

## Symposium I

# Sentinel Lymph Node Biopsy Using Tin Colloid RI and Blue Dye Method

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Axillary dissection has been considered essential for breast cancer staging because nodal metastasis is the most powerful predictive factor for recurrence. On the other hand, morbidity, such as lymphedema and shoulder dysfunction, may occur. Sentinel node biopsy is a good way to avoid unnecessary axillary dissection. We used tin colloid as a carrier of Tc99m tracer together with the blue dye method. The detection rate of the sentinel node was 27 cases out of 29 (90%) for the blue dye method, 10 cases out of 19 (53%) for the RI method, and 27 out of 33 (82%) for the combined method. The detection rate of the RI method was improved after adding the subcutaneous injection over the tumor from 45% before adding the subcutaneous injection to 82% after adding it. The false negative rate was 11% for the blue dye method, 0% for the RI method, and 10% for the combined method. This yields a sensitivity of 89% for the blue dye method, 100% for the RI method, and 90% for the combined method. Specificity was 100% for all three methods. Accuracy was 96% for the blue dye method, 100% for the RI method, and 96% for the combined method. There were two false negative cases. The average number of sentinel lymph nodes was 2.12 for the dye method, 1.66 for the RI method, and 1.95 for the combined method. There were three of 49 cases with identified parasternal lymph nodes by RI imaging. Lymphatic mapping using tin colloid may be useful for detecting sentinel nodes.

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Nodal metastasis is the best prognostic factor for breast cancer patients<sup>1)</sup>. Axillary dissection is considered to be a part of the breast cancer operation because nodal metastasis may not be fully diagnosed by imaging studies. Sentinel node biopsy is a promising method for predicting nodal metastasis although many problems still remain<sup>2)</sup>. One issue to be decided is the particle size of the colloid. Large colloid particles are preferable for detecting true sentinel nodes because they usually stay within the sentinel node without migrating<sup>3)</sup>. We report our experience with tin colloid combined with blue dye to detect sentinel lymph nodes (SLN).

## Patients and Methods

From September 1998 to March 2000, eighty-one patients underwent sentinel node biopsy using vital blue dye and radiocolloid. Demographic factors are listed in Table 1. Technetium 99m tin colloid was used as a radiocolloid. 99mTc tin colloid was injected in 0.5 ml quantities into three sites around the tumor and 0.2 ml was injected just over the tumor subcutaneously. Tin colloid was injected in the evening of the day before the operation. RI imaging was obtained as possible, three to four hours after the injection (Fig 1). Blue dye (1% isosulfan blue) was injected peritumorally three sites just before the operation, in a total amount of 2.5 ml. A gamma probe (Navigator) was used as a guide for detecting sentinel nodes. Backup axillary lymph node dissection was performed in all cases.

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Table 1. Demographic Factors

Age	52.7(33-88)	Tumor site	%
Tumor size		IUQ	9 (11.1)
1.0-2.0 cm	37	ILQ	12 (14.8)
2.1-3.0 cm	29	OUQ	37 (45.7)
3.1-5.0 cm	9	OLQ	13 (16.0)
5.1- cm	3	Areolar	3 (3.7)
others	3	others	7 (8.6)
mean	2.6 cm		
Operation			
mastectomy	35		
BCT	46		

IUQ, Inner upper quadrant; ILQ, Inner lower quadrant;  
OUQ, Outer upper quadrant; OLQ, Outer lower quadrant

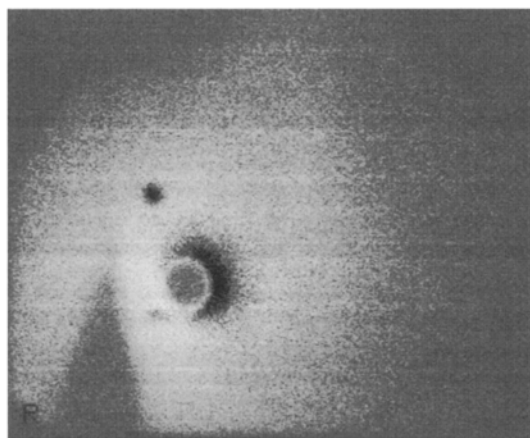


Fig 1. Images of the SLN with tin colloid

## Results

The detection rate of the sentinel node was 27 cases out of 29 (90%) for the blue dye method, 10 cases out of 19 (53%) for the RI method, and 27 out of 33 (82%) for the combined method (Table 2). The detection rate of the RI method was improved after adding the subcutaneous injection over the tumor; 15 out of 33 cases (45%) before adding the subcutaneous injection to 14 out of 17 cases (82%) after adding it. The overall detection rate increased in the last 50 cases compared with the first 31 cases. The false negative rate was 11% for the blue dye method, 0% for the RI method, and 10% for the combined method. This yields a sensitivity of 89% for the dye method, 100% for the RI method, and 90% for the combined method. The specificity was 100% for all three methods. Accuracy was 96% for the dye method, 100% for the RI method, and 96% for the combined method.

Table 2. Sensitivity and Specificity According to Method

	N	Success rate	False negative rate	Sensitivity	Accuracy
Overall	81	78%	9%	91%	97%
Late 50 cases	50	84%			
Dye method	29	90%	11%	89%	96%
RI method	19	53%	0%	100%	100%
Combined method	33	82%	10%	90%	96%

Table 3. False Negative Cases

Case No	Age	Tumor size	N	Tumor site	Detection technique	Nodal metastasis
1	88	1.9	0	E	Dye	3/9
2	56	2.2	0	C	Combined	2/14

There were two false negative cases (Table 3). There were no differences between SLN-identified cases and non-identified cases in terms of age, tumor size, tumor location, and histological type.

The average number of sentinel lymph nodes was 2.12 for the dye method, 1.66 for the RI method, and 1.95 for the combined method. There were three of 49 cases with identified internal mammary lymph nodes by RI imaging. There were no patients with sentinel nodes located in levels II or III.

## Discussion

Morbidity from axillary dissection, including arm edema, shoulder dysfunction, anesthesia of the upper arm, and seroma, are not infrequent. The average increase in size of the upper arm is about 2 cm postoperatively compared with preoperatively, regardless of the operative procedure<sup>4</sup>. Sensory disturbance of the medial region of the affected upper arm was present in all cases who underwent axillary dissection, although the extent of disturbance was smaller when the intercostobrachial nerve was preserved<sup>4</sup>. This morbidity led us to perform sentinel node surgery. The main difference of in our method and that of others<sup>5,6</sup> is the RI colloid. We used tin colloid labeled with Tc99m as a RI tracer. The detection rate for the SLN was 78% in this series. A learning curve for identifying SLN was reported by Guillian<sup>7</sup> and is widely accepted. The detection rate of the

Table 4. Skip Metastasis (cited from Morrow M<sup>11</sup> with revision)

Authors	No of Pts. with Ax meta.	Neg.level I /Pos. level II	Neg.level II /Pos. level III
Rosen et al	429	2	0.2
Veronesi et al	539	1.5	0.4
Smith et al	309	16	10
Danforth et al	65	29	3.1
Chevinsky et al	93	7	2
Boova et al	80	7.5	1.3
Ikeda et al	536	9	0.7

last 50 cases was 84% compared with 68% for the first 31 cases. The main reason for the failure to identify the SLN is a low detection rate by the RI method prior to performing the subcutaneous injection. We used tin colloid as a tracer. European investigators mainly use human albumin colloid<sup>6</sup> and American investigators mainly use sulfur colloid<sup>7</sup>. A greater than 90% detection rate has been reported by using these colloids<sup>8</sup>. The particle size of tin colloid is larger than these colloids, ranging from 500-1 000  $\mu$  m. Large colloids like tin colloid have been thought not to move into lymphatic drainage channels<sup>9</sup>. We realized that tin colloid can move into the lymphatic drainage system and into the lymph node. Sato et al<sup>10</sup> reported a 99% success rate for detecting SLN using tin colloid and blue dye in node negative patients. They also reported low identification rate without concomitant dye injection. Imoto also reported a low success rate with tin colloid injection into the peritumoral area<sup>11</sup>. The improvement of the visualization rate of the SLN after subcutaneous injection in our series is probably due to the abundant lymphatic network of the subcutaneous region. Once a large colloid moves into a lymph node, it remains there for a long time, so it is easy to detect true sentinel nodes even more than twelve hours after the injection. Even though the detection rate of the SLN is comparable between the blue dye method and the combined method, it is better to use the combined method because internal mammary lymph nodes are only detectable by

RI, although the implications of internal mammary lymph node metastasis has not been settled yet. We did not detect SLN in level II, although many authors report an average of 5% skip metastasis in cases with axillary dissection<sup>3</sup>. (Table 4) It is not clear whether the cause of the lack of skip metastasis to level II and III lymph nodes in this series is due to the difference in size between tin colloid and cancer cells. The mechanism of skip metastasis should be determined.

One of our cases who showed a false negative result was an 88-years-old woman who might have been too old for lymphatic mapping because of sclerotic lymphatics.

Analysing false negative cases is critical for determining the indications for SLN biopsy.

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