

Head and Neck Cancers in the New Era

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HPV – What is it?

Some details about what HPV is and how it is typically contracted

- Human Papilloma Virus
- Most people infected with HPV will not have any symptoms and their immune system will get rid of the infection without any treatment.
- In some cases, however, HPV can lead to cancer.
- Its a minority that will lead to cancer, but clearly HPV can cause one.

HPV = Human Papillomavirus

HPV is a very common virus; nearly 80 million people—about one in four—are currently infected in the United States.



Most HPV infections don't lead to cancer but certain types of HPV infection cause cancers. More than 100 varieties of human papillomavirus (HPV) exist.

High and Low risk of HPV subtypes

Low-risk infection

Causes warts on the skin, mouth or genitals.

High-risk infection

Can lead to cancer

Cervical is the most common type of cancer caused by HPV.

It can also cause head and neck cancer in both men and women.

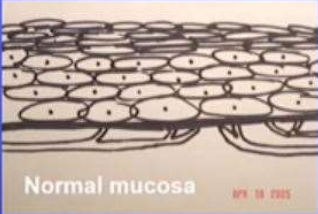
How is HPV Spread

- The skin or mucosa comes into contact with an infected person's skin or mucosa.
- For high-risk HPV, this usually occurs through sexual contact.
- Most HPV infections that cause head and neck cancer are spread through oral sex, and possibly by "open mouth" kissing

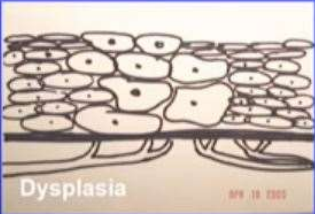
HPV – How it leads to Cancer

- Exposure to high-risk HPV infection
- Virus creates damage that eventually causes a tumor to grow. This process often takes many years
- Most head and neck cancers that happen are a result of HPV infection occur in the part of the throat that includes the base of tongue and the tonsils.


Carcinogenesis



Normal mucosa



Dysplasia



Carcinoma

https://youtu.be/3RaoE_YMf5Y

Human Papillomavirus (HPV) infection of epithelial cells.

Differentiation

Cornified

Granular

Supra-basal

Basal

Dermis

Normal epithelium

Viral infection

Dysplasia/ carcinoma in situ

Invasive cancer

HPV

Viral persistence

Clearance

Progression

Regression

Invasion

HPVs infect basal cells of squamous epithelia through sites of mechanical trauma. Infections with high-risk HPVs can lead to dysplasia and carcinoma in situ and to invasive squamous cell carcinoma. Progression is a rare and slow process and many lesions regress spontaneously.

HPV – How is this Cancer Different?

- How it tumors grow differently
- Some details on why cancers of this type are easier to treat
 - Age difference
 - Younger patients
 - Healthier
- Diagnosis and Prognosis
 - HPV related cancers treatment outcome is far better and more curable vs when its related to tobacco and alcohol

HPV and Oropharyngeal Cancer

Latency from infection:

Cervix (29 years) peak infection (20y) to cancer (49y)

HPV (10-30y) peak infection (25-30 and 55-60) and cancer 58y

HPV Vaccine impact expected by 2050

Age: 10 y younger on one study median age 57
(versus 61 for HPV -)

Gender: 76% male

Smaller primary: T1/T2 64% (versus 44% for
HPV -)

More Neck Nodes: N2/N3 in 69% (versus 51%
for HPV -)

Less likely to have a second primary: 6% versus
13%

Gender differences

- Males more likely to be infected
 - ? Increased number of sexual partners
 - ? Differences in immunologic response
 - ? Cervical exposure
- HPV 16
 - Cleared more slowly by males

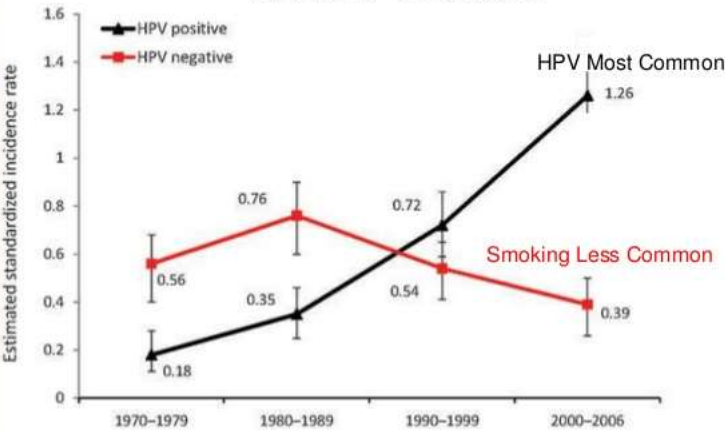
Head and Neck: Squamous Cell Carcinoma

- 6th most common cancer worldwide (600,000 cases/yr)
 - 4% of malignancies in USA 52,500cases/yr
 - Oropharynx
 - 14,000 cases/year in USA
 - Males > Females 3-4:1
 - Larynx
 - 12,000 cases/year
 - Alcohol/ Tobacco
 - Male > Female 5:1 (formerly 15:1)

	HPV-positive tumours	HPV-negative tumours
Anatomical site	Tonsil and base of tongue	All sites
Histology	Non-keratinised	Keratinised
Age	Younger cohorts	Older cohorts
Sex ratio	3:1 men	3:1 men
Stage	Tx, T1-2	Variable
Risk factors	Sexual behaviour	Alcohol and tobacco
Incidence	Increasing	Decreasing
Survival	Improved	Unchanging

Table 2: Differences between HPV-positive and HPV-negative head and neck squamous-cell carcinomas

Dramatic Rise in HPV + Tonsil Cancer



The HPV-head and neck cancer link

Evidence for a Causal Association Between Human Papillomavirus and a Subset of Head and Neck Cancers

Maura L. Gillison, Wayne M. Koch, Randolph B. Capone, Michael Spafford, William H. Westra, Li Wu, Marianna L. Zahurak, Richard W. Daniel, Michael Vigliani, David E. Symer, Keerti V. Shah, David Sidransky

- Retrospective analysis of 253 SCCa samples of head and neck
- 25% HPV positive (90% HPV-16)
- Oropharynx
- Poorly differentiated
- Less exposure to alcohol and tobacco exposure
- 59% reduced risk of death (vs HPV -)

Head and Neck Cancer – The Basics

- What anatomy is typically included and planned around in general
- Some general guidelines used
- Chains of nerves, fluids, and lymphatic systems
- What issues are there with irradiation in this region?

[Oropharynx](#) anatomy

Cancers caused by HPV

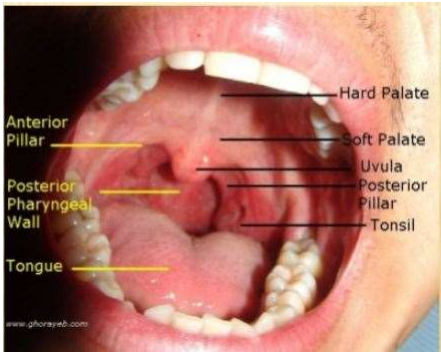
• Cervix	100%
• Anal	95%
• Oropharynx	70%
• Vaginal	65%
• Vulva	50%
• Penis	5%

In the US , 3% of all cancers in women and 2% of all cancers in men

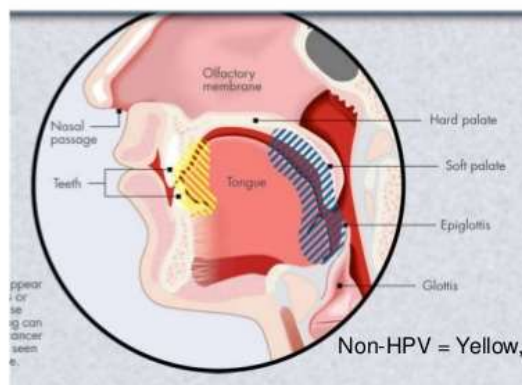


Subsites of the Oropharynx

- Soft palate- Hyoid
- Posterior pharyngeal wall
- 2/3 of Waldeyer's ring
 - Tonsillar complex
 - *Tonsil, tonsillar fossa,
 - anterior and posterior tonsillar pillars
- *Base of tongue
 - Beyond circumvallate papillae
 - Visualization challenging



HPV Infection and Cancer of the Oropharynx



Robert Miller MD

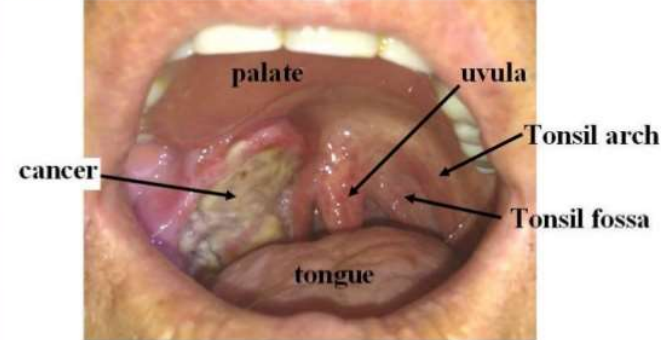
www.aboutcancer.com

Watch the video at <https://youtu.be/ISyagHODlvY>

Typical presentation

- Level II neck mass
- Minimal disease at "primary" site: tonsil or base of tongue
- Throat symptoms vague – Globus
 - Pain uncommon
 - Difficulty swallowing is uncommon
 - Voice changes uncommon
 - Visible lesion may be absent

Typical **smoking** related oropharynx cancer, presented with months of throat pain radiating into ear



In HPV + cancers the primary may be small and hard to see



Squamous Cell Carcinoma. This human papillomavirus-positive tumor presented as a diffuse erythroplakia of the left soft palate and tonsillar region.

HPV + Characteristics

- Neck mass
 - Cancer until proven otherwise in adults!!!
- Advance stage disease (3 or 4)
 - Nodal metastasis
 - Vague symptoms of primary site
- TNM findings
 - Small primary
 - Advanced nodal disease (cystic)

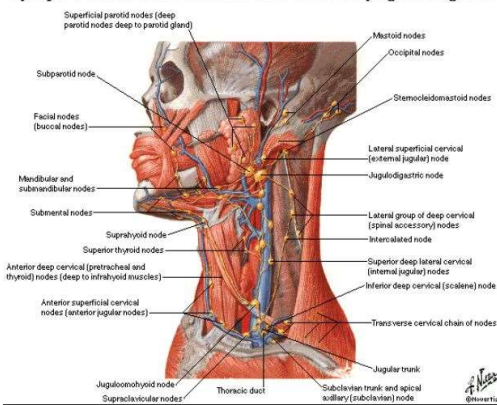
New ICON-S staging system was proposed for patients with HPV positive oropharyngeal cancer

Stage	TNM	5 Year Survival
Stage I	T1-2N0-1	85-88%
Stage II	T3 or N2	78-81%
Stage III	T4 or N3	53-65%

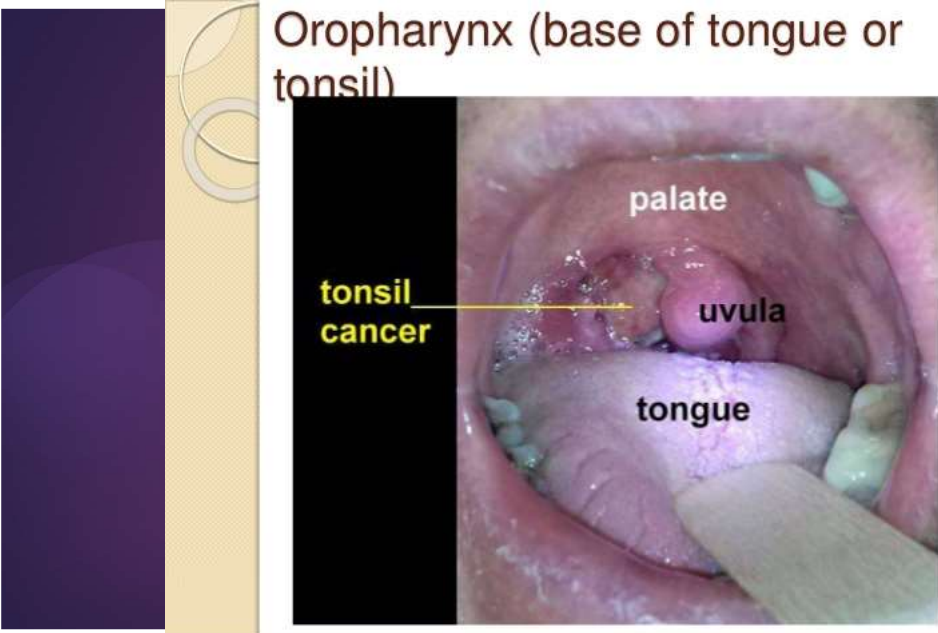
Cervical lymph nodes

- 300 lymph nodes in the head and neck
- ~ 30 – 40 % of total body lymphatics
- Embryological relation to venous system
- Mobile or Fixed?
- Tender to palpation?
- Change over time?

Lymph Vessels and Nodes of Oral and Pharyngeal Regions



Oropharynx (base of tongue or tonsil)



The Optima trail- Head and Neck Treatment

- Low-risk patients with favorable response receive low dose 50 Gy radiation
- Low risk patients with moderate response (30%-50%) received low dose 45Gy chemoradiation
- Low-risk patients with little to no response (>30%) received standard 75 Gy chemoradiation
- High-risk patients with favorable response received low-dose 45 Gy chemotherapy
- High-risk patients with favorable response receive standard 75 Gy chemoradiation

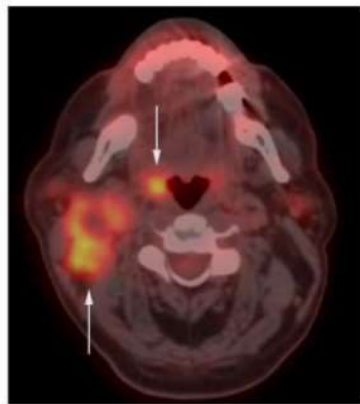
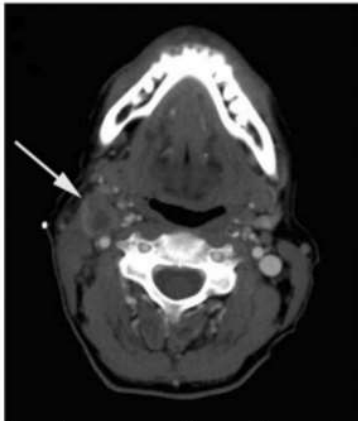
De-Escalation Trials for HPV...Can we use less chemotherapy or lower dose radiation and get the same result with less toxicity?



50 yo non-smoker, white male present with a lump in his left neck and the PET scan as noted

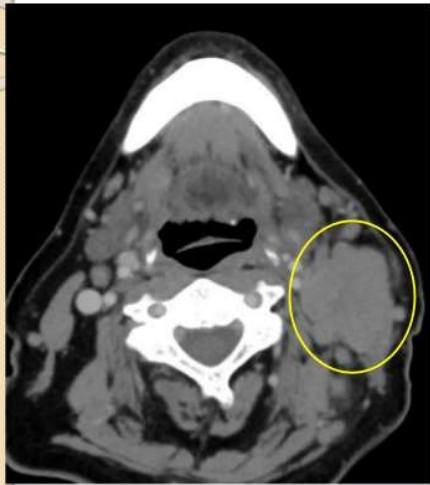


Typical Imaging for HPV Oropharynx Cancer



CT = large cystic node metastases PET = large neck mass with small primary in tonsil

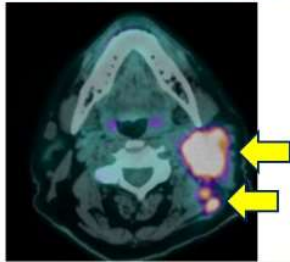
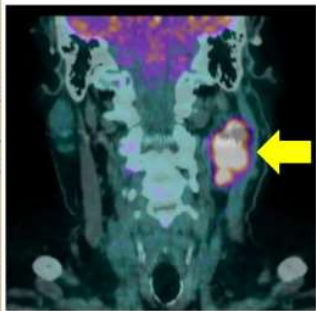
CT Scan Typical HPV + Patient



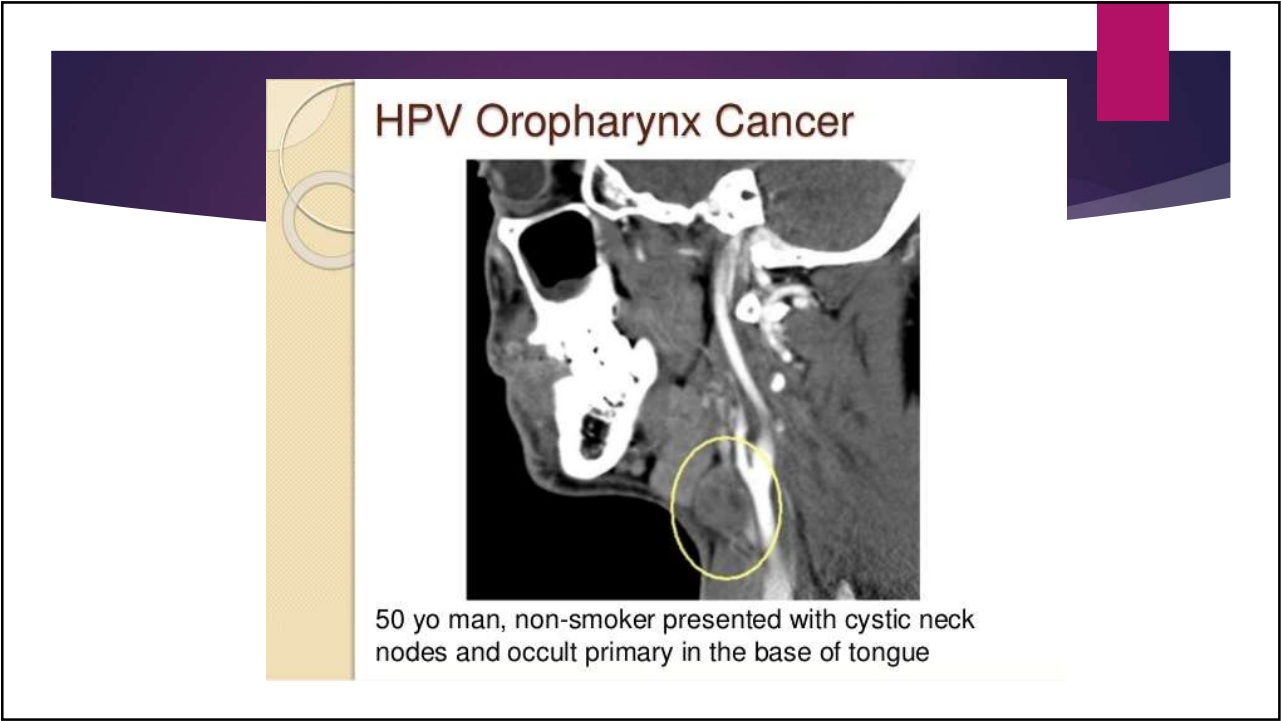
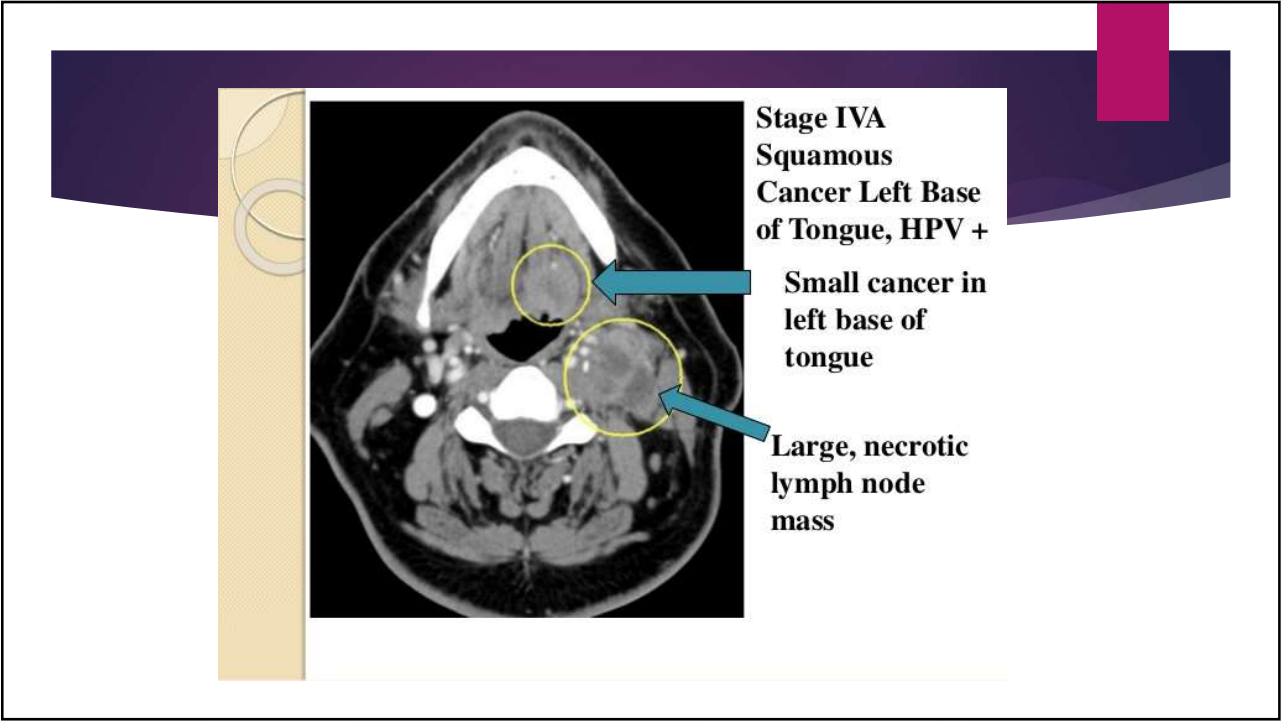
Large, Lobulated
neck mass of
lymph nodes
with no obvious
primary source

Neck biopsy =
squamous



**PET Scan Typical
HPV + Patient**



Large lymph
node
metastases in
the neck with
no obvious
primary
source



HPV Oropharynx Cancer



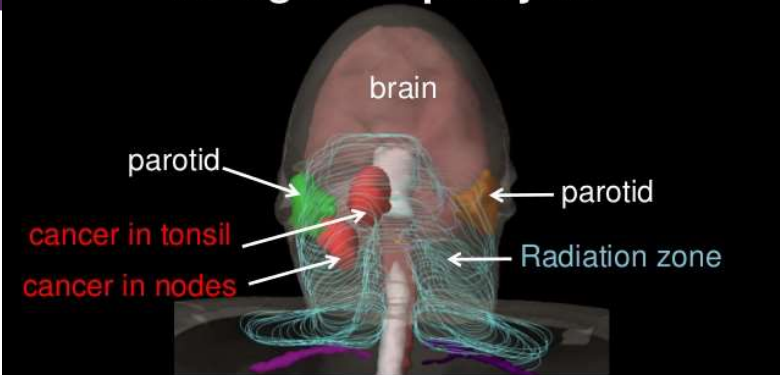
53 yo man with large cystic neck node and occult primary in base of tongue

Surgical Pathology Report

In Situ Hybridization Analysis

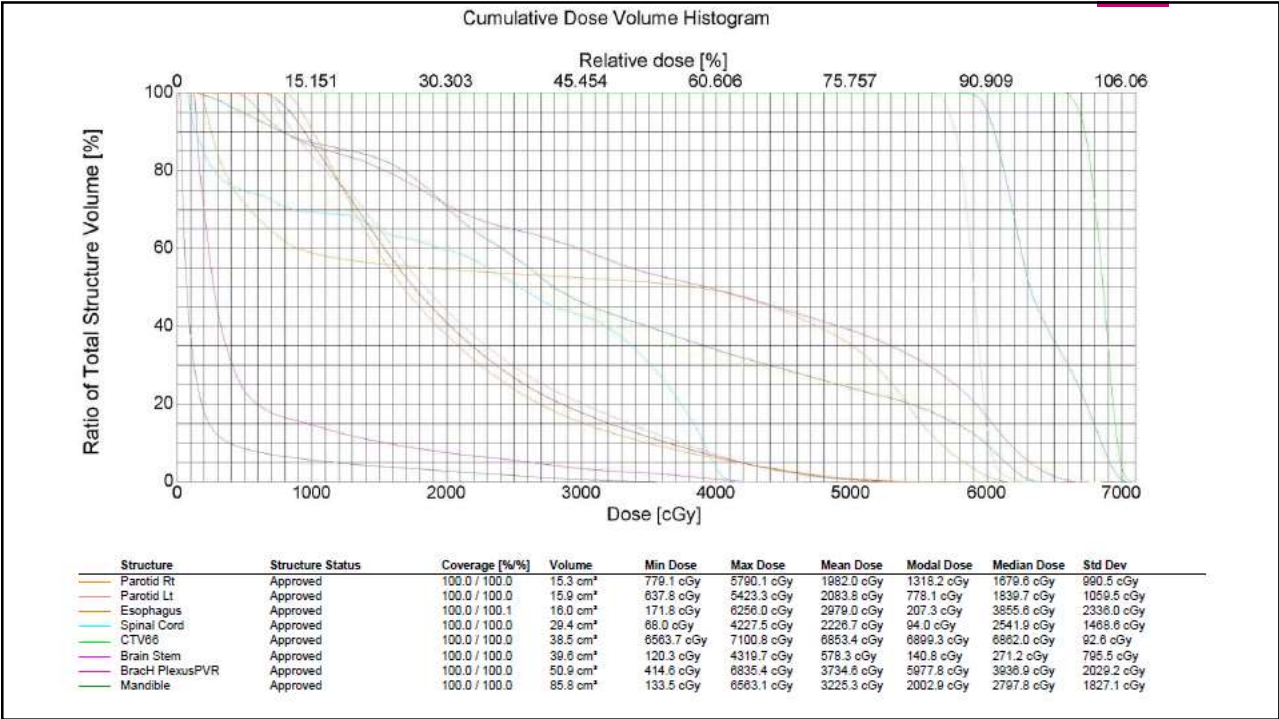
Marker	Result	Description
HPV (WSS)	Positive	HPV Wide Screen Spectrum
HPV (6/11)	Negative	Human Papilloma Virus Subtype 6/11, Low Risk
HPV (16/18)	Positive	Human Papilloma Virus Subtype 16/18, High Risk
HPV (31/33)	Negative	Human Papilloma Virus Subtype 31/33, High Risk

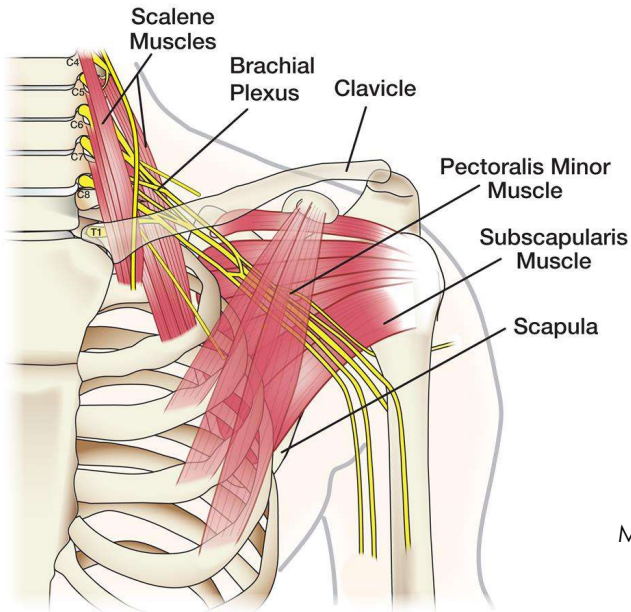
Typical Radiation Field for Cancer in Right Oropharynx



Part of the radiation includes the obvious cancer and other lymph node sites in the next but tries to spare normal structures like the parotid and brain

HPV Cancer – Head and Neck Planning Technique Walkthrough





Max total dose 63Gy

Short Term Side Effects of Radiation to the Throat and Neck



1. Skin irritation
2. Dry Mouth and changes in taste and possible problems with teeth
3. Sore throat and problems with swallowing and dehydration and possible need for a feeding tube
4. Pain management problems
5. Laryngitis
6. Fatigue

Long Term Side Effects of Radiation to the Throat and Neck



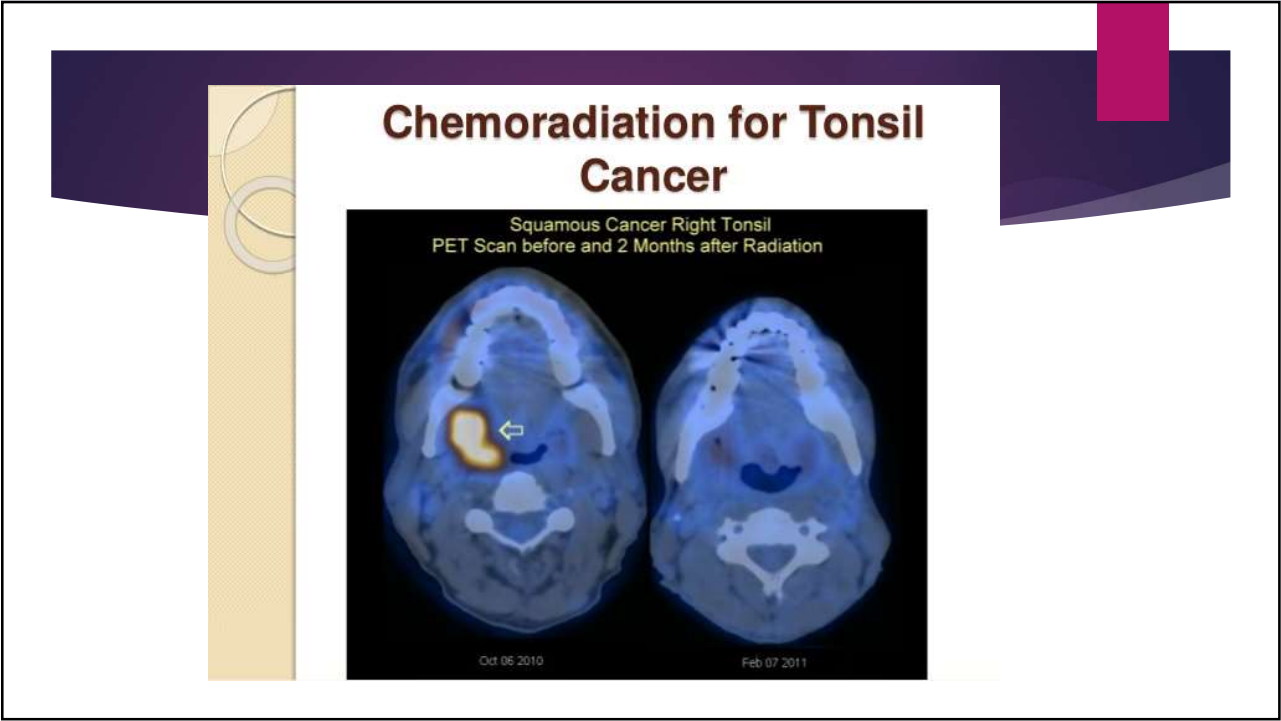
1. The dryness may be permanent, depending on the amount of saliva glands in the field
2. Teeth may be vulnerable to decay, and caution is need with future dental care to avoid jaw bone problems (osteonecrosis)
3. Problems with swallowing
4. Persistent hoarseness
5. Small risk of low thyroid
6. Carotid stenosis

Quick Response to Radiation combined with chemotherapy, Tonsil cancer gone by 2 ½ weeks



**Squamous
Tonsil Cancer**

**2.5 weeks after
chemoradiation**



Questions

Why You Should Worry about [HPV](#)