

Sentinel Lymph Node Biopsy using Isosulfan Blue Dye and Frozen Section in Early Breast Cancer - An Indian Perspective

Dr Paul Augustine¹, Dr Rexeena V. Bhargavan², Dr Prabhakaran U³, Dr Shafeek Shamshudeen⁴,
Dr Sindhu Nair⁵, Dr Kurian Cherian⁶

¹Additional Professor, Department of Surgical Services, Regional Cancer Centre, Thiruvananthapuram, Kerala, India

²Assistant Professor, Department of Surgical Services, Regional Cancer Centre, Thiruvananthapuram, Kerala, India

³M.Ch Trainee, Department of surgical services, Regional Cancer Centre, Thiruvananthapuram, Kerala, India

⁴Senior resident, Department of surgical services, Regional Cancer Centre, Thiruvananthapuram, Kerala, India

⁵Assistant Professor, Department of Pathology, Regional Cancer Centre, Thiruvananthapuram, Kerala, India

⁶Additional Professor, Department of surgical services, Regional Cancer Centre, Thiruvananthapuram, Kerala, India

Abstract: Sentinel lymph node biopsy (SLNB) is standard of care for axillary staging in node-negative breast cancer. SLNB is done using blue dye and /or radionucleotide. We aim to analyse our SLNB data using only blue dye. Retrospective analysis of prospective data of patients who underwent SLNB during study period was done. SLNB identification rate and sensitivity, specificity and false negativity rate of nodal frozen section was calculated. 50 female patients underwent SLNB. Identification rate was 96%. Sensitivity, specificity and negative predictive value of frozen section was 100%. SLNB with blue dye only with frozen section should suffice in early breast cancer.

Keywords: Sentinel lymph node; isosulphanblue ; frozen section; early breast cancer

1. Introduction and Literature Survey

Sentinel lymph node biopsy (SLNB) has revolutionized the management of the axilla in breast cancer patients. It has since become the standard of care for axillary staging in clinically node-negative breast cancer.^[1] A properly performed SLNB identifies patients who need further axillary clearance, while sparing others a potentially morbid axillary lymph node dissection (ALND)^[2]. Proper surgical technique in SLNB minimizes the risk of understaging and undertreating patients, which in turn influences outcome. SLNB can be done generally using blue dye and / or radionucleotide tracer. Although sentinel nodes draining the breast can be variably located, they are usually found within the lower axilla (level I)^[3]. Although excellent results are reported in single-institution series using either radioactive colloid or blue dye^[4], combined use of both tracers appears to be complementary, minimizing the false negative rate in most^[5-8], but not all studies^[9]. SLNB typically begins with injection of one or two tracers into breast skin or parenchyma either in the vicinity of the tumor or into the areolar plexus. These tracers enter lymphatic channels and passively flow to the draining lymph nodes. Sentinel lymph nodes are then identified as those first receiving drainage from the tumor by the presence of tracer and removed. SLNB false negativity rate is dependant on the surgical technique and the pathological assessment. We recently started SLNB in early clinically node negative breast cancer using isosulphan blue dye and frozen section. All patients with SLNB positive undergo completion axillary dissection of level I and II. We aim to analyse our SLNB data using only blue dye.

2. Material and Methods

This is an retrospective analysis of prospectively collected data of all patients who have undergone sentinel lymph node biopsy in the Department of Surgical Oncology, Regional Cancer Centre, Thiruvananthapuram, Kerala. All patients from the inception of the SLNB programme in November 2018 to February 2019 were studied. The data was collected prospectively. We aim to analyse our data of SLNB in early breast cancer. The objective of the study is to calculate the sentinel node identification rate and the sensitivity, specificity and false negativity rate of nodal frozen section vis a vis final histopathology.

3. Results

Our study includes 50 female patients with T1 or T2 primary breast cancer who were clinically N0. The patient and surgery characteristics are shown in Table 1.

Table 1: Patient and surgery characteristics

Age	
< 40 years	9
40 – 50 years	14
51 – 60 yrs	19
>60yrs	8
Clinical T stage	
Tx	6
T1	15
T2	29
Type of surgery	
Breast conservation surgery	47
Modified Radical Mastectomy	3

Age ranged from 25 to 69 years with median age of 51 years. All patients had histological proof of carcinoma breast. All patients underwent an ultrasound of the axilla and had no significant nodes on ultrasound. All underwent primary surgery. Six patients were post excision biopsy of the breast lump. Breast conservation surgery (BCS) was done in 47 patients and Modified Radical Mastectomy (MRM) in 3 patients. SLNB was done using only blue dye technique. All patients underwent SLNB using isosulphan blue dye injected periareolarly. Blue and enlarged nodes were sent for frozen section. SLNB characteristics are given in Table 2.

Table 2: Sentinel lymph node characteristics

Number of nodes identified	Number of patients
0	1
1	1
2	21
3	16
4	9
5	1
6	1
Sentinel lymph node frozen section	
Negative	40
Positive	8
Total	48
Frozen section versus final histology	
Frozen section negative, final histology negative	40
Frozen section negative, final histology positive	0
Total	40
Axillary dissection histology	
Nodes other than sentinel positive	3
Nodes other than sentinel negative	5
Total	8

The identification rate of SLNB was 96%. In one patient only enlarged nodes were identified and in another patient neither blue nor enlarged nodes were found. Both underwent axillary dissection. Both patients were NO on final histopathology. The mean sentinel node (SN) number was 2.8 with a range from 1 to 6. The mode was 2. SN was positive in 8 patients on frozen section and completion axillary nodal dissection of level I and II was done in all of them. SN was negative on frozen section in 40 and no further axillary dissection was done in them. No drain was placed in patients undergoing only SLNB. No patient developed any anaphylactic reaction or any other adverse reactions to the dye. All patients were discharged on the next day. All patients complained of bluish discoloration of urine postoperatively which settled in 2 to 3 days. No patient developed postoperative seroma requiring aspiration. No patient developed SLNB site wound infection. No patient with SLNB negative on frozen section had a positive node on final histopathology. Thus the sensitivity, specificity and negative predictive value of frozen section was 100%. In patients with SLNB positive who underwent completion axillary dissection, SN was the only positive nodes in 62.5% (5/8) while the rest had other nodes positive on axillary dissection.

4. Discussion

SLNB is currently the gold standard for the management of early stage node negative breast cancer. It is associated with

minimal morbidity as compared to axillary dissection with respect to lymphedema and shoulder dysfunction^[3]. SLNB can be done generally using a blue dye or a radionucleotide or both. Although excellent results are reported in single-institution series using either radioactive colloid or blue dye^[4], combined use of both tracers appears to be complementary, minimizing the false negative rate in most^[5-8], but not all studies^[9]. The use of isosulfan blue dye as a single agent in SLNB for breast cancer initially was reported by Giuliano and colleagues^[10] with sentinel node identification rates of 98%, without false-negative nodes. Isosulfan blue has shown a SLNB identification rate of 92% in a recent Thai study.^[11] In the Indian scenario many centres practice SLNB using both blue dye and radio isotope tracer^[12]. The limitations in the availability of radio isotope continues to be a hurdle in the usage of dual tracers in our country. However our preliminary results are very promising with a 96% identification rate using only isosulphan blue dye. A recent study from Indonesia has an identification rate of 91.7%^[13] using only dye tracer. Our study along with many others shows that single tracer is sufficient for identifying the SN and can be done in our setup.

Frozen section is commonly used during SLNB. The experience of the specialized pathologist counts greatly in the reporting as a false negative result may lead to repeat surgery if the final histopathology suggests lymph node metastasis. Our frozen section has a sensitivity, specificity and negative predictive value of 100%. Thus after final histology report no patient underwent repeat axillary surgery. The immediate advantage to our patients who underwent BCS with sentinel node is that there is not drain and hence the patient can go home and followup after the reports are ready. This decreases the emotional and economic strain on the patient and bystanders. The decrease in lymphedema and shoulder dysfunction in SLNB^[3] will be an added benefit to our patients also.

5. Future Scopes

There are many drawbacks of our study. We have studied only 50 patients. More numbers are required to definitely state that single tracer is sufficient. Secondly our procedures are done in a specialized cancer institute with highly experienced surgeons and pathologists. Whether these results will be achievable in non specialized centres is questionable. Long term follow is not available of our patients to identify axillary recurrence. However we believe that single tracer SLNB is feasible and should be offered to all patients with early node negative breast cancer. Long term follow up of our patients is planned and will be reported.

6. Conclusion

SLNB using isosulphan blue dye only has a high identification rate. The sensitivity, specificity and negative predictive value of frozen section is also high and SLNB with frozen section should suffice in early node negative breast cancer patients with negative sentinel node.

Reference

- [1] Lyman GH, Somerfield MR, Bosserman LD, et al. Sentinel Lymph Node Biopsy for Patients With Early-Stage Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. *J Clin Oncol* 2016; :JCO2016710947.
- [2] Rao R, Euhus D, Mayo HG, Balch C. Axillary node interventions in breast cancer: a systematic review. *JAMA* 2013; 310:1385.
- [3] Krag DN, Anderson SJ, Julian TB, et al. Technical outcomes of sentinel-lymph-node resection and conventional axillary-lymph-node dissection in patients with clinically node-negative breast cancer: results from the NSABP B-32 randomised phase III trial. *Lancet Oncol* 2007; 8:881.
- [4] Giuliano AE, Jones RC, Brennan M, Statman R. Sentinel lymphadenectomy in breast cancer. *J Clin Oncol* 1997; 15:2345.
- [5] Albertini JJ, Lyman GH, Cox C, et al. Lymphatic mapping and sentinel node biopsy in the patient with breast cancer. *JAMA* 1996; 276:1818.
- [6] McMasters KM, Tuttle TM, Carlson DJ, et al. Sentinel lymph node biopsy for breast cancer: a suitable alternative to routine axillary dissection in multi-institutional practice when optimal technique is used. *J Clin Oncol* 2000; 18:2560.
- [7] Cody HS 3rd, Fey J, Akhurst T, et al. Complementarity of blue dye and isotope in sentinel node localization for breast cancer: univariate and multivariate analysis of 966 procedures. *Ann Surg Oncol* 2001; 8:13.
- [8] Chagpar AB, Martin RC, Scoggins CR, et al. Factors predicting failure to identify a sentinel lymph node in breast cancer. *Surgery* 2005; 138:56.
- [9] He PS, Li F, Li GH, et al. The combination of blue dye and radioisotope versus radioisotope alone during sentinel lymph node biopsy for breast cancer: a systematic review. *BMC Cancer* 2016; 16:107.
- [10] Giuliano AE, Kirgan DM, Guenther JM, et al. Lymphatic mapping and sentinel lymphadenectomy for breast cancer. *Ann Surg* 1994;220(3):391–8 [discussion: 398–401].
- [11] Ratchaworapong, K., Thanawut, S., Yodavudh, S., et al. (2017). Rate of sentinel lymph node identification using isosulfan blue dye in breast cancer patients at CharoenkrungPracharak Hospital, Thailand. *Asian Biomedicine*, 8(4), pp. 517-524. Retrieved 9 May. 2018, from doi:10.5372/1905-7415.0804.322
- [12] Somashekhar SP, ZaveriShabber S, UdupaVenkatesh K, Venkatachala K, Parameshwaran, VasanThirumalai MM. Sentinel lymphnode biopsy in early breast cancer using methylene blue dye and radioactive sulphur colloid - a single institution Indian experience. *Indian J Surg*. 2008;70(3):111-9.
- [13] Brahma, B., Putri, R. I., Karsono, R., Andinata, B., Gautama, W., Sari, L., &Haryono, S. J. (2017). The predictive value of methylene blue dye as a single technique in breast cancer sentinel node biopsy: a study from Dharmais Cancer Hospital. *World journal of surgical oncology*, 15(1), 41. doi:10.1186/s12957-017-1113-8