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**Benefit of high-resolution, real-time color-imaging of lymphatic flow in sentinel lymph node biopsy**

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For qualitative and prognostic reasons, accurate detection of presence/absence of metastasis in sentinel lymph nodes (SLNs) is crucial for patients with primary cutaneous malignant melanoma (PCMM). Here we report sentinel lymph node biopsy (SLNB) in four cases with PCMM using a new high-resolution, near-infrared (NIR) fluorescence camera system for the real-time visualization of lymphatic flow and for the detection of SLNs. Patient 1 was a 76-year-old man with a primary tumor in the left sole. Patient 2 was a 40-year-old male with a primary lesion in the right thumb. Patient 3 was a 26-year-old woman with PCMM in the back. Patient 4 was a 71-year-old female with a primary tumor in the back.

We used a new NIR fluorescence visualization system (LIGHTVISION®, Shimadzu Corporation, Kyoto, Japan), which has two independent high-resolution image sensors. One is a CCD-NIR camera with a filter that allows only light of the NIR wavelength (above 820 nm) to pass. The other is a CCD-image sensor with the identical optical resolution for visualization the operation field of the same frame. Both video images are continuously displayed as 1920 x 1080-pixel full high-definition images on a monitor. We can choose two different frame rates of the images, 30 video frames or 60 video frames displayed per second. In case more real-time, smoother movement in the picture is important, 60 video frames per second is recommended.

Image processing allows us to superimpose the processed gray-scale fluorescence image onto the unadulterated, naked eye images. We are able to render a clearly identifiable false color to the gray-scale fluorescence signal in order to know reliably the localization of the lymphatic flow and the SLN.

In all four cases, preoperative lymphoscintigraphy performed one day before the resection surgery of the primary lesion and SLNB showed the accumulation of radioisotope signals in the regional lymph nodes. At the resection operation, we injected Patent blue and indocyanine green (ICG) around the primary lesions to detect the SLN. Using the new NIR camera system, we clearly visualized the real-time lymphatic flow and successfully performed SLNB (*figure 1*).

When SLNB first began to be applied to PCMM patients, detection rates of SLN were reported from 75 % to 90 %, and false-negative SLNB for metastasis (SLNs negative for metastasis, but other lymph nodes positive for metastasis) were reported in 1-2 % patients [1]. Later, the use of a radioactive colloid in combination with blue dye facilitated the precise detection of SLNs, detection rates of over 90 % [2, 3].

The lymphatic channels and SLNs in patients with skin tumors are often relatively superficially located compared with those in patients with tumors in other organs, such as the breast. Therefore, we can detect NIR fluorescence of the lymphatic flow from outside the body, and NIR fluorescence imaging could be particularly useful for SLNB in patients with PCMM. Indeed, NIR fluorescence imaging with ICG in combination with lymphoscintigraphy and Patent blue dye methods have been successfully used for SLN mapping in patients with PCMM [3, 4]. Very recently, a high-resolution, real-time NIR fluorescence imaging system was reported to be useful for the detection of SLN [5].

In the present pilot operations, the real-time demonstration of lymphatic flow was achieved using a newly developed NIR fluorescence visualization system. The previous NIR imaging systems display only low-resolution, black and white (or black and green) NIR images of the operation field [6, 7]. In contrast, the present system visualizes high-resolution, real-time naked-eye operation field images simultaneously with false-color NIR images and is able to superimpose them. Clear images of lymph vessels and lymph nodes with false color NIR signals enabled us to securely ligate lymph vessels, including small ones, and to resect SLNs precisely and safely. The disadvantage of the present system is that it occupies more space in the operation room than previous systems do. In all four cases of the present pilot operations, SLNBs in the inguinal or axillary area were performed accurately and smoothly without any postoperative lymphorrhea. The present cases suggest that the high-resolution real-time color imaging of lymphatic flow is highly beneficial for SLNB in PCMM patients.

**References**

**1.** Kapteijn BA, Nieweg OE, Liem I, *et al*. Localizing the sentinel node in cutaneous melanoma: gamma probe detection versus blue dye. *Ann Surg Oncol* 1997; 4: 156-60.

**2.** Gershenwald JE, Ross MI. Sentinel-lymph-node biopsy for cutaneous melanoma. *N Engl J Med* 2011; 364: 1738-45.

**3.** van der Vorst JR, Schaafsma BE, Verbeek FP, *et al*. Dose optimization for near-infrared fluorescence sentinel lymph node mapping in patients with melanoma. *Br J Dermatol* 2013; 168: 93-8.

**4.** Yokota K, Sawada M, Matsumoto T, Hasegawa Y, Kono M, Akiyama M. Lymphatic flow is mostly preserved after sentinel lymph node biopsy in primary cutaneous malignant melanoma. *J Dermatol Sci* 2015; 78: 101-7.

**5.** Göppner D, Nekwasil S, Jellestad A, Sachse A, Schönborn KH, Gollnick H. Indocyanine green-assisted sentinel lymph node biopsy in melanoma using the "FOVIS" system. *J Dtsch Dermatol Ges* 2017; 15: 169-78.

6. Korn JM, Tellez-Diaz A, Bartz-Kurycki M, Gastman B. Indocyanine green SPY elite-assisted sentinel lymph node biopsy in cutaneous melanoma. *Plast Reconstr Surg* 2014; 133: 914-22.

7. McGregor A, Pavri SN, Tsay C, Kim S, Narayan D. Use of indocyanine green for sentinel lymph node biopsy: case series and methods comparison. *Plast Reconstr Surg Glob Open* 2017; 5: e1566.

**Figure legends**

**Figure 1.** High-resolution real-time color imaging of lymphatic flow and SLNs: Cases 1 and 2.

In each panel, three real-time images of an identical frame in the operation field are displayed simultaneously on the monitor: a gray-scale fluorescence image (top left), an unadulterated, naked eye image (bottom left) and a merged image (right) of false color (green) fluorescence image and the unadulterated, naked eye image. **A**, **B**) Case 1. **A**) Lymphatic channels run through the flexor side of the left leg. **B**) SLN is clearly detected in the left inguinal area. **C**, **D**) Case 2. **C**) Lymphatic flow from the primary tumor on the right thumb is visualized sharply with the false green color. **D**) A SLN is clearly detected in the right axillary area.
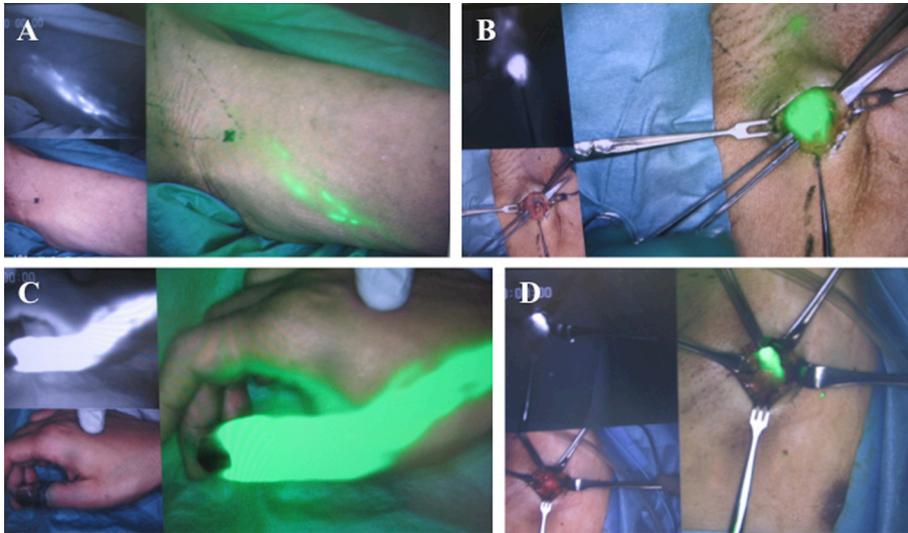
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