

Prospective Study of Axillary Reverse Mapping Using Indocyanine Green in Breast Cancer

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ABSTRACT

Background: Axillary Reverse Mapping (ARM) is an emerging technique aimed at preserving upper limb lymphatic drainage during axillary lymph node dissection (ALND) or sentinel lymph node biopsy (SLNB) in breast cancer surgery. The use of Indocyanine green (ICG), a near infrared fluorescent dye, has enhanced the visualization and identification of lymphatic pathways, potentially reducing the risk of lymphedema.

Methods: A prospective study using ICG for ARM, injecting into web space of ipsilateral upper limb intraoperatively. Near infrared fluorescence imaging was used intraoperatively to trace the lymphatic drainage pathways from the arm. Arm lymphatics and nodes were identified and FNAC and excision of node in the template of ALND done to assess the oncological safety.

Results: The application of ICG based ARM facilitated 96% of visualization of ARM lymphatics and 91% visualization of ARM nodes. The malignant positivity of ARM Node is 6% and 9% by FNAC and HPE respectively.

Conclusion: ICG guided ARM is a feasible and safe adjunct to axillary surgery in breast cancer. By enabling real time visualization of arm lymphatics, it allows surgeon to selectively preserve critical structures, minimizing the risk of lymphedema while maintaining oncological safety. Further investigation through larger studies with extended follow-up is needed to integrate this technique into routine practice.

Key-words: Axillary Reverse Mapping, Breast Cancer, Indocyanine Green, Lymph node dissection

INTRODUCTION

Carcinoma of the breast is the most common malignancy among Indian women ^[1]. Axillary lymph node status remains one of the most important prognostic factors in the management of breast cancer ^[2]. ALND and sentinel lymph node biopsy (SLNB) are the standard surgical procedures used for axillary staging.

However, ALND is associated with significant complications, including permanent hypesthesia or dysesthesia in the posterior aspect of the arm, painful neuroma, seroma formation, and, most notably, lymphedema ^[3,4].

Lymphedema of the arm is one of the most distressing and persistent complications following axillary surgery, with an even higher incidence when adjuvant radiotherapy is administered ^[5]. Although de-escalation of axillary surgery to SLNB has been adopted to reduce this risk, lymphedema still occurs in approximately 13% of cases ^[6].

ARM is a novel surgical technique introduced to identify and preserve arm lymphatics to reduce the incidence of lymphedema ^[7]. The procedure uses tracers such as

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methylene blue, radiotracers, or ICG, with ICG offering advantages such as superior visualization and fewer local complications [8,9]. In this study, we evaluate the feasibility of detecting ARM lymphatics and ARM nodes using ICG and assess the oncological safety of this technique in patients with breast cancer.

MATERIALS AND METHODS

Place and duration of study- The study included Patients who undergo ALND or SLNB with or without ALND for carcinoma breast in the Department of Surgical Oncology, Kidwai Memorial Institute of Oncology, Bangalore from 1 July 2023 to 31 July 2024.

Inclusion criteria

- Patients >18 years of age.
- Patients who undergo mastectomy or BCS with axillary lymph node dissection or sentinel lymph node biopsy with or without axillary lymph node dissection for carcinoma breast.
- Patient willing to participate in the study.

Exclusion criteria

- Patients not willing to participate in the study.
- Patient with history of allergy to ICG.
- Patients with previous history of ipsilateral arm surgery and ipsilateral axillary surgery.
- Patients who received radiation to axilla.

Methodology- With prior informed consent, 0.5ml(1mg/ml) diluted indocyanine green is injected into first and fourth web space of the ipsilateral upper limb just before opening clavipectoral fascia. A gentle massage was done at the injection site for a few minutes. During axillary dissection, clavipectoral fascia opened and the axilla was visualized using SPY-PHI imaging system at a wavelength of 805nm in white light, SPY fluorescence mode, overlay fluorescence mode and color-segmented fluorescence mode. The anatomical location of fluorescent lymphatics and nodes is documented. FNAC of Fluorescent ARM nodes will be done and removed only if they are present within the standard template of ALND and are sent separately for histopathological examination to look for metastasis and correlation with FNAC.

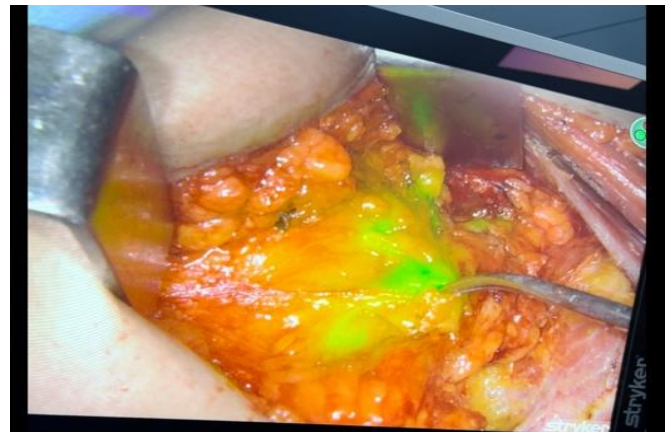


Fig. 1: The fluorescent ARM nodes

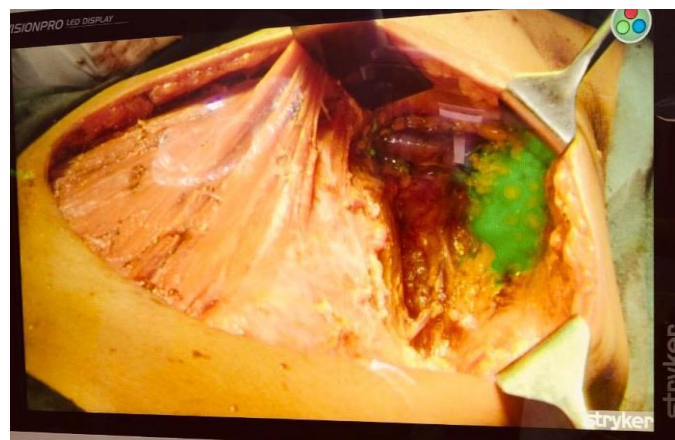


Fig. 2: Fluorescent ARM lymphatics

Statistical Analysis- Statistical analysis was performed using the IBM SPSS Statistics for Windows, version 25. The data collected was analyzed statistically using descriptive statistics namely mean, standard deviation, and percentage wherever applicable. Students t-tests and analysis of variance and covariance were used to analyze parametric variables. Chi-square test, Fisher's exact probability test and Multivariate logistic regression analysis were used to test qualitative measures. P-value of < 0.05 was considered statistically significant.

RESULTS

During the study period, 78 patients with unilateral breast cancer underwent surgery with ARM using ICG to assess detection of lymphatics, ARM node and oncological safety. 13(17%) patients underwent BCS + SLNB/ ALND and 65(83%) patients underwent MRM. Among them, 11(14%) patients had received NACT, and the rest (89%) underwent upfront surgery. The median age of patients is 54 years. Out of 78 patients, 15 (19%) belong to Stage I, 36 (46%) to Stage IIA, 22 (28%) to Stage IIB, and 5 (6%) to Stage IIIA (Table 1).

Table 1: Demography of the patients

Characteristics	No. of patients (%) (n= 78)
Early breast cancer	51(65%)
STAGAE I - T1 N0	15(19%)
STAGE IIA - T1N1	18(23%)
STAGE IIA - T2 N0	18(23%)
Locally Advanced Breast Cancer	27(35%)
Stage II B - T2 N1	22(28%)
Stage III A - T2N2	5(6%)
BCS	13(17%)
MRM	65(83%)
SLNB	07 (09%)
ALND	71(91%)
Age Group	
<50	33(42%)
>50	45(57%)

The fluorescent ARM lymphatics were found in 75 (96%) patients. ICG failed to detect ARM lymphatics in 4% (3) of patients. The location of most 81% (63) of the lymphatics to axillary vein is along and inferior to it. The infra-axillary lymphatics are within 1cm in 92% (58) cases. The ARM node is found in 91% (68) patients and most of them 81% (55) are single in number. The location of ARM node is in Zone D in all the cases and are related to

fluorescent lymphatics. 7% (5) of ARM nodes came positive for malignancy, all the nodes were present inferior to the axillary vein and lateral to LD pedicle. All Positive ARM nodes were found in Stage IIB and IIIA. There are no intraoperative anaphylactic complications observed. ICG pigmentation is seen in all the patients and resolved in 2-3 weeks without any tattooing (Fig. 3).

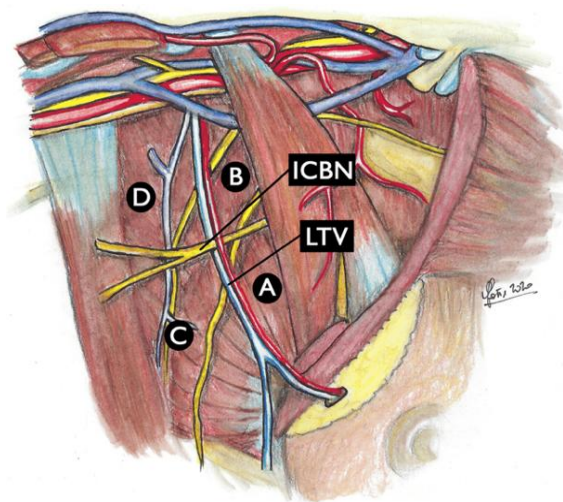


Fig. 3: Clough's classification of Axillary lymphnodes ^[6]

Table 2 shows that stage, mode of surgery or receiving NACT does not affect the detection of ARM lymphatics or

nodes. The higher the stage higher the detection of arm nodes.

Table 2: Identification of arm Lymphatics and Nodes

AJCC stage	No. of Pt	BCS + SLNB/ALND	MRM	NACT	Arm lymphatics present	Arm lymphatics absent	Arm node present	Arm node absent
Stage I	15	08	09	-	14	01	13	01
Stage IIA	32	04	28	-	30	02	26	04
Stage IIB	20	01	19	03	20	-	18	02
Stage IIIA	11	-	11	08	11	-	11	-

Table 3 shows that intraoperative FNAC was able to detect metastasis to ARM nodes in 05 (6%) patients.

Table 3: Identification of ARM Node Metastasis with FNAC

AJCC stage	ARM node present	FNAC positive	FNAC negative
Stage I	13	-	13
Stage IIA	26	-	26
Stage IIB	18	01	17
Stage IIIA	11	04	07

Table 4 shows that ARM node metastasis on final histopathology was seen in 7(9%) of patients and all the patients belong to stage IIB and IIIA.

Table 4: Identification of ARM metastasis on HPE

AJCC stage	No. of Pt	ARM positive	ARM negative
STAGE I	15	-	-
STAGE IIA	32	-	-
STAGE IIB	20	03	17
STAGE IIIA	11	04	07

DISCUSSION

The Axillary staging surgery with minimum morbidity is the goal of breast cancer management. The various de-escalation procedures like low axillary sampling, SLNB also carry 11-13% risk of lymphedema. In this background ARM technique was introduced to map and preserve arm lymphatics. The anatomy of arm lymphatics was delineated in a recent study by Thompson *et al.* [7] which helps in identifying and preserving the arm lymphatics. Indocyanine green dye is an alternative to methylene blue with advantages that, it allows the use of standard dual tracer SLNB and has fewer local complications.

Table 5 shows the comparison of studies using different techniques for ARM. Our findings support the growing body of literature demonstrating the effectiveness of ICG in ARM.

In our cohort of 78 patients, we achieved an ARM lymphatics identification of 96% and ARM nodal identification rate of 91%, consistent with prior reports by Wu *et al.* [8] (87.2%) Abbaci *et al.* [9] (94.5%) and Noguchi *et al.* [10] (85%). Both studies emphasized the superior detection rates of ICG, either alone or in combination with methylene blue or radiotracer. This shows the superiority of ICG over methylene blue in the detection of ARM nodes in the studies done in the same institute.

The oncological safety of ARM remains a crucial consideration. The metastasis rate in identified ARM nodes is 7% in our study which aligns with Wu *et al.* [8] reported a metastasis rate of 10.9%. The ARM nodal positivity is seen only in high nodal burden disease, and this low incidence reinforces that ARM can be safely performed in selected patients [11,12].

**Table 2:** Comparison of ARM studies

Study	Technique	Arm lymphatics	Arm node	ARNM node positive	ARNM node-positive (HPE)
Wu <i>et al.</i> [8]	ICG vs MB	-	87% (ICG)	-	10.9%
Abbaci <i>et al.</i> [9]	ICG	-	94.5%	-	19.4%
Noguchi <i>et al.</i> [10]	ICG (SLNB)	-	85%	-	32%
Narasannaiah <i>et al.</i> [13]	Methylene blue	-	73.2%	-	Higher
Our study	ICG	96%	91%	6%	9%

Incorporating FNAC enhances oncological safety by allowing real-time decision-making during surgery. ICG fluorescence imaging offers clear intraoperative visualization of lymphatics without radiation exposure, making it both surgeon and patient-friendly. Its compatibility with minimally invasive approaches also makes it suitable for modern breast surgery techniques. The incorporation of ICG in ARM has the potential to reduce postoperative lymphedema rates without compromising oncologic control, making it a valuable addition to the surgical armamentarium in breast cancer care. Identification of lymphatics is made sensitive and easier with ICG dye, which may help in combining lymphovenous anastomosis in further reducing lymphedema [14,15].

CONCLUSIONS

Axillary Reverse Mapping using indocyanine green is a promising technique that enhances intraoperative visualization of arm lymphatics during axillary surgery for breast cancer. Our study demonstrated a high detection rate of ARM lymphatics (96%) and nodes (91%), with a low incidence of metastasis in ARM nodes (9%), suggesting that ARM can be oncologically safe in early-stage and selected patients. The use of ICG provides real-time, radiation-free imaging, which aids in the identification and potential preservation of lymphatic pathways critical to reducing lymphedema. This technique may serve as a valuable adjunct to sentinel lymph node biopsy or axillary dissection, helping surgeons minimize postoperative morbidity without compromising oncologic outcomes. However, proper technique, including timing of injection and intraoperative mapping, is essential for accuracy.

Larger, multicentric studies with longer follow-up are required to validate these findings and establish guidelines for routine clinical application of ARM using ICG.

LIMITATIONS

The limitations of this study include early ICG administration, which may cause the dye to spread beyond the ARM node. Gadget availability and cost could limit wider application, and the follow-up for lymphedema was short, limiting long-term assessment. Additionally, there were no long-term oncological outcomes in the study.

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