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Oral Cavity Squamous Cell Carcinoma:  
Update in Staging & Treatment Recommendations

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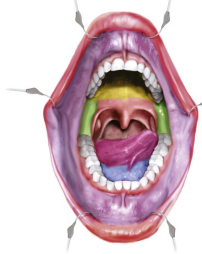
**Objectives**

- Overview of oral cavity anatomy & subsites
- Risk factors for oral cavity cancer
- Review AJCC 8<sup>th</sup> edition staging
- Treatment algorithms for oral cavity cancer
  - What is an adequate margin?
  - Who needs a neck dissection?

Poll #1

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**Anatomy of the Oral Cavity**



- 7 subsites of the oral cavity
- Oral tongue and base of tongue separated by **circumvallate papillae**
- Most common oral cavity cancer subsite?
  - Lips
  - (2<sup>nd</sup> most common is oral tongue)
- Least common oral cavity cancer subsite?
  - Buccal mucosa


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**Benign findings in the oral cavity**



**Geographic tongue –**

- “benign migratory glossitis”
- Loss of epithelium on the filiform papillae
- May be assoc with lower levels of salivary zinc



**Fissured tongue –**

- Benign finding
- May be associated with “burning” sensation
- Also may be assoc with zinc deficiency, or b12/folate


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**Benign findings in the oral cavity**



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**Malignancies in the oral cavity**



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### Oral cavity squamous cell carcinoma

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### Current prevalence of oral cavity cancer in the US

- Overall decline in oral cavity cancer incidence in the last few decades, largely due to decrease in tobacco use
- Unexplained increasing incidence in females, particularly < 40 years old
- Specifically oral tongue cancer incidence is increasing in younger individuals, without clear etiology
  - HPV DNA has not been readily detected in oral tongue cancers, unlike in oropharyngeal scc

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### Frequency of HPV in oral cavity squamous cell carcinoma

Priscilla Marinho de Abreu<sup>1</sup>, Anna Clara Gregório Co<sup>2</sup>, Pedro Leite Azevedo<sup>3</sup>, Isabella Bittencourt do Valle<sup>4</sup>, Natine Gadoli de Oliveira<sup>5</sup>, Sônia Alves Gouveia<sup>6</sup>, Melissa Freitas Cordero-Silva<sup>7</sup>, Siri Drummond Louro<sup>8</sup>, José Roberto Vasconcelos de Pódesta<sup>9</sup>, Jefferson Lera<sup>9</sup>, Agenor Sena<sup>9</sup>, Elisnauro Francisco Mendonça<sup>9</sup> and Sandra Lígia Viestorini von Zastler<sup>10</sup>

- Investigated the frequency of high-risk HPV in oral cavity SCC patients
- HPV DNA detected via PCR
- 90 specimen examined
- Only 3 tumors were positive for HPV via PCR (3.3%)

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### Low etiologic fraction for high-risk human papillomavirus in oral cavity squamous cell carcinomas

Mark W. Lingen<sup>1</sup>, Weihong Xiao<sup>2</sup>, Alessandra Schmitt<sup>3</sup>, Bo Jiang<sup>4</sup>, Robert Pickard<sup>5</sup>, Paul Kreinbrink<sup>6</sup>, Bayardo Perez-Ordóñez<sup>7</sup>, Richard C. Jordan<sup>8</sup>, Maura L. Gillison<sup>9,10</sup>

<sup>1</sup>Department of Pathology, University of Chicago, Chicago, IL, United States  
<sup>2</sup>Oral Oncology, The Ohio State University Comprehensive Cancer Center, Columbus, OH, United States  
<sup>3</sup>Department of Pathology, The Ohio State University Medical Center, Columbus, OH, United States  
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<sup>5</sup>Department of Otolaryngology, Pathology & Radiation Oncology, University of California San Francisco, San Francisco, CA, United States

- Retrospective case series to estimate the etiologic fraction of HPV in oral cavity SCC
- All tumors evaluated for p16 via immunohistochemistry (surrogate biomarker for HPV E7 oncoprotein function), but also for HPV DNA via in situ hybridization
- Results (n=409):
  - HR-HPV (high-risk HPV) E6/E7 expression found in 6% of cases
  - P16 did not serve as an appropriate surrogate diagnostic biomarker in the oral cavity (pos predictive value of ~40%)

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### Risk factors for oral cavity squamous cell carcinoma

- Tobacco use
- Heavy alcohol use
- Sun exposure (lip cancers)
- Betel nut chewing
- Immune-deficiency
- Periodontal disease or poor oral hygiene

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### Epidemiology of Head and Neck Squamous Cell Cancer Among HIV-Infected Patients

Gypsyamber D'Souza, PhD<sup>1</sup>, Thomas E. Carey, PhD<sup>2</sup>, William N. William Jr., MD<sup>3</sup>, Minh Ly Nguyen, MD<sup>4</sup>, Eric C. Ko, MD, PhD<sup>5</sup>, James Riddell IV, MD<sup>6</sup>, Sara I. Pai, MD, PhD<sup>7</sup>, Vishal Gupta, MD<sup>8</sup>, Heather M. Wallace, MS<sup>9</sup>, J. Jack Lee, PhD<sup>9</sup>, Gregory T. Wolf, MD<sup>9</sup>, Dong M. Shin, MD<sup>10</sup>, Jennifer R. Grandis, MD<sup>11</sup>, and Robert L. Ferris, MD, PhD<sup>11</sup> on behalf of the IHC SPORE HIV supplement consortium

- HIV-infected individuals known to have higher oral HPV infection (2-7% as opposed to 1% of gen pop) and higher incidence of HN cancer (2-3x)
- Case series of 94 HIV+ patients with HN cancer
  - Survival worse with CD4 <200 (median survival 16.1 vs 72.8 months)
  - Those with HPV+ tumors had higher CD4 counts, but all with history of low nadir CD4 cell counts (suggesting immunosuppression may have role EARLY in cancer process??)

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### Cancer

#### Risk of Oral Tongue Cancer Among Immunocompromised Transplant Recipients and Human Immunodeficiency Virus-Infected Individuals in the United States

Joseph E. Tota, PhD; Eric A. Engels, MD, MPH; Margaret M. Madeleine, PhD; Christina A. Clarke, PhD, MPH; Charles F. Lynch, MD, PhD; Ana P. Ortiz, PhD, MPH; Brenda Y. Hernandez, PhD, MPH; and Anil K. Chaturvedi, PhD

- Assessed risk of oral tongue cancer in 2 populations: **solid organ transplant & HIV-infected**
- They question if **immunosuppression (and a virally-induced tumor) may explain the increase in incidence of oral cavity ca** we are seeing in younger individuals
- Modest elevation** of SCC in transplant and HIV patients (standardized incidence ratio of ~2-3) -- **can not conclude that infection or exposure due to immunosuppression plays a profound role in the increase in oral tongue cancers we see epidemiologically.**

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### Chronic Periodontitis and the Risk of Tongue Cancer

Mine Tezal, DDS, PhD; Maureen A. Sullivan, DDS; Mary E. Reid, PhD; James R. Marshall, PhD; Andrew Hyland, PhD; Thom Loree, MD; Cheryl Lillis, BS; Linda Hauck, BA; Jean Wactawski-Wende, PhD; Frank A. Scannapieco, DMD, PhD

- Alveolar bone loss measured on panorex, representing chronic periodontitis
- Presence of alveolar bone loss (ABL) on radiograph suggests chronic disease, i.e. must have been present prior to cancer diagnosis
- ABL associated with risk of tongue cancer (OR 5.23, p<0.001)
- ABL remained significant independent of smoking status

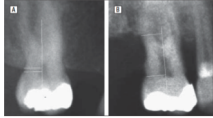
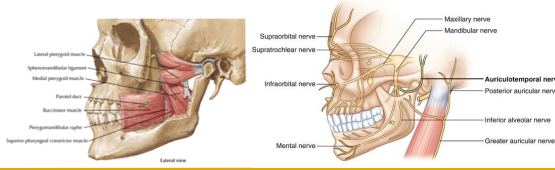


Figure. Illustration of the alveolar bone loss (ABL) measurements. A, radiograph depicting a molar tooth with no periodontitis history (ABL = 0.0 mm). B, radiograph depicting a molar tooth with severe periodontitis history (ABL = 7.31 mm).

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### Common presenting symptoms

- Painful ulcer / mass
- Difficulty chewing or eating
- Bleeding
- Weight loss
- Dysarthria
- Trismus
- Ear pain



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### Work-up of presumed oral cavity squamous cell carcinoma

- H&P<sup>a,b</sup> including a complete head and neck exam; mirror and fiberoptic examination as clinically indicated
- Biopsy<sup>c</sup>
- Quantify pack-years smoked, and advise all users to quit smoking.
- Screen for depression
- T3/T4 primary or ≥N1 nodal – PET/CT preferred
- Panorex recommended for oral cavity cancers requiring mandibulectomy or mandibulectomy, and also when post-op radiation is anticipated

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### Primary Tumor Staging for Oral Cancer and a Proposed Modification Incorporating Depth of Invasion

#### An International Multicenter Retrospective Study

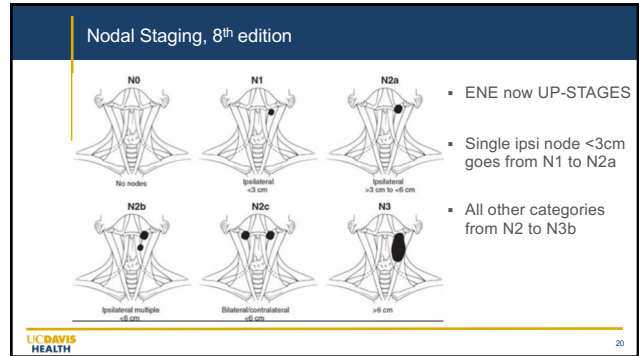
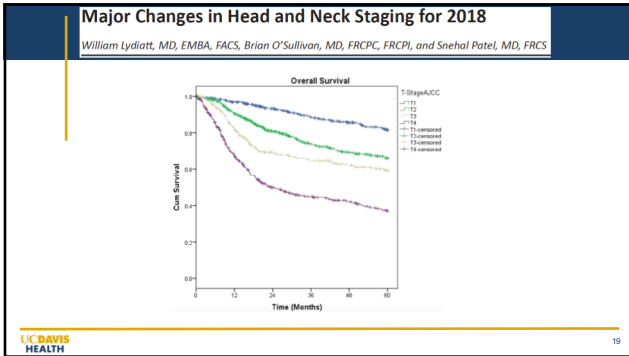
- AJCC 8<sup>th</sup> edition changes in staging was largely based on this multicenter retrospective study
- 3149 patients** with oral scc retrospectively evaluated from 11 cancer centers
- Assessed **DOI impact on disease-specific and overall survival** using multiple candidate staging systems
- Importantly also found that **tumor size** (AJCC 7<sup>th</sup> edition) was an **independent significant predictor of survival** after controlling for DOI

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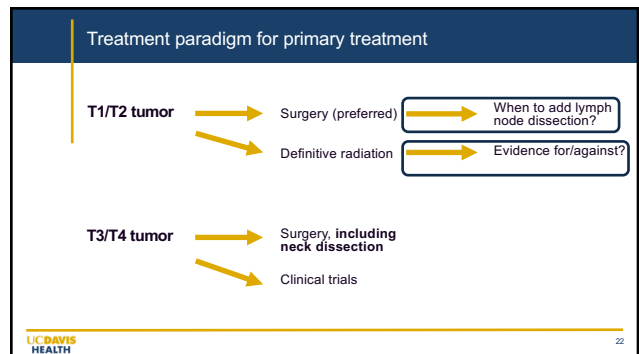
### AJCC 8<sup>th</sup> Edition – Staging Oral Cavity Cancers

T Category	T Criteria
Tx	Primary tumor cannot be assessed
Tis	Carcinoma in situ
T1	Tumor ≤2 cm, ≤5 mm DOI
T2	Tumor >2 cm, ≤5 mm DOI, or tumor >2 cm but ≤4 cm, and ≤10 mm DOI
T3	Tumor >4 cm or any tumor >10 mm DOI
T4	Moderately advanced or very advanced local disease
T4a	Moderately advanced local disease: (lip) tumor invades through cortical bone or involves the inferior alveolar nerve, floor of mouth, or skin of face (i.e., chin or nose); (oral cavity) tumor invades adjacent structures only (e.g., through cortical bone of the mandible or maxilla, or involves the maxillary sinus or skin of the face); note that superficial erosion of bone/tooth socket (alone) by a gingival primary is not sufficient to classify a tumor as T4
T4b	Very advanced local disease: tumor invades masticator space, pterygoid plates, or skull base and/or encases the internal carotid artery

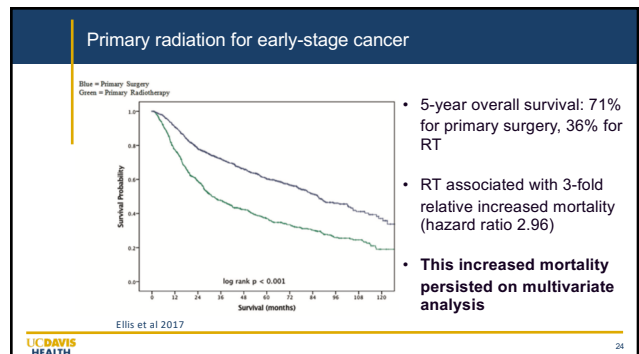
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- ### Nodal Staging, 8<sup>th</sup> edition
- Nx – cannot assess
  - N0 – no regional LN metastases
  - N1 – single, ipsilateral node,  $\le 3\text{ cm}$ , NO ENE
  - N2a – single, ipsilateral node  $\le 3\text{ cm}$  with ENE**, OR single node  $> 3$  but  $< 6\text{ cm}$ , no ENE
  - N2b – multiple, ipsilateral, all  $< 6\text{ cm}$ , no ENE
  - N2c – bilateral or contralateral, all  $< 6\text{ cm}$ , no ENE
  - N3a -  $> 6\text{ cm}$ , no ENE
  - N3b – single node  $> 3\text{ cm}$  with ENE**, or presence of multiple/contralateral/bilateral with ENE
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- ### Primary radiation for early-stage cancer
- Original Research—Head and Neck Surgery
- #### Primary Surgery vs Radiotherapy for Early Stage Oral Cavity Cancer
- Mark A. Ellis, MD<sup>1</sup>, Evan H. Graboyes, MD<sup>1</sup>, Amy E. Wollquist, MS<sup>1</sup>, David M. Neskey, MD<sup>1</sup>, John M. Kaczmar, MD<sup>1</sup>, Heather K. Schopper<sup>1</sup>, Anand K. Sharma, MD<sup>1</sup>, Patrick R. Morgan, MD<sup>1</sup>, Shaun A. Nguyen, MD<sup>1</sup>, and Terry A. Day, MD<sup>1</sup>
- National Cancer Database (NCDB) study
  - Identified 20,779 patients with stage 1/2 oral cavity cancer treated with either primary surgery or primary RT – 4.6% underwent primary RT
  - Factors identified with receiving non-preferred treatment
    - No insurance or public insurance (Medicaid or Medicare)
    - Age  $> 70$
    - Black race
    - Non-tongue subsite
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### IMRT in oral cavity cancer

Gabriela Studer<sup>1</sup>, Roger A Zwahlen<sup>2</sup>, Klaus W Graetz<sup>2</sup>, Bernard J Davis<sup>1</sup> and Christoph Glanzmann<sup>1</sup>

Address: <sup>1</sup>Department of Radiation Oncology, University Hospital Zurich, Rämistrasse 100, 8091 Zurich, Switzerland and <sup>2</sup>Department of Cancer-Surgical Surgery, University Hospital Zurich, Switzerland.  
Email: Gabriela Studer - gabriela.studer@usz.ch, Roger A Zwahlen - zwahlen@zank.unizh.ch, Klaus W Graetz - graetz@zank.unizh.ch, Bernard J Davis - bernard.davis@usz.ch, Christoph Glanzmann - christoph.glanzmann@usz.ch

- Assessed whether IMRT (as opposed to conventional 3D-CRT) resulted in improved locoregional control as primary treatment for oral cavity cancer

- 30 total patients underwent definitive IMRT
  - 6 T2
  - 3 T3
  - 12 T4
  - 9 treated for a recurrence
- 2-year local control 43%; disease-free survival 40% in definitive IMRT group
  - Significantly worse than adjuvant IMRT group (n=28) with local control rate 92% and disease-free survival 87%

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### Surgical approach for oral cavity squamous cell carcinoma

- Goal as a surgeon is to perform the best possible resection to hopefully *avoid adjuvant treatment* / additional toxicity for our patients
- Out of our control: ENE, PNI, LVI, etc.
- What we can control:
  - Adequate margins

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### Post-Resection Mucosal Margin Shrinkage in Oral Cancer: Quantification and Significance

RAJESH C. MISTRY, MS,\* SAJID S. QURESHI, MS, DNB, AND C. KUMARAN, MS, FRCS  
Department of Surgical Oncology, Tata Memorial Hospital, Ernest Borges Road, Patel, Bombay, India

- Included 27 patients with tongue and buccal mucosa cancer
- Measured in situ margin versus 30 minute post-resection margin
  - Placed suture at tumor edge & a second one at the margin
  - Measured in situ & compared this to the distance measured 30 minutes post-resection
- Noted significant "margin shrinkage" of 23.5% for tongue and 21.2% for buccal tumors

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### Tissue shrinkage

Table 2: Degree of shrinkage of surgical margins obtained from different anatomical sites

Authors (year)	Sample size	Sample Site	Shrinkage (%)
Mistry <i>et al.</i> , 2005 <sup>24</sup>	27	Buccal mucosa	21.2
		Tongue	23.5
Cheng <i>et al.</i> , 2008 <sup>25</sup>	41	Buccal mucosa, mandibular alveolar ridge, retromolar trigone	71.90
		Maxillary alveolar ridge and palate	53.33
		Tongue	42.14
El-Fol <i>et al.</i> , 2015 <sup>26</sup>	61	Buccal mucosa	66.7
		Tongue	35
		Floor of mouth	33.3
		Retromolar trigone	16.7
		Mandibular alveolus	15.4

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### Surgery for oral cavity squamous cell carcinoma

- Wide resection with **adequate margin** of normal tissue
  - What is defined as an adequate margin in the oral cavity?
  - Historically 5 mm
  - Recent data suggests margin of at least 1 mm is sufficient

- 423 patients retrospectively reviewed
- Tumor subsite:
  - 45% oral tongue
  - 21% alveolar ridge
  - 18% floor of mouth
  - 15% "other"

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### A Proposal to Redefine Close Surgical Margins in Squamous Cell Carcinoma of the Oral Tongue

JAMA Otolaryngology-Head & Neck Surgery | Original Investigation  
Daniella Karassawa Zanoni, MD, Jocelyn C. Migliacci, MA, Bin Xu, MD, PhD, Nora Katabi, MD, Pablo H. Montero, MD, Ian Garly, MD, PhD, Jatin P. Shah, MD, Richard J. Wong, MD, Ronald A. Gosssein, MD, Snehil G. Patel, MD

- Retrospective review of archived tumor specimen (n=381)
- Optimal cutoff associated with local recurrence free survival was 2.2mm
  - Patients with margin of 2.3 to 5 mm had similar LRFS as those with margin >5mm

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**Buccal mucosa carcinoma: surgical margin less than 3 mm, not 5 mm, predicts locoregional recurrence**

Shan-shen Zhou<sup>1</sup>, Han-yu Lin<sup>1,2</sup>, Feng-Chun Huo<sup>1</sup>, Moon-Sing Lee<sup>1,2</sup>, Hsu-Chueh Ho<sup>1</sup>, Yu-Chieh Su<sup>1</sup>, Chang-Chih Yen<sup>1</sup>, Cheen-Wei Hsu<sup>1</sup>, You-Cheng Wang<sup>1,2</sup>, Shyh-Jia Huang<sup>1,2</sup>

- Retrospective review of 134 patients with buccal carcinoma (110 included who received definitive surgery)
  - Only 29% (32/110) received surgery alone

While this refers to mucosal margins, others suggest radical surgery for buccal tumors as there is **not a great barrier for spread**

Theory: once tumor has encroached up on the buccinator muscle -> can easily infiltrate surrounding tissue

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**SQUAMOUS CELL CARCINOMA OF THE BUCCAL MUCOSA: ONE INSTITUTION'S EXPERIENCE WITH 119 PREVIOUSLY UNTREATED PATIENTS**

Eduardo M. Diaz, Jr., MD, FACS,<sup>1</sup> F. Christopher Holsinger, MD,<sup>1</sup> Edgar R. Zuniga, MD,<sup>2</sup> Diana B. Roberts, PhD,<sup>3</sup> Douglas M. Sorensen, MD<sup>2</sup>

- 119 patients included with buccal squamous cell carcinoma
  - 71% surgery alone; 22% adjuvant radiation, and 13% preop radiation

Overall 5 yr survival: ~63%

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**Nodal staging & Survival in buccal cancers**

- Presence of **regional mets** at time of **presentation increased mortality** (5 yr survival 70% vs. 49%)

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**Recurrence after buccal cancer treatment**

- 54 patients (45%) recurred, median time to recurrence = 8 mths (2-120 mths range)
- Buccinator muscle invasion, proximity to stenson's duct also had no significant effect on survival / locoregional control
- There was no statistically significant difference between T stage and survival**
- Salvage therapy successful in only 12 (22%) of patients w/ recurrences

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**Unit resection of buccal squamous cell carcinoma: Description of a new surgical technique**

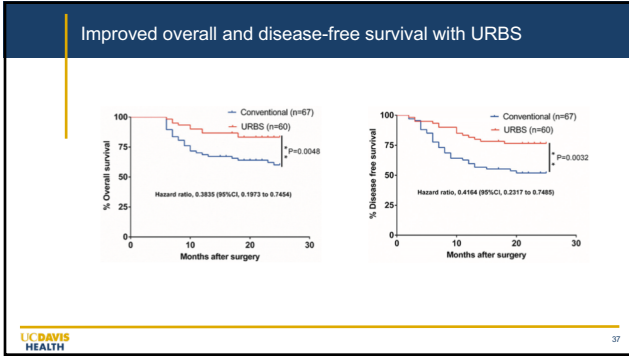
Zhen-Hu Ren<sup>1,2</sup>, Zhao-Jian Gong<sup>1</sup> and Han-Jiang Wu<sup>1</sup>

- Due to high recurrence rates of buccal tumors (33-57% reported), suggest a wide/unit resection
- Named a new approach, "Unit resection buccal surgery" (URBS) and compared this to conventional resection with (3-5mm margins)

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**Example of URBS**

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### Does Buccal Cancer Have Worse Prognosis Than Other Oral Cavity Cancers?

P. Ryan Camilon, BA; William A. Stokes, BS; Colin W. Fuller, MD, MS; Shaun A. Nguyen, MD, MA; Eric J. Lentzsch, MD

- SEER database study, identified 11,134 patients with oral cavity SCC – 825 buccal cancers (7.41%)
- Buccal cancer patients more likely to be **older** and **fewer presented with stage 1 tumors**
- Case-matched buccal cancers to other subsites of oral cavity and ended up with **817 matched pairs**

### Unmatched OS and DSS differences

Site	OS	Cumulative Survival
Oral	2-year	66.80%
	5-year	51.10%
Buccal	2-year	60.90%
	5-year	44.10%

- Appears that buccal SCC has worse OS & DSS than other oral cavity subsites
- P < 0.001

### Matched OS and DSS differences

Site	OS	Cumulative Survival
Oral	2-year	64.20%
	5-year	48.10%
Buccal	2-year	60.90%
	5-year	44.10%

- When controlled for age, stage, treatment, race, **significance was lost**
- P=0.113 for OS
- P=0.184 for DSS

### Treating the primary site

We mark out 1cm margins but **hope for at least 2mm margins** on final pathology (1mm considered “close” margin)

- Take into account possibility of “tissue shrinkage”

Buccal tumors historically thought to have worse prognosis than other subsites of oral cavity

- More rare in the US
- Overall & disease free survival appear to be driven by presence of nodal disease

### What about the neck?

#### ELECTIVE NECK DISSECTION FOR THE MANAGEMENT OF THE NO NECK IN EARLY CANCER OF THE ORAL TONGUE: NEED FOR A RANDOMIZED CONTROLLED TRIAL

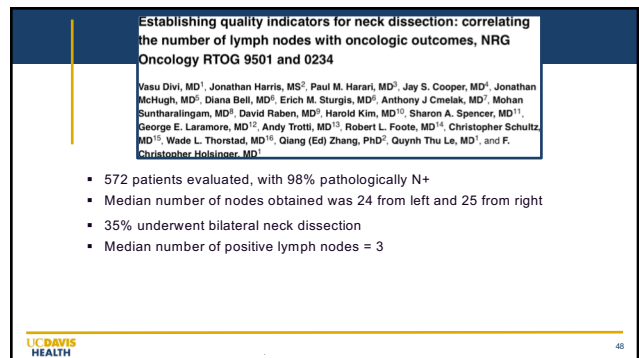
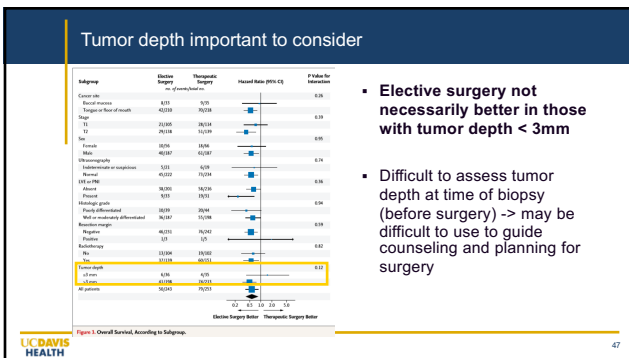
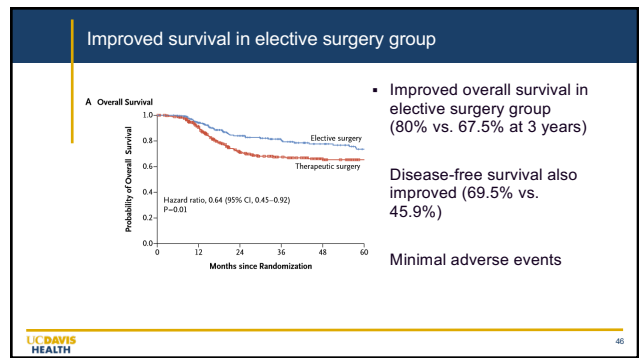
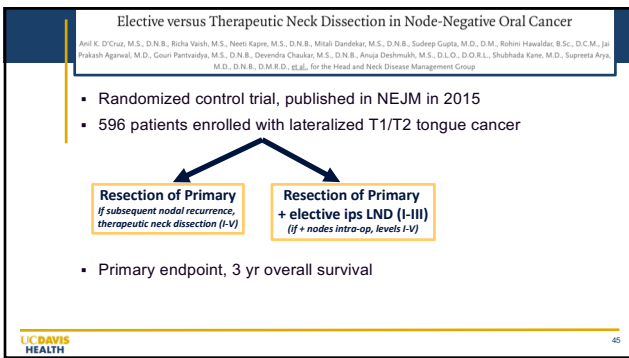
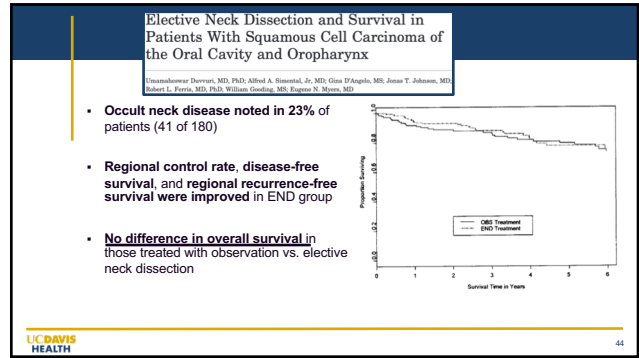
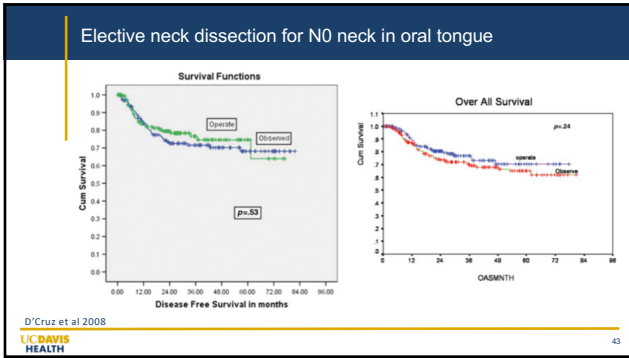
Anil K. D'Cruz, MS, DNB,<sup>1</sup> Ravichand C. Siddachari, MS, DNB, MRCS,<sup>1</sup> F. Gouri H. Pentvaliyil, MS, DNB, MRCS,<sup>1</sup> Devenendra A. Chaukar, MS, DNB, Mander S. Deshpande, MS, DNB,<sup>1</sup> Prithvishesh S. Pai, MS, DNB,<sup>1</sup> Parulak

**Table 1. Tumor characteristics: WW group versus END group.**

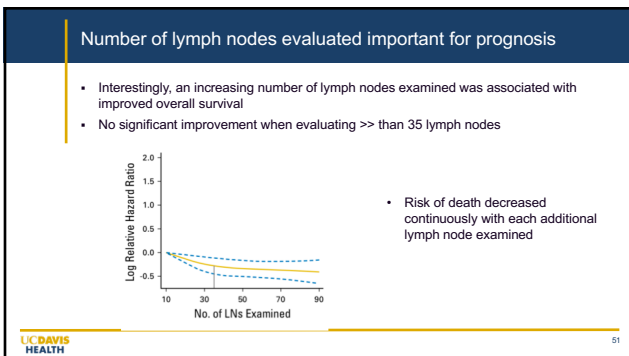
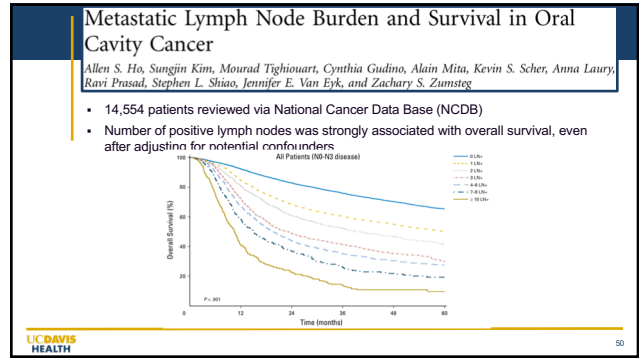
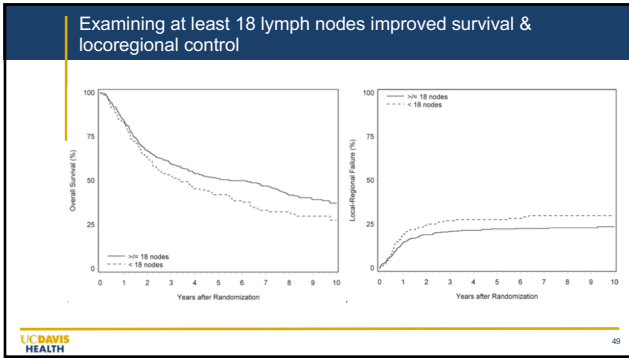
	WW group	END group
Tumor size		
T1	118 (59%)	69 (43.4%)
T2	82 (41%)	90 (56.6%)
Grade of differentiation		
Well differentiated	48 (24%)	30 (18.9%)
Moderately differentiated	132 (66%)	109 (66.6%)
Poorly differentiated	20 (10%)	20 (12.6%)
Perineural invasion		
No	181 (90.5%)	145 (91.2%)
Yes	19 (9.5%)	14 (8.8%)
Tumor thickness (mm) <sup>a</sup>		
≤4	217 (82.2%)	131 (83.2%)
>4	47 (17.8%)	26 (16.8%)
≤4	57 (18.0%)	50 (32.2%)
Surgical margins		
Positive	7 (3.5%)	4 (2.5%)
Negative	154 (76.5%)	146 (91.5%)
Close	9 (4.5%)	9 (5.7%)

Abbreviations: WW, well and watch; END, elective neck dissection. <sup>a</sup>Tumor thickness was unavailable in 14 patients.

- Lack of consensus** in otolaryngology community re: elective neck in **clinically N0 neck** for early stage tongue cancer
- Retrospective review** of 359 patients with T1/T2 tongue tumors who underwent either elective neck or watchful waiting
  - 200 in the WW group, 159 underwent END







### Sentinel Lymph Node Biopsy in N0 Squamous Cell Carcinoma of the Oral Cavity and Oropharynx

Robert D. Hart, MD; Joseph G. Nasser, MD, DDS; Jonathan R. Trites, MD; S. Mark Taylor, MD; Martin Balloch, MD; David Barnes, MD

- Study from 2005 assessing feasibility of sentinel lymph node biopsy for oral cavity/oropharyngeal cancer
- 20 patients enrolled
- Area surrounding tumor was infiltrated with technetium-99 sulfur colloid (radioactive tracer)

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### Table. Sentinel Lymph Node (SLN) Biopsy Study Results

Patient No.	Tumor Site	Tumor Stage	Location of SLN	SLN Histopathologic Status	Histopathologic Status of Neck Dissection* (No. of Nodes)
1	Buccal mucosa	T2	Level I	Negative	Negative (9/16)
2	Buccal mucosa	T4	Level I	Negative	Negative (9/5)
3	Retromolar trigone	T2	Level II	Negative	Negative (9/25)
4	Buccal mucosa	T2	Level III	Positive	Negative (9/24)
5	Tonsillar fossa	T1	Level II	Negative	Negative (9/15)
6	Floor of mouth	T3	Level I	Negative	Negative (9/31)
7	Buccal mucosa	T1	Level I	Negative	Negative (9/40)
8	Lateral tongue	T3	Level II	Positive	Negative (9/18)
9	Floor of mouth	T2	Level III	Positive	Positive (10/21)
10	Floor of mouth	T3	Level II	Negative	Negative (9/13)
11	Lateral tongue	T2	Level III	Negative	Negative (9/18)
12	Floor of mouth	T2	Level III	Negative	Negative (9/22)
13	Alveolar ridge	T3	Level II	Negative	Negative (9/22)
14	Buccal mucosa	T2	Level I	Negative	Negative (9/45)
15	Buccal mucosa	T2	Level II	Negative	Negative (9/23)
16	Oral vestibule	T1	Level I	Negative	Negative (9/5)
17	Buccal mucosa	T2	Level I	Negative	Negative (9/20)
18	Lateral tongue base	T2	Level I	Negative	Negative (9/20)
19	Lateral tongue	T2	Level II	Negative	Negative (9/21)
20	Lateral tongue	T4	Level II	Positive	Negative (9/13)
			Level III	Negative	

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### Sentinel Lymph Node Biopsy Accurately Stages the Regional Lymph Nodes for T1-T2 Oral Squamous Cell Carcinomas: Results of a Prospective Multi-Institutional Trial

Francisco J. Civantos, Robert P. Zitsch, David E. Schuller, Amit Agrawal, Russell B. Smith, Richard Nason, Guy Petruzzelli, Christine G. Gourin, Richard J. Wong, Robert L. Ferris, Adel El Naggar, John A. Ridge, Randal C. Panelli, Kausar Owzar, Linda McCall, Douglas B. Chelapa, Wendell G. Yarbrough, and Jeffrey N. Myers

- Prospective trial including 140 patients with T1/T2, N0 SCC of the oral cavity
- All underwent SLNB and then completion selective ND
- Primary end-point was **negative predictive value of SLNB**

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False negative rates

**Table 6.** Results Based on Central Pathology/IHC by Stage

Clinical Status	Clinical Stage				Total
	T1 (NPV = 1.0)		T2 (NPV = 0.94)		
	No.	%	No.	%	
TN	39	75.0	99	68.2	99
FN	0	0.0	4	4.5	4
True positive	19	26.0	24	27.3	37
Total	52		88		140

Abbreviations: IHC, immunohistochemistry; NPV, negative predictive value; TN, true negative; FN, false negative.

- Sentinel node biopsy more predictive of neck status for T1 than T2 tumors
- Negative predictive value was 94% with traditional H&E staining and improved to 96% with additional sectioning and immunohistochemistry

Laryngoscope, 2019 Jan;129(1):162-169. doi: 10.1002/lary.27523. Epub 2018 Oct 3.

Sentinel Lymph Node Biopsy Versus Elective Neck Dissection for Stage I to II Oral Cavity Cancer.

Cramer JD<sup>1</sup>, Sridharan S<sup>1</sup>, Ferris RL<sup>1</sup>, Duvvuri U<sup>1</sup>, Samant S<sup>2</sup>

- SLN has been incorporated in guidelines as an option instead of elective neck dissection, but utilization is still unclear
- Retrospective cohort study of T1/T2 oral cavity SCC (all N0)
- 8,328 patients identified via National Cancer Data Base
  - SLNB for 240 patients
  - Completion neck avoided in 63.8% (negative sentinel node)

**TABLE I.** Study Cohort Demographics and Clinical Characteristics.

Variable	SLNB (n = 240) N (%)	END (n = 8,088) N (%)	P Value*
Clinical T-stage			<0.001
T1	170 (70.8)	4,039 (49.9)	
T2	70 (29.2)	4,049 (50.1)	
Subsite			< 0.001
Lip	35 (14.6)	182 (2.3)	
Anterior tongue	134 (55.8)	4,839 (59.8)	
Upper or lower gum	12 (5.0)	618 (7.6)	
Floor of mouth	33 (13.8)	1,274 (15.8)	
Hard palate	2 (0.8)	116 (1.4)	
Buccal	14 (5.8)	557 (6.9)	
RMT or other mouth	10 (4.2)	502 (6.2)	
Depth			< 0.001
< 2 mm	20 (12.4)	252 (4.4)	
2-4 mm	19 (11.8)	366 (6.4)	
4-10 mm	35 (21.7)	1,396 (23.4)	
> 10 mm	87 (54.0)	3,732 (64.9)	

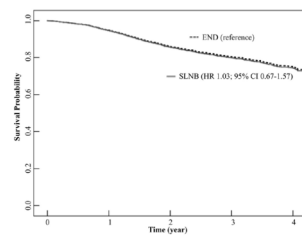
- More T1 tumors in SLNB group
- More lip cancers in SLNB group
- DOI was less in SLNB group

Comparing SLNB & END

**TABLE I.** Study Cohort Demographics and Clinical Characteristics.

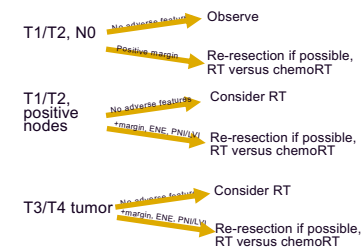
Variable	SLNB (n = 240) N (%)	END (n = 8,088) N (%)	P Value*
Lymphovascular invasion			0.01
Absent	225 (93.8)	7,173 (88.7)	
Present	15 (6.2)	913 (11.3)	
Extracapsular extension			0.12
Absent/not recorded	225 (95.7)	7,325 (93.1)	
Present	10 (4.3)	540 (6.9)	
Treatment summary			0.79
Surgical margins			
Negative	223 (93.3)	7,501 (93.8)	
Positive	16 (6.7)	500 (6.2)	

SLNB and END with similar survival probability



- No difference in overall survival between patients with SLNB and END
- Model controlled for DOI, margins, LVI, # of pos nodes, ENE, adjuvant treatment, etc

What happens after surgery?



### Effect of Time to Initiation of Postoperative Radiation Therapy on Surgically Managed Head and Neck Cancer

Evan M. Graboyes, MD<sup>1</sup>; Elizabeth Garrett-Mayer, PhD<sup>2</sup>; Mark A. Ellis, MD<sup>3</sup>; Anand K. Sharma, MD<sup>4</sup>; Amy E. Wahlquist, MS<sup>5</sup>; Eric J. Lentsch, MD<sup>1</sup>; Brian Nussenbaum, MD<sup>6</sup>; and Terry A. Day, MD<sup>7</sup>

- This study evaluates, via National Cancer Database (NCDB) review, whether earlier initiation of PORT (<4 weeks) has survival benefit & whether delay >6 weeks affects survival.
- 41,291 patients included - 44.7% initiated PORT within 6 weeks of surgery

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### Improved survival with PORT within 6 weeks of surgery

- Increasing delay of PORT > 6 weeks associated with progressively larger decreases in survival
- PORT < 4 weeks post-op (compared to 5-6 weeks) associated with significant improvement in overall survival in univariate analysis but **did not hold true in multivariate analysis** - Adjusted for age, race, comorbidity, insurance/income, primary site, staging, concurrent chemo.

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### Improved survival with PORT within 6 weeks of surgery

- The preferred time-interval between resection + radiation is  $\leq 6$  weeks

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### Who benefits from adding chemo?

Head Neck 2009 Oct 27;10:1443-50

Defining risk levels in locally advanced head and neck cancers: a comparative analysis of concurrent postoperative radiation plus chemotherapy trials of the EORTC (#22931) and RTOG (# 9501).

Berner J<sup>1</sup>, Cooper JS, Pajak TP, van Glabbeke M, Bourhis J, Forastiere A, Ozanne EM, Jacobs JB, Jansen J, Anzjak L, Lefebvre J.

Table 1. Summary of trials.

Disease characteristic and outcome endpoint	EORTC #22931 (N = 334)	RTOG #9501 (N = 409; 414 analyzed)
Characteristic		
Primary site		
Oral cavity	26%	27%
Oropharynx	30%	45%
Larynx	22%	21%
Hypopharynx	20%	10%
Other	1%	<1%
T classification		
T1-2	33%	39%
T3-4	60%	61%
Unknown	1%	0%
N classification		
N0-1	43%	6%
N2-3	57%	94%
Outcome endpoint, chemoradiotherapy vs RT		
Locoregional failure rate	3-y estimate, 19% vs 31% (p = 0.07)	3-y estimate, 22% vs 33% (p = 0.1)
Distant-free survival rate	3-y estimate, 47% vs 38% (p = 0.4)	3-y estimate, 47% vs 38% (p = 0.4)
Overall survival rate	3-y estimate, 53% vs 40% (p = 0.2)	3-y estimate, 56% vs 47% (p = 0.09)

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### ENE and positive margin -> Add chemo

In patients with ENE or positive margins, adding chemotherapy to post-op radiation improved locoregional control, disease-free and overall survival

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### Case #1

- 76 M with left lower lip squamous cell carcinoma
- ++ hx tobacco use
- Exam with the finding shown, as well as left level 1B palpable adenopathy

**Surgery:**  
Wide local excision lower lip cancer with bilateral neck dissections

**Pathology:**  
4.6cm poorly differentiated squamous cell carcinoma, negative margins (6mm), DOI 6mm  
76 lymph nodes evaluated, 5 positive (bilateral), largest 1.6cm, no ENE

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Case #1 – Staging? Poll #3

4.6cm poorly differentiated squamous cell carcinoma, negative margins (6mm), DOI 6mm

76 lymph nodes evaluated, 5 positive (bilateral), largest 1.6cm, no ENE

T3N2C

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Case #1 resection Poll #4

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Case #1 - JM

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Case #1 - JM

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Case #1 Poll #5

What next after surgery?

4.6cm poorly differentiated squamous cell carcinoma, negative margins (6mm), DOI 6mm

76 lymph nodes evaluated, 5 positive (bilateral), largest 1.6cm, no ENE

Adjuvant radiation

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Case #2

- 69 F with R tongue tumor with discomfort, difficulty eating, weight loss
- Never-smoker, + hx CML and bone-marrow transplant, on prednisone
- Biopsy + verrucous carcinoma

- Exam notable for finding shown →
  - Lateral tongue with ventral tongue and floor of mouth involvement
  - Separate from retromolar trigone, tongue base, alveolar ridge
  - No trismus

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Case #2 Poll #6

Treatment?  
Hemi-glossectomy, ipsilateral neck dissection, free flap reconstruction

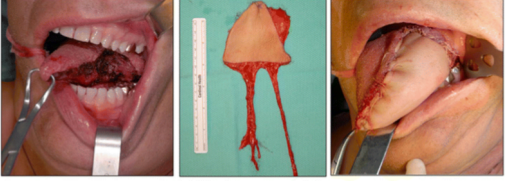
Path:  
3.9cm verrucous carcinoma, DOI 12mm, margins negative (4mm), no PNI or LVI

25 lymph nodes examined, 1 positive (1.7cm with ENE)

Stage?  
• T3N2a

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Case #2



Hemiglossectomy defect      Customized free flap      Reconstructed tongue

Idris et al 2018

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Case #2 Poll #7

- What next after surgery?

3.9cm verrucous carcinoma, DOI 12mm, margins negative (4mm), no PNI or LVI

25 lymph nodes examined, 1 positive (1.7 cm with ENE)

Adjuvant chemo-radiation

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Summary

- Unclear reason for why there is a **slight increase in incidence of oral cavity cancer in young women** (<40yrs old)
- Data suggest elective neck dissection for oral cavity cancers, with improved disease-free and overall survival
- Number of lymph nodes evaluated (and positive) appear to have a direct effect on survival outcomes
- Adjuvant radiation is recommended for larger tumors (T3/4) or smaller tumors with positive nodes or adverse features. Chemotherapy should also be added if ENE or positive margins are noted

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References

Full reference list can be provided upon request

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