

Sentinel lymph nodes identification in early breast cancer - peritumoral or subareolar injection of lymphotropic blue dye?

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Background. The sentinel lymph node (SLN) biopsy is a recently developed, minimally invasive method for staging the axilla in patients with early breast cancer. The authors investigated the optimal technique - peritumoral versus subareolar injection for the localization of the SLN.

Patients and methods. 192 procedures out of 238 ones were performed using a blue dye peritumoral injection at the early breast cancer site against 46, with a subareolar technique. All patients underwent sentinel node biopsy, followed by an axillary lymph node dissection.

Results. The SLN were metastatic in 69 out of 80 axillary positive patients that accounted for 86,3%. The sentinel node histology correctly predicted the axillary disease in 90,6% with a peritumoral injection versus 68,8 % with a subareolar lymphatic mapping.

Conclusions. This experience indicates that the peritumoral injection of blue dye is a more accurate than the subareolar one for axillary staging.

Key words: breast neoplasms; lymphatic metastasis; axilla; lymph nodes-pathology; biopsy; early breast cancer; sentinel lymph node biopsy

Introduction

Axillary staging operations in patients with breast cancer range from sampling with a blind biopsy alone to complete or with a total

lymph node dissection. The concept of the sentinel lymph node (SLN) has profound consequences for our understanding of the process of tumour cell spread.

The sentinel lymphadenectomy has been shown as an attractive technique in multiple studies, carried out recently as a part of ongoing effort to find a less invasive and still adequate method for axillary staging (N+ or N-) in the cases of early breast cancer. The first SLN or SLNs along the lymphatic pathways have never before been traced by the preoperative instillation, both of the blue dye¹ or ra-

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dioactive nanocolloid² peritumorally. The histological assessment of this "strategic spot" after the biopsy was compared with the results of the axillary dissection. The accuracy is reported to be up to 87-100%.¹⁻³

The extensive research of the lymphatic drainage and metastatic mapping led some authors up to the idea of employing the alternative approach, namely - the subareolar injection of radiocolloids, aiming the indication of the SLN.^{4,5}

There is no sufficient data in the literature related to subareolar mapping of SLN. Hence, the purpose of the current study was to examine the both methods comparatively and to submit the results of the analyses.

Patients and methods

During the period from February 1995 through June 2000, 238 women with primary early invasive, unilateral breast carcinoma (T₁₋₂, N₀₋₁, M₀) scheduled for the surgical treatment at our department were enrolled in this study. The median age of the group was 56.1 years (range 24 to 75).

We excluded pregnant or lactating women, those who had previously undergone biopsy or received radiotherapy to the axilla. Patients with multicentric or multiphocal breast carcinoma, mammographically confirmed, were also excluded. Informed consent was obtained in all cases.

The technique of lymphatic mapping and sentinel node biopsy included the following: in 192 patients, 2 ml of lymphotropic blue dye were injected immediately before the introduction of anaesthesia with a fine needle (21-22 G) around the tumour. In the majority of cases - 147 (76.6 %), Patent blue V (BYK Gulden) was applied, and 19 patients received Drimaren Brilliant blue (Fluka). The study also included 26 females with breast cancer in whom locoregional perioperative chemotherapy with Mitoxantrone (Novan-

trone, Wyeth-Lederle) was carried out. Two sites around the tumour were injected with 0.5 ml (1 mg) Mitoxantrone. It was established that Mitoxantrone dyes the lymphatic system very well, so this drug was used as a dye occasionally.

The rest 46 patients received the subareolar injections into two different zones by 0,5 - 1,5 ml each, into the respective quadrant where the carcinoma had been localized.

Preoperative lymphoscintigraphy was performed in 9 patients. ^{99m}Tc - sulphur colloid (Solco Lymphoscint, Sorin) with the particle average diameter of 50 nm was injected in the subareolar area in volume of 0,2 - 0,3 ml. The specific radioactivity of the injection zone was 20 mBq. Planar images - in frontal and inclined positions were obtained by rotative - gamma camera (Diacam, Siemens). The visualization achieved: the early one - at the 20-th minute and the late one - at the 120 to 180-th minute after the application, respectively.

In most of the cases - 201 (84,5%) a modified radical mastectomy was performed and in 37 (15,5%) - quadrantectomy with axillary dissection. Lymphadenectomy in 215 cases (90,3%) includes I, II and III axillary anatomic levels and in 23 cases (9,7%) with minimal size of the tumour (<1cm) - I and II levels. All nodes in the axillary dissection specimen were processed for histologic examination using hematoxylin and eosin (H&E). Immunohistochemical techniques to identify micrometastases were not performed.

Results

The median amount of the removed and examined lymph nodes is 12,6 (range 10-21). The identified blue-stained SLNs ranged 1 to 3, i.e. 1,5 per case at the average. Sentinel nodes were located on level I in 193 cases, in 34 cases - on level I and II, and in 11 cases SLN mapped only on level II.

Lymph node metastases had been found in

80 patients that accounted for 33,6% of the background - 64 of them from the group with peritumoral application of blue dye and 16 belonged to the group with subareolar application. Sixty-nine women (86,3%) had positive SLNs (Table 1).

Table 1. The axillary status of the two groups of patients studied

SLN	Lymph dissection		Total
	(+)	(-)	
Peritumoral			
(+)	58	-	58
(-)	6	128	134
Subareolar			
(+)	11	-	11
(-)	5	30	35
Total	80	158	238

SLN= sentinel lymph node

In most cases with mapped metastatic SLN the primary tumour is located in the lateral quadrants (53 cases). In 16 patients the carcinoma is localized centrally and in the rest 11 cases the tumour had medial location (Table 2).

After the preoperative lymphoscintigraphy hot spots were identified in 7 cases. In five women one SLN in each case were scanned in the axilla site zone on level I - as at the early so at the late stage of scanning. In other two patients with medial location of the tumour 1 sentinel node in each case was visualized in the area of ipsilateral lymphatic parasternal chain. With only two patients none SLN was visualized neither at the early nor at the late stage of the study most likely

due to microembolies in the lymphatic vessels, draining the tumour-bearing breast.

Discussion

Metastatic lymph nodes involvement proved to be the basic principal in the clinical strategic assignment and prognostication in cases of early breast cancer. The removal of the nodes from the levels I and II is a routine surgery operation when the primary breast cancer is diagnosed and thus, up to 98 % of the cases with positive axilla are identified.⁶ At the same time, the relatively high percentage (67-80%) with early disease with tested negative lymph nodes, as well as possible postoperative complications (lymphoedema), approved the necessity of a sentinel lymphadenectomy as an alternative to the lymph node dissection over the last decade.

The accuracy of this procedure is confirmed in numerous studies. There is a probability of only 0-6% of detecting false negative SLNs after the peritumoral application of blue dye or radiocolloids.^{1-3,6}

According to the results of the two studies of Klimberg et al. and Mertz et al., published so far, the exactness of 100% was reported to be achieved with 68 and 47 patients, respectively, who had received ^{99m}Tc sulfocolloid subareolar injection.^{4,5}

As to the accuracy after the peritumoral mapping, our results (90,6% of background) concur with those, performed by the other authors employing this method.

Simultaneously, some differences are ob-

Table 2. Location of the primary tumour in the cases with metastatic SLN

Localization	Peritumoral		Subareolar	
	Axilla (+)	SLN (+)	Axilla (+)	SLN (+)
Lateral	44	42	9	5
Central	12	11	4	4
Medial	8	5	3	2
Total	64	58 (90,6%)	16	11 (68,8%)

served between our results and figures, given in the literature, regarding the subareolar technique. We achieved 68,8% of diagnostic precision, using this method that appears to be much lower, in comparison to the percentage, presented in the other two studies, mentioned above.

These results may be explained as follows:

- The subareolar technique, being new and at its first stages, may give the accuracy which still remains debatable.
- The investigation was conducted up to now on an insufficient number of patients;
- Lymphatic drainage might be traced incompletely and further combination of blue dye and radiocolloids may raise the rate of strictness of this method;
- Metastatic SLN are not localized precisely by a microscope examination. We assume that in an additional immunohistochemical investigation micrometastases might be found.

In conclusion, the authors of the current study state that the peritumoral application of blue dye or radiocolloids technique is considered to be a reliable tool in determination of axillary status, verified histologically, whereas subareolar SLN mapping is still disputable and only further extending research would correctly evaluate its efficiency and positive/negative predictive values.

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