



## Original research

## Localization of sentinel lymph node in breast cancer. A prospective study



Antonio Marrazzo <sup>a, b, \*</sup>, Vincenzo Davide Palumbo <sup>b, c, d</sup>, Emilia Marrazzo <sup>b</sup>,  
 Pietra Taormina <sup>a</sup>, Giuseppe Damiano <sup>b</sup>, Salvatore Buscemi <sup>b</sup>, Giuseppe Buscemi <sup>b</sup>,  
 Attilio Ignazio Lo Monte <sup>b, c</sup>

<sup>a</sup> Breast Unit, Casa di Cura Macchiarella, Palermo, Italy

<sup>b</sup> Department of Surgical, Oncological and Stomatological Disciplines, University of Palermo, Palermo, Italy

<sup>c</sup> PhD Course of Surgical Biotechnologies and Regenerative Medicine, University of Palermo, Palermo, Italy

<sup>d</sup> Euromediterranean Institute of Science and Technology (IEMEST), Palermo, Italy

## ARTICLE INFO

## Article history:

Received 23 March 2014

Accepted 3 May 2014

Available online 24 May 2014

## Keywords:

Breast carcinoma

Skip metastases

Axillary sampling

## ABSTRACT

**Introduction:** Sentinel Lymph Node Biopsy (SLNB) is the standard of care for staging axillary lymph nodes in women with breast cancer and clinically negative nodes. It is associated with reduced arm morbidity, moderated or severe lymphoedema, and a better quality of life in comparison with standard axillary treatment. Unfortunately, skip metastases makes all minimally invasive approaches, such as axillary sampling, unreliable. The aim of the present clinical prospective study is to evaluate the position of SLN in an important number of cases and establish the real incidence of skip metastases in clinically node-negative patients.

**Patients and methods:** A cohort of 898 female patients with breast carcinoma was considered, from 2001 to 2008. Once SLN was localized, by means of radio-colloid or blue dye staining, and isolated, a biopsy was performed. Only those positive for metastases were submitted to axillary dissection.

**Results:** Only in nine cases a SLN was not isolated. We had 819 cases of first level SLN (group A) and 69 cases of second level SLN (group B). Considering all of 889 cases, SLN was localized in the second level in 69 patients (7.8%); but if we consider metastatic SLN alone (340 cases), it was in the second level in 23 subjects (6.8%). In total, we had a positive second level SLN in 2.3% of cases (23/889).

**Conclusion:** Second level SLN could be considered only an anomalous lymphatic axillary drainage and it does not linked to particular histological variants of the primitive tumour. In our study, skip metastases were recognized in only 2.6% of cases, therefore, whenever a SLN is not isolated for any reason, the first level sampling represent a viable operative choice.

© 2014 Surgical Associates Ltd. Published by Elsevier Ltd. All rights reserved.

## 1. Introduction

Sentinel Lymph Node Biopsy (SLNB) is the standard of care for staging axillary lymph nodes in women with breast cancer and clinically negative nodes. In particular, if the SLN is not metastatic, the patient will not undergo a complete axillary lymph-node dissection (ALND). Results from several trials and meta-analysis, indicate that total survival, disease-free survival and regional disease control are statistically equivalent between patients treated with complete axillary dissection and those who are not treated, after a negative SLNB [1–3]. SLNB is associated with reduced arm morbidity, moderated or severe lymphoedema, and a better quality

of life in comparison with standard axillary treatment [4]. An alternative technique to SLNB could be represented by axillary sampling, especially for those cases of difficult lymph node isolation or when SLNB cannot be performed. Unfortunately, this approach has not been accepted yet, because of skip metastases [5] which can localize in a second level lymph node, making staging unreliable. The present clinical prospective study was performed to evaluate the position of SLN in an important number of cases and establish the real incidence of skip metastases in clinically node-negative patients.

## 2. Patients and methods

From January 2001 to December 2008, 898 patients with breast carcinoma underwent conservative surgery and SLNB; only

\* Corresponding author. Department of Surgical, Oncological and Stomatological Disciplines, University of Palermo, Via del Vespro, 129, 90127 Palermo, Italy.

E-mail address: [antonio.marrazzo@unipa.it](mailto:antonio.marrazzo@unipa.it) (A. Marrazzo).

**Table 1**  
Lymph node histologic features after SLNB.

	Group A	Group B	<i>p</i>
Hyperplastic	454 (55.43%)	41 (59.4%)	N.S
Micrometastases	97 (10.5%)	6 (8.69%)	N.S
Macrometastases	220 (26.9%)	17 (24.6%)	N.S
Isolated tumoral cells	48 (5.9%)	5 (7.2%)	N.S

patients with positive sentinel nodes were submitted to axillary dissection. Of these 898 patients, 645 had SLN localization by both radio-colloid and blue dye, and 242 by radio-colloid only. A detailed report of both methods used to identify the SLN is provided by a previous trial conducted by the authors [6]. SLN was localized on the base of Berg classification [7]: lateral (level I), posterior (level II), or medial (level III) to the pectoralis minor muscle. While isolating the lymph node, operative time was recorded. A complete axillary dissection was performed when sentinel nodes resulted positive for metastases.

A non-parametric statistical analysis was used and categorical variables were evaluated using the chi-squares test or Fisher's exact test, where appropriate. A value of  $p > 0.05$  was considered significant.

### 3. Results

Only in nine cases a SLN was not isolated, whereas, for the remaining 889 patients, we had 819 cases of first level SLN (group A) and 69 cases of second level SLN (group B). The median age at the time of entering the study was 54 (range 30–80) for group B and 55 (range 30–82) for group A. The operative time to perform quadrantectomy and SLN biopsy was respectively 44.7 min range: 25–60 min) for group A and 44.8 min (25–60 min) for group B. Considering all of 889 cases, SLN was localized in the second level in 69 patients (7.8%); but if we consider metastatic SLN alone (340 cases), it was in the second level in 23 subjects (6.8%). In total, we had a positive second level SLN in 2.6% of cases (23/889). No statistically significant correlation was found between histopathological variables of patients with SLN localized at first level and those with second level SLN (see Table 1). Three-hundred and ten patients of group A (out of 317) and 23 of group B, with metastatic lymph nodes, underwent ALND. Tables 2 and 3 underline there was no statistical difference between the two groups, when Non Sentinel Lymph Nodes (NSLN) alone were considered.

### 4. Discussion

In the last year, thanks to several studies on sentinel node, we have better understood the anatomy of lymphatic drainage of the breast. Up to now, scientific literature has reported different lymphatic drainages for different areas of the breast. With the use of lymphatic mapping and the increased experience in SLNB, there

**Table 2**  
NSLNs involvement after ADLN in SLN positive patients.

	Group A	Group B	<i>p</i>
Micrometastases	81 (26.1%)	5 (21.7%)	N.S
Negative N			
Micrometastases	15 (4.8%)	1 (4.3%)	N.S
Positive N			
Macrometastases	94 (30.3%)	9 (39.1%)	N.S
Negative N			
Macrometastases	120 (38.7%)	8 (34.7%)	N.S
Positive N			

**Table 3**  
Number of positive LNs after ALND in SLN positive patients.

	Group A	Group B	<i>p</i>
Single metastatic SLN	175 (56.4%)	14 (60.8%)	N.S
Metastatic LNs <3	56 (18.1%)	3 (13.1%)	N.S
Metastatic LNs >3	79 (25.5%)	6 (26.1%)	N.S

is now increasing evidence-based support that the lymphatic vessels of the mammary gland drain through a few common afferent lymphatic trunks to specific axillary sentinel lymph nodes, regardless of tumour location [8,9]. Thanks to this new concept, indications for SLNB have been improved. For instance, currently, SLNB in multicentric and multifocal clinically node-negative breast cancer is feasible, with high sensitivity and specificity and low false-negative rates, and no axillary recurrence [10,11].

Interestingly, different authors have reported different rates of incidence of skip metastases. Gaglia et al. [12] reported an incidence of 19.2%; in Lloyd's study [13], the 1.6% of the whole group and the 3.2% of the positive node group showed positive LNs in Level II–III with no metastasis in Level I, whereas in other studies the incidence was 5.5% and 8.7% [14] and 7.9% and 14.6% [15], respectively. Rosen reported an overall incidence rate for skip metastases of 1.6% and 3% in positive node group [5], whereas Keskek [16] reported axillary skip metastases in 4.75% of the total and in 10% of those patients with axillary metastases.

Already in 1984, Pigott et al. [17] estimated that at least 10% of all women with carcinoma of the breast had been understaged by an axillary node sampling. That was because in 25% of cases the first level was skipped, being the metastasis present at the second or third level LNs (skip metastases).

Finally, Parmar et al. evidenced no statistical difference between false-negative rates of SLNB and axillary sampling [18].

In our case, we reported the presence of a SLN in 69 patients out of 889 or 7.7%, but considering only positive node group, we found 23 cases of second level SLN, equal to 2.6%. Therefore, the involvement of the lymph nodes occurs in a stepwise continuous fashion from periphery of the axilla in 97.4% of patients.

### 5. Conclusion

Second level SLN could be considered only an anomalous lymphatic axillary drainage and it does not linked to particular histological variants of the primitive tumour. In our study, skip metastases were recognized in only 2.6% of cases, therefore, whenever a SLN is not isolated for any reason, the first level sampling represent a viable operative choice.

### Funding

None declared.

### Ethical approval

No ethical approval was necessary (retrospective study).

### Conflicts of interest

None declared.

### Author contribution

Marrazzo A. designed the study, analysed data, wrote the article and gave the final approval.

Taormina P., and Marrazzo E. collected data, analysed data and wrote the article.

Palumbo V.D., Damiano G., Buscemi S., and Buscemi G. wrote the article.

Lo Monte A.I wrote the article.

## References

- [1] D.N. Krag, S.J. Anderson, T.B. Julian, 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.* 11 (2010) 927–933.
- [2] U. Veronesi, G. Viale, G. Paganelli, et al., Sentinel lymph node biopsy in breast cancer: ten-year results of a randomized controlled study, *Ann. Surg.* 251 (2010) 595–600.
- [3] I.M. Van der Ploeg, O.E. Nieweg, M.C. van Rijk, R.A. Valdés Olmos, B.B. Kroon, Axillary recurrence after a tumour-negative sentinel node biopsy in breast cancer patients: a systematic review and meta-analysis of the literature, *Eur. J. Surg. Oncol.* 34 (2008) 1277–1284.
- [4] R.E. Mansel, L. Fallowfield, M. Kissin, et al., Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: the ALMANAC trial, *J. Natl. Cancer Inst.* 98 (2006) 599–609.
- [5] P.P. Rosen, M.L. Lesser, D.W. Kinne, E.J. Beattie, Discontinuous or “skip” metastases in breast carcinoma. Analysis of 1228 axillary dissections, *Ann. Surg.* 197 (1983) 276–283.
- [6] A. Marrazzo, P. Taormina, A. Noto, et al., Localization of the sentinel node in breast cancer: prospective comparison of vital staining and radioactive tracing methods, *Chir. Ital.* 56 (2004) 621–627.
- [7] J.W. Berg, The significance of axillary node levels in the study of breast carcinoma, *Cancer* 8 (1955) 776–778.
- [8] T.M. Tuttle, M. Colbert, R. Christensen, et al., Subareolar injection of <sup>99m</sup>Tc facilitates sentinel lymph node identification, *Ann. Surg. Oncol.* 9 (2002) 77–81.
- [9] C. Chao, S.L. Wong, C. Woo, et al., Reliable lymphatic drainage to axillary sentinel lymph nodes regardless of tumor location within the breast, *Am. J. Surg.* 182 (2001) 307–311.
- [10] A. Marrazzo, P. Taormina, E. Marrazzo, et al., The Sentinel node biopsy is not contraindicated in multifocal breast carcinoma, *Eur. J. Oncol.* 16 (2011) 105–110.
- [11] A. Marrazzo, P. Taormina, E. Marrazzo, A.I.L. Monte, G. Buscemi, The accuracy of sentinel lymph-node biopsy in breast cancer after previous excisional biopsy, *Eur. J. Oncol.* 18 (2013) 57–61.
- [12] P. Gaglia, R. Bussone, B. Caldarola, M. Lai, A. Jayme, L. Caldarola, The correlation between the spread of metastases by level in the axillary nodes and disease-free survival in breast cancer. A multifactorial analysis, *Eur. J. Cancer Clin. Oncol.* 23 (1987) 849–854.
- [13] L.R. Lloyd, R.K. Waits Jr., D. Schroder, A. Hawasli, P. Rizzo, J. Rizzo, Axillary dissection for breast carcinoma. The myth of skip metastasis, *Am. Surg.* 55 (1989) 381–384.
- [14] R.S. Boova, R. Bonanni, F.E. Rosato, Patterns of axillary nodal involvement in breast cancer. Predictability of level one dissection, *Ann. Surg.* 196 (1982) 642–644.
- [15] J.Y. Sun, L.S. Ning, Axillary skip metastases in breast cancer, *Zhonghua Zhong Liu Za Zhi* 30 (2008) 352–355.
- [16] M. Keskek, S. Balas, A. Gokoz, I. Sayek, Re-evaluation of axillary skip metastases in the era of sentinel lymph node biopsy in breast cancer, *Surg. Today* 36 (2006) 1047–1052.
- [17] J. Pigott, R. Nicols, W.A. Maddox, C.M. Balch, Metastases to the upper levels of the axillary nodes in carcinoma of the breast and its implications for nodal sampling procedures, *Surg. Gynecol. Obstet.* 158 (1984) 255–259.
- [18] V. Parmar, R. Hawaldar, N.S. Nair, et al., Sentinel node biopsy versus low axillary sampling in women with clinically node negative operable breast cancer, *Breast* 22 (2013) 1081–1086.