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Identification of sentinel lymph node in breast cancer by lymphoscintigraphy and surgical gamma probe with peritumoral injection of scintimammographic agent "^{99m}Tc MIBI"

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The purpose of this study was to evaluate the efficacy of lymphoscintigraphy and the surgical gamma probe (SGP) with peritumoral injection of ^{99m}Tc MIBI in sentinel lymph node (SLN) detection in breast cancer regardless of whether metastatic or not. ***Method:*** Thirty patients with T1/T2 breast cancer had peritumoral injections of ^{99m}Tc MIBI (74 MBq/0.2 m*l* at 4 different locations) at 2, 6 and 24 hours before surgery. Anterior, anterolateral, and lateral spot images were taken at 10, 30, 45, 60 and 120 minutes. Counts were collected from the injection site, affected breast tissue, internal mammaries, axillary and supraclavicular regions, and the contralateral side. Peritumoral blue dye was also injected at surgery. The first lymph nodes with counts twice the background tissue and/or with blue dye uptake were surgically isolated, and histopathological evaluations were made. Modified radical mastectomy was performed on all patients. ***Results:*** 23/30 patients had lymph nodes in scintigrams and the sentinel lymph nodes were identified with SGP in 25/30 patients. ***Conclusion:*** Lymphoscintigraphy and subsequent SGP detection with peritumoral injection of ^{99m}Tc MIBI can be used for identifying SLN in breast cancer.

Key words: ^{99m}Tc MIBI, lymphoscintigraphy, surgical gamma probe, breast cancer, sentinel lymph node

INTRODUCTION

BREAST CANCER is a major health concern in women, and the 3 year survival rate is less than 85% for all stages.[1–3] Axillary lymph node status is the most important pathological determinant of prognosis in early breast cancer and total axillary lymphadenectomy is usually preferred[4–9] but the potential morbidity of axillary dissection is significantly high and may cause some serious problems.[10–12]

The sentinel lymph node is the first lymph node from which the tumor is drained, and it is the first to become involved in metastasis from the tumor. Identification of the sentinel lymph node plays an important role in surgical planning in the management of breast cancer.[13–15] If the sentinel lymph node(s) is not involved, complete axillary dissection may not be necessary, and this may reduce morbidity.

The sentinel lymph node can be identified with blue dye,[16,17] lymphoscintigraphy,[18–20] and the surgical gamma probe.[21–23]

In blue dye, 1–5 m*l* isosulfan blue is injected into the tumor just before the operation and is taken up by the lymphatic system. The blue dye shows the lymphatic drainage of the tumor, and blue stained nodes are accepted as the sentinel lymph nodes.

In lymphoscintigraphy, the radiopharmaceutical is injected peritumorally, intra-tumorally or intradermally and it is taken up by the lymphatic system. The region of lymphatic drainage of the tumor is evaluated and the first draining node of the tumor is accepted as a sentinel lymph node.

Surgical gamma probe (SGP) is a radioguided technique

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that enables the identification of sentinel lymph nodes during surgery. The radioactivity is detected by means of the surgical gamma probe. The nodes with the highest count rate are identified as the sentinel lymph node and dissected. The type of operation is decided according to the histopathological examination.

Radiocolloids, radiolabeled macromolecules and monoclonal antibodies are successfully used for lymphoscintigraphy and for SLN localization with SGP.

^{99m}Tc MIBI is a tumor seeking agent but the mechanism of tumoral uptake of this agent is not clear.[24–29] It is a successful agent for scintimammography and the lymph nodes were incidentally identified during scintimammography in a few studies.[30,31]

^{99m}Tc MIBI is used for lymphoscintigraphy with peritumoral injection in a very limited number of studies.[32]

In this study our aim was to evaluate the efficacy of ^{99m}Tc MIBI in SLN localization in breast cancers inspired by the observation that it is a good scintimammographic agent and lymph node uptake may occur during scintimammography.

MATERIALS AND METHODS

Thirty breast cancers staged as I and II preoperatively without any indication of axillary lymph node involvement underwent this study (32–61 years, mean age 46.4 ± 8.4). Informed consent was obtained from all the patients.

^{99m}Tc MIBI was injected in the peritumoral area at 4 different localizations 2–24 hours before the operation (2–6 hours after MIBI injection in 11 patients, 6–12 hours after injection in 13 patients, 12–24 hours after injection in 5 patients). Each injection was 74 MBq/0.2 m*l*. The images were taken immediately after injection at 10 min, 30 min, 45 min, 60 min, 120 min. Images were taken up to 24 hours to evaluate the wash out of MIBI in 5 patients (140 keV peak, GE starcam 3200, GE Camstar 4000I, 20% window, 10 minute images 256 matrix). Anterior, anterolateral and lateral images were obtained and evaluated qualitatively.

1–5 m*l* blue dye was injected peritumorally in 16/30 patients just before the operation and lymphatic channels were investigated visually.

Intraoperative localization of the sentinel lymph node was performed with a surgical gamma probe (Europrobe, the 140 keV photopeak of ^{99m}Tc was captured with a 20% window and probe sensitivity was 800 counts/sec/μCi ^{99m}Tc at contact).

All operations were performed by the same surgeon. The surgical gamma probe was covered with a sterile endoscopic probe cover. The breast mass, axillary, supraclavicular, infraclavicular, parasternal regions, rectus sheat and internal mammary regions were scanned with SGP. A hot spot was defined as a focus of increased activity and the node with the highest count and the closest to the tumor was identified as the sentinel lymph node. The radioactive node was removed and was also counted *ex-vivo*. Total axillary lymphadenectomy and modified radical mastectomy were performed on all the patients. All resected axillary tissues were scanned with the probe *ex-vivo* to detect any missing radioactive lymph nodes.

Histopathological analysis was performed by microscopic examination with hematoxylin-eosine.

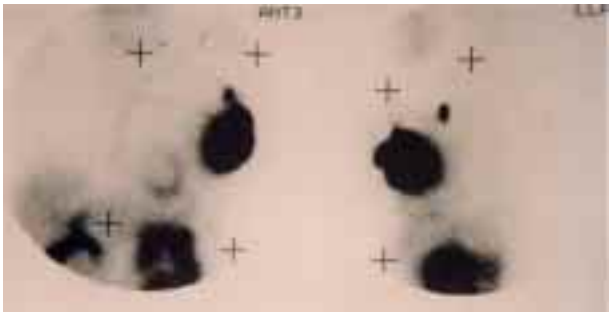

Fig. 2 A 33-year-old female with tumor in left lower inner quadrant. The lymph node and lymphatic channel were scanned at 2 hour images after peritumoral ^{99m}Tc MIBI injection.

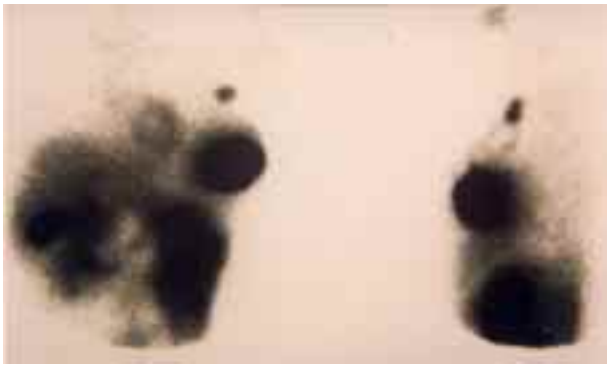

Fig. 1 A 51-year-old female who had adenocarcinoma in the left lower outer quadrant. The sentinel lymph node was identified clearly in the early image (30 minutes).

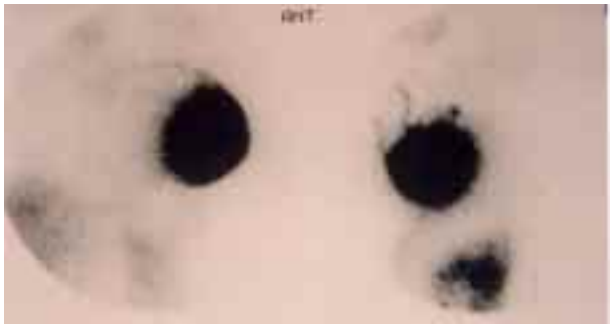

Fig. 3 A 37-year-old female, the tumor was localized in left upper outer quadrant. The sentinel lymph node was observed near the tumor and the lymphatic channels were identified also at 2 hour images.

Table 1 Tumor localization and results of lymphoscintigraphy, SGP and pathology in patients

No.	Age	Tumor localization	Lymphoscintigraphy	SGP	SLN metastasis
1	35	LUIQ	+	+	+
2	46	LLOQ	+	+	+
3	57	LUIQ	+	+	+
4	43	LLIQ	+	+	+
5	46	RLOQ	–	–	–
6	45	LIOQ	+	+	–
7	36	RUIQ	–	–	–
8	37	LUOQ	+	–	–
9	41	LMOQ	+	+	+
10	32	RUIQ	+	+	+
11	61	RUOQ	–	–	–
12	38	Right subareolar region	–	–	–
13	30	LUIQ	–	+	+
14	49	LUOQ	–	–	–
15	46	RLOQ	+	+	–
16	56	RUIQ	+	+	–
17	55	RUIQ	+	+	–
18	33	LLIQ	+	+	+
19	66	RLIQ	+	+	–
20	40	RUIQ	+	+	–
21	56	LUIQ	+	+	–
22	52	RUIQ	+	+	–
23	36	RLIQ	+	+	–
24	34	RLIQ	+	+	–
25	35	RUIQ	+	+	+
26	45	LUIQ	+	+	–
27	42	RUIQ	–	–	–
28	40	RUIQ	+	+	–
29	42	LUIQ	+	+	+
30	51	LLOQ	+	+	–

RUOQ: Right Upper Outer Quadrant, LUOQ : Left Upper Outer Quadrant, RLOQ: Right Lower Outer Quadrant, LLOQ: Left Lower Outer Quadrant, RUIQ: Right Upper Inner Quadrant, LLIQ: Left Lower Inner Quadrant, RLIQ: Right Lower Inner Quadrant, LUIQ: Left Upper Inner Quadrant, SGP: Surgical Gamma Probe, SLN: Sentinel lymph node

RESULTS

The image quality was good. The sentinel lymph nodes and lymphatic channels could be clearly detected (Figs. 1, 2 and 3).

Uptake of the lymph nodes started immediately after injection and reached its maximum in 2 to 6 hour images. The clearance of radiopharmaceutical from sentinel lymph node was fast and no lymph node activity was observed in the late images (24 hour images).

Blue dye was used in 16 of 30 patients. Lymph node(s) were detected with blue dye in 10 of 16 patients (62.5%) and all of them were also detected by lymphoscintigraphy and SGP. In 6 of 16 patients, no lymph nodes were detected with blue dye. But in one of them SLN was identified by lymphoscintigraphy and SGP but blue dye was negative.

The sentinel lymph nodes were clearly demonstrated in 23 of 30 patients with scintigrams. The axillary and internal mammary drainage was observed in 4 of 23 patients and 5 of 23 had only internal mammarian drainage. None of them had supraclavicular on infraclavicular lymph nodes.

The lymph nodes were detected at 30 minutes in 91.2% patients (21 of 23) at 60 minutes and up to 6 hours in 100% patients (23 of 23).

The sentinel lymph node was found in 25 of 30 patients with SGP (83.3%) and 10 of 25 (40%) had metastatic lymph nodes confirmed by pathological examination (Table 1).

DISCUSSION

Breast cancer is a major malignant tumor for women and axillary lymph node status is a significant pathological determinant of prognosis. The axillary lymphadenectomy is the most reliable procedure for staging and prognosis, but its morbidity is relatively high. If the sentinel lymph node is not involved, axillary lymphadenectomy may not be necessary.

Blue dye is commonly used for evaluation of lymphatic drainage and the rate of detection of SLN was reported as 41–98% and false negative results as 0–29%[16,17,41–45] which could be explained by the short residence of blue dye in SLN, In this study SLN was detected in 10 of 16 patients with blue dye and all of them were clearly observed with lymphoscintigraphy and SGP also. In one patient SLN was demonstrated with SGP and lymphoscintigraphy, but was not detected with blue dye. This false negative result was explained by a shorter residence time of blue dye in the nodes than ^{99m}Tc MIBI.

Nowadays, lymphoscintigraphy and subsequent surgical gamma probe are commonly used for detecting the sentinel lymph node. The results correlated well with studies using a combination of this technique with blue dye.[35–37]

^{99m}Tc MIBI is a successful tumor seeking agent and in a few studies lymph nodes were also detected during scintimammography.[30,31] The mechanism of tumoral uptake of this agent is not clear.[24–29] It is thought that this agent could be used to detect sentinel lymph nodes by peritumoral injection. Each injection was 74 MBq/0.2 m*l* at 4 different locations. We injected quite a large quantity of radioactivity to evaluate the washout of ^{99m}Tc MIBI from the lymphatic system in late images. Radiocolloids, radiolabeled macromolecules and monoclonal antibodies are commonly used for lymphoscintigraphy. The colloidal agents enter lymph channels through lymphatic capillaries passively, phagocytosis by macrophages.[18–23] Kramer observed that nonspesific macromolecules such as ^{99m}Tc HSA or ^{99m}Tc dextran generally had a shorter residence time in the nodes than colloids.[40] These agents enter lymph channels through lymphatic capillaries passively.

In this study, the injection was made into the peritumoral area. Since all the tumors were monocentric, we clearly identified the sentinel lymph nodes in early images. Previous studies demonstrated that there was no difference between intraparenchymal and subdermal injections for evaluation of the axillary region but intraparenchymal injection was more useful for evaluation of intramammary drainage.[35–37] Modified radical mastectomy was performed in all patients. The sentinel lymph nodes could not be identified clearly in the 24 hour images. Metastatic involvement was observed in 10 of 25 sentinel lymph nodes in pathological examination. No difference in washout was observed between metastatic and non-metastatic sentinel lymph nodes.

Our group is too small yet to change the type of operation but it is planned to make a decision about the type of operation in accordance with the pathological status of the sentinel lymph node.

Even though the sentinel lymph nodes could be identified by lymphoscintigraphy in 23 of 30 patients, they were detected with the probe in 25 of 30 patients. It was thought that lymph nodes which were small, calcified or closest to the tumor were not visible. Sentinel lymph nodes which were not visible with scintigrams and were detected by SGP (in 2 patients), were closest to the tumor and could not be differentiated from tumoral uptake in scintigrams.

In this study the efficacy of peritumoral MIBI injection for detection of sentinel lymph nodes with lymphoscintigraphy and SGP was evaluated. The sensitivity and specificity of peritumoral injection of ^{99m}Tc MIBI in lymphoscintigraphy was 92% and 71% respectively. The results are in correlation with studies using colloidal lymphoscintigraphic agents.[21–23,34–39] No immunopathological examination was performed in this study. It could be important for evaluation of metastasis. Since modified radical mastectomy was done in all patients we thought that no immunopathological examination was necessary.

^{99m}Tc MIBI was used for evaluation of the lymphatic drainage. It might be possible to correlate with other lymphoscintigraphic agents but injecting different radiopharmaceuticals into the same patient was not considered ethical.

In conclusion, ^{99m}Tc MIBI can also be used to identify sentinel lymph nodes, like colloidal and macromolecular agents when the interval between injection time and operation is short.

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