



# **SURGICAL OPTIONS FOR TREATMENT OF LYMPHEDEMA**

Alicia M. Jones, MHS, PA-C  
Memorial Sloan Kettering Cancer Center  
AAPA CME Conference

## Financial Disclosure

- No relevant financial relationship(s) exist

# Objectives



Recognize early symptoms/signs of lymphedema



Understand surgical options for lymphedema treatment



Determine a patient's candidacy for lymphatic surgery

# Overview of Lymphedema

- A chronic, progressive disease of the lymphatic system characterized by:
  - Swelling
  - Inflammation
  - Adipose hypertrophy
  - Fibrosis
- Primary vs. secondary



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Lymphedema  
affects  
5-6 million  
Americans



- 1 million Americans with Parkinson's Disease
  - <https://www.parkinson.org/Understanding-Parkinsons/Statistics>
- 3.1 million Americans with Inflammatory Bowel Disease (IBD)
  - <https://www.cdc.gov/mmwr/volumes/65/wr/mm6542a3.htm>
- 1.5 million Americans with Lupus
  - <https://www.lupus.org/resources/lupus-facts-and-statistics>
- 1 million Americans with Multiple Sclerosis (MS)
  - <https://www.nationalmssociety.org/About-the-Society/MS-Prevalence>

Dayan, Ly, Kataru, Mehrara. 2018. c. *Annu. Rev. Med.* 2018. 69:263-76



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# Overview of Lymphedema

- 1 in 6 patients undergoing treatment for solid tumor develop lymphedema
- Associated with:

<b>Breast</b> (most common cause in US)	Melanoma
Sarcoma	Gynecological tumors
Head and neck tumors	Urologic tumors

Cormier JN, Askew RL, Mungovan KS, et al. 2010. Lymphedema beyond breast cancer: a systematic review and meta-analysis of cancer-related secondary lymphedema. *Cancer* 116:5138-49

Petrek JA, Heelan MC. 1998. Incidence of breast carcinoma-related lymphedema. *Cancer* 83:2776-81



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# Lymphatic Anatomy

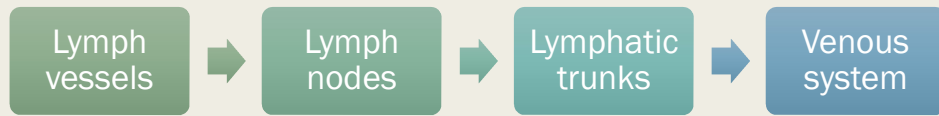
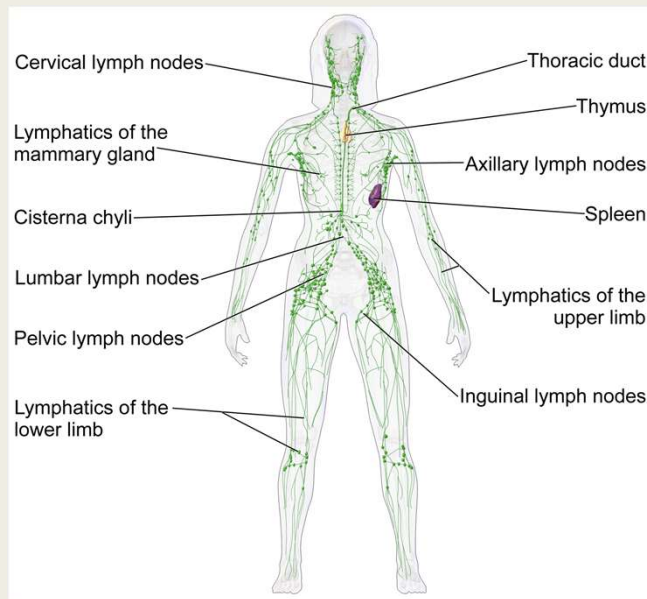
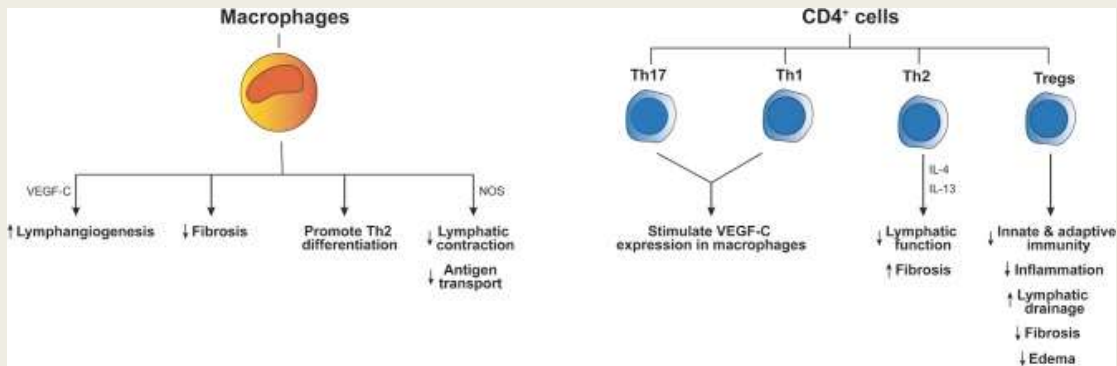
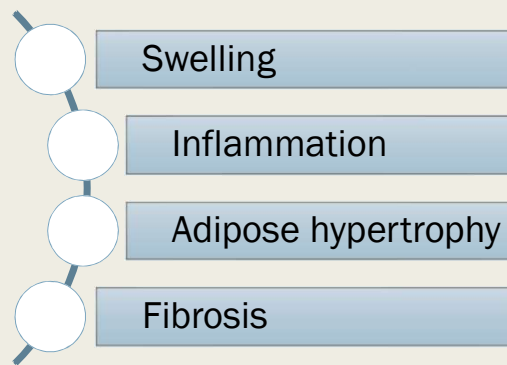


Photo: en.wikipedia.org/wiki/lymphatic\_system

# Pathophysiology of Lymphedema



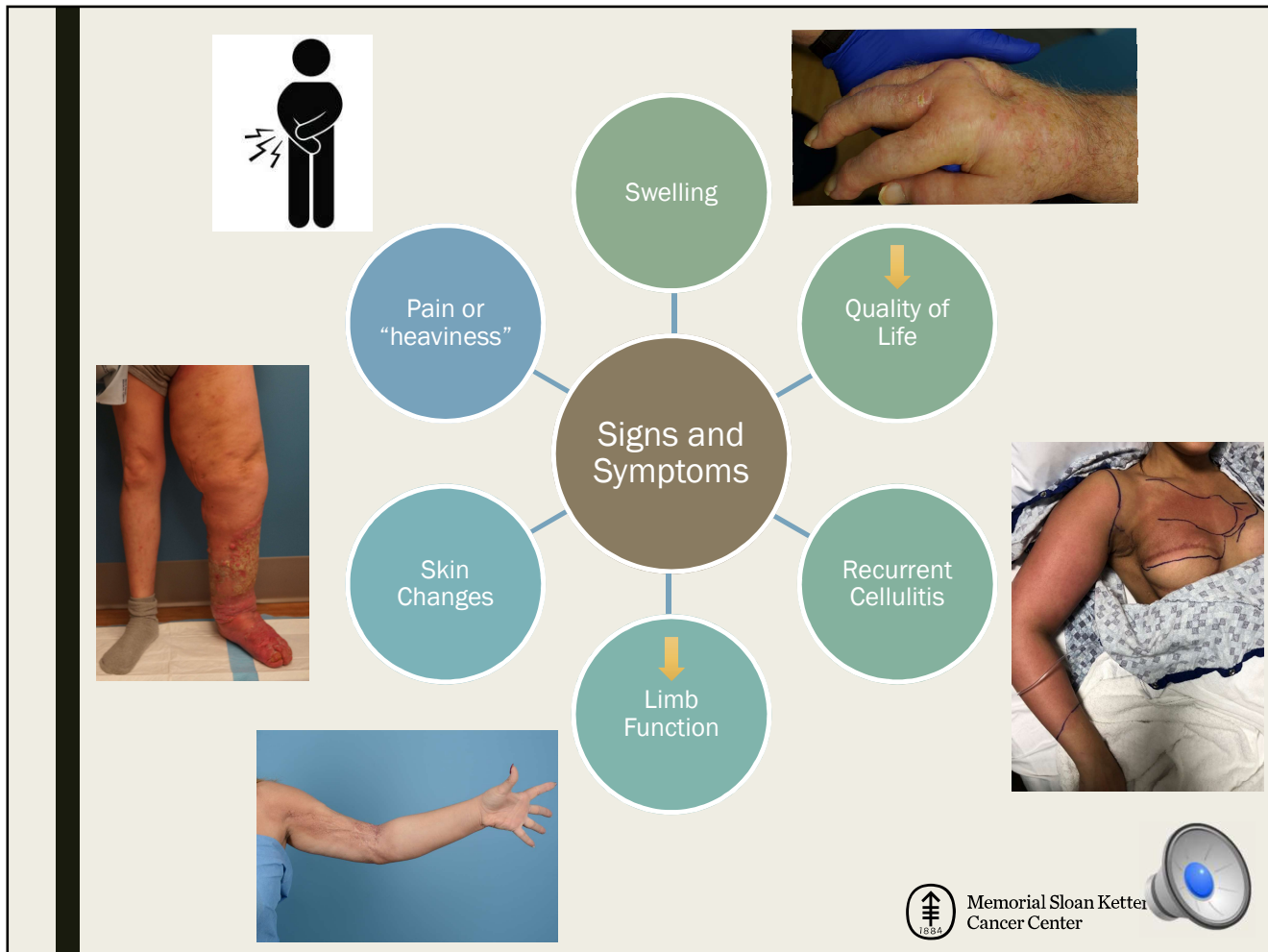


# Stages of Lymphedema

International Society of Lymphology (ISL) Staging



<b>Stage 0</b>	<b>Stage 1</b>	<b>Stage 2</b>	<b>Stage 3</b>
Left upper extremity	Right upper extremity	Right upper extremity	Right upper extremity



## Quality of Life Implications



Body image disturbances



Constant concern over cellulitis



Avoiding activities such as gardening, going to the beach, hiking, etc



Difficulty finding clothing that fits



Restrictions in ROM and mobility

TREATMENTS

## She Survived Breast Cancer, But Says A Treatment Side Effect 'Almost Killed' Her

February 19, 2018 · 4:50 AM ET

Heard on Morning Edition



PATTI NEIGHMOND



Virginia Harrod, an attorney and county prosecutor who lives in rural Kentucky, survived breast cancer, only to develop lymphedema, which sent her to the hospital three times with serious infections. A lymph node transplant helped restore her immune system.

Luke Sharrett for NPR

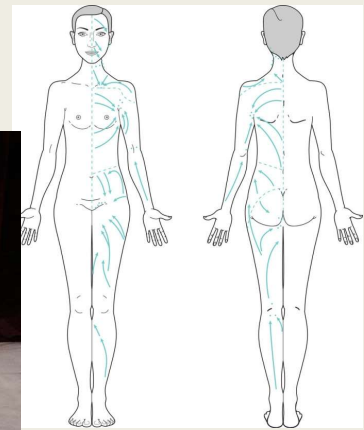
<https://www.npr.org/sections/health-shots/2018/02/19/585249587/she-survived-breast-cancer-but-says-a-treatment-side-effect-almost-killed-her>



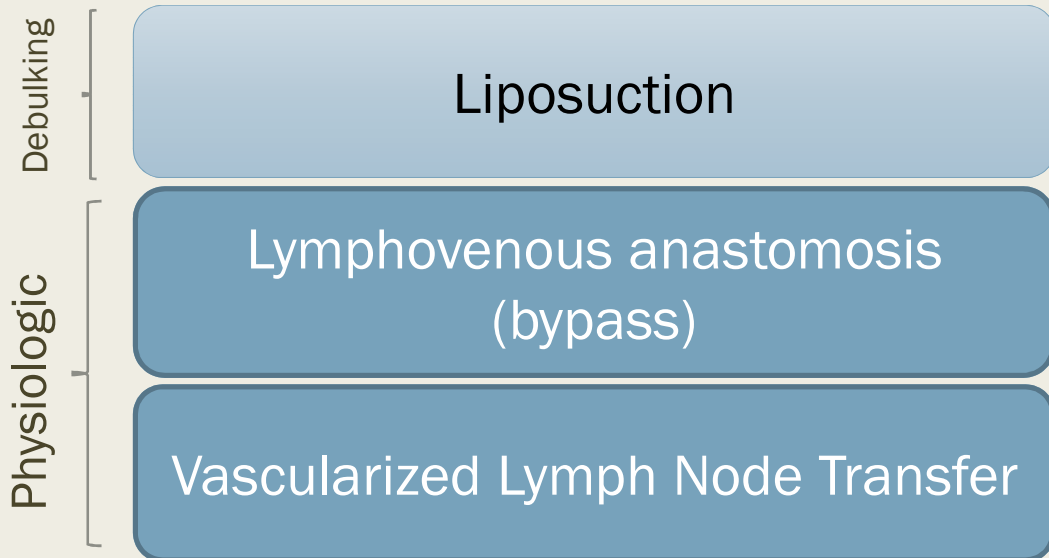
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# Conservative Management

- Complete Decongestive therapy
  - Lymphatic massage
  - Compression
- Weight loss and exercise



# Surgical Interventions

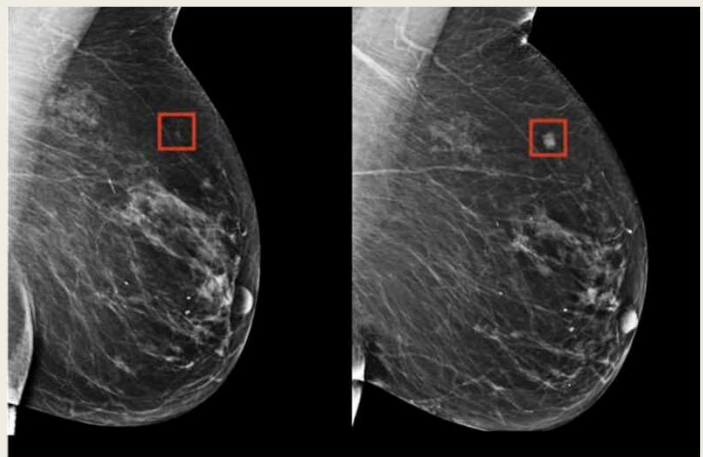


## Importance of Imaging workup

Before the late 1960s, breast cancer was diagnosed by clinical exam

Imaging dramatically improved survival through early detection.

Leading to development of biomarkers and targeting therapies.

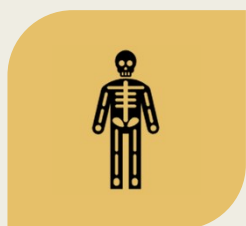


<https://www.rdmag.com/article/2019/05/new-deep-learning-model-finds-subtle-precursors-mammograms-predict-breast-cancer-risk>

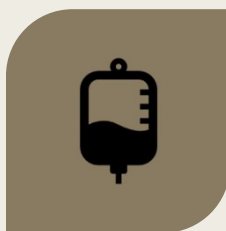


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# Imaging Workup



LYMPHOSCINTIGRAPHY

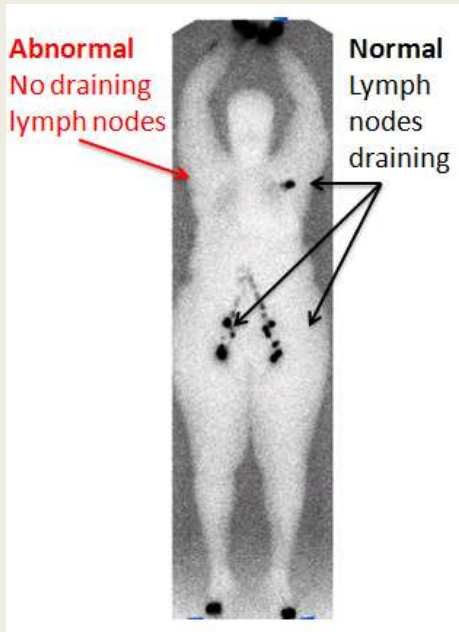


MRA



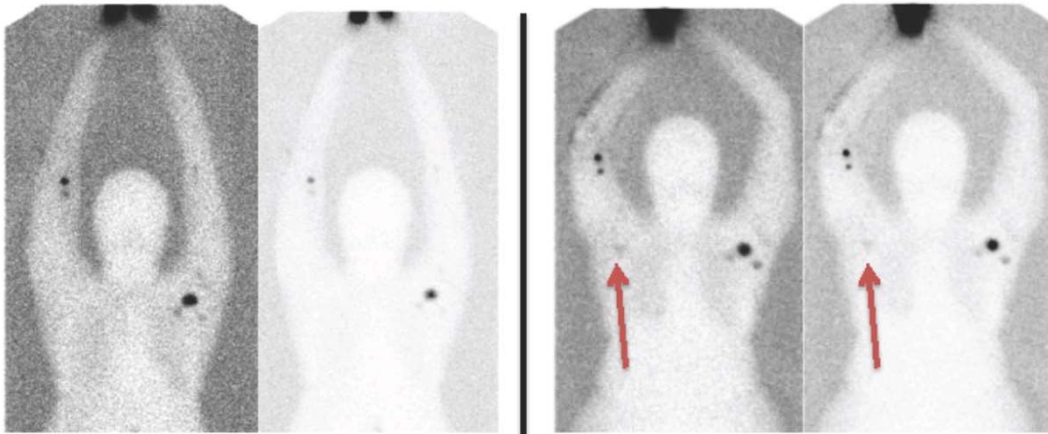
INDOCYANINE GREEN  
LYMPHANGIOGRAPHY  
(ICG)





## LYMPHOSCINTIGRAPHY

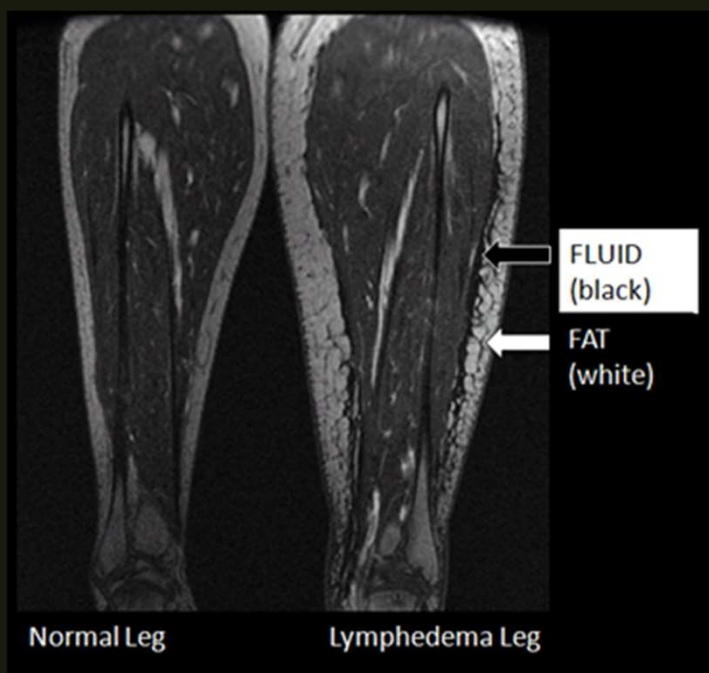
## Imaging- Lymphoscintigraphy



Pre Op

Post Op- showing uptake into the transplanted axillary lymphatic tissue

# MRA

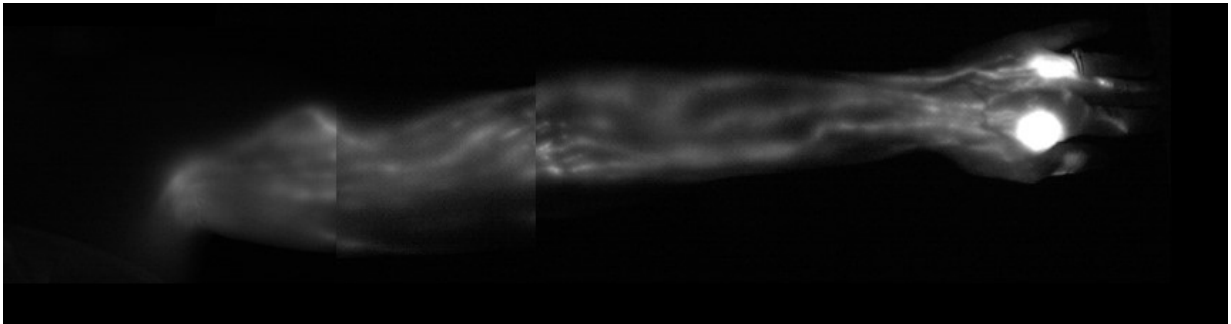




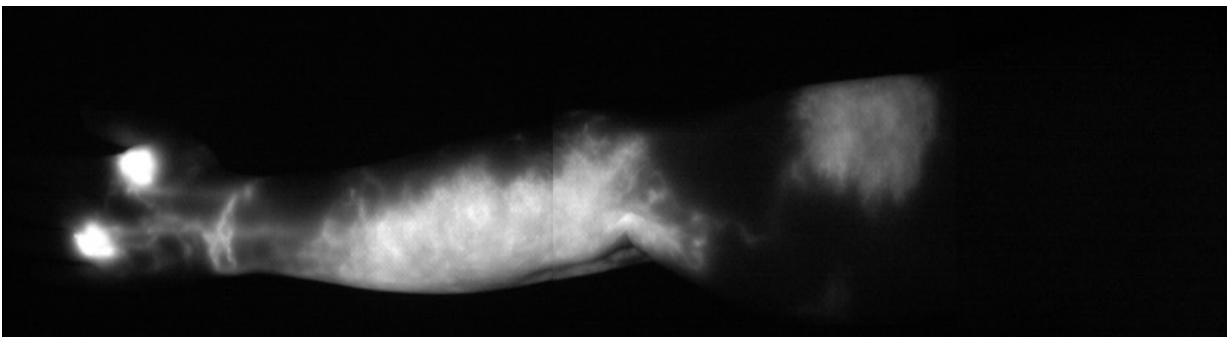
On clinical exam this patient is ISL stage 2

# ICG (indocyanine green lymphangiography)

Normal Lymphatics

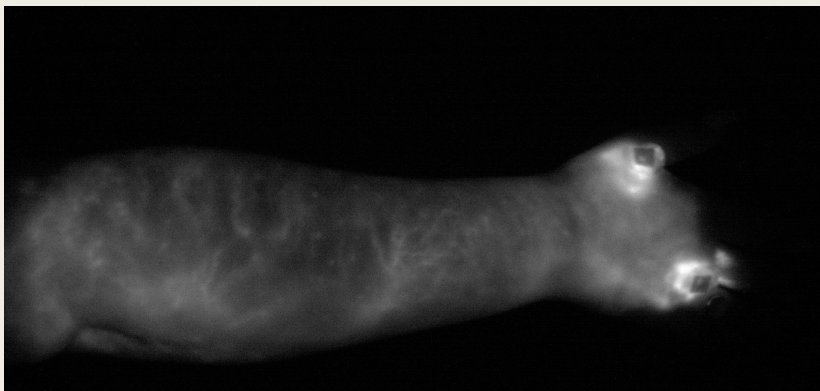


Abnormal Lymphatics – splash and stardust pattern





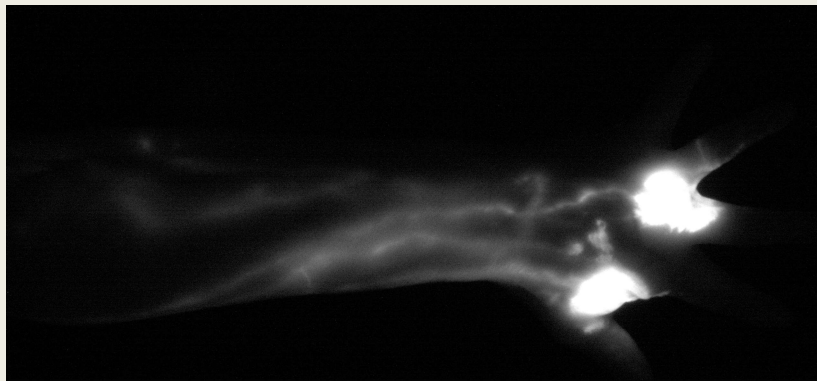
**Normal  
Lymphatics**  
(linear pattern)



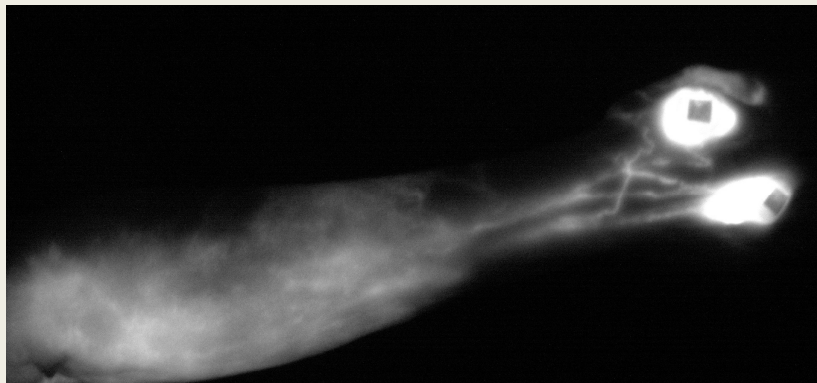
**Abnormal  
Lymphatics**  
(stardust pattern)



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**Normal  
Lymphatics**  
(linear pattern)

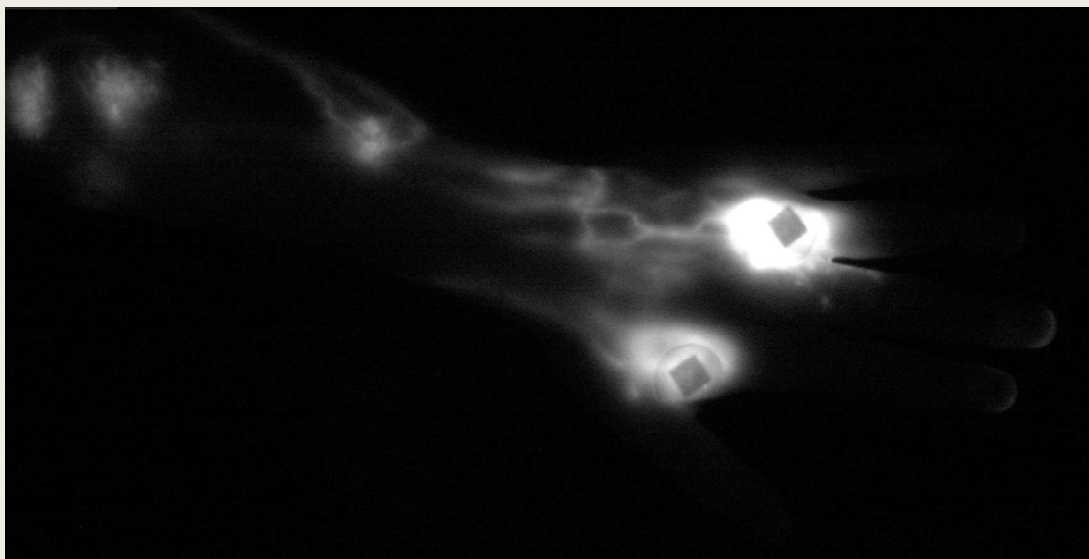


**Abnormal  
Lymphatics**  
(stardust pattern)



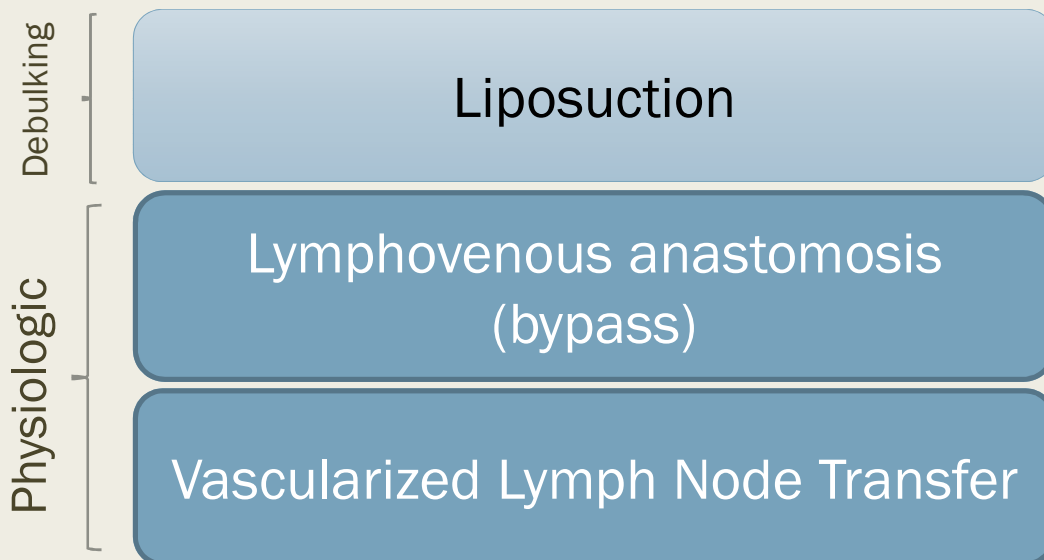
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**Abnormal  
Lymphatics**  
(splash pattern)





# Surgical Interventions



# Liposuction

- Debulking technique
- Indicated for more advanced, non-pitting lymphedema
- Patient must commit to lifetime compression for best results
- Outpatient surgery
- Complications: self limited paresthesias, wound healing issues



Preop

Postop



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# Liposuction



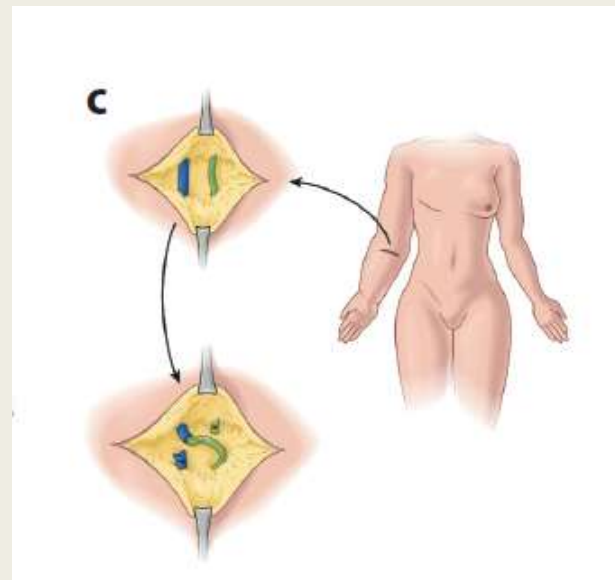
Hannson E., Brorson H. (2016) Liposuction of Lymphedema of the Extremities. In: Shiffman M., Di Giuseppe A. (eds) Liposuction. Springer, Berlin, Heidelberg

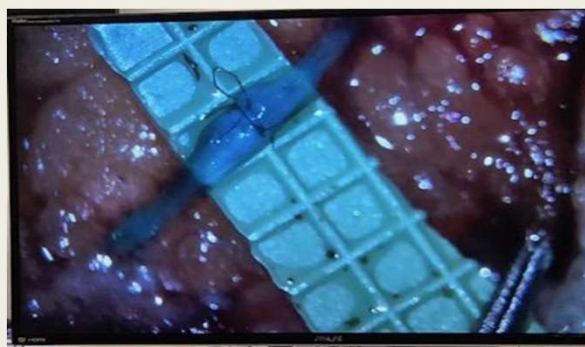
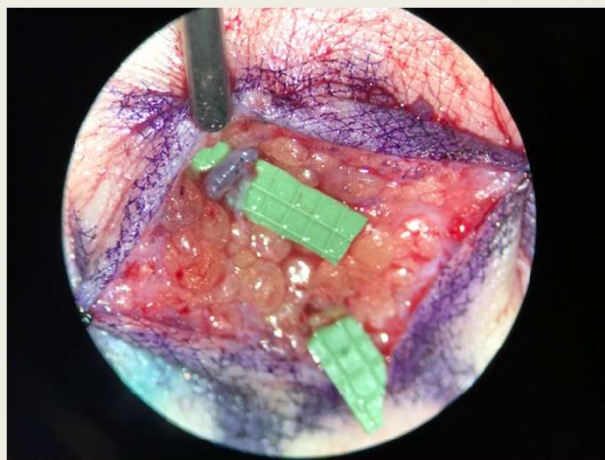


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## Lymphovenous anastomosis (Bypass)

- Microsurgical technique in which congested lymphatic is rerouted to nearby vein
- Most effective in early stage lymphedema
- Decrease excess fluid volume, does not address fat content
- Can also be done prophylactically



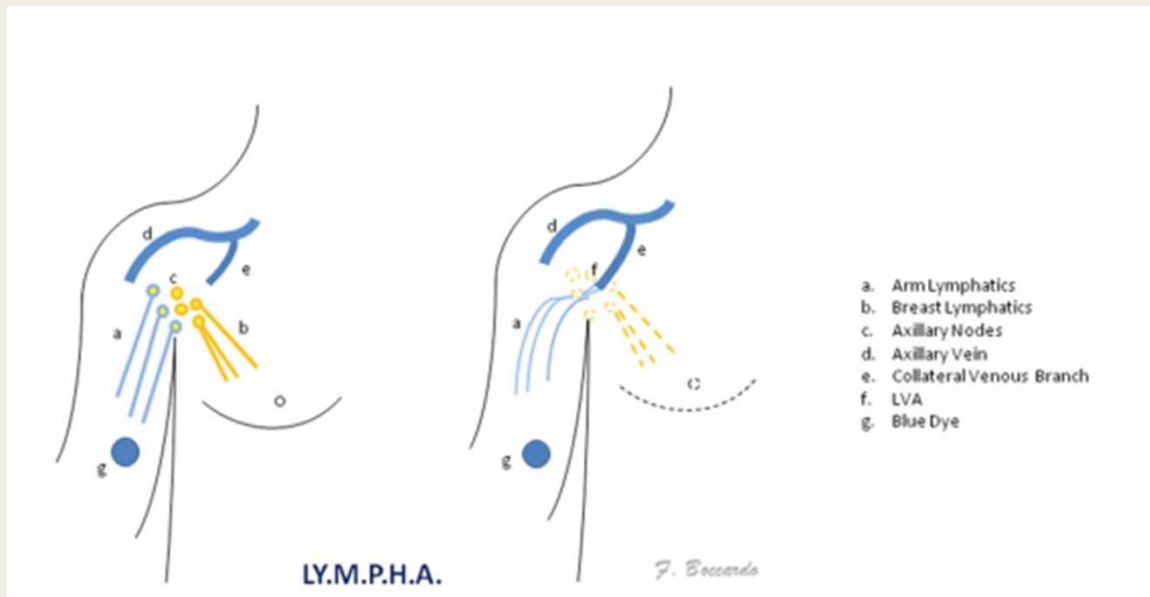


## Postop LVA

- 69 y/o female with history of right upper extremity lymphedema, related to breast cancer
- S/P LVA at two sites on right upper extremity
- Preop limb volume 48% difference
- 6 month postop 34% difference



# LYMPHA (LYmphatic Microsurgical Preventive Healing Approach)



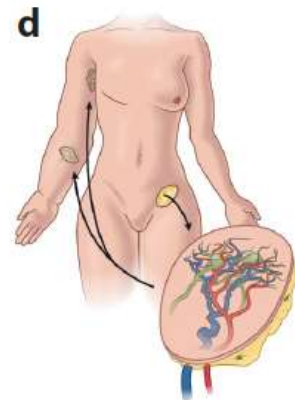
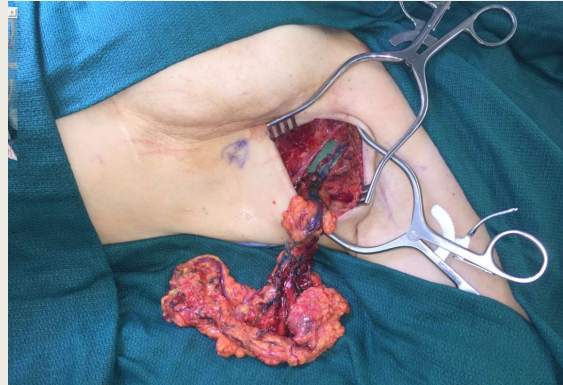
Boccardo et al. Lymphatic Microsurgical Preventing Healing Approach (LYMPHA) for Primary Surgical Prevention of Breast Cancer-Related Lymphedema: Over 4 years Follow up. *Microsurgery*, March 2014.



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## Vascularized Lymph Node Transfer/Transplant

- Microsurgical transfer of lymph nodes from one part of the body to the affected extremity
- Multiple donor site options
- Admission for 3-5 days
- Reverse lymphatic mapping
- Most effective in early stage lymphedema

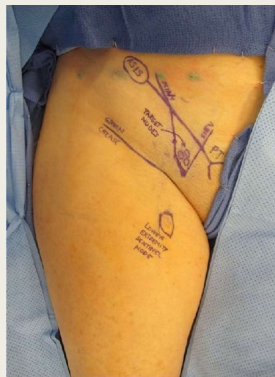




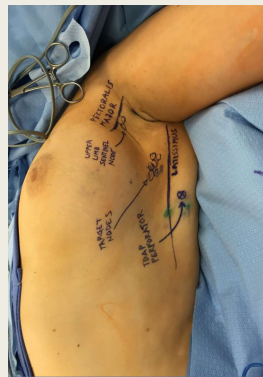
# Donor Sites



Supraclavicular



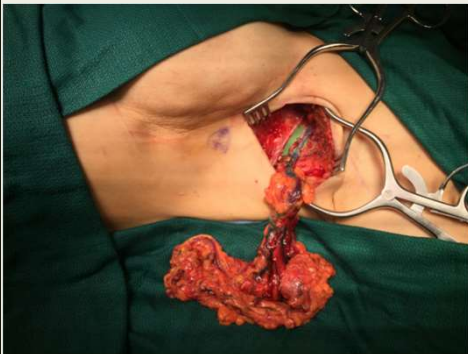
Groin



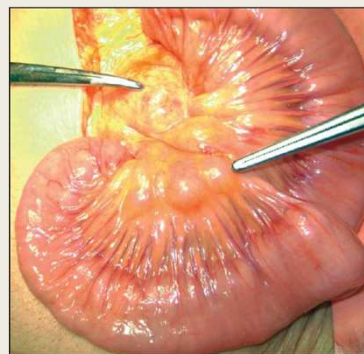
Axilla



Submental



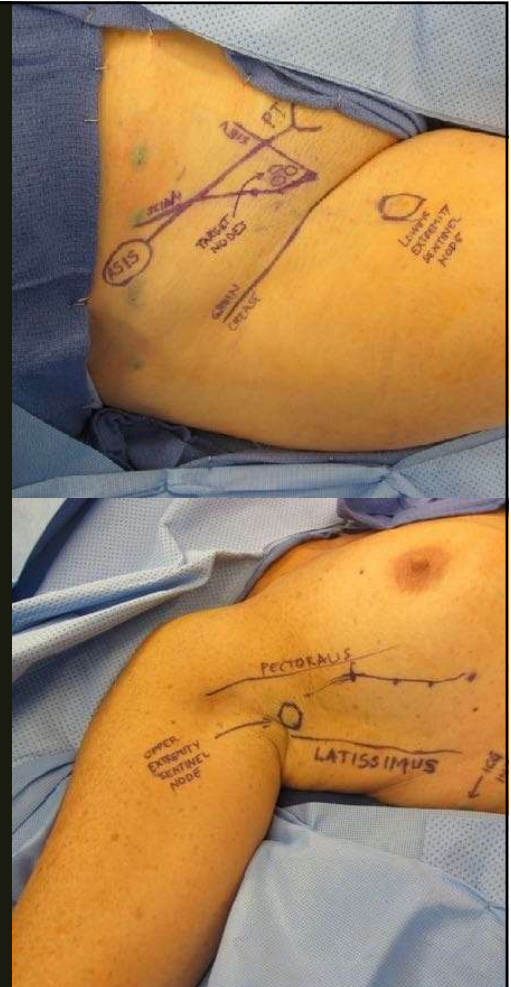
Omentum



Mesenteric

## Donor sites blood supply

- Axillary – thoracodorsal and lateral thoracic arteries
- Groin – superficial circumflex iliac artery
- Omentum – gastroepiploic vessels
- Supraclavicular – transverse cervical artery



## Ideal Candidate for lymph node transfer/transplant (LNT)

BMI < 30

No venous disease

No history of clotting issues

Early stage of lymphedema

Compliant with wrapping and therapy



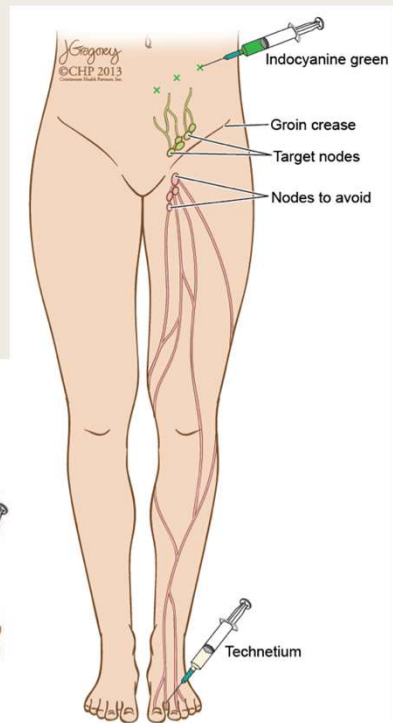
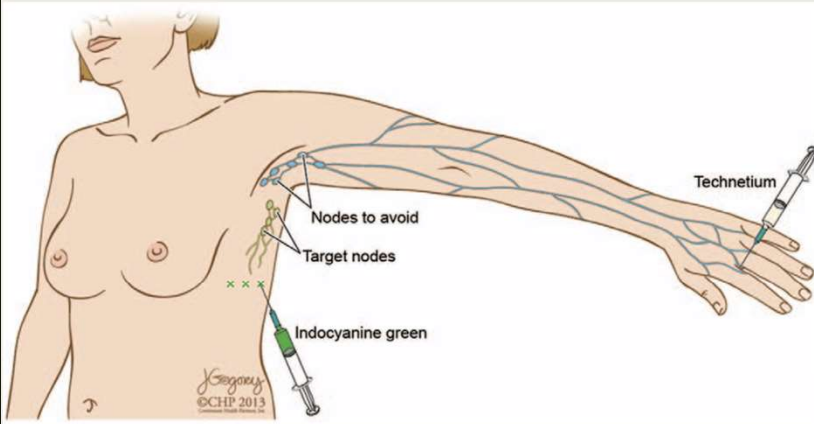
## How does it work?

- Lymphangiogenesis across a free flap
- Dr. Tobbia performed lymph node transplant in sheep
- Conclusion: lymphatic vessels grow into newly transplanted lymph nodes
  - *Lymph fluid removed from limb via pressure gradient*

Slavin SA, Upton J, Kaplan WD, et al. An investigation of lymphatic function following free-tissue transfer. *Plast Reconstr Surg.* 1997;99:730  
 Tobbia et al. Experimental Assessment of Autologous Lymph Node Transplantation as Treatment of Postsurgical Lymphedema. *Plastic and Reconstructive Surgery Journal.* September 2009. 777-786.

# How do you prevent donor site lymphedema?

## Reverse Lymphatic Mapping



Dayan & Smith, et al. "Reverse lymphatic mapping: a new technique to maximize safety in vascularized lymph node transfer." *Plastic and Reconstructive Surgery*. 2015, Jan, 135 (1): 277-85.

# The Risk of Donor Site Lymphedema is Real

**RECONSTRUCTIVE**

## Donor-Site Lymphatic Function after Microvascular Lymph Node Transfer

Tina P. Vuolteen, M.D.,  
Majja T. Maki, M.D., Ph.D.,  
Marko P. Seppänen, M.D.,  
Ph.D.,  
Erika A. Suominen, M.D.,  
Ph.D.,  
Anne M. Saaristo, M.D.,  
Ph.D.

*Turku, Finland*

**Background:** Lymphedema remains a challenging clinical problem that often lacks curative treatment options. Recent reports have shown that microvascular lymph node transfer from the groin area into axilla of lymphedematous patients may improve lymphatic drainage, but the effect on donor-site lymphatic flow has not been studied. These patients may be more prone to develop lymphedema at donor sites as well; therefore, the authors' aim was to evaluate postoperative donor-site lymphatic function.

**Methods:** The authors performed lymphatic groin flap transfer to the axilla in 13 lymphedema patients. In 10 patients, the lymph node transfer was performed simultaneously with lower abdominal breast reconstruction. Postoperative lymphatic vessel function of the donor site was evaluated by lymphoscintigraphy and limb circumference measurements. For semiquantitative evaluation of lymphatic drainage, a numerical transport index was used.

**Results:** In six of 10 patients, postoperative lymphoscintigraphy revealed minor changes in lymphatic flow of the donor-site limb. The transport index was considered slightly abnormal in two of 10 patients. None of the 13 patients had changes in lower limb circumferences during the 8- to 56-month follow-up.

**Conclusions:** Lymph node transfer can be easily combined with lower abdominal breast reconstruction, and the popularity of this technique is increasing rapidly. Even though none of our patients had developed symptoms of postoperative lymphedema, the results of the first lymphoscintigrams show that it is important to reduce the surgical trauma to the lymphatic flap donor site. (*Plast. Reconstr. Surg.* 130: 1246, 2012.)

**CLINICAL QUESTION/LEVEL OF EVIDENCE:** Therapeutic, IV.

**Therapeutic**

Chronic lymphedema, commonly caused by infection, surgery, or radiation therapy, remains a challenging clinical problem that often lacks curative treatment options. The incidence of lymphedema varies from 9 to 41 percent in patients who have undergone axillary lymph node dissection and from 1 to 10 percent in patients who have undergone sentinel lymph node biopsy.<sup>1-3</sup> The incidence of lymphedema after inguinal lymph node dissection in melanoma varies from 20 to 64 percent.<sup>4-6</sup> Conventional treatment options for chronic lymphedema aim at alleviating symptoms and are based mainly on physiotherapy and compression therapy, whereas reconstructive surgical treatment options have been limited.<sup>1</sup>

Late-stage lymphedema, accompanied by adipose tissue hypertrophy and fibrosis, can be managed with liposuction as a symptomatic treatment.<sup>7</sup> Recent studies have shown that autogenous microvascular lymph node transfer from the groin area into axilla or wrist of lymphedema patients may improve lymphatic drainage of the affected limb.<sup>8-10</sup> Because it is a fairly new technique, there has been concern about possible effects on the donor site. In previous studies, there have been no reports about postoperative lower limb lymphedema of the donor site after traditional groin flap operations or after lymph node flap transfers from the groin area.<sup>10-12</sup> According to anatomical studies,

followed by the wearing of elastic garments to stabilize the volume.<sup>13</sup>

Surgical treatment of lymphedema has been advocated as an alternative or adjunctive technique with the aim of "curing" the disease. Several categories of surgical procedures have been proposed to treat lymphedema, including excisional procedures [after intensive complete physiotherapy and cautious resection to remove excess limb flaps or lymphoedematous genital skin], liposuction, lymphatic reconstructions (lymphoedema anastomosis and lymphatic channel graft) and tissue-transfer procedures (autologous lymph node transplantation [ALNT] and autologous stem-cell transplantation).<sup>14</sup> Complications of the surgery are rarely mentioned in articles. Among the different types of surgery, ALNT essentially proposed to treat patients with cancer-related or primary lymphedema, can be responsible for

**Disclosures:** This study was supported by the Academy of Finland, the Turku University Foundation, Special Governmental Funding (EVO) allocated to Turku University Hospital, and the Paves and Eila Salonen Foundations. The authors have no potential conflicts of interest to declare.

From Plastic Surgery and the Department of Clinical Physiology and Nuclear Medicine, Turku University Hospital, and Turku PET Centre, Turku, Finland.  
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## Complications of Autologous Lymph-node Transplantation for Limb Lymphoedema

S. Vignes,<sup>1</sup> M. Blanchard, A. Yavoussou, M. Arrault

*Department of Vascular Medicine, Centre National de Référence des Maladies Vasculaires, Hôpital Européen (Paris), Hôtel Dieu (Paris), 75005 Paris, France*

**WHAT THIS PAPER ADDS**

This report concerns the complications arising after autologous lymph-node transplantation to treat primary or secondary upper- or lower-limb lymphoedema, including persistent iatrogenic lymphoedema of the limb corresponding to the donor-node site. Patients must be made aware of the potential risk of grafting before undergoing surgery.

**Objective:** This study aims to assess potential complications of autologous lymph-node transplantation (ALNT) to treat limb lymphoedema.

**Design:** Prospective, observational study.

**Method:** All limb-lymphoedema patients, followed up in a single lymphology department, who decided to undergo ALNT (January 2008–June 2012) independently of our medical team, were included.

**Results:** Among the 26 patients (22 females, four males) included, 14 had secondary upper-limb lymphoedema after breast-cancer treatment and seven had secondary and five primary lower-limb lymphoedema. Median (interquartile range, IQR) ages at primary lower-limb lymphoedema and secondary lymphoedema onset were 18.5 (13–30) and 47.4 (35–58) years, respectively. Median body mass index (BMI) was 25.9 (22.9–29.3) kg m<sup>-2</sup>. For all patients, median pre-surgery lymphoedema duration was 37 (24–60) months. Thirty-four ALNTs were transplanted into the 26 patients, combined with liposuction in four lower-limb-lymphoedema patients. Ten (38%) patients developed 15 complications: six, chronic lymphoedema (four upper limb, two lower limb), defined as >2-cm difference versus the contralateral side, in the limb on the donor lymph-node-site territory, persisting for a median of 40 months post-ALNT; four, post-surgical lymphoedema; one testicular hydrocoele requiring surgery; and four with persistent donor-site pain. Median (IQR) pre- and post-surgical lymphoedema volumes, calculated using the formula for a truncated cone, were, respectively, 1023 (633–1373) ml (median 3 (1–6) months) and 1058 (666–1506) ml (median: 40 (14–72) months; *P* = 0.73).

**Conclusion:** ALNT may engender severe, chronic complications, particularly persistent iatrogenic lymphoedema. Further investigations are required to evaluate and clearly determine its indications.

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Article history: Received 11 August 2012; Accepted 22 November 2012; Available online 8 January 2013

**Keywords:** Complication; Lymphoedema; Autologous lymph-node transplantation; Surgery

Lymphoedema is a chronic and often debilitating disorder caused by lymphatic insufficiency. It can be either primary or secondary, mainly after cancer treatment including surgery and/or radiotherapy. Lymphoedema management is based upon complete decongestive physiotherapy and is divided into two phases: the first, to reduce lymphoedema volume, and the second, to maintain the reduced volume. It includes multilayer low-stretch bandages to diminish lymphoedema volume, exercise and meticulous skin care

**Corresponding author:** S. Vignes, Department of Lymphology, Hôpital Européen, 11, rue Eugène Marix, 75015 Paris, France. Tel.: +33 1 40 30 61 91; fax: +33 1 40 30 61 84.  
E-mail address: svignes@hopital-europeen.paris.fr (S. Vignes).  
0167-4896/\$ – see front matter © 2012 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.  
http://dx.doi.org/10.1054/ejvs.2012.11056

Impaired donor site lymphatic function on lymphoscintigraphy but no clinical evidence of lymphedema

6/26 Patients with donor site lymphedema following lymph node transfer

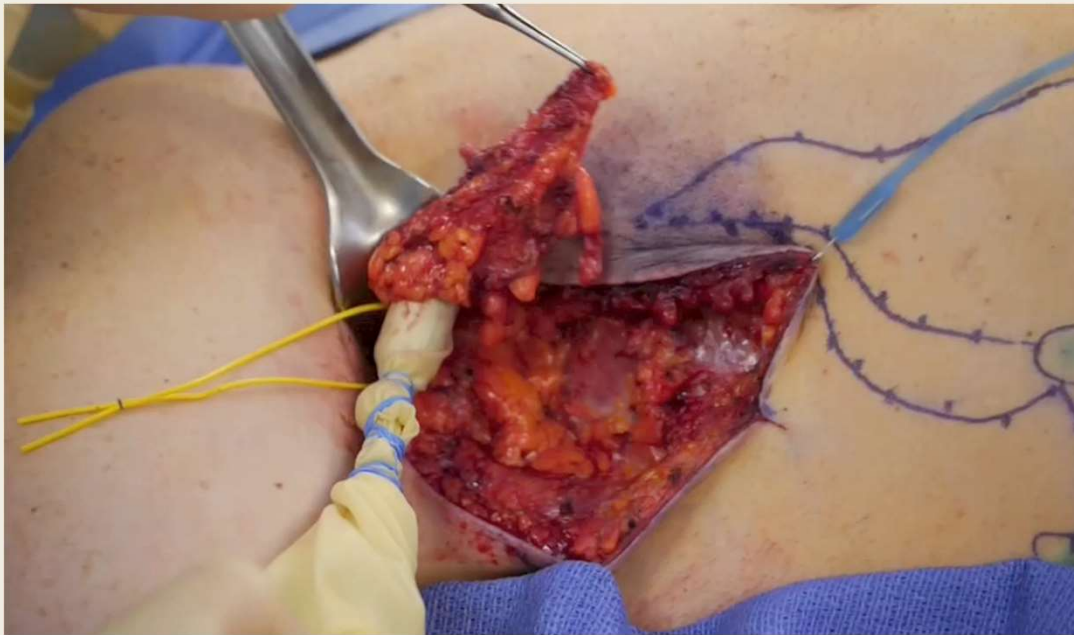


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**Localizing Thoracodorsal-based Lymph Nodes Using SPY**

**Injection of Indocyanine Green Into Chest & Back**

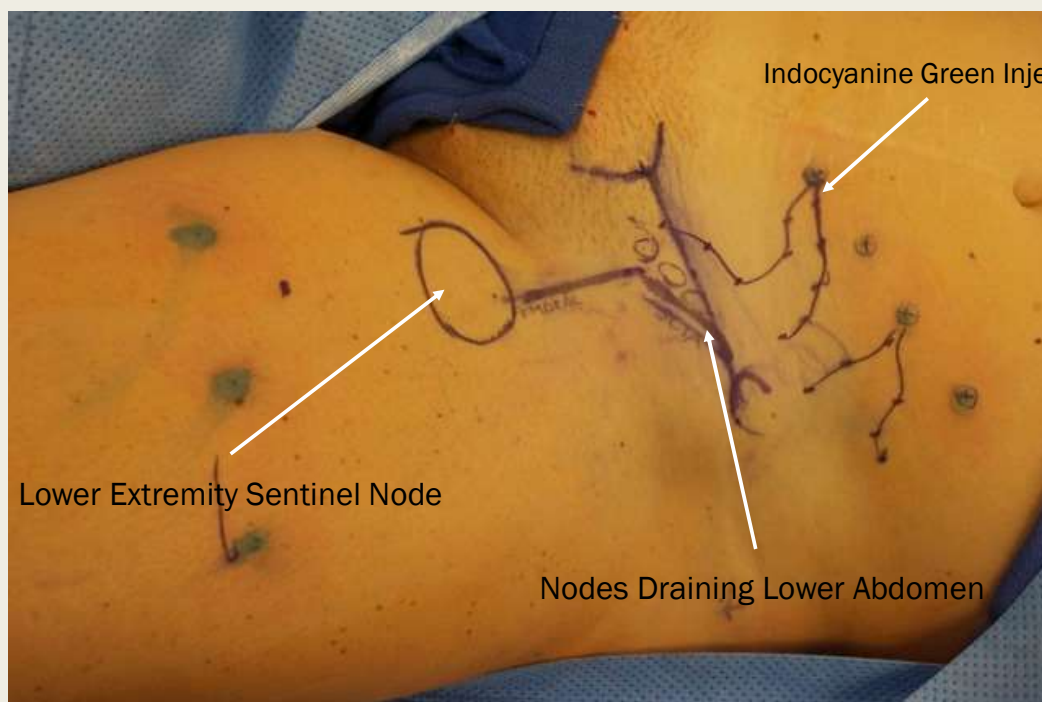


**Confirmation That We Have Not Harvested Lymph Nodes Draining Upper Extremity Using the Geiger Probe**









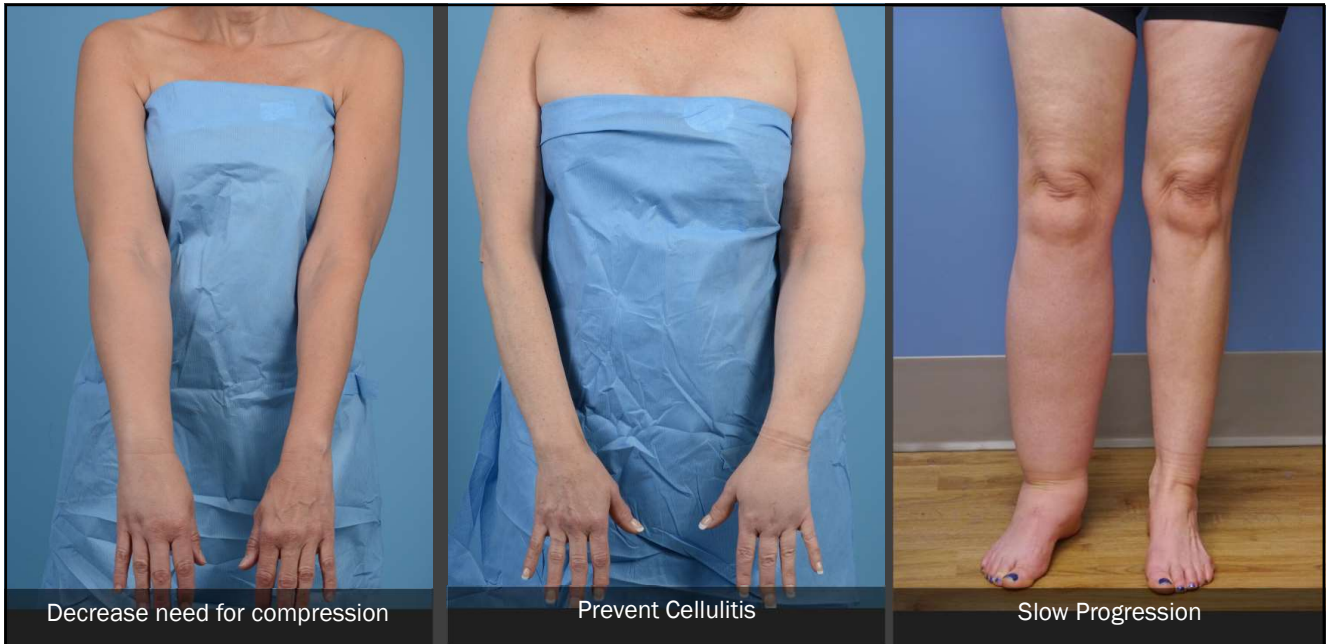


Importance of using reverse lymphatic mapping – can't rely on anatomic markings alone

## Why not just do LVA?

- LVA may not be feasible if lymphatics are scarred
- Connecting arteries and veins are more predictable
- Potential immunologic benefit of importing lymph nodes
- Patients with axillary radiation may have reduced ROM or contracture. We can bring in soft tissue to improve ROM





Decrease need for compression

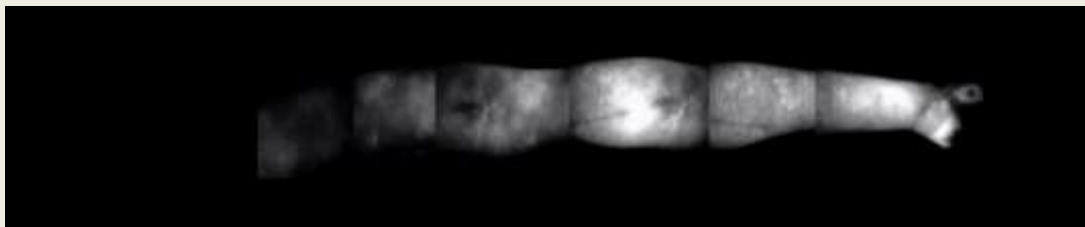
Prevent Cellulitis

Slow Progression

## PATIENTS PURSUE SURGERY FOR DIFFERENT CONCERNS

# Case Example 1

- 62 y/o female with RUE lymphedema
- s/p right lumpectomy, lymph node biopsy and radiation
- Patient in around the clock compression preop. 1 episode of cellulitis preop



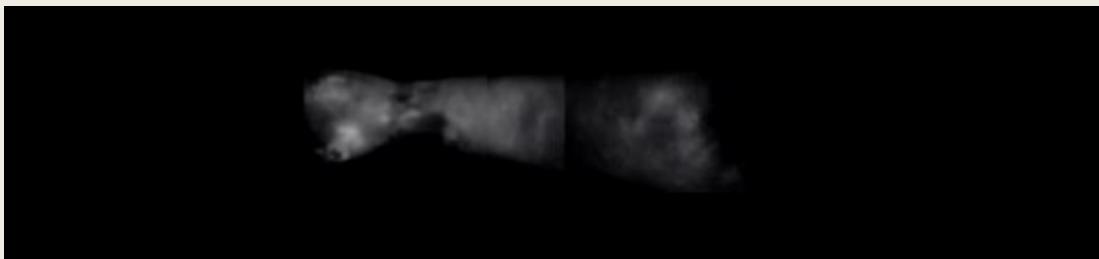


	Preop	2.5 years postop
BMI	22.3	21
Perometer volume % difference	44.4%	5%
L-Dex score	74.9	45.7



## Case Example 2

- 55 y/o female with LUE lymphedema
- s/p left mastectomy, axillary dissection and radiation 12 years prior to lymphedema surgery
- Preop: She wears compression 24/7. She has had 13 episodes of cellulitis preop, and took prophylactic abx



No ICG movement above the elbow preop



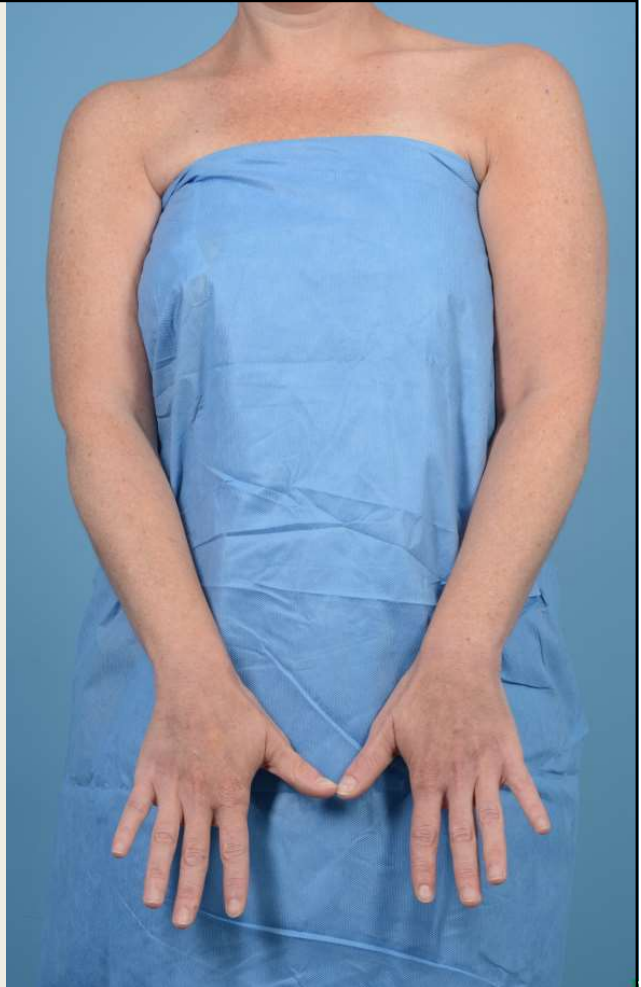
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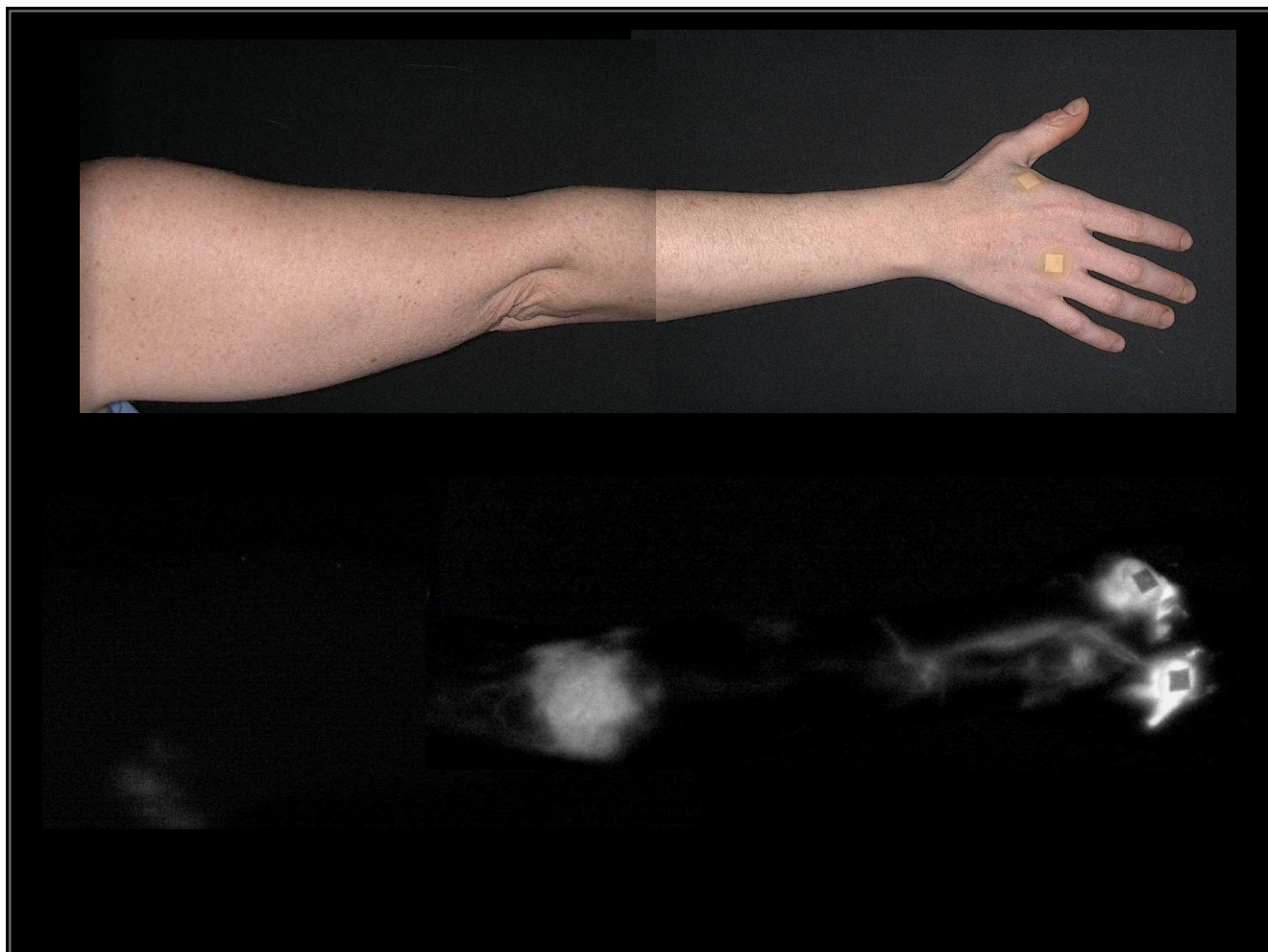


	Preop	4 years postop
Perometer volume difference	913	959
L-dex	70.1	55.3
Bmi	27.8	26
Cellulitis episodes	13	0

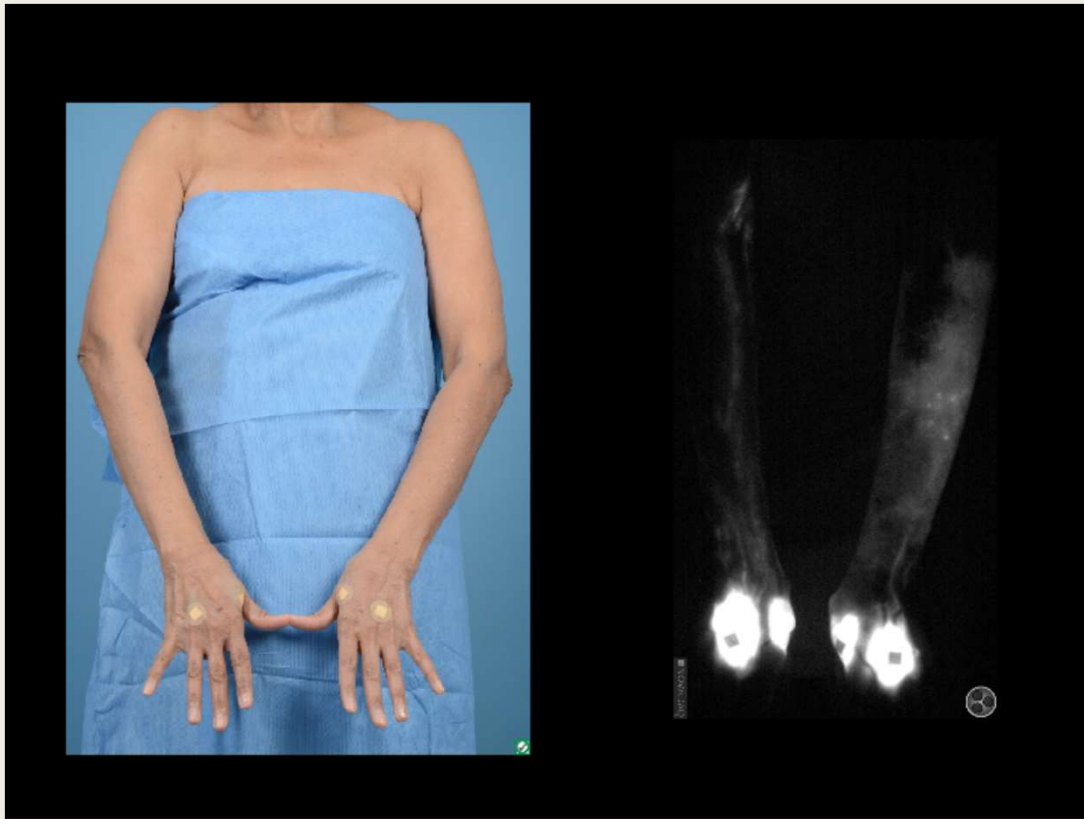
## Case Example 3

- 42 y/o female S/P right lumpectomy, axillary dissection and radiation
- Patient reports feeling of “heaviness” in the right upper extremity
- BMI 24.2
- Limb Volume difference 1%





## Importance of early recognition

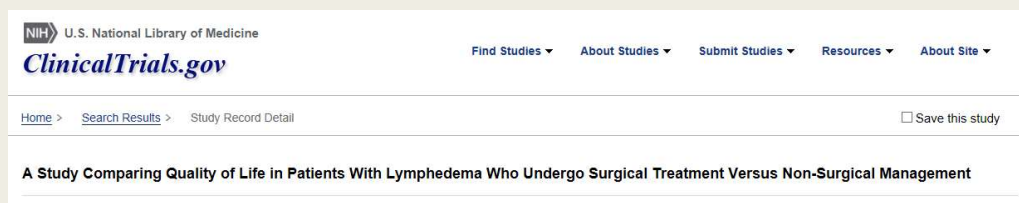




## LOWER EXTREMITY LNT RESULTS

## MSKCC clinical trials for surgical patients

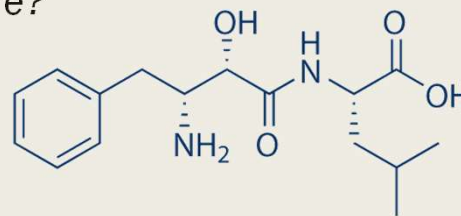
- A Prospective Study Comparing Quality of Life in Patients with Lymphedema Who Undergo Surgical Treatment Versus Non-Surgical Management
- Axillary Lymph Node Dissection with Immediate Lymphatic Reconstruction



The screenshot shows the ClinicalTrials.gov website interface. At the top left is the NIH logo and the text "U.S. National Library of Medicine". The main header is "ClinicalTrials.gov" in blue. To the right of the header are navigation links: "Find Studies", "About Studies", "Submit Studies", "Resources", and "About Site", each with a dropdown arrow. Below the header is a breadcrumb trail: "Home > Search Results > Study Record Detail". On the right side of the breadcrumb trail is a checkbox labeled "Save this study". The main content area displays the title of the study: "A Study Comparing Quality of Life in Patients With Lymphedema Who Undergo Surgical Treatment Versus Non-Surgical Management".

## Medical Treatments?

- Ketoprofen – anti-inflammatory thought to reduce swelling and recurrent infection risk
- Tacrolimus
- Ubenimex: Targets promotion of lymphangiogenesis
  - *Leukotriene B4 inhibits lymphangiogenesis in mouse tail models and is elevated in patients with lymphedema. Ubenimex is a medication which is an inhibitor of leukotrienes*
  - *Stanford University drug trial with Dr. Stanley Rockson*
  - *Results not reported yet*
- *Immunotherapy drugs in the future?*



Tacrolimus: Gardenier et al. Topical tacrolimus for the treatment of secondary lymphedema. *Nat Commun.* 2017; 8: 14335. doi: 10.1038/ncomms14345

Ketoprofen: Rockson et al. Pilot studies demonstrate the potential benefits of antiinflammatory therapy in human lymphedema. *JCI Insight.* 2018 Oct 18; 3(20): e123775. doi: 10.1172/jci.insight.123775

Ubenimex: <http://clinicaltrials.stanford.edu/browse-all-trials.html?ctid=NCT02700529>



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# Conclusions

- Recognition of lymphedema and progression
- Importance of early detection and early referral for surgical intervention
- Impact on quality of life
- Where to go from here?
  - *Medical therapy in conjunction with surgical options*
  - *Improvement of imaging techniques*
  - *Improvement in staging of lymphedema*



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**Contact info:**

Alicia Jones, MHS, PA-C

[jonesa@mskcc.org](mailto:jonesa@mskcc.org)

