OROPHARYNGEAL CANCER PREVENTION AND TREATMENT

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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

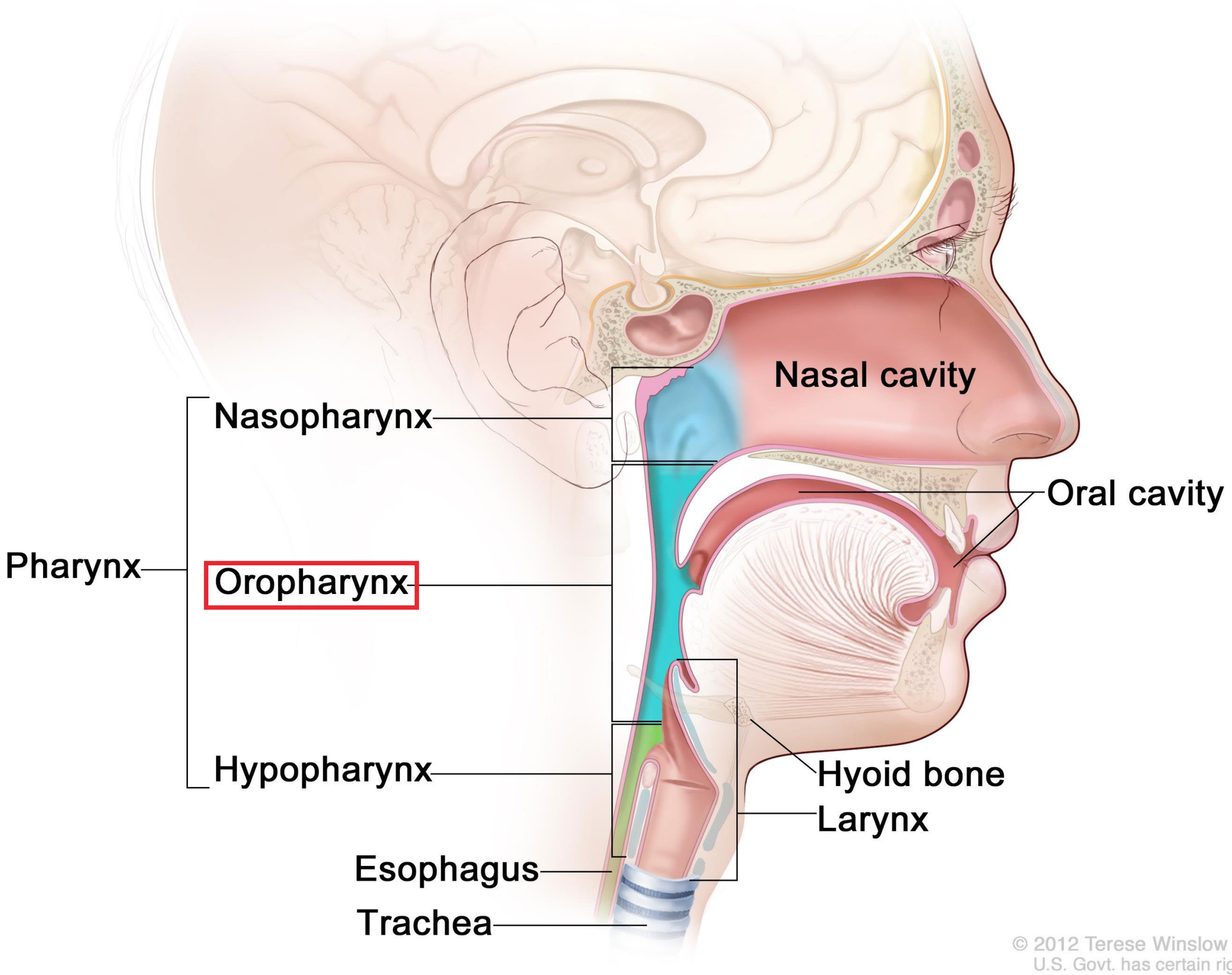
INTRODUCTION

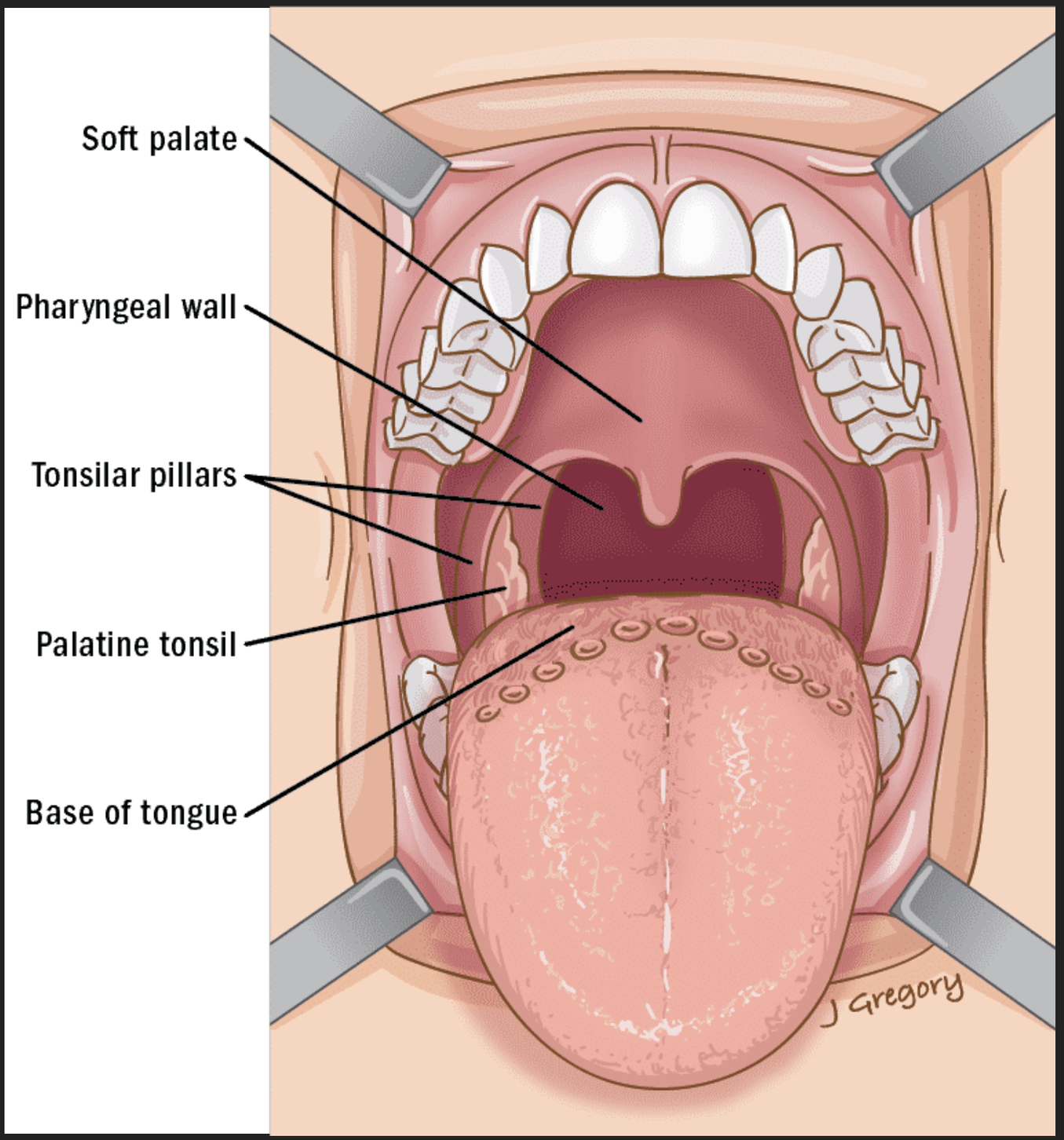
- Residency in Otolaryngology - Head & Neck Surgery at Mayo Clinic -2013-2018

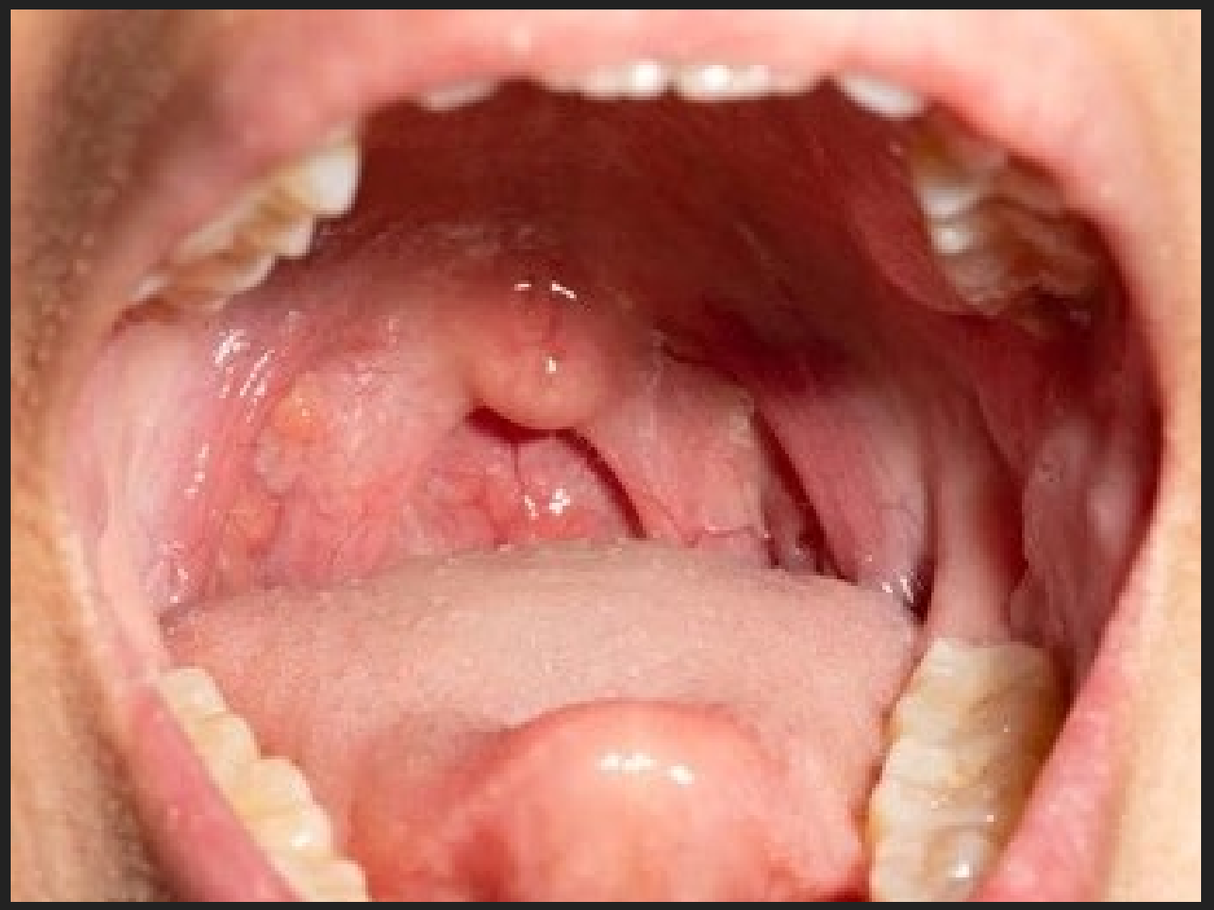
- Fellowship in Head & Neck Oncologic and Microvascular Reconstructive Surgery at Mount Sinai in New York City - 2018-2019

- CARTI Cancer Center 2019- present

Anatomy of the Pharynx




Soft palate
Pharyngeal wall
Tonsilar pillars
Palatine tonsil
Base of tongue
J Gregory



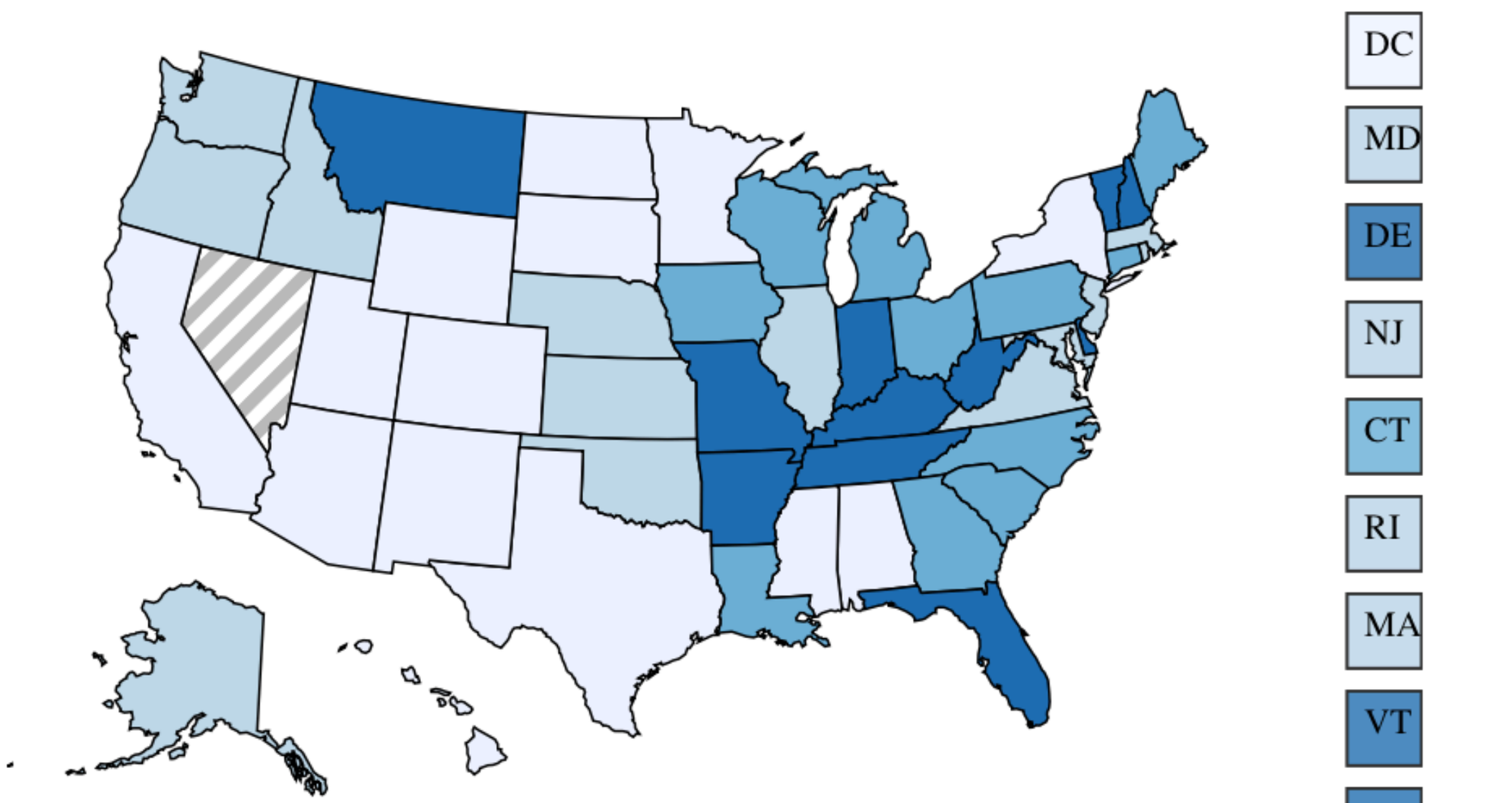
WHY OROPHARYNGEAL CANCER?

- Oropharyngeal squamous cell carcinoma is increasing in incidence
  - 2.7% per year in the United States (0.9% from 2017-2018)
  - 200% increase in prevalence from 1999-2015
- 70-80% of oropharyngeal cancers are HPV related
- Oropharyngeal cancer has now surpassed cervical cancer as the most common HPV-related cancer **(20,864 vs. 12,052)**

Oropharyngeal Squamous Cell Carcinoma, Male and Female, United States, 2018

Rate per 100,000 people

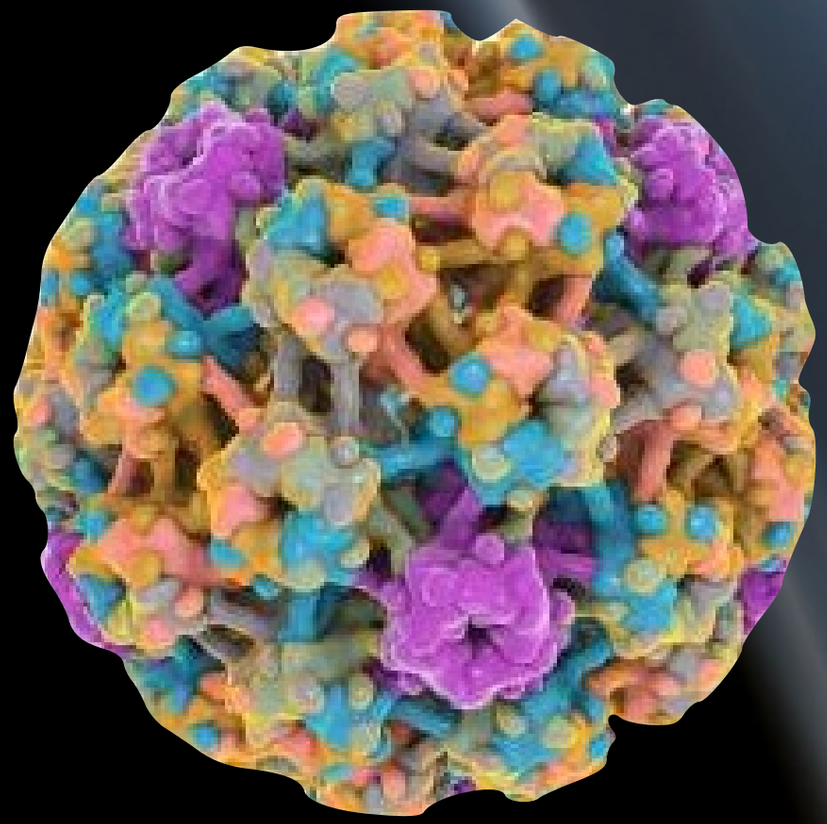
AR #3 in Nation



Rate per 100,000 people

No data | 3.0 - 4.7 | 4.8 - 5.3 | 5.4 - 5.7 | 5.8 - 7.0

CLINICAL PRESENTATION

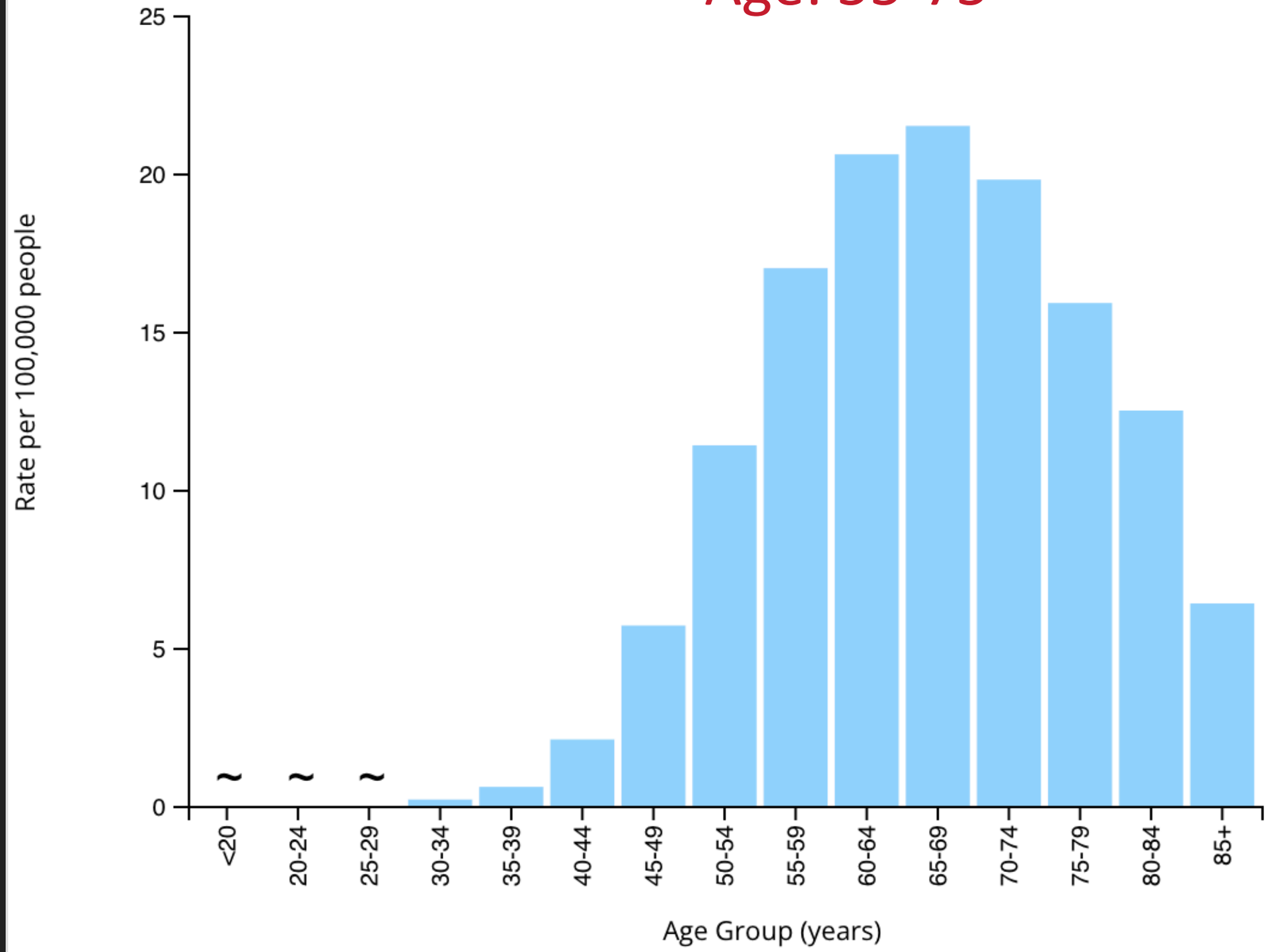


- HPV-related oropharyngeal cancers present in younger and healthier patients than previous tobacco and alcohol related cancers

Oropharyngeal Squamous Cell Carcinoma, Male and Female, United States, 2018

Rate per 100,000 people

Age: 55-75

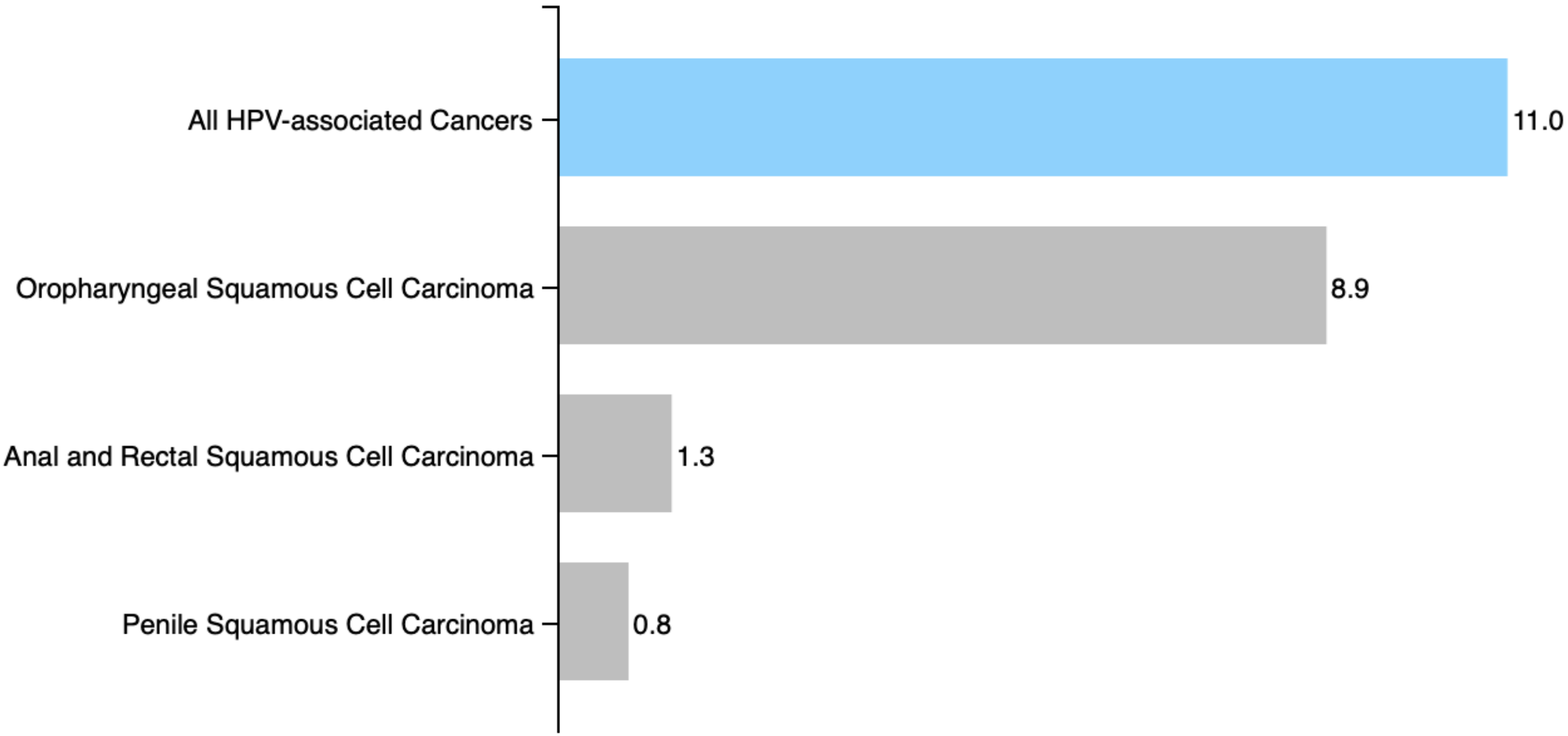


Rate of New HPV-associated Cancers by Cancer Type

HPV-associated Cancers, Male, United States, 2017
Rate per 100,000 men

Chart | Table | Export

Sex: M>>F

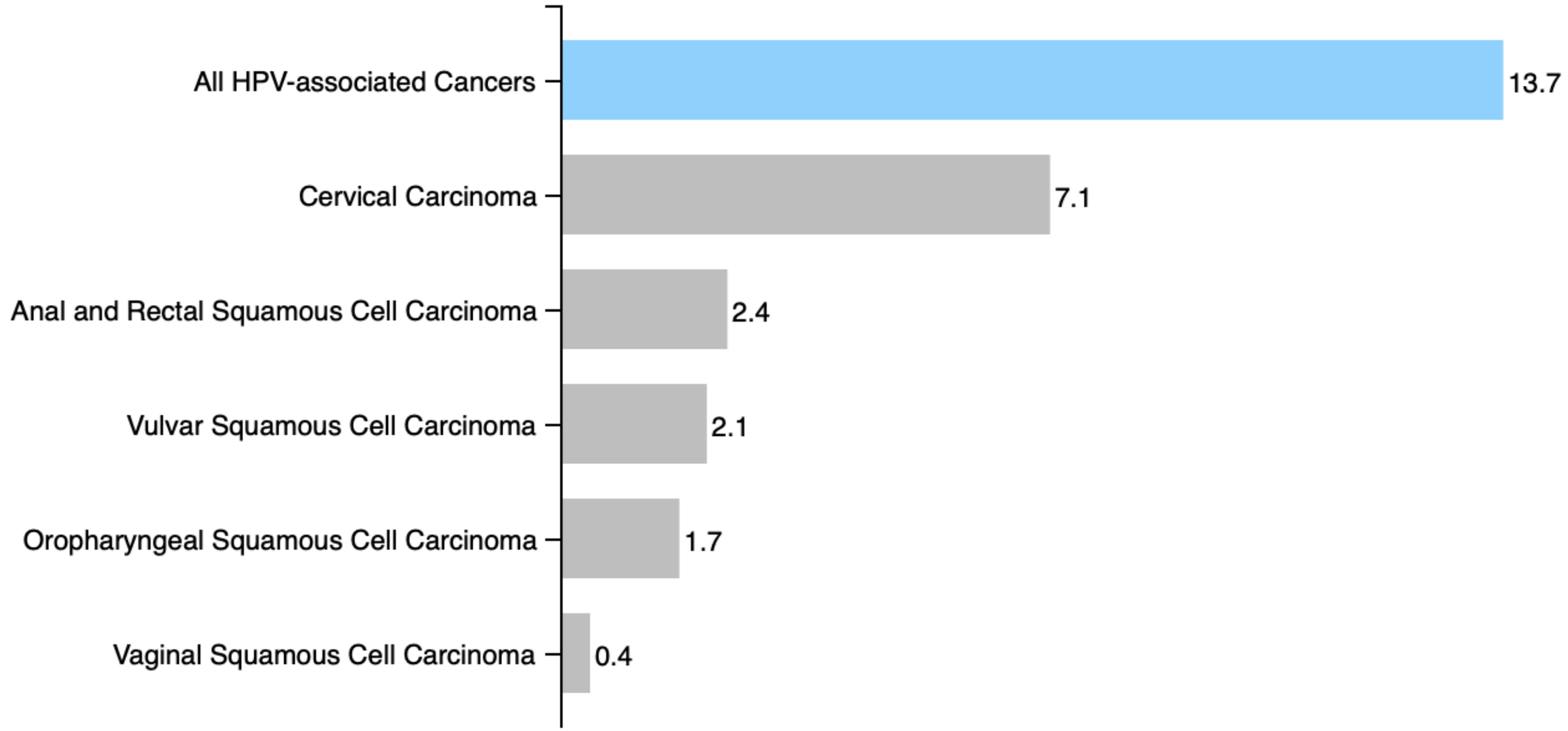


Rate of New HPV-associated Cancers by Cancer Type

HPV-associated Cancers, Female, United States, 2017
Rate per 100,000 women

Chart | Table | Export

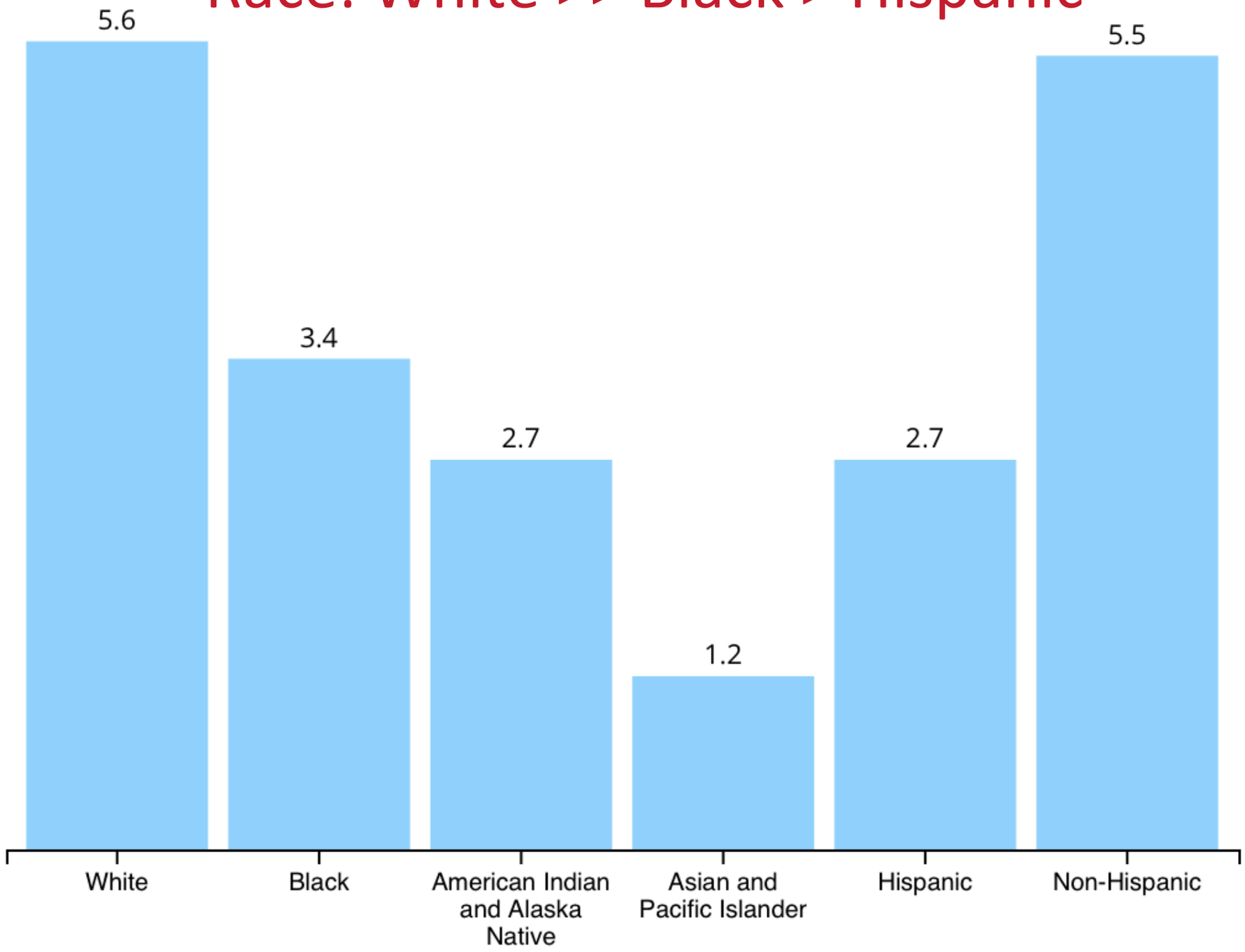
Sex: M>>F



Oropharyngeal Squamous Cell Carcinoma, Male and Female, United States, 2018

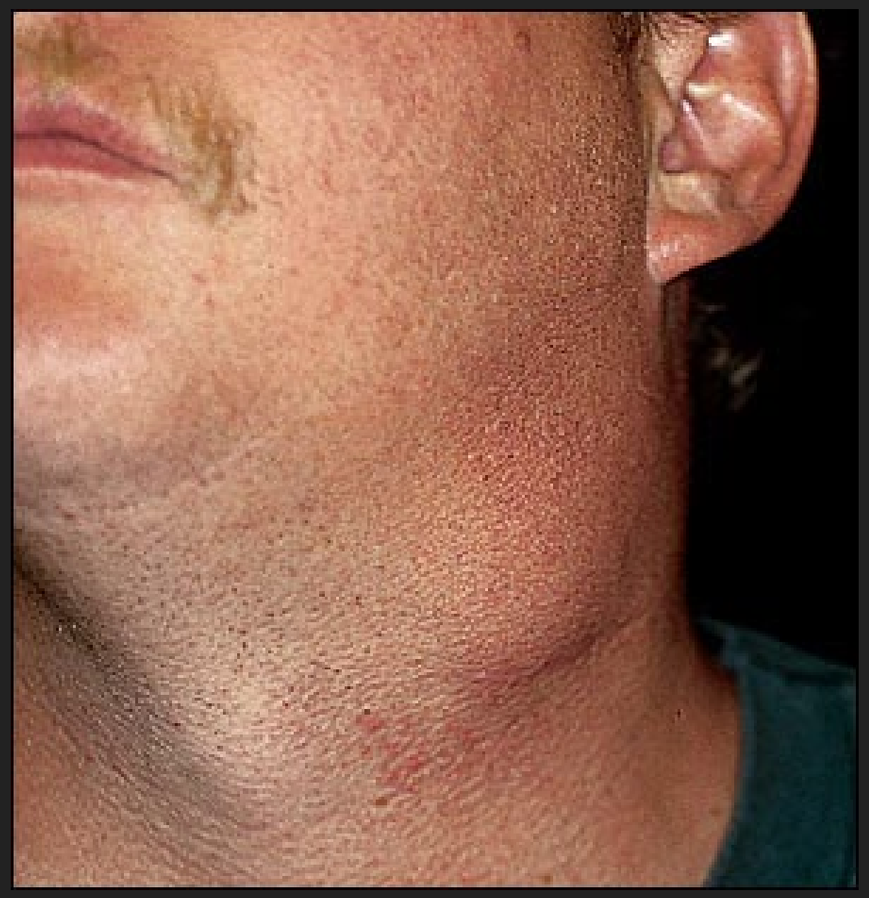
Rate per 100,000 people

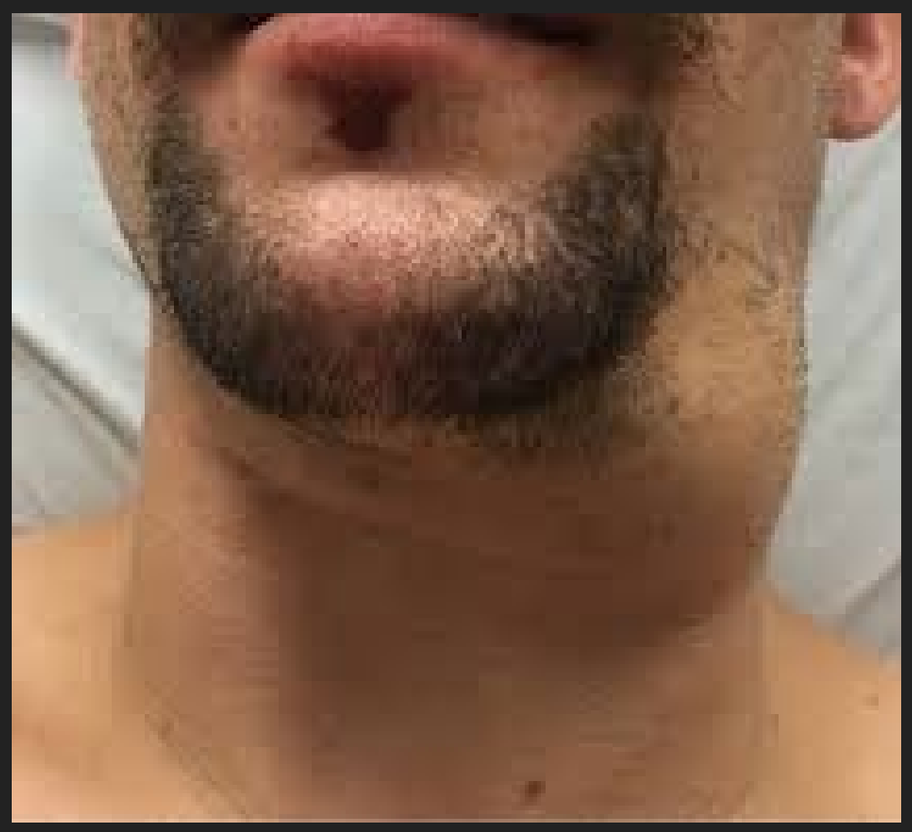
Race: White >> Black > Hispanic



SIGNS/SYMPTOMS

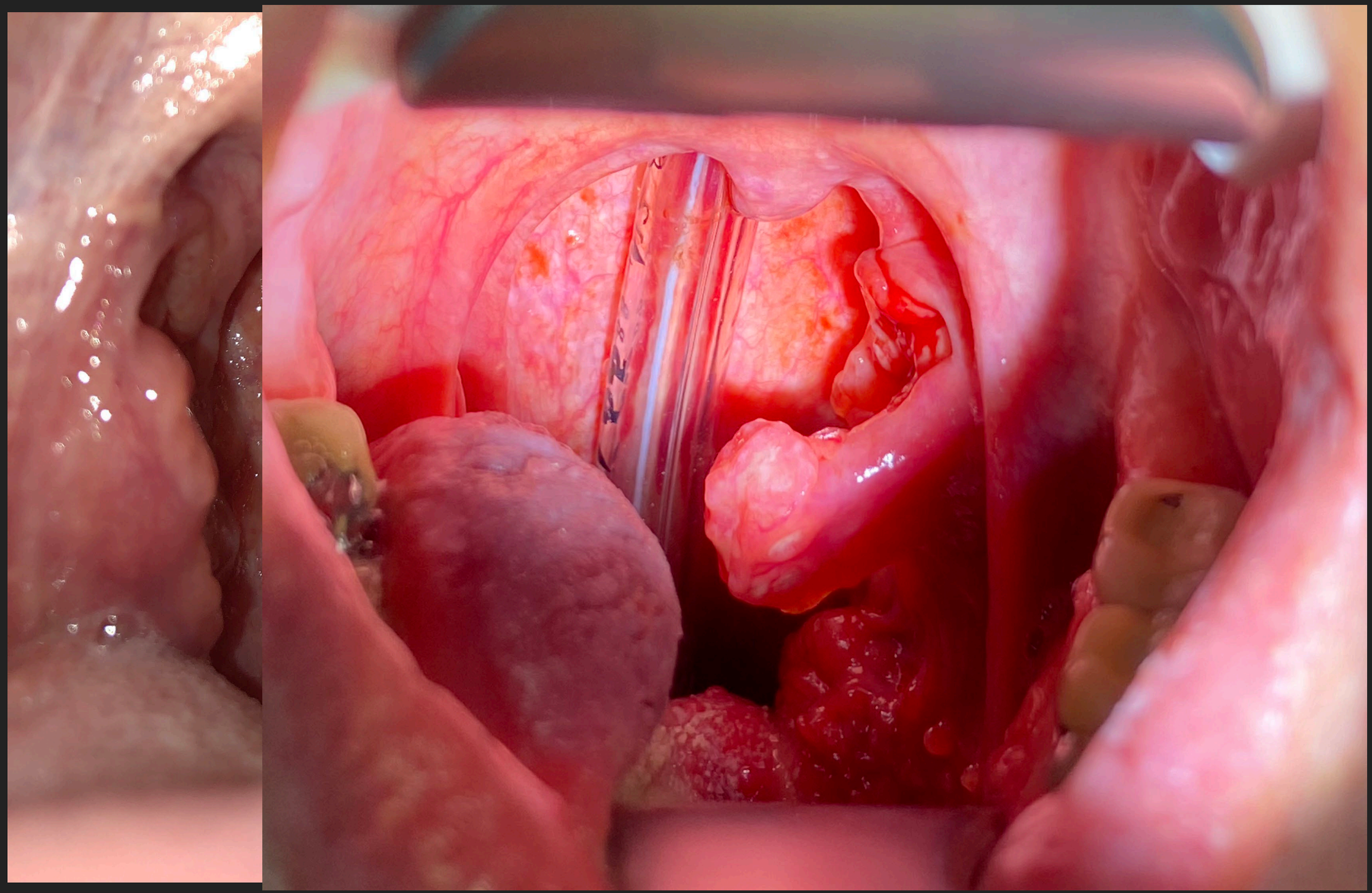
- The most common presentation is an asymptomatic neck mass
- Less common symptoms include:
  - Odynophagia
  - Otalgia
  - Trismus
  - Dysphagia
  - Weight loss
  - Voice changes
  - Velopharyngeal insufficiency





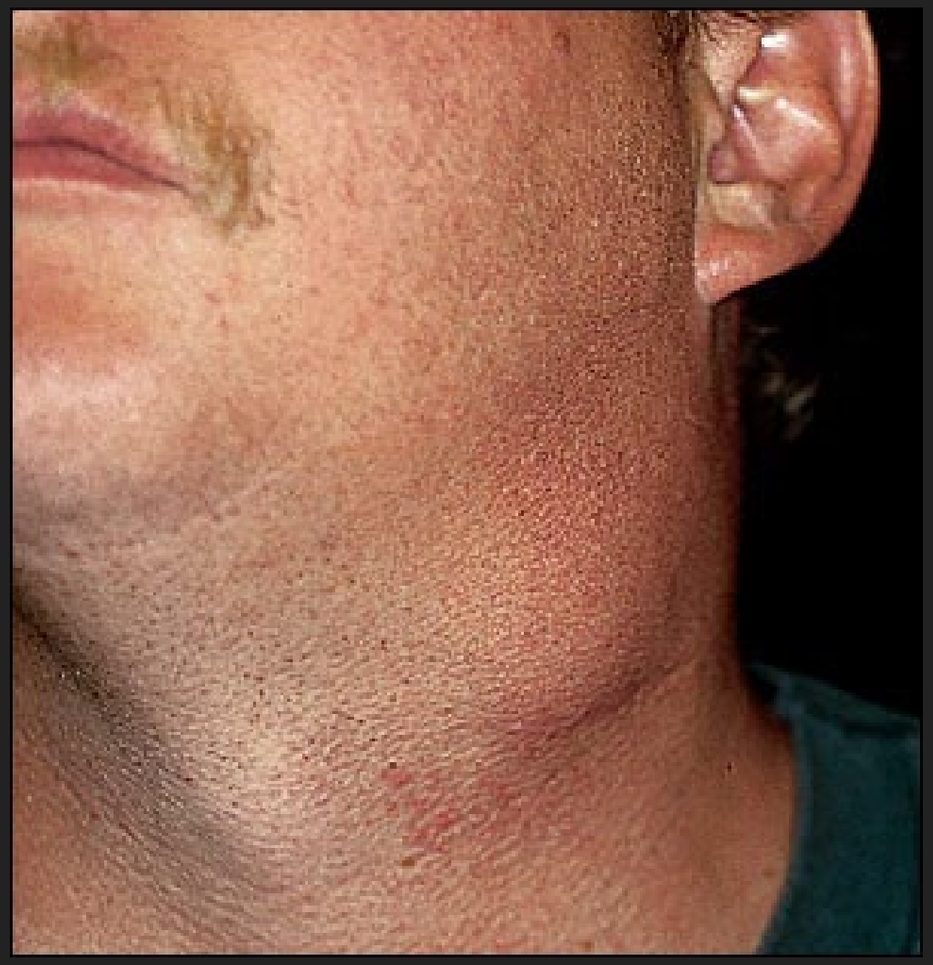
PHYSICAL EXAM

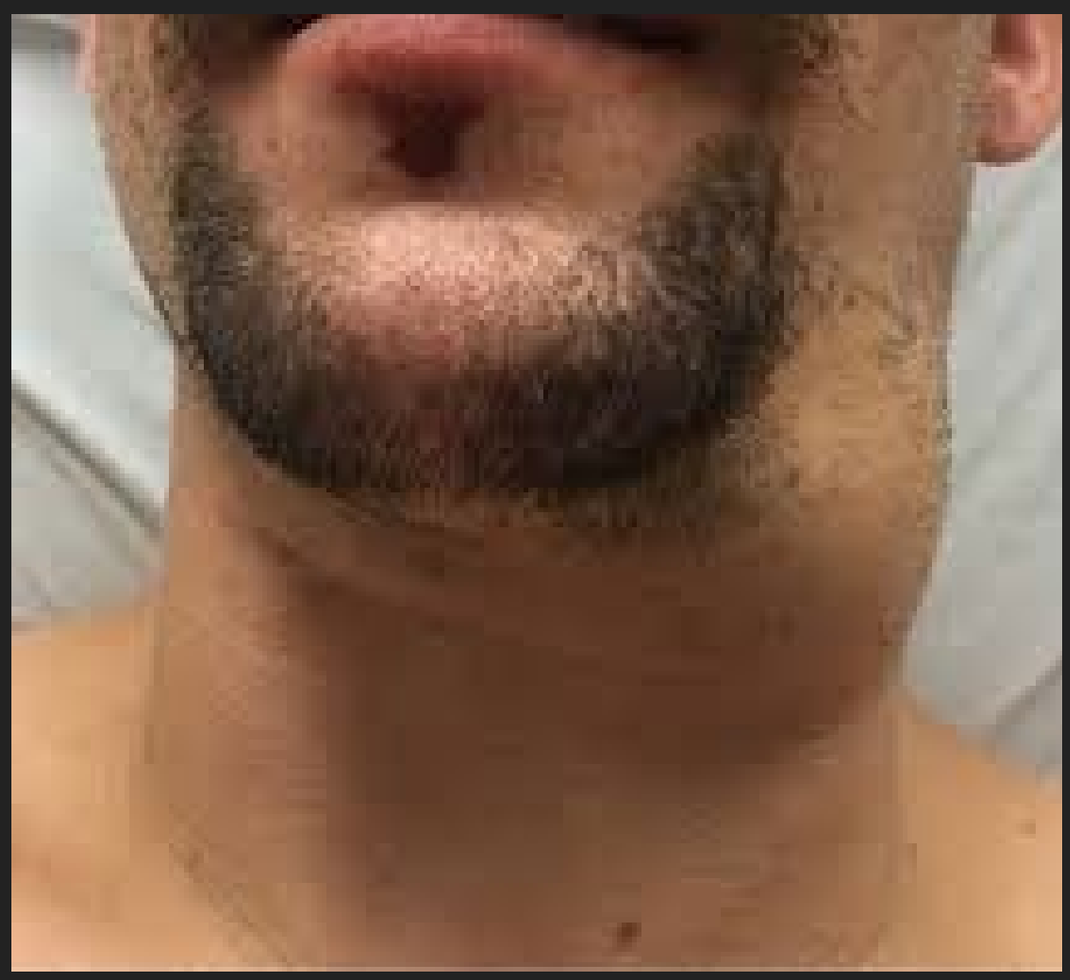
- Oropharyngeal exam



PHYSICAL EXAM

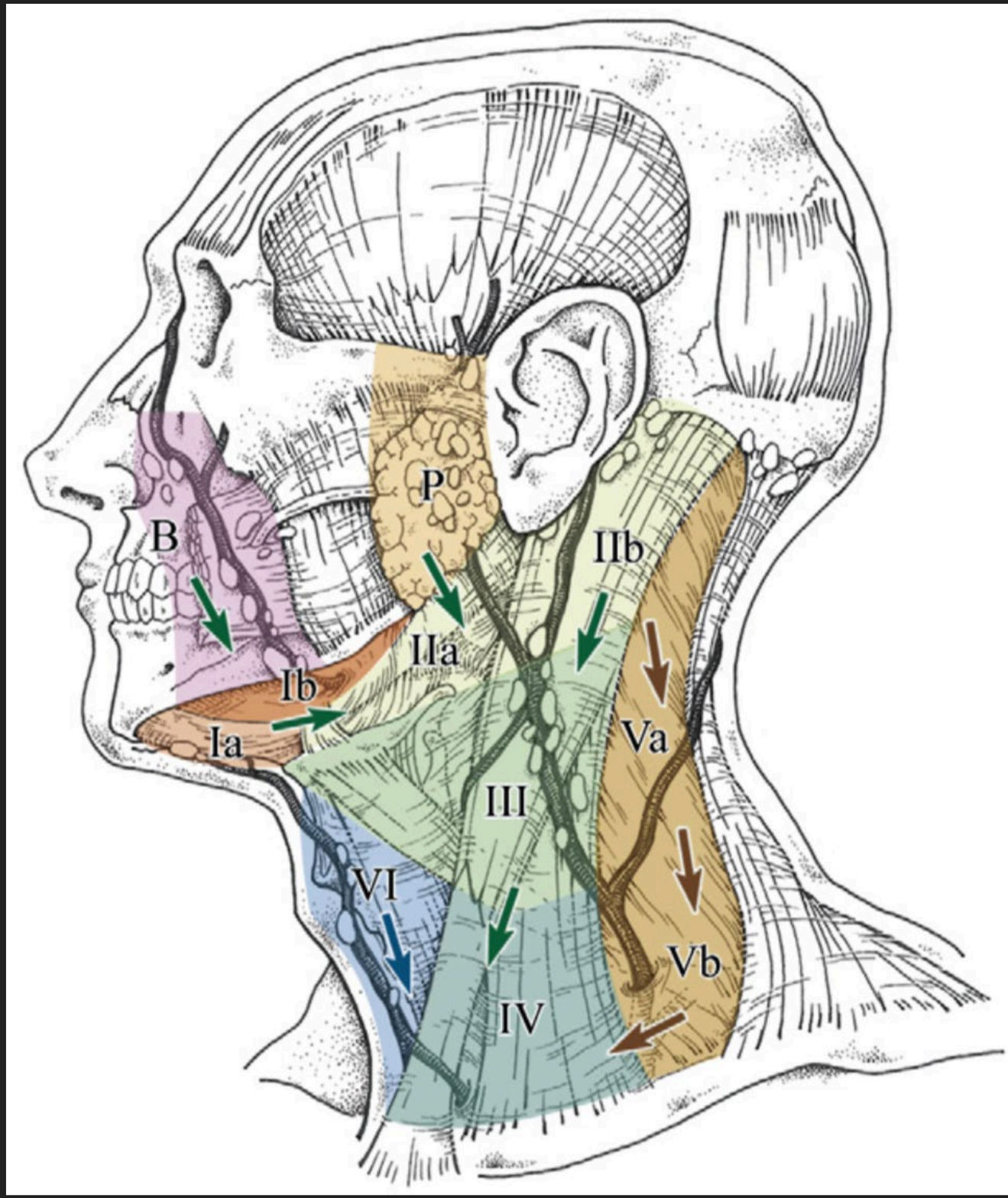
- Neck exam





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)	
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T0	No primary identified
T1	Tumor 2 cm or smaller in greatest dimension
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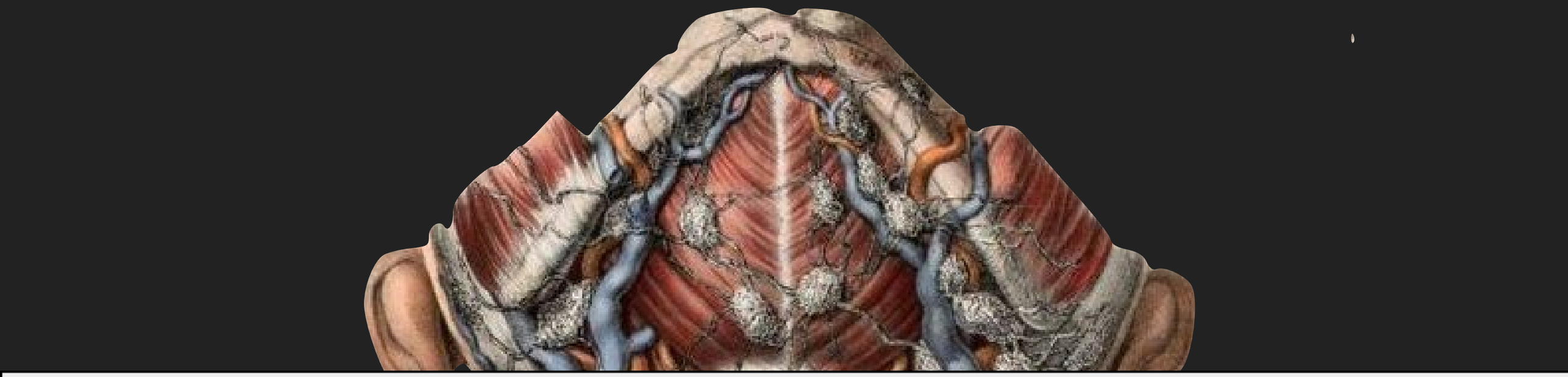
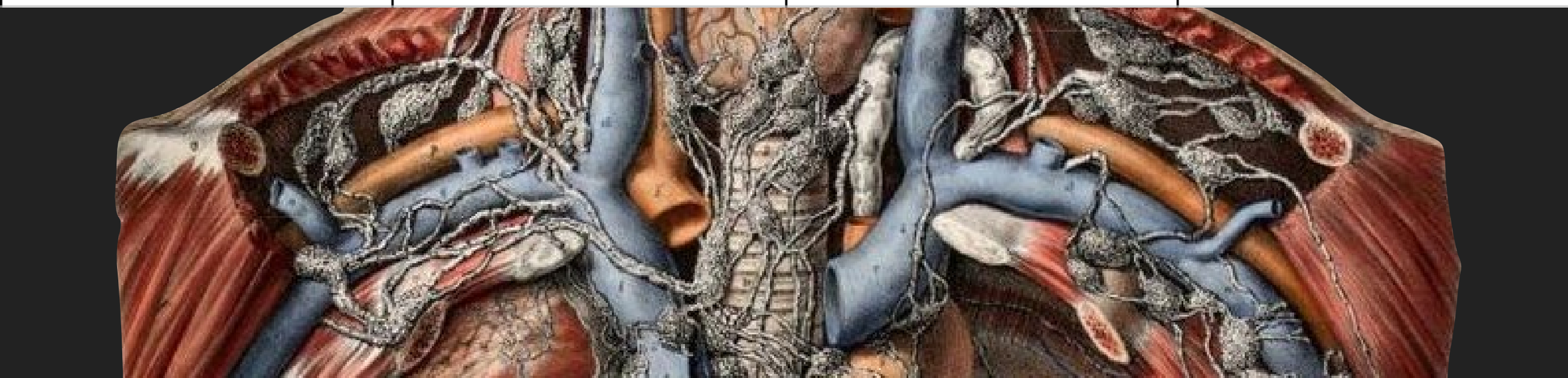
Regional lymph nodes (N) - Pathological N (pN)	
N category	**N criteria**
NX	Regional lymph nodes cannot be assessed
pN0	No regional lymph node metastasis
pN1	Metastasis in four or fewer lymph nodes
pN2	Metastasis in more than four lymph nodes

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



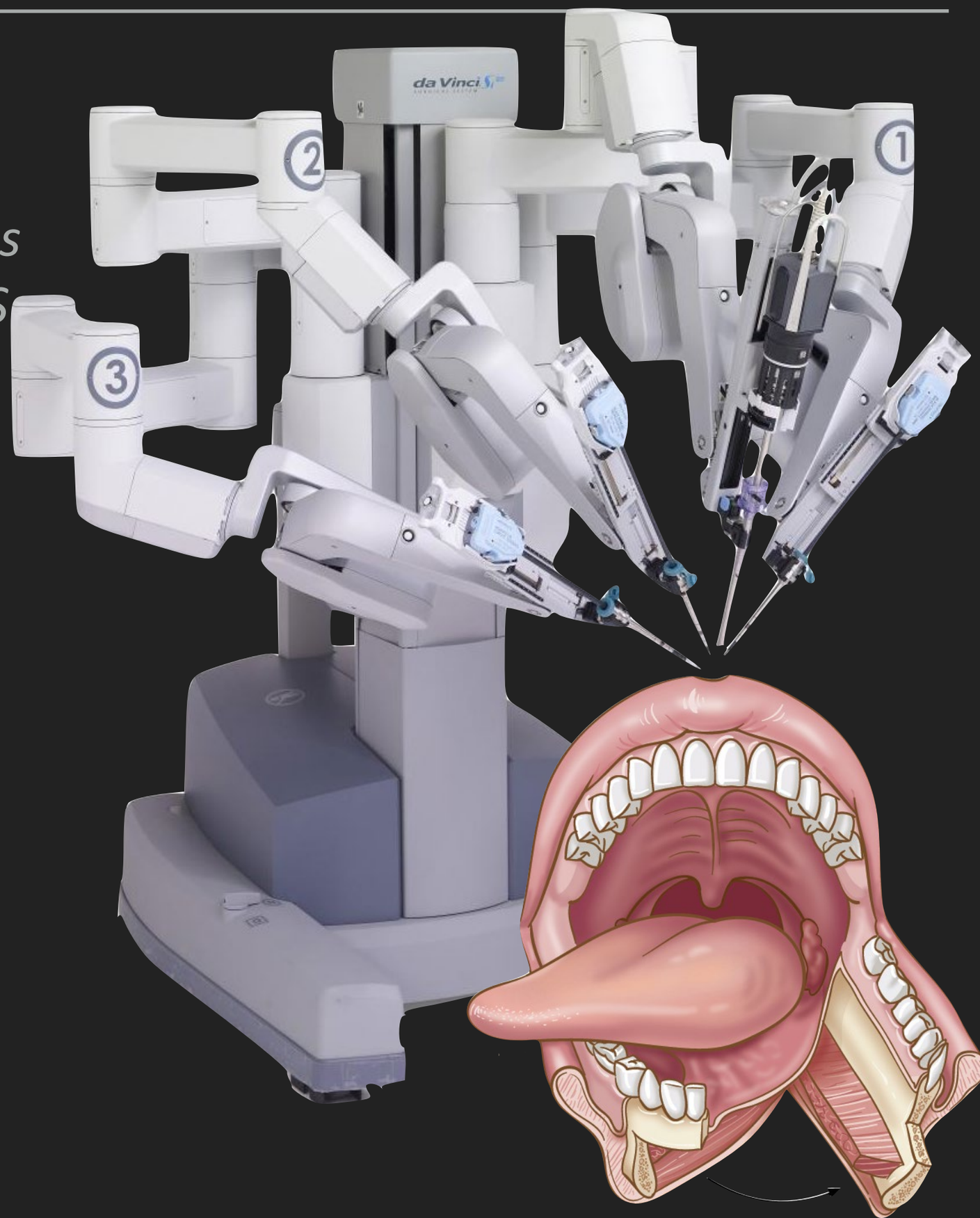
TREATMENT

TREATMENT

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

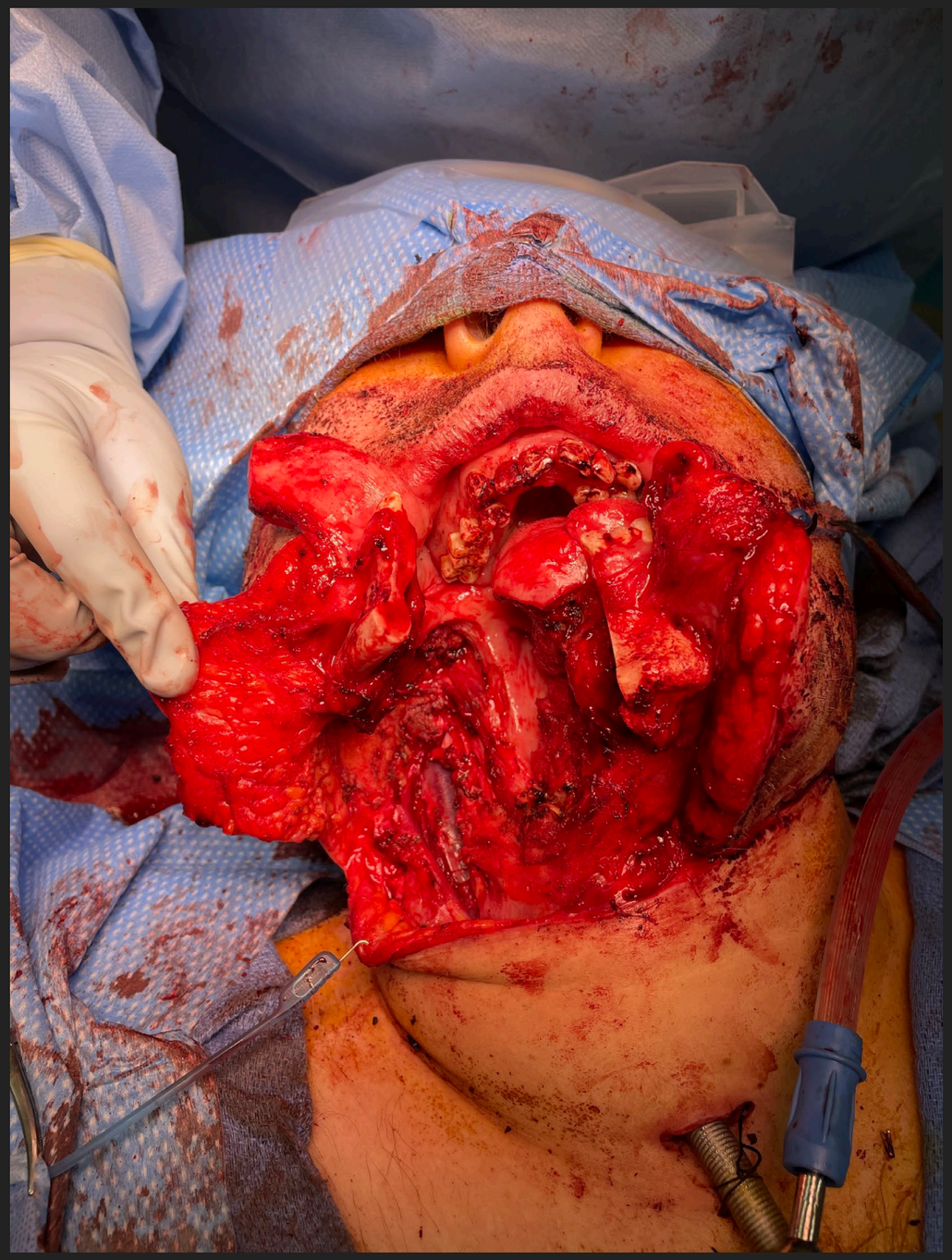
TRANSORAL ROBOTIC SURGERY (TORS)

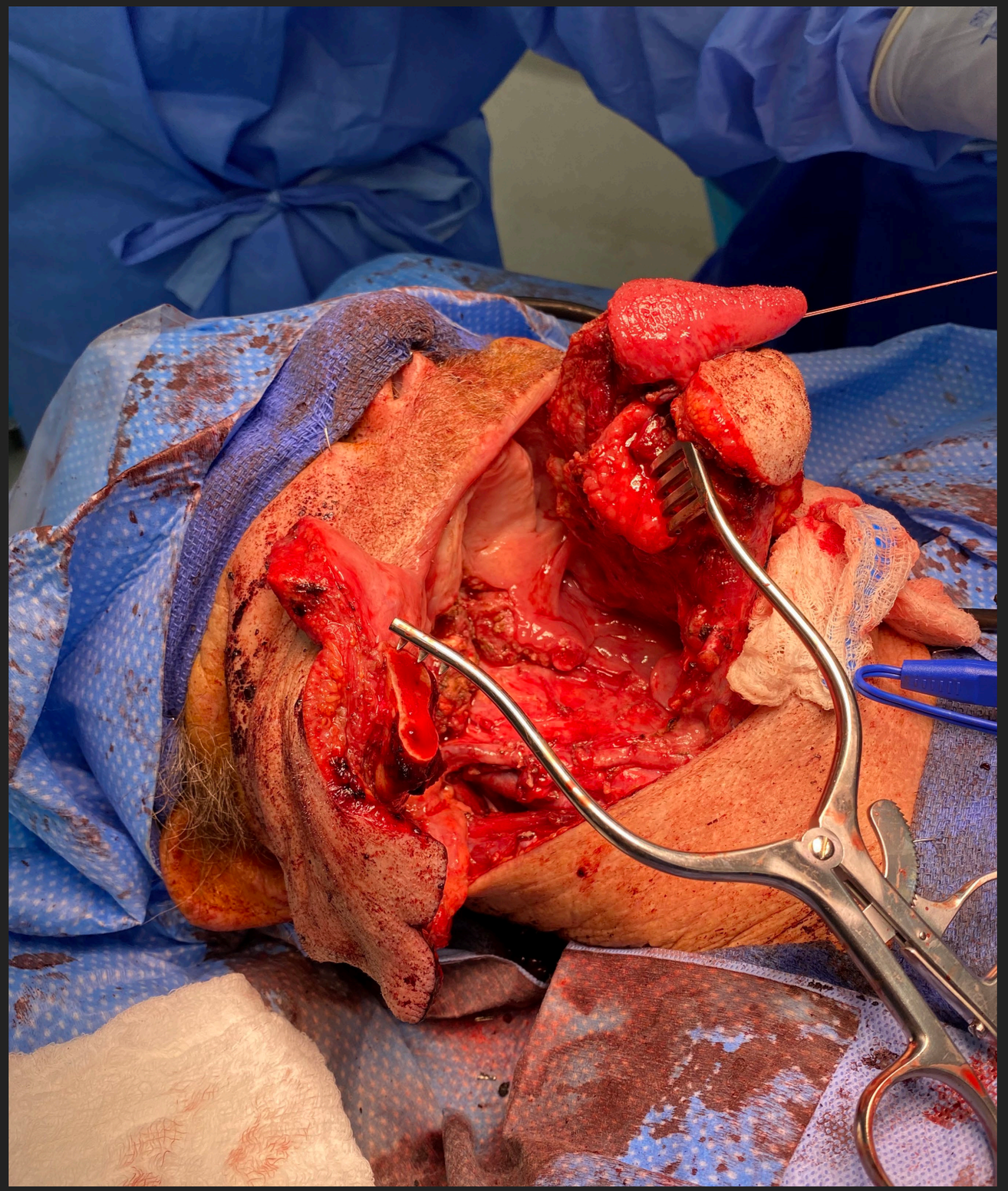
- *A combination of a change in the type of tumor and its growth pattern with advances in technology has made TORS possible*
- *What previously required splitting the jaw can now be done in a minimally invasive fashion through the mouth.*
- *Lower doses of radiation = fewer side effects and fewer long-term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



SURGERY

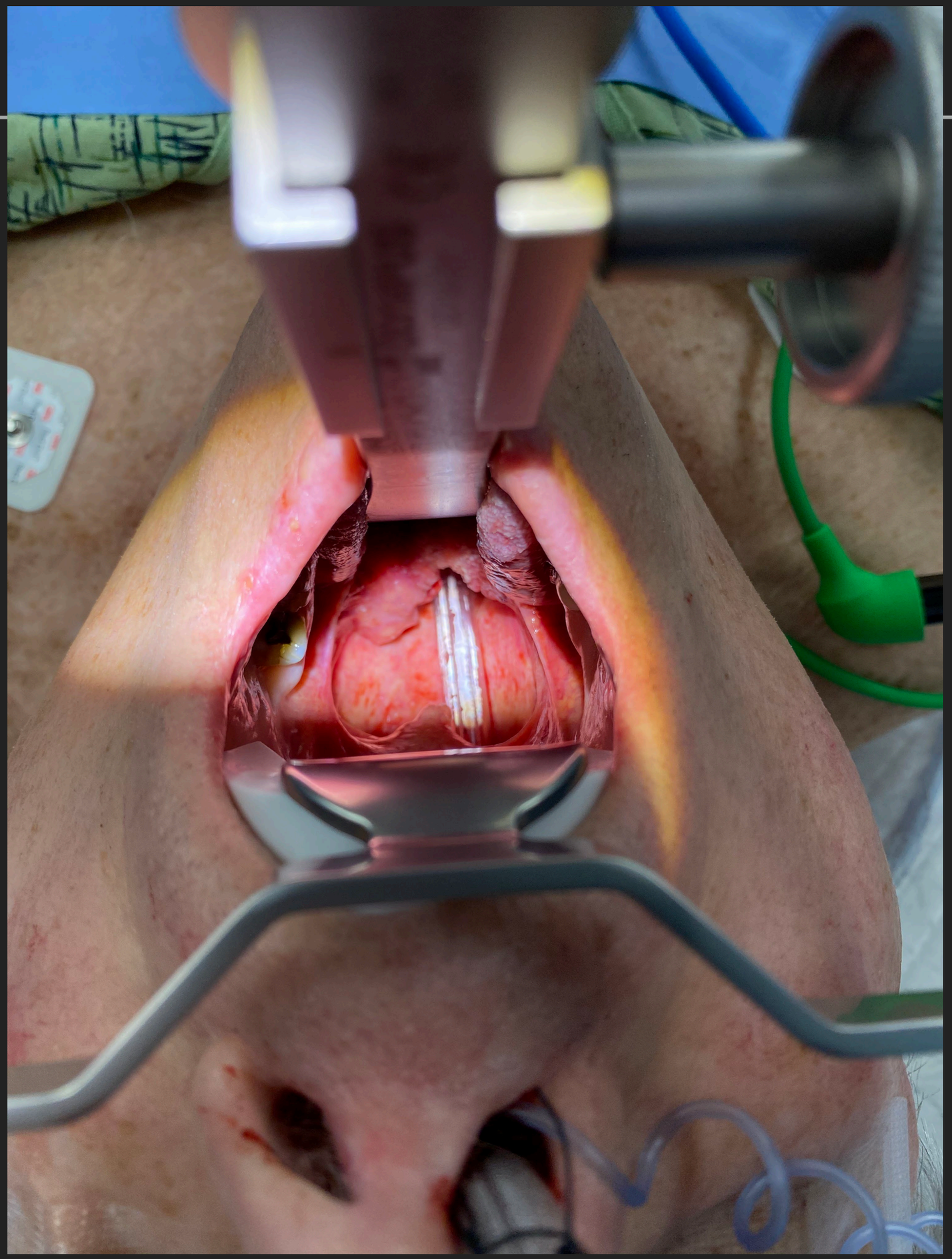
- Previous significantly more invasive approach



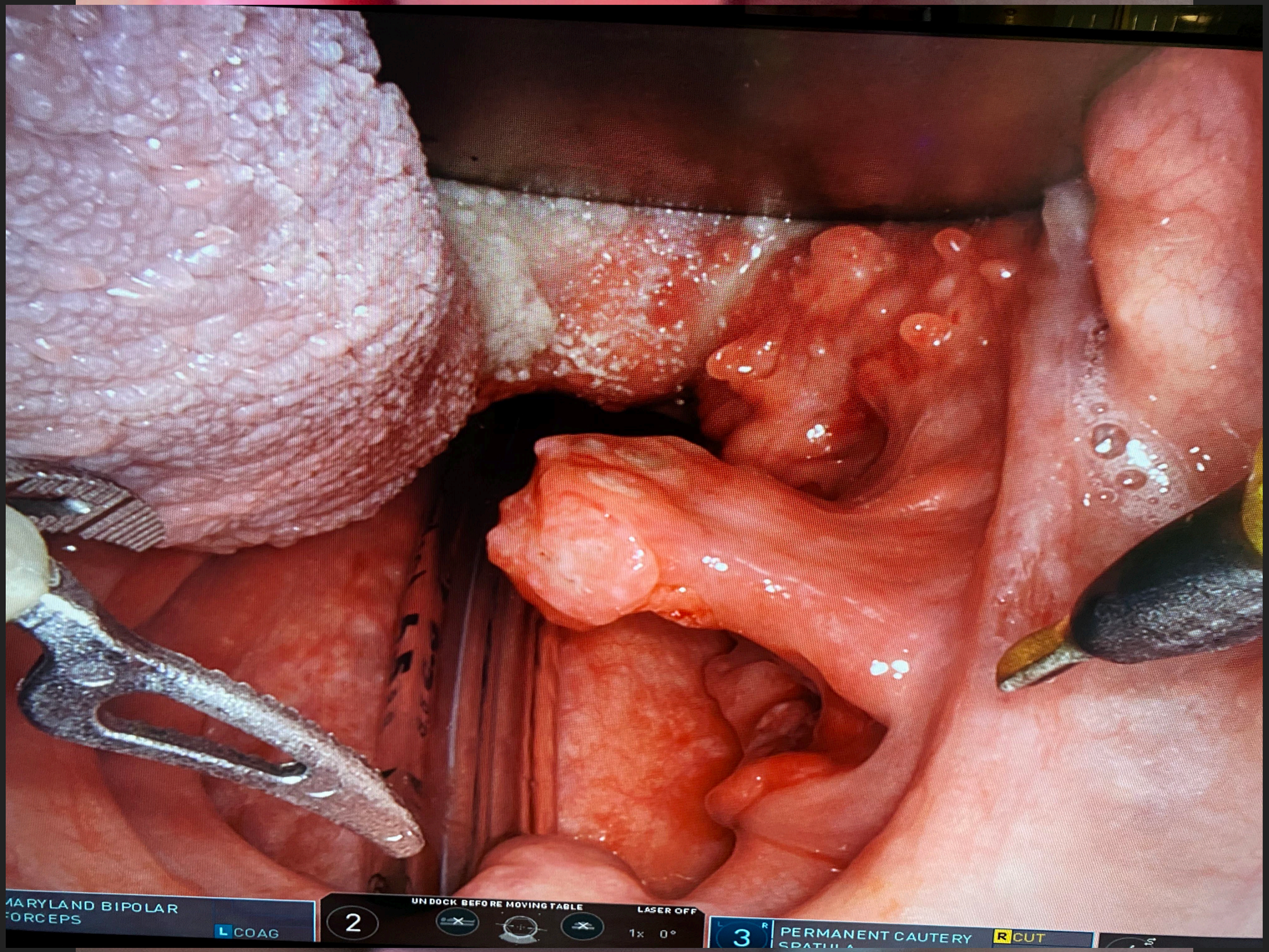


SURGERY

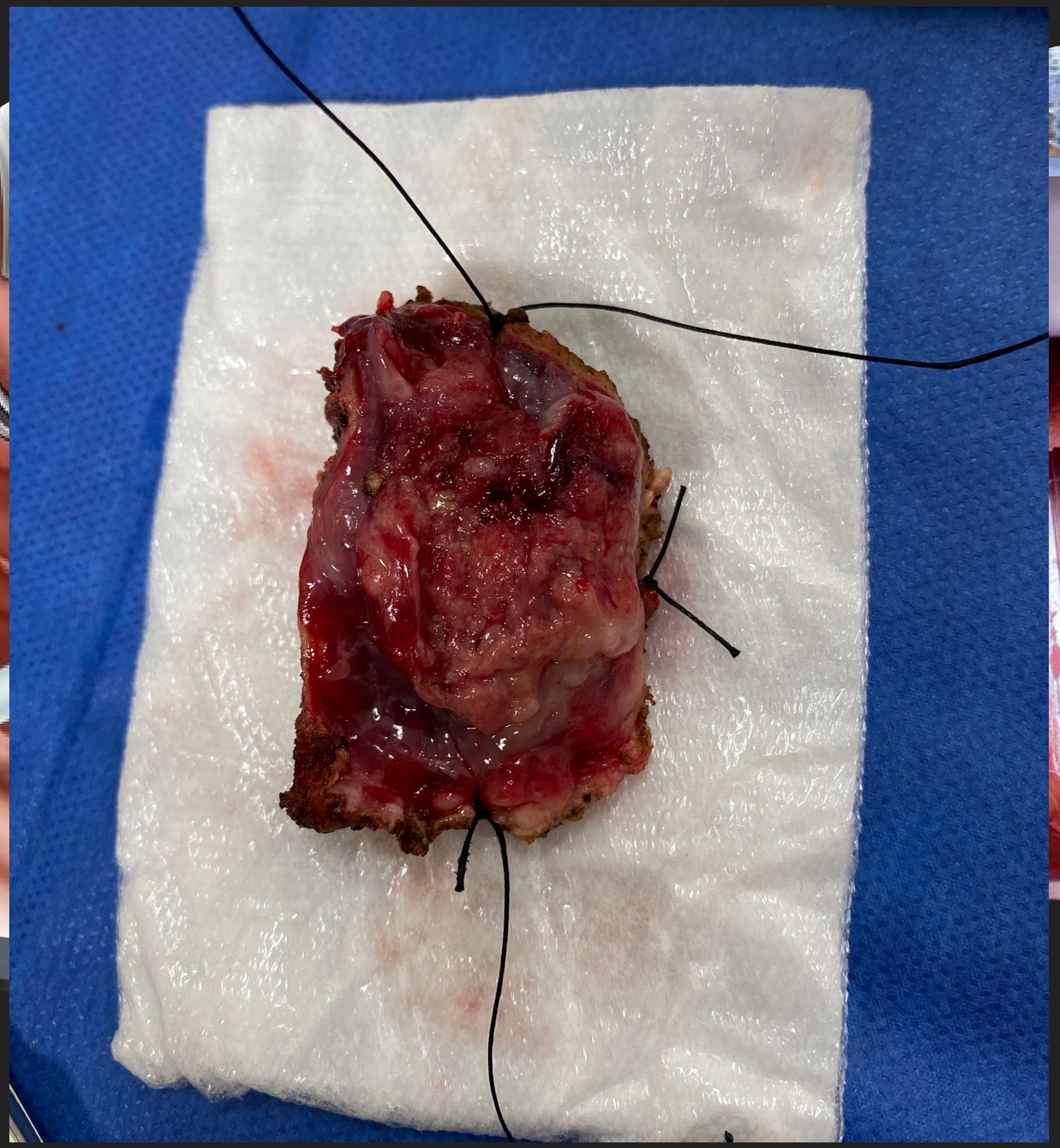
- Now less invasive removal through the mouth with a surgical robot

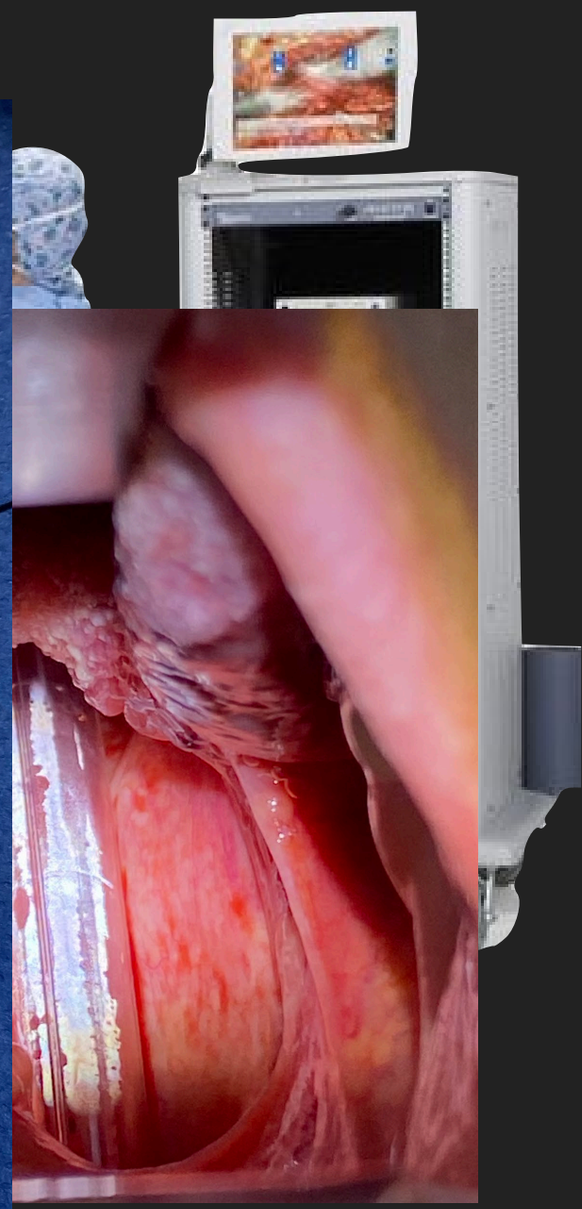


SURGERY

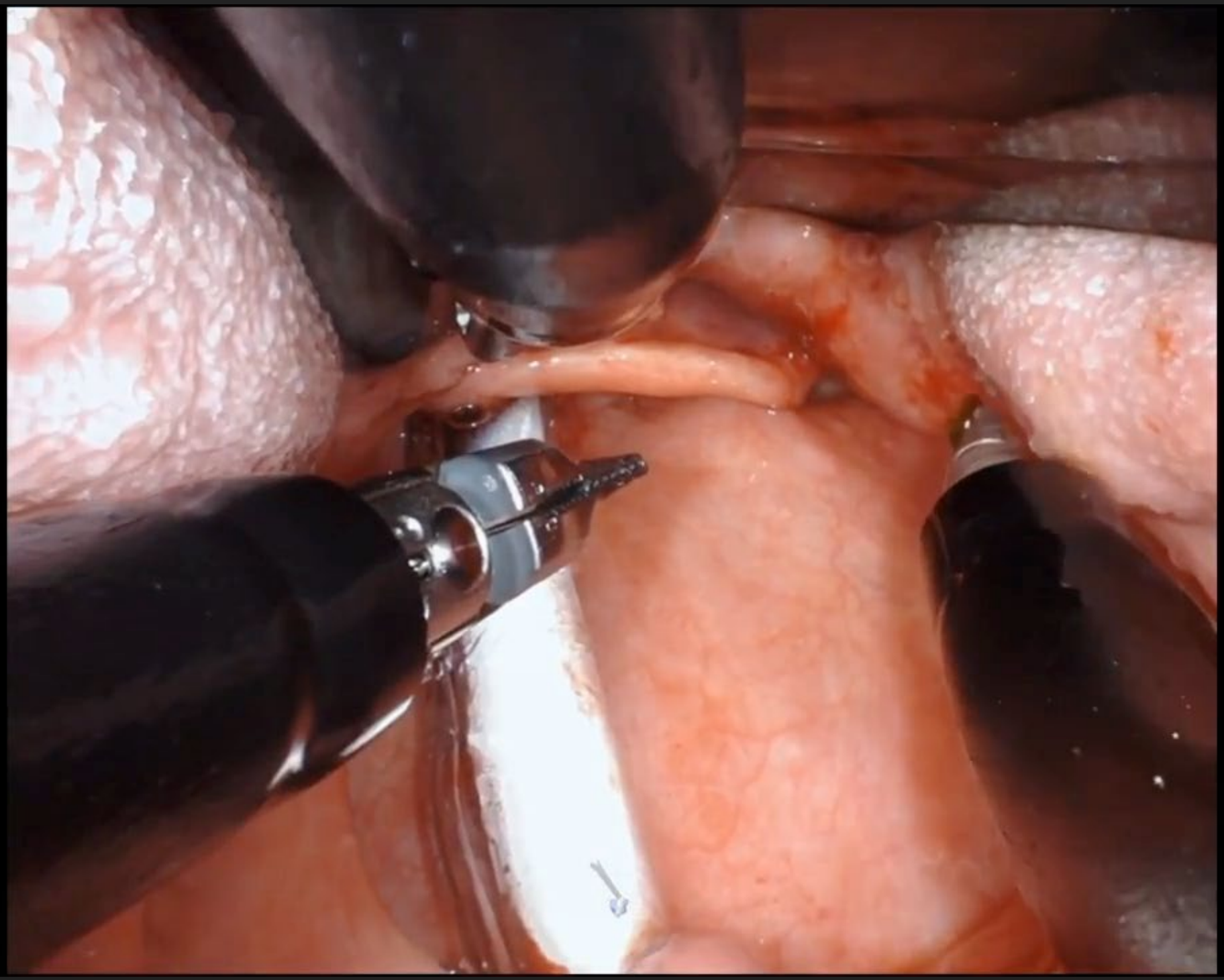

MARYLAND BIPOLAR
FORCEPS
L COAG
2
UN DOCK BEFORE MOVING TABLE
LASER OFF
1x 0°
3
R
PERMANENT CAUTERY
R CUT

HOW DOES TORS WORK?



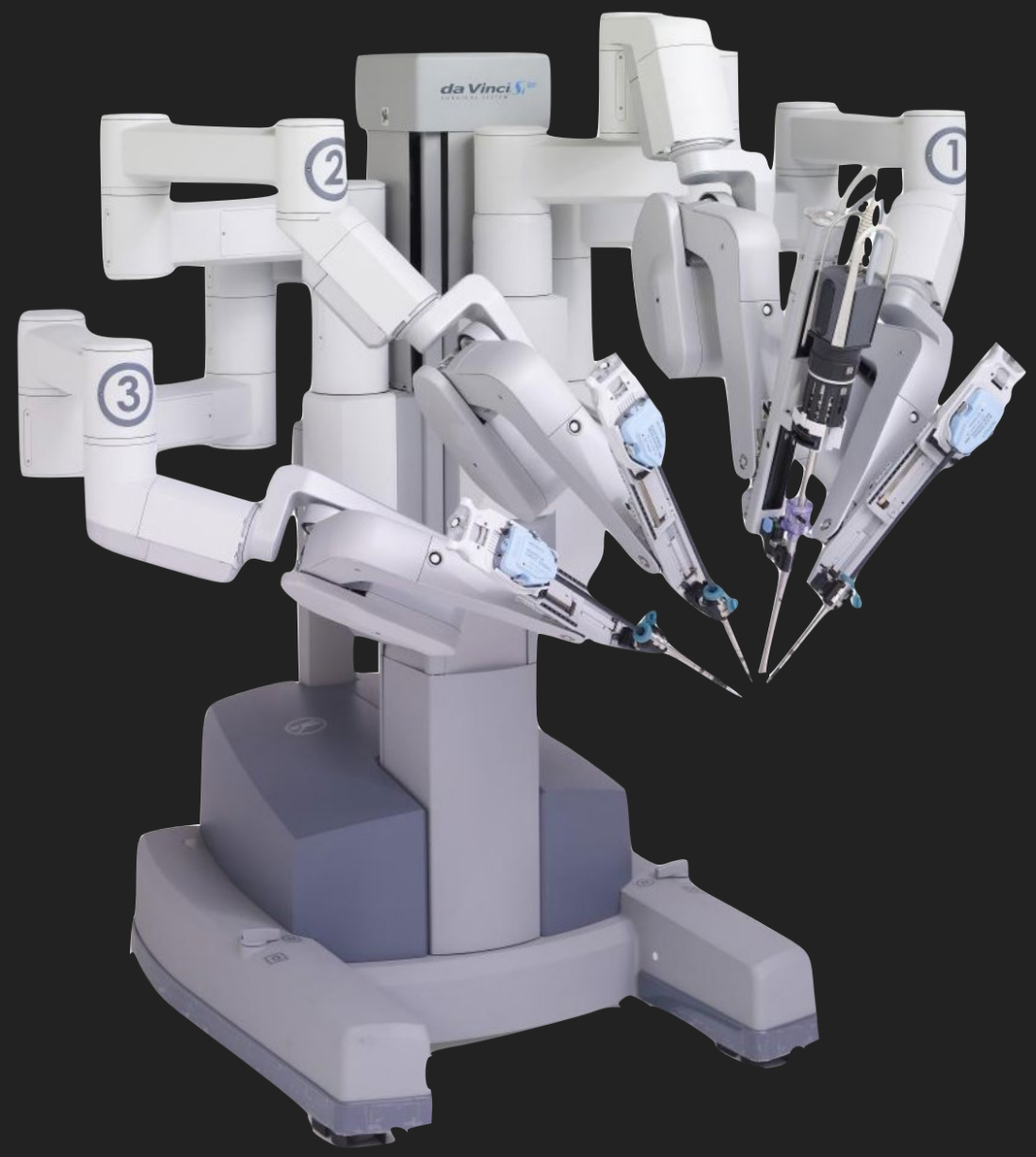


SURGICAL VIDEO



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



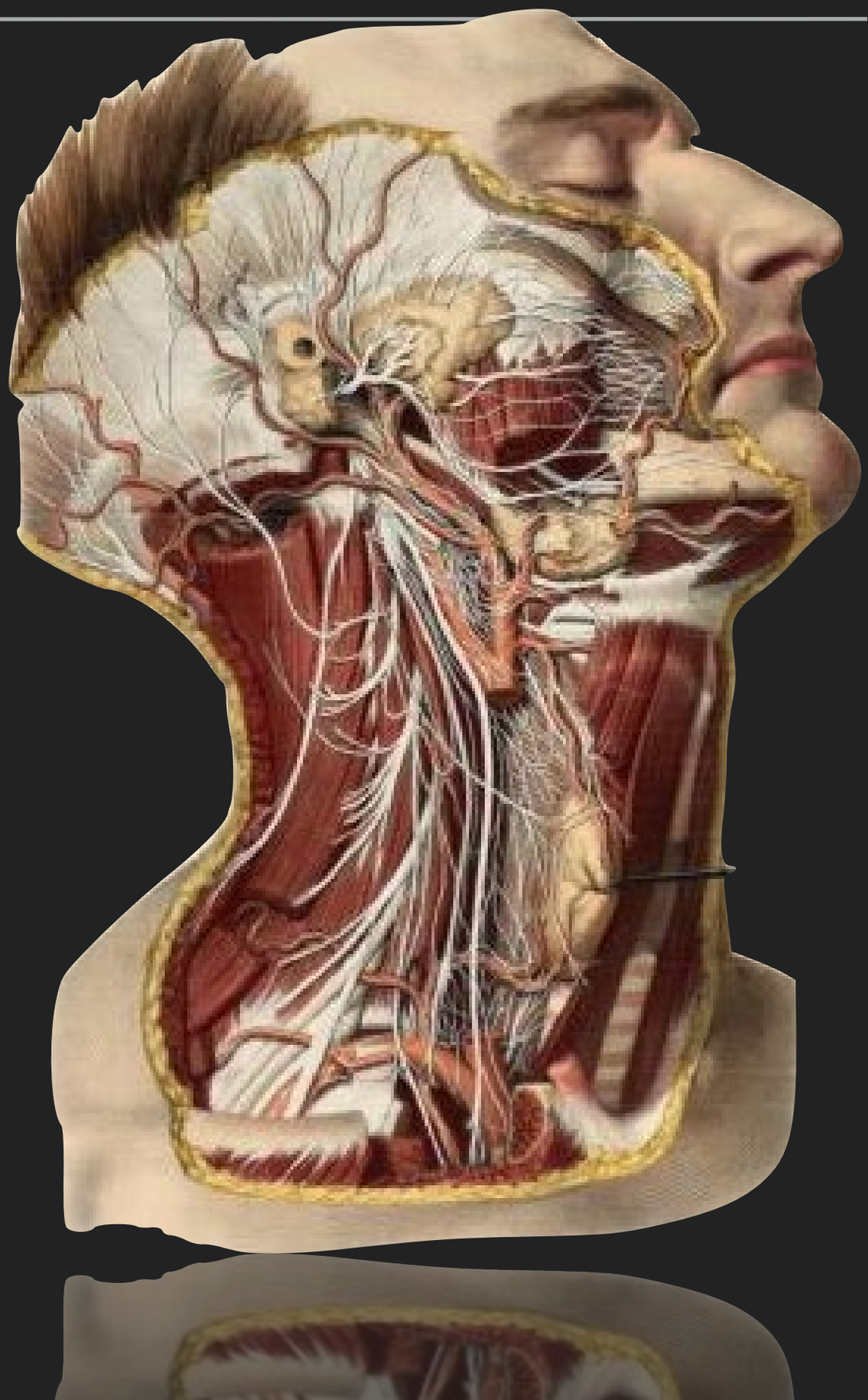
RADIATION/CHEMOTHERAPY

- 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

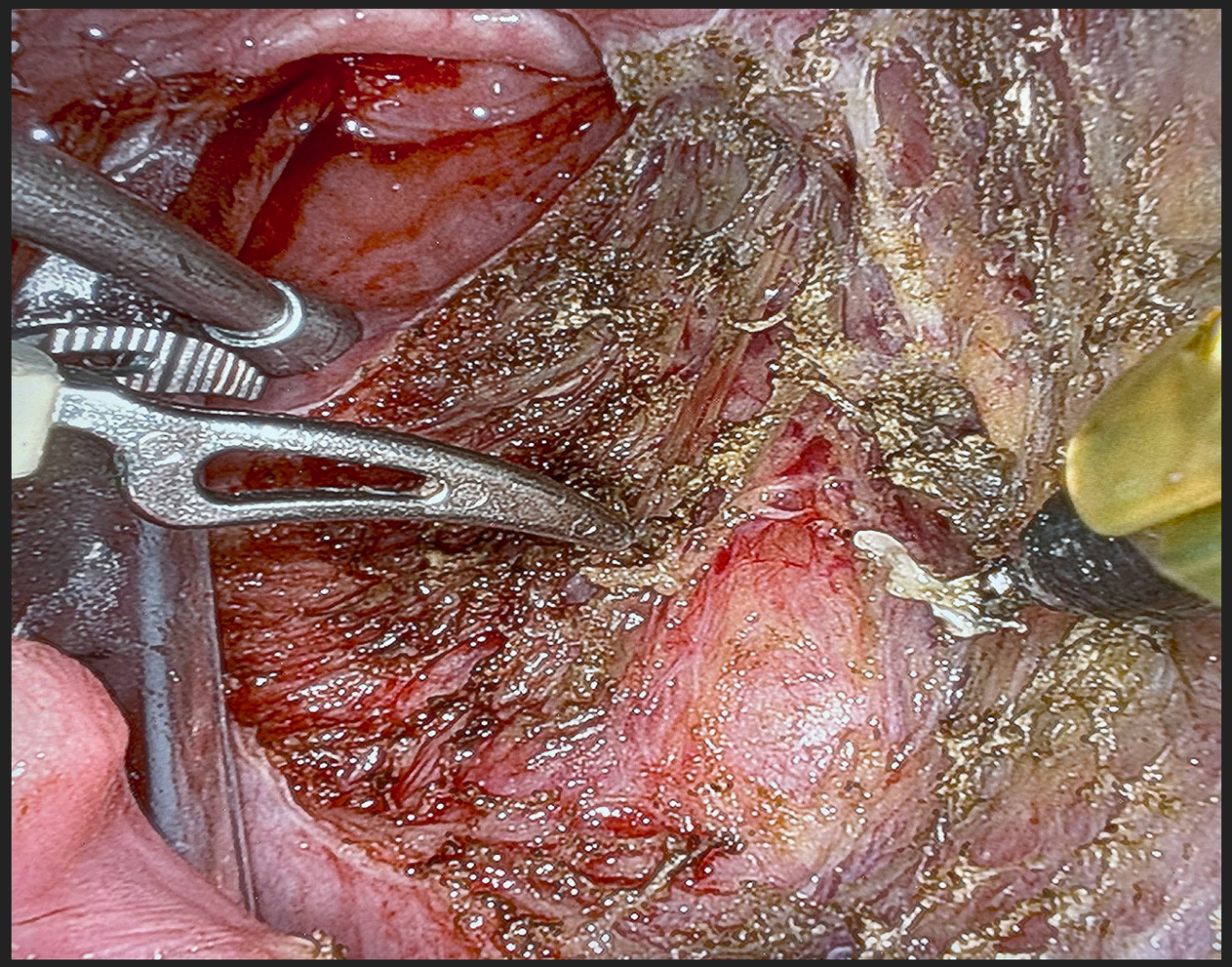
ONCOLOGIC OUTCOMES

- *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

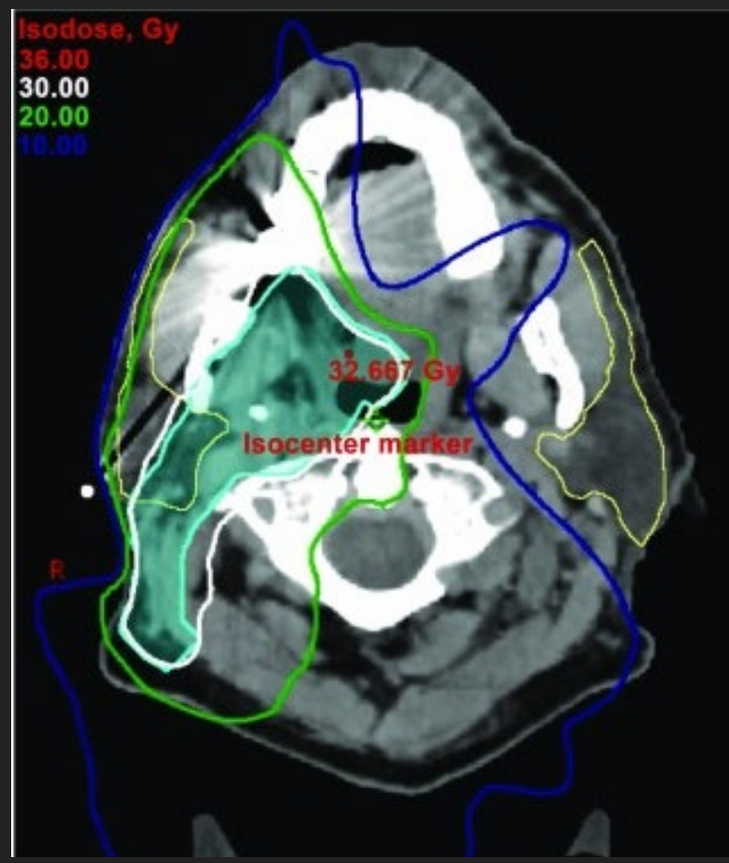
- *Short-term side effects*
  - **TORS:** *throat pain, dysphagia, VPI, aspiration (rare), risk of bleeding*
  - **Chemoradiation:** *throat pain, dysphagia, loss of taste, dry mouth, mucositis*
- *Long-term side effects:*
  - **TORS:** *VPI, trismus*
  - **Chemoradiation:** dry mouth, dysphagia, muscle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

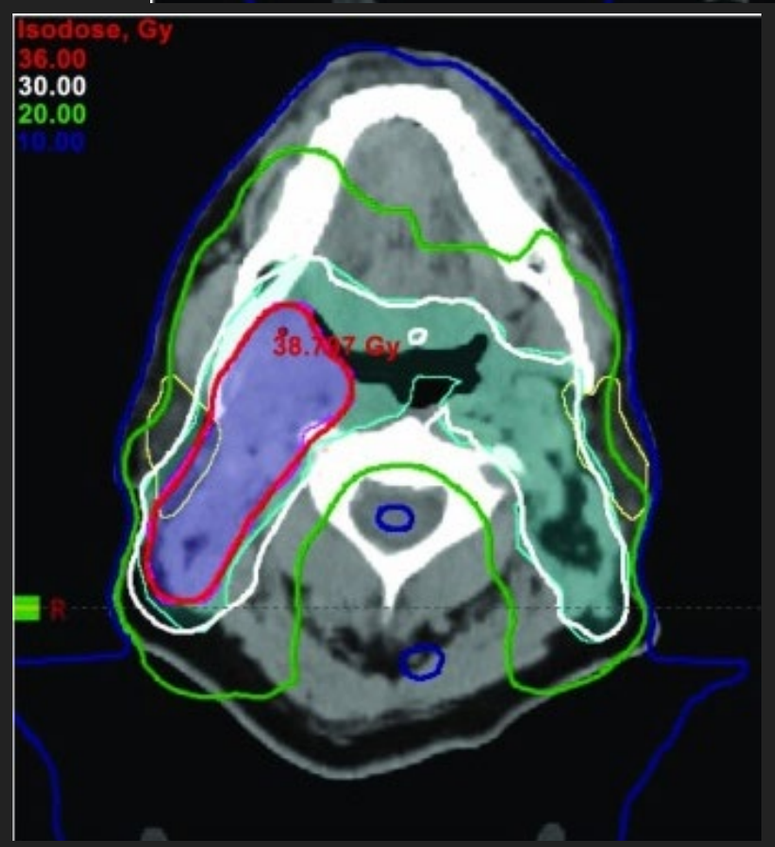


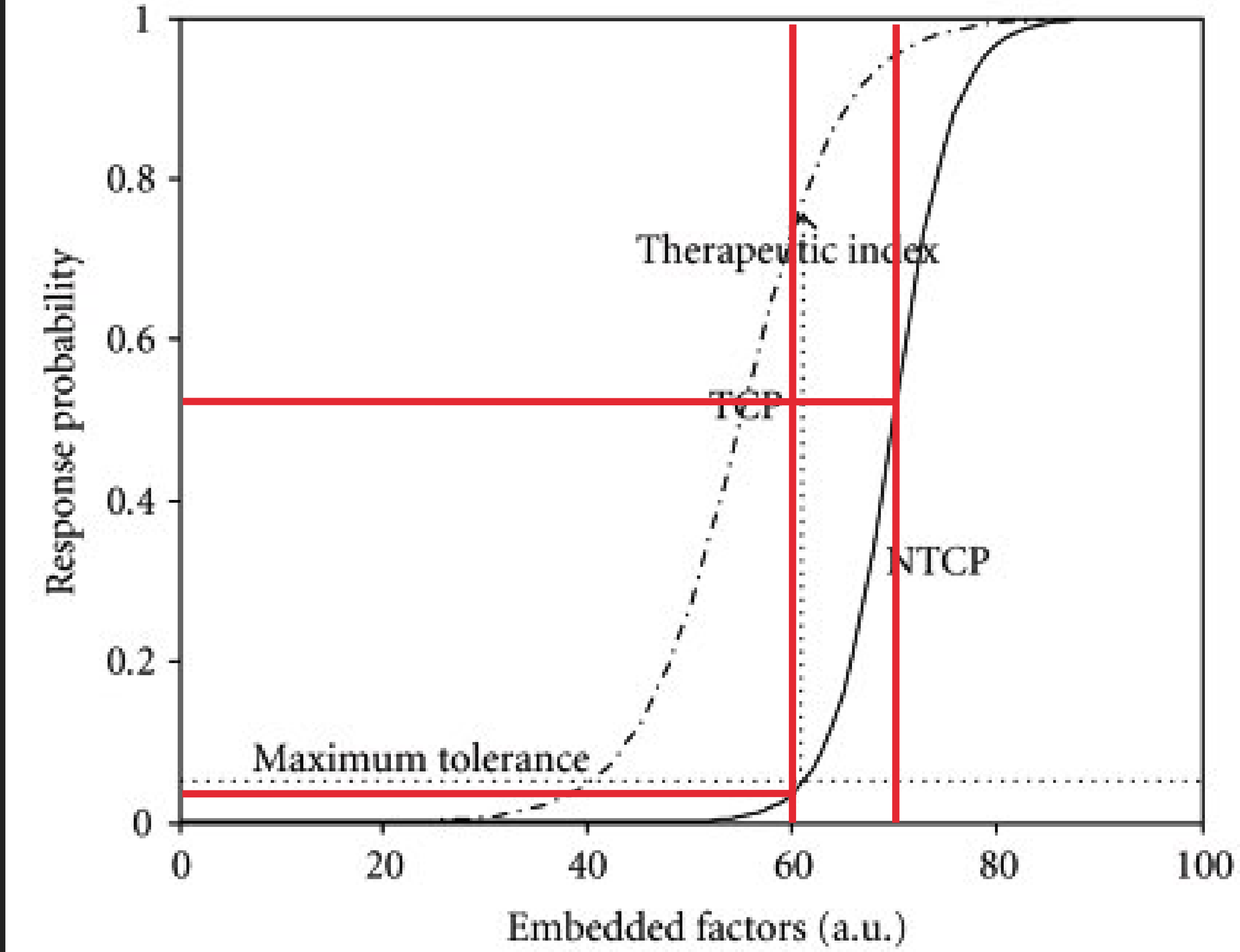
LOWER RADIATION DOSES TO REDUCE SIDE EFFECTS

- **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*






1
0.8
0.6
0.4
0.2
0
Response probability
0
20
40
60
80
100
Embedded factors (a.u.)
Therapeutic index
TCP
NTCP
Maximum tolerance

THE FUTURE - TREATMENT DEESCALATION

- Phase II clinical trial at Mayo Clinic
- Robotic surgery followed by **30-36Gy**
- The 2-year locoregional tumor control rate: **96.2%**
- Progression-free survival: **91.1%**
- Overall survival: **98.7%**
- Rates of grade 3 or worse toxicity at pre-RT and 1 and 2 years post-RT were 2.5%, 0%, and 0%
- XRT treatment finished in **2 weeks**

original report

Phase II Evaluation of Aggressive Dose De-Escalation for Adjuvant Chemoradiotherapy in Human Papillomavirus–Associated Oropharynx Squamous Cell Carcinoma

Daniel J. Ma, MD[1]; Katharine A. Price, MD[1]; Eric J. Moore, MD[1]; Samir H. Patel, MD[2]; Michael L. Hinni, MD[2]; Joaquin J. Garcia, MD[1]; Darlene E. Graner, SLPD[1]; Nathan R. Foster, MS[1]; Brenda Ginos, MS[1]; Michelle Neben-Wittich, MD[1]; Yolanda I. Garces, MD[1]; Ashish V. Chintakuntlawar, MBBS, PhD[1]; Daniel L. Price, MD[1]; Kerry D. Olsen, MD[1]; Kathryn M. Van Abel, MD[1]; Jan L. Kasperbauer, MD[1]; Jeffrey R. Janus, MD[1]; Mark Waddle, MD[3]; Robert Miller, MD[3]; Satomi Shiraishi, PhD[1]; and Robert L. Foote, MD[1]

abstract

PURPOSE The purpose of this study was to determine if dose de-escalation from 60 to 66 Gy to 30 to 36 Gy of adjuvant radiotherapy (RT) for selected patients with human papillomavirus–associated oropharyngeal squamous cell carcinoma could maintain historical rates for disease control while reducing toxicity and preserving swallow function and quality of life (QOL).

PATIENTS AND METHODS MC1273 was a single-arm phase II trial testing an aggressive course of RT de-escalation after surgery. Eligibility criteria included patients with p16-positive oropharyngeal squamous cell carcinoma, smoking history of 10 pack-years or less, and negative margins. Cohort A (intermediate risk) received 30 Gy delivered in 1.5-Gy fractions twice per day over 2 weeks along with 15 mg/m^2 docetaxel once per week. Cohort B included patients with extranodal extension who received the same treatment plus a simultaneous integrated boost to nodal levels with extranodal extension to 36 Gy in 1.8-Gy fractions twice per day. The primary end point was locoregional tumor control at 2 years. Secondary end points included 2-year progression-free survival, overall survival, toxicity, swallow function, and patient-reported QOL.

RESULTS Accrual was from September 2013 to June 2016 (N = 80; cohort A, n = 37; cohort B, n = 43). Median follow-up was 36 months, with a minimum follow-up of 25 months. The 2-year locoregional tumor control rate was 96.2%, with progression-free survival of 91.1% and overall survival of 98.7%. Rates of grade 3 or worse toxicity at pre-RT and 1 and 2 years post-RT were 2.5%, 0%, and 0%. Swallowing function improved slightly between pre-RT and 12 months post-RT, with one patient requiring temporary feeding tube placement.

CONCLUSION Aggressive RT de-escalation resulted in locoregional tumor control rates comparable to historical controls, low toxicity, and little decrement in swallowing function or QOL.

J Clin Oncol 37:1909-1918. © 2019 by American Society of Clinical Oncology

ASSOCIATED CONTENT

See accompanying Editorial on page 1854

Appendix

Data Supplement

Author affiliations and support information (if applicable) appear at the end of this article.

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Clinical trial information: NCT01932697.

INTRODUCTION

Human papillomavirus (HPV)–associated oropharyngeal squamous cell carcinoma (OPSCC) represents a demographically and biologically distinct disease compared with historical head and neck squamous cell carcinomas.[1,2] Patients are more likely to be younger and nonsmokers and have fewer medical comorbidities.[3] Furthermore, in vitro and in vivo experiments have demonstrated that these tumors are more sensitive to radiotherapy (RT) and chemotherapy compared with historical head and neck squamous cell carcinomas.[4-6] This combination of factors has led to markedly improved clinical outcomes after standard treatments.[7] For patients who are never-smokers, survival rates can be as high as 90% after standard therapy.[8] These high survival rates translate into a growing population of otherwise healthy, younger survivors who will live with treatment sequelae for a long time.

Standard treatment of HPV-associated OPSCC consists of either 7 weeks of RT (70 Gy) combined with concurrent cisplatin or surgery followed by 6 weeks of adjuvant RT (60 to 66 Gy) with or without cisplatin, depending upon risk factors.[9,10] Both approaches incur significant post-treatment sequelae. One third of patients or more will have long-term grade 3 or worse toxicities, such as xerostomia, dysphagia, neuropathy, neck fibrosis, or osteoradionecrosis.[11,12] In the context of a highly curable cancer with prolonged survival, clinical trials examining treatment de-escalation for reducing toxicity while preserving historically high cure rates are urgently needed.

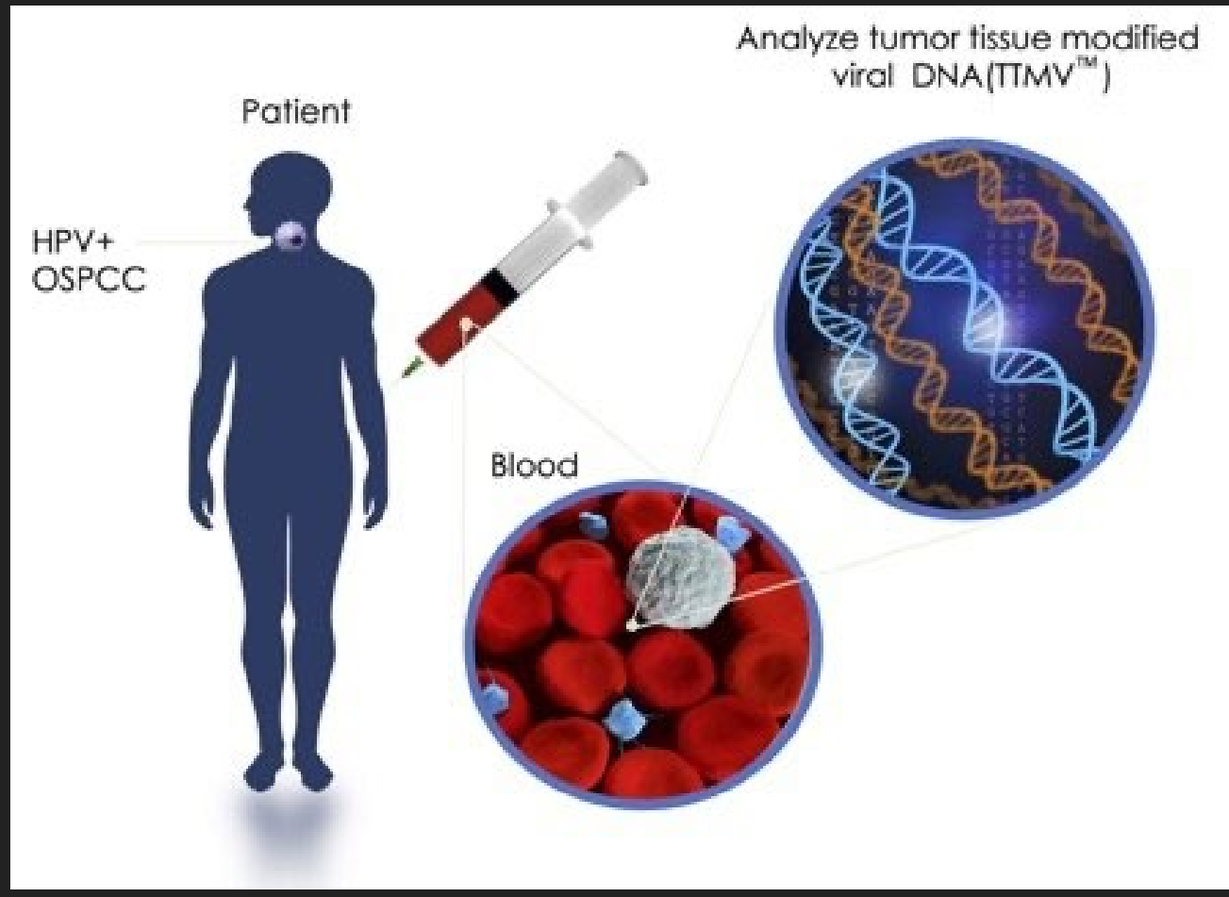
SURVEILLANCE AND PREVENTION

ADVANCED TUMOR MARKERS

- NavDx: new tumor marker that measures **circulating HPV tumor DNA** (HPV ctDNA)
- Can be measured at all post-treatment follow up visits
- Has been shown to catch recurrences months before imaging and conventional follow up

NAVERIS

- **>95%** sensitive
- **>99%** chance of being recurrence free if undetectable during follow up
- **CARTI** is only institution in Arkansas using this on every patient and it is **100%** free



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

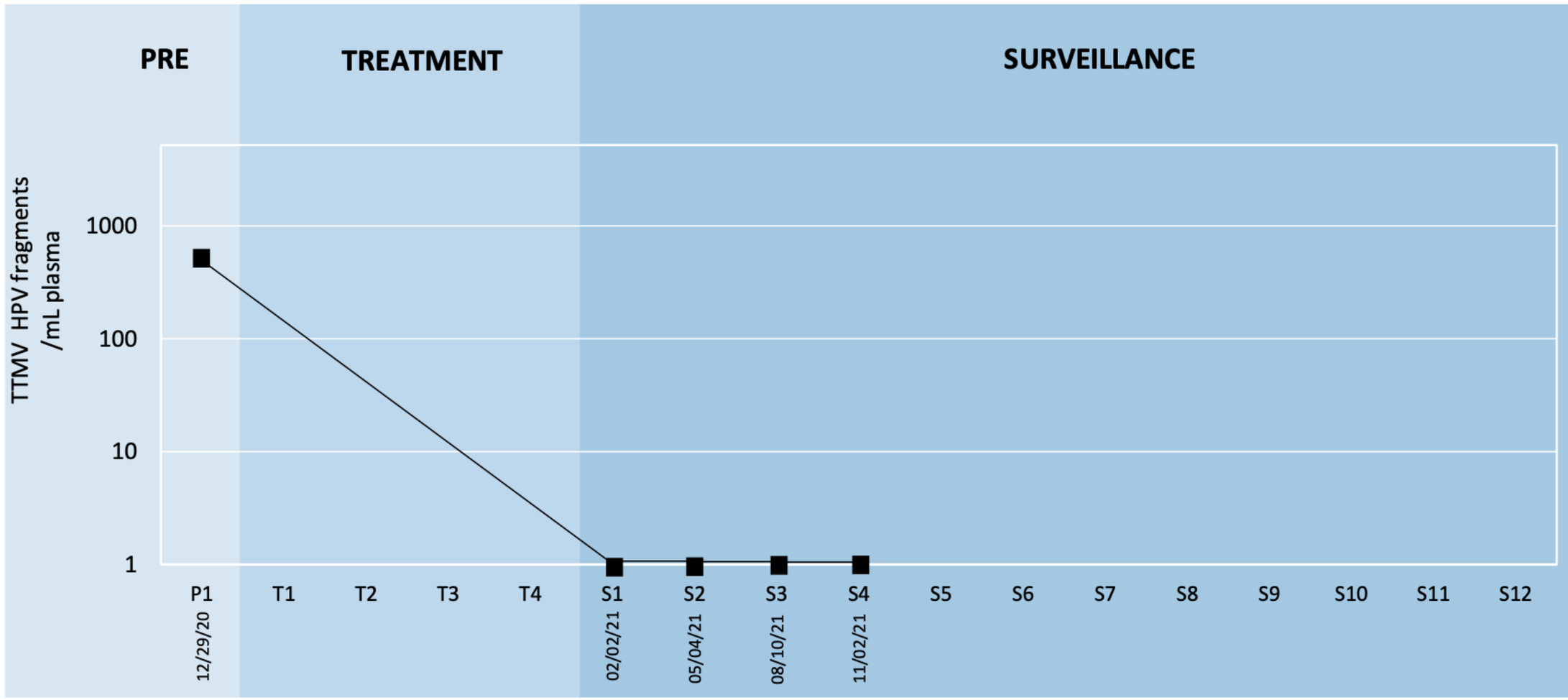
Contact Details

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

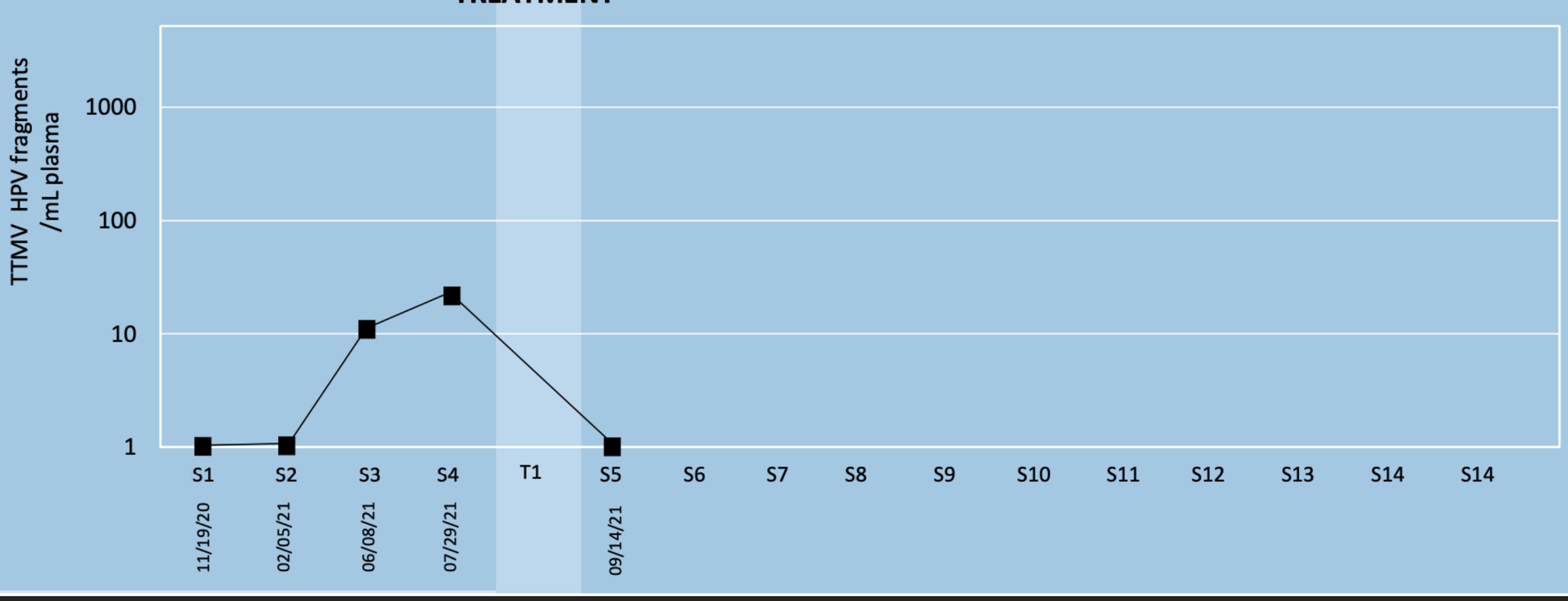
Physician:	John Sims
Facility:	CARTI
Address:	8901 CARTI Way Little Rock, AR 72205, USA
Additional Recipients:	

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

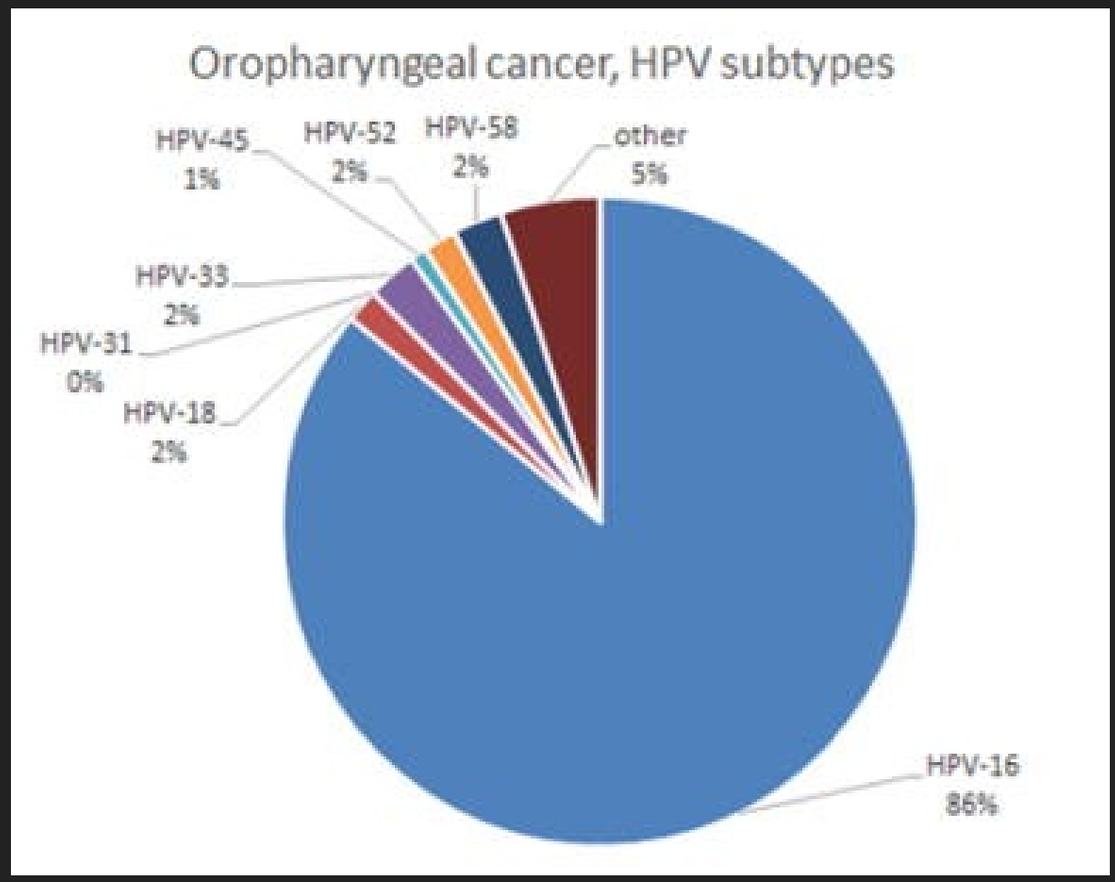
SURVEILLANCE

PRIMARY SURVEILLANCE | **SECONDARY TREATMENT** | **SECONDARY SURVEILLANCE**



PREVENTION

- *Gardasil 9 is now 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

- HPV-related head & neck cancer occurs in the **oropharynx** - most commonly the base of tongue and tonsils
- HPV-related oropharyngeal cancer is **rising in incidence** and is now the most common type of HPV-related cancer
- It most commonly presents as a **painless neck mass** in white males in their 55-75 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?