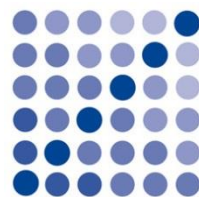




Laryngeal Cancer

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CENTRES

Certified
Head and Neck Cancer
Centre

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1. Overview

- Ca. 300 new cases/y. in CH (USA 2016: 13'500)
- 60% of all laryngeal cancer = Stad. III or IV
- Lower social class: ↗ and more advanced stages
- Mortality: ca. 1/3 of all cases
- Last 40 years: Incidence ↘ → but: 5 y.-OS ↘
(66% → 63%)!

2. Aetio-Epidemiology

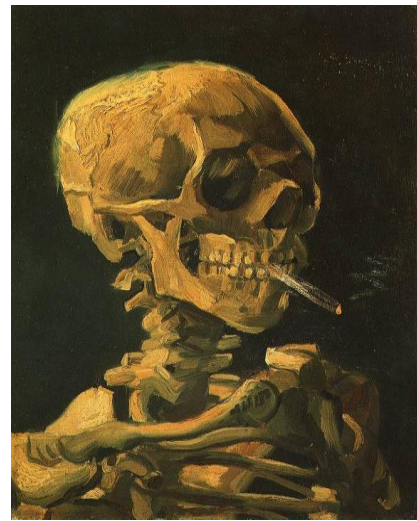
- Estimation: CH (2013): 254
USA (2016): 13'500
 - 1-4% of all malignancies
 - 25% of all head & neck malignancies
- Gender distribution:
 - 2016 - M:F = 5:1 (but 1990: 15-20:1)
→ CH/100'000:
1990: **19.3** / 2013: **5.5 (M)**
1990: **0.6** / 2013: **0.8 (F)**
- Age:
 - ↗ Prevalence at age 50 – 70 years



Aetio-Epidemiology

Number 1:

- Smoking



Smoking → Lineare relationship → Larynx cancer

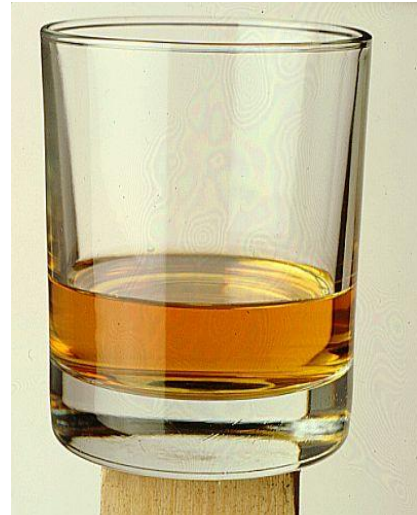
Smoker : Non-smoker = 15 : 1

Heaviest smoker : Non-smoker = 30 : 1

Number 2:

- Heavy alcohol consumers

Wine > 1.5 l/day: 34 x higher risk

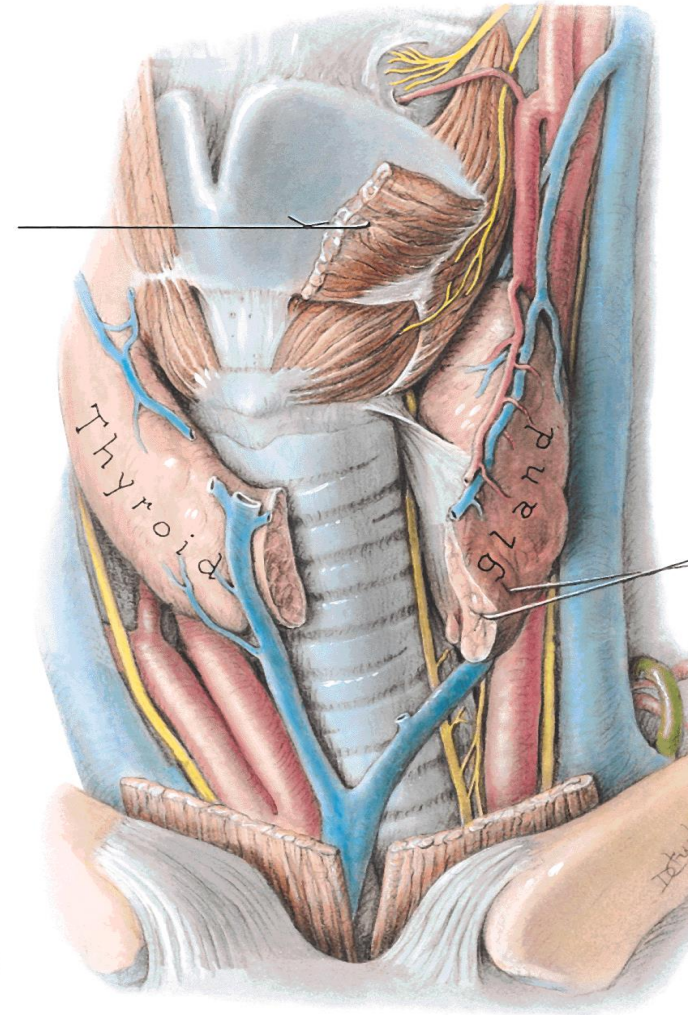


Aetio-Epidemiology

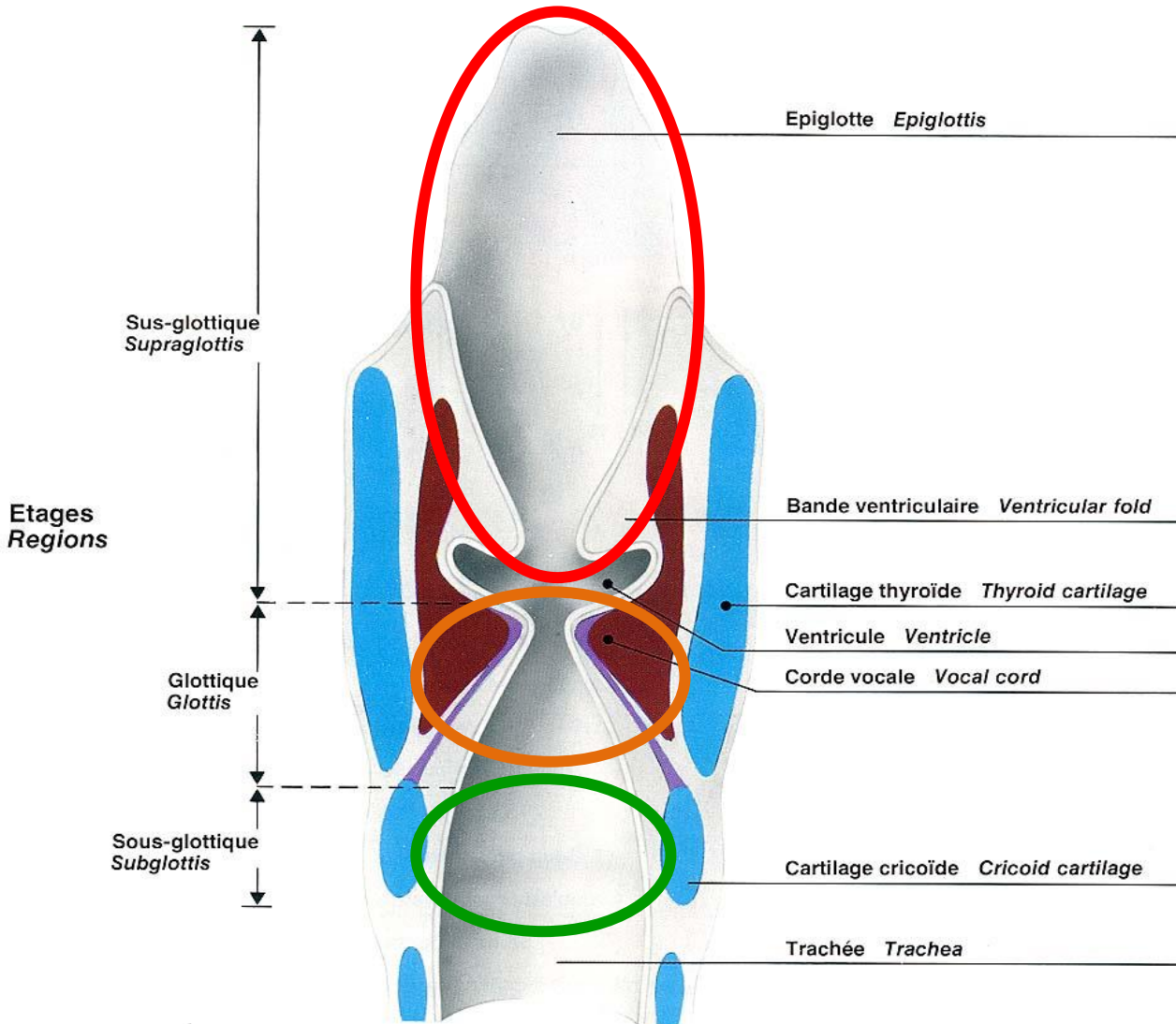
- Smoking
 - Alcohol
- Synergistic effect (90% S+A)**
- **Environmental factors** (asbestos, polycyclic aromatic hydrocarbons, textile dust)
 - **Human Papilloma Virus 16 & 18**
(Prevalence: 20-30% → biological and prognostic relevance yet unclear!)
 - **Gastro-esophageal reflux?** (controversial)

3. Laryngeal Anatomy

- Basic laryngeal functions:
 - **Respiration**
 - Keeping the «airtube» open
 - **Phonation**
 - Vocal folds
 - **Protection**
 - Aspiration: Vocal folds / Epiglottis
 - Trauma: Cartilage



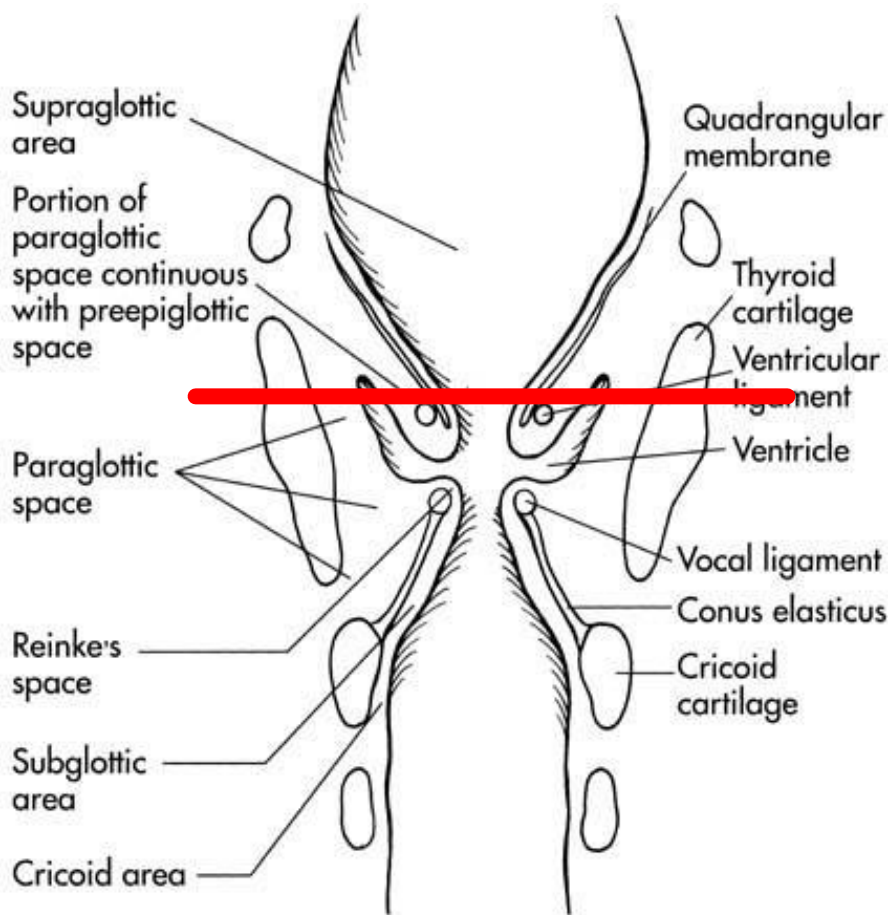
Anatomy



Anatomic sites:

- Supraglottic
- Glottic
- Subglottic

Tumor spread – Barriers



Extralaryngeal barriers:

- Thyroid and cricoid cartilages
- Membranes: thyro-hyoidal
hyo-epiglottic
crico-thyroidal

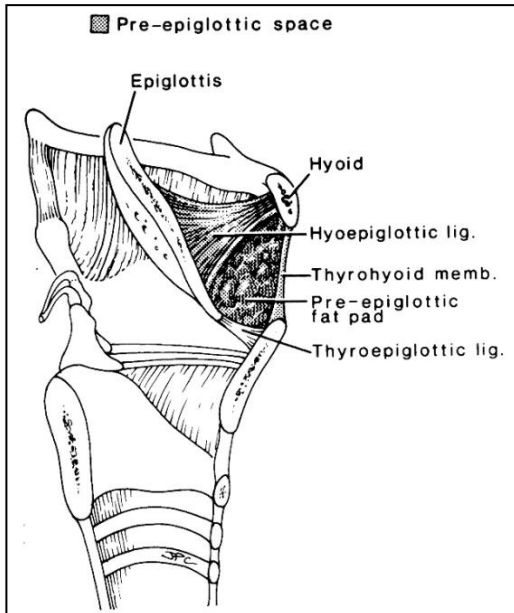
Intralaryngeal barriers:

- Quadrangular membrane
- Conus elasticus

Embryologically caused separation between supraglottis and glotto-subglottis

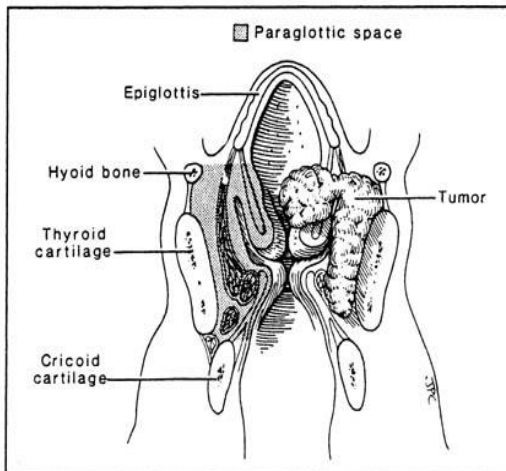
- Late tumor spread from supraglottis <> glottis

Tumor spread – Intrinsic spaces



Pre-epiglottic space

- Elastic epiglottis → foraminae → direct extension from supraglottic to preepiglottic
- Bilateral lymphatic basin +++



Paraglottic space

Tumor infiltration



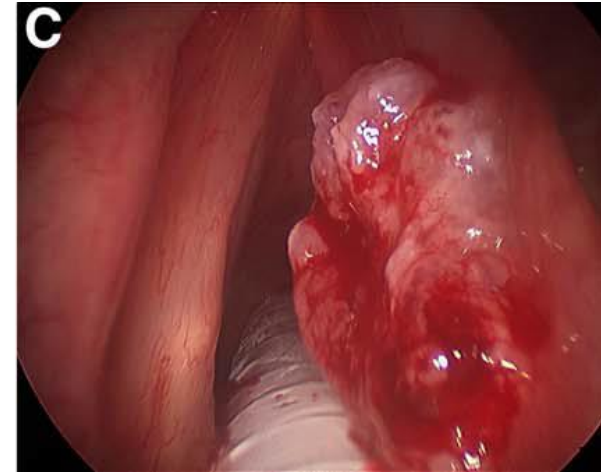
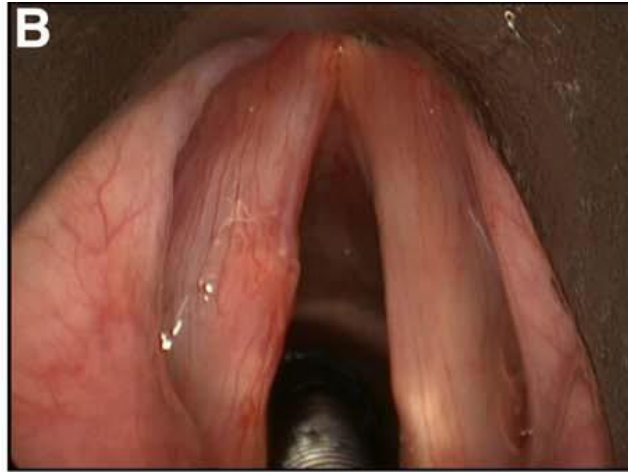
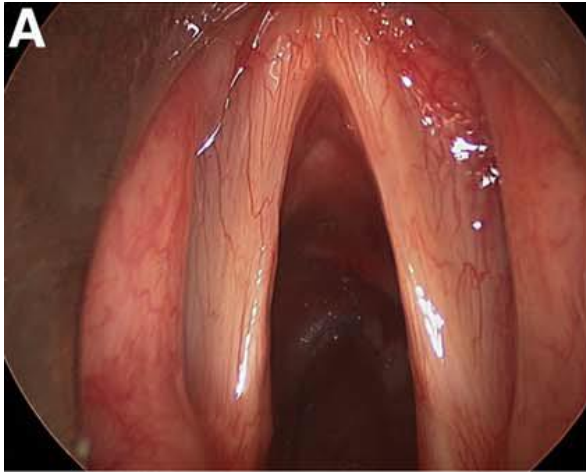
T3!

Pathways of Spread

Resume

- Laryngeal cancer tends to be contained within the larynx
- Direct spread:
 - **Via mucosa → continuous spread**
 - **In paraglottic / preepiglottic space**
 - **Through cartilage**
- Lymphatic drainage:
 - **Vocal folds:**
 - poor lymph. basin
→ no LN-Mets.
 - **Supraglottic / Subglottic**
 - rich lymph. basin
→ LN-Mets. ↗, bilateral

4. Macroscopic Aspects and Histopathology



A: normal

B: T1a

C: T2

Other aspects:

Hyperkeratosis

Leukoplakia / Erythroplakia

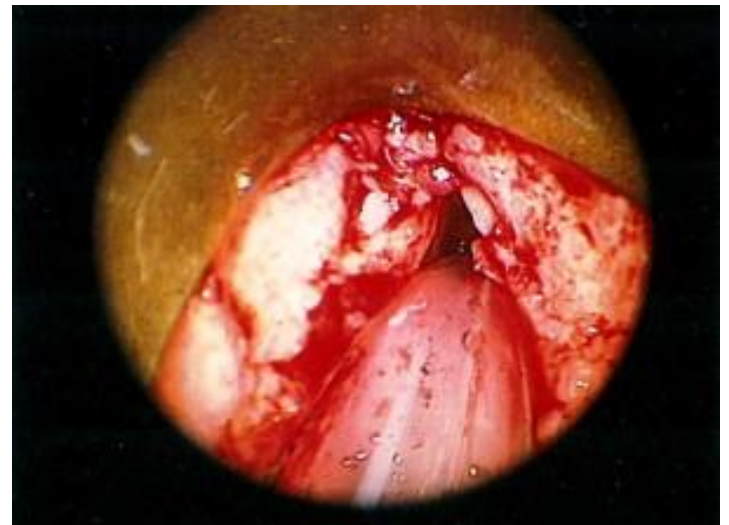
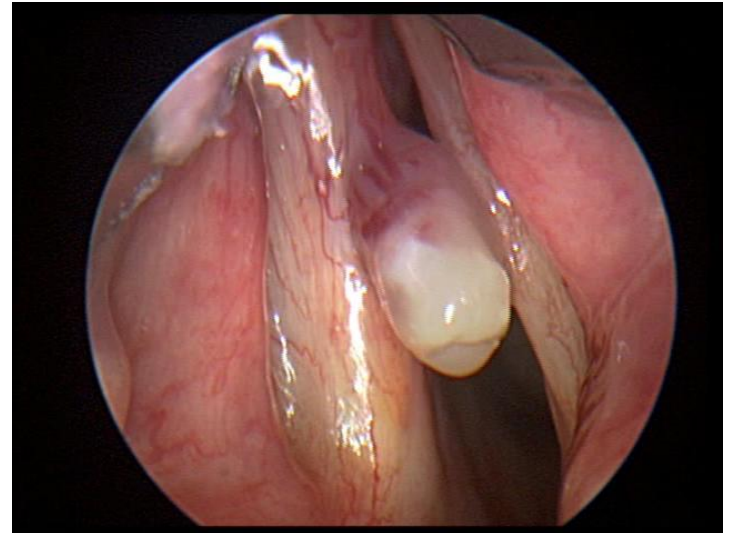
Exophytic

Ulcer

Macroscopic Aspects

Differential diagnosis

- Singer's nodules
- Polyps
- Papillomatosis
- Granuloma
- Granular cell - Tumor
- Cat scratch disease
- Sarcoidosis
- Wegener's Granulomatosis
- Tuberculosis



Histopathology

- Precancerous lesions
 - = Hyperkeratosis with atypia, Dysplasia, Ca in situ
- **>95%** = **Squamous cell carcinoma**
- **5%** = others
 - Neuroendocrine carcinoma
 - Fibrosarcoma
 - Chondrosarcoma
 - Adenocarcinoma
 - Adenoid-cystic carcinoma
 - Lymphoma
 - Benign tumors (very rare!)

5. Workup

- Symptoms and History
- ENT-Examination
- Imaging
- Diagnostic



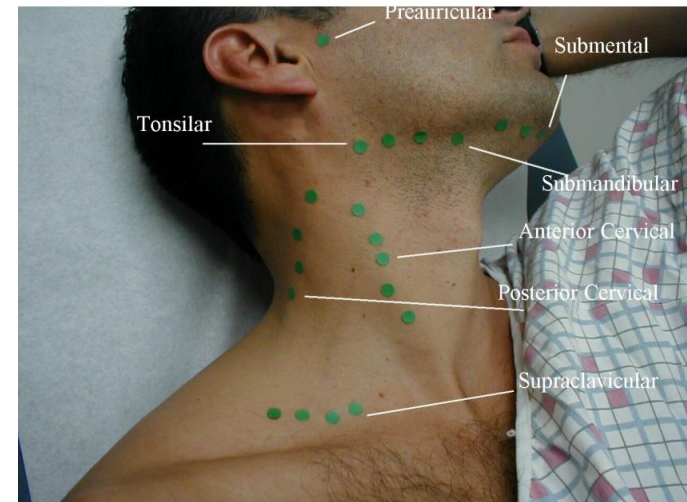
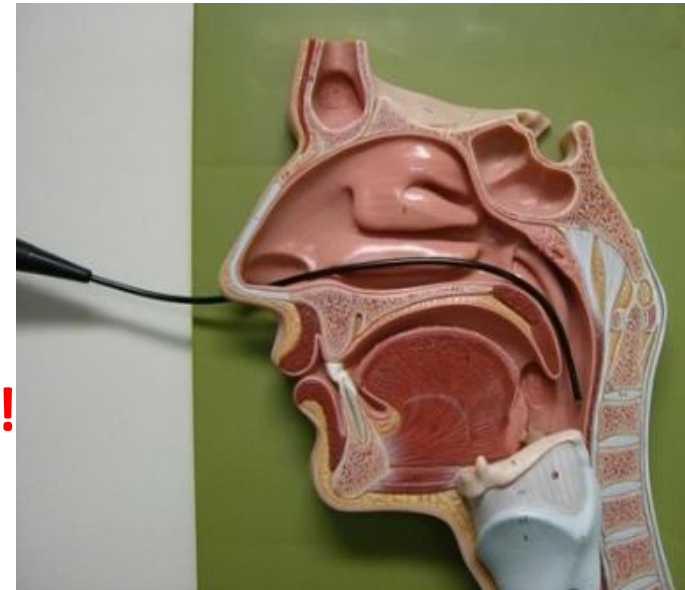
Symptoms

- Supraglottic localisation:
 - Otolgia
 - Dysphagia/Odynodysphagia
 - Haemoptysis
 - Aspiration
 - Cachexia
 - Neck mass
- Glottic localisation:
 - Early dysphonia
- Subglottic localisation:
 - Late dyspnea



ENT-Examination and History

- Assessment of risk factors
- Larynx- and Hypopharynx
 - **Laryngeal/vocal fold mobility? → T2/T3!**
- Base of tongue
 - **Palpation → Tumor extension → T4a!**
- Panendoscopy / Airway evaluation
- Nutritional status?
- Teeth status?



Radiology

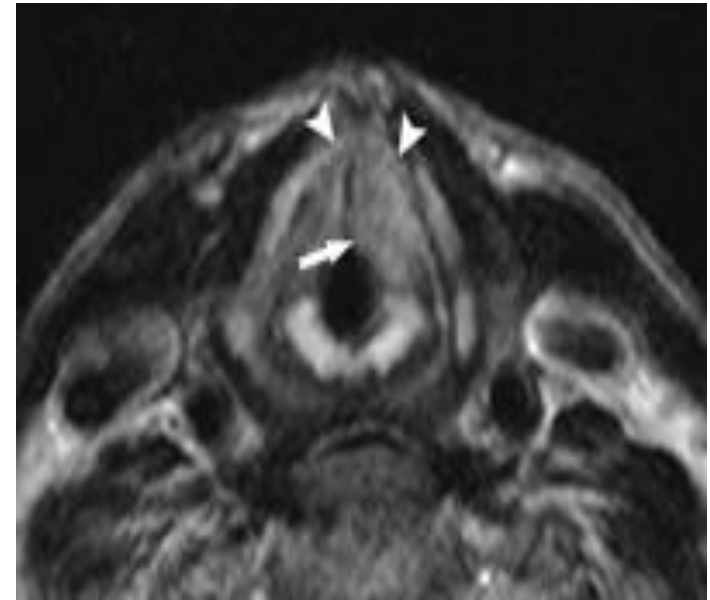
- **MRI and/or CT-Scan**

- Tumor extent (limitations of endoscopy)
- MRI: soft tissue invasion, nodal disease (ECS)
- CT: thyroid cartilage destruction
- **Cartilage infiltration: Specificity CT > MRI, but MRI interpretation has improved!**

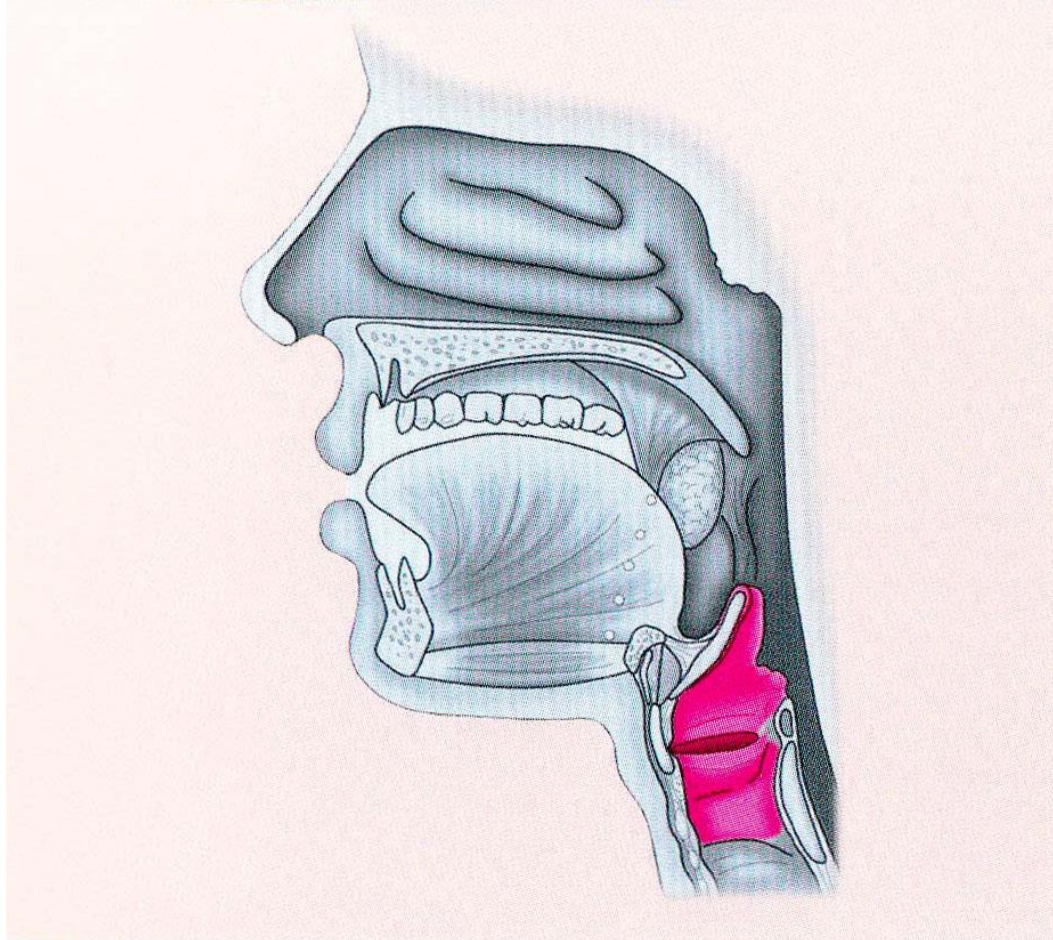


- **PET-CT**

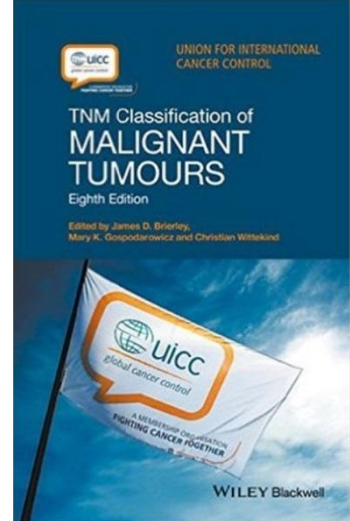
- Indication Stage III/IV
- Localisation of regional and systemic mets. (-30% in Stage II/IV)
- Differentiation between tumor and post-therapeutic changes
- **Study: PET-CT**
→ **Change of therapeutic strategy in 31%**



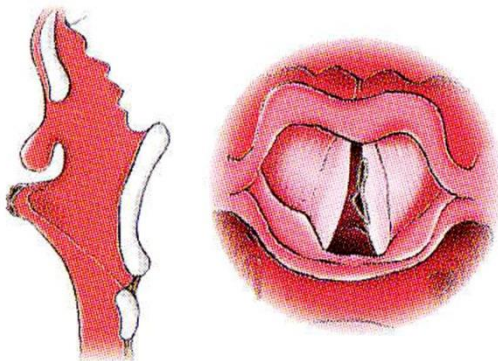
6. Staging



Staging UICC, TNM 8th, 2017



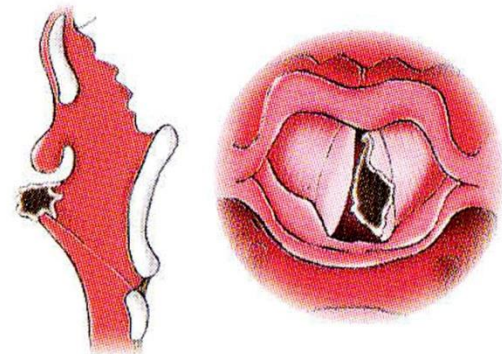
T1a



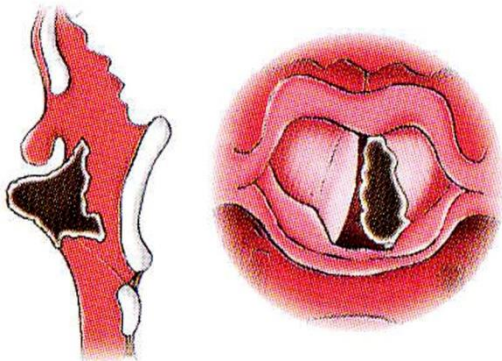
T1b



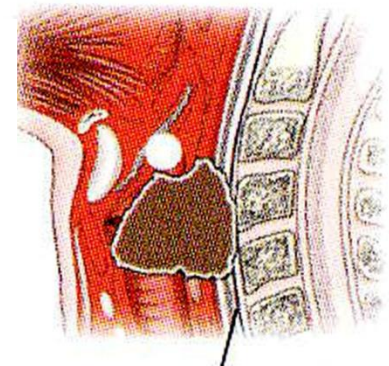
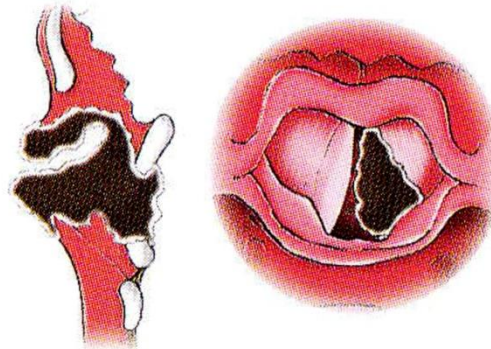
T2



T3



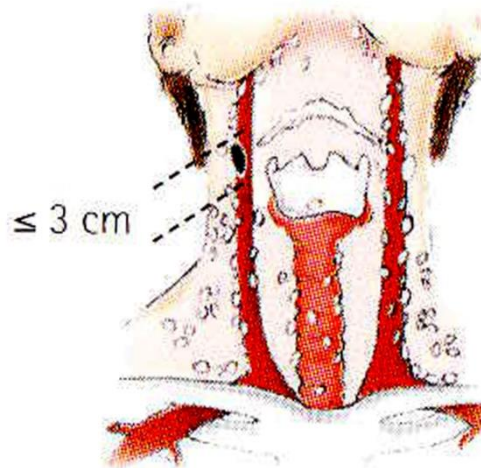
T4



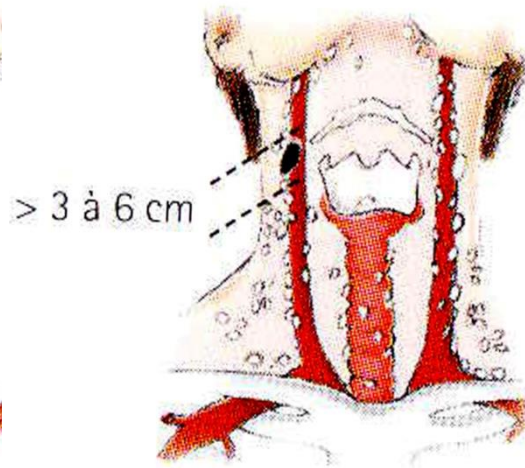
Fascia prévertébral

Staging UICC, TNM 8th, 2017

N1

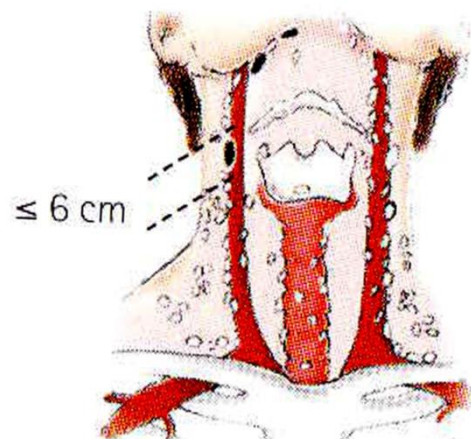


N2a

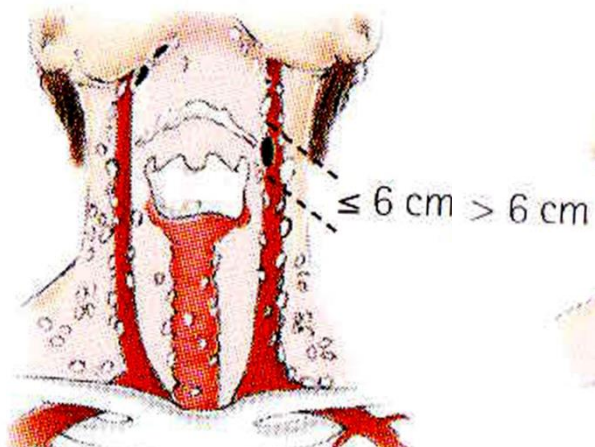


pN2a: $< 3 \text{ cm}$
with ECS

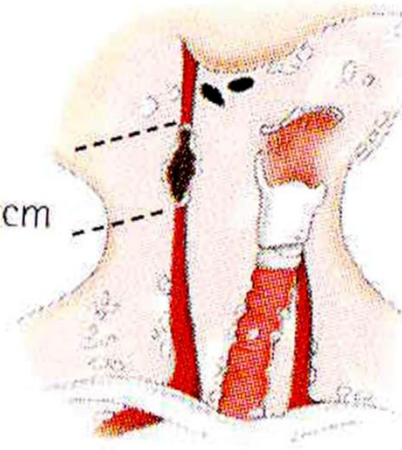
N2b



N2c



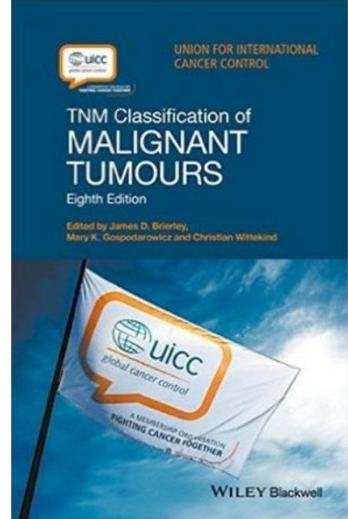
N3



cN3a: without
ECS

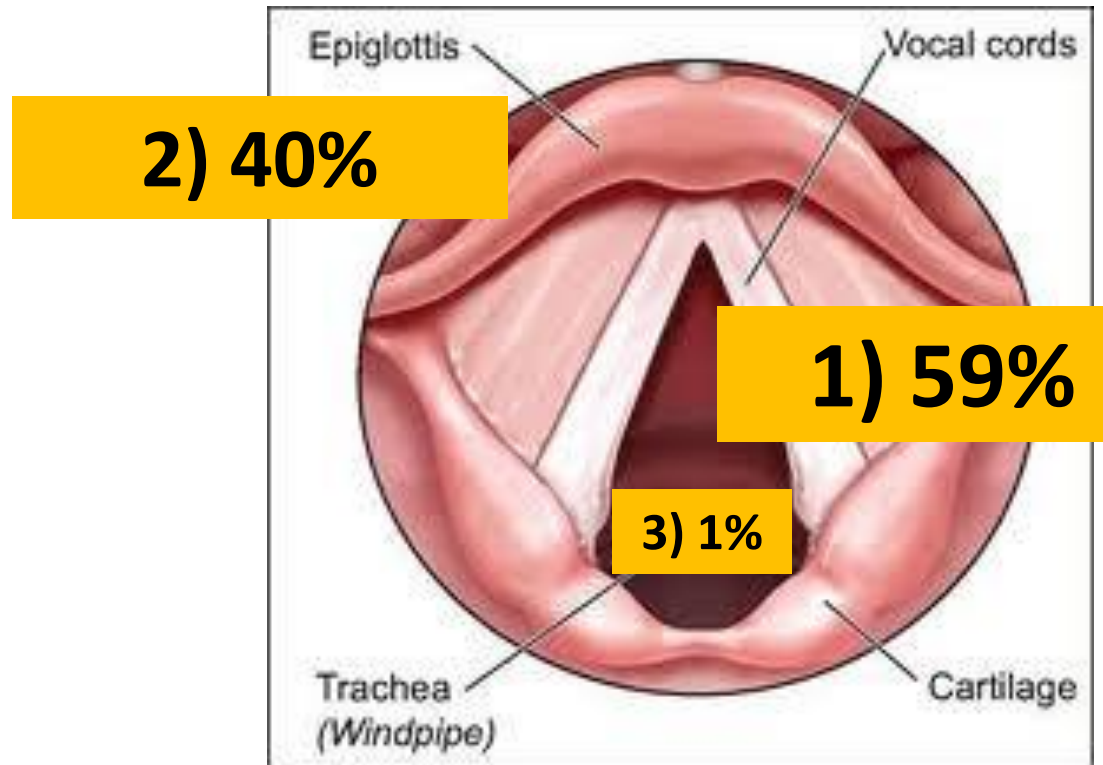
cN3b: all N
with ECS

pN3b: $> 3 \text{ cm}$
with ECS



Site-Distribution

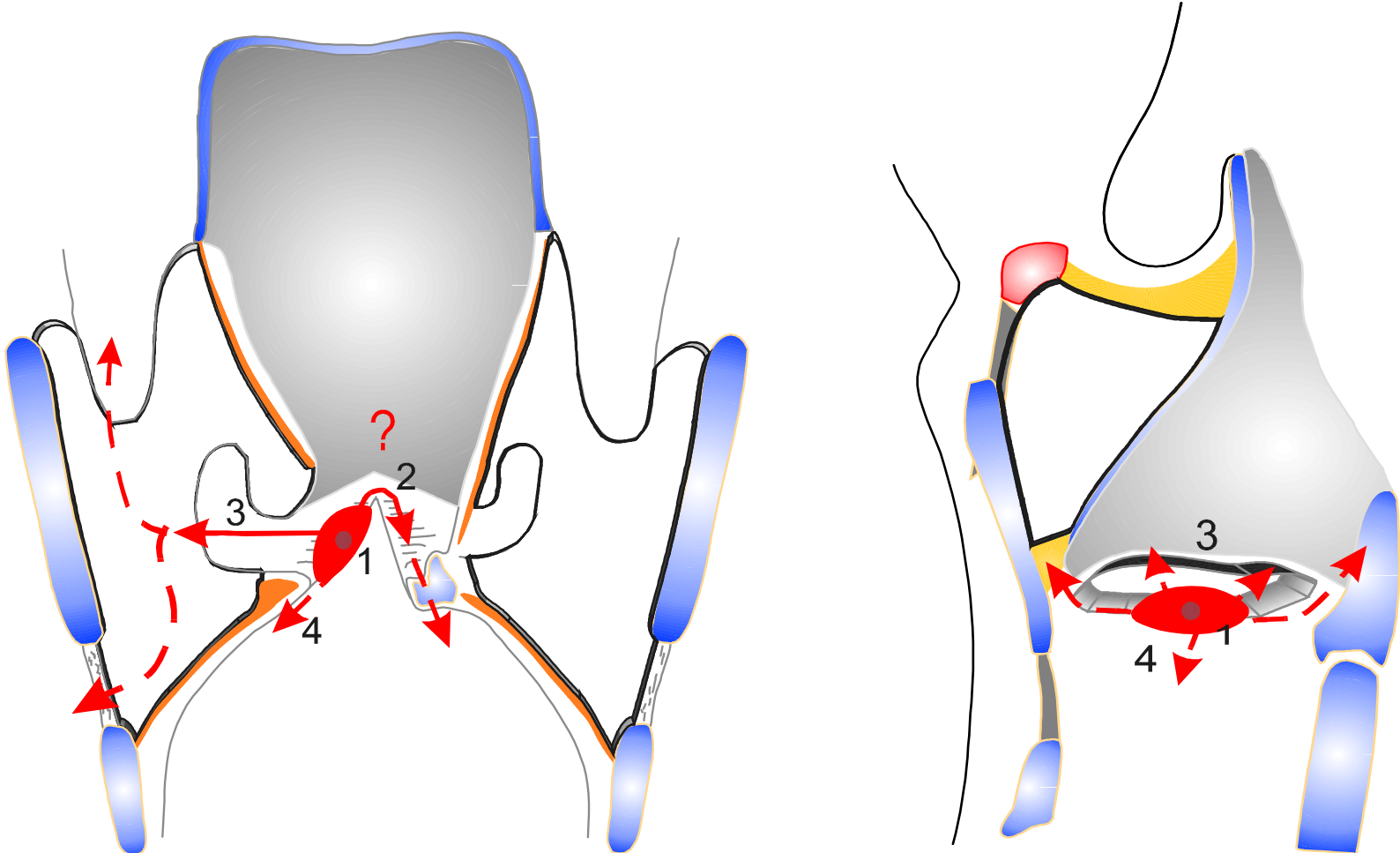
- Sites:
 - 1. Glottic
 - 2. Supraglottic
 - 3. Subglottic*



*(=true subglottic are very rare!)

Glottic Cancer

→ horizontal tumor spread: dysphonia!



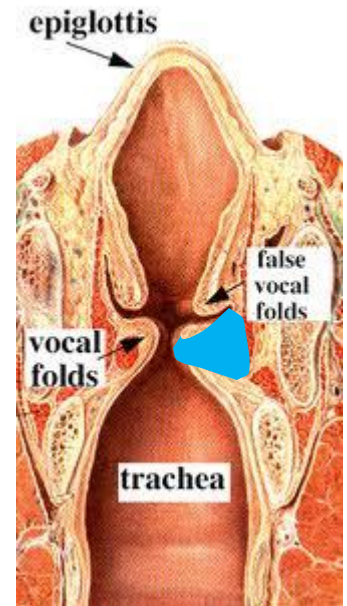
Glottic Cancer

- Biological aggressivity: \searrow (often G1-2)

- Slow progression, remains longer localized
- Early symptoms = dysphonia
- Sparse submucosal lymphatics \rightarrow LN-Mets. \searrow

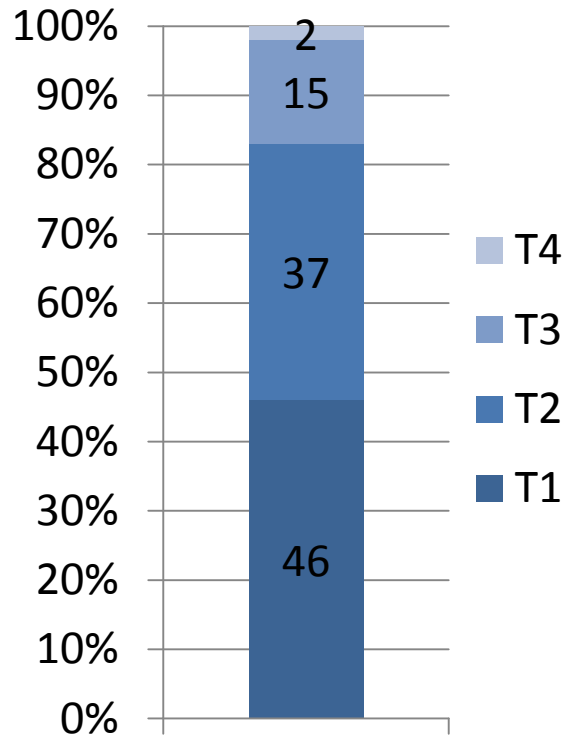
– T1	0-(5%) !!!
– T2	1.7 -8%
– T3	15-20%
– T4	30-65%

- Metastases only after infiltration of neighbour tissue with more lymphatics
- Horizontal and subglottic extension, supraglottic late (embryologic separation!)
- Immobility of the vocal folds caused by infiltration of musculature and paraglottic space!

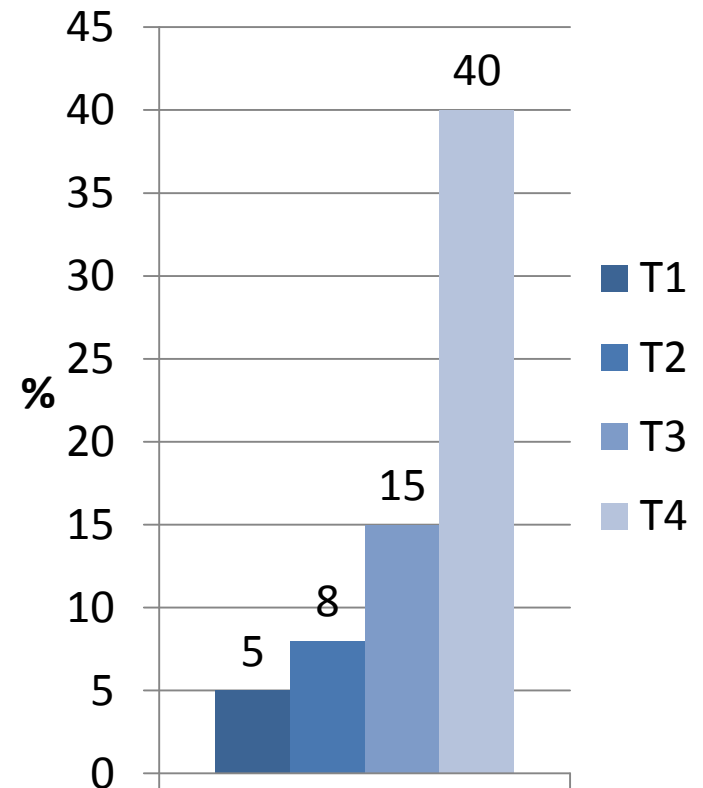


Glottic Cancer

**Glottic Cancer
T-Stages**

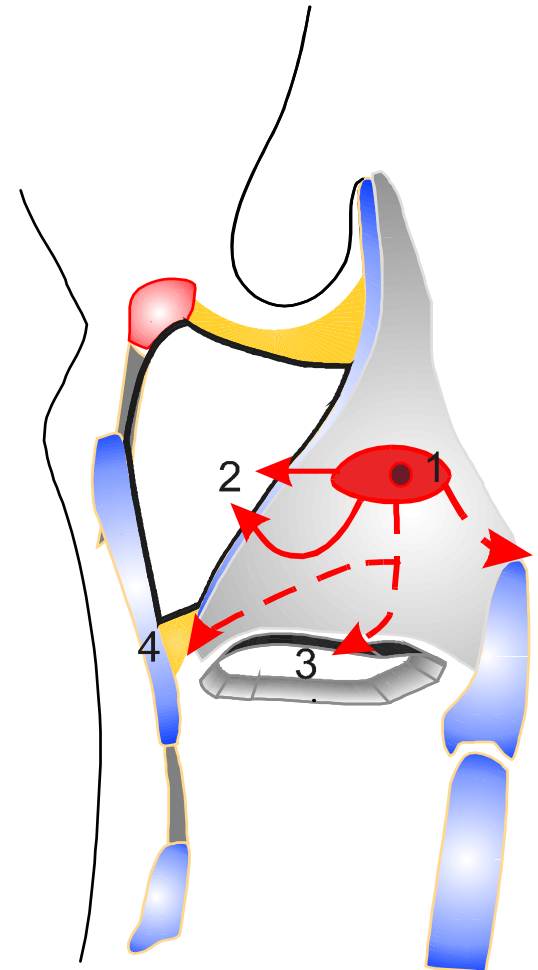
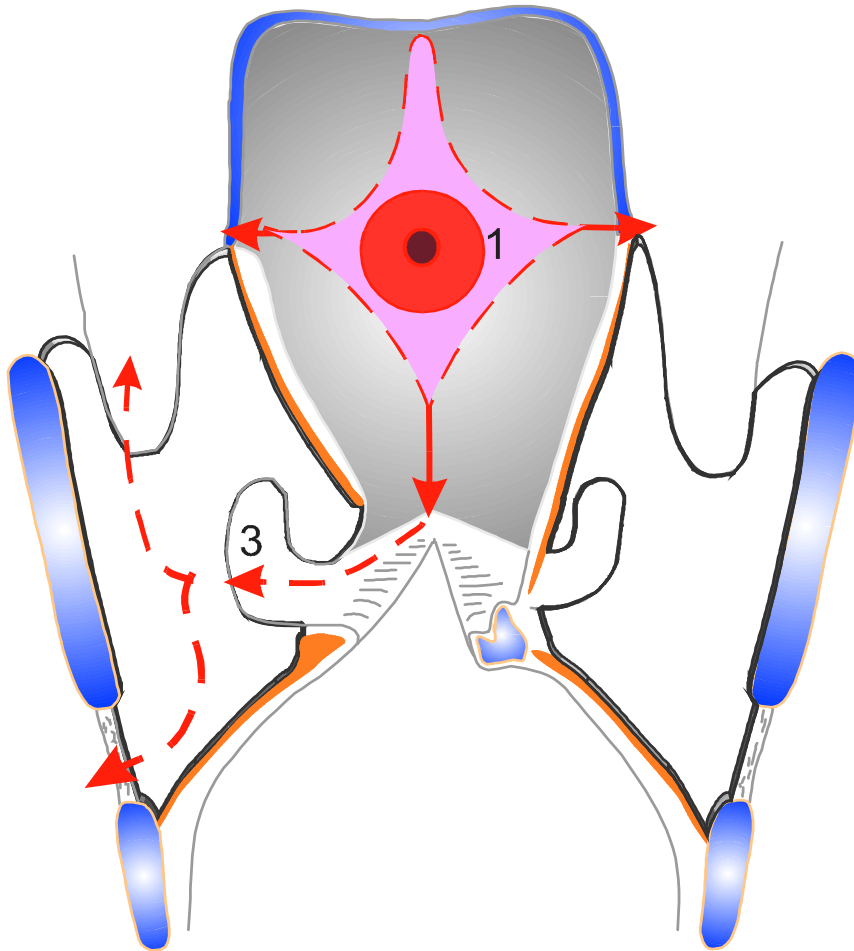


**Glottic Cancer
Frequency of LN-Mets.**



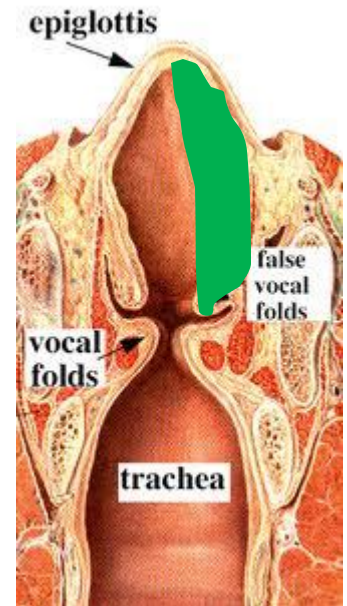
Supraglottic Cancer

→ late tumor spread to glottis!: no dysphonia



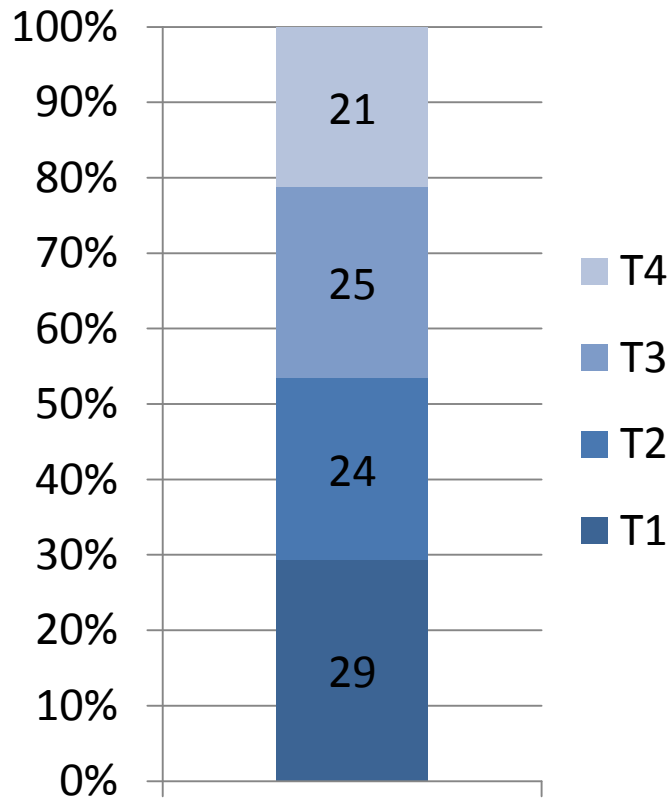
Supraglottic cancer

- Biological aggressivity: ↗ ↗
 - Continuous spread in pre-epiglottic space
 - Late symptoms: dysphonia, pain, dysphagia
 - LN-Metastases ↗
 - **55-60% clinical positive**
 - 16% bilateral, if N+
 - 37% kontralateral, if N+
- Direct extension to the hypopharynx, glosso-epiglottic fold and base of tongue

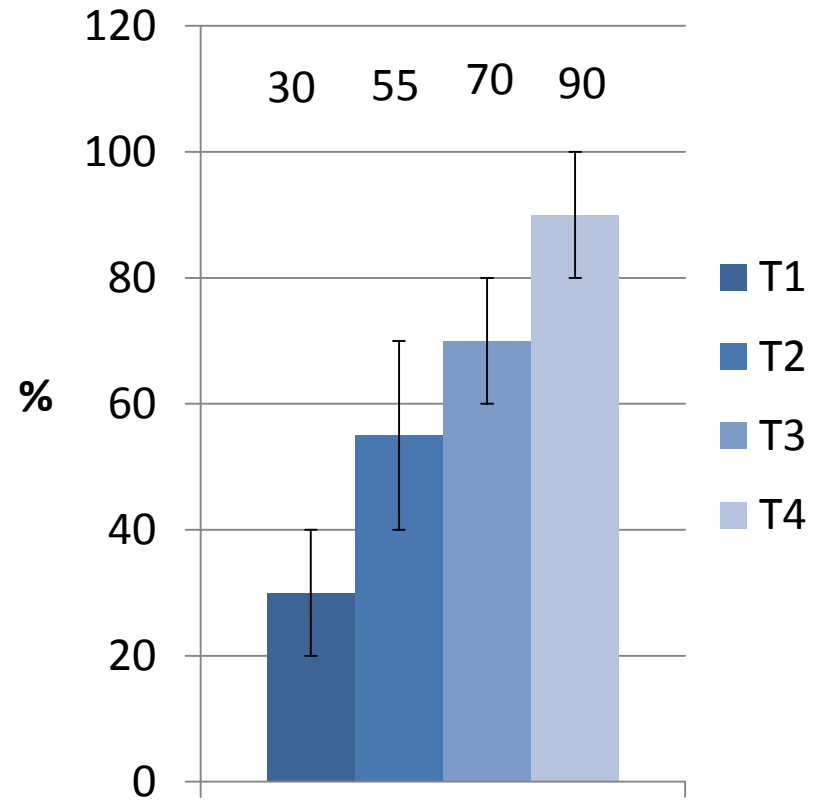


Supraglottic cancer

**Supraglottic Cancer
T-Stages**



**Supraglottic Cancer
Frequency of LN-Mets.**



Stage-Distribution

TNM-Stages	Distribution
Early Stage Tumors (I + II)	40%
Advanced Stage Tumors (III + IV)	60% LN-Mets.: -65% System. Mets.: -30%

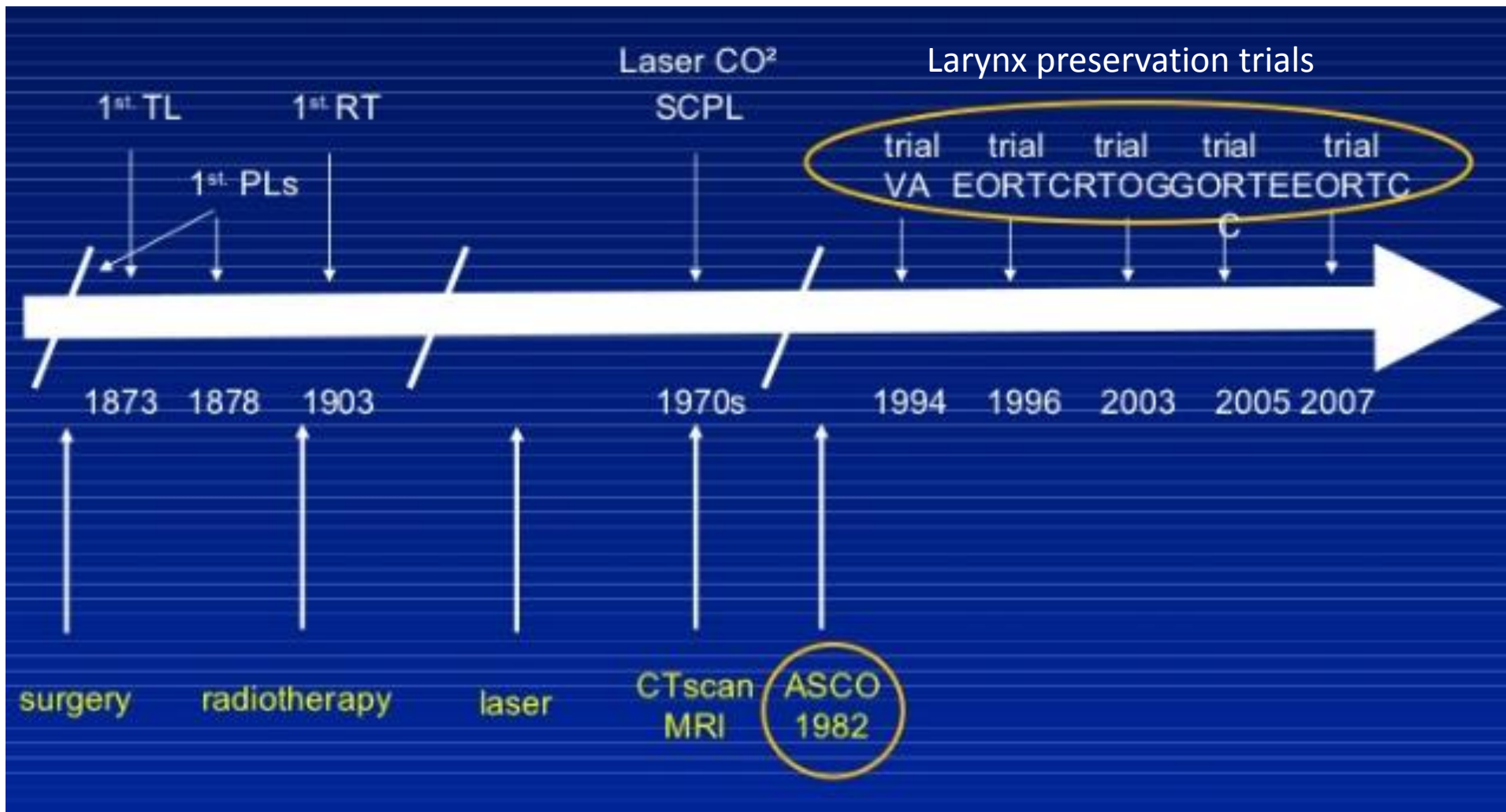
7. Treatment

- **Multidisciplinary Tumorboard!**



Larynx Cancer

Milestones in anti-larynx cancer treatment

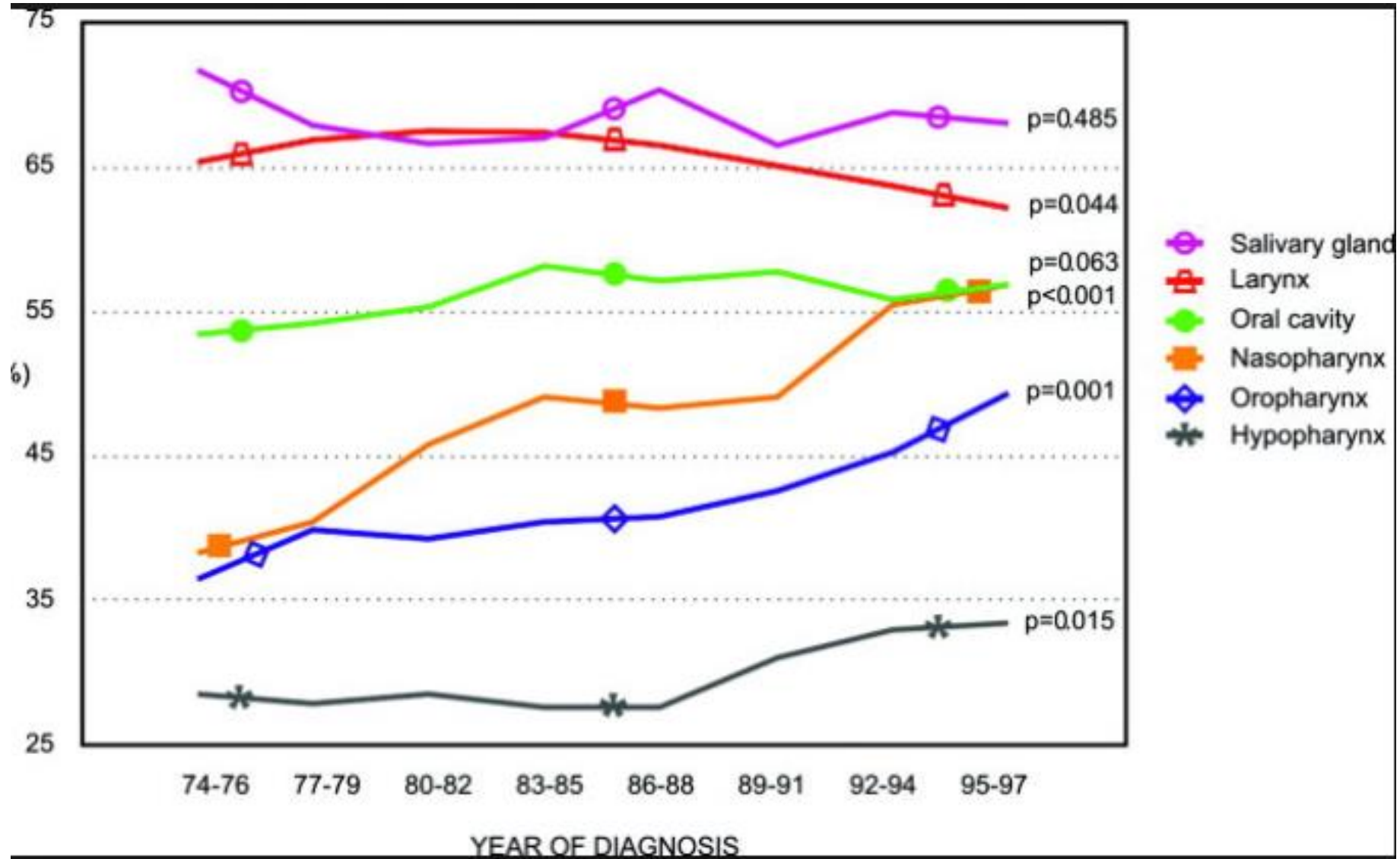


Standard Care - Principles

- **Standard of care for laryngeal cancer**
= +++ controversial!
 - RT alone
 - CXRT
 - Organ preserving surgical techniques
(transoral laser / transoral robotic surgery /
open partial laryngectomy /)
 - Total laryngectomy

Highly relevant:

OS for all cancer locations ↗ <-> OS for laryngeal cancer ↘



Principle treatments – T(umor)



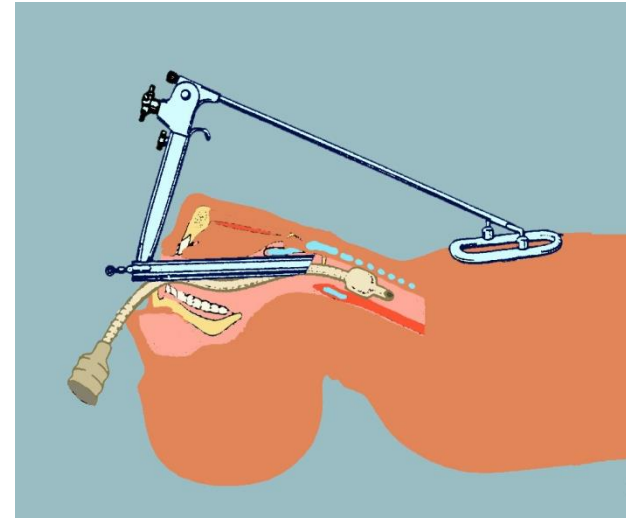
Principle treatments – T(umor)

- **Precancerous lesions**
- **Early Cancer - Glottic T1/2**
- **Early Cancer – Supraglottic T1/2**
- **Cancer T3**
- **Advanced Cancer T3/T4**

Precancerous lesions / Ca is

- **Surgery**

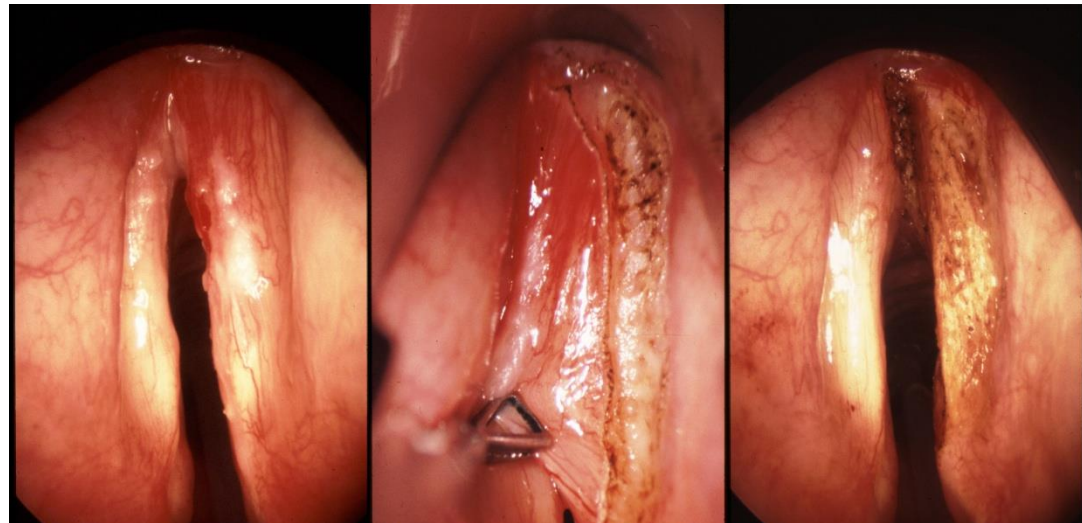
- Generous stripping / CO2-Laser
- Multiple treatments
- Vitalstaining with toluidin blue
- Rapid or frequent recurrence



- **Radiotherapy**

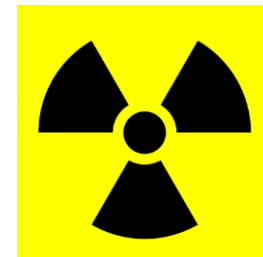
- Not primary choice of ttx.
- Failure ca. 10%
- No future option for RT T1-2

- **CAVE:** 15% of treated precancerous lesions will develop cancer



Early Cancer – Glottic T1/T2

- **Conservative surgery** (transoral CO2/open partial LE) or **Radiotherapy**
- ***No need*** for elective neckdissection/RT, if N0
- Surgical salvage possible: transoral / open partial LE / total LE
- Cure rates: RT and Surgery similar!
 - 5-y LC: Surgery 77-100% / RT 76-95%
 - 5-y DSS: Surgery 80-100% / RT 90-100%
 - Larynx pres.: Surgery 95% / RT 85-90%
 - (except anterior commissure: \searrow RT 5-y-LC 50-92%!)



=



adpic

Early Cancer – Glottic T1/T2

Factors influencing outcome

- **Factors that influence treatment outcome:**
 - T2 lesions are often unfavorable for transoral CO2 due to location/size
 - Anterior commissure involvement /subglottic extension hinders adequate transoral resection, but also difficult for RT → worse LC!
 - Complications of open partial LE: -8% (stenosis, bleeding, infection, aspiration)
 - Cure rates in T2: Surgery > RT
 - Outcome after different RT: **hyperfractionated** > normofractionated
- **Voice quality:** RT \geq transoral CO2 > open partial LE

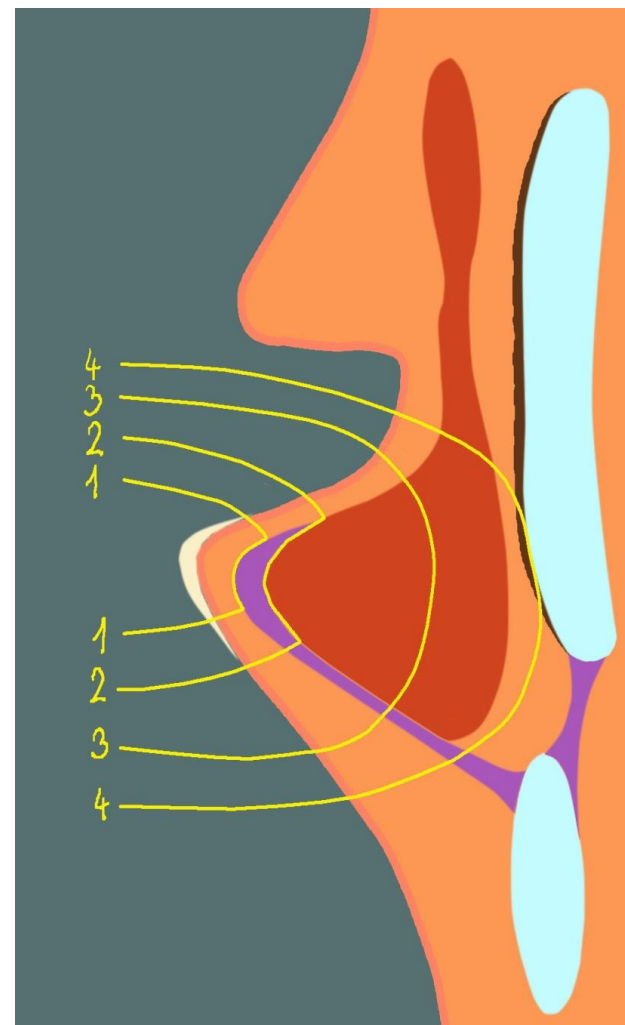
Mendenhall WM. Management T1-2 Glottic Carcinomas. Cancer, 2004

Agrawal N. Early Stage Laryngeal Cancer. Otol Clin N Am, 2008

Sjorgren EV. Voice outcome: RT vs CO2 Laser. Arch Otol HN Surg, 2008

Type of Endoscopic Cordectomies

- + Type V: anterior commissure and arytenoid region
- + Type VI: resection anterior commissure



Early Cancer – Glottic T1/T2

Meta-analyses and systematic reviews comparing the local control after RT and transoral CO2 of T1 and T2 glottic carcinomas

Author	Year	T stage	Analysis	Period	Trials	Patients	Conclusion
Higgins [21]	2009	T1, T2	M	?	25	6,491 2,213 TLM 4,278 RT	No difference between both therapeutic procedures
Feng [22]	2010	T1, T2	M	1990–2010	5	753 373 TLM 380 RT	No difference between both therapeutic procedures
Abdurehim [23]	2011	T1a	SR +M	1990–2010	10	1,445 765 TLM 680 RT	No difference between both therapeutic procedures
O'Hara [24]	2013	T1	SR	1948–2011	36	4,401 1,504 TLM 2,897 RT	No difference for T1a and T1b tumors between laser surgery and radiotherapy, tendency of better local control in T1b after radiotherapy

SR: systematic review, M: meta-analysis; TLM: transoral laser microsurgery; RT: radiotherapy, OR: odds ratio

Early Cancer – Glottic T1/T2

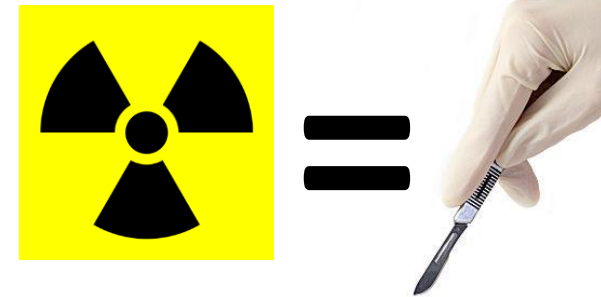
Meta-analyses comparing the voice quality after RT and transoral CO2 of T1 and T2 glottic carcinomas

Author	Year	T stage	Period	Trials	Patients	Conclusion
Cohen [39]	2006	T1	1966–2005	6	299 208 TLM 91 RT	Tendency of better voice after laser surgery
Higgins [21]	2009	T1,T2	?	9	554	Tendency of better voice after radiotherapy
Abdurehim [23]	2011	T1a	1990–2010	8	480 260 TLM 220 RT	Tendency of better voice after radiotherapy
Greulich [40]	2015	T1	1997–2013	8	362 157 TLM 207 RT	Tendency of better voice after radiotherapy

TLM: transoral laser microsurgery; RT: radiotherapy, OR: odds ratio

Early Cancer – Supraglottic T1/T2

- **Conservative surgery** (transoral CO2 and robotic /open partial LE) or **Radiotherapy**
- ***Need*** for elective neckdissection / RT, if >T1 N0
- Surgical salvage possible: transoral / open partial LE / total LE
- Cure rates: RT and Surgery similar!
 - 5-y LC: Surgery 73-100% / RT 60-100%
 - 5-y DSS: Surgery 82-91% / RT 83-100%
 - Larynx pres.: Surgery 85-87% / RT n.a.



Literature of RT alone in supraglottic early cancer is rare!

Early Cancer – Supraglottic T1/T2

Factors influencing outcome

- **Factors that influence treatment outcome:**
 - Highly related to pre-epiglottic / paraglottic space involvement (tumor volume!): T2 → T3
 - Complications of surgery: -13% permanent nutrition via PEG

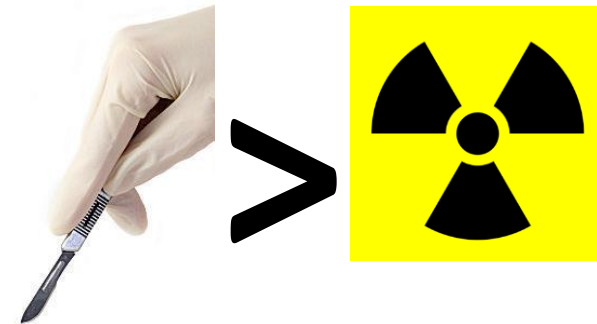
Early Cancer – Supraglottic T1/T2

Studies on the local control after transoral supraglottic partial CO2 resection of the last 10 years

Author	Year	T stage	Patients	Local control (%)	Time of measurement of the local control (months)
Grant [52]	2007	T1-T4	38	97	24
Roh [267]	2008	T1-T3	21	81	36
Chijiwa [268]	2009	T1-T3	161	86	60
Peretti [269]	2010	T1-T3	96	96	60
Perez-Delgado [270]	2010	T1-T3	53	81.1	60
Iro [271]	2011	T1-T2	137	91	60
Csanady [272]	2011	T1, T2	55	73	60
Hutcheson [273]	2012	T1-T3	5	100	24
Canis [51]	2013	T1-T2 T3 T4	118 104 55	85 82 76	60
Canis [49]	2014	T3	226	71.4	60
To [274]	2015	T1-T4	37	66 late stage 88 early stage	60
Wilkie [275]	2015	T1-T3	17	88	36

Cancer – T3

- **Conservative surgery** (transoral CO2 and robotic /open partial LE) or **Radiochemotherapy**
- ***Need*** for elective neckdissection/RT
- No literature with randomized trials comparing transoral CO2/ open partial LE vs. CXRT
- Surgical salvage possible: transoral / open partial LE / tLE
- Cure rates: RT and Surgery similar!
 - 5-y LC: Surgery 63-92% / RT 50%
 - 5-y DSS: Surgery 70-94% / RT 49-60%
 - Larynx pres.: Surgery 62-94% / RT 63%

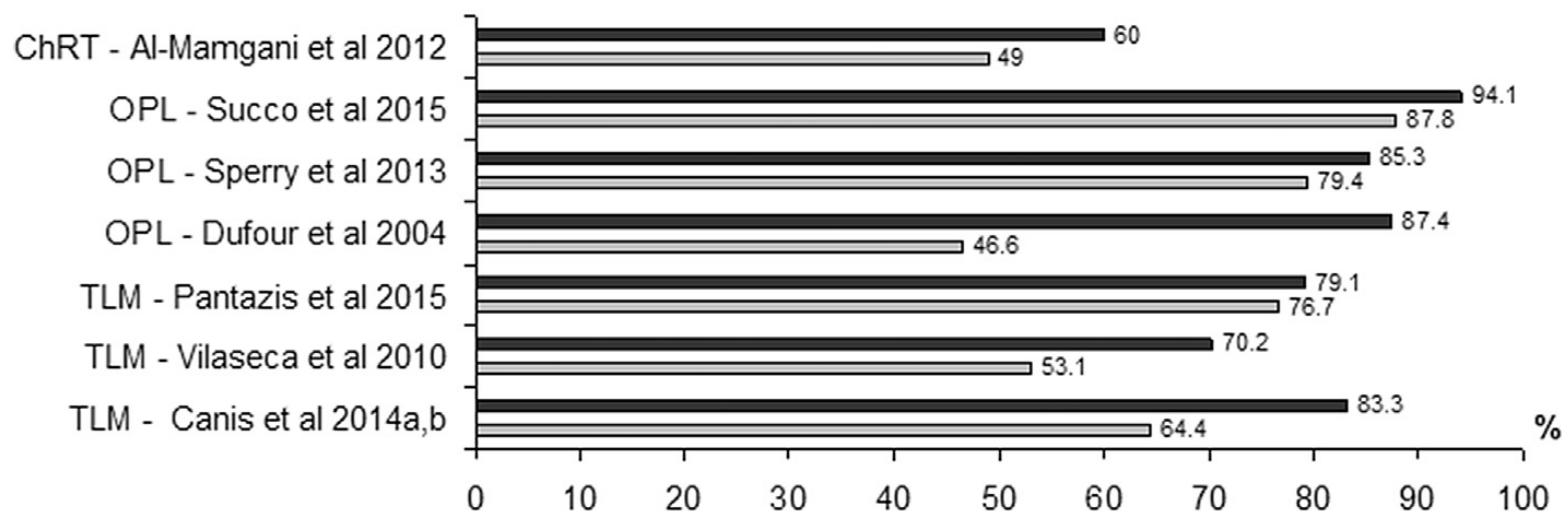


© adpic

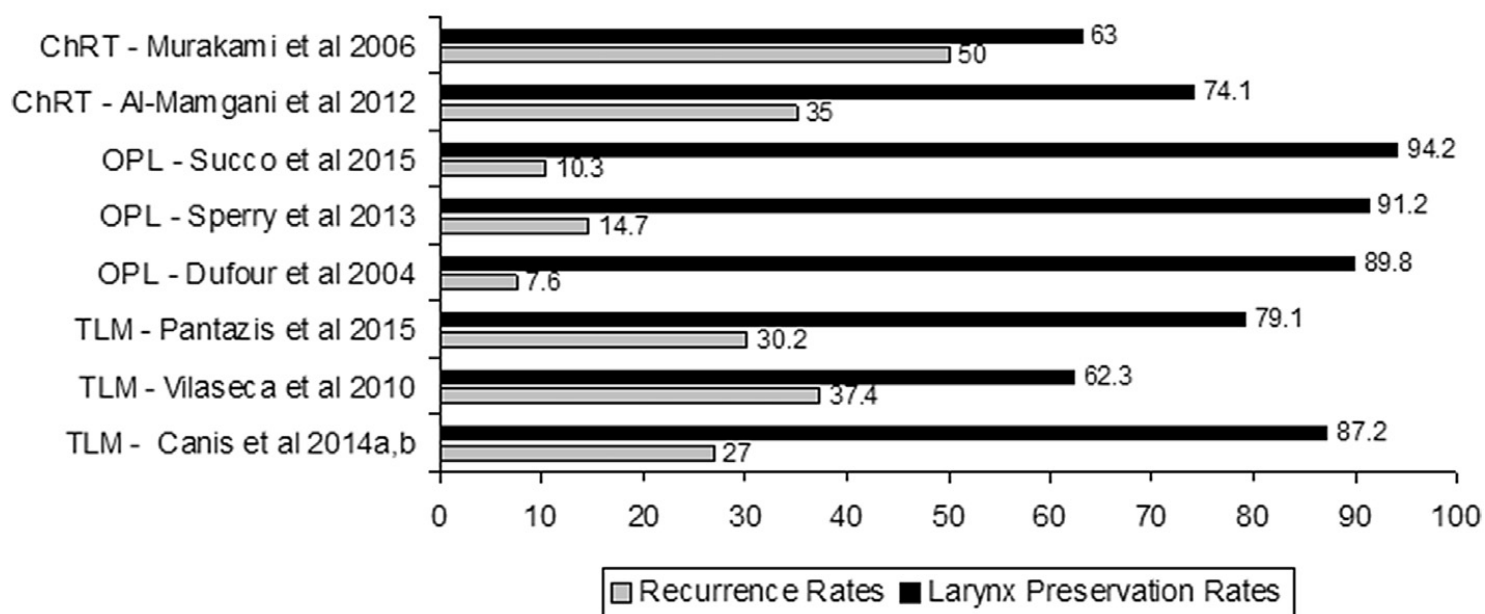
Mendenhall WM. Management T1-2 Glottic Carcinomas. Cancer, 2004

Agrawal N. Early Stage Laryngeal Cancer. Otol ClinN Am, 2008

5-year Overall Survival & Disease-specific Survival



5-year Larynx Preservation and Recurrence Rates



Cancer – T3

Factors influencing outcome

- **Factors that influence treatment outcome:**
 - Main contraindication for transoral / open partial LE:
 - Involvement of posterior commissure and/or both arytenoid cartilages
 - Tumor extension below upper border of the cricoid and cricoarytenoid joint invasion (fixed arytenoid)
 - Better prognosis for supraglottic tumors vs. glottic tumors in terms of local/regional control and larynx preservation in transoral CO2 surgery
 - Open partial LE > transoral CO2 (restricted exposure via transoral route)
→ maybe less difference with Robotic Surgery
 - Adjuvant RT necessary: 20-40%
- **Voice quality:**
 - RT >> transoral CO2 > Open partial LE

Riga M, et al. Systematic review T3 laryngeal cancer. EJSO, 2016

Ambrosch P, et al. Lasermikrochirurgie Larynxkarzinome. Onkologe, 2001

Canis M, et al. Transoral laser in larynx cancer T3. Head Neck, 2014

Cancer – T3

Studies on the local control after open vertical partial LE of the last 10 years

Author	Year	T stage	Procedure	Patients	Local control (%)	Time of measurement of the local control (months)
Brumund [82]	2005	T1-T3	FLPL	270	87.8	60
Dedivitis [276]	2005	T1-T2	FLPL	30	83.3	48
Bakhos [277]	2008	T1-T2	FAPL	23	87	60
Sachse [278]	2009	T1-T2	CHE, FLPL	68	86	60
Dong [83]	2009	T1-T2	FLPL	65	100	60
Mantsopoulos [279]	2012	T3	HLE; FLPL	66	86.9	60
Mantsopoulos [280]	2012	T2	VPL	128	93.9	60
Nie [281]	2015	T1, T2	VPL	58	94	36

FLPL: fronto-lateral partial laryngectomy; FAPL: fronto-anterior partial laryngectomy, CHE: chordectomy; HLE: hemilaryngectomy; VPL: vertical partial laryngectomy

Cancer – T3

Studies on the local control after open vertical partial LE of the last 10 years

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Cancer – T3

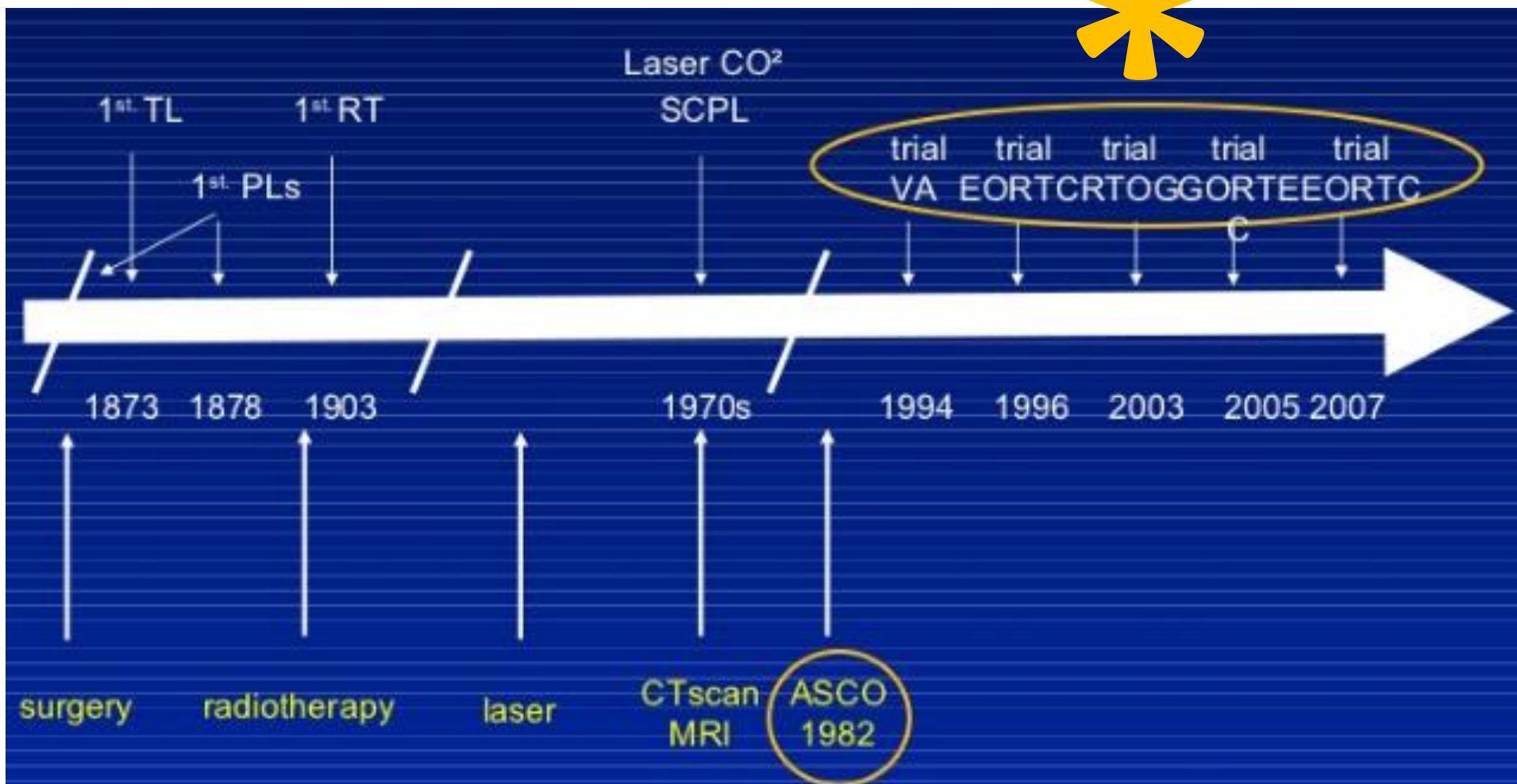
Studies on the local control after open horizontal partial laryngectomy of the last 10 years

Author	Year	T stage	Procedure	Patients	Local control (%)	Time of measurement of the local control (months)
Akbas [119]	2005	T1-T3	CHP	46	95.6	24
Bron [97]	2005	T2-T4	SCPL	75	92.5	60
Gallo [99]	2005	T1-T4	SCPL	253	92.5	60
Prades [106]	2005	T1-T3	HSL	110	90.3	30
Targa [100]	2005	T1-T4	CHP	81	86.4	53
Laudadio [102]	2006	T1-T4	SCPL	206	93.2	60
Lima [101]	2006	T3-T4	CHEP	43	85	60
Herranz [282]	2006	T1-T4	HSL	110	89.1	60
Farrag [283]	2007	T1-T4	SCPL	14	100	36
Sevilla [96]	2008	T1-T4	HSL	267	92	60
Bakhos [277]	2008	T1-T2	SCPL	19	83	60
Nakayama [207]	2008	T1-T4	SCPL	15	100	36
Laccoureye [284]	2008	T1-T3	HSL	95	93.4	60
Sun [285]	2009	T1-T4	SCPL	63	87	60
Sánchez-Cuadrado [286]	2011	T1-T3	SCPL	41	80	60
Pinar [112]	2012	T1-T4	SCPL	56	92.5	60
Mercante [115]	2013	T3	SCPL	32	96.2	60
Sperry [287]	2013	T2 T3	SCPL	23 28	100 96	60
Succo [104]	2015	T3-T4	HSL	555	90.6	60
Succo [103]	2015	T1-T2	HSL	216	97.5	60

CHP: cricothyroidopexy; CHEP: cricothyroid-epiglottopexy; SCPL: supracricoid partial laryngectomy; HSL: horizontal supraglottic laryngectomy

Advanced Cancer – T3/T4

- Organ preservation with induction CX → CXRT, CXRT or tLE?



Advanced Cancer – T3/T4

- **-1990s: organ preservation treatment protocols with CX and RT = alternative to tLE**

TABLE 1. Trials of Larynx Preservation

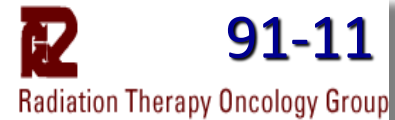
TRIAL	NAME	PHASE	STUDY ARM	RATE (TIME POINT)		
				DFS	OS	LARYNGEAL PRESERVATION
VALCSG 1991 ⁴⁰	VA Larynx Cancer Study	3	CF ×3 then RT	NR	68% (2 y)	66% (2 y)
			SX then RT	NR	68%	NA
Forastiere 2013 ⁶⁷	RTOG 91-11	3	CF ×3 then RT	20.4% (10 y)	39% (10 y)	67.5% (10 y)
			RT + C	21.6%	28%	81.7%
			RT	14.8%	32%	63.8%
Lefebvre 1996 ⁶⁶	EORTC	3	CF ×3 then RT	32% (5 y)	30% (5 y)	35% (5 y)
			SX then RT	27%	35%	NA
Lefebvre 2013 ⁷³	TREMPLIN	2	ICT ×3 then RT + C	91.7% (18 mo)	75% (3 y)	95% (3 mo)
			ICT ×3 then RT +CET	85.7%	73%	93%

Abbreviations: C, cisplatin; CET, cetuximab; CF, cisplatin and 5-fluorouracil; DFS, disease-free survival; EORTC, European Organization for Research and Treatment of Cancer; ICT, docetaxel, cisplatin, and 5-fluorouracil; NA, not applicable; NR, not reported; OS, overall survival; RT, radiotherapy; RTOG, Radiation Therapy Oncology Group; SX, surgery; TREMPLIN, induction chemotherapy followed by either chemoradiotherapy or biotherapy for larynx preservation; VALCSG, the US Department of Veterans Affairs Laryngeal Cancer Study Group.

Advanced Cancer – T3/T4

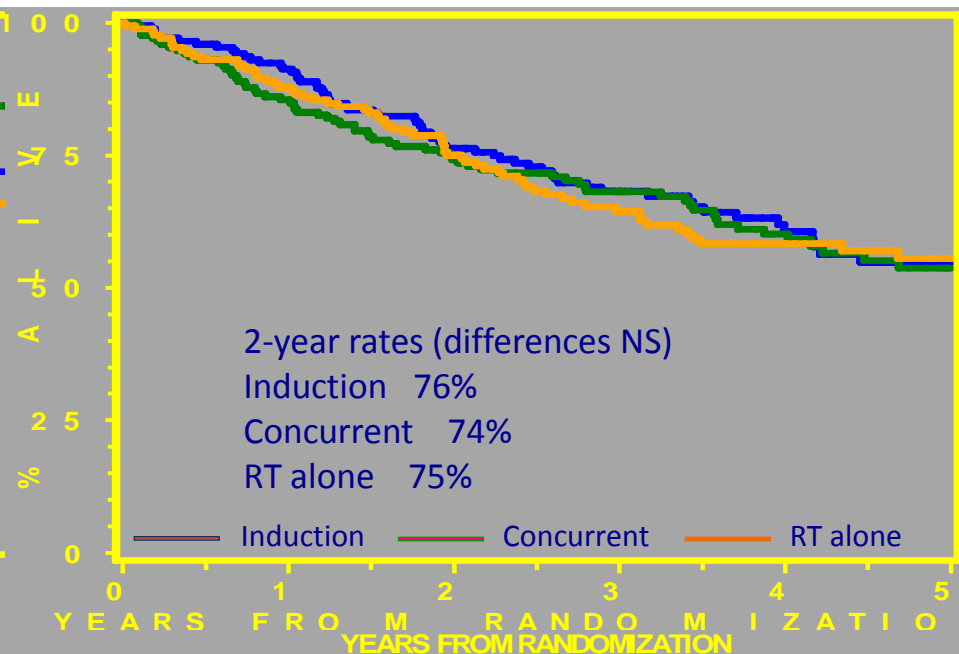
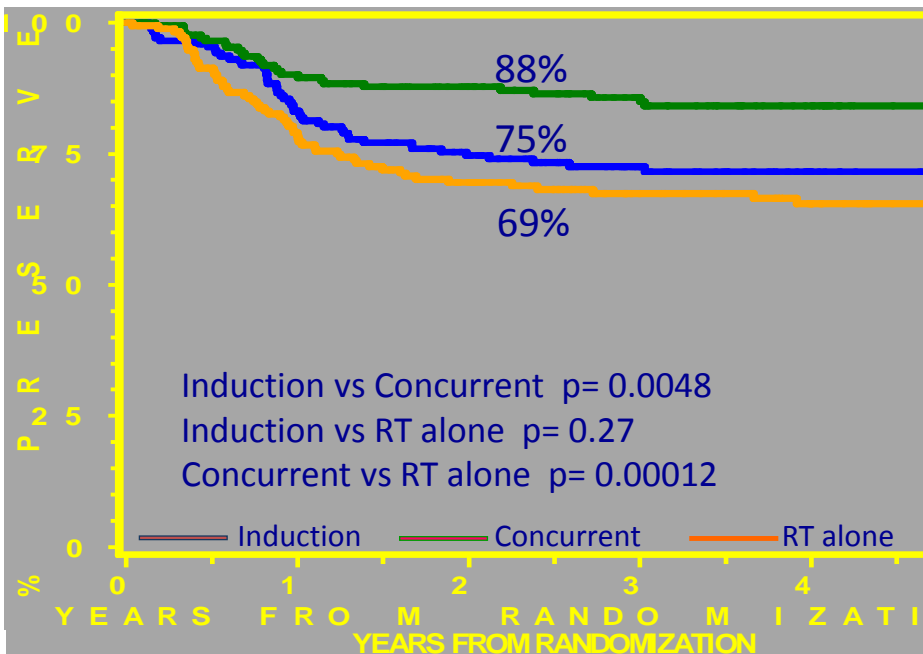
Outcome concerns

- Various randomized trials: OS CXRT = OS tLE
- All randomized trials: different protocols of CXRT, and not CXRT vs. tLE



Laryngeal Preservation

Overall Survival



Sanabria A, et al. Organ preservation with CXRT in advanced larynx cancer. *Auris Nasus Larynx*, 2017

Forastiere AA et al. RTOG 91-11: 3 non-surgical strategies for larynx preservation in advanced stage.

J Clin Oncol, 2013

Advanced Cancer – T3/T4

Outcome concerns

- No organ preservation protocol shows improvement in OS
- Long-term toxicity ↗: RTOG studies → 43% late grad 3-4 toxicities (swallowing and **larynx dysfunction**)
- Organ preservation → more relevant: functional organ preservation
- OS for all cancer locations ↗ ↔ OS for laryngeal cancer ↘

Question:

Approach developed by clinical trials → standard practice?

Advanced Cancer – T3/T4

Outcome concerns

Results of overall survival for population studies comparing CRT with laryngectomy in advanced laryngeal cancer.

Study	Database	5-Year overall survival for advanced tumors (%)		Adjusted hazard ratio for CRT
		CRT	Laryngectomy	
Chen et al. [13] ^a	NCDB	48	51	1.13 (1.06–1.21)
Megwalu and Sikora [14]	SEER	31	40	1.32 (1.22–1.43)
O'Neill et al. [15]	SEER	NR	NR	0.82 (0.68–0.99) ^b
Timmermans et al. [16]	NETHERLANDS CANCER REGISTRY (NCR) AND THE PALGA FOUNDATION DATABASE	42	48	1.27 (1.01–1.59)

NR: not reported.

^a 4-Year overall survival.

^b HR calculated to assess the effect of total laryngectomy.

Results of overall survival for primary observational studies comparing CRT with laryngectomy in advanced laryngeal cancer.

Study	Location	Number of patients	Overall survival for T4		Statistical significance
			CRT	Laryngectomy	
Dziegielewski et al. [17]	Canada	258	16	49	Yes
Karlsson et al. ^b [18]	Sweden/Scotland	176	42	58	No
Gourin et al. [19]	USA	451	25	55	Yes
Rosenthal et al. [20]	USA	221	48	60	Yes
Elegbede et al. [21]	USA	225	52	52	No
Rades et al. ^a [22]	Germany	122	66	75	No
Vengalil et al. ^b [23]	Canada	107	41	70	Yes

CRT: chemoradiotherapy.

^a 2-Year survival.

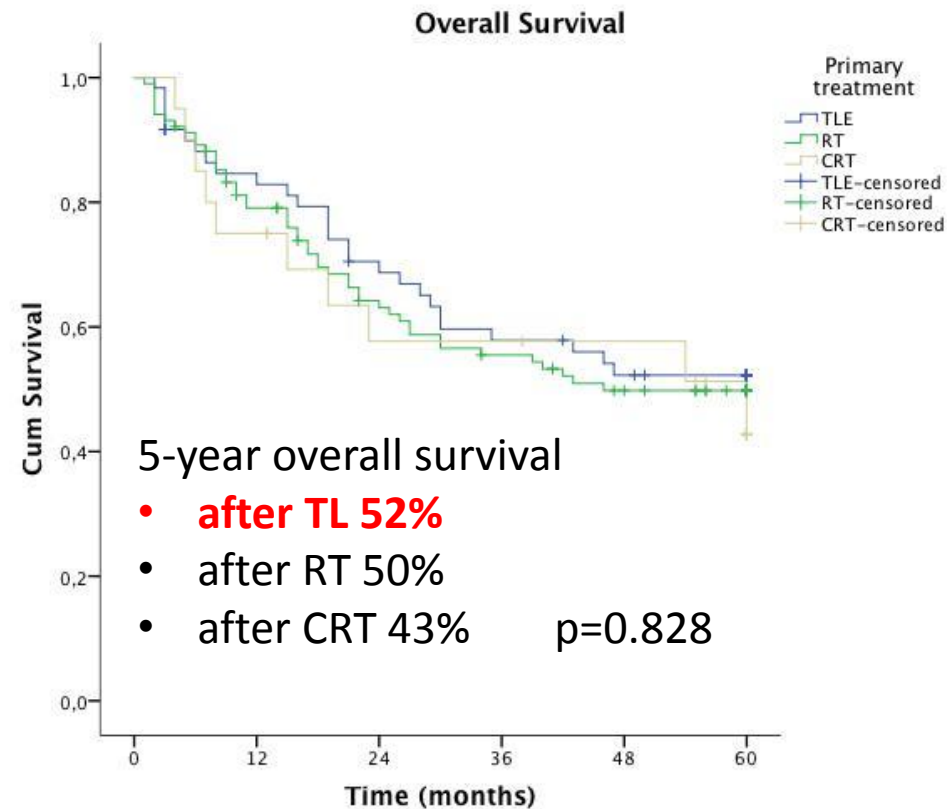
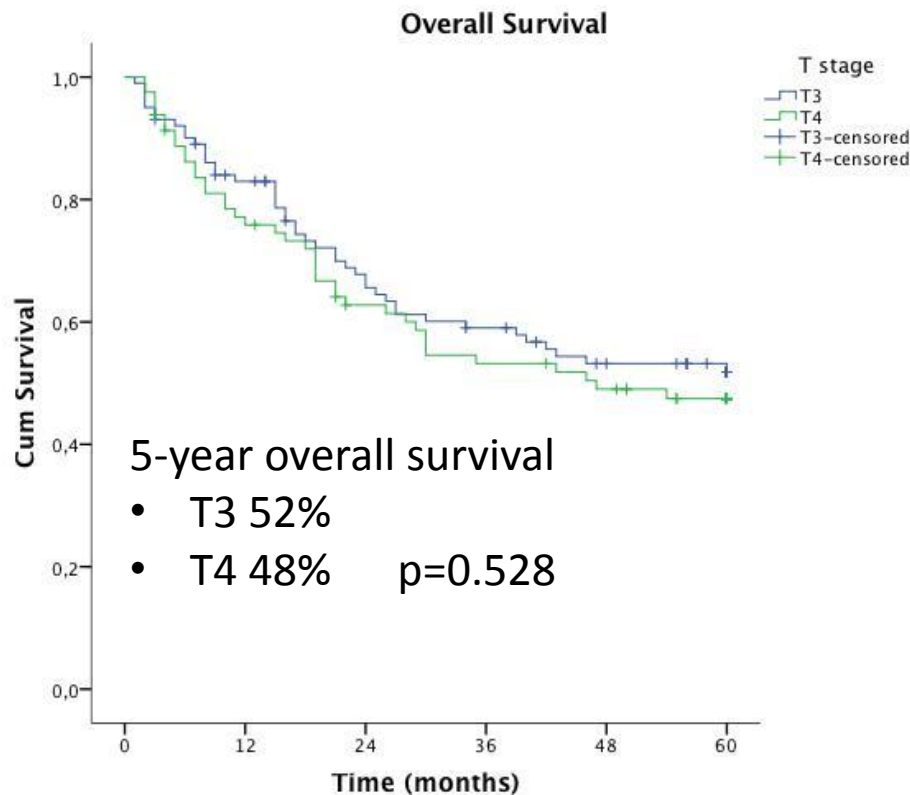
^b 3-Year survival.

Sanabria A, et al. Organ preservation with CXRT in advanced larynx cancer. Auris Nasus Larynx, 2017

Advanced Cancer – T3/T4

Outcome compared between RTCX and tLE?

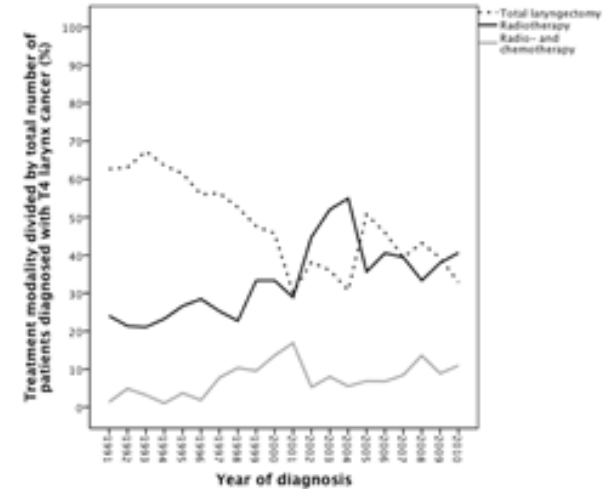
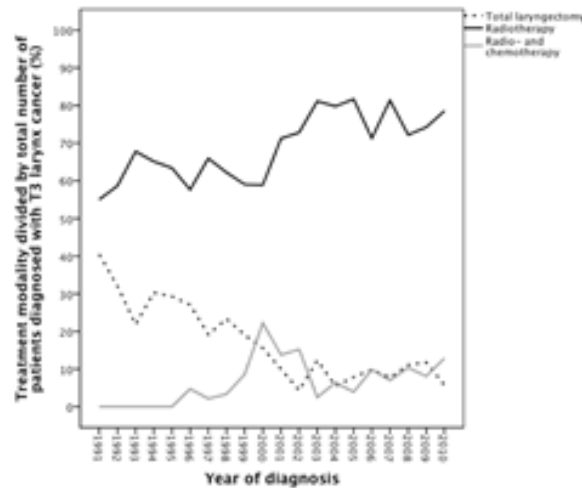
Overall survival of T3 and T4 laryngeal cancer (N=182)



Outcome compared between RTCX and tLE?

Time trends for therapy T3 (N=2072) and T4 (N=1722)

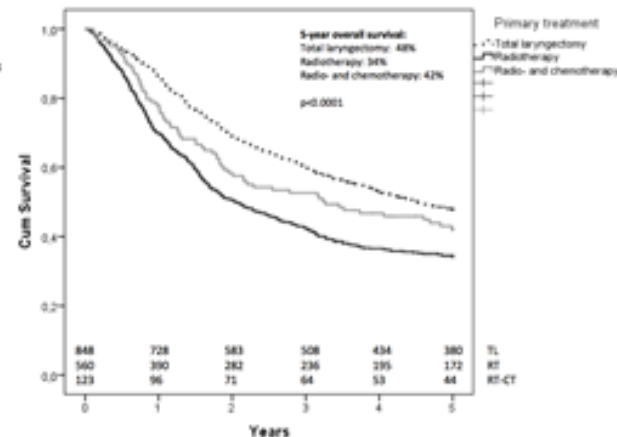
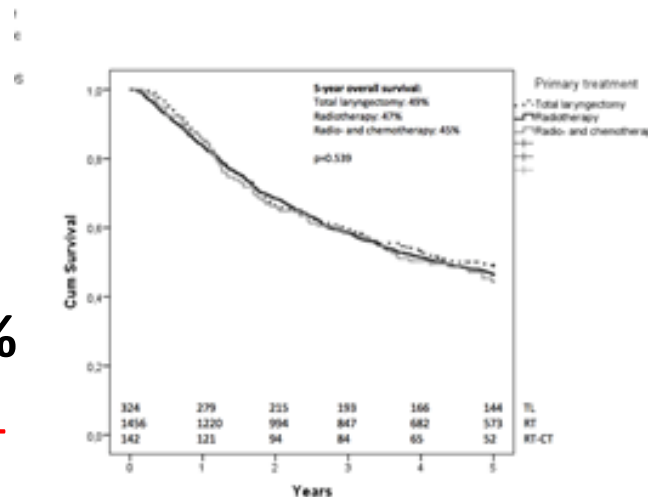
Decrease in total LT
since 1990



5-year overall survival T3 and T4 according to therapy

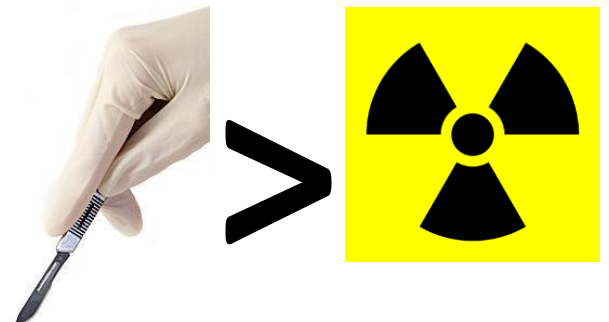
Decrease in 5-y OS

tLE +/- RT > RTCX > RT
48% 42% 34%
p<.0001



Advanced Cancer – T3/T4

- **Chemo-Radiotherapy vs. Total Laryngectomy**
- ***Need*** for elective neckdissection/RT
- Surgical salvage possible: open partial LE / tLE
- Cure rates:
 - 5-y OS: Surgery 49-60% / RT 16-52%
 - Larynx pres.: Surgery 0% / RT 66-93%



Advanced Cancer – T3/T4

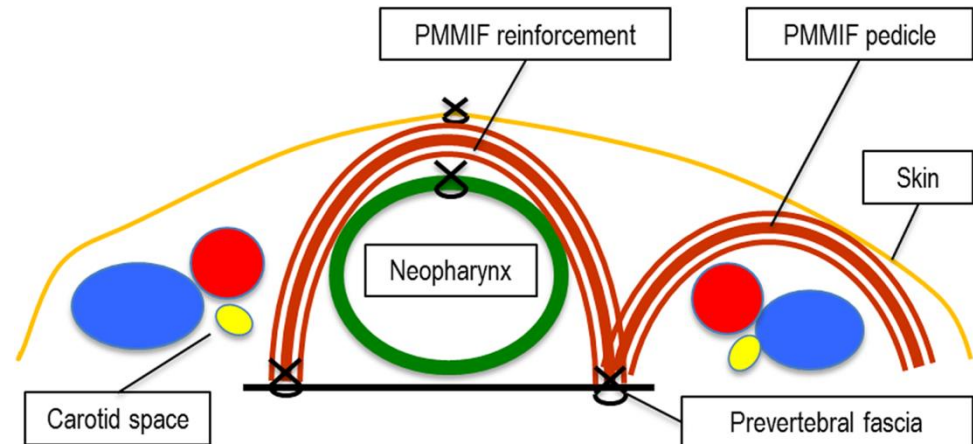
- **Factors that influence treatment outcome:**
 - Different RT schemes (IMRT; hyperfractionated; accelerated), combined modalities vs. well established tLE procedure
 - Post-tt. problems:
 - RT → swallowing problems +++, post-tt. dysfunctional larynx, chondroradionecrosis
 - tLE → tracheal breathing, bad voice dynamic, «no» smell
 - Increased complications in salvage surgery after CXRT
- **Voice quality:** RT > tLE

Advanced Cancer – T3/T4

Outcome concerns

Increased challenges of salvage tLE after failed organ preserving CXRT

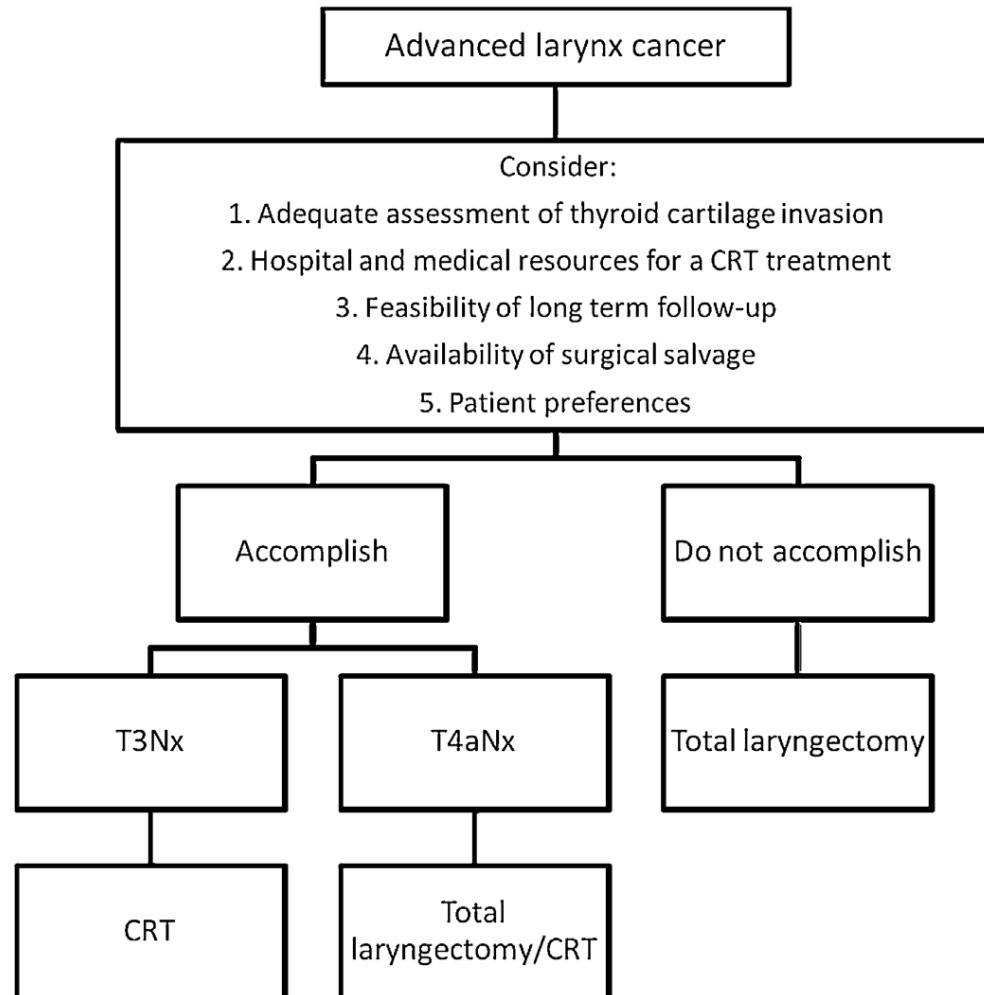
- Weber et. Arch Otolaryngol Head Neck Surg 2003: RTOG 91-11 study:
1/3 pharyngocutaneous fistulas
- Machtay et al. J Clin Oncol 2008. RTOG 91-11, 97-03, and 99-14:
43% severe late toxicity;
Older age, advanced T-stage, and larynx/hypopharynx primary site strong independent risk factors.
Neck dissection associated with increased risk of these complications
- Theunissen et al. Arch Otolaryngol Head Neck Surg. 2012 Neth. Cancer Inst.):
over a 10-year period (2000-2010)
25/217 (**11%**) of tLEs for a dysfunctional larynx!
- Necessity to use preventive surgical procedures, e.g. Pectoralis Major Myofascial Flap to cover carotids and pharyngeal suture line → Fistula ∨



Advanced Cancer – T3/T4

Treatment of advanced larynx cancer: to CUT or to CXRT?

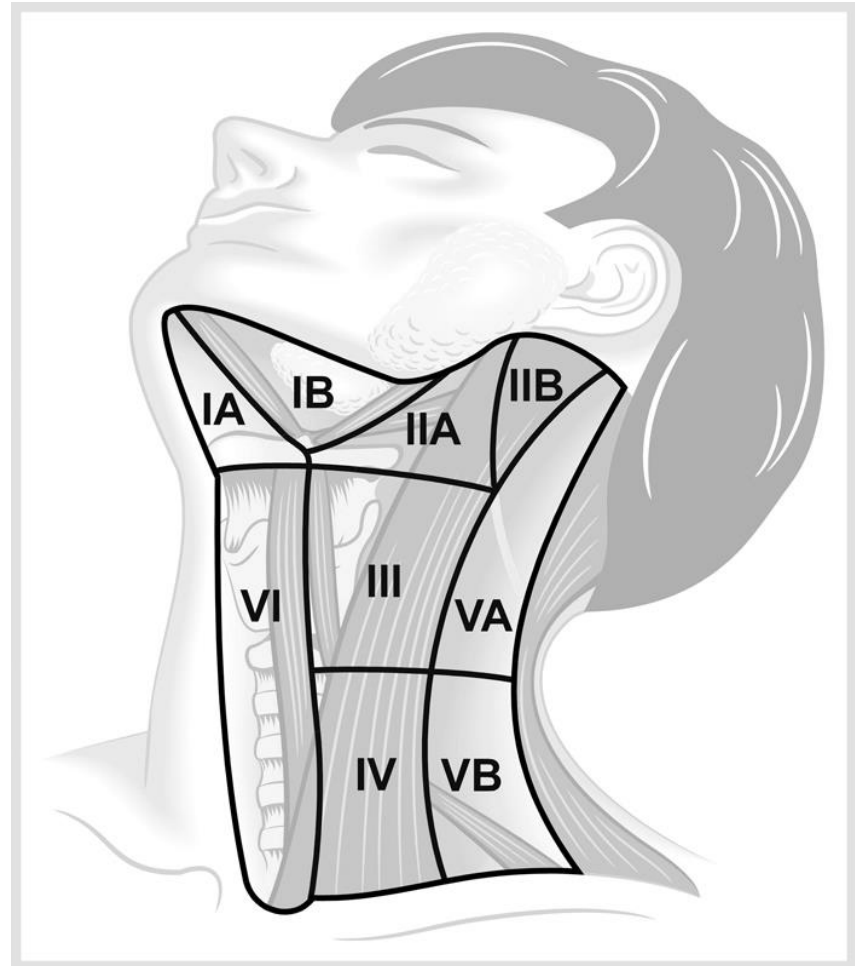
- Cure rates for present CXRT protocols are (still) not equivalent to those for tLE + postop RT:
 - significant lower OS, <50% chance of larynx preservation in T4, increased complication rates for salvage surgery
 - Anatomic + functional tumor-related tissue damage (T4) → ∩ functional recovery, with loss of lower airways protection as the main (chronic) problem
 - Thus, also in view of high success rates of vocal, pulmonary and olfactory rehabilitation after tLE, mostly limited swallowing problems after tLE, and documented lack of difference in QoL post organ preserving or sacrificing treatment,



...tLE still should be considered the treatment of choice in advanced (T4) larynx cancer

Principle treatments – N(eck)

- N0
- N+



Laryngeal Cancer

Treatment – Neck lymphnodes

- **T1 / T2 N0 glottic:** \emptyset ND or RT
- **> T2 / supraglottic / subglottic / >N0:** ND or RT

If surgery:

- Elective selective ND:
 - N0: Level IIA and III (+/- IV) (almost no occult mets. in IA/B ($\approx 0\%$), IIB (0.4%), IV (1.4-3.4%) and V ($\approx 0\%$))
- Therapeutic selective ND:
 - N+: Level II-IV (almost no occult mets. in I (2%) and V ($\approx 0\%$))
 - Level I and V only if mets. present
- Bilateral ND:
 - Tumor in midline and supraglottic
 - Tumor supraglottic and N+
 - N+ in Level VI
 - Controversial: N0 \rightarrow contralateral occult mets. <10%Level

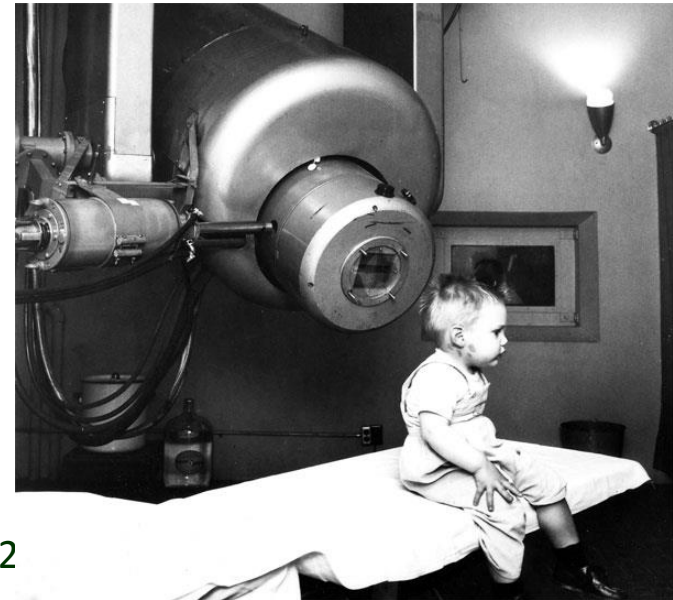
Adjuvant Radio- +/- chemotherapy

Indications

Post-operative RT	pT3-4a [†] pT3 pN1* Pn1 L1 V1 pN2-3*	*: ECE- †: favorable pT3 may be observed CXRT ma be discussed
Post-operative CXRT	pN+ ECE+ R+-Resection*	*if re-resection not possible

Additional CX:

Improved OS and DFS in ECE+ and R+



NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Head and Neck Cancers

Version 1.2017 — February 6, 2017

NCCN.org

Continue

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Schweizerische Gesellschaft für Oto-Rhino-Laryngologie, Hals- und Gesichtschirurgie
Société suisse d'Oto-Rhino-Laryngologie et de Chirurgie cervico-faciale
Società Svizzera di Oto-Rhino-Laringologia e di Chirurgia cervico-facciale

<http://www.orl-hno.ch>

Empfehlungen

für
die Betreuung (Abklärungen, Behandlung und
Nachsorge) von Patienten mit Karzinomen des
Kopf-Hals-Bereiches

Konsensus-Bericht
herausgegeben von der

Arbeitsgemeinschaft für Hals- und Gesichtschirurgie
der Schweizerischen Gesellschaft für ORL,
Hals- und Gesichtschirurgie

Ausgabe 2010

Redaktion

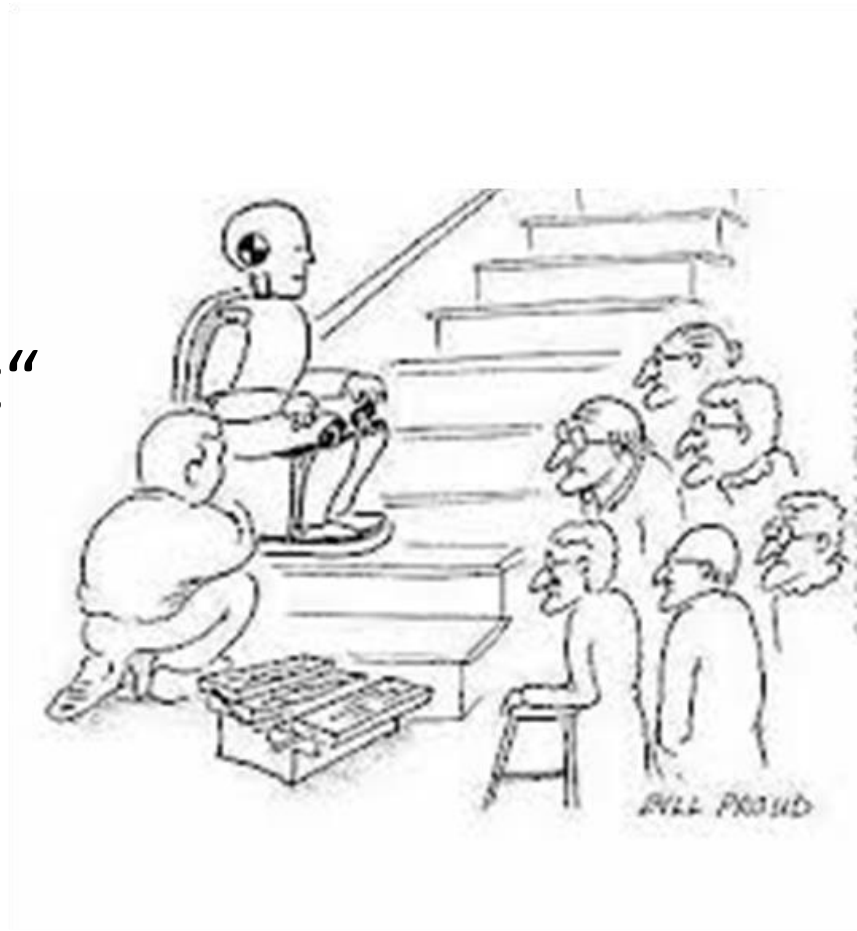
A. Arnoux / A. Arnold / P. Dulguerov / C. Fischer / R. Giger /
S. Hasenclever / G. Huber / W. Müller / Ph. Pasche / S. Stöckli / P. Zbären.

Ausgabe 2002: M. Wolfensberger / A. Arnoux / P. Zbären / D. Althaus / D.
Meier / P. Dulguerov / Ph. Pasche / W. Müller / M. Mauderli / S. Hasenclever /
H. Wespi / P. Schläpfer / S. Schmid.

8. Types of Surgery

1. Conservative procedures – Partial LE

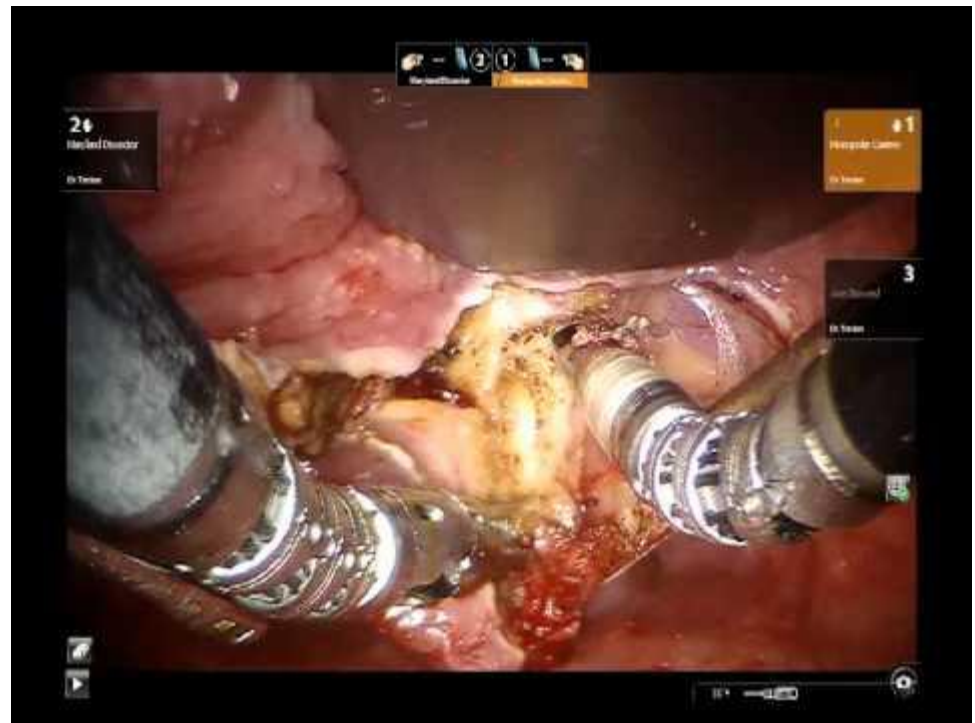
CAVE: „Ogura Stairway-Test“
(= climbing 2 stairs)



Laryngeal Cancer

Transoral Procedures

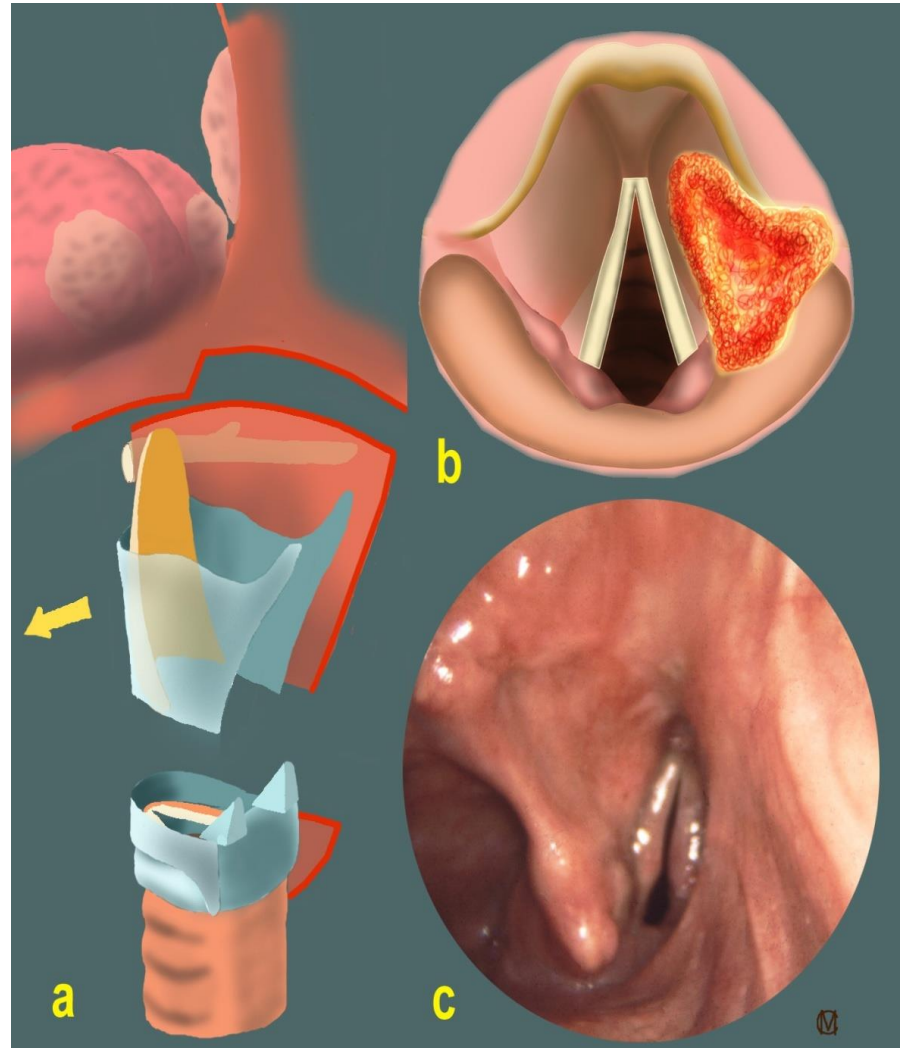
- Transoral procedures:
CO2 Laser / Da Vinci Robot



Laryngeal Cancer

Open Procedures

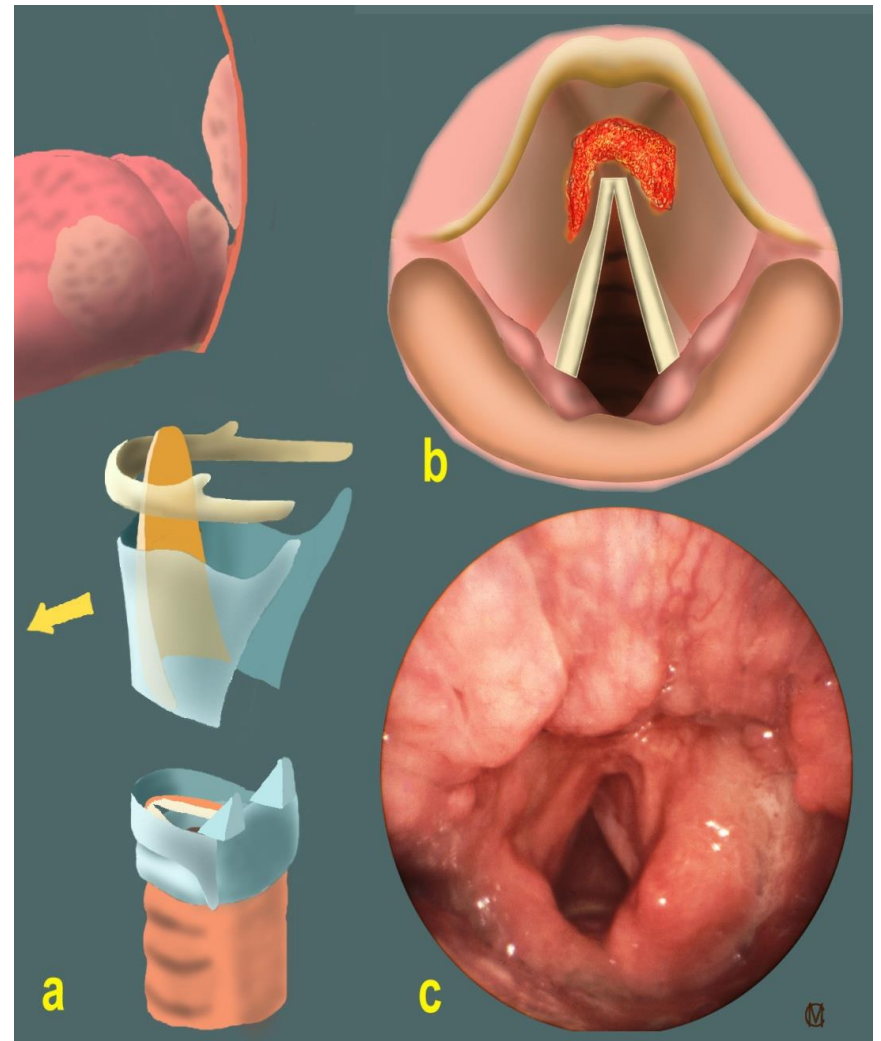
- Vertical Hemi-LE



Laryngeal Cancer

Open Procedures

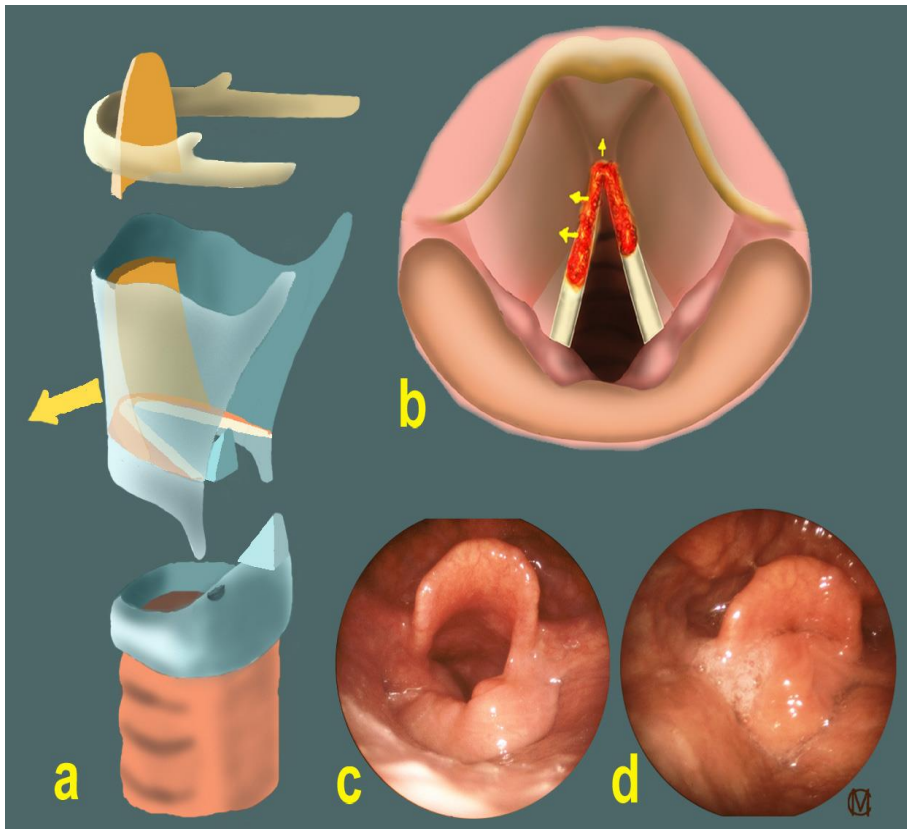
- Supraglottic LE



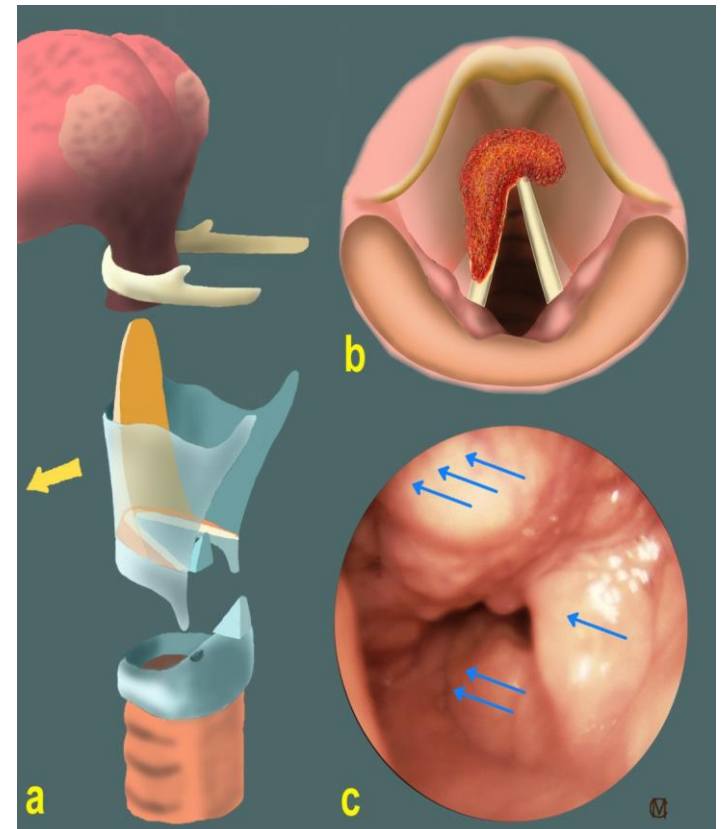
Laryngeal Cancer

Open Procedures

- Supracricoidal LE



Crico-Hyoido-Epiglotto-Pexy

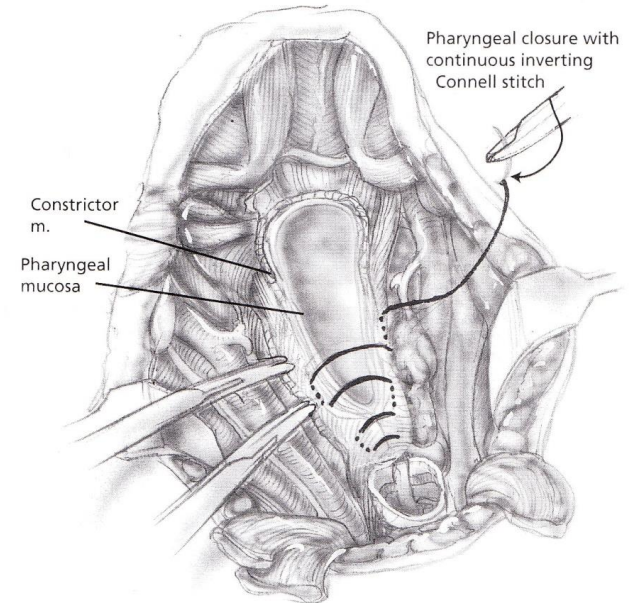
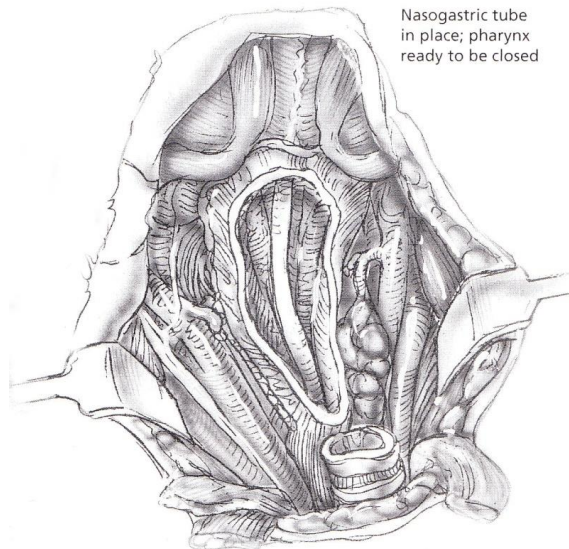
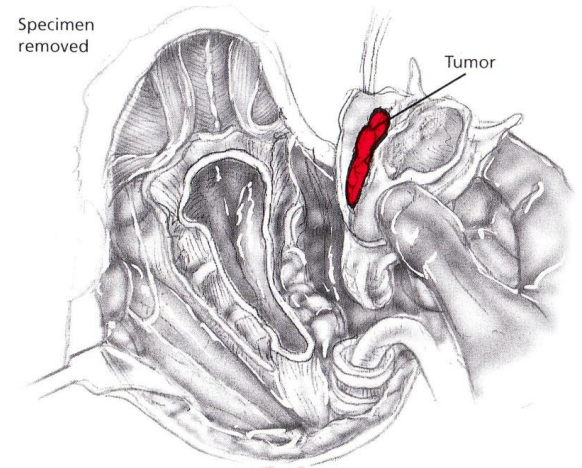
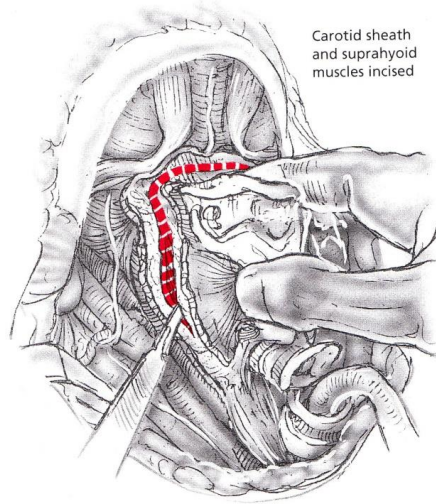


Crico-Hyoido-Pexy

Laryngeal Cancer

Total Laryngectomy

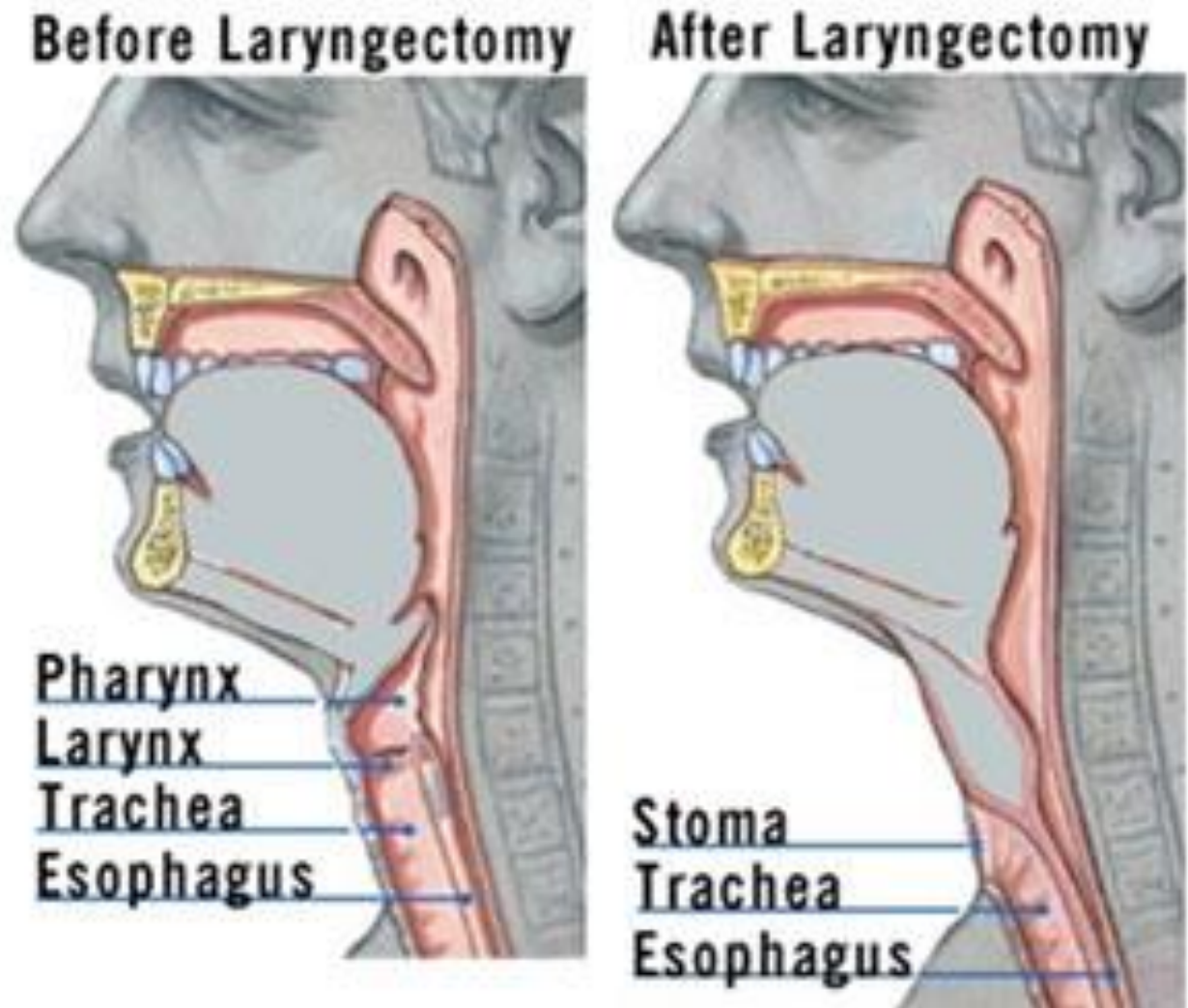
2. Total laryngectomy



Laryngeal Cancer

Total Laryngectomy

- Totale LE

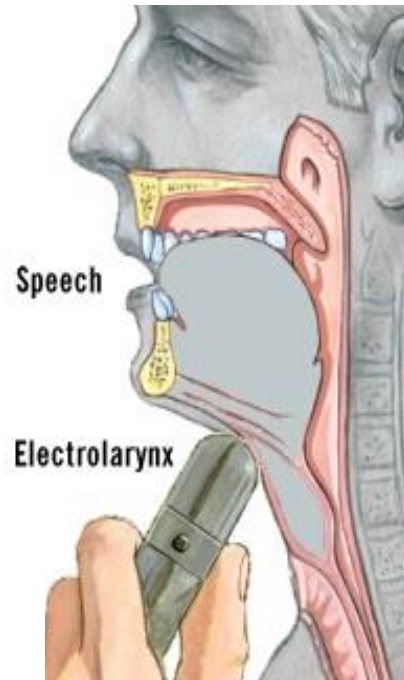


Laryngeal Cancer

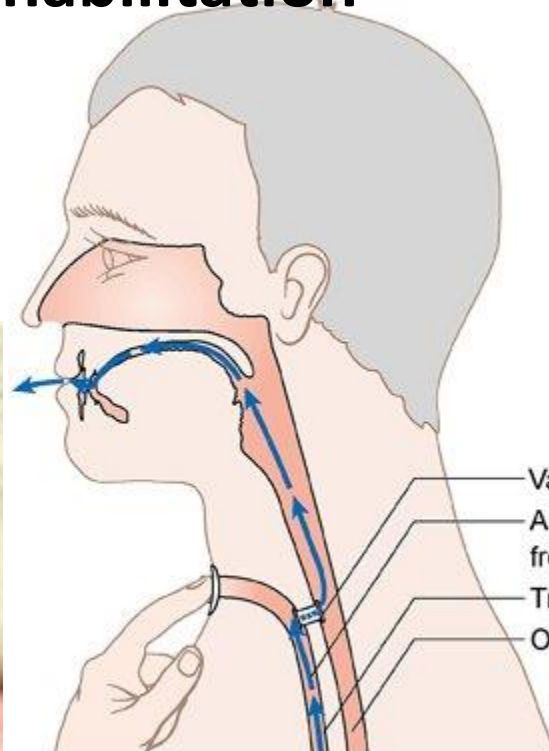
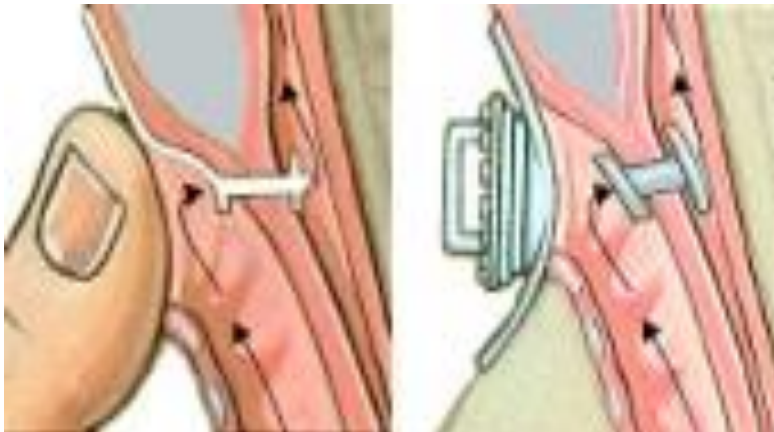
Voice Rehabilitation

1. Tracheostomal voice prosthesis
2. Electrolarynx
3. Esophageal voice rehabilitation

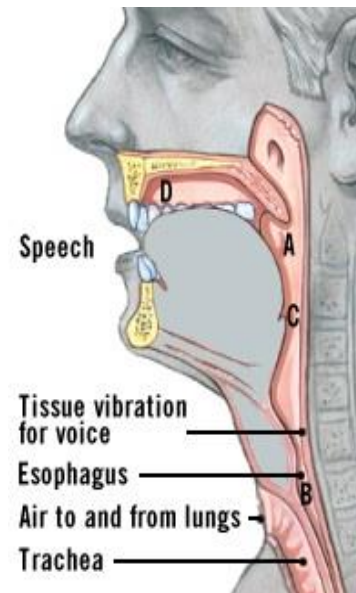
2.



1.



3.



9. Complications

- **CXRT-caused**

- Hypothyroidism /-parathyroidism
- Swallowing dysfunction (15%)
- Persistent xerostomia (⋮ IMRT technique)
- Caries
- Chondroradionecrosis
- Laryngeal fibrosis and synechiae

- **Surgery-caused**

- Bleeding/infections
- Dysphonia
- Swallowing dysfunction (stenosis)
- «Loss» of smell
- Fistulisation
- Permanent tracheotomy dependency after partial laryngectomy
- Hypothyroidism/-parathyroidism
- Mortality (1-2%)



10. Follow-up

- **Long-term follow-up**

- Early detection of relapse
- Early detection of 2. tumors (4%/y.)
- Cessation of tobacco and alcohol consumption
 - ↗ Improvement of outcome and survival
 - ↘ 2. tumor
- Management of complications (swallowing/speech)
- Evaluation of nutritonal conditions?
- Pain evaluation and treatment
- Psychological support

Follow-up

	1 y	2 y	3 y	4 y	5 y	> 5 y
ENT-examination	3 mth.	3 mth.	4 mth.	6 mth.	6 mth.	1 y.
Rx examination -loco-regional	4 mths/1 y: MRI/CT	2 y: MRI/CT	1x/y. low-dose CT, if smoker < 15 years			
-lung	1 y: CT	2 y: CT				
Panendoscopy + biopsy	if signs and symptoms of recurrence					
Dental monitoring	lifelong with topical fluoride treatment					
Thyroid hormone (if RT on neck)	2 x TSH	2 x TSH	1 x TSH			

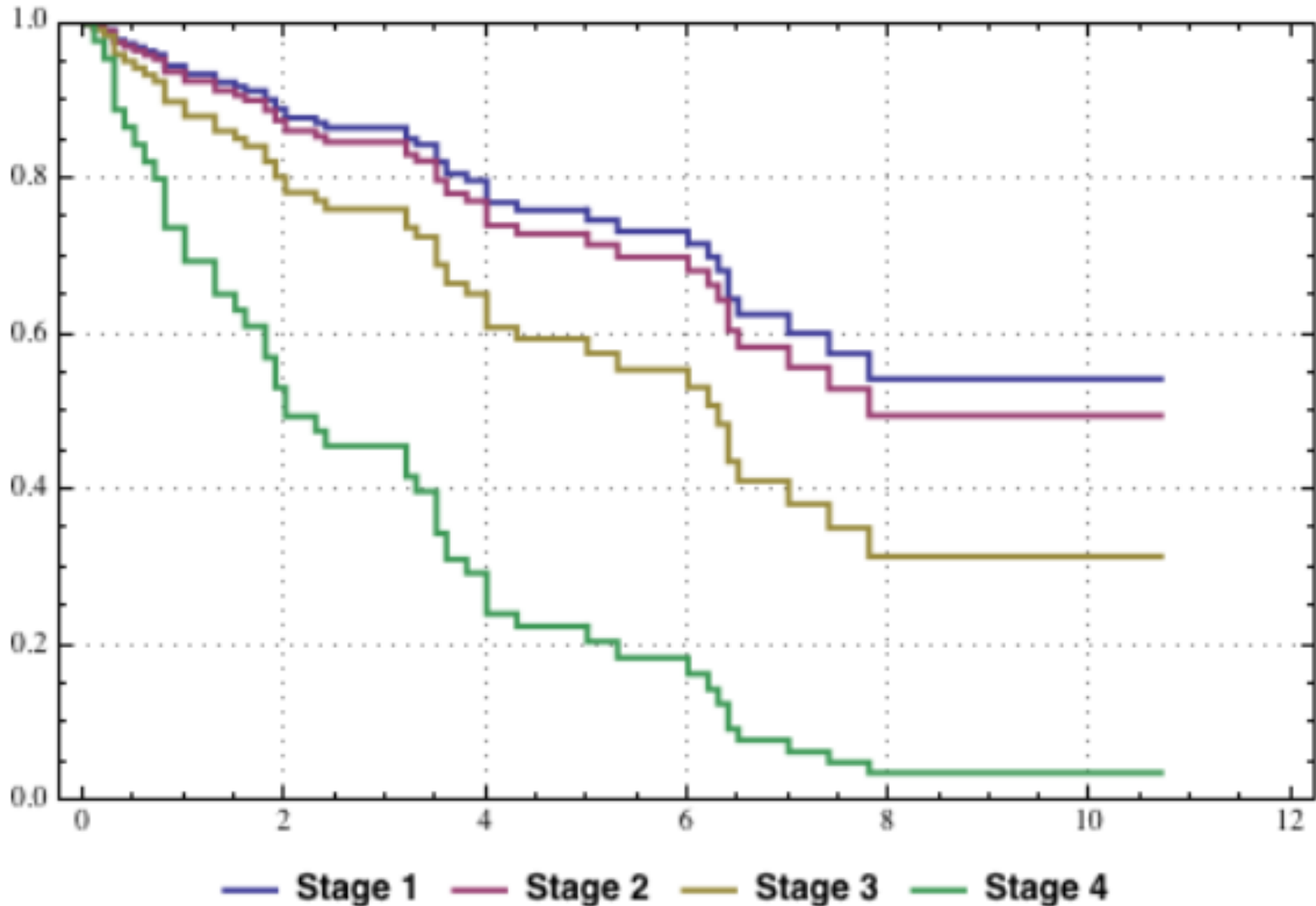
10. Outcome and Prognostic

Stage	5-y-overall survival
I	75%
II	70%
III	60%
IV	20%

Overall Survival depends the Tumor Stage

Larynx Cancer Survival by Stage

Males at Age 50



11. Treatment of Relapse

- Salvage-Therapy after CXRT
 - Surgery: (in chosen cases: transoral CO2/transoral robotic, open partial LE)
→ **most often total laryngectomy!**
 - Rate of complications 21-60%
 - Mortality <3%
 - 2-y relapse rate 33%
 - 5-y OS 30-86%
- Re-irradiation possible → toxicity ↗
- Palliative treatment: CX
Best supportive care



12. Future

- Randomized studies:
functional organ preservation vs. **tLE**
- Improvement of surgical techniques
(robotic surgery)
- Improvement of imaging techniques /
radiotherapy techniques
- Development of new treatment options:
immunotherapy

