Review Article

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Enhancing Diagnostic Precision and Treatment Effectiveness Using Indocyanine Green Lymphography in Lymphedema

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Indocyanine green (ICG) lymphography has rapidly emerged as a key imaging modality for improving the diagnosis and management of lymphedema. ICG lymphography offers superior sensitivity and detailed assessment of dermal backflow patterns, functional lymphatic channels, and collateral drainage routes. Evidence also supports its role in guiding targeted rehabilitation, including ICG-guided lymphedema treatment. Clinicians can enhance diagnostic precision and potentially improve therapeutic effectiveness by integrating ICG lymphography into clinical practice. This review summarizes current evidence on its clinical utility, highlighting how real-time visualization of superficial lymphatic pathways and lymph nodes allows for detection of dysfunction, and improved treatment planning. Future work should focus on standardizing protocols and developing quantitative metrics to expand its values in comprehensive lymphedema care.

Keywords: Lymphedema, Indocyanine green, Lymphography, Manual lymphatic drainage

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INTRODUCTION

Lymphedema is a chronic and progressive disease that significantly impacts patients' quality of life and function [1]. Indocyanine green (ICG) lymphography enables highly sensitive visualization of superficial lymphatic drainage and allows clinicians to assess lymphatic flow before and after lymphedema treatment. Although ICG lymphography is not yet formalized as a fully validated primary outcome measure, it has emerged as a highly promising tool for quantifying lymphatic function. ICG lymphography also contributes to the early identification and timely management of lymphedema by detecting lymphatic flow impairment at subclinical stage [2,3].

ICG dye was first photographed using near-infrared (NIR) imaging at Kodak Research Laboratories. It has traditionally been used for hepatic function testing, cardiovascular assessments, and retinal blood flow evaluation [4]. Clinically, its earliest and most widespread application in lymphatic imaging has been in sentinel lymph node mapping and intraoperative navigation for breast cancer [5]. Following early reports on lymphatic imaging and dynamic parameters such as propulsion velocity and contraction rate in both healthy individuals and patients with lymphedema [6,7], a rapidly expanding evidence of ICG lymphography has emerged as a reliable assessment tool for lymphedema diagnosis and monitoring [8].

In South Korea, ICG lymphography has been formally recog-

nized as a reimbursable diagnostic imaging modality for lymphedema since 2024, leading to rapid adoption across medical centers. In practice, its applications can be broadly categorized into three areas: diagnostic evaluation, assistive tool as image-guided treatment, and patient education. While diagnosis forms the foundation, the latter two are increasingly utilized in routine care. Given that lymphedema requires lifelong self-management, ICG lymphography serves as an effective educational tool by helping patients visually understand their condition, reinforcing motivation for self-care, and supporting more tailored management strategies. Although evidence on the role of ICG lymphography during lymphedema treatment is still evolving, personalized mapping of lymphatic pathways and real-time visualization of individual lymphatic dysfunction strongly suggest its potential benefit [9]. Furthermore, patients often gain clearer insight into their condition through imaging procedure, making ICG lymphography an invaluable adjunct for self-management guidance and clinical education.

In this review, we summarize the utility of ICG lymphography along with introducing our representative cases to illustrate how ICG lymphography can enhance diagnostic precision, support individualized lymphedema treatment and ultimately improve outcomes in patients with lymphedema.

THE BASICS OF ICG NIR FLUORESCENCE IMAGING

ICG is a tricarbocyanine dye having a molecular weight of 751.4 Da, soluble in water. It is classified as a relatively safe agent with no active metabolites, low toxicity and rapid biliary excretion [10]. Determining the optimal dose and concentration is essential for maximizing image quality. When the concentration is too low, visualization of the target region and fine lymphatic structures may be insufficient. Conversely, if the concentration is excessively high, the reduced molecular spacing can theoretically induce a quenching effect, whereby functional lymphatic channels lying beneath areas of segmental dermal backflow (DB) may become difficult to be identified [11]. When ICG dye is injected into the dermis, ICG rapidly binds to lipid-protein complexes, which facilitates its uptake to the lymphatic vascular compartment and drainage into superficial lymphatic vessels. When the excitement light illuminates with NIR light, the injected dye absorbs photons within NIR range and emits fluorescence that can be detected by NIR-sensitive imaging system (Fig. 1).

The quality of ICG lymphographic images depends largely on how efficiently photons emitted from activated fluorophores are collected after passing through biological tissues. ICG molecules function as fluorophores capable of repeated cycles of excitation and emission, theoretically producing thousands of photons per second. In addition, NIR excitation light induces minimal tissue autofluorescence, resulting in a high contrast-to-background ratio that facilitates visualization of superficial lymphatic vessels located just beneath the skin [12]. However, NIR photons possess relatively low energy and are highly susceptible to scattering within tissue. Consequently, despite the high theoretical photon count rate, the effective imaging depth remains limited, with reliable resolution generally restricted to approximately 3–4 cm below the skin surface. For this reason, ICG NIR fluorescence imaging is most widely used for applications involving superficial lymphatics [13].

Fig. 1. Near-infrared imaging system and representative indocyanine green lymphography visualization.

KEYNOTES FOR ICG GUIDED LYMPHATIC MAPPING

Improving patient experience with ICG lymphography

A major barrier to patient comfort during ICG lymphography is the pain caused by the low pH of the injected solution. Several alternative diluents have been explored to optimize both patient comfort and imaging reliability. Among them, ICG mixed with 5% dextrose has demonstrated a markedly improved pain, typically yielding Visual Analog Scale (VAS) of 0–1, while 5% albumin has also been investigated as a physiologically compatible option [14]. In our clinical practice, we adopted a hybrid approach administering a small amount of 2% lidocaine using a 30 gauge needle immediately before ICG injection, to minimized procedural discomfort while avoiding direct mixing of lidocaine with the ICG solution which have caused depressing effect of lymphatic contractility [15]. This strategy has effectively improved patient tolerance without compromising lymphatic imaging quality.

Protocols focusing on identification of an individual lymphatic drainage pathway

ICG-guided lymphatic mapping and manual lymphatic drainage (MLD) require careful attention to both anatomical visualization and functional assessment. Suami and colleagues demonstrated that the superficial lymphatic system is organized into distinct lymphosomes, territorial units by specific lymphatic collectors. Suami's cadaveric microdissection and dye-injection studies revealed that each lymphosome is separated by watershed lines and that lymphatic collectors run in consistent longitudinal patterns with limited cross-communication between territories [16]. Based on this principle, during ICG mapping, clinicians should assess which lymphosome the injection site belongs to, whether the expected collector pathway within that lymphosome remains intact, and whether drainage deviates into adjacent lymphosomes, indicating compensation or obstruction.

During the exam, initial observation should include monitoring the spontaneous movement of ICG to identify baseline propulsion patterns and potential stagnation zones. This was followed by MLD to facilitate the transit of ICG through functional superficial lymphatics, enabling clearer visualization of dynamic flow. Subsequently, detailed mapping and demarcation of superficial lymphatics can be performed (Fig. 2), real-time ICG visualization was then used to adjust MLD direction, pressure, and sequence for each patient, consistent with emerging evidence supporting personalized treatment strategies based on individual lymphatic drainage pathways rather than a stereotype anatomical approach [17].

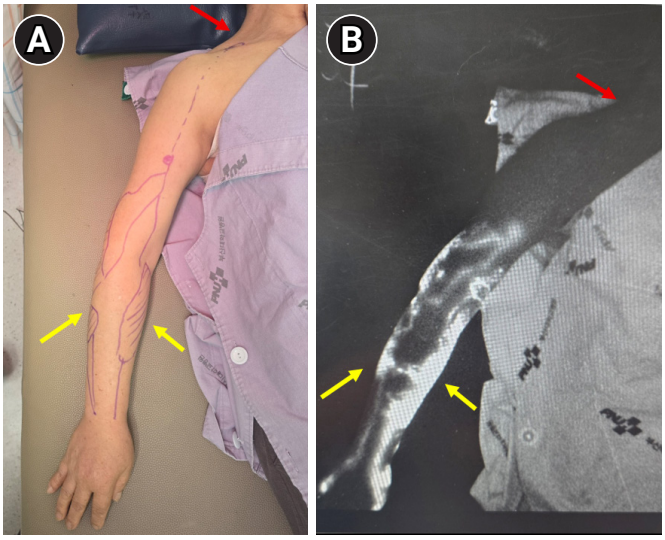

Fig. 2. Mapping superficial lymphatics and demarcation of dermal backflow (yellow arrows) in a breast cancer-related lymphedema patient (red arrow: final drainage pathway). (A) Surface mapping of superficial lymphatics and dermal backflow area projected onto the skin. (B) Corresponding indocyanine green lymphographic image of the patient.

INTERPRETING THE ICG LYMPHOGRAPHY FINDINGS

Interpreting ICG lymphography requires a systematic and anatomically informed approach. Precise mapping should document four key components: (1) preserved linear superficial lymphatic vessels; (2) presence of collateral or alternative pathway; (3) DB patterns with corresponding staging; and (4) subcutaneous pathways and fluid transport in advanced lymphedema. Real-time visualization allows the clinician to fine-tune the direction, sequence, and pressure of MLD based on each patient's unique lymphatic physiology rather than relying on conventional and uniform drainage patterns. Based on these principles, we propose the ICG-NIRS Image-Based Comprehensive Lymphedema Classification (Table 1), a structured framework consisting of three domains. First, patterns of ICG distribution are assessed by distinguishing functional and non-functional zones. Functional zones are defined by linear lymphatic flow with directional movement and are further characterized by

Table 1. ICG-NIRS Image-Based Comprehensive Lymphedema Classification

(1) Patterns of ICG distribution	
Functional zone	☐ Linear pattern with directional flow Velocity ☐ Rapid (<30 min) ☐ Delayed (30–60 min) ☐ Stagnant (>60 min) Visualized final drainage pathway ☐ Yes ☐ No
Non-functional zone	Proportion of dermal backflow areas relative to the total are _____ % ☐ Focal dermal backflow (e.g., elbow crease only) ☐ Segmental dermal backflow (e.g., forearm medial side) ☐ Regional dermal backflow (e.g., entire forearm) ☐ Extensive dermal backflow (e.g., forearm+arm) ☐ Diffuse dermal backflow (e.g., whole limb)
(2) Final drainage pathway analysis	
Original pathway	☐ Yes ☐ Partial ☐ No
Upper limb	☐ Ipsilateral clavicular ☐ Parasternal ☐ Intercostal ☐ Contralateral axilla ☐ Ipsilateral inguinal
Lower limb	☐ Popliteal ☐ Lower abdominal ☐ Upper lateral thigh ☐ Posterior thigh ☐ Gluteal ☐ Contralateral inguinal ☐ Axilla or parasternal
Breast	☐ Parasternal/internal mammary ☐ Intercostal/posterior scapular ☐ Clavicular ☐ Contralateral axilla ☐ Inferior/abdominal
(3) Severity grading system	
Grade 0 (Normal)	Normal linear lymphatic flow to axilla; no DB in breast
Grade 1 (Mild)	Localized DB in limb or peri-areolar region; >80% functional
Grade 2 (Moderate)	Regional DB or; delayed breast drainage
Grade 3 (Severe)	Diffuse DB involving limb or breast; <30% functional; alternative drainage dominant
Grade 4 (Very severe)	Whole-area DB with no detectable flow even after MLD

ICG, indocyanine green; DB, dermal backflow; MLD, manual lymphatic drainage.

flow velocity and the presence of a clearly visualized final drainage pathway. Non-functional zones are identified by DB, which is the proportion from the total limb area and categorized into focal, segmental, regional, extensive, or diffuse patterns based on anatomical distribution. Second, final drainage pathway analysis evaluates whether the original lymphatic pathway is preserved or identifies alternative drainage pathway. Their pathways are systemically classified according to anatomical regions, including upper limb (e.g., ipsilateral clavicular, parasternal, intercostal, contralateral axilla, ipsilateral inguinal), lower limb (e.g., popliteal, lower abdominal, upper lateral thigh, posterior thigh, gluteal, contralateral inguinal, or axillary/parasternal pathway), and breast (e.g., parasternal/internal mammary, intercostal/posterior scapular, clavicular contralateral axilla, or inferior/abdominal pathways). The identification of alternative drainage pathways is based on established anatomical lymphatic mapping concepts, including the lymphosome framework described by Hiroo Suami, which demonstrated that lymphatic flow follows distinct territories and can be rerouted through collateral pathways following disruption [17-19]. Finally, a severity grading system is applied based on the extent of DB, the proportion of functional lymphatic flow, and the dominance of alternative drainage pathways.

Preserved linear superficial lymphatic vessels

Preserved linear superficial lymphatic vessels indicate functional lymphatic channels with intact propulsion. These vessels often demonstrated rhythmic peristaltic contraction and direc-

tional flow, representing physiological drainage capacity. Mapping these linear structures helps determine whether the primary lymphosome-specific pathway remains patent and identifies potential targets for MLD to where lymph flow is directed. According to the MD Anderson Cancer Center (MDACC) ICG staging scale, the presence of continuous linear channels corresponds to stage 0–I, representing early or mild disease with preserved collecting lymphatics and minimal DB. As disease progresses beyond this stage, linear collectors become interrupted or completely absent, giving way to segmental or diffuse DB patterns (Fig. 3).

Despite the theoretical depth limitations of NIR fluorescence imaging, our anecdotal experience indicates that ICG lymphography can reliably visualize not only superficial lymphatic vessels but also lymph nodes located in the deep subcutaneous layers. As demonstrated in Fig. 4, drainage to the lateral humeral axillary lymph node was also well delineated in the upper arm. The epitrochlear lymph node within the antecubital fossa and along the medial aspect of the elbow was clearly identifiable, receiving lymphatic drainage from the ulnar side of the hand and forearm. Similarly, the popliteal lymph node, typically classified as a deep node in the posterior compartment, can be distinctly visualized in the lower limb. Even in the inguinal region, lymph nodes on the inferolateral aspect can be detected as they receive lymphatic drainage from the lower extremity. In such cases, where lymphatic function is relatively preserved, lymphatic flow remains functional, allowing clear visualization of lymphatic structures, including lymph nodes in the deep subcutaneous layer. However, as lymphedema progresses and lymphatic function deteriorates, visualization of these structures becomes less consistent and may be diminished. These observations support the expanding utility of ICG lymphography in mapping not only superficial lymphatics but also lymph nodes when they lie within the effective penetration depth of NIR light.

Presence of collateral or alternative drainage pathways

The identification of the lymphatic drainage pathway was an important parameter to determine treatment strategy, especially how to proceed MLD. ICG lymphography has capability to detect altered lymph drainage site in lymphedema (Fig. 5). Enhancement of ICG signal in the supraclavicular LN represented an alternative pathway at the same time as performing the MLD

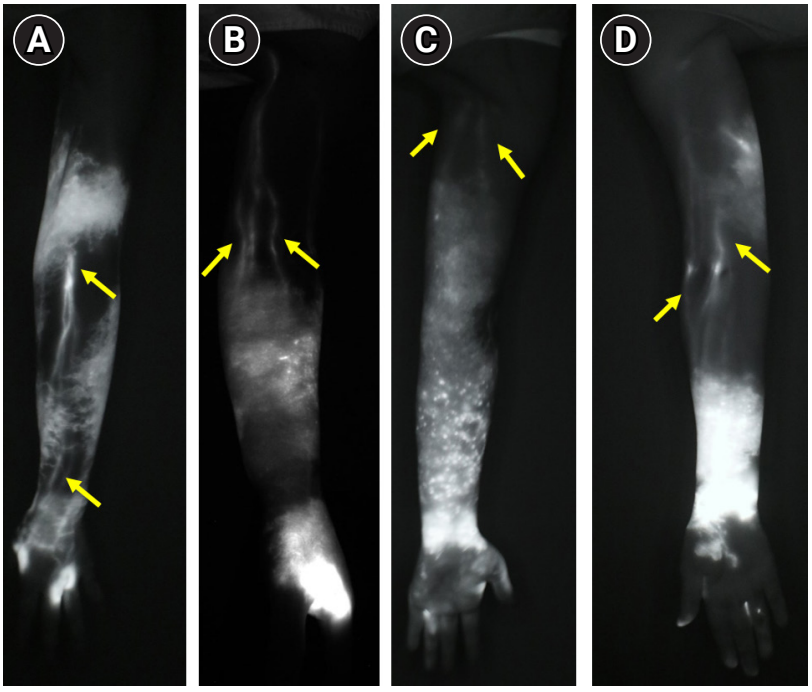

Fig. 3. Various dermal backflow patterns, expansion ranges, and the degree of functional lymphatic preservation patterns in the front upper limbs (arrows: preserved lymphatic vessels). (A) Extensive dermal backflow in the upper limb with preserved underlying functional lymphatic vessels. (B) Dermal backflow in the wrist and forearm with continuity to functional lymphatic in the proximal upper arm. (C) Extensive dermal back flow in the upper arm connected to the functional lymphatic vessel drainage toward axillary region. (D) Functional lymphatic vessel bridging dermal back flow in the proximal and distal upper limb.

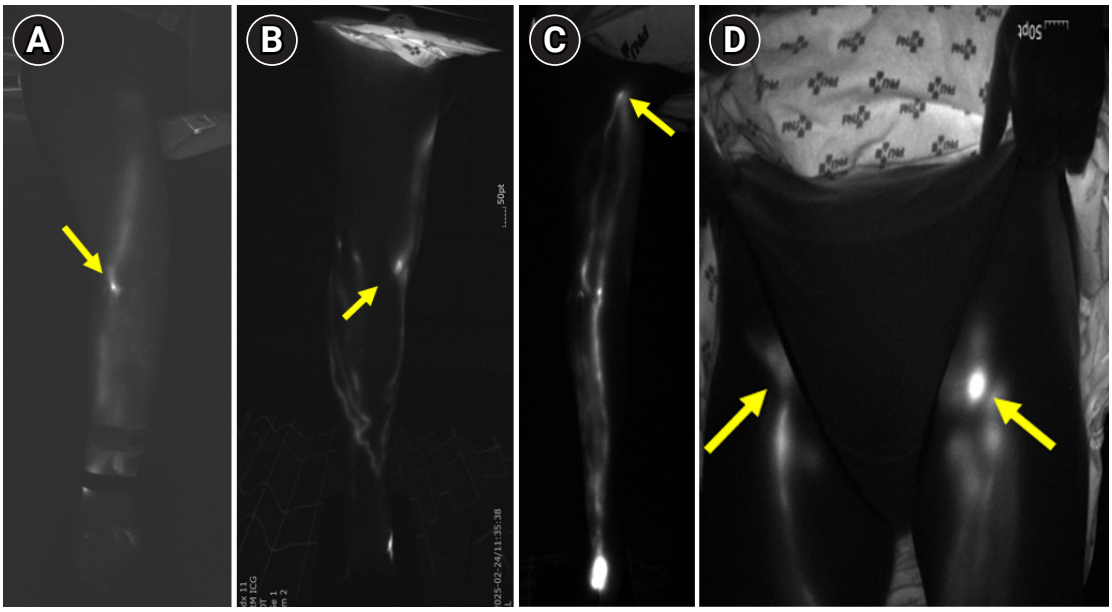

Fig. 4. Lymph node (LN) visibility (arrows) of indocyanine green lymphography of patients with early stage lymphedema. (A) Epitrochlear lymph node located in the antecubial fossa and medial aspect of elbow receiving lymphatic drainage from the ulnar-side-of the hand and forearm. (B) Popliteal LN located in the popliteal fossa and the efferent lymph vessels in the posterior thigh ascended upward and headed toward the inguinal LN. (C) Lymph fluid of upper limb drained to the lateral axillary LN. (D) Inguinal LN of inferolateral side with received lymph drain from lower limb.

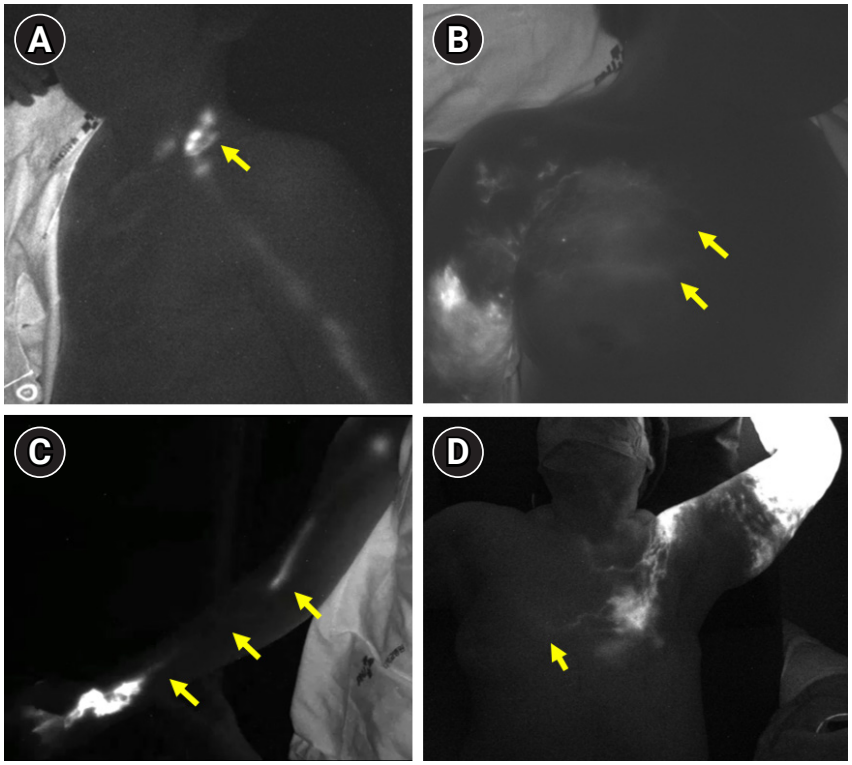

Fig. 5. Demonstration of alternative drainage pathways (arrows). (A) Enhancement of the supraclavicular lymph node at the same time as performing manual lymphatic drainage of the upper limb. (B) Alternative pathway draining to the parasternal site. (C) Connections between the superficial and deep lymphatic systems as a detour route. (D) Indocyanine green extended beyond the sagittal midline watershed and headed toward the contralateral axilla.

of the upper limb (Fig. 5A). In addition, alternative drainage can be observed to the parasternal site or extended beyond the sagittal midline watershed toward the contralateral axilla (Fig. 5B, 5D) In addition, alternative detour pathway may form between the superficial and deep lymphatic lymphatics. (Fig. 5C) Since identification of the alternative drainage site is important in determining the direction of MLD in addition to the diagnostic value, the imaging procedure should continue until confirmation of the final drainage pathway.

ICG lymphography is also useful to identify collateral routes in breast lymphedema cases after breast-conserving treatment. Several alternative lymphatic drainage pathways were identified when the primary axillary route was impaired, including parasternal, intercostal, clavicular and contralateral axilla [19]. In addition to these previously reported patterns, our observations identify an additional inferior/abdominal pathway, in which lymphatic flow diverges from the lateral or inferior breast and drains toward the abdominal or inguinal lymphatic territories (Fig. 6). This drainage pattern appears particularly when both axillary and parasternal drainage pathways were severely impaired, suggesting that the inferior/abdominal route functions as a dominant alternative pathway in severe breast lymphedema.

DB patterns with corresponding staging

DB has been specific image criterion for the diagnosis of lymphedema. DB represents a compensatory response of the body to redirect lymph fluid following lymphatic vessel injury. The pattern and distribution of DB correlate closely with the severity of lymphatic dysfunction, providing critical information for staging and clinical decision-making for treatment options [20]. DB forms a bridge between obstructed and patent lymphatic vessels, and also serves as a substitute route to transport lymph fluid following the obstruction of the superficial collecting vessels (Fig. 7) [21]. Lymphoscintigraphy and ICG lymphography have been taken on complementary roles to evaluate lymphatic function. Therefore, there was an essential need for the clinicians to determine the correlation of both examinations for obtaining comprehensive understanding. Yoon et al. [22,23] conducted two retrospective studies in lymphedema representing the DB severity stage on both examinations were very strongly correlated with substantial agreement. These studies confirmed that DB

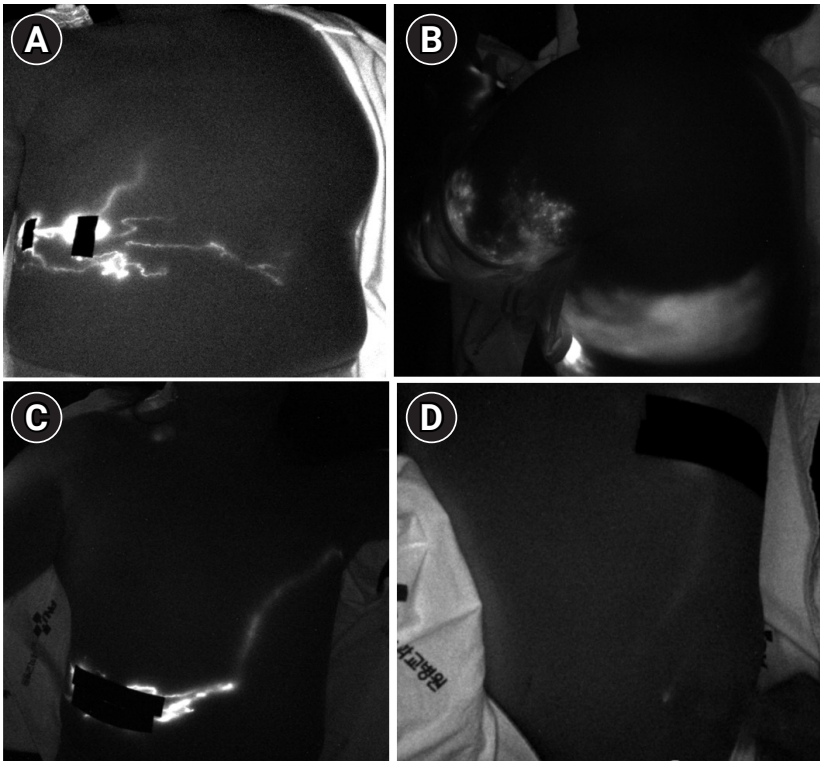

Fig. 6. Drainage pathway of breast lymphedema patients. (A) Ipsilateral axilla pathway. (B) Posterior/scapular pathway. (C) Contrallateral axilla pathway. (D) Parasternal/internal mammary pathway.

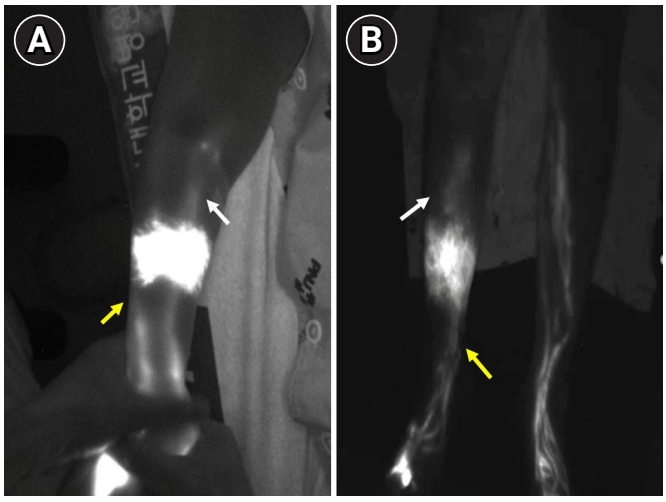

Fig. 7. Dermal backflow bridging the gap between the non-patent (yellow arrows) and patent vessels (white arrows).

corresponded to the lymph backflow from the collecting lymph vessels to the dermal lymphatics and thus both imaging modalities demonstrated the same information. The findings help to interpret the images of both tests in clinical practice.

Subcutaneous pathways and fluid transport in advanced lymphedema

In addition to the retrograde flow toward initial dermal lymphatics, diffusion of ICG exudates from the lymphatic vessels into the interstitial tissues can be seen simultaneously. In this condition, lymph drainage through the subcutaneous channel is considered as the main drainage route of lymph fluid. Therefore, MLD must be performed during ICG imaging to distinguish whether bridging DB from the obstructed lymphatic vessels to the adjacent patent lymphatic vessels or stagnant fluid in the subcutaneous channel. Identification of where the tissue fluid is located is useful for designing pneumatic devices for limb massage as well as for rational MLD in terms of dosage of external pressure [24]. The lymph fluid accumulated in the interstitial tissue mainly forms tissue channels within the subcutaneous tissue layer and along the fascia in patients with severe lymphedema. Since it is a stagnant fluid without a spontaneous propelling force, an increasing external force is essential to remove it [25].

IMAGE-GUIDED MLD

ICG lymphography enables clinicians to visualize superficial lymphatic structures in real time. Unlike traditional methods relying on anatomical assumptions or physical signs, ICG lymphography provides visualization of real-time motility and patency of superficial collectors, presence of DB, alternative drainage pathways, and functional response of lymphatic to various treatment modalities. This new image information allow to compose rehabilitation strategies, including MLD, compression, exercise, and patient self-management to be tailored according to each patient's unique lymphatic architecture in lymphedema rather than standardized, uniform protocol based on normal anatomy. Accordingly, image-guided approaches may offer a more physiologically informed basis for treatment planning.

MLD is a core component of lymphedema treatment and is known to promote lymph transport through enhanced superficial venous circulation, increasing uptake of interstitial fluid into functional lymphatic vessels, and reduction of skin fibrosis. Traditional MLD technique characterized by gentle and rhythmic strokes are usually applied along normal anatomical lymphatic routes [26]. However, recent systematic review has reported inconsistent evidence regarding treatment values of MLD, with some studies suggesting limited benefit beyond compression therapy in advanced lymphedema [27].

These discrepancies may be attributed to heterogeneity in MLD techniques, variability in disease severity, and the lack of individualized treatment planning based on objective lymphatic imaging. In this context, advances in lymphatic imaging have introduced the concept of image-guided MLD, in which real-time visualization of lymphatic function is incorporated into therapeutic decision-making. While direct evidence demonstrating superior clinical outcomes remains limited, preliminary studies suggest that ICG lymphography can enhance the understanding of patient-specific lymphatic flow patterns and may support more targeted and individualized interventions [28-30]. Most recent evidence suggest the ICG lymphography guided conservative management may lead to changes in treatment strategies and is associated with short-term improvement in objective measures [31]. However, these findings should be interpreted cautiously due to the lack of controlled comparisons. Therefore, further well-designed clinical studies are required to establish the long-term therapeutic effectiveness of this approach. Overall, image-guided MLD may be considered a physiologically informed and promising approach for individualized treatment planning but its clinical superiority over conventional methods has not yet been established.

CONCLUSION

The integration of ICG lymphography into routine lymphedema care represents an important advancement in both diagnostic precision and individualized rehabilitation. However, translating innovative technologies into clinical practice remains inherently complex. As ICG lymphography continues to demonstrate value in mapping patient-specific lymphatic architecture, guiding personalized treatment strategies, adequate training and organization readiness will be essential. Ultimately, embracing ICG lymphography within a structured implementation framework has the potential to improve diagnostic accuracy, optimize therapeutic approach, and enhance the overall quality of lymphedema care.

CONFLICTS OF INTEREST

Jin A Yoon is an Associate Editor of *Annals of Rehabilitation Medicine*. The author did not engage in any part of the review and decision-making process for this manuscript. Otherwise, no potential conflict of interest relevant to this article was reported.

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AUTHOR CONTRIBUTION

Conceptualization: Yoon JA, Suami H. Methodology: Yoon JA. Formal analysis: Yoon JA. Funding acquisition: Yoon JA. Project administration: Yoon JA, Suami H. Visualization: Yoon JA. Writing – original draft: Yoon JA. Writing – review and editing: Yoon JA, Suami H. Approval of final manuscript: all authors.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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