Hypopharynx Cancer

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Case Presentation

- **HPI:**
  - 75 year old male presents with 3 months of globus sensation.
- **ROS:**
  - Reports 1 month of hoarseness. Denies odynophagia, dysphagia, dyspnea, hemoptysis, otalgia, or weight loss.
- **PMHx:**
  - HTN, asthma, BPH
- **Social Hx:**
  - 3 pack-year smoking history, quit >50 years ago.
  - Drinks EtOH socially.
- **Fam Hx:**
  - Mother had endometrial cancer.

Case Physical Exam

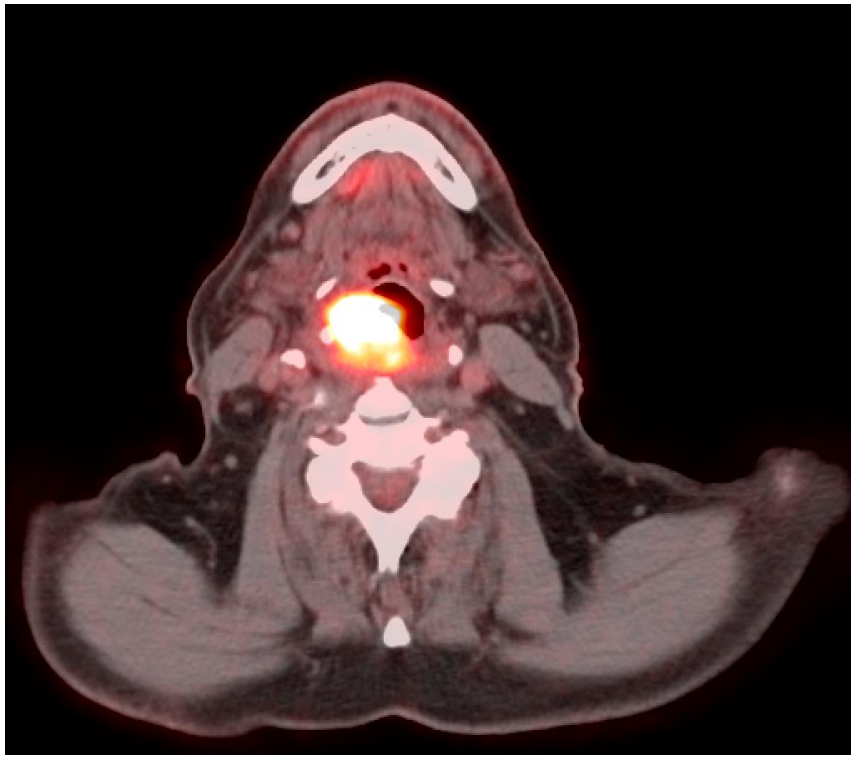
- No visible oral cavity or oropharynx lesions. CN II-XII intact.
- Enlarged, palpable right cervical level 2 and 3 lymph nodes.
- Direct Fiberoptic Nasopharyngolaryngoscopy (NPL)
  - Hypopharyngeal mass extending to the right arytenoids, pyriform sinus, lateral, and posterior walls.
  - Right vocal cord, false vocal cord, and right aryepiglottic folds are involved.

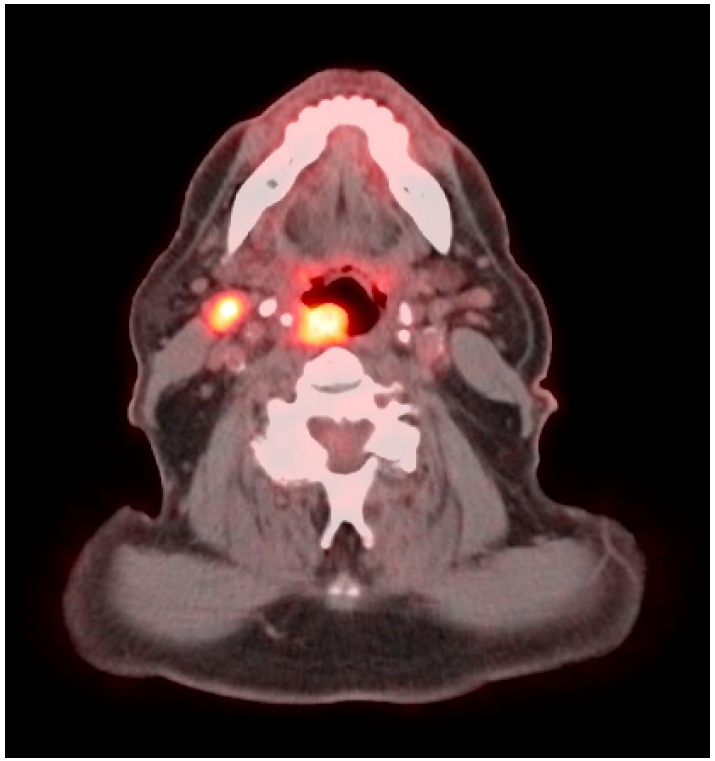
Case: CT neck w/ con

- Showed 2.6 x 2.6 x 4.2 cm right lateral and posterior wall hypopharynx mass.
- Multiple enlarged cervical right level 3 lymph nodes, all <3 cm.

Case: PET/CT

- PET redemonstrates previous findings. No distant disease noted.





Case Continued

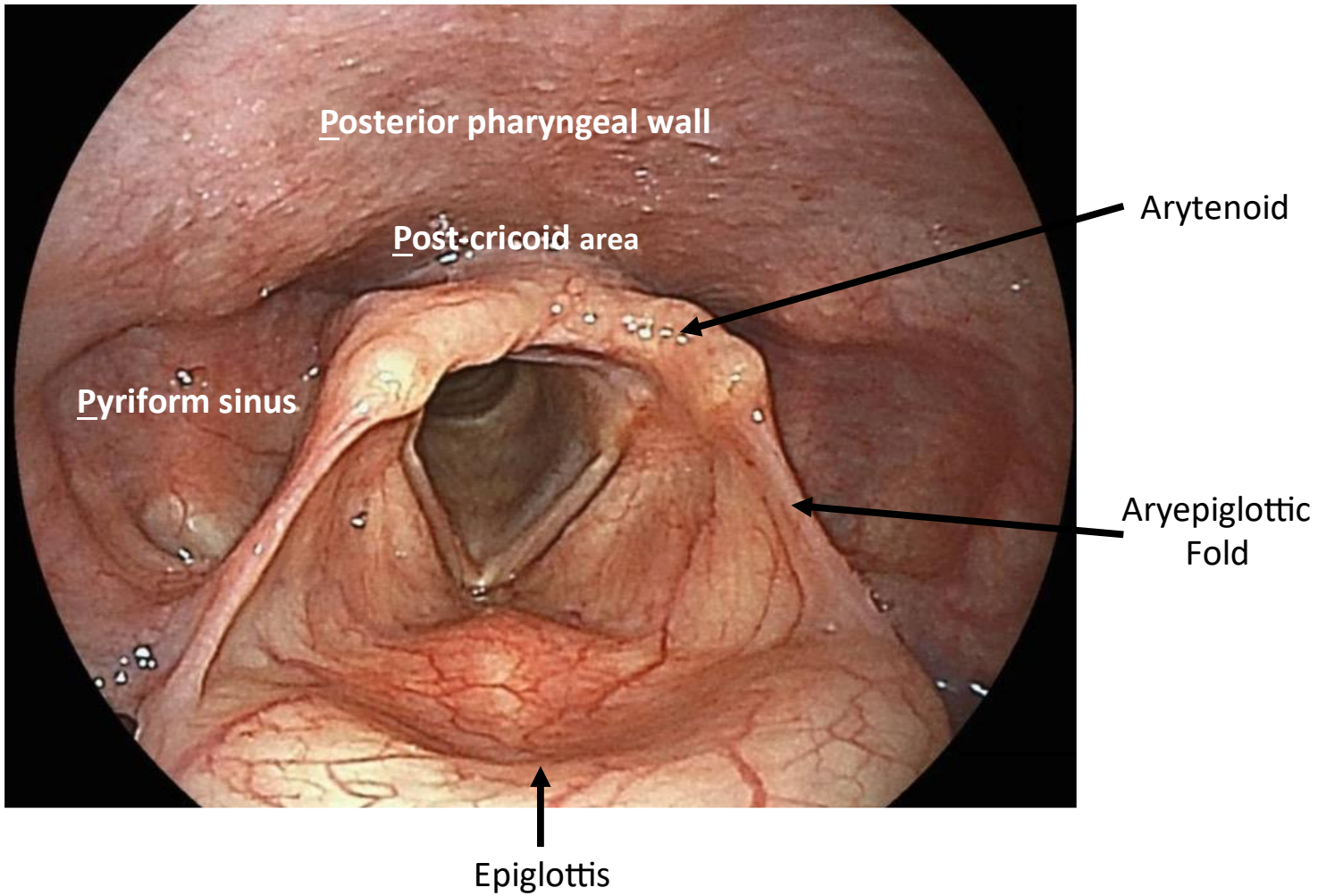
- Underwent panendoscopy and prophylactic tracheostomy. No additional lesions visualized.
- Biopsy of the mass showed poorly differentiated squamous cell carcinoma.
- After multi-disciplinary discussion at tumor board and reviewing treatment options with patient, plan to proceed with larynx preservation with definitive chemoRT with concurrent cisplatin.

Background

- Hypopharynx is located between the oropharynx and esophageal inlet.
- Substructures include (3 P's):
  - Pyriform sinus
  - Post cricoid
  - Posterior pharyngeal wall
- Distinct from larynx cancers with worse prognosis.
- ~3000 cases per year in the US

Presentation

- Piriform sinus (70%), posterior pharyngeal wall (25%), post-cricoid region (5%)
- Most commonly squamous cell carcinoma (95%), other histologies include adenoma, sarcoma, and lymphoma.
- Symptoms: Sensation of lump or discomfort in the throat, odynophagia, dysphagia, referred ear pain, voice hoarseness, pooling of secretions.
- 70% presents with LN involvement.


Posterior pharyngeal wall
Post-cricoid area
Pyriform sinus
Arytenoid
Aryepiglottic Fold
Epiglottis

Work-Up

- H&P with complete HN and fiberoptic exam
- Biopsy of primary site vs. FNA of neck
- CT w/ con +/- MRI w/ con of the neck
- EUA with panendoscopy
- CT chest, PET/CT for metastatic work-up
- Refer to dental, nutrition, speech therapy
- Multidisciplinary discussion

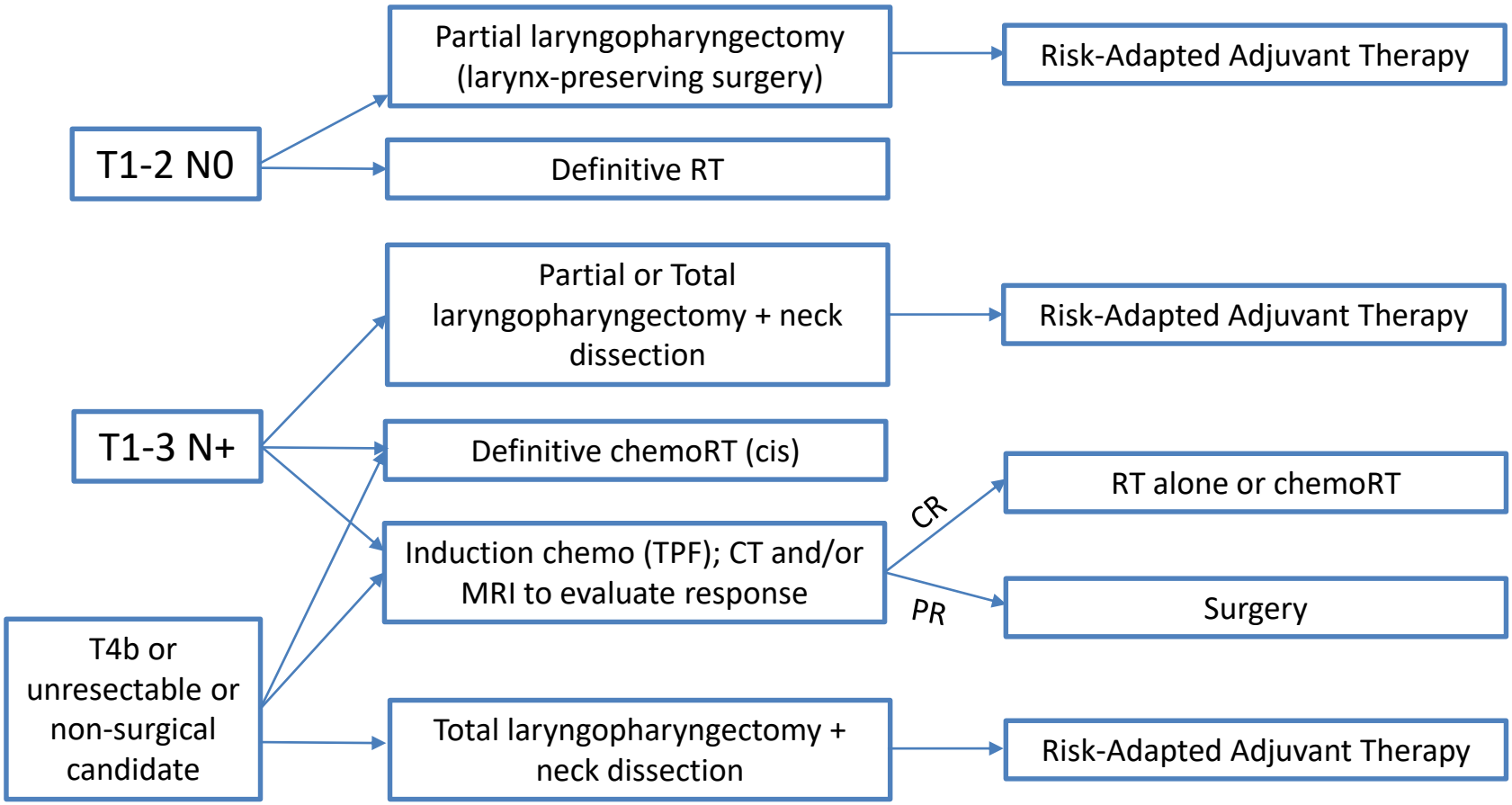
AJCC/UICC 8th Edition Staging

T1	Tumor limited to 1 HPX subsite and/or ≤2 cm
T2	Tumor invades >1 HPX subsite or adjacent subsite, or >2 cm but ≤4cm. No fixation of the hemilarynx
T3	Tumor >4 cm or with fixation of the hemilarynx or extension to esophageal mucosa
T4a	Moderately advanced local disease. Tumor invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, esophageal muscle, or central compartment soft tissue (prelaryngeal strap muscles, subcutaneous fat)
T4b	Very advanced local disease. Tumor invades prevertebral fascia, encases carotid artery, or involves mediastinal structures

N0	No regional LN involvement
N1	Single ipsi LN, ≤3 cm
N2a	Single ipsi LN, >3 cm and ≤6 cm
N2b	Multiple ipsi LN, ≤6 cm
N2c	Bilateral LN, ≤6 cm
N3a	Single or multiple LN, > 6 cm
N3b	Extranodal Extension

T	N	M	Group Stage
T1	N0	M0	I
T2	N0	M0	II
T3	N0	M0	III
T1, T2, T3	N1	M0	III
T4a	N0, N1	M0	IVA
T1, T2, T3, T4a	N2	M0	IVA
Any T	N3	M0	IVB
T4b	Any N	M0	IVB
Any T	Any N	M1	IVC

Management


T1-2 N0
Partial laryngopharyngectomy (larynx-preserving surgery)
Definitive RT
Risk-Adapted Adjuvant Therapy
T1-3 N+
Partial or Total laryngopharyngectomy + neck dissection
Definitive chemoRT (cis)
Induction chemo (TPF); CT and/or MRI to evaluate response
CR
PR
RT alone or chemoRT
Surgery
Risk-Adapted Adjuvant Therapy
T4b or unresectable or non-surgical candidate
Total laryngopharyngectomy + neck dissection
Risk-Adapted Adjuvant Therapy

Laryngeal preservation with induction chemotherapy for hypopharyngeal squamous cell carcinoma: 10-year results of EORTC trial 24891

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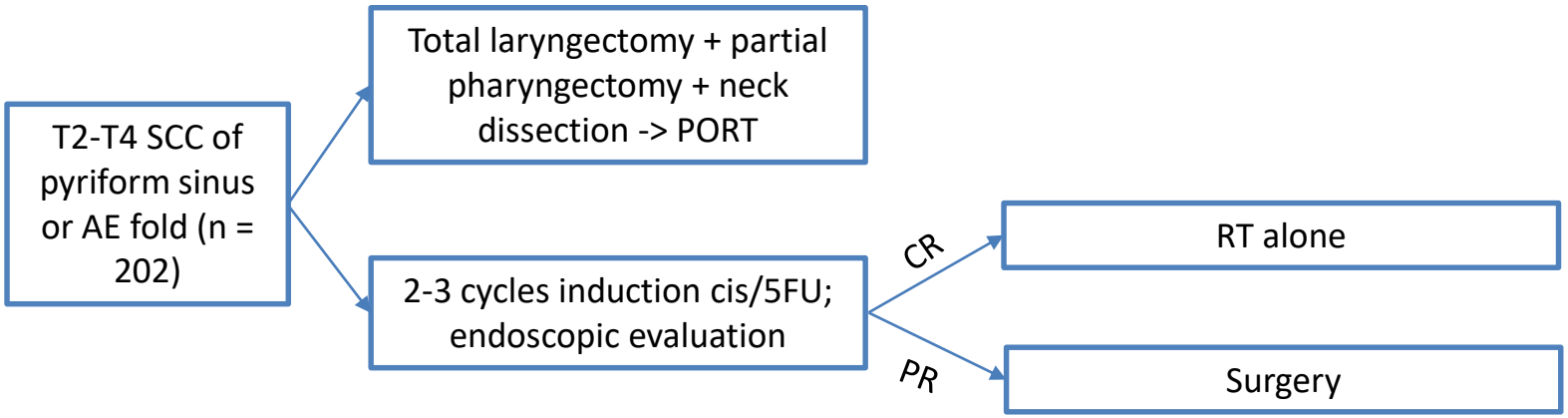
Received 24 June 2011; revised 7 December 2011; accepted 8 February 2012

- Randomized, phase III, non-inferiority study
- Endpoint: Overall survival



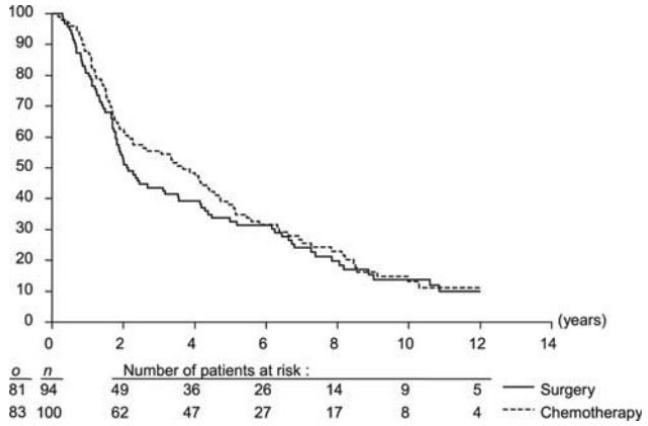


Figure 3. Overall survival. *o* is the number of events; *n* is the number of patients.

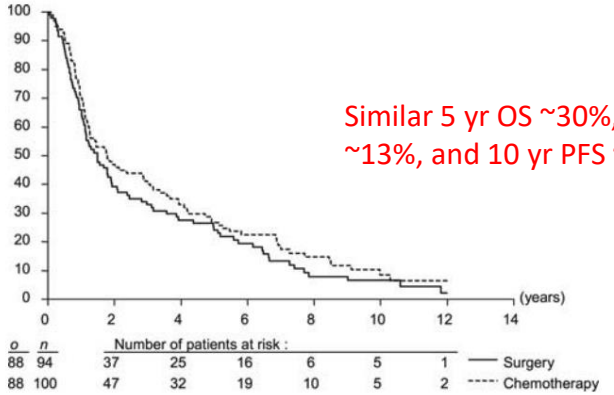


Figure 4. Progression-free survival (time to locoregional or distant recurrence, second cancer or death of any cause). *o* is the number of events; *n* is the number of patients.

Similar 5 yr OS ~30%, 10 yr OS ~13%, and 10 yr PFS ~8-10%

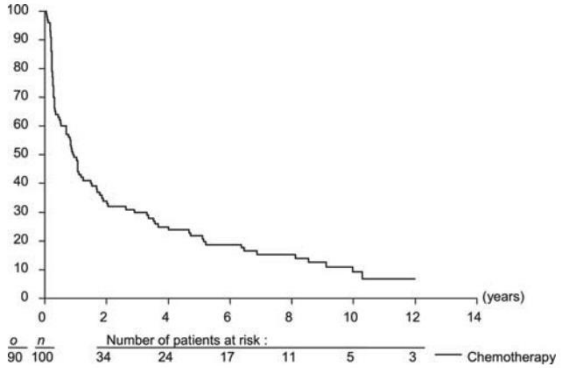


Figure 5. Larynx preservation [survival with preserved larynx; i.e. without local evolution or tracheotomy or feeding tube (i.e. larynx function preservation and local control)]. *o* is the number of events; *n* is the number of patients.

5 yr survival with functional larynx (SFL) ~22%, 10 yr SFL ~9%

Conclusion: ~2/3 of survivors with functional larynx after induction chemo + RT. Worse OS compared to larynx cancer.

Organ Preservation Studies

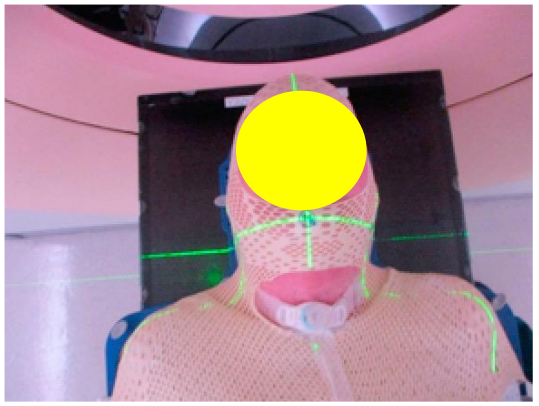
Table 1
Hypopharyngeal cancer organ preservation trial summary. IC: induction chemotherapy, RT: radiation therapy, S: surgery, IC: induction chemotherapy, TPF: docetaxel, cisplatin, and 5-FU, IC/RT: induction chemotherapy alternating with radiation therapy, CRT: chemoradiotherapy, P-RT: cisplatin with radiotherapy.

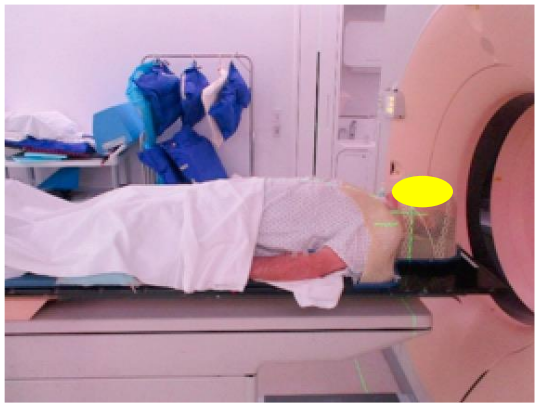
Trial	No. of patients	Anatomic subsite	Stage	Treatment arms	Larynx preservation rate	Follow up period	Overall survival
EORTC 24,891	202	Hypopharynx	Stage II-IV	IC → RT vs. S → RT	22% and 9% (survival with a functional larynx)	5 and 10 years	38% (5 yr) 13.1% (10 yr)
GORTEC 2000–01	213	Larynx and hypopharynx	Stage III and IV	IC → RT vs. TPF → RT	57% vs. 70%	3 years	60% vs. 60%
EORTC 24,954	450	Larynx and hypopharynx	Stage III and IV	IC → RT vs. Alternating IC/RT	48% vs. 52% (5 yr) 19% vs. 18% (10 yr)	5 and 10 years	53% vs. 60% (5 yr) 34% vs. 32% (10 yr)
TAX324	166	Larynx and hypopharynx	Stage III and IV	IC → CRT vs. TPF → CRT	32% vs. 52%	3 years	40% vs. 57%
Prades et al.	71	Piriform Sinus (T3N0M0)	Stage III-IV	IC → S or RT vs. P-RT	71% vs. 92% (1 yr) 68% vs. 92% (2 yr)	1 and 2 years	71% vs. 76% (1 yr) 47% vs. 51% (2 yr)
TREMPLIN	153	Larynx and hypopharynx	Stage III-IV	TPF → CRT vs. TPF → cetuximab + RT	93% vs 96%	3 months	85% vs. 86%
Steiner et al	172	Hypopharynx	Stage I-IVa	TLM Surgical Excision	99%	5 year	Stage I-II: 68% Stage III:64% Stage IVa: 41%

Garneau et al. *Oral Oncology 2018*

CT simulation

- CT simulation with 2 mm slice thickness
- IV contrast
- Custom mouthguard/TruGuard
- S/I borders: Top of skull to the carina
- Immobilization with thermoplastic HN mask
- Tape tracheostomy down with collar strip removed
- Neck extended to pull oral cavity/mandible out of field
- Shoulders down, arms at side





Contouring Pearls

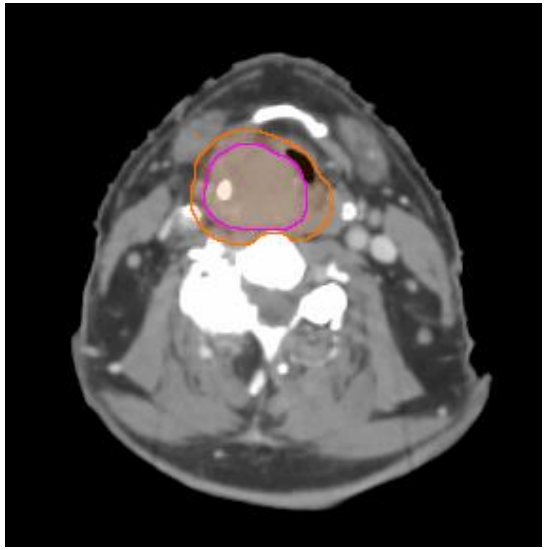
- **Dose:** 70 Gy/60-63 Gy/56 Gy SIB in 35 fx
  - ≤2 Gy per fx to minimize late toxicity risk
  - IMRT Preferred (Mok et al. *Head Neck 2015*)
- **CTV70**: GTV + 5 mm
- **CTV60-63**:
  - GTV + 10 mm; consider 15 mm S/I expansion for sub-mucosal spread (Ho et al. *Head Neck 1993*)
  - Bilateral level II-IV, RP LNs (1st echelon)
  - Ipsilateral IB, V, high level II LNs
  - Include entire HPX subsite involved, adjacent superior/inferior structures, entire larynx (hyoid to cricoid), pre-epiglottic fat, and prevertebral fascia
- **CTV56**:
  - Low risk LNs and contralateral 1st echelon if uninvolved
  - Include VI LNs if pyriform sinus apex involved, advanced stage, post-cricoid primary, or N+ neck

Case: Contours

- **Dose:** 70 Gy/63 Gy/56 Gy SIB in 35 fx
- **CTV70**: GTVp + 5 mm, GTVn + 5 mm
- **CTV63**:
  - GTV + 1 cm
  - ipsilateral level 1B LNs
  - bilateral level 2-4 and RP LNs
  - ipsilateral level 5 LNs
- **CTV56**:
  - Encompasses CTV63
  - Ipsilateral high level 2 LNs
  - Level VI LNs

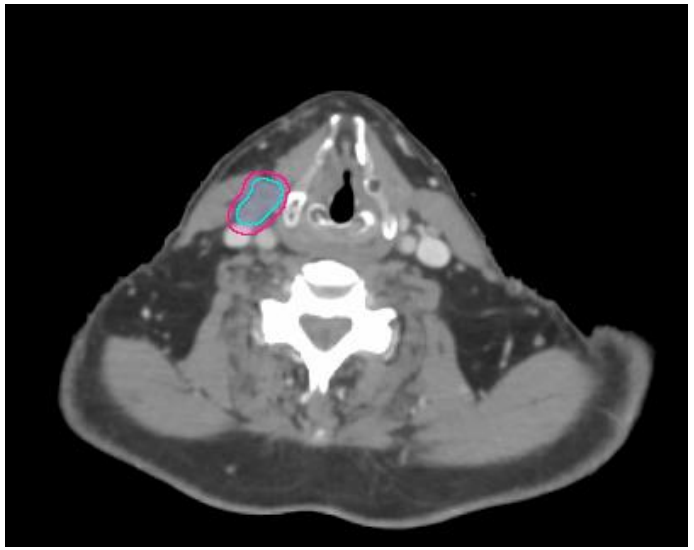
GTVp

CTVp = GTVp + 5mm

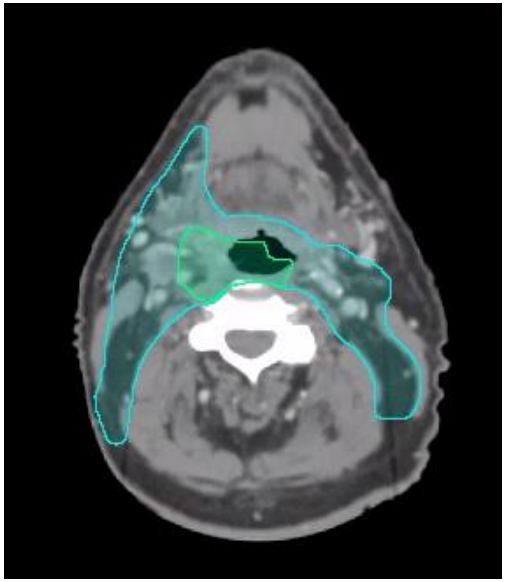


GTVn

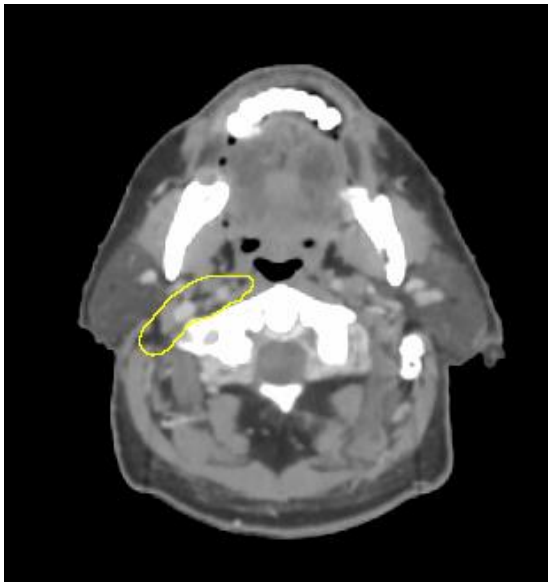
CTVn = GTVn + 5mm



Medium risk CTV
includes **GTV + 1 cm**



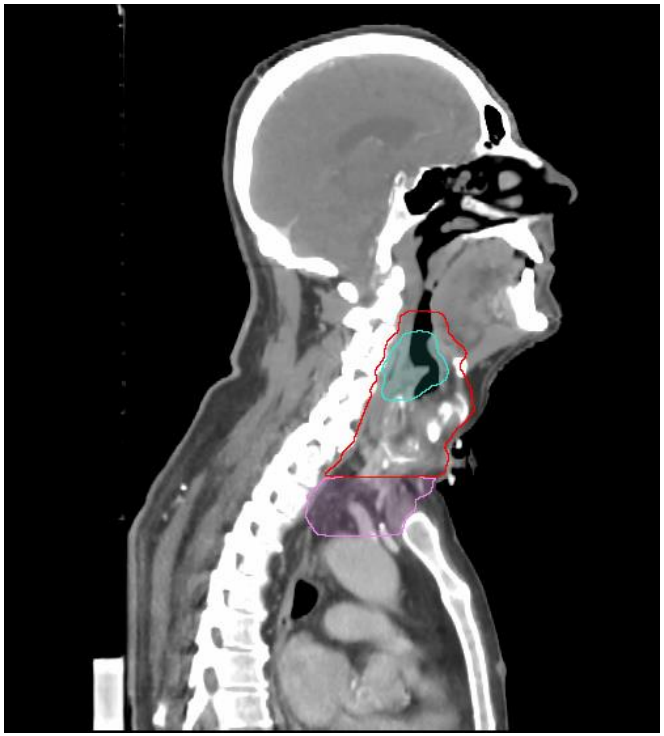
Asymmetric coverage of ipsilateral high level 2 lymph nodes in **low risk CTV**

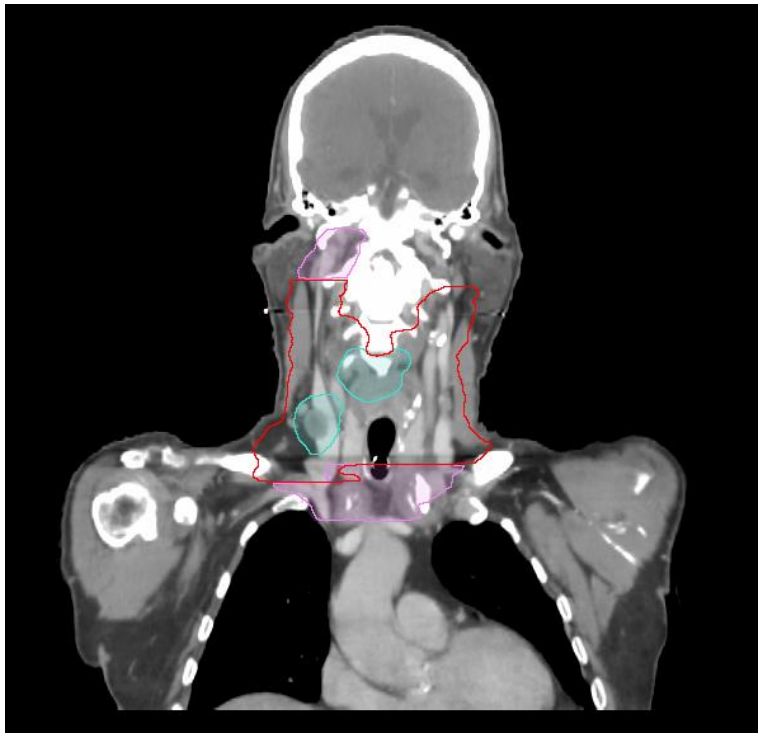


PTV high

PTV medium

PTV low

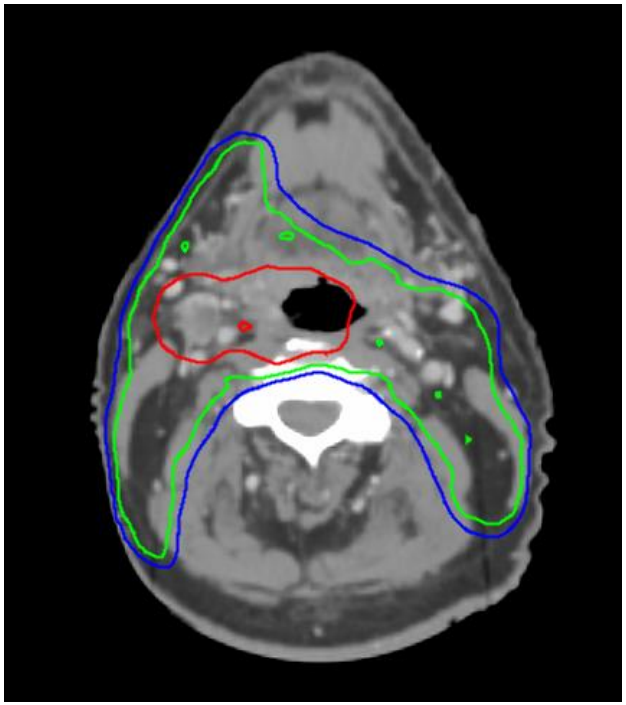


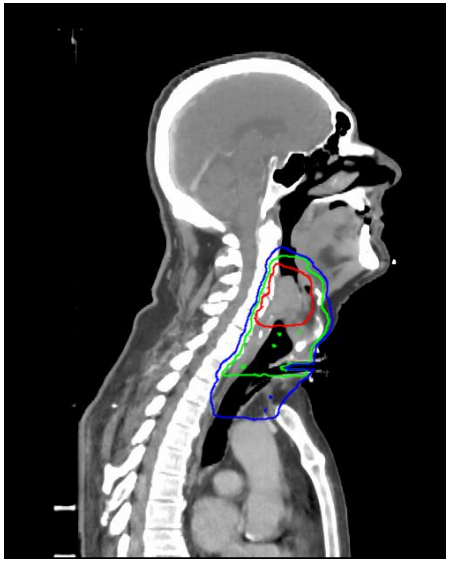


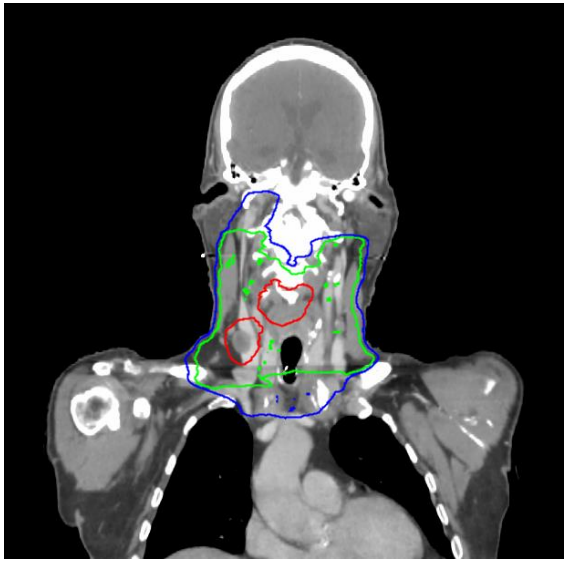
100% isodose line

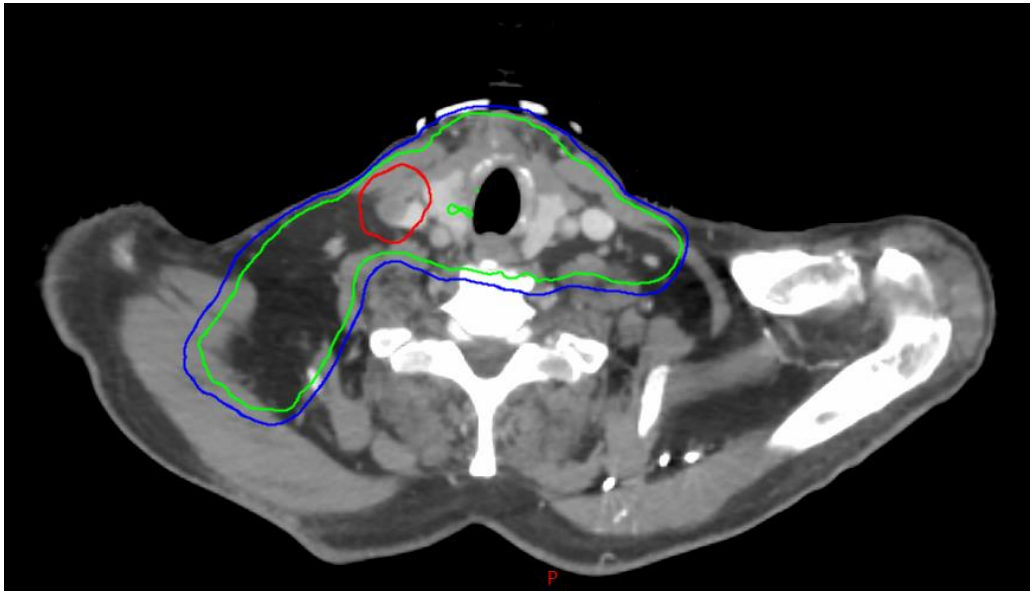
90% isodose line

80% isodose line



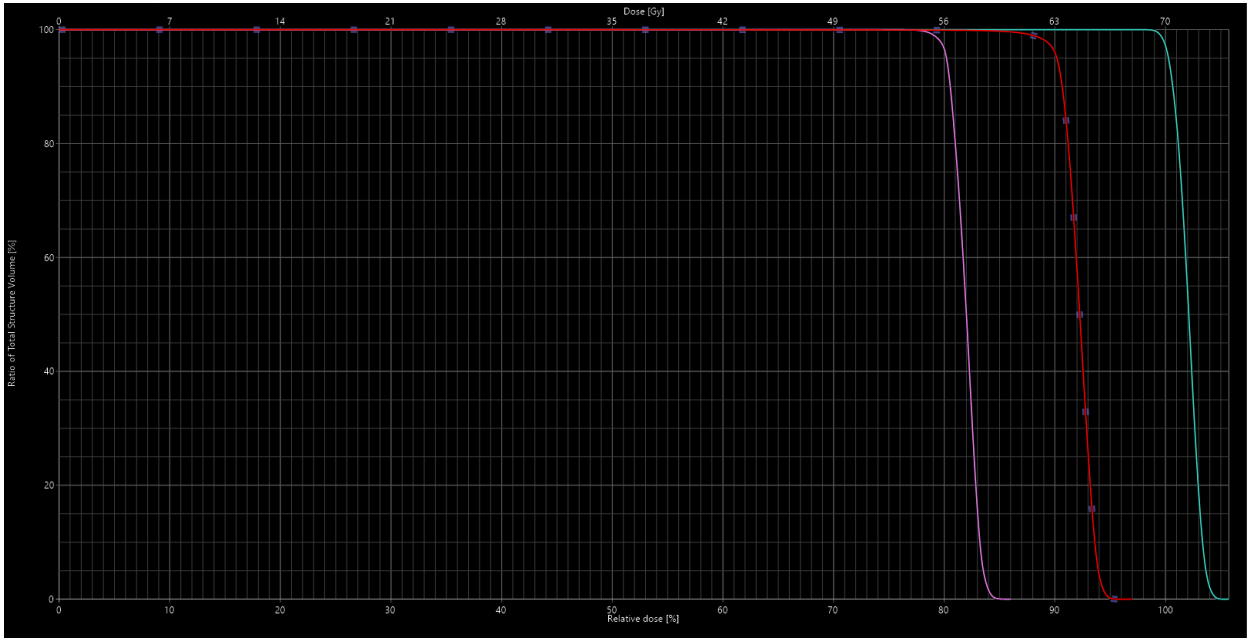






Dose Volume Histogram

PTV high
PTV medium
PTV low



Common HN OAR Constraints

Brain/Brainstem/Optic Nerve	Max <54 Gy
Brachial Plexus	Max <66 Gy
Cochlea	Mean ≤35 Gy
Esophagus	Mean <34 Gy
Eye	Max <50 Gy
Lens	Max <10 Gy
Larynx	Mean <35-40 Gy
Mandible	Max <70 Gy
Oral Cavity	Mean <40 Gy
Parotid Gland	Mean <26 Gy
Pharynx	Mean <50-55 Gy
Submandibular Gland	Mean <39 Gy

Follow-up

- PET/CT 3-6 mo after definitive RT/chemoRT
- H&P with complete HN exam and fiberoptic exam
  - Year 1: every 1-3 mo
  - Year 2: every 2-6 mo
  - Year 3-5: every 4-8 mo
  - >5 yrs: every 12 mo
- TSH every 6-12 mo after neck RT
- As indicated: Speech therapy, nutritional evaluation, depression surveillance, smoking cessation, alcohol counseling, lymphedema evaluation, dental evaluation, carotid stenosis evaluation.

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