Oncology-Related Lymphedema: Identification and Treatment for an Underserved, Chronic Condition

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Agenda

Review of the lymphatic system

Tissue assessment for lymphedema

How cancer affects the lymphatic system

Recognizing early signs and symptoms of cancer related lymphedema

Importance of early intervention

Comprehensive treatment of lymphedema

What is Lymphedema?

A **chronic, progressive condition** caused by a failure of the lymphatic system to adequately receive and transport fluid back into the cardiovascular circulation

Excessive **protein-rich fluid** accumulates in the interstitial spaces which leads to tissue changes and impaired immune function

What is the Lymphatic System?

Lymphatic vessels: span the entire body, lymph fluid travels throughout

Lymph nodes: 600–800 throughout the body.

Lymph fluid: clear to white fluid composed of

- Protein
- Fat
- Water
- Waste products (cellular debris)

Lymphoid tissue: important to immune system by producing/storing white blood cells

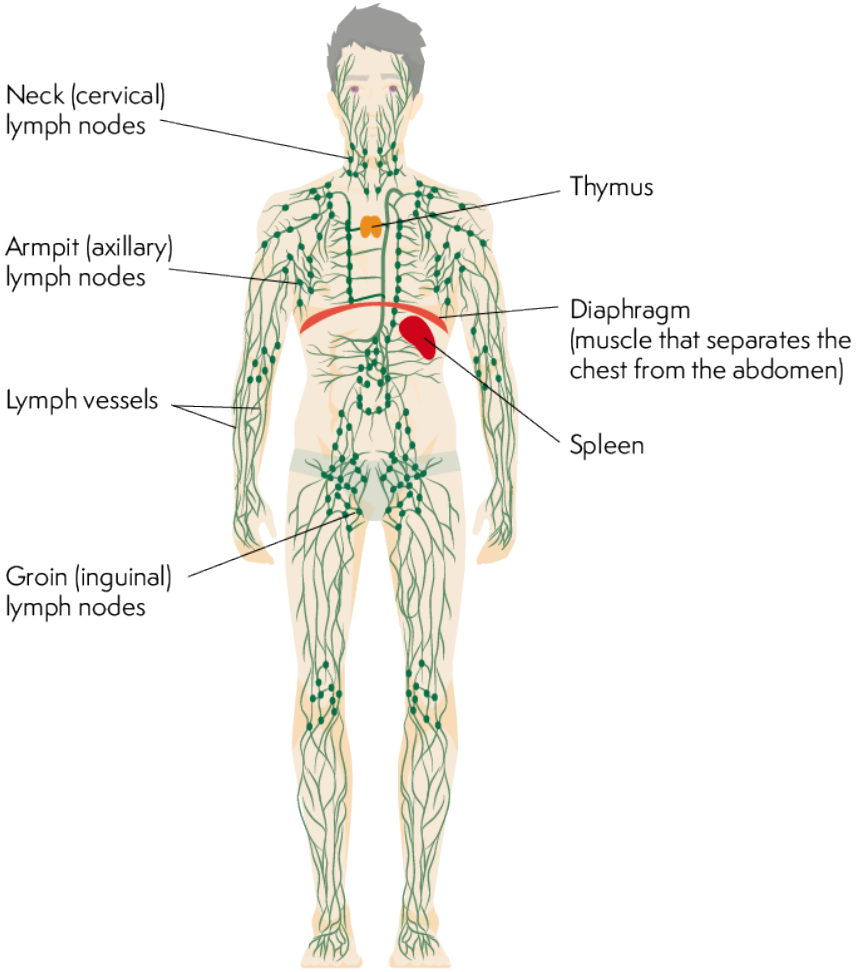


Photo Credit: Lymphoma Action

Lymphatic Vessels

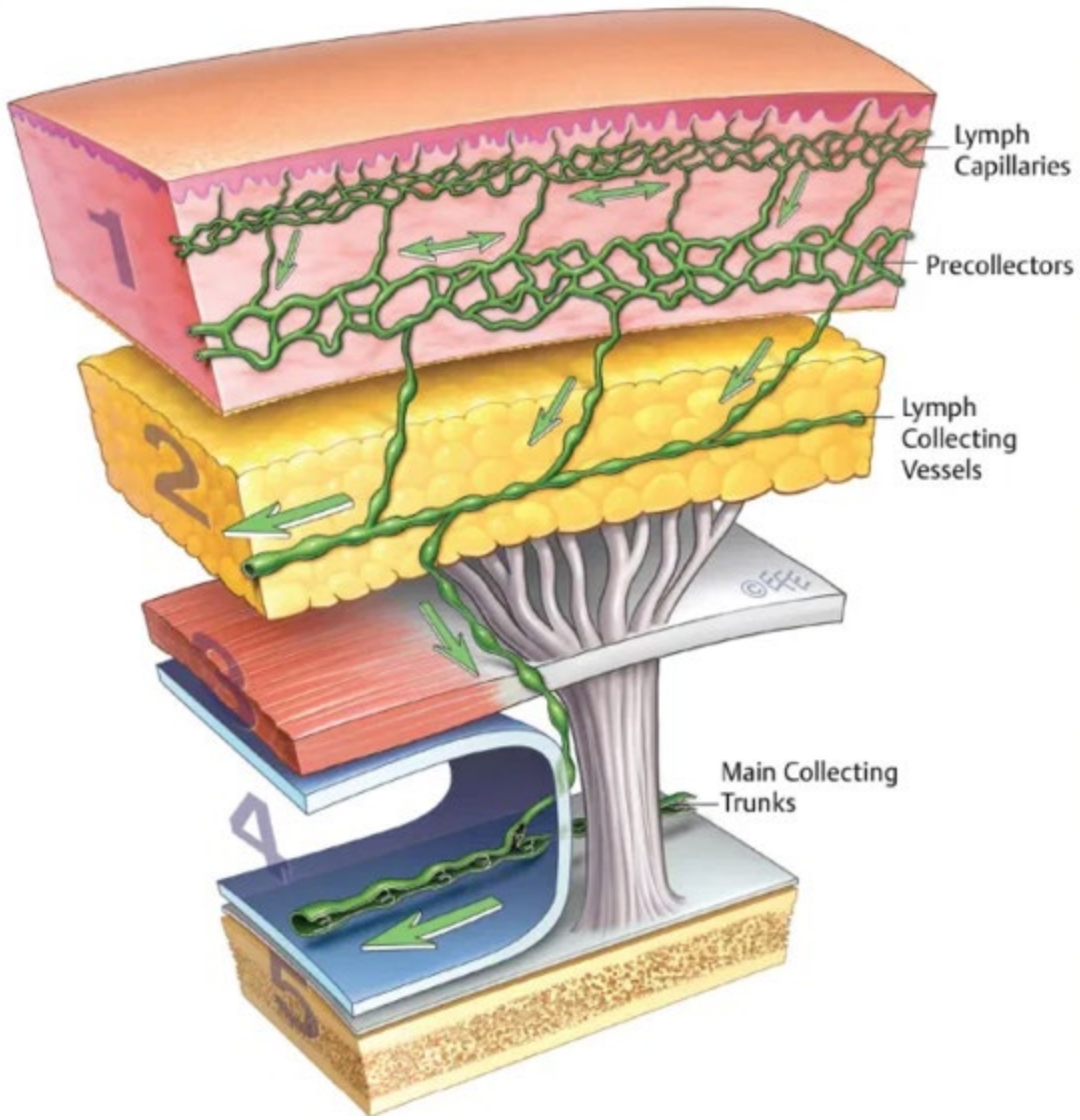
Lymph capillaries: Tiny vessels in the spaces between cells absorb extracellular fluid

Pre-collectors: Transports lymph fluid from capillaries to collectors

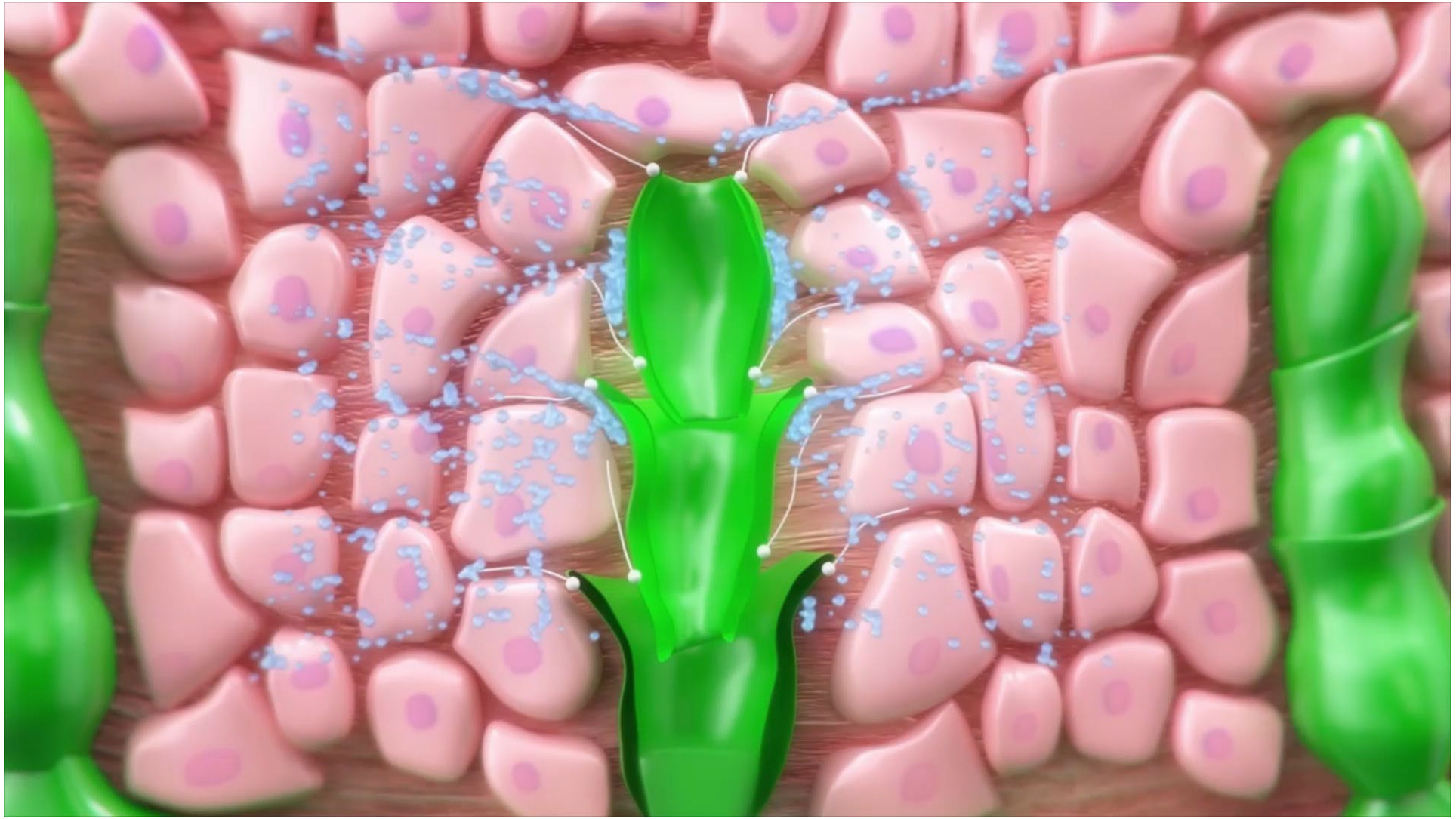
Lymph collectors: Valved vessels, contain smooth muscle which contract to drain fluid from skin, fat, muscle, joints, and ligaments

Trunks: Drain fluid from organs, extremities, and related quadrants of the trunk

Ducts: Large, deep vessels return lymph to circulation at the subclavian veins



Lymphatic Capillaries and Collectors



Lymphatic Trunks and Ducts

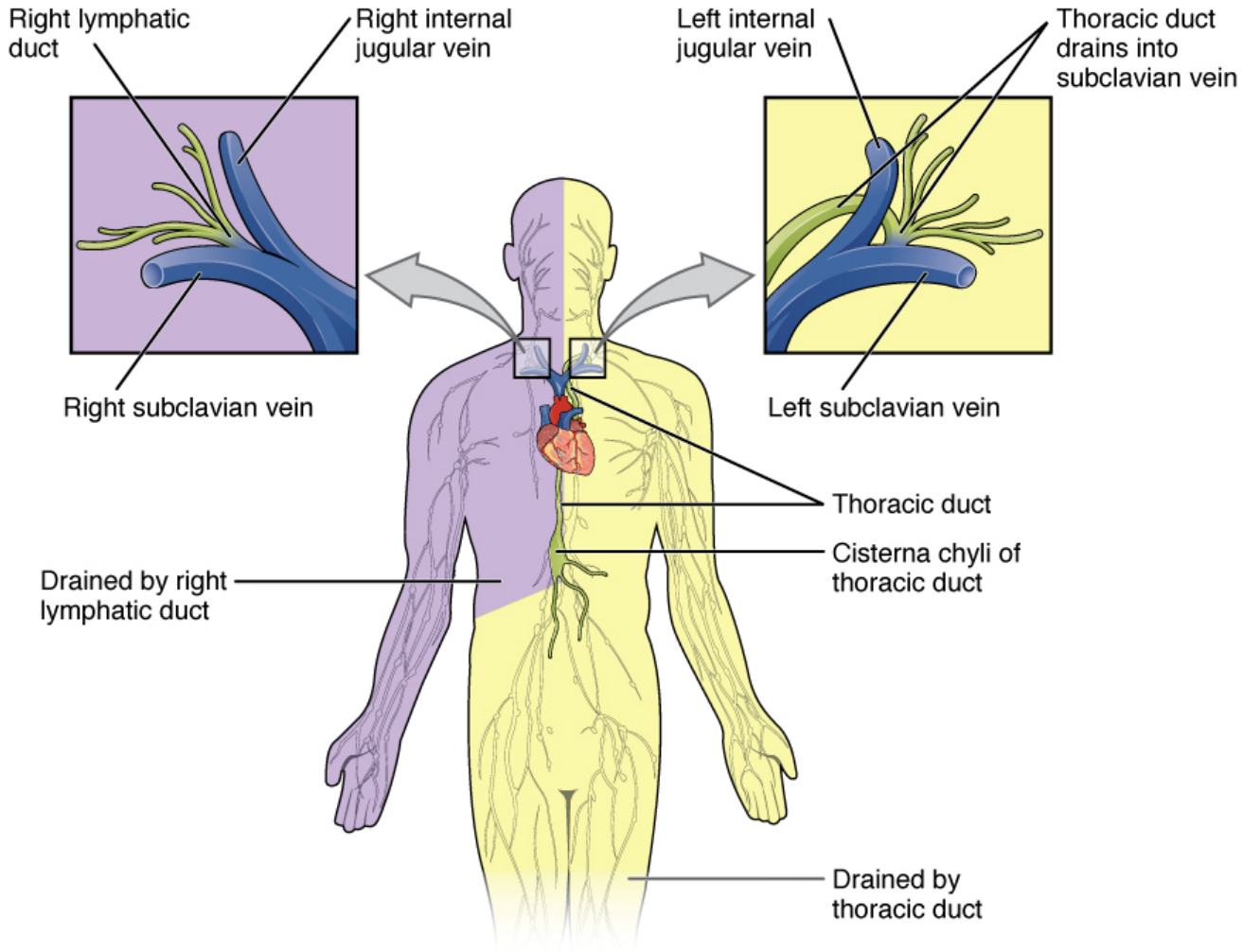
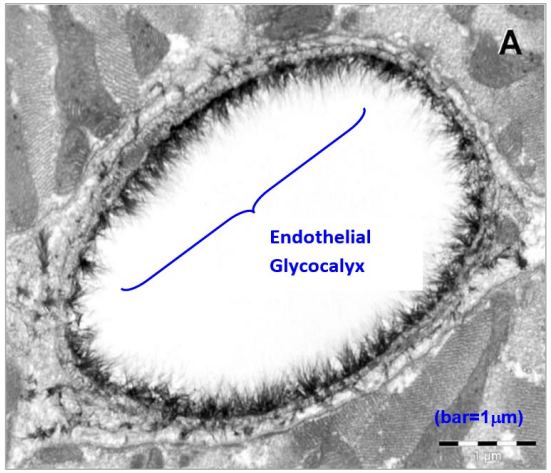
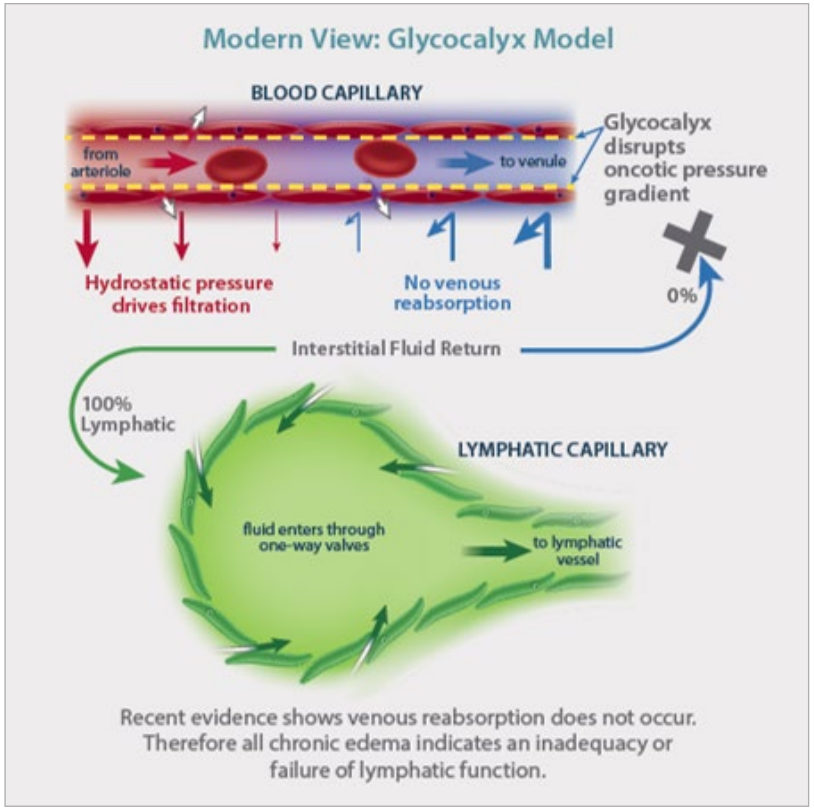


Photo credit: Illustration from Anatomy & Physiology, Connexions Web site. Jun 19, 2013.

Microcirculation and Importance of the Glycocalyx

All chronic edema represents failure of the lymphatic system to adequately manage excess fluid





Chappell D et al. Cardiovasc Res 2009; 88:388–96

Lymphedema Progression: Why Early Intervention Matters

Stage[1,2]	Intervention goals
Stage 0: latent or subclinical with no evident swelling ▪ Impaired lymphatic transport or subtle changes in tissue fluid or composition ▪ Patients commonly report feelings of heaviness, tightness or tingling ▪ May exist months or years before overt edema occurs	▪ **Reverse symptoms** ▪ **Prevent progression** ▪ **Improve quality of life** **Dynamic lymphatic insufficiency**
Stage 1: edema ▪ Early accumulation of high-protein fluid; pitting may occur ▪ Swelling is intermittent or subsides with limb elevation ▪ An increase in various types of proliferating cells may be seen	
Stage 2: fibrosis ▪ Swelling is evident; does not fully resolve with limb elevation ▪ Fibrosis and/or adipose tissue develops ▪ Pitting is evident until prevented by fibroadipose tissue in late stage[2]	▪ Manage symptoms ▪ Maintain or improve quality of life **Mechanical lymphatic insufficiency**
Stage 3: lymphostatic elephantiasis ▪ Further alterations in volume, skin character and thickness, further deposition of fat, fibrosis	▪ Limit infections ▪ Manage symptoms ▪ Maintain or improve quality of life

1. The International Society of Lymphology. The diagnosis and treatment of peripheral lymphedema: 2016 consensus document of the International Society of Lymphology. *Lymphology*. 2016;49(4):170–184.
2. Arm lymphedema images: DocHealer CC-SA 4.0

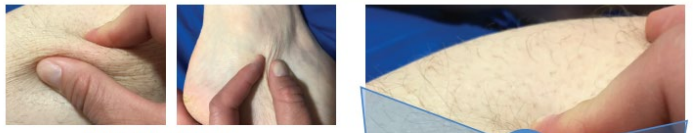
Tissue Assessment

Stemmer's sign

- Inability to lift the skin at the base of second toe
- Positive Stemmer's sign indicates lymphedema
- Negative Stemmer's sign does **not** rule out lymphedema

Bow tie test

- Healthy skin can be lifted and rolled to produce a bow tie of wrinkles when twisted[1]

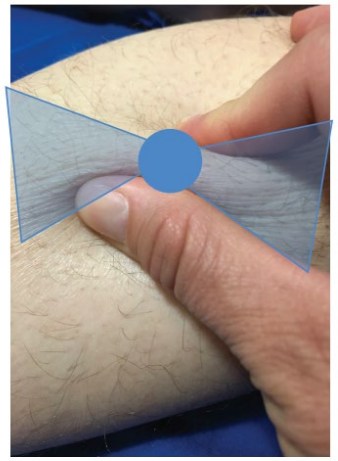


Negative Bjork Bow Tie Test

Positive Bjork Bow Tie Test

Alternate method Bjork Bow Tie Test

To perform the Bjork Bow Tie Test, in one maneuver, gently pinch, roll and twist the skin between the thumb and pointer finger, noting quality of tissue texture and thickness. Healthy skin can be lifted and pinched, should feel slippery between the layers when rolled and produce a 'Bow Tie' of wrinkles when twisted. Skin that tests positive for tissue texture changes will be thickened, less pliable, unable to be pinched and lifted, difficult to twist, and produce limited 'Bow Tie' of wrinkles. Negative test results include tissue that can be lifted, wrinkles when twisted and is of normal skin thickness for the tested body part.



Close up illustrating 'Bow Tie' of wrinkles

1. Bjork R, Ehmann S. S.T.R.I.D.E. Professional Guide to Compression Garment Selection for the Lower Extremity. *J Wound Care*. 2019;28(Sup6a):1-44. doi:10.12968/jowc.2019.28.Sup6a.S1

Positive Stemmer's Sign: Indicates Lymphedema

Negative Stemmer's Sign and Example Fibrosis Assessment

Cancer-related Lymphedema

Cancer Affects the Lymphatic System in Multiple Ways

Tumor

- Presence of tumor affects lymphatic fluid movement[1]

Surgery

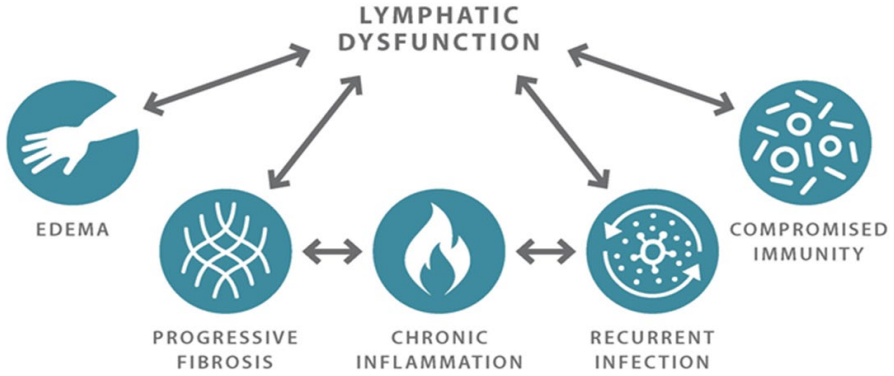
- Lymph node dissection increases risk for lymphedema[2]

Chemotherapy

- Fluid retention and decreased propulsion rate[4]

Radiation

- Depletion of WBCs in lymph nodes
- Lymph nodes become fatty/fibrotic
- Decreased lymphatic proliferation potential
- Interstitial fibrosis and scarring compressing lymphatic vessels[3]



Graphic adapted from Rockson. *Lymphat Res Biol.* 2013 Sep: 11 (3): 117-120.

All lead to mechanical insufficiency of the lymphatic system

1. Ridner SH, Dietrich MS, Niermann K, Cmelak A, Mannion K, Murphy B. A Prospective Study of the Lymphedema and Fibrosis Continuum in Patients with Head and Neck Cancer. *Lymphat Res Biol.* 2016 Dec;14(4):198-205.
2. Chaput G, Ibrahim M, Towers A. Cancer-related lymphedema: clinical pearls for providers. *Curr Oncol.* 2020;27(6):336-340.
3. Allam,O. et al. The impact of radiation on lymphedema: a review of the literature. Division of Plastic and Reconstructive Surgery, Yale University, New Haven, CT, USA . Dec 24, 2019
4. Johnson AR, Granoff MD, Lee BT, Padera TP, Bouta EM, Singhal D. The Impact of Taxane-based Chemotherapy on the Lymphatic System. *Ann Plast Surg.* 2019;82(4S Suppl 3):S173-S178. doi:10.1097/SAP.0000000000001884
5. Lee KT, Mun GH, Lim SY, Pyon JK, Oh KS, Bang SI. The impact of immediate breast reconstruction on post-mastectomy lymphedema in patients undergoing modified radical mastectomy. *Breast.* 2013 Feb;22(1):53-7.
6. Miller CL, Colwell AS, Horick N, Skolny MN, Jammallo LS, O'Toole JA, Shenouda MN, Sadek BT, Swaroop MN, Ferguson CM, Smith BL, Specht MC, Taghian AG. Immediate Implant Reconstruction Is Associated With a Reduced Risk of Lymphedema Compared to Mastectomy Alone: A Prospective Cohort Study. *Ann Surg.* 2016 Feb;263(2):399-405.

Prevalence of Lymphedema

20% of prostate cancer survivors[1]

Up to **70%** of gynecological cancer survivors[3]

Nearly **50%** of breast cancer survivors[2]

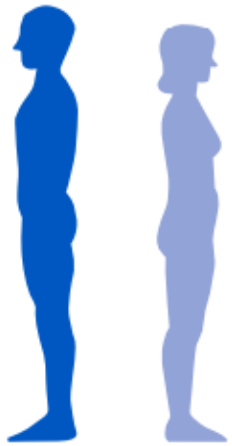
90% of head and neck cancer survivors[4]

1. Raskin: Journal of Urology 2019 2. Kohler LA, Mayrovitz HN, Phys Ther. 2020 3. Carlson JW, Kauderer J, Hutson A, et al., Gynecol Oncol. 2020 4. Ridner, S.H., et al., Lymphat Res Biol, 2016

Estimated New Cancer Cases in US: 2024

Estimated New Cases

Male			Female		
Prostate	299,010	29%	Breast	310,720	32%
Lung & bronchus	116,310	11%	Lung & bronchus	118,270	12%
Colon & rectum	81,540	8%	Colon & rectum	71,270	7%
Urinary bladder	63,070	6%	Uterine corpus	67,880	7%
Melanoma of the skin	59,170	6%	Melanoma of the skin	41,470	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	36,030	4%
Non-Hodgkin lymphoma	44,590	4%	Pancreas	31,910	3%
Oral cavity & pharynx	41,510	4%	Thyroid	31,520	3%
Leukemia	36,450	4%	Kidney & renal pelvis	29,230	3%
Pancreas	34,530	3%	Leukemia	26,320	3%
All sites	**1,029,080**		**All sites**	**972,060**	



American Cancer Society

1 in 8 women will develop breast cancer before age of 85

Incidence rates have increased ~0.6% per yr since the mid-2000s

Death rate decreased 42% from yrs 1989 to 2021

5-yr survival rate: 91%

American Cancer Society. Cancer Facts & Figures 2024. Atlanta: American Cancer Society; 2022. Cancer statistics. SEER. Retrieved November 1, 2024 from https://seer.cancer.gov/statistics/

Lymphatics of the Breast and Axilla

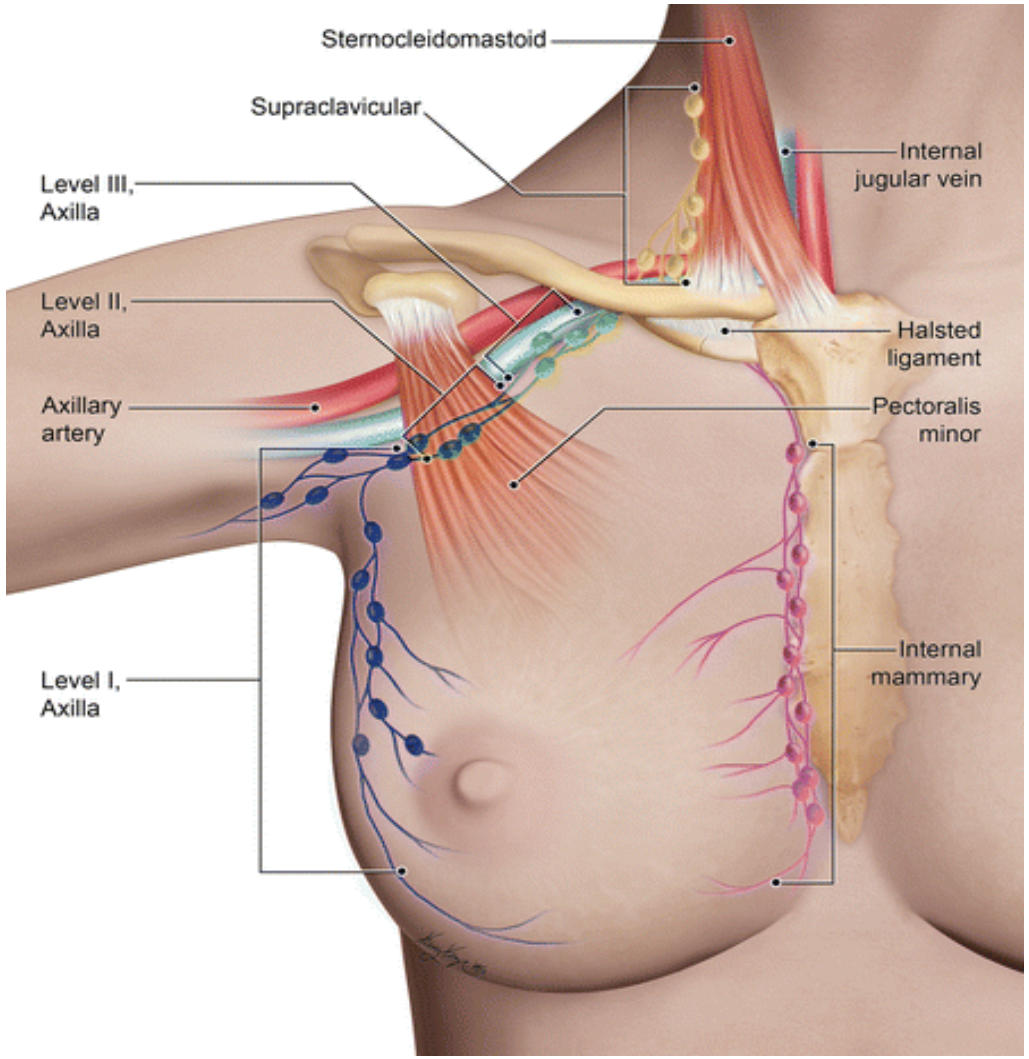


Photo credit: TheUrbanYou.com

Breast Cancer-related Lymphedema Signs and Symptoms

Pain in chest area, burning, aching or tingling	Trunk/back/shoulder area swelling and tingling	Arm swelling, tightness or heaviness with limited movement in shoulder/arm	Swollen breast, dimpled hair follicles on breast	Hand/finger swelling; tight fitting jewelry/rings

1. Fu MR, Axelrod D, Cleland CM, et al. Symptom report in detecting breast cancer-related lymphedema. *Breast Cancer* (Dove Med Press). 2015;7:345–352.
2. Sun, F., Skolny, M.N., Swaroop, M.N. et al. The need for preoperative baseline arm measurement to accurately quantify breast cancer-related lymphedema. *Breast Cancer Res Treat* 157, 229–240 (2016).

Patient Symptom Report: BCRL

Arm symptoms

- ☐ Arm swelling
- ☐ Arm heaviness
- ☐ Arm firmness
- ☐ Increased arm temperature
- ☐ Seroma formation (fluid buildup under the surface of the skin)
- ☐ Arm tightness
- ☐ Limited arm movement
- ☐ Tingling in affected arm
- ☐ Arm aching
- ☐ Limited fingers movement
- ☐ Limited elbow movement
- ☐ Limited wrist movement
- ☐ Limited shoulder movement
- ☐ Stiffness in the affected arm
- ☐ Burning in the affected arm
- ☐ Arm redness
- ☐ Numbness in the affected arm
- ☐ Tenderness in the affected arm
- ☐ Pain in the affected arm

Trunk symptoms

Note: *Differences in bra fit, including indentation at bands/straps or changes in band and cup size, are common indicators of truncal swelling.*

Breast, chest and collarbone area:

- ☐ Swelling or puffiness
- ☐ Heaviness or fullness
- ☐ Tightness or firmness
- ☐ Dimpled hair follicles on breast; orange peel appearance

Side and axilla (armpit):

- ☐ Swelling or puffiness
- ☐ Heaviness or fullness
- ☐ Tightness or firmness
- ☐ Feeling of a "ball" preventing arm from resting at side
- ☐ Feeling of a cord pulling with motion

Shoulder and back:

- ☐ Swelling or puffiness
- ☐ Heaviness or fullness
- ☐ Tightness or firmness
- ☐ Limited range of motion
- ☐ Pain

Patient-reported symptoms are instrumental in diagnosing early-stage lymphedema,[1] especially when pre-treatment measurements are not available.[2]

1. Fu MR, Axelrod D, Cleland CM, et al. Symptom report in detecting breast cancer-related lymphedema. *Breast Cancer* (Dove Med Press). 2015;7:345–352.
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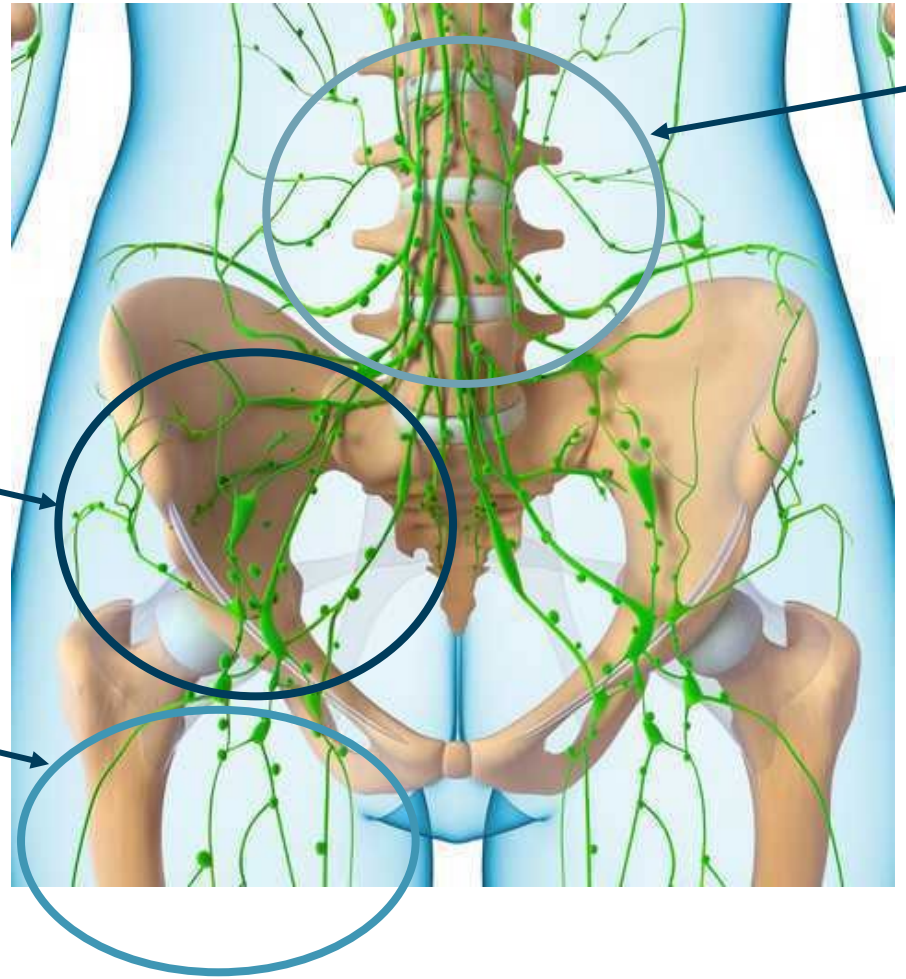
Lymphatics of the Pelvic Region

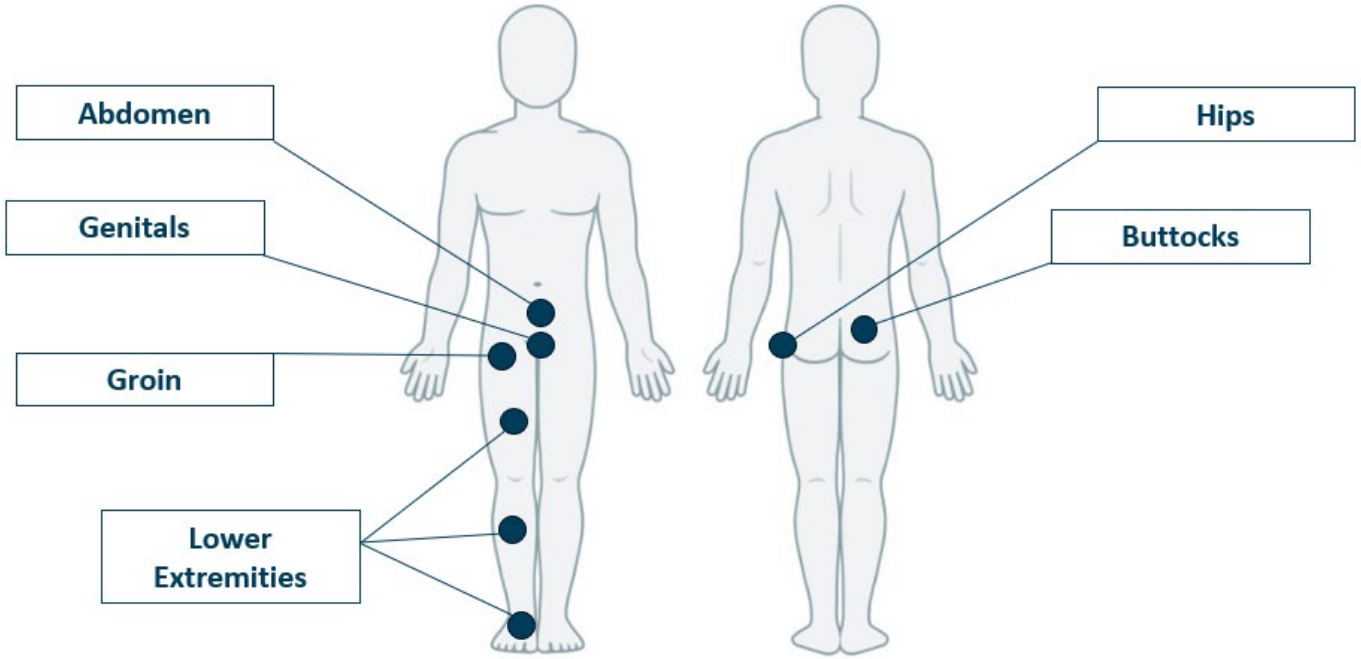
Pelvic nodes
Cervical, endometrial, vaginal, ovarian, bladder, prostate cancers

Inguinal nodes
Vulvar and vaginal cancers



Lumbar/Para-aortic
Endometrial, cervical, ovarian, kidney cancers

Locations of Pelvic Cancer-related Lymphedema



Identifying Lymphedema: Signs and Symptoms (Gynecological)

Gynecological cancer treatment-related lymphedema patient symptom screener.

CHECK ALL THAT APPLY

Abdominal area	☐ Heaviness in abdomen	☐ Persistent bloating
	☐ Firmness across abdomen	☐ Tingling/numbness in abdomen
	☐ Underwear band fitting tighter	☐ Pitting across waistband
Genital area	☐ Bowel/bladder dysfunction	☐ Sexual dysfunction
	☐ Vaginal/vulvar swelling	☐ Vulvar fullness/heaviness
	☐ Vulvar pressure	☐ Sensation of sitting on something
Legs	☐ Heaviness in thighs/legs	☐ Tingling/numbness in thighs/legs
	☐ Tightness in thighs/legs	☐ Aching in thighs/legs
Skin	☐ Skin firmness/tissue changes	☐ Rash/skin irritation inner thigh up to stomach

Identifying Lymphedema: Signs and Symptoms (Prostate)

Prostate cancer treatment-related lymphedema patient symptom screener.

CHECK ALL THAT APPLY		
Abdominal area	☐ Heaviness in abdomen ☐ Pitting across waistband	☐ Firmness across abdomen ☐ Underwear band fitting tighter
Genital area	☐ Scrotal swelling ☐ Genital fullness	☐ Sexual dysfunction ☐ Bowel/bladder dysfunction
Legs	☐ Heaviness in thighs/legs ☐ Tingling/numbness in thighs/legs	☐ Tightness in thighs/legs
Skin	☐ Skin firmness/tissue changes	☐ Persistent bloating

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Internal and External Lymphedema Following Head and Neck Cancer Treatment

Most common internal locations

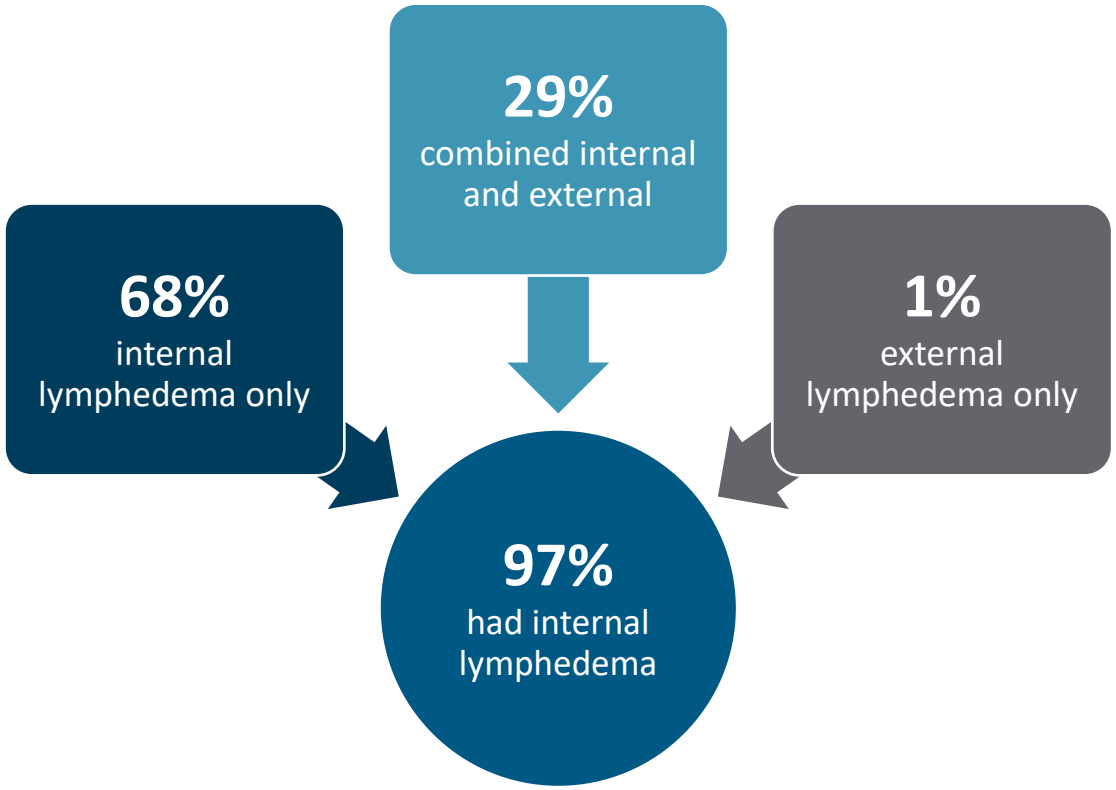
- Epiglottis
- Arytenoids
- Pharyngoepiglottic folds
- Aryepiglottic folds

Most common external locations

- Submental region
- Neck

Higher severity of internal and external LE

- More severe dysphagia
- Poorer-patient reported outcomes
- Need for more diet modifications



Jeans, C, Ward, EC, Brown, B, et al. Association between external and internal lymphedema and chronic dysphagia following head and neck cancer treatment. *Head & Neck*. 2021; 43: 255– 267. https://doi.org/10.1002/hed.26484

Head and Neck Cancer (HNC) in the United States

The NCI estimated prevalence in 2024

4%
of all cancers

New cases:
71,110

Deaths:
16,110

Males affected more than females 2.7:1

Lymphatics of the Head and Neck

Lymphatic vessels

- Divided into two major groups

Superficial vessels

- Drain lymph from scalp, face and neck into superficial ring of lymph nodes at junction of the neck and head

Deep vessels

- Arise from deep cervical lymph nodes
- Converge to form L and R jugular lymphatic trunks

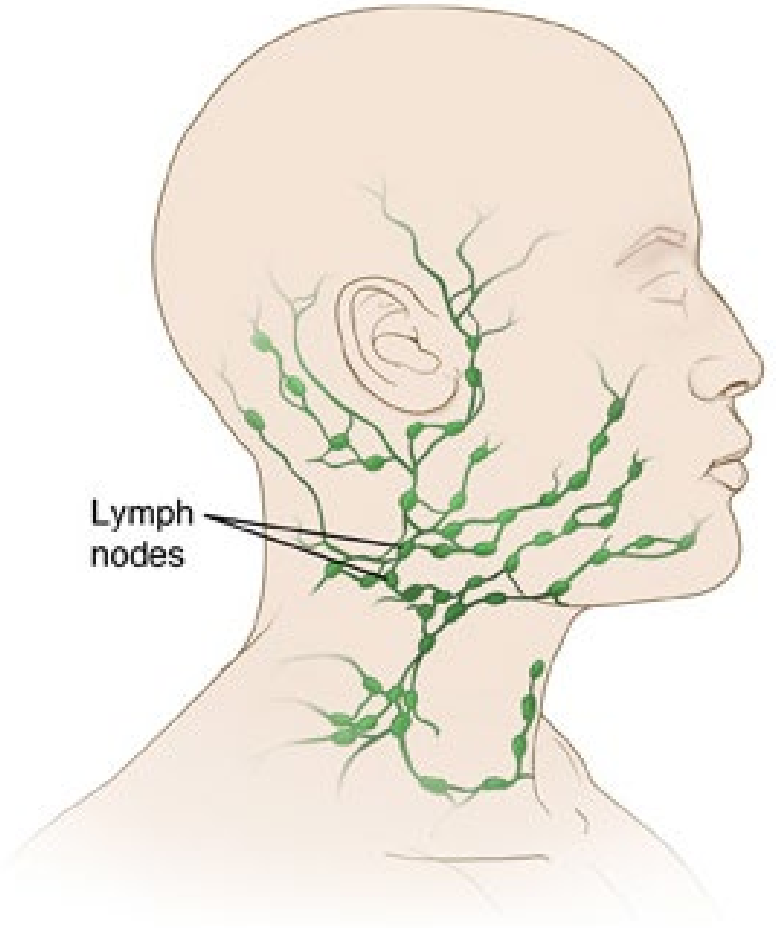


Photo credit: Spectrum Health Lakeland Ear, Nose and Throat

Screening for/Assessing Lymphedema: Imaging (CT/MBS/Scope/FEES)

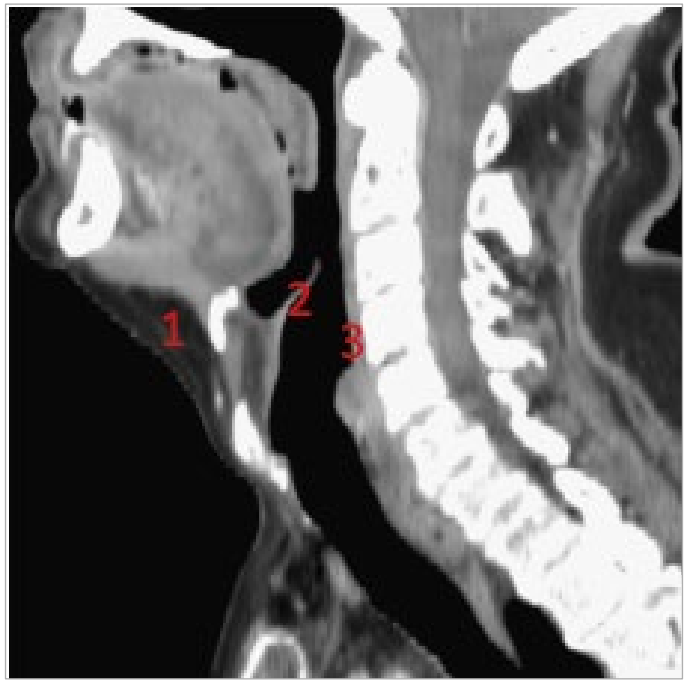


Fig. 1. Baseline CT scans

1. No submental fat
2. Epiglottis not thick
3. No prevertebral soft tissue swelling at C3 (posterior pharyngeal wall)

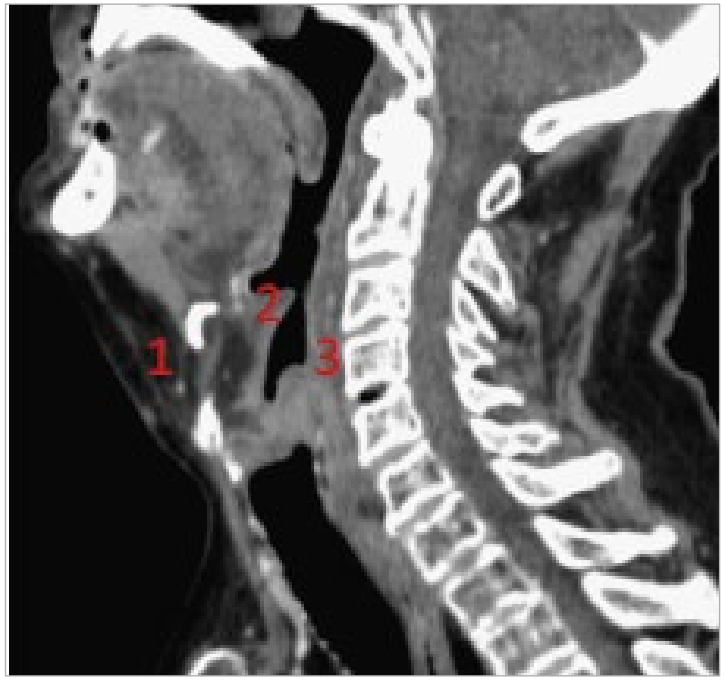


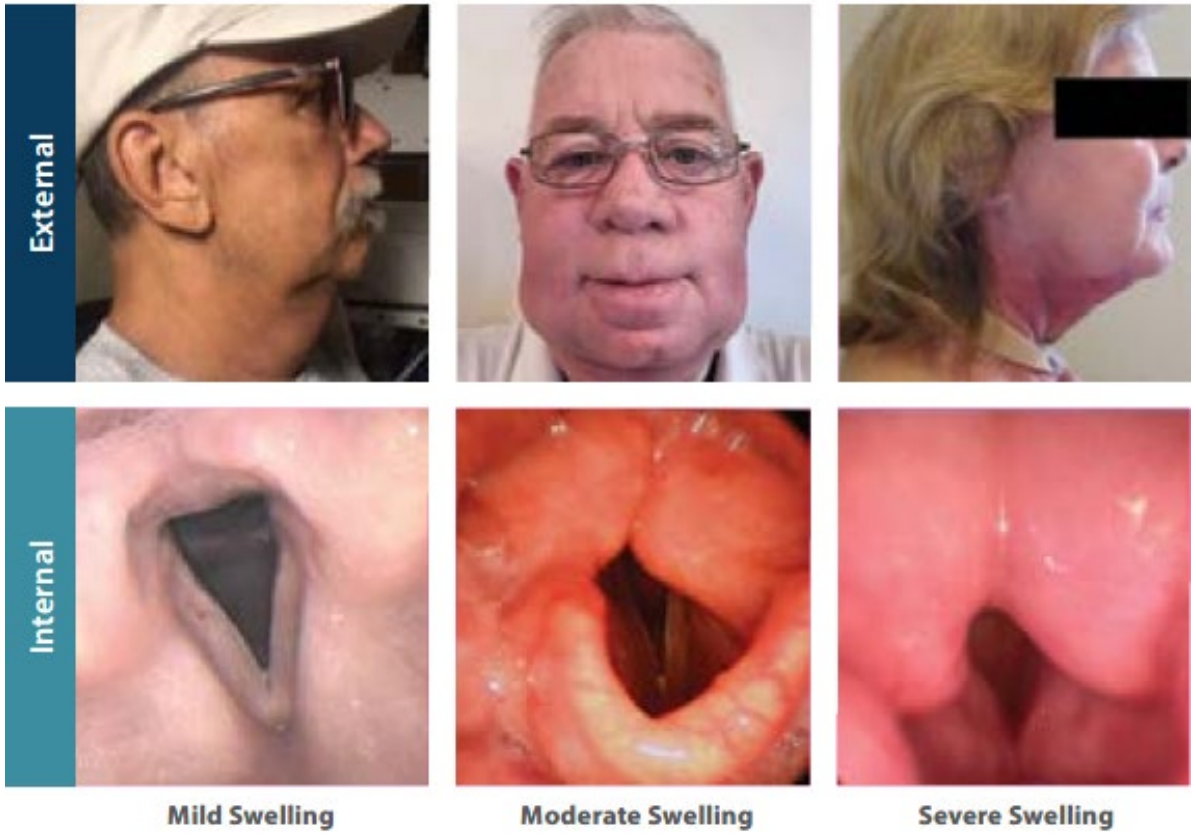
Fig. 2. Seven-month post treatment scans

1. Submental tissue changes
2. Epiglottis thickened
3. Prevertebral soft tissue swelling at C3 (posterior pharyngeal wall)

Deng J, et al. Assessment and measurement of head and neck lymphedema: State-of-the-science and future directions. *Oral Oncology.* 2018 51 (431-437)

Head and Neck Cancer-related Lymphedema Signs and Symptoms

- Swelling (external and internal)
- Intraoral/external edema
- Fibrosis/adhesions
- Pain (internal/external)
- Impaired swallow (dysphasia)
- Impaired communication
- Decreased head/neck, UE, shoulder ROM
- Trismus (mouth opening 35 mm or less)[1]
- Xerostomia/dry mouth



1. van der Geer SJ, van Rijn PV, Kamstra JI, Roodenburg JLN, Dijkstra PU. Criterion for trismus in head and neck cancer patients: a verification study. Support Care Cancer. 2019 Mar;27(3):1129-1137. doi: 10.1007/s00520-018-4402-z.

NCCN Guidelines® Call for More Proactive Consideration and Intervention

Recommendations of note from the Survivorship Guidelines (V 3.2021)

1. Early detection/diagnosis is key for optimal lymphedema management; identify patients in stages 0 and 1 which are more responsive to management

2. Screen survivors for swelling, feeling of heaviness, fatigue, or fullness at each visit, providing further evaluation and education if symptoms are noted

3. Provider education and recommendations to the survivor should include
   - Importance of reporting signs, symptoms or infections to the healthcare team
   - Physical activity and supervised resistance training may improve symptoms
   - Consideration of compression garments, MLD and pneumatic compression for ongoing home management

National Comprehensive Cancer Network. Survivorship (Version 3.2021). https://www.nccn.org/professionals/physician_gls/pdf/survivorship.pdf. Accessed December 12, 2021.

Lymphedema Treatment

Complete Decongestive Therapy (CDT) for Lymphedema Management

Lymphedema is a chronic, progressive disease: Requires early intervention

Chronic care model needed for long term management vs episodic care (or curative model)

Phase I: In-clinic 2–4 week duration	Phase II: Self-care lifetime duration
Goal: Decongest/reduce volume	**Goal: Maintain reduction/minimize progression**
Daily treatments ▪ Manual lymph drainage (MLD) ▪ Compression bandaging ▪ Exercise ▪ Skin and nail care/precaution ▪ Patient education in self-care	**Ongoing therapy** ▪ Self-MLD or pneumatic compression device ▪ Compression garments and/or bandaging ▪ Exercise ▪ Skin and nail care

Neither MLD or compression garments should be stand-alone treatment, most effective when combined

Lasix/diuretics, if used primarily to treat LE edema without CHF, can worsen edema and fibrosis as these draw water from the tissues but leave behind protein molecules

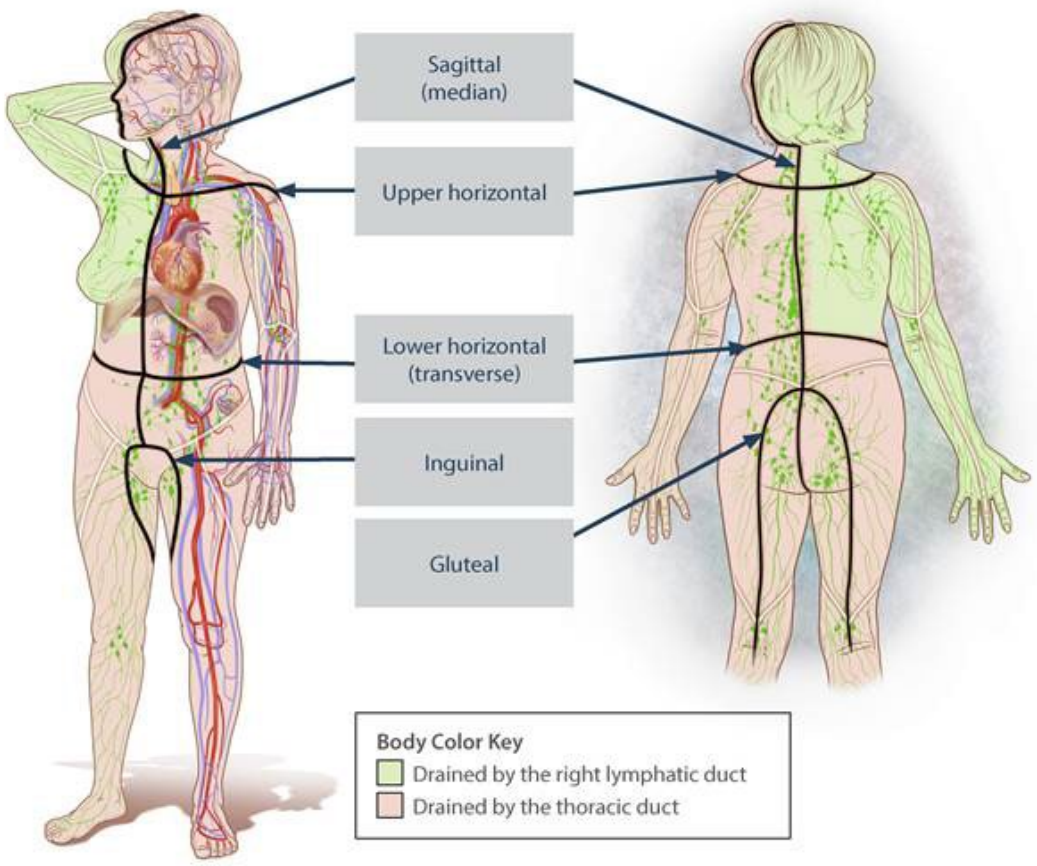
Manual Lymph Drainage (MLD)

Treatment starts with proximal decongestion working distally in small segments followed by movement of fluid distal to proximal

Gentle, short strokes to stretch skin opening superficial lymphatic capillaries and to stimulate the lymphatic system

Lymphatic Watersheds

Represent linear areas on the skin that separate territories.
Direction of flow is determined by lymphatic watersheds.



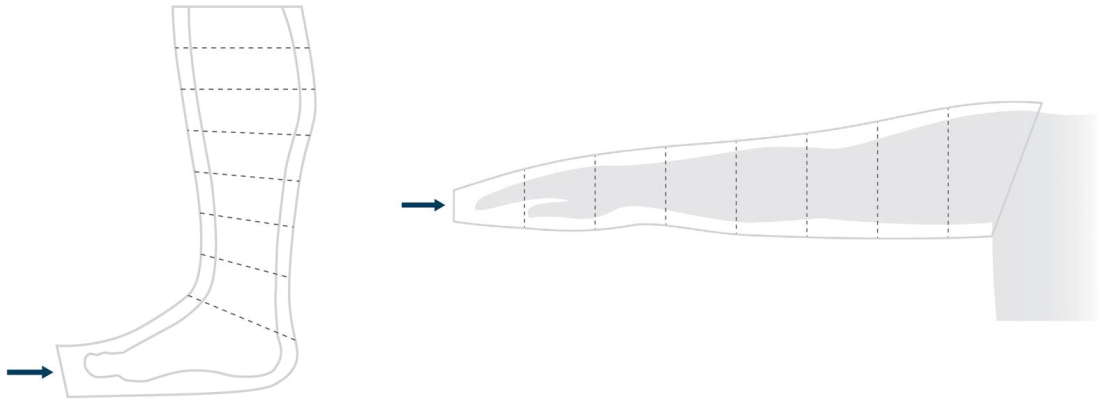
Basic Pneumatic Compression Device (E0651)

Fewer chambers

Designed to direct lymph fluid distal to proximal

Different pressure options may be available

Non-programmable



Advanced Pneumatic Compression Device (E0652)

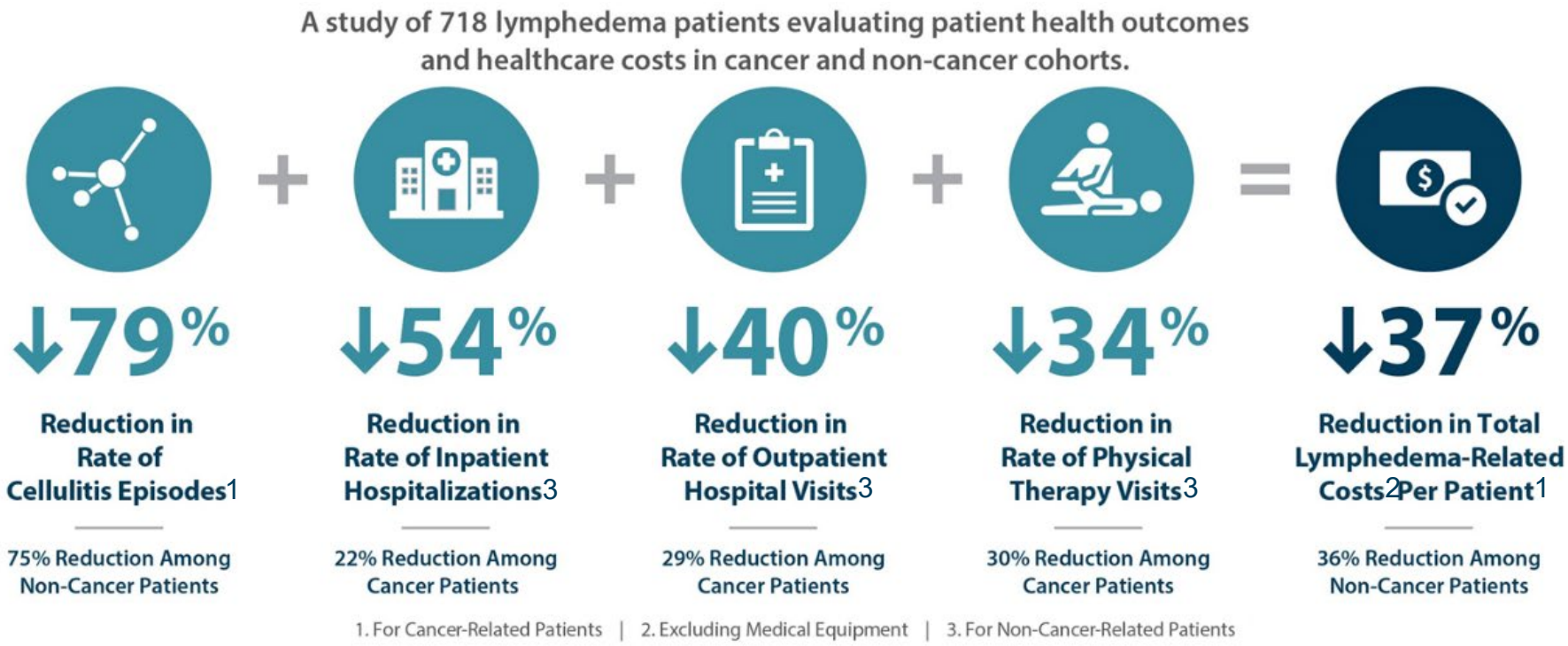
Provides truncal/proximal clearance

Works proximal to distal to decongest, then distal to proximal to drain

More chambers to better stimulate the lymphatics

Programmable/customizable treatment - ability to adjust the pressure manually in the individual compartments as well as the time spent in an area

Advanced Pneumatic Compression Demonstrated Reductions in Key Adverse Events, Healthcare Utilization and Costs



Karaca-Mandic, P. et al. (2015) The Cutaneous, Net Clinical, and Health Economic Benefits of Advanced Pneumatic Compression Devices in Patients with Lymphedema. JAMA—Dermatology, Oct. 2015.

Gradient Compression Bandaging Supplies

Compression Garments

Off the shelf circular knit knee high

Off the shelf flat knit (Solaris ExoStrong)

Custom/made to measure flat knit

Custom flat knit

Compression glove

Inelastic velcro (CircAid)

Nighttime compression (Juzo Night)

Donning gloves

Key Takeaways

Lymphedema is a chronic, progressive condition requiring daily management to prevent progression to later stages, further skin changes, and infection.

Comprehensive lymphedema management should be individualized and may include

- Patient education
- MLD/pneumatic compression
- Compression garments and/or bandaging
- Exercise/physical activity
- Skin and nail care

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