

An anatomical drawing of a human head and neck, showing the skull, facial features, and the complex network of muscles and nerves in the neck. The drawing is rendered in a detailed, scientific style with various colors like brown, tan, and grey. In the background, there is a faint pencil sketch of a landscape with trees and a horizon line. The text is overlaid on a dark grey semi-transparent box on the right side of the image.

HEAD & NECK CANCER PREVENTION AND TREATMENT

JOHN R. SIMS, M.D.

HEAD & NECK ONCOLOGIC AND MICROVASCULAR
RECONSTRUCTIVE SURGEON

 CARTI CANCER CENTER

INTRODUCTION

- ▶ Grew up in Conway, AR



- ▶ Medical school at University of Arkansas for Medical Sciences (UAMS) - 2009-2013



INTRODUCTION

- ▶ Fellowship in Head & Neck Oncologic and Microvascular Reconstructive Surgery at Mount Sinai in New York City - 2018-2019



- ▶ Residency in Otolaryngology - Head & Neck Surgery at Mayo Clinic -2013-2018





▶ CARTI Cancer Center 2019- present

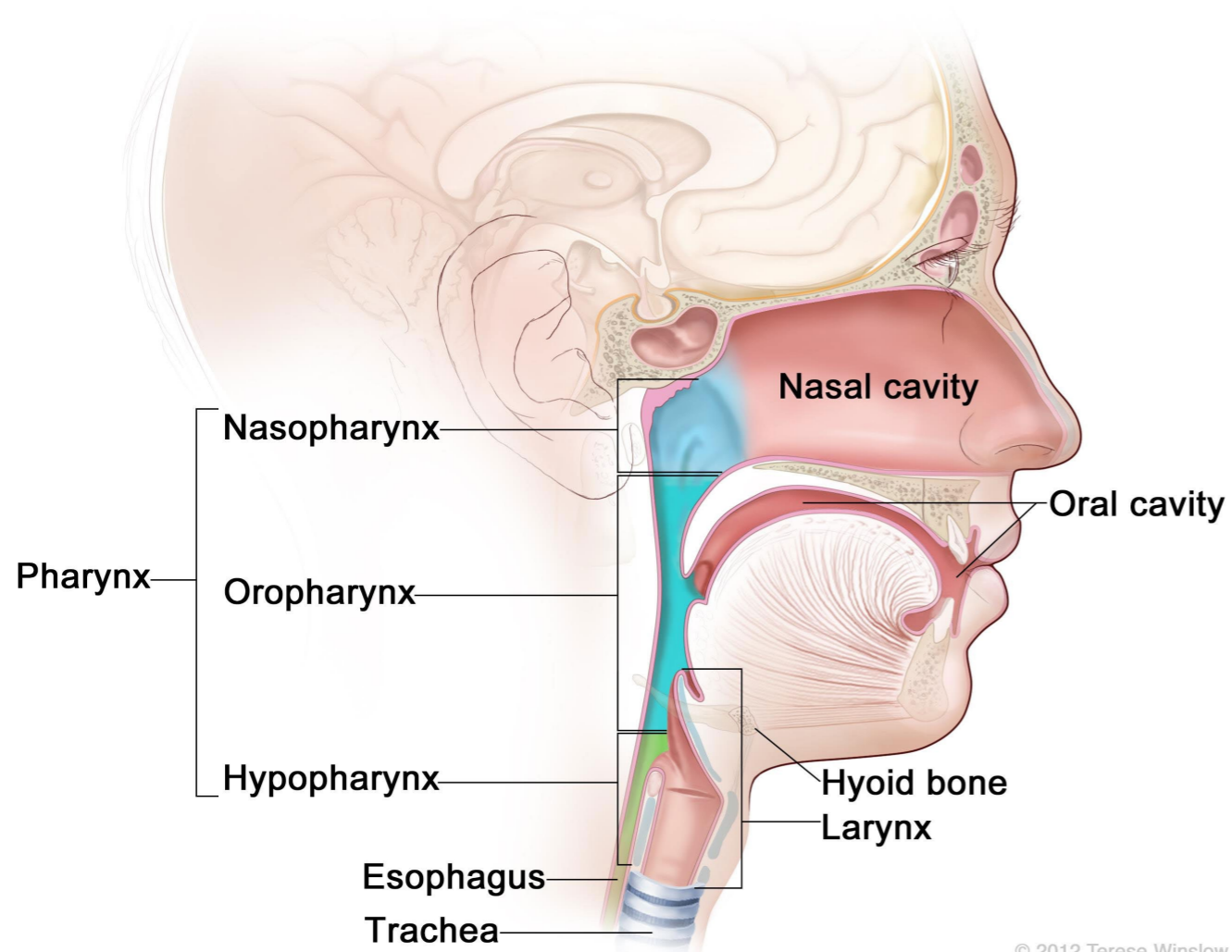


WHAT IS HEAD & NECK CANCER?

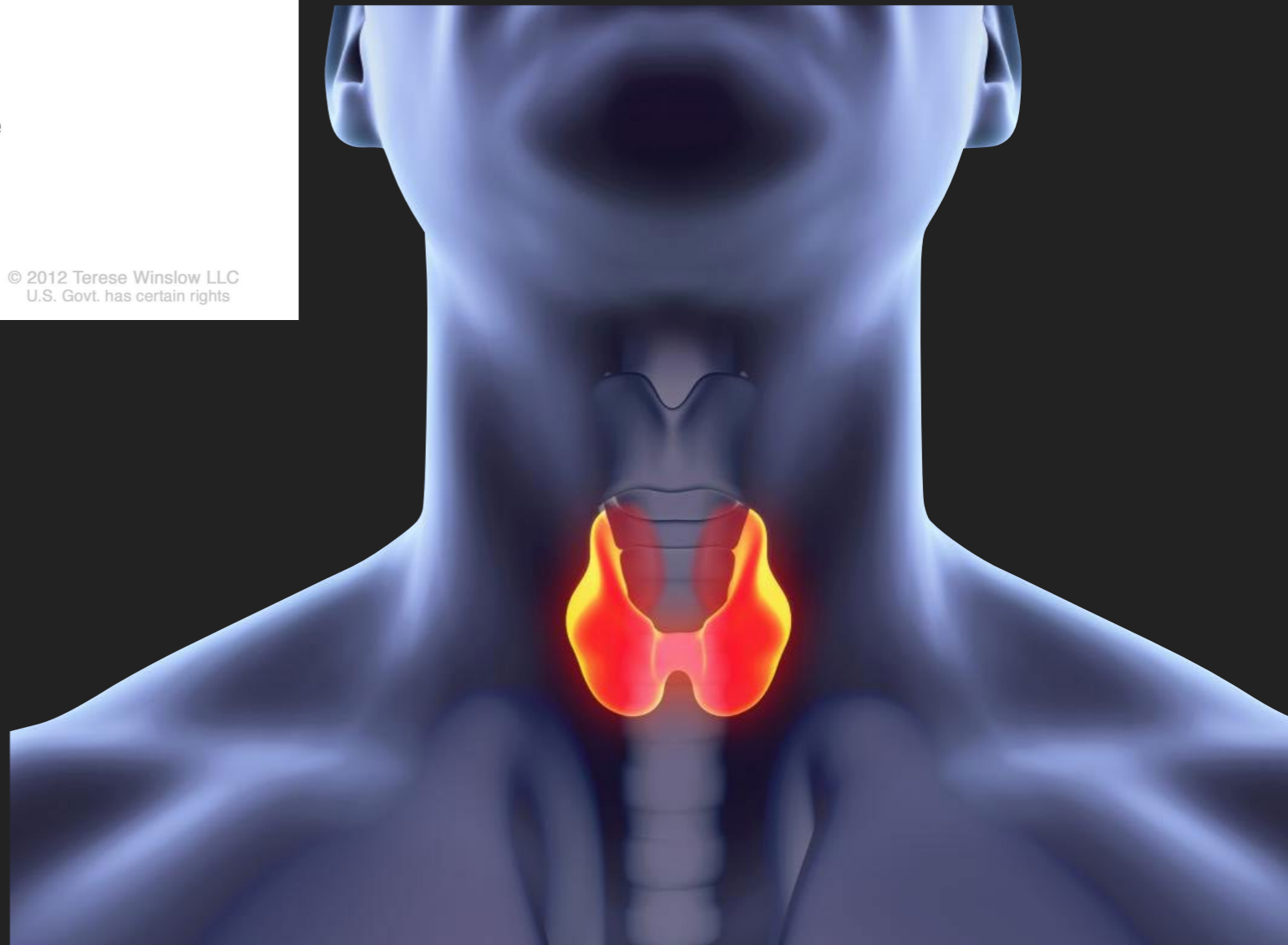
Estimated New Cases

			Males	Females			
Prostate	180,890	21%			Breast	246,660	29%
Lung & bronchus	117,920	14%			Lung & bronchus	106,470	13%
Colon & rectum	70,820	8%			Colon & rectum	63,670	8%
Urinary bladder	58,950	7%			Uterine corpus	60,050	7%
Melanoma of the skin	46,870	6%			Thyroid	49,350	6%
Non-Hodgkin lymphoma	40,170	5%			Non-Hodgkin lymphoma	32,410	4%
Kidney & renal pelvis	39,650	5%			Melanoma of the skin	29,510	3%
Oral cavity & pharynx	34,780	4%			Leukemia	26,050	3%
Leukemia	34,090	4%			Pancreas	25,400	3%
Liver & intrahepatic bile duct	28,410	3%			Kidney & renal pelvis	23,050	3%
All Sites	841,390	100%	All Sites	843,820	100%		

Anatomy of the Pharynx



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CLINICAL PRESENTATION

DEMOGRAPHICS AND RISK FACTORS

- ▶ Classic Demographic
 - ▶ >60 years old
 - ▶ M>F
- ▶ Risk Factors
 - ▶ Smoking and all forms of tobacco use
 - ▶ Alcohol abuse

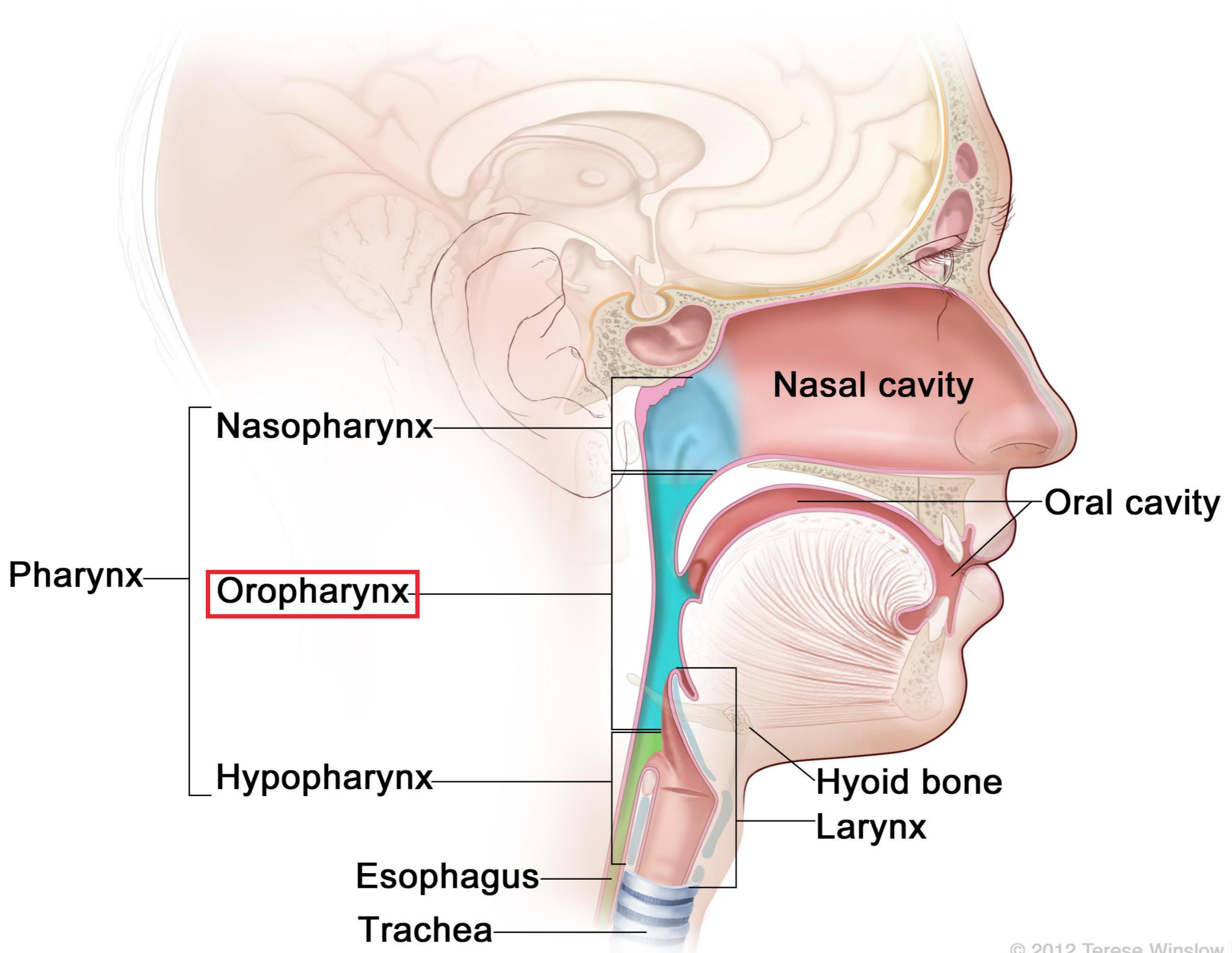


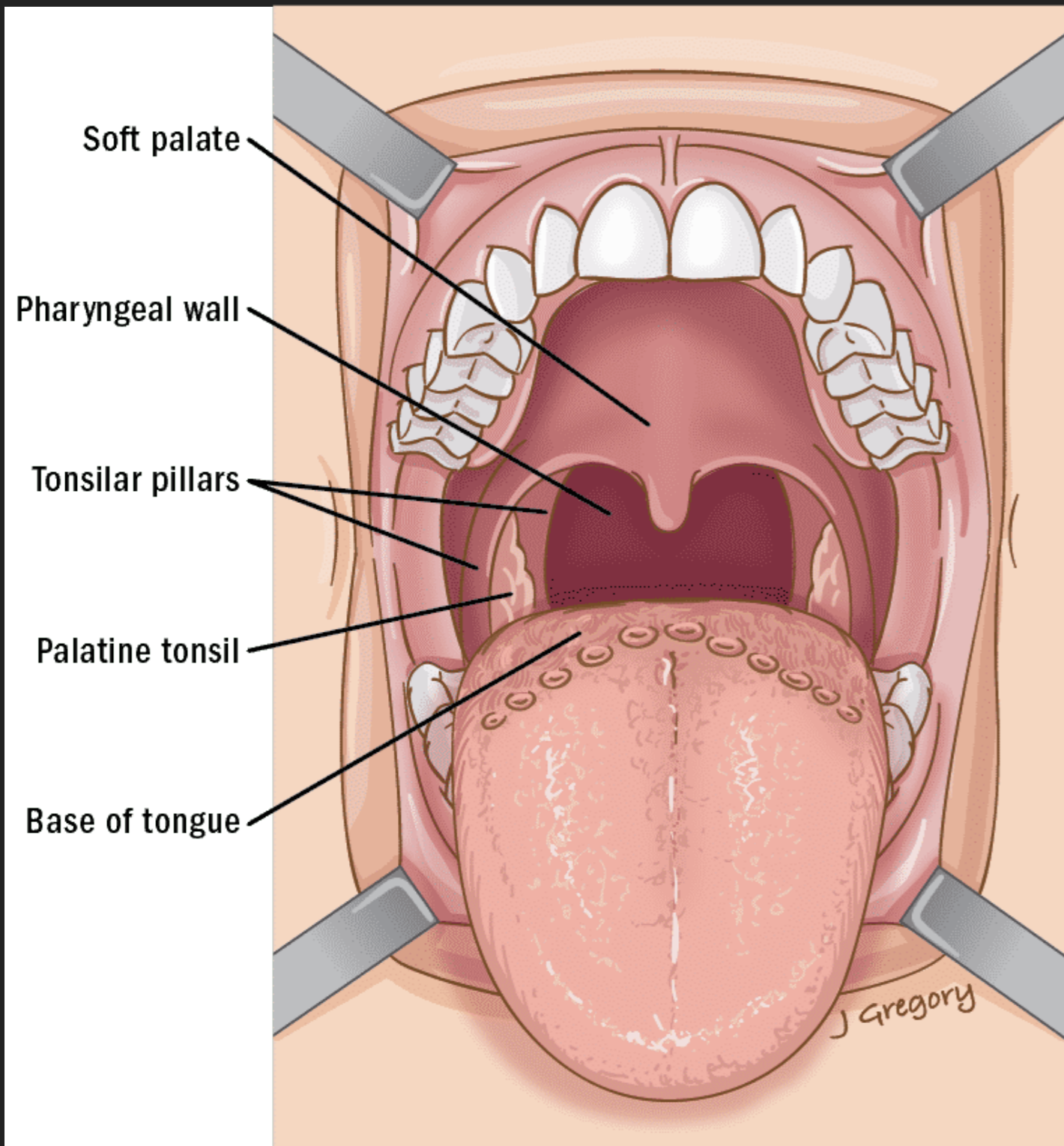
SIGNS/SYMPTOMS

- ▶ Ulcer or lesion anywhere in the mouth
 - ▶ >3 weeks
 - ▶ Not healing
 - ▶ Painful
 - ▶ Bleeding
- ▶ Neck mass
- ▶ Other symptoms:
 - ▶ Odynophagia
 - ▶ Change in speech
 - ▶ Trismus
 - ▶ Dysphagia
 - ▶ Weight loss
 - ▶ Velopharyngeal insufficiency



Anatomy of the Pharynx





- ▶ Oropharyngeal squamous cell carcinoma is increasing in incidence
- ▶ 80% of oropharyngeal cancers are HPV related
- ▶ Oropharyngeal cancer has now surpassed cervical cancer as the most common HPV-related cancer (20,747 vs. 10,853)

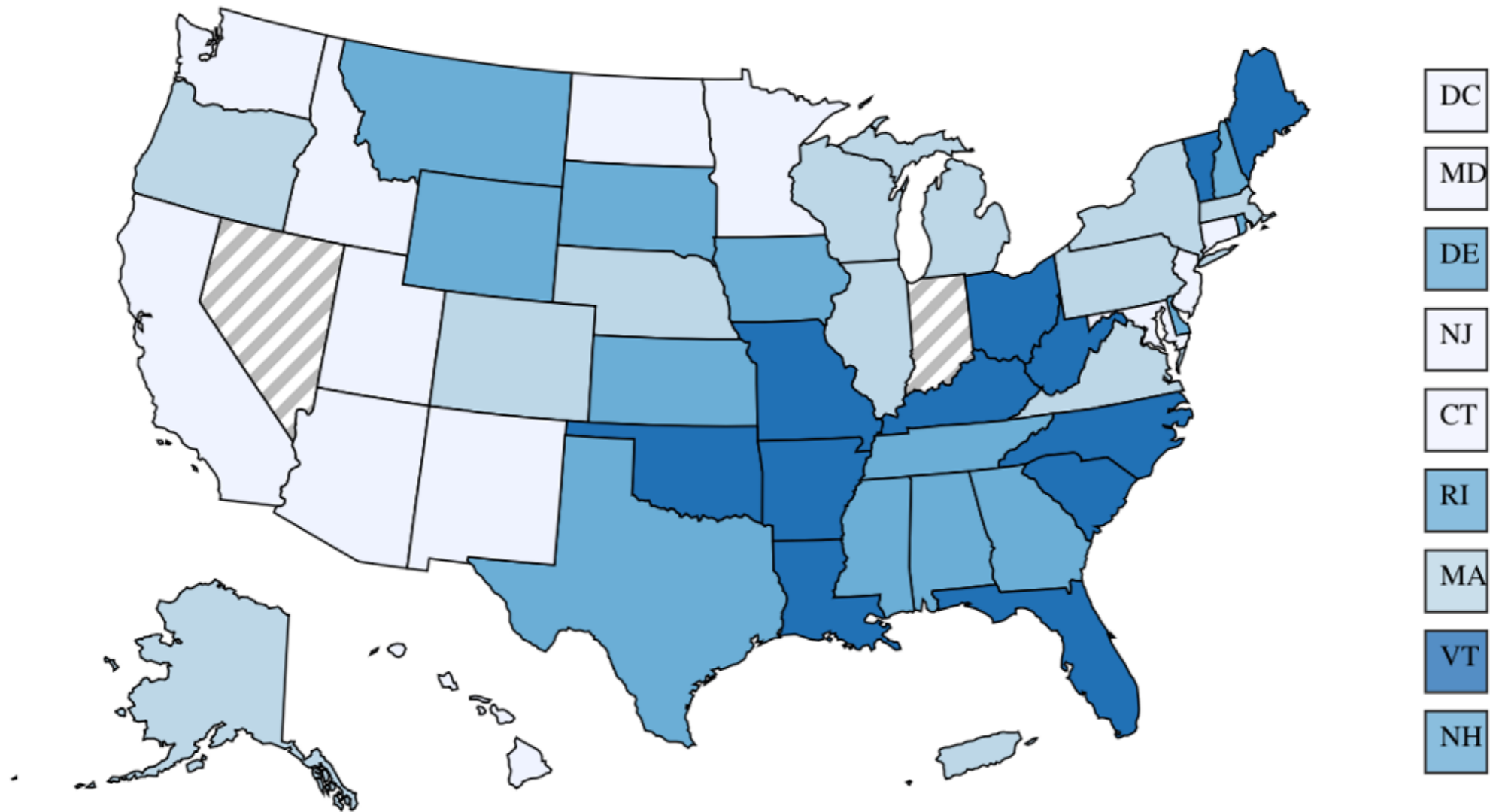
WHY OROPHARYNGEAL CANCER?

Cancer Type	Age-Adjusted Rate	Case Count	Population
All HPV-associated Cancers	11.8	45,531	319,590,911
Cervical Carcinoma	6.5	10,853	162,239,308
Oropharyngeal Squamous Cell Carcinoma	5.0	20,747	319,590,911
Vulvar Squamous Cell Carcinoma	2.0	4,176	162,239,308
Anal and Rectal Squamous Cell Carcinoma	1.9	7,622	319,590,911
Penile Squamous Cell Carcinoma	0.7	1,272	157,351,603
Vaginal Squamous Cell Carcinoma	0.4	861	162,239,308

Rate of New HPV-associated Cancers By State

All HPV-associated Cancers, Male and Female, United States, 2020

Rate per 100,000 people



Rate per 100,000 people



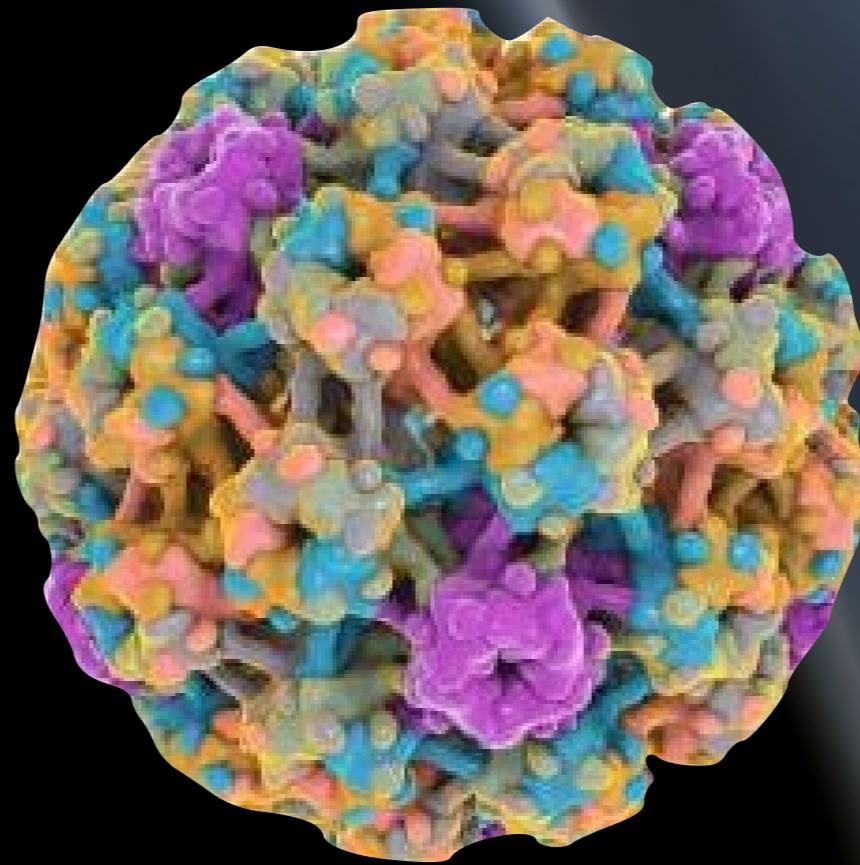
No data/data not presented

7.7 - 10.5

10.6 - 12.0

12.2 - 13.0

13.2 - 16.3



- ▶ HPV-related oropharyngeal cancers present in younger and healthier patients than previous tobacco and alcohol related cancers

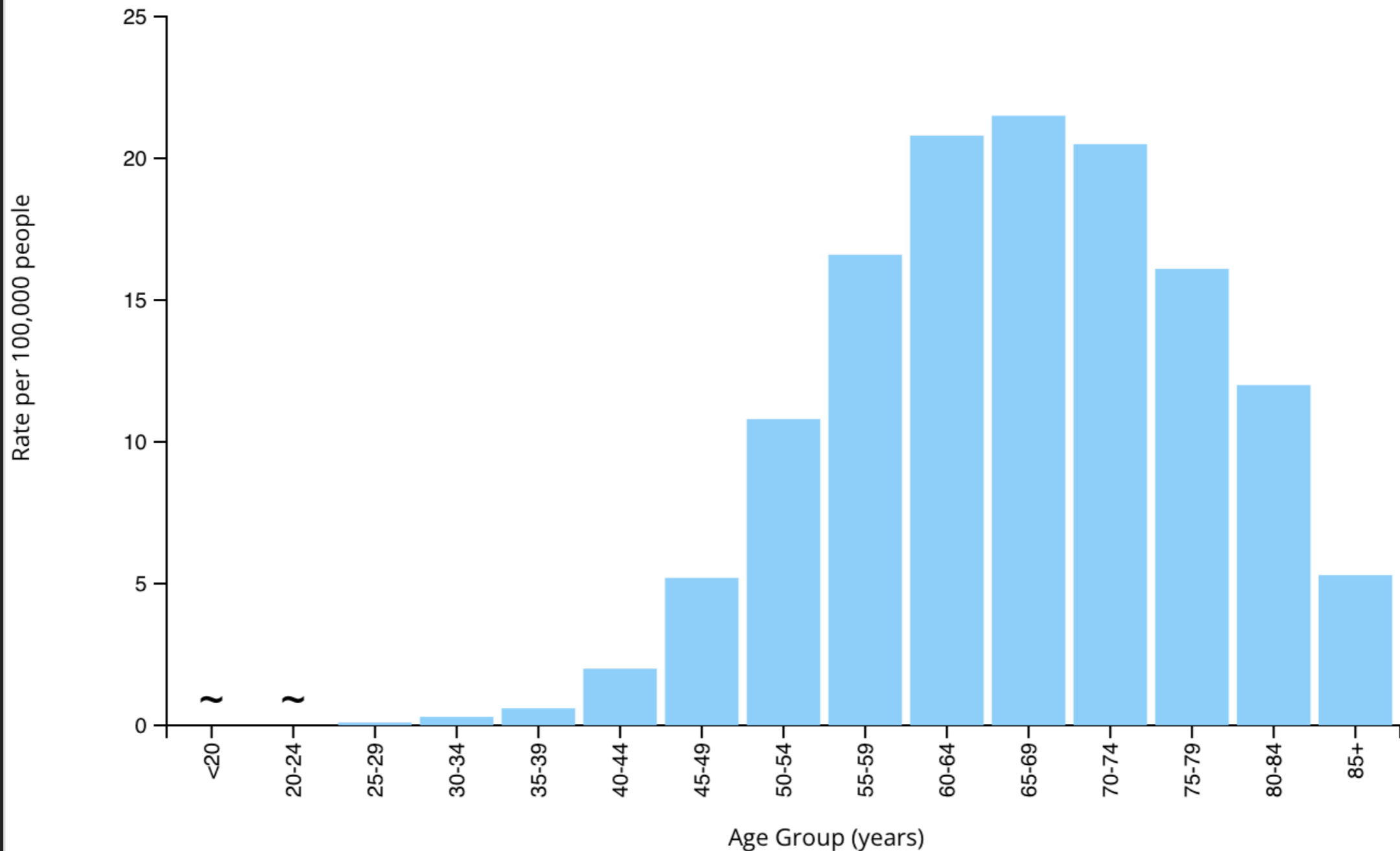


Rate of New HPV-associated Cancers By Age Group (years)

Oropharyngeal Squamous Cell Carcinoma, Male and Female, United States, 2020
Rate per 100,000 people



Age: 55-79

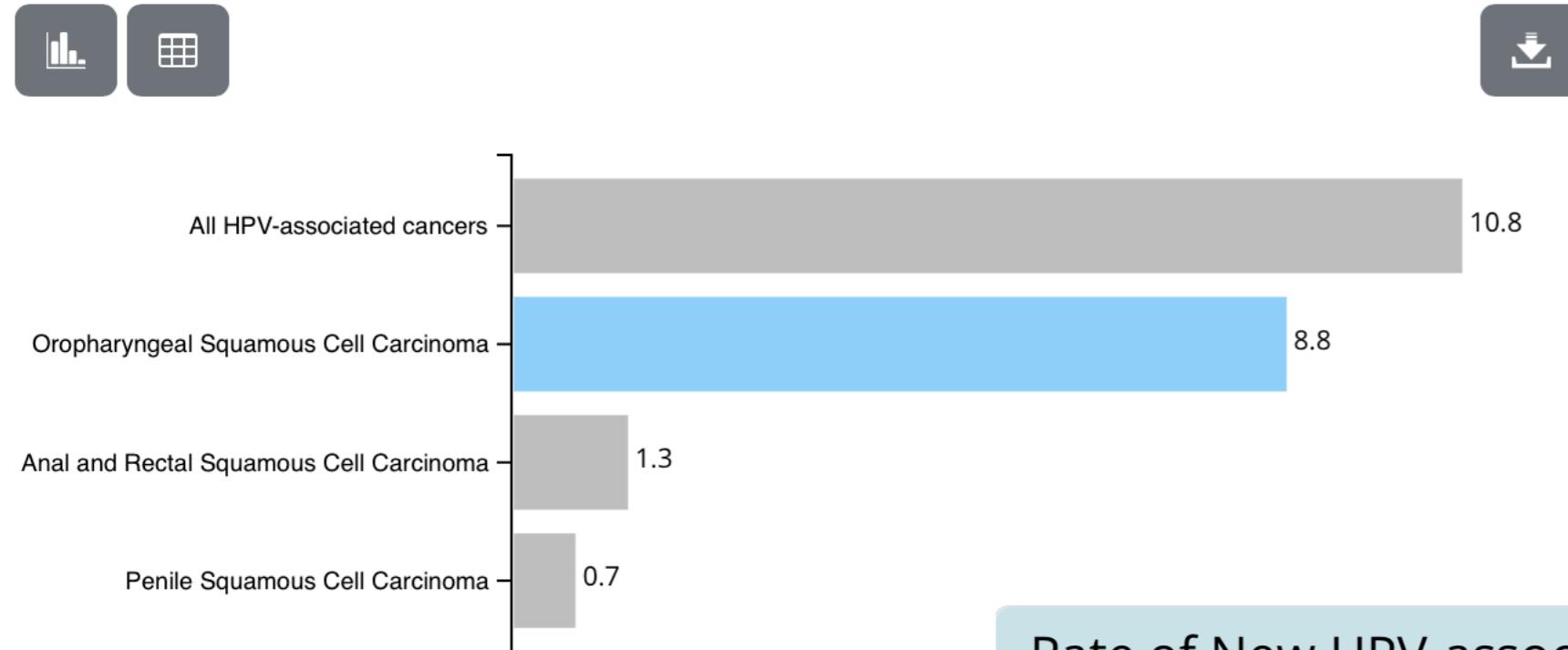


~ Data are suppressed for less than 16 cases

Rate of New HPV-associated Cancers by Cancer Type

Oropharyngeal Squamous Cell Carcinoma, Male, United States, 2020

Rate per 100,000 men

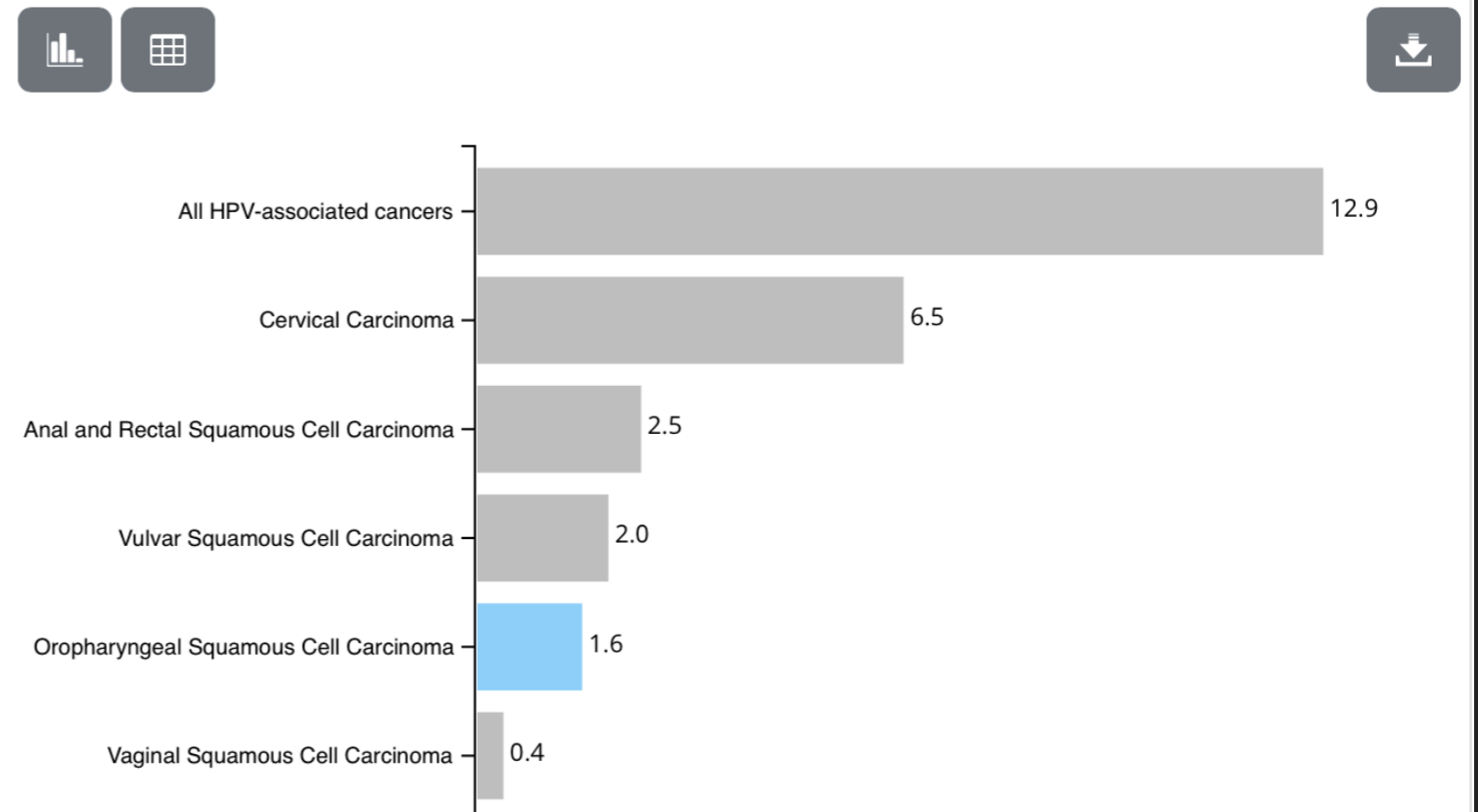


Sex: M>>F

Rate of New HPV-associated Cancers by Cancer Type

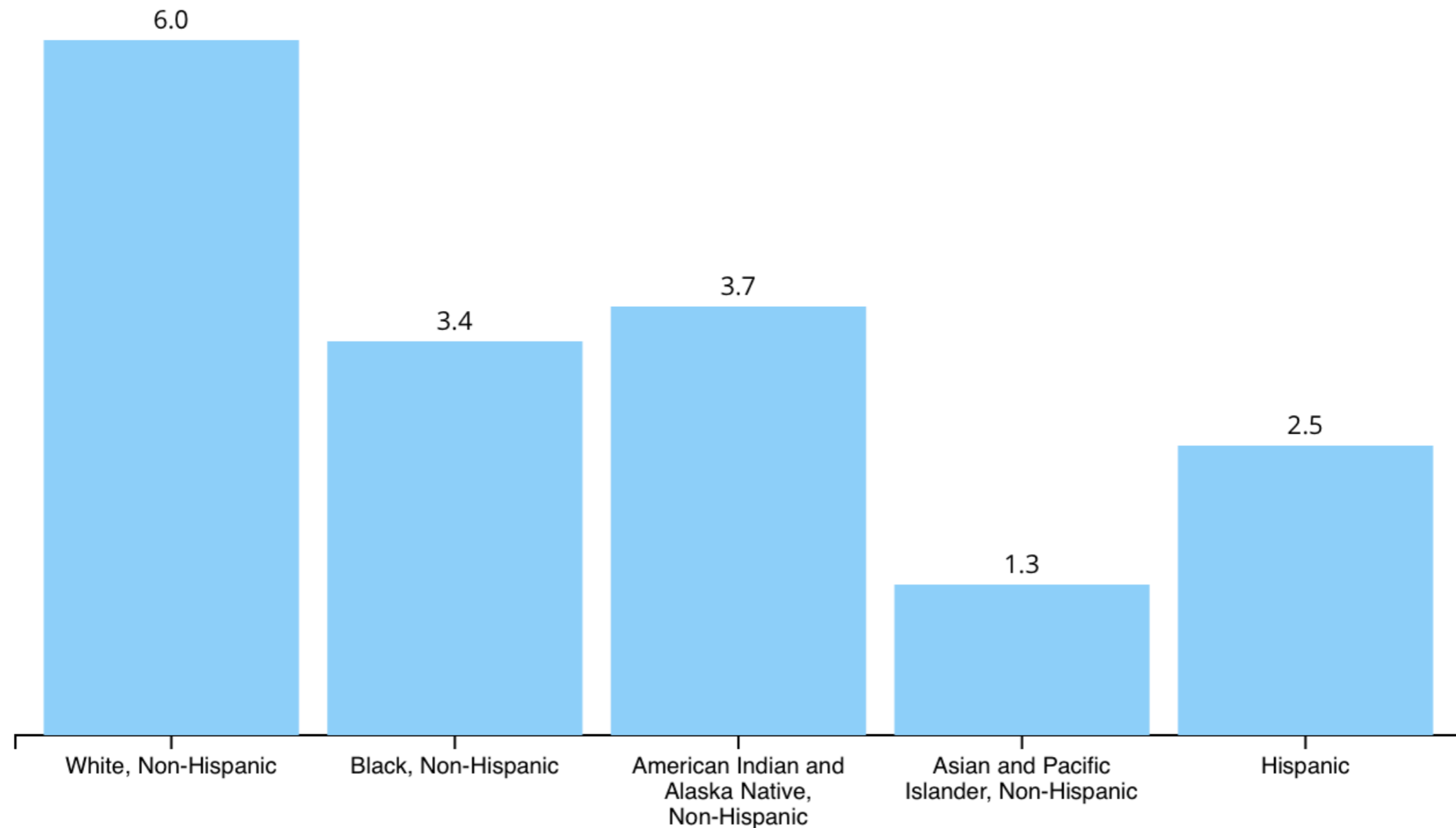
Oropharyngeal Squamous Cell Carcinoma, Female, United States, 2020

Rate per 100,000 women



Rate of New HPV-associated Cancers By Race and Ethnicity

Oropharyngeal Squamous Cell Carcinoma, Male and Female, United States, 2020
Rate per 100,000 people



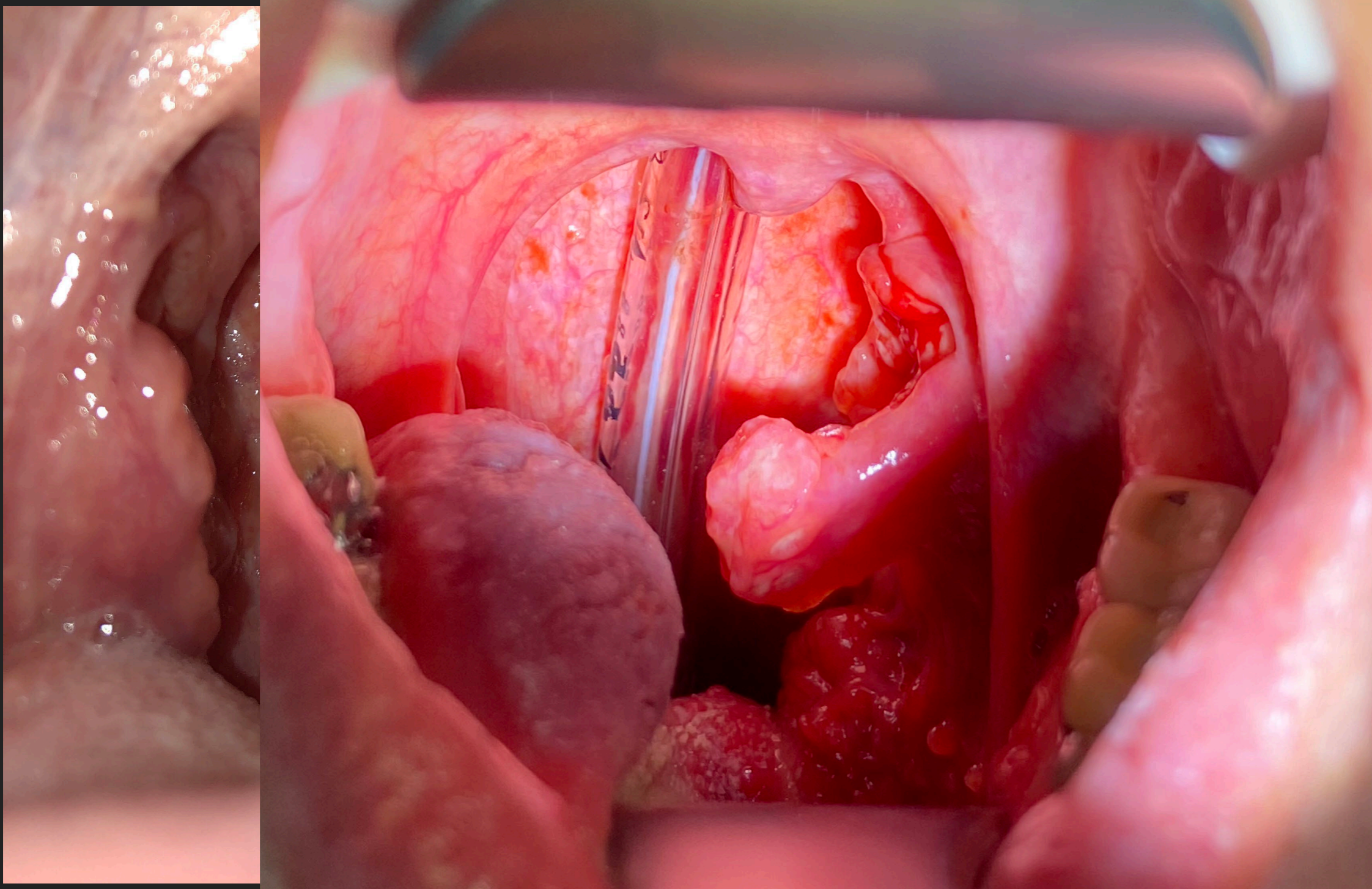
SIGNS/SYMPTOMS

- ▶ The most common presentation is an asymptomatic neck mass
- ▶ Less common symptoms include:
 - ▶ Odynophagia
 - ▶ Otalgia
 - ▶ Trismus
 - ▶ Dysphagia
 - ▶ Weight loss
 - ▶ Voice changes
 - ▶ Velopharyngeal insufficiency



PHYSICAL EXAM

- ▶ Oropharyngeal exam



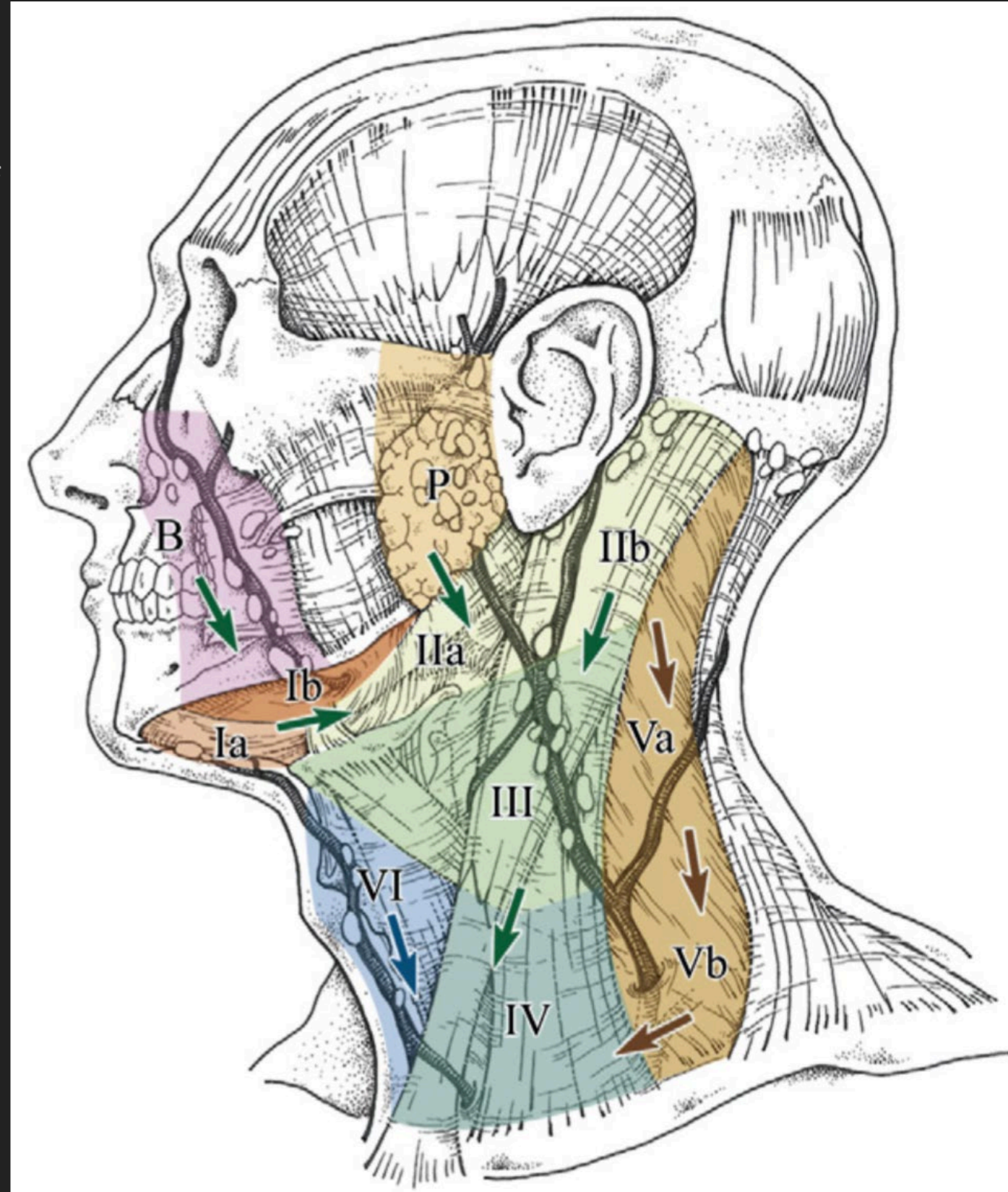
PHYSICAL EXAM

- ▶ Neck exam



LYMPHATIC PATHWAYS

- ▶ **Level I**
 - ▶ a - lower lip, anterior alveolus, anterior FOM, tip of tongue, buccal mucosa
 - ▶ b - Oral cavity, anterior nasal cavity, submandibular gland, midfacial face skin
- ▶ **Level II** - Oropharynx, oral cavity, nasopharynx, nasal cavity, larynx, hypopharynx
- ▶ **Level III** - Oropharynx, oral cavity, nasopharynx, larynx, hypopharynx
- ▶ **Level IV** - Oropharynx, larynx, hypopharynx, upper esophagus, thyroid
- ▶ **Level V** - Nasopharynx, posterior scalp skin, thyroid
- ▶ **Level VI** - Thyroid, larynx, hypopharynx, upper esophagus
- ▶ **Other:**
 - ▶ **Buccal/Facial** - frontal scalp, facial and nasal skin, septum, eyelids
 - ▶ **Parotid** - Lateral/upper facial and scalp skin, parotid gland
 - ▶ **Retropharyngeal** - Nasopharynx, oropharynx, palate, nasal cavity, middle ear
 - ▶ **Mastoid/Occipital** - parietal and occipital scalp, auricular skin



STAGING

HPV-related oropharyngeal carcinoma TNM clinical staging AJCC UICC 8th edition

Primary tumor (T)

T category	T criteria
T0	No primary identified
T1	Tumor 2 cm or smaller in greatest dimension
T2	Tumor larger than 2 cm but not larger than 4 cm in greatest dimension
T3	Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis
T4	Moderately advanced local disease. Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible or beyond.*

* Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.

Regional lymph nodes (N) - Clinical N (cN)

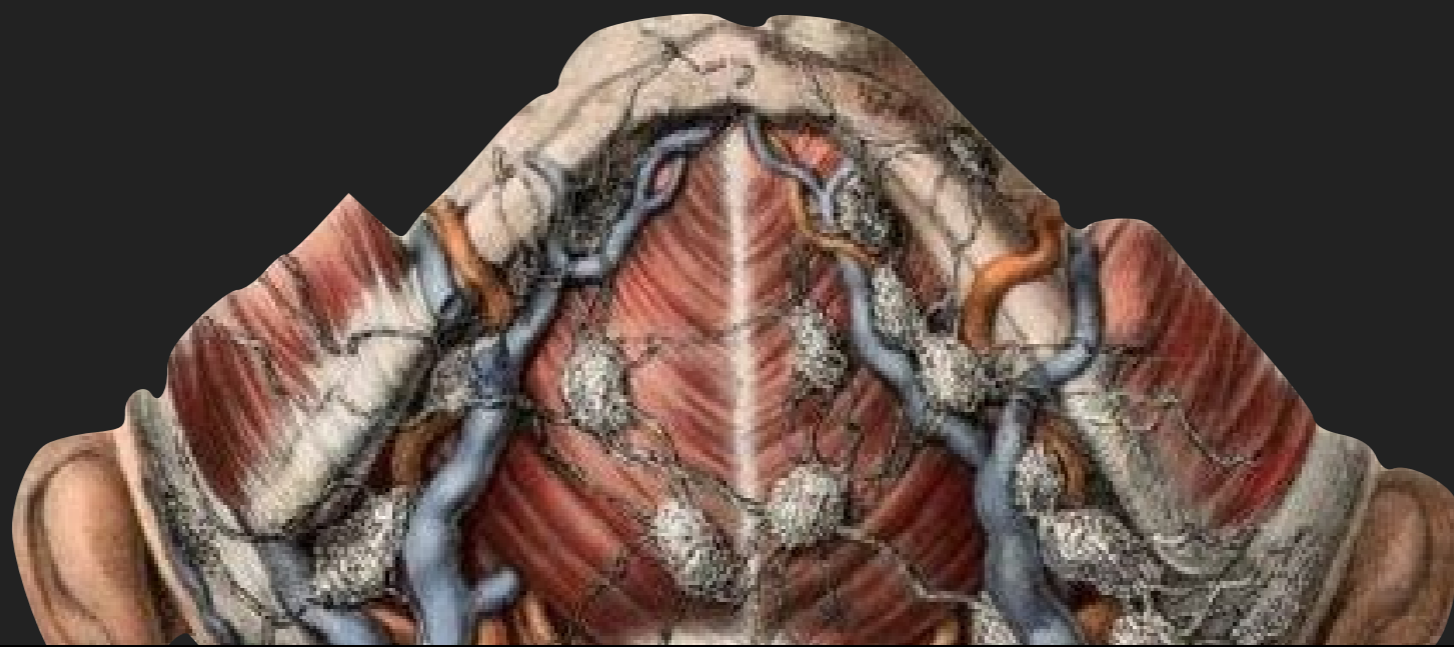
N category	N criteria
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	One or more ipsilateral lymph nodes, none larger than 6 cm
N2	Contralateral or bilateral lymph nodes, none larger than 6 cm
N3	Lymph node(s) larger than 6 cm

Distant metastasis (M)

M category	M criteria
M0	No distant metastasis
M1	Distant metastasis

HPV related oropharyngeal carcinoma TNM pathologic staging AJCC UICC 8th edition

Primary tumor (T)	
T category	T criteria
T0	No primary identified
T1	Tumor 2 cm or smaller in greatest dimension
T2	Tumor larger than 2 cm but not larger than 4 cm in greatest dimension
T3	Tumor larger than 4 cm in greatest dimension or extension to lingual surface of epiglottis
T4	Moderately advanced local disease. Tumor invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible or beyond.*
* Mucosal extension to lingual surface of epiglottis from primary tumors of the base of the tongue and vallecula does not constitute invasion of the larynx.	
Regional lymph nodes (N) - Pathological N (pN)	
N category	N criteria
NX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in four or fewer lymph nodes
pN2	Metastasis in more than four lymph nodes
Distant metastasis (M)	
M category	M criteria
M0	No distant metastasis
M1	Distant metastasis



Prognostic stage groups - Pathological

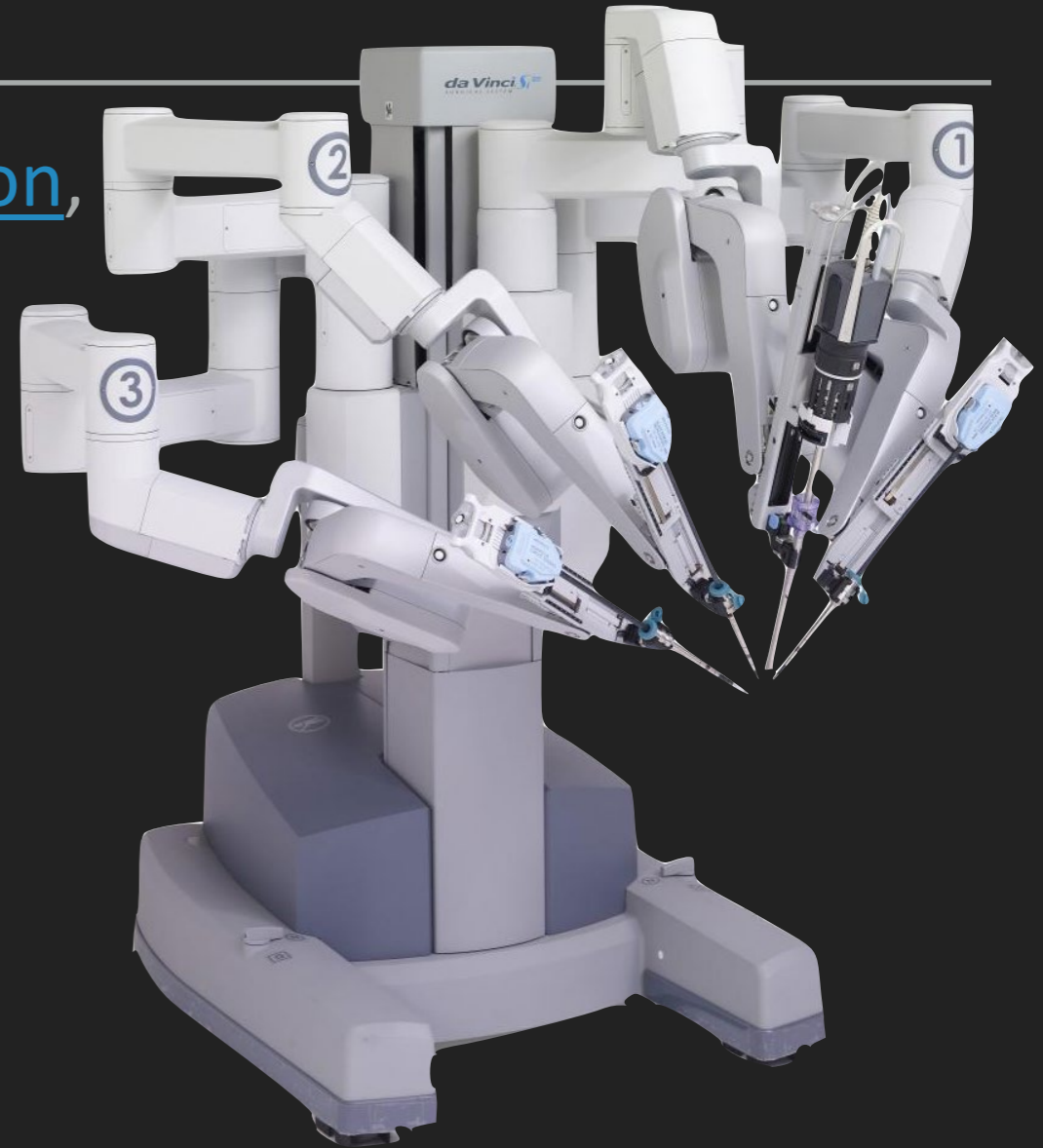
When T is...	And N is...	And M is...	Then the stage group is...
T0, T1, or T2	N0, N1	M0	I
T0, T1, or T2	N2	M0	II
T3 or T4	N0, N1	M0	II
T3 or T4	N2	M0	III
Any T	Any N	M1	IV



TREATMENT

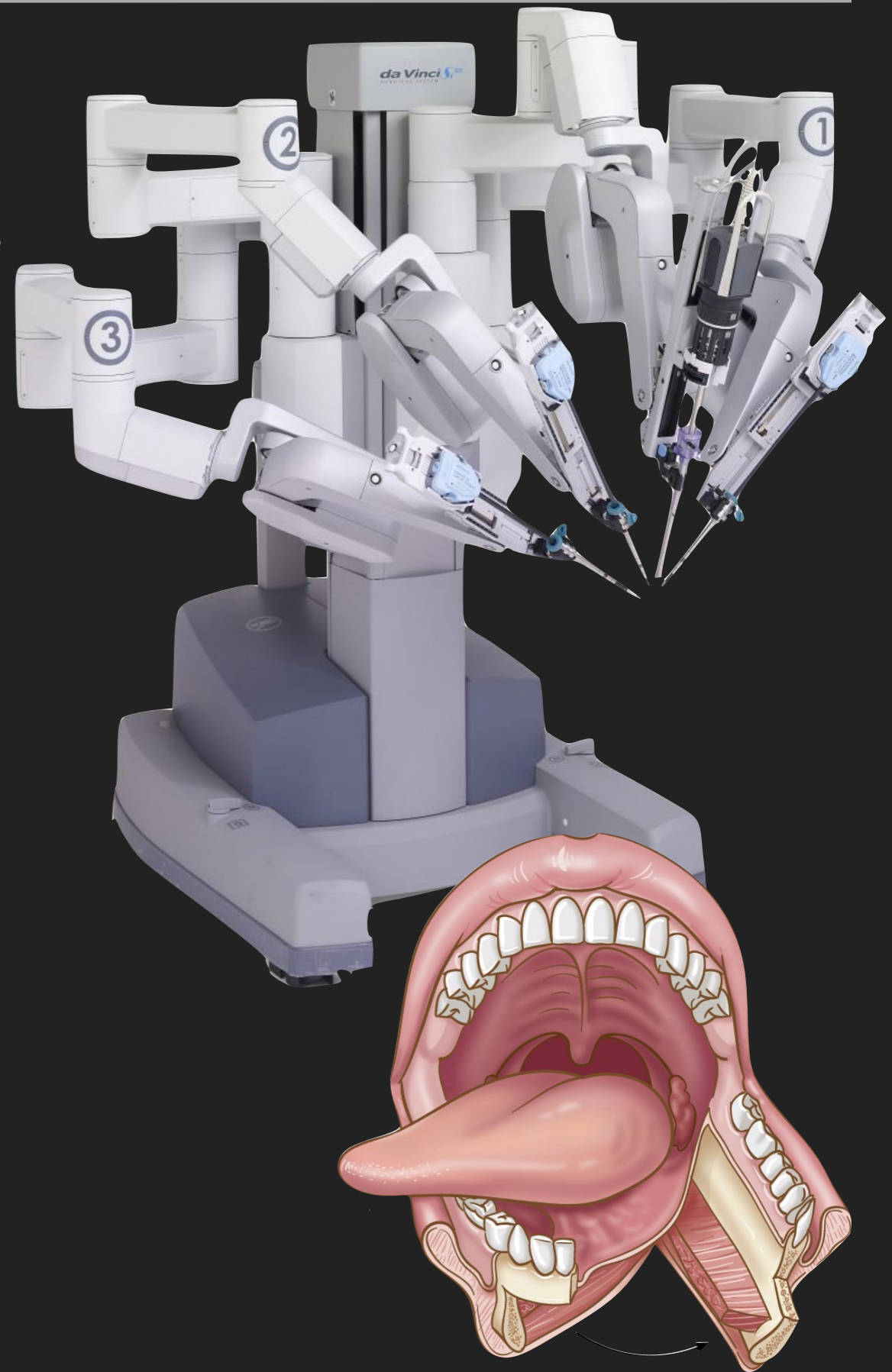
TREATMENT

- ▶ Treatment involves either Surgery, Radiation, Chemotherapy, or a combination of these three



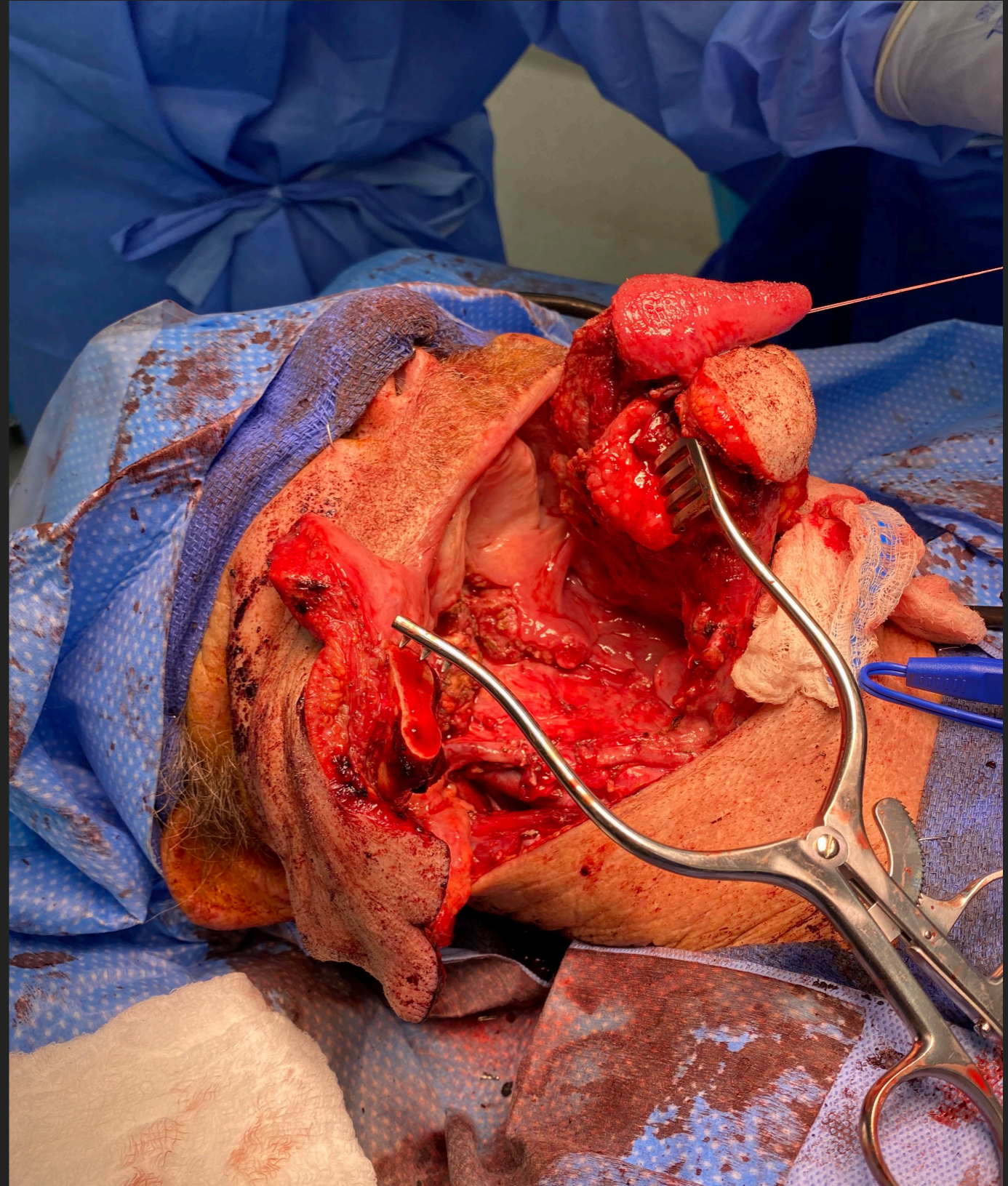
TRANSORAL ROBOTIC SURGERY (TORS)

- ▶ *A combination of a change in the type of tumor and its growth pattern with advances in technology has made TORS possible*
- ▶ *What previously required splitting the jaw can now be done in a minimally invasive fashion through the mouth.*
- ▶ *Lower doses of radiation = fewer side effects and fewer long-term complications*



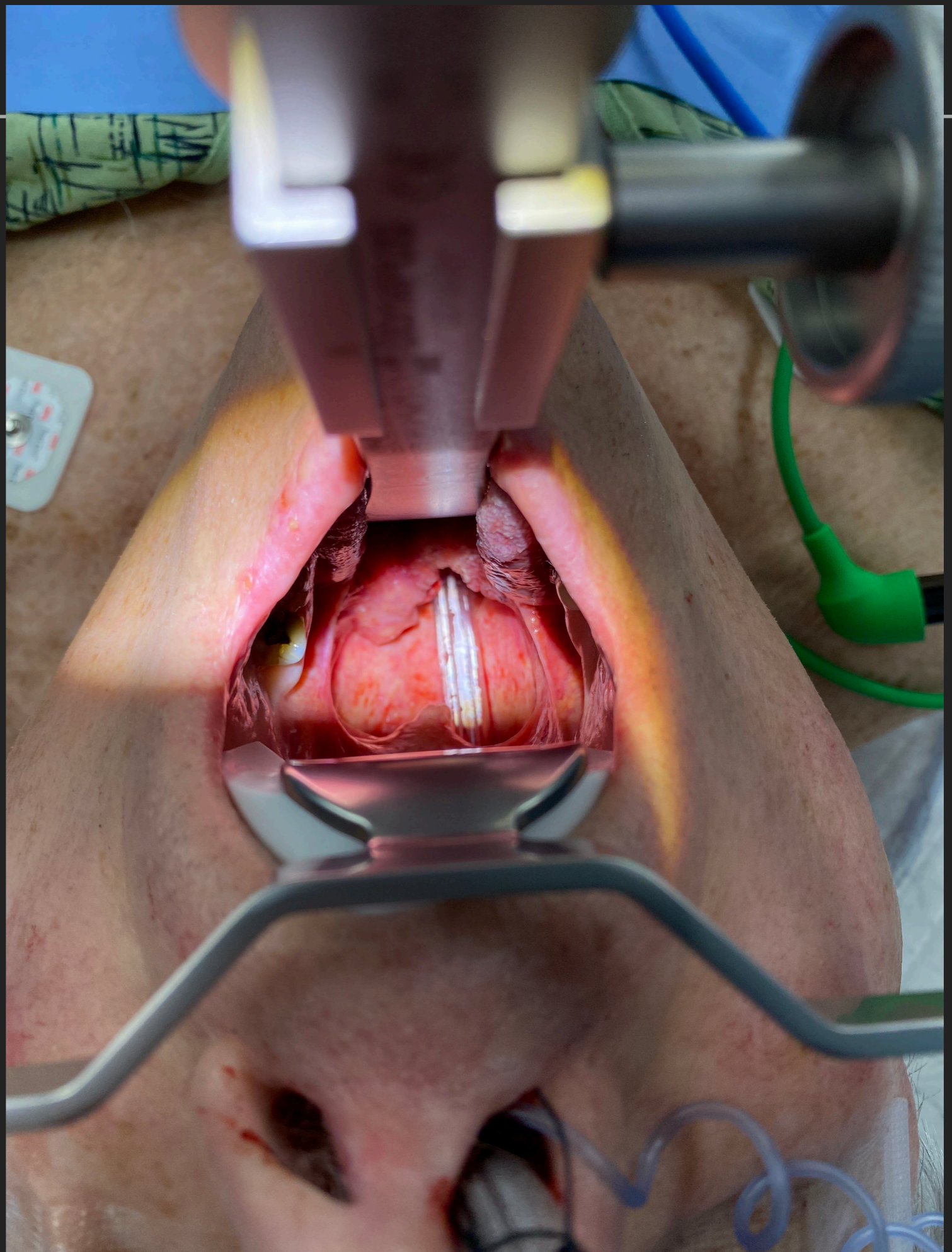
SURGERY

- ▶ Previous significantly more invasive approach

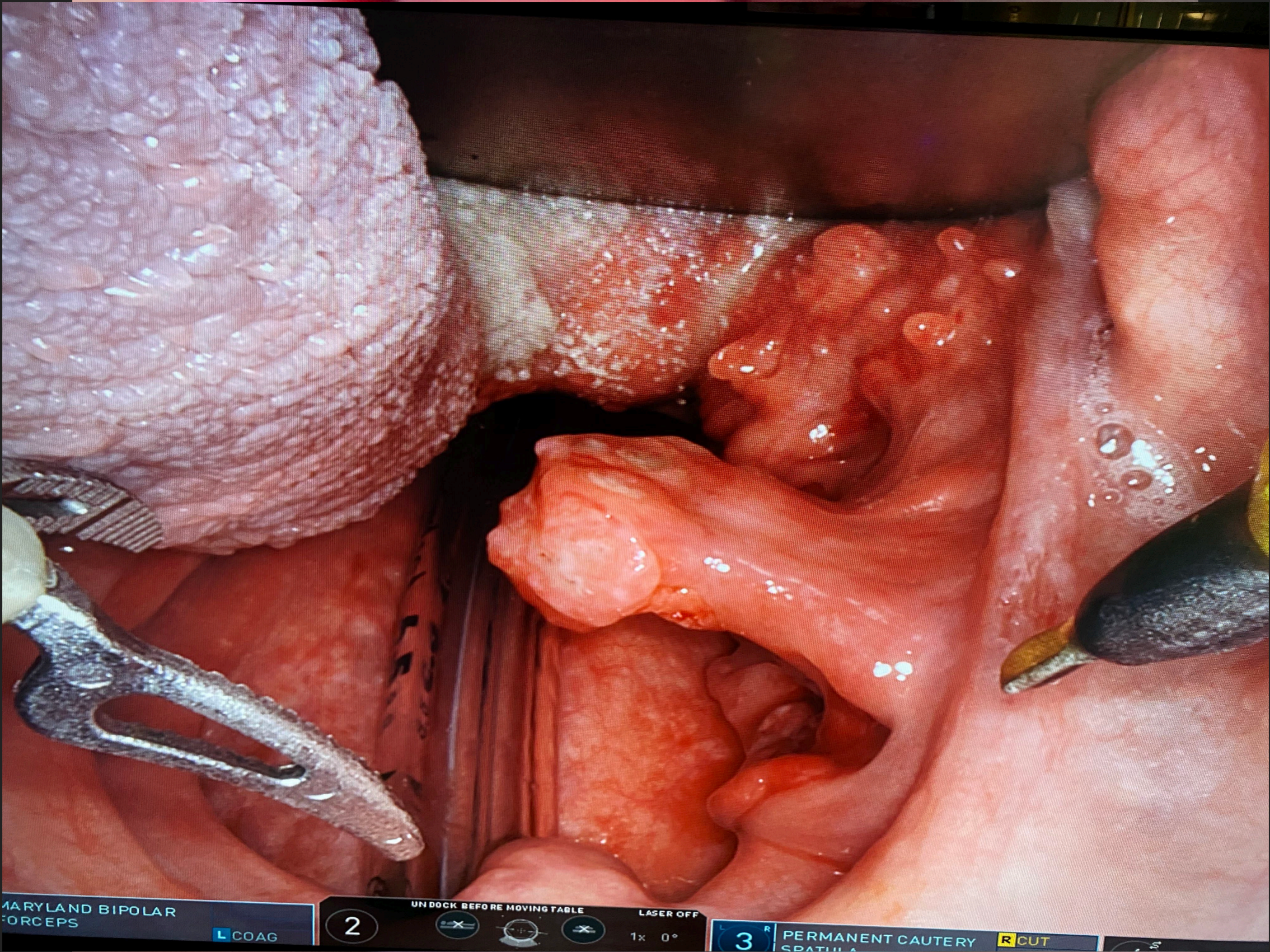


SURGERY

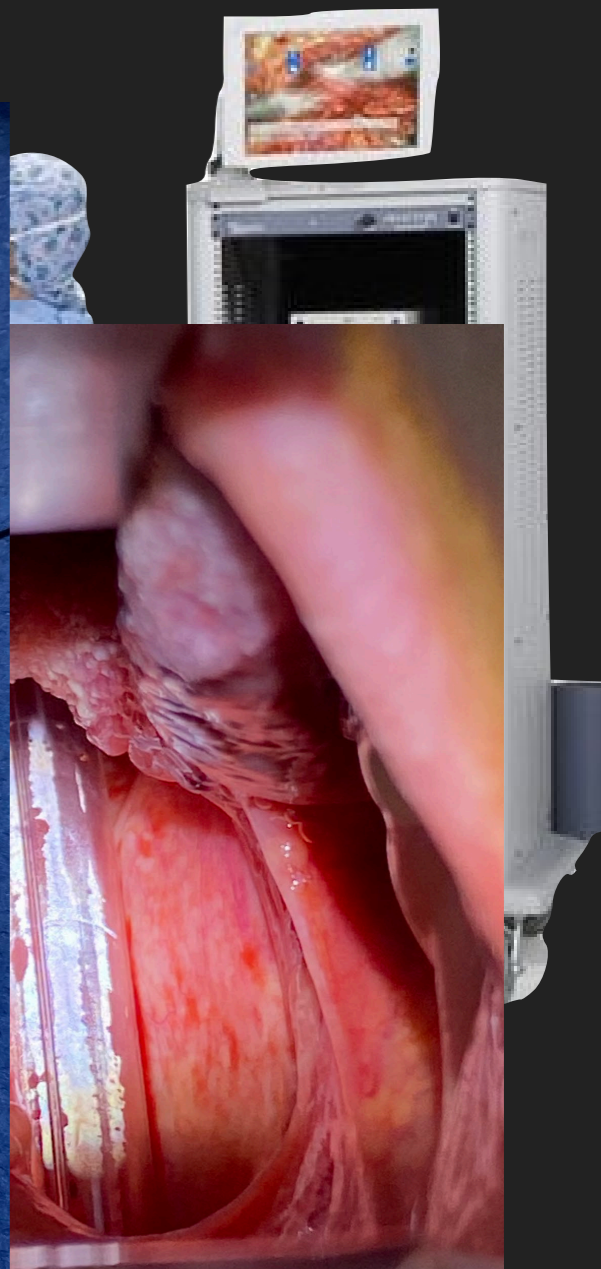
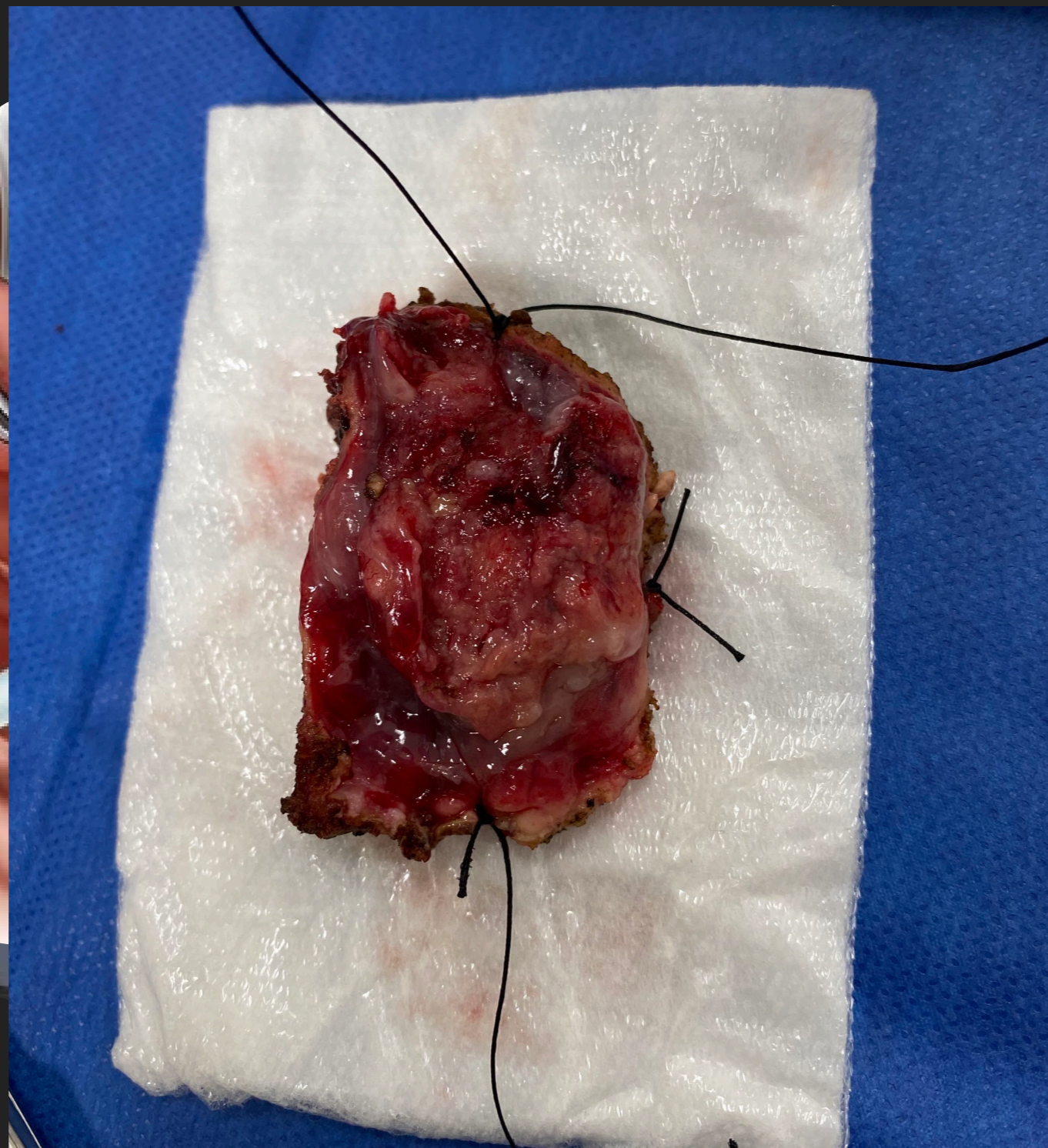
- ▶ Now less invasive removal through the mouth with a surgical robot



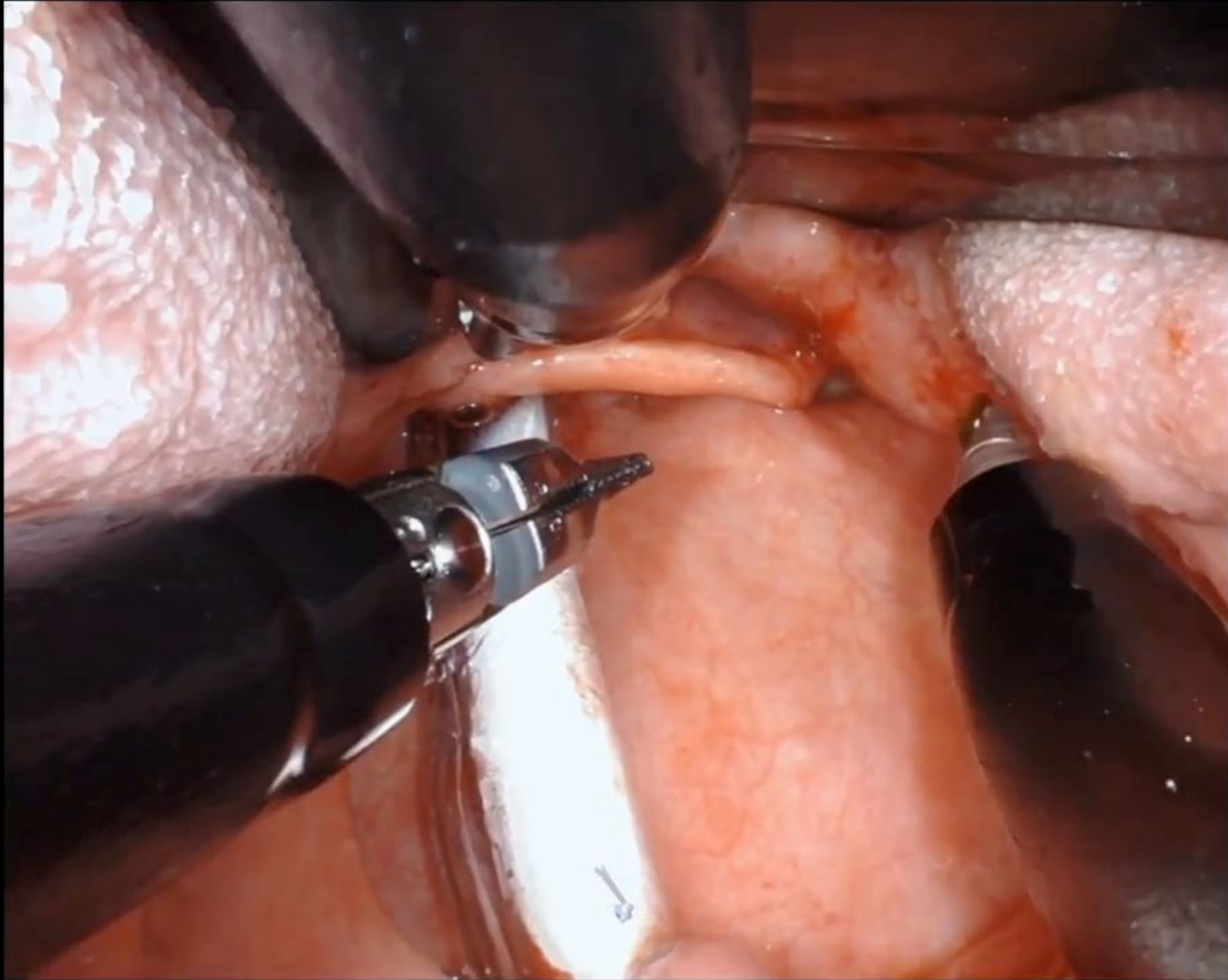
SURGERY



HOW DOES TORS WORK?

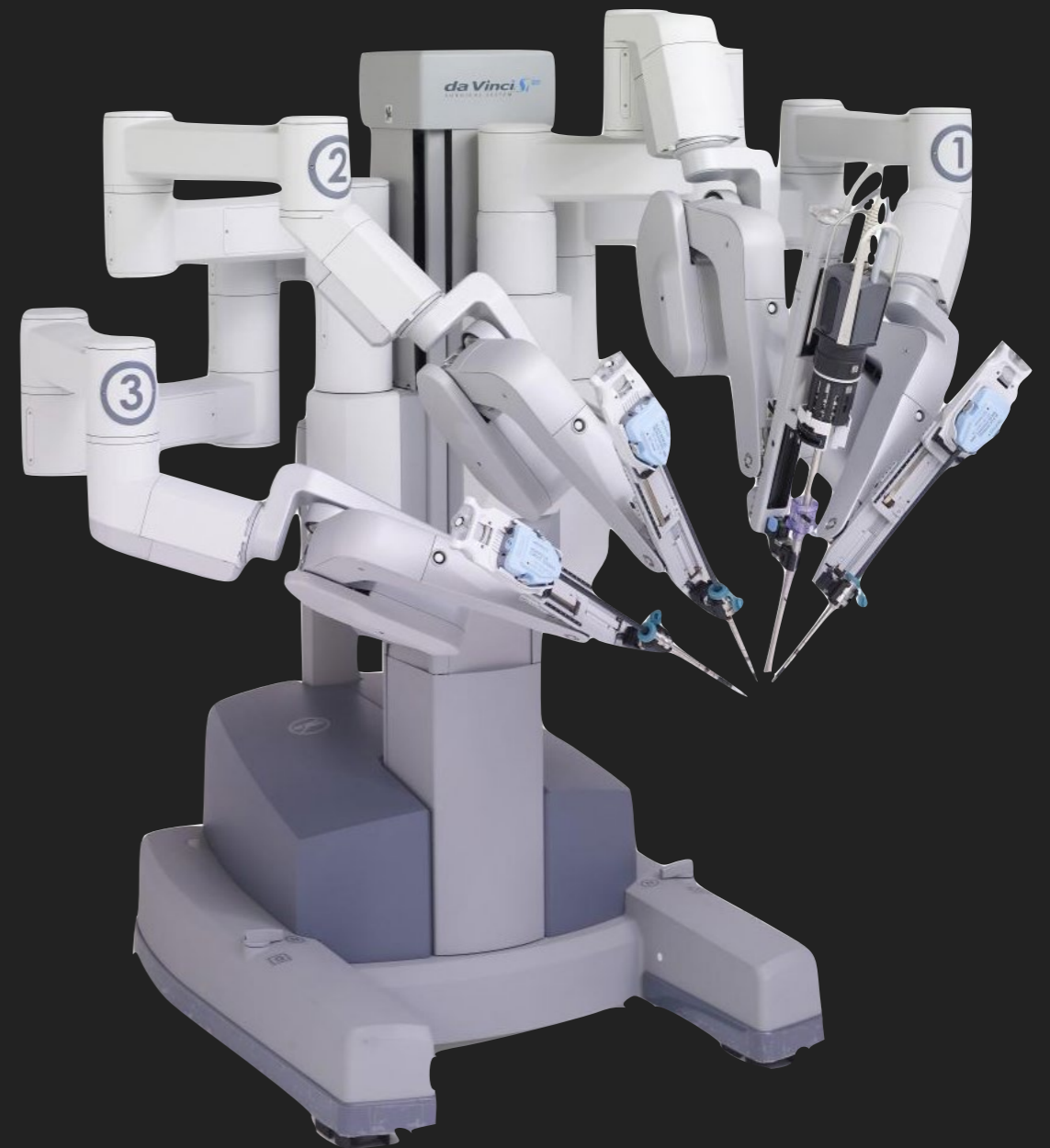


SURGICAL VIDEO



SURGERY

- ▶ Advantages of TORS over previous open approaches:
 - ▶ Shorter hospital stays (1-2 days vs. 1-2 weeks)
 - ▶ Fewer complications
 - ▶ Quicker recovery
 - ▶ Equally as effective



RADIATION/CHEMOTHERAPY

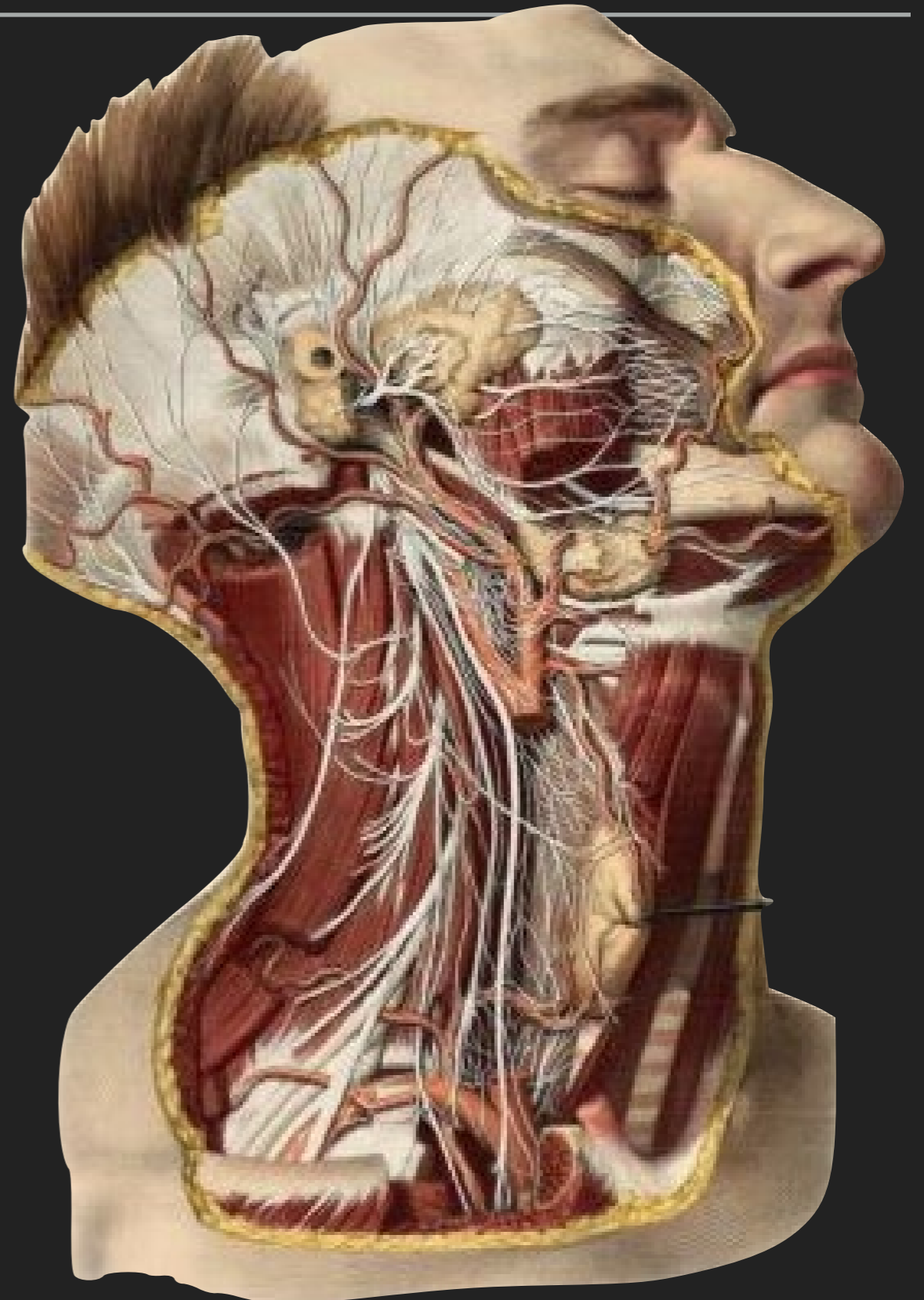
- ▶ Primary chemotherapy and radiation is an acceptable alternative to surgery
- ▶ Advances in radiation therapy with more targeted treatments (IMRT/Proton-beam) have decreased side effects
- ▶ Indications:
 - ▶ Large tumors unresectable with TORS
 - ▶ Patients unable to come off anticoagulation medications
 - ▶ Significant palatal involvement
 - ▶ Etc.



OUTCOMES

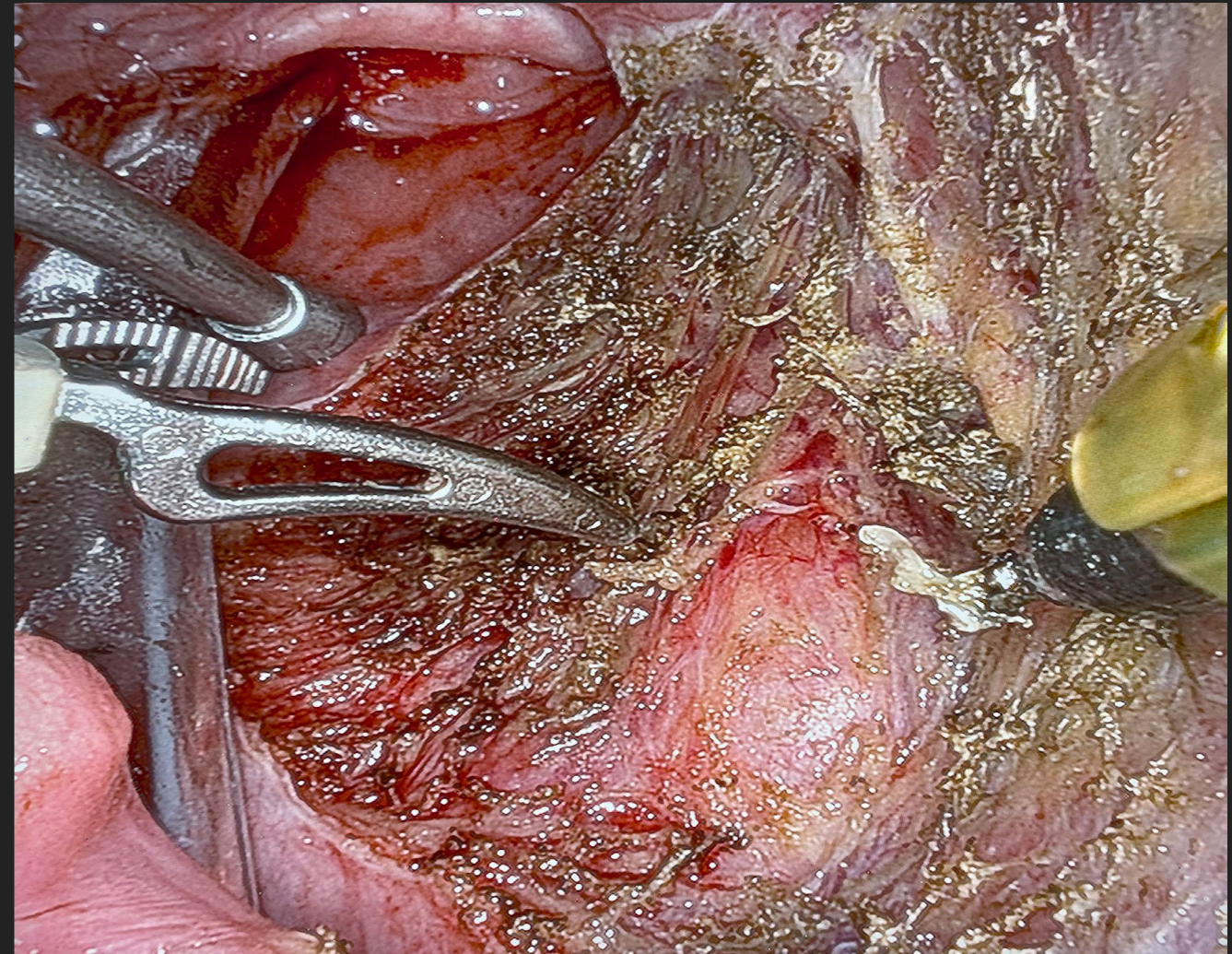
ONCOLOGIC OUTCOMES

- ▶ *Survival:*
 - ▶ **TORS: 81-100% Overall Survival and 90%-95% Cancer Specific Survival 2-3 years**
 - ▶ **Chemoradiation: 69-100% Overall Survival and 77%-96% Cancer Specific Survival 2-3 years**
- ▶ *Recurrence Rates:*
 - ▶ **TORS = 91-96% 3 year RFS**
 - ▶ **Chemoradiation = 77-87% 3 year RFS**



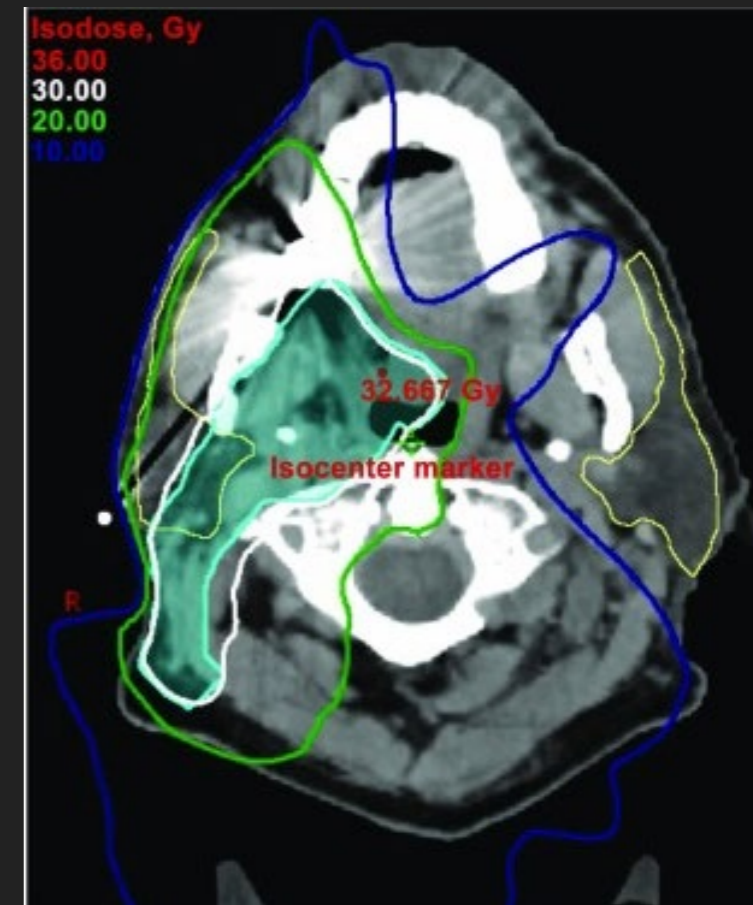
FUNCTIONAL OUTCOMES & TREATMENT SIDE EFFECTS

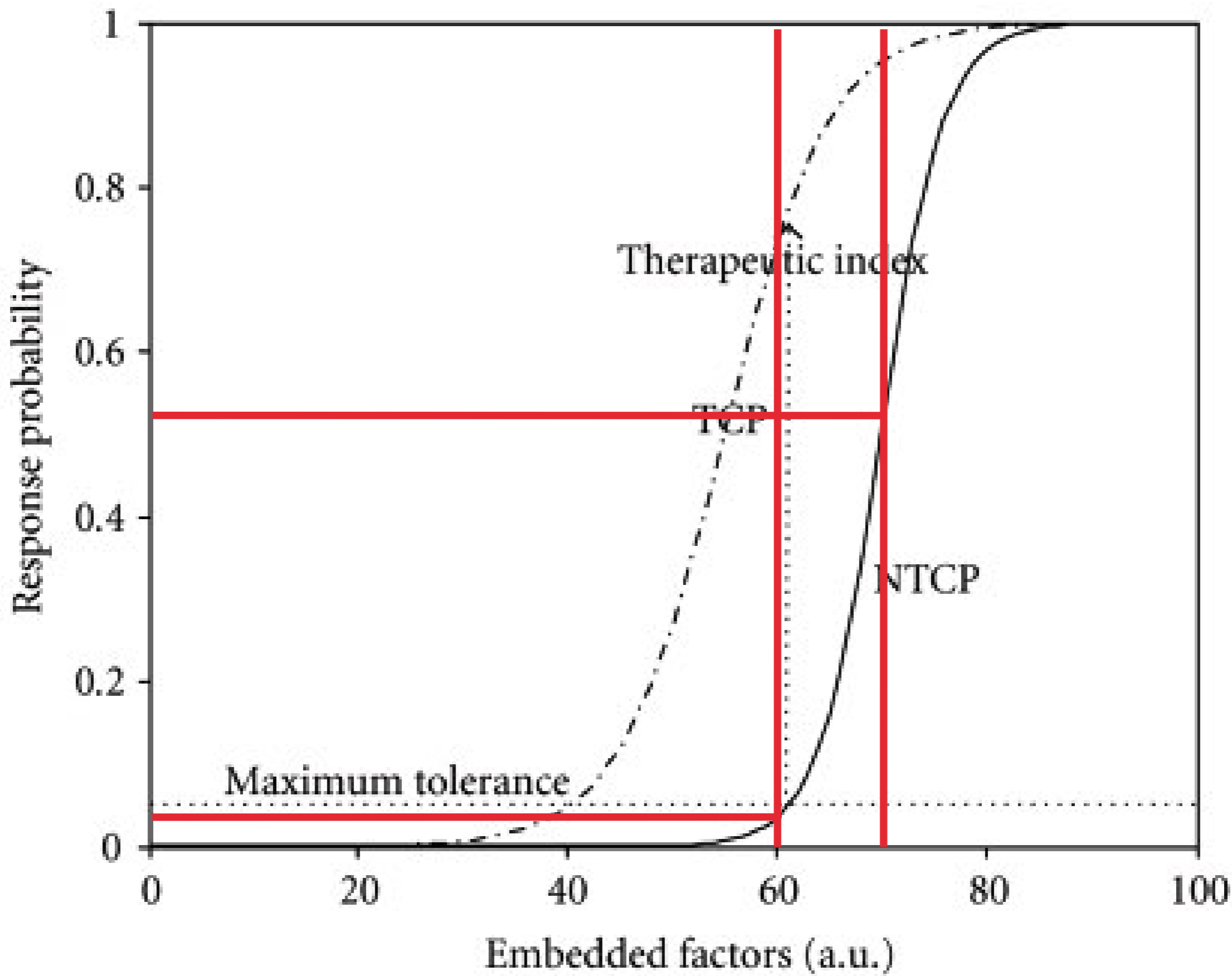
- ▶ *Short-term side effects*
 - ▶ **TORS:** *throat pain, dysphagia, VPI, aspiration (rare), risk of bleeding*
 - ▶ **Chemoradiation:** *throat pain, dysphagia, loss of taste, dry mouth, mucositis*
- ▶ *Long-term side effects:*
 - ▶ **TORS:** *VPI, trismus*
 - ▶ **Chemoradiation:** *dry mouth, dysphagia, muscle spasm, osteoradionecrosis*



LOWER RADIATION DOSES TO REDUCE SIDE EFFECTS

- ▶ Primary chemoradiation dose: **70 Gy**
- ▶ Post robotic surgery radiation dose: **60 Gy**
- ▶ *Advantages of up-front robotic surgery:*
 - ▶ *lower doses of radiation*
 - ▶ *avoiding chemotherapy*
 - ▶ *potentially avoiding radiation all together*
 - ▶ *saves radiation for potential recurrence*





THE FUTURE - TREATMENT DEESCALATION

Table 5 | Trials investigating de-escalation or replacement of chemotherapy and/or radiotherapy in HPV+ OPSCC

Study	Study cohort	Treatment	Outcomes	Toxicity profile	Ref.
MC1273 (2019)	80 patients with ≤10 pack-year smoking history, negative margins; cohort B included patients with extranodal extension	Cohort A: 30 Gy RT plus docetaxel (15 mg/m ²) Cohort B: extranodal extension to 36 Gy	2-year locoregional tumour control 96.2%, PFS 91.1%, OS 98.7%	Grade ≥3 toxicities before RT in 2.5% of patients, no grade ≥3 toxicities at 1 or 2 years after RT	196
NCT01530997 (2015)	43 patients with T0–3 N0–2c M0 disease and a minimal smoking history	60 Gy IMRT with concurrent cisplatin (30 mg/m ²)	3-year locoregional control 100%, distant MFS 100%, DSS 100%	Grade ≥3 dysphagia in 39%, grade ≥3 mucositis in 35%; chemotherapy-related grade ≥3 toxicities included haematological events (11%), nausea (18%) and vomiting (5%)	201
Quarterback and Quarterback 2b (2021)	24 and 65 patients; stage III/IV disease without distant metastases (per AJCC 7th edn staging)	Quarterback: three cycles of induction chemotherapy; responders randomized 2:1 to receive 56 Gy (rdCRT) or 70 Gy (sdCRT) RT with concurrent carboplatin (AUC 1.5) Quarterback 2b: 56/50.4 Gy IMRT	Combined rdCRT arms: 2-year LRC, PFS and OS 87.4%, 84.4% and 90.6%	No therapy-related mortality, minimal long-term consequences (to be reported)	246
ORATOR (2019)	68 patients, ≥18 years of age with ECOG PS 0–2, stage T1–2 N0–2 tumours; stratification by p16 status	70 Gy IMRT with high-dose cisplatin (100 mg/m ²) or modified cisplatin, cetuximab or carboplatin, for patients with N1–2 tumours or TORS plus ND with 1 cm margins (± adjuvant CRT)	MDADI score (swallowing-related QOL at 1 year): 86.9 vs 80.1 in the RT vs TORS plus ND groups, respectively.	Grade ≥3 dysphagia in 18% vs 26, grade ≥3 hearing loss in 18% vs 0%, grade ≥3 post-operative haemorrhage and bleeding (oral cavity) each in two patients in the TORS plus ND group	213
ORATOR2 (2021)	61 patients with stage T1–2 N0–2 (AJCC 8th edn) tumours	De-intensified IMRT (60 Gy ± chemotherapy) vs TORS plus ND (± adjuvant 50 Gy IMRT)	Estimated 2-year OS 100% vs 89.2% in the IMRT vs TORS plus ND arms, respectively	Grade 2–5 toxicities in 67% of patients in the RT arm and 71% in the TORS plus ND arm. Study terminated early owing to treatment-related mortality and unacceptable PFS in the TORS plus ND arm	247

An overview of ongoing trials is provided in Supplementary Information. AUC, area under the curve; AJCC, American Joint Committee on Cancer; CRT, chemoradiotherapy; DSS, disease-specific survival; ECOG, Eastern Co-operative Oncology Group; HPV, human papillomavirus; IMRT, intensity-modulated radiotherapy; LRC, locoregional control; MDADI, MD Anderson Dysphagia Inventory; MFS, metastasis-free survival; ND, neck dissection; OPSCC, oropharyngeal squamous cell carcinoma; QOL, quality of life; PFS, progression-free survival; PS, performance status; rdCRT, reduced-dose chemoradiotherapy; RT, radiotherapy; sdCRT, standard-dose chemoradiotherapy; TORS, transoral robotic surgery.

THE FUTURE - TREATMENT DEESCALATION

Table 6 | Trials investigating de-escalation of adjuvant therapy in HPV⁺ OPSCC

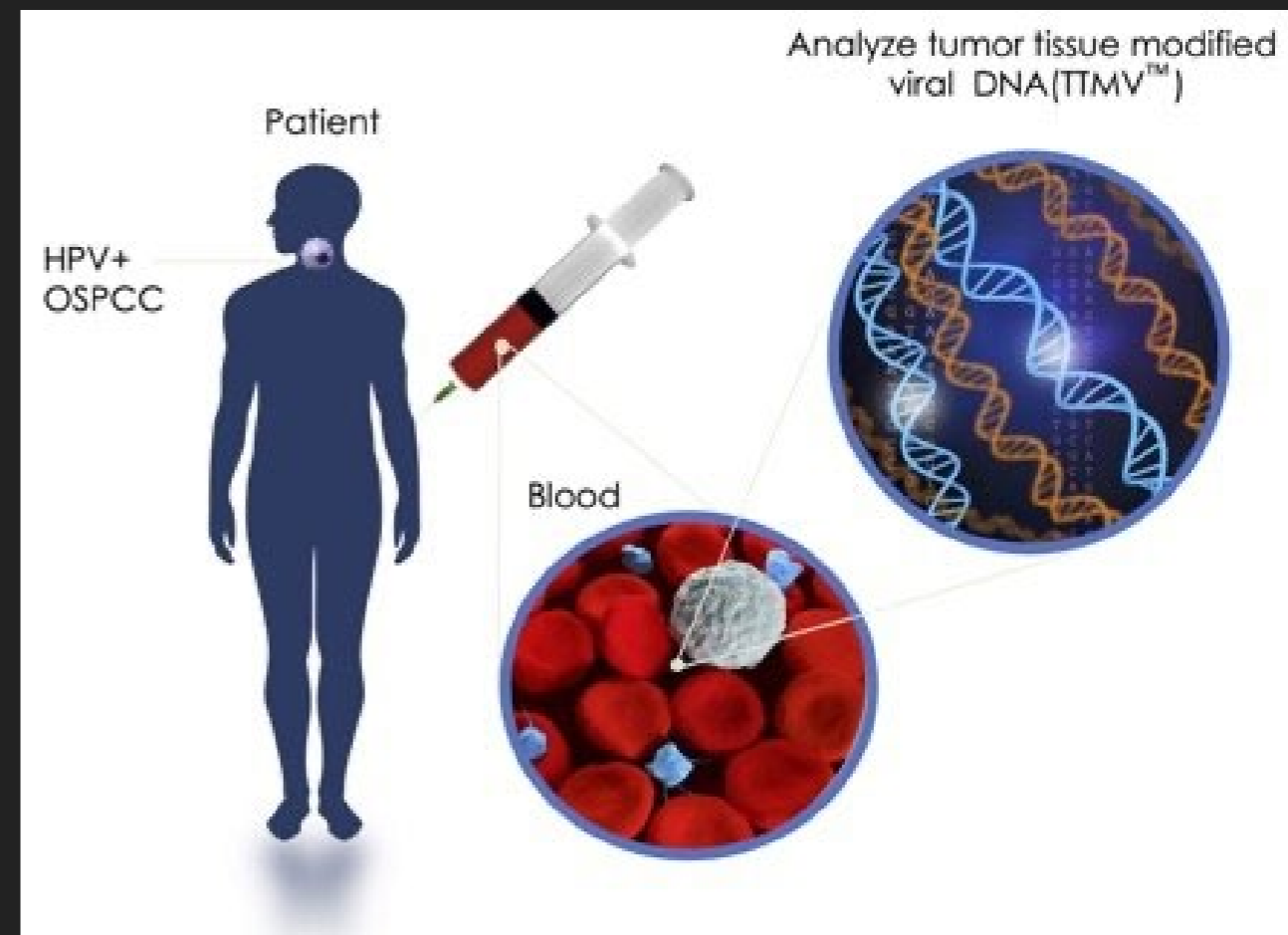
Study	Cohort	Treatment	Outcomes	Toxicity profile	Ref.
SIRS (2021)	54 patients with stage I, II, III and intermediate stage IVa (T1 N0–2b, T2 N0–2b, AJCC 8th edn) disease, with stratification based on pathological prognosis (based on ECS, LVI, PNI)	TORS with follow-up monitoring for patients with a good prognosis (group 1); reduced-dose adjuvant RT or CRT based on risk status for patients with a poor prognosis (group 2 or 3)	mPFS 91.3%, 86.7% and 93.3% for groups 1–3, respectively, at a median follow-up duration of 43.9 months	Group 1: dysphagia in 37%, severe pain in 29.6%, anxiety in 11.1%; group 2: altered taste/dysgeusia in 100%, xerostomia in 66.6% and severe pain in 66.6%; group 3: dysphagia in 100%; pain in 100%; dysarthria in 50.0%	248
E3311 (2021)	495 patients with cT1–2 stage III/IV disease (AJCC 7th edn)	TORS only (group A); TORS with low-dose IMRT (group B) or TORS with standard-dose IMRT (group C) or TORS with standard-dose IMRT with concurrent cisplatin or carboplatin (group D)	2-year PFS 96.6%, 94.9%, 96.0% and 90.7% in arms A–D, respectively	17% of patients had grade 3–4 AEs following TORS; grade 3–4 AEs observed in 0%, 15%, 24% and 60% in groups A–D, respectively, common AEs included oral mucositis and dysphagia	200
AVOID (2020)	60 patients with pT1–pT2 N1–3 disease with favourable prognostic features underwent TORS at the primary site	Adjuvant RT omitting the tumour bed	2-year local control 98.3%; 2-year OS 100%	AEs in 30%: including radiation dermatitis (13.33%), oral mucositis (5.00%) and dysphagia (3.33%)	249

An overview of ongoing trials is provided in Supplementary Information. AEs, adverse events; AJCC, American Joint Committee on Cancer; CRT, chemoradiotherapy; ECS, extracapsular spread; HPV, human papillomavirus; IMRT, intensity-modulated radiotherapy; LVI, lymphovascular invasion; mPFS, median progression-free survival; OPSCC, oropharyngeal squamous cell carcinoma; OS, overall survival; PNI, perineural invasion; PFS, progression-free survival; RT, radiotherapy; TORS, transoral robotic surgery.

SURVEILLANCE AND PREVENTION

ADVANCED TUMOR MARKERS

- ▶ NavDx: new tumor marker that measures **circulating HPV tumor DNA (HPV ctDNA)**
- ▶ Can be measured and all post-treatment follow up visits
- ▶ Has been shown to catch recurrences months before imaging and conventional follow up
- ▶ **>95%** sensitive
- ▶ **>99%** chance of being recurrence free if undetectable during follow up



**Tumor Tissue-Modified
Virus (TTMV)[™]**

Not Detected

TTMV-HPV-16 fragments/
mL plasma

Report Details

Issued: 10 Nov 2021
Sample: Blood
Collection: 02 Nov 2021

Receipt: 03 Nov 2021

Contact Details

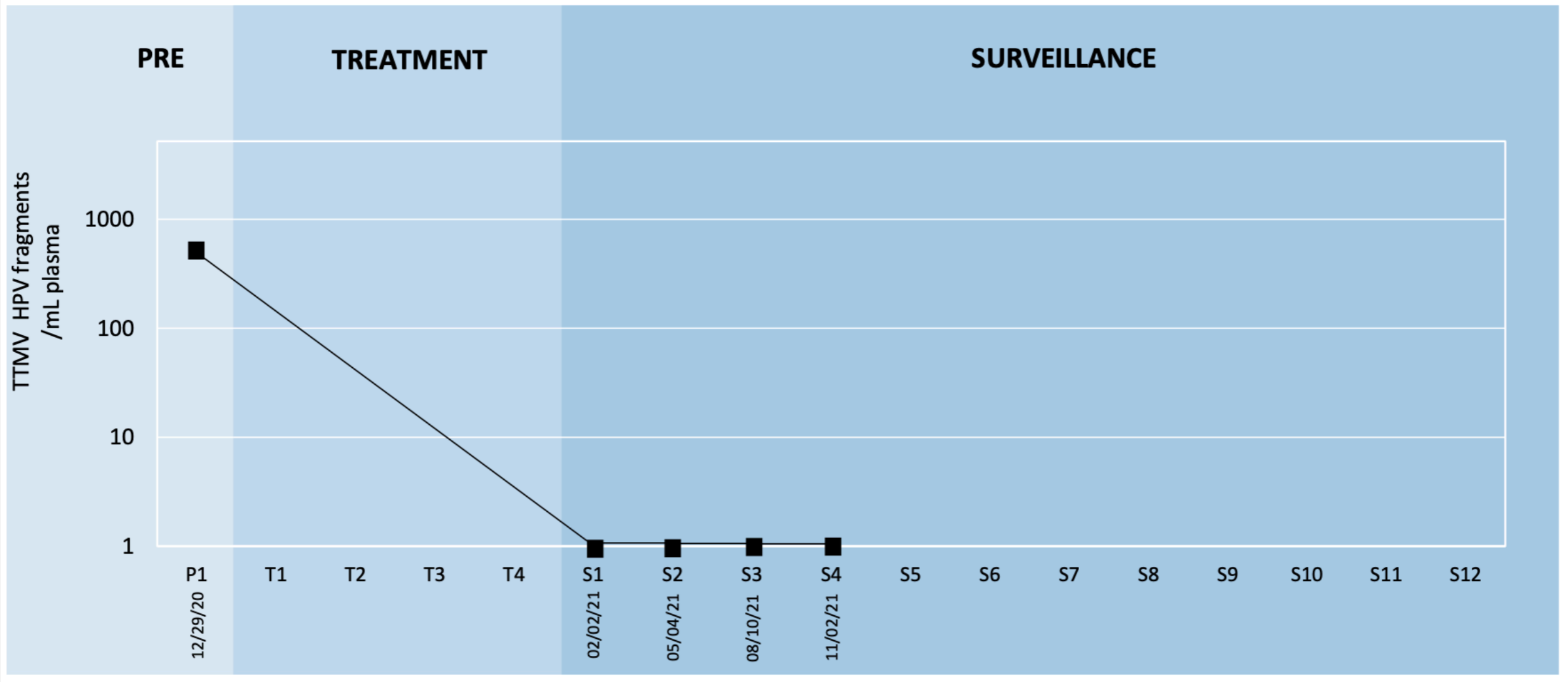
Physician: John Sims
Facility: CARTI
Address: 8901 CARTI Way
Little Rock, AR 72205, USA

Additional Recipients:

Clinical Details

ICD 10 Code: C10.9, Oropharynx cancer
Tumor p16 Status: Positive
Pre-Treatment TTMV-HPV Status: Positive, TTMV-HPV-16
FFPE NavDx Test Result: N/A

SURVEILLANCE



**Tumor Tissue-Modified
Virus (TTMV)[™]**

Not Detected

TTMV-HPV-16 fragments/
mL plasma

Report Details

Issued: 17 Sep 2021
Sample: Blood
Collection: 14 Sep 2021

Receipt: 15 Sep 2021

Contact Details

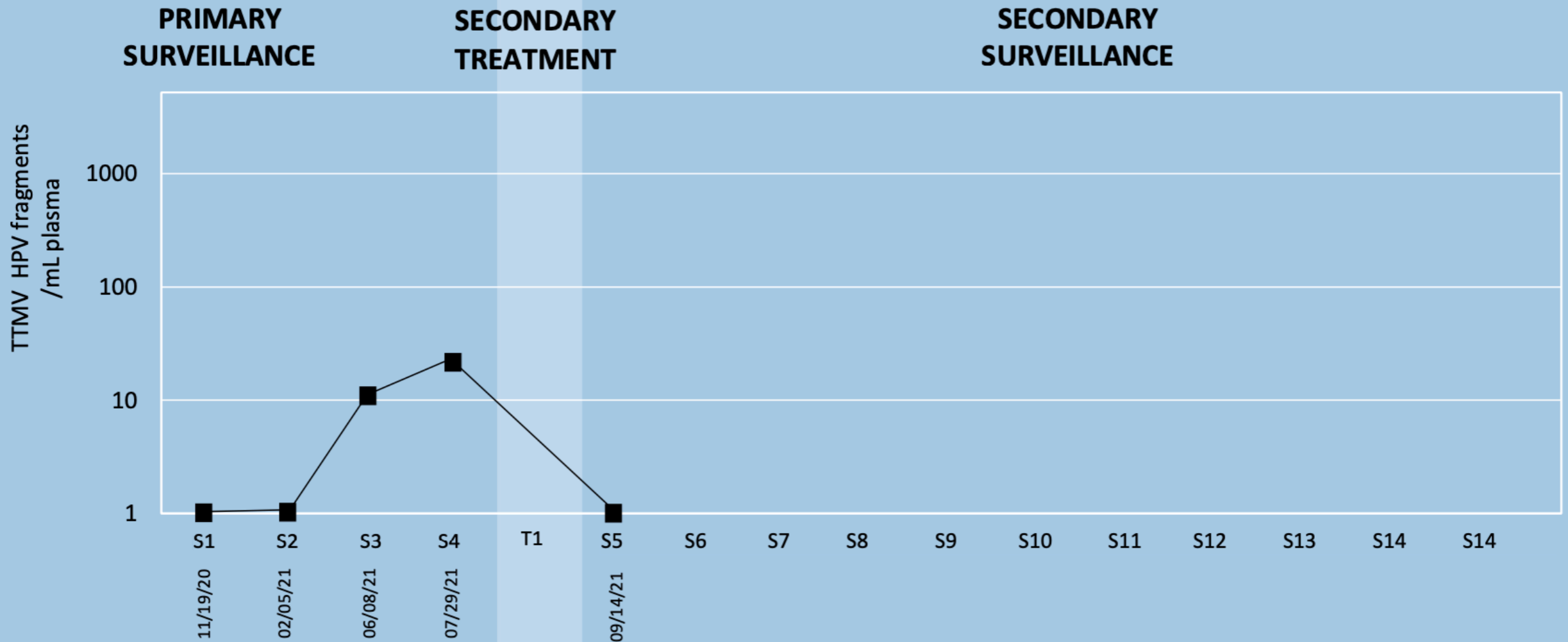
Physician: John Sims
Facility: CARTI
Address: 8901 CARTI Way
Little Rock, AR 72205, USA

Additional Recipients:

Clinical Details

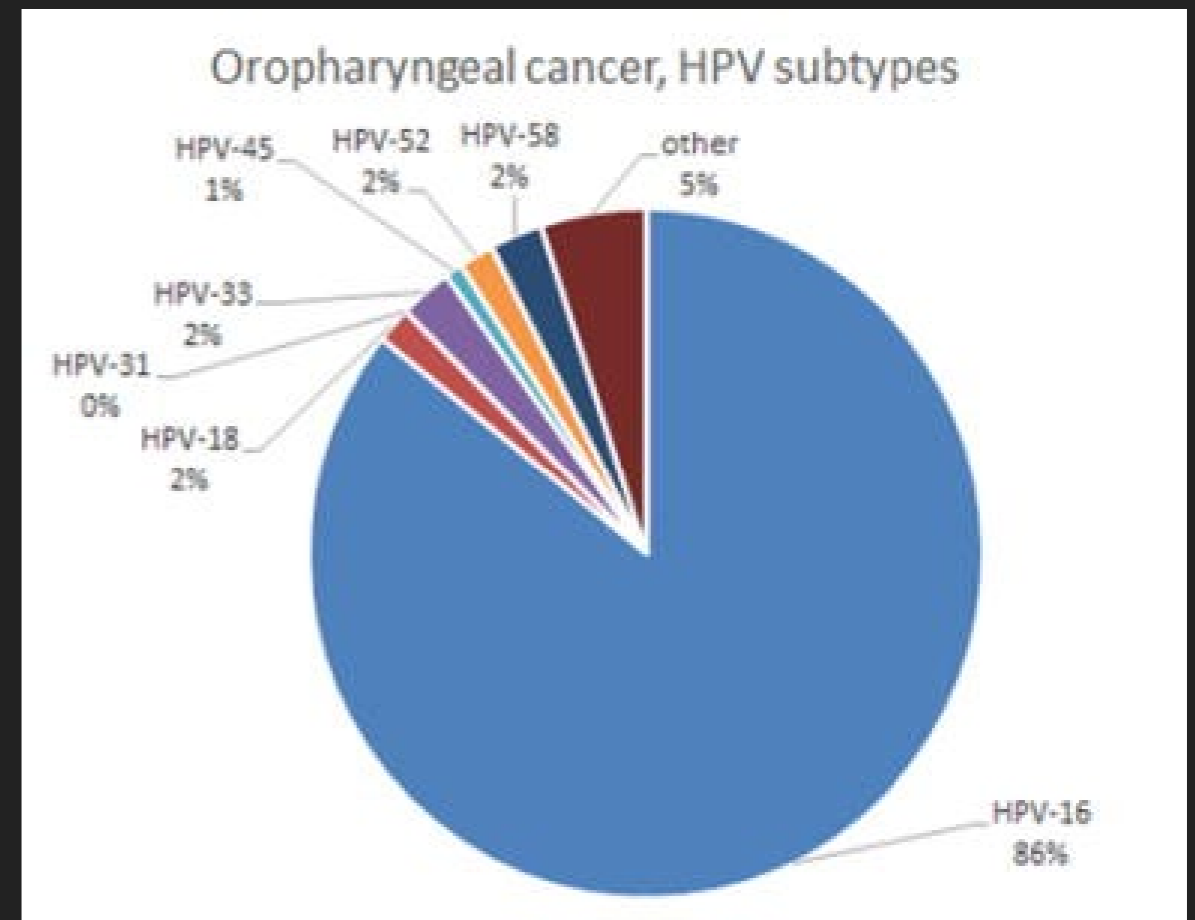
ICD 10 Code:	C10.9, Oropharynx cancer
Tumor p16 Status:	Positive
Surveillance TTMV-HPV Status:	Positive, TTMV-HPV-16
FFPE NavDx Test Result:	N/A

SURVEILLANCE



PREVENTION

- ▶ *Gardasil 9 is FDA approved for prevention of HPV-related head and neck cancers (oropharyngeal cancers)*
 - ▶ *Vaccinates against 6, 11, **16**, and 18 as well as types 31, 33, 45, 52, and 58*
- ▶ *Very safe with few if any side effects*
- ▶ *HPV vaccination has been associated with a decrease in the subsequent prevalence of oral HPV infection.*
- ▶ *One study of over 2000 patients showed that unvaccinated patients were 15x more likely to have HPV type 16, 18, 6, 11 in oral washes than vaccinated patients*



SUMMARY

- ▶ The typical presentation for an **oral cavity cancer** is a painful, non healing ulcer in an older adult with risk factors of tobacco and alcohol
- ▶ HPV-related head & neck cancer occurs in the **oropharynx** - most commonly the base of tongue and tonsils
- ▶ HPV-related oropharyngeal cancer is now the most common type of HPV-related cancer
- ▶ It most commonly presents as a **painless neck mass** in white males 55-79 years old
- ▶ Treatment options include minimally invasive **transoral robotic surgery (TORS)**, **radiation**, **chemotherapy**, or a combination of these 3
- ▶ Multiple deescalation trials are currently underway looking at reducing treatment without sacrificing oncologic outcomes
- ▶ Novel **HPV-targeted tumor markers** allow for improved post-treatment surveillance
- ▶ **Widespread vaccination has the potential to prevent and eventually eradicate HPV-related oropharyngeal cancer**

THANK YOU!



QUESTIONS?

