Detection of Sentinel Lymph Node in Breast Carcinoma Using A Combined Injection Tecnique

MEME KANSERİNDE SENTİNEL LENF NODU SAPTANMASINDA KOMBİNE ENJEKSİYON TEKNİĞİ

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Abstract

Objective: The comparison of different injection techniques of Tc-99m nanocolloid for the diagnosis of sentinel lymph node in patients with breast carcinoma.

Material and Methods: Fifty-nine patients who were admitted to the surgery clinic with the diagnosis of breast carcinoma were included in the study. Tc-99m nanocolloid was injected peritumoral or pericaviter to 16 patients, combine to 35 patients, intratumoral to 8 patients. Sentinel lymph node localization was established with a gamma probe and blue dye during surgery. Forty seven patients underwent sentinel lymph node biopsy and axillary lymph node dissection, 12 patients underwent only sentinel lymph node biopsy. Sentinel lymph node was established in 50 patients by gamma probe during surgery. Three injection techniques were compared with chi-square statistical technique. All dissected lymph nodes were evaluated histopathologically.

Results: Success rate of peritumoral or pericaviter, combine and intratumoral injection techniques were calculated 75% (12/16), 91% (32/35) and 75 % (6/8), respectively. Lymph node metastases were established in 13 patients both sentinel lymph node and axillary lymph node. Lymph node metastases were established in only sentinel lymph node in 3 patients. There were 3 false negative results. There was no statistically significant difference between the groups ($p>0.05$).

Conclusion: Though there was no statistically significant difference, the success percentages of combined injection technique was higher than the others.

Key Words: Breast carcinoma, sentinel lymph node, Tc-99m nanocolloid, gamma probe

Özet

Amaç: Meme kanseri saptanan hastalarda sentinel lenf nodu tespiti için kullanılan Tc-99m nanokolloid'in farklı enjeksiyon tekniklerinin karşılaştırılması.

Gereç ve Yöntemler: Cerrahi polikliniğine başvuran meme kanseri saptanan 59 hasta çalışmaya dahil edildi. Operasyondan önce Tc-99m nanokolloid 16 hastaya peritümöral veya perikaviter, 35 hastaya kombine, 8 hastaya ise intratümöral olarak enjekte edildi. Operasyon esnasında sentinel lenf nodu lokalizasyonları gama prob ve mavi boya kullanılarak saptandı. 47 hastaya sentinel lenf nod biyopsisi ve aksiller lenf nod disseksiyonu, 12 hastaya ise sadece sentinel lenf nod biyopsisi uygulandı. 50 hastada sentinel lenf nodu gama prob ile başarılı olarak çıkarıldı. Üç enjeksiyon tekniğinin başarısı ki-kare testi kullanılarak karşılaştırıldı. Çıkarılan tüm lenf nodları histopatolojik olarak değerlendirildi.

Bulgular: Peritümöral veya perikaviter, kombine ve intratumoral enjeksiyon tekniklerinin sentinel lenf nodunu saptamadaki başarı oranları sırasıyla %75 (12/16), %91 (32/35) ve %75 (6/8) olarak hesaplandı. 13 hastada hem sentinel lenf nodunda hem de aksiler lenf nodlarında metastaz saptanırken, 3 hastada sadece sentinel lenf nodunda metastaz saptandı. 3 yanlış negatif sonuç izlendi. Enjeksiyon grupları arasında istatistiksel olarak anlamlı fark bulunamadı ($p>0. 05$).

Sonuç: İstatistiksel olarak gruplar arasında anlamlı fark saptanmamakla birlikte, meme kanserinde sentinel lenf nodunun saptanmasında kombine yöntemin diğer iki yönteme göre daha başarılı olduğu görülmüştür.

Anahtar Kelimeler: Meme kanseri, Sentinel lenf nodu, Tc-99m nanokolloid, Gama prob

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Sentinel lymph node (SLN) is the first lymph node of the tumor's lymphatic drainage. The excision of this node called SLN biopsy, gives information about the tumoral infiltration of SLN. The exclusion of metastasis in SLN makes the regional lymph node dissection unnec-

essary.[1-4] Only the 30% and 10% of the axillary lymph node (ALN) dissection is positive in palpable breast carcinomas and non-palpable breast carcinomas, respectively. This brings out a 70-90 % unnecessary ALN dissection.[5,6] The complications of ALN dissection are ipsilateral arm edema, hematoma, neuropathy and infections. Therefore, SLN biopsies can prevent unnecessary surgery and related complications.

Localization of SLN was first described by David Krag and his colleagues in 1993 using Tc-99m sulphurcolloid and peritumoral injection.[7] Although many studies have been performed in this field until now, there are still controversies concerning the diameter of the colloid, the site and volume of the injection. The site of the injection can be subdermal, intradermal, peritumoral, intratumoral or subareolar. The subdermal injection method was described by Veronesi et al, but Cox et al declared that subdermal lymph drainage will not completely reflect the parenchymal lymphatic drainage of the breast and they advocated peritumoral injection as a better method.[8,9] Therefore, combined injection technique such as peritumoral and subdermal, peritumoral and intradermal have been used in order to reflect both parenchymal and superficial lymphatic drainage of the breast tissue. In these studies it has been reported that axillary, intramammarial and infraclavicular lymphatic drainage of tumor can be shown by combined injection technique.[10]

In this study we used three different injection techniques for the localization of SLN in breast carcinoma. Our aim was to establish the success rates of peritumoral or pericaviter (PT), peritumoral or pericaviter and intradermal (combine, PT+ID) and intratumoral (IT) injections techniques and to compare their usefulness in the localization of SLN.

Material and Methods

Fifty nine female patients who were admitted to the surgery clinic between November 1998 and March 2004 with the diagnosis of T1 or T2, N0, M0 breast carcinoma were included in the study. Tc-99m nanocolloid (Nycomed Amersham SorinS.r.I., with colloidal diameter $\leq$ 80 nm) was injected PT to 16, PT+ID to 35 and IT to 8 patients before the surgery. PT injections were made in 4 quadrants which are 0.5 cm away from the tumor. The injected activity and the volume were 7.4 MBq (200 μCi) and 0.5 cc respectively. PT+ID injections were given as peritumoral or if the tumor was previously excised, pericaviter (7.4 MBq/0.5 cc) to 4 quadrants which are 0.5 cm away from the tumor and intradermal (7.4 MBq/0.1 cc) to the skin overlying the tumor. IT injections were done directly into the tumor (7.4 MBq/0.5 cc). Lymphoscintigraphy was performed to 46 patients (7PT, 35PT+ID, 4IT) and dynamic imaging from anterior view, anterior and lateral prone static images were obtained up to two hours. Dynamic imaging was obtained to detect the first lymph node of the tumor's lymphatic drainage. A double head gamma camera (Siemens MULTISPECT II) with low energy all purpose collimator was used for imaging. Ninety dynamic images (each for 2 seconds) and 5 minute static images (at 5^{th}, 15^{th}, 30^{th} minutes and first and second hour) were obtained. A scintimammographic pallet was used for prone images. The skin overlying the SLN was marked with an unerasable pen using a gamma probe (Navigator GPS, with a probe head diameter 14 mm and energy spectrum between 27-364 keV, maximum count rate 25000 cps and detector material CdTe) while the patient was in surgical position in whom SLN was detected by lymphoscintigraphy. Lymphoscintigraphy could not be performed in 13 patients due to the lack of enough time for imaging before the surgery. The operational field was searched circularly and linearly with the gamma probe for SLN activity and also blue dye (isosulphan blue, subdermal injection) was used during the surgery. Breast protecting surgery, SLN biopsy and ALN dissection were performed to 47 patients. 12 patients underwent to only breast protecting surgery and SLN biopsy with no ALN dissection. SLN was successfully excised 54 in patients and sent for histopathologic diagnosis. Standard cross-sections and routine hemotoxylene-eosin staining were performed for histopathologic examination. In tumor negative cases all SLNs were examined with deep serial

cross-sections. Immunohistochemical cytokeratin was performed to two sections of different levels and micrometastases were searched. Tumor negative SLNs were accepted to be non-metastatic after immunohistochemical staining.

The success rates of different injection techniques for detection of SLN were calculated and the success rates of three injection techniques were compared with chi-square statistical technique (SPSS 11.00).

Results

The mean age of 59 patients was 53±13 (50±14 in PT groups, 58±14 in ID group, and 54±12 in PT + ID group). There was no statistical significant difference between the age groups (p>0, 05). The histopathological results of the 59 patients were 47 invasive ductal carcinoma, 4 invasive lobular carcinoma, 3 invasive ductal and lobular carcinoma, 2 mucinous carcinoma, 1 tubular carcinoma, 1 medullary carcinoma, 1 papillary carcinoma of the breast. Table 1 and 2 summarizes the detected SLN and success rate of different injection techniques. Twelve SLN (11 PT+ID, 1 PT) was shown by dynamic images. One hundred five SLN was successfully excised in 54 patients. No uptake was seen either in the axilla or outside of axillary bed in 6 of 46 patients by lymphoscintigraphy. In 2 of 6 patients, SLN was found by gamma probe and blue dye, in 1 was found only by blue dye. They were detected and excised with the use of gamma probe and blue dye in 32 (9 PT, 18 PT+ID, 5 IT), (61 SLN), with gamma probe alone 18 (3 PT, 14 PT+ID, 1 IT), (37 SLN), with blue dye alone in 4 (2PT, 2IT), (7 SLN) patients. Neither intraoperative gamma probe, nor blue dye was positive for SLN in 5 (2 PT, 3 PT+ID) patients. All of these patients had complete ALN dissection. ALN were positive in 3 of 5 and negative 2 of 5. Of 105 SLN, 1 was located in intramammarial lymph chain (PT+ID) and 104 (21 PT, 69 PT+ID, 14 IT,) were located in axillary region. There was more than one SLN in 28 patients.

The histopathologic results of SLNs and ALNs were summarized in Table 3. There were 3 false negative results. There was no statistical significant difference between the groups (p>0, 05).

Images of PT, PT+ID and IT injection technique were shown in Figures 1, 2 and 3, respectively.

Discussion

The injection technique of the radiocolloid for the detection of SLN in breast carcinoma is still a debate. Peritumoral and subdermal injections were among the most frequently used techniques until today. Subdermal injection technique was first described by Veronesi et al.[8] They injected serum albumin subdermally in 163 patients with breast carcinoma and reported a success rate of 97.5% for

Table 1. SLN detection in three injection techniques by lymphoscintigraphy.

	PT		PT + ID		IT	
	SLN (+)	SLN (-)	SLN (+)	SLN (-)	SLN (+)	SLN (-)
Lymphoscintigraphy	5	2	32	3	3	1
Success rate	5/7 (71 %)		32/35 (91 %)		3/4 (75 %)	

Table 2. SLN detection and success rate in three injection techniques by gamma probe.

	PT		PT + ID		IT	
	SLN (+)	SLN (-)	SLN (+)	SLN (-)	SLN (+)	SLN (-)
Gamma probe	12	4	32	3	6	2
Success rate	12/16 (75 %)		32/35 (91 %)		6/8 (75 %)	

Table 3. Histopathologic results of SLNs and ALNs.

	SLN Metastases (+)	SLN Metastases (-)	Total
ALN Metastases (+)	13	3	16
ALN Metastases (-)	3	23	26
Total	16	26	42

SLN localization. Borgstein et al also advocate that lymphatic pathways of both the subdermal and the tumoral region drain into the same lymphatic region.[11] They have injected radiocolloid peritumorally and the blue dye subdermally on 33 patients and shaped that they drain into the same

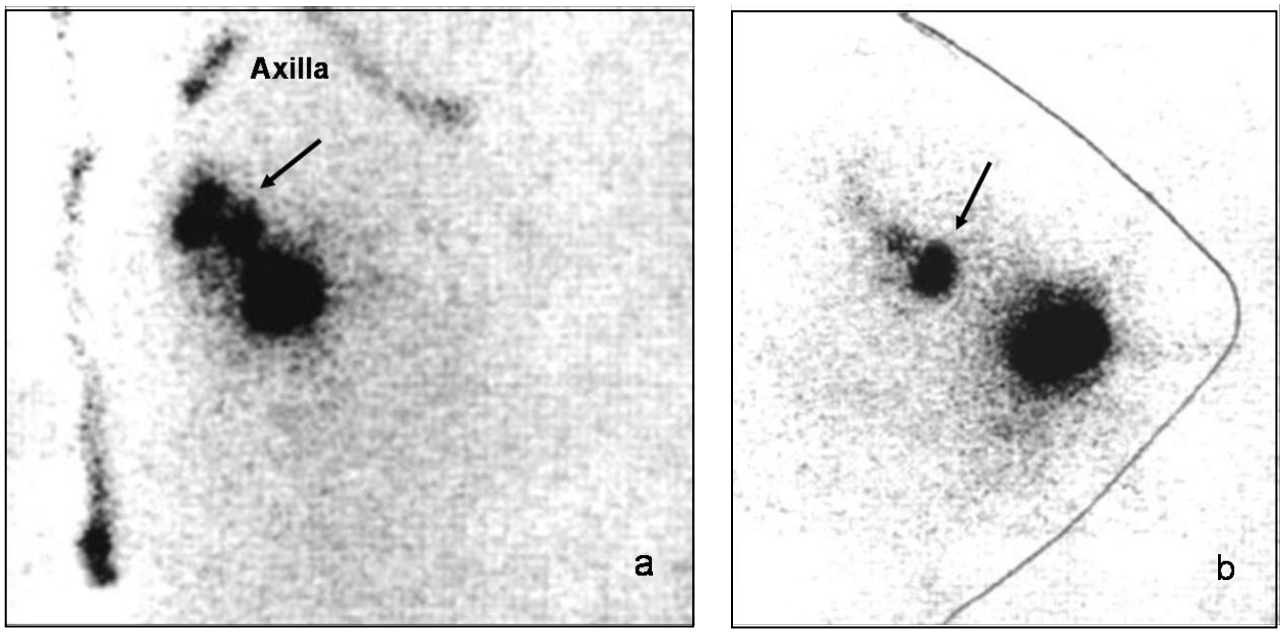

Figure 1. Peritumoral injection technique. Anterior **(a)** and lateral **(b)** images showing increased activity in right axillary region corresponding to SLN (black arrows).

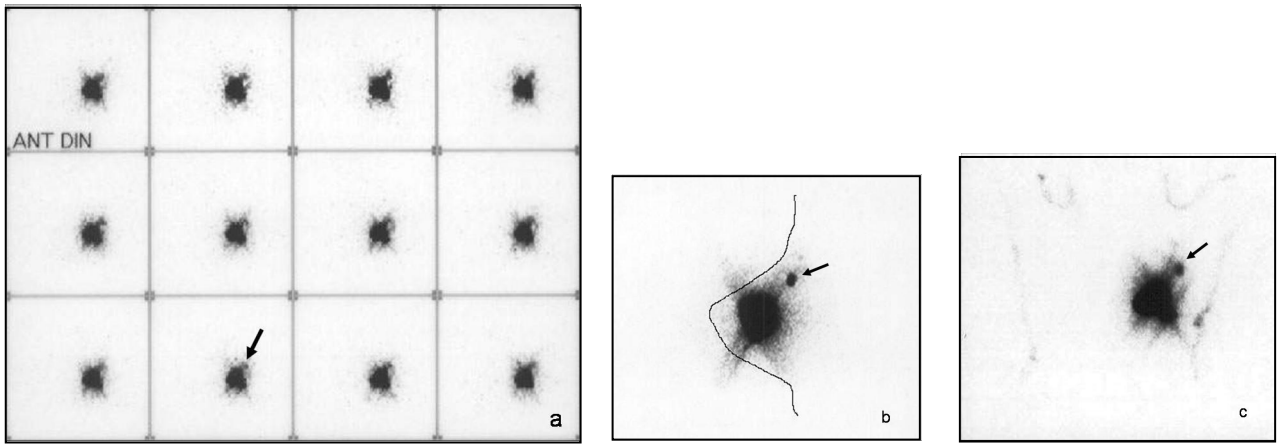

Figure 2. Peritumoral and intradermal injection technique. Dynamic **(a)**, lateral **(b)** and anterior **(c)** images shows a SLN (black arrows) on the left axillary region.

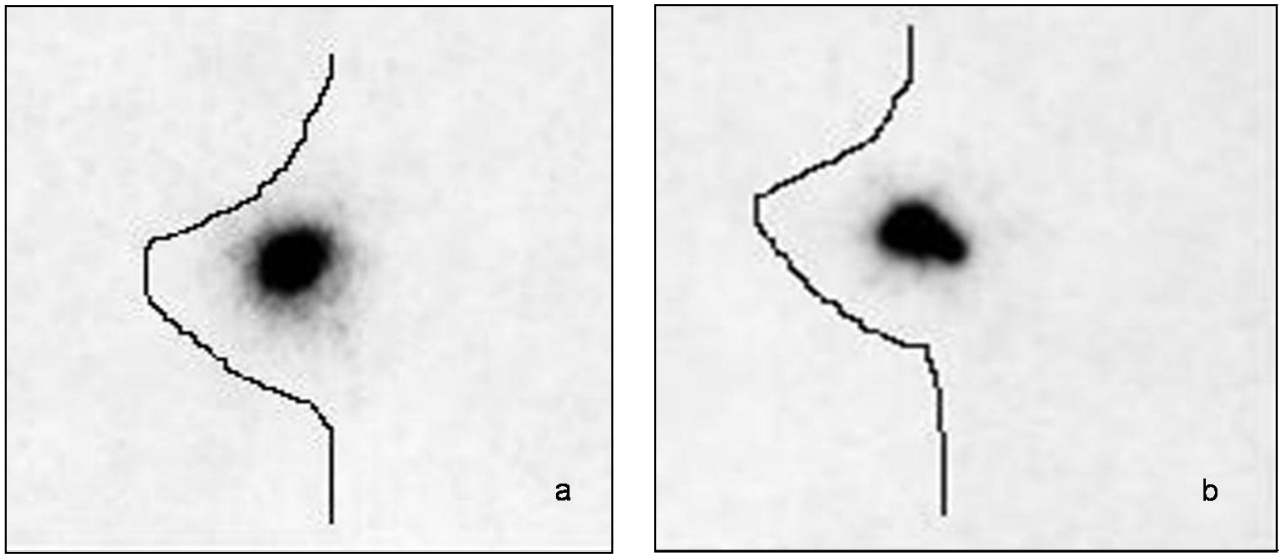

Figure 3. Intratumoral injection technique. There was no activity of corresponding to SLN in early **(a)** and late **(b)** (2hour) images.

lymph node.[11] Subdermal injection can be useful especially when the tumor is superficial and palpable. However there is still a debate on the topic if subdermal lymphatic drainage reflects the parenchymal lymphatic drainage of the breast. From this point of view some authors advocate the peritumoral injection technique.[9] Some other comparative studies declare that peritumoral injection technique is especially successful in detecting intramammarial lymph nodes,[12-15] while some studies demonstrated that subdermal injection technique is more successful than peritumoral injection.[16,17] Alazraki et al reported 98% and 96% success rates with subdermal and peritumoral injections, respectively.[12] Mateos et al declared a 100% success rate with subdermal injection technique and 98% with peritumoral.[13] Motomura et al compared the subdermal versus intradermal injection techniques and showed a success rate of 92.7% and 100%, respectively.[18] On the other hand the success rates of intratumoral injection were declared to be between 87-97% in some studies.[19-21] In addition, Pelosi et al. reported 98.3% and 90.5% success rate with periareolar and subdermal/peritumoral injections, respectively.[22]

In a study of Feezor et al which is similar to our study they showed the success rates 98.5%, 83.3% and 100% for intradermal injection, peritumoral injection and combined teqnique, respectively.[10] In our study we used PT, PT+ID and IT injection techniques and according to our results the success rates for SLN detection were 75%, 91% and 75% respectively. Our results demonstrate that combined PT+ID injections are the best for SLN detection. On the other hand, low success rates of PT and IT injection techniques may be related to number of patient in these groups.

PT injections better demonstrate non-axillary lymph nodes.[12-14] ID injections demonstrate axillary lymph nodes better than other technique because the dermal and the parenchymal lymphatics of the breast join at the level of subaerolar lymphatic plexus and drain into the axillary region.[12-14] In this respect combined PT+ID injections give chance to demonstrate the axillary, intramammarial and infraclavicular lymph nodes. On the other hand IT injections alone decrease the success rate for demonstrating axillary lymph nodes.

We could not perform lymphoscintigraphy for all the patients. But we had chance to perform lymphoscintigraphy to all our patients whom PT+ID injection technique was used with a success rate of 91% (32/35, Table 1). Lymphoscintigraphy was negative in 3 patients. Lymphatics can become infiltrated with tumor cells and do not allow the passage of radionuclide in the patients whom can

not establish by lymphoscintigraphy, gamma probe and blue dye.

Performing lymphoscintigraphy before surgery brings some advantages; first, it exactly localizes SLN for surgeons. Secondly, it prevents skipping of intramammarial SLN. Additionally one has the chance to mark the location of SLN to overlying skin. Therefore we propose to perform lymphoscintigraphy to all patients in whom SLN will be searched.

We conclude that, though there was no statistically significant difference, the success percentages of combined injection technique for SLN detection was higher than PT or IT injection alone. The combination of peritumoral and intradermal injection technique was a reliable method of sentinel lymph node detection in breast cancer. We think that new studies including more patients in subgroups are needed to reach statistically significant result.

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