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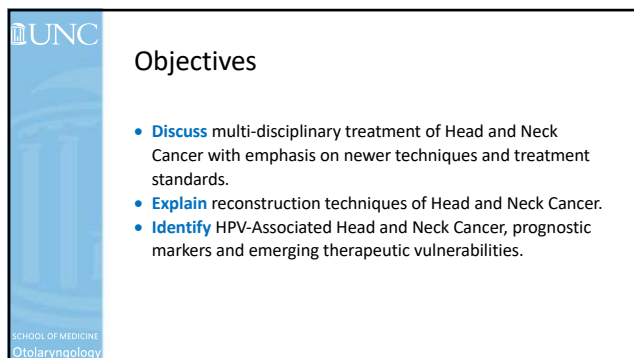
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## Head and Neck Cancer - Overview

- Many in US not aware of HN cancer
- > 60,000 cases per year in U.S.
- Vast majority SCC (squamous cell carcinoma)
- HNC classified by subsites –decreases recognition of problem
 

Larynx  
Oropharynx  
Oral Cavity  
Hypopharynx

Nasopharynx – HPV and EBV associated  
Sinonasal – HPV associated  
Thyroid – WDTC and anaplastic  
Salivary – many histologies
- 2 main molecular subtypes ofHNSCC based on causative agent
  - Tobacco-associated
  - HPV-associated



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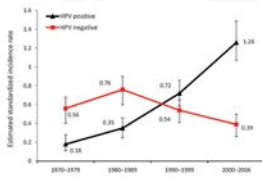
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### Tobacco HNSCC is decreasing HPV+ HNSCC is increasing

- Overall incidence HNSCC decreasing (1973-2004)
  - Associated with trend of decreased tobacco
- Oropharyngeal SCC (OPSCC) increasing
  - Younger patients
  - Decreased or absent traditional risk factors – Tobacco/ETOH
  - Annual change (1973-2004) - 0.8%



Chaturvedi et al. J Clin Oncol. 26:632-639, 2008  
Sturgis et al. Cancer. 115:1425, 2007  
Torjorn Ramqvist & Tina Dallanin



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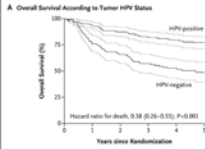
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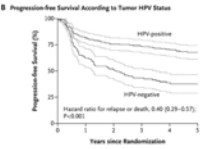
### Survival HPV+ vs. HPV(-) HNSCC

#### A Overall Survival According to Tumor HPV Status



| Years since Randomization | 0   | 1   | 2   | 3   | 4   | 5  |
|---------------------------|-----|-----|-----|-----|-----|----|
| HPV positive              | 206 | 181 | 179 | 165 | 151 | 73 |
| HPV negative              | 117 | 89  | 76  | 63  | 51  | 22 |

#### B Progression-free Survival According to Tumor HPV Status



| Years since Randomization | 0   | 1   | 2   | 3   | 4   | 5  |
|---------------------------|-----|-----|-----|-----|-----|----|
| HPV positive              | 206 | 168 | 155 | 148 | 136 | 65 |
| HPV negative              | 117 | 75  | 59  | 49  | 37  | 15 |

Ang KK et al. N Engl J Med 2010;363:24-35

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### HPV- and tobacco-associated HNSCC are distinct diseases

| HPV(+) HNSCC   | HPV(-) HNSCC   |
|--|--|
| <ul style="list-style-type: none"> <li>- Younger patients</li> <li>- Risk factor                             <ul style="list-style-type: none"> <li>- Sexual transmission of HPV</li> </ul> </li> <li>- More responsive to therapy</li> <li>- ~75-85% cure rate</li> <li>- Conserved gene alterations                             <ul style="list-style-type: none"> <li>- TRAF3, CYLD</li> <li>- E2F1, FGFR3</li> </ul> </li> <li>- Distinct gene expression profile</li> <li>- More methylated genome</li> </ul> | <ul style="list-style-type: none"> <li>- Older patients</li> <li>- Risk factor                             <ul style="list-style-type: none"> <li>- Tobacco, alcohol</li> </ul> </li> <li>- Less responsive to therapy</li> <li>- &lt;50% cure rate (advanced stage)</li> <li>- Conserved gene alterations                             <ul style="list-style-type: none"> <li>- P53, p16, EGFR, FGFR1, cyclin D1, myc</li> </ul> </li> <li>- Distinct gene expression profile</li> <li>- Less methylated genome</li> </ul> |

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### Head and Neck Cancer - Overview

#### Tobacco-associated HNSCC

Occurs at all subsites – OC, larynx most common

Incidence in U.S. is decreasing

- Because smoking decreasing

Advanced tumors poor prognosis

- <50% cure

Treatment modalities

- Surgery
- Radiation +/- concurrent chemotherapy

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
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### Head and Neck Cancer - Overview

#### HPV-associated HNSCC

- Occurs at oropharynx (almost exclusively)
- Incidence in U.S. is increasing
  - Now more than 25% of HNSCC
- Better prognosis than tobacco associated
  - 70-80% cure
- Treatment modalities
  - Surgery
  - Radiation +/- concurrent chemotherapy



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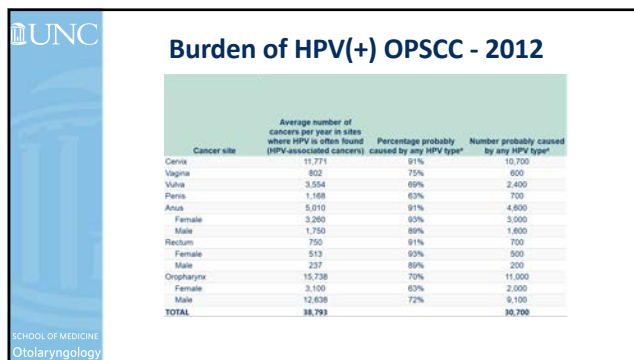
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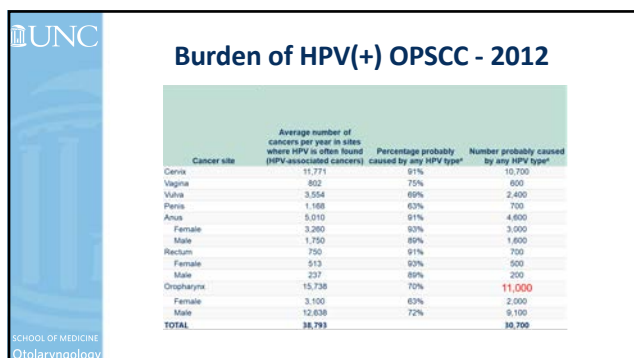
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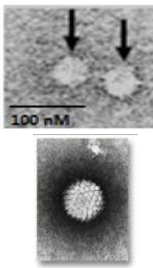
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**HPV Vaccine**

- Prevents CIN of uterine cervix and urogenital condylomas
- Very effective and long lasting
- Currently recommended (9-valent, Gardasil-9) vaccine
  - 7 oncogenic + 2 benign types
  - HPV16
- Decreases oral HPV infection to prevent HNSCC



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### Multi-Disciplinary Care HNSCC

- Includes many groups for patient care
  - OHNS (ENT), Med Onc, Rad Onc, Radiology, Pathology, Oral Medicine, SLP, Nursing (OR, Hospital, Clinic), Nutrition, APPs, Social Work, Navigators, Smoking Cessation, Addiction Services, Pain Management, Schedulers, Respiratory Therapist, Fellows, Residents, etc.
- Associated with improved survival
- Associated with better functional outcomes



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### Division of Head and Neck Oncology

  
Samir Patel, MD, FACS  
Division ChiefTrevor Hackman, MD,  
FACSCatherine Lumley, MDJeffrey Blumberg, MD,  
FACS

  
Mark Weissler, MD, FACSWendell Yarbrough, MD,  
MMHC, FACSTravis Schrank, MD, PhDCatie Voegler, MSPAS, PA-C



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### Head and Neck Medical Oncology

  
Shetal Patel, MD, PhDSiddharth Sheth, MDJared Weiss, MD



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### Head and Neck Radiation Oncology



Bhisham Chera, MD



Colette Shen, MD, PhD



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### Department of Pathology



Susan Maygarden, MD



Fredrick Askin, MD



Danielle Samulski, MD



Bart Singer, MD



Scott Smith, MD



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### Division of Radiology



Valerie Jewell, DO, FACR, FAOCR



Benjamin Huang, MD



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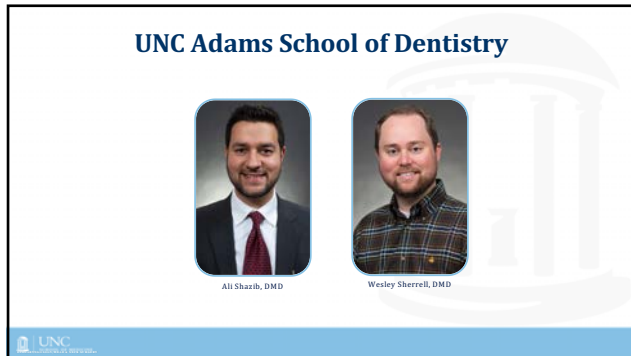
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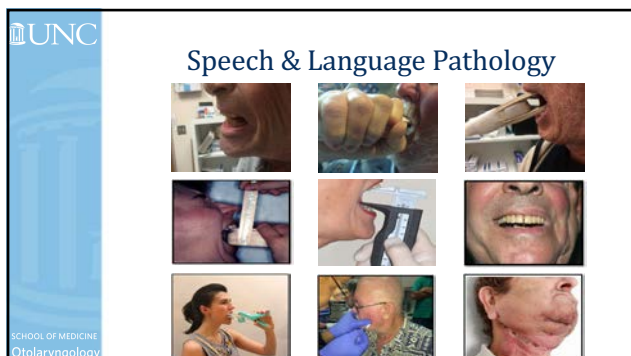
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| Active Therapeutic HNSCC Trials |  |   |   |  |   |
|---------------------------------|--|---|---|--|---|
| Squamous Cell Carcinoma         | ACTIVE TRIALS  |   |   |  |   |
|                                 | Induction  | Definitive  | Adjuvant  | 1L R/M   | ≥2L R/M   |
|                                 | <a href="#">NCT01623416</a><br>(M. Flores / J. Weis)<br>Carboplatin+Durva<br>for induction tx of<br>resectable HNSCC   | <a href="#">NCT01551376</a><br>(S. Green / J. Chao)<br>P53 status<br>and circulating<br>free HPV DNA for<br>management of<br>HPV+ OPSCC | <a href="#">NCT01277276</a><br>(J. Barnes / S. Sheth)<br>Phase I<br>Study of Durva (MEDI<br>4736) with Radiotherapy<br>for the adjuvant<br>treatment of<br>intermediate risk<br>HNSCC     | <a href="#">NCT01709100</a><br>(J. Barnes / S. Sheth)<br>Rando, Ph II/III Trial of<br>RT+Durva vs RT+Cetux in<br>Pts with Locoregionally     | <a href="#">NCT01711007</a><br>(M. Flores / J. Chao)<br>Ph I/II<br>Study of SBTR3<br>Activated SABR Patients<br>w/ any HNSCC or NSCLC |
|                                 | <a href="#">NCT02788277</a><br>(J. Chao)<br>A Phase II trial of the<br>addition of<br>pembrolizumab<br>and olaparib to definitive<br>chemoradiation in locally<br>advanced head and neck<br>squamous cell carcinoma<br>(HNSCC) |   | <a href="#">NCT01613346</a><br>(J. Barnes / S. Sheth)<br>Ph II/III Trial of Adjuvant<br>KRT with Cisplatin vs.<br>Docetaxel-Cetuximab vs.<br>Cisplatin-Atezolizumab in<br>high risk HNSCC | <a href="#">NCT01709100</a><br>(Weiss)<br>Phase II study of HPV-16<br>EG/ET and Pembrolizumab<br>in 1L R/M high risk HPV16<br>HNSCC          | <a href="#">NCT01711007</a><br>(M. Flores / J. Chao)<br>Phase 2 Study<br>Evaluate Efficacy & Safety<br>of Lymphocytes (LN-145)        |
|                                 | <a href="#">NCT01709100</a><br>(J. Chao)<br>Yale SPORE<br>(Yarborough)<br>Window Trial of 5-AZA or<br>Nivo or Nivo+5-AZA in<br>Resectable HPV+ HNSCC   |   |   | <a href="#">NCT01709100</a><br>(J. Garbarino / J. Chao)<br>Phase I Study of<br>Intratumorally<br>administered SL-172154<br>for CSCC and SCCN |   |

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### OHNS RESIDENTS 2020-2021



OHNS RESIDENTS 2020-2021

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### Clinical Fellowships

**Facial Plastics**  
Director: Dr. Madison Clark  
Current Fellow: Deanna Menapace, MD



**Neurotology (2 year)**  
Director: Dr. Kevin Brown  
Current Fellow: A. Morgan Selleck, MD



**Pediatric Otolaryngology**  
Director: Dr. Lauren Kilpatrick



**Rhinology/Skull Base**  
Director: Dr. Charles Ebert  
Current Fellows: Craig Miller, MD  
Justin Morse, MD



**Head & Neck/Microvascular Reconstruction**  
AHNS-accredited  
Director: Dr. Trevor Hackman  
Current Fellow: Andrew Coniglio, MD



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## Goals of Head & Neck Cancer Reconstruction

### Head and Neck Area is Complex

- Functionally important
  - Along with healing, restoration of function is the **first goal**
  - Eating, Breathing, Vision, Facial expression, Talking
- High-value real estate
  - Airway
  - Brain
  - Eyes
  - Lips/nose/eyelids/etc.
  - Tongue
  - Palate
- Cosmetically important area
  - Difficult to cover
  - Scars and deformity visible
  - Nerve defects (facial) obvious
- Many types of tissues required
  - Bone
  - Muscle
  - Epithelia/skin
  - Tendon
  - Nerves



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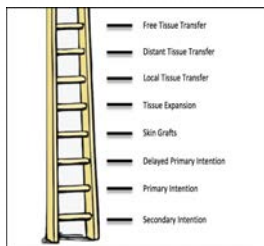
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## Head & Neck Cancer Reconstruction

### Reconstructive Ladder

- Balance between simplicity and results
- Patient considerations
  - Health status and age
  - Need for post-operative radiation
  - Available adjacent tissue and quality
- Type of tissue needed
  - Bone, filler, epithelial lining



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## Skin graft/alloderm



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Local flap – Cross lip



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Regional pedicled flap reconstruction



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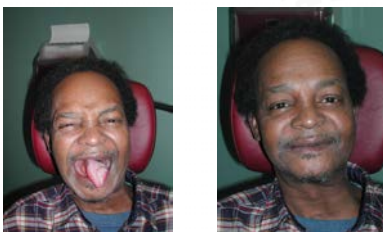
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Post op: Regional flap reconstruction



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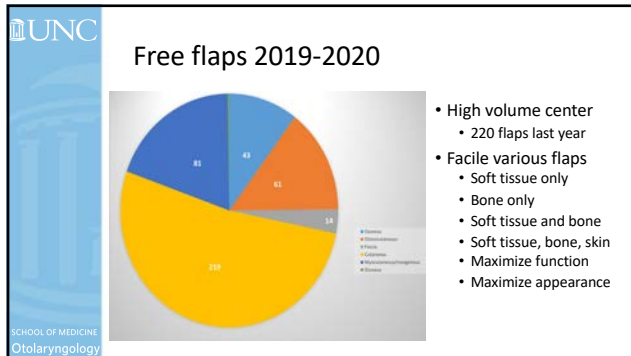
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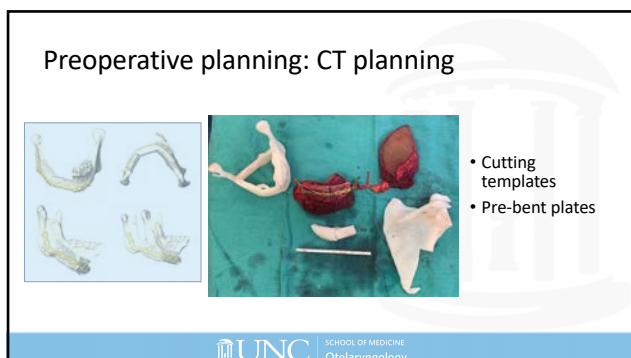
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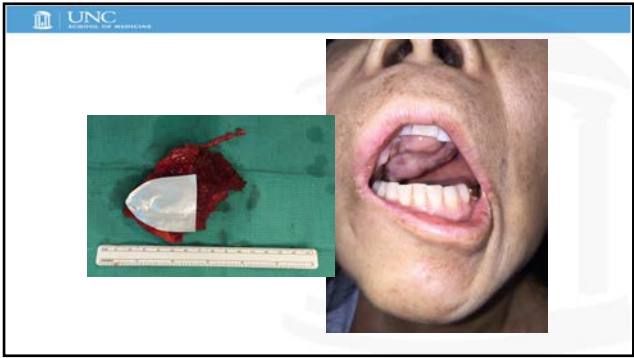
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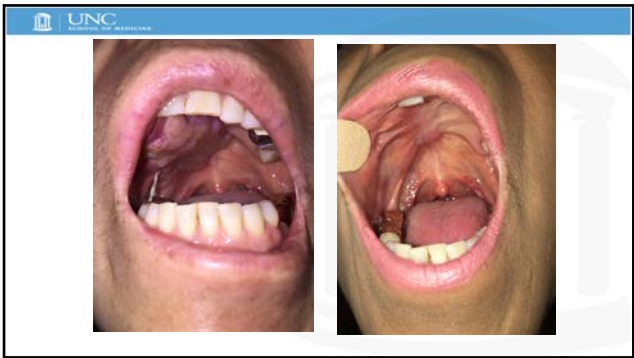
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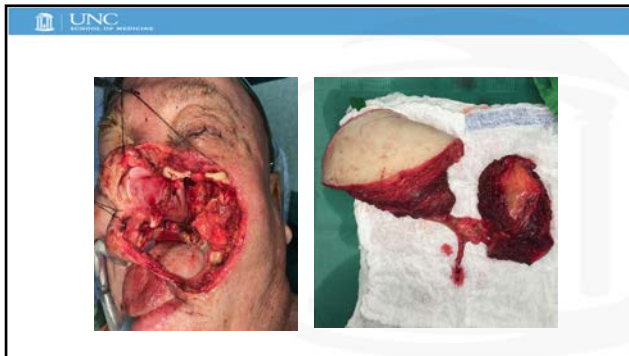
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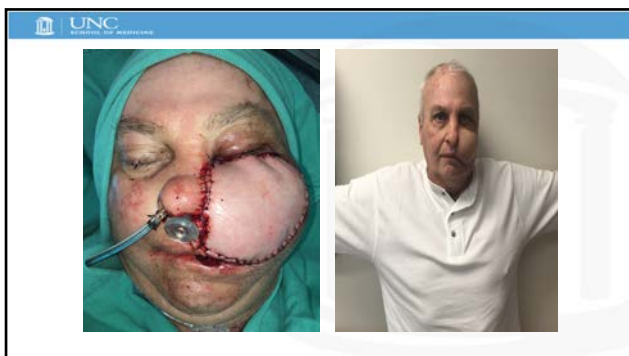
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### Practice Gaps: HPV+ HNSCC

- Identify patients with good or poor outcomes
  - Currently smoking history > 10 pack years
  - Overtreating some patients / Undertreating others?
- How do we safely de-intensify therapy
  - Surgery – TORs with post op therapy guided by path
  - Radiation – decrease dose or fields
  - Neoadjuvant therapy
  - New therapies targeting molecular vulnerabilities
- Early diagnosis of HPV+ HNSCC

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### Practice Gaps: HPV+ HNSCC

- Identify patients with good or poor outcomes
  - Currently smoking history > 10 pack years
  - Overtreating some patients / Undertreating others?
- How do we safely de-intensify therapy
  - Surgery – TORs with post op therapy guided by path
  - Radiation – decrease dose or fields
  - Neoadjuvant therapy
  - New therapies targeting molecular vulnerabilities
- Early diagnosis of HPV+ HNSCC

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### De-escalation of therapy

- Decreasing dose or delivery of chemotherapy and radiation
- Minimizing invasiveness of surgery
  - Transoral robotic surgery (TORS)
- No prognostic markers to choose patients for de-escalation therapy

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### TORS for OP cancer



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### TORS: Operative view



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### HPV+ OPSCC: Post TORS



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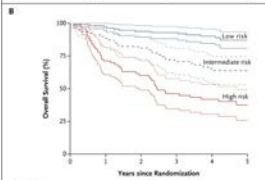
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### Smoking history is only indicator of survival HPV+ HNSCC



|                   | 0   | 1   | 2   | 3   | 4  | 5  |
|-------------------|-----|-----|-----|-----|----|----|
| No. at Risk       | 114 | 111 | 106 | 102 | 95 | 46 |
| Low risk          | 79  | 70  | 64  | 54  | 44 | 24 |
| Intermediate risk | 79  | 70  | 64  | 54  | 44 | 24 |
| High risk         | 79  | 70  | 64  | 54  | 44 | 24 |

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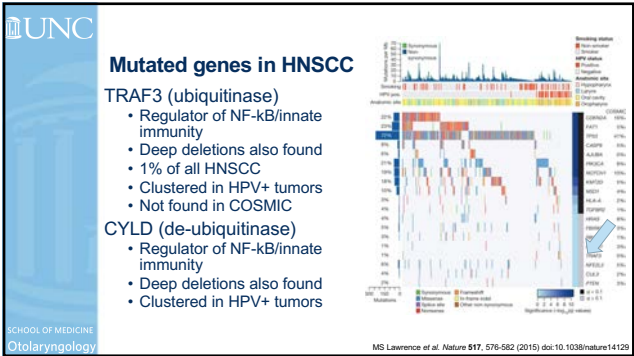
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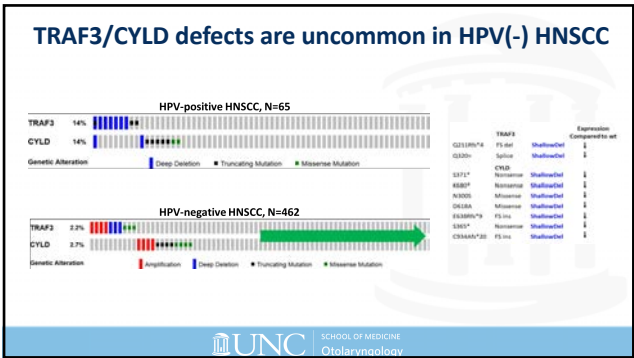
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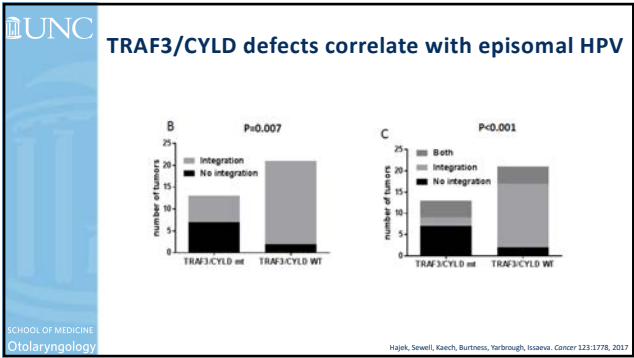
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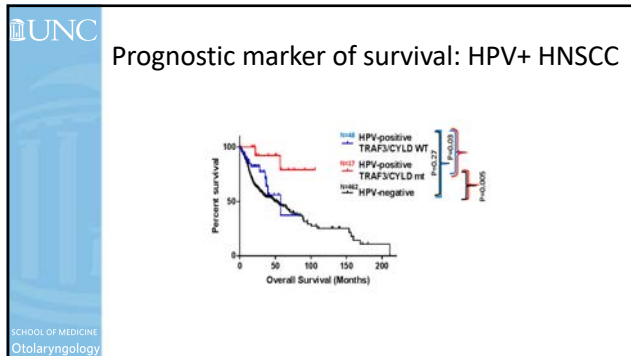


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Salivary Cancer

Many types of salivary tumors

- 1<sup>st</sup> goal to remove tumor
  - 2<sup>nd</sup> goal preserve facial function
  - 3<sup>rd</sup> goal scar and contour

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Salivary Cancer

- Many tumor types
- 1<sup>st</sup> goal to remove tumor
  - 2<sup>nd</sup> goal preserve facial function

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### Salivary Cancer

- Many tumor types
- 1<sup>st</sup> goal to remove tumor
  - 2<sup>nd</sup> goal preserve facial function
- But appearance important
- Typical neck face incision
  - Scar and soft tissue defect

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### Salivary tumors/cancer

- Facelift incision

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### Salivary tumors/cancer

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Salivary tumors/cancer



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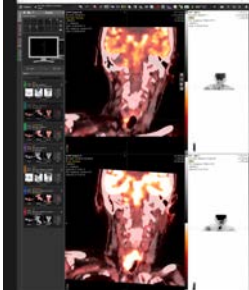
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UNC Anaplastic Thyroid

- Most aggressive thyroid cancer
- Rare, but more than 50% of thyroid cancer mortality
  - mOS 6 mos
- Associated with invasion of airway

**Targeted therapy if BRAF mutant**

- 45% BRAF mutant
- MEKi + BRAFi Therapy for unresectable or distant metastases
- Continue therapy until resectable



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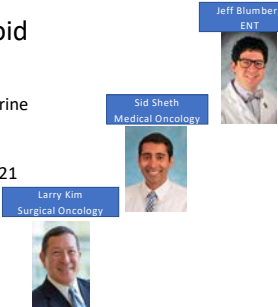
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UNC Anaplastic Thyroid

- Integrated clinical and research team
- Multi-disciplinary endocrine tumor board
- Clinical trial opening for advanced disease Q2 2021



Jeff Blumberg  
ENT

Sid Sheth  
Medical Oncology

Larry Kim  
Surgical Oncology

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### UNC Head & Neck Oncology Lab

Natalia Isaeva

Gary Bellinger

Hina Rehmani

Damir Alzhanov

Travis Schrank

Andrew Prince

Wesley Stepp

Vaccine/Immunology/Therapy

Blossom Damania

John Serody

Jared Weiss

Wesley Stepp

Alison McBride

Cary Moody

UNC HN Surgery

Samip Patel

Mark Weissler

Trevor Hackman

Jeff Blumberg

Catherine Lumley

Travis Schrank

NF-κB

Albert Baldwin

Marty Mayo

p53

Yue Xiong

Jennifer Pietenpol

Weaver Lab

Previous Lab Members

Xinyuan Lu

Hanbing An

Amy Whigham

Jonathan Law

Jialiang Wang

Adam Zanation

Brandee Brown

Carol Shores

Asel Biktasova

Michael Chang

Bea Carbone

Kathy Yu

Jonathan Moss

Yale Head & Neck and SPORE

Barbara Burtress

Karen Anderson

Joseph Contessa

Mark Lemmon

Benjamin Judson

Saral Mehra

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#10 ranked ENT department in the NATION

#1 ranked program in the Southeastern U.S.

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Otolaryngology

BEST HOSPITAL

University of North Carolina Hospitals ranked #1 in 6 adult specialties and 4 pediatric specialties

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