



REVIEW ARTICLE

# Artificial intelligence and lymphedema: State of the art

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## ABSTRACT

**Background:** Lymphedema practice is facing many challenges. Some of these challenges include eradication of tropical lymphedema, preclinical diagnosis of cancer-related lymphedema, and delivery of appropriate individualized care. The past two decades have witnessed an increasing implementation of artificial intelligence (AI) in health-care services. The nature of the challenges facing the lymphedema practice is suitable for AI applications.

**Aim:** The aim of this study was to explore the current AI applications in lymphedema prevention, diagnosis, and management and investigate the potential future applications.

**Methods and Results:** Four databases were searched: PubMed, Scopus, Web of Science, and EMBASE. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analysis as our basis of organization. Our analysis showed that several domains of AI, including machine learning (ML), fuzzy models, deep learning, and robotics, were successfully implemented in lymphedema practice. ML can guide the eradication campaigns of tropical lymphedema by estimating disease prevalence and mapping the risk areas. Robotic-assisted surgery for gynecological cancer was associated with a lower risk for the lower limb lymphedema. Several feasible models were described for the early detection and diagnosis of lymphedema. The proposed models are more accurate, sensitive, and specific than current methods in practice. ML was also used to guide and monitor patients during the rehabilitation exercises.

**Conclusion:** AI offers a variety of solutions to the most challenging problems in lymphedema practice. Further, implementation into the practice can revolutionize many aspects of lymphedema prevention, diagnosis, and management.

**Relevance to Patients:** Lymphedema is a chronic debilitating disease that is affecting millions of patients. Developing new modalities for prevention, early diagnosis, and treatment are critical to improve the outcomes. AI offers a variety of solutions for some of the complexities of lymphedema management. In this systematic review, we summarize and discuss the latest AI advances in lymphedema practice.

## 1. Introduction

Lymphedema is a chronic debilitating condition caused by lymphatic transport dysfunction [1]. In the primary lymphedema, the pathology is exclusively limited to lymph vessels, while in secondary lymphedema, the pathology may involve lymph vessels, lymph nodes, or both. Primary lymphedema is caused by three disorders: congenital hereditary lymphedema, familial lymphedema praecox, and lymphedema tarda [1]. Secondary lymphedema is caused by destruction or obstruction of the lymphatic system by infections, malignancy, trauma, surgery, and irradiation [1,2].

Lymphatic filariasis (LF) is the most common cause of lymphedema, with over fifty million patients worldwide [3]. However, in the developed world, breast cancer-related

lymphedema accounts for most cases of secondary lymphedema and can occur up to 20 years after surgery [4].

Lymphedema is considered incurable once established [5]. Conservative treatment is the standard of care and usually consists of manual lymphatic drainage, compressive therapy, skin hygiene, and rehabilitation exercises [6].

The current practice of lymphedema is facing many challenges. First, the eradication of LF from endemic regions is faced with many difficulties. Despite delivering over seven billion doses of chemotherapeutic agents and thousands of eradication campaigns, over 800 million people remain at risk [3]. Second, the early detection of lymphedema is difficult as most patients are asymptomatic during the initial stages. Finally, many of the methods used in diagnosis lack the required sensitivity, accuracy, and technical and economic feasibility, which adds to the complexity of the management. Artificial intelligence (AI) can be implemented in lymphedema practice to solve some of these challenges.

Today, many domains of AI, including machine learning (ML), fuzzy model (FM), robotics, and natural language processing (NLP), have become an essential component of patient care [7]. ML is ideal for tasks that depend on pattern recognition to make a specific clinical conclusion. For example, supervised ML can be used to automate EKG and X-ray images to reach a diagnosis [8]. NLP can create chatbots to interact with patients to deliver healthcare services. Robotics is becoming more integrated in the surgical practice, for example, robotic staging and robotic-assisted surgery are now widely accepted as the standard of care in many institutions [9,10].

Since the nature of the challenges that face lymphedema practice are very suitable for AI applications as pattern recognition and analysis of raw data, we have conducted this systematic review to investigate the current applications of AI in lymphedema practice.

## 2. Methods

### 2.1. Information sources, search strategy, and eligibility criteria

We used four electronic databases to run an all-time search: PubMed (including MEDLINE), Scopus, EMBASE, and Web of Science. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analysis as our basis of organization (Figure 1). The details of the search in each database can be found in the supplementary material. We ran our search in August 2021 with the following inclusion criteria: (1) English language, (2) full-text available, (3) studies reporting use of one or more domains of AI in prevention, (4) diagnosis, or (5) treatment of lymphedema. We have excluded editorials, reviews, and papers of which the full-text was not available.

### 2.2. Study selection and data collection process

Two authors searched independently, and the duplicates were removed using EndNote (Clarivate Analytics).

After filtering the studies based on titles, abstracts were, then, screened according to the eligibility criteria. Then, the remaining studies were screened based on full-text readings. The third author solved any conflicts between the first two authors.

## 3. Results

After the initial search yielded 257 results, 66 underwent abstract screening and full-text screening resulting in 15 studies included in the final analysis (one study was excluded after full-text screening as it was discussing an irrelevant topic to our review).

Table 1 summarizes the included studies chronologically, with the earliest at the top ( $n=15$ ). For each study in our sample, we have summarized the type of AI used, clinical implications, challenges, and comments.

### 3.1. Synthesis of evidence

ML was reported in 12 studies [11-22], robotics were reported in two studies [9,23], and FM was reported in a single study [24]. ML estimated the prevalence, geographical distribution, and risk factors of LF in four studies [15,17,19,21]. ML measured changes of *Wuchereria bancrofti* (WB) before and after mass treatment by comparing immunoglobulin G (IgG) curves [12]. In another study, an ML predictive model estimated the prevalence and geographical distribution of podoconiosis in an endemic area [14]. FM predicted the risk of developing post-operative lymphedema and classified its severity to standardize rehabilitation programs for each clinical stage [24]. Robotic-assisted surgery for endometrial and cervical cancer was associated with a lower incidence of post-operative lower limb lymphedema in two retrospective studies [9,23].

Preclinical identification of lymphedema in breast cancer survivors using the upper body function ML evaluation model was attempted in one study [11]. In another study, Chiang *et al.* introduced a feasible model of monitoring postoperative lymphatic exercises performed by breast cancer survivors [13]. Fu *et al.* trained an ML model to detect lymphedema status based on the symptoms reported by the patients [16]. The model successfully detected lymphedema status with an accuracy, sensitivity, and specificity of more than 90% [16]. Kistenev *et al.* combined multi-photon imaging and ML to diagnose and stage lymphedema with a 96% accuracy by estimating subcutaneous collagen disorganization [18]. Finally, ML diagnosed lymphedema by measuring foot and arm volume in two studies [20,22]. Although these models are more feasible than the current methods used in practice, further research is required for clinical validation.

## 4. Discussion

### 4.1. Eradication of tropical lymphedema

LF, also known as elephantiasis, is a parasitic disease transmitted by mosquitos infected with larvae [25]. LF is the most common cause of secondary lymphedema worldwide, with over fifty million infected patients and over 800 million at risk of infection [3,26]. Moreover, LF is the most common cause of permanent disfigurement and the second most common cause of disability worldwide, with over forty million being disfigured or disabled due to the disease [25].

**Table 1.** Summary of the included studies.

Author and Date	Description of AI	Clinical Relevance	Technical Challenges/Study Flaws	Summary/Comments
Vicentini et al.[24] (2011)	FM	Clinical and functional assessment for classifying the risk of developing lymphedema and its severity.	Validation by testing in actual patients is needed.	The proposed model allows standardization of rehabilitation programs, and the assistance level required by patients at every clinical stage.
Moreira et al.[11] (2015)	ML	Early/preclinical identification of lymphedema In breast cancer survivors via an upper body function evaluation model.	Although more feasible than traditional methods of early lymphedema detection, the results need validation by comparing to the results of methods currently in practice.	Early identification of lymphedema would permit early intervention which can improve the long term outcomes.
Zanagnolo et al.[9] (2016)	Robotics	Robotic-assisted hysterectomy for cervical cancer was associated with lower risk of postoperative lymphedema than open surgery.	This is a retrospective study. A stronger evidence should be obtained from an RCT.	Robotic radical hysterectomy is safe, feasible, and is associated with improved outcomes including post-operative lymphedema.
Arnold et al.[12] (2017)	ML	Measuring changes in transmission of Wuchereria bancrofti before and after mass treatment by comparing IgG curves in repeated cross sectional surveys.	<ul style="list-style-type: none"> <li>• Mean antibody levels do not reflect a direct epidemiologic transmission parameter.</li> <li>• Lack of a universal reference for antibody titers makes it challenging to compare means across different studies.</li> </ul>	This model could be used to evaluate the success of elimination programs by accurately estimating pathogen transmission rates.
Chiang et al.[13] (2018)	ML	Monitoring and providing feedback to breast cancer patients performing postoperative lymphatic rehabilitation exercises.	Validation of the system requires comparing the model with the gold-standard methods in practice.	The proposed model is more feasible than the other motion capture systems in practice.
Deribe et al.[14] (2018)	ML	Estimating prevalence and geographical distribution of Podoconiosis in Cameroon using ML predictive model.	<ul style="list-style-type: none"> <li>• Data collection may have introduced geographical bias to the study.</li> <li>• Some confounders were not accounted for as economic status and personal hygiene.</li> </ul>	Accurate estimation of prevalence guide eradication and treatment plans of endemic communicable disease.
Eneanya et al.[15] (2018)	ML	Mapping lymphatic filariasis risk area in Nigeria using ML predictive model.	-	Accurate mapping of the risk area is critical for the vector eradication campaigns.
Fu et al.[16] (2018)	ML	Detection of lymphedema status based on real-time symptom report.	<ul style="list-style-type: none"> <li>• The study depended on self-reported lymphedema status rather medical records.</li> <li>• Expanding the spectrum of data to include lymph volume is required to train and improve the algorithm predictive ability.</li> </ul>	The proposed model detected lymphedema with an accuracy, sensitivity, and specificity of >90%
Eneanya et al.[15] (2019)	ML	Mapping the prevalence of lymphatic filariasis in Nigeria.	<ul style="list-style-type: none"> <li>• Selection bias towards more accessible sampling sites.</li> <li>• The nocturnal nature of the blood test may have confounded the results.</li> </ul>	Accurate prediction of prevalence is essential for mass treatment campaigns.
Kistenev et al.[18] (2019)	ML	Diagnosis and staging of lymphedema by estimating collagen disorganization using mltiphoton imaging and ML.	<ul style="list-style-type: none"> <li>• The sensitivity and specificity of the test were not reported.</li> <li>• The ability of detecting preclinical lymphedema was not tested.</li> </ul>	The proposed model diagnosed lymphedema with a 96% accuracy.
Agarwal et al.[23] (2019)	Robotics	Robotic-assisted surgery for endometrial cancer was associated with less incidence of postoperative lymphedema than open surgery.	• A retrospective study. Stronger evidence should be obtained from an RCT.	Robotic-assisted surgical staging for uterine cancer and is associated with fewer short-term and long-term complications.
Mayfield et al.[19] (2020)	ML	Estimating prevalence of lymphatic filariasis in Samoa by using a combination of geostatistics and ML.	• The data used to train the model were not randomly sampled which may bias the predictions.	Predicting prevalence of lymphatic filariasis is critical for the mass-treatment campaigns in endemic regions.

Table 1. (Continued)

Author and Date	Description of AI	Clinical Relevance	Technical Challenges/Study Flaws	Summary/Comments
Chausiaux et al.[20] (2021)	ML	Evaluation of foot volume to detect lymphedema.	• The device was tested on healthy volunteers and for validation, it should be tested on patients with lower limb edema.	The proposed model is more feasible and as accurate as the standard methods.
Kwarteng et al.[21] (2021)	ML, DL	Recognizing risk factors of lymphatic filariasis in Ghana.	• The proposed model did not consider important risk factors that could improve predictions.	The findings of the study are critical for vector elimination and treatment campaigns.
Notash et al.[22] (2021)	ML	Measurement of lymphedema arm volume.	• The study did not report sensitivity or specificity of the proposed model.	The proposed model is more feasible than standard methods.

AI, artificial intelligence; FM, fuzzy model; ML, machine learning; DL, deep learning; RCT, randomized clinical trial.

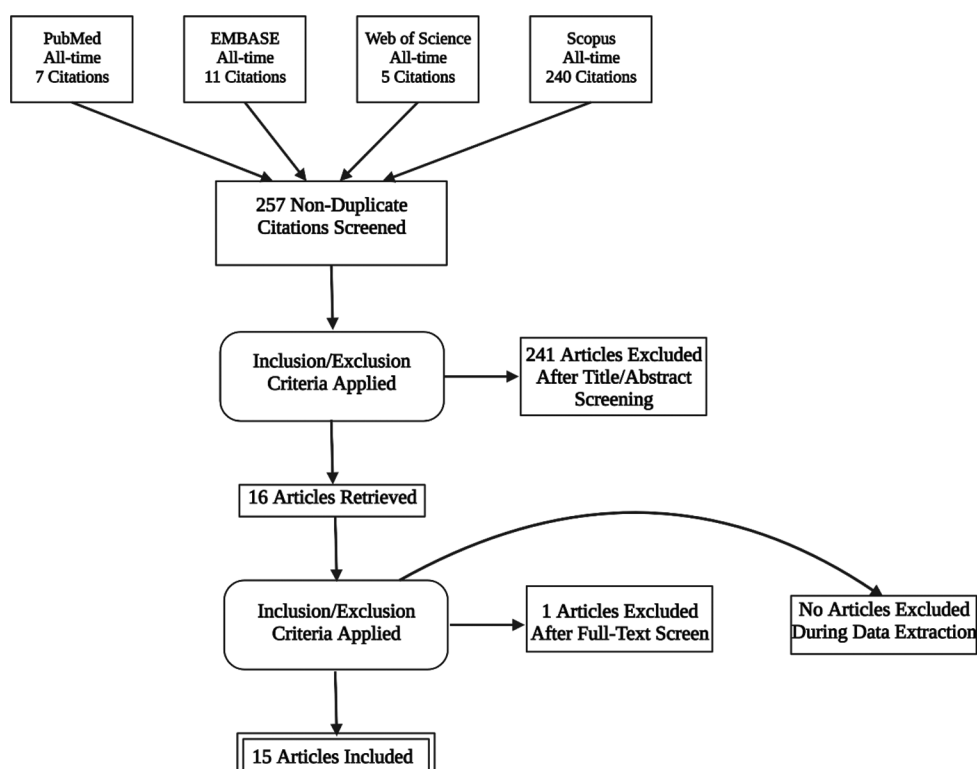


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis flow chart diagram. Created with biorender.com.

WB is a nematode that causes 90% of LF cases worldwide [25]. *Brugia malayi* and *Brugia timori* are other nematode worms that are less common than WB and cause 10% of LF cases [25]. WB infects humans, who are the exclusive hosts, through mosquito bites. The larvae enter the human body through the bite wound and migrate to the lymphatic vessels. After 6–12 months, the larvae mature into adult worms and reproduce in the lymphatic vessels resulting in microfilariae (MF). MF, then, moves to the patient's blood vessels, with a nocturnal preference to the superficial vasculature, and infects the mosquitoes. MF, then, matures into larvae inside the mosquito and the cycle repeats (Figure 2) [27].

The economic burden of LF is heavy and exclusively limited to the developing countries that already lack resources and potent healthcare strategies [27]. Although the World Health

Organization (WHO) set a goal in 1997 to completely eliminate the disease by the year 2020, 100 millions of people are still at risk and 10 millions are infected, disfigured, or disabled [3,25]. Eradication of LF requires long years of extensive efforts, scientific research, and ample resources [28]. Since 2000, the WHO has delivered 7.7 billion chemotherapy doses as a part of its mass drug administrations (MDAs) in the endemic countries [3]. These campaigns aim to achieve a target of elimination as a public health problem (EPHP) in the endemic areas. EPHP is achieved when a target of 1% MF prevalence is reached. Unfortunately, achieving EPHP did not eliminate the disease in many endemic areas. The transmission appears to be controlled with many factors that are difficult to predict, leading to the elimination targets and strategies being revisited by the experts [29].

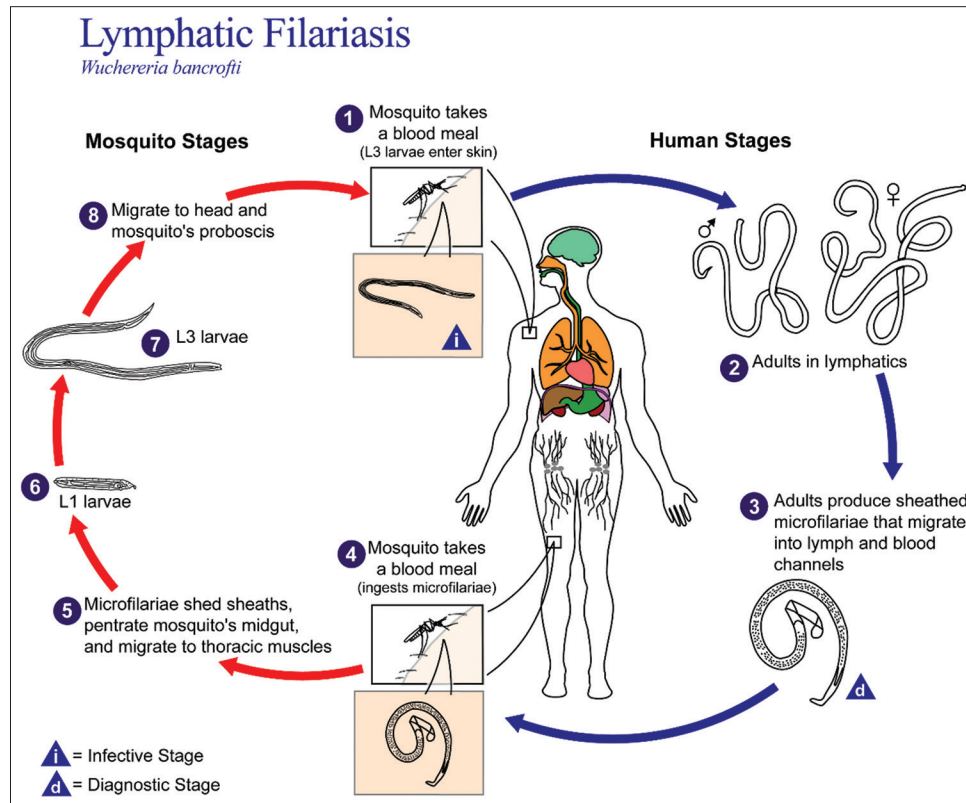


Figure 2. *Wuchereria bancrofti* life cycle.

As a result, attention is now turning to AI as a potential solution to LF eradication challenges. AI's predictive and pattern recognition powers can be used to estimate the prevalence, geographical distribution, and risk factors of LF. In addition, AI can monitor the response to MDAs and predict the remaining endemic pockets. Arnold *et al.* pioneered the first AI model using ensemble ML to monitor tropical disease transmission, including LF, from quantitative analysis of antibody levels [12]. Ensemble ML depends on a set of classifier algorithms to achieve higher predictive performance than any ML algorithm alone [30]. The advantage of ensemble ML is that it reduces the risk of choosing a single classifier algorithm with poor performance [30]. The ensemble algorithm used by Arnold *et al.* is called "super learner" and it utilizes cross-validation to combine many different algorithms into a single prediction [12]. Arnold *et al.* employed multiple cross-sectional surveys to obtain age-dependent IgG curves before and after MDAs. The antibody curves are then fit in ensemble ML to control potential confounders by including additional covariates. The method provided a sensitive and accurate measure of changes in transmission, especially in young children. The results obtained from the model suggest that quantitative IgG levels can be used for pathogen exposure monitoring in populations with very high or very low transmissions [12]. Furthermore, this model proved that IgG level could be effectively implemented as an additional measure of EPHP to avoid recurrence of transmission in endemic areas following MDAs.

Enyanea *et al.* used pre-intervention occurrence data from survey sites across Nigeria, environmental and geographical data,

quantile regression forest ML model, and ensemble ML to map the ecological niche of LF, estimate the baseline prevalence, and quantify the number of people at risk of infection [15,17]. The ensemble model that was used was built using seven algorithms, namely, generalized linear model, surface range envelopes, multivariate additive regression splines, artificial neural networks, generalized boosted regression modeling, random forest, and maximum entropy ecological niche models. These algorithms were fitted in a computational framework called Biodiversity Modeling. Their maps revealed that northern Nigeria was more environmentally suitable for LF than the rest of Nigeria. In addition, the model predicted that 3.3 million people are infected, while 110 million are at risk of infection [15,17]. These models provide the decision-makers with accurate information to guide the elimination efforts and become invaluable in limited-resource settings.

Podoconiosis, also known as endemic non-filarial elephantiasis, is a neglected tropical disease caused by exposure of bare feet to red clay soil [31]. The mineral particles from the soil trigger an inflammatory response in genetically susceptible people, leading to lymphedema and fibrosis [31,32]. Podoconiosis has the potential to be quickly eradicated by promoting footwear and general cleanliness; however, confident estimations of the global burden of the disease and its geographical distribution are lacking [33]. Deirbe *et al.* used two ML algorithms, namely, generalized boosted regression tree modeling and random forest, and geostatistical analysis to predict the burden and distribution

of podoconiosis in Cameron. The model revealed that the disease is widely distributed throughout the country with over 5 million people at risk [14]. As in any eradicable disease, mapping the disease distribution allows for directing preventive measures to the population at risk.

#### 4.2. Early detection/diagnosis

The clinical course of lymphedema is slow and develops over months to years [5]. The pathophysiology of lymphedema involves cycles of fluid accumulation and inflammation resulting in fibrosis and irreversible lymphedema [34]. Clinically, lymphedema starts with subclinical volume accumulation (Stage 0); in this stage, the patients may complain of limb heaviness. However, most patients are asymptomatic. If the left untreated, this can progress to clinically evident lymphedema that resolves completely with prolonged limb elevation (Stage 1). Subsequently, intradermal fibrosis occurs due to chronic inflammation, resulting in a reduced ability of the skin to indent (Stage 2). In this stage, patients present with clinically evident lymphedema that does not resolve with limb elevation. Stage 2 is characterized by a positive Stemmer sign (inability to pinch the dorsal skin of fingers) and increased susceptibility to skin infections. Finally, further fibrosis and fluid accumulation result in lymphostatic elephantiasis (Stage 3). In this stage, patients present with little or no pitting and the Stemmer sign becomes more evident. Lymphostatic elephantiasis is characterized by recurrent cellulitis and a small yet real risk of life-threatening complications as lymphangiosarcoma, lymphoma, and Kaposi sarcoma [34-36].

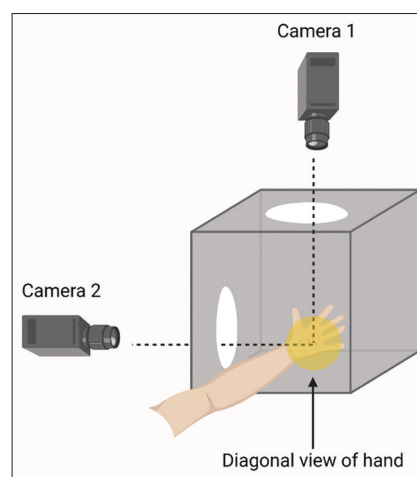
Although lymphedema is considered incurable, early intervention can prevent or slow progression to irreversible stages [34]. A meta-analysis conducted by Shah *et al.* demonstrated that early detection and intervention were associated with favorable outcomes [36]. However, this endeavor is challenged by the subtle nature of the early lymphedema that makes it clinically undetectable even for the most experienced eyes. In addition, the ability of the traditional edema evaluation techniques, such as water displacement method and circumferential measurements, to detect early lymphedema is questionable [18]. Although the last few years have witnessed the introduction of new diagnostic models for the early detection, including magnetic resonance imaging, bioelectrical impedance analysis, infrared perometry, and dual-energy X-ray absorptiometry, most of these models lack technical and economic feasibility. Moreover, staging lymphedema is currently largely subjective, leading to vagueness and uncertainty, which add to the complexity of management. This is where AI solutions can be effectively implemented in lymphedema care by offering feasible and accurate methods for early detection, diagnosis, staging, and rehabilitation.

The first model was proposed by Vicentini *et al.*, who used an FM to classify the risk and severity of lymphedema objectively. The proposed fuzzy system used clinical and functional criteria that the Brazilian Society of Lymphology recommended as input variables using severity scales as “low, intense,” and “low, partial,

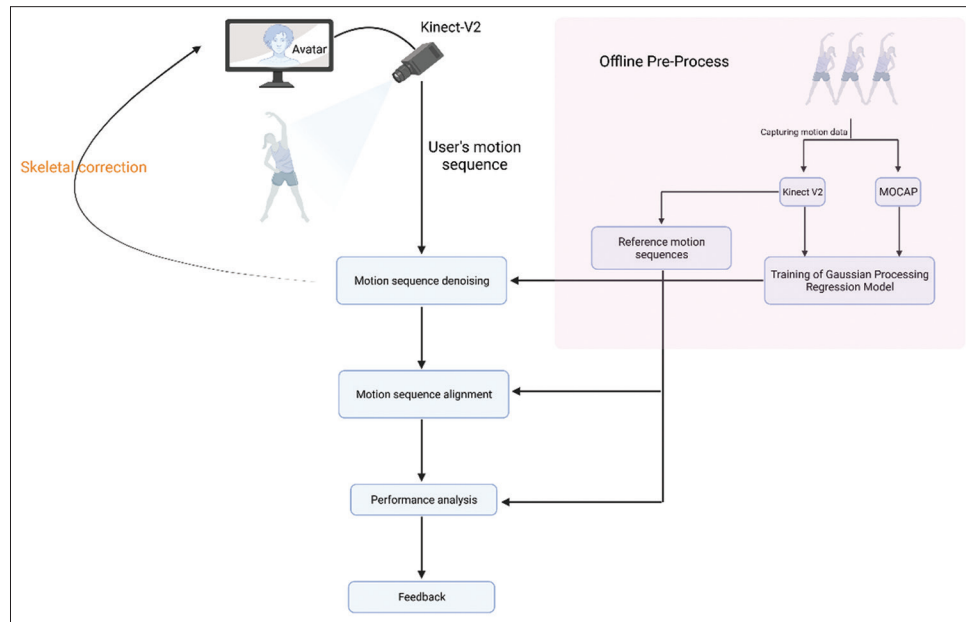
total.” These criteria are pitting, skin changes, Stemmer sign, reversibility, and joint involvement. The model uses a group of “IF-THEN” fuzzy rules to quantitatively assess the lymphedema stage while considering the overlap between classes. This model differs from the conventional score systems in that it permits the overlap between different classes as it accepts different degrees of severity for every input. This means that the model reports its results qualitatively and quantitatively. This fuzzy assessment allows standardization of the rehabilitation program and the degree of patient assistance for each stage, improving the outcomes substantially [24].

Moreira *et al.* tested three ML algorithms, namely, Fisher Linear Discriminant Analysis, the Naive Bayes Classifier, and Support Vector Machines (SVMs) to preclinically detect lymphedema in breast cancer survivors [11]. BCRL causes significant impairment of upper body function. Therefore, detecting subtle impairment of upper body function can help in the preclinical detection of lymphedema. Kinect features of upper body motion are captured, and a supervised ML algorithm uses the extracted data to build a predictive classification model that can accurately detect subclinical lymphedema changes [11]. The best performance was obtained using the SVM classifier, with a miss-classification error of 0.19.

Another promising model was described by Kestenev *et al.* A combination of multi-photon imaging and SVM was used to build a model that can diagnose lymphedema with high accuracy based on estimating collagen disorganization in the tissue. Two-photon images were obtained from patients with stage 2 lymphedema and healthy volunteers. Mathematical models from the images were built using feature extraction methods. The characteristics of collagen fibers were, then, evaluated using variable vision edge detector algorithms including Sobel operator, Canny edge detector, Laplacian of Gaussian, and mathematical morphology. Collagen structural disorganization was then quantified using gradient image analysis. Finally, a trained SVM predicted lymphedema status based on the data



**Figure 3.** Horizontal-vertical image scanning (HVIS) tool described by Notash *et al.* [22] to obtain accurate arm volume measurements Created with biorender.com.



**Figure 4.** Scheme of a Kinect-based in-home exercise system described by Chiang *et al.* [13] Created with biorender.com.

extracted from the images. Although the model's ability to detect preclinical lymphedema was not tested, the concept of diagnosing lymphedema from tissue structure disorganization holds high promise in the early diagnosis [18].

BCRL can develop immediately and up to 20 years after surgery [4]. Therefore, breast cancer survivors should be continuously monitored for lymphedema signs to implement early intervention if necessary. Unfortunately, most patients will not seek medical attention until a noticeable swelling develops. At this stage, lymphedema is clinically evident (stage 1 or more), and the interventions are less effective, which leads to poor outcomes [37].

The recent advances in information and communication technologies allow patients to access many healthcare services in the comfort of their homes. Services such as video consultations, websites, and health applications are implemented to diagnose and manage a broad-spectrum of clinical conditions with high success rates [38]. Fu *et al.* used a combination of telehealth services and AI to create a tool for real-time detection of lymphedema [16]. In the proposed system, the patients use a web-based telehealth system to report their symptoms. An ANN used the data reported in the survey to predict lymphedema status. The system was able to predict lymphedema with an accuracy of 93.7%. Since the accuracy of the proposed tool is higher than the current methods in practice, this tool can significantly improve the outcomes for BCRL patients by achieving early lymphedema detection from home. Notash *et al.* [22] created a horizontal-vertical image scanning tool to obtain accurate arm volume measurements (Figure 3). An evolutionary ensemble feature selection learning comprising different base learners (K-nearest neighbors, SVM, adaptive neurofuzzy inference system, Decision Tree, and Naïve Bayes) was used to detect lymphedema using the obtained measurements with high accuracy.

### 4.3. Rehabilitation

Lymphatic rehabilitation exercises are one practical approach to treat lymphedema conservatively and an essential component of complete decongestive therapy. Performing the rehabilitation exercises correctly are vital to achieve positive outcomes. However, lymphedema exercises can be challenging to some patients and are usually performed under the supervision of physical therapists or nurses. Although several motion capture systems already exist, they are not practical for clinical use as they require the patient to wear a tight suit and perform the exercise in a particular room equipped with many cameras [13]. Therefore, a feasible system should be inexpensive, accurate in detecting patient's movement, usable at home, and provide interactive feedback to guide the patient. Chiang *et al.* [13] developed a system that uses a Kinect sensor and a motion capture system to capture the patient's movements while exercising (Figure 4). A probabilistic supervised ML framework (Gaussian process regression model) that was previously trained will, then, denoise the collected measurements before providing the patient with the feedback. The system guided patients with a risk of BCRL while performing their exercises. The system could accurately evaluate the patients' movements in real-time and provide the patients with instant feedbacks while performing the exercise.

### 4.4. Robotic-assisted surgery

Robotic-assisted surgery is becoming more popular in the field of gynecologic oncology. It offers a safe and effective approach for staging and treatment of cervical and endometrial cancer [10]. In general, robotic-assisted surgery for gynecological cancers is considered not different or safer regarding postoperative complications [10]. One retrospective study that compared outcomes of robotic-assisted hysterectomy

for cervical cancer versus open surgery reported a statistically significant lower incidence of postoperative lower limb lymphedema [9]. Another retrospective study compared robotic-assisted surgery for endometrial cancer versus open surgery reported the exact lower incidence of postoperative lymphedema [23]. Unfortunately, strong evidence from randomized clinical trials is still lacking.

## 5. Conclusion

ML can accelerate the eradication of tropical lymphedema. The predictions obtained from ML models guide the eradication campaigns and provide the decision-makers with valuable information on how and where their resources should be directed. Moreover, ML can monitor the elimination and predict the remaining pockets of infection in endemic regions. Variable models were described for the early detection of lymphedema to improve the outcomes. Combining ML models with telehealth services allow patients at risk of lymphedema to closely monitor the development of lymphedema in the comfort of their homes. ML was used along with a movement capturing system to monitor patients while exercising and provide instant feedback. Finally, robotic-assisted surgery for gynecological malignancies can lower the risk of post-operative lower limb lymphedema.

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Figure 2 is in the public domain of Center of Disease Control. The image was released in the public domain with ID#3425 and is free of any copyright restrictions. Graphical abstract and Figures 1, 3, and 4 were created using biorender.com.

## Conflict of Interest

The authors report no conflicts of interest.

## References

- [1] Warren AG, Brorson H, Borud LJ, Slavin SA. Lymphedema: A Comprehensive Review. *Ann Plast Surg* 2007;59:464-72.
- [2] Wheeler ES, Chan V, Wassman R, Rimoin DL, Lesavoy MA. Familial Lymphedema Praecox: Meige's Disease. *Plast Reconstr Surg* 1981;67:362-4.
- [3] World Health Organization. Lymphatic Filariasis: Key Facts. Geneva: World Health Organization; 2021.
- [4] Petrek JA, Senie RT, Peters M, Rosen PP. Lymphedema in a Cohort of Breast Carcinoma Survivors 20 Years After Diagnosis. *Cancer* 2001;92:1368-77.
- [5] The Diagnosis and Treatment of Peripheral Lymphedema. Consensus Document of the International Society of Lymphology. *Lymphology* 2003;36:84-91.
- [6] Oremus M, Dayes I, Walker K, Raina P. Systematic Review: Conservative Treatments for Secondary Lymphedema. *BMC Cancer* 2012;12:6.
- [7] Deo RC. Machine Learning in Medicine. *Circulation* 2015;132:1920-30.
- [8] Noorbakhsh-Sabet N, Zand R, Zhang Y, Abedi V. Artificial Intelligence Transforms the Future of Health Care. *Am J Med* 2019;132:795-801.
- [9] Zanagnolo V, Minig L, Rollo D, Tomaselli T, Aletti G, Bociolone L, et al. Clinical and Oncologic Outcomes of Robotic Versus Abdominal Radical Hysterectomy for Women with Cervical Cancer: Experience at a Referral Cancer Center. *Int J Gynecol Cancer* 2016;26:568-74.
- [10] Krill LS, Bristow RE. Robotic Surgery: Gynecologic Oncology. *Cancer J* 2013;19:167-76.
- [11] Moreira R, Magalhães A, Oliveira HP. A Kinect-based System to Assess Lymphedema Impairments in Breast Cancer Patients. In: *Lecture Notes in Computer Science (Including Subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics)*. Berlin, Germany: Springer; 2015. p. 228-36.
- [12] Arnold BF, van der Laan MJ, Hubbard AE, Steel C, Kubofcik J, Hamlin KL, et al. Measuring Changes in Transmission of Neglected Tropical Diseases, Malaria, and Enteric Pathogens from Quantitative Antibody Levels. *PLoS Negl Trop Dis* 2017;11:e0005616.
- [13] Chiang AT, Chen Q, Wang Y, Fu MR. Kinect-based in-home Exercise System for Lymphatic Health and Lymphedema Intervention. *IEEE J Transl Eng Health Med* 2018;6:4100313.
- [14] Deribe K, Cano J, Njouendou AJ, Eyong ME, Beng AA, Giorgi E, et al. Predicted Distribution and Burden of Podoconiosis in Cameroon. *BMJ Global Health* 2018;3:730.
- [15] Eneanya OA, Cano J, Dorigatti I, Anagbogu I, Okoronkwo C, Garske T, et al. Environmental Suitability for Lymphatic Filariasis in Nigeria. *Parasit Vectors* 2018;11:513.
- [16] 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.
- [17] Eneanya OA, Fronterre C, Anagbogu I, Okoronkwo C, Garske T, Cano J, et al. Mapping the Baseline Prevalence of Lymphatic Filariasis Across Nigeria. *Parasit Vectors* 2019;12:440.
- [18] Kistenev YV, Borisov AV, Nikolaev VV, Vrazhnov DA, Sandykova EA, Kurochkina OS. Application of Multiphoton Imaging and Machine Learning to Lymphedema Tissue Analysis. *Biomed Optics Exp* 2019;10:3353-68.
- [19] Mayfield HJ, Sturrock H, Arnold BF, Andrade-Pacheco R, Kearns T, Graves P, et al. Supporting Elimination of Lymphatic Filariasis in Samoa by Predicting Locations of Residual Infection using Machine Learning and Geostatistics. *Sci Rep* 2020;10:20570.
- [20] Chausiaux O, Williams G, Nieznański M, Bagdu A, Downer P, Keyser M, et al. Evaluation of the Accuracy of a Video and Ai Solution to Measure Lower Leg and Foot Volume. *Med Dev Evid Res* 2021;14:105-18.



- [21] Kwarteng EV, Andam-Akorful SA, Kwarteng A, Asare DB, Quaye-Ballard JA, Osei FB, Duker AA. Spatial Variation in Lymphatic Filariasis Risk Factors of Hotspot Zones in Ghana. *BMC Public Health* 2021;21:230.
- [22] Notash AY, Bayat P, Haghghat S, Notash AY. Evolutionary Ensemble Feature Selection Learning for Image-based Assessment of Lymphedema Arm Volume. *Concurrency and Computation: Practice and Experience*. United States: John Wiley & Sons Ltd.; 2021.
- [23] Agarwal R, Rajanbabu A, Goel G, Unnikrishnan UG. A Comparison of the Clinical Outcomes in Uterine Cancer Surgery After the Introduction of Robotic-assisted Surgery. *J Obstet Gynaecol India* 2019;69:284-91.
- [24] Vicentini P, Del Perez MC, Araujo E. Fuzzy Lymphedema Assessment Based on Clinical and functional Criteria: IEEE International Conference on Fuzzy Systems, United States: IEEE; 2011. p. 2708-13.
- [25] Lourens GB, Ferrell DK. Lymphatic Filariasis. *Nurs Clin North Am* 2019;54:181-92.
- [26] Grada AA, Phillips TJ. Lymphedema: Pathophysiology and Clinical Manifestations. *J Am Acad Dermatol* 2017;77:1009-20.
- [27] Centers for Disease Control and Prevention. Lymphatic Filariasis: Epidemiology and Risk Factors. United States: Centers for Disease Control and Prevention; 2021.
- [28] Huang X, Deng X, Kou J, Liu X, Wang H, Cheng P, et al. Elimination of Lymphatic Filariasis in Shandong Province, China, 1957-2015. *Vector Borne Zoonotic Dis* 2020;20:875-81.
- [29] Davis EL, Reimer LJ, Pellis L, Hollingsworth TD. Evaluating the Evidence for Lymphatic Filariasis Elimination. *Trends Parasitol* 2019;35:860-9.
- [30] Polikar R. Ensemble Based Systems in Decision Making. *IEEE Circ Syst Mag* 2006;6:21-44.
- [31] Korevaar DA, Visser BJ. Podoconiosis, a Neglected Tropical Disease. *Neth J Med* 2012;70:210-4.
- [32] Price EW, Bailey D. Environmental Factors in the Etiology of Endemic Elephantiasis of the Lower Legs in Tropical Africa. *Trop Geogr Med* 1984;36:1-5.
- [33] Deribe K, Cano J, Trueba ML, Newport MJ, Davey G. Global Epidemiology of Podoconiosis: A Systematic Review. *PLoS Negl Trop Dis* 2018;12:e0006324.
- [34] Lawenda BD, Mondry TE, Johnstone PA. Lymphedema: A Primer on the Identification and Management of a Chronic Condition in Oncologic Treatment. *CA Cancer J Clin* 2009;59:8-24.
- [35] Ruocco V, Schwartz RA, Ruocco E. Lymphedema: An Immunologically Vulnerable Site for Development of Neoplasms. *J Am Acad Dermatol* 2002;47:124-7.
- [36] Shah C, Arthur DW, Wazer D, Khan A, Ridner S, Vicini F. The Impact of Early Detection and Intervention of Breast Cancer-related Lymphedema: A Systematic Review. *Cancer Med* 2016;5:1154-62.
- [37] McLaughlin SA, Bagaria S, Gibson T, Arnold M, Diehl N, Crook J, et al. Trends in Risk Reduction Practices for the Prevention of Lymphedema in the First 12 Months After Breast Cancer Surgery. *J Am Coll Surg* 2013;216:380-9.
- [38] Ekeland AG, Bowes A, Flottorp S. Effectiveness of Telemedicine: A Systematic Review of Reviews. *Int J Med Inform* 2010;79:736-71.

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