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Original Contribution

THE ROLE OF PATENT BLUE V IN REVERSE AXILLARY MAPPING IN PATIENTS UNDERGOING SENTINEL AXILLARY LYMPH NODE BIOPSY FOR BREAST CANCER - INITIAL RESULTS

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ABSTRACT

Purpose: The main purpose of this study is to research the initial experience with Patent Blue V as a tracer for reverse axillary mapping during sentinel lymph node biopsy for breast cancer and look into the lymphedema rates. **Methods:** We analyzed the first consecutive patients who underwent sentinel axillary lymph node dissection with ICG in combination with reverse axillary mapping with Patent Blue V for the period from May 2023 to January 2024 at our clinic. **Results:** Thirteen patients were included. Patent Blue V (reverse axillary mapping tracer) was found intraoperatively in only two patients (15%). ICG (sentinel lymph node biopsy tracer) was found in 100% of the patients. No lymphedema of upper limb was found with a mean follow-up of 4.2 months. **Conclusions:** The use of Patent Blue V seems not to be an efficient method for reverse axillary mapping with a success rate of 15% in this study. The use of another tracker for reverse axillary mapping is appropriate. However, no upper extremity lymphedema is reported in patients after sentinel lymph node biopsy in this study.

Key words: breast cancer, sentinel lymph node biopsy, ICG, reverse axillary mapping, Patent Blue V

INTRODUCTION

Sentinel lymph node biopsy (SLNB) has become a standard in the axillary surgical management of breast cancer in indicated patients (1-3). Although, in terms of lymphedema rates, SLNB is proven to be superior to axillary lymph node dissection, lymphedema occurs after SLNB in up to 8 % (4-9). Upper limb lymphedema is the most common and one of the most severe late complications after surgery and/or radiotherapy for breast cancer. The incidence varies widely, reaching up to 75% (9-11). It depends on the type of surgery (axillary lymph node dissection or sentinel axillary lymph node biopsy - SLNB), BMI, and consequent infection (12-14). Currently, several techniques have been developed with different tracers for sentinel lymph node biopsy - indocyanine green (ICG), dye method (Patent Blue V, etc.), radioisotopes - technetium 99 alone or in combination with dye (dual technique), carbon dye and magnetic tracers (15-20). The aim of reverse axillary mapping is the preservation of the lymph nodes responsible for the lymph flow of the upper limb. For our study, we chose a combination of sentinel lymph node tracing with ICG and reverse axillary mapping with Patent Blue V. ICG is a tricarbocyanine that, when emitted with near-infrared (NIR) light with a wavelength of 800-820 nm fluoresces. The dye has a short half-life, it is almost 100% excreted via the liver, and no adverse reactions have been reported with its use. On the other hand, by the use of Patent Blu V, the lymph nodes responsible for the upper limb lymph flow are identified and preserved. The main objective of the current study is to investigate, through the application of two methods, SLNB and RAM with Patent Blue V, the possibility of achieving a better quality of life in patients without the occurrence of lymphedema as a postoperative complication.

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MATERIALS AND METHODS

We analyzed the first consecutive patients with this technique for the period from May 2023 to January 2024 at our clinic. Thirteen patients underwent sentinel axillary lymph node dissection in combination with reverse axillary mapping during the study period. For sentinel lymph node biopsy, peritumoral injection of 2 ml 2.5% solution of ICG 20 minutes prior to skin incision was used. For reverse axillary mapping, a 2ml 2.5 % solution of Patent Blue V was injected subcutaneously on the anterior edge of the deltoid muscle 10 minutes prior to skin incision. All procedures were performed by the same surgeon with experience in sentinel lymph node biopsy and using Patent Blue V as a tracer.

To objectify the occurrence of upper limb lymphedema, we measured the circumference of the upper limb every 10 cm, starting from the fingertip. The results preoperatively were compared with 3, 6, and 12 months postoperatively.

RESULTS

For the period from May 2023 to January 2024, 13 SLNB in combination with RAM were performed for indicated patients with breast carcinoma. All of them were women, with a mean age of 66.5 ± 6.3 years. Surgery was performed after neoadjuvant treatment in 2 patients. Patent Blue V was found intraoperatively in only two patients (15%). In both patients, the lymph nodes were part of the lateral axillary lymph node group (first level). In all patients, the sentinel lymph nodes were found by fluorescence of ICG; in 9 of these patients (69%), the sentinel lymph nodes were part of the central group, and in the remaining 4 patients (31%) were part of the pectoral lymph nodes. Non-sentinel lymph nodes were visualized and excised in 5 (38%) of the patients, due to macroscopic enlargement (>10mm). None of the patients had an accumulation of Patent Blue V and ICG in the same lymph node (Crossover). No postoperative complications were recorded in the early postoperative period. When patients were followed up for the occurrence of postoperative lymphedema, no edema of the upper extremity was found **(Table 1).** The mean follow-up was 4.2 months.

Table 1. *Arm measurements*

Distance from finger tips	Diamer (cm)	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Patient 12	Patient 13
0-10 cm	preop.	16	18	17	16	16	19	17	17	18	16	18	19	19
	3rd month	17	18	17	18	16	18	17	17	18	16	18	18	19
	6th month	17	18	16	18	16	19	17	16	18	17	18	19	19
11-20 cm	preop.	15	15	16	13	13	15	12	13	14	13	15	15	16
	3rd month	15	15	17	14	14	15	13	14	14	14	15	15	16
	6th month	15	15	17	14	14	15	13	13	15	15	15	14	16
21-30 cm	preop.	22	22	25	21	13	25	18	19	21	20	21	22	21
	3rd month	21	23	24	20	14	24	18	19	21	21	22	22	21
	6th month	22	23	26	21	14	25	18	20	21	20	21	23	22
31-40 cm	preop.	23	23	25	22	20	26	22	23	22	21	25	22	24
	3rd month	24	23	24	22	21	26	22	23	21	22	24	21	25
	6th month	24	23	26	23	20	27	22	23	21	21	25	21	24
41-50 cm	preop.	27	28	27	26	22	33	25	25	21	26	27	33	25
	3rd month	27	29	28	26	22	33	24	25	22	26	27	33	24
	6th month	28	29	28	26	21	34	25	26	22	26	28	34	25
51-60 cm	preop.	30	33	35	30	22	36	30	27	26	30	33	35	30
	3rd month	30	33	34	31	21	36	31	27	26	31	33	34	31
	6th month	30	33	35	31	22	36	31	27	26	31	33	35	31

DISCUSSION

Lymphedema is a common complication after breast cancer surgery. Sentinel lymph node biopsy and reverse axillary mapping both aim to lower the rate of postoperative lymphedema. There are not any strict guidelines on how to perform the surgical technique and which tracer should be used. The time of the application, the interval between the application and the operation, and the surgeon himself are factors

related to the identification of the lymph nodes. However, body mass index, age, histological type of breast cancer, and neoadjuvant chemotherapy can play a role (21).

Different studies use different classifications of the axillary lymph nodes. Most common is dividing axillary lymph nodes into three levels: 1st level, lymph nodes located lateral to the lateral margin of the minor pectoralis muscle; 2nd level, lymph nodes located between the medial and lateral margin of the minor pectoralis muscle and the interpectoral lymph nodes; 3rd level, lymph nodes located medial to the medial margin of the minor pectoralis muscle (22). The other one which is proposed by Clough et al. is based on lateral thoracic vein and second intercostobrachial nerve (23). Even though those classifications are most commonly used, we decided to divide lymph nodes according to topographic anatomy into 5 groups – medial, lateral, posterior, central and apical. Some studies show that most of the lymph nodes in ARM are located between axillary vein and second intercostobrachial plexus (68%) or between the inferolateral side of the axillary and the thoracodorsal vessels in 58.76% of the patients (21, 24). Some of the studies use blue dye for ARM. They register between 29% to 90% success rate [25]. The mean lymph node yield is between 1 and 2.5 according to other studies using blue dye. Crossover with the sentinel lymph node is 4% (21, 24, 26, 27).

The main aim of axillary surgery for breast cancer is staging. The paradigm of complete axillary clearance has changed to sentinel lymph node biopsy. Even though, lymphedema as a complication of axillary surgery can occur. Reverse axillary mapping (RAM) was introduced to identify and preserve the limb-draining lymphatics with the help of a dye (21, 25, 28). RAM is a procedure that is easier to be performed in axillary lymph node dissection (ALND) due to a better view of the whole axillary region. It is challenging in SLNB, especially in high-BMI patients.

The Patent Blue V dye technique (used alone) is proven to be inferior to radioisotopes or ICG for sentinel axillary lymph node biopsy (15, 20, 29). Hence, the blue dye technique alone is not recommended for SLNB. In our study, we used Patent Blue V as a tracer for RAM and it showed a low success rate (15%).

The discussion what is the management if a sentinel lymph node is found and it is also responsible for upper extremity lymph flow (dye from axillary mapping is also present – Crossover) is still open. The same discussion is relevant when crossover in ALND and RAM occurs, although most studies recommend leaving the lymph node in situ if it is not enlarged.

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CONCLUSION

The use of Patent Blue V seems not to be an efficient method for reverse axillary mapping with a success rate of 15% in this study. The use of another tracker for reverse axillary mapping is appropriate. However, no upper extremity lymphedema is reported in patients after sentinel lymph node biopsy in this study.

Abbreviations:

SLNB – sentinel lymph node biopsy
ALND – axillary lymph node dissection
RAM – reverse axillary mapping

REFERENCES

1. S. Zahoor, A. Haji, A. Battoo, M. Qurieshi, W. Mir, and M. Shah, “Sentinel Lymph Node Biopsy in Breast Cancer: A Clinical Review and Update,” *jbc*, vol. 20, no. 3, pp. 217–227, Sep. 2017, doi: 10.4048/jbc.2017.20.3.217.
2. F. Cardoso *et al.*, “Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†,” *Ann. Oncol.*, vol. 30, no. 8, pp. 1194–1220, Aug. 2019, doi: 10.1093/annonc/mdz173.
3. M. L. Telli, W. J. Gradishar, and J. H. Ward, “NCCN Guidelines Updates: Breast Cancer,” *J. Natl. Compr. Cancer Netw. J Natl Compr Canc Netw*, vol. 17, no. 5.5, pp. 552–555, 2019, doi: 10.6004/jnccn.2019.5006.

4. U. Veronesi *et al.*, "Sentinel Lymph Node Biopsy in Breast Cancer: Ten-Year Results of a Randomized Controlled Study," *Ann. Surg.*, vol. 251, no. 4, 2010, [Online]. Available: https://journals.lww.com/annalsofsurgery/fulltext/2010/04000/sentinel_lymph_node_biopsy_in_breast_cancer_.3.aspx.
5. A. D. Purushotham *et al.*, "Morbidity after sentinel lymph node biopsy in primary breast cancer: results from a randomized controlled trial.," *J. Clin. Oncol. Off. J. Am. Soc. Clin. Oncol.*, vol. 23, no. 19, pp. 4312–4321, Jul. 2005, doi: 10.1200/JCO.2005.03.228.
6. T. Ashikaga *et al.*, "Morbidity results from the NSABP B-32 trial comparing sentinel lymph node dissection versus axillary dissection," *J. Surg. Oncol.*, vol. 102, no. 2, pp. 111–118, Aug. 2010, doi: https://doi.org/10.1002/jso.21535.
7. G. Gill and T. S. T. G. of the R. A. C. of S. (RACS) and N. C. T. Centre, "Sentinel-Lymph-Node-Based Management or Routine Axillary Clearance? One-Year Outcomes of Sentinel Node Biopsy Versus Axillary Clearance (SNAC): A Randomized Controlled Surgical Trial," *Ann. Surg. Oncol.*, vol. 16, no. 2, pp. 266–275, 2009, doi: 10.1245/s10434-008-0229-z.
8. P. Del Bianco *et al.*, "Morbidity comparison of sentinel lymph node biopsy versus conventional axillary lymph node dissection for breast cancer patients: Results of the sentinella–GIVOM Italian randomised clinical trial," *Eur. J. Surg. Oncol.*, vol. 34, no. 5, pp. 508–513, May 2008, doi: 10.1016/j.ejso.2007.05.017.
9. R. E. Mansel *et al.*, "Randomized Multicenter Trial of Sentinel Node Biopsy Versus Standard Axillary Treatment in Operable Breast Cancer: The ALMANAC Trial," *JNCI J. Natl. Cancer Inst.*, vol. 98, no. 9, pp. 599–609, May 2006, doi: 10.1093/jnci/djj158.
10. U. Veronesi *et al.*, "A Randomized Comparison of Sentinel-Node Biopsy with Routine Axillary Dissection in Breast Cancer," *N. Engl. J. Med.*, vol. 349, no. 6, pp. 546–553, Aug. 2003, doi: 10.1056/NEJMoa012782.
11. D. N. Krag *et al.*, "Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial.," *Lancet. Oncol.*, vol. 11, no. 10, pp. 927–933, Oct. 2010, doi: 10.1016/S1470-2045(10)70207-2.
12. S. G. Rockson, "Lymphedema after Breast Cancer Treatment," *N. Engl. J. Med.*, vol. 379, no. 20, pp. 1937–1944, Nov. 2018, doi: 10.1056/NEJMcp1803290.
13. J. M. Armer and B. R. Stewart, "Post-breast cancer lymphedema: incidence increases from 12 to 30 to 60 months.," *Lymphology*, vol. 43, no. 3, pp. 118–127, Sep. 2010.
14. N. R. Taghian, C. L. Miller, L. S. Jammallo, J. O'Toole, and M. N. Skolny, "Lymphedema following breast cancer treatment and impact on quality of life: A review," *Crit. Rev. Oncol. Hematol.*, vol. 92, no. 3, pp. 227–234, 2014, doi: https://doi.org/10.1016/j.critrevonc.2014.06.004.
15. A. Zada *et al.*, "Meta-analysis of sentinel lymph node biopsy in breast cancer using the magnetic technique," *Br. J. Surg.*, vol. 103, no. 11, pp. 1409–1419, Oct. 2016, doi: 10.1002/bjs.10283.
16. N. Wei *et al.*, "Sentinel lymph node biopsy with carbon nanoparticle suspension after neoadjuvant chemotherapy for breast cancer patients.," *Ann. R. Coll. Surg. Engl.*, vol. 103, no. 10, pp. 752–756, Nov. 2021, doi: 10.1308/rcsann.2021.0084.
17. X. Qin, M. Yang, and X. Zheng, "Comparative study of indocyanine green combined with blue dye with methylene blue only and carbon nanoparticles only for sentinel lymph node biopsy in breast cancer," *astr*, vol. 97, no. 1, pp. 1–6, Jun. 2019, doi: 10.4174/astr.2019.97.1.1.
18. T. Sugie *et al.*, "Evaluation of the Clinical Utility of the ICG Fluorescence Method Compared with the Radioisotope Method for Sentinel Lymph Node Biopsy in Breast Cancer.," *Ann. Surg. Oncol.*, vol. 23, no. 1, pp. 44–50, Jan. 2016, doi: 10.1245/s10434-015-4809-4.
19. J. Goonawardena, C. Yong, and M. Law, "Use of indocyanine green fluorescence compared to radioisotope for sentinel lymph node biopsy in early-stage breast cancer: systematic review and meta-analysis," *Am. J. Surg.*, vol. 220, no. 3, pp. 665–676, 2020, doi:https://doi.org/10.1016/j.amjsurg.2020.02.001.
20. C. L. Nguyen *et al.*, "Novel Dual Tracer Indocyanine Green and Radioisotope Versus Gold Standard Sentinel Lymph Node

Biopsy in Breast Cancer: The GREENORBLUE Trial," *Ann. Surg. Oncol.*, vol. 30, no. 11, pp. 6520–6527, 2023, doi: 10.1245/s10434-023-13824-6.

21. S. Jena, S. Bhattacharya, A. Gupta, and N. K. Sinha, "Axillary Reverse Mapping in Patients Undergoing Axillary Lymph Node Dissection: A Single Institution Experience From India.," *Cureus*, vol. 13, no. 7, p. e16462, Jul. 2021, doi: 10.7759/cureus.16462.
22. A. Puthangot, C. Chintamani, and M. Tandon, "Evaluation of Axilla With Sentinel Lymph Node Biopsy (Using Methylene-Blue) and Reverse Axillary Mapping (Using Fluorescein) to Validate Optimum and Safe Axillary Dissection in Breast Cancer.," *Cureus*, vol. 15, no. 9, p. e45267, Sep. 2023, doi: 10.7759/cureus.45267.
23. R. Cirocchi *et al.*, "New classifications of axillary lymph nodes and their anatomical-clinical correlations in breast surgery," *World J. Surg. Oncol.*, vol. 19, no. 1, p. 93, 2021, doi: 10.1186/s12957-021-02209-2.
24. J. W. Han, Y. J. Seo, J. E. Choi, S. H. Kang, Y. K. Bae, and S. J. Lee, "The efficacy of arm node preserving surgery using axillary reverse mapping for preventing lymphedema in patients with breast cancer.," *J. Breast Cancer*, vol. 15, no. 1, pp. 91–97, Mar. 2012, doi: 10.4048/jbc.2012.15.1.91.
25. A. H. Narasannaiah *et al.*, "Reverse Axillary Mapping in Breast Cancer Using Blue Dye: A Tertiary Setup Experience.," *Cureus*, vol. 13, no. 10, p. e18576, Oct. 2021, doi: 10.7759/cureus.18576.
26. M. A. Beek, P. D. Gobardhan, E. G. Klompenhouwer, H. J. T. Rutten, A. C. Voogd, and E. J. T. Luiten, "Axillary reverse mapping (ARM) in clinically node positive breast cancer patients.," *Eur. J. Surg. Oncol. J. Eur. Soc. Surg. Oncol. Br. Assoc. Surg. Oncol.*, vol. 41, no. 1, pp. 59–63, Jan. 2015, doi: 10.1016/j.ejso.2014.09.012.
27. C. Boneti *et al.*, "Scientific Impact Award: Axillary reverse mapping (ARM) to identify and protect lymphatics draining the arm during axillary lymphadenectomy.," *Am. J. Surg.*, vol. 198, no. 4, pp. 482–487, Oct. 2009, doi: 10.1016/j.amjsurg.2009.06.008.
28. X. Shao, B. Sun, and Y. Shen, "Axillary reverse mapping (ARM): where to go," *Breast Cancer*, vol. 26, no. 1, pp. 1–10, 2019, doi: 10.1007/s12282-018-0886-0.
29. M. C. Peek, T. Kovacs, R. Baker, H. Hamed, A. Kothari, and M. Douek, "Is blue dye still required during sentinel lymph node biopsy for breast cancer?," *Ecancermedicalscience*, vol. 10, p. 674, 2016, doi: 10.3332/ecancer.2016.674.