# Head and Neck Cancers

OPEN EDUCATIONAL RESOURCES

2019-03-25

# Head and Neck Cancers

James Liebmann
*University of Massachusetts Medical School*

Ali Akalin
*University of Massachusetts Medical School*

Liana Puscas
*Duke University*

Andrew Chen
*University of Massachusetts Medical School*

Richard S. Pieters
*University of Massachusetts Medical School*

***See next page for additional authors***



## Recommended Citation

Citation: Liebmann J, Akalin A, Puscas L, Chen A, Pieters RS. Head and Neck Cancers. In: Pieters RS, Liebmann J, eds. Cancer Concepts: A Guidebook for the Non-Oncologist. Worcester, MA: University of Massachusetts Medical School; 2019. doi:10.7191/cancer_concepts.1021.

# Head and Neck Cancers

**Authors**
James Liebmann, Ali Akalin, Liana Puscas, Andrew Chen, and Richard S. Pieters

**Keywords**
head and neck cancers

**Comments**
This project has been funded in whole or in part with federal funds from the National Library of Medicine, National Institutes of Health, under Contract No. HHSN276201100010C with the University of Massachusetts, Worcester.

# Head and Neck Cancers

James Liebmann, MD
Ali Akalin MD, PhD
Liana Puscas, MD, MHS
Andrew Chen MD
Richard S. Pieters, MD

Citation: Liebmann J, Akalin A, Puscas L, Chen A, Pieters RS. Head and Neck Cancers. In: Pieters RS, Liebmann J, eds. Cancer Concepts: A Guidebook for the Non-Oncologist. Worcester, MA: University of Massachusetts Medical School; 2019. https://doi: 10.7191/cancer_concepts.1021

This project has been funded in whole or in part with federal funds from the National Library of Medicine, National Institutes of Health, under Contract No. HHSN276201100010C with the University of Massachusetts, Worcester.



## Summary and Key Points

1. A variety of different malignancies fall into the category of "Head and Neck Cancers". This chapter focuses on upper aerodigestive tract cancer.
2. Tobacco and alcohol use and human papillomavirus infection are common causes of head and neck cancers.
3. Most head and neck cancers are squamous cell carcinomas.
4. Treatment of head and neck cancers commonly requires some combination of surgery, radiation, and chemotherapy. Close cooperation between otolaryngologists, radiation oncologists, and medical oncologists is mandatory for successful treatment of these cancers.
5. Preservation of organ function in addition to cure of cancer, is an important goal of treatment.
6. Any patient with persistent symptoms of sore throat, hoarseness, difficulty swallowing or an enlarged cervical lymph node should be evaluated for possible head and neck cancer.

## Clinical Cases

Case 1

A 65-year-old man complains of several months of progressive right sided throat pain, with development of a progressive right earache and progressive pain on swallowing over the last few days. He reports it hurts to swallow, even water, and has lost about 20 pounds over the last few months. He is an executive at a large company, denies use of tobacco or recreational drugs in any form, except occasional wine or beer. He runs marathons, but recently has become exhausted after running less than 3 miles.

On physical examination, he is six feet tall and weighs 180 pounds. A 2 cm mobile firm, non-tender mass in the right upper neck just posterior to the angle of the mandible. A 2 x 3 cm mass is visible along the right lateral oropharyngeal wall and base of tongue. His voice is normal (Figure 1a).

CT of the neck was obtained for preliminary assessment (Figure 1a). PET/CT was then obtained to evaluate for local and distant metastatic disease which demonstrates the two masses and no evidence of further spread (Figure 1b). Biopsy of the oropharyngeal mass shows squamous cell carcinoma, which also stains with P16 immunostain, a surrogate marker for the presence of HPV in the tumor cells (Figure 1c, d, e, and f). HPV high risk molecular test performed later revealed the presence HPV 16 DNA in this tumor.

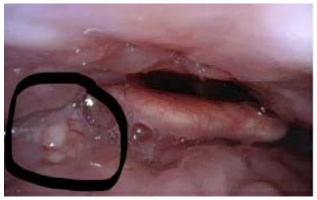

**Figure 1a.** Photograph of right lateral oropharyngeal wall and base of tongue. Image courtesy of Duke University Division of Head and Neck Surgery and Communication Sciences.

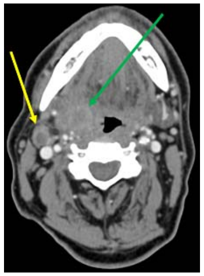

**Figure 1b**. CT of the neck shows a mass along the right lateral oropharyngeal wall in the region of the palatine tonsil (green arrow). Adjacent to the mass a pathologic appearing level 2A lymph node with necrosis (yellow arrow), located just posterior to the angle of the mandible. Image courtesy of the University of Massachusetts Medical School, Department of Radiology.

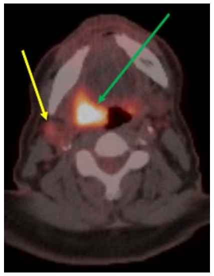

**Figure 1c.** PET/CT of the neck was obtained to further confirm CT findings and evaluate for other potential sites of local and distant metastatic disease. The above image shows increased metabolic uptake in the right palatine tonsillar mass (green arrow) and in the pathologic right level 2A lymph node (yellow arrow). No other areas of abnormal uptake were seen in the remainder of the body. Of note, mild increased metabolic uptake in the left palatine tonsil is within normal physiologic range. Image courtesy of the University of Massachusetts Medical School, Department of Radiology.

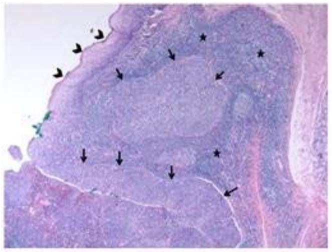

**Figure 1d.** (H&E stain, 40X magnification): Invasive SCC of the oropharynx showing normal squamous mucosa in the left upper corner of the picture (arrowheads). Nests of malignant cells (arrows) are seen infiltrating into the lamina propria with lymphoid tissue (stars). Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

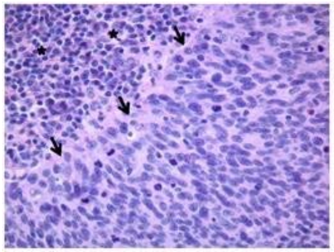

**Figure 1e.** (H&E stain, 400X magnification): On higher magnification, a nest of malignant squamous cells (arrows) with hyperchromatic, enlarged nuclei and multiple mitotic figures. Note the presence of lymphoid stroma (stars) in the left upper corner of the picture. Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

**Figure 1f.** (P16 immunostain stain, 40X magnification): The malignant squamous cells (arrows) are positive for P16 immunostain, a surrogate marker for the presence of HPV in the tumor cells. Note that benign squamous mucosa (arrowheads) and lymphoid stroma (stars) are negative for P16 immunostain. Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

Case 2

A 50-year-old woman complains of oral pain; her dentist notes a mass along the undersurface of the tongue, extending onto the floor of mouth and refers her to an oral surgeon. She reports a 3 pack/day tobacco history since age 13, and drinks 2 shots of Bourbon and at least a six pack of beer/day. The oral surgeon palpates a mass in the floor of mouth fixed to the mandible (Figure 2a). Biopsies of the lesion shows grade 3 squamous cell carcinoma (Figure 2b & c). Palpation of the neck is unremarkable, and PET/CT confirms that the area of increased uptake is confined to the anterior tongue/floor of mouth lesion (Figure 2d & e).

**Figure 2a.** Photograph of the lesion in floor of mouth. Image courtesy of Duke University Division of Head and Neck Surgery and Communication Sciences.

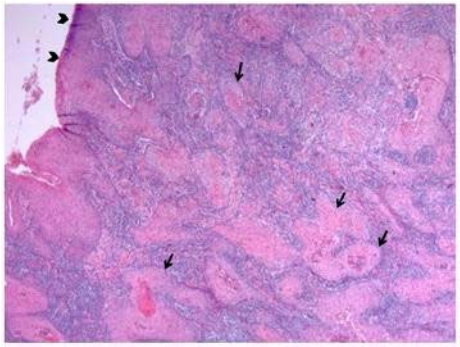

**Figure 2b.** (H&E stain, 40X magnification): Invasive keratinizing squamous cell carcinoma of the tongue showing normal squamous mucosa in the left upper corner of the picture (arrowheads). Nests of malignant cells (arrows) are seen infiltrating into the submucosa and muscle fibers of the tongue (stars). Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

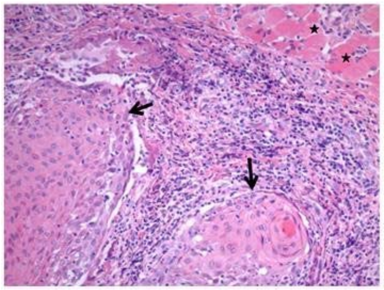

**Figure 2c.** (H&E stain, 400X magnification): Nests of squamous cell carcinoma cells (arrows) and muscle fibers (stars) Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

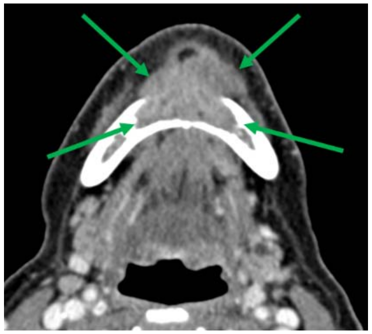

**Figure 2d**. CT of the neck demonstrates a soft tissue mass (green arrows) along the anterior floor of the mouth that erodes into the mandible. Image courtesy of the University of Massachusetts Medical School, Department of Radiology.

**Figure 2e.** PET/CT demonstrates metabolic uptake in the tumor (green arrow). No pathologic lymph nodes were identified. Image courtesy of the University of Massachusetts Medical School, Department of Radiology.

Case 3

A 40-year-old Chinese American man who reports he was born in a rural fishing village in southern China noted a painless lump in the right neck, nasal speech quality and sore throat. His physician noted that apparent tumor on the soft palate, ordered a contrasted enhanced CT of the neck, and referred him to an otolaryngologist. CT scan of the neck demonstrated a mass in the nasopharynx, invading the soft palate and protruding into the oropharynx (Figure 3a). Adenopathy of the right upper neck and submandibular region was also identified (Figure 3b). A fine needle aspirate of the submandibular node was performed, demonstrating malignant appearing squamous cells (Figure 3c). Biopsy of the lesion in the nasopharynx shows poorly differentiated squamous cell carcinoma (Figure 3d, e & f).

**Figure 3a.** CT of the neck demonstrates a mass originating in the nasopharynx (green arrow) extending caudally to invade the soft palate (yellow arrow) and prolapse into the oropharynx (blue arrow). Image courtesy of the University of Massachusetts Medical School, Department of Radiology.

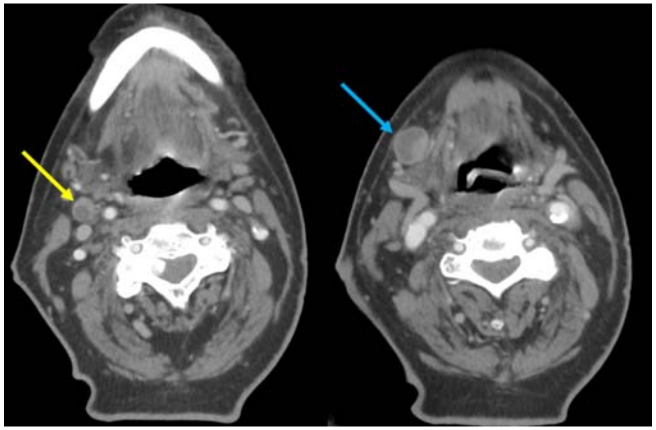

**Figure 3b.** CT of the neck demonstrates pathologic lymph nodes in the right upper neck, level 2A (yellow arrow), and right submandibular region, level 1B (blue arrow). Image courtesy of the University of Massachusetts Medical School, Department of Radiology.

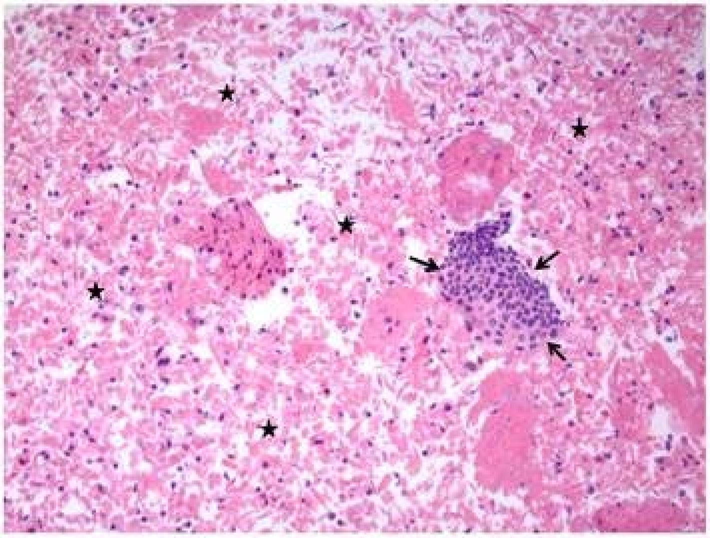

**Figure 3c.** (H&E stain of cell block, 100X magnification): A cluster of malignant squamous cells (arrows) in a background of nuclear and keratin debris (stars) Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

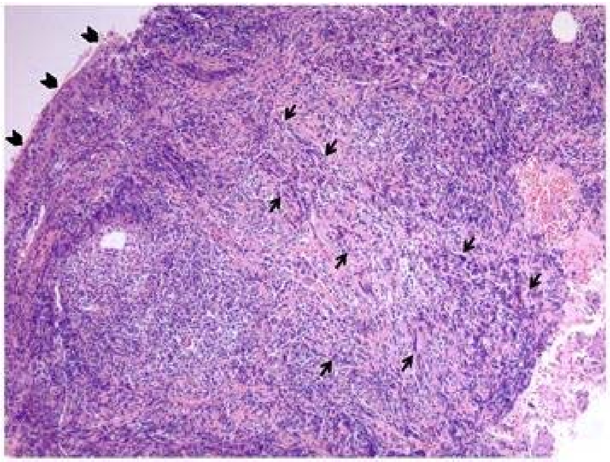

**Figure 3d.** (H&E stain, 40X magnification): Invasive poorly differentiated squamous cell carcinoma of the nasopharynx. Normal mucosa is seen in the left upper corner (arrowheads). Nests and cords of infiltrating tumor cells are present in the submucosa (arrows). Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

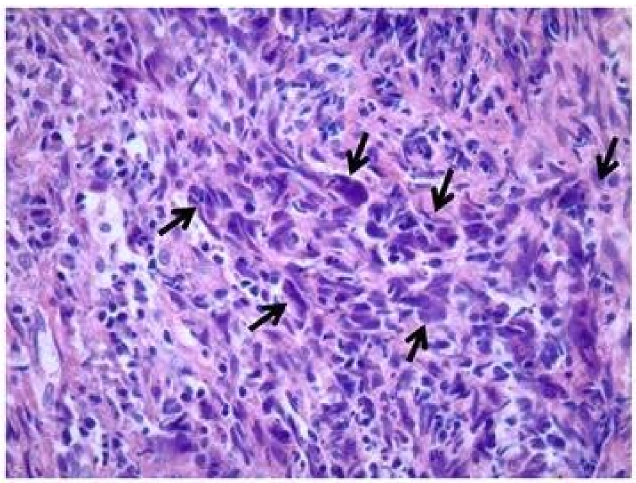

**Figure 3e.** (H&E stain, 400X magnification): On higher magnification, infiltrating malignant squamous cells (arrows) with hyperchromatic, enlarged nuclei are seen in the stroma. Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

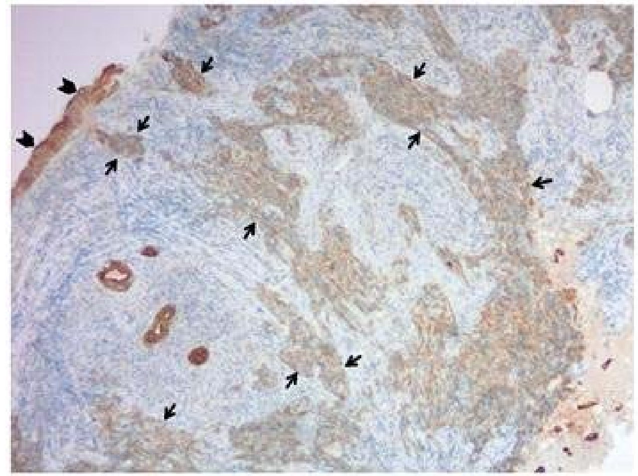

**Figure 3f.** (Pancytokeratin immunostain, 40X magnification): Pancytokeratin immunostain highlights both benign epithelial cells (arrowheads, left upper corner) and malignant cells (arrows) in the submucosa. Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

## Introduction

Head and neck cancers include cancers of the skin, thyroid and upper aerodigestive tract including the lip, oral cavity, oropharynx, nasopharynx, larynx, paranasal sinuses, salivary glands, and carcinomas of unknown primary origin found in cervical lymph nodes. Oncologists recognize the tremendous disparity in tumors collected under the rubric of “head and neck cancer” and appreciate that a full understanding of the malignancies in this category requires consideration of the characteristics of individual tumors.

This chapter focuses on cancers of the upper aerodigestive tract which are most often squamous cell carcinomas arising from the squamous epithelium that lines the tract. Overall though, these cancers are uncommon, accounting for only 3% of all malignancies in the United States (US). In 2018 64,700 new cases of oral cavity, oropharynx and larynx cancer will be diagnosed and 13,700 people are expected to die from this group of malignancies. (By comparison, 54,000 new cases of thyroid cancer and 234,000 new cases of lung cancer are expected.)[1]

Despite their heterogeneity, there are similarities in the therapeutic approaches to the different head and neck cancers. All modalities of anti-cancer treatment– surgery, radiation, and chemotherapy– are frequently employed against these cancers. In addition to cure, organ preservation is a major concern of treatment because of the integral function of the structures involved with these tumors. Given the complex issues involved in treatment, head and neck cancers provide a perfect example of the need for a multi-disciplinary approach to cancer and the invaluable role that tumor boards play in planning treatment.

This chapter is intended to provide an overview of head and neck cancers. Etiology, pathology, staging, and principles of treatment will be reviewed. Individual sites of cancer will be discussed only as examples to illustrate larger principles.

## Etiology

In the US, head and neck cancers are strongly associated with tobacco use, including smoking, dipping, and chewing. Alcohol use is also strongly associated with these cancers, and the effect of tobacco and alcohol together is exponential, not simply additive, in increasing the risk for developing these cancers. Other organic substances that can come in contact with oral and nasal mucosal surfaces for long times (e.g., inhaled wood dust, the juice from betel nut chewing) are also known risk factors. All of these carcinogenic substances can bathe the epithelium throughout the mouth, nose, pharynx, and larynx and increase the risk of cancers developing at more than one site. This phenomenon is known as field cancerization.

Viruses also play a role. Oncogenic strains of human papilloma virus (HPV) (notably HPV 16) can cause head and neck cancers especially in the tonsils and the base of tongue (both part of the oropharynx). Cancers caused by HPV tend to arise in patients about 10 years sooner than non-HPV associated cancers and are less likely to arise in smokers and heavy drinkers. Interestingly, such cancers also tend to respond better to treatment and have a better prognosis than head and neck cancers not associated with HPV. The number of cases of HPV+ oropharyngeal cancers has been increasing rapidly in the United States, with the number of cases essentially doubling from1999 to 18,917 cases in 2015, when it was the most common HPV+ cancer in the United States. The rate of increase has been far greater in males than females; 82% of the HPV+ cancers occurred in men.[2.] Epstein-Barr virus is associated with nasopharyngeal carcinoma.

## Screening

Because head and neck cancer is so uncommon compared to other malignancies, patients and health care providers do not often think of this as the cause of a sore throat or an enlarged lymph node. Any patient with persistent sore throat, hoarseness, dysphagia (difficulty swallowing), odynophagia (painful swallowing) or enlarged cervical lymph node lasting more than three months should be referred to an otolaryngologist for evaluation. It is appropriate for the primary care provider to prescribe antibiotics or antireflux medications as initial therapy because most patients will suffer from routine ailments. However, longer lasting symptoms, especially in adults over 40 or in patients with a history of tobacco and/or alcohol use, should trigger referral to an otolaryngologist-head and neck surgeon for detailed physical exam. Of note, tobacco is also a strong risk factor for lung cancer, so anyone with head and neck squamous cell carcinoma (SCCA) in the setting of tobacco use should also undergo a chest X-ray as a basic screen for lung cancer.

## Pathology

Most head and neck cancers arise from the epithelial lining, the most common histopathologic type being SCCA (Figure 4a and 4b).
A significant exception to this is carcinomas of the salivary glands, which are frequently adenocarcinomas (Figure 5a and 5b). Minor and major salivary glands are scattered throughout the upper aerodigestive tract so the tumors arising in salivary glands must remain in the differential diagnosis along with less common malignancies such as mucosal melanomas (Figure 6a and 6b) while evaluating patients with head and neck cancers.

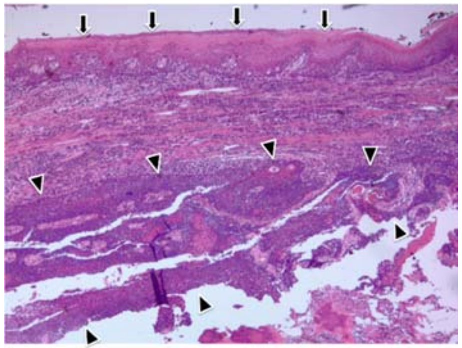

**Figure 4a.** (H&E stain, 20X magnification) A representative picture from a case with squamous cell carcinoma of gingiva. Normal squamous mucosa is shown in the upper portion of the picture (arrows) and infiltrating malignant squamous cells below it (arrow heads). Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

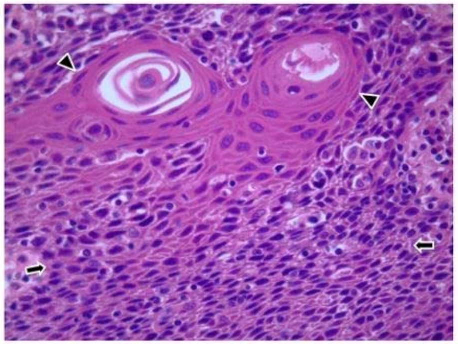

**Figure 4b.** (H&E stain, 400X magnification) Sheets of infiltrating malignant squamous (arrows) cells with hyperchromatic and enlarged nuclei. Squamous cell carcinoma cells are focally trying to form keratin pearls (arrow heads). Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

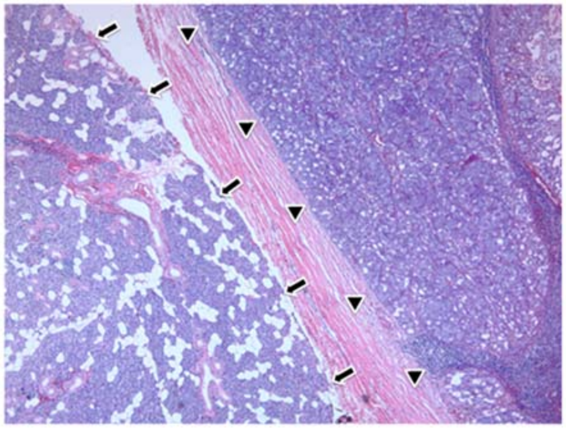

**Figure 5a.** (H&E stain, 20X magnification) A representative picture from a case with acinic cell adenocarcinoma of salivary gland. Normal salivary gland is on the left (delineated by arrows) and the tumor is on the right (delineated by arrowheads). Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

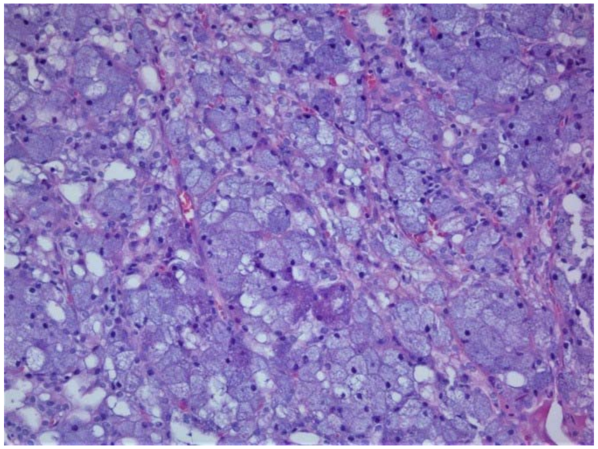

**Figure 5b.** (H&E stain, 200X magnification) Sheets of malignant tumor cells with purple granular cytoplasm (zymogen granules) consistent with salivary gland serous acini differentiation. Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

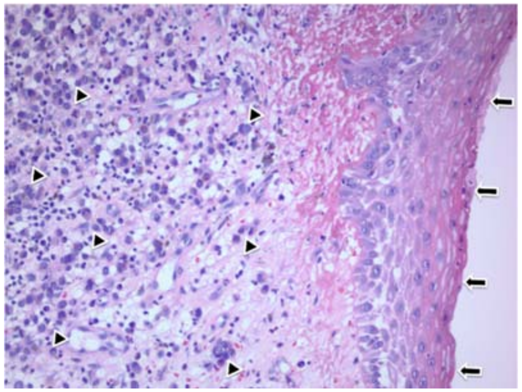

**Figure 6a**. (H&E stain, 20X magnification) A representative picture from a case with malignant melanoma of the palate. Normal squamous mucosa is shown in the right side of the picture (arrows) and infiltrating malignant melanoma cells in the left side (arrow heads). Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

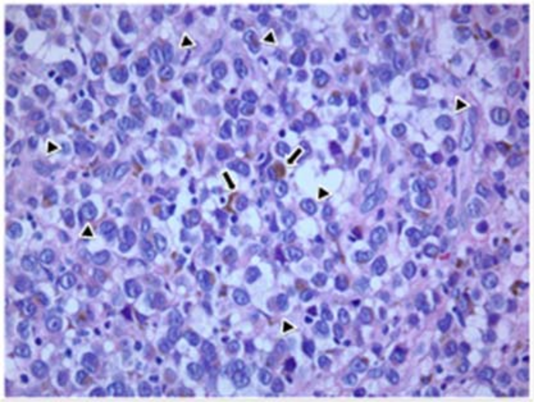

**Figure 6b.** (H&E stain, 400X magnification). Sheets of infiltrating malignant melanoma (arrowheads) cells with hyperchromatic and enlarged nuclei and prominent nucleoli. Melanin pigment (arrows) is seen in the cytoplasm of some tumor cells. Image courtesy of the University of Massachusetts Medical School, Department of Pathology.

### Prognostic Factors

The stage of the cancer, the response to the initial treatment course and Human Immunodeficiency Virus (HIV) status are important prognostic factors. Advanced tumors, recurrent cancer and cancer in the setting of HIV positive serology all portend a worse prognosis. SCCA arising from HPV has a better prognosis than non-HPV SCCA. Immunosuppression after organ transplant is a very important prognostic factor for skin cancers.

### Staging

Staging of head and neck cancers differs from many other solid tumors because of the propensity for these tumors to spread locally. Distant spread (e.g., to bones, lungs, liver, etc.) is less common than direct extension of tumors into adjacent structures. Similarly, death from these cancers is frequently due to complications from extensive tumor burden in the head, face, or neck. These complications include aspiration and malnutrition from an inability to swallow, and exsanguination from tumor erosion into an artery.

Since the extent of local disease is critical to staging, a good otolaryngology exam is mandatory, and is supplemented with diagnostic imaging. Endoscopy can provide direct visualization of the superficial mucosal detail of the tumor (Figure 7) while diagnostic imaging provides assessment of the depth of tumor, involvement of adjacent structures, and metastatic disease (Figure 8). Modalities typically used for head and neck imaging include computed tomography (CT) (Figure 9a, b & d-f), magnetic resonance imaging (MRI) (Figure 10), and positron emission tomography with computed tomography (PET/CT) (Figures 9c & 11). A thorough clinical exam and appropriate imaging are important in the diagnosis and staging of head and neck cancers.

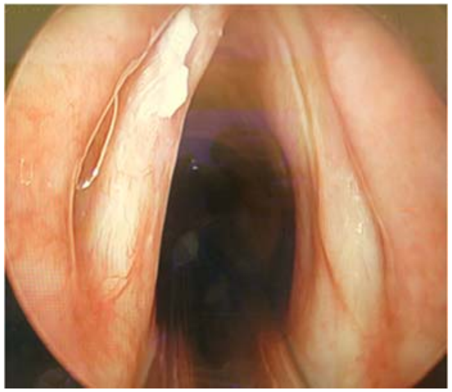

**Figure 7.** Endoscopic image of a T1 Squamous cell carcinoma of the True Vocal Cord. A cancer in this location is highly unlikely to metastasize, even to regional nodes, because of the lack of lymphatic channels in the true vocal cords. Image courtesy of Duke University, Department of Otolaryngology.

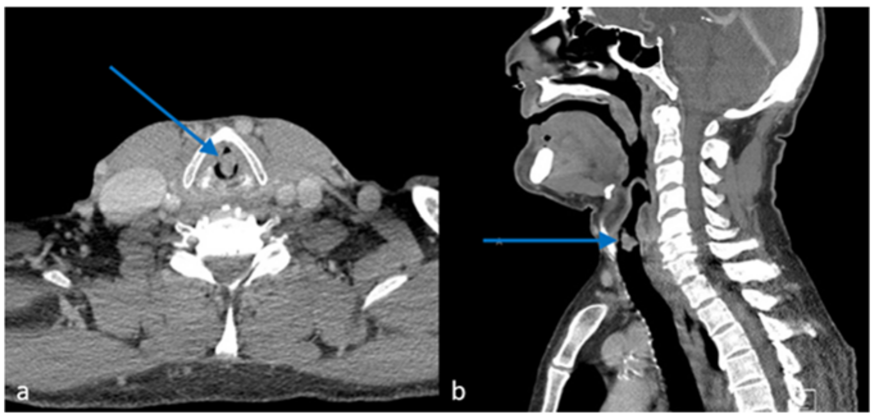


**Figure 8.** Axial (a) and sagittal (b) CT of the neck with contrast demonstrate a vocal cord polyp (blue arrow) protruding into the larynx from the right true vocal cord. The patient had a long history of smoking and alcohol use with worsening hoarseness of the voice. The patient was hospitalized in respiratory distress. The polyp caused a ball valve effect making expiration progressively more difficult. Pathology revealed a squamous cell carcinoma. After excision, breathing returned to normal and hoarseness significantly improved. Image courtesy of University of Massachusetts Medical School, Department of Radiology.

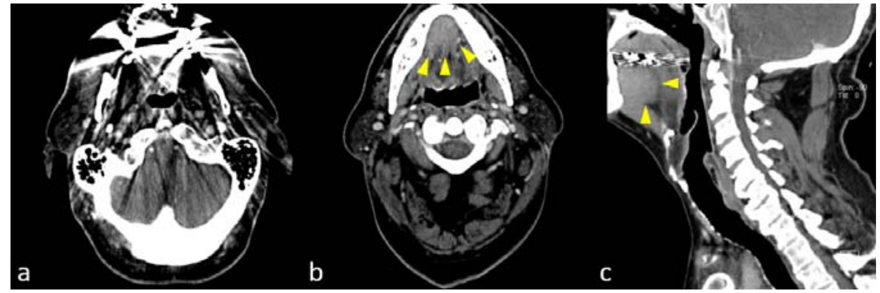


**Figure 9a**. Axial (a & b) and sagittal (c) CT of the neck with contrast shows a lesion in the oral cavity along the ventral surface of the tongue. While clinically obvious by direct visualization of the mucosa, a combination of clinical and radiologic imaging is often necessary for staging. Note in Figure 9a, the oral cavity is obscured by metallic streak artifacts from dental fillings and implants. Without the clinical information of an oral cavity lesion, the artifacts would have made detection of this squamous cell carcinoma more challenging and potentially missed by imaging alone. Figure 9b (caudal to Figure (a) and 9c demarcate the margins of this pathology proven squamous cell carcinoma (yellow arrowheads). Image courtesy of University of Massachusetts Medical School. Department of Radiology.

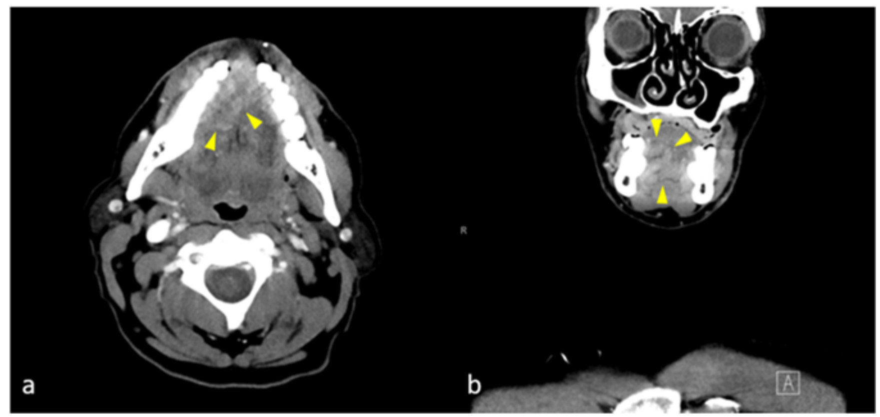


**Figure 9b**. Axial (a) and sagittal (b) CT of the neck with contrast show a subtle ulcerative lesion along the right ventral surface of the tongue (yellow arrowheads). While the superficial mucosal detail of this ulcerative lesion is better identified by direct visualization, imaging is helpful to evaluate the depth of local invasion of the soft tissues as well as possible bone and lymph node involvement. Image courtesy of University of Massachusetts Medical School, Department of Radiology.

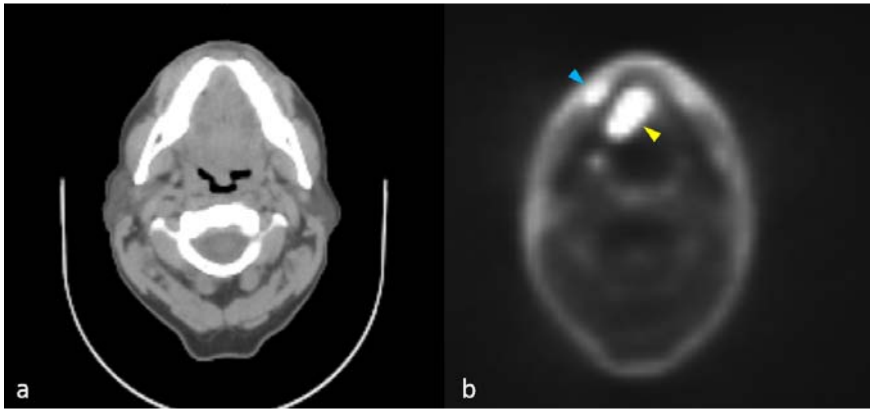


**Figure 9c.** PET/CT images from the above patient shows hypermetabolic activity in the region ulceration (yellow arrowhead). A. CT is unremarkable. b. PET image of same level: Unexpectedly, increased metabolic activity was also seen along the buccal surface of the mandible (blue arrowhead). This lesion had extended submucosally across the gingival surface and was not clinically evident. Image courtesy of University of Massachusetts Medical School. Department of Radiology.


**Figure 9d.** Sagittal CT of the neck in Figure 9da shows a transglottic mass involving the supraglottic, glottic, and subglottic larynx (yellow arrowhead). A total laryngectomy was performed Figure 9db. Tracheostomy and nasogastric tubes have been placed. Image courtesy of the University of Massachusetts Medical School. Department of Radiology.

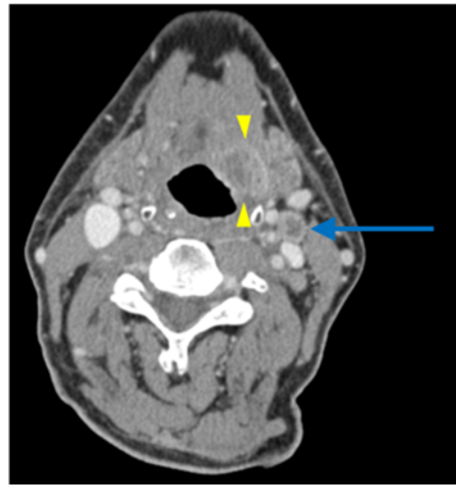

**Figure 9e.** Axial CT of the neck with contrast shows an ulcerative lesion at the left tongue base (yellow arrowheads) with a pathologic necrotic level 2A lymph node (arrow). Image courtesy of the University of Massachusetts Medical School, Department of Radiology.

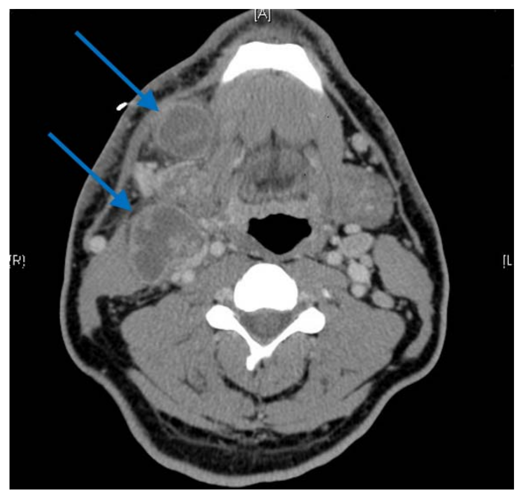


**Figure 9f.** Pathologically enlarged lymph nodes with central necrosis (arrows) are demonstrated on this contrast enhanced CT of the neck. In a young adult without a history of smoking or alcohol abuse, there is increased likelihood that this is HPV related which tends to have a better prognosis. Image courtesy of the University of Massachusetts Medical School, Department of Radiology.

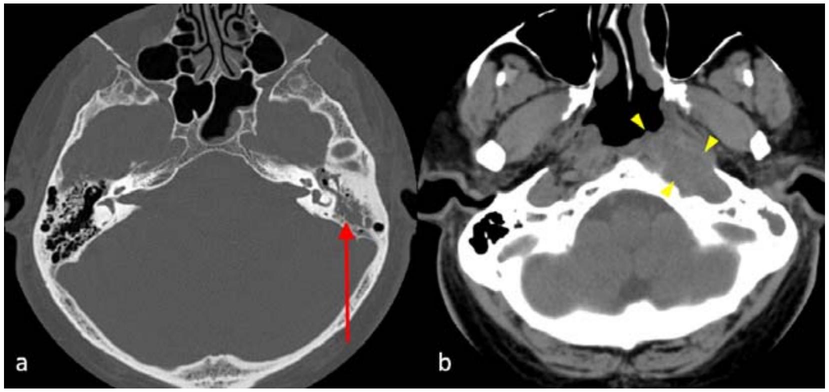


**Figure 10a.** CT of the temporal bones in a patient with chronic left ear pain. a: demonstrates fluid in the left middle ear cavity and mastoid air cells (red arrow). b: A mass was identified at the skull base along the left nasopharynx and retropharyngeal space (yellow arrowheads) obstructing the Eustachian tube. Image courtesy of the University of Massachusetts Medical School, Department of Radiology.

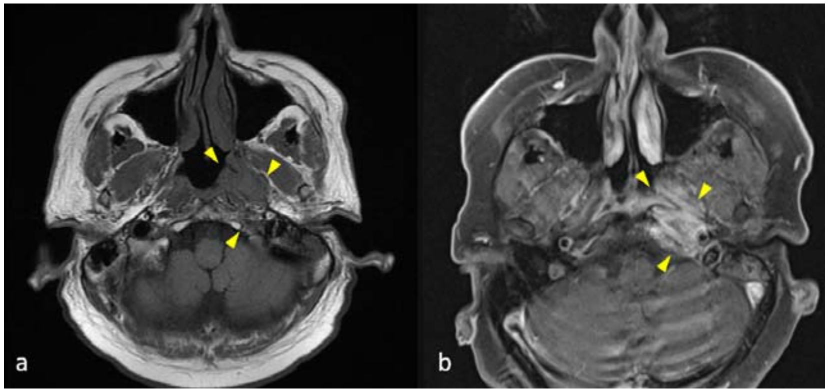


**Figure 10b.** MRI of the above patient better delineates the margins of this mass. Figure 10ba is a T1 image showing the soft tissue mass infiltrating and displacing the normal fat around the left nasopharyngeal mucosa and retropharyngeal space (yellow arrowheads). Figure 10bb is a T1 fat saturated post contrast image shows corresponding abnormal enhancement of this region and skull base of this infiltrative lesion. Image courtesy of the University of Massachusetts Medical School. Department of Radiology.

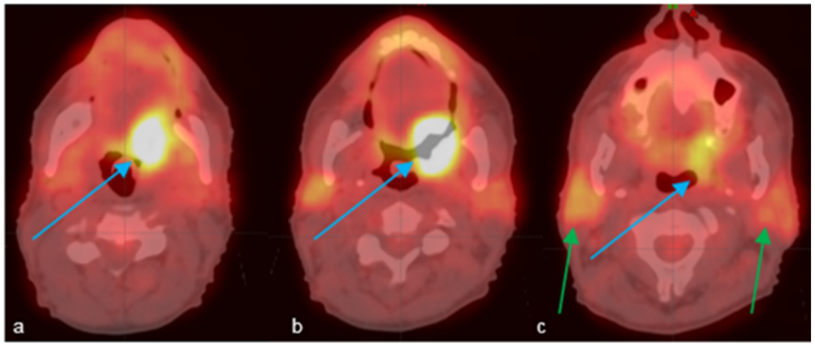


**Figure 11.** CT/PET PET is fused into CT image set and color enhanced on radiation oncology treatment planning system. Cancer of lateral wall of oropharynx: a: Lower extent of disease, note uninvolved epiglottis (arrow) b: Middle of disease, note base of tongue (arrow) with anterior tonsillar pillar/soft palate posterior to tongue c: Superior extent of disease, blue arrow points at tonsil. Green arrows point at inflamed parotid gland on right and intraparotid nodes on left. Image courtesy of the University of Massachusetts Medical School, Department of Radiation Oncology.

The current positron emitter used in PET, 18F-glucose, is readily taken up by many cancers of the head and neck, but also by inflammatory cells and the normal brain. Hence, it may be difficult at times to distinguish a lymph node involved with tumor from an inflamed lymph node on PET[3.] (Figure 11c). In this case a needle biopsy such as a fine needle aspiration (FNA) of the lymph node can be very helpful (Figure 12).

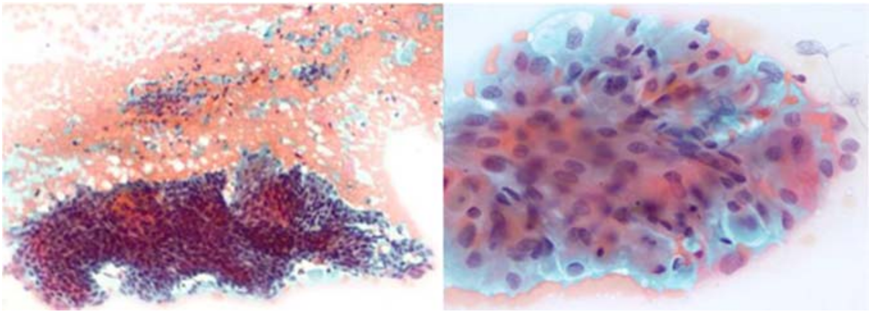

**Figure 12.** Aspiration biopsy (cytology, left image 100X, right image 400X magnification) of squamous cell carcinoma. Image courtesy of University of Massachusetts, Department of Pathology.

As with any cancer patient, a distant metastatic workup must also be performed. Head and neck cancer, both SCCA and other histologic types, are most likely to spread first to regional lymph nodes, less commonly to the lungs and then to the liver and other sites.

The staging system currently used for many head and neck cancers is located here. Note that Stage IV disease can occur in the absence of distant spread of tumor. Either bulky cervical lymphadenopathy or tumor invasion into structures adjacent to the primary organ constitutes Stage IV disease, as does distant metastatic disease.

### Principles of Treatment

Most head and neck cancers that have not spread beyond cervical lymph nodes are potentially cured with current treatments. However, once these cancers have spread into distant sites, such as lungs, bone, or liver, they are incurable and treatment is largely palliative. Current curative treatments will employ some combination of regional therapy using surgery and/or radiation, frequently with chemotherapy that is either given before radiation treatment ("induction" chemotherapy) or concurrent with radiation therapy One of the main principles of treatment is to minimize treatment modalities in an attempt to mitigate negative effects on function (i.e. utilizing surgical or non-surgical therapies alone to effect cure).

In addition to the goal of cure, another major treatment goal is preserving the functions of the structures involved by these tumors. Organ preservation protocols involving radiation +/- chemotherapy allow for anatomic preservation of structures within the upper aerodigestive tract. The function of these organs is rarely completely normal after radiation, but the majority of patients are able to breathe and swallow, keep their larynx and avoid permanent tracheostomy and gastrostomy tubes.

Currently, radiation or surgery appear to do equally well for most small (Stage I or II) head and neck tumors. In general, more extensive tumors are best treated with induction chemotherapy followed by concurrent chemotherapy and radiation with surgery reserved for tumors that do not achieve complete remission. An exception to this general rule are cancers of the oral cavity which have a better survival rate if surgery is performed first followed by radiation +/- chemotherapy.

### Surgery

The goal of surgery is to completely remove all of the cancer while preserving as much uninvolved tissue as possible (Figure 13).

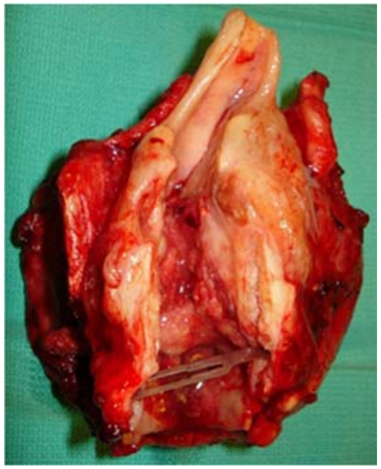

**Figure 13.** Gross image of total laryngectomy specimen, showing a large cancer of the larynx originating from the right side. Image courtesy of Duke University, Department of Otolaryngology.

Due to the confined anatomic region of the head and neck, margins are much closer than in other areas of the body and sacrifice of adjoining tissue can have a significant impact on patient function. In addition to surgical removal of the primary cancer, patients with higher stage tumors also require neck dissection to remove the lymph node beds that drain the primary site. In these cases, neck dissections are both therapeutic (by removing the lymph nodes) and staging (by establishing the extent of disease). However, recent data suggests that complete response (CR) on post treatment PET/CT scan of initially node positive head and neck cancer predicts excellent long-term disease free survival, and that neck dissection can be safely avoided in patients achieving CR.[4.]

Immediate reconstruction after cancer resection is of prime importance to allow patients to return to swallowing and speaking. Local, regional and distant free tissue flaps are essential components of the surgical care of many of these patients. Patients may require temporary tracheostomy and nasogastric feeding tubes as they heal from surgery, and fistulas caused by a breakdown in the pharynx with leakage of saliva into the neck are of special concern because they prohibit oral intake and delay healing.

Surgery can be used as solitary treatment of early stage cancer. In more advanced cases or if pathological evaluation reveals signs of more aggressive cancer (such as perineural or lymphovascular invasion), surgery is often followed by radiation therapy with or without chemotherapy to increase the chances for cure. Surgical salvage is used when patients have undergone nonsurgical treatment for their cancers but suffer from persistent or recurrent disease. Surgery in the post-radiation setting is associated with increased wound healing problems but does provide an effective cure in many cases.

### Radiation Therapy

Radiation therapy (RT) may be used as a solitary treatment modality for early stage tumors or as first line therapy in combination with chemotherapy for more advanced disease. RT is also given after surgery when the primary tumor is large or has aggressive features or there are multiple lymph nodes involved with cancer. Radiation has the great advantage of organ preservation but does have some significant side effects like loss of salivary function, possible permanent lymphedema, possible radionecrosis of the mandible and permanent alteration in swallowing from scar tissue that may develop in the pharynx and neck musculature. Intensity Modulated Radiation Therapy (IMRT) allows for targeted delivery of radiation to the tumor site with smaller doses to the surrounding structures. This allows for greater preservation of salivary and swallowing functions that are essential to maintaining a good quality of life for head and neck cancer patients.

In general, RT lasts for 5-7 weeks depending on the stage of the cancer and whether the radiation is being given as first line therapy or in a postsurgical setting. Patients usually do not have many side effects the first four weeks of therapy. Fatigue, mucositis and other side effects may present toward the end of treatment and continue for several weeks after completion of RT.

RT for T1 true vocal cord cancer involves a tiny field encompassing only the larynx; for a T2 laryngeal cancer, only first echelon lymph nodes are treated. (Figure 14a & b). While patients will have a sore throat during treatment, these treatments are usually very well tolerated. Late effects are largely restricted to voice changes, although professional singers have sometimes been able to return to professional singing after RT to the larynx.

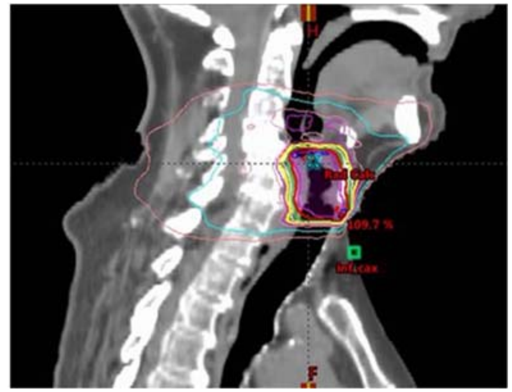

**Figure 14a.** True vocal cord treatment volume. Yellow line illustrates 100% dose line, or edge of treatment field for treatment of T1 TVC cancer. Image courtesy of the University of Massachusetts Medical School, Department of Radiation Oncology.

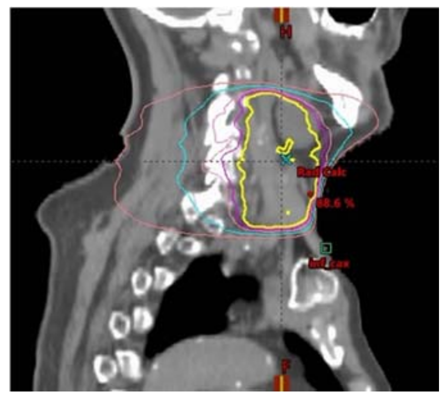

**Figure 14b.** True vocal cord nodal treatment volume for a T2 N0 TVC cancer. Yellow line again illustrates edge of treatment field. Dose for treatment of N0 nodal volume is less than that required for gross disease, so the TVC volume shown in Figure 11a is treated to higher dose. Image courtesy of the University of Massachusetts Medical School, Department of Radiation Oncology.

Treatment of large volumes (Figure 15) of the upper aerodigestive tract is much more difficult, with dry mouth, and loss of taste often interfering with hydration and nutrition. Some patients may require placement of a temporary feeding tube if they are unable to maintain oral intake and occasionally some patients require a tracheostomy tube because of airway edema. For those patients treated with radiation alone or in combination with chemotherapy, maintaining oral intake (even if a temporary feeding tube is necessary) is essential to preserving long-term swallowing function. Avoiding treatment breaks is essential for optimizing chance of cure, and adequate nutrition is a critical piece of the supportive care required to get patients through RT treatment.

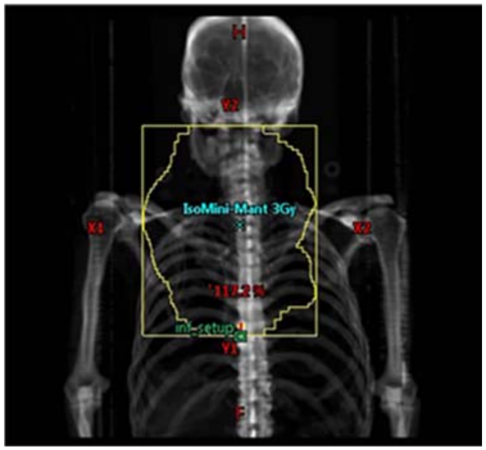


**Figure 15.** Simple AP treatment field for palliation of massive tumor in the base of tongue. The entire upper aerodigestive tract is in the treatment volume. Image courtesy of the University of Massachusetts Medical School, Department of Radiation Oncology.

The most important late effect for patients' quality of life is severe dry mouth, which also can lead to issues with cavities and loss of teeth. For this reason, evaluation by a dentist or oral surgeon expert in the management of RT patients should occur as early in initial work-up as possible. The degree of dryness depends on the volume of remaining functional salivary gland tissue. IMRT permits sparing of, for example, the contralateral parotid gland (when possible), which significantly decreases severity of dry mouth (Figure 16). Except for early laryngeal cancer without lymph node metastases, IMRT has become standard of care for head and neck cancer treatment.

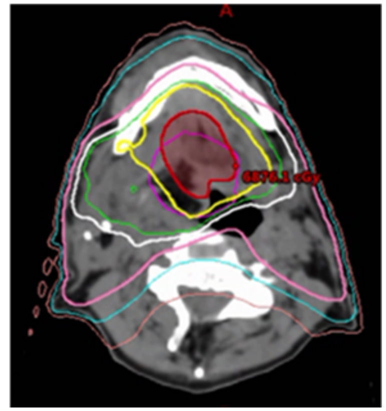

**Figure 16a.** IMRT treatment plan CT slice for Stage III, T3N0 squamous cell carcinoma of base of tongue. Yellow line is 7000 cGy, the prescription dose for the primary tumor (red). The radiation oncologist felt tumor arose on right, therefore the right nodal volume was at greater risk, so has elected to relatively spare the left parotid and adjacent lymph nodes. Image courtesy of the University of Massachusetts Medical School, Department of Radiation Oncology.

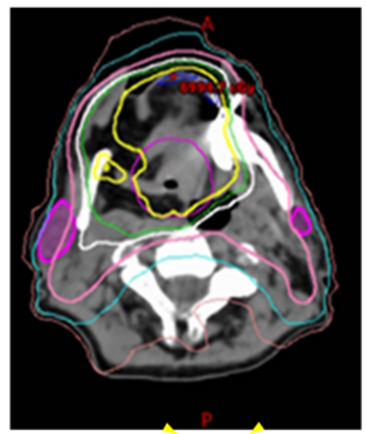

**Figure 16b.** Treatment plan CT slice superior to the slice in 13a, showing relative sparing of left parotid (parotids are pink volumes adjacent to mandible). Image courtesy of the University of Massachusetts Medical School, Department of Radiation Oncology.

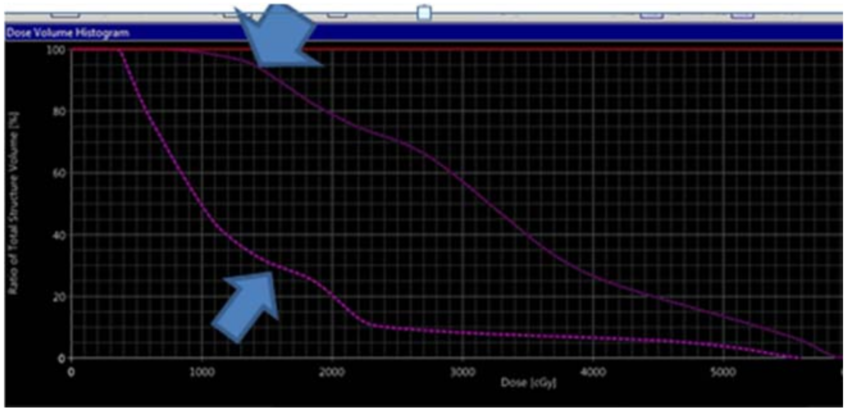


**Figure 16c.** Dose Volume Histogram (DVH) demonstrating relative sparing of left parotid (thin arrow) compared to left (thick arrow). Y axis is % of volume of the particular organ, and x axis is dose in cGy. Parotid tissue tolerance for continued salivary function is 1500cGy. Arrows both point at 1500 cGy and show that greater than 90% of right parotid will receive in excess of this dose, while only 30% of the left one will. Image courtesy of the University of Massachusetts Medical School. Department of Radiation Oncology.

## Chemotherapy

Chemotherapy alone is not a mainstay for treatment of head and neck cancers but may be used in a solitary fashion for palliation of disease. The main role of chemotherapy is to sensitize the tissue to increase the effectiveness of radiation. Thus, it may be used as an initial treatment prior to radiation in the form of induction chemotherapy or simultaneous with radiation in the form of concurrent chemotherapy. Platinum-based drugs are most commonly used as sensitizing agents, but small-molecule inhibitors and monoclonal antibody agents also comprise an important role in certain head and neck cancer treatment protocols.

## Outcome

Outcome is reported for each disease site separately, by stage. For example, 5-year relative survival rates for supraglottic cancer were 59.0% for localized disease, 53% for regional disease (positive lymph nodes, and 34% for distant disease (distant metastases) in 1995-96. True vocal cord cancer 5-year survival was 90% for Stage I disease, 74% for Stage II, 56% for Stage III disease, and 44% for Stage IV disease in the same period.[5.] And most of the T1 and T2 true vocal cord patients retained their larynx. Close follow-up by physicians trained in direct or at least indirect visualization of the larynx and physical examination of the head and neck is very important, as regional recurrences may be salvaged for long term disease-free survival if the recurrences are found early. But locally advanced recurrences are almost always treated with palliative intent (Figure 17).

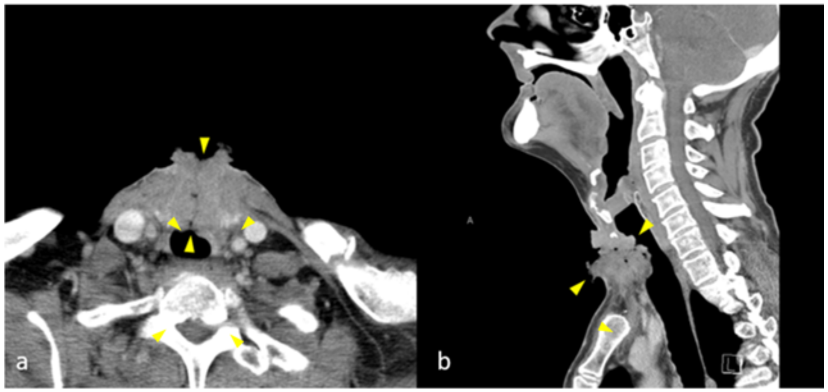


**Figure 17**. Axial (a) and sagittal (b) CT of the neck with contrast images shows pathology proven squamous cell carcinoma recurrence (yellow arrowheads) which occurred outside of the irradiated area. Long term surveillance of patients with head and neck cancers is advised. This patient had a transoral robotic supraglottic laryngectomy and adjuvant radiation. One year later he developed a fungating mass that obliterated his tracheostomy tract, projecting out through the skin and posteriorly into the trachea. Image courtesy of the University of Massachusetts Medical School, Department of Radiology.

## Conclusion

Cancers of the upper aerodigestive tract are most often SCC. Tobacco and alcohol are the leading causes; recently an epidemic of HPV cancers, particularly of the oropharynx has developed. It is hoped that HPV vaccination may decrease the incidence of this disease in the future.

Management of these cancers requires a full multidisciplinary team: otolaryngologist, radiation oncologist, medical oncologist, diagnostic radiologist, qualified dentist/oral surgeon, nutritionist and social worker at a minimum. While these cancers, especially the HPV+ ones, appear in patients from all walks of life and economic statuses, the importance of tobacco and especially alcohol in the lives of many patients means that their life situations are often very complicated, requiring considerable social support during treatment.

The fact that these cancers are less likely to spread beyond the neck means that even very advanced malignancies are often curable, so late effects are an important consideration in treatment decisions. And many of these patients will live to experience second, third and fourth cancers of the aerodigestive tract.

## Thought Questions

1. A 48-year-old man whose wife of 20 years recently underwent treatment for cervical cancer presents with left-sided sore throat for two months and an enlarged left neck lymph node noticed approximately one month later. What is the likely diagnosis?

   Your answer:

   **Expert Answer**

2. A 65-year-old woman receiving concurrent chemo/radiation therapy for an oropharyngeal SCCA is having significant trouble with swallowing. What is the best way to maximize her long term swallowing function?

   Your answer:

**Expert Answer**

Maintain oral intake even if a temporary feeding tube is necessary.

Some patients develop such significant mucositis or impairment of their pharyngeal musculature that it is very difficult for them to continue eating and drinking while undergoing radiation. Patients may require a nasogastric tube to avoid dehydration and significant weight loss. However, the key to long term swallowing function is to maintain oral intake, even if most nutrition is temporarily provided via non-oral means.

3. A patient has Stage II oropharyngeal cancer with known indications for radiation therapy. The patient desires surgery first followed by radiation to maximize his chances for cure. What will you tell him?

   Your answer:

**Expert Answer**

## Glossary

Aerodigestive tract- The oral and nasal cavities and throat, and some people include the trachea and esophagus, through which air, food and liquids pass

Exsanguination- Severe blood loss, sufficient to cause death

Field cancerization– Atypia ranging from mild abnormality to invasive cancer that affects a wide area of an anatomic region usually involving multiple sites to various degrees

Transglottic- A cancer which involves both false cord and true vocal cord, extending through the laryngeal ventricle.

## References


1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin. 2018; 68(1):7-30.
2. Van Dyne EA, Henley SJ, Saraiya M, Thomas CC, Markowitz LE, Benard VB. Trends in human papillomavirus-associated cancers - United States, 1999-2015. MMWR Morb Mortal Wkly Rep. 2018;67(33):918-924.
3. Troost EG, Vogel WV, Merkx MA, et al. 18F-FLT PET does not discriminate between reactive and metastatic lymph nodes in primary head and neck cancer patients. J Nucl Med. 2007; 48(5):726-735.
4. Thariat J, Ang KK, Allen PK, et al. Prediction of neck dissection requirement after definitive radiotherapy for head-and-neck squamous cell carcinoma. Int J Radiat Oncol Biol Phys. 2012;82(3):e367-74.
5. American Cancer Society. Laryngeal and Hypopharyngeal Cancer: Early Detection, Diagnosis and Staging. https://www.cancer.org/cancer/laryngeal-and-hypopharyngeal-cancer/detection-diagnosis-staging/survival-rates.html