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DRAINAGE PATTERN OF THE UPPER MEDIAL QUADRANT OF THE BREAST IN YOUNG HEALTHY WOMEN AFTER SUBDERMAL INJECTION: A LYMPHSCINTIGRAPHIC STUDY

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ABSTRACT

This study examines the lymphatic drainage after injection of a radiotracer in the upper medial quadrant of the right breast in young healthy female subjects. Most studies concerning lymphatic drainage pathways have focused on the upper lateral quadrant of the breast because of the high incidence of carcinoma in this quadrant while the drainage pattern of the medial quadrant has been less studied. We injected radiotracer (Human Serum Albumin labeled with 99 technetium) subdermally into the upper medial quadrant of the right breast tissue of 33 young healthy female volunteers and obtained static images with a scintillation camera briefly after injection and approximately one hour after injection. We identified lymphatic pathways in 82.8% of our subjects, lymph nodes in 79.3% and in 3.4%, a sentinel lymph node was found in the internal mammary chain. In early images, lymph nodes were visualized in 65.5% of subjects while in 17.2% of subjects, lymphatic vessels only appeared on later images.

Keywords: sentinel, lymph node, lymphatics, breast, lymphscintigraphy, lymphatic mapping, healthy subjects

A variety of methods of lymphatic mapping are used to identify the sentinel lymph node (SLN). The radiotracer approach involves injection of a radiopharmaceutical followed by pre-operative scintillation counter imaging or by an intra-operative handheld probe for localizing the radioactive lymph node. Studies using pre-operative imaging found a SLN in 89%, 63.2%, 36%, and 73% of the patients, and using the handheld probe enhanced the localization of the SLN up to 94%, 81.2%, 84.8% and 81%, respectively (1-4).

However, no standardized technique exists to locate the SLN. Different parameters may influence the success rate, e.g., location of the tumor, multifocal tumors, time between injection and imaging, diameter of the particles, dose and volume of the tracer, location and depth of the injection, age, and prior treatment(s). In addition, periareolar, subareolar, intradermal, or subcutaneous injections are based on the principle that the breast and the overlying skin share the same lymphatic drainage, and peri- or intratumoral injection sites are also used.

With the introduction of the SLN, knowledge of the anatomy of the breast lymphatics assumed more importance. The physiological concept of the SLN is based on the idea that tumor cells spread via lymphatics in a sequential pattern, meaning that first level I axillary nodes will be invaded. However, skip metastases have been described in 12% (5) to 23.7% of patients (6), and Veronesi et al (7) have postulated that this finding is due to anatomical variances.

It is believed that tumors of the lateral quadrant drain towards axillary lymph nodes and those of the medial quadrant towards the

internal mammary chain (8), but some studies have shown the involvement of both nodal basins from a tumor located in the medial breast quadrant.

Jansen et al (9) found a higher percentage of SLN in the internal mammary chain in patients with a medial quadrant tumor (12/45) compared to patients with a lateral quadrant tumor (9/68). Van der Ent et al (10) found in 65 of 256 patients (25.3%) supplementary "hot spots" in the internal mammary chain with patients presenting with a central or medial located primary tumor (63%) or a primary tumor in the lateral quadrant of the breast (37%). Other hot spots were located in the intersternal spaces (five of the eleven patients with metastases in the internal mammary chain had the primary tumor in the lateral quadrant, five in the upper medial and 1 in the lower medial quadrant). Reintgen et al (11) and Johnson et al (12) found a drainage pattern to the axilla and the internal mammary chain in 10% of patients. However, location of the tumor was not specified. In a study of Uren et al (8) (n = 34), two of the six medial quadrant tumors drained to the axilla and 5 of 18 lateral quadrant tumors to the internal mammary chain. In a sequential study of 2001 (13) (n = 159), these numbers became 21 out of 29 and 33 out of 82, respectively. Only one study of Vendrell-Torné et al (14) reported on the breast drainage pattern in healthy subjects. Of the 250 patients investigated, 50 breasts were injected in the upper medial quadrant and axillary lymph nodes were involved in 94%, internal mammary lymph nodes in 62%, and supraclavicular lymph nodes in 6%.

Most previous studies have been performed in patients with breast cancer, and most studies concentrated on the upper lateral quadrant of the breast because the high incidence of carcinoma in this area. Therefore, we aimed to visualize both the lymphatic pathways and SLN after subdermal injection of a radiotracer in the upper medial quadrant of the breast in healthy volunteers.

SUBJECTS, MATERIALS, AND METHODS

Thirty-three healthy female volunteers (mean age 22.4 years, mean height 167.4 cm, mean weight 60.2 kg) entered the study after informed consent. The results of 4 subjects were lost during processing. Ethical approval for the study was obtained from the Ethics committee (OG 16-20001014D) of the Vrije Universiteit Brussel.

The radiotracer (Human Serum Albumin labeled with 99 technetium, type Sorin Nanocoll, by Nycomed Amersham Sorin, Italy) was injected subdermally into the middle of the upper medial quadrant of the right breast. The same surgeon made the injection in each subject using a volume of 0.2-0.3 ml and a dose of 3.5 mCi. After injection, a local soft circular massage was performed at the injection site for five minutes to facilitate uptake into regional lymphatics. Fourteen minutes after injection, anterior and right oblique position images were obtained using a Multispect 2 Gamma Camera System (Siemens) with a low energy collimator. Sixty minutes after injection, three static images were obtained: anterior, anterior with flood (to outline the body contour), and right oblique anterior (ROA) image. The three radioactive markers were placed at the midclavicular region, on the xiphoid process, and in the middle of the axilla in order to facilitate the location of the SLN. Axillary nodes were subdivided into three levels: level I located at the lateral site of the pectoralis minor muscle; level II nodes under this muscle; and level III nodes at the medial site of the pectoralis minor muscle.

RESULTS

Fig. 1 displays the anterior, anterior with flood, and right oblique anterior images obtained one hour after injection. We successfully identified a SLN in 82.8% of the subjects. In 41.4%, the tracer migrated to level I axillary lymph nodes, in 34.5%, hot spots were visualized at level II axillary lymph nodes, and in 1 subject, additional hot spots were detected in the internal mammary chain and in supraclavicular lymph nodes. Results are summarized in *Table 1*. In 65.5% of the women, the SLN was visualized within

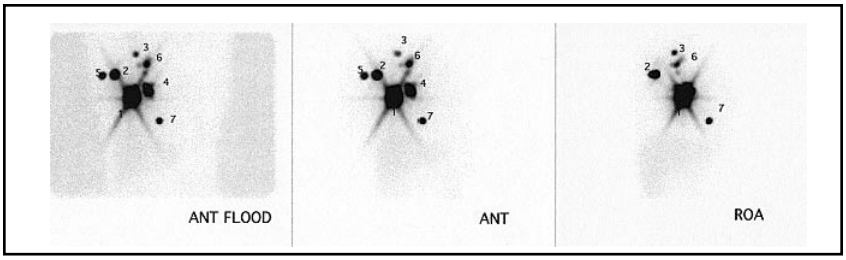

Fig. 1: Images (anterior with flood, anterior, and right oblique anterior) of one subject obtained one hour after injection. Legend: 1 Injection site; 2 hot spot level I; 3 hot spot Level II; 4 hot spot towards internal mammary chain; 5 axillary mark; 6 midclavicular mark; 7 xiphoid mark.

15 minutes after tracer injection and in 17.2% the SLN appeared later (*Table 2*).

DISCUSSION

In other studies using Tc99m-nanocolloid to depict the SLN in patients with breast cancer (9,10,15-20,22), the SLN was successfully identified in 94.5% of the cases using radioactive doses and the volumes varied between 3.7 and 370 MBq and 0.2 to 6 ml. In our study, the SLN was found in 82.8% only and we utilized a dose of 0.5 - 3.5 mCi (129.5 MBq).

According to Valdès Olmes et al (20), a minimum dose of 65 MBq is necessary to visualize the sentinel node while Tanis et al (21) used a minimum dose of 100 MBq. Increasing the tracer dose enhances the success of identifying the sentinel node. Because we were dealing with healthy subjects, we chose a lower irradiation dose and this factor may be why our SLN detection is somewhat lower. Our injected volume of 0.2-0.3 ml was used in order to minimize disturbance of regional lymph flow and was consistent with other studies (15,21,22).

After tracer administration, a local soft circular massage was performed at the injection site to enhance uptake into regional lymphatics. A recent study of Shenoy et al (23) has shown that a massage of the injection site did not improve the SLN detection rate or biopsy time, but it may reduce the number of false negative SLN.

Another point of discussion is the injection depth. We used a subdermal injection which is the same as in other studies (2,15-17,19,22,24). The SLN was successfully identified in these studies in 95.5% of subjects. It must be mentioned that in several studies, the SLN was detected during the surgical procedure, using a gamma probe, improving the chance of finding a SLN, because of the higher density of lymphatics in the skin, compared with the breast parenchyma. Intradermal, intraparenchymal, subareolar, or subdermal injections lead to the same SLN, indicating that the lymphatics of the breast are regional, not point specific (25). Additionally, some investigators have reported that the drainage pattern to the internal mammary chain cannot be detected using an intra- or subdermal injection (10,16). Shen et al (26) compared lymphatic drainage patterns and sentinel node localization after a dermal and an intraparenchymal (IP) injection: after dermal injection 16% of the subjects showed a drainage pattern different from the IP injection, and after IP injection, 3% showed a drainage pattern different from dermal injection. In 84% of the dermal and in 96% of the IP injections, an axillary sentinel node was found, extra-axillary (contralateral axillary, suprasternal, internal mammary, apical axillary, and internal mammary) sentinel nodes were identified in 26% (8 of 31) of the dermal injections and in 5% (5 of 97) of the IP injections.

Estrougie et al (27) has described the chances of an internal mammary chain SLN for a primary tumor in each quadrant. A tumor in the upper inner quadrant has a risk

TABLE 1
Anatomic Distributions of Sentinel Node in 29 Women

	#	%
Axillary, level I	12	41.4%
Axillary, level II	10	34.5%
Axillary, level III	1	3.4 %
Internal mammary	1	3.4 %
Subclavicular	0	0 %
No sentinel node visualized	5	17.2%

TABLE 2
Time of Appearance of the Sentinel Node in 29 Women

	#	%
Before 15 minutes	19	65.5%
After 15 minutes	5	17.2%
No sentinel node visualized	5	17.2%

of 31% of having an internal mammary chain SLN, the lower inner quadrant 53%, the outer upper quadrant 11%, the outer lower quadrant 30% and central lesions 25%. The risk of tumor-positive internal mammary chain SLN is 13% for primary tumors in the UIQ, 9% LIQ, 16% UOQ, 23% LOQ and 31% in case of central lesions. In this study, we found only one subject with drainage in the direction of the internal mammary chain from the UIQ (3.4%).

The reason why the SLN could not be visualized in some subjects is not clear and many different factors can influence the success rate of the sentinel technique. A possible explanation can be delayed uptake of the tracer, so that the chosen imaging time of one hour is not sufficient. According to Tanis et al (21), delayed imaging up to 23 hours can lead to detecting SLN. SLNs which are close to the injection site are also difficult to differentiate because of the signal from the injection site (28,29). Sentinel nodes of the internal mammary chain could be missed after an injection in the upper medial quadrant if the radiologist did not look closely enough.

A study by Cox et al (30) investigating the influence of age and BMI on the chance of failure in SLNB showed that every increase of 1 year of age or one unit of BMI decreased the chance of success by approximately 5%. The mean BMI was 29.54 in failed patients and 26.42 in successfully mapped patients. In our study the mean BMI of all subjects was 21.36, the BMI of patients with an identified SLN was 20.98 and the BMI of non-visualized SLN was 23.47.

We conclude from our results that subdermal injection of tracer in the middle of the upper medial quadrant of the breast of healthy female subjects results in drainage to the internal mammary chain in 3.4% of the cases.

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