



# Lymphatic Mapping with Multi-Lymphosome Indocyanine Green Lymphography in Legs with Lymphedema

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## Abstract

It is observed that the locations of the most functional lymphatic vessels in the lymphedematous limbs can differ significantly from those in healthy limbs. The aim of this study was to elucidate the lymphatic map of lymphedematous limbs. We retrospectively analyzed 59 patients (118 limbs) with lower limb lymphedema. Fifty-five were women and four were men. The mean age and duration of lymphedema was 62.4 and 7.7 years, respectively. For the lateral thigh lymphosome, we injected indocyanine green (ICG) at the lateral knee and measured the distance (Dt) between the anterior superior iliac spine (ASIS) and the point where the lymphatic vessels crossed the reference line (the line connecting the ASIS and the patellar center). For the lateral calf lymphosome, we injected ICG at the lateral ankle and measured the distance (Dc) between the inferior patellar border and the point where the lymphatic vessels crossed the reference line (the anterior border of the tibia). In the lateral thigh, the mean Dt was  $30.4 \pm 0.6$  cm (range, 0–41 cm) and the distribution peaked at approximately 30 cm from the ASIS. In the calf, the mean Dc was  $13.1 \pm 0.9$  cm (range, –11 to 32 cm). The distribution of lymphatic vessel locations was highly variable. We could establish the lymphatic map in the lymphedematous legs. The distribution of lymphatic vessels in the thigh and lower legs had one and two peaks, respectively.

## Keywords

- ▶ lymphedema
- ▶ lymphosome
- ▶ ICG
- ▶ lymphatic mapping
- ▶ indocyanine green

Lymphaticovenous anastomosis (LVA) is a minimally invasive surgical method that can be performed with a small incision under local anesthesia to treat lymphedema.<sup>1–6</sup> Among several examinations including lymphoscintigraphy,<sup>7</sup> indocyanine green (ICG) lymphography,<sup>8,9</sup> lymphatic ultrasonography,<sup>10–18</sup> or lymphatic magnetic resonance imaging,<sup>19,20</sup> the most common examination performed as a preoperative examination for LVA is ICG lymphography. Conventionally, ICG was injected only at the distal points of the affected limbs (e.g., interdigital web spaces, toe web spaces, or ankles).<sup>8</sup> To observe more lymphatics, we proposed multi-lymphosome ICG lymphography, in which

we injected ICG at the dorsum of the foot, the lateral ankle, and the lateral knee, and named the lymphatic vessels in each lymphosome as the saphenous, lateral calf, and lateral thigh lymphatics, respectively.<sup>21–25</sup>

In the current study, we performed multi-lymphosome ICG lymphography in lymphedematous patients and attempted to establish a lymphatic map. This map will contribute not only to surgeons but also to therapists who perform manual lymph drainage. This study aimed to elucidate the lymphatic map of lymphedematous limbs.

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We retrospectively analyzed 59 patients (118 limbs) who underwent LVA for lower limb lymphedema under local anesthesia between September 2020 and June 2021. Among the participants, 55 were women and 4 were men (–Supplementary Table S1 [available in the online version only]). The mean age and duration of lymphedema were 62.4 years (range, 21–87 years) and 7.7 years (range, 1–34 years), respectively.

In multi-lymphosome ICG lymphography, we injected ICG (0.5% Diagnogreen, Daiichi Pharmaceutical, Tokyo, Japan) at three lymphosomes subdermally and observed the lymphatic pathway with the Photodynamic Eye camera (Hamamatsu Photonics, Hamamatsu, Japan) immediately after injection.<sup>19–21</sup> We recorded the location of the lateral calf and lateral thigh lymphatics only, because the route of the saphenous lymphatics is always at the medial leg.

For the lateral thigh lymphosome, we injected 0.05 mL of ICG at the mid-lateral thigh at the superior patellar border. We connected the anterior superior iliac spine (ASIS) and the patellar center to form the reference line. We measured the distance (Dt) between the ASIS and the point where the lymphatic vessels crossed the reference line (–Fig. 1A).

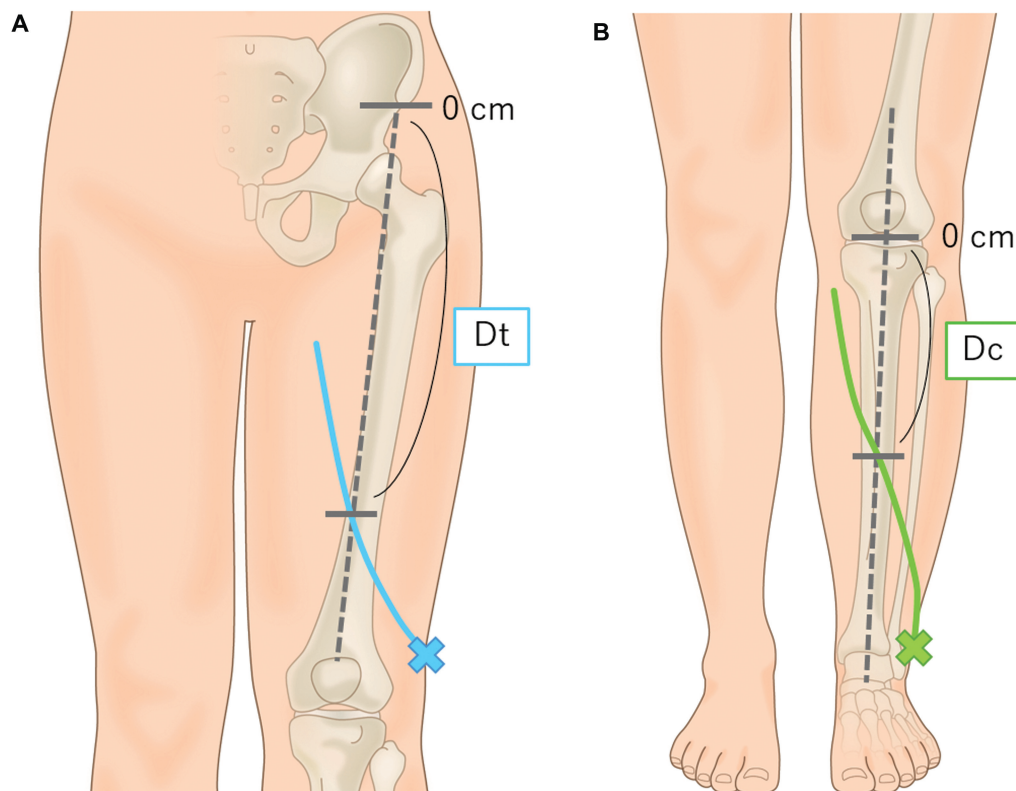
For the lateral calf lymphosome, we injected 0.05 mL of ICG at the superior border of the lateral malleolus. We defined the anterior border of the tibial bone and its extension

as the reference line. We measured the distance (Dc) between the inferior patellar border and the point where the lymphatic vessels crossed the reference line (–Fig. 1B). If the lymphatic vessels crossed the reference line at the proximal point from the inferior patellar border, the Dc value was negative.

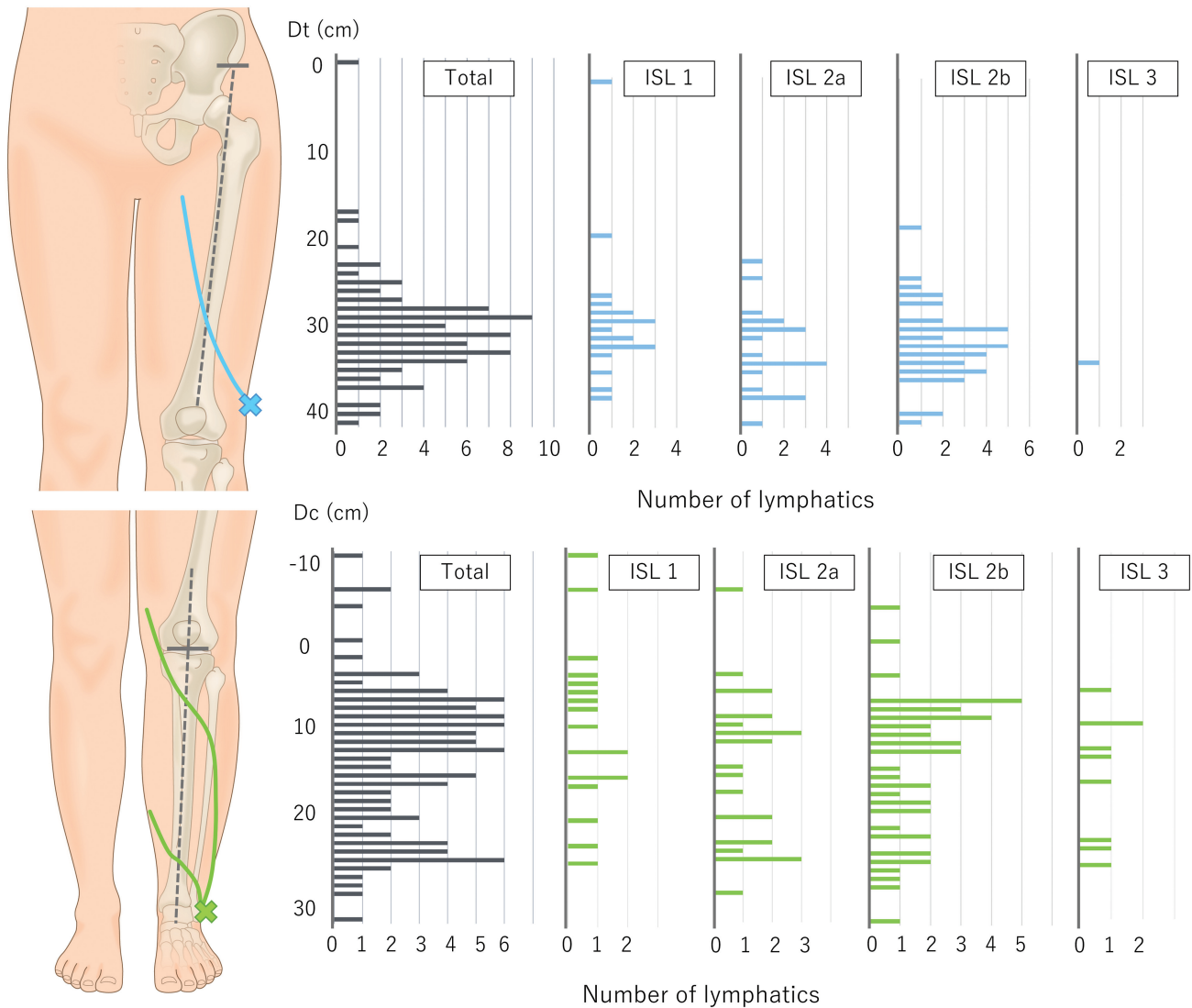
If pleural lymphatic vessels were observed in one lymphosome, we recorded all the vessels. If no lymphatic vessels crossed the reference line, we recorded “not applicable (N/A).” If the lymphatic vessels ran from the ankle to the posterior side of the calf, we recorded a “posterior pattern.”

In the lateral thigh lymphosome, we observed 78 lymphatic vessels in 72 limbs. Forty-six limbs had “N/A” results. The mean Dt was  $30.4 \pm 0.6$  cm (range, 0–41 cm). The distribution of lymphatic vessels is shown in –Fig. 2 (above). The distribution peaked at approximately 28 to 34 cm from the ASIS. Therefore, the lymphatic vessels are likely located on the lateral side of the reference line in the area distal to this point. In contrast, lymphatic vessels in the area within 22 cm from the ASIS are seldom located at the lateral side of the reference line.

In the calf, 107 lymphatic vessels were observed in 88 limbs. We recorded “N/A” and “posterior pattern” in 30 and 9 limbs, respectively. The mean Dc was  $13.1 \pm 0.9$  cm (range, –11 to 32 cm). The distribution of lymphatic vessels is shown



**Fig. 1** Schematic images of the lymphatic mapping. (A) For the lateral thigh lymphosome, we injected indocyanine green (ICG) at the mid-lateral thigh at the superior patellar border (blue cross). The reference line connected the anterior superior iliac spine (ASIS) and the patellar center (gray dotted line). We measured the distance (Dt) between the ASIS and the point where the lymphatic vessels crossed the reference line. (B) For the lateral calf lymphosome, we injected ICG at the superior border of the lateral malleolus (green cross). The reference line was defined as the anterior border of the tibia and its extension (gray dotted line). We measured the distance (Dc) between the inferior border of the patella and the point where the lymphatic vessels cross the reference line. If the lymphatic vessels crossed the reference line at the proximal point from the inferior border of the patella, Dc was indicated by a negative number.



**Fig. 2** The distribution of the lymphatic vessels. Above: The distribution had a peak at around 30 cm from the anterior superior iliac spine (ASIS). In the area 20 cm proximal to the ASIS, the lymphatic vessels seldom crossed the reference line. Below: The distribution of lymphatic vessel locations was highly variable. In the lower legs, the lymphatic vessels ran laterally in a wide range, from the ankle to the knee joint. ISL, International Society of Lymphology.

in **Fig. 2** (below). The distribution of lymphatic vessel locations was highly variable. In the lower legs, the lymphatic vessels ran on the lateral side over a wide range from the ankle to the knee joint.

The body mass indices (BMIs) of those with lymphatic vessels observed and those with “N/A” results were 22.5 and 23.1 kg/m<sup>2</sup>, respectively, in the thigh, with no significant difference by Student’s *t*-test ( $p = 0.409$ ). Also, the BMIs were 22.5 and 23.6 kg/m<sup>2</sup>, respectively, in the calf, with no significant difference ( $p = 0.192$ ).

One of the limitations of this study was that we evaluated only the lymphatic vessels that originated from two points on the legs (the lateral ankle and the lateral knee). In reality, there may have been more lymphatic vessels, which should be a topic for future research.

We established a lymphatic map to indicate the variation in where the lymphatic vessels may be located in the lymphedema-affected limb. We hope that the results of

the current study will help health care providers involved in the treatment of lymphedema.

#### Authors’ Contributions

H.H. and M.M. substantially contributed to the study conceptualization, data analysis, interpretation, and manuscript drafting. Both authors critically reviewed and revised the manuscript draft and approved the final version for submission.

#### Ethical Approval

This study was approved by the JR Tokyo General Hospital Ethical Committee (approval number: 30-8).

#### Patient Consent

All patients were informed about the advantages and disadvantages of ICG lymphography and provided written consent.

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None.

**Conflict of Interest**

None declared.

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