Breast Cancer (2012) 19:343–348
DOI 10.1007/s12282-011-0286-1

ORIGINAL ARTICLE

# Transcutaneous detection and direct approach to the sentinel node using axillary compression technique in ICG fluorescence-navigated sentinel node biopsy for breast cancer

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Received: 2 April 2011 / Accepted: 5 June 2011 / Published online: 2 July 2011
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**Abstract**

*Background* Indocyanine green (ICG) fluorescence navigation is a useful option in sentinel node biopsy (SNB) for breast cancer. However, several technical difficulties still exist. Since the sentinel node (SN) cannot be recognized over the skin, subcutaneous lymphatic vessels (LVs) must be carefully dissected without injury. In addition, the dissecting procedures are often interrupted by turning off the operating light during fluorescence observation. In this report, we introduce a new approach using the axillary compression technique to overcome these problems.

*Materials and methods* In the original procedure of the ICG fluorescence method, the subcutaneous lymphatic drainage pathway from the breast to the axilla was observed in fluorescence images, but no signal could be obtained in the axilla. When the axillary skin was compressed against the chest wall using a plastic device, the signals from the deeper lymphatic structures could be observed. By tracing the compression-inducible fluorescence signal towards the axilla, transcutaneous detection and direct approach to the SN were achieved. The benefit of this approach is that there is no risk of injury of LVs, and the procedures are interrupted less frequently by fluorescence observation. The axillary compression technique was used in 50 patients with early breast cancer.

*Results* SNs were successfully removed in all patients. Transcutaneous detection and direct approach were possible in 47 patients. This approach was also effective in obese patients.

*Conclusions* Axillary compression technique is a simple way to facilitate the surgical procedures of ICG fluorescence-navigated SNB for breast cancer.

**Keywords** Breast cancer · Sentinel node biopsy · Lymphatic mapping · ICG · Axillary compression technique

## Introduction

Sentinel lymph node biopsy (SNB) is an established approach for axillary staging in breast cancer [1–4]. Radioactive colloids and/or blue dye are used as tracers. The radioisotope (RI) method is surgeon-friendly, allowing subcutaneous navigation to the sentinel node (SN), but requires expensive equipment and protection measures for radiation, which are not always available. On the other hand, the dye method is convenient and safe, but technically difficult to learn. Indocyanine green (ICG) fluorescence navigation is a useful option for this purpose [5]. Fluorescence imaging can visualize subcutaneous lymphatic drainage pathways from the breast to the axilla over the skin. A surgeon can decide the site of skin incision precisely, and recognize ICG containing lymphatic vessels and lymph nodes with high sensitivity and specificity during the dissection, even when they are embedded in the fatty tissue. Therefore, less training is required before one can achieve a more satisfactory result than with the conventional dye method. Several clinical studies have reported that ICG fluorescence navigation provided results

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comparable to those with the RI method [6–9]. However, several technical difficulties still exist. First, since the penetration depth of fluorescent light is limited to 1 cm, the lymphatic vessels (LVs) and lymph nodes (LNs) in the axilla lying deeper than 1 cm cannot be recognized over the skin. Therefore, the subcutaneous LV must be carefully dissected until the SN is found. If any LV is injured, further fluorescence navigation will be difficult because of ICG contamination in the surgical field. It is sometimes difficult in overweight or obese patients for the same reason. Second, the light of the operating room must be dimmed during the fluorescence observation to prevent the contamination of near-infrared light. In this report, we introduce a new approach using an axillary compression technique to overcome these problems.

## Materials and methods

### Instruments and surgical procedures

An infrared fluorescence imaging system (Photodynamic Eye, Hamamatsu Photonics, Japan), which consists of light-emitting diodes (LED) set at 760 nm as a light source, and a charge-coupled device camera with a cut filter set for below 820 nm as a detector, was used to obtain near infrared (NIR) fluorescence images. The original procedure of the ICG fluorescence method has been described elsewhere [5]. Briefly, 5 mg/1 ml of ICG is injected intradermally into the periareolar skin. After a few seconds, subcutaneous lymphatic drainage towards the axilla is observed with fluorescence images. The signal disappears beyond the lateral edge of the pectoralis major muscle, where the subcutaneous LV runs deep into the axillary space. After a small skin incision is made at this point, the LV is dissected until the SNs are reached under the guidance of fluorescence images. It is important not to injure the LVs during the dissection. Otherwise, owing to the fluorescence signal of ICG spilling into the surgical field, further dissection becomes difficult. Several fluorescent spots observed around the first encountered node are dissected en bloc with the surrounding fatty tissue. LNs in the dissected specimen are isolated and investigated under an infrared camera. All fluorescent nodes are regarded as SNs and examined with frozen sections.

The principle of the axillary compression technique is shown in Fig. 1. The fluorescence signal of a subcutaneous LV becomes invisible where it runs deeper in the axillary space (Fig. 1a). When the axillary skin is compressed against the chest wall with a transparent plastic device (Hamamatsu Photonics, Japan) (Fig. 2), a fluorescence signal appears at the bottom of the device because the LV or the LN comes near to the surface. As shown in Fig. 1b, c, the shape and intensity of the compression-inducible fluorescence signal depend on the underlying structure. Typically, a linear-shaped and sharp signal represents an LV (b), and a round-shaped and intense signal represents an LN (c). Transcuataneous lymphatic mapping can be undertaken by tracing the compression-inducible fluorescence signal towards the axilla. The first pressure-inducible, round, and intense fluorescence signal is supposed to be the first SN. It usually takes several minutes after ICG injection until an adequate amount of ICG is accumulated in the SNs. A skin incision is made at the estimated site, and the SN is directly approached without dissecting the LV. The dissecting procedure is as simple as severing the subcutaneous tissue and the axillary fascia towards the fluorescent signal. As the dissection plane becomes deep, the intensity of the fluorescence signal from the SN increases. The LED output need to be decreased when the

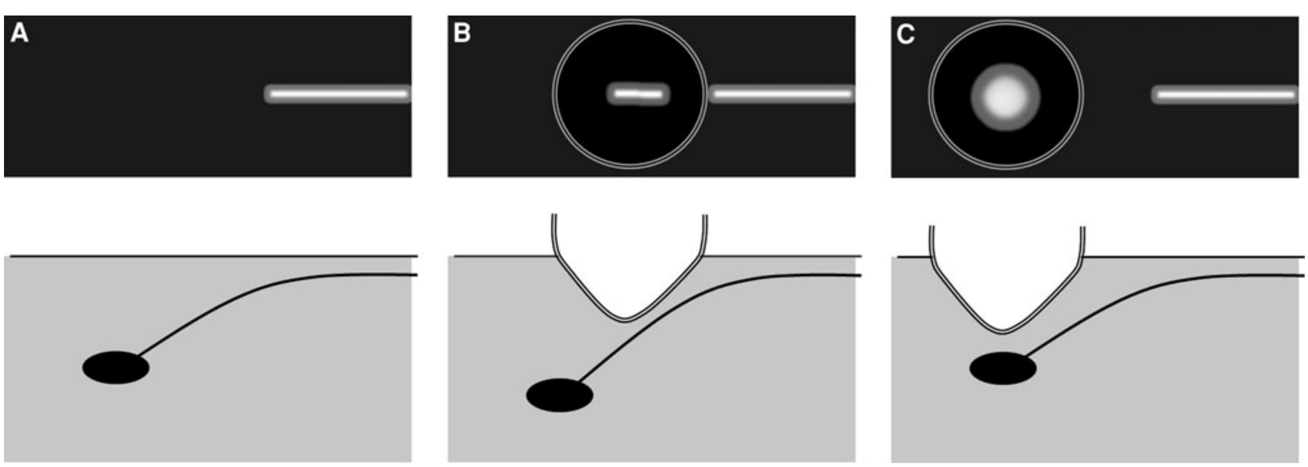


**Fig. 1** **a** Fluorescence signal of a subcutaneous lymphatic vessel becomes invisible where it runs deeper in the axillary space. **b** When the axillary skin is compressed against the chest wall with a transparent plastic device, a fluorescence signal appears at the bottom of the device. A linear-shaped and sharp signal represents a lymphatic vessel. **c** A round-shaped and intense signal represents a lymph node

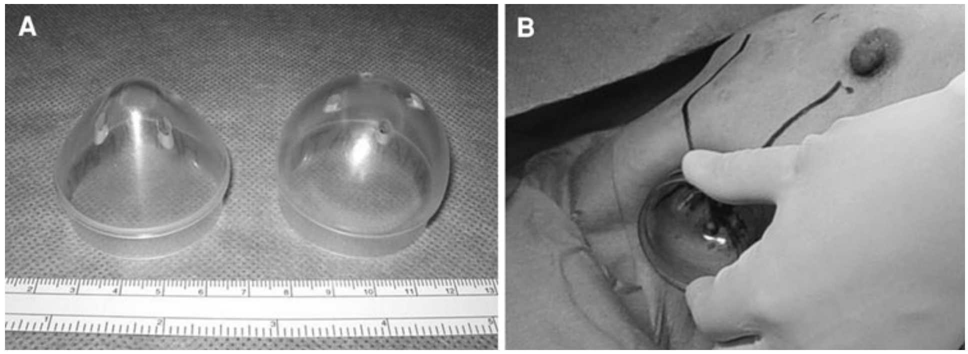


**Fig. 2** **a** We used two types of compression devices, which were a hemispheric bowl with a diameter of 4 cm (*right*) and a cone-shaped device (*left*). **b** The axillary skin was compressed against the chest wall by a plastic compression device

**Table 1** Results of sentinel node biopsy using axillary compression technique

| | No. of patients | No. of SNs average (range) | Duration (min) | Success rate of direct approach[a] |
|---|---|---|---|---|
| All cases | 50 | 3.6 (1–8) | 22.9 | 47/50 |
| BMI | | | | |
| <25 | 38 | 3.8 (2–7) | 23.7 | 35/38 |
| ≥25 | 12 | 3.3 (1–8) | 25.6 | 12/12 |
| Age | | | | |
| <65 | 24 | 3.7 (2–8) | 21.8 | 24/24 |
| ≥65 | 26 | 3.6 (1–5) | 26.2 | 23/26 |

[a] In three cases, where the direct approach was not successful, an axillary LV was first detected and then traced to SNs as the original method. Finally, SNs were successfully removed in all cases

fluorescence signal become too high. When the fluorescent nodes are extracted out of the wound, a subcutaneous LV draining to the nodes can be observed using a fluorescence image to ensure that the SNs are correctly excised. In most cases, when the first SL was pulled out of the wound with the surrounding fatty tissue, a few more fluorescent nodes were observed in the fat. We excised these nodes with the fatty tissue as a lymphatic basin. In order to clearly observe these SNs and draining LV without injury, it is important to widely open the axillary fascias and adequately pull them out of the wound by freeing the adjacent vessels and nerves. Electrical dissection was useful to minimize ICG contamination in the surgical field. In cases where only one node could be removed, the axillary space was observed again by fluorescence to determine whether any fluorescent nodes were left after removal of the first node. The following procedures are the same as the original method.

### Patients

The axillary compression technique was used in 50 patients with clinically node-negative breast cancer who underwent SNB from January 2008 to August 2009 in Nara Social Insurance Hospital. The mean age was 63.1 (41–93), and the body mass index (BMI) was 22.9 (17.6–36.4). The mean tumor size was 1.6 (0.5–3.5) cm. Fifteen patients were operated on by an attending physician, and the other 35 by a surgical resident under supervision.

## Results

Compression-inducible fluorescence signal in the axilla could be observed in all cases. Transcutaneous identification and direct approach to the SNs were successfully carried out in 47 cases. In the three other cases, where the SNs could not be directly approached, an axillary LV was first detected and then traced to the SNs following the original method. Finally, SNs were successfully removed in all cases. The average number of dissected nodes was 3.6 (1–8), and six were metastatic. It took 24.1 (10–47) min to remove the SNs after ICG injection. Transcutaneous detection and direct approach to the SN were also effective in 12 patients with BMIs greater than 25. Three cases of unsuccessful results were non-obese and elderly patients (Table 1).

Figure 3 shows the case of a 35-year-old female with a BMI of 17.6. Subcutaneous lymphatic drainage was observed, and the signal disappeared at the lateral edge of the pectoralis major muscle (a). Beyond the disappearing point, a linear-shaped fluorescence signal was seen by compression, representing an LV (b). Upon tracing towards the axilla, a round-shaped intense fluorescence signal was then observed and supposed to be the signal from the SN (c). A skin incision was made, and the subcutaneous tissue was dissected until an SN was exposed without tracing the LV (d). An LV draining to the SN was observed when the fluorescent node was extracted from the wound (e).

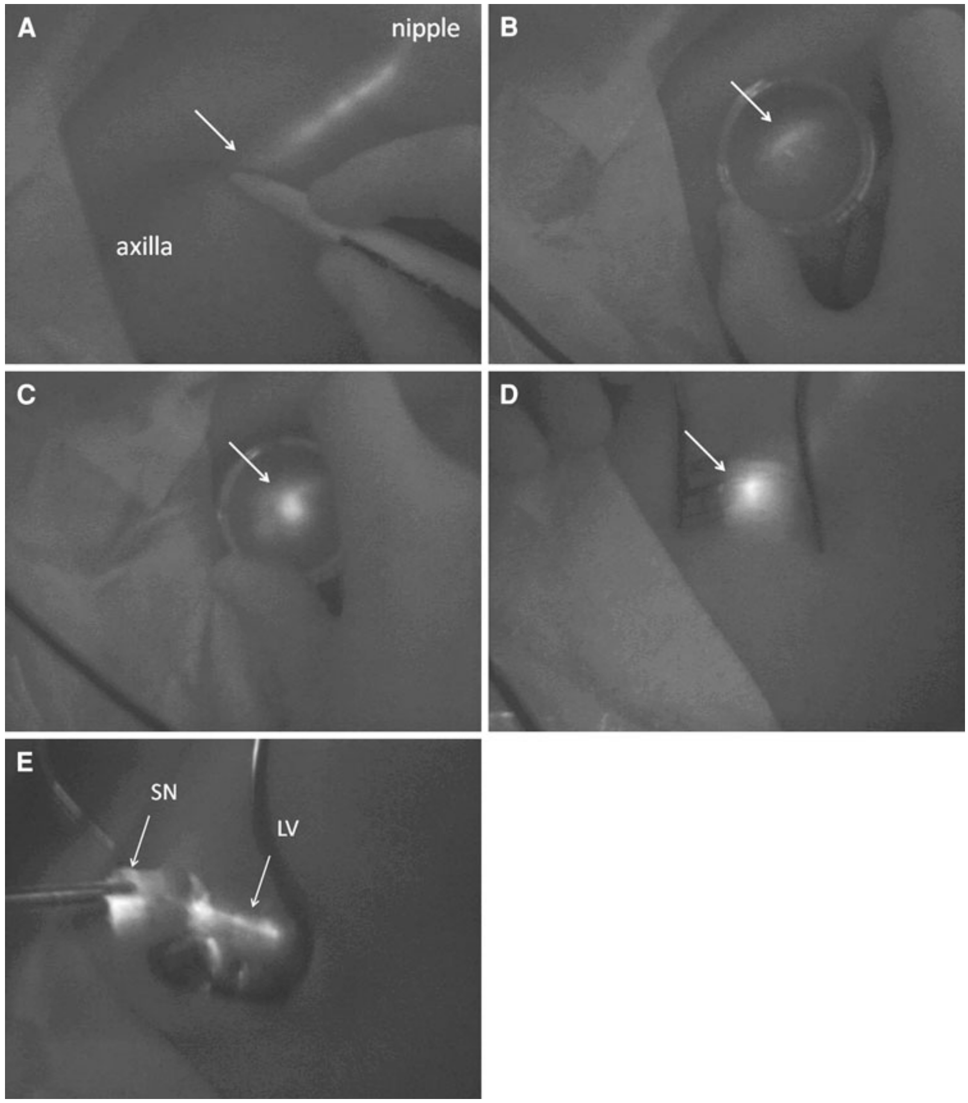


**Fig. 3** Fluorescence images in a 35-year-old female with a BMI of 17.6. **a** Subcutaneous lymphatic drainage was observed, and the signal disappeared beyond the lateral edge of the pectoralis major muscle (*arrow*). **b** A linear-shaped fluorescence signal was seen by compression, representing a lymphatic vessel (*arrow*). **c** A round-shaped intense fluorescence signal was observed, representing a sentinel node (*arrow*). **d** After skin incision, the sentinel node showed more intense fluorescence signal (*arrow*). **e** A lymphatic vessel (*LV*) draining to the sentinel node (*SN*) was observed

Figure 4 shows the case of a 71-year-old patient with a BMI of 31.4. Subcutaneous LVs were difficult to follow towards the axilla owing to thick subcutaneous fat (a). However, compression-inducible fluorescent signal could be observed in the axilla (b), and a direct approach to the SN was possible (c).

## Discussion

ICG has characteristic fluorescence spectra in the NIR wavelengths ranging from 700 to 900 nm, which is called "an optical window" [10]. This is advantageous for clinical applications because the NIR light can penetrate deep into the tissue without being absorbed by hemoglobin or water [11, 12]. However, when applied to living tissue, light scattering becomes an important issue [13, 14]. The fluorescent excitation and emission are attenuated by scattering when passing through the tissue. Fat droplets in the axilla are the main scatterers [15, 16]. In a preliminary experiment, ICG fluorescence signal at a depth of 1 cm in the phantom was detectable, but the detection became more difficult as the depth increased. LNs under the axillary fascia, lying deeper than 1 cm, cannot be detected over the skin in most cases. The attenuation of the fluorescence intensity is determined mainly by the scattering coefficient of the tissue and the distance between the detector and the SN. When the axillary skin is compressed against the chest wall, the SN comes close to the skin surface and the fluorescence signal becomes detectable. The scattering coefficient of the tissue is not increased much by compression. At the start of this study, we used a transparent hemispheric bowl with a diameter of 4 cm as a compression device [17], but lately we have preferred a cone-shaped device, which is more suitable to detect the shape and intensity of the compression-inducible fluorescence signal.

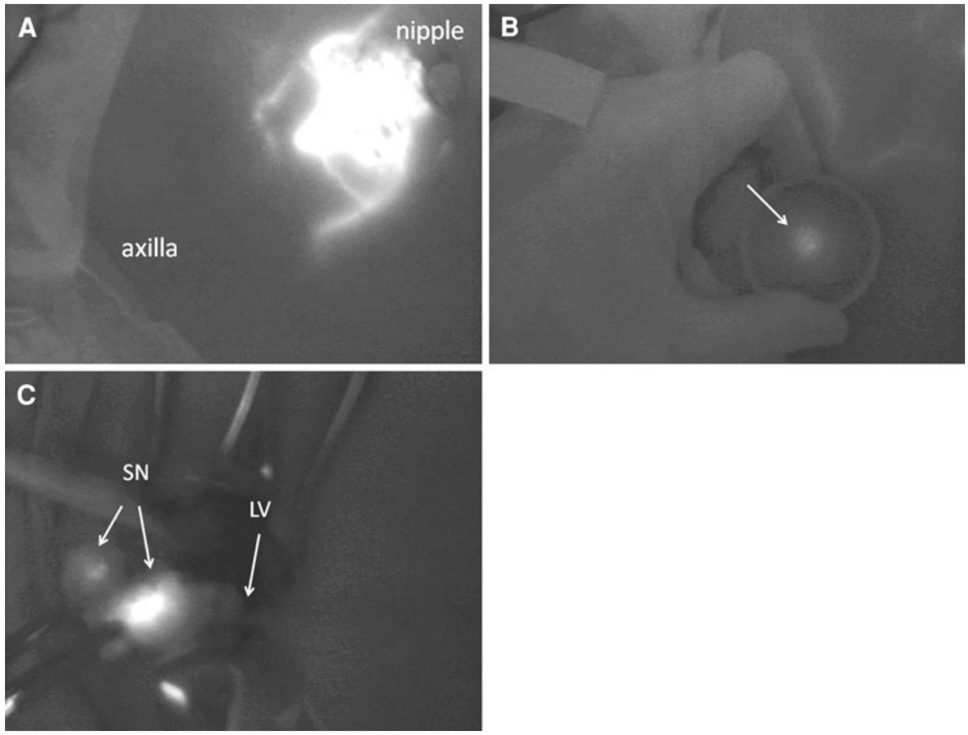


**Fig. 4** Fluorescence images in a 71-year-old patient with a BMI of 31.4. **a** Subcutaneous lymphatic vessels were difficult to follow towards the axilla. **b** Compression-inducible fluorescent signal (*arrow*) could be observed in the axilla. **c** Direct approach to the sentinel node was possible. *SN* sentinel node, *LV* lymphatic vessel

The axillary compression technique enables not only visualization of deep lymphatic structures, but also discrimination of an LN from an LV by considering the shape and intensity of the compression-inducible fluorescence signal. Transcuataneous detection and a direct approach to the SN bring several technical advantages. First, the surgical procedure is simple and similar to that of the RI method. Since there is no need to trace LVs, the risk of injury is very low. It is feasible even for a surgeon who is inexperienced in SNB. Second, it is also easy to estimate the location of the SN in obese patients. In the original method, much effort was sometimes required to follow the LV in thick fatty tissue. Third, the direct approach reduces the frequency of having to observe a fluorescence image because of the technical simplicity. There was one drawback of the original ICG fluorescence method in that the operating room light needed to be dimmed for every fluorescence observation. Using this technique, the dissecting procedure was not interrupted as frequently as before by switching on and off the light.

Intraoperative axillary lymphatic mapping is helpful to select the fluorescent nodes to be removed. One of the criticisms against the ICG fluorescence method is that too many fluorescent nodes may be removed [5, 17]. Since ICG is drained faster than RI colloid and detection by fluorescence is much more sensitive than inspection, many nodes were sometimes observed to be fluorescent. As the number of removed nodes increases, the risk of postoperative lymph edema and the discomfort perceived by patients may increase. Therefore, it is important to determine the first SN in such cases. By applying the axillary compression technique, it is easy to determine the first SN receiving lymphatic drainage from the breast. Usually, a few more nodes following the first node were additionally removed to prevent false-negative results [18].

In conclusion, ICG fluorescence image navigation is a useful option for SNB for breast cancer. The axillary compression technique is a simple way to improve the surgical procedure of the ICG fluorescence method.

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