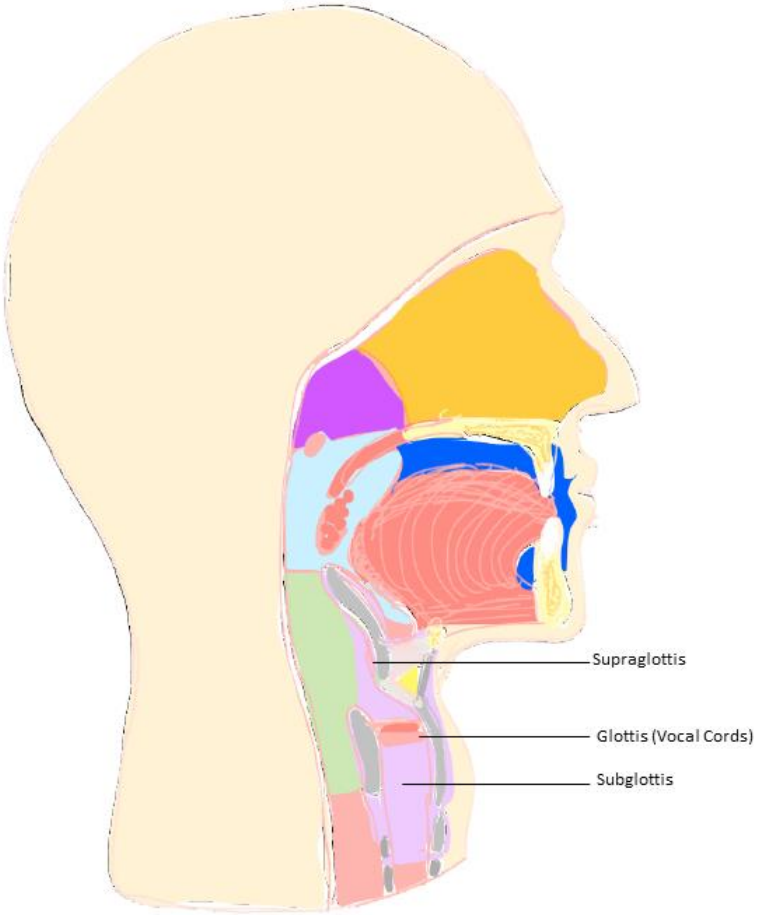
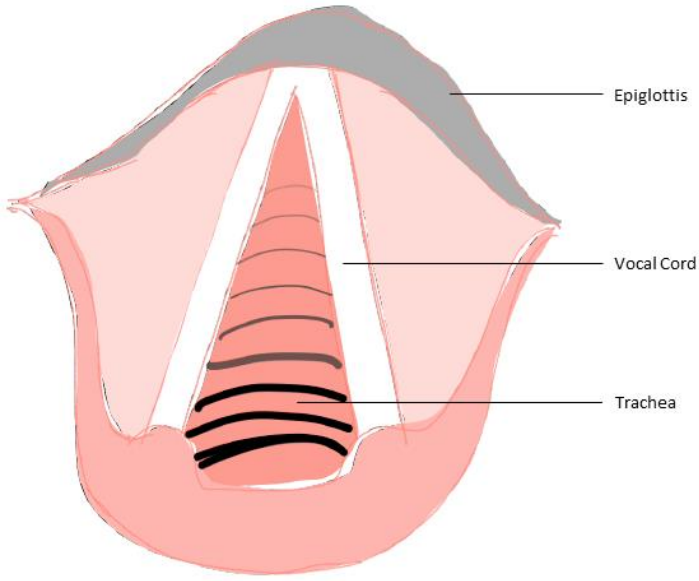
Larynx

a. Anatomy
    i. The larynx, or voice box, is composed of cartilage, muscle and a mucosal lining. The cartilage skeleton can be seen and felt externally and is often referred to as the “Adam’s Apple.” These structures serve to create your voice but the main function of the larynx is to protect the lungs from aspiration (food and water entering the lungs). Internally, the larynx contains vocal cords and the epiglottis. The epiglottis is a flap of cartilage that folds over the larynx while swallowing to protect the airway from aspiration. The epiglottis stays open during breathing so air can pass easily.
    ii. Involvement of these important anatomical structures by cancer causes voice changes and difficulty swallowing.
    iii. The hypopharynx is intimately related to the larynx. In fact, distinguishing larynx and hypopharynx may be difficult if a cancer involves overlapping sites. Fortunately, the treatments are often very similar.

    iv. Squamous cells make up the lining, also known as the mucosa, of the larynx. That is why squamous cell carcinoma is the most common type of larynx cancer.


Supraglottis
Glottis (Vocal Cords)
Subglottis

Glottis


Epiglottis
Vocal Cord
Trachea

b. Risk Factors
    i. Tobacco use is the most common risk factor associated with cancer of the larynx
        1. Alcohol can have an additive effect
    ii. Occupational exposures
        1. Sulfuric acid
c. Symptoms
    i. Hoarseness, chronic sore throat, ear pain, pain with swallowing, difficulty swallowing, difficulty breathing, chronic cough, weight loss, and coughing up blood
d. Diagnosis
    i. Diagnosis of a cancer within the larynx (voice box) is often first suspected with patients reporting voice changes, coughing up blood or swallowing difficulties. Once an abnormality is observed, a biopsy will be required to confirm the diagnosis. This can occasionally be accomplished in the clinic with specialized equipment. To effectively biopsy and evaluate the extent of the laryngeal cancer, you may require biopsy under general anesthesia in the ambulatory outpatient setting. Prior to scheduling your biopsy under general anesthesia, a complete head and neck exam including in-office fiberoptic camera exam to visualize the tumor growth and palpation of neck lymph nodes will be performed. Patients presenting with a neck, mass may undergo a needle biopsy in the office setting or under radiologic image guidance.
    ii. Your doctor may also order a variety of medical imaging:
        1. Computerized tomogram imaging (CT scan)
        2. Magnetic resonance imaging (MRI)
        3. Positron emission tomography (PET)

        These images will help to further delineate the extent of the cancer. Different types of imaging help to visualize different anatomic structures Intravenous contrast enhanced CT scan and MRI can identify abnormalities in the larynx or neck that suggest a primary tumor or lymph node metastases. PET imaging is a special technology that identifies a glucose (sugar) molecule being absorbed by the cancer cells and help localize the tumor in other parts of the body. CT scan imaging of the chest may be required to visualize any spread of disease to the lungs.
e. Staging
    i. The American Joint Committee on Cancer (AJCC) has created a staging system (TNM staging)
    ii. to help guide treatment. The staging system groups cancers into stages based on their anatomic extent. The staging helps to determine the optimal treatment for a specific cancer, and provides information about expected survival rates.

iii. The staging system includes information about the extent of the original or local tumor (T classification or primary tumor extent), spread to lymph nodes (N-classification or nodal metastases), and spread to distant parts of the body (M classification or distant metastases). The T staging system is further refined into three subsites (supraglottis, glottis, subglottis) based upon its location relative to the vocal cords (glottis). More advanced tumors impair normal movement of the vocal cords, or involve multiple subsites within the larynx.

iv. Combinations of T, N and M-classifications produce an overall stage. There are 4 overall staging groups (Stage 1-4). As the AJCC TNM stage number increases so does the disease burden. More advanced cancers lead to worse survival rates. Factors that play a role in the overall stage include: destruction of nearby structures (ie. tongue base, extralaryngeal invasion, thyroid cartilage destruction, involvement of the paraspinal musculature or esophagus and blood vessels of the neck) and involvement of lymph nodes within the neck.

v. Lymph nodes are small oval shaped structures found within the fat of the neck that harbor immune cells that filter and fight infection and disease.. Cancer cells from the larynx detach from the primary tumor, and travel through lymphatic vessels becoming trapped in lymph nodes where they start to grow. Once a larynx cancer spreads to lymph nodes, it is considered more advanced, and is considered overall stage 3 or higher. In addition, the number of abnormal lymph nodes and their size is important. Sometimes, the cancer in a lymph node grows out of the lymph node, a property known as extranodal extension (ENE). Extranodal extension (ENE) is defined as cancer that has breached the outside capsule of the involved lymph node. In general, the demonstration of ENE suggests a cancer is aggressive, and intensification of treatment should be considered.

Primary Tumor Stage: Supraglottic Larynx	
Stage	Description
Tx	Primary tumor cannot be assessed
Tis	Carcinoma *in situ*
T1	Tumor limited to one subsite of the supraglottis with normal vocal cord mobility
T2	Tumor invades more than one subsite of supraglottis or glottis or an adjacent site without fixation of the larynx
T3	Tumor limited to the larynx with vocal cord fixation; **and/or**, Invasion of any of the following: postcricoid, preepiglottic space, paraglottic space, or inner cortex of thyroid cartilage
T4a	Tumor invades through outer cortex of thyroid cartilage; **and/or**, invades tissues beyond the larynx
T4b	Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures

Primary Tumor Stage: Glottic Larynx	
Stage	Description
Tx	Primary tumor cannot be assessed
Tis	Carcinoma *in situ*
T1a	Tumor limited to one vocal cord
T1b	Tumor involves both vocal cords
T2	Tumor extends to supraglottis and/or subglottis with normal or impaired mobility
T3	Tumor limited to the larynx with vocal cord fixation; **and/or**, Invasion of paraglottic space and/or inner cortex of thyroid cartilage
T4a	Tumor invades through outer cortex of thyroid cartilage; **and/or**, invades tissues beyond the larynx
T4b	Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures

Primary Tumor Stage: Subglottic Larynx	
Stage	Description
Tx	Primary tumor cannot be assessed
Tis	Carcinoma *in situ*
T1	Tumor limited to the subglottis
T2	Tumor extends to vocal cords with normal or impaired mobility
T3	Tumor limited to the larynx with vocal cord fixation; **and/or**, Invasion of paraglottic space and/or inner cortex of thyroid cartilage
T4a	Tumor invades through outer cortex of thyroid cartilage; **and/or**, invades tissues beyond the larynx
T4b	Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures

Regional Nodal Stage: Larynx	
Clinical Stage	Description
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral node, 3 cm or smaller and ENE (-)
N2a	A single ipsilateral node larger than 3 cm but not larger than 6 cm and ENE (-)
N2b	Metastases in multiple ipsilateral lymph nodes, none larger than 6 cm and ENE (-)
N2c	Metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm and ENE (-)
N3a	Metastasis in a lymph node larger than 6 cm and ENE (-)

N3b	Metastasis in any nodes and ENE (+)

Regional Nodal Stage: Larynx	
Pathologic Stage	Description
Nx	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis in a single ipsilateral node, 3 cm or smaller and ENE (-)
N2a	Metastasis in a single ipsilateral node 3 cm or less and ENE (+); **or**, A single ipsilateral node larger than 3 cm but not larger than 6 cm and ENE (-)
N2b	Metastases in multiple ipsilateral lymph nodes, none larger than 6 cm and ENE (-)
N2c	Metastasis in bilateral or contralateral lymph nodes, none larger than 6 cm and ENE (-)
N3a	Metastasis in a lymph node larger than 6 cm and ENE (-)
N3b	Metastasis in a single ipsilateral node larger than 3 cm and ENE (+); **or**, Multiple ipsilateral, contralateral or bilateral nodes, any with ENE (+); **or**, A single contralateral node any size and ENE (+)

AJCC Prognostic Stage Groups: Larynx	
Pathologic Stage	Description
0	TisN0M0
I	T1N0M0
II	T2N0M0
III	T3N0M0, T1-3N1M0
IVA	T4aN0-1M0, T1-4aN2M0
IVB	Any T, N3, M0; **or**, T4b, any N, M0
IVC	Any T, any N, and M1

f. Treatment
   i. Fortunately, there are several effective treatment options for larynx cancer. Treatment selection typically depends on the exact location of the tumor, the stage of the tumor and how well the larynx is functioning.
   ii. Early Stage Larynx Cancer (Stages 1 & 2)

1. Early stage larynx cancer is typically treated with either surgery or radiation. Larynx preservation, without the need for a total laryngectomy is the rule. Occasionally, both treatment types may be required.
2. Surgical removal of larynx cancer through the mouth is possible for some early larynx cancers. Transoral laser microsurgery (TLM) is an effective tool for early larynx cancers. Transoral robotic surgery may be considered. External neck incisions are not required for removal of the larynx cancer; however, incisions are needed to remove lymph nodes in the neck. Not every patient is a candidate for TLM. Patients must meet specific criteria that ensure the best results. Potential risks of TLM include injury to the teeth and gums, injury to the trachea or esophagus, airway fire, bleeding, swallowing difficulties and hoarse voice. These surgeries are highly specialized, and consultation with a surgeon with a vast experience should be considered.
3. Removal of part of the larynx may be considered in selected early stage cancers. These operations are chosen for patients with slightly larger tumors and inadequate access to the tumor through the mouth. These operations are known as open partial laryngectomy. The portion of the larynx with the cancer is removed through an incision in the neck. A temporary tracheostomy and feeding tube are often required, and voice quality and swallowing function are not as favorable as with transoral approaches. However, the operation achieves high success rates in properly selected patients, and may be preferred to a total laryngectomy.
4. Laryngectomy is more commonly needed for advanced larynx cancers but is occasionally necessary for early stage tumors in certain locations or early tumors in patients who have failed other treatments. Laryngectomy requires complete removal of the voice box, which is not reversible. Patients who undergo a laryngectomy will have a permanent stoma or opening in the neck for breathing. Most patients are eventually able to maintain their nutrition by mouth without a feeding tube.
5. Radiation therapy is a common and effective tool for treating early larynx cancers. Typically, treatments are given every day, five days per week, for up to 7 weeks. A customized mask is created for patients prior to treatment to target the radiation. Side effects of radiation treatment include red/sore skin, sore throat, oral sores, voice box swelling, and difficulty with swallowing.
6. Chemotherapy, which is a broad term for intravenous or orally administered anti-cancer medications, is typically reserved for advanced laryngeal cancers. Immunotherapy, a newer class of medications that takes advantage of the immune properties of tumors, is typically reserved for patients with incurable larynx cancer.

iii. Advanced Stage Laryngeal Cancer (Stages 3 & 4)

iv. Advanced stage larynx cancers are typically treated with at least two treatments (surgery and radiation or radiation and chemotherapy). Usually, minimally

invasive surgical techniques such as TLM and robotic surgery are not recommended in advanced stage cancers.

v. Radiation and chemotherapy are often used as part of what is referred to as an "organ preservation" approach. The goal of the treatment is to cure the cancer while anatomically preserving the larynx. Laryngeal functions include breathing, speech, and swallowing food and liquids safely. Patients with advanced larynx cancers may have a poorly functioning larynx as a result of the tumor-related destruction of the larynx. When a larynx is not functioning properly to separate breathing and swallowing functions, it is considered a "non-functioning larynx." The patient may require a tracheostomy to breathe and a feeding tube to eat. They are unlikely to regaining normal function with organ preservation approaches. Removal of the diseased organ surgically is usually recommended in a surgery known as a total laryngectomy which results in a permanent opening or tracheostoma in the neck. In this operation, the windpipe is permanently attached to an opening in the skin, and the throat is attached to the esophagus. Breathing and swallowing functions are permanently surgically separated. While laryngectomy leaves the patient with a permanent stoma (hole) in the neck, most patients are able to eat and rehabilitate their communication. As patients are not able to use their own voice, patients may eventually use a tracheoesophageal puncture device (TEP), electrolarynx or text-to-talk devices to communicate.
vi. Reconstructive surgery is sometimes required during laryngectomy surgery. Tissue used for reconstruction can come from the chest wall, shoulder, wrist, thigh or other location depending on the tumor location and the individual surgeon's preferences.
vii. Once surgery is complete, the final pathology result will direct what additional treatments may be required. Most patients with advanced larynx cancer undergoing surgery who have not had radiation before will require post-operative radiation therapy. Post-operative chemotherapy is also sometimes recommended in combination with radiation therapy for very advanced cases.
viii. Organ preservation with chemoradiation: For many patients with advanced larynx cancer, non-surgical treatment with radiation and chemotherapy without surgery may be good option. These treatments are usually combined, with patients receiving chemotherapy infusions once per week while also undergoing daily radiation treatments. The most common chemotherapy drugs administered are cisplatin or carboplatin. Radiation plus chemotherapy can be quite effective for many advanced larynx cancers, and many patients may be able to avoid a laryngectomy. Side effects can include sore throat, sore mouth, trouble swallowing, weight loss, kidney disfunction, nerve damage, hearing loss, skin irritation, voice box swelling and fatigue.
ix. If the larynx cancer is determined to be incurable to due metastases or involvement of vital unresectable structures, chemotherapy alone and/or immunotherapy may be administered. Typically, these treatments are meant to minimize symptoms and slow tumor progression rather than cure the disease.

g. Survival
    i. Survival from laryngeal cancer are directly related to the cancer stage. Early stage cancers tend to respond better to treatment than later stage cancers. Delays in diagnosis and treatment may contribute to poorer outcomes. Staging differs based on which part of the larynx is affected, but typically, smaller tumors that involve just one or two components of the larynx, and have not spread to lymph nodes are classified as Stage I or Stage II cancers. Larger tumors that begin to grow into the major cartilages of the larynx or that causes one of the vocal cords to be paralyzed are Stage III cancers. Tumors that grow outside of the larynx are Stage IV cancers. If you have a cancer that has spread to lymph nodes in the neck, the cancer is automatically Stage III or higher, no matter the size of the tumor in the larynx. According to the American Cancer Society, Stage I and II cancers have a 5-year survival of 60-83%, depending on the location of the tumor in the larynx. When the cancer has spread to lymph nodes in the neck (Stage III), the 5-year survival is around 50%. Stage IV laryngeal cancers typically carry of 5-year survival of less than 50%.
    ii. Your physician will help determine what type of treatment is best based on the location of the cancer, the stage of the cancer, and the type of symptoms that you have prior to treatment (voice changes, trouble swallowing, trouble breathing, etc.).
    iii. Early side effects of treatment depend on the type of treatments. Patients with early laryngeal cancers who are treated with surgery may expect to have some voice changes and some difficulty swallowing that improve with time and speech therapy. Depending on the procedure, patients may require a temporary tracheotomy. A tracheostomy is a tube placed into the windpipe, which allows patients to breath when there is swelling in the voice box that would otherwise make breathing difficult. When the swelling improves, the tracheotomy may be removed, and the opening in the windpipe closes. Occasionally, a temporary feeding tube (either in the stomach or in the nose) may be required if there is significantly difficulty with swallowing after surgery.
    iv. Patients with early cancers that are treated with radiation may have less voice changes but could still have some trouble with swallowing due to pain, throat dryness, and other side effects from radiation. Another common side effect from radiation for laryngeal cancer is lymphedema. This term refers to swelling of skin of the neck. There are specialized treatments to help improve lymphedema that are often conducted by physical therapists. As with patients who undergo surgical treatment for laryngeal cancer, some patients who are treated with radiation require temporary feeding tubes. Speech therapists can help with swallowing after treatment is completed, but some patients lose their ability to swallow, are unable to take a diet by mouth and require feeding tubes permanently.
    v. For the most advanced laryngeal cancers, or for cancers that return after radiation therapy, treatment may involve complete removal of the voice box as mentioned above. Patients who undergo total laryngectomy are permanent neck

breathers and no longer have a voice box with which to talk. In many cases, laryngectomy patients are able to swallow normally. There are also several ways for laryngectomy patients to learn how to speak after having the voice box removed, including use of an electrolarynx, esophageal speech, or having a trachea-esophageal prosthesis placed. Specialized speech therapists train laryngectomy patients in each of these types of speech replacements, depending on what the patient capabilities and preference after completing treatment. Some patients with TEP speech rehabilitation have near normal voices, but TEP speech requires motivation to pick up a new skill.

h. Surveillance/Survivorship
    i. Surveillance: As with any cancer, there is a risk that larynx cancer will come back ('recur') after treatment. 'Surveillance' means that your doctor(s) will monitor you after treatment with a combination of physical examination and imaging studies in order to detect disease that has recurred. Protocol details will vary from institution to institution. Patients will be followed for at least 5 years once completing your cancer treatment. Once cleared by the treating physician, patients may transition into a cancer surveillance/survivorship clinic, often run by an advanced practice provider (APP) that is well trained in head and neck cancer surveillance.
        1. Physical examination: Your doctor(s) will examine you according to the following schedule:
            a. Year One: every 1-3 months
            b. Year Two: every 2-6 months
            c. Years Three through 5: every 4-8 months
            d. After 5 years: every 12 months or as needed.
        2. Imaging: The timing and type of imaging you have will be based on your doctor's judgment.
            a. Baseline imaging within 6 months of completing treatment.
            b. Imaging may include CT scans, PET/CT scans, MRI, or sometimes ultrasound.
            c. Additional imaging will be based on your symptoms, exam, and your doctor's judgment.
    ii. Survivorship: Larynx cancer and its treatment can affect many areas of your health and quality of life. 'Survivorship' refers to caring for your health and well-being from the moment you receive your diagnosis, and for the rest of your life. Depending what your treatment involves, important parts of survivorship for larynx cancer may include:
        1. Speech and swallowing evaluation and therapy: This is typically with a Speech-Language Pathologist, or SLP, with expertise in speech and swallowing for head and neck cancer patients.
            a. Swallowing: Safe swallowing is important for your health and quality of life. Poor swallowing function, called 'dysphagia', can lead to health problems such as pneumonia or malnutrition, and may lead to the need for a feeding tube for nutrition. You may

also be referred to a dietician for guidance on how to maintain adequate nutrition.

b. Esophageal stricture: You may be at risk for narrowing of your esophagus, called an 'esophageal stricture'. This can be diagnosed with a swallowing X-ray. Some patients benefit from having their esophageal stricture stretched.
c. Speech: Rehabilitation of your speaking is important for your communication and quality of life. If you have had a total laryngectomy, a SLP specialist can help you learn about options for voice rehabilitation.

2. Oral and dental health: Larynx cancer and its treatment can have a major impact on your teeth, taste, saliva and jaw bone.
    a. Dental cleaning and care: Larynx cancer patients should establish care early after diagnosis, ideally before treatment, with a dentist who has experience in head and neck cancer. Some dental work may be necessary prior to treatment. In the long term, patients should have routine cleaning and examination. Routine fluoride treatments may be recommended.
    b. Radiation and dental health: Radiation can be detrimental to your dental health. It is especially important for patients who undergo radiation to have regular dental care and excellent dental hygiene.
    c. Dry mouth: Dry mouth, or 'xerostomia', is common after radiation therapy and can have a significant negative impact on quality of life. There is no cure for xerostomia. If you have xerostomia, you can decrease the symptoms by staying hydrated, using salivary substitutes, and maintaining excellent dental hygiene.
    d. Chondronecrosis of the larynx: Patients who undergo radiation are at risk for damage to the larynx or voicebox. The cartilage of the larynx which preserves the structural integrity of the voicebox becomes severely damaged and dysfunctional. The larynx no longer separates breathing and swallowing functions. Saliva and foods go into the breathing passages, causing coughing, choking and pneumonia. Patients may not be able to take their nutrition by mouth, due to the severity of the swallowing problem. In severe cases, they may require surgical removal of a dysfunctional larynx which is causing life threatening pneumonias due to aspiration.
    e.
    f. Trismus: Surgery and radiation can cause difficulty opening your mouth, called trismus. This can interfere with dental care and with eating. Ask your doctor about ways to improve your mouth opening, such as stretching exercises.

3. Thyroid function testing: If you have had radiation therapy or surgery for larynx cancer, you have an increased risk of low thyroid function, or 'hypothyroidism'. Symptoms of hypothyroidism may include fatigue, weight gain, constipation and depression. Your thyroid function should be tested every 6-12 months to determine whether you need treatment with thyroid hormone supplementation.
4. Tobacco use:
    a. Most head and neck cancers are associated with tobacco use, especially smoking cigarettes.
    b. Continued tobacco use after treatment is associated with worse survival and higher risk of other cancers, among many other negative health effects.
    c. It is important to know that quitting tobacco at any time will improve your overall health and chances of survival from head and neck cancer.
    d. If you still use tobacco after head and neck cancer treatment, we strongly encourage you to consider quitting. Your doctor can help you find resources, including medications and counseling programs, that have been proven to help.
5. Lymphedema: Lymphedema is swelling of the soft tissue that is common for patients who have had surgery and/or radiation. Specialized Physical Therapy called Lymphedema Therapy provide massage, compression garments, exercises and skin care, is available and can significantly improve lymphedema.
6. Shoulder dysfunction: Many head and neck cancer survivors have shoulder dysfunction, including decreased range of motion, weakness and stiffness as a result of surgery and/or radiation. Physical therapy is very helpful in improving shoulder function. If you have problems with your shoulder, ask your doctor about a referral to a physical therapist.
7. Obstructive sleep apnea: Survivors of head and neck cancer treatment are at risk for obstructive sleep apnea (OSA) because of changes to the upper airway anatomy. Symptoms may include daytime sleepiness, snoring, gasping or choking during sleep, daytime headaches, and irritability. OSA is diagnosed with a sleep study, and there are several options for treatment. Discuss your risk of OSA with your doctor, to decide whether you should have a sleep study.
8. Carotid artery stenosis evaluation: Radiation therapy to the neck increases the risk of carotid artery narrowing (stenosis) later in life. Carotid artery stenosis increases the risk of stroke. If you have had radiation to your neck, ask your doctor about an ultrasound to look for carotid artery stenosis.
9. Mental and sexual health: Head and neck cancer and its treatment can result in cognitive dysfunction, anxiety, depression, body image concerns, and changes in sexual function and desire. If you suffer from any of these,

you are not alone. Ask your doctor about meeting with a mental health professional to determine whether counseling and/or medication may be helpful for you.

10. Hearing evaluation: Head and neck cancer treatments, especially with certain chemotherapy drugs, can cause hearing loss. If you have decreased hearing, you should have a hearing test to evaluate your hearing and determine whether you may benefit from hearing augmentation, such as with a hearing aid.

i. Questions for your doctor
    i. Before/during treatment:
        1. What types of treatment are recommended (such as surgery, radiation, and/or chemotherapy)?
        2. Why are these treatments best (best chance of cure, best chance of swallowing function, best chance to preserve my voice)?
        3. Are there any other treatment options that I should learn about, such as clinical trials?
        4. Should I see a dentist before treatment begins?
        5. How long will treatment take? How long will it take to fully recover after treatment?
        6. What are the risks and side effects of each part of treatment? Which side effects are temporary, and which might be permanent?
        7. Will I need a feeding tube or a breathing tube (tracheostomy)? Will they be temporary or permanent?
        8. What will my swallowing, speech and breathing be like after treatment?
        9. If you are having a total laryngectomy:
            a. What are my options for voice rehabilitation?
            b. What permanent activity restrictions will I have?
        10. Will I have any other functional problems after treatment?
        11. Will I be able to keep doing my job after I've recovered?
    ii. After treatment:
        1. Should I have any imaging studies?
        2. When should my next follow-up appointment be, and with whom?
        3. Should I have my thyroid function tested?
        4. Should I be referred to a speech and language pathologist (SLP), and or to a physical or occupational therapist?
        5. Am I receiving appropriate dental care?
        6. Should I have a sleep study?
        7. Do I need a carotid artery ultrasound?
        8. Should I have a hearing test?