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Lymphedema Imaging and AI: A Review of Diagnostic Modalities, Biomarkers, and Clinical Integration

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ABSTRACT

Lymphedema, a chronic lymphatic disorder characterized by swelling, fibrosis, and adipose tissue accumulation, requires precise, stage-specific imaging for effective diagnosis and management. This review evaluates conventional imaging modalities, including indocyanine green lymphography (ICG-L), lymphoscintigraphy, magnetic resonance imaging (MRI), and computed tomography (CT), alongside emerging artificial intelligence (AI) applications to enhance diagnostic accuracy and treatment planning. We analyze their capabilities in assessing lymphatic function and tissue changes through quantitative biomarkers, comparing their strengths across disease stages. ICG-L excels in detecting early lymphatic dysfunction, while MRI and CT provide detailed visualization of advanced fibrotic and adipose changes. AI-driven tools, such as automated segmentation and biomarker quantification, show promise in improving tissue characterization and supporting surgical planning. However, clinical integration of AI is hindered by data heterogeneity, lack of interpretability, and regulatory challenges. To address these, we propose a strategic framework incorporating federated learning for privacy-preserving model training, explainable AI for clinical transparency, and standardized imaging protocols. Future efforts should prioritize multicenter validation and harmonized guidelines to enhance reproducibility and ensure equitable, scalable adoption of advanced imaging technologies for lymphedema management worldwide.

1. Introduction

Lymphedema, a chronic and progressive disorder, arises from impaired lymphatic drainage, causing accumulation of protein-rich interstitial fluid, primarily in the limbs. This leads to persistent swelling, discomfort, recurrent infections, and, in advanced stages, irreversible tissue changes like fibrosis and adipose tissue proliferation (1-3). Globally, lymphedema affects 140–250 million people, posing a significant burden on healthcare systems and diminishing patients' quality of life(4, 5).

The condition is classified as primary, due to congenital lymphatic malformations, or secondary, resulting from acquired damage from cancer treatments, surgery, trauma, or infection. Secondary lymphedema is especially prevalent among cancer survivors, with incidence rates up to 50% in patients treated for breast, gynecologic, prostate, or melanoma malignancies, depending on lymph node dissection or radiation extent (6, 7).

Despite its prevalence, lymphedema is often underdiagnosed due to its insidious onset and lack of standardized diagnostic criteria. Early symptoms are frequently misattributed to other causes, delaying intervention. Traditional diagnostic methods, such as limb circumference measurement and water displacement, lack sensitivity for detecting subclinical or early-stage disease (8). This highlights the need for objective, reproducible, and sensitive diagnostic tools to enable early detection and effective management.

Medical imaging plays a critical role in lymphedema management, evolving from basic anatomical visualization to advanced modalities that assess lymphatic structure and functional techniques, such as lymphoscintigraphy(LSG), near-infrared fluorescence lymphography with indocyanine green (ICG-L), Dynamic contrast-enhanced magnetic resonance lymphangiography (DCE-MRL), and high-frequency ultrasonography, which offer distinct advantages based on disease stage and clinical goals (9, 10). However, the lack of standardized imaging protocols and limited comparative studies restricts their optimal application(3).

Emerging technologies, such as artificial intelligence (AI), and radiomics, show significant potential to enhance diagnostic accuracy, reproducibility, and efficiency (11). AI-driven tools, including automated segmentation and pattern classification, can improve early detection and personalize treatment strategies. Yet, their clinical integration faces challenges, such as the need for large, annotated datasets, external validation, and regulatory approval (12, 13).

Recent progress in imaging standardization and artificial intelligence makes this review particularly timely. Over the past few years, the development of reproducible MRI and CT protocols for lymphatic and soft-tissue evaluation, together with advances in deep learning based multimodal segmentation and portable fluorescence imaging, has transformed the diagnostic landscape for lymphedema (11-13). These innovations have improved quantitative tissue assessment, reduced operator dependence, and expanded access to early detection in low-resource settings. Therefore, a comprehensive synthesis that integrates conventional imaging, quantitative biomarkers, and AI-driven approaches is needed to support standardized and equitable clinical implementation.

Prior reviews have examined individual imaging modalities or early AI applications but lack a comprehensive synthesis of conventional and advanced techniques, standardized protocols, or quantitative biomarkers (2). Comparative analyses of modalities and practical frameworks for AI integration remain limited. This review systematically evaluates conventional imaging modalities (lymphoscintigraphy, ICG lymphography, DCE MRL, ultrasonography) and emerging AI technologies for lymphedema diagnosis and management. It compares their diagnostic performance, emphasizes the role of quantitative biomarkers in staging and treatment planning, and proposes a strategic framework for integrating AI into clinical practice to improve early detection, personalized care, and global accessibility.

Table 1. Comparative Summary of Previous Reviews on Lymphedema Imaging Modalities and Computational Advancements

Study (Year)	Scope of Review	Main Deficiencies	Gap Highlighted	Contribution of Current (our) Review
Nagy et al., 2023(Medicina)(14)	Anatomical imaging modalities (ICG-L, MRI, CT, US)	Lacked comprehensive synthesis; no AI or quantitative biomarker discussion	Limited to qualitative comparison of modalities	Integrates conventional imaging with AI-based quantification and stage-specific diagnostics
Salehi et al., 2022(MRI of Lymphedema)(15)	MRI-focused narrative review	Focused only on MRI; no cross-modal assessment or AI framework	Missing multimodal or comparative standardization	Provides cross-modality performance comparison and unified biomarker framework
Rai et al., 2025(BJR Precision Oncology)(16)	Imaging and Management in oncology	Emphasized oncology context; minimal computational or biomarker detail	No systematic comparison of functional vs structural modalities	Expands to quantitative, AI-enhanced imaging and universal staging integration
Jayasree et al., 2025 (Prog. Biomed. Eng.)(2)	Computational and ML methods for lymphedema detection	Insufficient clinical and imaging context; focused mainly on algorithms	Lacked linkage between imaging biomarkers and clinical utility	Aligns computational methods with imaging biomarkers and clinical relevance
Mohos et al., 2024 (CRC Press Handbook)(10)	Overview of lymphoscintigraphy & ICG techniques	No stage-based or quantitative comparative analysis	Absence of unified framework across diseases stages	Introduces multimodal, stage-specific algorithmic evaluation and standardization targets

2. Pathophysiology of Lymphedema and Its Imaging Implications

Lymphedema is a chronic condition caused by impaired lymphatic drainage, leading to the accumulation of protein rich interstitial fluid, chronic inflammation, fibrosis, and adipose tissue proliferation (17).

On a molecular level, lymphedema progression involves chronic inflammation and impaired lymphangiogenesis. Dysregulation of vascular endothelial growth factor-C (VEGF-C) and its receptor VEGFR-3 reduces lymphatic vessel formation, while persistent macrophage infiltration releases cytokines such as TNF-α and IL-6 that promote fibrosis and adipose tissue deposition. These biological alterations correspond to imaging findings such as increased dermal thickness, tissue stiffness, and reduced lymphatic transport observable on ultrasound, MRI, and LSG. These progressive tissue changes correlate with the International Society of Lymphology (ISL) staging system (Stages 0–III), which informs imaging modality selection and treatment strategy(18).

In the subclinical phase (Stage 0), lymphatic dysfunction occurs without visible swelling, providing a critical window for early intervention. Functional imaging, such as ICG-L and LSG, detects delayed lymphatic transport, enabling preemptive management (19). In Stages I and II, reversible edema progresses to early fibrosis and fat deposition, which are effectively visualized using high-frequency ultrasound and magnetic resonance imaging (MRI). These modalities reveal dermal thickening and increased T2 signal intensity indicative of edema (20). In Stage III, irreversible tissue remodeling, marked by extensive fibrosis and structural distortion, requires advanced structural imaging, such as CT and DCE-MRL, to assess lymphatic architecture and guide surgical planning (21, 22). This progression reflects a clinically recognized pattern where imaging approaches are stratified by disease stage and the depth of lymphatic involvement, aligning diagnostic goals with modality characteristics.

The choice of imaging modality depends on the depth and nature of lymphatic involvement. ICG-L and ultrasound excel in evaluating superficial lymphatics, making them ideal for early-stage assessments. In contrast, MRI and CT are better suited for deep lymphatic and tissue characterization in advanced stages (23). Primary lymphedema, often due to congenital malformations, and secondary lymphedema, commonly acquired post-cancer treatment, exhibit distinct imaging features. For example, ICG-L may show linear lymphatic patterns in primary lymphedema, while secondary lymphedema often presents with dermal backflow.

The clinical decision flowchart in Figure 1 illustrates modality selection based on disease stage and etiology, prioritizing functional imaging (e.g., ICGL, lymphoscintigraphy) in early stages and structural imaging (MRI, CT) in advanced disease. Advanced techniques, such as optical coherence tomography (OCT), ultrasound elastography, and Dixon or diffusion weighted MRI, enhance precision in staging and monitoring by quantifying tissue composition and lymphatic flow (24, 25). For instance, Dixon MRI quantifies fat fraction, a key biomarker for Stage II progression, while ultrasound elastography measures tissue stiffness associated with fibrosis (26, 27). Figure 2a provides state specific imaging guidance, highlighting representative features

and modality recommendations tailored to clinical objectives, such as diagnosis, staging, or surgical planning.

Pediatric and head-and-neck lymphedema present unique diagnostic challenges. In children, congenital or syndromic forms require low-dose protocols and high-resolution modalities to avoid radiation exposure and capture small lymphatic channels. Head-and-neck cases, often secondary to surgery or radiotherapy, demand imaging sequences with reduced motion and metal artefacts. Techniques such as ICG-L and DCE-MRL are particularly valuable for these anatomically complex regions, offering both structural and functional insight.

Integration of artificial intelligence (AI) and radiomics enhances diagnostic reproducibility and supports personalized care. AI-driven segmentation improves identification of lymphatic vessels in ICG-L, while radiomics quantifies tissue changes, such as fibrosis ratio (> 25% for advanced disease), to inform treatment decisions (2). These advancements, combined with standardized imaging protocols, hold promise for optimizing lymphedema management across diverse clinical settings while maintaining consistency with contemporary staging-aligned imaging approaches.

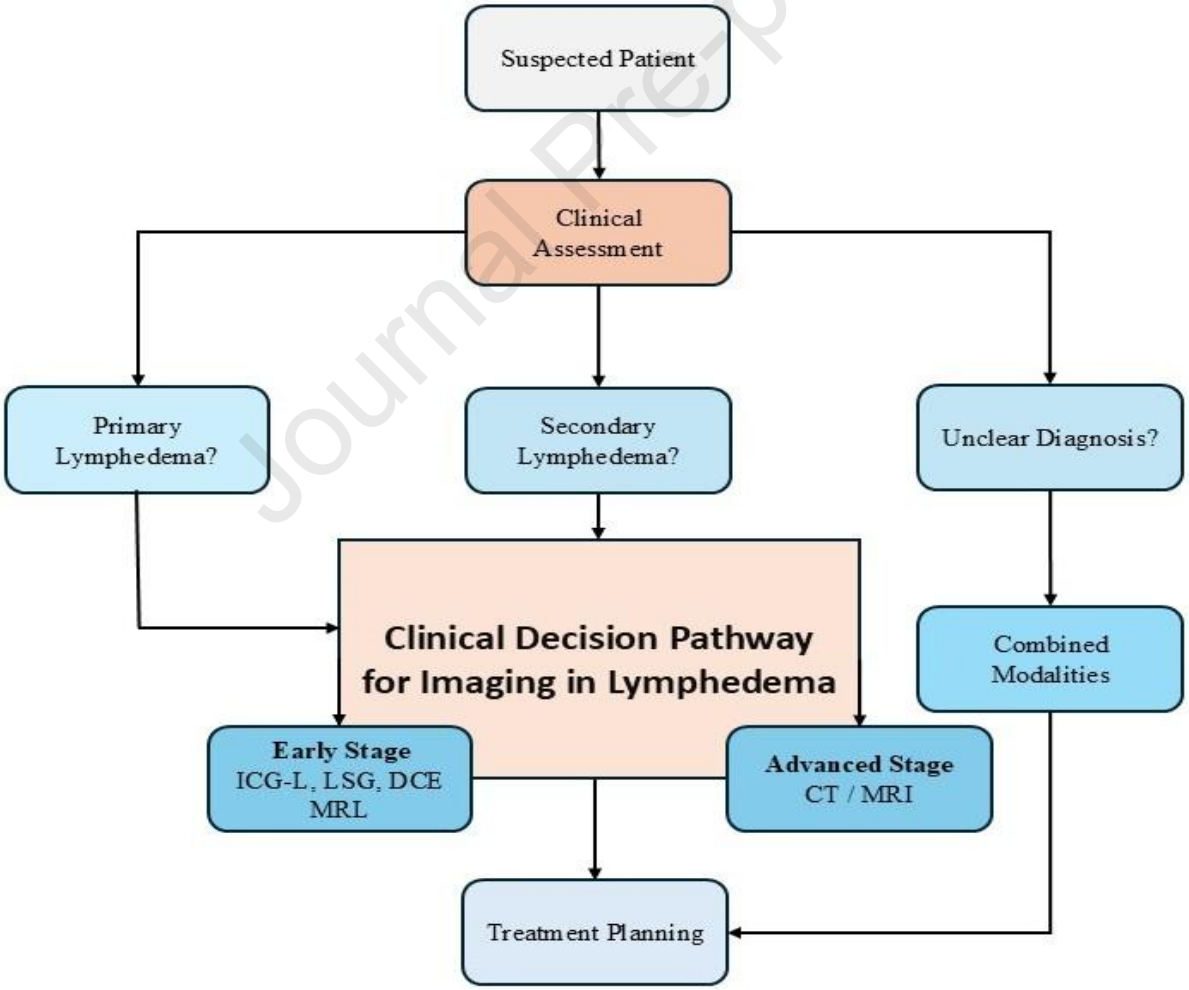


Figure 1: Clinical decision flowchart for lymphedema imaging based on suspected patient assessment. The process begins with clinical assessment, followed by differentiation into primary lymphedema, secondary lymphedema, or unclear diagnosis. For primary lymphedema, in addition to imaging with modalities like ICG-L, LSG, DCE-MRL, and MRI, genetic testing is also conducted to identify congenital causes. Secondary lymphedema is further stratified into early stage (ICG-L, LSG, DCE-MRL) and advanced stage (CT/MRI) for tailored imaging. Cases with unclear diagnosis may require combined modalities. The pathway culminates in treatment planning based on imaging results.

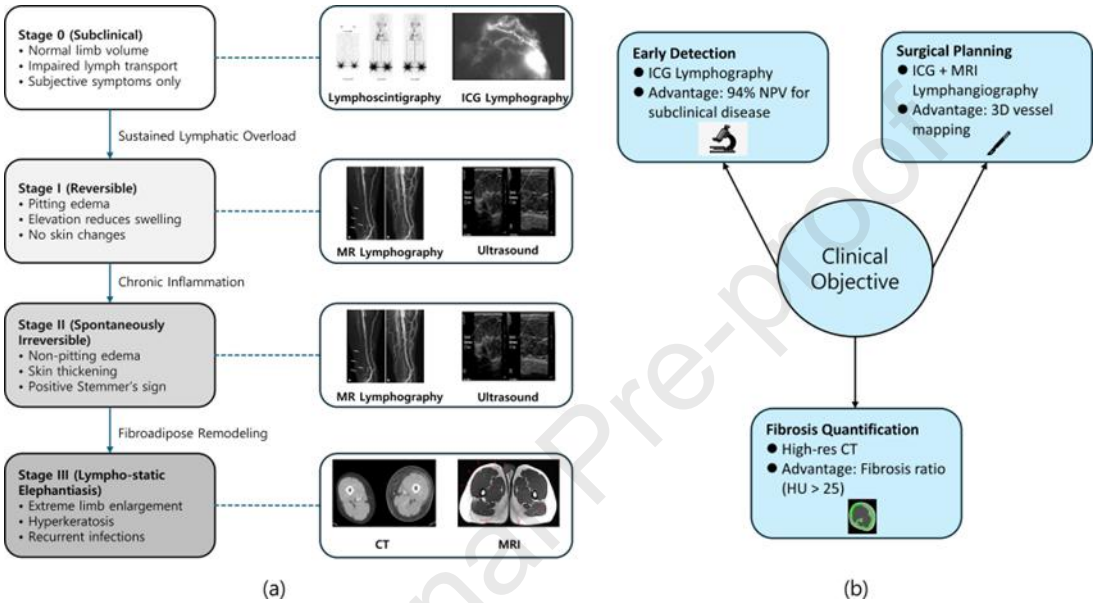


Figure 2: Stage-specific imaging guidance for lymphedema: (a) Representative imaging features by stage, including delayed lymph flow (Stage 0), dermal thickening (Stage I II), and fibrosis (Stage III). (b) Modality recommendations tailored to clinical objectives, such as diagnosis, staging, or surgical planning

3. Comparative Analysis of Imaging Modalities in Lymphedema

Recent advances in imaging technologies have significantly enhanced diagnostic precision, staging accuracy, and treatment planning for lymphedema. Imaging modalities can be broadly categorized into functional and structural approaches, each offering complementary insights into lymphatic transport, tissue remodeling, and disease progression. This section provides a comparative evaluation of commonly employed imaging tools, organized by functional purpose and clinical applicability.

3.1. Functional Imaging Techniques

Functional imaging assesses lymphatic flow dynamics, dermal backflow, and drainage pathways. These modalities are especially valuable for detecting early or subclinical lymphedema and for evaluating therapeutic responses.

3.1.1. Lymphoscintigraphy

Lymphoscintigraphy is widely regarded as the functional reference standard for diagnosing lymphedema. It involves intradermal injection of a radiotracer, typically technetium-99mTc labeled sulfur colloid (100–200 nm) or nano colloid, which is taken up by lymphatic vessels and transported to regional lymph nodes. The movement of the tracer is monitored over time using a gamma camera to assess lymphatic flow dynamics and identify anatomical disruptions (26). Figure 3 illustrates radiotracer dynamics over time.

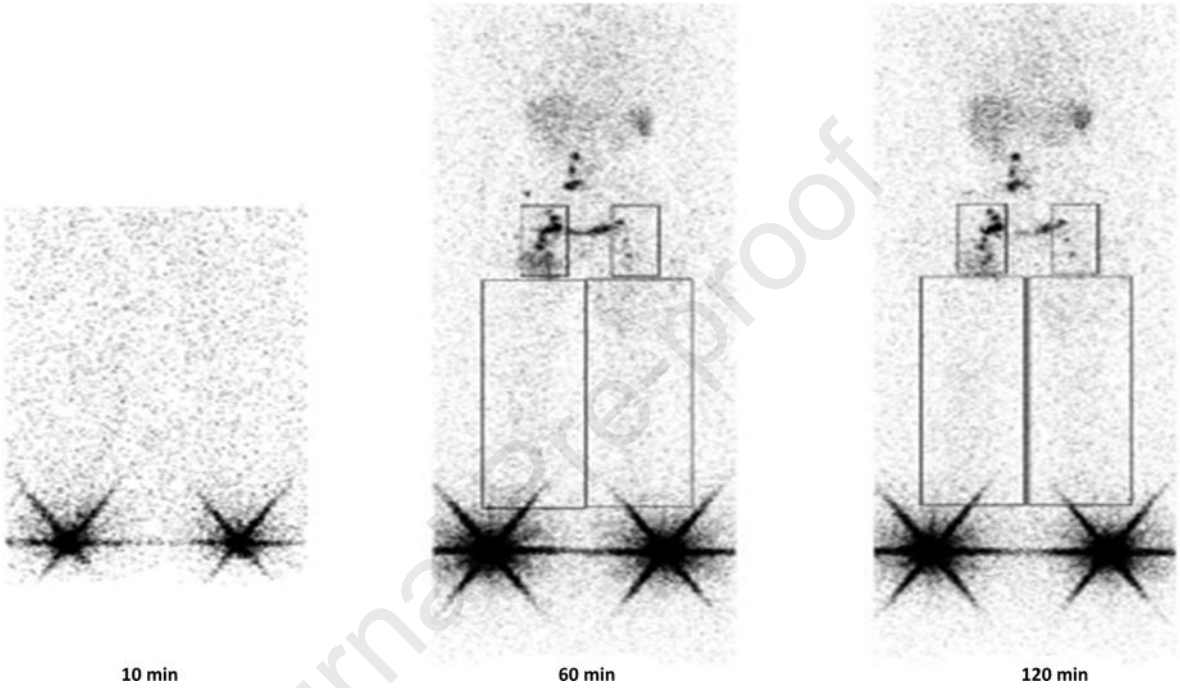


Figure 3: Sequential lymphoscintigraphy images captured at 10-, 60-, and 120-minutes post-injection, illustrating radiotracer migration from the injection sites in the lower extremities to pelvic and abdominal lymphatic channels. Outlined regions highlight progressive nodal uptake and delineate evolving drainage pathways.

This modality provides valuable information on lymphatic transport, dermal backflow, collateral vessel formation, and nodal uptake. It enables differentiation between primary and secondary lymphedema and assists in disease staging. Parameters such as the transport index (TI), time to peak tracer uptake, and interlimb asymmetry are commonly used quantitative metrics for evaluating severity and guiding treatment decisions (28, 29). Despite its clinical utility, lymphoscintigraphy is limited by low spatial resolution, long acquisition times, and reliance on ionizing radiation. Procedural variability, including differences in injection site, radiotracer formulation, and imaging protocol, further hampers reproducibility across institutions. Additionally, the technique may fail to detect early or subclinical disease, particularly in patients with only partial lymphatic dysfunction or asymptomatic limbs. To address these limitations, hybrid imaging approaches such as single-photon emission computed tomography/computed

tomography (SPECT/CT) have been introduced. SPECT/CT enables the integration of functional and anatomical information, thereby enhancing lesion localization and staging accuracy (30). However, its widespread adoption remains constrained by cost, availability, and the need for specialized facilities. In summary, while lymphoscintigraphy remains essential for functional lymphatic assessment, especially in advanced or equivocal cases, its diagnostic role is increasingly complemented by higher-resolution modalities such as ICG lymphography and MR lymphangiography (2, 31, 32).

3.1.2. Indocyanine Green (ICG) Lymphography

Indocyanine green (ICG) lymphography is a minimally invasive, near-infrared fluorescence imaging technique that enables high-resolution, real-time visualization of superficial lymphatic architecture. Following intradermal injection of a small volume of ICG dye, typically at the dorsal hand or foot, the dye binds to plasma proteins and is absorbed by the lymphatic vessels. The emitted fluorescence is captured using a near-infrared camera, allowing dynamic assessment of lymphatic flow patterns and dermal backflow. ICG lymphography is particularly effective in the early stage or subclinical lymphedema, detecting functional impairment before structural changes become evident. Flow patterns observed on ICG imaging are typically classified into four categories: linear, splash, stardust, and diffuse, corresponding to increasing severity of lymphatic dysfunction. This stratification facilitates clinical staging and surgical planning, particularly for physiologic procedures such as lymphaticovenous anastomosis (LVA) (33, 34). Compared to lymphoscintigraphy, ICG lymphography offers superior spatial and temporal resolution for superficial lymphatic structures. Studies have demonstrated that ICG can detect lymphatic abnormalities in 100% of symptomatic limbs (typically Stage I–II, with dermal backflow patterns present) and over 60% of asymptomatic limbs in high-risk cohorts (e.g., post-cancer treatment patients), surpassing the sensitivity of lymphoscintigraphy in early-stage disease (14, 26, 34). Despite its advantages, ICG lymphography has limitations. Its imaging depth is restricted to approximately 1–2 cm, limiting visualization of deep lymphatic vessels and central drainage pathways. Interpretation remains largely qualitative and operator-dependent, although quantitative frameworks such as transit time and backflow area are under active development. Additionally, ICG is contraindicated in patients with iodine or dye hypersensitivity, although adverse reactions are rare (35, 36).

3.1.3. Dynamic contrast-enhanced MRI (DCE-MRI) and Magnetic Resonance Lymphangiography

DCE-MRI is an advanced imaging technique that tracks the temporal distribution of gadolinium-based contrast agents to evaluate tissue perfusion and capillary permeability. In the context of lymphedema, DCE-MRI enables the assessment of both lymphatic function and structural alterations, serving as a bridge between purely functional and anatomical imaging.

It captures rapid sequential images after contrast injection, enabling time-intensity curves that reflect microvascular leakage, interstitial diffusion, and lymphatic drainage. These parameters help differentiate between active lymphedema (with ongoing fluid accumulation) and chronic fibrotic disease. Quantitative biomarkers such as time to peak enhancement, wash-in/wash-out rates, and area under the curve (AUC) have shown potential in distinguishing disease severity and monitoring response to therapy (37, 38).

An extension of this approach, DCE-MRL, focuses on the dynamic visualization of lymphatic structures and flow. Following subcutaneous or intradermal contrast injection, it enables real-time assessment of dermal backflow, lymphatic stasis, and collateral vessel formation. This is particularly useful in evaluating lymphatic transport capacity and identifying dysfunctional or tortuous lymphatic pathways, aiding in pre-surgical planning for procedures such as LVA or VLNT.

In early-stage lymphedema, both DCE-MRI and MRL detect perfusion abnormalities and delayed lymphatic uptake before structural damage sets in. In advanced disease, they reveal fibrotic zones, impaired clearance, and microcirculatory disruption (39). When combined with multiparametric sequences like T2-weighted imaging, DIXON, and diffusion tensor imaging, they offer comprehensive assessment of both structure and function.

These techniques require rapid imaging sequences, patient cooperation, and contrast use, which may limit applicability in patients with renal impairment. Interpretation also demands standardized post-processing and trained radiologists. Despite these limitations, DCE-MRI and MRL are valuable functional imaging tools for diagnosing, staging, and managing lymphedema, with growing relevance in clinical and research settings(30)

3.2. Structural Imaging Techniques

Structural imaging plays a critical role in visualizing tissue-level changes such as fibrosis, adipose deposition, and lymphatic vessel remodeling. These techniques are particularly important in intermediate to advanced disease stages.

3.2.1. Magnetic Resonance Imaging (MRI)

MRI serves as a cornerstone in the structural evaluation of lymphedema, providing high-resolution, three-dimensional visualization of tissue morphology without ionizing radiation. It enables precise assessment of dermal thickening, subcutaneous fibrosis, adipose deposition, and fascial changes, which are critical for disease staging and treatment planning. Using high-field systems (1.5T–3.0T) and dedicated sequences, MRI allows accurate differentiation between fluid-dominant and fibrotic stages of lymphedema.

Key imaging protocols include T2-weighted sequences for detecting interstitial fluid and edema, DIXON-based fat water separation for quantifying adipose infiltration, and T1-weighted imaging for evaluating dermal and fascial thickening. Diffusion tensor

imaging (DTI) can further provide microstructural information related to fibrosis and collagen deposition, enhancing staging precision(40, 41). A visual overview of these imaging biomarkers is shown in Figure 4.

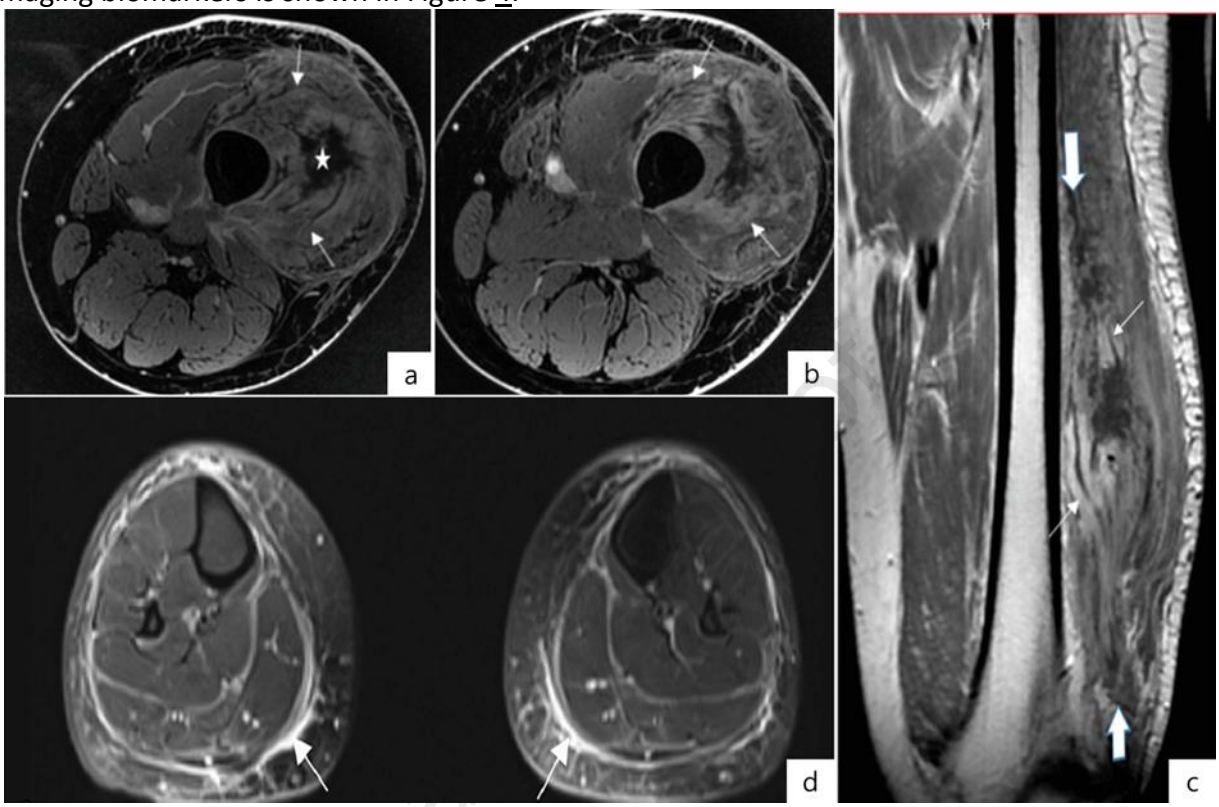


Figure 4: Representative MRI findings in early-stage lymphedema adapted from (42, 43). (a) Axial T2-weighted image shows high signal soft tissue edema (white star) and mild skin thickening (arrowheads). (b) Gadolinium-enhanced axial image demonstrates fascial enhancement. (c) Coronal T1-weighted image reveals subcutaneous infiltration (thin arrows) and fascial thickening (bold arrows). (d) Fat-suppressed axial post-contrast image highlighting deep fascia thickening (arrows).

These multiparametric assessments facilitate longitudinal monitoring of disease progression and objective evaluation of treatment efficacy.

MRI findings typically evolve with disease severity. Early-stage lymphedema shows increased dermal and subcutaneous T2 signal intensity with preserved tissue planes, while advanced disease demonstrates fascial thickening, trabecular patterning, and heterogeneous fibrosis. Quantitative biomarkers, including fat fraction, skin thickness, and fibrosis index, have shown strong correlations with clinical severity scores and can serve as reproducible indicators for outcome assessment (35, 36). In preoperative contexts, MRI assists in identifying optimal intervention zones by delineating fibrotic and fatty components and differentiating viable from non-viable tissues. It also provides valuable baseline information for postoperative monitoring following physiological or excisional surgical procedures.

Recent advances have highlighted the potential of low-field MRI (typically <1.5T) for lymphedema evaluation. While lower signal-to-noise ratio (SNR) remains, a technical limitation compared to high-field systems, low-field MRI offers practical benefits including lower cost, quieter operation, reduced susceptibility to metal artifacts, and enhanced accessibility in resource-constrained settings. These systems are increasingly used for soft tissue assessment in musculoskeletal and peripheral vascular disorders and may reliably detect lymphedema-related changes such as edema, fat infiltration, and fibrosis. Moreover, the reduced specific absorption rate (SAR) improves safety for patients with implants or sensitivity to RF-induced heating. Although validation studies in lymphedema are limited, improvements in image reconstruction and artifact correction could make low-field MRI a feasible alternative for structural imaging for early detection where high-field access is limited (44, 45).

Despite its advantages, MRI presents certain limitations. Scan duration, cost, and the requirement for experienced interpretation may restrict accessibility in low-resource settings. Additionally, its sensitivity to motion artifacts and the absence of lymphatic-specific contrast agents due to regulatory restrictions, cost constraints, limited supply in low-resource regions, or patient-specific contraindications such as renal impairment, allergy, or pregnancy can affect delineation accuracy (46, 47). Nevertheless, MRI has demonstrated high sensitivity and moderate-to-high specificity in detecting characteristic structural changes of lymphedema, particularly in distinguishing fibrotic remodeling from reversible edema. As such, it remains a highly effective structural imaging tool for comprehensive lymphedema evaluation. By providing reproducible, high-resolution assessment of tissue composition and pathological remodeling, it supports precision diagnosis, staging, and individualized clinical management (32).

3.2.2. Computed Tomography (CT)

Computed tomography (CT) plays a complementary role in the evaluation of lymphedema, particularly in the assessment of chronic fibrotic and adipose tissue remodeling. While CT is not a first-line modality for functional lymphatic imaging, it offers high spatial resolution and quantitative anatomical assessment, making it valuable in the staging and longitudinal monitoring of advanced disease (48). CT imaging can identify hallmark features of lymphedema, including dermal thickening, subcutaneous edema, fat hypertrophy, and fascial distortion. It is particularly useful for differentiating lymphedema from other conditions with similar clinical presentations, such as lipomatosis, deep vein thrombosis, or post-surgical edema. Axial and coronal reconstructions provide precise measurements of tissue thickness and volume, enabling objective evaluation of disease extent (49). Quantitative parameters derived from CT, such as the fibrosis ratio, subcutaneous thickness, and limb volume asymmetry, have shown strong correlations with clinical severity, as shown in Figure 5

For instance, a fibrosis ratio exceeding 25% is considered indicative of advanced-stage lymphedema, while interlimb volume asymmetry greater than 12% is commonly used to identify pathologic swelling. Post-processing techniques, including 3D volumetric

analysis and reticulation mapping, further enhance diagnostic granularity. One of the emerging applications of CT in lymphedema care is the use of CT-based indices to guide surgical intervention. In particular, the maximum reticulation index and fibrosis mapping can assist in distinguishing candidates for physiologic versus excisional procedures. Additionally, dynamic contrast-enhanced CT (4D-CT) is under investigation for evaluating lymphatic flow in real time, although its clinical use remains limited. Despite its diagnostic strengths, CT has several limitations (50). The use of ionizing radiation restricts its application in younger or high-risk populations, and soft tissue contrast is inferior to that of MRI. Repeated exposure is also a concern for long-term monitoring. Nevertheless, the wide availability, rapid acquisition time, and strong quantitative capabilities of CT make it a valuable tool, especially in resource-limited settings or when MRI is contraindicated. In summary, CT imaging provides robust anatomical detail and quantitative biomarkers for assessing tissue changes in lymphedema, offering clinical utility in diagnosis, staging, and pre-surgical planning when appropriately integrated with other modalities(51-53).

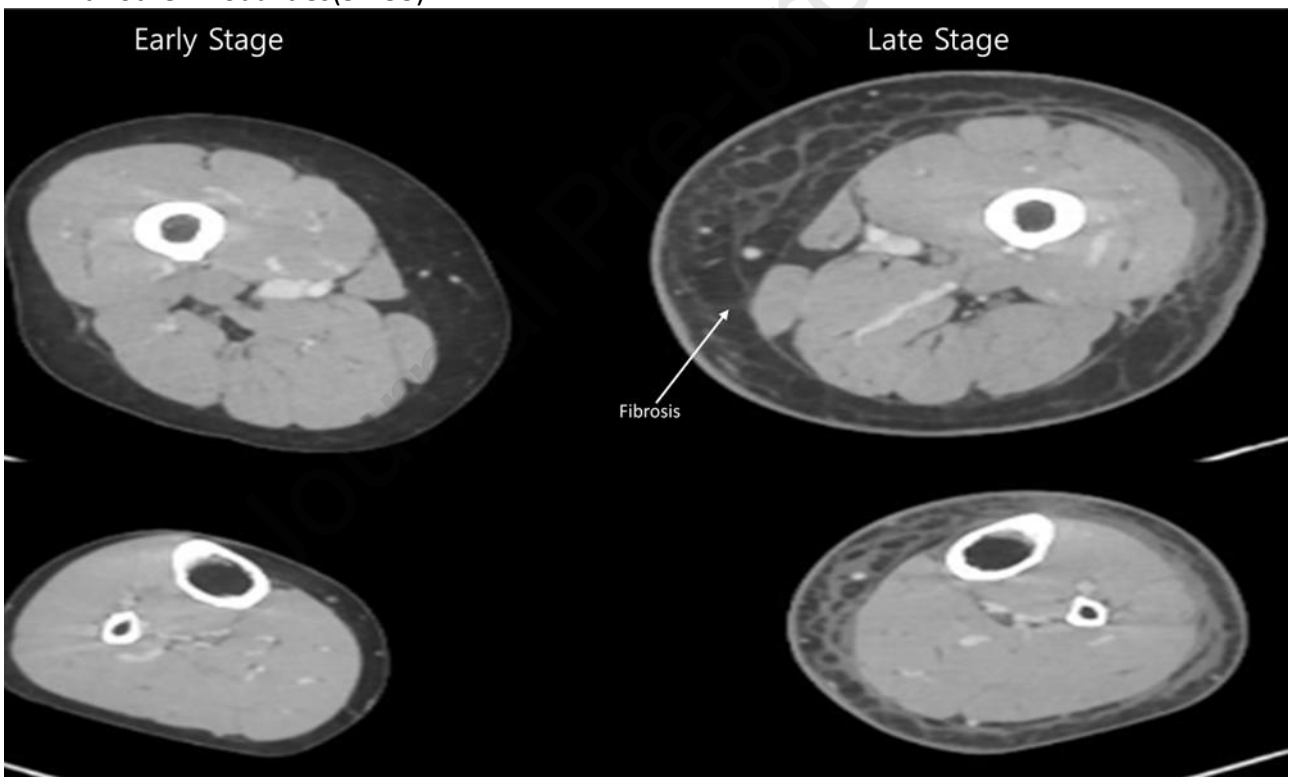


Figure 5: Representative axial CT images illustrating disease progression. Left panels: early-stage lymphedema with preserved architecture. Right panels: late-stage Fibrosis and increased tissue density (arrows).

3.2.3. Ultrasound elastography

Ultrasound is a widely accessible, non-invasive modality that provides valuable anatomical insights in lymphedema assessment. High-frequency ultrasound can detect

dermal thickening, subcutaneous edema, and the characteristic honeycomb pattern of the subcutis. These findings support clinical staging and treatment monitoring (54).

Doppler ultrasound aids in ruling out differential diagnoses such as venous insufficiency or deep vein thrombosis. Elastography, an advanced technique, can assess tissue stiffness and may help quantify fibrosis in chronic cases (55).

While limited in visualizing lymphatic vessels and functional flow, ultrasound remains useful for serial evaluation, especially in resource-limited settings.

3.3. Multimodal and Scenario-Driven Strategies

A scenario-driven framework is vital for optimal diagnostic performance, aligning imaging strategies with clinical objectives, disease stages, and healthcare resources

For instance, ICG lymphography offers high sensitivity and a negative predictive value of up to 94% in early-stage disease (49). When integrated with MR lymphangiography, it enables comprehensive visualization of both superficial and deep lymphatic systems, which is essential for preoperative planning, particularly in procedures such as lymphatic venous anastomosis (LVA) (56).

In resource-limited settings, ultrasound and elastography provide accessible alternatives for fibrosis detection and disease monitoring. In contrast, high-resource environments may leverage advanced MRI and CT protocols for precise staging and operative planning. Bioimpedance spectroscopy complements imaging by quantifying extracellular fluid volume, particularly for tracking response to decongestive therapy (57, 58). The cost and availability of imaging tools remain key determinants of diagnostic strategy worldwide. Functional imaging modalities such as ICG lymphography and ultrasound offer high diagnostic yield at relatively low cost, making them suitable for low- and middle-income settings. In contras advanced modalities such as DCE MRI and CT provide comprehensive assessment but require substantial infrastructure and expertise. Implementing tiered diagnostic frameworks where resource efficient modalities are used for screening and advanced imaging reserved for complex cases can optimize clinical outcomes while ensuring equitable access (59, 60). A concise comparison of the diagnostic performance and practical attributes of each imaging modality is presented in **Table 2**, summarizing their relative sensitivity, specificity, radiation exposure, and cost. This overview complements the preceding discussion by highlighting how different modalities align with clinical needs and resource settings.

A visual summary of modality selection across disease stages is presented in Figure 2b.

Table 2. Comparative Summary of Imaging Modalities in Lymphedema

Modality	Type	Sensitivity (%)	Specificity (%)	Radiation Exposure	Cost	Key Advantages	Main Limitations
Lymphoscintigraphy (61)	Functional	High	High	Yes (low)	High	Quantitative lymphatic transport; established	Low resolution; lengthy procedure; radiation
ICG Lymphography (62)	Functional	High	High	No	High	Real-time superficial mapping; high sensitivity	Operator-dependent; limited depth (1–2 cm)
DCE-MRI / MRL (37)	Functional + Structural	Moderate to high	Moderate	No	High	Deep lymphatic and soft tissue visualization; quantitative biomarkers	Cost; long scan time; contrast contraindications
CT (48)	Structural	Moderate to high	Low	Yes (moderate)	Moderate	High spatial resolution; quantitative fibrosis metrics	Radiation exposure; limited soft-tissue contrast
Ultrasound / Elastography (63)	Structural	Moderate	Moderate	No	Low	Portable; non-invasive; accessible	Operator-dependent; limited functional data

Quantitative metrics derived from these imaging modalities, such as fat fraction, fibrosis ratio, and volume asymmetry, are increasingly used to assess disease severity and guide treatment. A summary of these key biomarkers, along with their clinical applications and diagnostic thresholds, is provided in **Table 3**. The integration of artificial intelligence and molecular imaging into this clinical framework, further elaborated in

Section 4, is expected to enhance diagnostic precision, enable automation, and support scalable personalized care.

Table 3. Quantitative Biomarkers in Lymphedema Assessment

Biomarker / Metric	Imaging Modality	Clinical Application	Key Findings / Thresholds
Fat Fraction	MRI (Dixon, T2)	Differentiates adipose proliferation from early edema	Fat fraction >30% in chronic cases (40, 41)
Fibrosis Index / Ratio	CT (Deep learning or Manual)	Measures tissue fibrosis; guides surgery candidacy	Ratio >25% indicates advanced-stage lymphedema (51-53)
Skin / Subcutaneous Thickness	CT, MRI, Ultrasound	Indicates staging, therapy monitoring	Thickness >15 mm linked to Stage II/III (64)
Volume Asymmetry	MRI, CT (3D recon), Ultrasound	Assesses inter-limb difference; staging	>10–12% discrepancy clinically significant (65)
ICG Flow Patterns	ICG Lymphography	Visual staging (linear, splash, stardust, diffuse)	AI classifiers >95% accuracy for stage prediction (14, 34).
ICG Transit Time / Backflow Area	ICG Lymphography	Quantitative functional evaluation	Metrics under validation; useful for AI training (35, 36)
Composite Scores (e.g., Lymphedema Staging Index)	Multimodal (MRI + CT + ICG)	Standardized diagnosis and monitoring	Integrates volume, fat, fibrosis, and flow pattern (46, 47)

4. Artificial Intelligence Applications in Lymphedema Imaging

Artificial intelligence (AI) is advancing lymphedema imaging by embedding automation, reproducibility, and data-driven objectivity into diagnostic and therapeutic workflows. Using deep learning (DL) and machine learning (ML) techniques, AI facilitates high-precision segmentation and classification that underpin robust clinical decision-making. Radiomics, which extracts quantitative imaging features from standard modalities, serves as a bridge enabling these AI models to translate complex visual data into structured inputs for disease stratification and monitoring. The schematic flow of this AI-enabled imaging pipeline is illustrated in **Figure 6**.

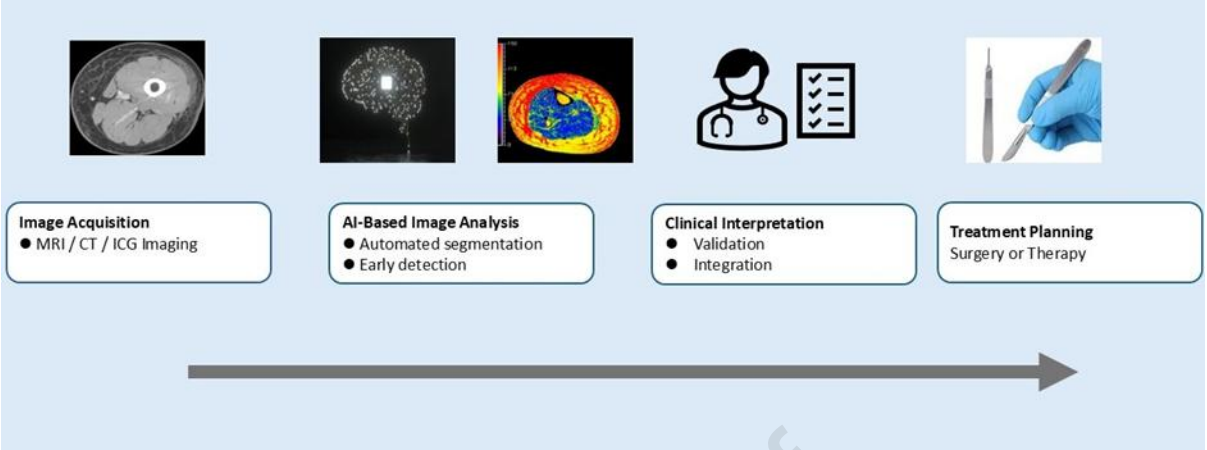


*Figure 6: Workflow for AI-assisted imaging in lymphedema. The process begins with **Image Acquisition** using MRI, CT, or ICG imaging modalities. This is followed by **AI-Based Image Analysis**, where automated segmentation and early detection are performed. Next, **Clinical Interpretation** involves validating AI outputs and integrating them into clinical understanding. Finally, **Treatment Planning** is conducted, guiding surgical or therapeutic interventions.*

4.1. Automated Segmentation for Tissue Quantification

Manual segmentation remains a limiting factor in clinical practice due to high time demands and inter-observer variability. Convolutional neural networks (CNNs), particularly U-Net variants, have become the gold standard for automating segmentation across modalities. These models delineate fat, muscle, and fibrotic tissues with high fidelity, enabling standardized volumetric assessment and supporting downstream analyses.

In computed tomography (CT), Na et al. (53). applied a U-Net++ architecture with an EfficientNet-B7 encoder to segment lower extremity tissues in 118 gynecologic cancer patients. The model achieved Dice Similarity Coefficients (DSCs) of 0.945–0.999 and volumetric similarity (VS) exceeding 0.97, supporting surgical planning and longitudinal monitoring via a custom graphical interface. Son et al. (51) utilized a SegNet model for fibrosis-specific segmentation in 27 patients with chronic unilateral lymphedema, reporting a DSC of 0.738 and a strong correlation with bioelectrical impedance (r = 0.875), underscoring its potential for early fibrosis detection.

In magnetic resonance imaging (MRI), which offers superior soft-tissue contrast, Nowak et al. (66) implemented a DL pipeline on 3D Dixon MR lymphangiography in 45 patients, achieving DSCs of 0.989 and 0.994 for subcutaneous and subfascial compartments, respectively. This enabled reliable quantification of limb asymmetry, critical for staging and treatment assessment. Abts et al. (67) extended segmentation to the head and neck region using ResNet and UNETR models, demonstrating feasibility for radiation-induced lymphedema detection in post-treatment cancer patients.

Ultrasound and emerging modalities have also seen AI integration. Goudarzi et al. (68) deployed a graph-supervised CNN for automated segmentation of tissue layers in BCRL arm ultrasounds, while Shokouhifar et al. (69) employed an ensemble DL model and depth camera to quantify arm volume with high accuracy (R = 0.992 vs. water displacement), providing a non-contact, hygienic alternative for serial assessment.

4.2. AI-Based Classification and Differential Diagnosis

AI models also exhibit strong performance in disease classification, leveraging either direct image-based features or derived radiomic attributes. These approaches support diagnostic accuracy, disease differentiation, and early detection.

In image-based classification, Lewsirirat et al. (70) trained CNNs, including EfficientNetV2, on 1,622 clinical photographs to distinguish lymphedema from other etiologies such as venous insufficiency and systemic edema. The model achieved 78.6% accuracy, outperforming human readers (62.7%), with Grad-CAM-based heatmaps enhancing interpretability. Nomura et al. (71)demonstrated opportunistic screening by training a ResNet-34 model on pelvic CT slices at the greater trochanter level, achieving an AUC of 0.967 for lymphedema detection in gynecologic cancer patients.

Radiomics-driven classification provides a higher-dimensional analysis. Textural and intensity-based features extracted from segmented regions can stratify disease stages and predict treatment response. Although still emerging, these models suggest promise for integrating imaging biomarkers into routine staging algorithms.

Non-imaging approaches also contribute. Fu et al. (72) used ML models, including artificial neural networks (ANNs), to classify symptom reports from 355 breast cancer survivors. The ANN achieved 93.75% accuracy, 95.65% sensitivity, and 91.03% specificity, enabling remote, real-time monitoring of lymphedema risk.

4.3. AI-Assisted Clinical Decision Support

AI-enabled segmentation and classification systems collectively form the foundation of clinical decision support (CDS) in lymphedema imaging. By transforming imaging data into quantitative, reproducible metrics, these models provide clinicians with actionable insights that enhance staging accuracy, treatment selection, and longitudinal monitoring. Automated volumetric quantification of fat, muscle, and fibrotic tissue allows objective tracking of disease progression and post-surgical recovery. Tissue-specific maps generated by CNN-based models help identify optimal surgical or physiological intervention zones, guiding procedures such as lymphaticovenous anastomosis and vascularized lymph node transfer(53) (51) (66). AI classifiers that integrate radiomic features, clinical parameters, and dynamic flow data assist in distinguishing lymphedema from mimicking conditions such as venous insufficiency and lipedema. These systems enable early disease recognition and risk stratification, supporting personalized follow-up intensity (70) (71). When segmentation- and classification derived features are combined within multimodal machine learning frameworks including CT, MRI, and clinical data predictive models can automatically

stage lymphedema, estimate fibrosis burden, and forecast therapy response (53) (49, 71). Furthermore, AI-assisted lymphography video analysis enables dynamic visualization of lymphatic flow patterns and obstruction points, offering a functional complement to static imaging (73, 74). This integrated approach translates AI predictions into quantitative decision indices, improving reproducibility across institutions and enabling evidence-based management. Table 4 summarizes key AI studies, detailing models, datasets, and performance metrics.

Table 4. key AI studies, detailing models, datasets, and performance metrics.

Primary AI Task	Study & Source	Modality	AI Approach / Model	Key Objectives	Key Performance Metrics	Clinical Relevance
Segmentation & Quantification	Na et al., Eur Radiol (2025) (53)	CT	U-Net++, EfficientNet-B7	Automated segmentation of fat, muscle, fibrosis	DSC 0.945–0.999	Surgical planning, volumetric monitoring
	Nowak et al., Eur Radiol (2023) (66)	MRI (Dixon)	Custom DL Pipeline	Tissue volume/asymmetry assessment	DSC 0.989 (SCT), 0.994 (SFT)	Objective staging and monitoring
	Son et al., Sci Rep (2022) (51)	CT	SegNet	Quantitative estimation of fibrosis	DSC 0.738; Corr. with BIS: 0.875	Early fibrosis detection
	Abts et al. (2024) (67)	MRI (Head/Neck)	ResNet, UNETR	Automated segmentation for HNC lymphedema	DSC up to 0.75	Detection in complex anatomy
	Goudarzi et al., IEEE TBME (2023)(68)	Ultrasound	GSCNN	Tissue layer segmentation in BCRL	Model DSC 0.87 ± 0.11	Portable, automated US monitoring
	Shokouhifar et al., Biomed Signal Proc	3D Camera	THENDEL (Ensemble DL)	Automated arm volume measurement	MAE 36.7 mL, R = 0.992	Hygienic, real-time volume quantification

	Contr (2023) (69)					
Classification & Diagnosis	Lewsirirat et al., Sci Rep (2025) (70)	Clinical Photos	EfficientNetV2	Differentiate lymphedema from other edemas	Accuracy 78.6% (Human: 62.7%)	Triage and differential diagnosis
	Nomura et al., Sci Rep (2023) (71)	CT	ResNet-34	Screening for LEL from routine CT	AUC 0.967, Accuracy 92.9%	Opportunistic screening
	Fu et al., mHealth (2018) (72)	Symptom Reports	ANN, SVM, Decision Trees	Early detection via symptom reports	Accuracy 93.75%, Sens. 95.65%	Cost-effective, remote risk detection

5. Limitations and Challenges

Despite significant advancements, several challenges hinder the full clinical integration of AI in lymphedema imaging. Data heterogeneity is a primary concern, as most models are trained on small, single-center datasets, limiting generalizability. For example, AI models trained on Western populations may underperform in Asian cohorts due to differences in body composition or disease presentation, necessitating diverse, multi-center datasets (75). Inconsistent labeling criteria for fibrosis, lymphatic flow patterns, and segmentation boundaries across institutions further undermine reproducibility and cross-study comparability (76). Additionally, the diagnostic accuracy of operator-dependent modalities such as ultrasound and ICG lymphography varies with procedural technique and user expertise, with reported inter-observer variability of 15–20% due to differences in injection site, probe pressure, and image interpretation. Establishing standardized acquisition protocols and adopting quantitative indices such as transit time, flow area, or elasticity measures can improve reproducibility and reduce subjective bias across clinical settings (77).

Another challenge lies in multimodal integration. Imaging techniques such as MRI, CT, and ICG lymphography vary significantly in spatial resolution, contrast dynamics, and acquisition parameters. This heterogeneity makes it difficult to develop AI systems that perform consistently across modalities. Addressing this requires harmonization strategies like intensity normalization, inter-modality registration, and standardized

annotation protocols to ensure training data compatibility and model robustness (15, 78).

The issue of interpretability and clinician trust remains central. Deep learning models, often perceived as opaque, have limited transparency, which hampers clinical acceptance. While tools like Grad-CAM have made some progress in visualizing decision pathways, they are insufficient for clinical implementation. Techniques like SHAP(SHapley Additive exPlanations) and LIME Local Interpretable Model-agnostic Explanations offer more quantitative feature explanations and can enhance interpretability, but these methods are not yet routinely integrated into clinical workflows (79, 80).

Regulatory, ethical, and technical constraints further obstruct adoption. Regulatory bodies lack standardized evaluation metrics and validation frameworks for AI tools in lymphedema care, resulting in minimal external validation and limited approvals. Ethically, the lack of algorithmic transparency raises concerns about accountability and informed consent. Technically, variability in imaging hardware, protocols, and annotation quality reduces the reproducibility and portability of AI solutions.

Financial and infrastructural barriers are also significant. The cost of establishing and maintaining the necessary AI infrastructure including high-performance computing resources, secure data storage, integration software, and trained personnel can be prohibitive, especially for resource-limited settings. The absence of clear reimbursement frameworks for AI-driven diagnostics further limits institutional incentives for adoption, necessitating health economic assessments to demonstrate cost-effectiveness(81, 82).

Interoperability poses an additional hurdle. Many EMR and PACS platforms operate on outdated, proprietary systems incompatible with AI software, obstructing integration into routine clinical workflows. A shift toward standardized data formats (HL7, FHIR) and middleware capable of secure, real-time data exchange is essential to address this limitation (83, 84).

Privacy and data governance remain critical concerns. Legal regulations such as HIPAA and GDPR restrict centralized data aggregation, limiting collaborative AI development. Federated learning offers a decentralized alternative, enabling institutions to train shared models without exposing sensitive data. Moreover, reinforcement learning and generative models such as GANs (Generative Adversarial Networks) can generate high-quality synthetic data to augment small datasets, simulate rare lymphedema cases, and improve model robustness without compromising patient privacy. These approaches may become essential for overcoming the persistent limitations of real-world clinical data scarcity(85, 86).

Finally, algorithmic bias and equity concerns must be addressed. Diagnostic accuracy can vary significantly across demographic groups due to differences in subcutaneous fat, skin tone, or tissue properties, especially in modalities like MRI and ICG. These disparities can propagate health inequities unless AI models are trained on demographically diverse datasets and undergo continuous performance audits to detect

and correct bias. Without these safeguards, the clinical implementation of AI risks perpetuating existing disparities rather than mitigating them (87).

Figure 6 outlines a workflow for overcoming these challenges through data standardization, ethical AI deployment, and infrastructure development.

6. Strategic Framework for Clinical Integration

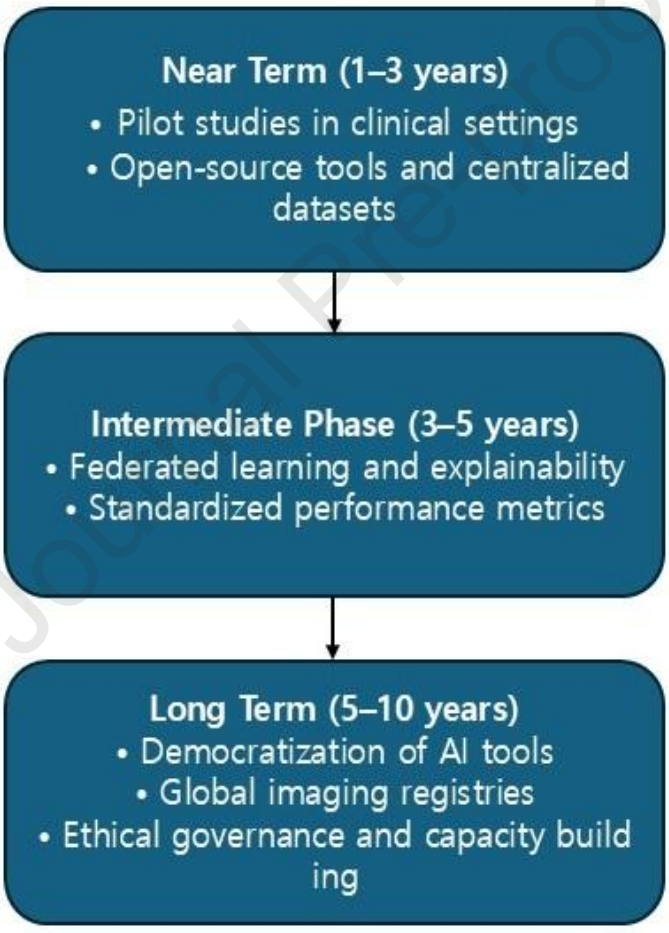
To overcome the above limitations, a structured, phased roadmap is essential to guide the safe, scalable, and equitable clinical integration of AI into lymphedema imaging. This strategy prioritizes harmonization, transparency, regulatory readiness, and global accessibility. In the near term (1–3 years), AI deployment should begin in well-equipped clinical settings, focusing on pilot studies that capture real-world feedback and usage patterns. Concurrent development of open-source annotation tools and segmentation standards will facilitate consistency across centers. Establishing centralized benchmarking datasets, particularly those including diverse demographics and imaging modalities, is critical to ensure reproducibility and to enable cross-comparison of model performance(12) (13).

During the intermediate phase (3–5 years), federated learning frameworks must be expanded to allow collaborative model development across institutions without compromising patient data, ensuring compliance with global regulations like GDPR and HIPAA (88). This approach supports generalizability and addresses regional disparities in model accuracy. Integration of explainable AI modules such as SHAP, LIME, and Grad-CAM into clinical PACS and EMR systems can provide interpretability at the point of care, increasing clinician trust and fostering adoption. Regulatory bodies and professional societies should simultaneously create standardized performance metrics, validation protocols, and approval pathways tailored for AI applications in lymphedema imaging. This includes defining acceptable thresholds for accuracy, reproducibility, and interpretability in segmentation, classification, and clinical decision-support tasks(75) (79).

In the long term (5–10 years), democratization of AI tools will be essential to reach low-resource and underserved settings. Emerging innovations like portable near-infrared fluorescence imaging devices and low-field MRI systems (≤ 0.55 T) offer scalable, cost-effective solutions for early-stage lymphedema detection and monitoring (44, 45, 89). These can be combined with lightweight, cloud-compatible AI models optimized for low-bandwidth environments, delivering expert interpretation through teleconsultation. The use of synthetic data generated by generative adversarial networks (GANs) can supplement training data for rare disease presentations or minority populations, improving model robustness while preserving privacy. Reinforcement learning can further optimize decision-support algorithms for diverse clinical workflows (90) (91). Standardized imaging registries with global participation and structured metadata will enable continuous learning, model retraining, and transparent cross-validation. Ethical governance must underpin this ecosystem. Fairness audits

should be routinely conducted to detect algorithmic bias across sex, ethnicity, or BMI strata. Transparent model documentation and auditing frameworks are essential to address disparities and ensure accountability. Data privacy frameworks must evolve to support secure, distributed model training and responsible data sharing (85) (86).

Capacity building will also be critical. Training programs for radiologists, technologists, and healthcare workers must emphasize AI literacy, clinical interpretation of AI outputs, and workflow integration. These initiatives will support sustainable implementation and long-term institutional alignment(92, 93). Finally, clinical effectiveness should be quantified using operational outcomes such as staging accuracy, diagnostic latency, inter-rater agreement, and patient outcomes. These metrics will provide evidence for reimbursement models and policy formulation, ensuring AI adoption advances both precision medicine and health equity (94).



Flowchart for Strategic Framework for Clinical In integration

7. Conclusion

This review underscores the critical role of stage-specific imaging in lymphedema management, highlighting that no single modality is universally effective across all disease stages. Indocyanine green lymphography excels in detecting early lymphatic dysfunction, while magnetic resonance lymphangiography and computed tomography provide essential insights into advanced fibrotic and adipose changes. Artificial intelligence enhances these modalities by automating the quantification of biomarkers, such as fat fraction and fibrosis ratio, potentially improving diagnostic accuracy by up to 20% and refining surgical planning. To unify staging and monitoring practices, quantitative imaging biomarkers offer a cohesive framework across the disease continuum tracking progression from early lymphatic dysfunction to irreversible fibrosis. Standardized metrics such as dermal backflow area, lymphatic vessel diameter, fat thickness, and tissue water content allow for reproducible assessments and inter-study comparability. However, inconsistent biomarker application and fragmented imaging protocols hinder reproducible, high-quality care. To address these gaps, establishing multicenter registries and collaborative clinical trials is imperative. These initiatives should focus on validating AI-assisted quantification tools, harmonizing imaging protocols, and building longitudinal datasets stratified by etiology, stage, and treatment response. Future research should also prioritize imaging innovations tailored to underserved groups, including pediatric, gynecologic, and head-and-neck cancer populations. Promoting equity through subsidized MRI access and clinician training in low-resource settings is essential to ensure global diagnostic reach. By integrating validated AI tools, standardized biomarkers, and coordinated research infrastructure, lymphedema care can advance toward precision staging, earlier intervention, and improved patient outcomes.

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9. References

1. Bowman C, Rockson SG. The role of inflammation in lymphedema: a narrative review of pathogenesis and opportunities for therapeutic intervention. International journal of molecular sciences. 2024;25(7):3907.

2. Jayasree K, Vijaykumar D. A comprehensive review of computational diagnostic techniques for lymphedema. Progress in Biomedical Engineering. 2025.

3. Kondra K, Stanton E, Salibian AA, Patel KM. Imaging in lymphedema management: A narrative review of preoperative assessment & surgical planning. Annals of Breast Surgery. 2024;8.

4. Buki LP, Rivera-Ramos ZA, Kanagui-Muñoz M, Heppner PP, Ojeda L, Lehardy EN, et al. "I never heard anything about it": Knowledge and psychosocial needs of Latina breast cancer survivors with lymphedema. Women's Health. 2021;17:17455065211002488.
5. Földi M, Földi E, Strößenreuther C, Kubik S. Földi's textbook of lymphology: for physicians and lymphedema therapists: Elsevier Health Sciences; 2012.
6. Cucinella G, Di Donna MC, Casarin J, Schivardi G, Multinu F, Borsellino L, et al. Lower limb lymphedema after surgical staging for endometrial cancer: Current insights and future directions. Taiwanese Journal of Obstetrics and Gynecology. 2024;63(4):500–5.
7. Vargo M, Aldrich M, Donahue P, Iker E, Koelmeyer L, Crescenzi R, et al. Current diagnostic and quantitative techniques in the field of lymphedema management: a critical review. Medical Oncology. 2024;41(10):241.
8. İyigün ZE, Ozmen T, İlgün S, Nakipoğlu C, Özkurt E, Çelebi F, et al. Evaluation of Long-Term Lymphedema Rate in Patients With Subclinical Lymphedema Diagnosed in the Preoperative Period via Bioimpedance. European Journal of Breast Health. 2025;21(1):40.
9. Carroll BJ, Singhal D. Advances in lymphedema: An under-recognized disease with a hopeful future for patients. Vascular Medicine. 2024;29(1):70–84.
10. Mohos B, Tzou C-HJ, Gloviczki P. Imaging modalities for diagnosis and treatment of lymphedema. Handbook of Venous and Lymphatic Disorders: CRC Press; 2024. p. 717–29.
11. Eldaly AS, Avila FR, Torres-Guzman RA, Maita K, Garcia JP, Serrano LP, et al. Artificial intelligence and lymphedema: State of the art. Journal of Clinical and Translational Research. 2022;8(3):234.
12. Kondylakis H, Kalokyri V, Sfakianakis S, Marias K, Tsiknakis M, Jimenez-Pastor A, et al. Data infrastructures for AI in medical imaging: a report on the experiences of five EU projects. European radiology experimental. 2023;7(1):20.
13. Ozcan BB, Patel BK, Banerjee I, Dogan BE. Artificial intelligence in breast imaging: challenges of integration into clinical practice. Journal of Breast Imaging. 2023;5(3):248–57.
14. Nagy BI, Mohos B, Tzou C-HJ. Imaging modalities for evaluating lymphedema. Medicina. 2023;59(11):2016.
15. Salehi BP, Sibley RC, Friedman R, Kim G, Singhal D, Loening AM, et al. MRI of

Lymphedema. J Magn Reson Imaging. 2023;57(4):977–91.
16. Rai P, Mahajan A, Shukla S, Pokar N. Imaging and management of lymphedema in the era of precision oncology. Br J Radiol. 2025;98(1169):619–29.
17. Brown S, Dayan JH, Kataru RP, Mehrara BJ. The vicious circle of stasis, inflammation, and fibrosis in lymphedema. Plastic and reconstructive surgery. 2023;151(2):330e–41e.
18. Brouillard P, Murtomäki A, Leppänen V-M, Hyytiäinen M, Mestre S, Potier L, et al. Loss-of-function mutations of the TIE1 receptor tyrosine kinase cause late-onset primary lymphedema. The Journal of clinical investigation. 2024;134(14).
19. Manrique OJ, Bustos SS, Ciudad P, Adabi K, Chen WF, Forte AJ, et al., editors. Overview of lymphedema for physicians and other clinicians: a review of fundamental concepts. Mayo Clinic Proceedings; 2022: Elsevier.
20. Lee E, Biko DM, Sherk W, Masch WR, Ladino-Torres M, Agarwal PP. Understanding lymphatic anatomy and abnormalities at imaging. Radiographics. 2022;42(2):487–505.
21. Salibian AA, Yu N, Patel KM. Staging approaches to lymphatic surgery: techniques and considerations. Journal of Surgical Oncology. 2025;131(1):12–21.
22. Kim C, Ali H, Tsai LL, Bulman J, Singhal D, Carroll B, et al. Evaluation of primary lymphedema with intranodal lymphangiography. Cardiovascular and Interventional Radiology. 2024;47(2):238–44.
23. Bernas M, Al-Ghadban S, Thiadens SR, Ashforth K, Lin WC, Safa B, et al. Etiology and treatment of cancer-related secondary lymphedema. Clinical & Experimental Metastasis. 2024;41(4):525–48.
24. Schaapman JJ, Tushuizen ME, Coenraad MJ, Lamb HJ. Multiparametric MRI in patients with nonalcoholic fatty liver disease. Journal of Magnetic Resonance Imaging. 2021;53(6):1623–31.
25. Zhang T, Feng Z, Zhang Y, Li C, Huang Z, editors. Piezoelectrical Micro-Tapper based Three-Dimensional Optical Coherence Elastography for In Vivo Dermatology Applications. 2024 IEEE Ultrasonics, Ferroelectrics, and Frequency Control Joint Symposium (UFFC-JS); 2024: IEEE.
26. Figueroa BA, Lammers JD, Al-Malak M, Pandey S, Chen WF. Lymphoscintigraphy versus indocyanine green lymphography—which should be the gold standard for

lymphedema imaging? Lymphatics. 2023;1(1):25–33.
27. Bernardo R, Domingues JP, Bernardes R, Morgado M, Batista A, editors. Evaluation of skin care products using optical coherence elastography. Optical Elastography and Tissue Biomechanics X; 2023: SPIE.
28. Bhattacharya A, Mathur Y, Laroiya I, Bal A, Sharma S, Mittal BR. Abstract B042: Sentinel lymph node detection in breast cancer: Comparison of blue dye and filtered Technetium 99m sulphur colloid radiotracer injection. Cancer Research. 2023;83(2_Supplement_2):B042–B.
29. Fearn NR, Dylke ES, Bailey D, Kilbreath SL. Lymphoscintigraphy as an outcome measurement for conservative upper limb lymphedema treatments: a systematic review. Lymphatic Research and Biology. 2022;20(3):248–59.
30. Yoon H-J, Woo K-J, Kim J-Y, Kang SY, Moon BS, Kim BS. The added value of SPECT/CT lymphoscintigraphy in the initial assessment of secondary extremity lymphedema patients. Scientific Reports. 2023;13(1):19494.
31. Friedman R, Bustos VP, Pardo J, Tillotson E, Donohoe K, Chatterjee A, et al. Superficial and functional imaging of the tricipital lymphatic pathway: a modern reintroduction. Breast cancer research and treatment. 2023;197(1):235–42.
32. Pieper C, Wagenpfeil J, Henkel A, Geiger S, Köster T, Hoss K, et al. MR lymphangiography of lymphatic abnormalities in children and adults with Noonan syndrome. Scientific Reports. 2022;12(1):11164.
33. Brezgyte G, Mills M, van Zanten M, Gordon K, Mortimer PS, Ostergaard P. A systematic review of indocyanine green lymphography imaging for the diagnosis of primary lymphoedema. British Journal of Radiology. 2025;98(1168):517–26.
34. Li Q, Tang Q, Luo K, Zhang S, Zhou X, Yang Y, et al. Comparative analysis of the International Society of Lymphology and Taiwan Lymphoscintigraphy Staging systems: correlation, reliability, and a quantitative severity index in extremity lymphedema. Quantitative Imaging in Medicine and Surgery. 2025;15(3):1822.
35. Liu M, Zhang Y, Li X, Hao Q, Li B, Wang R. MRI-based volume measurement methods for staging primary lower extremity lymphedema: a single-center study of asymmetric volume difference-a diagnostic study. BMC Musculoskeletal Disorders. 2023;24(1):810.
36. Liu M, Li B, Hao K, Zhang Y, Hao Q, Li X, et al. Quantitative evaluation of primary

lower extremity lymphedema staging using MRI: a preliminary study. Quantitative Imaging in Medicine and Surgery. 2023;13(8):4839.

37. Dong F, Li J, Wang J, Yang X. Diagnostic performance of DCE-MRI radiomics in predicting axillary lymph node metastasis in breast cancer patients: A meta-analysis. Plos one. 2024;19(12):e0314653.

38. Yu Y, Chen R, Yi J, Huang K, Yu X, Zhang J, et al. Non-invasive prediction of axillary lymph node dissection exemption in breast cancer patients post-neoadjuvant therapy: A radiomics and deep learning analysis on longitudinal DCE-MRI data. The Breast. 2024;77:103786.

39. Facondo G, Bottero M, Goanta L, Farneti A, Faiella A, D'Urso P, et al. Incidence and predictors of lower extremity lymphedema after postoperative radiotherapy for prostate cancer. Radiation Oncology. 2025;20(1):41.

40. Engelke K, Chaudry O, Gast L, Eldib MA, Wang L, Laredo J-D, et al. Magnetic resonance imaging techniques for the quantitative analysis of skeletal muscle: State of the art. Journal of orthopaedic translation. 2023;42:57–72.

41. Crescenzi R, Donahue PM, Garza M, Lee CA, Patel NJ, Gonzalez V, et al. Elevated magnetic resonance imaging measures of adipose tissue deposition in women with breast cancer treatment-related lymphedema. Breast cancer research and treatment. 2022;191(1):115–24.

42. Cren P-Y, Penel N, Cordoba A, Decanter G, Gaboriau L, Ben Haj Amor M. Myositis ossificans circumscripta after surgery and radiotherapy and during sunitinib treatment: a case report. Journal of Medical Case Reports. 2022;16(1):454.

43. Kim J, Lee LH. Diagnostic Utility of Magnetic Resonance Imaging in Eosinophilic Fasciitis: A Case Report and Review of Literature. Cureus. 2023;15(4):e37899.

44. Pogarell T, Heiss R, Janka R, Nagel AM, Uder M, Roemer FW. Modern low-field MRI. Skeletal radiology. 2024;53(9):1751–60.

45. Tian Y, Nayak KS. New clinical opportunities of low-field MRI: heart, lung, body, and musculoskeletal. Magnetic Resonance Materials in Physics, Biology and Medicine. 2024;37(1):1–14.

46. Sanderson J, Tuttle N, Box R, Reul-Hirche H, Laakso E-L. Localised Objective Characterisation Assessment of Lymphoedema (LOCAL): Using High-Frequency Ultrasound, Bioelectrical Impedance Spectroscopy and Volume to Evaluate Superficial

Tissue Composition. Diagnostics. 2024;14(15):1616.
47. Bundred N, Foden P, Riches K, Morris J, Evans A, Todd C, et al. Prospective Study of criteria for Lymphoedema diagnosis, development of new Composite index for diagnosis and prediction model. European Journal of Cancer. 2018;92:S38–S9.
48. Lee DG, Lee S, Kim KT. Computed tomography-based quantitative analysis of fibrotic changes in skin and subcutaneous tissue in lower extremity lymphedema following gynecologic cancer surgery. Lymphatic Research and Biology. 2022;20(5):488–95.
49. Rai P, Mahajan A, Shukla S, Pokar N. Imaging and management of lymphedema in the era of precision oncology. British Journal of Radiology. 2025;98(1169):619–29.
50. Werner R, Szkitsak J, Madesta F, Büttgen L, Wimmert L, Sentker T, et al. Clinical application of breathing-adapted 4D CT: image quality comparison to conventional 4D CT. Strahlentherapie und Onkologie. 2023;199(7):686–91.
51. Son H, Lee S, Kim K, Koo K-i, Hwang CH. Deep learning-based quantitative estimation of lymphedema-induced fibrosis using three-dimensional computed tomography images. Scientific Reports. 2022;12(1):15371.
52. Kim S-Y, Bae H, Ji HM. Computed tomography as an objective measurement tool for secondary lymphedema treated with extracorporeal shock wave therapy. Annals of rehabilitation medicine. 2015;39(3):488–93.
53. Na S, Choi SJ, Ko Y, Urooj B, Huh J, Cha S, et al. Automated CT segmentation for lower extremity tissues in lymphedema evaluation using deep learning. European Radiology. 2025:1–11.
54. Montazeri G, Rohban N, Sotoudeh M, Massarrat S. Abdominal ultrasound combined with laboratory tests as a reliable, easily accessible and cost-effective way of assessing the stages of liver fibrosis and cirrhosis. Archives of Iranian Medicine. 2022;25(2):118–23.
55. Canales-Lachén E, Asunsolo Á, Manrique OJ, Blázquez J, Holguín P, Maldonado AA. The use of ultrasound imaging for upper extremity lymphedema after breast cancer: a systematic review. Journal of Reconstructive Microsurgery. 2023;39(02):102–10.
56. Yasunaga Y, Nakajima Y, Mimura S, Yuzuriha S, Kondoh S. Magnetic resonance lymphography as three-dimensional navigation for lymphaticovenular anastomosis in patients with leg lymphedema. Journal of Plastic, Reconstructive & Aesthetic Surgery.

2021;74(6):1253–60.
57. Lippi L, Turco A, Moalli S, Nascimben M, Curci C, de Sire A, et al. Quantitative assessment of upper-limb volume: implications for lymphedema rehabilitation? Applied Sciences. 2023;13(17):9810.
58. Cihoric M, Kehlet H, Højlund J, Lauritsen M, Kanstrup K, Foss N. Bioimpedance spectroscopy fluid analysis in acute high-risk abdominal surgery, a prospective clinician-blinded observational feasibility study. Journal of Clinical Monitoring and Computing. 2023;37(2):619–27.
59. Brezgyte G, Mills M, van Zanten M, Gordon K, Mortimer PS, Ostergaard P. A systematic review of indocyanine green lymphography imaging for the diagnosis of primary lymphoedema. Br J Radiol. 2025;98(1168):517–26.
60. O'Connor JP, Tofts PS, Miles KA, Parkes LM, Thompson G, Jackson A. Dynamic contrast-enhanced imaging techniques: CT and MRI. Br J Radiol. 2011;84 Spec No 2(Spec Iss 2):S112–20.
61. Cheng M-H, Pappalardo M, Lin C, Kuo C-F, Lin C-Y, Chung KC. Validity of the novel Taiwan lymphoscintigraphy staging and correlation of Cheng lymphedema grading for unilateral extremity lymphedema. Annals of surgery. 2018;268(3):513–25.
62. Mihara M, Hara H, Araki J, Kikuchi K, Narushima M, Yamamoto T, et al. Indocyanine green (ICG) lymphography is superior to lymphoscintigraphy for diagnostic imaging of early lymphedema of the upper limbs. PloS one. 2012;7(6):e38182.
63. Forte AJ, Huayllani MT, Boczar D, Cinotto G, Ciudad P, Manrique OJ, et al. The basics of ultrasound elastography for diagnosis, assessment, and staging breast cancer-related lymphedema: a systematic review of the literature. Gland Surgery. 2020;9(2):589.
64. Maita K, Garcia JP, Torres RA, Avila FR, Kaplan JL, Lu X, et al. Imaging biomarkers for diagnosis and treatment response in patients with lymphedema. Biomarkers in Medicine. 2022;16(4):303–16.
65. Zhao Y, Ding Y, Lau V, Man C, Su S, Xiao L, et al. Whole-body magnetic resonance imaging at 0.05 Tesla. Science. 2024;384(6696):eadm7168.
66. Nowak S, Henkel A, Theis M, Luetkens J, Geiger S, Sprinkart AM, et al. Deep learning for standardized, MRI-based quantification of subcutaneous and subfascial tissue volume for patients with lipedema and lymphedema. European Radiology. 2023;33(2):884–92.

67. Abts T, Mulder S, Ramezani S, Wahid K, Fuller CD. Automated Lymphedema Detection: A Multi-Observer Deep-Learning Approach. 2024.
68. Goudarzi S, Whyte J, Boily M, Towers A, Kilgour RD, Rivaz H. Segmentation of arm ultrasound images in breast cancer-related lymphedema: a database and deep learning algorithm. IEEE Transactions on Biomedical Engineering. 2023;70(9):2552–63.
69. Shokouhifar A, Shokouhifar M, Sabbaghian M, Soltanian-Zadeh H. Swarm intelligence empowered three-stage ensemble deep learning for arm volume measurement in patients with lymphedema. Biomedical Signal Processing and Control. 2023;85:105027.
70. Lewsirirat T, Titijaroonroj T, Apichonbancha S, Uthatham A, Suwanruangsri V, Suwan N, et al. Deep learning-based classification of lymphedema and other lower limb edema diseases using clinical images. Scientific Reports. 2025;15(1):12453.
71. Nomura Y, Hoshiyama M, Akita S, Naganishi H, Zenbutsu S, Matsuoka A, et al. Computer-aided diagnosis for screening of lower extremity lymphedema in pelvic computed tomography images using deep learning. Scientific Reports. 2023;13(1):16214.
72. Fu MR, Wang Y, Li C, Qiu Z, Axelrod D, Guth AA, et al. Machine learning for detection of lymphedema among breast cancer survivors. Mhealth. 2018;4:17.
73. Ozmen BB, Pandey SK, Schwarz GS. Artificial Intelligence-Based Indocyanine Green Lymphography Pattern Classification for Management of Lymphatic Disease. Plast Reconstr Surg Glob Open. 2024;12(8):e6132.
74. Kim J, Kim H, Yoon YS, Kim CW, Hong S-M, Kim S, et al. Investigation of artificial intelligence integrated fluorescence endoscopy image analysis with indocyanine green for interpretation of precancerous lesions in colon cancer. PLoS One. 2023;18(5):e0286189.
75. Busnatu Ș, Niculescu A-G, Bolocan A, Petrescu GE, Păduraru DN, Năstasă I, et al. Clinical applications of artificial intelligence—an updated overview. Journal of clinical medicine. 2022;11(8):2265.
76. Rengan V, Lalwani D, Bhat S, Sundaram PM. Enhancing Dataset Quality for AI in Radiology: Challenges and Solutions. Journal of Gastrointestinal and Abdominal Radiology. 2025;8(01):003–4.
77. Nagy BI, Mohos B, Tzou CJ. Imaging Modalities for Evaluating Lymphedema. Medicina (Kaunas). 2023;59(11).

78. Fortin J-P, Cullen N, Sheline YI, Taylor WD, Aselcioglu I, Cook PA, et al. Harmonization of cortical thickness measurements across scanners and sites. NeuroImage. 2018;167:104–20.
79. van Der Vegt A, Campbell V, Zuccon G. Why clinical artificial intelligence is (almost) non-existent in Australian hospitals and how to fix it. Medical Journal of Australia. 2023.
80. Hassan SU, Abdulkadir SJ, Zahid MSM, Al-Selwi SM. Local interpretable model-agnostic explanation approach for medical imaging analysis: A systematic literature review. Computers in Biology and Medicine. 2025;185:109569.
81. Grover V, Dogra M. Challenges and Limitations of Explainable AI in Healthcare. Analyzing Explainable AI in Healthcare and the Pharmaceutical Industry: IGI Global Scientific Publishing; 2024. p. 72–85.
82. Mansoor I, Ortiz JG, Rector M. Generative AI in Clinical Research: Regulatory Submissions, Clinical Data Management, and Beyond. AMWA Journal: American Medical Writers Association Journal. 2024;39(1).
83. Tejani AS, Cook TS, Hussain M, Sippel Schmidt T, O'Donnell KP. Integrating and adopting AI in the radiology workflow: a primer for standards and integrating the healthcare enterprise (IHE) profiles. Radiology. 2024;311(3):e232653.
84. Carlos Ferreira J, Elvas LB, Correia R, Mascarenhas M. Enhancing EHR Interoperability and Security through Distributed Ledger Technology: A Review. Healthcare (Basel). 2024;12(19).
85. Firdaus M, Rhee K-H, editors. Towards trustworthy collaborative healthcare data sharing. 2023 IEEE International Conference on Bioinformatics and Biomedicine (BIBM); 2023: IEEE.
86. Attya SM, Jumaa DA, Hwezy NNK, Sajid WA, Khaleefah AM, Zhyrov G, et al., editors. Harnessing Federated Learning for Secure Data Sharing in Healthcare Systems. 2024 36th Conference of Open Innovations Association (FRUCT); 2024: IEEE.
87. Koçak B, Ponsiglione A, Stanzione A, Bluethgen C, Santinha J, Ugga L, et al. Bias in artificial intelligence for medical imaging: fundamentals, detection, avoidance, mitigation, challenges, ethics, and prospects. Diagnostic and interventional radiology. 2025;31(2):75.
88. Nigri A, Ferraro S, Wheeler-Kingshott CAG, Tosetti M, Redolfi A, Forloni G, et al.

Quantitative MRI harmonization to maximize clinical impact: the RIN–neuroimaging network. Frontiers in Neurology. 2022;13:855125.

89. Hussain I, Rial C, Boza J, Tompkins S, Branen J, Giordano J, et al. Design of a handheld and portable fluorescence imaging system for quantitative detection of pregnancy-specific biomarkers in cattle. Analytical and Bioanalytical Chemistry. 2024;416(18):4101–9.

90. Jiang S, Bukhari SM, Krishnan A, Bera K, Sharma A, Caovan D, et al. Deployment of artificial intelligence in radiology: Strategies for success. American Journal of Roentgenology. 2025;224(2):e2431898.

91. Vlăsceanu GV, Tarbă N, Voncilă ML, Boiangiu CA. Selecting the right metric: A detailed study on image segmentation evaluation. BRAIN Broad Research in Artificial Intelligence and Neuroscience. 2024;15(4):295–318.

92. Doherty G, McLaughlin L, Hughes C, McConnell J, Bond R, McFadden S. Radiographer Education and Learning in Artificial Intelligence (REAL-AI): A survey of radiographers, radiologists, and students' knowledge of and attitude to education on AI. Radiography. 2024;30:79–87.

93. Abràmoff MD, Roehrenbeck C, Trujillo S, Goldstein J, Graves AS, Repka MX, et al. A reimbursement framework for artificial intelligence in healthcare. NPJ Digit Med. 2022;5(1):72.

94. Hogg HDJ, Martindale APL, Liu X, Denniston AK. Clinical Evaluation of Artificial Intelligence-Enabled Interventions. Invest Ophthalmol Vis Sci. 2024;65(10):10.

Highlights

- Review of imaging (ICG, MRI, CT, lymphoscintigraphy) for lymphedema diagnosis and staging.
- Quantitative biomarkers: fat fraction >30%, fibrosis ratio >25% indicate severity.
- AI aids segmentation (Dice >0.945), classification, clinical reporting.
- Challenges: data heterogeneity, interpretability, regulations.
- Framework: explainable AI, federated learning, standardized protocols for adoption.