

# Breast cancer surgery under the shadow of COVID-19: Quest for optimal axillary management after neo-adjuvant chemotherapy

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The disastrous COVID-19 pandemic caused great challenges in regard to medical and surgical management worldwide. Surgeons are currently responsible to serve infected patients and to treat non-deferrable oncologic cases in an optimal way. In all circumstances, oncologic safety must be the priority. Particularly in patients converted to cN0 after neo-adjuvant chemotherapy (NAC), sentinel lymph node biopsy (SLNB) is an option; however, the evaluation of axilla is a challenge.

## 1 | STUDY DESIGN

After COVID-19 outbreak, lymphoscintigraphic evaluations were canceled and we initiated a modified algorithm of targeted axillary dissection (TAD; marking metastatic node with a clip before NAC and resecting node during SLNB) and SLNB via dual-agent mapping of ICG (indocyanine green) and patent blue dye (PB) to spare cN0 patients from devastating consequences of ALND at our institution. Herein, our data about this hybrid technique without radiocolloid are presented. As primary outcome, rate of SLN identification, and as secondary outcome number, pathologic status and discordance between SLNs and clipped nodes were evaluated.

## 2 | SURGICAL TECHNIQUE

After induction of anesthesia, periareolar injection of fluorescent ICG (2 mL-2.5 mg/mL) (DID; Samsung) and PB was followed by massage. Once fluorescence visualized (SPY; Novadaq) in axilla, the

precise spot was marked to design incision. With ICG detecting probe (Europrobe3), fluorescent avid nodes excised with attention to ligate each lymphatic. Specimen radiography was coupled with second-look US in case of the absence of clip in imaging. Frozen section (FS) analysis of SLNs was standard surgical practice. Fluorescent and/or blue nodes were defined as "sentinel" irrelevant to clip presence.

## 3 | RESULTS

The clinicopathologic characteristics of 12 cN0 patients are summarized in Table 1. SLN was identifiable with ICG + PB in 10/12 patients (83%). The median lymph node harvest was 4 nodes (range 0-12). The clipped node was one of SLNs in 10 cases (83%). In two out of 12 cases, clipped nodes were found via second-look US. The dual tracer mapping with TAD indicated ALND for four patients (33%) due to failure of dual-agent mapping in two cases, positive SLNs in FS for one case, and in final pathology for another case. In ten cases,  $\geq 3$  SLNs were identified. There was pathologic concordance between clipped and SLNs in 9 out of 10 cases (90%). Dual mapping method identified totally 39 SLNs. Three SLNs were positive in FS and 6 out of 39 SLNs in final pathology. In regard to metastasis, 50% was only ICG, 33% was both ICG and PB, and 16% was only PB positive (Table 2). The overall FNR for dual-agent mapping was 25% on FS, and sensitivity for nodal metastasis was 75% (Table 3).

Under the siege of COVID-19, various resources had to be sacrificed to save lives. However, we have to serve our best to cancer

**TABLE 1** Clinicopathologic characteristics

Characteristics	
Mean Age	46 (range:30-60)
Menopausal status	
Premenopausal	6
Postmenopausal	6
Histology	
Invasive ductal carcinoma	8
Invasive lobular carcinoma	3
Mucinous	1
Breast Surgery	
Breast-conserving Surgery	10
Mastectomy	2
Axillary surgery	
SLNB	9
SLNB + ALND	3
Pathologic T stage	
pCR	3
Non-pCR	9
Pathologic N stage	
pCR	8
Non-pCR	4
Lymphovascular Invasion	
Positive	4
Negative	8
Subtype	
HR-positive	5
HER2-positive	3
TNBC	2
Ki 67 (%)	
<20%	3
>20%	9
Grade	
I	3
II	7
III	2

Abbreviations: ALND, axillary lymph node dissection; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; N, nodal, pCR, pathologic complete response; PR, progesterone receptor; SLNB, sentinel lymph node biopsy; T, tumor.

patients. Fluorescent imaging is a competing technology challenging the standard procedure of SLNB with radioactivity in centers without accessibility to lymphoscintigraphy with the limited data in the setting of NAC.<sup>1</sup> The most controversial issue in regard to SLNB after NAC is FNR. Prospective trials encouraged dual mapping, achieving at least 3 SLNs, incorporating immunohistochemistry and TAD to decrease FNR (<10%).<sup>2-5</sup> However, ALND is the only option when failed to identify clip intraoperatively. This issue could be

**TABLE 2** Number of SLNs identified via ICG, PB, and clip

SLN	Metastatic	Non-metastatic	N (%)
ICG + PB+	2 (33%)	8 (24%)	10 (25%)
ICG + PB-	3 (50%)	12 (36%)	15 (38%)
ICG-PB+	1 (16%)	13 (39%)	14 (35%)
ICG-PB-Clip+	2 patients excluded (ALND)	-	-
Total SLN	6 (100%)	33 (100%)	39 (%100)

Abbreviations: ALND, axillary lymph node dissection; ICG Indocyanine green; PB patent blue; SLN sentinel lymph node.

**TABLE 3** SLN harvest to detect axillary metastasis on intraoperative pathology

Characteristic	ICG + PB (n = 12)	SLN:<3 nodes (n = 2)	SLN:≥3 nodes (n = 10)	Clipped node alone (n = 12)
Frozen Section Analysis				
True positives	3	0	2	3
False positives	0	0	0	0
True negatives	8	0	8	8
False negatives	1	2	0	1
Sensitivity for nodal metastasis	75%	-	%100	75%
False-negative rate (%)	25%	%100	-	25%
Final Pathologic Analysis				
True positives	4			
False positives	0			
True negatives	8			
False negatives	0			
Sensitivity for nodal metastasis	%100			
False-negative rate (%)	0			

Abbreviations: ICG, Indocyanine green; PB patent blue; SLN sentinel lymph node.

addressed via intraoperative sonography which helped us to avoid ALND. Moreover, confirmation of metastasis in clipped node via FS generated ALND indication and spared us from secondary surgery. In addition, the recommended SLN harvest was achieved to optimize FNR which was 25% in FS, decreasing to null when combined with TAD in final pathology. ICG mapping determined metastasis in 83% of our cases. However, PB achieved this goal in 49%. The limitations of presented study with low sample size and no follow-up require interpreting results with caution. Moreover, higher number of SLNs identified with ICG might have possible side effects including lymphedema.

NAC has potential to deescalate axillary surgery in patients converted to cNO. Therefore, techniques designed to predict axillary status during COVID-19 pandemic have great value. In this regard,

clipping metastatic node, dual-agent mapping, and intraoperative sonography are vital. Whether the replacement of radiocolloid with ICG in this setting will depend upon its validation via larger series, the demonstration of clinical advantages of presented hybrid technique, in terms of yielding adequate SLN harvest and acceptable FNR, is considerable. Shared decision-making with patients is of paramount importance.

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