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Author(s)	Ebihara, Yuma; Kato, Hiroaki; Narita, Yoshiaki; Abe, Masaru; Kubota, Reiko; Hirano, Satoshi
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**Case report**

Detection of Sentinel lymph node with a novel near-infrared fluorescence spectrum system and  
indocyanine green fluorescence in patients with early breast cancer: First clinical experience

Yuma Ebihara PhD<sup>1,2</sup>, Hiroaki Kato PhD<sup>3</sup>, Yoshiaki Narita PhD<sup>3</sup>, Masaru Abe PhD<sup>3</sup>, Reiko Kubota  
PhD<sup>3</sup>, Satoshi Hirano PhD<sup>1</sup>

<sup>1</sup> Department of Gastroenterological Surgery II, Faculty of Medicine, Hokkaido University, Sapporo,  
Japan

<sup>2</sup> Division of Minimally Invasive Surgery, Hokkaido University Hospital, Sapporo, Japan

<sup>3</sup> Department of Thoracic Surgery, Teine Keijinkai Hospital, Sapporo, Japan

Corresponding author

Yuma Ebihara,

Email: yuma-ebi@wc4.so-net.ne.jp

Division of Minimally Invasive Surgery, Hokkaido University Hospital, North 15 West 7, Kita-ku,  
Sapporo 0608638, Hokkaido, Japan.

Telephone: +81 11 706 7714; Fax: +81 11 706 7158

## **Abstract**

Background: Sentinel lymph node biopsy (SLNB) for early breast cancer is common, and many studies have reported its usefulness with indocyanine green (ICG). However, in the case of sentinel lymph node (SNs) identification using ICG, it is difficult to accurately identify the fluorescence signal of SNs through the skin because of the weakening of the signal due to the intervening tissue thickness. In this study, we examined whether fluorescence spectroscopy can detect weaker fluorescence signals and accurately identify SNs that have accumulated ICG.

Methods: Six women with early breast cancer and clinically confirmed negative axillae were recruited. The periareolar region was subcutaneously injected with ICG (1 ml, 5 mg/mL). The identification rate of SNs in the skin was studied using the novel fluorescence spectroscopy (Lumifinder™, ADVANTEST, Tokyo, Japan).

Results: Lumifinder™ was able to identify 100% of SNs in the skin (6/6 patients). In addition, for SNs identification in deeper axillary areas, pressing the probe tip against the body surface allows clearer fluorescence observation.

Conclusion: Novel fluorescence spectroscopy (Lumifinder™) may overcome the problem of SLNB using ICG for breast cancer.

## **Key words**

Sentinel lymph node biopsy, breast cancer, indocyanine green, fluorescence spectroscopy

1       The indocyanine green (ICG) fluorescence sentinel lymph node biopsy (SLNB) method for early  
2 breast cancer is increasingly used in breast cancer centers because it is more accurate than blue dye  
3 and avoids the administrative complications of radioisotopes [1]. However, the depth of tissue that can  
4 be observed using ICG fluorescence is approximately 3-10 mm from the skin surface, and SNs may  
5 not be identifiable from the skin surface [2]. The use of a novel fluorescence spectrum measurement  
6 system (Lumifinder™, ADVANTEST, Tokyo, Japan) (Fig.1) can measure a much weaker ICG  
7 fluorescence signal and is expected to overcome the problems of SNs identification using ICG [3].

8       In this study the usefulness of Lumifinder™ in SLNB using ICG for early-stage breast cancer  
9 was examined. Six female patients with early breast cancer and clinically confirmed negative axilla  
10 were recruited from the Department of Breast Surgery of the Department of Thoracic Surgery of Teine  
11 Keijinnkai Hospital between June 2021 and July 2021. The inclusion criteria were as follows: 1)  
12 primary breast cancer confirmed by core needle biopsy, 2) absence of enlarged axillary lymph nodes  
13 as verified by palpation or breast ultrasound examination, and 3) absence of distant metastasis. The  
14 exclusion criteria were as follows: 1) pregnancy or lactation, 2) primary breast cancer confirmed by  
15 open biopsy, 3) preoperative radiotherapy in the breast area, 4) history of axillary surgery, and 5)  
16 allergy to iodine. Each dose of ICG consisted of 25 mg of the powdered form which was dissolved in  
17 5 ml sterilized water originally prepared by the manufacturer, and the mass concentration of the  
18 solution was 5 mg/ml. The peri-areolar region was subcutaneously injected with 1 ml indocyanine

1 green (ICG). After a 5-minute massage, SN stained with ICG was detected using Lumifinder™ from  
2 the surface of the skin. This study was approved by the independent ethics committee of Teine  
3 Keijinkai Hospital (3-022109-00), and informed consent was obtained from all patients.

4 The median age of the patients was 70 years (range, 64-82) years. The median operative  
5 time was 132.5 min. (range, 95-165) and the median blood loss was 0 ml. The median time for SN  
6 identification was 20 min. (range, 14-48) and the number of SN detected was 2.5 (range, 1-5). There  
7 were no cases of postoperative complications ( $\geq$  Clavien-Dindo classification [4,5] II). The median  
8 length of hospital stay after surgery was 4.5 days (range, 1-6 days). Lumifinder™ was able to identify  
9 SNs in the skin at a detection rate of 100 % (6/6 patients). In observation from the skin, SNs could not  
10 be identified with a handheld camera imaging device (PDE-NEO; Hamamatsu Photonics, Hamamatsu,  
11 Japan) in all cases (Fig. 2). In addition, for identification of SNs in deeper axillary areas, pressing the  
12 probe tip against the body surface facilitated clearer observation of fluorescence (Fig. 3). Currently,  
13 SLNB must be performed using a viewing monitor instead of directly observing the operating field,  
14 and a fluorescence imaging system with a near-infrared camera is required.

15 Novel fluorescence spectroscopy (Lumifinder™) can overcome the problems of SLNB  
16 using ICG for breast cancer, such as deeper SN identification from the skin and manipulation during  
17 monitoring. This report will contribute to further improvements in the identification rate of SLNB  
18 using ICG.

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## Figure legends

Fig. 1: The fluorescence spectroscopy (Lumifinder™, ADVANTEST, Tokyo, Japan). The system can display the fluorescence spectrum in real-time, the fluorescence intensity is indicated by high and low tones. The Y-axis is fluorescence intensity (a.u. arbitrary units) and the X-axis is wavelength (nm).

Fig. 2: A; Sentinel lymph node biopsy for early breast cancer with handheld camera imaging device (PDE-NEO; Hamamatsu Photonics, Hamamatsu, Japan). The identification of sentinel lymph nodes from the skin with PDE-NEO. The interruption of lymphatic vessels is observed (Arrow). The circle shows the axillary areas. B,C; Sentinel lymph node biopsy for early breast cancer with fluorescence spectroscopy (Lumifinder™, ADVANTEST, Tokyo, Japan). B; This system is capable of measuring the spectrum of ICG fluorescence signal, and can measure the weaker fluorescence signal. And the accurate identification of sentinel lymph nodes (SNs) from the skin was possible. C; It was possible to press the probe against the skin and identify deeper axillary SNs.





