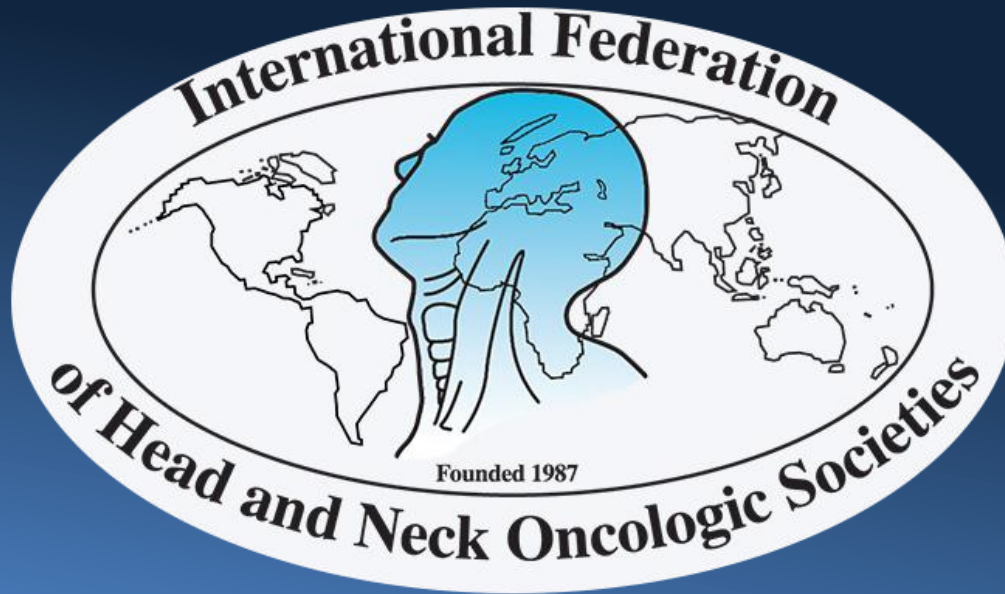




The International Federation of Head and Neck Oncologic Societies

Current Concepts in Head and Neck Surgery and Oncology 2018



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Larynx Preservation - Non surgical-radiation therapy

Sandro V Porceddu

Director, Radiation Oncology Research
Princess Alexandra Hospital, Brisbane, Australia
Professor of Medicine, University of Queensland

What do these animals have in common with the human larynx?



descended larynx for vocalisation

Laryngeal Cancer

- Billroth performed the first laryngectomy in 1873
- Röntgen discovered x-rays 1895 & Pierre and Marie Curie discovered radium in 1898
- Between 1920-1940 radiation therapy was the treatment of choice for his type of laryngeal cancer

Giacomo Puccini

1858-1924



- In 1924 Puccini diagnosed with laryngeal cancer while working on the opera *Turandot*
- Treated with the Columbia Apparatus – radium needles

Giacomo Puccini

1858-1924

“What an ordeal! God help me. This treatment will last no less than six weeks, it is terrible... I feel as though I have bayonets in my throat!”

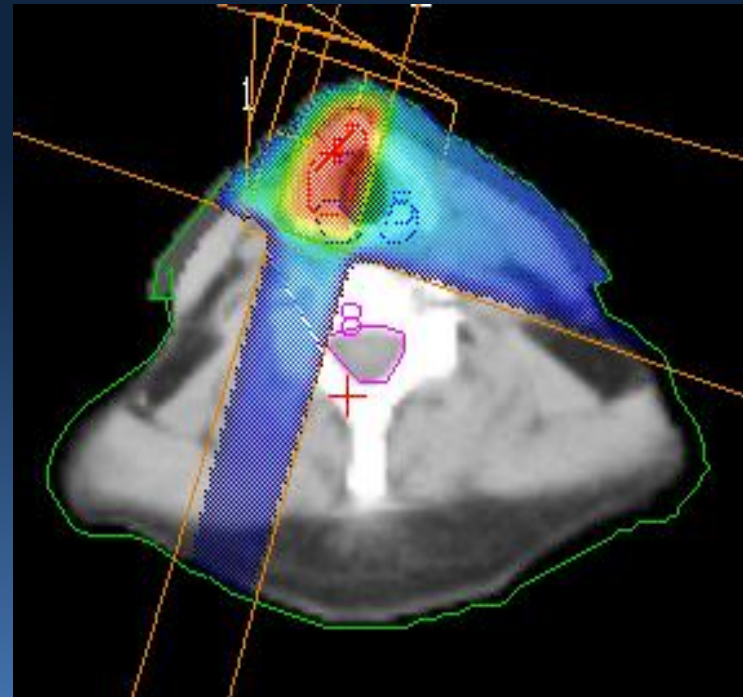
Puccini died shortly after due to myocardial infarct brought on by a massive haemorrhage

External Beam Radiation Therapy

Standard Parallel Opposed



Highly Conformal



DEFINITIVE:

RT Alone

- Tis, N0: 60.75 Gy (2.25 Gy/fraction) to 66 Gy (2.0 Gy/fraction)
- T1, N0: 63 Gy (2.25 Gy/fraction) to 66 Gy (2.0 Gy/fraction)
- T2, N0: 65.25 (2.25 Gy/fraction) to 70 Gy (2.0 Gy/fraction)

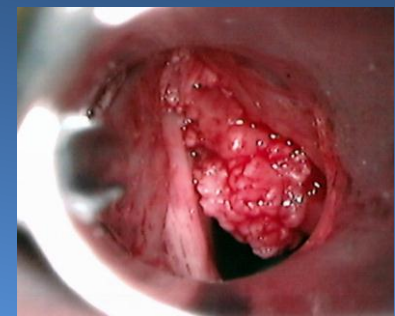
Larynx preservation with radiotherapy

- Early laryngeal cancer
- Locally advanced laryngeal/hypopharyngeal cancer
- Case examples
- Radiotherapy contouring guidelines

EARLY LARYNGEAL CANCER

Early Laryngeal Cancer

- Spectrum of disease
 - T1 & T2
- Favourable disease
 - T2 glottis with extension onto supra- or subglottis, superficial & normal cord mobility
- Unfavourable disease
 - T2 glottis with deep extension and/or impaired mobility



Larynx Preservation Options

- Radiation Therapy
- Endoscopic Surgery
 - Trans Oral Laser microsurgery (TOLMS)
 - Trans Oral Robotic Surgery (TORS)
- Open partial laryngectomy

Early Laryngeal Cancer

		Radiotherapy		Transoral Excision
5yr Local Control	T1	85-95%	T1	83-93%
	T2	68-80%	T2	73-89%
5 yr DSS	T1	93-98%	T1	96-99%
	T2	70-88%	T2	83-97%

Voice Quality Outcome

- Systematic review of functional outcome TOLM & RT
- 880pts; 448 TOLM, 442 RT
- Vocal outcomes (subjective analysis); 12 studies no difference, 3 superior RT
- Voice disability (patient perception); 5 studies no difference, 3 conflicting results
- Lack of uniformity of assessment of voice quality
- Neither modality clearly superior

Voice Quality Outcome

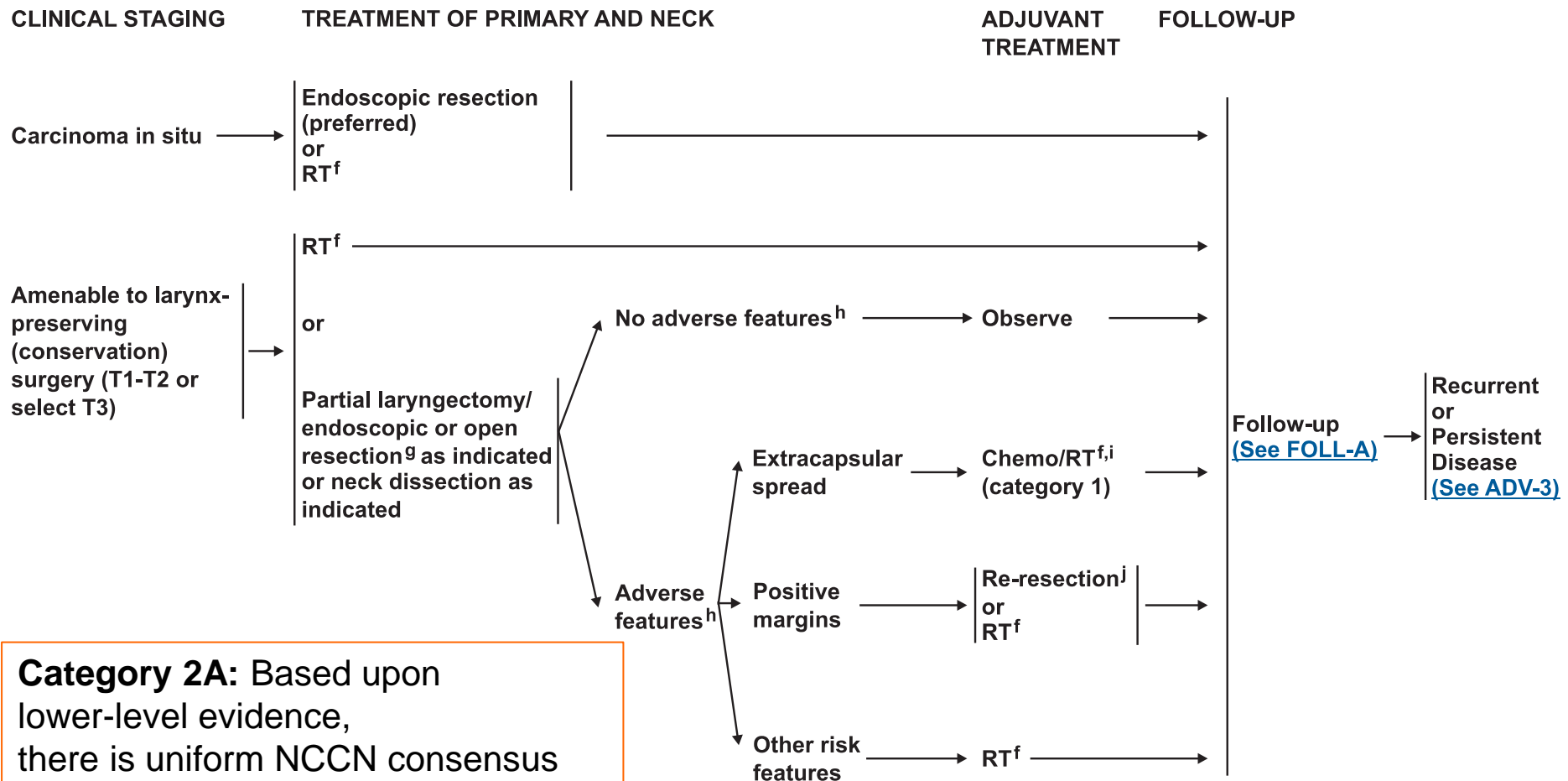
- Meta-analysis Voice Handicap Index (VHI) after treatment for T1 Glottic cancer with either RT or Laser (Laser=208, RT=91)
- No difference in VHI
- Regardless of treatment modality voice quality is dependant on initial disease extent and amount of tissue removed

Is RT obsolete in early glottic larynx cancer?

- Given the comparable outcomes
 - Cure rates
 - Voice Quality
- Not accounting for
 - Cost-effectiveness comparisons
 - Patient preference
- Accepting the convenience of endoscopic resection
- Endoscopic resection is the preferred choice

NCCN Guidelines 2018

Glottic cancer



Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate

Is radiation therapy obsolete in early laryngeal cancer?

- Radiotherapy may no longer be the preferred initial choice
 - comparable outcomes both in local control & voice quality
 - relative low morbidity
- RT still has a role in selected cases
 - unfavourable anatomy
 - medically not suitable
 - widespread in-situ changes
 - deeply infiltrative
 - multiply failed laser procedures
 - patient preference

**LOCALLY ADVANCED
LARYNGEAL/HYPOPHARYNGEAL
CANCER**

Surgery/PORT vs chemo-radiotherapy

Guiding Principles in Management

- Functional outcome
 - Is it worth preserving?
 - What is the functional deficit
- Likelihood of clear macroscopic/microscopic margins
- Expected control rates & toxicities
- Aim to use the least number of modalities to obtain the required clinical outcome
- Biological characteristics of the tumour
 - chemo-responsive (to neoadjuvant)
 - recurrent disease

Larynx Preservation

- Early larynx preservation studies
 - VA study NEJM 1991
 - EORTC (*Lefebvre JL et al*) JNCI 1996
- Induction chemotherapy (Cisplatin/5FU)
 - Responders had definitive RT
 - Non-responders had surgery/PORT
- Larynx preservation rate 66% at 2 years
- No measure of functional outcomes
- No difference in survival

RTOG 91-11

Eligibility

- Stage III-IV SCC glottic or supraglottic larynx
- Surgical treatment would require total laryngectomy
- T1 excluded
- Large-volume T4 disease defined as a tumor penetrating through the cartilage or extending more than 1 cm into the base of the tongue were excluded

Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer

RTOG 91-11

3-arm randomised study (n=547)

Induction cisplatin/5FU
concurrent ChemoRT*
88%

2 year intact larynx

PR/RT → 75%

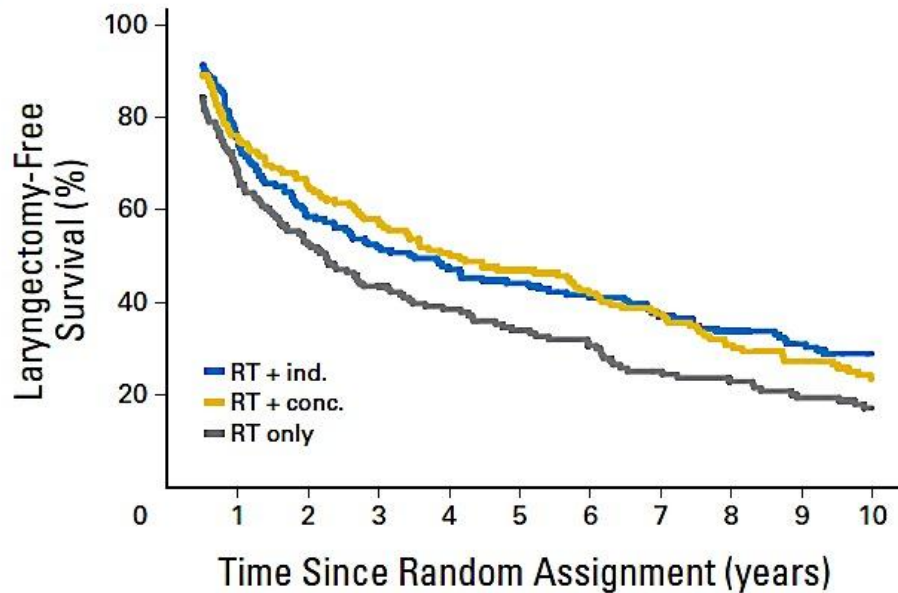
RT alone
70%

- *cisplatin 100mg/m² weeks 1, 4 & 7
- 70Gy over 7 weeks to gross disease

Overall survival no difference

RTOG 91-11 10-year follow up

Primary Endpoint LFS

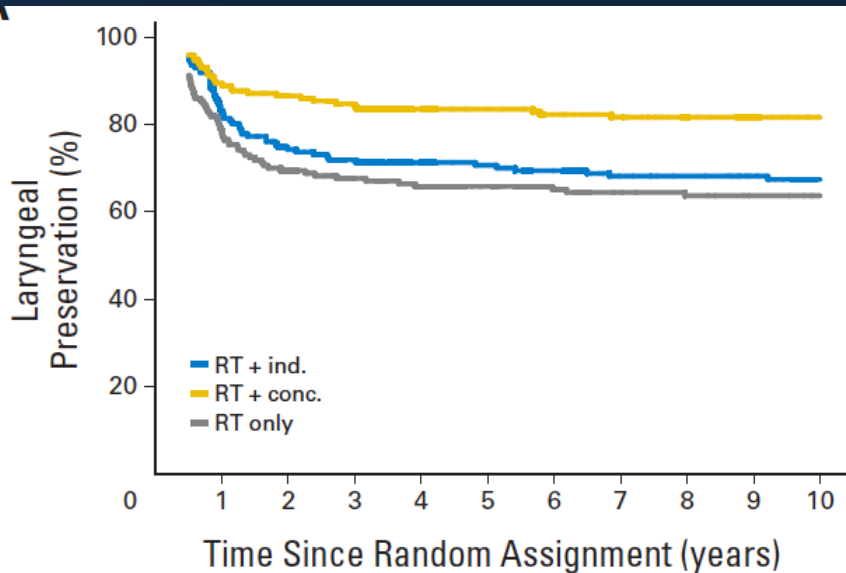


No. at risk	0	1	2	3	4	5	6	7	8	9	10
RT + ind.	174	130	98	87	78	72	65	56	51	44	37
RT + conc.	174	130	111	96	83	76	67	58	45	38	30
RT only	172	116	88	70	62	52	46	35	32	27	24

	10 yr LFS	p-value
RT + ICT	28.9	p=0.02
RT + cCT	23.5	p=0.03
RT	17.2	

RTOG 91-11 10-year follow up

Larynx preservation (LP)



No. at risk	0	1	2	3	4	5	6	7	8	9	10
RT + ind.	174	130	98	87	78	72	65	56	51	44	37
RT + conc.	174	130	111	96	83	76	67	58	45	38	30
RT only	172	116	88	70	62	52	46	35	32	27	24

	10 yr LP	p-value
RT + ICT	67.5	
RT + cCT	81.7	p=0.02
RT	63.8	p<0.001

- No difference in survival
- No difference in late effects
- Deaths not attributed to larynx cancer or treatment were higher in the concomitant arm

Functional outcome

- Alive, disease free, retained larynx, over 2-5yrs

	RT - ICT	RT - cCT	RT
Impaired speech/voice quality	3-9%	4-8.5%	5-8.5%
Soft foods only	13-14%	17-24%	10-17%
Liquids only	<4%	<4%	<4%
Inability to swallow	<3%	<3%	<3%

*no substantive differences in quality of function, but limited numbers

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A S C O S P E C I A L A R T I C L E

Use of Larynx-Preservation Strategies in the Treatment of Laryngeal Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update

Arlene A. Forastiere, Nofisat Ismaila, Jan S. Lewin, Cherie Ann Nathan, David J. Adelstein, Avraham Eisbruch, Gail Fass, Susan G. Fisher, Scott A. Laurie, Quynh-Thu Le, Bernard O'Malley, William M. Mendenhall, Snehal Patel, David G. Pfister, Anthony F. Provenzano, Randy Weber, Gregory S. Weinstein, and Gregory T. Wolf

Larynx-preservation guidelines for laryngeal cancer

Larynx-preservation approaches for appropriately selected patients does not compromise survival

No LP approach offers survival advantage vs surgery/PORT

T1-2

Larynx preservation
Endoscopic resection or RT

T3 (non-extensive) and T4

Larynx-preservation surgery,
CRT or RT alone offer potential
LP without survival detriment

T3(extensive) and T4a
& poor pretreatment
laryngeal function

Better survival rates and
QoL may be achieved
with total laryngectomy

Laryngeal/Hypopharyngeal Ca

T3N0 Supraglottic SCC

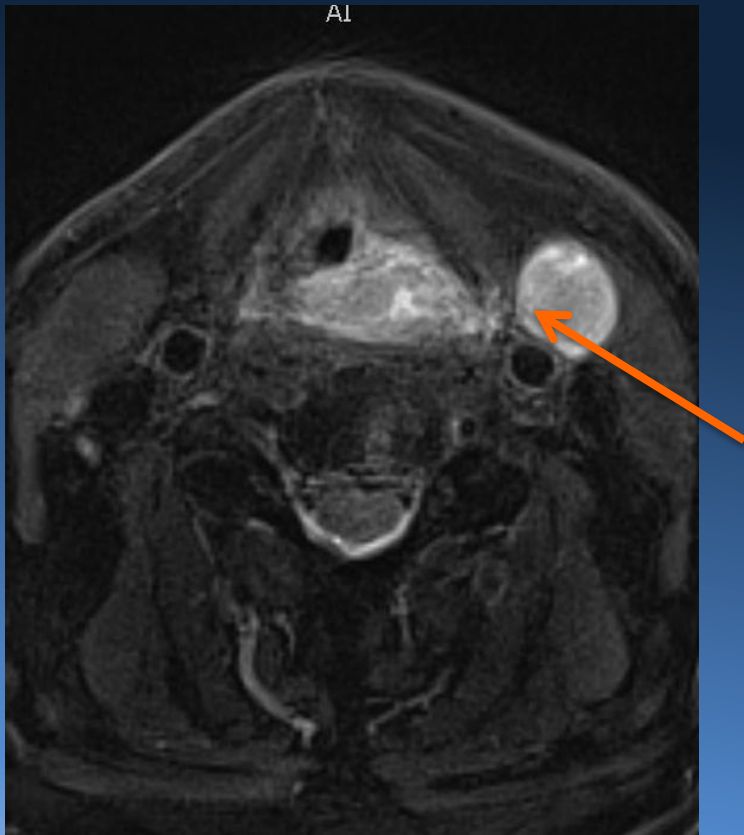


Preservation

- No extension through laryngeal cartilage or into soft tissues
- Swallowing function intact
- At least one cord mobile
- Airway reasonable
- Voice worth preserving
- ECOG ≤ 2
- *Lower threshold for offering CRT for supraglottic ca due to lower rate of long term swallowing issues and greater control rates*

Laryngeal/Hypopharyngeal Ca

T4N2a hypopharyngeal SCC

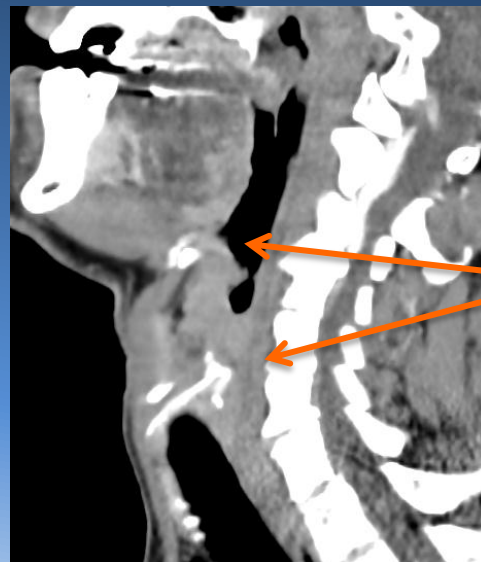


Non-preservation

- Destroyed laryngeal cartilage/structures
- Extension through laryngeal cartilage and/or soft tissues
- Aspirating (Fluid/solids)
- Fixed bilateral cords
- Severe airway compromise
- Marked poor voice quality
- ECOG 3
- *Lower threshold for offering surgery for hypopharyngeal ca due to greater rate of long term swallowing issues and lower control rates*

Induction preservation case

T3N2b Hypopharyngeal SCC



- 46 year old man
- 60 pack years
- Bulky left neck mass
- No airway obstruction
- No dysphagia
- No weight loss
- ECOG 0
- Left level III 4x3cm nodal mass
- Mass involving left piriform sinus extending to base of tongue and immobile left cord

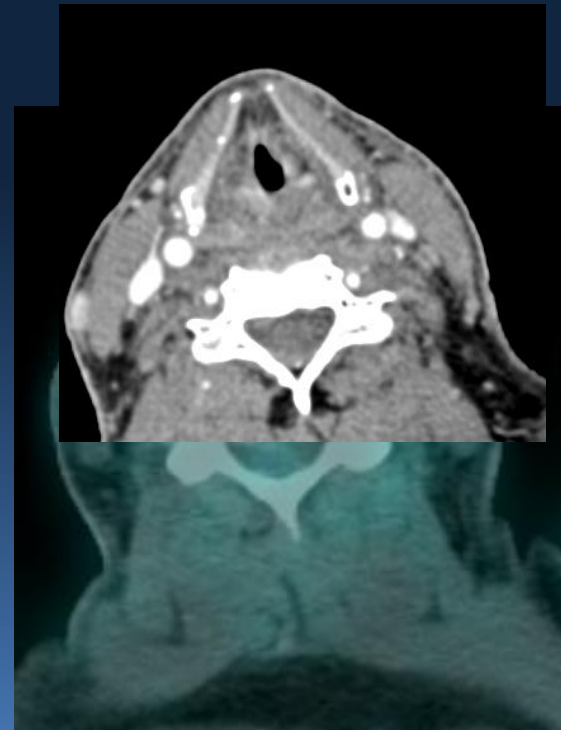
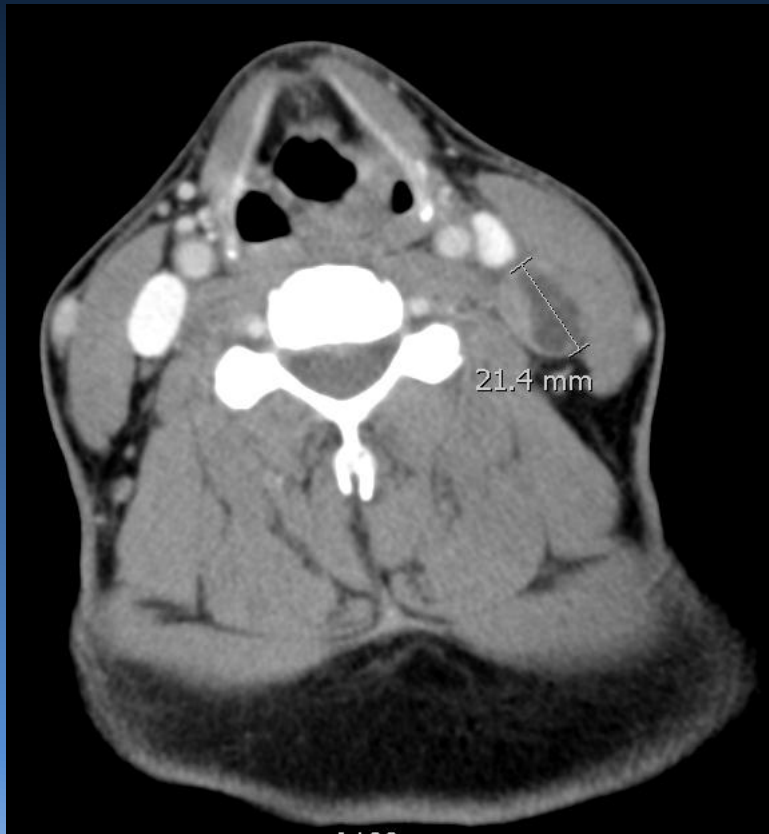
Induction chemotherapy - TPF

- Borderline organ preservation cRT
- High risk nodal N2c/N3

T3N2bM0 Hypopharyngeal SCC

Post x2 cycles of TPF

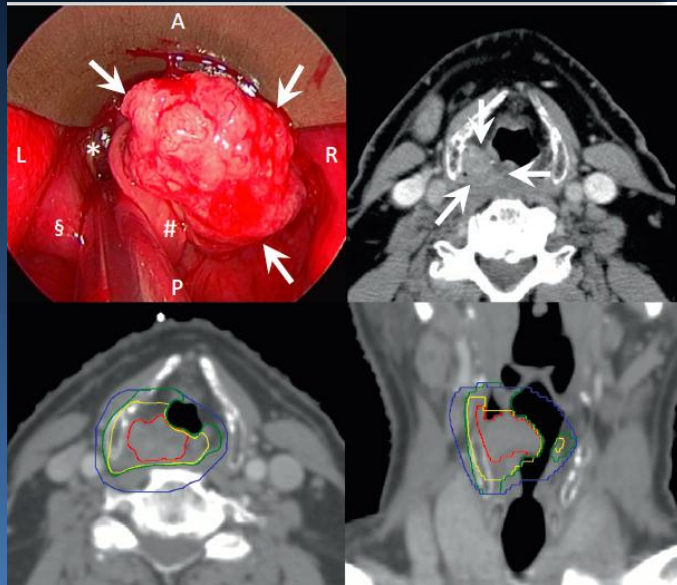
Concurrent HD cisplatin/70Gy



Contouring guidelines

(Gregoire V et al Radiother Oncol 2018)

T2 Right Piriform Sinus Ca



Gross Tumour Volume (GTV)

Blue contour = 10mm isotropic expansion on GTV

Green contour = 10mm isotropic expansion on GTV with cropping = CTV2

Yellow contour = 5mm isotropic expansion on GTV with cropping = CTV1

Primary Tumour CTV =
5mm + 5mm on GTV-p

- CTV1 = 5mm GTV-p
- CTV2 = 5mm + CTV1
- Cropping off anatomic boundaries/air cavities

Concluding remarks

- Radiotherapy still has a role in early laryngeal cancer
- Concomitant radiotherapy is superior to radiotherapy alone in preserving larynx
- Induction chemotherapy has a role in selected cases for larynx-preservation treatment
- Careful selection for larynx preservation based on disease extent and organ function warranted