Imaging in lymphedema management: a narrative review of preoperative assessment & surgical planning

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Background and Objective: Imaging is an invaluable resource in modern medicine, particularly during patient selection and preoperative planning. Given the microscale of lymphedema surgery, the field is heavily reliant on imaging technologies. This review highlights the current status of these applicable innovations focusing on preoperative assessment and surgical planning.

Methods: The following databases were queried to identify articles for inclusion: PubMed, Cochrane, Web of Science, and Embase. With the exception of articles included to provide historical context and background, database searches were limited to articles published in the last 6 years [2017–2022]. The main goal of this search was to identify well-designed large-cohort studies that provide evidence-based conclusions on imaging modalities for lymphedema diagnosis, treatment, and monitoring of disease progression/resolution.

Key Content and Findings: Lymphoscintigraphy has been a mainstay for diagnosing lymphedema and visualizing lymphatic function. While this imaging modality is safe, minimally invasive, and easy to perform, there is a lack of standardized protocol with poor image quality, making for heterogeneity in the literature. Indocyanine green (ICG) lymphography provides excellent spatial resolution of superficial lymphatics throughout the extremity, providing for rapid diagnosis and staging of lymphedema. Deeper lymphatics in more advanced disease may be missed given limited penetration. Magnetic resonance (MR) lymphography provides excellent diagnostic information regarding spatial references, fluid:fat ratios, and secondary lymphedema changes; however, it is expensive, time-consuming, and requires the expertise of a Radiologist to protocol and execute. Ultra-high frequency ultrasound provides real-time, non-invasive, and high-quality information on lymphatic vessels for staging and operative planning while expanding bypass candidacy to patients with deeper lymphatics undetectable on ICG lymphography. Limitations include operator dependence and machine availability.

Conclusions: Preoperative image-guided planning is of tremendous benefit in modern surgery, and different modalities can provide complementary findings to formulate a comprehensive treatment plan. Lymphedema surgeons should be flexible and willing to embrace change as imaging modalities and treatment protocols continue to evolve in this exciting field.

Keywords: Lymphoscintigraphy; indocyanine green lymphography (ICG lymphography); magnetic resonance lymphography (MR lymphography); ultra-high frequency ultrasound

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Introduction

Background

The ever-evolving field of imaging technologies has provided tremendous insight into modern medicine, especially in surgical specialties. From patient selection and preoperative planning to intraoperative targeting and postoperative monitoring, radiologic innovations allow surgeons to provide more tailored care and precise interventions.

Rationale and knowledge gap

Given the microscopic yet diffuse structures inherent to lymphedema surgery, the field is heavily reliant on imaging technologies. Patients with lymphedema typically undergo multiple different forms of imaging during their workup with the most common techniques being lymphoscintigraphy, indocyanine green (ICG) lymphography, magnetic resonance (MR) lymphography, and ultra-high frequency ultrasound.

Objective

As such, this review highlights the current status of these innovations focusing on preoperative assessment and surgical planning for patients with lymphedema. We present the following article in accordance with the Narrative Review reporting checklist (available at https://abs.amegroups.com/article/view/10.21037/abs-22-40/rc).

Methods

The following databases were queried for relevant published studies over the last 6 years, from 2017–2022: PubMed, Cochrane, Web of Science, Embase. Some select older studies were included to provide historical context and background; however, the main focus of our search was to identify more recent publications. Search terms to identify studies included: lymphoscintigraphy; indocyanine green lymphography; magnetic resonance lymphography; ultrasound lymphography. Only publications in the English language were included. Both review articles and original articles were reviewed. Two reviewers critiqued manuscripts and selected papers for inclusion with consensus obtained through discussion with additional authors when warranted. A summary of the overall search strategy can be found in *Table 1*.

Lymphoscintigraphy

First introduced in 1950, lymphoscintigraphy has been a mainstay for diagnosing lymphedema and visualizing lymphatic function (1,2). Following injection of a technetium-99m (^{99m}Tc)-labeled tracer, the lymphatic drainage can be mapped along the channels, leading to the lymph node basin. Both quantitative metrics regarding nodal update as well as qualitative analysis on imaging visualization provide valuable information to the lymphatic surgeon regarding lymphedema treatment.

Lymphoscintigraphy is also widely used in breast and melanoma surgery for identification of sentinel lymph nodes following intradermal tracer injection. While this imaging modality is safe, minimally invasive, and easy to perform, there is a lack of standardized protocol with poor image quality, making for heterogeneity in the literature. Several scoring systems have been developed for diagnosis, categorization, and treatment allocation of lymphedema, but the objective quantifiable metrics alone cannot

Table 1 Search strategy summary

Items	Specification
Date of search	15 September 2022
Databases and other sources searched	PubMed, Cochrane, Web of Science, Embase
Search terms used	Lymphoscintigraphy; indocyanine green lymphography; magnetic resonance lymphography; ultrasound lymphography
Timeframe	1982–2022
Inclusion criteria	English language
Selection process	Studies were selected by two authors; to meet inclusion with consensus obtained through discussion with additional authors

replace the subjective qualitative components inherent to lymphoscintigraphy.

Recent literature has aimed to validate this gold standard diagnostic modality. Yoon et al identified a strong positive correlation between lymphoscintigraphy severity stage and arm dermal backflow (ADB) stage on ICG lymphography, demonstrating that these two techniques can synergistically evaluate lymphedema severity to better guide treatment planning (3).

Lymphatic fluorescence imaging: indocyanine green lymphography

ICG lymphography uses the near-infrared spectrum of light to capture the fluorescence of injected indocyanine green dye (4). Much like lymphoscintigraphy, ICG lymphography has applications in breast surgery for lymph node identification (3). However, in 2007, ICG lymphography successfully imaged extremity lymphatics in real time with clear visualization of the superficial lymphatics, including superficial precollectors and deeper subcutaneous collectors, thereby paving the way for another safe, simple, and minimally invasive imaging modality for assessment of lymphedema with enhanced spatial resolution (5).

ICG lymphography is widely used as a diagnostic tool, both for staging and guiding treatment planning with respect to patient selection. Injection of ICG dye into the intradermal web spaces reveals the drainage pattern of the lymphatic vessels draining that area or lymphosome (6,7). In patients without lymphatic obstruction, superficial linear channels will trace from the injection site along the lymphatic pathways to the nodal basin. In the setting of secondary lymphedema, a proximal obstruction leads to increased pressures in the lymphatic system resulting in lymphatic dilation and vessel insufficiency. Yamamoto *et al.* characterized a severity scale of progressive lymphatic disruption and congestion (7). Initially, obstruction causes deeper collections to flow retrograde into the superficial precollectors (Splash) with progressive vertical retrograde flow in a punctate pattern (Stardust) followed by horizontal bleeding into a diffuse dilated capillary network (Diffuse).

Resultant staging classification scores help standardize lymphedema severity and allocate decision making and treatment planning (8). Yamatoma *et al.* described six stages based on the extent of dermal backflow, starting with no backflow and progressing to diffuse backflow of the entire limb (9). Chang *et al.* (10) similarly detailed a four-stage classification system based on dermal backflow while also detailing the presence of linear lymphatic channels that can be bypassed; stage I reflects many patent lymphatics with minimal dermal backflow while progressive stages correlate with decreasing patency and increased dermal backflow (11). Patients with early-stage disease and intact lymphatic channels are often good candidates for lymphovenous bypass (12). Conversely, patients with late-stage disease and diffuse backflow are poor candidates for bypass, but rather, might benefit from vascularized lymph node transfer. As such, ICG lymphography not only provides information regarding diagnosis and preoperative planning, but also indirectly provides information regarding postoperative success following lymphedema surgery.

Intraoperative ICG lymphography is invaluable for on-table planning of lymphovenous bypasses. Intradermal webspace injections reveal dermal backflow from proximal lymphatic disruption. The surgeon can subsequently plan incisions distal to these areas to capture affected lymphatic channels to reroute and bypass the congested lymphosomes. ICG lymphography can also evaluate bypass patency as demonstrated by fluorescence in the proximal vein, both in the immediate as well as the delayed postoperative setting, though more rarely in the latter.

Given the vast diagnostic and planning capability of ICG lymphography, this modality remains one of the most utilized imaging techniques in lymphedema surgery. Drawbacks include limited penetration, which can miss deeper lymphatics in more advanced disease and areas of increased tissue thickness, and a paucity of information regarding fluid:fat ratios of the limb.

MR lymphography

MR lymphography utilizes a water-soluble gadolinium-based contrast that is injected in the intradermal web spaces of the limb. Two sequences are typically used for imaging, though protocols vary: (I) a T2 weighted fat suppressed sequence that localizes areas of dermal backflow and edema; (II) and a 3-dimensional T1 sequence that images the actual lymphatic channels themselves (13,14). With this complementary imaging, the surgeon can not only spatially quantify the extent and severity of lymphedema, but also, identify lymphatic channels and nodes while determining the fatty versus fluid tissue composition of the extremity. This modality also depicts changes in surrounding skeletal muscle as well as any other secondary changes to lymphedema.

Much like ICG lymphography, MR lymphography can be of use for preoperative planning for lymphovenous bypass. Using fixed landmarks on the extremity, underlying lymphatic channels and adjacent veins can be translated to the skin surface by way of the excellent spatial resolution offered by MR lymphography (13,15). This tends to be a less commonly utilized technique compared to on-table ICG lymphography, yet MR lymphography remains a great tool for staging and guiding decision making when considering surgical intervention for patients with lymphedema.

Valuable information regarding fluid and fat composition ratios may drastically change patient allocation and surgical planning (16). MR lymphography delineates a fat dominant extremity from a fluid dominant extremity; the former would benefit more from reductive procedures and less from physiologic fluid procedures, whereas the latter might be a candidate for bypass or a vascularized lymph node transplant (17). As with ICG lymphography, absent channels on MR may similarly guide decision making away from lymphovenous bypass and toward vascularized lymph node transfer. Decision making pathways, such as the New Brussels Approach to Limb Lymphedema Surgery, harness the anatomical benefits of MR lymphography to guide intervention and treatment of lymphedema (8).

While MR lymphography has many benefits, including anatomical accuracy, spatial awareness, and details regarding fluid:fat ratios, it is an expensive and time-consuming modality requiring Radiology expertise for creating, executing, and interpreting protocols.

Ultrasound

More recently, high frequency ultrasound probes have provided real-time identification of lymphatic channels. In 2015, Drs. Koshima, Yoshimatsu, Hayashi and colleagues described mapping lymphatic vessels with high frequency ultrasound probes around 19 Megahertz (18). This paved the way for the ultra-high frequency ultrasound, with probes up to 70 Megahertz and axial resolution of 30 microns, allowing for further enhancement of microscopic structures (19). Hayashi and colleagues subsequently compared lymphatic identification using high frequency and ultra-high frequency probes, with striking improvement in the quality of images for vessel evaluation at higher frequencies (20).

Unlike MR lymphography, ultrasound easily differentiates lymphatics from venules as the former lacks flow velocity that is fast enough to be seen on color doppler mode. Veins also tend to compress more easily than lymphatics and have a mosaic pattern in B-mode secondary to flow, which is not seen in lymphatics (21). Accordingly, ultrasound serves as a useful staging and decision-making tool while also assisting in planning of lymphovenous bypass.

One of the most important factors in the success of lymphovenous bypass is lymphatic vessel quality. Lymphatic disease initially starts with dilatation of ectatic vessels with increased pressure, which subsequently leads to progressively worsening degrees of sclerosis and wall thickening, eventually occluding the lumen and obscuring lymphatic flow through the vessel. Lymphosclerosis is difficult to assess preoperatively yet can be visualized intraoperatively and histologically; however, ultra-high frequency ultrasound has been shown to depict the degree of dilation and severity of wall thickening preoperatively (22). Bianchi and colleagues demonstrated excellent correlations between histological characteristics and ultrasound findings, thereby making this the only non-invasive modality to evaluate the ultra-fine structures of lymphatics preoperatively (23).

The enhanced capabilities of ultra-high frequency ultrasound to detect lymphatics beyond that of ICG lymphography may expand criteria for lymphovenous bypass in certain patients, as demonstrated by Dr. Cha and colleagues (24). Superficial lymphatic collectors in deep fat may be difficult to assess on ICG lymphography given increased tissue thickness and severe dermal backflow in patients with advanced disease. However, new ultrasound advances may broaden candidacy for bypass to patients otherwise excluded based on ICG lymphography alone.

Ultra-high frequency ultrasound is also a valuable intraoperative imaging modality, allowing surgeons to precisely identify lymphatics in real time as well as their diameter, wall thickness, and proximity to venule branches, thereby optimizing on-table bypass planning (21). Ultrasound assisted bypasses have also identified deeper lymphatics with large diameters and with more rapidity than non-ultrasound assisted bypasses.

While ultra-high frequency ultrasound has a myriad of benefits, there is a fair amount of operative dependence, and this ultra-high frequency probe is not widely available.

Conclusions

The many imaging modalities employed in lymphedema surgery reflect the complexity of this pathology and its variable treatment paradigms. Not all patients may benefit from the same intervention, and individualized treatment plans may be required for each patient and each limb. Preoperative image-guided planning is a tremendous benefit in modern surgery, and different modalities can provide complementary findings to formulate a comprehensive treatment plan. Lymphedema surgeons should be flexible and willing to embrace change as imaging modalities and treatment protocols continue to evolve in this exciting field.

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