

The Need for Skin Pen Marking for Sentinel Lymph Node Biopsy: A Comparative Study

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ABSTRACT

Introduction: There is a consensus in the literature that sentinel lymph node biopsy is the standard procedure for axillary staging in early stage (I and II) breast cancer patients. Usually during lymphoscintigraphy, the location of the sentinel lymph node is marked on the skin by an indelible ink. In this study we evaluated this issue in our patients.

Methods: 40 patients with the clinical diagnosis of early stage breast cancer (stage I or II) were included into the study. All patients received periareolar intradermal injections of 18.5 MBq Tc-99m antimony sulfide colloid 2-4 hours before the surgery and 2 ml patent blue V dye in a subdermal and periareolar fashion during surgery. The patients were divided randomly into two groups (20 patients in each group). In group I, the anterior and lateral locations of the sentinel lymph node were marked on the skin with an indelible ink. In group II, no skin marking was used. A sentinel node was defined as any blue node or any node with an ex vivo radioisotope count of twofold or greater than the axillary background. All patients underwent standard axillary lymph node dissection after sentinel node biopsy.

Results: Mean age and tumor size were not significantly different between groups. SLN detection rate and number of detected SLNs were not significantly different either ($P>0.05$). Number of detected lymph nodes was 1.24 ± 0.43 and 1.28 ± 0.61 in group I and II of the patients, respectively. False negative rate (negative SLN and positive axillary nodes) for both groups were 0%.

Conclusion: Although marking the location of the sentinel lymph node on the skin with an indelible ink can guide the surgeon during surgery, it can not increase the sentinel lymph node detection rate or improve the results of sentinel lymph node biopsy.

Key words: Sentinel lymph node, Tc-99m antimony sulfide colloid, lymphoscintigraphy, Skin marking

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INTRODUCTION

There is a consensus in the literature that sentinel lymph node biopsy is the standard procedure for axillary staging in early stage (I and II) breast cancer patients (1-4). This technique significantly reduced the complications of axillary lymph node dissection such as lymphedema of the upper limb (5).

Sentinel lymph node biopsy usually involves injection of a special radiopharmaceutical (which migrates through lymphatic channels) and use of surgical gamma probe for detection of sentinel lymph node during surgery. This technique is usually combined with injection of a blue dye during surgery which is claimed to improve the overall detection rate of sentinel lymph node (6-8).

In the nuclear medicine departments after injection of the radiotracer, usually lymphoscintigraphy image sets are obtained. Lymphoscintigraphy can increase detection rate for melanoma in which the location of sentinel lymph node can be unpredictable (9, 10). Lymphoscintigraphy is also routinely performed for breast cancer patients. It can show the nuclear medicine specialist whether the sentinel lymph node is visible or not and also can show unusual locations of sentinel lymph nodes (such as internal mammary chain). However its contribution in detection rate of the sentinel lymph node is debated (11-13).

Usually during lymphoscintigraphy, the location of the sentinel lymph node is marked on the skin by an indelible ink (14, 15). Although this practice is in use all around the world, to the extent of our knowledge no study has been evaluated its contribution in sentinel lymph node biopsy. In this study we evaluated this issue in our patients.

METHODS

Forty patients with the clinical diagnosis of early stage breast cancer (stage I or II) were included into the study. The diagnosis of breast cancer was confirmed before surgery

by core needle biopsy. A commercial antimony sulfide colloid kit (AEOI, Tehran, Iran) was used and the labeling and quality control procedures were performed according to the manufacturer's instructions. All patients received periareolar intradermal injections of 18.5 MBq Tc-99m antimony sulfide colloid (16). All injections were done 2-4 hours before surgery and gentle massage was applied to the injection site subsequently.

2 minutes post-injection images were acquired on anterior, anterior oblique, and lateral views (3 minutes/image, 64×64 matrix) using a dual head gamma camera (E.CAM siemens), equipped with a parallel hole low energy high resolution collimator. In case of non-visualization of the sentinel lymph node, delayed imaging up to 180 minutes was performed.

The patients were divided randomly into two groups (20 patients in each group). In group I, the anterior and lateral locations of the sentinel lymph node were marked on the skin with an indelible ink. In group II, this was not performed.

In the operating room, 2 ml patent blue V dye was injected in a subdermal and periareolar fashion to all patients. A surgical gamma probe (RMD navigator GPS system) was used for detection of sentinel lymph nodes during surgery. A sentinel node was defined as any blue node or any node with an ex-vivo radioisotope count of two fold or greater than the axillary background. All patients underwent standard axillary lymph node dissection after sentinel node biopsy. All harvested lymph nodes underwent step sectioning at three levels (2mm apart) followed by standard hematoxylin and eosin (H & E) staining.

The study was approved by the local ethical committee and all patients gave an informed written consent before inclusion into the study.

Statistical analysis

Continuous variables are described by the mean value \pm SD. Fisher's exact test, χ^2 test, and Student's t test were used to compare

two groups according to the variable type. $P < 0.05$ was considered significant.

RESULTS

Demographic data of the patients is shown in Table 1. No significant difference was noted between two groups regarding these characteristics ($p > 0.05$).

The results of sentinel lymph node biopsy in studied groups are shown in Table 2. SLN detection rate and number of detected SLNs were not significantly different between two groups ($P > 0.05$). False negative rate (negative SLN and positive axillary nodes) for both groups were 0%.

Table 1: Demographic and clinical data of the studied groups.

	Group I	Group II
Total number of patients	20	20
Age	34±8	35±7
Tumor size	2.0±1	2.1±0.9
Tumor location		
Upper outer	9	10
Upper inner	3	3
Lower outer	2	2
Lower inner	2	2
Central	4	3
Histological type		
Invasive ductal	16	17
Invasive lobular	4	3
Axillary lymph node metastasis	7	8

Table 2: Comparison of results of sentinel lymph node biopsy between studied groups.

	Group I	Group II
Total number of patients	20	20
Detection rate	95% (19/20)	95% (19/20)
False negative rate	0%	0%
Number of detected lymph nodes	1.24±0.43	1.28±0.61

DISCUSSION

Pre-operative lymphoscintigraphy is usually accompanied by marking the location of sentinel lymph node on skin by an indelible ink (14, 15). The marks are intended to guide the surgeon during operation for sentinel lymph node biopsy.

Some studies have suggested that pre-operative lymphoscintigraphy imaging can improve sentinel lymph node detection for breast cancer (17, 18). It can also be of value for surgeons in the learning curve and in patients with problematic sentinel lymph node localization during surgery (such as obese patients) (19). Some studies suggest that a negative preoperative lymphoscintigraphy can predict sentinel lymph node detection failure during surgery (19, 20). Blue dye has been recommended for these patients. Not all studies agree with the above-mentioned advantages of the lymphoscintigraphy images and some claim that this technique neither can improve sentinel lymph node detection rate nor can predict failure during surgery (11-13).

Although many authors have studied different aspects of pre-operative lymphoscintigraphy in breast carcinoma, to the extent of our knowledge no study has been performed to evaluate the value of the skin marking for sentinel lymph node biopsy procedure. Skin marking can be helpful when extra-axillary lymph node harvesting is planned to be performed (21, 22). However this approach is believed to be excessively invasive and is not recommended by all experts (12). In addition, the rate of extra-axillary sentinel lymph node detection using superficial injection of the radiotracers is extremely low (23). Another problem with marking sentinel lymph node on skin in breast cancer is the proximity of the injection site to the sentinel node. This can decrease the accuracy of skin marking significantly, especially for the tumors in the upper lateral quadrants (12). In many cases, marking is difficult regardless of the tumor location due

to little space under the detectors of the gamma camera (15).

Detection rate and false negative rate were not statistically different in our studied groups which show that using skin markers can not improve the surgeon success for sentinel lymph node detection. No extra-axillary lymph node was detected in our patients, which can be attributed to the superficial injection of the tracer we used in our study. This fact also limited the use of skin marking in our study.

CONCLUSION

Although marking the location of the sentinel lymph node on the skin with an indelible ink can guide the surgeon during surgery, it can not increase the sentinel lymph node detection rate or improve the results of sentinel lymph node biopsy.

REFERENCES

1. Zavagno G, De Salvo GL, Scalco G, Bozza F, Barutta L, Del Bianco P et al. A randomized clinical trial on sentinel lymph node biopsy versus axillary lymph node dissection in breast cancer: results of the Sentinella/GIVOM trial. *Ann Surg* 2008; 247(2):207-213.
2. Mansel RE, Fallowfield L, Kissin M, Goyal A, Newcombe RG, Dixon JM et al. Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC Trial. *J Natl Cancer Inst* 2006; 98(9):599-609.
3. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Ashikaga T 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(10):881-888.
4. Veronesi U, Paganelli G, Viale G, Luini A, Zurrada S, Galimberti V et al. A randomized comparison of sentinel node biopsy with routine axillary dissection in breast cancer. *N Engl J Med* 2003; 349(6):546-553.

5. Purushotham AD, Upponi S, Klevesath MB, Bobrow L, Millar K, Myles JP et al. Morbidity after sentinel lymph node biopsy in primary breast cancer: results from a randomized controlled trial. *J Clin Oncol* 2005; 23(19):4312-4321.
6. Aarsvold JN, Alazraki NP. Update on detection of sentinel lymph nodes in patients with breast cancer. *Semin Nucl Med* 2005; 35(2):116-128.
7. Zanzonico P, Heller S. The intraoperative gamma probe: basic principles and choices available. *Semin Nucl Med* 2000; 30(1):33-48.
8. Bostick PJ, Giuliano AE. Vital dyes in sentinel node localization. *Semin Nucl Med* 2000; 30(1):18-24.
9. Albertini JJ, Cruse CW, Rapaport D, Wells K, Ross M, DeConti R et al. Intraoperative radiolymphoscintigraphy improves sentinel lymph node identification for patients with melanoma. *Ann Surg* 1996; 223(2):217-224.
10. Thompson JF, Uren RF, Shaw HM, McCarthy WH, Quinn MJ, O'Brien CJ et al. Location of sentinel lymph nodes in patients with cutaneous melanoma: new insights into lymphatic anatomy. *J Am Coll Surg* 1999; 189(2):195-204.
11. Tanis PJ, Valdés Olmos RA, Muller SH, Nieweg OE et al. Lymphatic mapping in patients with breast carcinoma: reproducibility of lymphoscintigraphic results. *Radiology* 2003; 228(2):546-551.
12. McMasters KM, Wong SL, Tuttle TM, Carlson DJ, Brown CM, Dirk Noyes R et al. Preoperative lymphoscintigraphy for breast cancer does not improve the ability to identify axillary sentinel lymph nodes. *Ann Surg* 2000; 231(5):724-731.
13. Tuthill LL, Reynolds HE, Goulet RJ Jr. Biopsy of sentinel lymph nodes guided by lymphoscintigraphic mapping in patients with breast cancer. *Am J Roentgenol* 2001; 176(2):407-411.
14. Buscombe J, Paganelli G, Burak ZE, Waddington W, Maublant J, Prats E et al. Sentinel node in breast cancer procedural guidelines. *Eur J Nucl Med Mol Imaging* 2007; 34(12):2154-2159.
15. Laasanen MS, Heikkinen JO, Saarakkala S, Paajanen H. Localization of sentinel nodes in breast cancer: novel method and device to help pen marking of active nodes during gamma camera imaging. *Phys Med Biol* 2005; 50(7):49-54.
16. Shabani GA, Hamzeh H, Najafi R. Production of ^{99m}Tc -Antimony Sulfide Colloid for lymphoscintigraphy. *Iran J Nucl Med* 2003; 19:65-57.
17. Borgstein PJ, Pijpers R, Comans EF, van Diest PJ, Boom RP, Meijer S. Sentinel lymph node biopsy in breast cancer: guidelines and pitfalls of lymphoscintigraphy and gamma probe detection. *J Am Coll Surg* 1998;186(3):275-283.
18. Reintgen D, Cox C, Haddad F, Costello D, Berman C. The role of lymphoscintigraphy in lymphatic mapping for melanoma and breast cancer. *J Nucl Med* 1998 Dec;39(12):22N, 25N, 32N, 36N.
19. Goyal A, Mansel RE. Does imaging in sentinel node scintigraphic localization add value to the procedure in patients with breast cancer? *Nucl Med Commun* 2005; 26(10):845-847.
20. Veronesi U, Paganelli G, Viale G, Galimberti V, Luini A, Zurrida S et al. Sentinel lymph node biopsy and axillary dissection in breast cancer: results in a large series. *J Natl Cancer Inst* 1999; 91(4):368-373.
21. Uren RF, Howman-Giles RB, Thompson JF, Malouf D, Ramsey-Stewart G, Niesche FW et al. Mammary lymphoscintigraphy in breast cancer. *J Nucl Med* 1995; 36(10):1775-1780.
22. Valdés Olmos RA, Hoefnagel CA, Nieweg OE, Jansen L, Rutgers EJ, Borger J et al. Lymphoscintigraphy in oncology: a rediscovered challenge. *Eur J Nucl Med* 1999; 26(4 suppl):S2-S10.
23. Fleming FJ, Hill AD, Kavanagh D, Quinn C, O'Doherty A, Collins CD et al. Intradermal radioisotope injection optimises sentinel lymph node identification in breast cancer. *Eur J Surg Oncol* 2003; 29(10):835-838.