Journal of BUON **14:** 251-257, 2009

ORIGINAL ARTICLE

Is anterior oblique view alone in surgical position sufficient for preoperative sentinel lymph node mapping in breast cancer? A quantitative comparative analysis with conventional views

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Summary

Purpose: *Since the anterior projection alone has several limitations in the conventional preoperative sentinel lymph node (SLN) mapping, multiple projections including anterior oblique (AO) view are preferred. There are many AO acquisition techniques described in the literature but none of them creates an image which fully reflects the surgical perspective. We aimed to compare the AO view in the surgical position with the conventional projections according to quantitative parameters.*

Patients and methods: *Sixty female breast cancer patients entered the study. Two hours after the radiotracer injection, preoperative SLN mapping at anterior, lateral and 35° AO projections in surgical position was performed. For each projection, mapping success rate (MSR), the mean number of SLNs, lymphatic channel visualization rate, image contrast and distance measurements between each SLN and between the SLNs and the injection site were recorded.*

Results: *The best MSR and image contrast for the first and the consecutive axillary SLNs were found at the AO projection. The longest distance between the injection site and the SLNs and between the two SLNs were observed at the AO views. Although the AO view gave the best results for intramammary SLNs the difference was not statistically significant from the anterior view.*

Conclusion: *The 35° AO view in the surgical position was superior to the anterior and lateral projections. Therefore, the simple 4-min AO view in the surgical position may entirely reflect the surgeon's perspective and could be used safely alone in the preoperative lymphatic mapping for breast cancer patients.*

Key words: acquisition projection, breast cancer, lymphoscintigraphy, sentinel lymph node, surgical position

Introduction

The main acquisition projection of the conventional preoperative SLN mapping is the anterior projection [1]. However, lymphatic mapping at the anterior projection alone has several limitations and today nuclear medicine departments prefer multi-projectional imaging that is combined with lateral and/or anterior oblique projections [1,2]. There are many AO acquisition techniques reported in the literature. However, none of them created an image which fully reflected the surgical perspective [1, 3-9].

The purpose of this study was to compare the 35° AO view in the surgical position with the anterior and lateral views according to quantitative parameters such as the MSR, the image contrast value and the distance measurements.

Patients and methods

Patients

Sixty women with biopsy-proven AJCC stage T1 (n= 46) or T2 (n= 8) invasive breast cancer or patients with ductal carcinoma *in situ* (DCIS) (n= 6) were in-

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Received 14-07-2008; Accepted 25-10-2008

vestigated in this study. Mean age was 54.5±12.8 years (range 32-80). Diagnostic biopsy was performed either by needle (n=39) or excision (n=21). Mean tumor size was 14.9±6.4 mm (range 5-30).

The lymphoscintigraphy protocol was approved by the institutional ethical committee. Because the gamma rays from the outside the patient's body lead to erroneous calculation, patients with Co-57 or Tc-99m flood source transmission images were not included.

SLN identification rate and the mean number of SLNs of the axillary and extra-axillary lymphatic basins, lymphatic channel visualization rate, image contrast values of SLNs and distance measurements between each SLN and between the SLNs and the injection site were recorded.

Radiotracer injection

In all cases, combined intradermal and intraparenchymal radiotracer injection technique was performed.

In medial and outer quadrant tumors, deep injection entailed 18.5 MBq (0.5 mCi) of 99mTc-nanocolloid (Nanocoll, Amersham Health, Italy) in a volume of 0.5 mL injected parenchymally in 4 depots (total 74 mBq, 2 mL) into the normal breast tissue surrounding the primary tumor or the excisional biopsy cavity using a 0.45 × 13 mm (26 G, 1/2") needle. For central or upper outer quadrant tumors, periareolar deep injections were made into the normal breast tissue just outside the areolar border at 4 sites around the areola.

The superficial technique consisted of 7.4 MBq (0.2 mCi) of 99mTc-nanocolloid in a volume of 0.2 mL injected intradermally at the breast quadrant over the tumor site or at 12-o'clock position at the periareolar region.

In non-palpable tumors, ultrasound, wire or skin marking guidance were used.

Lymphoscintigraphy

In all patients, static images were obtained at the anterior (A), 35° AO, and lateral (L) projections 2 hours after radiotracer injection. All images were acquired in supine position using a single-head, large field-of-view gamma camera (XRT Camstar, GE, USA) with a low-energy high-resolution collimator (4-min acquisition in a 256×256 matrix). In all patients, the arm on the tumor site was abducted at an angle of 90ΌI (to simulate surgical position) during 35° AO imaging. In patients with oversized breasts, manual inferior-medial and lateral displacements of the breast were performed for the evaluation of axillary and internal mammary lymphatic basins. A Tc-99m point source was used to outline the body contour of the patients.

Axillary lymph nodes were ordered as 1st (the hottest), 2nd, 3rd and 4th-5th according to the radioactivity levels of each lymph node.

Quantitative parameters

For each projection, MSRs were calculated for the axillary and extra-axillary SLNs and for the lymphatic channels.

For the delineation of the border of the injection sites and other quantitative measurements, intensity of each view was set to 1-2% of the maximum count intensity.

Image contrast values for each axillary and extra-axillary hot lymph nodes were calculated according to the following formula by drawing identical regions-of-interest over the lymph nodes and adjacent background tissue for all projections (Figure 1).

$$\text{Image contrast} = ({}_{\text{total count}}\text{SLN} - {}_{\text{total count}}\text{Background}) / {}_{\text{total count}}\text{Background}$$

Because the edge detection of the lymph nodes might be difficult, we used the center instead of the border of the lymph nodes for a measurement origin (Figure 1). Hence, the following measurements were performed:

A. (mm)= distance between the centre of each lymph node and the nearest border of the injection site.

B. (mm)= distance between the centers of the first and the second lymph nodes.

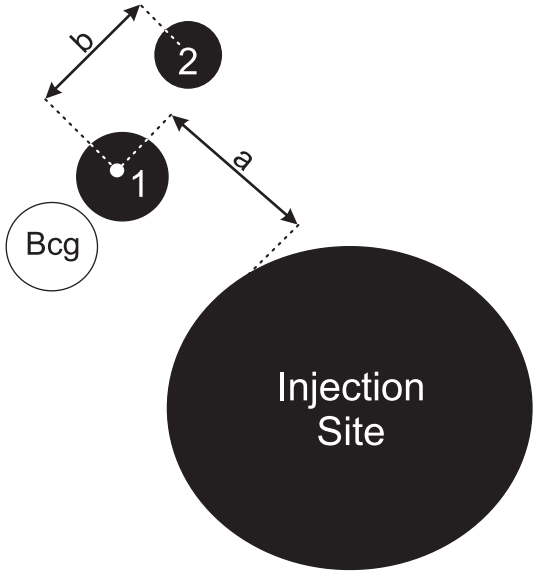

Figure 1. Schematic drawing of the injection site, the first (1) and the second (2) SLNs, and the background (Bcg). **a:** Distance between the lymph node and the nearest edge of the injection site; **b:** Distance between the two lymph nodes.

Statistical analysis

Statistical analysis was done with the use of Graph Pad InStat version 3.00 for Windows (GraphPad Software, San Diego California USA). Based on compared data, Fisher's exact test, unpaired *t*-test, Mann-Whitney U test and ANOVA were used. P-value less than 0.05 was accepted as statistically significant.

Results

Mapping success rates

For the first SLN, MSR of the A, L and AO projections were 80%, 98% and 100%, respectively (Figure 2). The AO view also gave the best identification rates for the 2nd and the consecutive axillary lymph nodes (Table 1). Parallel to the MSR, the mean number of detected SLNs in A, L and AO projections were 1.6, 1.7 and 2.4, respectively; the AO oblique projection showed significantly higher number of SLNs than the other projections ($p < 0.05$; Figure 2). The highest number of SLNs was detected with the periareolar radiotracer injection for all projections. In patients with periareolar injection, the average numbers of SLNs were 1.8, 1.9 and 2.8 for A, L and AO projections, respectively ($p < 0.05$). For the mean number of detected SLNs, none of the projections was affected by the site of injection except the A projection. At the A projection, outer quadrant injections significantly decreased the number of SLNs ($p < 0.05$). Although the A projection showed a higher failure rate (20%) for the demonstration of the first SLN, the site of injection did not

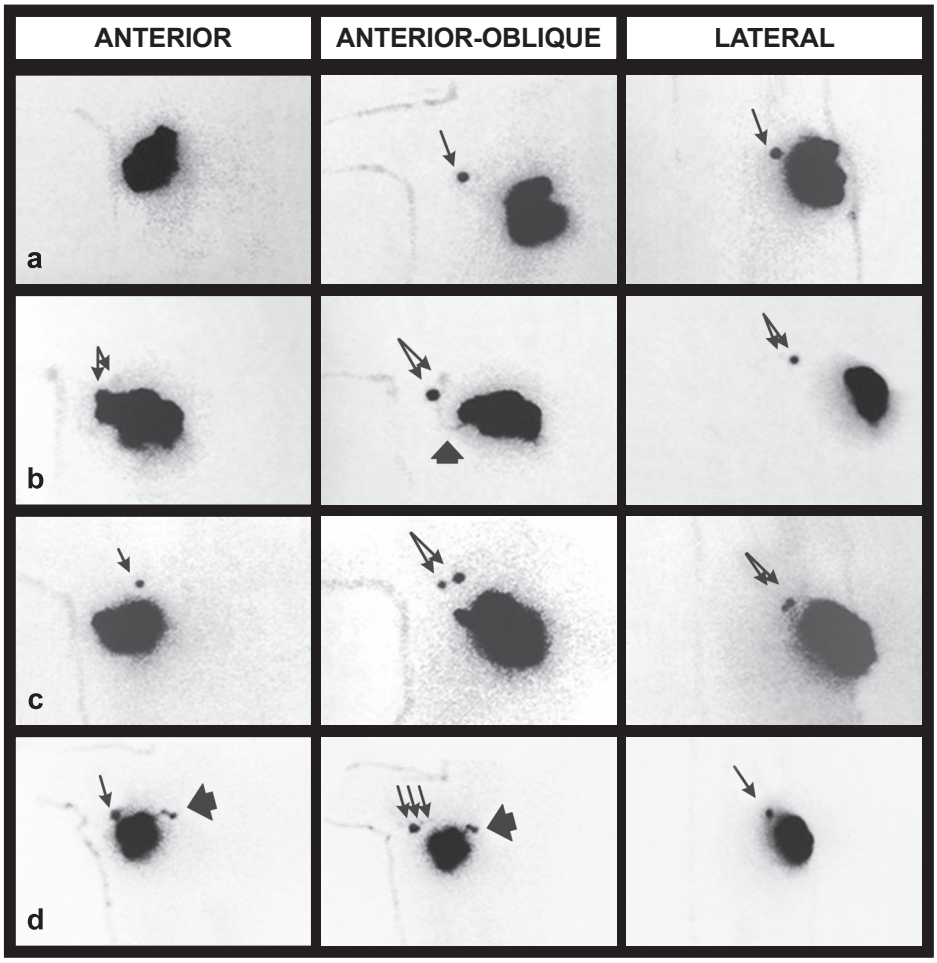

Figure 2. Static lymphoscintigraphy images - at anterior, 35° anterior-oblique, and lateral projections - of 4 different cases. In cases a and b, anterior images did not demonstrate any clear axillary SLN. However, anterior-oblique projection definitely showed single or multiple axillary nodes in these cases (arrows). In case b, lymphatic channel was only visualised at anterior-oblique projection (arrowhead). Anterior-oblique projection showed more axillary foci than the anterior projection in cases c and d (arrows). As shown in case d, internal mammary SLNs appeared similarly in anterior and anterior oblique projections (arrowhead).

Table 1. Mapping success rates of the 3 projections for the axillary and extra-axillary SLNs (patients, n= 60)

	A		*L*		*AO*		*A vs. L*	*A vs. AO*	*L vs. AO*
	n	*%*	*n*	*%*	*n*	*%*			
1st LN	48	80	59	98	60	100	*	*	–
2nd LN	30	50	32	53	49	82	–	*	*
3rd LN	14	23	6	10	24	40	–	–	*
4th + 5th LN	2	3	4	7	10	17	–	*	–
Internal-MSLN	10	17	0	0	9	15	NA	–	NA
Intra-MSLN	3	5	6	10	7	12	–	–	–
Lymphatic channel	13	22	4	7	20	33	*	–	*

A: anterior view, L: lateral view, AO: 35° anterior oblique, LN: lymph node, Internal-MSLN: internal mammary sentinel LN, Intra-MSLN: intramammary sentinel LN, NA: not available
*: p value < 0.05, –: p value > 0.05

significantly deteriorate the MSR. The failure rates at the A projection were 19%, 19% and 22% for periareolar, inner and outer quadrant injections, respectively (p >0.05).

The results of the extra-axillary lymph node detection are summarized in Table 1. Intramammary SLNs (intra-MSLN) were detected at all projections. Identification rates of AO, L and A projections were 12%, 10%, and 5%, respectively (p > 0.05). Internal mammary SLNs (internal-MSLN) were demonstrated only at the A and AO projections (17% and 15%, respectively; p >0.05).

The lymphatic channel visualization rates at AO, A and L projections were 33%, 22% and 7%, respectively. The success rate of L projection was significantly lower than the other projections (p < 0.05).

Image contrasts

The average image contrast values for the first axillary SLN were 10.7, 9.6 and 22.4 for A, L and AO projections, respectively. Overall, the AO projection gave significantly higher contrast values than A and L projections (p <0.05). Contrast values of the 2nd and the next SLNs are given in Table 2.

The site of the radiotracer injection significantly affected the contrast values, especially at A and L projections. The highest contrast values were obtained by the periareolar injection at all projections, (C: 14.1, 13.7 and 31.6, for A, L and AO projections, respectively). Outer quadrant injection significantly decreased the contrast at the A projection (C=6.8, p < 0.05), whereas inner quadrant injections significantly decreased the contrast at the L projection (C: 4.1, p <0.05). At the AO projection, the contrast was slightly decreased by the inner quadrant injection. However, this change was not statistically significant (C: 16.8, p >0.05).

Generally, the extra-axillary SLNs' image contrast values were smaller than the axillary SLNs' values at each projection (Table 2). The average contrast values of internal-MSLNs were 3.3 and 2.4 for A and AO projections, respectively (p > 0.05). And the mean contrast values of intra-MSLNs were 1.3, 2.4, and 4.7 for A, L and AO projections, respectively. Image contrast at AO projection was significantly higher than A projection for intra-MSLNs (p < 0.05).

Distance measurements

As shown in Table 3, the distance between the 1st and the 2nd axillary SLN ("b") and the distance between these SLNs and the injection site ("a") were longer with the AO projection rather than other projections. Although the shortest distance between the axillary SLNs and the injection site ("a") was measured at the A projection, L projection gave the shortest value for distance between the 1st and the 2nd SLN ("b"). In addition to these comparisons, we investigated the relationship between the "a" values of the 1st SLN and the site of the

Table 2. Mean image contrast values of axillary and extra-axillary SLNs for the 3 projections

	A (range)	*L (range)*	*AO (range)*	*A vs. L*	*A vs. AO*	*L vs. AO*
1st LN	10.67 (0.23-49.8)	9.57 (0.45-48.57)	22.41 (0.68–206.65)	–	*	*
2nd LN	4.28 (0.33-17.33)	4.99 (0.18-20.33)	7.56 (0.75–42.92)	–	*	*
3rd LN	3.53 (0.09-8.91)	6.95 (1.36-10.15)	5.97 (3.98-29.70)	*	–	–
4th + 5th LN	3.60 (1.88-5.38)	2.52 (1.22-3.57)	5.01 (0.99-15.56)	–	–	–
Internal-MSLN	3.34 (0.51-12.14)	–	2.35 (0.29-6.27)	NA	–	NA
Intra-MSLN	1.25 (0.64-1.78)	2.44 (0.26-5.46)	4.68 (1.16-8.51)	–	*	–

For abbreviations see footnote of Table 1

Table 3. Distance measurements between the SLNs and injection site ("a") and between the 1st and the 2nd SLNs ("b") for the 3 projections

	A	*L*	*AO*	*A vs. L*	*A vs. AO*	*L vs. AO*
	Mean, mm (range)					
a - 1st LN	37.7 (0-93)	44.2 (0-110)	67.4 (9-125)	–	*	*
a - 2nd LN	24.11 (0-55)	31.10 (0-56)	42.28 (11-94)	*	*	*
a - Internal-MSLN	41.5 (7-69)	–	35.9 (15-69)	NA	–	NA
a - Intra-MSLN†	14.2 (4-30)	31.6 (23-43)	30.5 (17-38)	NA	NA	NA
b	22.6 (0-61)	17.1 (0-48)	25.7 (9-71)	*	–	*

a: distance from the SLN to the injection site, b: distance between the 1st and the 2nd SLNs
†statistical analysis was not performed because of too few values
For the rest of the abbreviations see footnote of Table 1

radiotracer injections. In patients with inner quadrant injection, the "a" values were 42.3, 49.3 and 76.0 mm at L, A and AO projections, respectively. These values were 47.4, 39.6 and 70.3 mm for periareolar injections, and 45.1, 27.7 and 59.3 mm for outer quadrant injection. According to these results, the site of the radiotracer injection did not significantly affect the distance between the 1st SLN and the injection site for each projection except the A projection. At the A projection, "a" value was significantly lower in the outer quadrant injection than the inner quadrant injection ($p < 0.05$).

The mean "a" values for the internal-MSLNs were 41.5 mm at the A projection and 35.9 mm at the AO projection ($p > 0.05$). The AO and the L projections gave identical distances for the intra-MSLNs (30.5 and 31.6 mm, respectively).

Discussion

Since the first introduction of SLN mapping, both nuclear medicine and breast surgeon's experience and procedural data are gradually increasing. Under the light of this collective data, we were faced with the dilemma of whether or not to perform preoperative lymphoscintigraphic mapping [10]. Today, some of the breast surgeons conclude that surgical gamma probe is good enough for SLN biopsy and preoperative radionuclide mapping is not really necessary [11-13]. On the contrary, nuclear medicine physicians who focused on the SLN biopsy recommended not only the conventional but also the more sophisticated preoperative mapping protocols to improve the success of the SLN biopsy [3,4,6-9,14,15].

It is known that the preoperative radionuclide SLN mapping is one of the most important predictors of successful SLN biopsy [13,16-18]. It decreases: (a) the learning period of breast surgeon; (b) the time duration of the biopsy; (c) the false-negative procedures; and (d) it increases the accuracy of SLN biopsy with axillary and extra-axillary SLNs [2,13,16-21]. However, lymphoscintigraphy has some technical limitations depending on the imaging technique. In the literature, there are many lymphoscintigraphy-negative but gamma probe-positive cases, and these are good examples to demonstrate the insufficiency of the existing techniques [2,13,22]. The mismatches between the two modalities are generally explained with the higher radiation sensitivity of the probes. However, improvable causes - such as "shine through effect" and soft tissue attenuation- can also lead to a false - negative lymphoscintigraphy [1,3]. To eliminate these technical artefacts, various factors have been investigated such as the type of collimators (medium or low energy), different patient positions (supine, prone, modified supine, oblique or upright), various acquisition projections (multiple projections, 30°, 45° or 60° AO, L or stereoscopic) and the multimodality imaging such as SPECT/CT systems [1,3,4,6,7,9,14,15,23,24].

Krynyckyi et al. from Mount Sinai hospital suggested obtaining A and L projection images as first-step approach and recommended oblique views as an alternative to lateral views [1]. Similarly, other investigators demonstrated the necessity of oblique projections for better diagnostic accuracy [3,4,24]. Although the advantages of AO imaging were not new [5], only few studies quantitatively analyzed its benefits [4,25]. These studies were generally focused on the "hottest" axillary SLNs and unfortunately neither less radioactive axillary nodes nor extra-axillary lymph nodes were studied quantitatively in the literature. Krynyckyi et al. not only reported the usefulness of the oblique view, but also pointed to the importance of the arm position [1,8]. Although the position of the arm in lymphoscintigraphy should approximate the one used during surgery, the effectiveness of AO view in surgical position is not analyzed yet.

In this study, the 35° AO view in the surgical position was compared with the conventional A and L projections by objective parameters such as MSR, image contrast and distance measurements.

The AO view used in the present study was simple but slightly different from the previously studied oblique protocols [3,4,6,7,9,14]. As demonstrated in previous

studies, the AO projection was useful and its impact increased with some modifications such as multiple AO imaging, modified AO imaging with triangular foam wedge, imaging in upright or sitting position or using medium energy collimator. However, Ichihara et al. reported that, despite the usefulness of these modified imaging techniques, an additional view in the supine position was essential since SLN detection with the gamma probe was performed in the supine position during surgery [14].

Lymphoscintigraphy was the "road map" for the surgeon [2] and acquired images should fully reflect the surgeon's perspective during the surgery. Therefore, in this study 35° AO view was acquired in the supine position and the arm on the tumor site was abducted at an angle of 90° to simulate the exact surgical position. The skin was marked in the same position which was nearly the identical to the surgeon viewpoint.

Similar to the previous reports about standard or modified oblique techniques [3,4,6,7,9,14], our results showed that the AO view in surgical position was superior to the A and L projections with higher MSR, higher image contrast and longer distance between the injection site and the 1st SLN. In our patient group we did not have any patient whose oblique view was negative for axilla, although the other views were positive.

Because the hottest axillary node is not always the 1st (sentinel) lymph node [26], we quantitatively analyzed either the less radioactive axillary or the extra-axillary lymph nodes in this study. In general, the AO projection gave the higher MSR for the subsequent axillary lymph nodes with better contrast values. The best separation between the 1st and the 2nd SLN was observed with AO imaging.

Although the A view showed the relatively better MSR, image contrast and distance measurement from the injection site for the internal-MSLNs, this difference was not statistically significant in our small patient population. None of the internal-MSLNs was detected by the L view. In the detection of intra-MSLNs, all projections showed similar MSR. However, the AO projection gave the higher image contrast for these SLNs.

Despite the controversies and lack of clear consensus elective radiotherapy for internal-MSLNs may be considered in axillary node-positive breast cancer patients. However, the major concern for irradiation of internal-SLNs is the increased risk for cardiac toxicity [27]. Meanwhile, detailed and precise mapping in order to localize lymph nodes by AO view may lessen the potential complications and bring a new implication to CT-based radiotherapy planning in order to define the treatment volumes [28-31].

The site of the radiotracer injection did not significantly decrease the success rate of the AO projection. However, performances of the A and L views changed significantly with the site of injection. The lymphatic channel visualization rate which was an important factor for the SLN determination [23] was higher in the AO projection.

"Shine through" effect and soft tissue attenuation were the independent factors which affected the success of SLN mapping [1,3,15]. Previous studies investigated various modifications of oblique imaging (upright/sitting position, modified oblique views with use a wedge or multi-angle views) to overcome these problems [1]. The rationale for these modified techniques was that injection sites move to a more inferior location away from the SLNs [1,7]. In our study, the periareolar injection technique was systematically used for tumors located in the upper outer quadrant and these tumors did not cause any specific problem. During the acquisition, inferior-medial breast displacement was routinely used in patients with oversized breast. This simple manoeuvre minimized the attenuation of the breast tissue and the "shine through" effect of the injection site.

Conclusions

Our results showed that the 35° AO view in surgical position was superior to the A and L projections with higher MSR, higher image contrast, better spatial separation of axillary SLNs, and favorable extra-axillary SLN identification rates. We think that simple and single 4-min 35° AO view in the surgical position, which entirely reflects the surgeon's perspective, could be used safely alone in the preoperative lymphatic mapping in patients with breast cancer.

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