Symposium I

Sentinel Lymph Node Biopsy in Breast Cancer Using Blue Dye with or without Isotope Localization

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Background: The purpose of this study was to determine the feasibility of sentinel lymph node (SLN) biopsy using blue dye with or without isotope localization to predict the presence of axillary and internal mammary lymph node (IMN) metastases in patients with breast cancer. We also investigated whether multiple sectioning of the SLN could improve the accuracy of frozen section examination.

Method: One-hundred twenty-six patients underwent dye-guided or dye- and gamma probe-guided SLN biopsy followed by complete axillary lymph node dissection (ALND). No ALND was performed in the 14 patients with small tumors and a negative SLN. In addition, 69 patients underwent IMN biopsy.

Results: The axillary SLN was identified in 123 of 140 (88%) patients. An accuracy rate of 90% was obtained by frozen section examination of the SLN, which increased to 100% in patients examined with a greater number of sections. Lymphatic flow to the IMN and/or a radioactive hot spot in the IMN was found in 9 of 102 (9%) patients, while a hot node was detected using a gamma probe in only 2 of these patients. No involvement of the IMNs was found histologically in these 9 patients. IMN involvement was found in 7 of 61 (11%) patients without lymphatic flow to the IMNs or a hot spot by lymphoscintigraphy or who did not undergo lymphoscintigraphy.

Conclusion: ALND can be avoided in patients with small breast cancers and a negative SLN. SLN biopsy guided by lymphatic mapping is unreliable for identifying metastases to IMNs.


Key words: Breast cancer, Lymph node metastases, Sentinel lymph node biopsy

Studies done 20 years ago established that breast-conserving treatment is an effective alternative to total mastectomy for small breast cancers. Breast conservation currently is the accepted treatment for most patients with clinical stage I or II invasive breast cancer. In an effort to further reduce operative morbidity, intraoperative lymphatic mapping and sentinel lymph node (SLN) biopsy is being evaluated as an alternative to axillary lymph node dissection (ALND) in clinically node-negative breast cancer patients, and several reports have documented the success of this minimally invasive alternative to routine ALND in selected patients. In the near future, SLN biopsy is likely to replace ALND as the procedure of choice for assessing axillary disease in patients with early-stage breast cancer.

Because SLN technology is evolving rapidly, variation in technique is widespread and a standard procedure has not yet become accepted. Controversies remain concerning the optimal method for identifying the SLN and for detecting micrometastases within it. Particularly, immediate and reliable intraoperative information regarding the status of the SLN would be beneficial for deciding whether to perform complete ALND at the time of the initial operation. However, the accuracy of SLN diagnosis using frozen sections varies. Moreover, limited ability to map the internal mammary lymph node (IMN) chain is considered an important drawback of SLN biopsy for staging purposes. Therefore, additional studies are needed to assess the feasibility of using SLN biopsy to detect axillary and internal mammary disease in patients with breast cancer.

We performed this study to determine the fea-
sibility of SLN biopsy using blue dye with or without isotope localization to detect the presence of axillary and IMN metastases from breast cancer. Moreover, we investigated whether multiple sectioning of the SLN could improve the accuracy of frozen section examination.

Patients and Methods

Patients and Treatment

A total of 140 patients with TIS or clinical stage I or II breast cancer (TNM classification) were enrolled in the study between February 1996 and December 1999, after giving informed consent as approved by the local ethical committee at the Kanazawa University School of Medicine. Patients with primary tumors larger than 5.0 cm in greatest diameter (T3) or metastatic axillary nodes fixed to one another or to adjacent tissue (N2) were excluded. Other exclusion criteria included a history of previous axillary lymph node biopsy, multiple primary breast tumors, and pregnancy. Patients with palpable axillary nodes (N1a, N1b) were included because clinical evaluation of axillary nodes in these patients frequently is inaccurate and inconsistent. Patients with TIS were included because microinvasion and lymph node metastases may occur in these patients. After SLN biopsy using blue dye with or without radioisotope, a complete ALND (level I-III) was performed in 126 patients. However, we did not perform ALND in 14 additional patients with small cancers (< 1.5 cm) and a negative SLN. Therefore, the diagnostic accuracy of the SLN biopsy was evaluated in 126 patients, while the identification of the SLN was examined in all 140 patients.

Dye-Guided Method

The technique of SLN biopsy using blue dye has been described previously. This was performed during the first phase of the study between February 1996 and February 1998. After induction of general anesthesia, 4 mL of 1% patent blue dye (CI 42045; Wako Pure Chemical Industries, Ltd., Osaka, Japan) was injected with a 25-gauge needle, 5 to 15 minutes prior to the surgical procedure. The injections were performed at the 12, 3, 6, and 9 o'clock positions into the breast tissue around the tumor or biopsy cavity. Blunt dissection was performed until a lymphatic tract or blue-stained node was identified. The dye-filled tract was dissected to the first blue lymph node. If possible, the tract was followed proximally to the edge of the breast tissue to ensure that the identified lymph node was the most proximal (i.e. the SLN). Using blue dye, the SLN was defined as the most proximal lymph node with any visible blue staining. The SLN was removed via mastectomy or axillary incision.

Preoperative Lymphoscintigraphy

During the second phase of the study between March 1998 and April 1999, 3 mCi of 99m-techne
tetium (99m-Tc) human serum albumin (HSA) (Dai-ichi Radioisotope Laboratory Co., Ltd., Tokyo, Japan) in a volume of 0.3 mL of saline was injected into the subdermal tissue above the primary tumor or biopsy cavity. Preoperative lymphoscintigraphy with anterior projection was performed 10 minutes and 1 hour after the injection using a gamma camera (ECAM; Siemens-Toshiba, Nasu, Japan). The injection site was shielded with lead to enhance visualization of an axillary or internal mammary lymph node. The jugular notch and the xyphoid process were used as anatomical landmarks. Lymphoscintigraphy using 99m-Tc HSA was also performed in some patients during the first phase of the study between February 1996 and February 1998. During the third phase of the study between May 1999 and December 1999, 1 mCi of 99m-Tc tin colloid (Nihon Mediphysics, Tokyo, Japan) in 4 mL of saline was injected into the subdermal tissue above the primary tumor or biopsy cavity. Lymphoscintigraphy was similarly performed 1 hour and 4 hours after the injection using a gamma camera. When the node was localized, the overlying skin was marked with indelible ink to facilitate intraoperative node detection.

Dye- and Gamma Probe-Guided Method

The technique of SLN biopsy using blue dye and radioisotope has been described previously. Patients were transported to the operating room 1.5 hours after the injection of 99m-Tc HSA or the day after the injection of 99m-Tc tin colloid. After induction of general anesthesia, 4 mL of 1% patent blue dye was injected with a 25-gauge needle into the peritumoral area 5 to 15 minutes prior to the surgical procedure. Routine transcutaneous probing of the axillary, internal mammary, and supraclavicular basins was performed using a handheld gamma-detection probe (C-Trak; Care-Wise...