UC DAVIS HEALTH

Updates in Surgical Management in Head and Neck Cancer
November 11, 2023

MEDICAL CENTER

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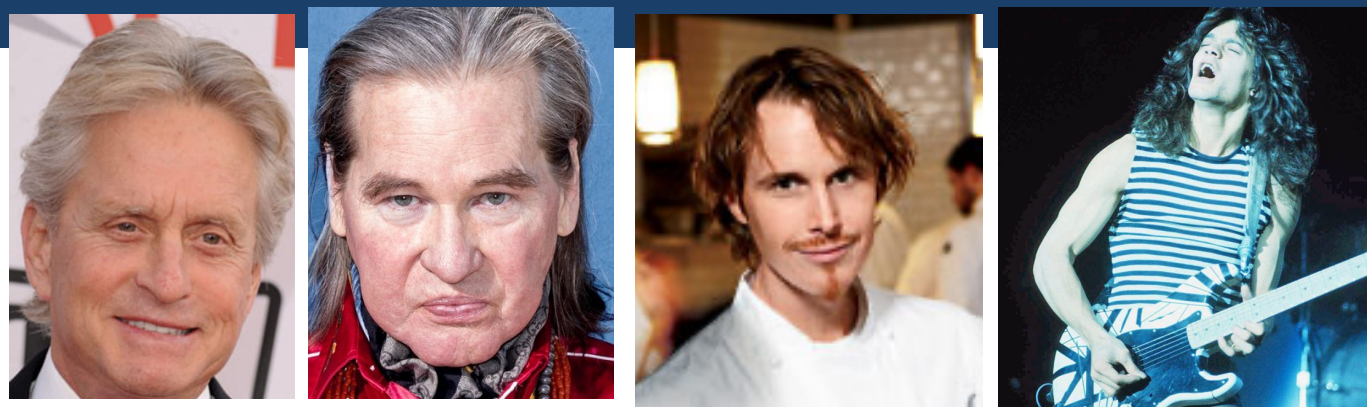
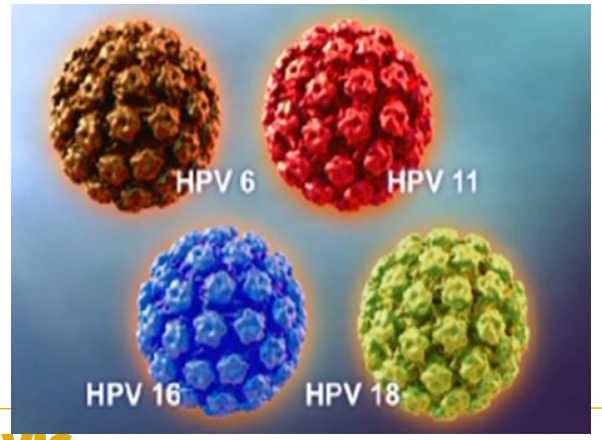
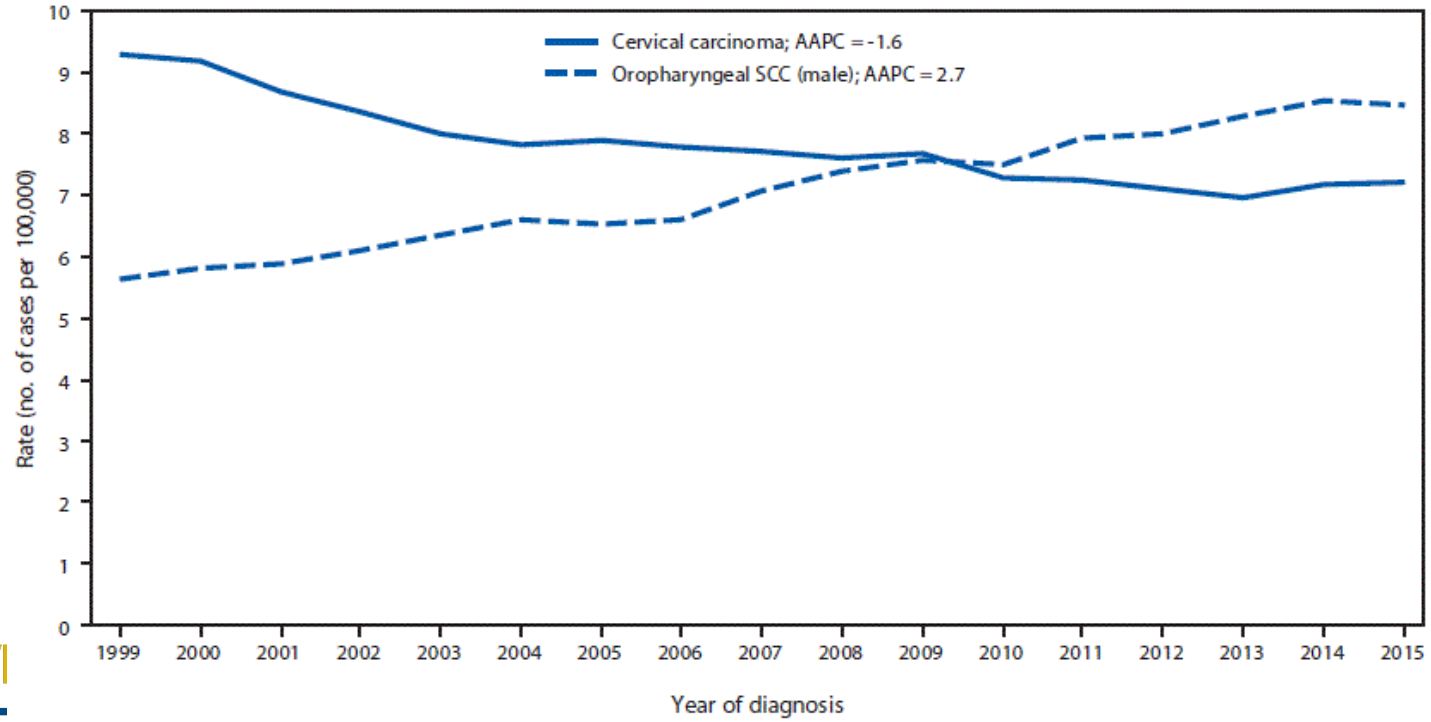
Background

- 6th most common cancer worldwide
- >60,000 cases and >10,000 deaths in US annually
- Traditionally caused by tobacco and alcohol
- HPV-related head and neck cancers among fastest rising cancers in incidence
- Survival is poor in advanced cases (~50%), and has not improves substantially in decades







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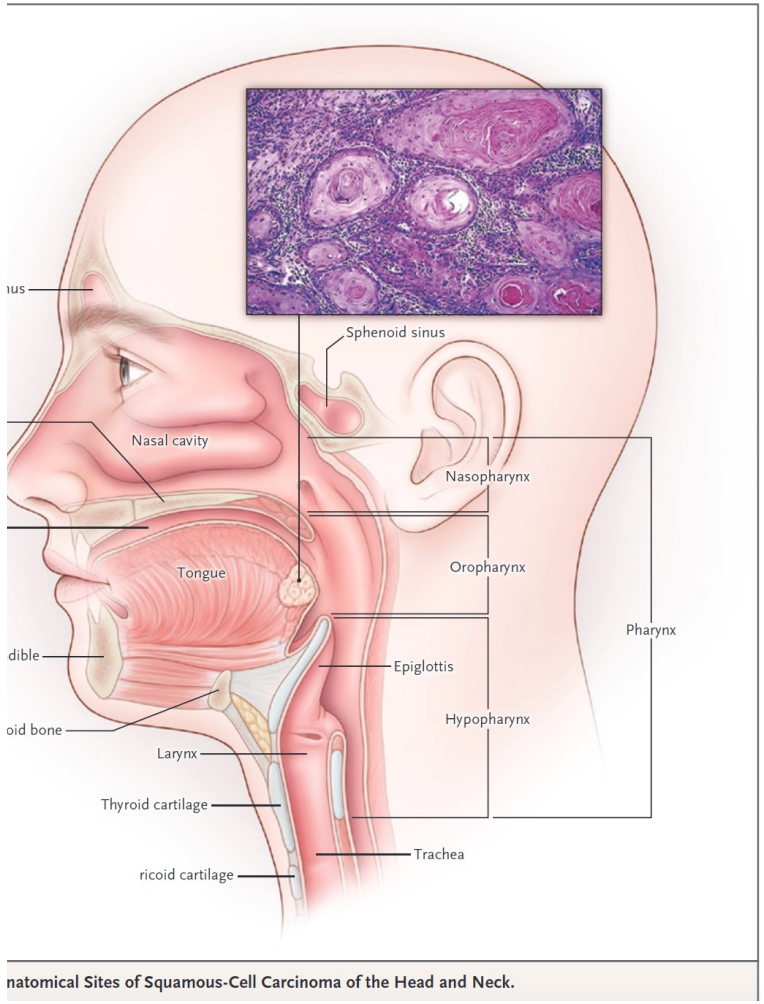
Background

National Comprehensive Cancer Network®

- Often multidisciplinary management with Radiation Oncology and Medical Oncology
- Primary surgery is indicated for:
  - Oral cavity cancers (***preferred***)
  - Oropharynx cancers
  - Larynx cancers (***preferred for T4 or nonfunctional larynx)***
  - Salivary gland cancers (***preferred***)
  - Thyroid cancer (***preferred***)
  - Cutaneous (***preferred***)
  - Salvage surgery after (chemo)radiation



natomical Sites of Squamous-Cell Carcinoma of the Head and Neck.

Chow. *NEJM*. 2020

Surgery for Head and Neck Cancer

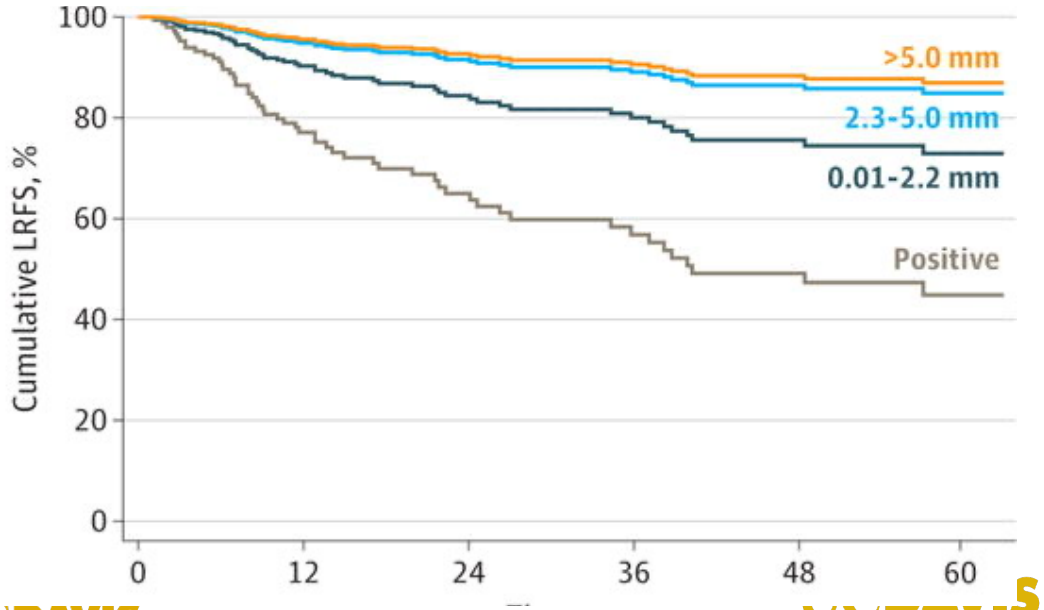
- Primary tumor resection
  - Surgical margins and pathology
  - Surgical cancer intraoperative assessment
  - Transoral robotic surgery
- Addressing the nodal basin
  - Neck dissection
  - Sentinel lymph node biopsy
- Surgical reconstruction
- Neoadjuvant therapy
  - Keynote 689
- Adjuvant therapy
  - Keynote 630, RTOG1216

Surgery for Head and Neck Cancer

- A caution for close margins

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

Daniella Karassawa Zanoni, MD[1]; Jocelyn C. Migliacci, MA[1]; Bin Xu, MD, PhD[2]; Nora Katabi, MD[2]; Pablo H. Montero, MD[1]; Ian Ganly, MD, PhD[1]; Jatin P. Shah, MD[1]; Richard J. Wong, MD[1]; Ronald A. Ghossein, MD[2]; Snehal G. Patel, MD[1]



CLINICAL REVIEW

WILEY

Stratification of surgical margin distances by the millimeter on local recurrence in oral cavity cancer: A systematic review and meta-analysis

Kurtis Young BS[1,2] | Hannah Bulosan BS[1] | Carley C. Kida BA[1] | Arnaud F. Bewley MD[2] | Marianne Abouyared MD[2] | Andrew C. Birkeland MD[2]

Effect size of each study | Confidence interval of effect size

TABLE 4 The effect of 1 mm surgical margin incremental distances on LR

Parameter	Sample size	Risk for LR (risk ratio)	Confidence interval (95%)	*p*-value[a]
Margin status				
Negative margins (≥5 mm)	1450	1		
Positive/close (>5 mm)	765	2.09	1.53–2.86	**<0.001**
Margin threshold				
0.0–0.9	275	2.96	2.15–4.07	**<0.001**
1.0–1.9	179	2.01	1.29–3.13	**<0.001**
2.0–2.9	116	2.17	1.73–2.73	**<0.001**
3.0–3.9	126	1.81	1.81–1.21	**<0.001**
4.0–4.9	69	0.98	0.52–1.85	0.96

Note: Bolded values significant $p < 0.05$.

[a]*p*-value for association as determined from meta-analysis.

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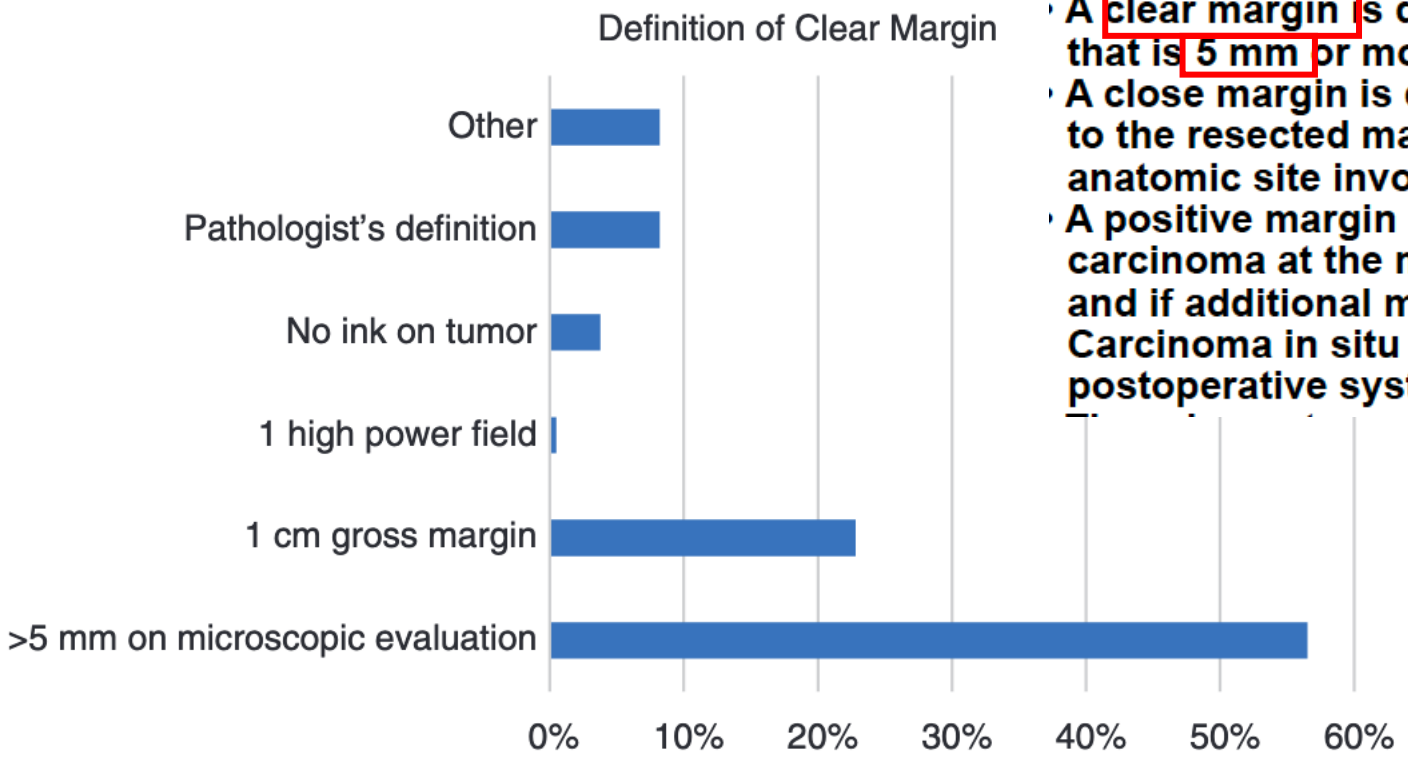
Surgery for Head and Neck Cancer

- A caution for close margins

- AHNS Survey (2021):



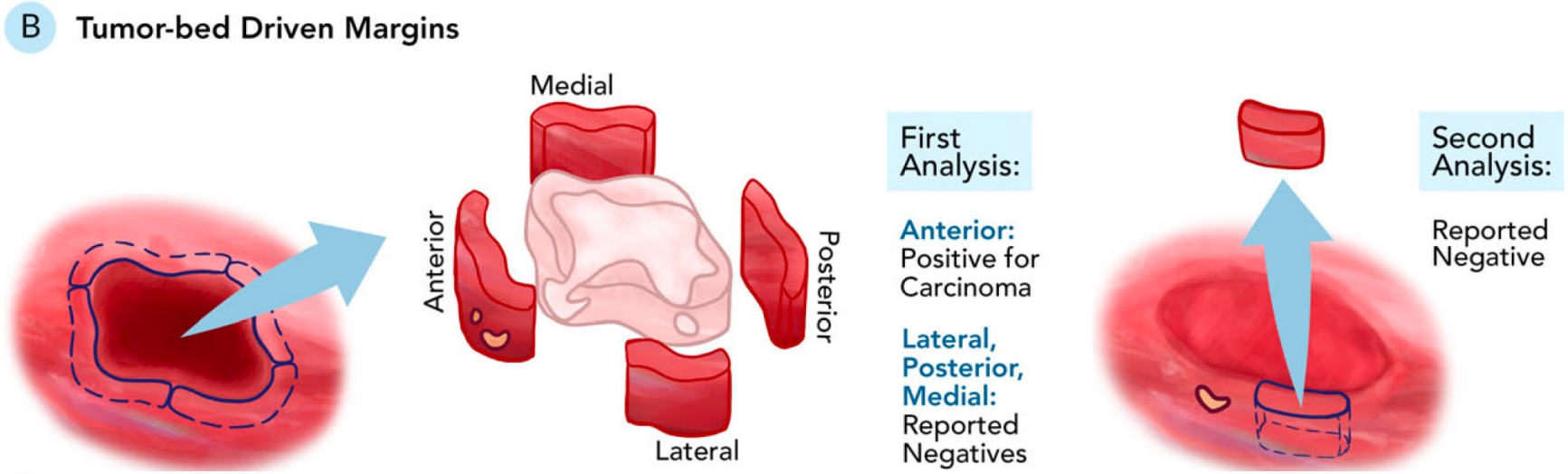
National Comprehensive Cancer Network®

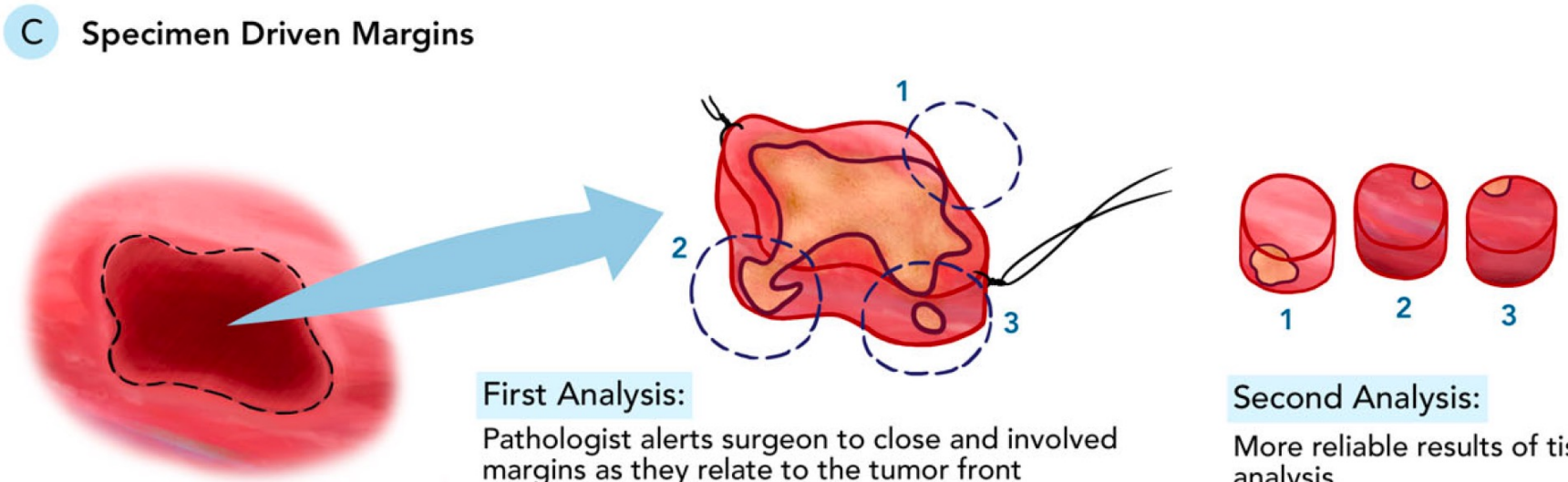
- **A clear margin is defined as the distance from the invasive tumor front that is 5 mm or more from the resected margin.**
- **A close margin is defined as the distance from the invasive tumor front to the resected margin that is less than 2–5 mm, depending on the anatomic site involved.**
- **A positive margin is defined as carcinoma in situ or as invasive carcinoma at the margin of resection. If carcinoma in situ is present and if additional margins can be obtained that is the favored approach. Carcinoma in situ should not be considered an indication for concurrent postoperative systemic therapy/RT.**

Bulbul et al. *Laryngoscope˄2021*

Surgery for Head and Neck Cancer

- Tumor bed versus specimen margins





Kain, Birkeland, et al. *Laryngoscope, 2019*

Surgery for Head and Neck Cancer

- Tumor bed versus specimen margins

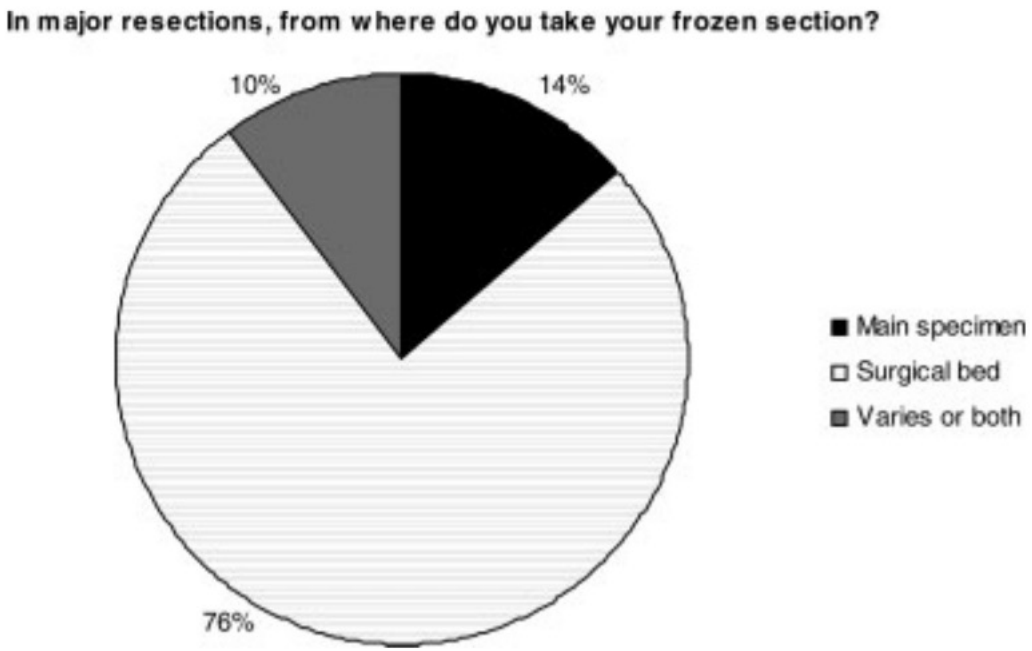


FIGURE 5. Choice of sample site for frozen section.

2005

Do you take margin samples from the main specimen or the tumor bed?

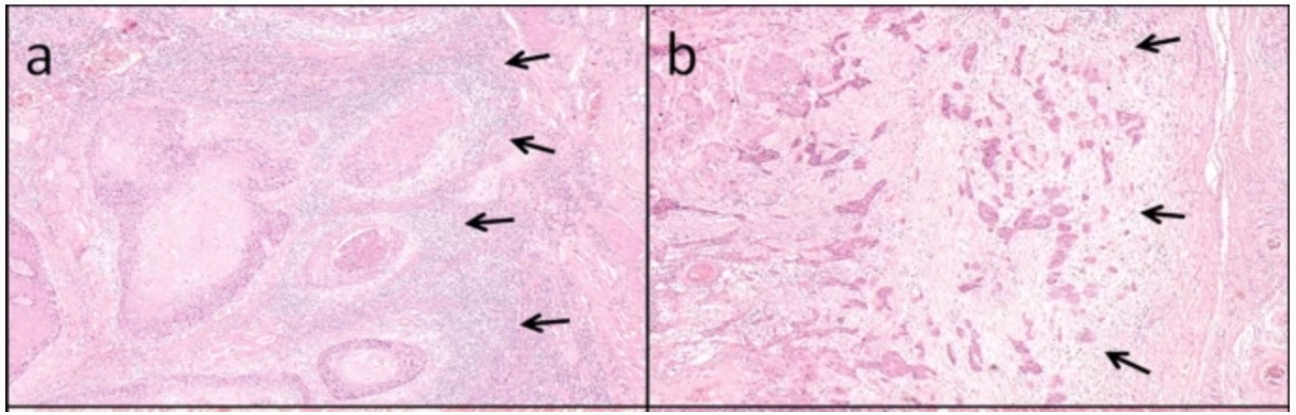
Main specimen	55
Tumor bed	45

2021

Meier et al. Head Neck 2005
Bulbul et al. *Laryngoscope*ˆ*2021*

Surgery for Head and Neck Cancer

- Challenges for achieving negative margins
  - New pathologic variables
    - Worst pattern of invasion



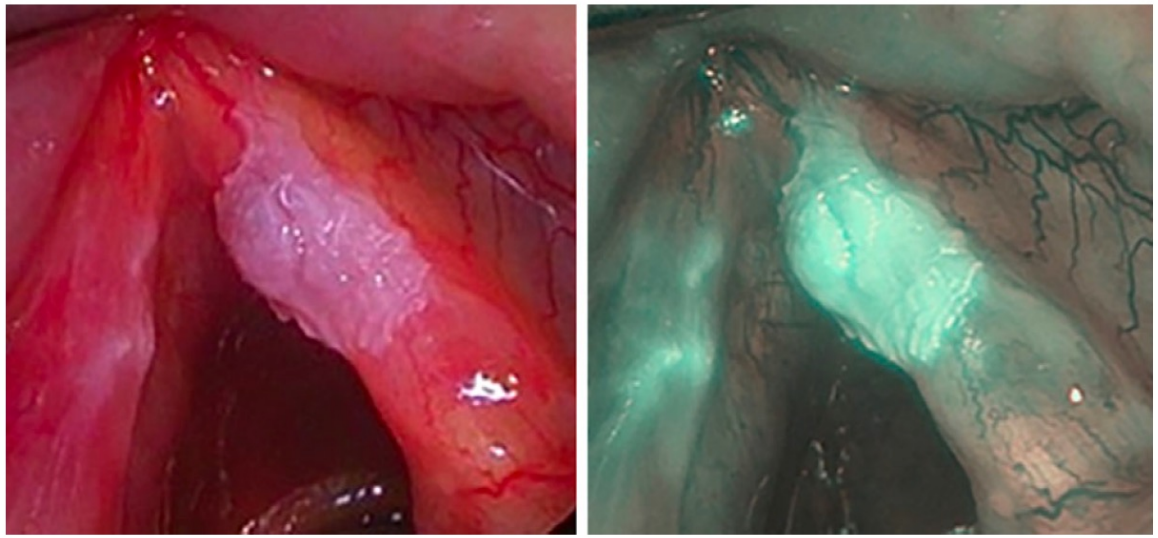
Variable	Definition
WPOI	
Type 1	Pushing border
Type 2	Finger-like growth
Type 3	Large separate islands, more than 15 cells per island
Type 4	Small tumour islands, 15 cells or fewer, per island
Type 5	Tumour satellites, ≥1 mm from main tumour or next closest satellite

Rahman et al. Head Neck Path, 2020

Surgery for Head and Neck Cancer

- ***All exploratory***

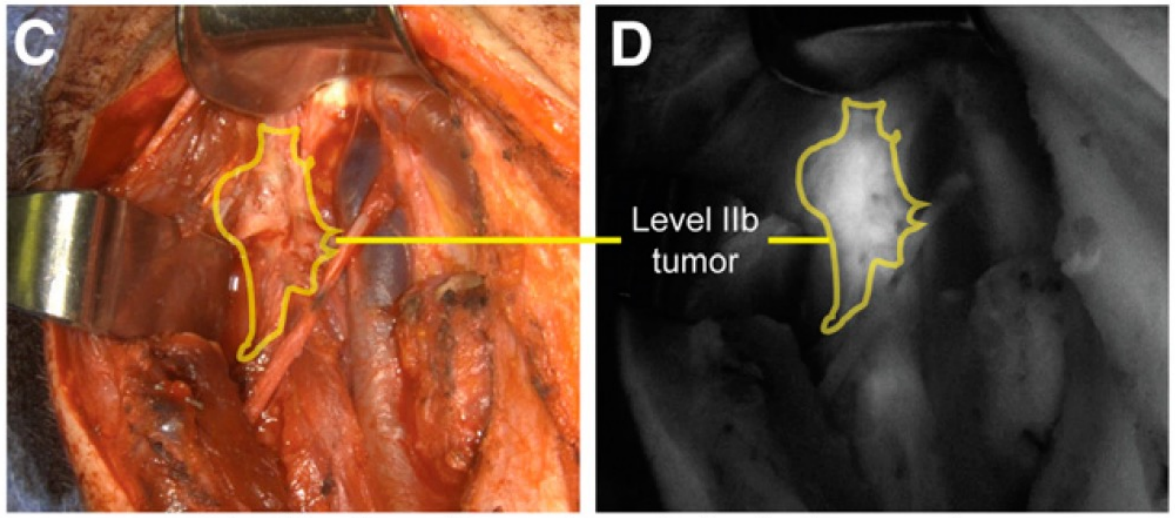
- Intraoperative margin assessment
  - Adjuvant techniques
    - MOHs
    - Indocyanine Green
    - Ultrasound
    - VELscope
    - Narrow band imaging



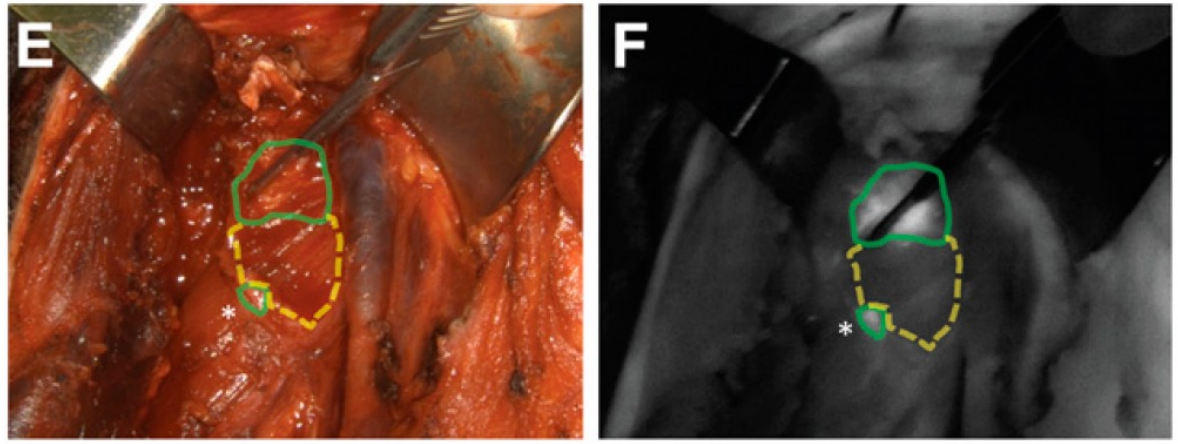
- Investigational techniques
  - Raman spectroscopy
  - Tissue autofluorescence
  - Tagged agents
  - Molecular margins

Surgery for Head and Neck Cancer

- Tagged agents



Identification of tumor boundaries in deep neck musculature



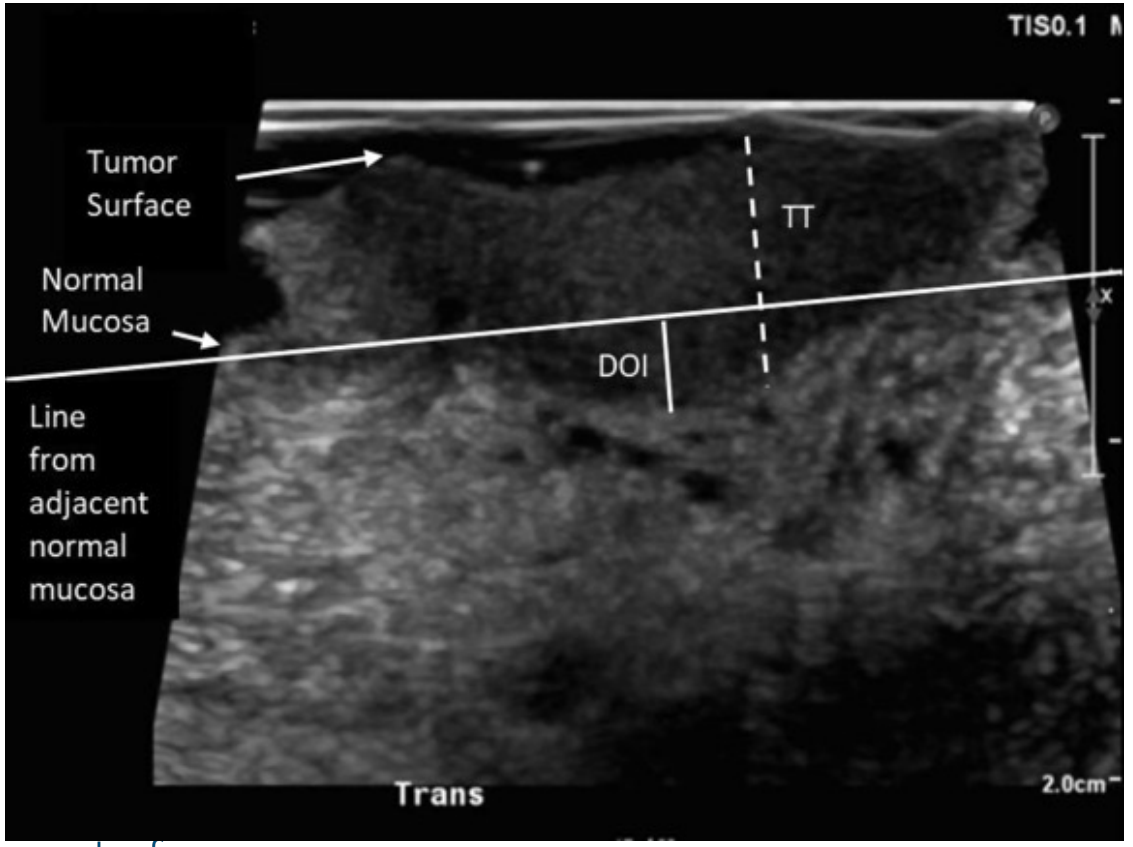
Detection of residual disease

Van Keulen, Birkeland, et al. *J Nuc Med, 2019*
Van Keulen, Birkeland, et al. *Clin Cancer Res, 2019*

Surgical margins in head and neck cancer

- Ultrasound
  - Opportunity to better assess deep margin
  - Most usable for oral tongue
  - No significant difference

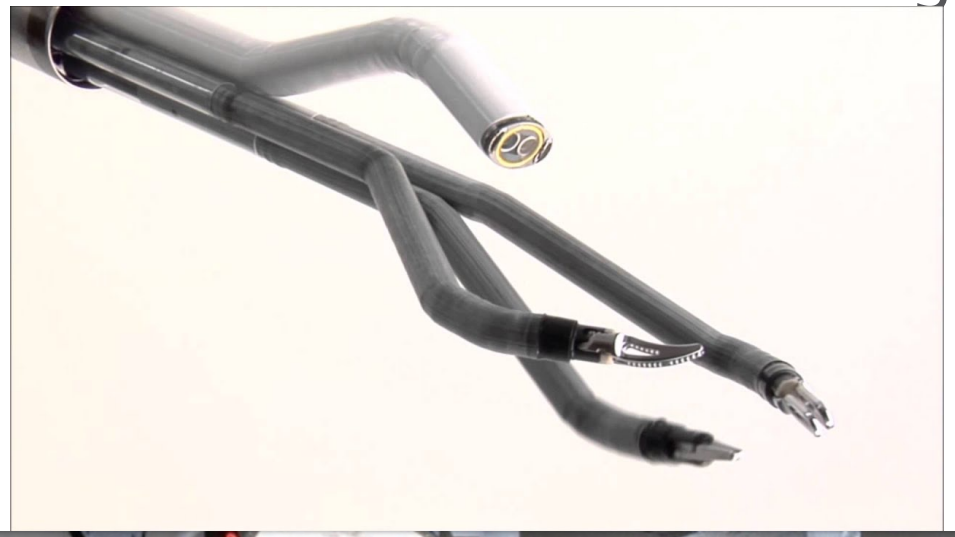
Characteristic	US-guided Resection (N = 23)	No Ultrasound (N = 21)	p-value
>5 mm	18 (78%)	14 (67%)	0.39
<5 mm	5 (22%)	7 (33%)	
Deep Margin (mm), mean ± SD	8.5 ± 4.9	6.7 ± 3.8	0.18

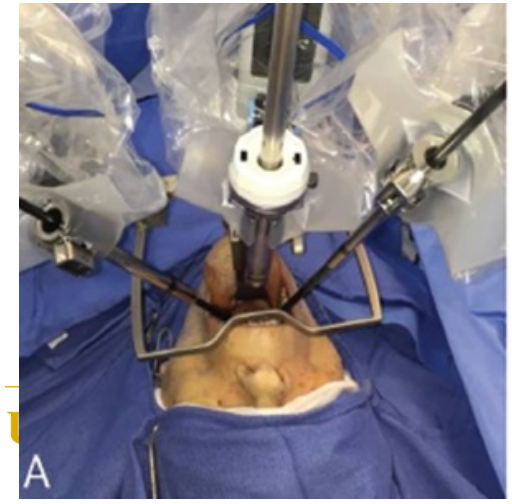


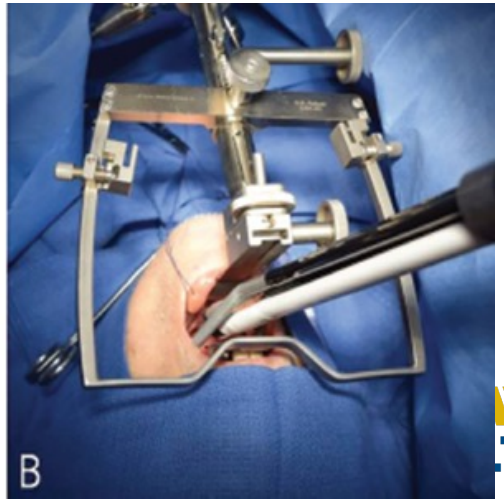
Bulbul et al. *Oral Oncol*, 2021

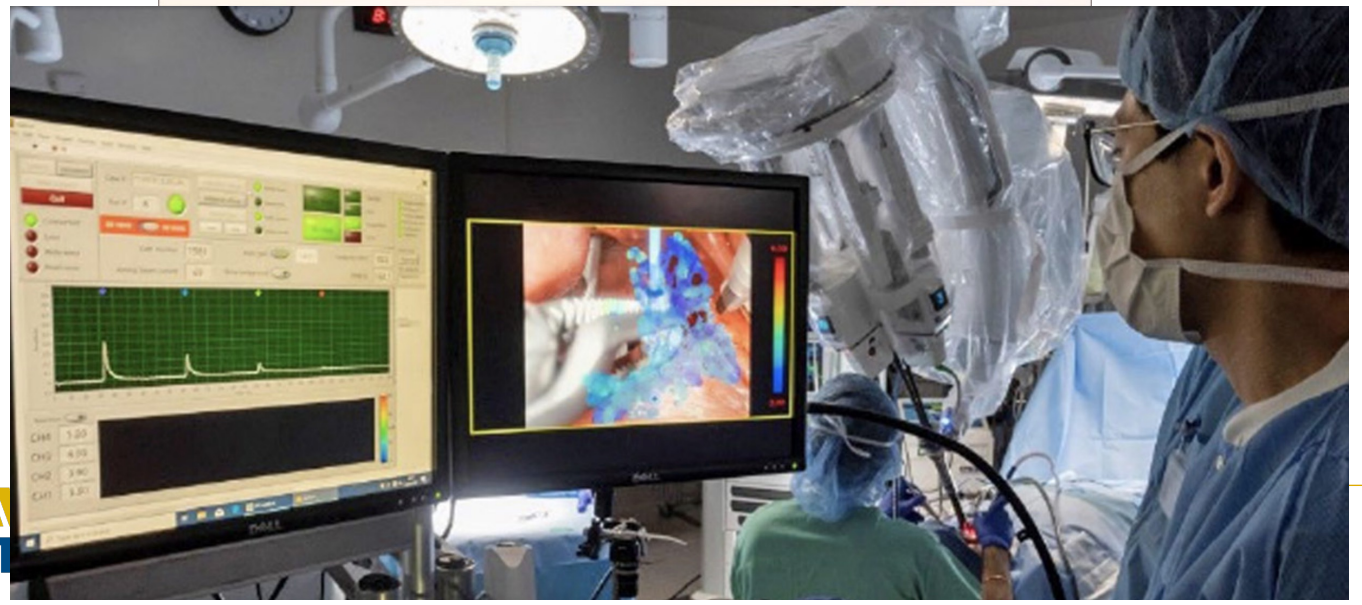
Surgery for Head and Neck Cancer

- Surgery for Oropharynx Cancer: Transoral Robotic Surgery



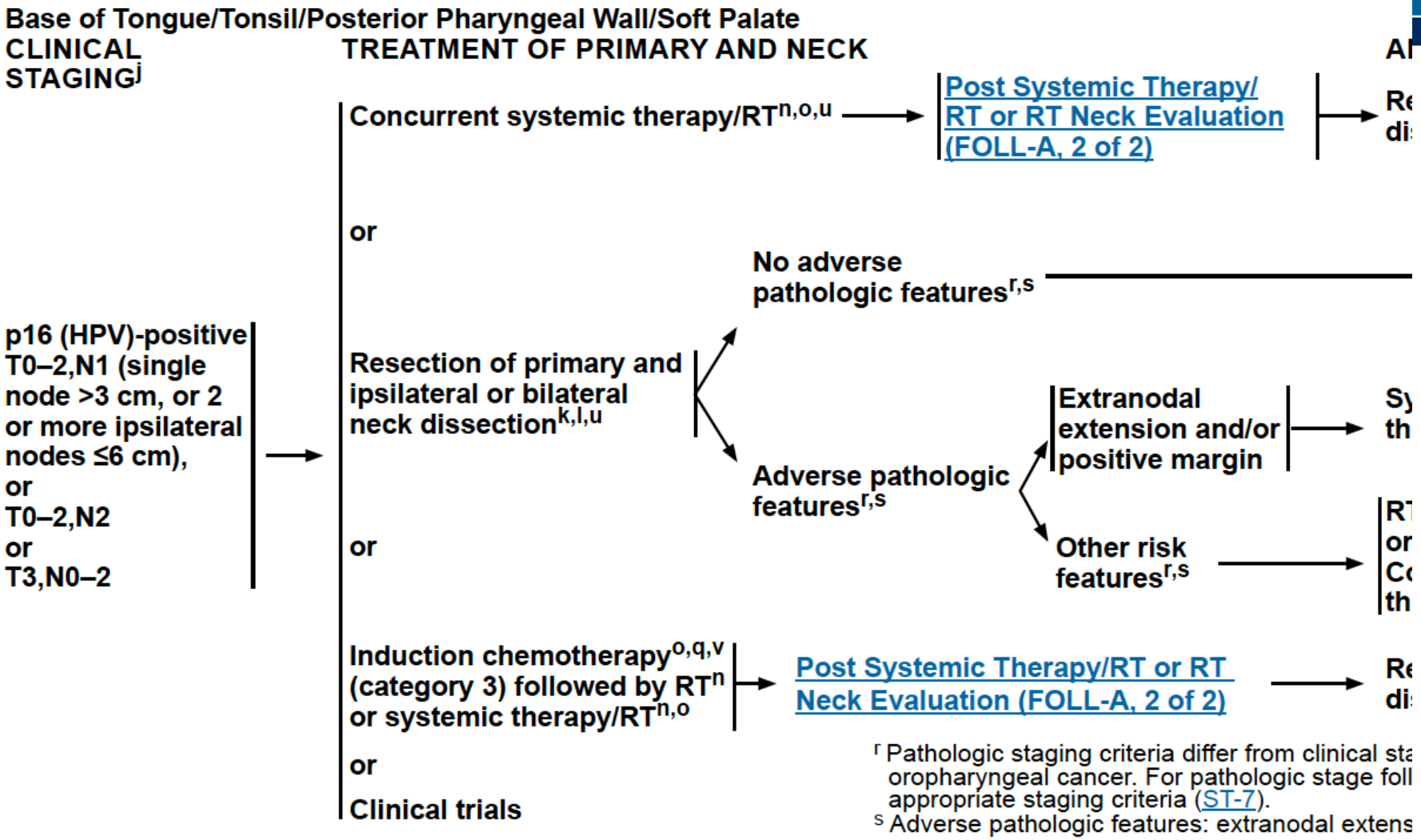






Surgery for Head and Neck Cancer

National Comprehensive Cancer Network®

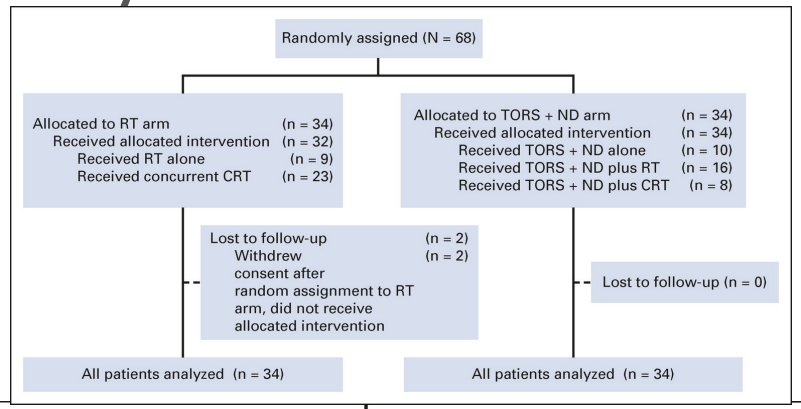


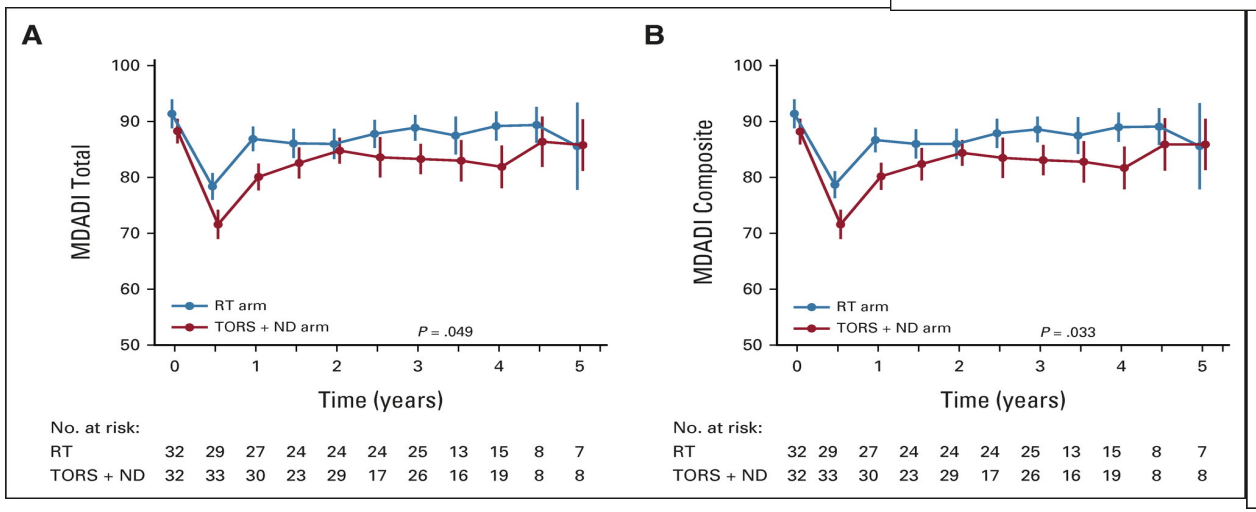
Surgery for Head and Neck Cancer

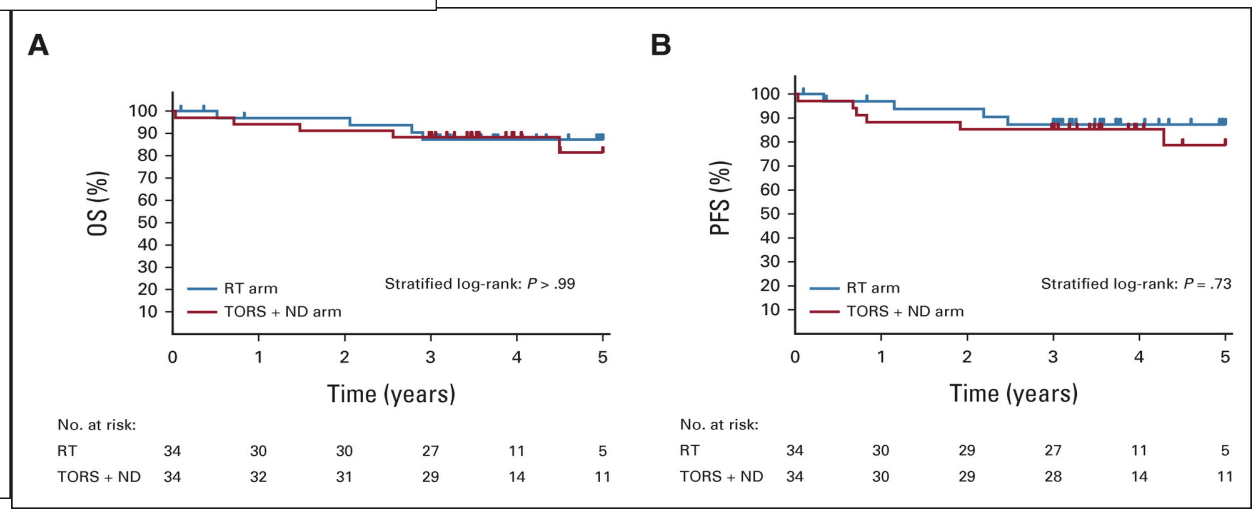
- Surgery for Oropharynx Cancer: Transoral Robotic Surgery

Surgery for Head and Neck Cancer

- Surgery for Oropharynx Cancer: Transoral Robotic Surgery
  - ORATOR trial







Published in: Anthony C. Nichols; Julie Theurer; Eitan Prisman; Nancy Read; Eric Berthelet; Eric Tran; Kevin Fung; John R. de Almeida; Andrew Bayley; David P. Goldstein; Michael Hier; Khalil Sultanem; Keith Richardson; Alex Mlynarek; Suren Krishnan; Hien Le; John Yoo; S. Danielle MacNeil; Eric Winquist; J. Alex Hammond; Varagur Venkatesan; Sara Kuruvilla; Andrew Warner; Sylvia Mitchell; Jeff Chen; Martin Corsten; Stephanie Johnson-Obaseki; Michael Odell; Christina Parker; Bret Wehrli; Keith Kwan; David A. Palma; *Journal of Clinical Oncology* 2022 40866-875.
DOI: 10.1200/JCO.21.01961
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Surgery for Head and Neck Cancer

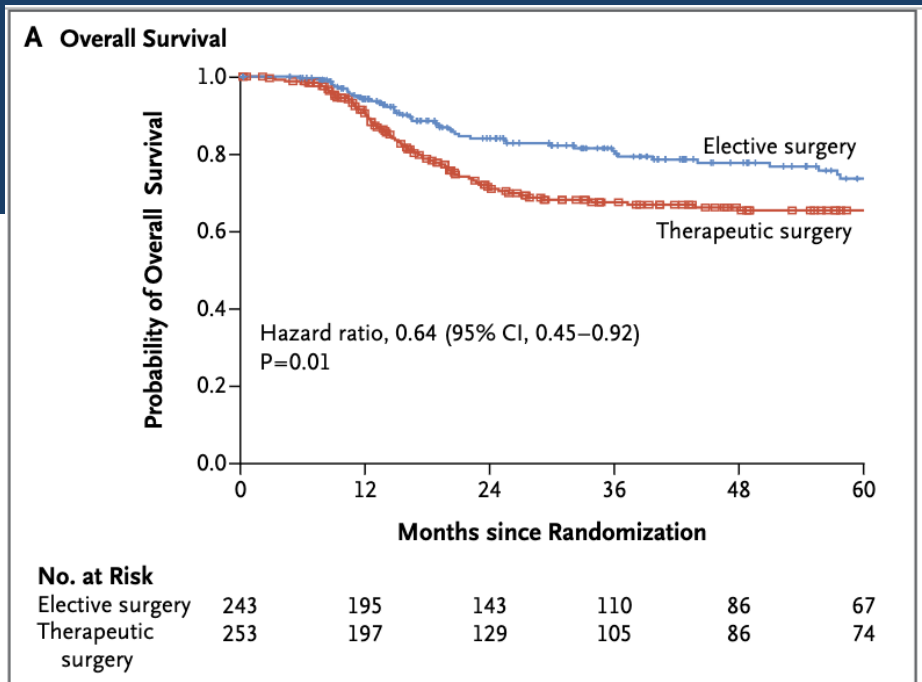
- Assessing Nodal Basin for Oral Cancer
  - Best level 1 evidence is to surgically address the nodal basin in N0 necks

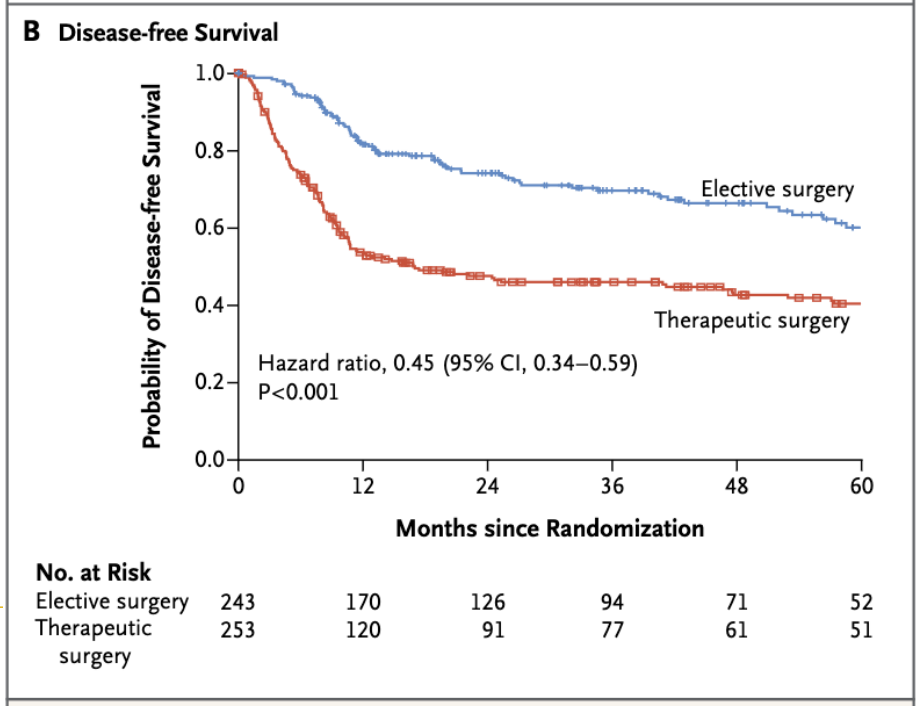
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Elective versus Therapeutic Neck Dissection in Node-Negative Oral Cancer

Anil K. D'Cruz, M.S., D.N.B., Richa Vaish, M.S., Neeti Kapre, M.S., D.N.B.,





Surgery for Head and Neck Cancer

- Sentinel Lymph Node Biopsy
  - Melanoma
  - Merkel cell carcinoma
  - *cT1-2N0 oral cavity SCCa

NRG-HN006
SCHEMA

STEP 1 REGISTRATION
Early Stage Oral Cavity Cancer (T1-2N0; AJCC 8th ed.)

PET/CT study* (central read)

STEP 2 REGISTRATION

PET/CT Negative

PET/CT Positive

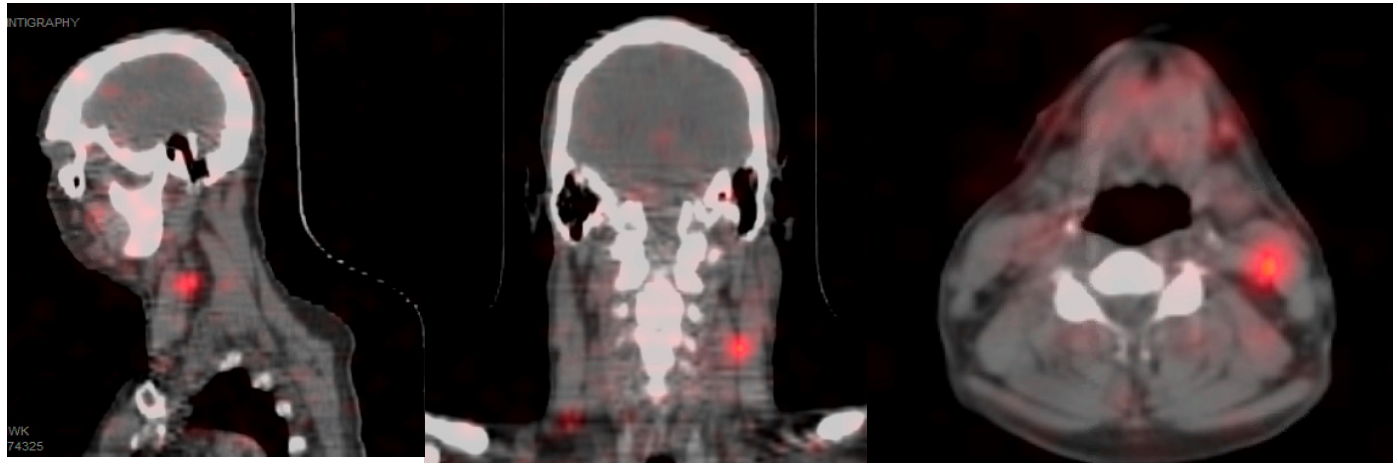
STRATIFICATION
Clinical & Radiographic T-stage (T1 vs. T2)
Zubrod Performance Status (0 vs 1-2)

RANDOMIZATION**

Record neck pathology findings.***
Patient goes off study

Arm 1†
Sentinel Lymph Node (SLN) Biopsy

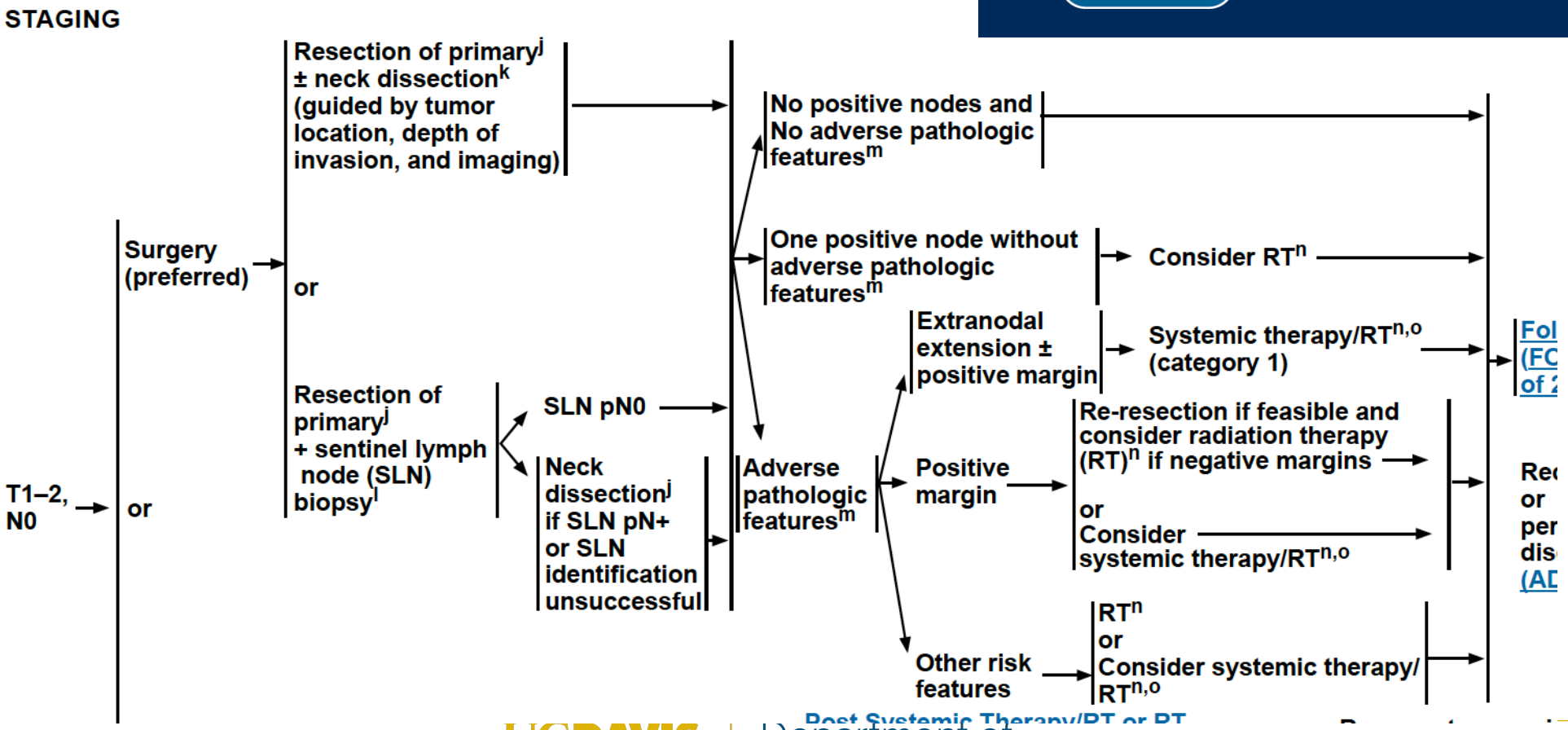
Arm 2†
Elective Neck Dissection (END) (Control)



Surgery for Head and Neck Cancer

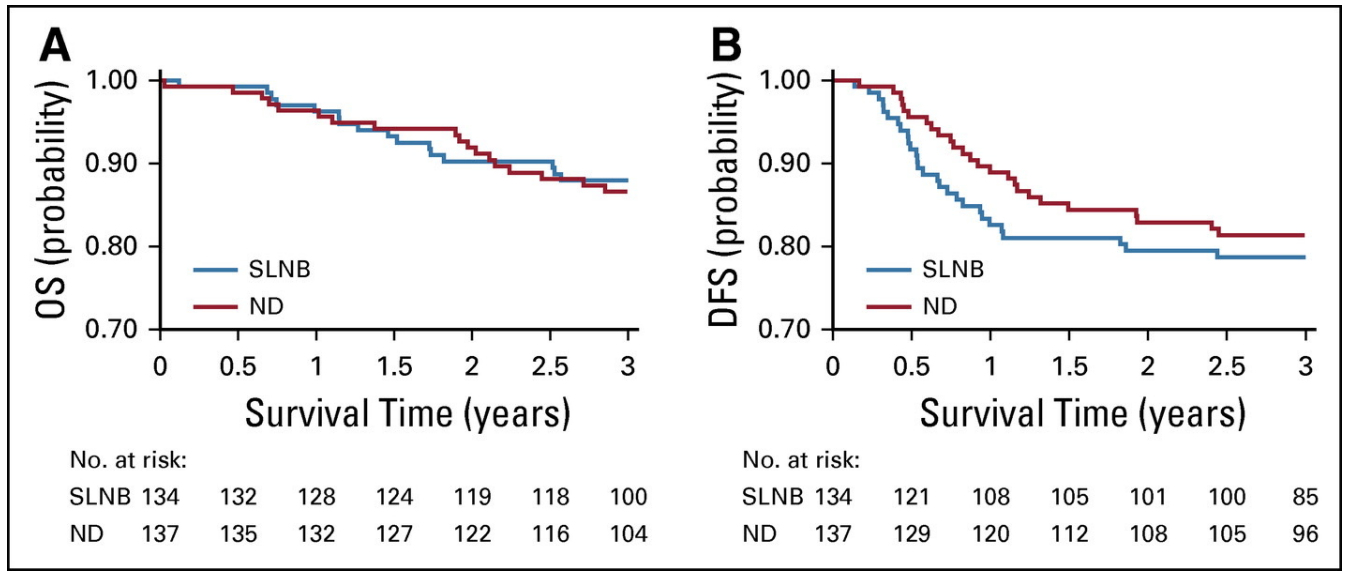
- Sentinel Lymph Node Biopsy
  - *cT1-2N0 oral cavity SCCa

NCCN National Comprehensive Cancer Network®



Surgery for Head and Neck Cancer

- Sentinel Lymph Node Biopsy
  - *cT1-2N0 oral cavity SCCa
  - Trial in Japan (JCO 2021)



RESULTS

Pathologic metastasis-positive nodes were observed in 24.8% (34 of 137) and 33.6% (46 of 134) of patients in the ND and SLNB groups, respectively ($P = .190$). The 3-year overall survival in the SLNB group (87.9%; lower limit of one-sided 95% CI, 82.4) was noninferior to that in the ND group (86.6%; lower limit 95% CI, 80.9; P for noninferiority < .001). The 3-year disease-free survival rate was 78.7% (lower limit 95% CI, 72.1) and 81.3% (75.0) in the SLNB and ND groups, respectively (P for noninferiority < .001). The scores of neck functionality in the SLNB group were significantly better than those in the ND group.

CONCLUSION

SLNB-navigated ND may replace elective ND without a survival disadvantage and reduce postoperative neck disability in patients with early-stage OCSCC.

Published in: Yasuhisa Hasegawa; Kiyoaki Tsukahara; Seiichi Yoshimoto; Kouki Miura; Junkichi Yokoyama; Shigeru Hirano; Hirokazu Uemura; Masashi Sugasawa; Tomokazu Yoshizaki; Akihiro Homma; Kazuaki Chikamatsu; Mikio Suzuki; Akihiro Shiotani; Takashi Matsuzuka; Naoyuki Kohno; Masakazu Miyazaki; Isao Oze; Keitaro Matsuo; Shigeru Kosuda; Yasushi Yatabe; *Journal of Clinical Oncology* 2021 392025-2036.
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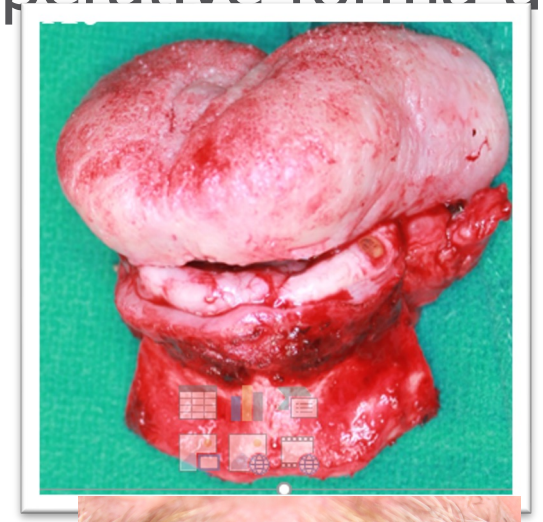
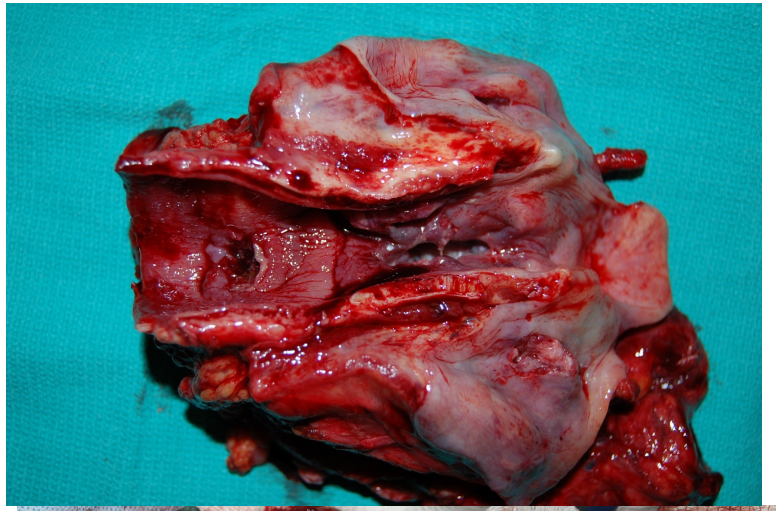
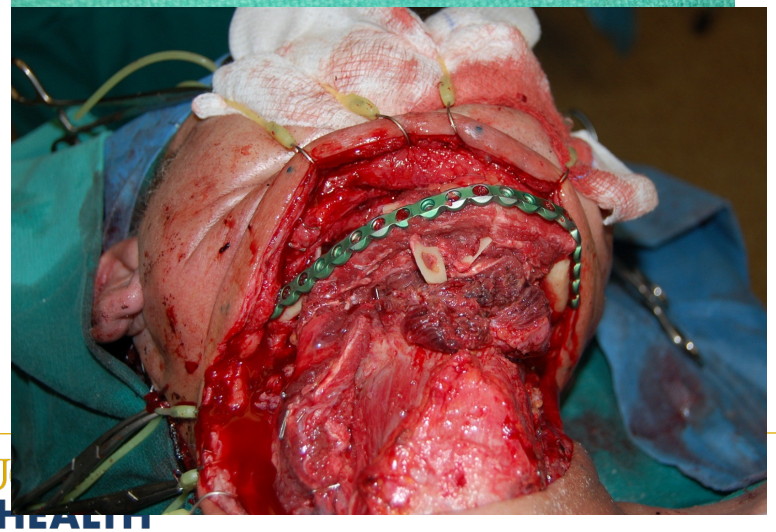
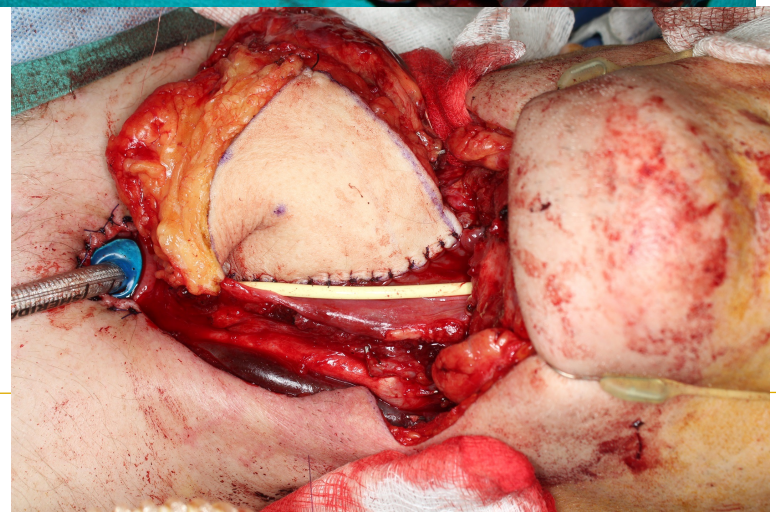
Surgery for Head and Neck Cancer

- Surgical Reconstruction
  - Achieve postoperative forma and function



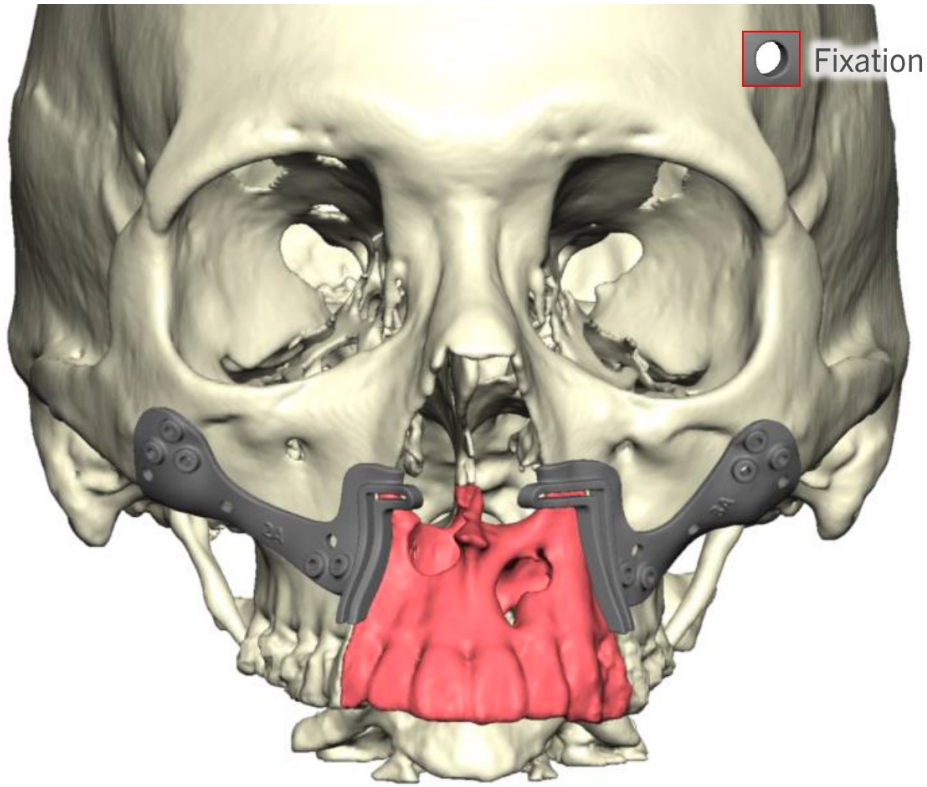


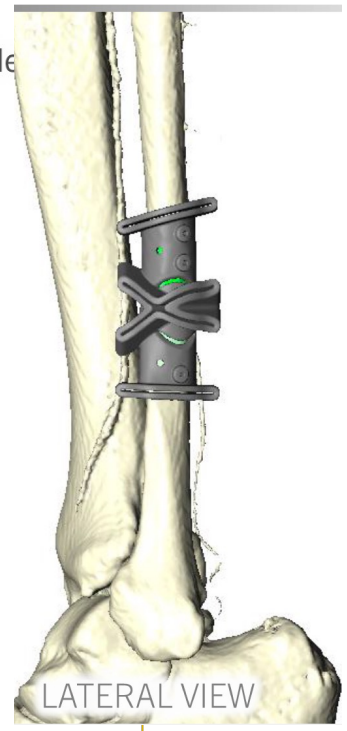


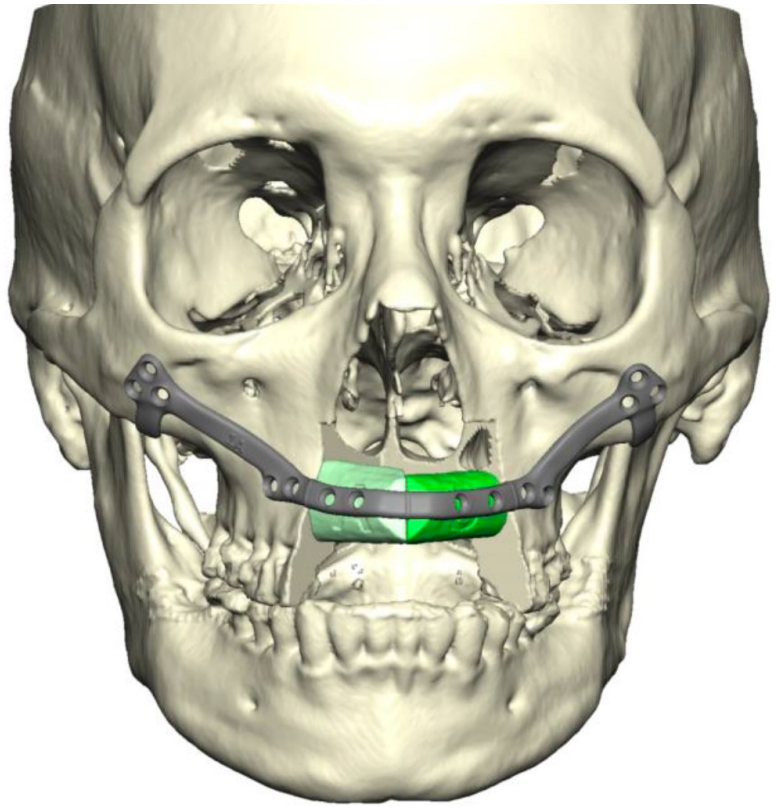


Surgery for Head and Neck Cancer

- Surgical Reconstruction
  - 3-D planning and reconstruction
  - Enhance postoperative function (e.g. dental restoration)







Surgery for Head and Neck Cancer

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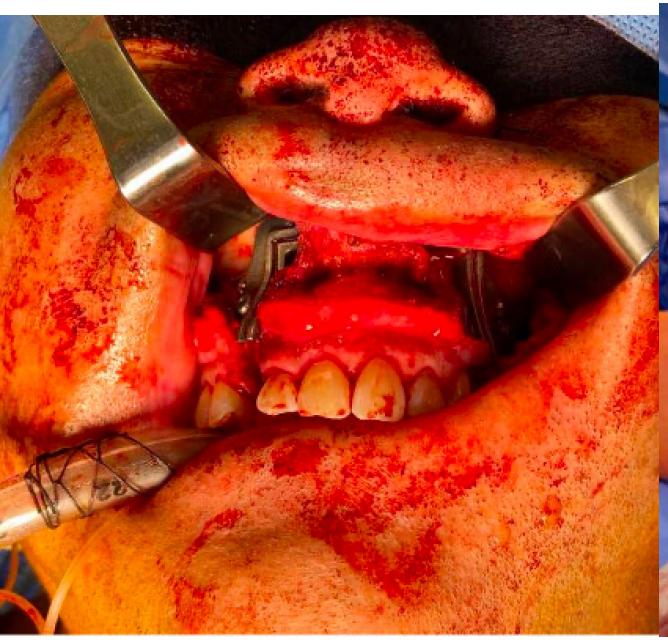
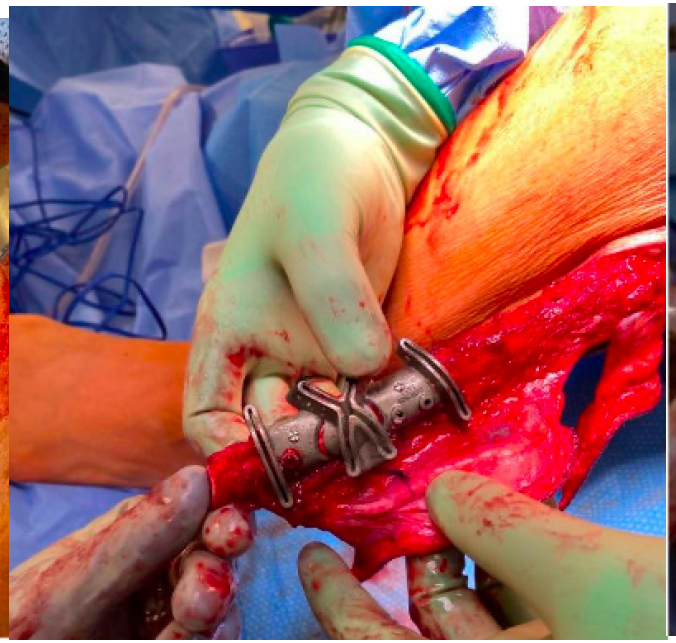
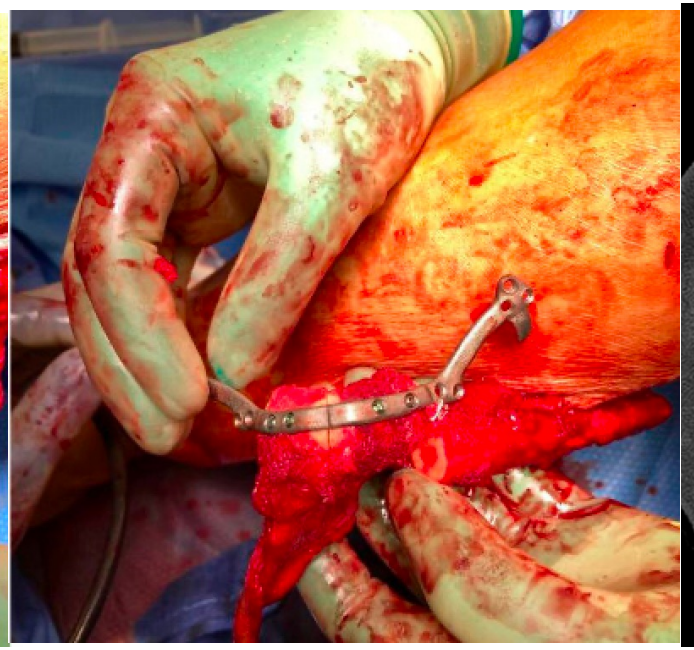
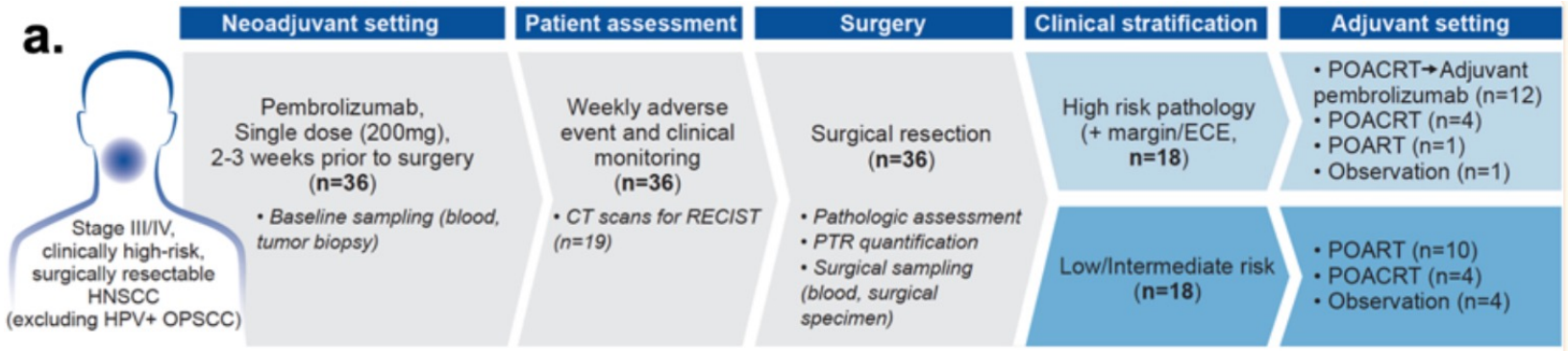
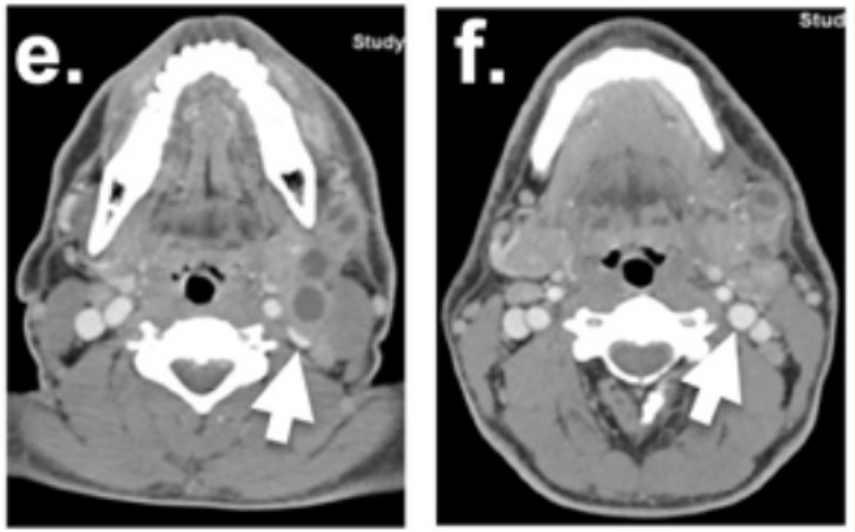





Surgery for Head and Neck Cancer

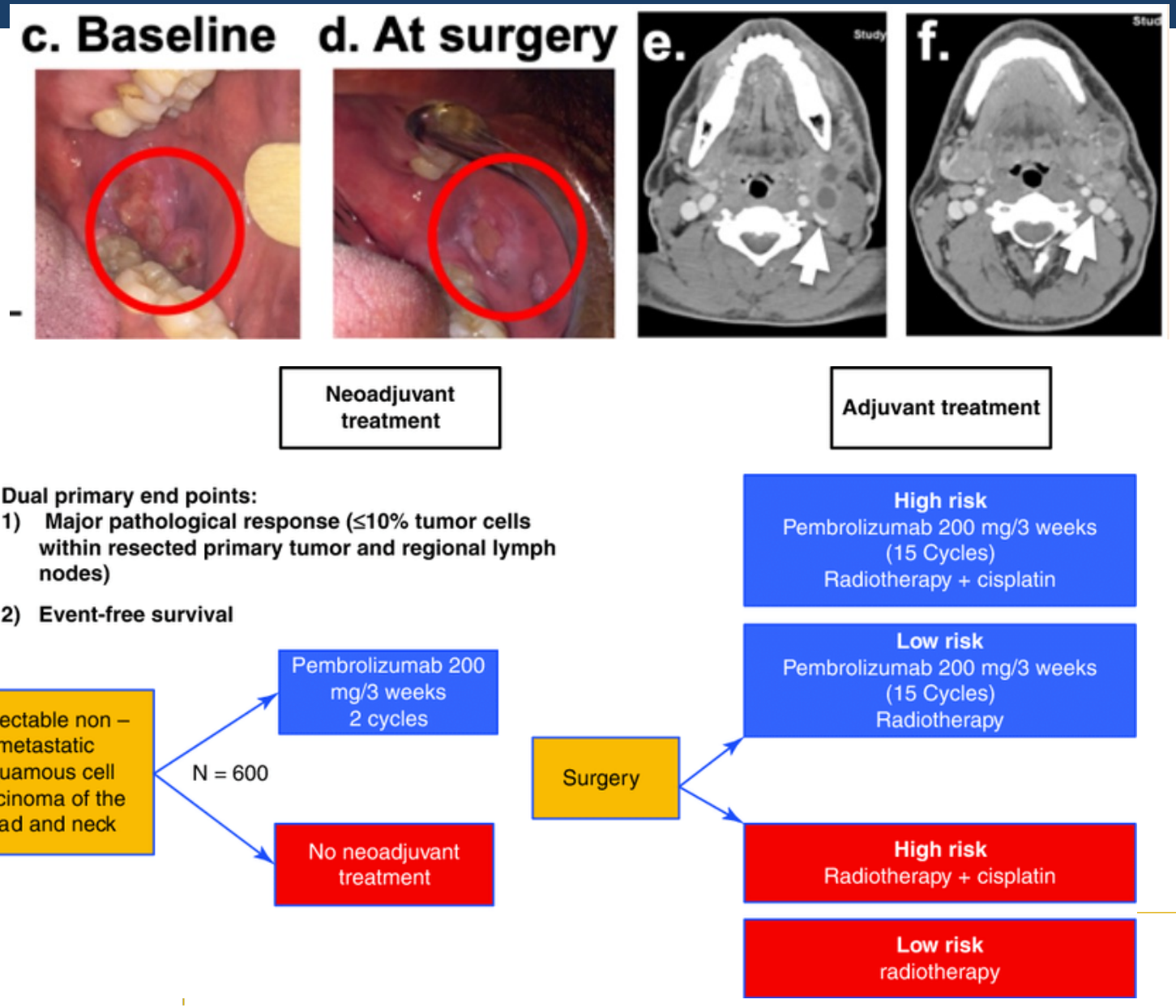
- Uppaluri et al. Clin Cancer Res, 2020
  - Single cycle pembrolizumab before surgery
    - Any pathologic response: 44%
      - 8/36 patients> 50% response
      - 8/36 patients: 10-49% response
      - 0/36 pCR





Surgery for Head and Neck Cancer

- Neoadjuvant therapies
  - Reduce morbidity
  - Improve survival
- KEYNOTE-689
  - resectable, stage III/IVA HNSCC
  - Phase III trial
  - 704 enrollment



Surgery for Head and Neck Cancer

- Adjuvant therapies
  - Improve survival
  - Reduce morbidity
- KEYNOTE-630: Locally advanced high-risk cutaneous SCCa after surgery and radiation
  - Phase III trial
  - 570 enrollment
  - 1:1 IV pembrolizumab (400 mg Q6W) or placebo for up to 9 cycles (~1 year)

Surgery for Head and Neck Cancer

- Adjuvant therapies
  - Reduce morbidity
  - Improve survival
- RTOG-1216
  - After primary surgery
  - Stage III/IV HNSCC with ***ENE*** or ***positive margin***
  - Phase III trial
  - 684 enrollment

    Weekly cisplatin *vs.*

    Weekly docetaxel + cetuximab *vs.*

    Weekly cisplatin + atezolizumab Q3W for up to 8 doses

Surgery for Head and Neck Cancer

- Questions?
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