

## Sentinel lymphoscintigraphy in patients with breast cancer undergoing excisional biopsy

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Some small tumors of the breast cannot be diagnosed by needle biopsy, and an excisional biopsy is occasionally needed for the diagnosis. Sentinel node navigation surgery is frequently suitable for patients with such small breast cancers. The purpose of this study was to compare sentinel lymphoscintigrams in breast cancer patients who had previously undergone excisional biopsy with sentinel lymphoscintigrams in patients undergoing no excisional biopsy. We also investigated the possibility of clinical application of the sentinel node navigation procedure in the former group of patients. **Methods:** Sentinel lymphoscintigrams of 43 patients with breast cancer undergoing excisional biopsy were compared to those of 116 patients without excisional biopsy. Lymphoscintigrams were obtained by using intradermal and/or subdermal injections of technetium-99m labeled phytate at 2 points on each side of the dermal incision in patients after excisional biopsy. Injections were performed at 2 points of the skin over the tumor in the patients who had not undergone excisional biopsy. **Results:** Axillary lymph nodes were visualized in 42 of 43 patients undergoing excisional biopsy (98%) and in 115 of 116 patients without excisional biopsy (99%). The number of visualized axillary nodes was 1 to 5 (mean  $\pm$  SD = 2.1  $\pm$  1.0) and 1 to 5 (mean  $\pm$  SD = 1.9  $\pm$  1.0) in the two groups, respectively. No significant difference was determined between the two groups. Parasternal lymph nodes were depicted in 3 patients after excisional biopsy who had the tumor in the outer half of the breast, in contrast to 4 without excisional biopsy who had the tumor in the inner half. Intramammary hot spots were observed in 5 patients after excisional biopsy and in 2 without excisional biopsy. Lymphatic vessels were observed in 23 patients (53%) who had the excisional biopsy, and in 37 (32%) who did not have the biopsy. The former figure was significantly higher than the latter ( $p < 0.02$ ). **Conclusion:** Sentinel node navigation surgery for axillary nodes was shown to be possible in patients undergoing excisional biopsy. However, the visualization of parasternal nodes, intramammary hot spots and lymphatic vessels tended to increase in number, and care must be exercised in the management of these patients.

**Key words:** breast cancer, excisional biopsy, sentinel node, lymphoscintigraphy

### INTRODUCTION

SENTINEL NODE NAVIGATION SURGERY has been developing into an important technique in early breast cancer for avoiding postoperative complications. Observational studies have confirmed the usefulness of the sentinel node

concept in breast cancer surgery.<sup>1,2</sup> Some small tumors of the breast cannot be diagnosed by needle biopsy alone, and excisional biopsy is occasionally needed for the diagnosis. Sentinel node navigation surgery is frequently suitable for patients with such small breast cancers. The purpose of this study was to compare sentinel lymphoscintigrams in breast cancer patients who had previously undergone excisional biopsy with sentinel lymphoscintigrams in patients undergoing no excisional biopsy. At the same time, the feasibility of the clinical application of the sentinel node navigation procedure in those patients undergoing excisional biopsy was studied.

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## PATIENTS AND METHODS

Sentinel lymphoscintigraphy was performed in 159 women with clinical stage Tis or T1–2, N0 breast cancer<sup>3</sup> from October 2001 to July 2003. Lymphoscintigrams of 43 patients with breast cancer who had previously undergone excisional biopsy were compared to those of 116 patients undergoing no excisional biopsy. The mean ages of the two groups were 53.6 years (39–78) and 55.4 (29–79), respectively. Informed consent was obtained from all patients. Intervals between the biopsy and the lymphoscintigram were 8 to 58 days with a mean of 22.4. Lymphoscintigraphy was performed using a Toshiba GCA-7200 A/DI attached with a low energy general purpose

collimator, or a Siemens E.CAM attached with a low & middle energy general purpose collimator. Lymphoscintigrams were obtained 0.5 to 2, 4 to 6, or 16 to 20 hours after intradermal and/or subdermal injections of technetium-99m labeled phytate (111–148 MBq) at 2 points on each side of the dermal incision in patients undergoing excisional biopsy. Intervals between injections and imaging were decided according to the operation schedule. Injections were performed at 2 points of the skin over the tumor in the patients who had not undergone excisional biopsy. Imaging directions were anterior, oblique and

**Table 1** The number of patients with visualized axillary nodes

	Biopsy	Nonbiopsy
0.5–2 hours	1/2 (50%)	6/6 (100%)
4–6 hours	11/11 (100%)	39/39 (100%)
16–20 hours	30/30 (100%)	70/71 (99%)
Total	42/43 (98%)	115/116 (99%)

The intervals are the hours between injections and imaging.

**Table 2** The number of visualized axillary nodes

	Biopsy	Nonbiopsy
0.5–2 hours	3	1–3 (1.7)
4–6 hours	1–3 (2.0)	1–5 (2.0)
16–20 hours	1–5 (2.2)	1–5 (1.8)
Total	1–5 (2.1)	1–5 (1.9)

The arithmetic mean of the numbers is enclosed in parentheses.

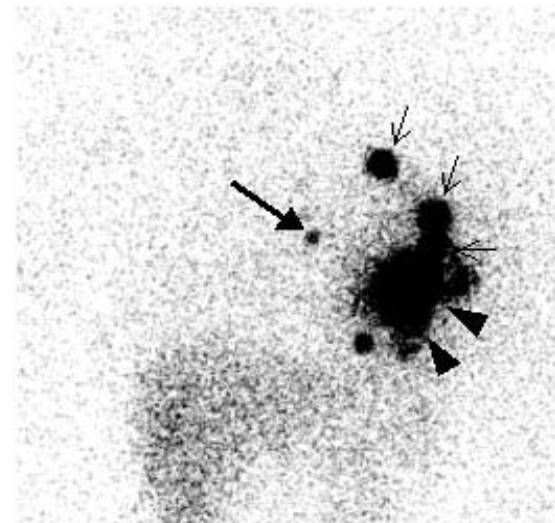
**Table 3** The site of visualized hot spots according to the location of breast cancer

	Biopsy Patients			Nonbiopsy Patients		
	Inner (15 pts)	Subareola (2)	Outer (26)	Inner (38)	Subareola (6)	Outer (72)
Axillary LN	15	2	25	38	5	72
Parasternal LN			3	4		
Supraclavicular LN	1			2		
Intramammary HS			5	2		

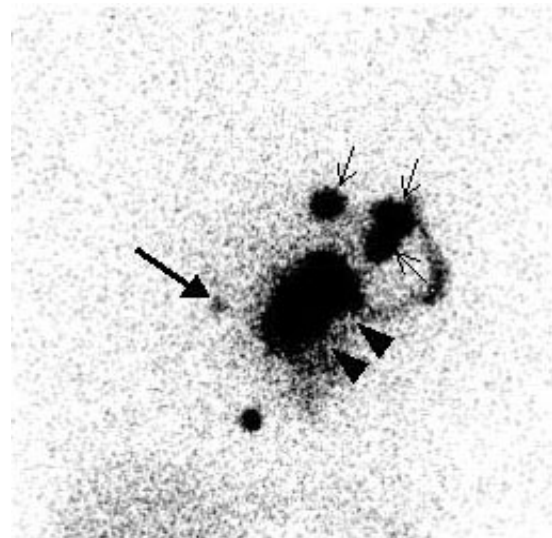
The numbers of patients are enclosed in parentheses.  
pts: patients, LN: lymph node, HS: hot spot

**Table 4** The number of patients with visualized lymphatic vessels

	Biopsy	Nonbiopsy
0.5–2 hours	0/2 (0%)	2/6 (33%)
4–6 hours	7/11 (64%)	11/39 (28%)
16–20 hours	16/30 (53%)	24/71 (34%)
Total	23/43 (53%)	37/116 (32%)

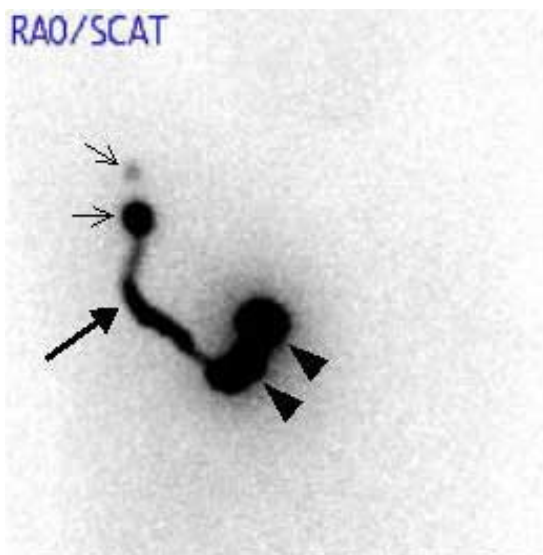


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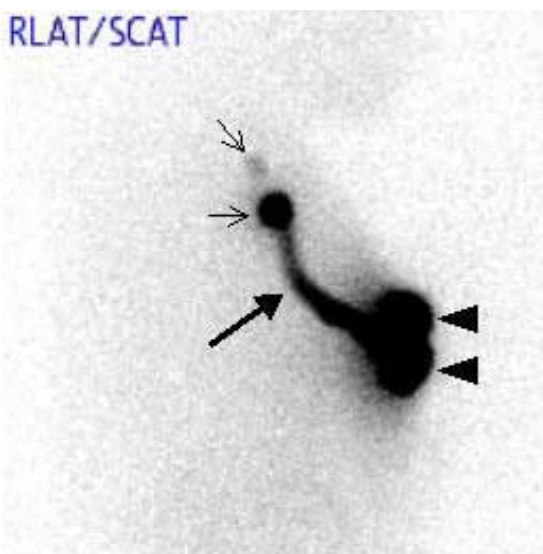


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**Fig. 1** Sentinel lymphoscintigrams of a 51-year-old female with left breast cancer. (A) Anterior view. (B) Left anterior oblique view. Arrowheads, a large arrow and small arrows indicate injection sites, the parasternal lymph node and the axillary nodes, respectively.



A



B

**Fig. 2** Sentinel lymphoscintigrams of a 41-year-old female with right breast cancer. (A) Right anterior oblique view. (B) Right lateral view. Arrowheads, a large arrow and small arrows indicate injection sites, the lymphatic vessel and the axillary lymph nodes, respectively.

lateral views. The arm of the involved side was lowered on the anterior view and raised on the oblique and lateral views. The body contours were outlined using scattered photons.<sup>4</sup> The differences in the numbers of visualized axillary nodes between patients after excisional biopsy and patients without excisional biopsy were analyzed using the Student's t-test, and the differences between visualization frequencies of lymphatic vessels in the two groups were compared using the  $\chi^2$  test. Differences of  $p < 0.05$  were considered to be significant.

## RESULTS

Axillary lymph nodes were visualized in 42 of 43 patients undergoing excisional biopsy (98%), and in 115 of 116 patients without excisional biopsy (99%). According to intervals between injections and imaging, the number of patients with visualized axillary nodes is shown in Table 1. Of 2 patients whose axillary nodes were not observed by lymphoscintigrams, one patient after excisional biopsy had the lesion in the axillary tail. The axillary node was not depicted probably due to the "shine-through" produced by the excess radioactivity from the area of injections, and the 3 sentinel nodes were detected by a gamma-detection probe during surgery. The other patient without excisional biopsy had involved lymph vessels and lymph nodes. Overall, the number of visualized axillary nodes was from 1 to 5 (mean  $\pm$  SD =  $2.1 \pm 1.0$ ) in those with excisional biopsy, and 1 to 5 (mean  $\pm$  SD =  $1.9 \pm 1.0$ ) in those without excisional biopsy. There was no significant difference between the two groups. Table 2 shows the number of visualized axillary nodes according to the interval between injections and imaging. The summary of visualized hot spots is shown in Table 3 according to the site of breast cancer. Parasternal lymph nodes were depicted in 3 patients after excisional biopsy who had the tumor in the outer half of the breast, compared to 4 without excisional biopsy who had the tumor in the inner half. Intramammary hot spots were observed in 5 patients after excisional biopsy against 2 in those without excisional biopsy. Lymphatic vessels were observed in 23 patients (53%) who had the biopsy, compared to 37 (32%) who did not have the biopsy. The former figure was significantly higher than the latter ( $p < 0.02$ ). According to intervals between injections and imaging, the number of patients with visualized lymphatic vessels is shown in Table 4.

### Case Presentations

Figure 1 exhibits sentinel lymphoscintigrams of a 51-year-old female with left breast cancer which was located in the outer half region of the breast. She had previously undergone excisional biopsy. Three axillary lymph nodes, one parasternal node and one intramammary hot spot are observed.

Figure 2 shows sentinel lymphoscintigrams of a 41-year-old female with right breast cancer which was located in the subareolar region. One lymphatic vessel toward the axillary lymph node is clearly observed in this patient who had excisional biopsy.

## DISCUSSION

Recently, sentinel node navigation surgery has been adopted for early breast cancer patients with clinically negative (N0) axillary lymph nodes. On the other hand, excisional biopsy is essential for patients with small breast tumors that are not diagnosed by needle biopsy.

Sentinel node navigation procedures must be performed in patients with such early breast cancer. Whether it is also applicable for patients with breast cancer undergoing excisional biopsy is an important question. Though there are a few reports concerning the use of sentinel node navigation surgery in patients after excisional biopsy, there is no consensus on this matter.<sup>5-7</sup> A definitive evaluation is sought because there are many patients who undergo excisional biopsies due to a small tumor of the breast.

With regard to the injection site for sentinel lymphoscintigraphy, peritumoral injections have generally been used.<sup>8,9</sup> However, intradermal and/or subdermal injections over the tumor have also been used,<sup>10,11</sup> due to the evidence of lymphatic communications between the mammary gland and overlying skin.<sup>12</sup> McMasters et al.<sup>13</sup> reported that dermal injections were associated with sentinel lymph nodes that were more radioactive than with peritumoral injections and minimized the false-negative rates. Therefore, the intradermal and/or subdermal injections over the tumor were used in the present study. In point of fact, peritumoral injections were impossible in patients after excisional biopsy.

In the present study, we compared sentinel lymphoscintigrams in breast cancer patients with or without excisional biopsies. If sentinel lymphoscintigraphy had been performed before and after excisional biopsy in the same patient, we could have determined whether or not the lymphoscintigrams depicted the same lymph nodes. However, excisional biopsies were carried out to diagnose the properties of tumor and we did not perform lymphoscintigraphy before and after excisional biopsy in the same patient for ethical reasons. Our study demonstrated that there was no significant difference between patients after excisional biopsy and patients without excisional biopsy, on the visualized frequency and the visualized number of axillary lymph nodes. The two groups of patients were rather different in terms of the number of patients, due to the fact that we compared patients within the same time period. Therefore, in order to optimize accuracy, we compared patients after excisional biopsy with 45 consecutive patients without excisional biopsy. Through this comparison, it was confirmed that there was no significant difference between the two groups.

Our results would suggest that the axillary nodes, which were visualized by using intradermal and/or subdermal injections at 2 points on each side of the dermal incision in patients after excisional biopsy, were still sentinel nodes. Parasternal lymph nodes were not depicted in patients without excisional biopsy who had the tumor in the outer half of the breast. However, these nodes were visualized in those patients after excisional biopsy who had the tumor in the outer half of the breast. Intramammary hot spots were observed in comparatively more patients having excisional biopsy than in those patients who did not have excisional biopsy. These hot spots were

interpreted as pooling of radionuclides which originated from lymphatic disruption and/or the space arising out of tumorectomy, as well as being intramammary lymph nodes. Lymphatic vessels were frequently visualized in patients after excisional biopsy. Because of the above-mentioned findings, lymphatic flows were thought to be partially changed by the excisional biopsy. According to the interval between the time of excisional biopsy and sentinel lymphoscintigraphy, there is a difference in the degree of fibrous scarring and it is possible that visualized lymph nodes change in number and the visualization of lymphatic vessels changes in frequency. Excisional biopsy patients are still small in number and the influence of the interval on lymphoscintigraphic images will require future study.

Observational studies have been performed in all of the patients in this study. The observation periods ranged from 15 to 37 months. Although recurrence has not been detected in the regional lymph nodes, two patients had distant metastases. One patient had multiple bone metastases and the other had multiple pulmonary metastases. These patients had not undergone excisional biopsy before the sentinel lymphoscintigraphy. Extended observational studies hereafter will be necessary for the validation and acceptance of the sentinel node navigation surgery in patients with breast cancer after excisional biopsy, as well as in patients undergoing no excisional biopsy.<sup>2</sup> If sentinel node navigation surgery can be adapted for use in more patients, postoperative complications should decrease proportionately.

## CONCLUSION

The sentinel node navigation procedure for axillary nodes was shown to be possible in patients undergoing excisional biopsy. Following an increase in the number of patients who will undergo breast-conserving surgery without dissection of axillary lymph nodes, we expect a decrease in postoperative complications. However, the visualization of parasternal nodes, intramammary hot spots and lymphatic vessels tended to increase in number and care must be exercised in their management.

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