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Original Article

Sentinel Node Biopsy Using Laparoscopic Camera and Monitor – A Novel Technique in Breast Cancer Patients

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Abstract

Introduction: Axillary staging based on sentinel lymph node biopsy (SLNB) became the gold standard in early-stage breast cancer management avoiding complete axillary dissection in more than 70% of cases. The radioisotope Technetium-99m in combination with methylene blue became the gold standard for SLNB with a detection level of up to 96%. Indocyanine green (ICG) is a relatively non-toxic and inexpensive water soluble molecule. It's use in breast cancer has been proposed as the only recommended alternative to the use of radioisotope by the breast surgery community. A meta-analyses showed that ICG-SLNB in breast cancer had a high detection rate for SLN and was reliable for the detection of SLN metastasis and used to perform adequate axillary staging in hospitals where a nuclear medicine service is not available and is also cheaper than radioisotopes.

Materials and Methods: The aim of the study is to demonstrate the safety and feasibility of the SLNB method using ICG as the only tracer using laparoscopic camera and monitor. This is a prospective single institution study conducted between 2023-2025 comprising 23 consecutive patients diagnosed with stage I-III breast cancer(n=23) who underwent surgery for the primary and the axilla.

Results: Sentinel node was the only positive node in 1 patient(4.3%).Both sentinel and other regional nodes were positive in 3 patients(13.04%).Node positive disease with negative sentinel nodes was observed in 1 patient(4.34%) with a sentinel node detection rate of 95.7%. The costs involved in the procedure was only for the ICG significantly lower than that of Tc99m.No costs involved for the fluorescent probe as the laparoscopic camera and monitor is utilized for the identification of sentinel nodes.

Conclusion: The technique of using laparoscopic camera and monitor for performing ICG sentinel node biopsy in breast cancer patients is feasible and needs further studies for standardisation.

Key words: Axillary dissection, Indocyanine green, Laparoscopic camera, Metastasis, Sentinel node biopsy

INTRODUCTION

Axillary staging based on sentinel lymph node biopsy (SLNB) became the gold standard in early-stage breast cancer management. It avoids complete axillary dissection in more than 70% of cases.[1-3] Radioisotope Technetium-99 in combination with methylene blue had a detection level of up to 96%,[4,5] posing it a gold standard approach. Indocyanine green (ICG) is an innovative molecule with varied medical applications in the field of oncological surgery. The injection of ICG in the surroundings of the cancer is a method for detecting the sentinel lymph node in tumors of different sites, such as the colon, prostate, uterus, and oropharynx.[6] Its use in breast cancer has been proposed in recent years by the breast surgery community. The European Society of Medical Oncology and the Japanese Breast Cancer Society define ICG as the only recommended alternative to the use of radioisotopes.[7-9] ICG has a relatively better cost profile and safety profile than the blue dyes (BDs) without a change in the oncological yield, even during implementation as a new operative technique.[10] The use of a routinely available

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laparoscopic camera and monitor further reduces the cost by replacing the need for the near-infrared camera and video display. The aim of the study is to demonstrate the safety and feasibility of the SLNB method using ICG as the only tracer, using a laparoscopic camera and monitor.

MATERIALS AND METHODS

Study Design and Participants

This is a prospective single-institution study conducted between 2023 and 2025, comprising 23 consecutive patients diagnosed with stage I-III breast cancer (n = 23) who underwent surgery for the primary and the axilla by a single surgical oncologist.

Inclusion Criteria

1. Patients with early-stage breast cancer and no axillary lymph node metastasis
2. Patients with axillary nodal metastasis and no systemic metastasis treated with neoadjuvant chemotherapy
3. Patients of all ages, irrespective of their menopausal status, were included.

Exclusion Criteria

1. Patients with previous breast surgeries
2. Patients with a history of allergy to dyes
3. Patients with metastatic disease at presentation
4. Patients with poor performance status.

Surgical Technique

At the time of surgery, after anesthesia and immediately before the incision, 4 mL of Indocyanine® 25 mg/10 mL (Aurogreen, India) was injected subdermally into the peri-areolar area at 9'o clock position. Movement of ICG in the lymphatic ducts was facilitated by manual massage for 5 min.

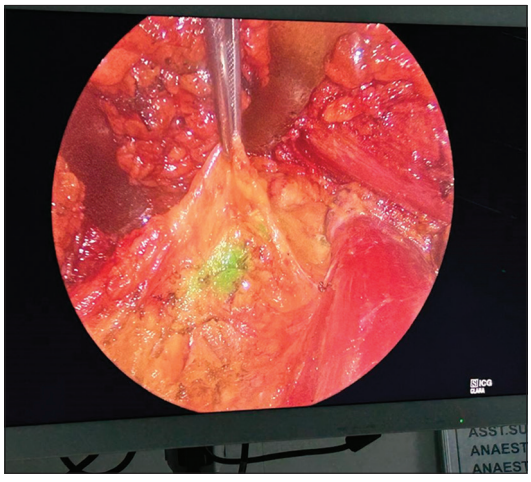

Figure 1: The laparoscopic monitor with an indocyanine green-positive sentinel node

Fluorescence of ICG was elicited and detected by the Karl Storz Laparoscopic camera IMAGE1 S 4U RUBINA, OPAL1 NIR/ICG with the real-time FI overlay mode in the 32" 4K monitor (3840 × 2160 pixel resolution) [Figure 1]. Lymphatic drainage was visualized in real-time on the laparoscopic monitor, and the fluorescence followed from the injection site toward the axilla. Sentinel lymph node (SLN) mapping and biopsy were proceeded through either a breast or axillary incision. Assessment of the surgical field using the laparoscopic camera was applied continuously throughout the surgical exploration. Fluorescent lymphatic channels were dissected and followed to the first ICG-avid lymph node. Fluorescent lymph nodes ("ICG-positive") were then localized and excised [Figure 2]. SLN removal continued until no residual fluorescence was visible in the axilla. ICG fluorescence was well made out in the laparoscopic 4K monitor as a greenish fluorescence. Axillary lymph nodal dissection (ALND) was completed in all patients, as this is a new surgical technique adopted with due consideration to the surgeon's learning curve.

The procedure was done after obtaining informed consent for the procedure from all the patients in accordance with institutional ethics.

Histopathological Assessment

ICG-positive nodes and a complete axillary nodal dissection sample were sent for routine histopathology examination separately. The frozen section of the sentinel nodes was not performed as axillary nodal dissection was done in all patients as part of this study.

Outcomes

Primary outcomes were the number of SLNs identified, the sentinel node biopsy detection rate, and the rate of failed mapping. Secondary outcomes were the costs associated with this technique.

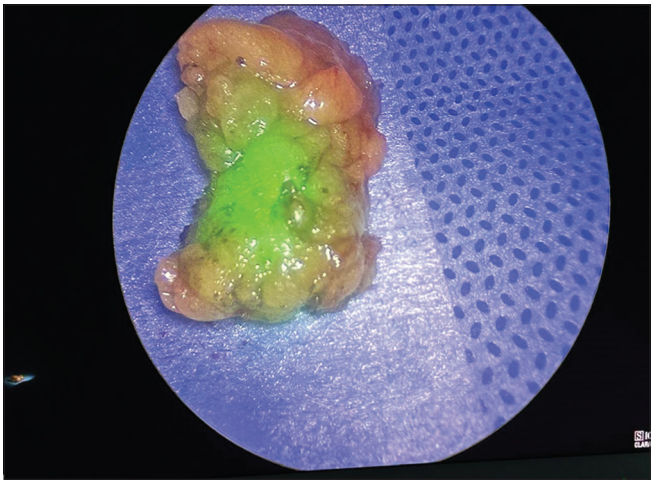

Figure 2: The indocyanine green-positive sentinel node

Demographic information included age, menopausal status, parity, tumor type, and neoadjuvant therapy. Intraoperative information included the type of breast surgery and the number of nodes identified with the technique. Post-operative information included hospital admission duration, complications (adverse reactions and anaphylaxis to tracers), significant complications related to SLN biopsy (Clavien-Dindo grade ≥III), T status, number of metastatic lymph nodes on histopathology, and follow-up visit information up to 90 days postoperatively.

RESULTS

The mean age of the patients was 47.86 (range 29–71years). The age distribution is 0–49 years (34%), 50–69 years (56%), and >70 years (8.6%). Nine patients (39.1%) were premenopausal, and 14 patients were postmenopausal (60.9%). 16 patients were estrogen receptor (ER) positive (69.56%). Progesterone receptor (PR) positivity was present in 13 patients (56.52%). Parity distribution is as follows: Nulliparous – 1 patient (4.3%), Uniparous – 2 patients (8.6%), and multiparous – 20 patients (86.9%). Two patients had pathological complete response in the primary (8.6%), 11 patients had T1 disease (47.82%), 8 patients had T2 disease (34.7%), and 1 patient (4.3%) had T3 disease and ductal carcinoma *in situ* (DCIS). Regarding the receptor status, 16 patients were ER positive (69.56%), 15 patients (65.2%) were PR positive, and human epidermal growth factor receptor 2 (Her2) positivity was observed in 12 patients (52.17%). Invasive ductal histology was the predominant histology in 19 patients (82.6%), followed by mixed type in 2 patients (8.6%) and one each in invasive lobular and DCIS subtypes. Seven patients (30.43%) underwent breast conservation surgery with oncoplastic reconstruction, and 16 patients (69.56%) underwent modified radical mastectomy. Nine patients (39.1%) underwent neoadjuvant chemotherapy, and 14 patients (60.86%) underwent upfront surgery. The clinicopathological characteristics are shown in Table 1.

Table 1: The clinical characteristics of the patients

Clinical characteristics	No. of cases	%
Total	23	
Age at diagnosis		
0–49	8	34
50–69	13	56
>70	2	8.6
Menopausal Status		
Premenopausal	9	39.1
Postmenopausal	14	60.9
Parity		
Nulliparous	1	4.3
Parous	2	8.6
Multiparous	20	86.9
T Status		
T0	2	8.6
T1	11	47.82
T2	8	34.7
T3	1	4.3
T (is)	1	4.3
IHC		
Estrogen receptor		
Positive	16	69.56
Negative	7	30.4
Progestrone receptor		
Positive	15	65.2
Negative	8	34.78
HER 2 NEU		
Positive	12	52.17
Negative	10	43.47
Tumour type		
Invasive ductal	19	82.6
Invasive lobular	1	4.3
DCIS	1	4.3
Mixed	2	8.6
Type of surgery		
MRM	16	69.56
BCS	7	30.43
No of patients		
Post-NACT	9	39.1
Straight surgery	14	60.86

DCIS: Ductal carcinoma *in situ*, NACT: Neoadjuvant chemotherapy, MRM: Modified radical mastectomy, BCS: Breast-conserving surgery, HER 2 NEU: Human epidermal growth factor receptor 2

The total number of sentinel nodes harvested was in the range of 0-16 lymph nodes (mean – 3.08). The total number of positive sentinel lymph nodes was in the range of 0–5 lymph nodes (mean – 0.73). the total number of nodes harvested in the completion axillary lymph node dissection was in the range of 9–48 lymph nodes (mean – 23 nodes). The total number of positive lymph nodes harvested was 55 nodes, with a mean of 2.39. The total number of sentinel node positive patients was 4 (17.3%), and the total number of node positive patients after complete nodal dissection was 9(39.1%). No sentinel nodes were evident due to failed mapping in 4 patients (17.3%). The sentinel node was the only positive node in 1 patient (4.3%). Both sentinel and other regional nodes were positive in 3 patients (13.04%). Node-positive disease with negative sentinel nodes was observed in 1 patient (4.34%) with a sentinel node detection rate of 95.7%. Both sentinel and total lymph nodes were negative for metastatic deposits in 14 patients (60.86%). The characteristics of the sentinel nodes are shown in Table 2.

The statistical analysis was done by standard descriptive statistics.

The costs involved in the procedure were significantly lower for the ICG than those of Tc99m. No extra cost was involved for the infrared camera, as the laparoscopic camera and monitor were utilized for the identification of sentinel nodes.

Table 2: The characteristics of the sentinel nodes

Total no of node-positive patients	9	39.1%
Total no of sentinel lymph node positive patients	4	17.3%
No evident sentinel lymph node (failed mapping)	4	17.3%
Fibro fatty tissue in the sentinel lymph node biopsy	4	17.3%
Only the sentinel lymph node positive	1	4.3%
Sentinel lymph nodes and regional lymph nodes positive	3	13.04%

The duration of hospital stay was 3 days for all the patients. There were no significant complications associated with the use of ICG. All the patients are being followed up till date.

DISCUSSION

ICG is water-soluble, relatively non-toxic, and inexpensive. It rapidly combines with plasma albumin and α-1-lipoprotein on intravenous injection, generating near-infrared light that penetrates into tissues under the excitation of exotic light with a wavelength of 750–810 nm. Since the mid-1950s, ICG has been used in clinical practice as a diagnostic drug. ICG enables the formation of clear fluorescence imaging (FI) during surgery, which achieves the visualization of the surgical field and real-time tracer drainage of lymphatic and lymph nodes through the near-infrared imaging system equipment. ICG has the ability to be gathered in tumor tissues, displaying the boundary of the tumors clearly, owing to the enhanced permeability and retention effect of solid tumors, potentiating complete resection of the tumor.[11] In our study, Karl Storz Laparoscopic camera Image1 S 4u Rubina, OPAL1 NIR/ICG with the real-time FI overlay mode was used for FI to identify the sentinel lymph nodes (SLN).

SLN biopsies are useful for staging breast cancer and predicting the likelihood of disease spread to other non-sentinel axillary nodes and beyond, with considerable evidence. The average incidence of skip metastases is just 5% among patients without clinically apparent metastases,[2,12-15] as in our study. SLN biopsy is associated with fewer complications and less morbidity than ALND,[14-16] with no increase in axillary or distal cancer recurrence[15-19] and survival rates that are at least as good as with total ALND.[15,18,19] Only 1 patient (4.3%) had skip metastases with the sentinel node being negative but positive axillary lymph nodes on final histopathology in our study.

BD and 99mTc have long been used to identify SLNs. Either 99mTc or the combination of 99mTc and BD is considered standard of care. Access to radioisotopes and the equipment and personnel required for their use is non-universal. Due to the need for injection hours or the day before surgery, the need to involve nuclear medicine personnel, radiation exposure to patients and healthcare personnel, using 99mTc can be problematic.[20,21] Lymphoscintigraphy does not provide real-time visualization of lymph nodes as the surgeons dissect areas previously identified as radioactively hot. Both BD and ICG-FI circumvent the limitations of 99mTc. As documented in previously published meta-analyses, only ICG-FI attains SLN detection results like those observed with 99mTc.[7,22-28] In our study, only ICG was used as a sole agent, as we had a lack of access to Tc99m at our center. The results in our study are on par with the use of a combination of Tc99m and BD.

The costs involved with a new technology compared to the current "gold standard" are a key consideration in its widespread adoption. FI, including the costs of the ICG drug and the dedicated camera, incurs additional expenditure. Cattin *et al.* found that the tracer combination of ICG-Radioactive Imaging (ICG-RI) was more expensive than BD-Radioactive Imaging (BD-RI). Higher initial outlay costs, as well as the recurrent cost of the ICG drug, may pose financial challenges in the adoption of ICG-RI. ICG fluorescence as a single technique would be less expensive than BD-RI. Hospital infrastructure to accommodate radioactive materials, specialist staff for lymphoscintigraphy, and patient travel would incur additional costs with the use of RI.[28] ICG is cheaper than radioisotopes, facilitating the performance of adequate axillary staging in hospitals where a nuclear medicine service is not available, as in our setup. The good safety profile and the results of a meta-analysis in terms of accuracy in detecting the SLNs make ICG a reliable alternative to standard methods for SLN mapping. ICG is preferable to BD-RI from a cost perspective alone. The use of a laparoscopic camera and monitor, as in our study, obviated the need for an ICG FI camera, further lowering the consequent costs involved. The only expense in our study was for the procurement of ICG.

A meta-analysis showed that ICG-SLNB in breast cancer had a high detection rate for SLN and was reliable for the detection of SLN metastasis.[6] In a meta-analysis by Zhang *et al.*,[19] studies including 2594 breast cancer patients showed that the ICG-guided SLN detection rate was 98% (95% confidence interval [CI]: 0.96–0.99) and the sensitivity was 92% in diagnostic performance in the presence of metastases (95% CI: 0.85–0.96).[29] Another meta-analysis aimed to compare the diagnostic performance of ICG with standard tracers (both BD and RI) regarding SLNB in breast cancer patients, which yielded no statistically significant difference between ICG and RI for SLN detection rate. This implies that ICG-SLNB is a reliable tool for SLN detection compared with the standard RI method. The detection rate was significantly different

between ICG and BD.[26] The sentinel node detection rate was 95.7% in our study.

Sarun *et al.* demonstrated that a higher number of SLNs are removed per patient in ICG-SLNB than in standard methods. Whether the increased number of SLNs yielded by ICG-SLNB is secondary to adjacent lymph nodes staining from ICG leakage or ICG-SLNB rendering better axillary staging compared with the standard methods needs further investigation. The result from this study supported the use of ICG. The detection rate and number of SLNs removed from ICG proved the safety and feasibility of this technique.[26] The total number of sentinel nodes harvested was in the range of 0–16 lymph nodes (mean – 3.08) in our study.

The Karl Storz VITOM HD System, an exoscope using extracorporeal magnification coupled with a high-definition fluorescence camera system, was utilized to trace ICG to perform SLNB before breast surgery. In our study, a Karl Storz Laparoscopic HD camera was used to identify the sentinel nodes after ICG injection. Utilization of a laparoscopic camera for sentinel node biopsy, as in our study, needs further standardization with future studies as an alternative to hand held ICG fluorescent camera.

The ease of administration and relatively non-toxic profile of ICG make it an ideal choice over the BDs. The oncological safety is also not compromised in the hands of well-trained high-volume breast surgical oncology units. The ready availability of a laparoscopic camera in the operation theater as part of minimally invasive surgical oncology procedures makes it a suitable choice for ICG sentinel node detection, obviating the need for the near-infrared camera and monitor. The novelty of the study lies in the incorporation of the laparoscopic unit as a new eye-opener in performing breast oncological surgery.

The limitation of our study is the small sample size and the lack of an established technique for the use of a laparoscopic camera to detect ICG-positive sentinel nodes in patients undergoing axillary staging surgery for breast cancer.

CONCLUSION

The technique of using a laparoscopic camera and monitor for performing sentinel node biopsy in breast cancer patients is feasible from the oncological and cost aspects. The use of ICG alone for sentinel node biopsy in breast cancer patients using stand-alone laparoscopic units needs further studies.

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