epidermal growth factor receptor, LVI lymphovascular invasion

In the Baker et al.<sup>20</sup> study, the only two significant predictors of finding three or more SLNs after NAC were younger age (< 50 years) and cN1 status at presentation. In the study from the DFCI/BWCC group, the median number of SLNs was also four, and older age and low grade were the only significant predictors of inadequate mapping.<sup>17</sup> In our study, older age was associated with decreased odds of adequate mapping, but this did not reach statistical significance (OR 0.88, 95% CI 0.77–1.01;  $p = 0.07$ ). On multivariable analysis, the only significant predictors of inadequate mapping were higher BMI and LVI. The influence of BMI on SLN mapping has been described in the upfront surgery setting,<sup>21,22</sup> with decreased lymphatic flow due to the increased fatty tissue in the breast hypothesized as the mechanism.<sup>22</sup> The relationship between LVI and the number of SLNs identified is less well described. In the SENTINA trial, the absence of LVI was not predictive of a higher SLN detection rate,<sup>9</sup> and studies of other types of primary cancers, such as melanoma, have found the presence of LVI to be associated with an increased number of SLNs.<sup>23</sup> In the setting of NAC, it is possible that the death of tumor cells in lymphatic vessels leads to fibrosis of these lymphatic channels with failure to take up blue dye or radioactivity, leading to identification of a fewer number of SLNs.

Although the exact mechanisms behind the association of higher BMI and LVI with failure to achieve adequate mapping remain to be elucidated, patients with these characteristics have a significantly increased risk of inadequate mapping. Of the 42 cases with inadequate mapping in our study, 18 (43%) had nodal pCR and could have been potentially spared ALND. Alternative mapping strategies independent of the number of SLNs retrieved may be useful in patients with preoperative characteristics unfavorable for SLNB mapping. In an unplanned analysis of the ACOSOG Z1071 study, the FNR for patients in whom the metastatic node was clipped at diagnosis and retrieved at the time of surgery was 6.8%.<sup>24</sup> The combination of SLNB with retrieval of the clipped node, termed targeted axillary dissection (TAD), has also been shown to be associated with a low FNR.<sup>25</sup> This approach is not without technical challenges, as failure to identify the clip, due to migration into the perinodal fat, has been reported in 3–30% of cases, with variation according to the localization technique used.<sup>26–28</sup> Nevertheless, TAD may be useful in groups of patients at increased risk for inadequate mapping. Unfortunately, the concordance between pathological prognostic findings on core biopsy and final specimen is limited,<sup>29</sup> and although LVI was the only pathological factor predictive of both inadequate mapping and failure to avoid ALND, it was present on core biopsy in only 101/213 cases (47%), which limits the application of our findings.

Among patients with adequate mapping, 41% achieved nodal pCR and were spared ALND. Our rate of nodal pCR is consistent with the results of the ACOSOG Z1071 trial.<sup>30</sup> We identified HER2+ and TN receptor status, high grade, ductal and apocrine histology, and absence of LVI as predictors of ALND avoidance. As reported in other studies, patients with HER2+ and TN tumors were more likely to achieve nodal pCR and be spared ALND compared with HR+/HER2– tumors.<sup>3,7,30</sup> Dominici et al.<sup>7</sup> reported a nodal downstaging rate of 74% in HER2+ patients treated with trastuzumab only, with no difference based on estrogen receptor status. Our downstaging rate in the HER2+ group, where all patients received dual anti-HER2 therapy, was 63%, with a significant difference according to the hormone receptor status (78% in the HR-/HER2+ group vs. 55% in the HR+/HER2+ group;  $p = 0.001$ ). This is consistent with our previous report<sup>3</sup> and with the results of the NeoSphere trial that showed a higher rate of pCR in HR–, HER2+ tumors treated with dual anti-HER2 therapy.<sup>31</sup> In univariate analysis, micropapillary histology was associated with a lower rate of nodal pCR (OR 0.26, 95% CI 0.11–0.59;  $p = 0.001$ ), but this did not remain significant in multivariable analysis, likely due to the limited number of cases.<sup>32</sup> Micropapillary tumors are known to be associated with poor prognosis<sup>33</sup> and poor response to NAC.<sup>32</sup> In our study, the rate of ALND avoidance in this histotype was low, at 28%, second only to the rate of ALND avoidance in the lobular histotype (17%).

In this study, we demonstrate that, with standard surgical techniques and modern NAC regimens, more than 40% of clinically node-positive patients avoided ALND. This rate is likely to increase with the use of new agents, alone or in combination with chemotherapy, which have been shown to increase the rate of pCR.<sup>34,35</sup> Although prospective trials have documented the accuracy of SLN biopsy after NAC, all patients underwent ALND to determine the FNR of the procedure. To the best of our knowledge, this is the first large study examining how often ALND is avoided in node-positive patients with the NAC approach, and examining an optimized SLNB procedure with the use of dual mapping and retrieval of three or more SLNs, as endorsed by national and international guidelines as well as expert panels.<sup>36–38</sup>

The strengths of this study include its large sample size, use of homogenous preoperative systemic therapy regimens, and standardized pathologic assessment and operative techniques, while the limitations of this study include the fact that it was carried out at a single institution with dedicated surgeons and pathologists in which the SLNB procedure is highly standardized, which may limit generalizability. Data on regional recurrence after omitting

ALND in patients who achieve nodal pCR are limited.<sup>39</sup> Follow-up of this cohort will provide further evidence on the safety of this approach.

## CONCLUSIONS

In this large consecutive cohort of node-positive patients treated with NAC, three or more SLNs were retrieved in 93% of cN0 patients post-NAC with the use of dual tracer mapping. ALND was avoided in 41% of patients who achieved nodal pCR and had three or more SLNs retrieved. Women with higher BMI and LVI had lower rates of adequate mapping and represent a group of patients in whom retrieval of the clipped lymph node may help to reduce the need for ALND. The correlation of LVI with axillary downstaging and SLNB identification rate should be further explored. Our results demonstrate that NAC reduces the need for ALND in clinically node-positive patients of all subtypes.

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