Management of early laryngeal and hypopharyngeal cancers

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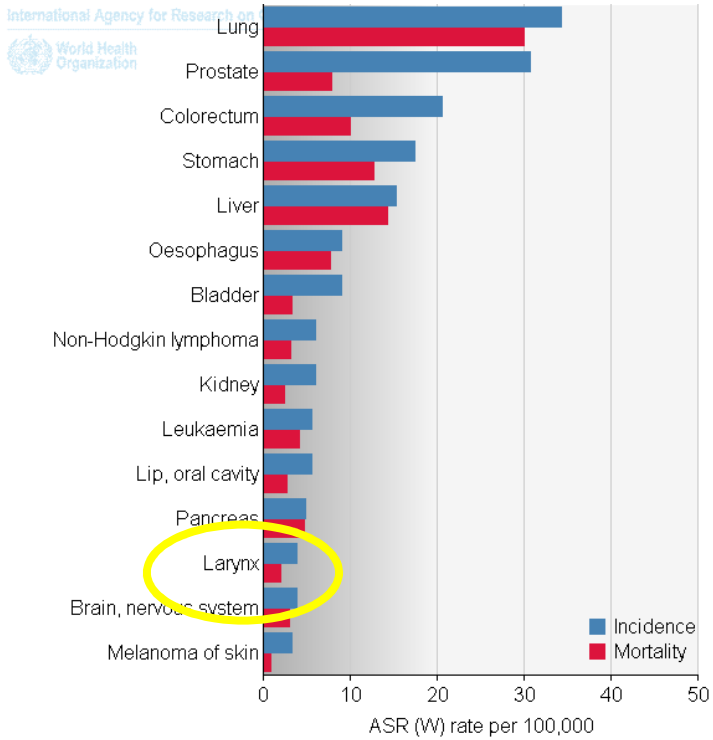
World War 1 History

- 1886 – Crown Prince Frederick, Germany developed Laryngeal cancer.
- Advised Laryngectomy. Refused.
- Died 1888
- Succeeded by Kaiser Wilhelm II, who along with Otto von Bismark – Military rule in Germany.
- Led World war I

Could a Radiation oncologist have prevented World War I?



Globocan, 2012

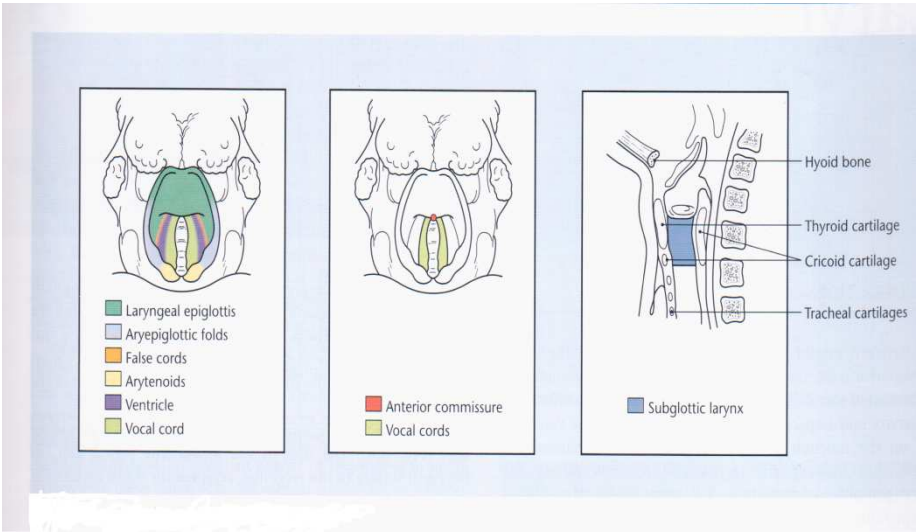
- 11,000 new cases of laryngeal cancer per year in the U.S.
- Accounts for 25% of head and neck cancer and 1% of all cancers
- Most prevalent in the 6^{th} and 7^{th} decades of life
- 4:1 male predilection; Downward trend post WWII
- Due to increasing public acceptance of female smoking

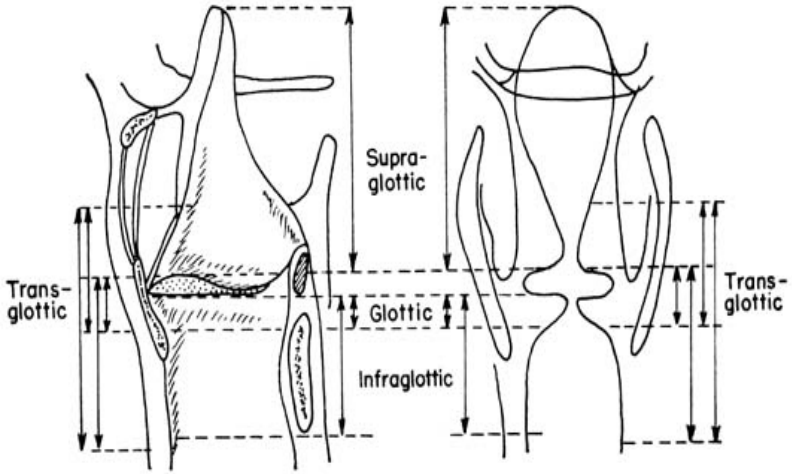
Sub-sites

Supraglottic - Epiglottis
- AE fold
- Arytenoid
- False cords
- Ventricles

Glottic - Vocal cord

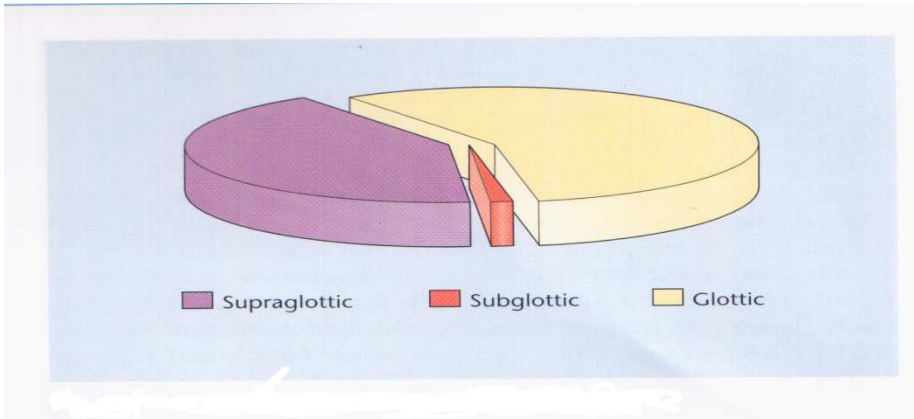
Subglottic





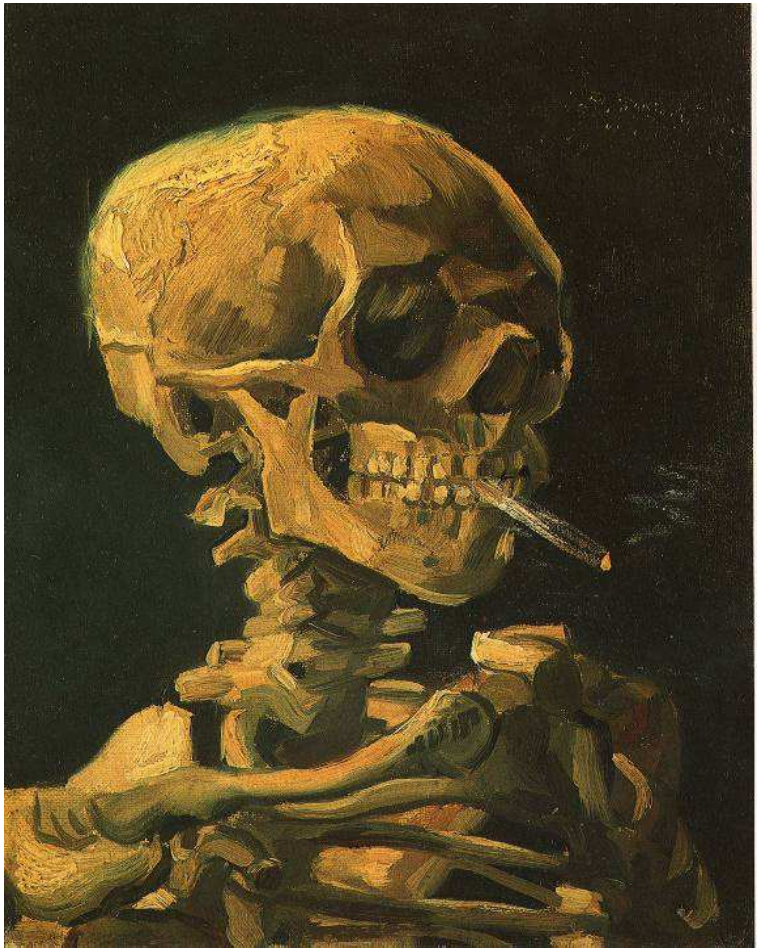
Subtypes

- Glottic Cancer: 59%
- Supraglottic Cancer: 40%
- Subglottic Cancer: 1%



- Most subglottic masses are extension from glottic carcinomas

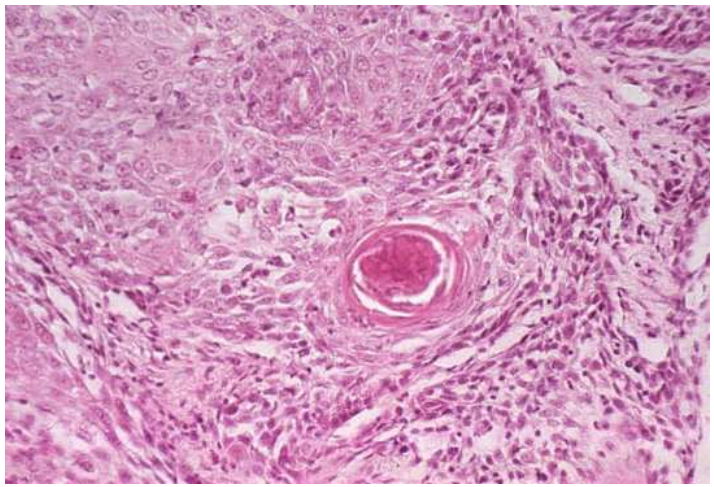
Risk Factors



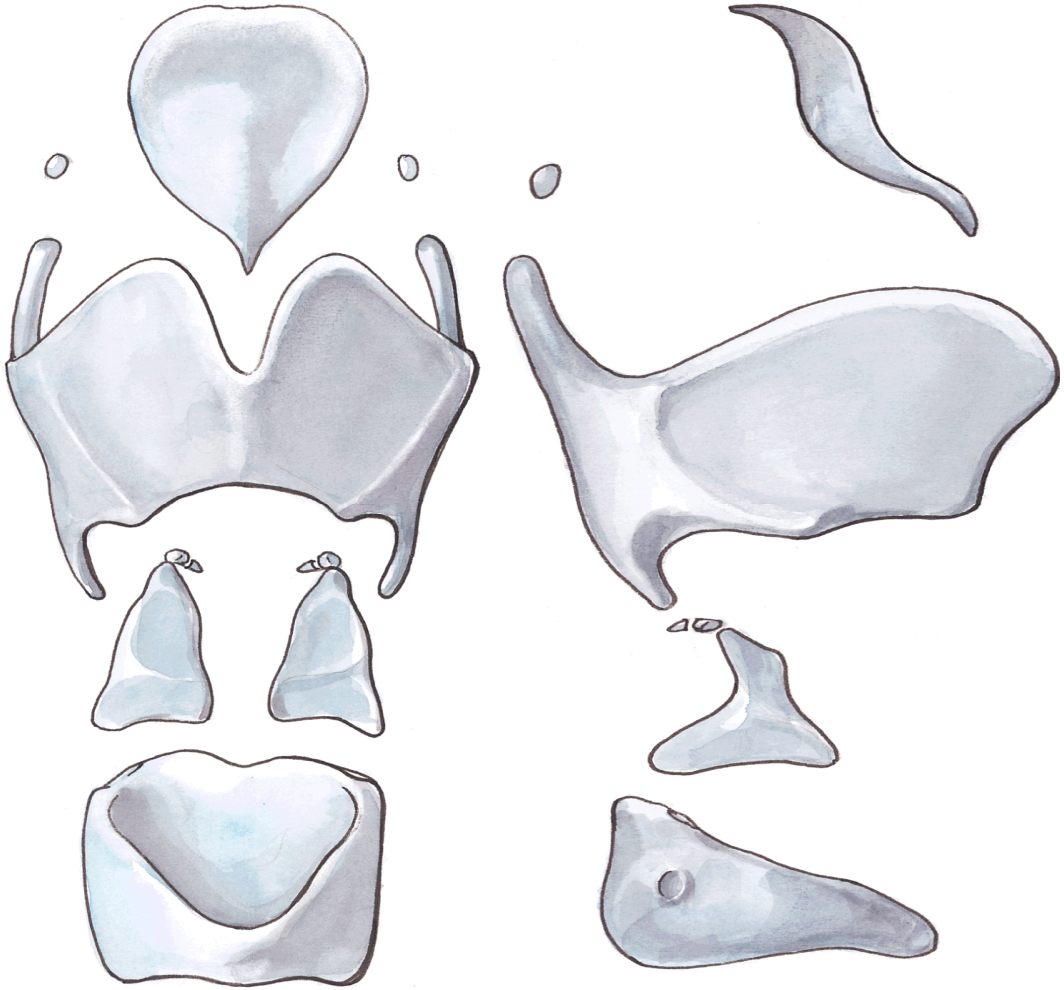
90% of patients with laryngeal cancer have a history of both

Histological Types

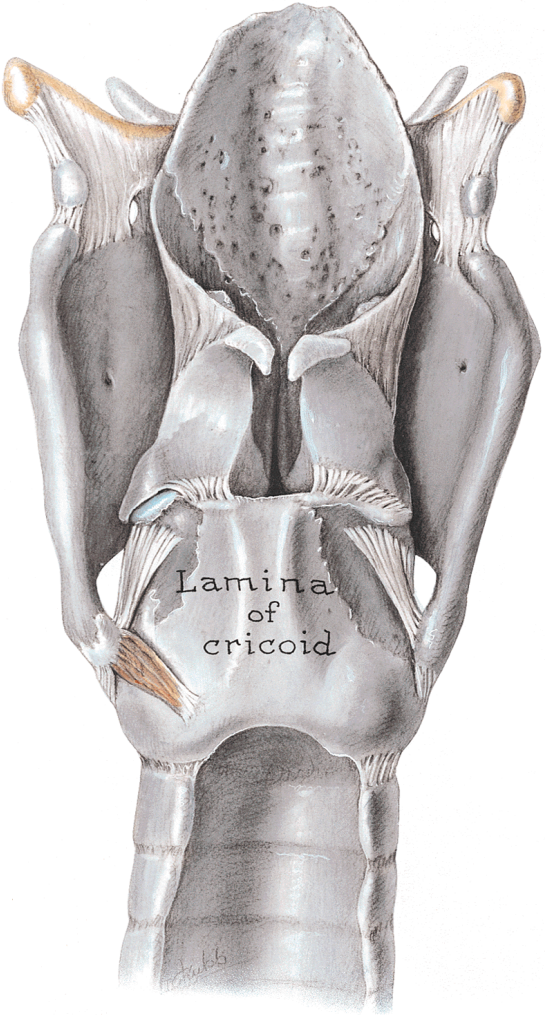
- 85-95% - squamous cell carcinoma
- Histology linked to tobacco and alcohol abuse
- Characterized by epithelial nests surrounded by inflammatory stroma
- Keratin Pearls - pathognomonic

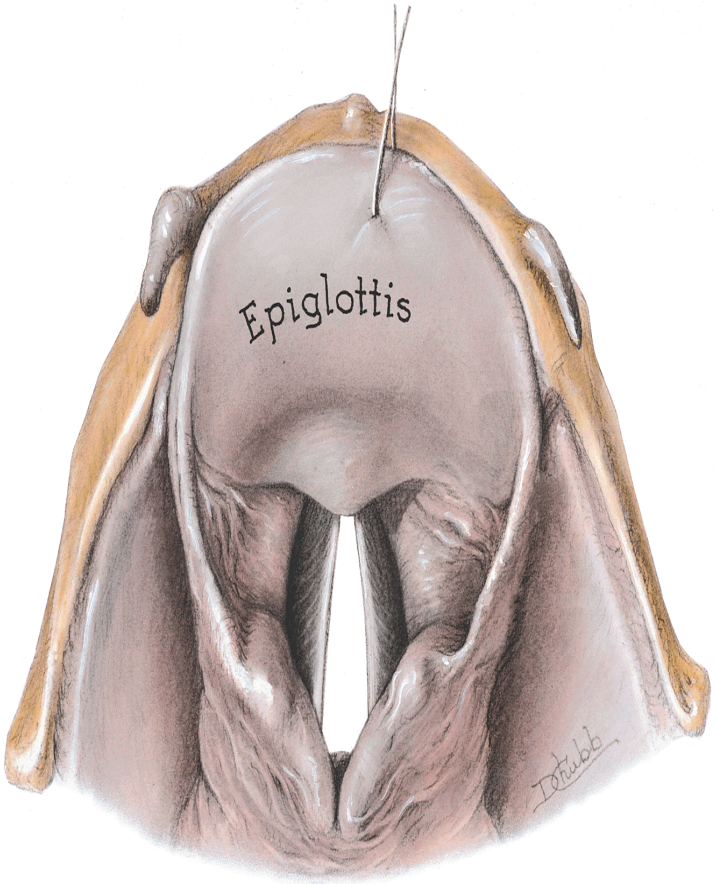


Anatomy

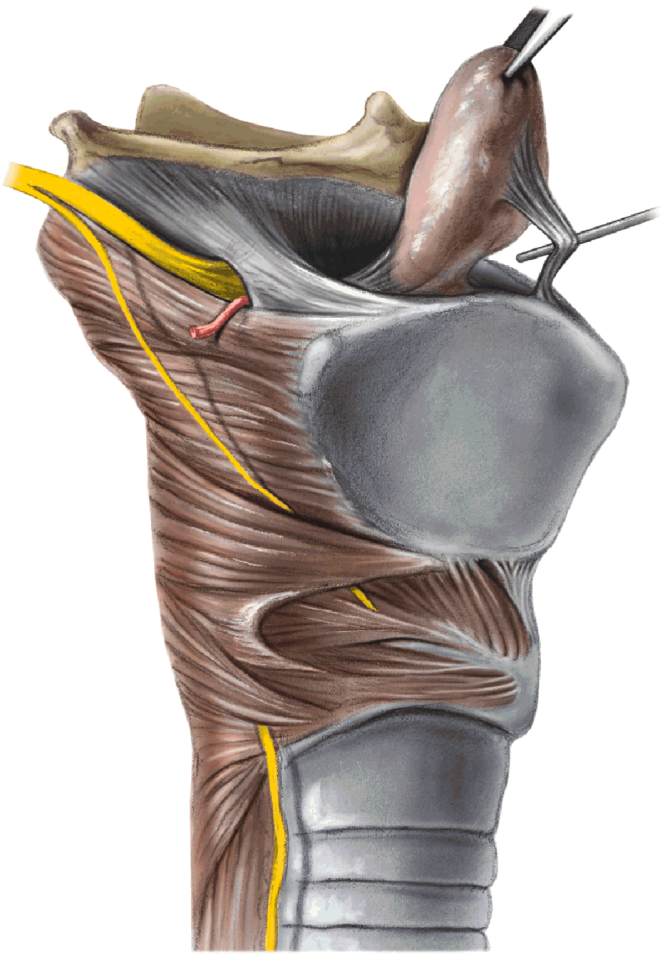


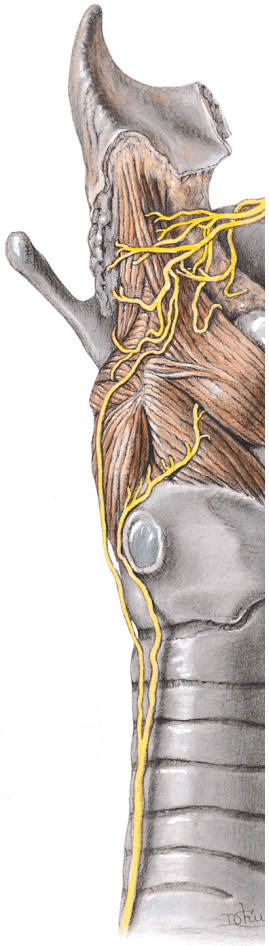
Anatomy

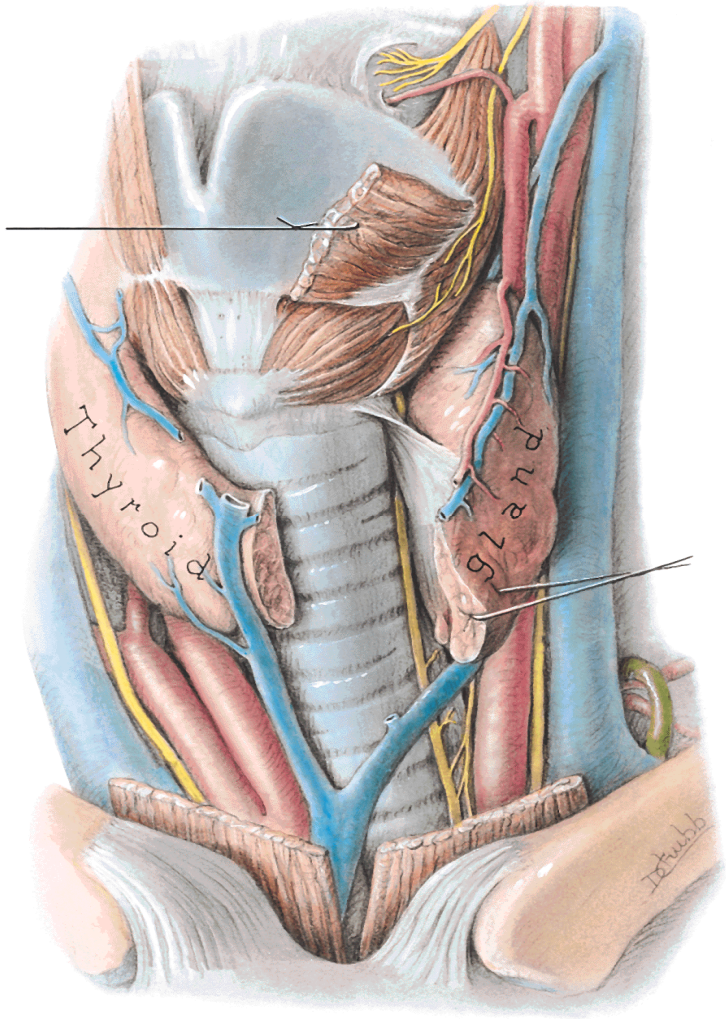




Anatomy







Natural History

- Supraglottic tumors more aggressive:
  - Pre-epiglottic space/ LN/ hypopharnyx, glossoepiglottic fold and tongue base
- Glottic tumors grow slower and metastasize late - paucity of lymphatic drainage
- Metastasize after they have invaded adjacent structures with better drainage
- Subglottic space extension - poor prognosis
- Increases chance of B/L LN & mediastinal extension

Presentation

- Hoarseness
  - Most common symptom
  - Small irregularities in the vocal fold and chronic use of tobacco and alcohol – change in voice

Supraglottic tumors - dysphagia

Methods of determining gross tumor

- Visual inspection
- Palpation
- Endoscopy
- CT scan –axial, sagittal and coronal reconstructs
- T2 MRI
- PET scans

Clinical evaluation

- Indirect mirror exam and/or flexible laryngoscope evaluation
- Videostrobe laryngoscopy may be needed to follow up these subtler lesions

Goals:

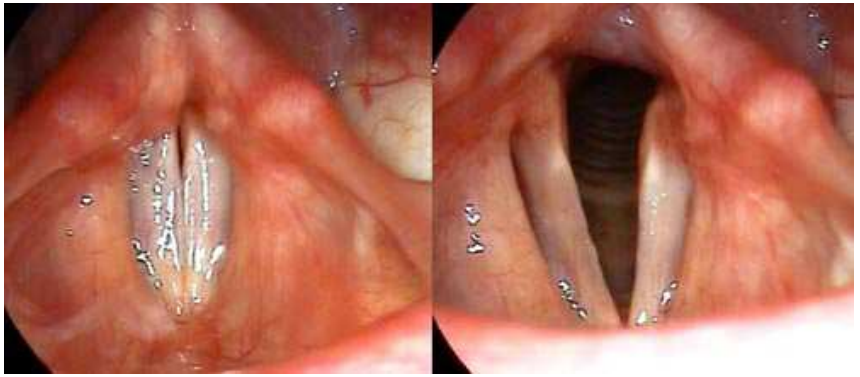
- to confirm histopath
- Map the disease & regional nodes & potential metastatic disease
- Stage the lesion

Indirect Laryngoscopy

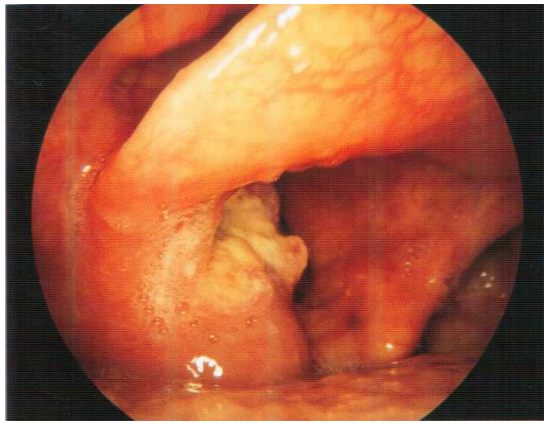
- Overview of larynx / hypopharynx.
- Excellent color & depth perception

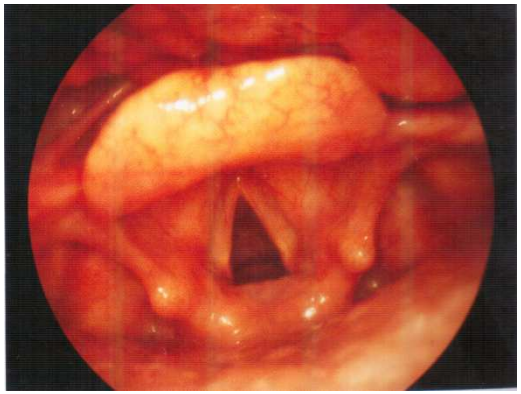
Disadvantage:

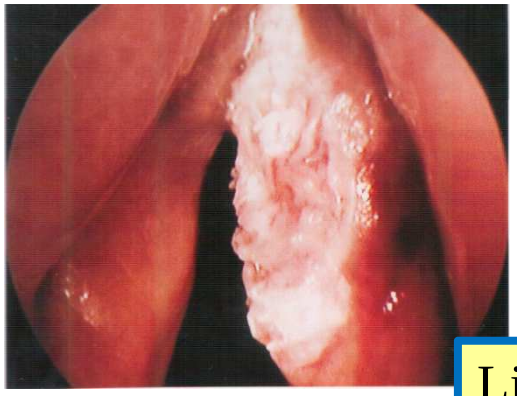
- difficult patients
- hidden areas



Malignant lesions can appear as friable, fungating, ulcerative masses or be as subtle as changes in mucosal color







Direct laryngoscopy

Standard of care

- extent of the disease
- vocal cord mobility
- visualise hidden areas
- Palpate crico aryetenoid joint
- biopsy –obvious & suspicious areas

Rigid telescopic examination – 90^0/ 70^0

Advantages: - simple

- added magnification
- better optical resolution
- higher sensitivity
- better contrast

Flexible fibre optic endoscopy

Limitation of endoscopy – PES/PGS/ Cartilage involvement

Staging- Primary Tumor (T)

TX	Minimum requirements to assess primary tumor cannot be met
T0	No evidence of primary tumor
Tis	Carcinoma in situ

Staging- Supraglottis

T1	Tumor limited to one subsite of supraglottis with normal vocal cord mobility
T2	Tumor involves mucosa of more than one adjacent subsite of supraglottis or glottis, or region outside the supraglottis (e.g. mucosa of base of the tongue, vallecula, medial wall of piriform sinus) without fixation
T3	Tumor limited to larynx with vocal cord fixation and or invades any of the following: postcricoid area, preepiglottic tissue, paraglottic space, and/or minor thyroid cartilage erosion (e.g. inner cortex)
T4a	Tumor invades through the thyroid cartilage and/or invades tissue beyond the larynx (e.g. trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus)
T4b	Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures

Staging- Glottis

T1	**Tumor limited to the vocal cord (s) (may involve anterior or posterior commissure) with normal mobilty**
T1a	**Tumor limited to one vocal cord**
T1b	**Tumor involves both vocal cords**
T2	**Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility**
	paraglottic space, and/or minor thyroid cartilage erosion (e.g. inner cortex)
T4a	**Tumor invades through the thyroid cartilage, and/or invades tissues beyond the larynx (e.g. trachea, soft tissues of the neck including deep extrinsic muscles of the tongue, strap muscles, thyroid, or esophagus**
T4b	**Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures**

AJCC 6th edition, 2006 – T2a –with cord mobility & T2b – with impaired mobility

Aim of treatment – desirable end points

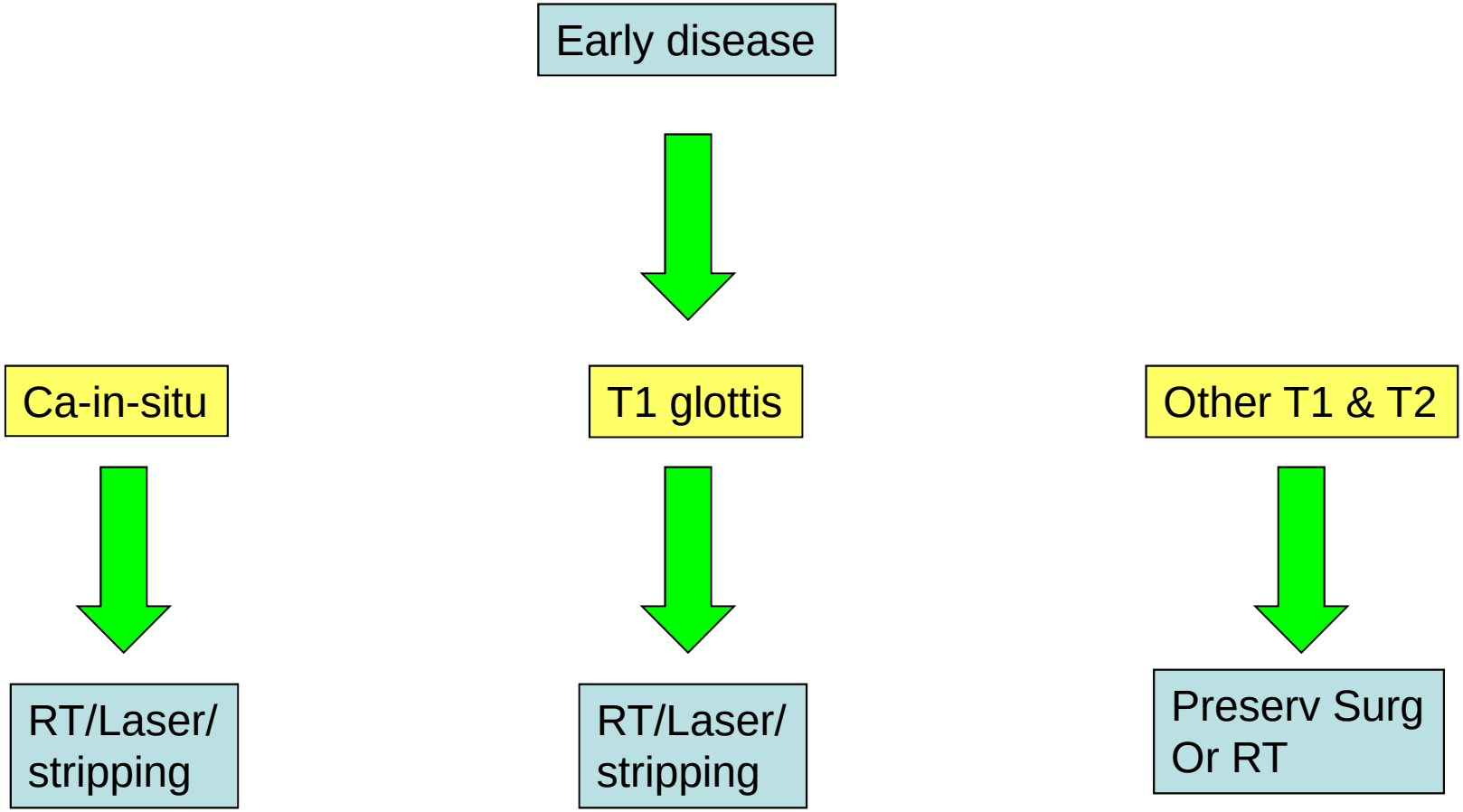
- **Local control**
- **Organ preservation**
- Organ preservation possible by surgery and radiotherapy
- Organ preservation ≠ Function preservation
- Functions – speech, deglutition and breathing.

Patient related factors influencing decision

-KPS
-Co-morbidities
-Tracheostomy
-Age

Nutritional support required before, during and after radiation treatment.

Decision tree – stagewise management



- N0 – No treatment in T1 and select T2 glottic cases. Single modality treatment.

ORL

Review

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Laser Surgery versus Radiotherapy for T1–T2N0 Glottic Cancer: A Meta-Analysis

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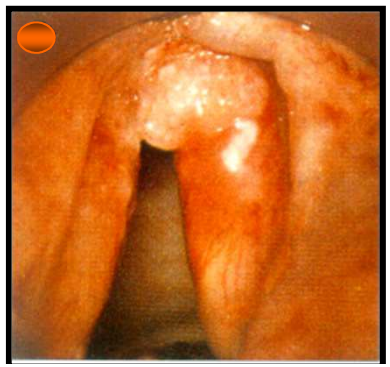
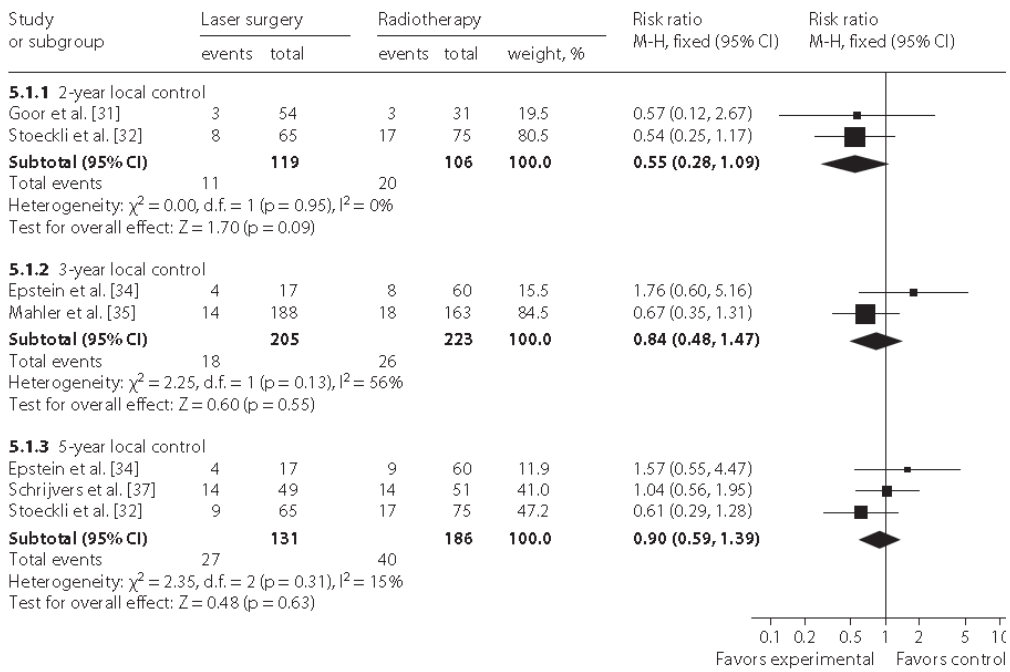
- CO2 laser
- Accurate review of margins difficult
- AC – not adequately dissected
- Residual hoarseness +





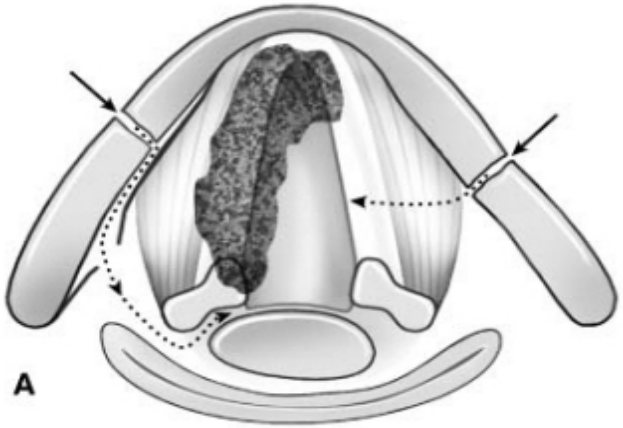
Study or subgroup	Laser surgery events	Laser surgery total	Radiotherapy events	Radiotherapy total	weight, %	Risk ratio M-H, fixed (95% CI)
5.1.1 2-year local control						
Goor et al. [31]	3	54	3	31	19.5	0.57 (0.12, 2.67)
Stoeckli et al. [32]	8	65	17	75	80.5	0.54 (0.25, 1.17)
Subtotal (95% CI)		**119**		**106**	**100.0**	**0.55 (0.28, 1.09)**
Total events	11		20			
Heterogeneity: $\chi^2 = 0.00$, d.f. = 1 (p = 0.95), $I^2 = 0\%$						
Test for overall effect: Z = 1.70 (p = 0.09)						
5.1.2 3-year local control						
Epstein et al. [34]	4	17	8	60	15.5	1.76 (0.60, 5.16)
Mahler et al. [35]	14	188	18	163	84.5	0.67 (0.35, 1.31)
Subtotal (95% CI)		**205**		**223**	**100.0**	**0.84 (0.48, 1.47)**
Total events	18		26			
Heterogeneity: $\chi^2 = 2.25$, d.f. = 1 (p = 0.13), $I^2 = 56\%$						
Test for overall effect: Z = 0.60 (p = 0.55)						
5.1.3 5-year local control						
Epstein et al. [34]	4	17	9	60	11.9	1.57 (0.55, 4.47)
Schrijvers et al. [37]	14	49	14	51	41.0	1.04 (0.56, 1.95)
Stoeckli et al. [32]	9	65	17	75	47.2	0.61 (0.29, 1.28)
Subtotal (95% CI)		**131**		**186**	**100.0**	**0.90 (0.59, 1.39)**
Total events	27		40			
Heterogeneity: $\chi^2 = 2.35$, d.f. = 2 (p = 0.31), $I^2 = 15\%$						
Test for overall effect: Z = 0.48 (p = 0.63)						

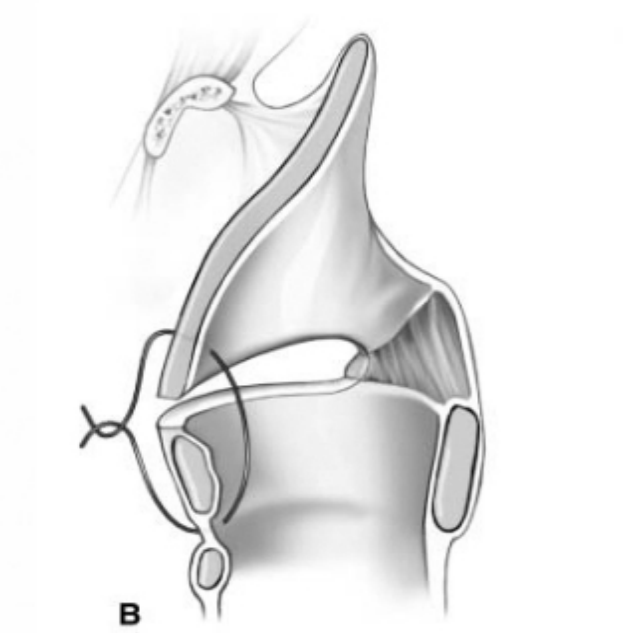
Stripping/ cordectomy

- Tis lesions
- T1a &b lesions
- Strong consideration for RT in Tis lesion post stripping recurrence
- Web formation
- Voice quality diminishes on repeated stripping
- Median time to rec 2-3yrs. Need close follow up.

Univ of florida, Gainsville. Fein et al, IJROBP 1993; 27(2):379-384

Laryngeal preservation surgery – partial laryngectomy





- T2 (esp unfavourable) lesions
- Expensive; skill
- Voice quality – poor

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JOURNAL OF CLINICAL ONCOLOGY

ASCO SPECIAL ARTICLE

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

David G. Pfister, Scott A. Laurie, Gregory S. Weinstein, William M. Mendenhall, David J. Adelstein, K. Kian Ang, Gary L. Clayman, Susan G. Fisher, Arlene A. Forastiere, Louis B. Harrison, Jean-Louis Lefebvre, Nancy Leupold, Marcy A. List, Bernard O. O'Malley, Snehal Patel, Marshall R. Posner, Michael A. Schwartz, and Gregory T. Wolf

- T1 /T2 – suitable for OP. RT or surgery - 85-95% cures.
- Surgery - shorter treatment period; worse voice outcomes; RT as reserve
- RT- 6-7 wks.
- T1/T2 – RT = Larynx preserv Sx
- T1/T2 – No elective nodal RT
- T1/T2 SGL – Treat the neck

Management of T1–T2 Glottic Carcinomas

William M. Mendenhall, M.D.[1]
John W. Werning, M.D.[2]
Russell W. Hinerman, M.D.[1]
Robert J. Amdur, M.D.[1]
Douglas B. Villaret, M.D.[2]

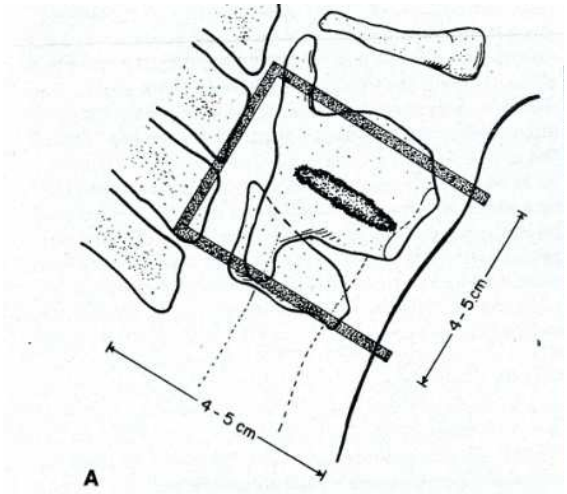
[1] Department of Radiation Oncology, University of Florida College of Medicine, Gainesville, Florida.

[2] Department of Otolaryngology, University of Florida College of Medicine, Gainesville, Florida.

T1–T2 glottic carcinomas may be treated with conservative surgery or radiotherapy. The goals of treatment are cure and laryngeal voice preservation. The aim of the current study was to review the pertinent literature and discuss the optimal management of early-stage laryngeal carcinoma. Literature review indicated that the local control, laryngeal preservation, and survival rates of patients were similar after transoral laser resection, open partial laryngectomy, and radiotherapy. Voice quality depended on the extent of resection for patients undergoing surgery; results for patients undergoing laser resection for limited lesions were comparable to the corresponding results for patients receiving radiotherapy, whereas open partial laryngectomy yielded poorer results. Costs were similar for laser resection and radiotherapy, but open partial laryngectomy was more expensive. Patients with well defined lesions suitable for transoral laser excision with a good functional outcome were treated with either laser or radiotherapy. The remaining patients were optimally treated with radiotherapy. Open partial laryngectomy was reserved for patients with locally recurrent tumors. ***Cancer*** **2004;100:1786–92.**

Radiotherapy

- UK - RT standard of care – TIS, T1/2
- Parallel opp fields
- T1- 5cm – thyroid promontory to lower border C5
- T2 -6cm – Hyoid to cricoid



No IMRT done routinely!

Steps of Larynx (T1/2) Radiotherapy

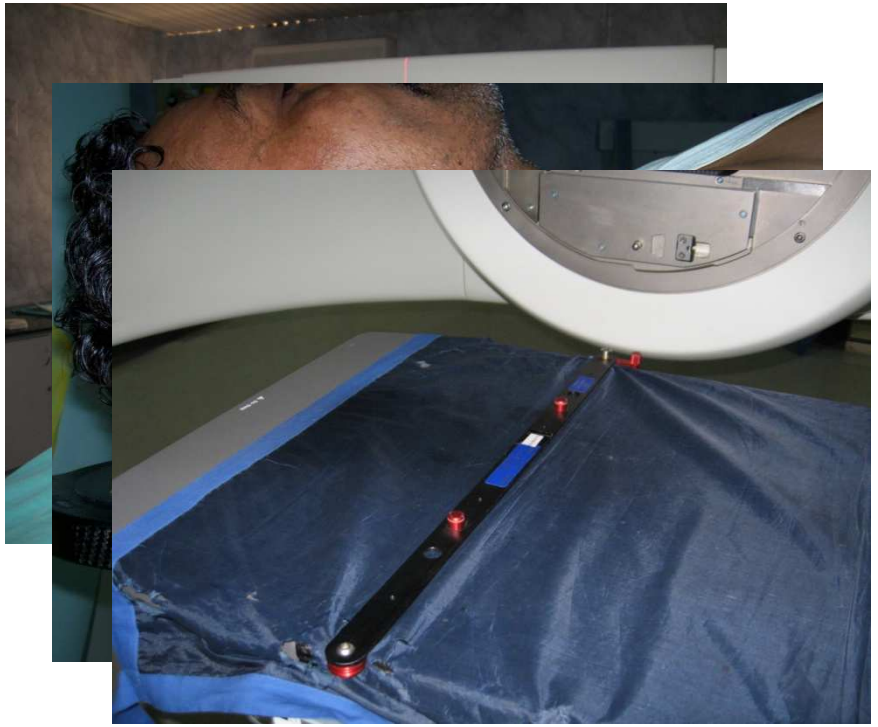
Patient counseling

Patient positioning and Immobilization

- Simulation and/or Imaging
- Target definition & planning
- Treatment delivery

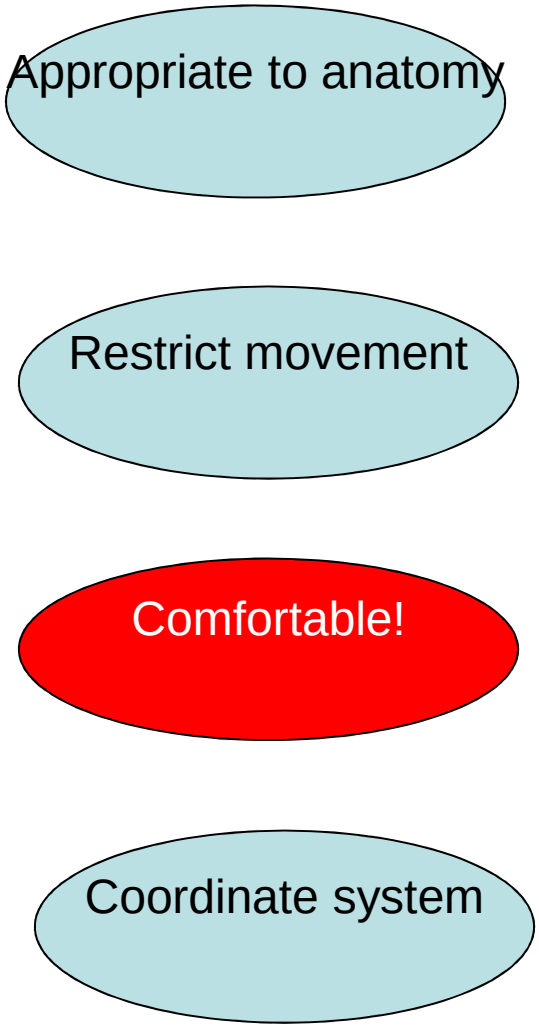
Patient poitioning

- Comfortable
- Supine
- Neutral head position
- Laser alignment
- Indexing



Patient positioning devices

Immobilization



What are the problems in immobilization?

- Neck rest versus neck shape
- Loosening of cast due to weight loss
- Difficult individual patient positioning
- Short neck

Gap between neck, upper thorax and table with standard neck rest

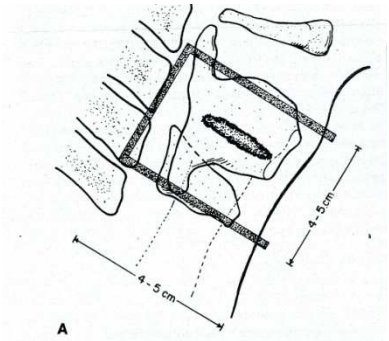
Wrong neck rest

What do radiation portals depend upon?

- Location of the primary and stage
- LN- location, size and laterality

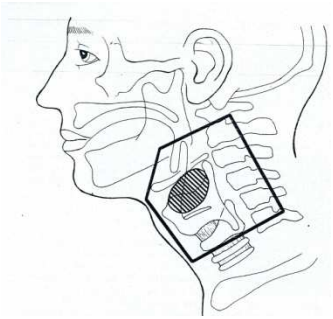
T1 Glottis

Thyroid notch to Cricoid
Post - individual



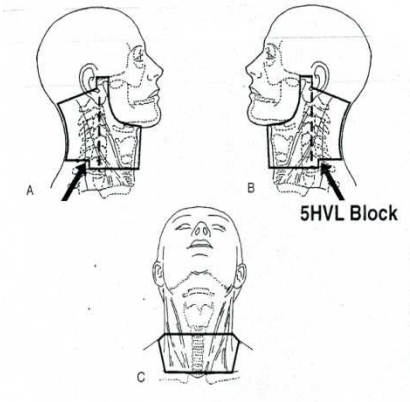
T2 Glottis

Hyoid to Cricoid
Post - individual



Others

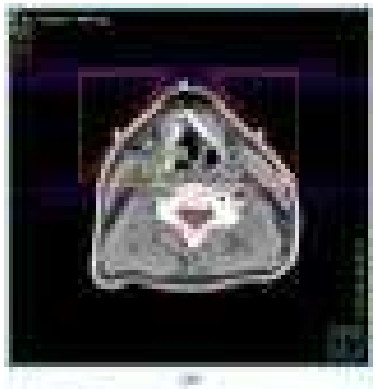
3 field plan
C1 to clavicle
Post - individual

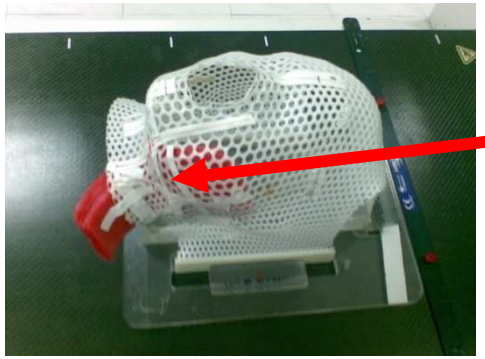


Beam energy and accessories

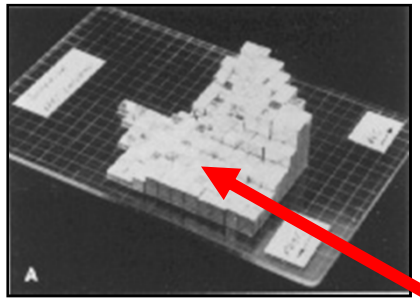
- 4- 6Mev
- Cobalt-60

- 10-20deg
  Wedge pair

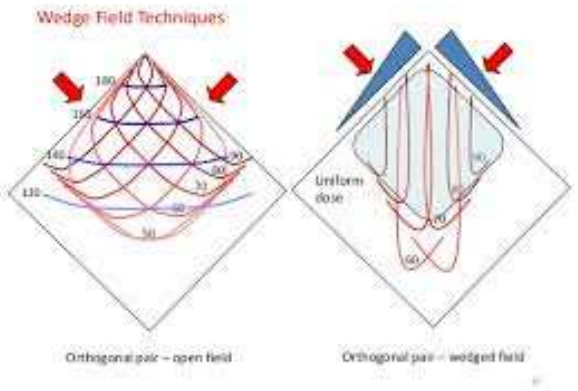




Bolus



Missing tissue
Compensator



Khan et al. Radiation Oncology 2012, 7:193
http://www.ro-journal.com/content/7/1/193

RADIATION ONCOLOGY

RESEARCH Open Access

Definitive radiotherapy for early (T1-T2) Glottic Squamous cell carcinoma: a 20 year Cleveland clinic experience

Mohammad K Khan[1*], Shlomo A Koyfman[2], Grant K Hunter[2], Chandana A Reddy[2] and Jerrold P Saxton[2]

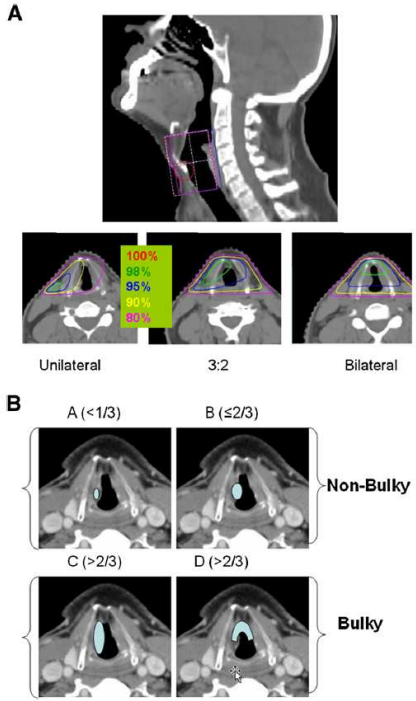
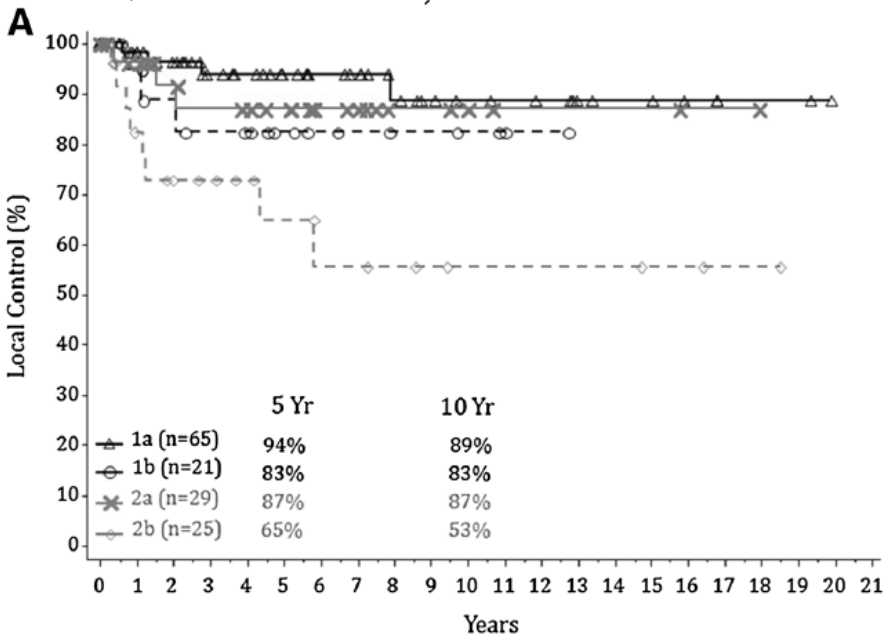
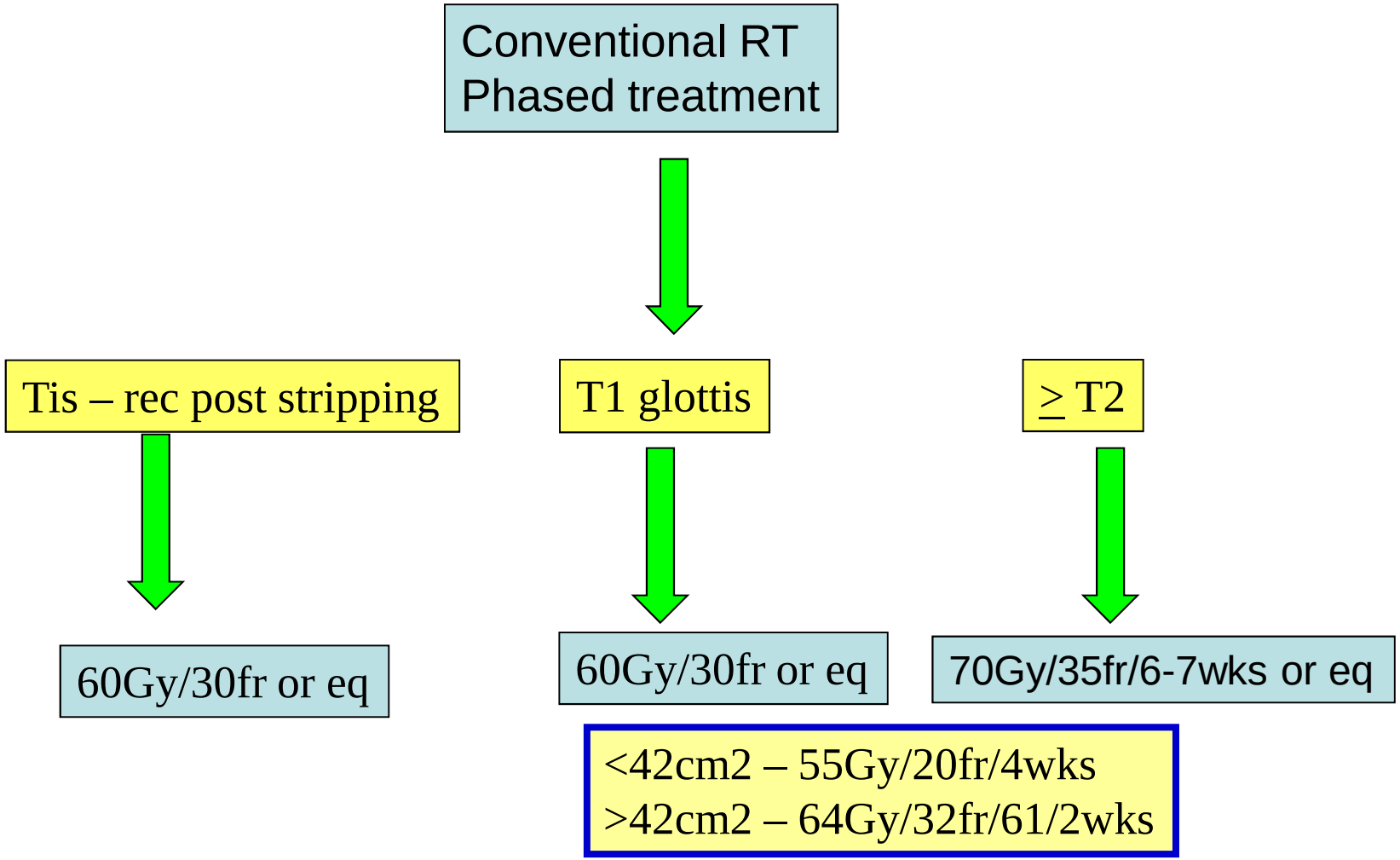


Figure 1 Example of Arrangement & Weighting of Fields (1A) and Comparison of Non- Bulky vs. Bulky Tumor (1B).



Radiation dose scedules



Status of IMRT in early glottic ca.

No sparing of vital structures – not recommended routine clinical setting

Published in final edited form as:
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SIMPLE CAROTID-SPARING INTENSITY-MODULATED RADIOTHERAPY TECHNIQUE AND PRELIMINARY EXPERIENCE FOR T1–2 GLOTTIC CANCER

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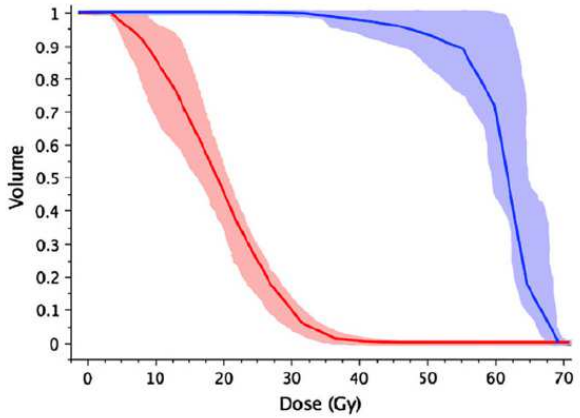


Fig. 1.
Composite carotid artery dose–volume histogram ($n = 6$) showing mean (solid line) and 95% confidence interval (shaded region) for virtual plans (red = intensity-modulated radiotherapy, blue = opposed laterals).

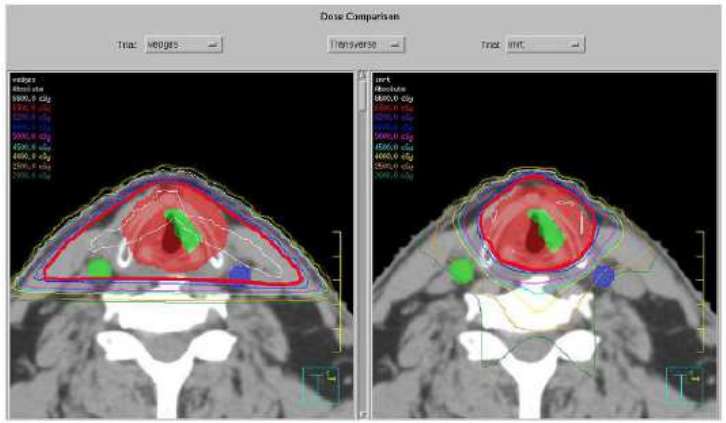


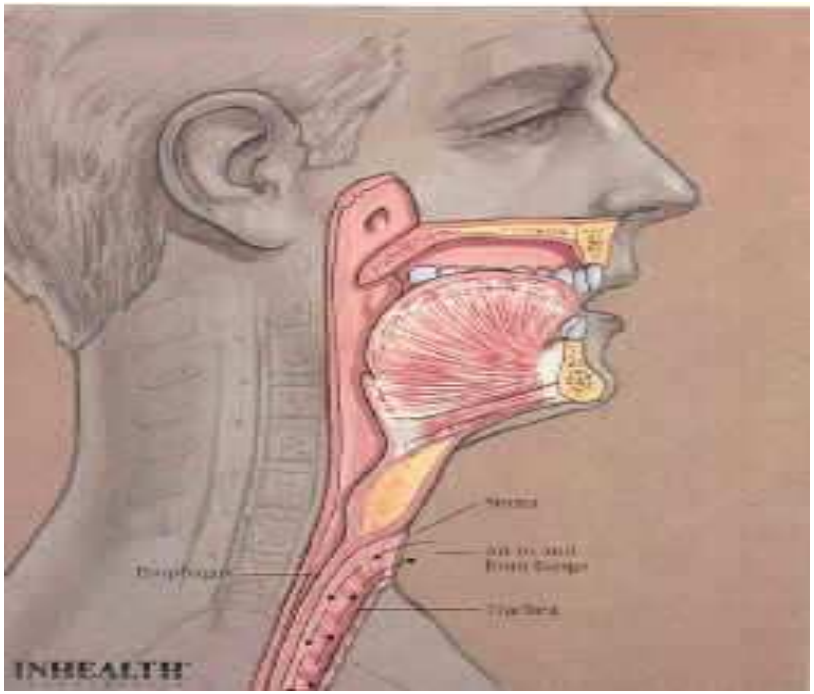
Fig. 2.
Stereotypic isodose plans for (a) lateral field setup and (b) intensity-modulated radiotherapy.

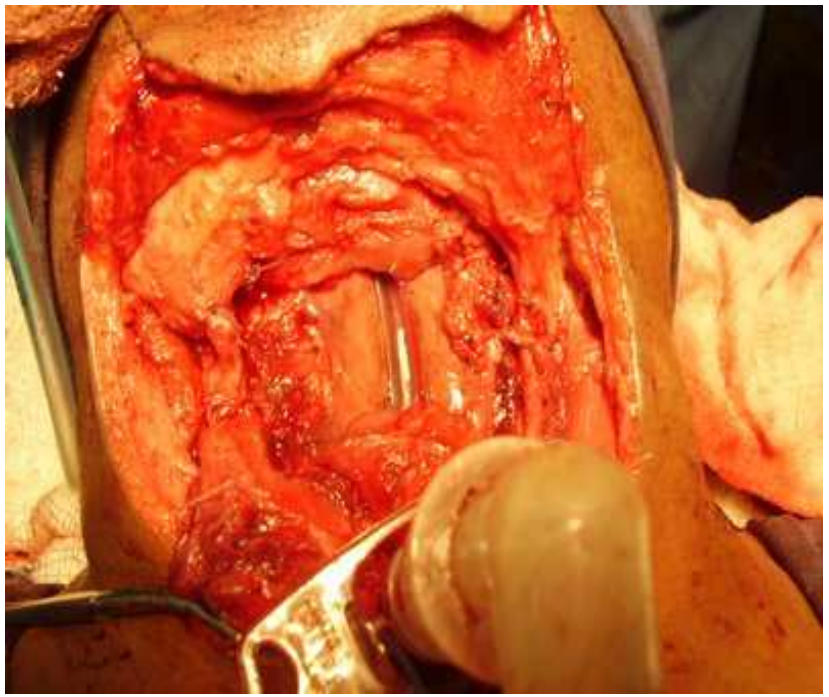
Reasons for failure

- Diffuse Tis lesions
- Ant commissure failure with megavolatge beam underdosage – **Bolus; No shell cut outs; No wedge.**
- Short neck – high shoulder – **Use of wedge oblique arrangement.**

Total Larygectomy - Salvage

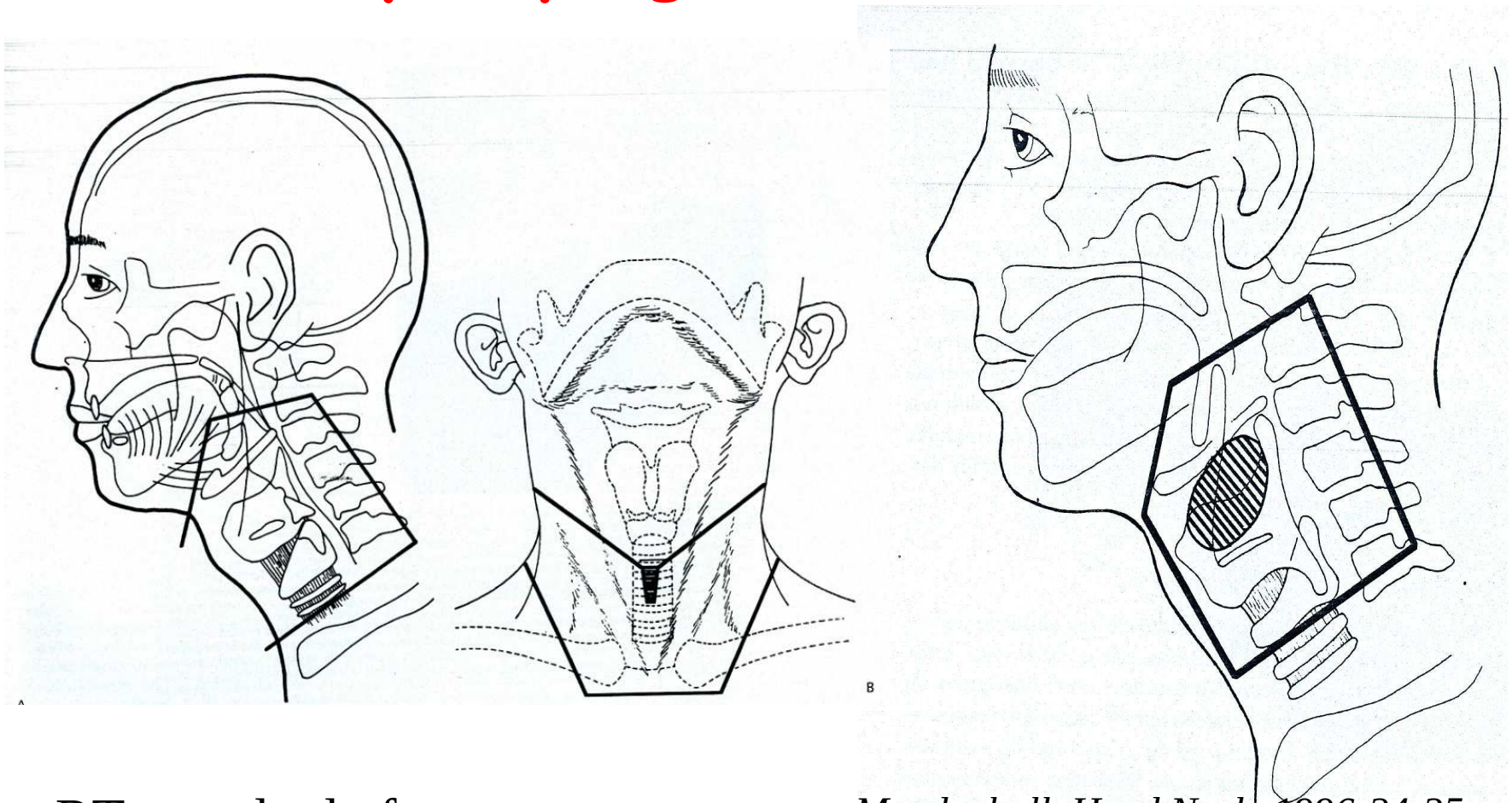
- Post RT failures





- Speech rehabilitation –TEP; electro larynx; eso speech

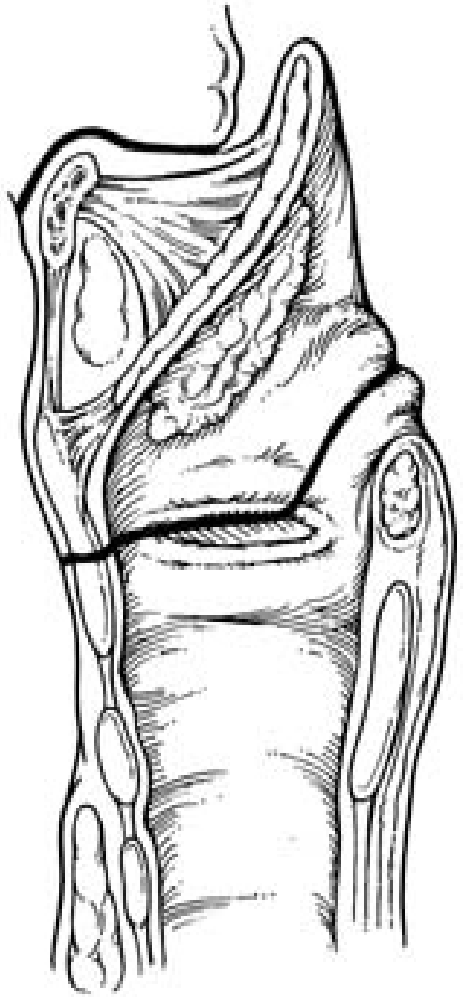
Early Supraglottic carcinoma



Mendenhall, Head Neck, 1996:24-35

- RT standard of care
- Cover bilateral lymph nodes – level II -IV
- 5 year LC rate T1 -100%; T2 -83%

Supraglottic laryngectomy

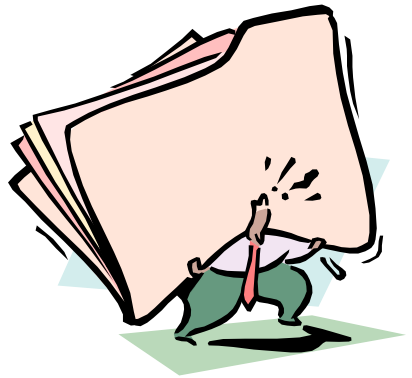


- Select group
- T1,2, or 3 if only by preepiglottic space invasion
- Mobile cords
- No anterior commissure involvement
- Good cardiac & pulmonary reserves
- No tongue base disease past circumvallate papillae
- Apex of pyriform sinus not involoved

Outcome – Glottis & Supraglottis

5 year survival	
Stage I	>95%
Stage II	85-90%

Conclusions



- Worst complication is tumor recurrence
- Pre treatment assessment & staging crucial
- Radiotherapy = Laryngeal preservation surgeries
- Results excellent. Pay attention to disease, planning and treatment delivery

Carcinoma of the Hypopharynx – early tumors

Hypopharynx- Anatomy

- Lies behind and lateral to larynx from hyoid bone to crico pharyngeal junction at C6 level.
- Larynx indents anterior wall of hypopharynx to form horse shoe shaped hollow cavity which forms the central aerodigestive pathway and two lateral fossae ie : pyriform sinuses.

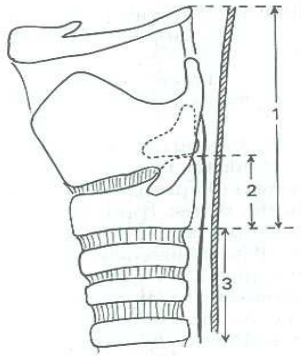


Fig. 2.8.2. Lateral view of larynx.
1, Posterior pharyngeal wall.
2, Postcricoid region.
3, Cervical oesophagus.

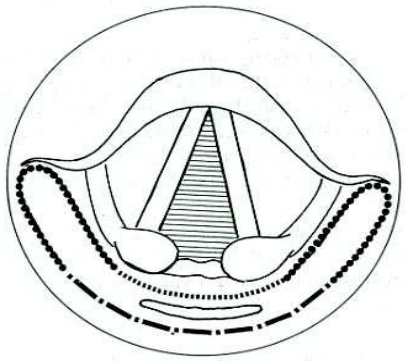


Fig. 2.8.1. The areas of the hypopharynx.
●●●●●, Pyriform fossa.
■■■■■, Postcricoid region.
■▬■▬■, Posterior pharyngeal wall.

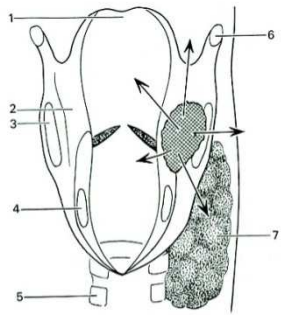
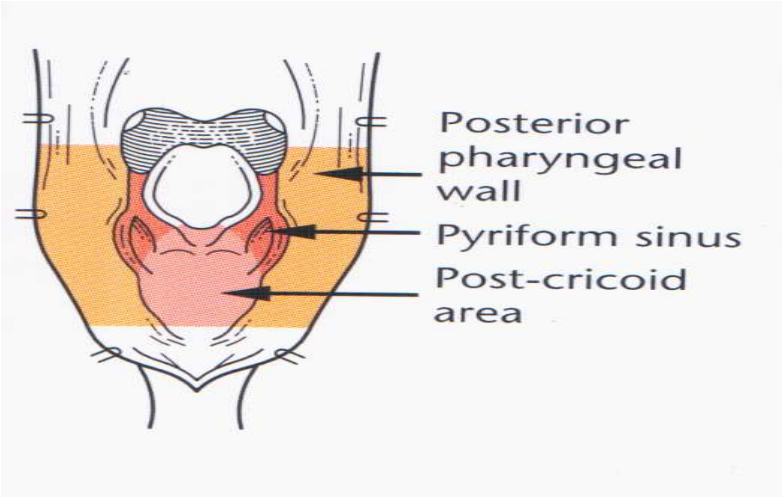


Fig. 2.8.3. Routes of spread of tumours of the pyriform fossa. (By courtesy of Heinemann Books.)
1, Epiglottis. 5, Trachea.
2, Pyriform fossa. 6, Hyoid bone.
3, Thyroid cartilage. 7, Thyroid gland.
4, Cricoid cartilage.

Hypopharynx- pathology

• Pyriform fossa	- 75-80%
• Post. Pharyngeal wall	- 15-20%
• Post cricoid	- 5%

- 95% cases - squamous cell carcinoma
  - 33% - non keratinising
  - 40% - poorly differentiated
- Minor salivary gland tumors
- Sarcomas
- lymphoma



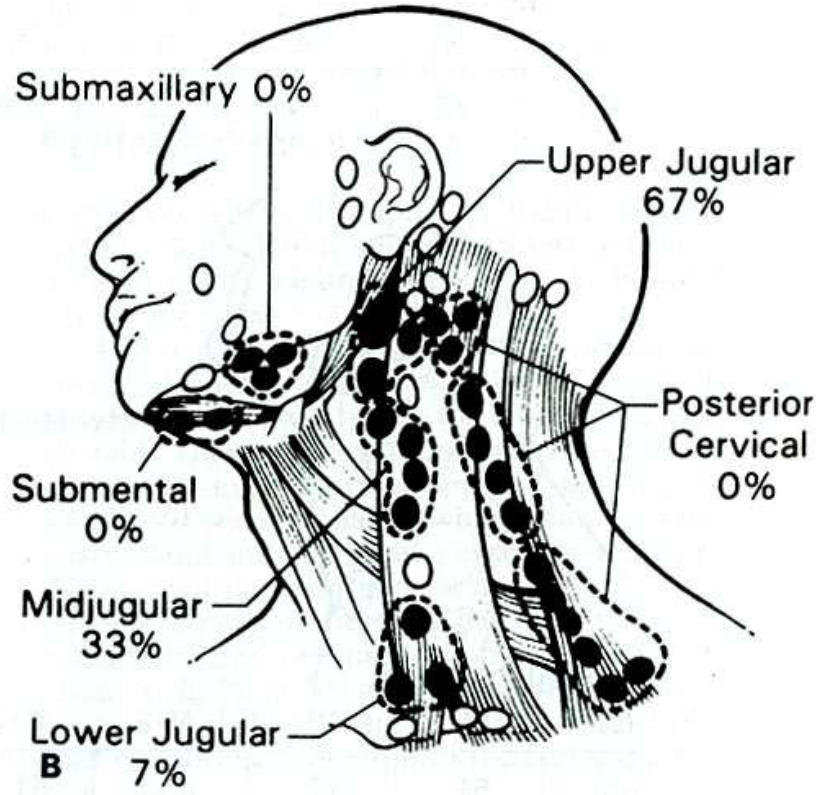
Hypopharyngeal cancer- aetiology

- Clinically inaccessible region
- Aggressive in behavior; Abundant lymphatic drainage
- Field cancerisation-12-20 % multiple synchronous
- Nutritionally depleted patients
- Tobacco (smoked/ chewed); Alcohol –co-carcinogen
- Nutritional- deficiency of B-carotenoids, iron deficiency anemia (asso . with dysphagia and glossitis asPlummer Wilson or PKB syndrome

Lymph node involvement after elective neck diss. In N0 neck-2/3 in T1-T2

- Pyriform fossa
  - Incidence of nodal involvement - 75%
  - Bilateral nodal involvement - 10-14%
  - Clinical N0 neck, found positive - 40-50%

    Retropharyngeal nodes +ve in 40% patients with PFF and post. Pharyngeal wall lesions



Hypopharynx- natural history

- Advanced disease at presentation
- Distant mets follow locoregional relapse
- Skip lesions
- Early esophageal spread
- Lymphatic
  - Most common level II followed by level III
  - Involvement of level I, IV, V uncommon

Hypopharynx- distant spread

- Distant metastasis
  - 20-30% with in two years despite treatment
  - RTOG analysed effect of locoregional control on distant metastasis
  - Locoregional control at 6 months associated with reduction in incidence of mets.- 43-40%
  - Most common sites – lungs, mediastinal nodes, liver, bone

Cancer Hypopharynx- symptomatology

- Mild non specific **sore throat**
- Vague discomfort on swallowing
- Neck mass as sole finding in 25% cases
- Referred otalgia characteristic of ca PFF
- Salivary drooling, blood streaked saliva
- Significant wt. loss, poor ODH
- Hoarseness- cricoid, inter-arytenoid space, post-cricothyroid muscles OR Hot potato voice OR Nasal voice

Cancer Hypopharynx-work up

- History
- Physical examination (general, neck, laryngeal crepitus)
  - I.L examination
- Flexible endoscopy and biopsy
- Hemogram, Clinical chemistry
- Imaging barium swallow, chest X Ray,Xray soft tissue neck,
- CT/MRI/USG neck
- FNAC from LN mass

Cancer Hypopharynx- staging

- Tx Primary tumor can not be assessed
- T0 No evidence of primary tumor
- Tis Carcinoma in situ
- T1 Limited to one subsite of hypopharynx, < 2 cm
- T2 More than one subsite or involving an adjacent site or 2-4 cm, without fixation of larynx
- T3 More than 4 cm or With fixation of larynx
- T4 Tumor invades adjacent structures of neck (soft tissues, prevertebral fascia, esophagus, thyroid or cricoid cartilage, thyroid gland)

Cancer Hypopharynx- surgery

- Conservation surgery – size and location, fixity of nodes, medical condition of patient
- **Contraindication**
  - Transglottic extension (mucosa of AE fold and paraglottic space)
  - Cartilage invasion
  - Vocal fold paralysis
  - Pyriform apex or post cricoid invasion
  - Extension beyond laryngeal framework
- Unilateral neck dissection

Hypopharyngeal ca. -RT

Pyriform sinus
T1,T2 lesions

Irradiation alone
or surgery (PLP+ U/L ND) +/- RT

Posterior Pharyngeal wall
T1,T2 lesions

Irradiation alone
or surgery (PLP+ U/L ND) + RT +/- CT

Post cricoid –early lesion

Optimal treatment yet to be defined

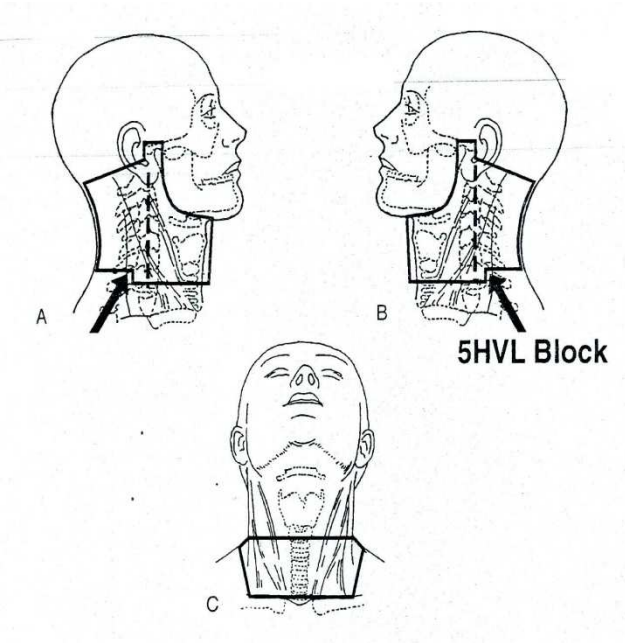
Cancer Hypopharynx-Radiotherapy

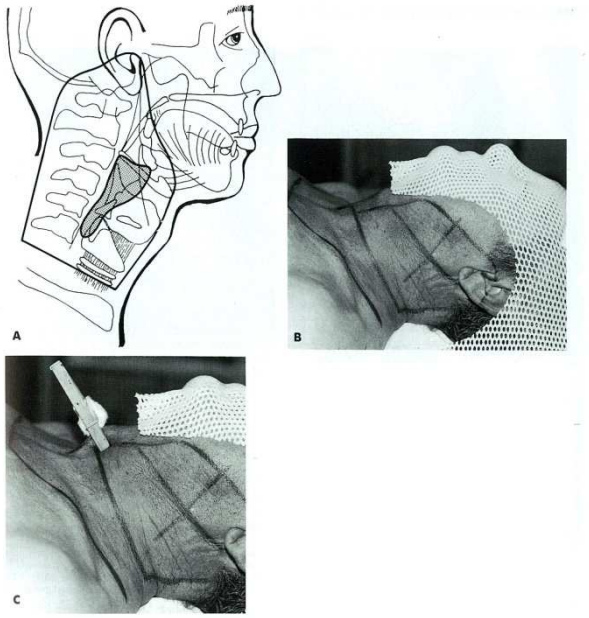
- RT alone
  - Small superficial lesions PFS
  - Mendenhall et al reported 64% control in T1/2 lesions (65 - 70Gy in 7 weeks)
  - Best results with
    - Lesions confined to one or two walls
    - Lack bulk
    - Not infiltrate larynx or destroy thyroid cartilage

Cancer Hypopharynx- RT technique

- Larynx, pharynx ,neck
- Base of skull to clavicle (PC – 5cm prox esophagus)
- Dose – 70Gy/ 35fr/7wks or eq.

- **Postoperative**
  - Dose – 60Gy/ 30fr/6wks. 3 field technique
  - Anterior shield not used





Conformal RT

- Advantageous as they effectively treat horse shoe shaped target volume
- GTV-grossly visible/palpable extent of primary tumor with metaststic l. node
- CTV- GTV +regions of potential microscopic disease ie; upper middle and lower jugular l. nodes, SA and RP lymph nodes ,RP space ,thyroid and criciod cartilage,SC L. node +/- upper mediastinal l. nodes
- PTV- CTV +1.5 cm margin

Cancer Hypopharynx- Results

- Overall cure rates for hypopharyngeal tumours – 55%
- Local disease – 80%
- Regional disease – 43%
- Distant disease – 20%
- 5 –year disease free survival rates
  - A-E fold - 66%
  - PFF - 55%
  - Post.pharyngeal wall - 49%

Sequalae

- ❖ Acute effects
  - Mucositis (major limitation)-sore throat, dysphagia, hoarseness
  - Dysguesia and xerostomia
  - Laryngeal edema
- ❖ Late
  - Late laryngeal chondronecrosis – 2-4%
  - Severe laryngeal edema requiring tracheostomy – 6%
  - Subcutaneous fibrosis
- ❖ Mortality 1-3% with RT alone,5-6% with surgery +RT
  - Aspiration ,pharyngeal stricture causing cachexia, asphyxia d/t laryngeal edema ,carotid blow out

Thank you