Treatment of oral cavity carcinomas

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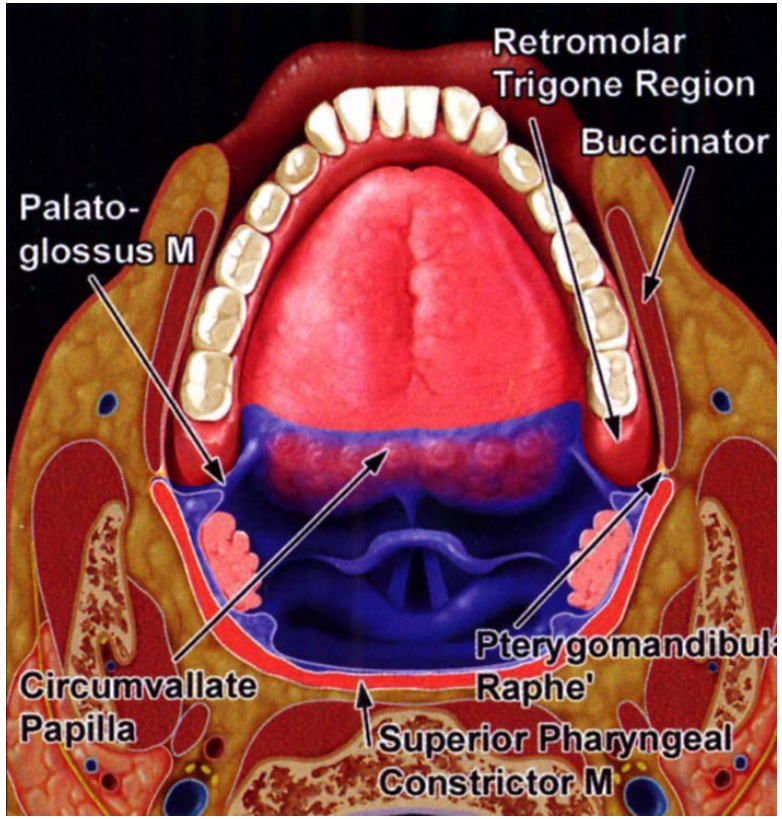
USZ Universitäts Spital Zürich

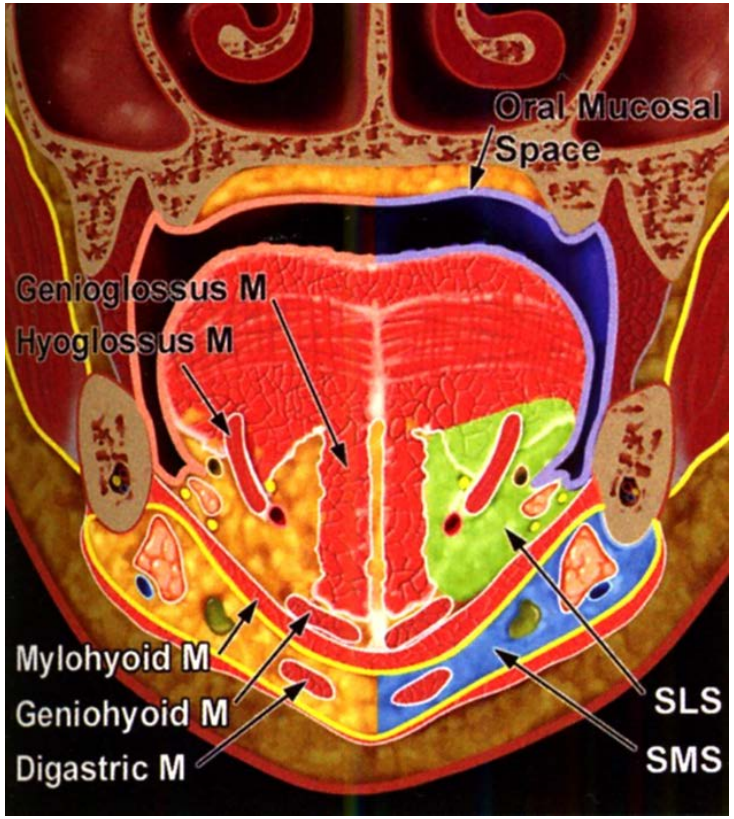
Learning objectives

Focus on

1. Epidemiology of oral cavity cancer in Switzerland
2. Diagnostic of oral cavity cancer
3. Relevant aspects of the TNM classification of neoplasms of the oral cavity
4. Parameters for treatment decisions

Oral cavity and subsites

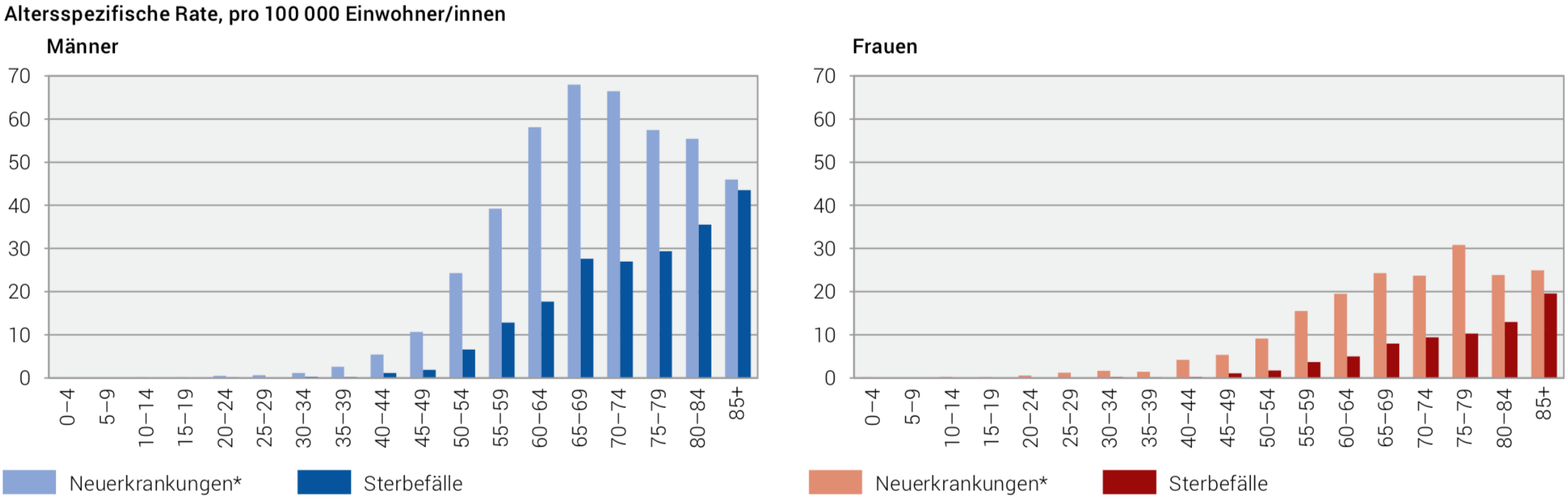




- lips
- 2/3 of the tongue
- buccal mucosa
- gingiva
- hard palate
- retromolar trigone
- floor of the mouth

from Harnsberger Diagnostic Imaging Head and Neck, Amirsys 2004

Annual new cases and death rate in Switzerland



* Neuerkrankungen geschätzt aufgrund der Daten der Krebsregister

Quellen: NKRS – Neuerkrankungen; BFS – Sterbefälle

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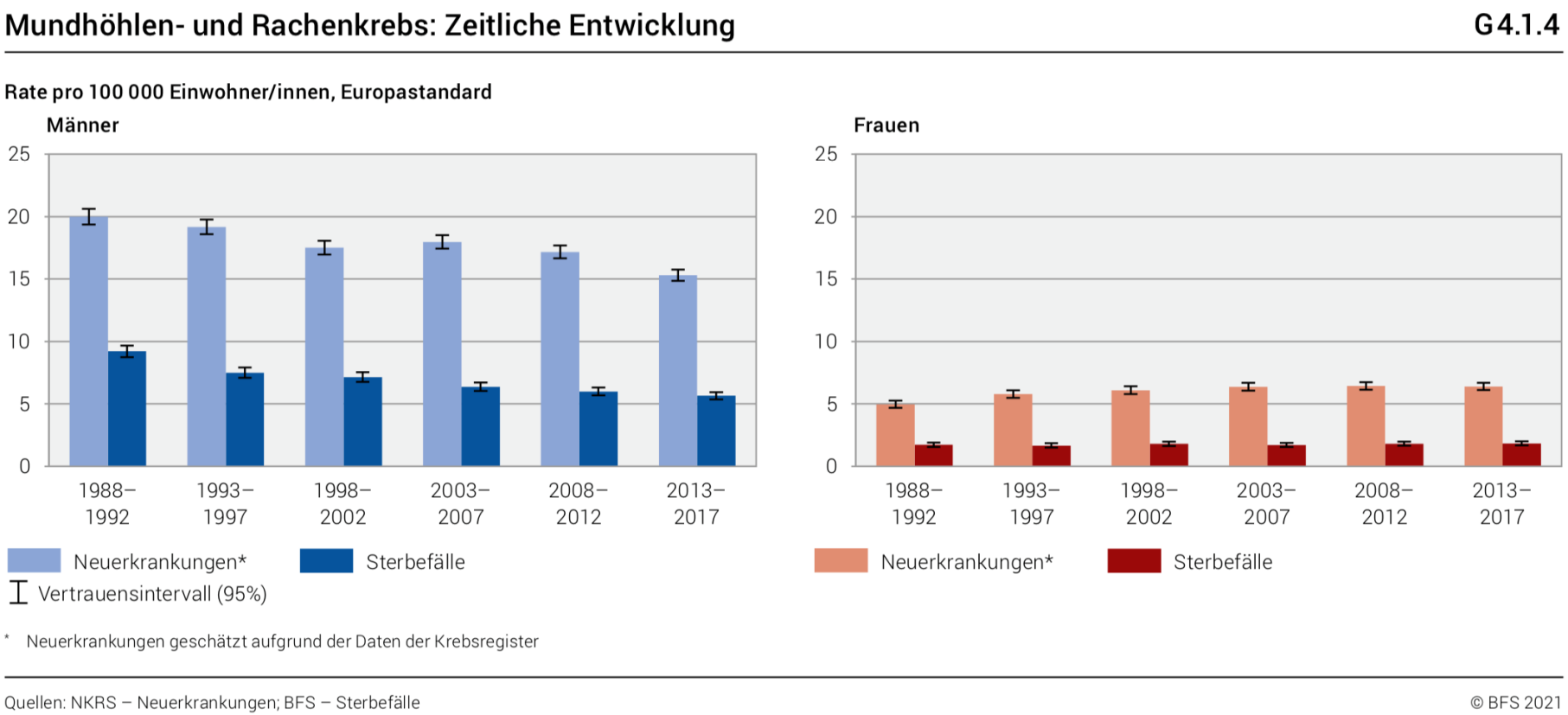
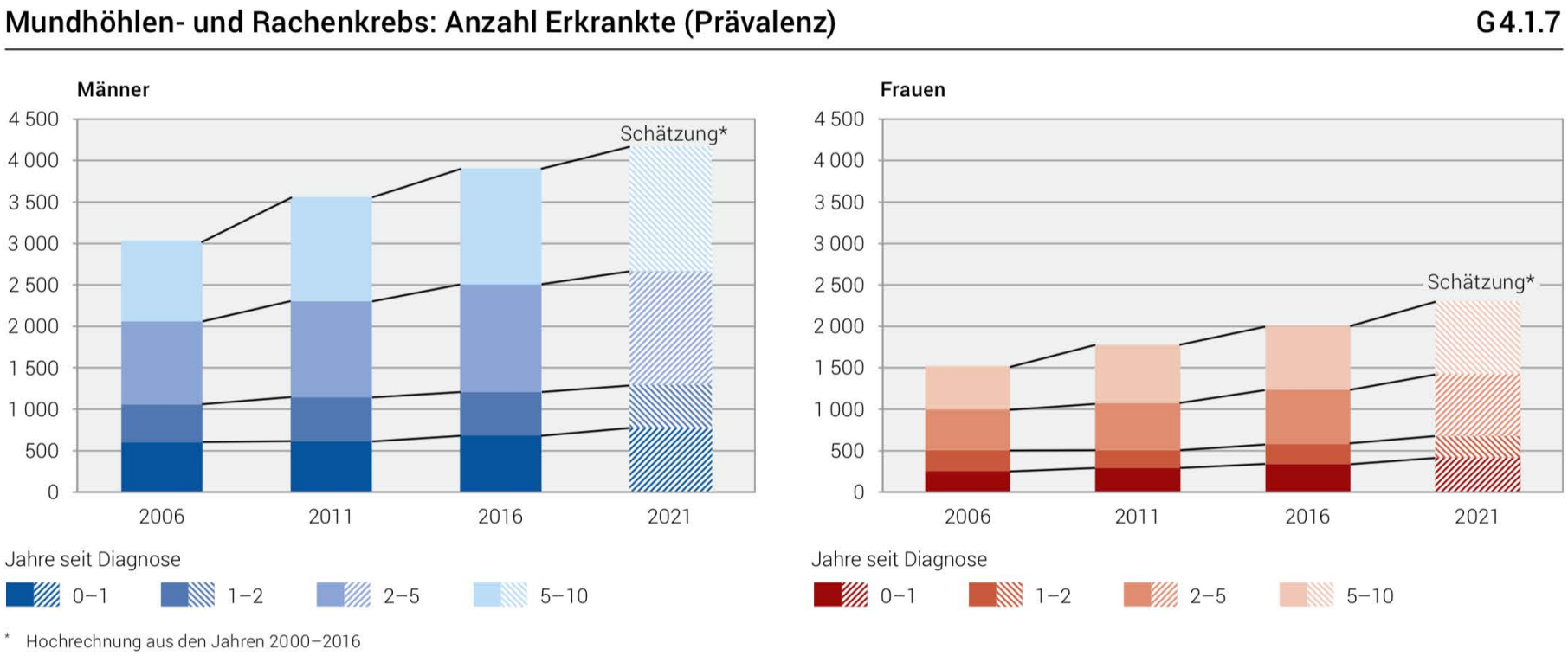
Development in the past 30 years

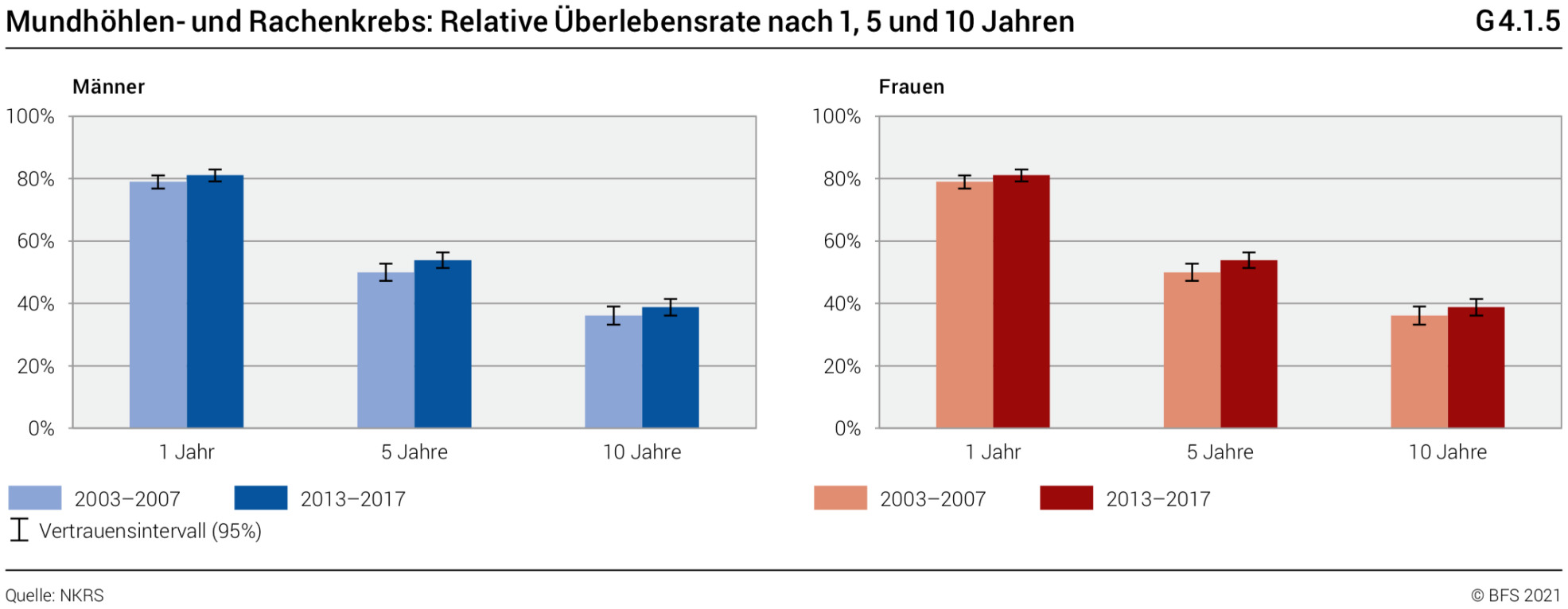


-> Inzidenz leicht rückläufig

Prevalance


Mundhöhlen- und Rachenkrebs: Anzahl Erkrankte (Prävalenz)
G 4.1.7
Männer
Frauen
4 500
4 000
3 500
3 000
2 500
2 000
1 500
1 000
500
0
Schätzung*
2006
2011
2016
2021
Jahre seit Diagnose
0–1
1–2
2–5
5–10
* Hochrechnung aus den Jahren 2000–2016
Quelle: NKRS
© BFS 2021

Survival



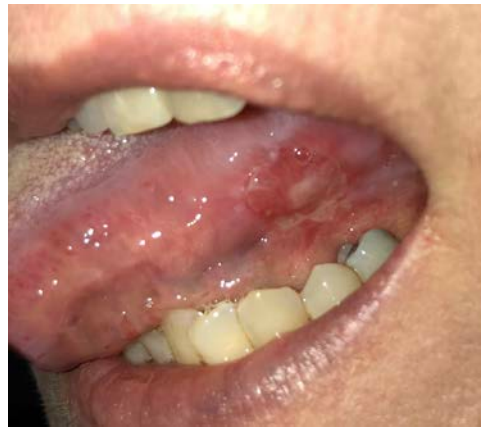
Five year overall survival 50%

How to diagnose oral cancer?

Signs and Symptoms?

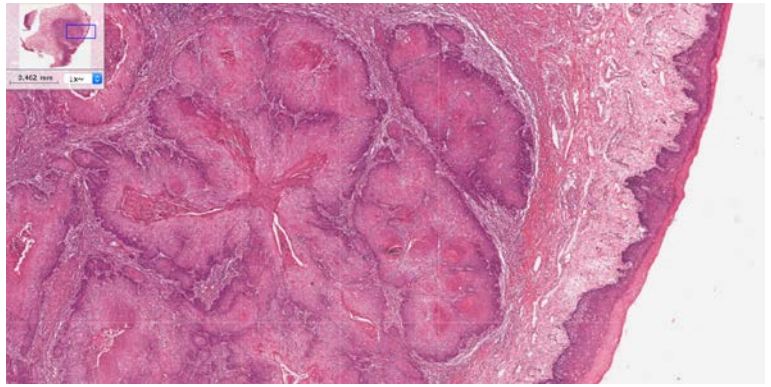
- A lip or mouth sore that doesn't heal
- A white or reddish patch on the inside of your mouth
- Loose teeth
- A growth or lump inside your mouth
- Mouth pain
- Ear pain
- Difficult or painful to articulate or swallowing

How to diagnose oral cancer?



Further diagnostic steps?

- Case history
  - Risk factors (smoking, alcohol), symptoms (articulation, pain, food intake, loss of weight) medical record, medication
- ENT exam
- Biopsy in local anesthesia if applicable
- Imaging
- Panendoscopy



Squamous cell cancer

NCCN Guidelines Version 2.2019
Cancer of the Oral Cavity

NCCN Guidelines Index
Table of Contents
Discussion

Buccal mucosa, floor of mouth, anterior tongue, alveolar ridge, retromolar trigone, hard palate

WORKUP

- H&P[a,b] including a complete head and neck exam; mirror and fiberoptic examination as clinically indicated
- Biopsy
- As clinically indicated:
  - Chest CT (with or without contrast)[c]
  - CT with contrast and/or MRI with contrast of primary and neck
  - Consider FDG-PET/CT[d]
  - Examination under anesthesia (EUA) with endoscopy
  - Preanesthesia studies
  - Dental/prosthodontic evaluation,[e] including Panorex or dental CT without contrast
  - Nutrition, speech and swallowing evaluation/therapy[f]
- Multidisciplinary consultation as indicated

CLINICAL STAGING

- T1-2, N0 → See Treatment of Primary and Neck (OR-2)
- T3, N0 → See Treatment of Primary and Neck (OR-3)
- T1-3, N1-3 → See Treatment of Primary and Neck (OR-3)
- T4a, N0-3 → See Treatment of Primary and Neck (OR-3)
- T4b, N0-3 or Unresectable nodal disease or Unfit for surgery → See Treatment of Very Advanced Head and Neck Cancer (ADV-1)
- Metastatic (M1) disease at initial presentation → See Treatment of Very Advanced Head and Neck Cancer (ADV-2)

[a]H&P should include documentation and quantification (pack years smoked) of tobacco use history. Smoking cessation counseling as clinically indicated. All current smokers should be advised to quit smoking, and former smokers should be advised to remain abstinent from smoking. For additional cessation support and resources, smokers can be referred to the NCCN Guidelines for Smoking Cessation and www.smokefree.gov.
[b]Screen for depression (See NCCN Guidelines for Distress Management).
[c]Chest CT is recommended for advanced nodal disease to screen for distant metastases, and for select patients who smoke to screen for lung cancer. See NCCN Guidelines for Lung Cancer Screening.
[d]See Discussion.
[e]See Principles of Dental Evaluation and Management (DENT-A).
[f]See Principles of Nutrition: Management and Supportive Care (NUTR-A).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

Imaging algorithm oral cavity

- **MRI**
  - for soft tissue delineation, perineural spread, transspatial extension
- **CT**
  - for edentulous parts, cortical bone, skull base
  - for critical ill or for noncooperative patients, MR noncompatible pacemaker
- **PET-CT**
  - In T3/T4, N+ patients
- **Ultrasound (with fine needle aspiration cytology)**
  - Neck staging

Diagnostische Richtlinie für Vorstellungen am Tumorboard des Kopf-Hals-Tumorzentrum (KHTZ)

(exkl. Schilddrüsentumoren)

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- Für die Erstvorstellung am Tumorboard des Kopf-Hals-Tumorzentrums ist der untenstehende diagnostische Algorithmus **obligat**.
- Unvollständig abgeklärte Patienten werden nur in Ausnahmefällen und nach Rücksprache vorgestellt.
- Bei der Anmeldung sind **Vorerkrankungen und Vorbehandlungen** anzugeben

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Verdacht auf Kopf-Hals-Tumor
inkl. Rezidive und Zweittumore

Verdacht auf Schleimhautkarzinom

Bioptische Sicherung
- Biopsie des Primärtumors zwingend. Falls Tumor nicht ohne Narkose zugänglich: Endoskopie +/- Panendoskopie (Indikation für Panendoskopie siehe unten)
- Bei nicht eindeutigen Lymphknotenmetastasen und regionären Rezidiven: FNP
- p16-Bestimmung bei pharyngealen Tumoren, falls p16 positiv: HPV-DNA Bestimmunng
- EBV-Bestimmung bei nasopharyngealen Tumoren

Bildgebung

Larynx:	T1-T2 N0: CT Hals mit Feinschicht Larynx + Low dose CT Thorax T3-4 oder N+ oder Rezidiv: PET-CT + bei Bedarf MR Hals
Pharynx/ Mundhöhle:	T1-T2 N0: MR Hals + Low dose CT Thorax T3-4 oder N+ oder Rezidiv: PET-CT + bei Bedarf MR Hals bei Knocheninfiltration inkl. Feinschicht-CT Kiefer +/- Angio-CT Beine
Nase/NNH:	T1-T2 N0: MR NNH* + Feinschicht-CT NNH + Low dose CT Thorax T3-4 oder N+ oder Rezidiv MR NNH* + PET-CT inklusive Feinschicht-CT NNH

*Gemäss Zurich sinonasal tumour protocol

Endoskopie/ Panendoskopie
Endoskopie in Narkose zur Tumorevaluation bei allen Tumoren
Zusätzlich Ösophagoskopie und Bronchoskopie im Sinne einer Panendoskopie bei:
- Risikofaktoren (Nikotin, Alkohol)
- Carcinoma of unknown primary: inklusive Tonsillektomie und Biopsie von Auffälligkeiten im PET-CT

Verdacht auf anderes Karzinom (Speicheldrüsen, Haut, andere)

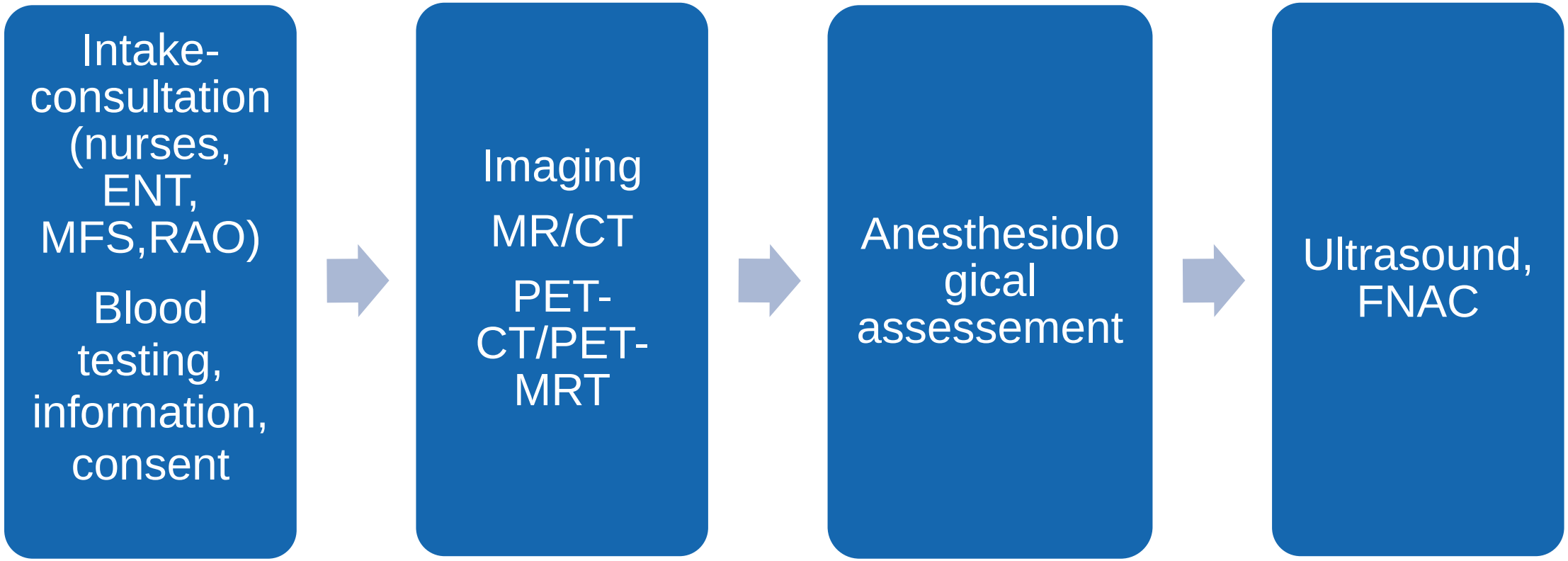
Bioptische Sicherung
Falls Tumor nicht ohne Narkose zugänglich: Endokopie in Vollnarkose
Tumor der Grossen Speicheldrüsen: Feinnadelpunktion

Bildgebung

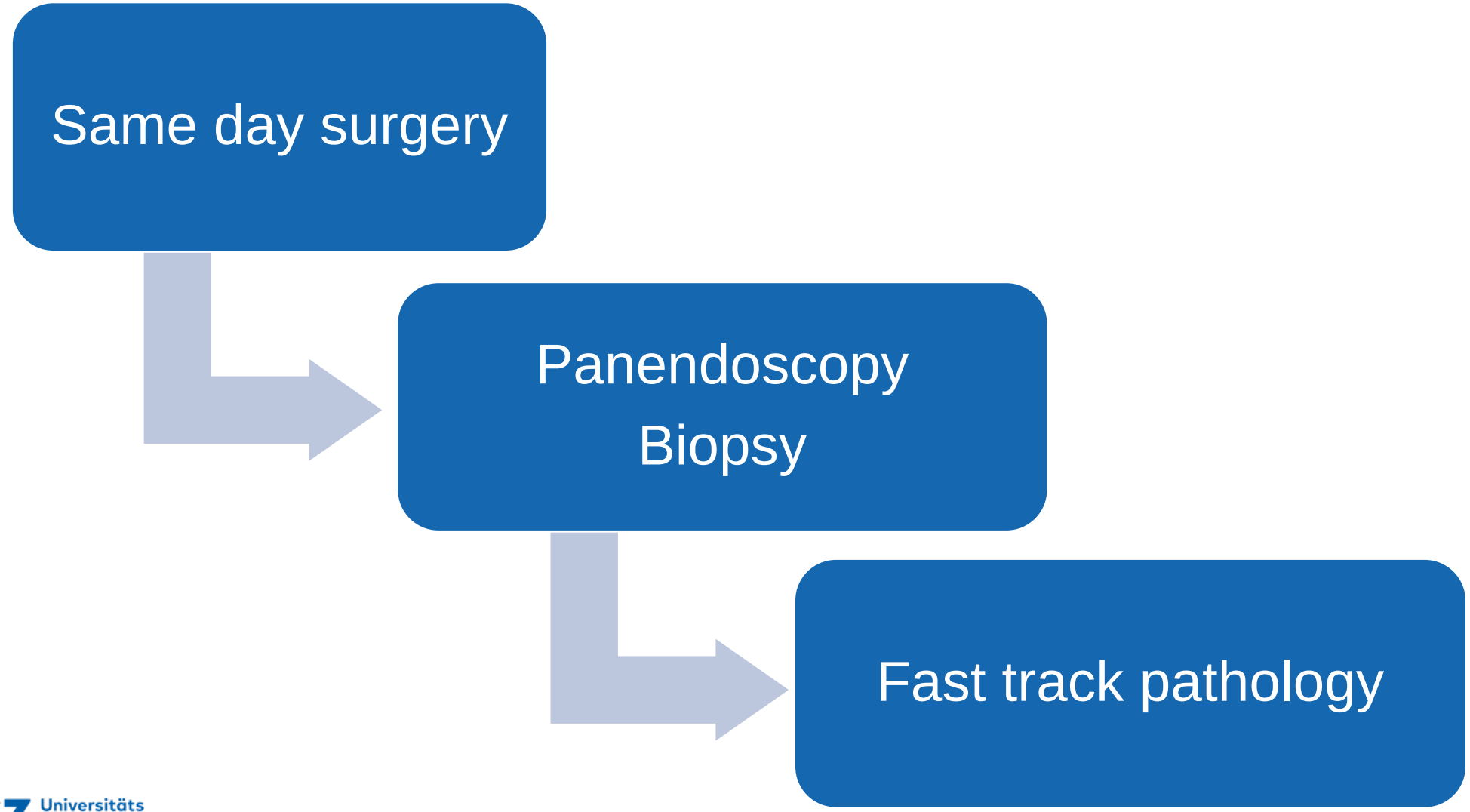
Speicheldrüsen:	Falls Zytologie unklar und T1-T2: MR Hals Falls Zytologisch low-grade Tumor: MR Hals Falls zytologisch oder klinisch high-grade Karzinom wahrscheinlich: MR Hals + PET-CT
Haut (Spinaliom):	T1-T2 N0: Sonografie Hals -> keine Tumorboardvorstellung T3-4 und/oder N+: PET-CT + bei Bedarf MR Hals -> Hauttumorboard
Andere:	Lokal begrenzter Befund: MR + Low dose CT Thorax Ausgedehnter Primarius oder N+: MR + CT-Thorax oder PET-CT

Anmeldung Tumorboard
Intern: via KISIM -> Tumordokumentation (VOLLSTÄNDIG ausgefüllt gemäss Weisung)
Extern: via Email: **halschirurgie@usz.ch** zuhanden Dr. S. Müller / PD Dr. M. Broglie-Däppen

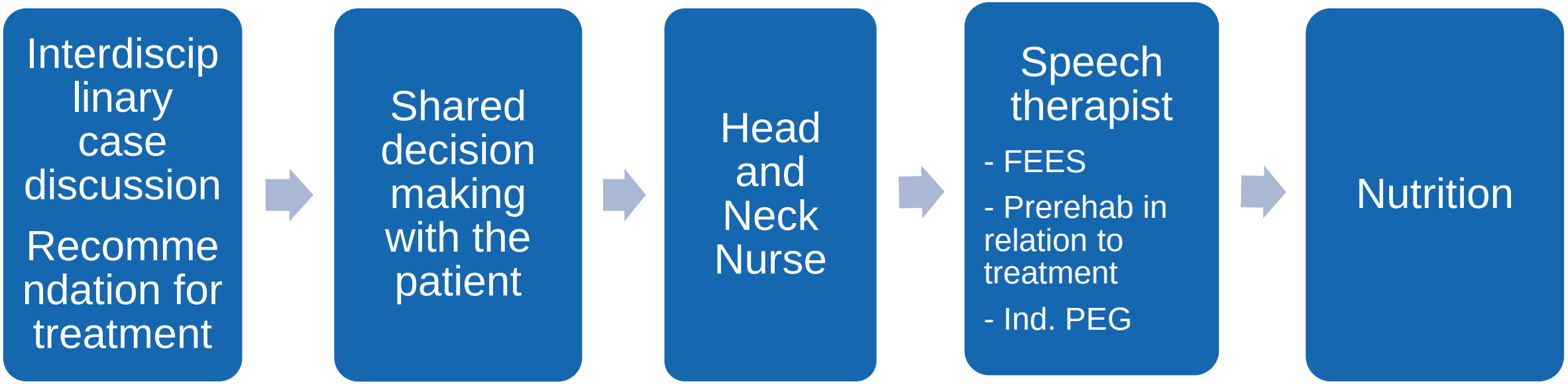
Fast track tumor evaluation in Zurich
Day 1



Day 2


Same day surgery
Panendoscopy
Biopsy
Fast track pathology

Day 3



Further evaluation if indicated
- Dentist
- Audiometry

Therapeutic principles in oral cavity cancer

Dependent on

1. **tumor size**
2. **tumor stage**
3. **Previous treatment**
4. **Patient factors (Comorbidities, preferences)**

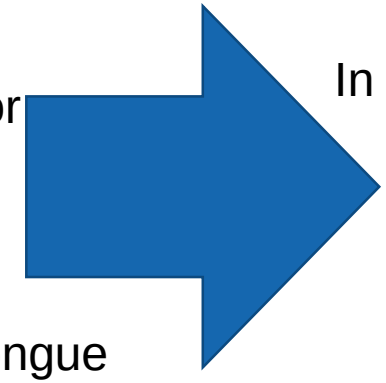
Treatment decisions should include the treatment of the primary tumor and the neck

1. Elective neck treatment (risk of occult metastases, usual lymphatic drainage) by sentinel node biopsy (T1/T2cN0) or elective Neck Dissection (Level I-III)
2. Therapeutic neck treatment in case of nodal involvment

Important questions to define treatment in oral cancer

Questions

- Tumor localisation
- TNM Category
  - T: Depths of invasion versus tumor thickness
  - Infiltration of further structures?
    - Bone: Mandible / maxilla
    - Muscle: intrinsic / extrinsic tongue muscles / pterygoid muscle
    - Salivary glands
    - Nerves: perineural spread
  - N-category / ENE



Consequences

Access?

In T3/T4 tumors adjuvant radiotherapy

- Bony reconstruction (free flap)
- Reconstruction of soft tissue (free flap)
- Connection between the oral cavity and the neck
- R0-Resection achievable? Adjuvant treatment?

- In N+ tumors adjuvant radiotherapy, in ENE even adjuvant radiochemotherapy

Surgery is the preferable treatment option in

Oral cavity

- **Surgery**
  - **T1/T2 surgical resection, secondary healing**
  - **T3/T4 surgical resection, reconstruction (bony, soft tissue)**

Function preservation?

Indications for adjuvant RT / RCT

Adjuvant RT

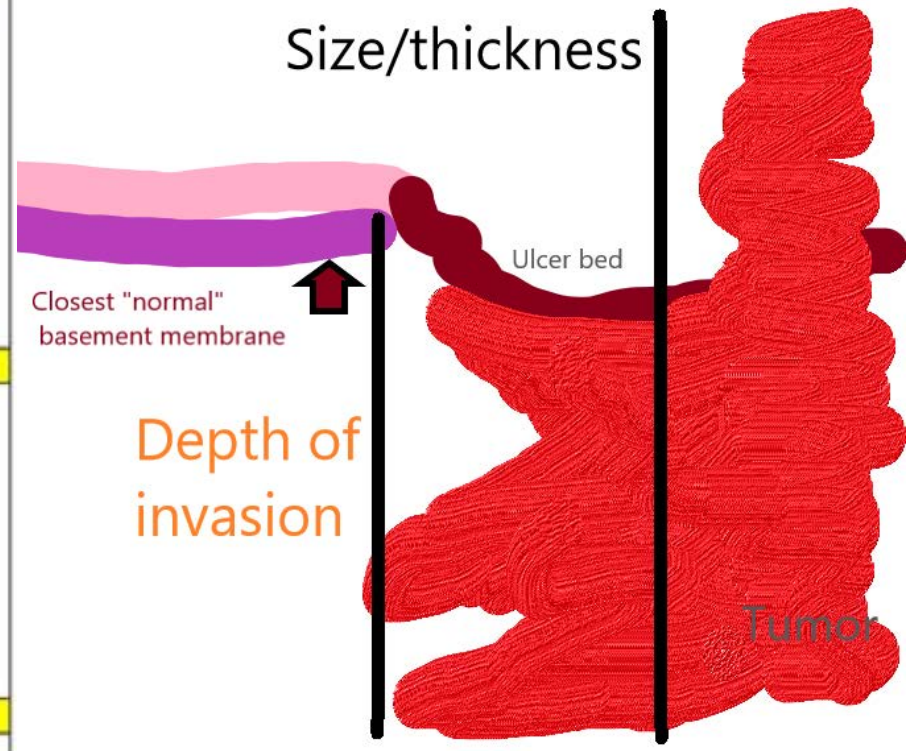
- T3/T4
- Perineural spread, Lymphangiosis
- multiple positive lymph nodes (> N1)

Adjuvant RCT

- R1/R2 Resection (positive margins)
- Extranodal extension

Bernier, Cooper 2004

Change	7th Ed. (2010)	8th Ed. (2017)		
		Oral Cavity	HPV- Oropharynx	HPV+ Oropharynx
T-stage	**T0**: no primary **T1**: size ≤2cm **T2**: size 2-4cm **T3**: size >4cm **T4:** ○ **T4a**: moderately advanced (extrinsic tongue muscle involvement constituted T4a) ○ **T4b**: very advanced	• **T0** deleted • **T1:** size ≤2cm and **DOI ≤5mm** • **T2:** size ≤2cm and **DOI 5-10mm** or size 2-4cm and **DOI ≤10mm** • **T3:** size >4cm or **>10mm DOI** • **T4a** extrinsic tongue muscle infiltration now deleted	• **T0** deleted	• **T0** if proven p16+ disease without evidence of primary tumor • All locally advanced combined to **T4**
		Clinical N-stage		
	N0: no LN involved **N1**: single ipsi LN ≤3cm in size **N2:** ○ **N2a**: single ipsi LN, 3-6cm in size ○ **N2b**: multiple ipsi LNs, all ≤6cm in size ○ **N2c**: any bi or ctr LNs, all ≤6cm in size **N3**: any LN >6cm in size	• **N1-N2** is same as previous and **ENE(-)** • **N3** now with subcategories: ○ **N3a** is previous N3 (size >6cm) and **ENE(-)** ○ **N3b** is any **ENE(+)**, either clinical or radiographic		• Previous N1, N2a combined to **N1 (≤6cm with or without ENE)** • Previous N2b, N2c combined to **N2**
		Pathological N-stage		
		• Microscopically evident ENE(+) LNs results in upstaging		• **N1**: ≤4 LNs involved • **N2**: >4 LNs involved • **N3** deleted
Stage grouping	Clinical or pathological TNM used for same grouping system	Same as previous		**Separate clinical and pathological TNM groupings**



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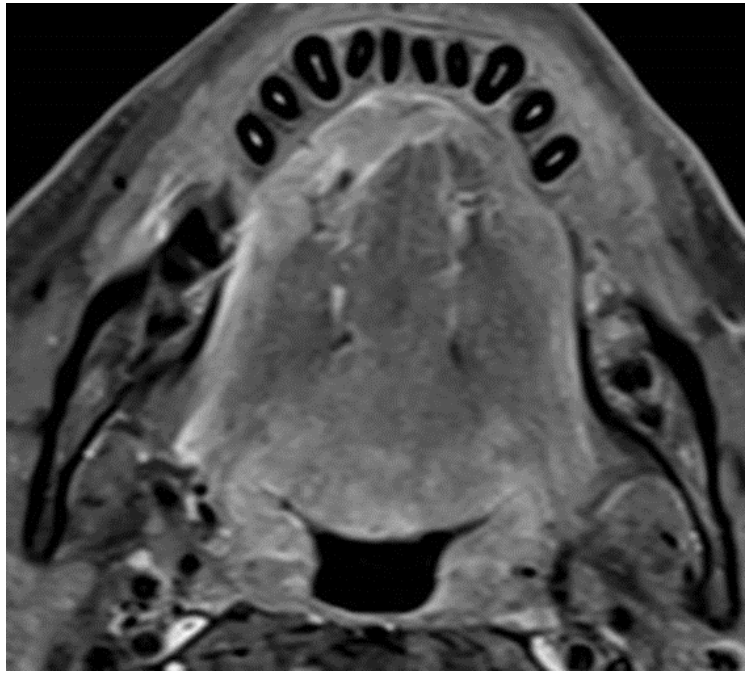
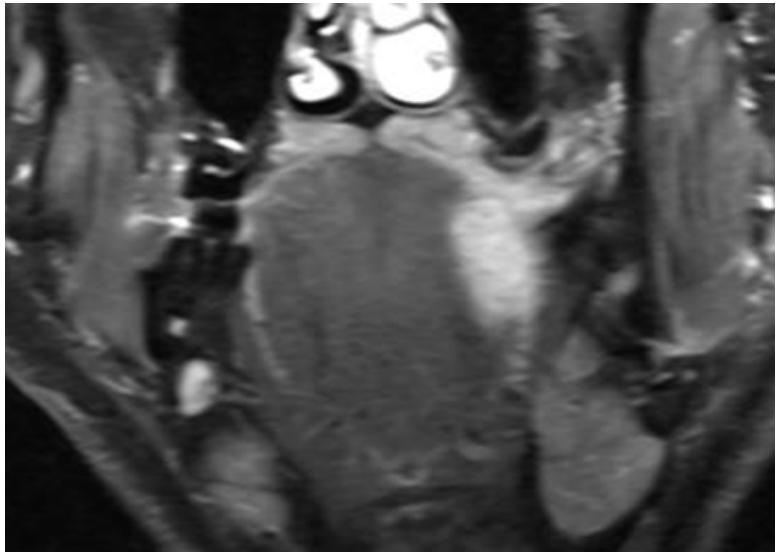
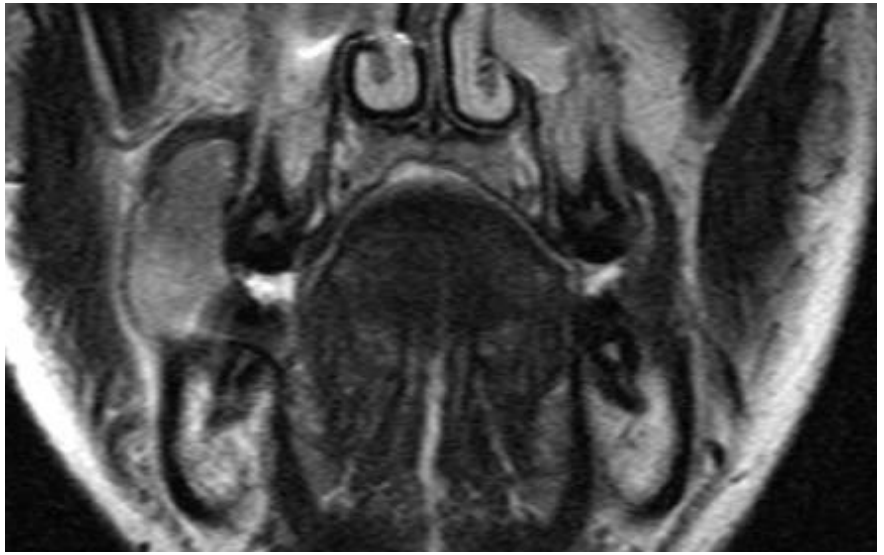
Oral cancer – tumor localisation



Floor of mouth

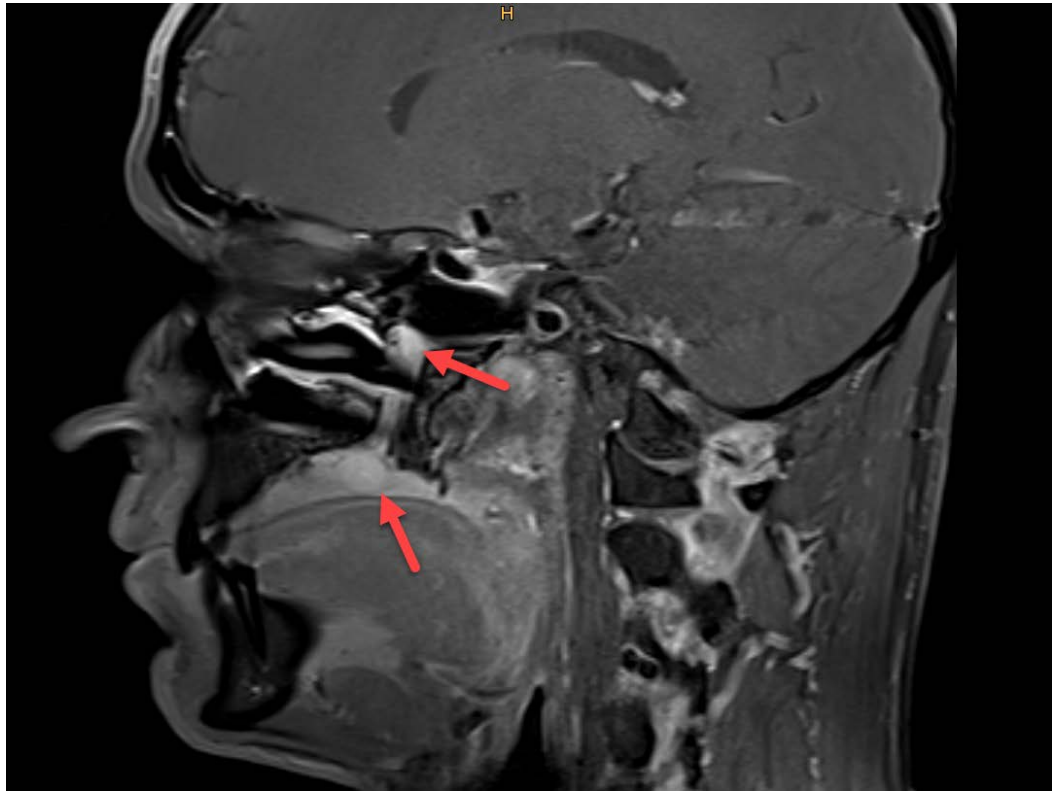


lateral tongue

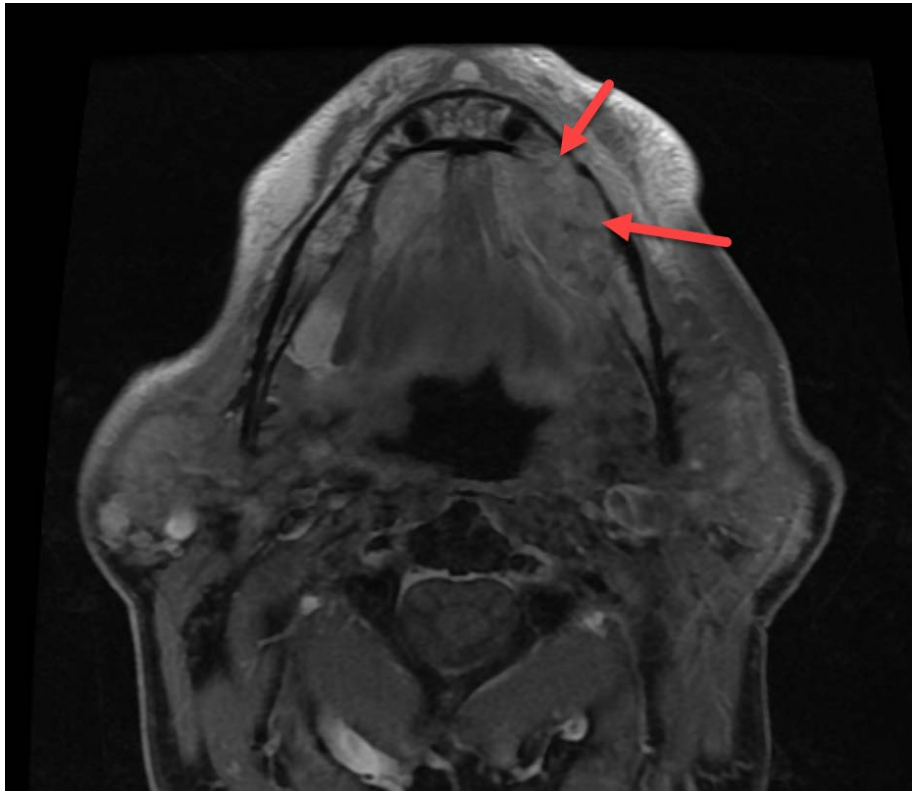


buccal mucosa

Oral cancer – infiltration of further structures?



T1 Sag with KM

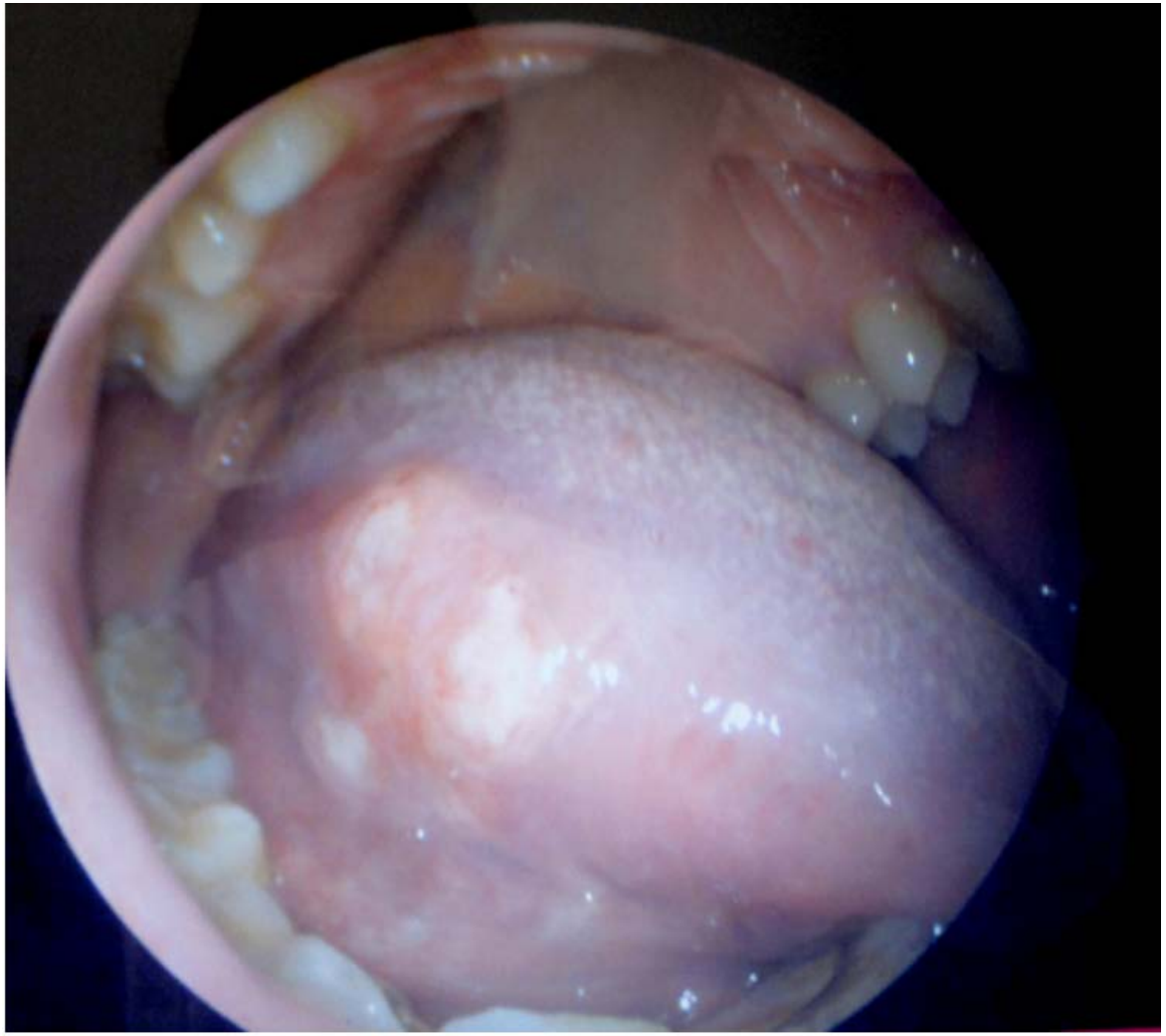


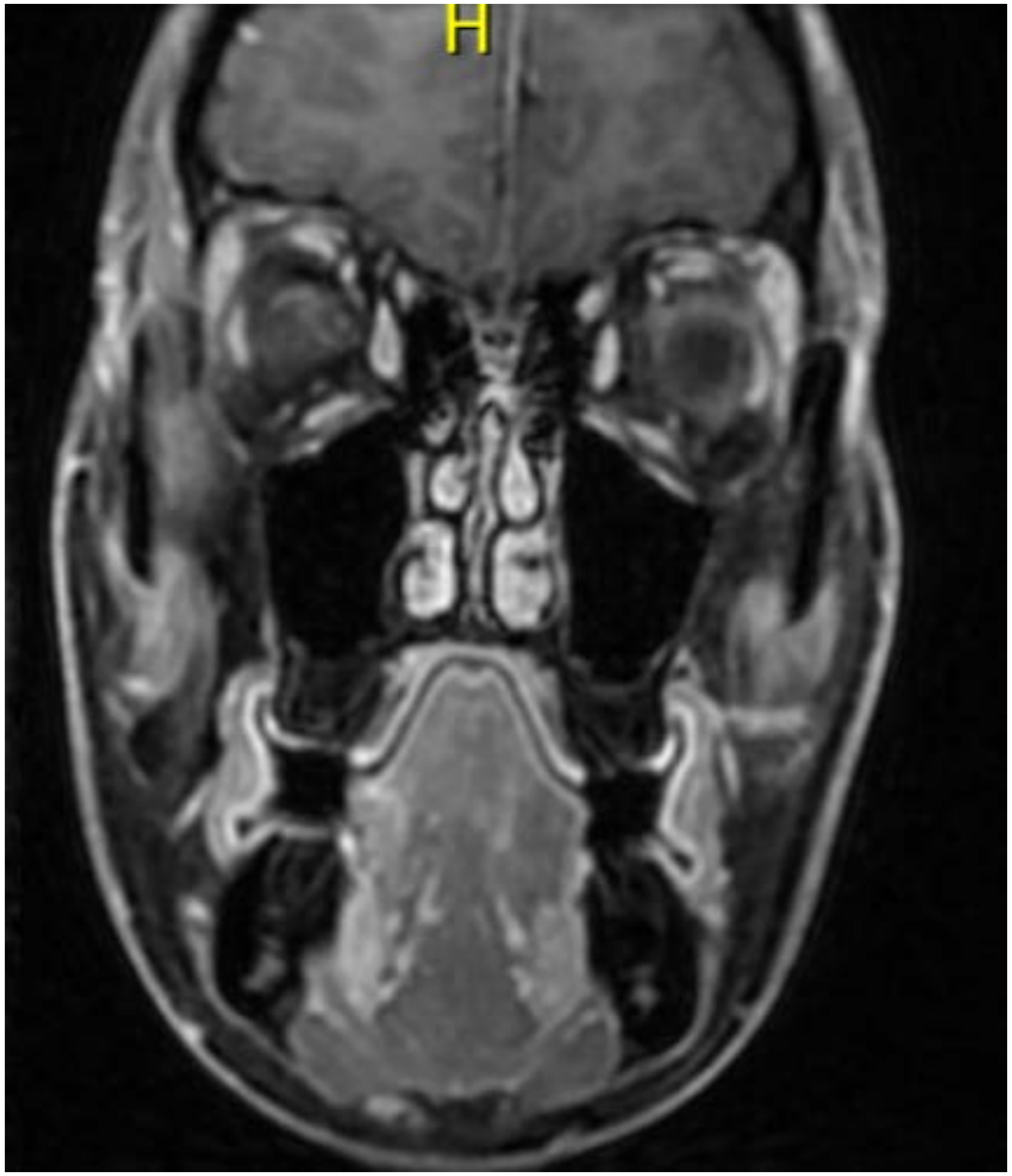
T1 axial GD Fat sat

34 years old women

- Painful sore on the left boarder of the tongue that does not heal for six weeks
- No risk factors

- Biopsy: squamous cell cancer

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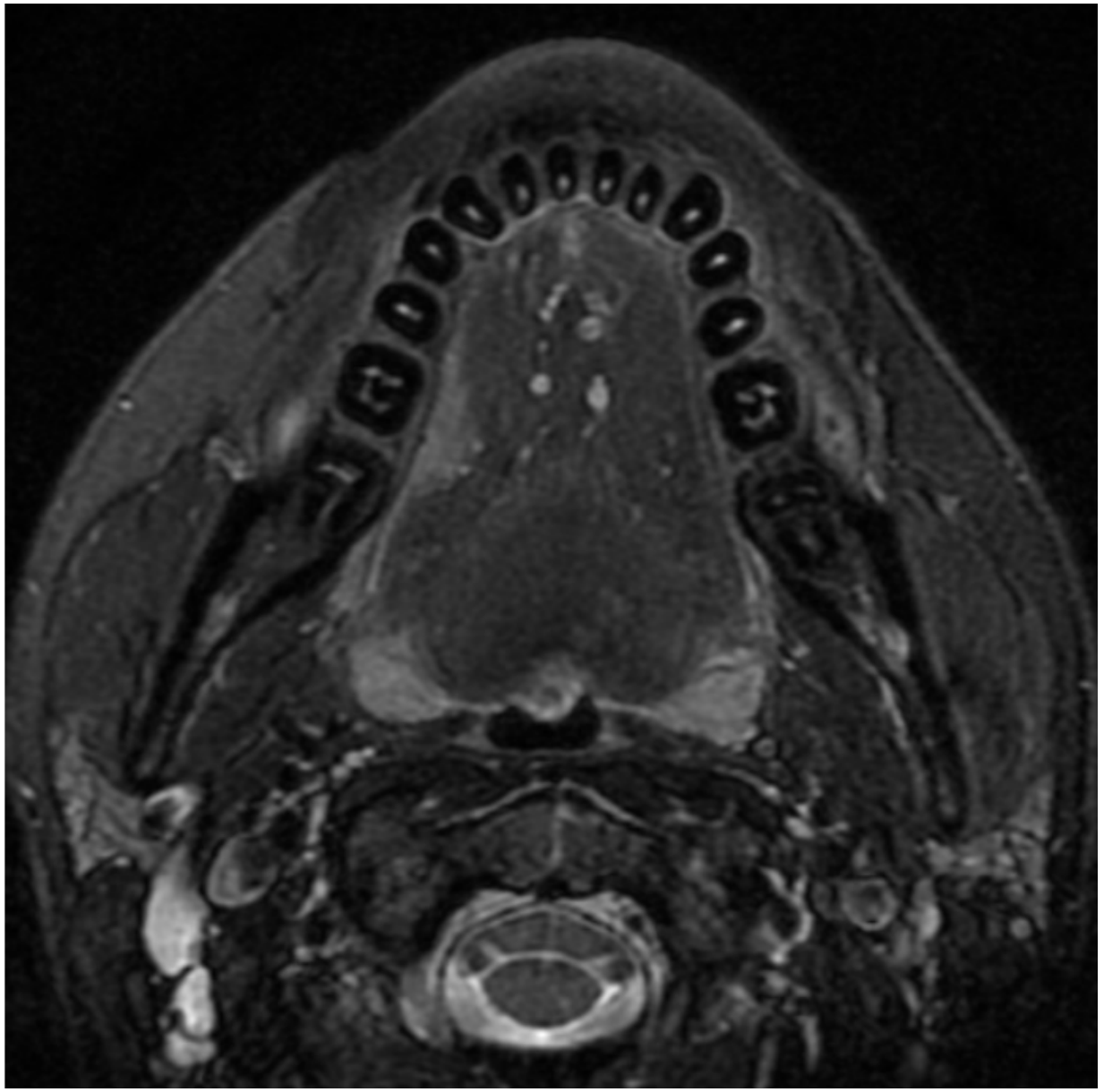
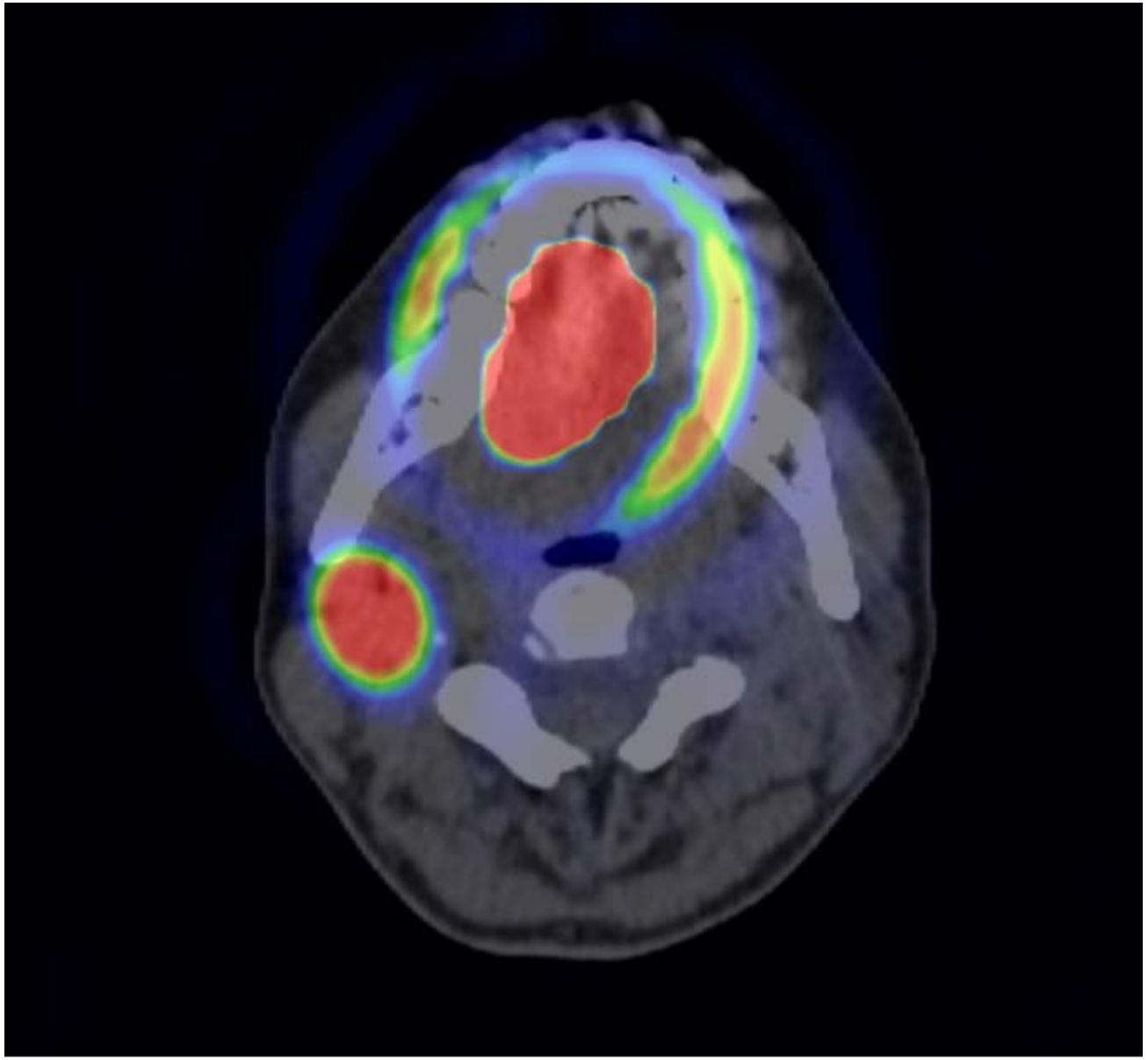
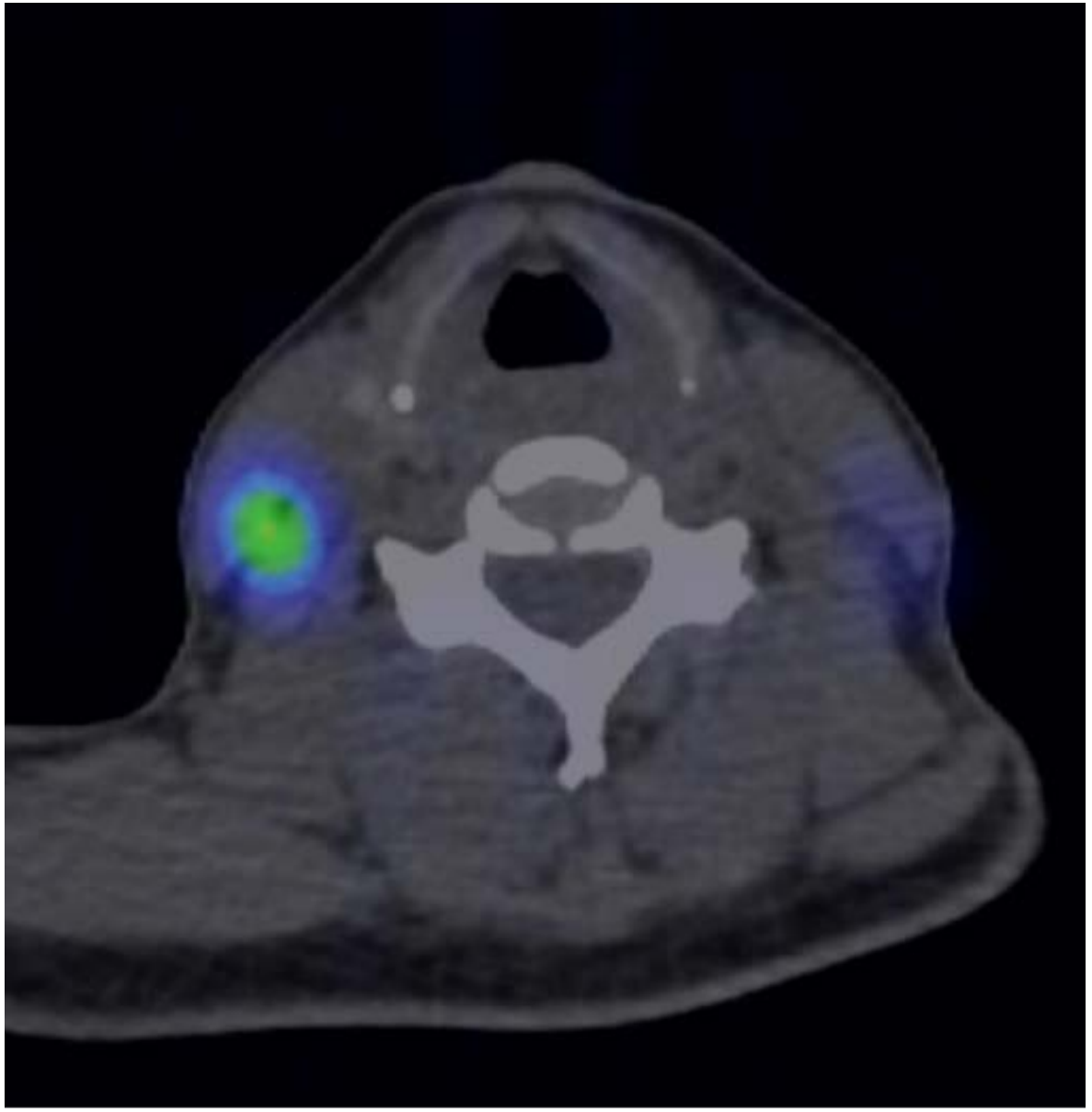






Diagnose

B 2017.8785-55: Resektat (Zungenrand rechts): Mässig bis wenig differenziertes, verhornendes Plattenepithelkarzinom (G2-3) mit ausgedehnter peritumoraler chronischer Entzündung.
Horizontale Ausdehnung 1,4 cm. Maximale Invasionstiefe 0,7 cm.
Keine Lymph- oder Blutgefässinvasion.
Keine Perineuralscheideninfiltration.

Kein Karzinom an den Resektionsrändern nachgewiesen.
Abstände zu den Präparaträndern: Anterior 2 mm, Zungenoberfläche 4,5 mm, mundbodenwärts 3 mm, zur Tiefe 3 mm, übrige Ränder >5 mm.
Bezüglich definitive Abstände vergleiche bitte Nachresektat unter B17.87907

TNM-Klassifikation (8. Auflage, 2017): pT2 V0 L0 G3.
Bezüglich pN-Status vergleiche bitte B17.87903-906

Ergänzende TNM-Klassifikation: pN0(sn)(0/4).

B 2017.87907: Nachresektat (Zungenrand rechts): Tumorfreie Schleimhaut und Muskelgewebe.

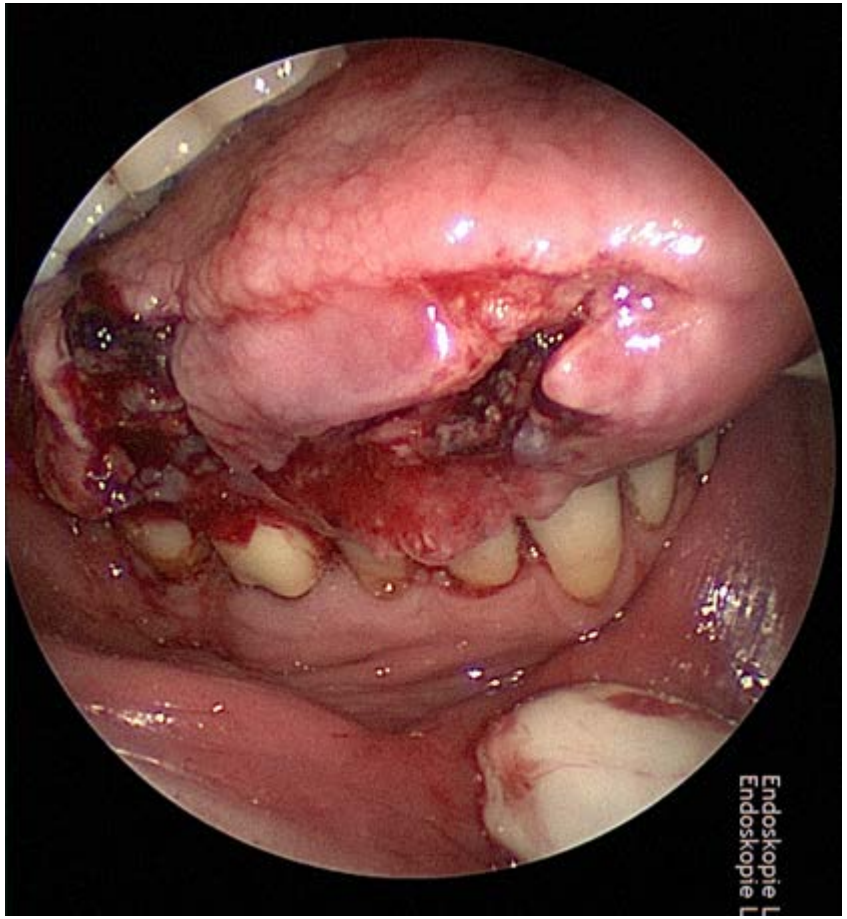
Further Treatment?

59 year old male

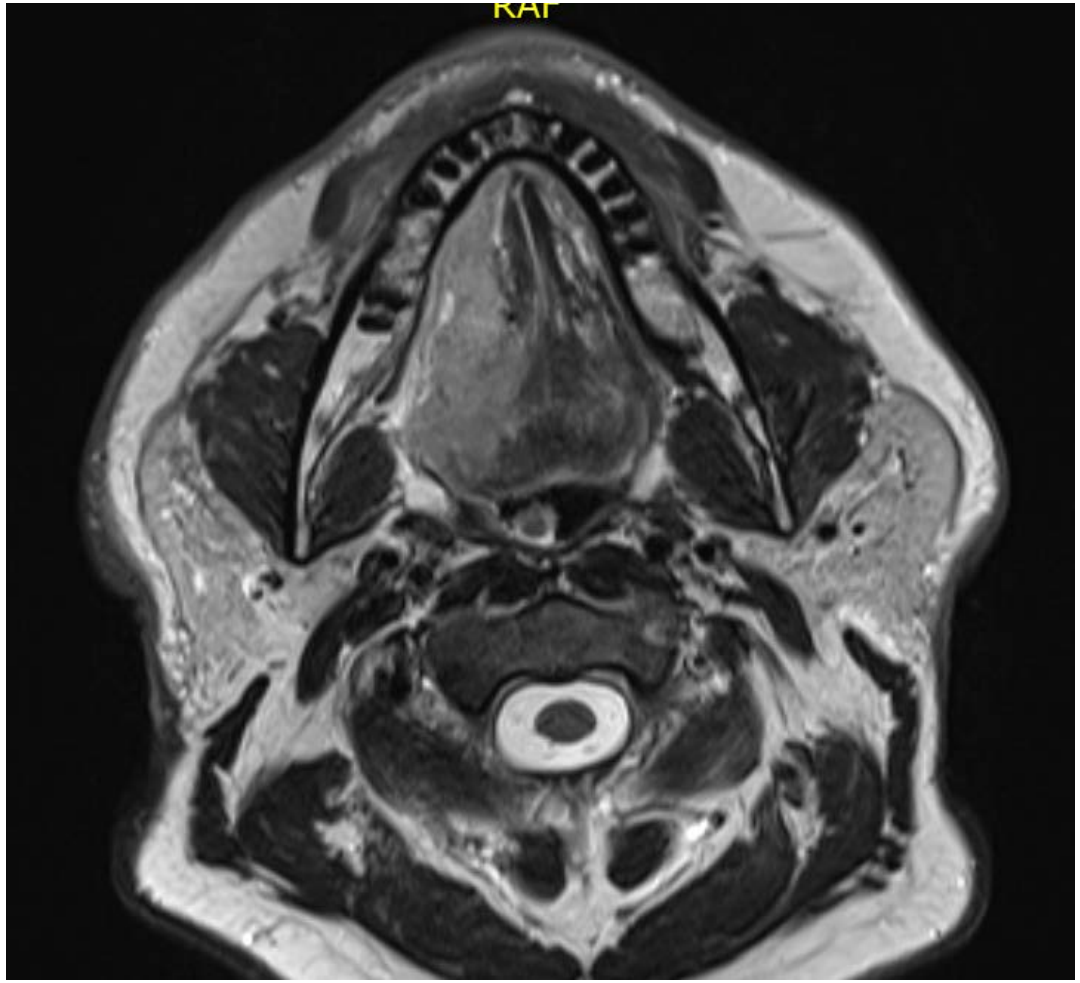
ulcerative mass at the lateral boarder of the tongue

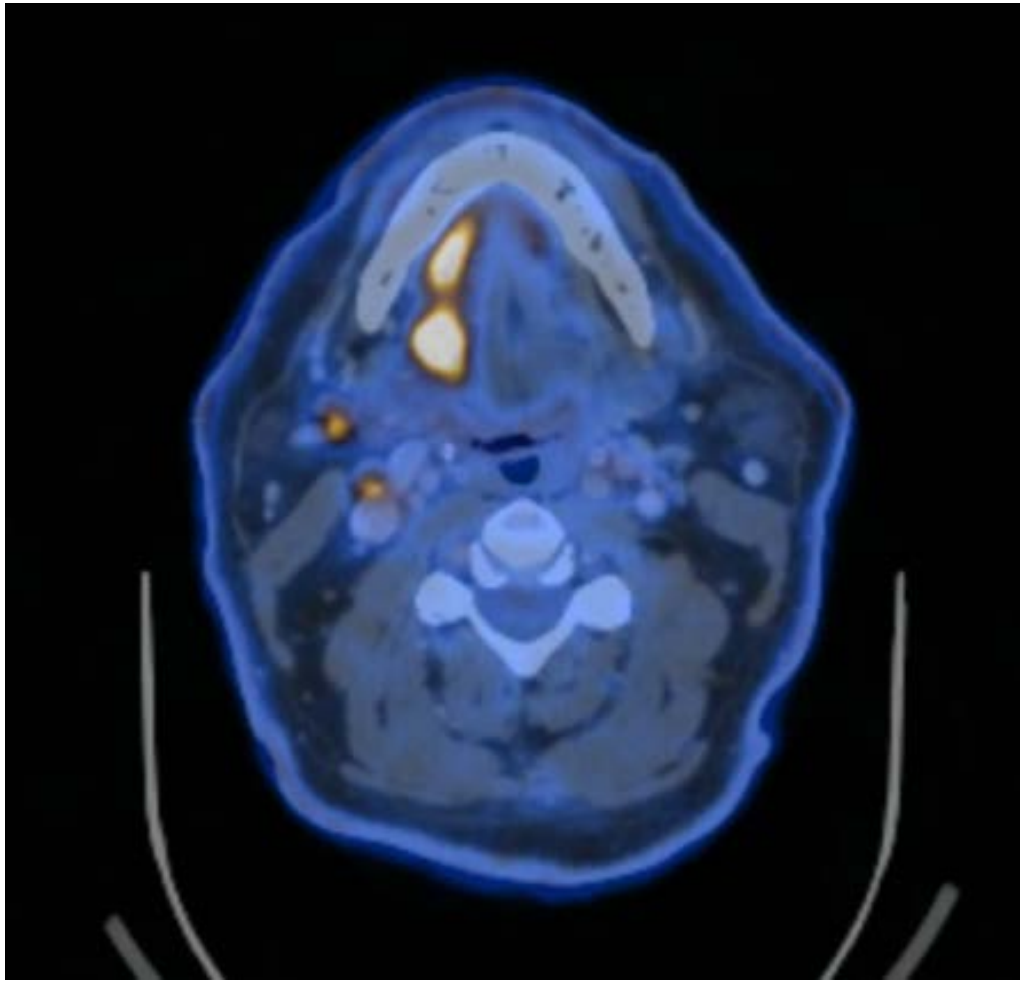
Progressive articulation difficulties and pain

Biopsy: squamous cell cancer

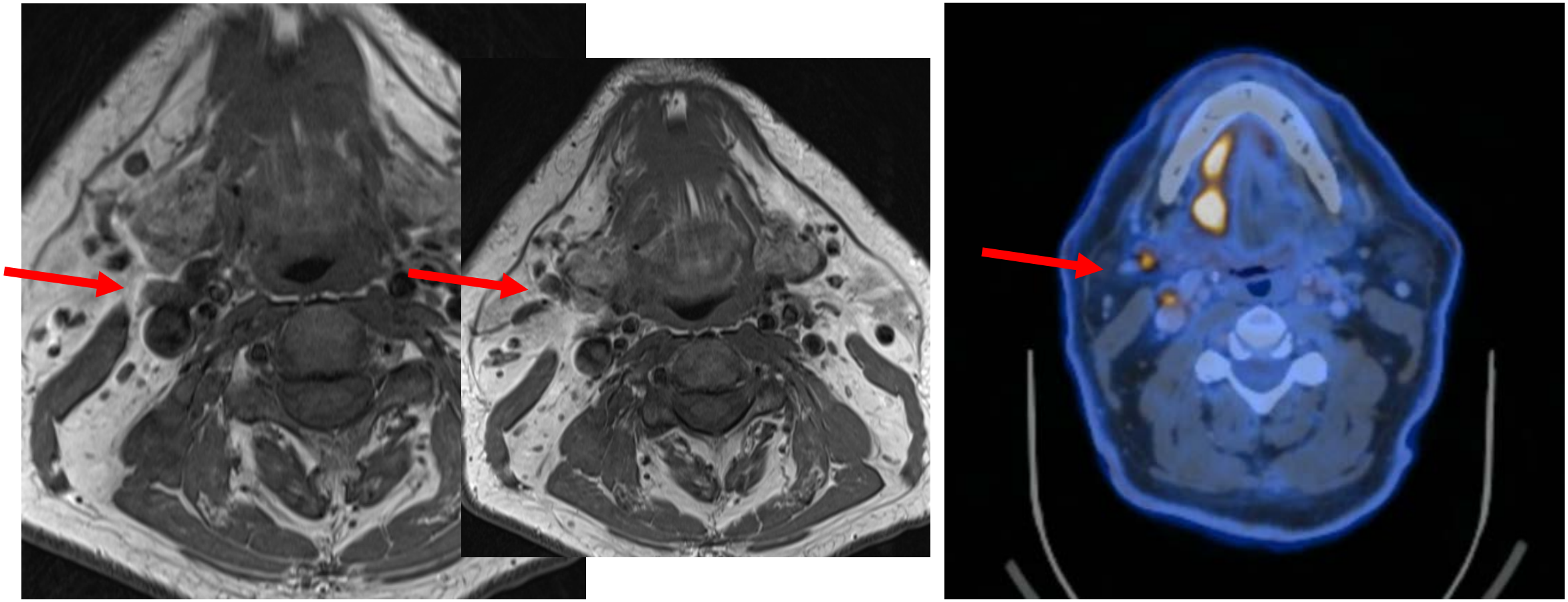


Primary tumor

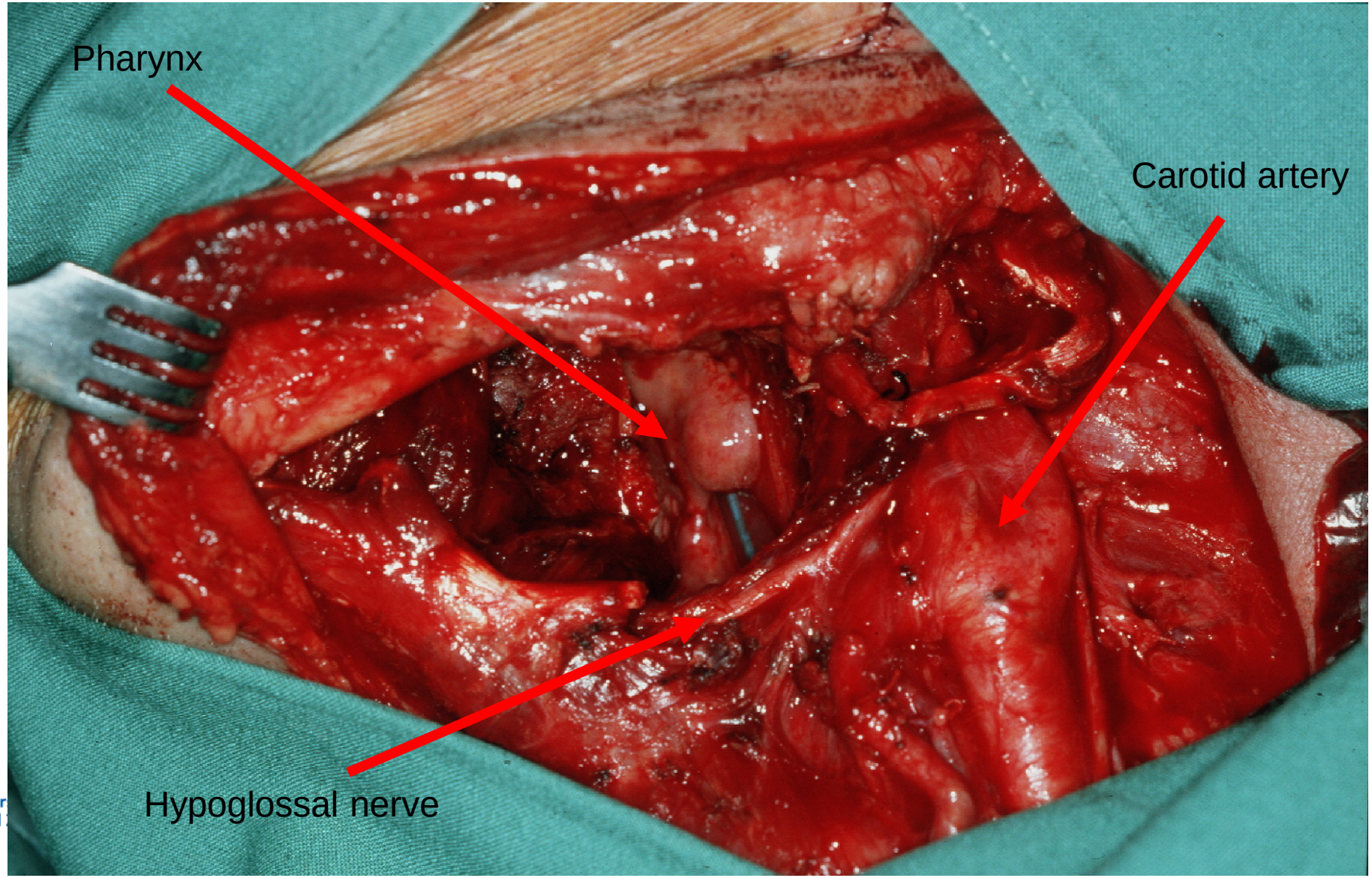




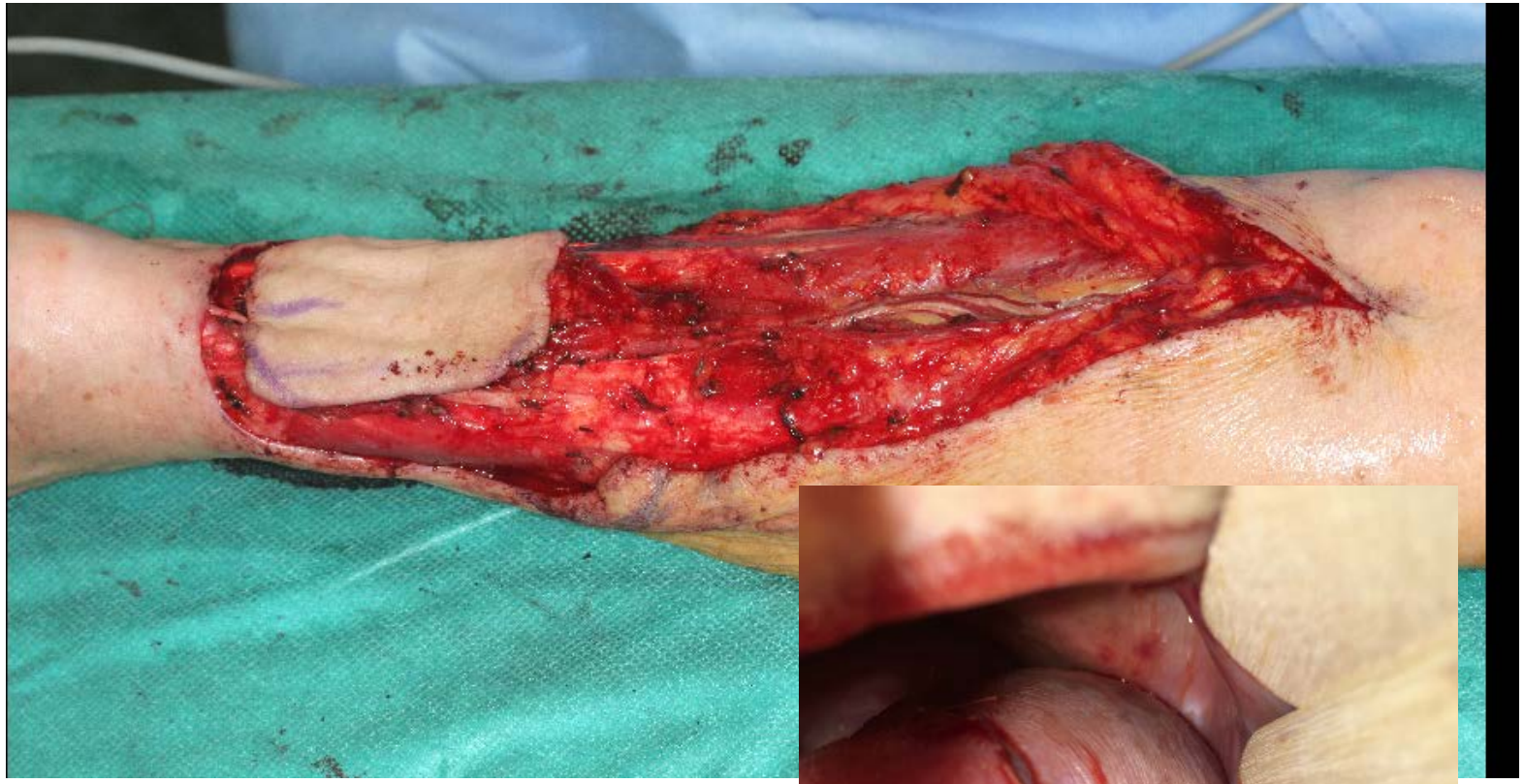
Neck

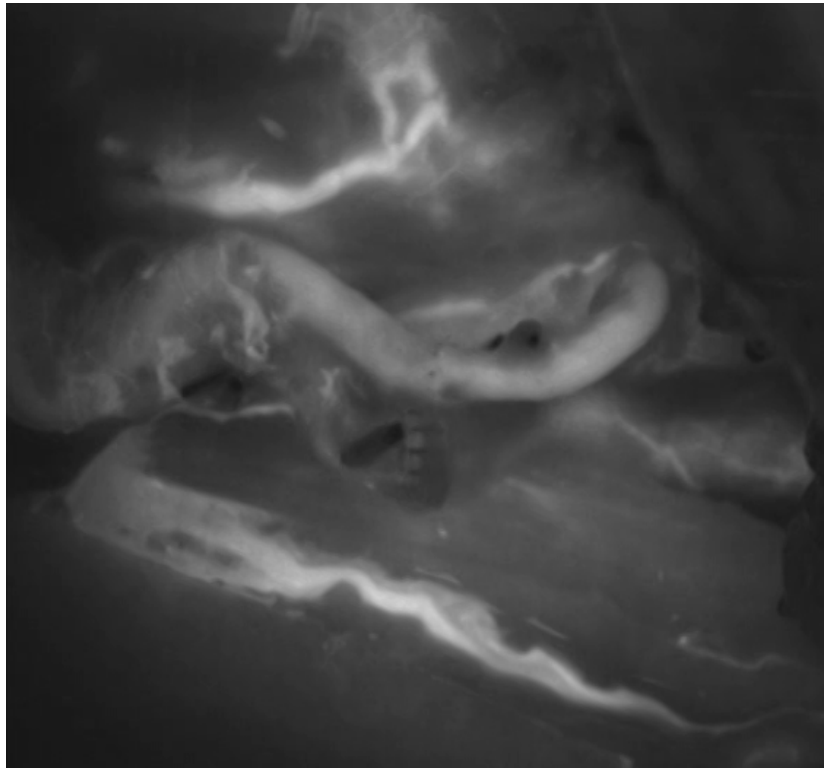


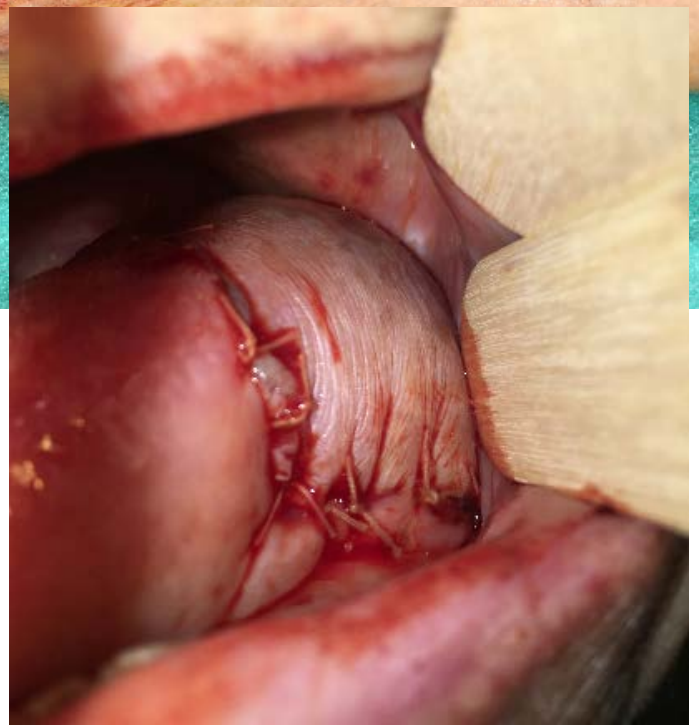
Transcervical approach



Reconstruction with radial forearm flap







Histology report

Diagnose
B 2021.8769: Exzisat (fascialer LK rechts):
Plattenepithelkarzinom-Metastase in einem von zwei Lymphknoten (1/2).
Max. Metastasendurchmesser: 1,2 cm.
Fokale extrakapsuläre Extension nachgewiesen, minimaler Abstand zur Präparateoberfläche 0,6 cm.

B 2021.8770: Resektat (Glandula submandibularis):
Tumorfreies Speicheldrüsengewebe mit dilatierten Ausführungsgängen.

B 2021.8771: Neck dissection Präparat (rechts Level IIB):
Plattenepithelkarzinom-Metastase in einem von drei Lymphknoten (1/3).
Max. Metastasendurchmesser: 0,2 cm.
Keine extrakapsuläre Extension nachgewiesen.

B 2021.8772: Neck dissection Präparat (Level I-IV rechts):
Plattenepithelkarzinom-Metastase in fünf von neun Lymphknoten (5/9).
Max. Metastasendurchmesser: 1,5 cm.
Extrakapsuläre Extension nachgewiesen, minimaler Abstand zur Präparateoberfläche 0,4 cm.

B 2021.8776: Neck dissection Präparat (links Level I-III):
Plattenepithelkarzinom-Metastase in einem von 22 Lymphknoten (1/22).
Max. Metastasendurchmesser: 0,3 cm.
Keine extranodale Extension.
Karzinomfreies Speicheldrüsengewebe mit mikroskopisch kleinem benignen sogenannten onkozytären Zystadenom.

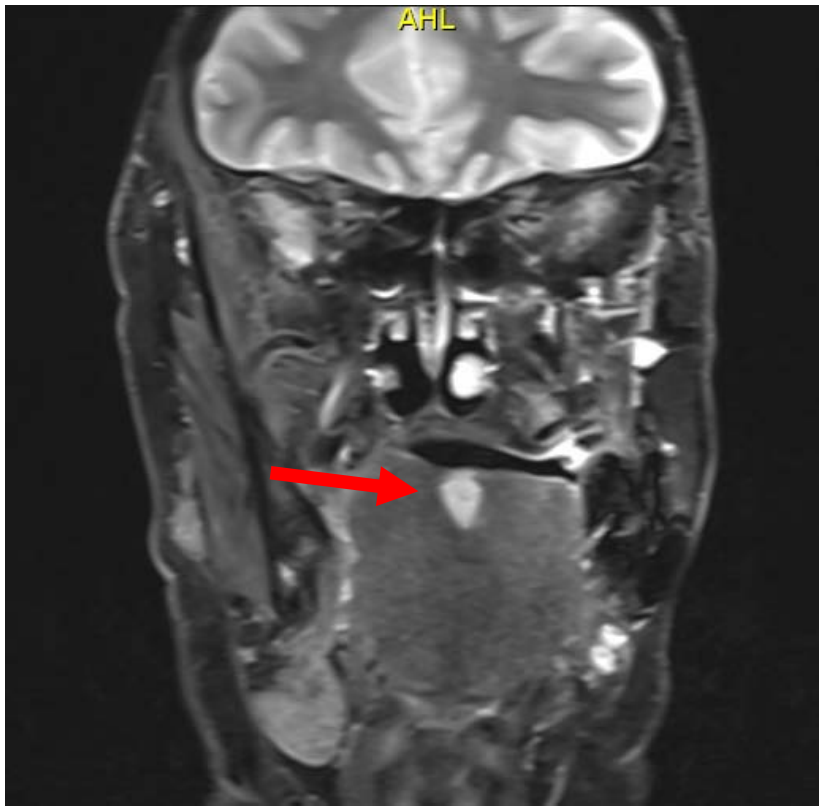
TNM-Klassifikation (8. Auflage, 2020): pT3, pN3b (8/37), L0, V1, Pn1, R (siehe Kommentar)

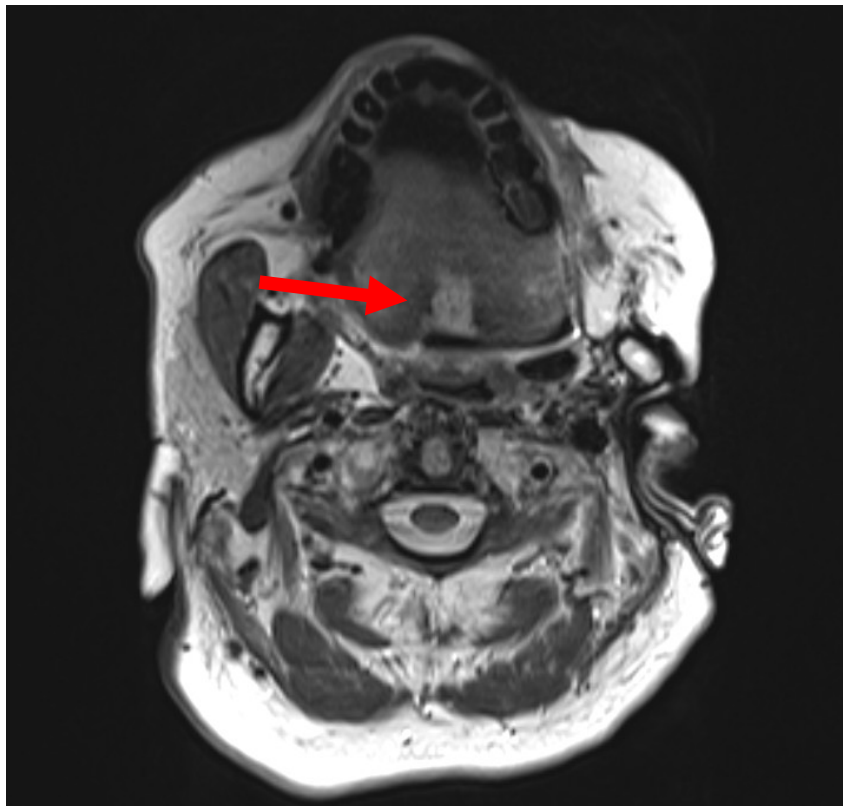
pN3b (8/37), ENE → adjuvant RCT indicated

74 year old lady

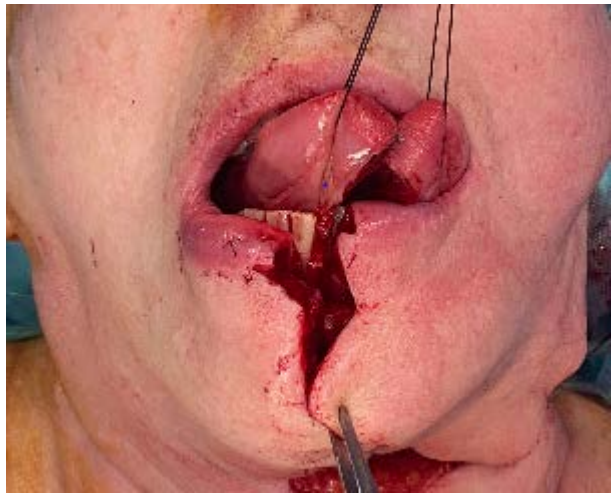
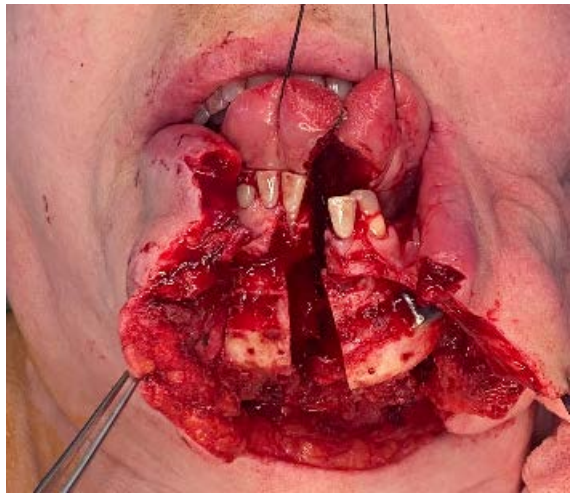
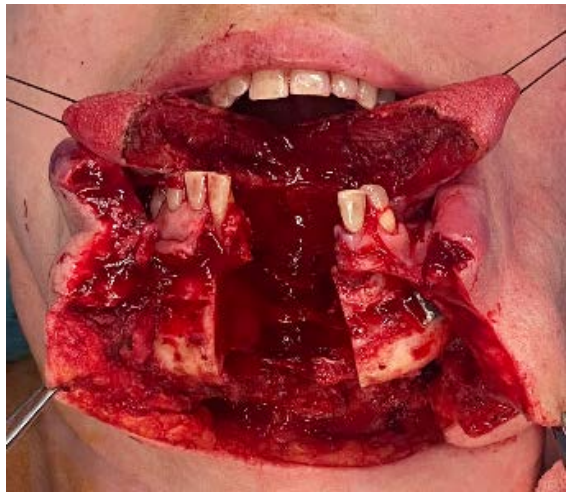
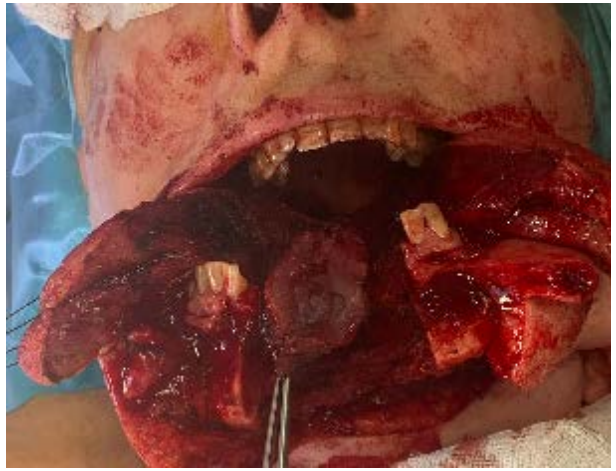
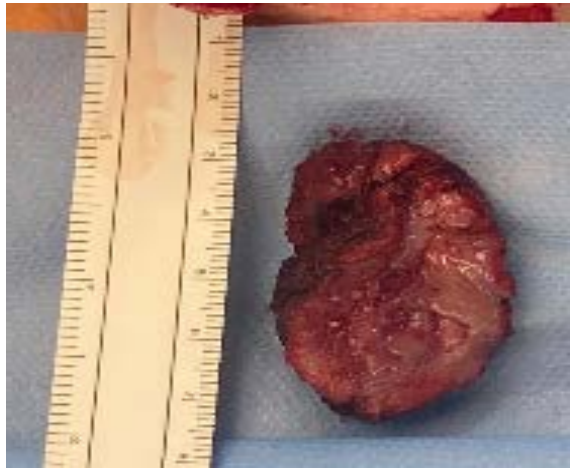
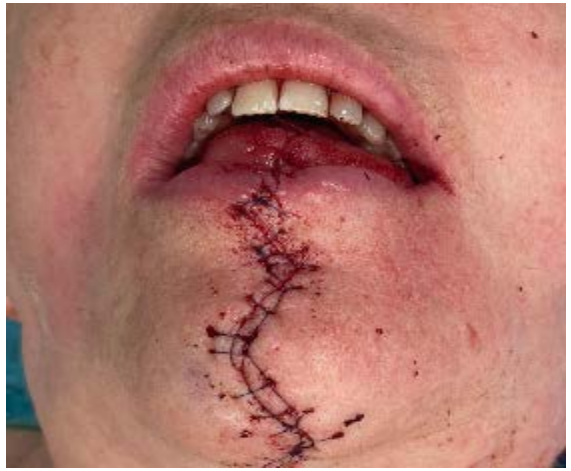
Squamous cell cancer of the posterior tongue in the midline

- Previous treatment with surgery and adjuvant radiotherapy due to an advanced stage parotid gland cancer
- Further radiotherapy not recommended





Transmandibular tumor resection

Tumor surveillance

Nachsorgeschema Kopf-Hals-Tumorzentrum

USZ Universitäts Spital Zürich

Lokalisierte & low-risk Tumore

Definition

Schleimhautkarzinome: T1-T2 N0
Speicheldrüsenkarzinome: T1-T2 N0 low-grade Karzinome
Hautkarzinome: Schema nicht anwendbar bei T1-T2 N0 M0 Hautkarzinomen. Diese müssen durch Dermatologen kontrolliert werden.
Andere Tumore: low-grade Sarkome

Jahr n. Therapieabschluss	Jahr 1					Jahr 2				Jahr 3		Jahr 4		Jahr 5		Jahr >5
Monat n. Therapieabschluss	2	3	6	9	12	15	18	21	24	30	36	42	48	54	60	>60
Klinische Untersuchung	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Jährlich in HNO-Praxis
Phoniatrische Untersuchung (Larynx-& Hypopharynxkarzinom)	Bei unklaren Befunden der Stimmbänder oder schlechter Beurteilbarkeit															
MR Hals (Ausnahme: Larynx) CT Feinschicht (nur Larynx)		■			■				■							
CT Thorax low dose					*				*		*		*		*	*Jährlich durch HA
Sonographie			■	■			■									
TSH (nur nach RT)					■				■		■		■		■	
EBV Titer (Nasopharynx Ca)		■			■				■							

Fortgeschrittene & high-risk Tumore, Rezidive

Definition

Schleimhautkarzinome: T3 und T4 oder N+, alle Rezidive
Speicheldrüsenkarzinome: Alle high-grade Karzinome + T3 und T4 oder N+ low-grade Karzinome, alle Rezidive
Hautkarzinome: T3 und T4 (Ausnahme: Basaliome) oder N+
Andere Tumore: SNUC, high-grade Sarkom, Schleimhautmelanom, Ästhesioneuroblastom

Jahr n. Therapieabschluss	Jahr 1					Jahr 2				Jahr 3		Jahr 4		Jahr 5		Jahr >5
Monat n. Therapieabschluss	2	3	6	9	12	15	18	21	24	30	36	42	48	54	60	>60
Klinische Untersuchung	■	■	■	■	■	■	■	■	■	■	■	■	■	■	■	Jährlich in HNO-Praxis
Phoniatrische Untersuchung (Larynx-& Hypopharynxkarzinom)	Bei unklaren Befunden der Stimmbänder oder schlechter Beurteilbarkeit															
PET-MR Ganzkörper		■		■		■			■							
CT Thorax low dose											*		*		*	*Jährlich durch HA
Sonographie			■		■		■	■								
TSH (nur nach RT)					■				■		■		■		■	
EBV Titer (Nasopharynx Ca)		■			■				■							

*Nur aktive Raucher und Ex-Raucher >20py mit Rauchstopp vor <10 Jahren, sowie Adenoid-zystisches Speicheldrüsenkarzinom

Prognosticators?

5 year Overall and Disease free survival dependent on

- T-stage (depth of invasion)
- N-stage (extranodal extension)
- Margin status
- Vascular invasion
- Perineural invasion

Zanoni et al, oral oncology 2020

Outcome?

5 year Overall and Disease free survival 64.4% and 79.3% respectively

Stage I OSCC 5y OS and DSS 79.7% and 93.4% respectively

Zanoni et al, Oral oncology 2020

Stage IVb OSCC 5y OS and DSS 37.9% and 54.3% respectively

Disease recurrence 32.3%, Salvage rate 26.5%

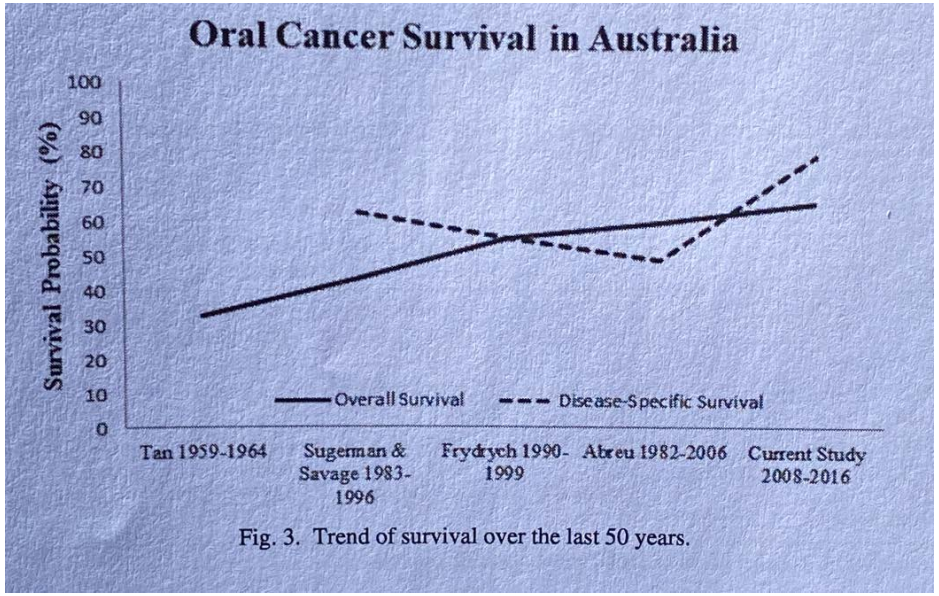


Fig. 3. Trend of survival over the last 50 years.

Liu T et al, Med Oral Pathol Oral Radiol 2021

Take home message

1. **Diagnostic work up** in oral cancer include **Panendscopy, MRI** for soft tissue delineation, perineural spread, transspatial extension and **CT** for cortical bone and skull base and **FDG-PET-CT** in advanced stages
2. Therapeutic principle is surgical resection with or without reconstruction and adjuvant radiotherapy in advanced stages
3. Treatment decision dependent on **tumor size (depth of invasion), tumor stage (nodal involvement, extranodal extension), prognostic factors (margin status,** Margin status, vascular invasion, perineural invasion) and **previous treatment**
4. **Survival has improved over time with** 5 year OS and DSS of 64.4% and 79.3% respectively due to multimodal treatment approach

Questions?