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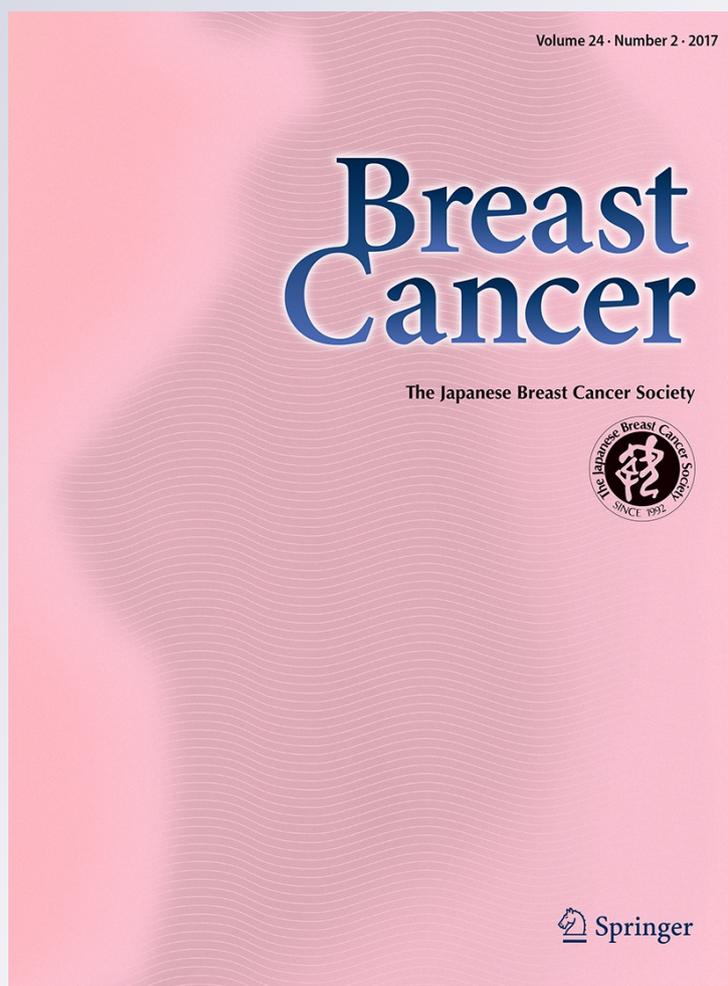
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Patterns of clinical practice for sentinel lymph node biopsy in women with node-negative breast cancer: the results of a national survey in Japan

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Abstract

Purpose Sentinel lymph node (SLN) biopsy is now accepted as the standard of care for axillary staging in women with node-negative breast cancer. Currently, dye, radioisotope (RI), and fluorescence indocyanine green (fICG) are tracers available. Importance of these three tracers has been recognized for SLN biopsy but the trend for SLN mapping has not been reported. Aim of this national wide survey was to evaluate practice patterns of SLN biopsy in Japan.

Methods This survey was conducted to examine the clinical practice of SLN biopsy in centers where one or more Japanese Breast Cancer Society (JBCS) board-certified surgeons practice breast cancer care. Their responses were recorded from 1 to 30 Oct 2014 and received by mail or fax in Japan. The questionnaire included three items: the number of breast cancer patients treated per year, the number of SLN biopsy procedures in a single year, and the methods for SLN detection.

Results A total of 412 responses excluding the 63 centers that do not perform the surgery were analyzed. Out of them, 206 (50 %) centers had a gamma probe, 118 (29 %) had an NIR fluorescence imaging system, and both were

available at 49 (12 %) of the centers. Neither RI nor fICG was available in 137 (33 %). The dye method was preferentially used in private hospitals. In 412 centers, a total of 36,221 patients underwent SLN biopsy per year and 23,038 (64 %) received radioactive tracer. fICG was co-applied with RI in 83 and 13 % of patients, respectively. Single mapping with RI alone was used in only 4 % of patients. The non-radioactive method was used for routine SLN biopsy in 13,183 (36 %) patients [8533 (24 %) for dye alone and 4650 (12 %) for fICG alone].

Conclusions A radioactive tracer was used in 64 % of women with early breast cancer for SLN biopsy while approximately 24 % received dye alone, which was especially prevalent in PHs. The fICG was used in only 12 % as a non-radioactive method but incentive package for fICG by national health insurance plan could increase the number of NIR imaging systems and improve the sensitivity for SLN biopsy in Japan.

Keywords Breast cancer · Sentinel lymph node biopsy · Radioisotope · Dye · Indocyanine green

Introduction

Sentinel lymph node (SLN) biopsy is now accepted as the standard of care for axillary staging in women with node-negative breast cancer. Currently, dye, radioisotope (RI) or the dual-tracer method, involving both, are the standard techniques for SLN mapping [1]. ICG is a widely used green dye for assessing liver function and cardiac output. This amphiphilic molecule quickly binds to plasma proteins in the vascular components and serves as a new, useful imaging tool for use with near infrared (NIR) fluorescence imaging systems [2]. This NIR imaging can visualize the lymphatic

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channels through the skin and guide the surgeon to the SLN in the axillary basin [3, 4]. Previous studies show increasing evidence that the fluorescence ICG (fICG) method is safe and can achieve high SLN detection comparable with the RI method [5–8]. Based on these findings, the fICG method is recommended for SLN biopsy by the Japanese Breast Cancer Society (JBCS) clinical practice guidelines (recommendation grade B). Importance of three tracers including RI, dye, and fICG has been recognized for SLN biopsy but the trend for SLN mapping has not been reported. In this study, we conducted a national survey of SLN mapping and evaluated practice patterns of SLN biopsy.

Patients and methods

This survey was conducted to examine the clinical practice of SLN biopsy in centers where one or more JBCS board-certified surgeons practice breast cancer care. Their responses were recorded from 1 to 30 Oct 2014 and received by mail or fax in Japan. The questionnaire included institution information (institution name, department name, respondent, date of response), number of primary breast cancer patients, and number of each SLN biopsy practices (RI alone, dye alone, fICG alone, RI with dye, and RI with fICG).

Results

The questionnaires were sent to 699 centers where one or more members of the JBCS practiced and answers are received from 475 (68 %) of these centers. The response rate for the questionnaire items are 68 % for institution information, 67.8 % for number of primary breast cancer patients, and 67.7 % for number of each SLN biopsy

practices. As 63 centers had no surgical management, remaining 412 were subject to final analysis for this study. These 412 centers were classified into four main categories: 6 comprehensive cancer centers (CC), 78 university hospitals (UH), 205 public community hospitals (PCH), and 123 private hospitals/clinics (PH). Response rates of CC, UH, PCH, and PH were 88, 44, 91, and 63 %, respectively. The median number of breast cancer patients per year was 309 for CC, 138 for UH, 87 for PCH, and 48 for PH and the median number of SLN biopsy practices per year was 228 for CC, 94 for UH, 63 for PCH, and 40 for PH. In terms of device availability, 206 (50 %) centers had a gamma probe and the installation rate for this device was 100 % in CC, 78 % in UH, 52 % in PCH, and 28 % in PH. Of 412 centers, 118 (29 %) had an NIR fluorescence imaging system, and both were available at 49 (12 %) centers. Neither RI nor fICG were available in 137 (33 %) (Table 1). Of those 137 centers, CT lymphangiography and Sonazoid bubble combined with blue dye were applied in 23 and 1 of the centers, respectively. In 412 centers, a total of 36,221 patients underwent SLN biopsy per year and 23,038 (64 %) received radioactive tracer. As shown in Fig. 1, dye and fICG were co-applied with RI in 83 and 13 % of patients, respectively. Single mapping with RI alone was used in only 4 % of patients. The non-radioactive method was used for routine SLN biopsy in 13,183 (36 %) patients [8533 (24 %) for dye alone and 4650 (12 %) for fICG alone]. Among the non-RI methods, fICG occupied in 35 %.

Discussion

This survey demonstrated the variation in the techniques used in SLN biopsy in routine clinical practice in Japan. The standard techniques used in SLN biopsy are the RI

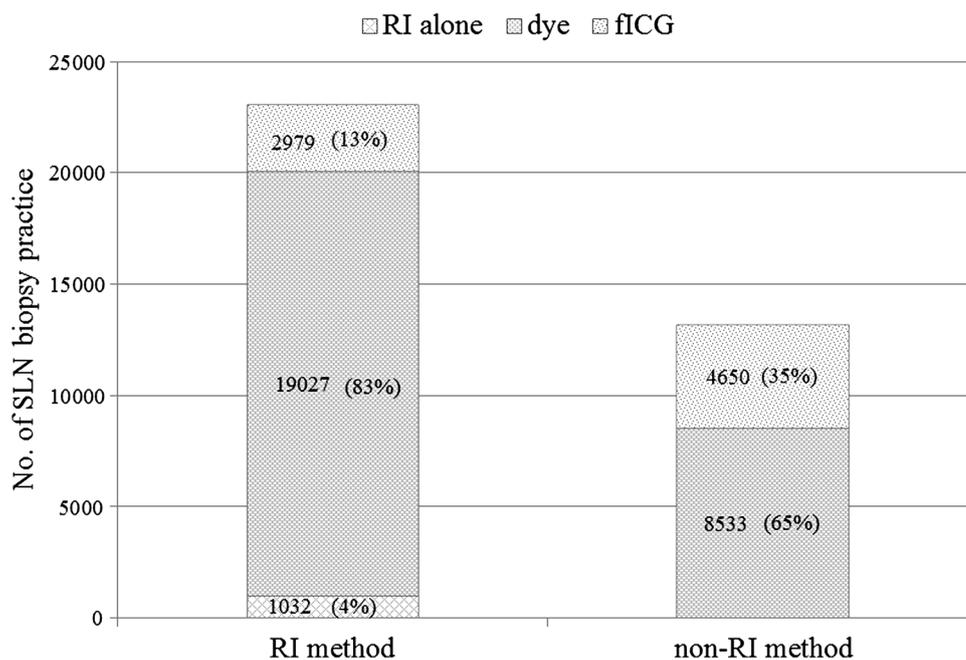
Table 1 Patients and technique for SLN mapping in the centers

	N (%)	# of primary breast cancer patients/year [median (range)]	# of SLN biopsy practices/year [median (range)]
Centers			
Comprehensive cancer centers	6 (1.5 %)	309 (108–906)	228 (75–803)
University hospitals	78 (18.9 %)	138 (40–917)	94 (25–696)
Public community hospitals	205 (49.8 %)	87 (1–545)	63 (0–392)
Private hospitals	123 (29.9 %)	48 (1–579)	40 (0–487)
Devices available for			
Radio active mapping	206* (50 %)		
NIR mapping	118* (29 %)		
Neither RI nor NIR mapping	137 (33 %)		

* Both radioactive mapping and NIR imaging are available in 49 (12 %) centers

SLN sentinel lymph node, NIR near infrared

Fig. 1 Practice patterns of procedures for SLN biopsy *RI* radioisotope, *fICG* fluorescent indocyanine green, *SLN* sentinel lymph node



method and/or the dye method. The NIR fluorescence imaging with ICG was developed for non-radioactive and real-time mapping for SLN biopsy. The results of previous studies have developed this novel technique as clinical practice for SLN detection of early breast cancer without nodal involvement [9–13]. For clinically node-positive patients, SLN biopsy following primary systemic therapy (PST) resulted in rather high (13–14 %) false negative rate [14, 15]. Kyoto Breast Cancer Consensus Conference 2014 highlighted procedures of SLN biopsy after PST [16]. There was a general agreement that dual mapping using dye and RI should be used for SLN biopsy after PST in patients with a positive node at presentation. Moreover, NIR fluorescence imaging can offer advantages for SLN detection after PST in terms of the number of SLNs harvested.

The RI method has some drawbacks including logistical and legislative issues. Applicability of RI is restricted to high-volume centers where radioactive materials are acquired and used in a nuclear medicine department. In this survey, half of the centers had a gamma probe and the installation rate for this device was the lowest in PH (28 %). In terms of detection techniques for SLN biopsy, two-thirds of patients received a radioactive tracer, and the dual mapping with RI and dye was common. Additional use of fICG accounted for 13 % in the RI method. These results indicated that the majority of high-volume centers, including CC and UH, used the higher detection methods for SLN, while the dye method was still predominant in PHs. In this survey, the installation rate of NIR imaging systems is approximately 30 %, and about a quarter of

patients underwent SLN biopsy using fICG. As establishing centers for the RI method is a large financial burden for most PHs, SLN mapping with fICG could be an alternative method for more accurate axillary staging [17]. Moreover, a sustainable supply of radioactive material is an issue due to its expanding usage and the decommissioning of old nuclear power plants. Exploration of non-radioactive tracers including fICG is warranted for more precise SLN biopsies in Japan.

In conclusion, 64 % of women with early breast cancer underwent SLN biopsy using a radioactive tracer, while approximately 24 % received dye alone, which was especially prevalent in PHs. An incentive package for fICG by national health insurance plan could increase the number of NIR imaging systems and improve the sensitivity for SLN biopsy in Japan.

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Compliance with ethical standards

Conflict of interest All authors declare that there are no conflicts of interest.

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