The Role of SPECT/CT in Detection and Localization of Sentinel Lymph Node in Breast Cancer

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Abstract • Objectives: The purpose of this study was to compare SPECT/CT and planar lymphoscintigraphy in detecting hot nodes. Methods: In this retrospective study, planar and SPECT/CT lymphoscintigraphy were performed in 119 consecutive women with invasive breast cancer. Both images were assessed for the number of lymph nodes and their anatomical site. Hot nodes were categorized based on the classification used by surgeons as level I, II, III nodes. In addition, pathology reports were retrieved which provided additional information concerning the characteristics of the lesions missed or detected by either or both imaging modalities. Results: SPECT/CT detected hot nodes in 81 (66%) patients, while planar lymphoscintigraphy detected hot nodes in 70 (58.8%) patients. SPECT/CT and planar imaging had 38 (32%) patients in common where they did not detect any hot nodes. According to histopathology, 15 (12.6%) out of 36 patients with negative lymphoscintigraphic sentinel node identification on both modalities had nodal metastasis. The higher lymph node detection rate by SPECT/CT was significant (p = 0.019). Conclusion: When compared to planar lymphoscintigraphy, SPECT/CT refines preoperative lymph node detection and thus (N) staging. As such, we recommend that SPECT/CT ought to be performed in a particular set of patients, for it improves localization of the draining nodes, detects nodes missed on planar, and excludes false positives in cases of lymphatic/blood vessel radiotracer accumulation.

Keywords: SPECT/CT; sentinel lymph node, breast cancer

Résumé • Objectifs : Comparer la SPECT CT à la lymphoscintigraphie planaire conventionnelle dans la détection de ganglions chauds hypercaptants. Méthodes : Étude rétrospective sur 119 cas de cancer mammaire invasif référés pour recherche de ganglions sentinelles par lymphoscintigraphie planaire et par SPECT CT. Le nombre et le site anatomique des ganglions positifs ont été évalués pour les deux modalités. La catégorisation des ganglions hypercaptants a été basée selon la classification chirurgicale en stades ganglionnaires I, II, III. Les rapports de pathologie ont été consultés afin d’obtenir une évaluation supplémentaire des caractéristiques des lésions détectées ou non par chaque modalité. Résultats : Des ganglions chauds hypercaptants ont été découverts chez 81 (66%) patientes par SPECT CT, et chez 70 (58,8%) patientes par lymphoscintigraphie planaire. SPECT CT et imagerie planaire n’ont pas détecté de ganglions chauds hypercaptants chez 38 (32%) patientes. En se basant sur les données histopathologiques, 15 (12,6%) des 36 patientes avec lymphoscintigraphie négative ont présenté une atteinte ganglionnaire métastatique sur les deux modalités. La détection du nombre de ganglions par SPECT CT était significativement supérieure (p = 0,019). Conclusion : Par comparaison à la lymphoscintigraphie planaire conventionnelle, la SPECT CT améliore la détection de ganglions sentinelles en préopératoire (stade N). Nous recommandons donc d’avoir recours à la SPECT CT dans des cas particuliers, notamment pour améliorer la localisation du drainage ganglionnaire, détecter les ganglions non visualisés sur les images planaires conventionnelles et exclure les faux positifs en cas de stagnation du radiotracer dans les vaisseaux sanguins ou les chaînes lymphatiques. Mots-clés : SPECT CT; ganglion sentinelle; cancer du sein

Introduction

Sentinel lymph node biopsy (SLNB) for staging breast cancer has had momentous reverberations since its introduction back in 1996. It enabled us to shift from axillary lymph node dissection (ALND) to a relatively minimal invasive procedure with less postoperative morbidity. The risks of lymphedema, limited mobility, and sensory disturbances in the arm with ALND have been well established. Whilst in SLNB when a positive sentinel lymph node is detected, often the nodal basin is dissected only [1]. Furthermore, it has been shown that SLND achieves the same overall survival, disease-free survival, and regional control as ALND [2].

The most common region of breast lymphatic drainage is the axilla. However, Estourgie et al. demonstrated just how various breast drainage sites can be which include: internal mammary chain, supraclavicular, interpectoral, and intramammary nodes. Moreover, numerous lymphatic drainage patterns may result from tumors located

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in the same breast region [3]. Therefore, it is essential to optimize visualization of the primary tumor’s lymphatic drainage track.

Hybrid single photon emission computed tomography camera with integrated CT (SPECT/CT) and planar lymphoscintigraphy’s imaging technique are similar whereby both use gamma ray detection. Nevertheless, the latter is limited in comparison to SPECT/CT by the lack of 3D imaging information and absence of anatomical landmarks which make planar lymphoscintigram interpretation limited. Moreover, SPECT/CT also has the advantage of attenuation and scatter correction which results in a better contrast and resolution [4].

The purpose of this study was to compare SPECT/CT and planar lymphoscintigraphy by summarizing our experience with 119 consecutive breast cancer patients.

PATIENTS AND METHODS

Patient population
In this retrospective study, as per hospital protocol, planar and SPECT/CT lymphoscintigraphy were performed in 119 consecutive women with invasive breast cancer. They had neither clinical evidence of axillary lymph node metastasis (N0) nor remote metastasis (M0). The mean age of the patients was 52 years (range, 29-81 years).

Lymphoscintigraphic technique
Two to six hours prior to surgery, a dose of 74 MBq (2mCi) 99mTc-nanocolloid, divided into two equal aliquots of 0.5 ml each, was administered as a periareolar injection by a nuclear medicine physician. Planar imaging was performed 1 hour after injection of the radiopharmaceutical. Anterior, lateral, and oblique projections were obtained. SPECT/CT images were acquired immediately after the planar images. A SPECT/CT emission/transmission study was performed using a hybrid system composed of a dual-head gamma camera with low-energy high-resolution collimators, namely the BrightView XCT, and a flat panel X-ray detector (Philips).

SPECT acquisition of the chest was performed with the following parameters: matrix size 128x128, 180° in the anterior L-mode rotation, 3.75° angle steps and 30s time frame. The CT detector consists of 384 crystals and photodiodes mounted on the gantry-rotating module.

The overall acquisition time of a SPECT/CT study was 25 min. After reconstruction, the SPECT images were corrected for attenuation and scatter. Both SPECT and CT axial 5-mm slices were generated using the BrightView XCT software (Philips). Fusion of the SPECT and CT images was performed on Intellispace portal workstations (Philips).

Scintigraphic interpretation
Evaluation of hot nodes was performed by two certified nuclear medicine physicians in a consensus reading. A hotspot was defined as any focal area of significant increased uptake. Planar and SPECT/CT images were interpreted separately and blindly to each other. Both images were assessed for the number of lymph nodes and their anatomical site: axillary, pectoral, retropectoral, or intramammary.

Patients were staged according to the American Joint Committee on Cancer 7th edition for Breast Cancer Staging [5]. Furthermore, hot nodes detected on SPECT/CT were categorized based on the classification used by surgeons as level I, II, III nodes. Level I nodes are located lateral to the pectoralis muscle. Level II nodes are located within the medial and lateral margins of pectoralis minor muscle. Level III nodes include those located in the axilla medial to the pectoralis minor muscles, interpectoral nodes located between the major and minor pectoralis muscles, intramammary nodes located within the breast tissue, internal mammary nodes, and supraclavicular nodes [3].

Intraoperative sentinel lymph node identification
An intraoperative hand-held probe (Neoprobe 2000; Neoprobe Corp) is used to identify the site with the highest counts along the lymphatic basin. A patent blue dye (purified trypan blue isotonic sterile solution: 0.75 ml of a 0.055% solution per syringe) is injected similarly to the colloid injection. A blue node or even a blue duct may assist the probe in identifying sentinel lymph nodes intraoperatively. At AUBMC, SLNB is indicated in any T stage with no detectable LN in the axilla on ultrasound.

Chart review
Patient medical records were reviewed for any surgical history involving the breast and whether the patient had undergone neo-adjuvant treatment or not. In addition, pathology reports were retrieved which provided additional information concerning the characteristics of the lesions missed/detected by either or both imaging modalities. Surgical history involving the breast was negative for 102/119 (85.7%) of our patients. Six (5%) patients had bilateral implants. A single patient had positive surgical history for each of the following procedures: breast reduction, right breast lumpectomy, left breast lumpectomy, right breast mastectomy, left breast mastectomy, right breast partial mastectomy, excisional biopsy of the right breast, excisional biopsy of the left breast, and left breast quadrantectomy. Two patients had right breast quadrantectomy prior to presentation. Only 10 (8.4%) patients had a positive history of receiving neo-adjuvant therapy, while 109 (91.6%) patients did not. Four patients had a history of lymph node dissection.

Statistical analysis
Statistical analysis was performed on the SPSS software (release 23.0; SPSS Inc.) for Windows (Microsoft). Quantitative data were described as mean, range (minimum - maximum), percentages and measurements were made in centimeters (cm). The difference in the lymph node detection rate between planar and SPECT/CT lymphoscintigraphy was tested using Fisher’s exact test.
RESULTS

SPECT/CT detected hot nodes in 81 (68%) patients distributed as follows:
- 117 axillary lymph nodes in 77 patients
- 9 pectoral lymph nodes in 3 patients
- 10 retropectoral lymph nodes in 6 patients
- 1 intramammary lymph node in a single patient.

Meanwhile, planar lymphoscintigraphy detected hot nodes in 70 (58.8%) patients:
- 100 axillary lymph nodes in 67 patients
- 7 pectoral lymph nodes in a single patient
- 3 retropectoral lymph nodes in 2 patients
- 0 intramammary lymph node.

These results are summarized in Tables I & II.

Using the Fisher’s exact test to compare both imaging techniques, the SPECT/CT lymph node detection rate was significantly higher ($p = 0.019$).

SPECT/CT and planar imaging had 38 (32%) patients in common where they did not detect any hot nodes. Planar had a negative result for 47 patients in total. However, 2 positive planar lymphoscintigrams turned out to be skin contamination when visualized on SPECT/CT (Figure 1). Thus, planar imaging had 9 false negatives and 2 false positives as compared to SPECT/CT. Those same 2 patients had positive SPECT/CT mapping which were missed on planar (Figure 2). As a result, SPECT/CT was able to detect hot nodes in 11 patients that were missed on planar.

According to histopathology, a total of 37 patients had positive sentinel lymph nodes on pathology. Fifteen (12.6%) out of 36 patients with negative lymphoscintigraphic sentinel node identification had nodal metastasis.

The pathology findings in those patients were as follows: 1 sentinel positive in 4 patients with micrometastasis sizes of 0.6 mm, 1 mm, 1.9 mm, 2 mm. Another sentinel axillary was positive for macrometastasis (more than 2 mm) in 7 patients. Moreover, 2 sentinel lymph nodes were positive in 3 patients and 3 sentinel positive lymph nodes in another patient.

Patient’s primary breast tumor lesion pathology and T-stage are summarized in Tables III & IV. The surgeon classification of our patients was as follows: 61 patients were level I, 6 patients were level II, 10 patients were level III, 4 patients were level I and II, one patient was level I, II and III. Finally, one last patient was level I and III (summarized in Table V).

Concerning the 11 patients that were missed by planar but detected on SPECT/CT, they had the following surgical classification: 9 patients were level I, and 2 patients were level II.

![Figure 1](image)

Anterior and oblique projections on planar (a) reveal a suspicious focal increased uptake at the level of the right internal mammary lymph node (thin arrow). Low dose CT, SPECT and fused images (b) revealed these hot spots to be skin contamination (thick arrow).
Staging breast cancer patients necessitates an accurate identification of the extent of lymph node involvement. Before the introduction of SPECT/CT, several improvements in planar imaging techniques have been described. These changes include alterations in colloid particle concentration, amount of radiotracer, time of imaging (early versus delayed), a second injection of the radiopharmaceutical, and post injection massage [6-9]. They have resulted in a high sensitivity of lymphoscintigraphy; however, planar imaging remains to have its limitations. In planar imaging, when a peritumoral injection site is chosen, a node close to the site can be masked due to the strong activity of the radiopharmaceutical. This phenomenon is referred to as a “shine through” [10]. Moreover, planar imaging cannot distinguish superimposed nodes [11]. Often planar imaging depicts what seems to be a nodal uptake only to be identified on SPECT/CT as a false positive due to skin contamination. This may have been identified on lateral view; however, since this was a retrospective study, after archive retrieval, no lateral view was found for this patient. This has been documented in two patients in our study. Lerman et al. [12] had 14 false positive foci out of 329, 7 of which were skin contamination.

The higher patient and lymph node detection rates by SPECT/CT were significant \( (p < 0.001) \). Our results echo those of a prospective multicenter International Atomic Energy Agency study [13]. Furthermore, SPECT/CT improved the visualization rate from 59% to 68%. A similar
rate of increase is noted by van der Ploeg et al. [14] and Borrelli et al. [15] where the increase was from 84% to 92% and 53.3% to 53.3%, respectively. The confidence of visualization is noted as well (Figure 3). Moreover, SPECT/CT did not miss any lesion that was seen on planar. However, one intramammary lymph node was detected on SPECT/CT which was missed on planar. In this particular case of ours, it did not affect overall management, primarily since it was negative as per histopathology and secondarily, it was not a skipped metastasis since other lymph nodes were positive on imaging as well. Nevertheless, the significance of this observation lies in the fact that skip metastasis has been documented in other studies. Interpectoral and intramammary nodes were identified in five patients on SPECT/CT by Lerman et al. [12]. Interpectoral nodes are a pathway by which metastasis may occur in level III nodes without disease at levels I and II. Furthermore, SPECT/CT has proven to be a valuable asset in the surgical technique. A study done by van der Ploeg et al. [14] analyzed SPECT/CT outcome on surgical technique which showed that it allowed to avoid an incision in two patients, facilitated more precise incision in 48 patients, and resulted in an extra incision in six patients.

We had negative SPECT/CT lymphoscintigraphy results in 38 (32%) patients. It is fundamental to understand the variables that play a role in lymphoscintigraphy mapping. Injection of the radiopharmaceutical 2-6 hours prior to surgery may not be ample time for tracer uptake. In addition, it has been reported that tumoral involvement of the sentinel lymph node may not allow the passage of the tracer [16]. Furthermore, patients who have a history of reduction mammoplasty, axillary surgery, and lumpectomy are associated with altered lymphatic drainage which would result in a negative lymphoscintigraphy study. Estourgie et al. have shown that excisional biopsy of breast lesions changed drainage patterns in 45% of the patients with axillary sentinel nodes and in 80% of the patients with internal mammary sentinel nodes [17].

Despite all of the advantages of SPECT/CT, its utilization is limited for it requires additional time which may diminish patient workflow and it exposes the patient to an extra dosage of radiation. In addition, the increase of visualization rate in our study was no more than 9%. However, the benefit of a SPECT/CT was noted in patients with unusual lymphatic drainage pattern and those with planar images difficult to interpret would benefit the most of an additional SPECT/CT.

CONCLUSION

When compared to planar lymphoscintigraphy, SPECT/CT refines preoperative lymph node detection and thus (N) staging. As such, we recommend that SPECT/CT ought to be performed in a particular set of patients, for it improves localization of the draining nodes, detects nodes missed on planar, and excludes false positives in cases of lymphatic/blood vessel radiotracer accumulation.

Figure 3
Anterior projection on planar shows a sentinel hot lymph node (thin arrow) with a possible second hot lymph node on the oblique view (a).
Low dose CT, SPECT and fused images (b) confirm the presence of two hot drainage axillary lymph nodes (thick arrows).

CONFLICT OF INTEREST
The authors have no conflict of interest to disclose.

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