Laryngeal Cancer
...From early to late

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Overview

- Epidemiology
- Staging & Survival
- Early stage laryngeal cancer
  - Management
    - Endoscopic
    - Role of radiation
- Late stage laryngeal cancer
  - Management
    - Open surgery
- Innovation

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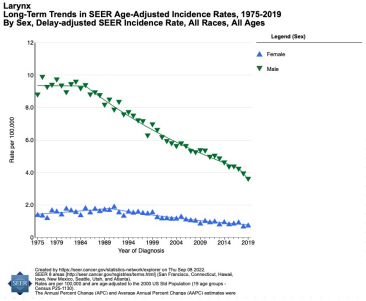
Epidemiology



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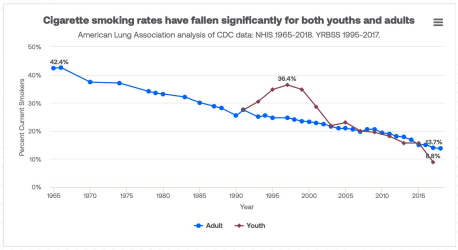
Epidemiology



Ref: - https://www.lung.org/research/trends-in-lung-disease/tobacco-trends-brief/overall-tobacco-trends

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Epidemiology

Multicenter Study > Laryngoscope. 2020 Mar;130(3):E108-E115. doi: 10.1002/lary.28067. Epub 2019 May 15.

The rising rate of nonsmokers among laryngeal carcinoma patients: Are we facing a new disease?

Hagit Shoffel-Havakuk [1,2], Karla O'Dell [3], Michael M Johns 3rd [3], Lindsay Reder [4], Margarita Popova [3], Doron Halperin [5], Edit Feldberg [6], Yonatan Lahav [5]

- N = 330
  - N = 75 (22.7%) non smokers
  - Glottic level
  - 60.2 ± 17.5 years
  - ? etiology

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Supraglottic SCC T staging

T1: Tumor limited to one subsite* of supraglottis with normal vocal cord mobility

T2: Tumor invades mucosa of more than one adjacent subsite* of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx

T3: Tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, PES, PGS, inner cortex thyroid cartilage

T4a: Tumor invades through the thyroid cartilage, and/or extends into soft tissues of the neck, thyroid, and/or esophagus

T4b: Invades prevertebral space, encases carotid artery, invades mediastinal structures

*Subsites include the following:
- ventricular bands (false cords)
- arytenoids
- suprahyoid epiglottis
- infrahyoid epiglottis
- aryepiglottic folds (laryngeal aspect)

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Glottic SCC T staging

T1: Tumor limited to vocal cord(s) (may involve anterior or posterior commissure) with normal mobility

- 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

T3: Tumor limited to the larynx with vocal cord fixation and/or invasion of PGS and/or inner cortex of thyroid cartilage

T4a: Tumor invades through outer cortex of thyroid cartilage and/or to other tissues beyond the larynx (e.g., trachea, soft tissues of neck, including thyroid, pharynx, strap muscles, esophagus)

T4b: Invades prevertebral space, encases carotid artery, invades mediastinal structures

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Subglottic SCC T staging

T1: Tumor limited to the subglottis

T2: Tumor extends to vocal cord(s) with normal or impaired mobility

T3: Tumor limited to larynx with vocal cord fixation

T4a: Tumor invades through outer cortex of thyroid cartilage and/or to other tissues beyond the larynx (e.g., trachea, soft tissues of neck, including thyroid, pharynx, strap muscles, esophagus)

T4b: Invades prevertebral space, encases carotid artery, invades mediastinal structures

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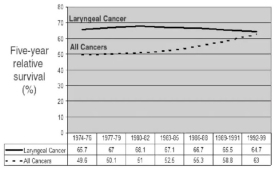
Survival



	1974-76	1977-79	1980-82	1983-85	1986-88	1989-1991	1992-99
Laryngeal Cancer	65.7	67	68.1	67.1	66.7	66.5	64.7
All Cancers	49.6	50.1	51	52.6	55.3	58.8	63

Trends in 5-Year Relative Survival Rates* (%) by Race and Year of Diagnosis, United States

ALL RACES

	1975 TO 1977	1987 TO 1989	2004 TO 2010
Larynx	66	66	63†
Oral cavity & pharynx	53	54	66†

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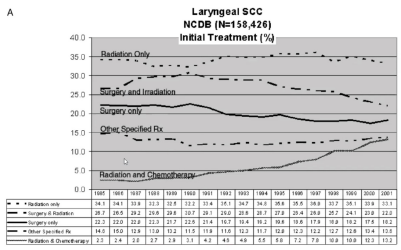
Survival

A



	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
Radiation only	34.1	34.1	33.8	32.3	32.8	32.2	33.4	35.1	34.7	34.3	35.6	35.5	36.8	33.7	36.1	33.9	33.1
Surgery & Radiation	28.7	28.5	29.2	29.6	29.8	30.7	28.1	29.0	28.8	28.7	27.8	28.4	28.8	28.7	24.1	27.8	27.2
Surgery only	32.3	32.0	32.8	33.3	31.7	32.5	31.4	30.7	30.4	30.2	30.8	29.6	27.9	31.9	32.8	27.6	30.2
Other Specified Rx	14.0	15.0	12.9	13.0	12.2	11.5	11.9	11.0	12.3	11.7	12.8	12.3	12.2	12.7	12.8	12.4	13.0
Radiation & Chemotherapy	2.3	2.4	2.0	2.7	2.9	3.1	4.2	4.5	4.8	5.5	6.0	7.2	7.8	10.2	10.9	12.3	13.2

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Survival

Veteran's Affairs – 1991 NEJM

- Total Laryngectomy + RT vs. Induction chemo + RT
- 64% Larynx Preservation with chemo-RT
- ***Equivalent survival:***
  - 68% 2-year survival in both groups

INDUCTION CHEMOTHERAPY PLUS RADIATION COMPARED WITH SURGERY PLUS RADIATION IN PATIENTS WITH ADVANCED LARYNGEAL CANCER

The Department of Veterans Affairs Laryngeal Cancer Study Group*

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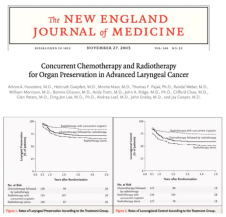
Survival

Three Arms:

1. Induction Chemo + RT
2. Concomitant Cisplatin + RT
3. RT Alone

Endpoint: Larynx Preservation

- **88% w/ concurrent. OS 54% → 45% Laryngectomy Free at 5 years.**
- 75% w/ induction
- 70% w/ RT alone



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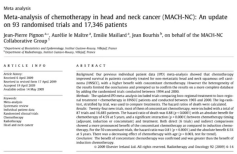
MACH-NC: 2000 and 2009

1. *Concomitant chemoradiation*
2. *Platinum based regimen*


Meta-analysis

Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 93 randomised trials and 17,346 patients

Jean-Pierre Pignon[a,*], Aurélie le Maître[a], Emilie Maillard[a], Jean Bourhis[b], on behalf of the MACH-NC Collaborative Group[a]

[a]Department of Biostatistics and Epidemiology, Institut Gustave-Roussy, Villejuif, France
[b]Department of Radiotherapy, Institut Gustave-Roussy, Villejuif, France

ARTICLE INFO

ABSTRACT

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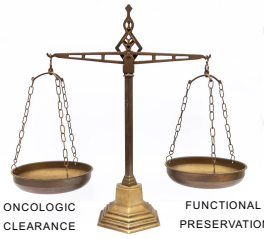

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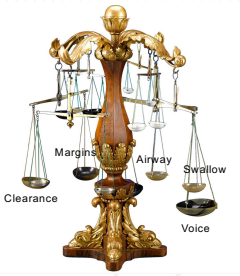

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Tis

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Tis

Level of abnormal maturation (WHO 2005)	WHO 2005 classification [61]	SIN classification [60]	Ljubljana classification [59]	Amended Ljubljana classification [58]	WHO 2017 [8]
	Squamous hyperplasia	Squamous hyperplasia	Squamous hyperplasia	Low-grade SIL	Low-grade dysplasia
Lower 1/3	Mild dysplasia	SIN 1	Basal/parabasal hyperplasia		
1/3 to 1/2	Moderate Dysplasia	SIN 1 or 2	Atypical hyperplasia	High-grade SIL	
Upper 1/2–3/4		SIN 2			High-grade dysplasia*
Full thickness	Severe dysplasia				
	Carcinoma in situ		Carcinoma in situ	Carcinoma in situ	

Ref: - Eckel, H.E., Simo, R., Quer, M. et al. European Laryngological Society position paper on laryngeal dysplasia Part II: diagnosis, treatment, and follow-up. Eur Arch Otorhinolaryngol ***278,*** *1723–1732 (2021). https://doi.org/10.1007/s00405-020-06406-9*

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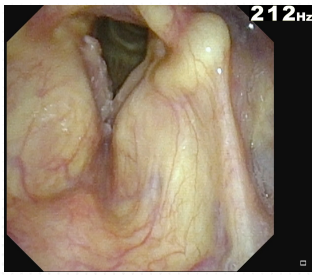
Case 1

73 year old male

- Dysphonia 4 months
- Non smoker
- Non drinker



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Role of Stroboscopy

– Good at diagnosing benign mid membranous lesions

– Does not reliably predict the presence of malignancy or depth of invasion

Ref: - Colden D., Zeitels S.M., Hillman R.E., et al: Stroboscopic assessment of vocal fold keratosis and glottic cancer. Ann Otol Rhinol Laryngol 2001; 110: pp. 293-298

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Case 1

COLLECTION DATE: 04/08/2022
Surgical Pathology Report

SPECIMEN SOURCE:

A. F.S. - RIGHT VOCAL CORD LESION
B. RIGHT VOCAL CORD LESION
C. RIGHT ANTERIOR MARGIN
D. RIGHT POSTERIOR MARGIN
E. RIGHT DEEP MARGIN

DIAGNOSIS:

A, B. Right vocal cord lesion (excision): Fragments of at least in situ squamous cell carcinoma, highly suspicious for invasion

C. Right anterior margin (excision): In situ squamous cell carcinoma

D. Right posterior margin (excision): Negative for dysplasia and carcinoma

E. Right deep margin (excision): Negative for carcinoma

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Utility of Laryngeal Margins

- All surgical margin positivities predict tumor recurrence
- BUT T1–T2 glottic tumors completely excised within negative margins may relapse
  – Recurrence rates ranging from 3.1 to 22.8%

Ref: - Fiz, I. , Koelmel, J. & Sittel, C. (2018). Nature and role of surgical margins in transoral laser microsurgery for early and intermediate glottic cancer. Current Opinion in Otolaryngology & Head and Neck Surgery, 26 (2), 78-83. doi: 10.1097/MOO.0000000000000446.

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Case 1

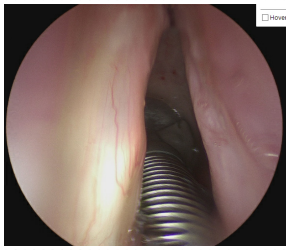
Microdirect laryngoscopy with cordectomy

DIAGNOSIS:

A. Right anterior vocal cord (biopsy): High-grade squamous
dysplasia, superficial strip. The base of the lesion is not well
represented for evaluation of invasive growth.

B. Right vocal cord (excision): Negative for tumor and dysplasia

C. Right anterior vocal cord (excision): Negative for tumor and
dysplasia



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ELS Cordectomy Classification

Classification	Description	Schematic Representation
Type I	Subepithelial	
Type II	Subligamental	
Type III	Transmuscular	
Type IV	Total cordectomy	
Type Va	Extension to the anterior commissure	–
Type Vb	Extension to the arytenoid cartilage	

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ELS Cordectomy Classification

Type Vc	Extension to the false vocal fold	
Type Vd	Extension to the subglottis	
Type VI	Anterior commissure and petiole of the epiglottis	

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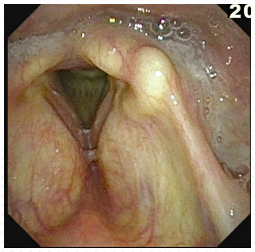
Case 1



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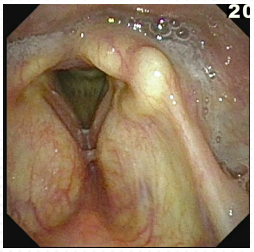
Case 1



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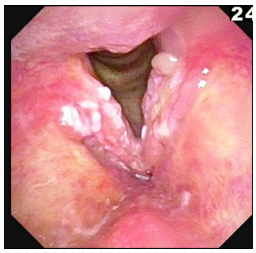
Case 2

60 year old male

- Dyspnonia 4 years
- 30 pack year smoking history
- Drinks 12 beers/week



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Case 2

Microdirect laryngoscopy with biopsy

A. MID LEFT VOCAL CORD
B. ANTERIOR LEFT VOCAL CORD
C. LEFT VOCAL PROCESS
D. MID RIGHT VOCAL CORD

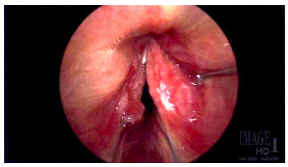
DIAGNOSIS:

A. Mid left vocal cord (biopsy): High grade squamous dysplasia. An invasive component is not identified.

B. Anterior left vocal cord (biopsy): High grade squamous dysplasia. An invasive component is not identified.

C. Left vocal process (biopsy): At least high grade squamous dysplasia. An invasive component cannot be excluded in this specimen.

D. Mid right vocal cord (biopsy): High grade squamous dysplasia. An invasive component is not identified.



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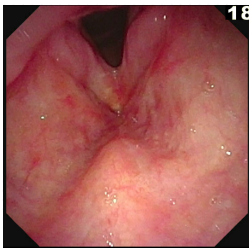
Case 2



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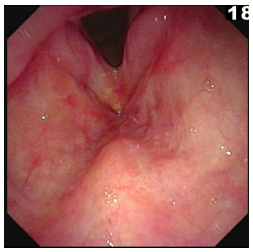
Case 2



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Surgery Vs RT - Survival

J Otolaryngol Head Neck Surg. 2016 Aug 2;45(1):42. doi: 10.1186/s40463-016-0155-1.

Comparison of survival between radiation therapy and trans-oral laser microsurgery for early glottic cancer patients; a retrospective cohort study.

De Santis RJ[1], Poon I[2], Lee J[2], Karam I[2], Enepekides DJ[3], Higgins KM[4].

CONCLUSION: No difference was demonstrated in the 5-year disease-specific survival, disease-free survival, and total laryngectomy-free survival, between the RT and TLM treatment groups. Additionally, both groups showed similar 5-year survival after stratifying by confounding variables.

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Surgery Vs RT - Voice

J Voice. 2019 Mar;33(2):176-182. doi: 10.1016/j.jvoice.2017.10.018. Epub 2017 Dec 8.

Long-term Voice Outcome Following Radiation Versus Laser Microsurgery in Early Glottic Cancer.

Ma Y[1], Green R[2], Pan S[1], McCabe D[1], Goldberg L[1], Woo P[3].

CONCLUSIONS: This is the first multi-modality voice analysis to suggest TLM results in better LTVO than XRT in GRBAS score and objective voice analysis but not in self-perception. These differences may reflect the progressive effects of XRT on glottic tissue. A randomized controlled study is required to confirm our findings.

Otolaryngol Head Neck Surg. 2015 May;152(5):811-9. doi: 10.1177/0194599815577103. Epub 2015 Apr 2.

Voice outcomes following radiation versus laser microsurgery for T1 glottic carcinoma: systematic review and meta-analysis.

Greulich MT[1], Parker NP[2], Lee P[1], Merati AL[3], Misono S[4].

CONCLUSION: VHI scores were comparable following transoral laser microsurgery and radiation therapy for T1 glottic carcinoma in the current literature, suggesting no clinically significant difference in functional voice outcomes between treatment types.

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Surgery Vs RT - Cost

Comparative Study > Acta Otolaryngol. 2020 Nov;140(11):954-958.
doi: 10.1080/00016489.2020.1788723. Epub 2020 Jul 17.

Radiotherapy versus laser microsurgery in the treatment of early glottic cancer

Yolanda Lois-Ortega [1], Fernando García-Curdi [1], José Miguel Sebastián-Cortés [2], Félix De Miguel-García [3], Héctor Vallés-Varela [2], Ana Muniesa-Del Campo [4]

Results: It was found that radiation therapy was approximately four times more expensive than TLM.

Conclusions: This study suggests that TLM should be the preferred treatment option for treating early glottic cancer in Canada as it is the most economical and has been shown in previous studies to be as effective as radiation therapy in both cure rates and quality of life.

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Case 3

62 year old male

- Dysphonia 3 months
- Smoker
- Direct microlaryngoscopy (Referring surgeon)
  - SCC, moderately differentiated

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Case 3

DIAGNOSIS:

A. Deep margin: Negative for tumor

B. Posterior margin: Negative for tumor

C. Anterior margin: Negative for tumor

D. Right vocal cord lesion: Focus of in-situ squamous cell carcinoma (1 mm). No invasive component identified. Subepithelial tissues with chronic inflammation and fibrosis.


IMG001

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Case 3

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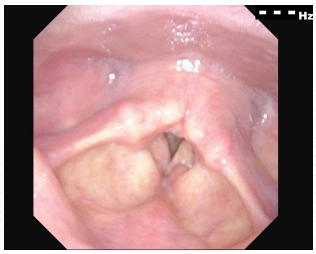
Case 3



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Open Partial Laryngeal Surgery

- Limited indications now
  - Increased morbidity
  - Inferior outcomes (cf TOL)
- Indications
  - Poor endoscopic access
  - Limited recurrence post-RT

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Surgical Options

- Vertical
  - Vertical Partial Laryngectomy
- Horizontal
  - Horizontal Supraglottic Laryngectomy
  - Supracricoid Laryngectomy

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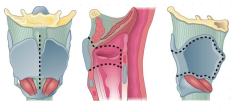
VPL

Indications
- Lesion of mobile cord up to AC or to vocal process
- Subglottic extension <5mm

Outcomes
- T1 local control >90%
- T2 local control <80%

Cautions
- AC involvement
- Extension beyond glottis
- Impaired cord mobility



Variants
- Frontolateral
- Posterolateral
- Extended

Reconstruction
- Strap muscle rotation
- Imbrication

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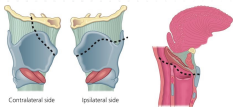
SUPRAGLOTTIC LARYNGECTOMY

Resects:
- Epiglottis (+/- hyoid), pre-epiglottic space, thyrohyoid membrane, upper ½ thyroid cartilage, supraglottic mucosa

Indications
- Supraglottic lesion
- True VCs mobile
- No cartilage invasion
- 5mm clear of AC

Outcomes
- >90% control for T1/T2



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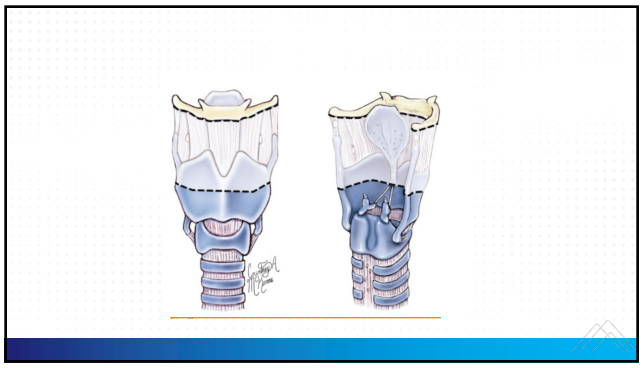

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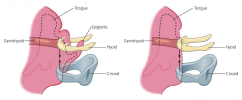
SUPRACRICOID LARYNGECTOMY

2 options

- CHEP- glottic lesion
  - T1b with AC involvement
- CHP- supraglottic lesion
  - Supraglottic lesion extending to glottis
  - T3 transglottic lesion with impaired mobility of 1 VC



Significant speech/swallowing issues

- NGT 30-365 days
- TL in 10%

High success rates

- Excision of B/L paraglottic spaces, pre-epiglottic space and thyroid cartilage

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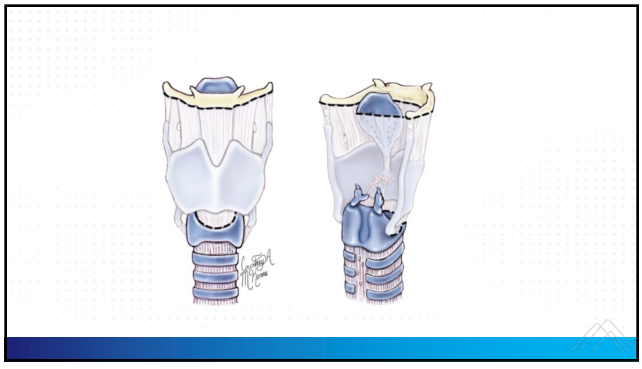

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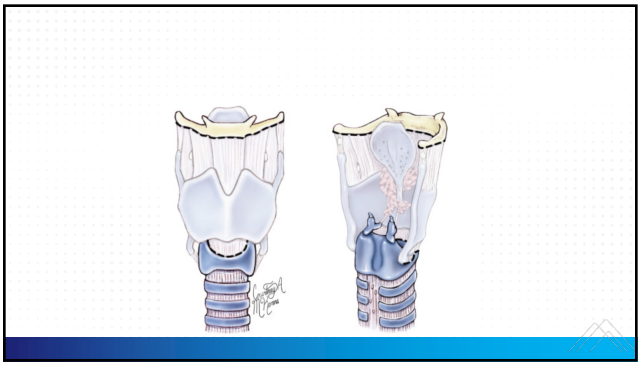

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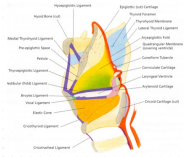
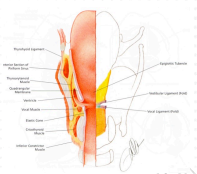
MEMBRANES OF THE LARYNX

Extrinsic

- Thyrohyoid
- Hyoepiglottic
- Cricotracheal
- Aryepiglottic





Intrinsic

- Quadrangular membrane
- Conus elasticus

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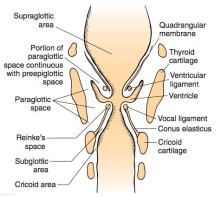
INTRINSIC MEMBRANES

Quadrangular membrane

- Epiglottis to arytenoid/corniculate
- Covered with mucosa to form AE fold
- Separates larynx and hypopharynx



Conus elasticus

- Cricoid cartilage
- Thyroid-arytenoid
- Free edge is vocal ligament

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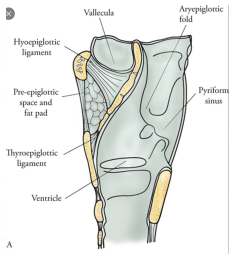
LARYNGEAL SPACES

Pre-epiglottic space

- Thyroid cartilage/thyrohyoid membrane
- Epiglottis/thyroepiglottic lig
- Hyoepiglottic lig



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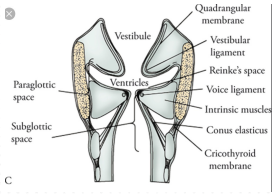
LARYNGEAL SPACES

Paraglottic space

- Thyroid cartilage
- Conus elasticus
- Cricoid cartilage
- Quadrangular membrane
- Pyriform fossa



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RELEVANCE

- Membranes prevent spread of cancer
  - Supraglottic tumors access pre-epiglottic space via glandular perforations in epiglottis
- Once into the spaces can spread quickly
  - Paraglottic and pre-epiglottic are continuous
  - Transglottic tumors
- Important to recognize for accurate staging

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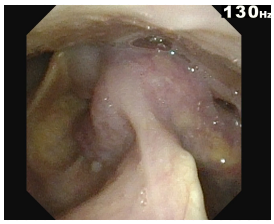
Case 4

73 year old male

- Dysphonia 6 weeks
- PMHx Lung Cancer
- Ex smoker, drinker, WTC



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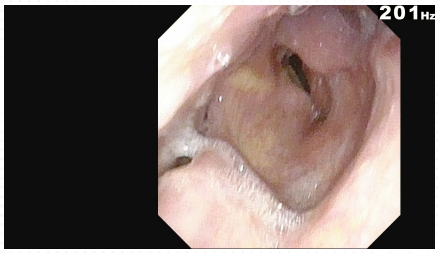
Case 4



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RT Descalation Larynx

- No evidence
- Subject to further investigation!

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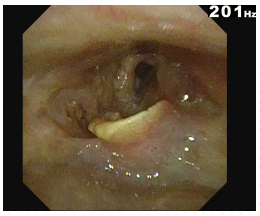
Case 5

60 year old male

- PMHx T4N1M0 transglottic SCC HPV negative
- Treated with ChemoXRT + Immunotherapy
- Tracheostomy but then decannulated
- Prior to completion of immunotherapy hospitalized for pneumonia likely due to aspiration
- Tracheostomy and PEG
- Repeat PET scan demonstrated avidity



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Case 5

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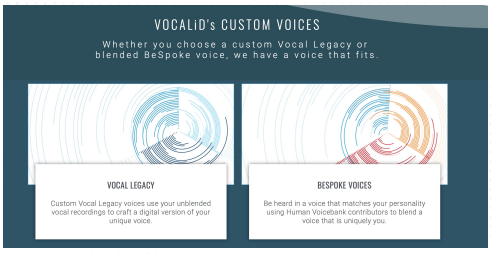
Voice Rehabilitation – Present & The Future



https://vocalid.ai

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Swallow Rehabilitation – Present & The Future

Present

- Swallow Therapy
- Surgery
  - Dilation
  - Botox

Future

- CN Stimulation?

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Laryngeal Chondrosarcoma

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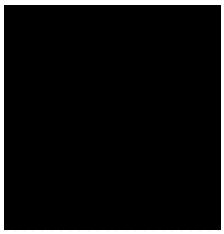
Case 6

54 year old male

- Dysphonia 2 years
- Outside workup including CT and biopsy demonstrated a low grade chondrosarcoma
- Referred in for partial laryngeal surgery



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Case 6

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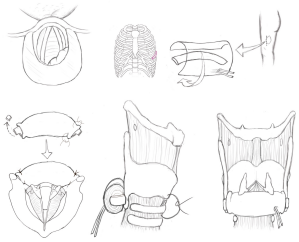
Rib Graft + Fascial Free Flap Reconstruction



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Case 6

65

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The Mount Sinai Team

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66

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Summary

- Always consider the oncologic and functional
  - Voice, airway and swallow
- Know your trials
- Be proficient at management of early to late
  - Endoscopic
  - Open
- Think innovatively

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