

Lymphedema and Fibrosis in Head and Neck Cancer

Survivors: Manifestations and Assessment

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Educational Goals

- To describe **clinical manifestations** of lymphedema and fibrosis in head and neck cancer survivors
- To discuss **clinical assessment** of lymphedema and fibrosis in head and neck cancer survivors

Untreated or Under-treated Lymphedema



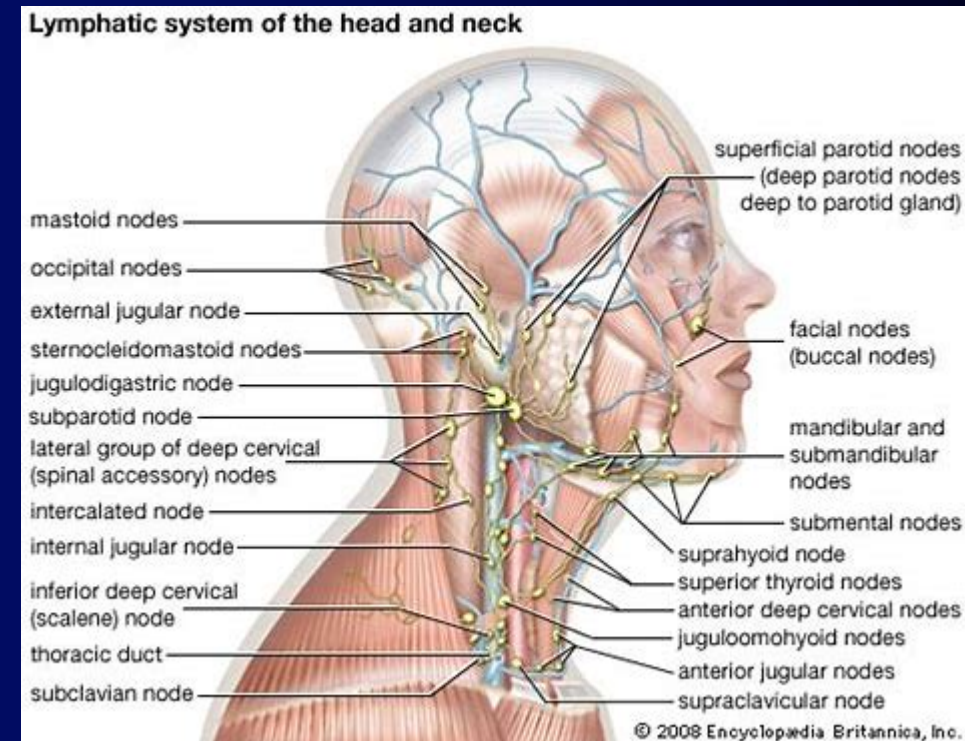
- Lymphedema results in - Disfigurement – Pain – Disability

Head and Neck Cancer Statistics

- **65,410** new cases in the U.S.A. in 2019
- Epidemic of **HPV-associated** cancer
 - 70-80% of oropharyngeal cancer
- Over **half a million** survivors in the U.S.A.
- The **sixth** most common type of cancer worldwide

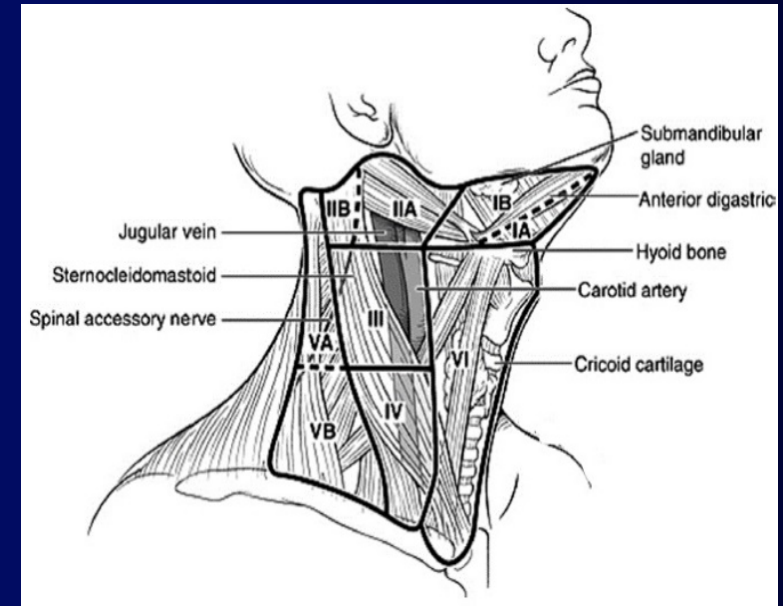
Physiology

- Head and neck requires massive lymph drainage to maintain vital functions
 - 300 lymph nodes
 - 1/3 of the total amount in the human body

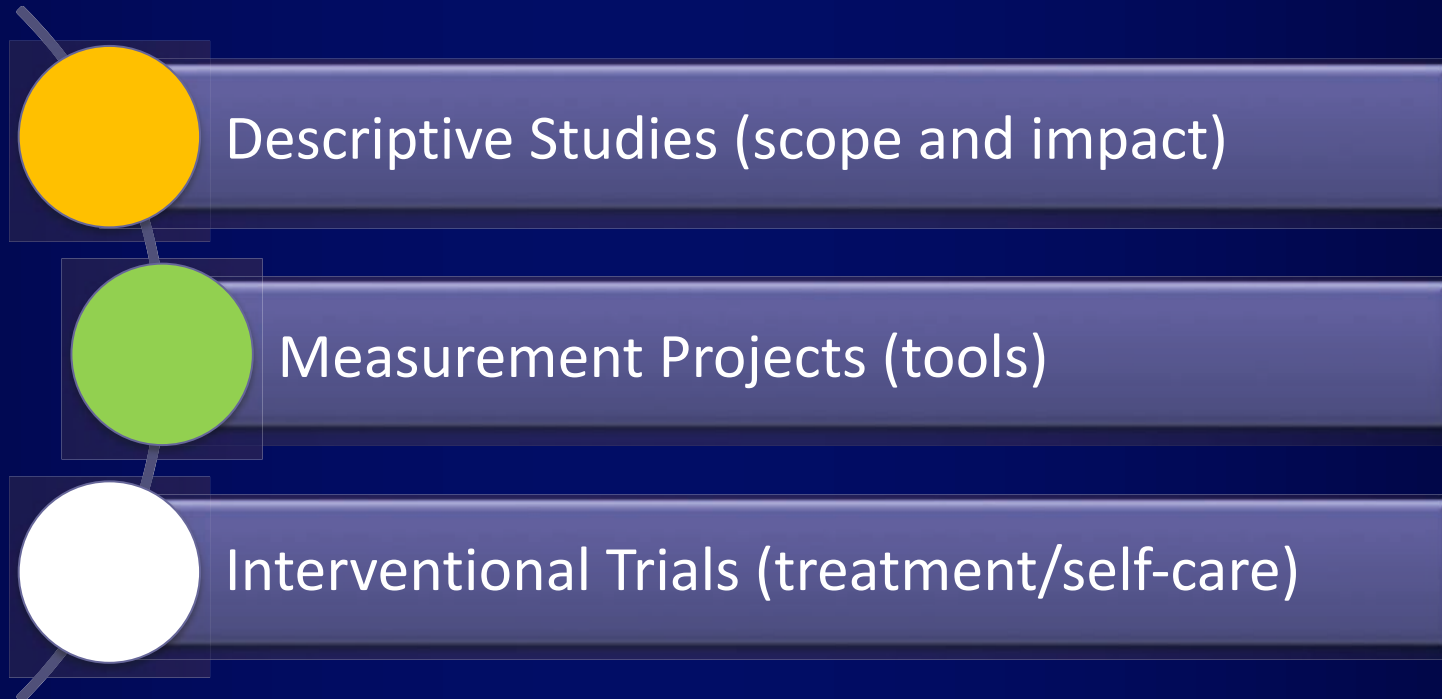


Treatment Related Effects on Lymph Flow

- Surgery
 - Removal of lymph nodes
 - Transection of lymph channels
 - Decreased muscular contraction
- Radiation therapy
 - Fibrosis of lymph nodes
 - Scarring of lymph channels
 - Decreased muscular contraction
- A goal of therapy is to eliminate nodal disease



Research Projects



Study 1 (Quantitative) –

Impact of Lymphedema in Patients with Head and Neck Cancer

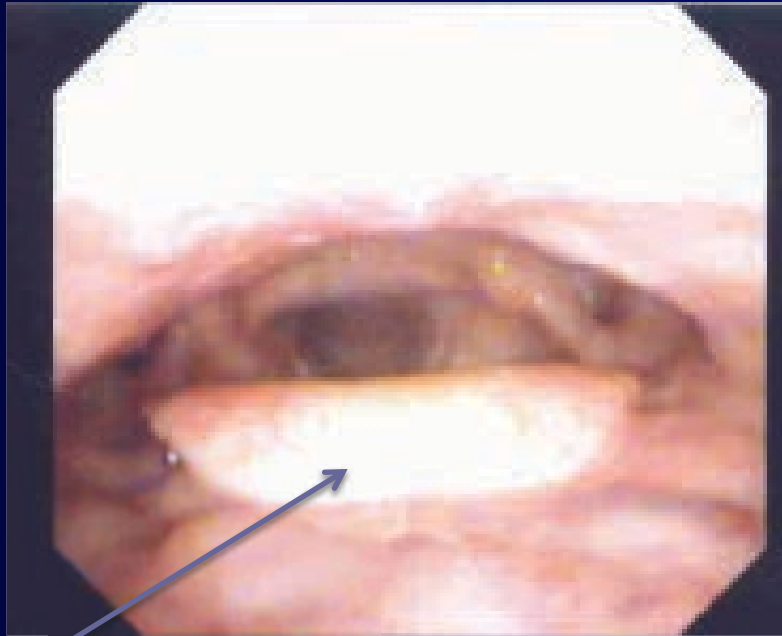
Funded by Oncology Nursing Society Foundation in United States

External Lymphedema



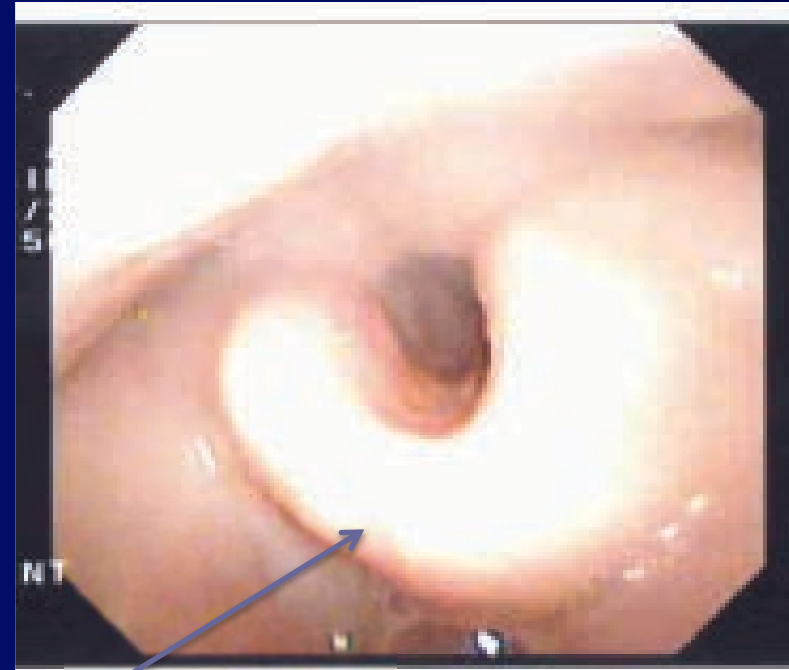
patient permission obtained

Internal Lymphedema



Epiglottis

No Lymphedema



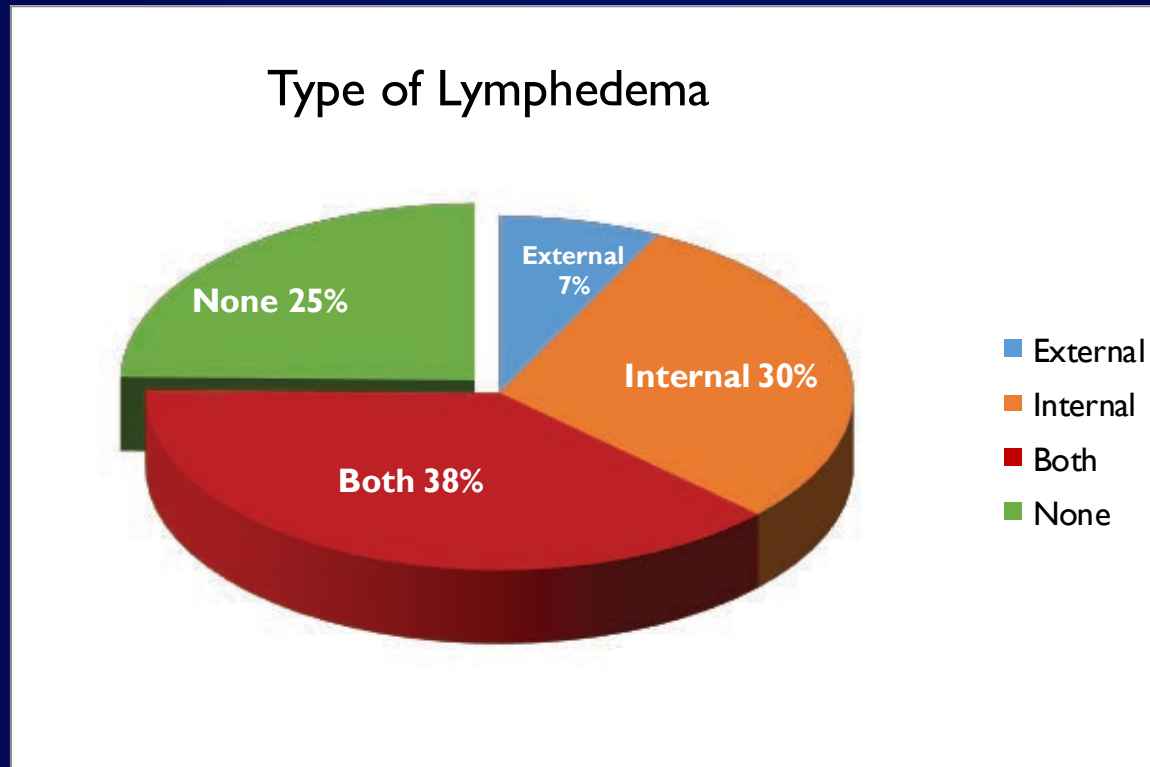
Epiglottis

Severe Lymphedema

Epiglottis Function

<https://www.youtube.com/watch?v=t17JeebmBPM>

Prevalence



Deng, J. Ridner, S.H., Dietrich, M.S., Wells, N., Wallston, K.A., Sinard, R.J., Cmelak, A.J., & Murphy, B.A. (2012). Prevalence of secondary lymphedema in patients with head and neck cancer. *Journal of Pain and Symptom Management*, 43(2), 244-252.

Physical Symptom Burden

Associations between Lymphedema Severity and VHNSS Scores

Lymphedema Severity	Standardized Coefficients Beta or R-square Change (<i>p</i> -value)							
	Sample size (n)	Swallowing	Nutrition	Mucous /Dry mouth	Pain	Voice	Dentition	Hearing
External lymphedema	100	0.32 (.001)	0.27 (.007)	0.29 (.004)	0.03 (.790)	0.12 (.226)	0.17 (.084)	-0.05 (.600)
Internal Lymphedema	78	0.23 (.042)	0.18 (.113)	0.27 (.016)	0.22 (.047)	0.30 (.008)	0.07 (.548)	0.02 (.833)
Combined lymphedema	79	0.13 (.003)	0.12 (.008)	0.13 (.004)	0.05 (.134)	0.09 (.030)	0.01 (.669)	0.01 (.700)

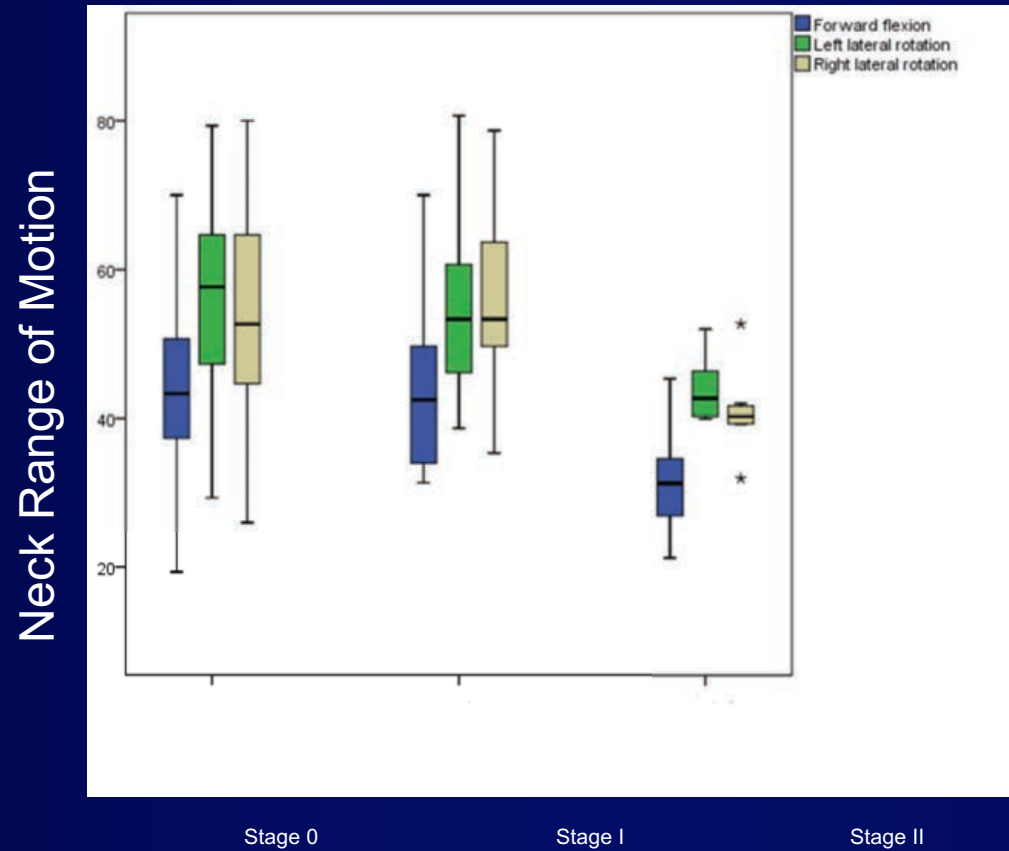
Note: (1) Beta or R-square Change is highlighted if $p < 0.05$.

Psychological Symptom Burden

- Altered appearance
- Body image disturbance
- Anxiety

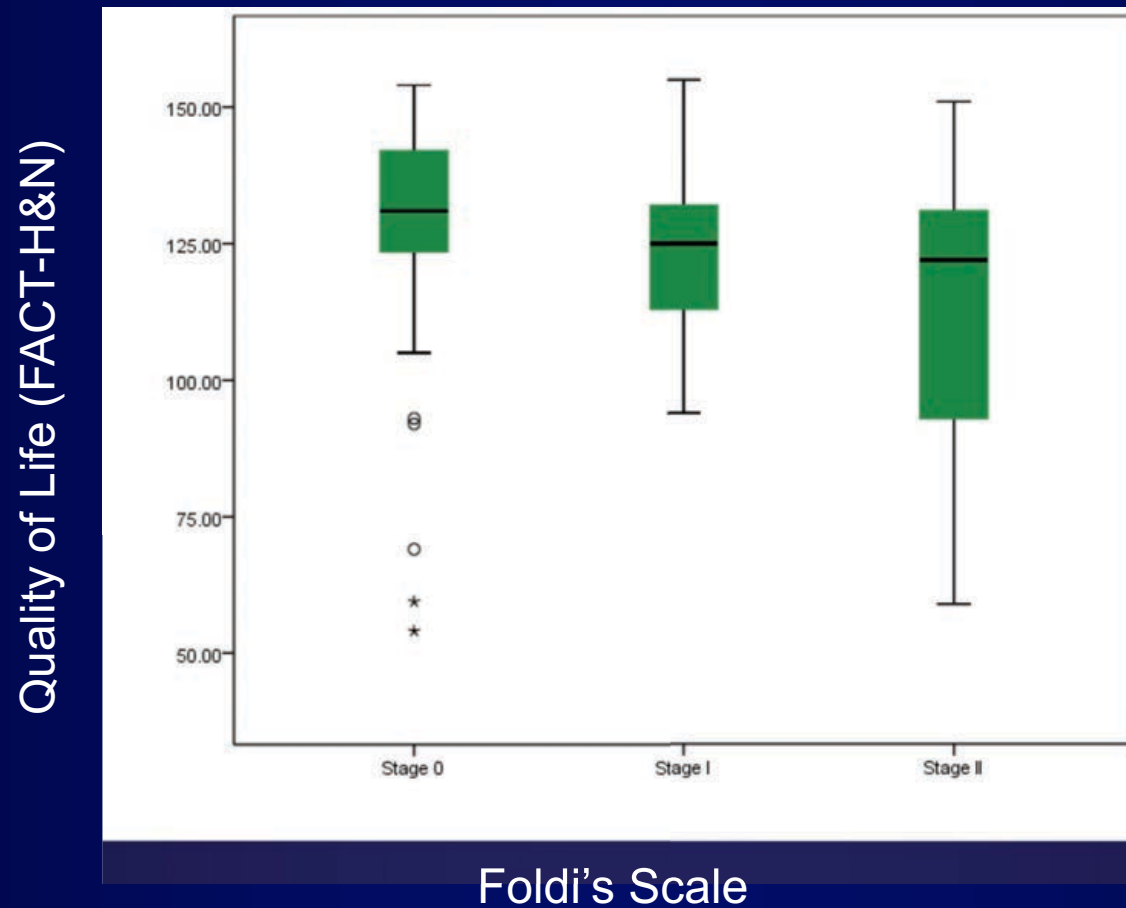


Function Impact – Neck Range of Motion



Foldi's Scale

Quality of Life Impact (FACT-H&N)



P= .005

Summary

- Lymphedema in patients with HNC
 - Frequent
 - Substantial symptom burden
 - Decreased functional status
 - Decreased overall quality of life

Study 2 (Qualitative) –
Symptom Experience in Head and Neck Cancer
Patients with Lymphedema

Funded by Vanderbilt Office of Clinical and Translational
Scientist Development

Symptoms

- Symptoms are the most common reason people seek health care
- Symptoms are felt or noticed by a patient
- Symptoms may not be captured by anyone else
- Symptoms are important for early identification of a disease

Interview Guide (2/21 questions)

- Can you tell me about when you first noticed lymphedema/swelling?
- What symptoms did you have with the lymphedema/swelling?

Temporal Onset

- 70% of participants: first noticed facial or neck swelling/lymphedema **within three months** following either surgery or radiation therapy
- 20% of participants: identified by oncologists
- 10% of participants: noticed before HNC therapy

Situational Factors



Symptoms/Complaints

- Tightness
- Discomfort
- Tenderness
- Numbness
- Tingling
- Spasm
- Pressure
- Throbbing



Symptoms/Complaints

- Impaired speech
- Impaired eating
- Difficulty swallowing
- Breathing difficulties
- Blurred vision
- Problems opening mouth



*Altered
Functions*

Symptoms/Complaints

- Pain
- Stiffness
- Limited neck/shoulder ROM
- Limited driving
- Limited swimming



*Neck-Shoulder
Musculoskeletal
Impairments*

Symptoms/Complaints

- Skin texture change
- Loose skin
- Skin color change
(hyper- or hypo-pigmentation) •



*Skin
Changes*

Symptoms/Complaints

- Altered appearance
- Negative self-image
- Fear
- Anxiety
- Acceptance
(swelling as part of life)



*Psychosocial
/ Symptoms*

Study 3 – Internal Lymphedema: Correlation with Dysphagia

- Hypothesis:
 - Dysphagia is in part due to soft tissue swelling of pharyngeal and laryngeal structures secondary to lymphedema
- Is this distinction important?
 - Yes....
 - Mechanism
 - Prevention
 - Treatment

Internal Lymphedema: Correlation with Dysphagia

- 81 HNC patients
 - VHNSS v 2.0: including -13 swallowing/nutrition-related questions grouped in 3 clusters: swallow solids, swallow liquids, nutrition
 - External lymphedema: Foldi's scale (physical exam)
 - Internal lymphedema: Patterson scale (endoscopic exam)
 - Modified-barium swallow study (MBSS) rated by:
 - Dysphagia Outcome and Severity Scale (DOSS)
 - In combination with swallow evaluation, by National Outcomes Measurement System (NOMS)
- Examinations performed at varied time points to assess the lymphedema spectrum, from baseline to 18 months post-therapy

Correlation of VHNSS Subscales with Internal Lymphedema by Patterson Scale

Patterson Scale Site	VHNSS Swallow solids	VHNSS Swallow liquids	VHNSS Nutrition
Epiglottis	.39, p = .004	.36, p = .009	.36, p = .007
Pharyngoepiglottic folds	.41, p = .003	.35, p = .12	.41, p = .002
Aryepiglottic folds	.53, p < .001	.44, p = .001	.41, p = .003
Arytenoids	.39, p = .004	.31, p = .023	.35, p = .009
False vocal cords	.41, p = .003	.24, p = .081	.24, p = .084
Pyramiform sinus	.46, p < .001	.37, p = .005	.49, p = .002
Base of tongue	.22, p = .107	.34, p = .010	.42, p = .001

No correlations exist between VHNSS and external lymphedema (p>0.20)

Correlation of Internal Lymphedema by Patterson Scale with Objective Swallow Evaluation

Patterson scale site	NOMS	DOSS
Epiglottis	.44, p = .002	.30, p = .029
Pharyngoepiglottic folds	.50, p = .001	.33, p = .015
Aryepiglottic folds	.47, p = .001	.32, p = .018
Arytenoids	.44, p = .002	.36, p = .006
False vocal cords	.42, p = .004	.34, p = .011
Pyriiform sinus	.44, p = .002	.35, p = .009

NOMS/DOSS ratings correlated with external lymphedema (p<0.01)

Clinical Implications

- HNC patients with lymphedema experience **multiple symptoms**
- Some of symptoms may be **unique indicators** of this pathophysiological condition
- Potential **situational factors** and possible risk reduction strategies for head and neck lymphedema

Clinical Implications

- Clinicians should educate HNC patients about symptoms associated with lymphedema
- Clinicians should inquire HNC patients about lymphedema-related symptoms and provide adequate supportive care to diminish symptom burden

Measurement Issues: Lessons Learned

- No “Gold Standard” available
- Multiple methods explored
- Limitations to all measurement tools

Measurement Projects

- Patient-Reported Outcome Measure (PRO)
- Clinician-Reported Outcome Measure (CRO)
- Imaging Techniques



Lymphedema Symptom Intensity and Distress Survey-Head & Neck (sample)

Instructions: Please read each of the symptoms and **circle yes or no** to indicate whether you have had this symptom **over the past week**. If you circle **yes**, please indicate the **severity** of this symptom and the **bother** of this symptom.

Over the past week have you had the following symptoms in <i>your head and neck</i> :																						
Symptom	Yes/No		Severity							Bother												
1. Feeling uncomfortable in your head or neck	Yes	No	Slight							Severe	Slight							Severe				
			1	2	3	4	5	6	7	8	9	10	1	2	3	4	5	6	7	8	9	10
2. Heaviness	Yes	No	Slight							Severe	Slight							Severe				
			1	2	3	4	5	6	7	8	9	10	1	2	3	4	5	6	7	8	9	10
3. Tightness	Yes	No	Slight							Severe	Slight							Severe				
			1	2	3	4	5	6	7	8	9	10	1	2	3	4	5	6	7	8	9	10
4. Firmness or hardness of your skin	Yes	No	Slight							Severe	Slight							Severe				
			1	2	3	4	5	6	7	8	9	10	1	2	3	4	5	6	7	8	9	10
5. Stiffness	Yes	No	Slight							Severe	Slight							Severe				
			1	2	3	4	5	6	7	8	9	10	1	2	3	4	5	6	7	8	9	10

Manifestations – Symptom Assessment Tool

Most Common Complaints

- Feeling uncomfortable in head and neck
- Tightness
- Firm or hard skin
- Stiffness
- Tenderness
- Limited movement
- Problems swallowing
- Voice changes
- Feel like something stuck in throat
- Feeling tired
- Feel like people are staring at me



Table 1 Symptom Prevalence Differences ($p < 0.05$)

Frequency of Symptoms	LE (%) (N=23)	No LE (%) (N=23)	<i>p-value</i>
Altered sensation			
Numbness of the face/neck skin	34.8	8.7	0.032
Heaviness of the face/neck skin	21.7	0.0	0.018
Warmth of the face/neck skin	17.4	0.0	0.036
Pain without head/neck movement	17.4	0.0	0.036
Neck – Shoulder musculoskeletal/skin symptoms			
Swelling in face	17.4	0.0	0.036
Swelling in neck	21.7	0.0	0.018
Head and neck-specific functioning			
Problems swallowing mashed food	39.1	9.1	0.019
Trouble breathing	26.1	0.0	0.009
Blurred vision	21.7	0.0	0.018
Systemic symptom			
Feel worse when flying in air plane	25.0	0.0	0.017

Clinician-Reported Outcome Measures

- Four scales available
 - Two for head and neck lymphedema
 - CTCAE Lymphedema Scale –H&N (v3.0)
 - ACS Lymphedema Scale –H&N
 - Two for general lymphedema
 - Foldi's Scale
 - CTCAE Fibrosis Scale (v3.0)

Development Project

-Head and Neck External Lymphedema-Fibrosis Assessment Criteria (HN-LEF)

- Method: Two-phase Study
 - Development phase (15 expert participants)
 - Preliminary test phase (30 patient participants)
- Findings
 - Head and Neck Lymphedema Scale
 - Good content/face validity
 - Acceptable inter-rater reliability
 - (83% exact agreement, 100% within 1 grade,
 - $kappa= 0.752, p < .001$)
 - Further studies for psychometric testing justified

Type	Descriptors
Type A	No visible tissue swelling; palpable thickening and/or tightness of dermis
Type B	<p>Visible soft tissue swelling; involved tissues are soft to touch; tissue swelling is reducible and fluctuates in severity</p> <p><u>Grade:</u> Mild – visible soft tissue swelling on close inspection Moderate – easily visible swelling that significantly alters normal tissue contours Severe – extreme or massive tissue swelling</p>
Type C	<p>Visible soft tissue swelling; involved tissues are firm to touch; tissue swelling is non-reducible and persistent</p> <p><u>Grade:</u> Mild – visible soft tissue swelling on close inspection Moderate – easily visible swelling that significantly alters normal tissue contours Severe – extreme or massive tissue swelling</p>
Type D	<p>Firm tissues with increased density and decreased compliance in the absence of swelling</p> <p><u>Grade:</u> Mild – palpable firmness of soft tissues Moderate – soft tissues are extreme hard and have a woody texture Severe – fibrosis associated with contracture</p>

Type:
Description of some *physical characteristics* of the soft tissue abnormalities observed by physical exam

Grade:
Description of the *severity* of the soft tissue abnormalities

Clinical Use of HN-LEF - Protocol Development

- Clinical training: Working with HNC medical oncologists
- Procedures: Patient interview and physical examination
- Documentations: Table and figures



Protocol Development

- Patient Interview (sample)

- Have you experienced any swelling or firmness in your head or neck area as a result of your tumor or treatment?
- Does swelling change or fluctuate throughout the day?
- Please tell me if anything (e.g., specific activities) aggravates the swelling.

Protocol Development

- Physical Examination (sample)

- Wash hands or clean hands using antiseptic hand wash
- Ask patient for permission to palpate face and neck
- Make sure patient is sitting comfortably, facing the examiner, and have patient remove glasses or necklace if needed
- Visual inspection
- Palpation
- Then use HN-LEF Grading Criteria to determine the types and grades of LEF
- Wash hands or clean hands using antiseptic hand wash

Head and Neck External Lymphedema and Fibrosis Documentation Sheet

Start time: _____

History:

1. Since being diagnosed head and neck cancer (HNC) or end of HNC treatment, have you experienced any swelling in your head and neck area (using the same order listed in the Documentation Sheet, e.g., around eyes, cheek)?

Please document patient-reported swelling sites: _____

2. Does swelling change or fluctuate throughout the day? (also, check if swelling increases or decreases and at what time of day)

___ No; ___ Yes, please specify: _____

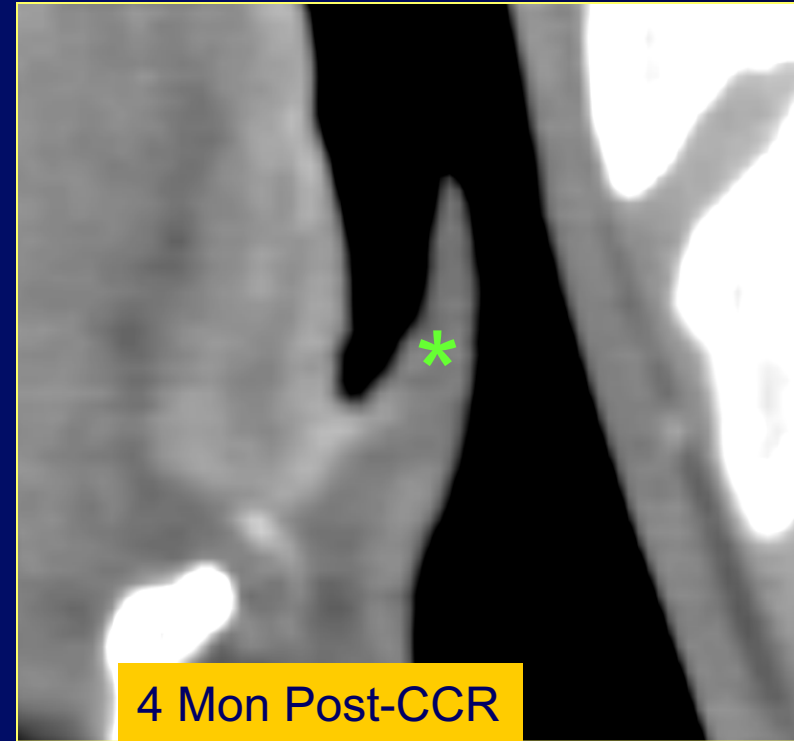
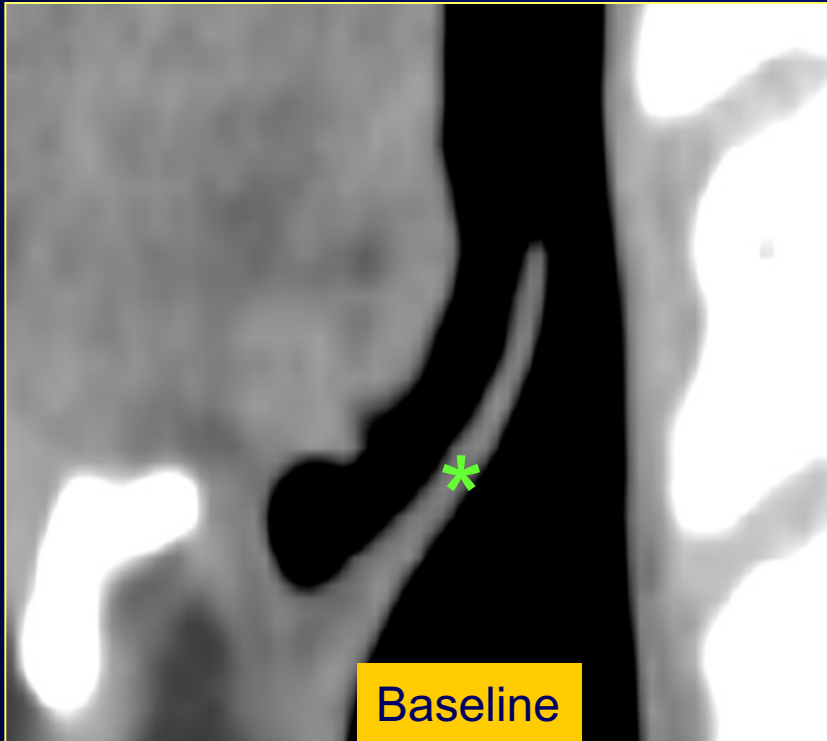
Sites of Tissue Swelling/Fibrosis	Type	Grade
Left Peri-orbital Region		
Right Peri-orbital Region		
Left Cheek		
Right Cheek		
Submental Region		

Imaging Techniques

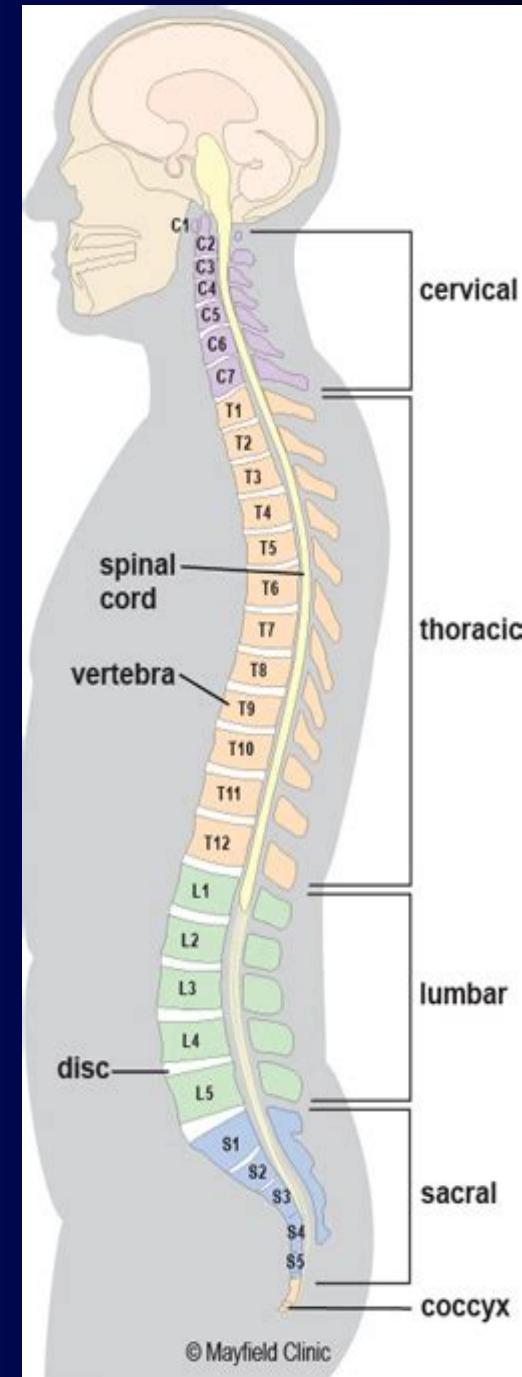
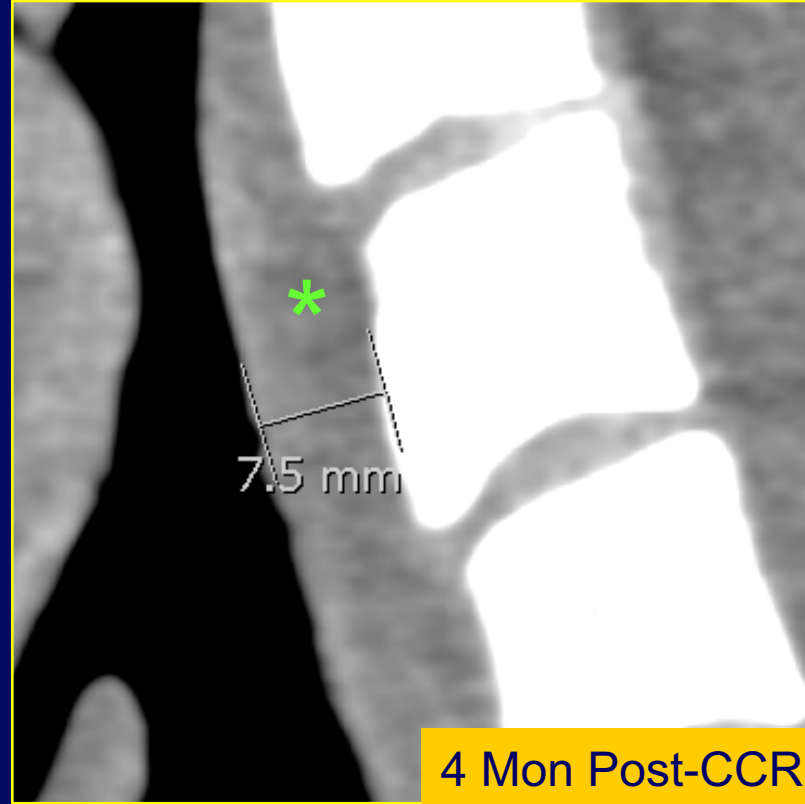
- CT Scan

- Goal: To develop a measurement tool to quantify CT changes after HNC treatment
 - Reliable assessment sites
 - Easy to use
 - Standardized criteria

Epiglottis Thickness



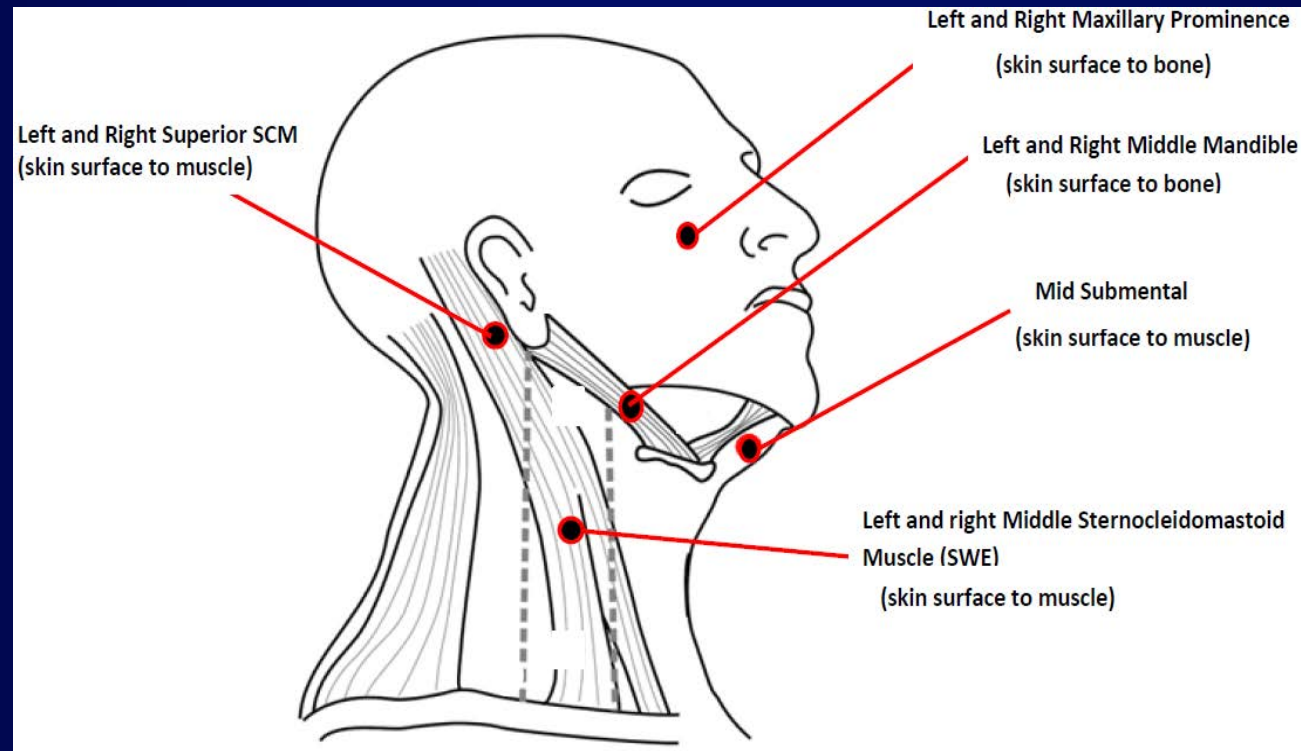
Prevertebral Soft Tissue Thickness



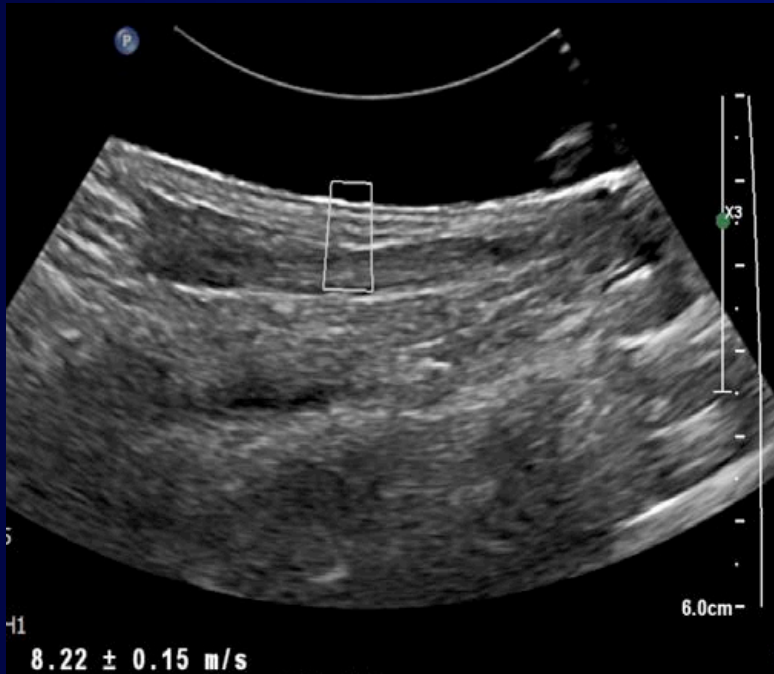
Imaging Techniques

- Ultrasound Measure

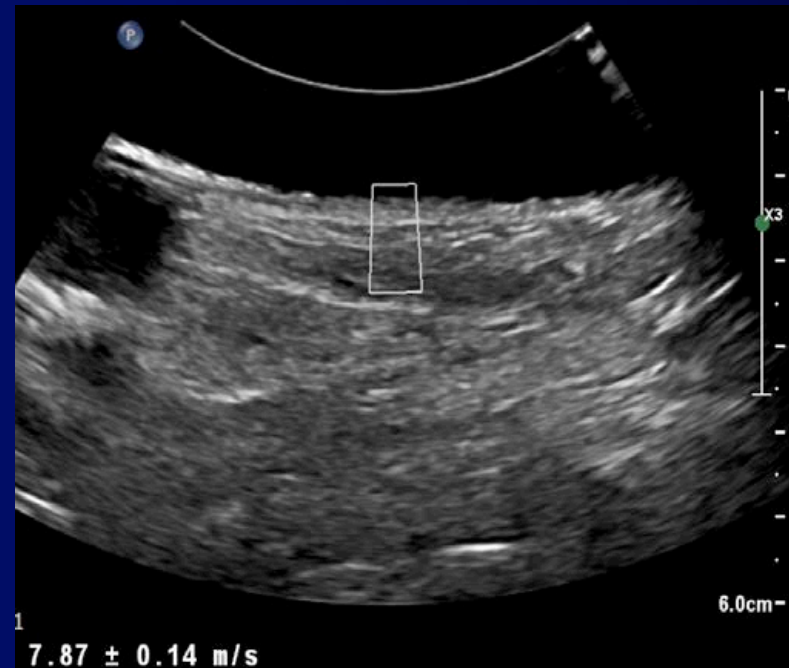
- Anatomical Sites and Measurement Distances



Ultrasound Elastography



Left Middle SCM



Left Superior SCM

- Notes:
1. The box (region of interest) within each image shows how measurement of shear wave velocity on each anatomical site was made. The calculated shear wave velocity (mean \pm standard deviation) is shown within each image.
 2. SCM: Sternocleidomastoid Muscle.

Establishing Lymphedema and Fibrosis Measures in Oral Cancer Patients

(NIH/NIDCR R01, PI Deng)

- Goal: To assess and compare patient-reported, clinician-reported, and imaging measures of LEF across the trajectory of treatment, recovery, and survival
- Design: Prospective, longitudinal
- Population: Patients with locally advanced oral cavity or oropharyngeal cancer

Feasibility and Preliminary Efficacy of Yoga in Head and Neck Cancer Survivors

- NIH/NCI R21
- Design: Wait-list control RCT, >3 months post-treatment
- Intervention: 8-week hatha yoga
- Assessment: baseline, 4-week, and 8-week
- Major findings (n=40):
 - Feasibility: recruitment/retention rate, satisfaction and no AEs
 - Efficacy: shoulder ROM ($p<.05$), pain ($p<.005$), and anxiety ($p=.015$)

Lymphedema Management Project

(American Cancer Society Research Scholar Grant, PI Deng)

- Challenges for lymphedema management
 - Lymphedema: incurable, chronic, progressive
 - Intensive lymphedema therapy
 - Long-term self-care

Patient Barriers

– Lymphedema Self-Care

Lack of Guidelines

Lack of Monitoring

Limited Knowledge

Lack of Training on
Skills for Self-Care

Lack of Motivation

Low Self-Efficacy

Difficult in
Integrating into
Daily Routine

March is

L. Y. M. P. H. E. D. E. M. A.

Awareness Month

