Lymphology 51 (2018) 13-17

ARE PRE-OPERATIVE LYMPHOSCINTIGRAMS NEEDED FOR LOCALIZATION PRIOR TO SENTINEL NODE BIOPSY?: AN AUDIT TO ENSURE SAFE PRACTICE AND TO PROVIDE ANOTHER VIEW

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ABSTRACT

Traditionally lymphoscintigrams are taken after injection of peri-areolar Technetium-99m (Tc-99m) to quantify sentinel nodes before biopsy (SNB). However, recent research suggests that scintigraphy is not an essential adjunct. For service improvement, we stopped using lymphoscintigraphy so as to minimize delay to operating theater and reduce demand on the Nuclear Medicine Department. We audited early outcomes to ensure quality was maintained. 100 consecutive patients undergoing SNB with lymphoscintigrams were investigated. Lymphoscintigrams were reported by Consultant Radiologists. Reported node count (RNC) was compared to biopsied node count (BNC) using Cohen's kappa statistic. Lymphoscintigrams were then discontinued, and the results on the next 69 consecutive patients undergoing SNB were analyzed. The BNC was then compared to BNC in patients having lymphoscintigrams. Of the first 100 patients, RNC ranged from 0-5 (mean=1.84, mode=1) and BNC from 1-4 (mean=1.89, mode=1). 90% of lymphoscintigrams were performed on the day of surgery. Cohen's Kappa statistic was 0.34 (95%CI = 0.195 to 0.482, i.e., Fair agreement). RNC was zero in two cases, but SNB was successful. Of 69 patients in the second group with no scan, BNC ranged from 0-4 (mean=1.80, mode=2). There were two cases of failed localization and no significant difference between BNC with or without scans (p=0.16). Sentinel node positivity rate was 36% for those with scans and 25.3% for those without scans, which was not significant (chi-squared, p=0.11). These results correlate to previously published studies. Correlation between RNC and BNC was only in fair agreement, and negative lymphoscintigrams did not result in failed SNB localization. Our study suggests that BNC without scans is safe and effective. Removing the lymphoscintigram will result in measurable cost savings, saving of clinical time (no delay to operating room while waiting for scan or multiple journeys to hospital), freeing the scanner for other scans, and allowing additional time for radiology physicians and staff.

Keywords: imaging, lymphoscintigraphy, sentinel node, breast cancer

Sentinel node biopsy (SNB) is the current standard method for staging the axilla in patients with clinically node negative breast cancer (1). In cases of melanoma, a lymphoscintigram can be useful since the sentinel node can be distant, and this method was then transferred when SNB was adopted for breast cancer. However, the breasts mostly drain only to the axillary nodes with some

drainage to supraclavicular, infraclavicular, interpectoral, intramammary and internal mammary nodes, and this makes the role of biopsy of non-axillary nodes uncertain. Additionally, studies have shown that it does not benefit the patient (2).

The most commonly used method of identifying the sentinel node(s) is to inject technetium colloid (Tc-99m) in the peri-areolar area of the quadrant of the breast containing the tumor. One single injection of 20mBq is carried out for same day surgery or 40mBq if the day before. This is then followed by a lymphoscintigram using a gamma camera (Siemens symbia-T), which identifies the position and number of sentinel nodes. The scan is performed at 20 minutes but if there is no uptake seen, the scan can be repeated up to a few hours later. Views are taken laterally and anteriorly. Oblique views are occasionally used if the tracer is not seen. A hand held gamma probe is also employed to mark the nodes pre-operatively. The process after Tc-99m injection can therefore be timely and costly. If the scan is performed on the day of surgery, it can delay the patient's travel to the operating theater.

We undertook an analysis of other studies looking at outcomes of SNB with lymphoscintigraphy, and they concluded that it is not necessary. Rather than comparing groups who did and did not have scans, we chose to look at clinical practice when a scan has been performed to see if it influences the number of nodes biopsied. Our intention was to discover whether the scan is actually clinically relevant. Further, we audited outcomes after scanning has been stopped in a second cohort.

A study in 2000 of over 800 patients compared those who did to those who did not receive a scan pre-operatively. There was no difference in false negative rate, detection rate, or number of sentinel nodes removed between the groups (3). This result was confirmed in a similar comparison study of over 500 patients (4). A smaller study of only 50 patients found that if the lymphoscintigram was negative (i.e., no nodes shown), localization at operation was still possible further demonstrating that the scan does not add to the procedure (5). Additional studies have also shown no benefit of lymphoscintigraphy. A study of over 100 patients where the surgeon was blinded to the scan showed that successful SNB was possible in 99% of cases, and the scan revealed only 3% more nodes (6).

METHODS

As part of institutional audit registered locally, 100 consecutive female patients with breast cancer undergoing SNB with lymphoscintigram were analyzed retrospectively. Our institution uses the combined radiocolloid and Patent V blue dye method for identifying sentinel nodes.

Biopsied node count (BNC) was defined as the number of nodes identified by surgeon as sentinel node on blue dye score and radioactivity count. Sentinel nodes were removed according to the definition of a sentinel node (7): the hottest node; any blue node; any node at the end of a blue lymphatic channel; any node that has ex vivo counts greater than 10% of the hottest node; any palpably suspicious node. Nodes were then sent for OSNA analysis (One Step Nucleic Acid Amplification, Sysmex UK) or for histologic examination if the nodes were too small for immediate analysis. The results from OSNA were interpreted as follows: one positive = micrometastasis, two positive = macrometastasis.

Reported node count (RNC) was defined as the number of nodes seen on the scan reported by Consultant Radiologists with expertise in breast oncology blinded to the BNC. The scans were reported on the same day as the scan was performed by one radiologist. RNC was compared to BNC using Cohen's kappa statistic. Other patients who had SNB without scan, for example due to technical problems, in the same period were also analyzed. RNC can be subjective as displayed in *Fig. 1.*

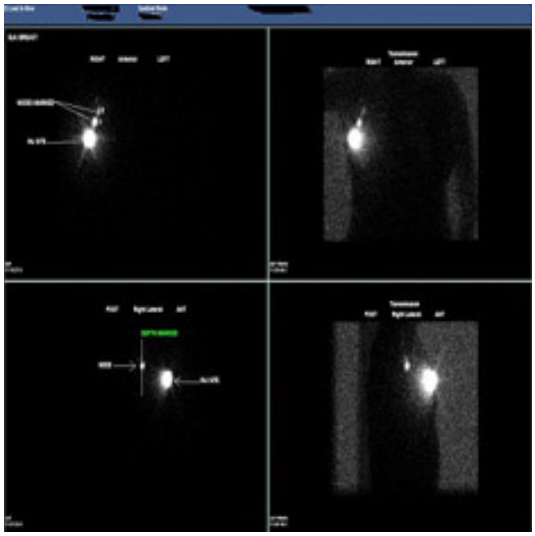

Fig. 1 Traditional lymphscintigram after peri-areolar injection of Tc-99m. Note the ambiguity of number of nodes as seen in the different projections from the same patient.

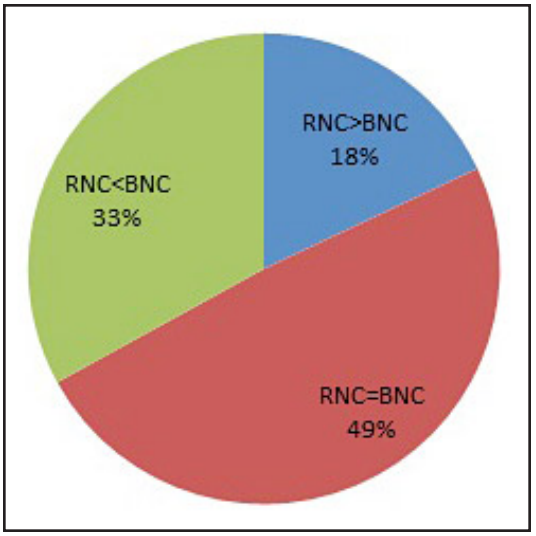

Fig. 2. Results from 100 cases comparing reported node count (RNC) to sentinel node biopsy node count (BNC), note just less than 50% agreement

The results of the RNC compared to BNC were then presented and discussed at a multidisciplinary meeting, and it was agreed to eliminate the scans. Subsequently, the next cohort of consecutive patients undergoing SNB alone was collected and analyzed.

The BNC was normally distributed, therefore compared using a Student's t-test.

RESULTS

In the first phase, data from 100 female patients, aged 64.68 ± 12.02 years (mean±standard deviation) were analyzed. All procedures were unilateral. RNC ranged from 0-5 (mean=1.84 ± 1.01, mode=1), and 90% of lymphoscintigraphy was performed on the day of surgery.

BNC was calculated from operative and histological data. Nodes that were classified as non-sentinel (i.e., neither blue or radioactive) were not included in the count. BNC ranged from 1-4, mean=2.0 ± 0.95, mode=1. RNC was zero in two cases but SNB was successful. Cohen's Kappa statistic was used to analyze the correlation between the RNC and BNC, and was 0.34 (95% CI = 0.195 to 0.482; <0.2 is considered poor agreement, 0.21-0.4 fair, 0.41-0.6 moderate, 0.61-0.8 strong, > 0.8 near complete agreement) *(Fig. 2)*.

In the same time frame, 14 female patients had Tc-99m colloid injection without lymphoscintigrams. These patients did not have scans because of scanner unavailability, and SNB localization was possible in all.

In the second phase, 69 female patients underwent SNB deliberately without a pre-operative lymphoscintigram. All cases were unilateral. BNC ranged from 0-4 (mean=1.80 ± 0.88, mode=2). There was no statistical significance of BNC between the scan and no scan group (p=0.156). When the 14 patients without scans from the first phase were also included in analysis (i.e., 100 with scan vs 83 with no scans), there was still no statistical significance (p=0.158). Failed localization rate of patients with scans was 0% despite two scans showing no axillary uptake. There were two cases of failed localization in

TABLE 1
Outcomes of SNB With and Without Lymphscintigram

BNC	A: With scan (n=100)	B: No scan (n=69)	C: All no scan (n=83)	P value
Mean	2.0 ± 0.95	1.80 ± 0.88	1.80 ± 0.88	p=0.156 (A:B) p=0.158 (A:C) t-test
Localization rate	100% (despite 2 failed scans)	97.10%	97.59%	n/a
Node positivity rate (all)	36	21	25	p=0.11 (A:C) Chi-squared test
Node positivity rate (macromets)	21	9	11	p=0.06 (A:C) Chi-squared test

patients without scans. Detection rate for sentinel node was 97.59%. Sentinel node results in patients with scans yielded 15 patients with micrometastases and 21 patients with macrometastases (overall node positive rate 36%). Sentinel node results in patients without scans demonstrated 12 patients with micrometastases and nine patients with macrometastases (overall node positive rate 25.3%). The difference was not significant between scan and no scan groups (Chi-squared test, p=0.11 overall for all metastases, p=0.06 for macrometastases only) *(Table 1)*.

DISCUSSION

Our results correlate to previously published studies supporting the idea that not obtaining a lymphoscintigram did not change BNC. Correlation between RNC and BNC was only in fair agreement, and negative lymphoscintigrams did not result in failed SNB localization, a conclusion that has been documented previously (8). The low agreement may be because the scan could show more than four nodes but it is standard practice to remove no more than four nodes (9). This is unlikely to be the cause in this study as BNC was higher than RNC in a third of cases. The scans were not double read, and there can be ambiguity in scans leading to inaccurate RNC (*Fig.1*).

To safely exclude lymphoscintigrams from clinical practice, it needs to be ensured that failed localization rates do not rise above an accepted standard, and also that the positive sentinel node rate should not fall significantly. The detection rate of SNB without scans remains higher than the guidelines from the ALMANAC trial (96.1%) (10) and the prospective international multicenter AMAROS study (97%) (11). Furthermore, if the lymphoscintigram shows no uptake (i.e., negative scan), blue dye alone can still detect sentinel nodes in 85.6% of cases (10).

The sentinel node positivity rate compares to that from the ALMANAC trial (12). The rate appeared to drop when the scans were stopped but this failed to reach statistical significance. This was despite the same technique for analysis of the nodes, and the BNC was not statistically different between groups.

CONCLUSION

Scanning by the use of lymphoscintigraphy was only introduced into breast surgery as it had been shown to be useful for other cancers (e.g., melanoma) and helped to validate the technique. Based on the

lymphatic drainage of the breast, uncertainties in the role of extensive axillary surgery, and the results of this audit and study, we conclude that lymphoscintigrams should no longer be used in routine practice. There may, however, still be a role for lymphoscintigraphy in patients who are unable to receive blue dye (13), those who have had previous axillary or breast surgery, and those who have received neoadjuvant therapy.

In addition to measurable savings in the lymphoscintigram cost, there are also the repercussions of time savings (no delay to operating room while awaiting scan or multiple journeys to hospital), freeing up the scanner for other scans, and recovery of time for the radiologist. However, it would still be prudent to further audit the SNB detection rates and node positivity rates when not using lymphoscintigrams in a larger series and in an alternative setting for replication.

CONFLICT OF INTEREST AND DISCLOSURE

All authors declare that no competing financial interests exist.

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