



Title	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
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1 **Case report**

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

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1 **Abstract**

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

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

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

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

17 **Key words**

18 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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5 **Figure legends**

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

9

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

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