Clinical relevance and refinement of the sentinel node procedure in breast cancer and melanoma
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CHAPTER 4

INTRATUMORAL VERSUS INTRAPARENCHYMAL INJECTION TECHNIQUE FOR LYMPHOSCINTIGRAPHY IN BREAST CANCER

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INTRODUCTION

The best injection technique for the sentinel node procedure in breast cancer patients is still being debated. Periareolar, subareolar and subcutaneous injections provide good sentinel node identification results for the axilla but are associated with a low incidence of non-axillary drainage. A recent study by Shen et al. showed a significant difference in lymphatic drainage and sentinel node localization between dermal and intraparenchymal tracer administration. At our institute, an intratumoral injection technique is used. This method has not been compared with peritumoral or other intraparenchymal injection techniques in a randomized trial so far. Recently, we have come across a case in which a patient with a non-palpable lesion received an intraparenchymal tracer injection by accident and an intratumoral injection the next day. A different drainage pattern was visualized on the two sets of images.

CASE REPORT

A 55-year old woman presented with a 1.5 cm non-palpable suspicious left breast lesion detected by screening mammography that showed microcalcifications in a density. The primary tumor was located in the upper outer quadrant. Fine needle aspiration cytology showed malignant cells. The patient was scheduled for wide local excision and sentinel node biopsy. On the day before surgery around 9:00 AM, Tc-99m-nanocolloid (Nanocoll®, Amersham Cygne, Eindhoven, the Netherlands) was injected under ultrasound guidance into an ultrasound-dense lesion in the upper outer quadrant of the left breast (Figure 1). A volume of 0.2 ml and a radioactivity dose of 127.7 MBq were administered. Static imaging was performed at 30 minutes, two hours and four hours post-injection with simultaneous transmission scanning using a $^{57}$Co flood source to outline the body contour. Both anterior and lateral images with hanging breast were obtained with use of a dual-head gamma camera (ADAC Vertex®, Milpitas, California, U.S.A.). The last lymphoscintigraphic image (four-hour scan) showed two axillary sentinel nodes and four axillary second-echelon nodes. No sentinel nodes were visualized outside the axilla (Figure 2).

Figure 1. Ultrasound image of the dense (benign) lesion in which the first dose of Tc-99m-nanocolloid was injected.
After the last scintigraphic image, a localization procedure was performed to place a catheter for intratumoral administration of patent blue dye. A more extensive description of this technique has been published elsewhere. An 18G needle with a catheter (Secalon®, Ohmeda, Swindon, UK) was loaded with a X-shaped hookwire (Cook, Bjaeverskov, Denmark). The needle was inserted and positioned in the same ultrasound-dense lesion under local anesthesia using ultrasound. Mammograms in a cranial-caudal and medial-lateral direction were made to confirm the correct position of the catheter. Unfortunately, these showed an incorrect location of the hookwire and catheter (Figure 3; position A). They had been positioned in another lesion, known from the mammography and judged as benign. The malignant lesion was located more medial and deeper in the breast, although within the same quadrant. The distance between the two lesions was approximately 3 cm.
Because the radioactive tracer had been injected in the wrong ultrasound-dense lesion, a new plan was made with consultation of the surgeon, the nuclear physician and the radiologist. The change of plan was discussed with the patient and carried out with her permission. A new hookwire with catheter was placed into the true primary tumor (Figure 3; position B). The first catheter was removed, leaving only its hookwire in place.

The next day at 8:40 AM, a second dose of 128.6 MBq Te-99m-nanocolloid was administered through the catheter in a volume of 0.2 ml. Anterior and lateral images were obtained after three hours in a similar fashion as the day before (Figure 4). The lateral image showed the same axillary sentinel nodes. However, two additional extra-axillary sentinel nodes were seen on the anterior scan. One was located in the intramammary chain, the other within the breast.

The patient was subsequently brought to the operation room. At 12:40 PM, 1.4 ml of patent blue dye (Blue Patenté V, Laboratoire Guerbet, Aulnay-sous-Bois, France) was administered through the catheter. The sentinel nodes were identified and harvested after careful dissection of blue lymphatic vessels and detection of radioactivity with a gamma ray detection probe (Neoprobe® 2000, Johnson & Johnson Medical, Hamburg, Germany). A total of three axillary sentinel nodes, four internal mammary chain sentinel nodes and one medial intramammary sentinel node were harvested. Both hookwires were removed together with the suspicious lesion.

Pathological evaluation included hematoxylin-eosin and immuno-histochemical staining (CAM 5.2, Becton Dickinson, San Jose, California, U.S.A.). No metastatic disease was seen in any of the sentinel nodes. The primary tumor was a 2.0-cm poorly differentiated ductal carcinoma in situ and was completely excised.

**Figure 4. Preoperative anterior and lateral lymphoscintigraphic images, three hours after the second (intratumoral) injection of the Tc-99m-nanocolloid. 1=Injection site, C=correctly positioned catheter through which the radioactive tracer was administered, 1=two axillary sentinel nodes, 2=parasternal sentinel nodes, 3=medial intramammary sentinel node.**
DISCUSSION

The purpose of lymphoscintigraphy for lymphatic mapping is to demonstrate the lymphatic drainage pathway of the neoplasm. To be more precise, there are five specific reasons to perform lymphoscintigraphy. These are to indicate the drainage basin, to determine the number of sentinel nodes, to differentiate these first-tier nodes from subsequent nodes, to locate sentinel nodes outside the usual nodal basins and to mark the location of a sentinel node on the skin. The relevance of lymphoscintigraphy has been acknowledged by others.\(^4^,5\)

This case shows the difference in lymphoscintigraphic imaging between two different injection sites in the same patient. The first injection of radioactive tracer cannot be regarded as peritumoral because it was administered approximately 3 cm away from the primary tumor. Both injections were however located within the same quadrant, and therefore a comparison between intratumoral and intraparenchymal injection is more appropriate.

We have described our hypothesis on the finding of more extra-axillary sentinel nodes in non-palpable breast cancer patients in a recent study.\(^3\) The percentage of visualized extra-axillary sentinel nodes in non-palpable breast cancer patients was 43% and differed significantly from the visualization rate in palpable tumors (24%). Paganelli et al. have also found a high incidence of drainage to the internal mammary chain when they injected the tracer underneath the primary breast tumor.\(^6\) Anatomical studies dealing with the arrangement of the breast lymphatics show that internal mammary nodes and interpectoral nodes are supplied by retromammarian lymphatics.\(^7\) These lymphatics arise from the breast lobules, run on the surface of the pectoral fascia and accompany penetrating blood vessels on their way through the pectoral and intercostal muscles. The finding that only a deep tracer injection will visualize extra-axillary sentinel nodes supports the observation that deep lymphatics from the dorsal part of the breast drain to these nodes. This may also be the explanation for the difference in drainage in the case described above, where the second injection was administered into the tumor and therefore deeper in the breast. This case supports our contention that lymphatic watersheds do exist in the breast and underlines the importance of a tracer administration into or close to the tumor.\(^8\)

REFERENCES
