

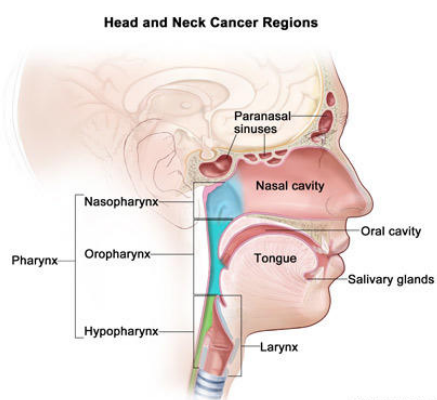


Disclosures

DISPOSISJON

- DEFINISJON
- EPIDEMIOLOGI OG ETIOLOGI
- UTREDNING
- KIRURGISK BEHANDLING
- OPPFØLGING
- PROGNOSE
- FREMTIDEN

DEFINISJON



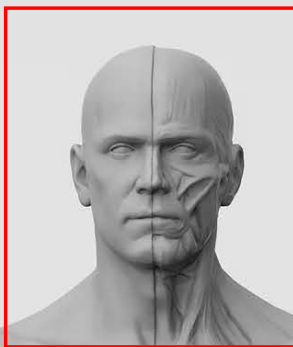
Plateepitelkarsinom > 90%

DEFINISJON

Parenchymatøs

- Thyroidea
- Spyttkjertler

Lymfeknuter



Hud

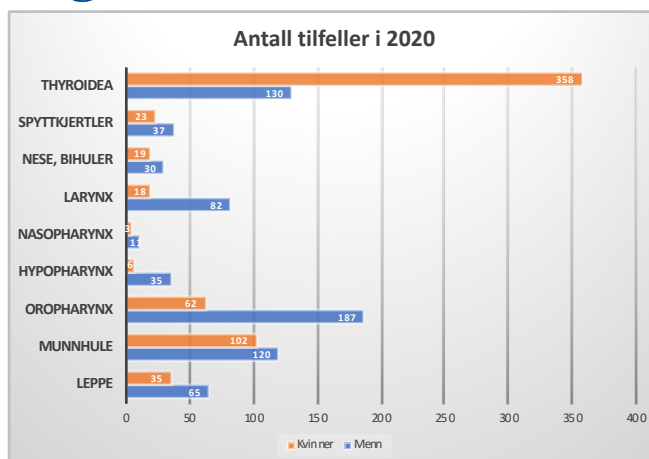
- Malignt melanom:
 - Hode-hals (ca 30 % av 2000)
- Non-melanom hud cancer (totalt ca 2000 pr år)
 - 3/4 av lokalisert i hode-hals

EPIDEMIOLOGI OG ETIOLOGI

Globalt:	890 000/år
Norge:	700/år (eksludert thyroidea)
Gjennomsnittsalder:	65 år
Menn >> kvinner	

Bray et al. CA Cancer J Clin 2018
Cancer Registry of Norway. Cancer in Norway 2020.

Tall fra Norge



Cancer Registry of Norway. Cancer in Norway 2020.

EPIDEMIOLOGI OG ETIOLOGI

- Økt incidens av oropharynx cancer

- HPV +

USA 1980 16,3%

USA 2000 72,7%

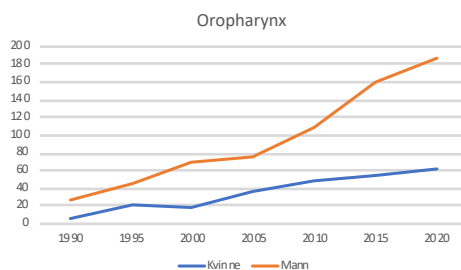
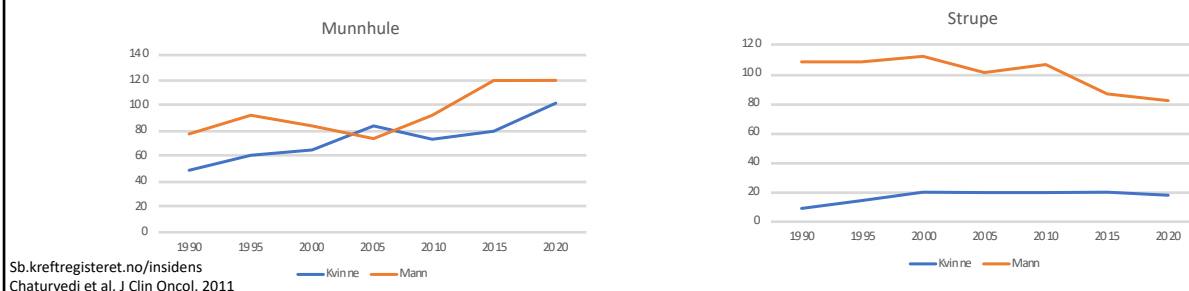


Foto: Colourbox.com

Sb.kreftregisteret.no/insidens
Gillison et al. J Clin Oncol. 2015

EPIDEMIOLOGI OG ETIOLOGI

- Økt antall kvinner med tungecancer
- Redusert incidens av tobakk-relatert sykdom



EPIDEMIOLOGI OG ETIOLOGI



Epstein-Barr Virus (EBV)

Human papillomavirus (HPV)



Argiris et al. Lancet. 2008

UTREDNING

- Sykehistorie
- Klinisk undersøkelse
- Våken-skopi
- Narkose-skopi
- Prøvetakning
- Radiologi



TNM
Guidelines



Behandling

Sykehistorie

VARSELSSYMPTOM – Screening på «organsystem»

- Sår, belegg eller tumor
- Tumor colli hos voksne
- Stemmeendring, heshet
- Dysfagi
- Odynofagi, trismus, tenner som løsner, proteser som ikke lenger passer etc.
- Otalgi (referert smerte)
- Nasalstenose, ny, særlig ensidig (sinusitt)
evt. med sekresjon, blodig sekresjon?
- Ensidig og vedvarande sekretorisk otitt
- Hjernenerveaffeksjon



WEEKS

Klinisk undersøkelse + skopi



Vevsprøver - FNAC

- Highly sensitive, specific and accurate
- Tandon et al. Systematic review and metaanalysis. Head Neck 2008

Results

Systematic review identified 30 studies; 3459 FNAC aspirates from all head and neck sites were included. Overall results were as follows: sensitivity, specificity, accuracy, positive predictive value (PPV), and negative predictive value (NPV) were 89.6%, 96.5%, 93.1%, 96.2%, and 90.3%, respectively. Two thousand seven hundred two head and neck aspirates were included in our institutional review. Sensitivity, specificity, PPV, NPV, and accuracy were 89.5%, 98.5%, 97.3%, 94.0%, and 95.1%, respectively.

Radiologi

- CT hals og thorax
- Ultralyd
- MR – bløtvev, spyttkjertler, perinevral vekst?
- PET CT – origo, utbredelse, “avklaring av utilgjengelige lesjoner”, responseevaluering



TNM

- TNM angis i stadium I-IV
 - Lavt stadium (I-II)
 - Avansert stadium (III-IV)

Hensikt

Planlegging av behandling

Yte prognostisk informasjon

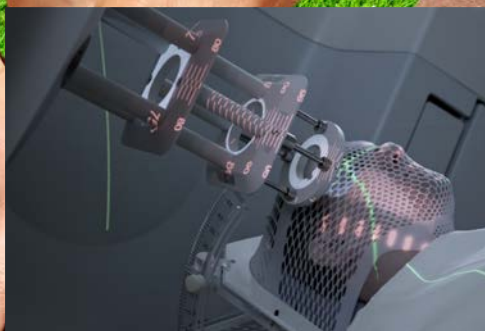
Objektiv mål på utbredelse for sammenlikning i studier

«Globalt språk»

BEHANDLING



Foto: Instagram operasjonssykepleierne



BEHANDLING

○ Lavt stadium (I-II) 30-40%

Tabel 4. Behandlingsmodalitet ved forskjellige stadier

Stadium	I	II	III	IV
TNM	T1, N0	T2, N0	T1, N1	T2, N1
T position	Monoterapi:			Kombinationsbehandling:
N position	Kirurgi, evt. strålebehandling			Kirurgi og strålebehandling

○ Avansert stadium (III-IV) >60%

DAHANCA: Nationale retningslinier for Mundhulekræft 2016

BEHANDLING

- Multidisiplinært team møte
 - Før eller etter behandlingsvalg?
 - *Kirurg, onkolog* (medisinsk og stråle), *patolog, radiolog, kreftsykepleier, tannlege/oralkirurg, ernæringsfysiolog, logoped, sosionom, fysioterapeut etc.*
 - Assosiert med bedret prognose.

Eskander et al. Laryngoscope 2014



BEHANDLING

- | | |
|---|---|
| <ul style="list-style-type: none"> ○ Primær kirurgi <ul style="list-style-type: none"> ○ Leppe ○ Munnhule ○ (Orofarynx T1) ○ (Hypofarynx T1) ○ Larynx T1, T4 ○ Nese, bihuler ○ Spyttkjertler ○ Halsglandelmetastaser <ul style="list-style-type: none"> ○ Avhengig av origo ○ Origo incerta N1 | <ul style="list-style-type: none"> ○ Primær stråleterapi (kjemo) <ul style="list-style-type: none"> ○ Oropharynx ○ Hypopharynx ○ Nasopharynx ○ Larynx T2-T3 ○ T4b ○ Halsglandelmetastaser <ul style="list-style-type: none"> ○ >N1 |
|---|---|



Onkologisk behandling

○ Primær stråleterapi + (kjemo)

- Kurative doser 60-70 Gy
- Elektive doser 45-50 Gy
- Cisplatin*
- EGFR**

○ Strålesensitizers

○ Adjuvant stråleterapi (kjemo)***

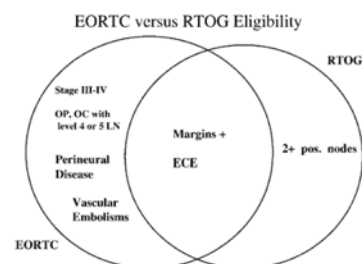


FIGURE 1. Eligibility criteria in EORTC 22931 and RTOG 9501 trials. OP, oropharynx; OC, oral cavity; LN, lymph node; ECE, extracapsular extension.

*Pignon et al. MACH-NC Radiother Oncol 2009

**Blanchard et al. MACH-NC Ann Oncol 2016

** Bonner et al. NEJM 2006

*MACH-NC > 17 000 pas med lokalavansert sykdom.

Konkomitant CRT absolutt reduksjon i 5-års dødelighet på 6,5%

***Bernier et al. Head Neck 2005

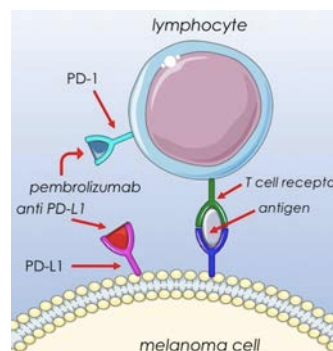
***Bernier et al. NEJM 2004

***Cooper et al. NEJM 2004

Onkologisk behandling

○ Ikke-kurabel

- Palliativ stråleterapi
- Div. kjemoterapi
 - EXTREME*
- Immunoterapi**



Modified from: National Cancer Institute website, <https://www.cancer.gov/news-events/cancer-currentsblog/2015/pembrolizumab-nsclc> and Servier Medical Art website, <http://smart.servier.com/>

*Vermorken et al. NEJM 2008

**Burtneess et al. The Lancet 2019 - Pembrolizumab

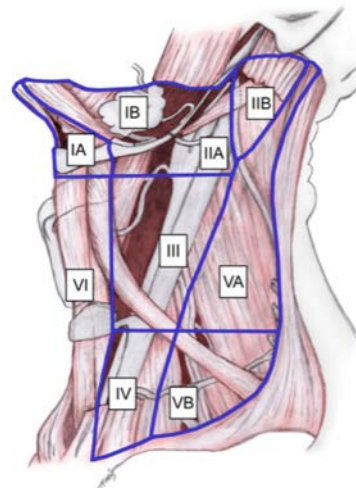
**Ferris et al. Oral Oncol 2018 - Nivolumab

KIRURGISK BEHANDLING

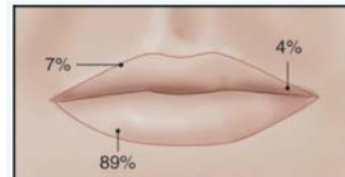
Praktiske eksempler

Halsglandeldisseksjon

- Elektiv
- Terapeutisk
- Klassifisering basert på involverte LK-stasjoner og omfang
 - **Selektiv**
 - Eks. Supraomohyoidalt I-II-III
 - **Radikal**
 - Regio I-V +/- IJV, CNXI, SCM



Leppe



Females
5%
Males
95%

Jatin Shah's Head and Neck Surgery and Oncology 4th ed.

Munnhule - tunge

T – Primary Tumour

TX Primary tumour cannot be assessed

To No evidence of primary tumour

Tis Carcinoma in situ

T1 Tumour 2 cm or less in greatest dimension and 5 mm or less depth of invasion*

T2 Tumour 2 cm or less in greatest dimension and more than 5 mm but no more than 10 mm depth of invasion or Tumour more than 2 cm but not more than 4 cm in greatest dimension and depth of invasion no more than 10 mm

T3 Tumour more than 4 cm in greatest dimension or more than 10 mm depth of invasion

T4a (*Lip*) Tumour invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin (of the chin or the nose)

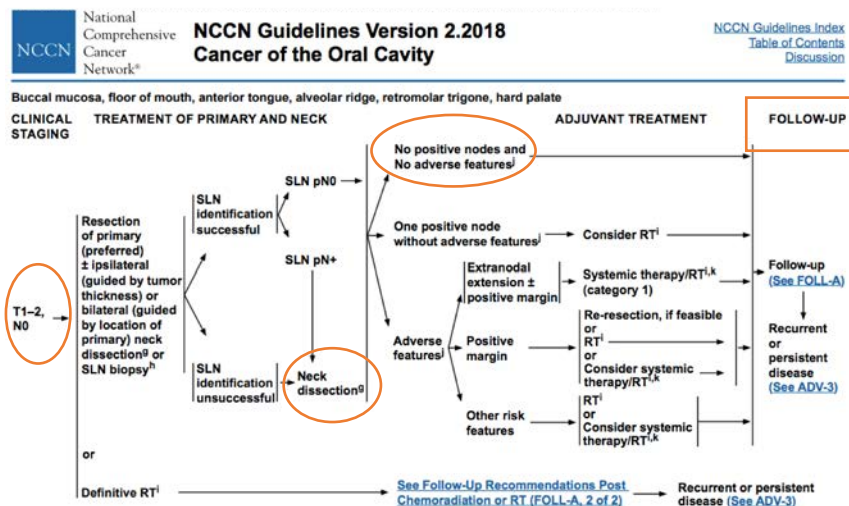
T4a (*Oral cavity*) Tumour invades through the cortical bone of the mandible or maxillary sinus, or invades the skin of the face

T4b (*Lip and oral cavity*) Tumour invades masticator space, pterygoid plates, or skull base, or encases internal carotid artery

Tabel 4. Behandlingsmodalitet ved forskellige stadier

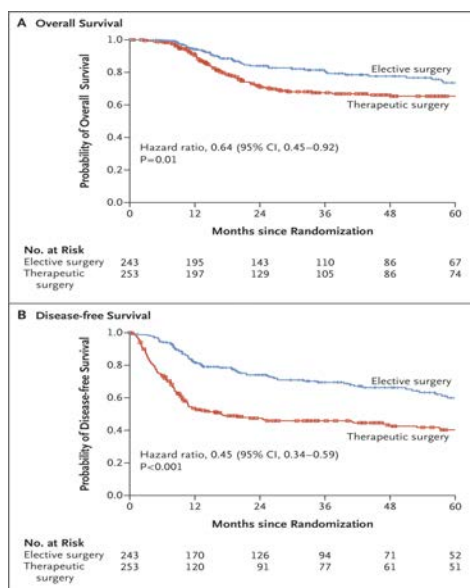
Stadium	I	II	III				IV
TNM	T1,N0	T2, N0	T1,N1	T2,N1	T3, N0	T3, N1	≥T4, ≥ N0
T position	Monoterapi:				Kombinationsbehandling:		
N position	Kirurgi, evt. strålebehandling				Kirurgi og strålebehandling		

DAHANCA: Nationale retningslinier for Mundhulekræft 2016



Munnhule

Elective versus Therapeutic Neck Dissection in Node-Negative Oral Cancer



D'Cruz et al. NEJM 2015





Foto: T. Osnes Presentasjon: Kreft i hovud og hals 2018

Obturator

Gjennoppretter skillet mellom munnhule og nese/bihule

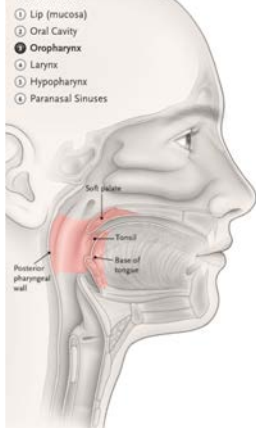


Oropharynx

Treatment Options for Squamous-Cell Carcinoma of the Head and Neck

TUMOR SITES

- ① Lip (mucosa)
- ② Oral Cavity
- ③ **Oropharynx**
- ④ Larynx
- ⑤ Hypopharynx
- ⑥ Paranasal Sinuses



EARLY STAGE

LOCALLY ADVANCED STAGE

Description

Includes base of tongue, tonsil, posterior pharyngeal wall, soft palate

Small primary tumors with no or minimal lymph-node involvement

Immunohistochemical testing for p16 (a marker for human papillomavirus [HPV] positivity) must be performed; p16 expression (representing HPV-positive disease) and no p16 expression (HPV-negative disease) are treated similarly, according to the relative downstaging of p16-positive (HPV-associated) disease in the AJCC 8th edition cancer staging manual

No p16 expression (HPV-negative disease)

Stages I and II without nodal disease (T1 or T2, N0) and stage III with minimal nodal disease (T1 or T2, N1)

Positive p16 expression (HPV-associated disease)

Stage I disease (T1 or T2, N0)

Initial Treatment of the Primary Tumor

OPTION 1

Consider enrollment in clinical trials when feasible

Primary definitive radiotherapy alone (common)

or

Consider concurrent systemic therapy with radiotherapy for bulky T2 disease (especially in HPV-positive disease) and N1 disease

OPTION 2

Surgical resection of the primary tumor: minimally invasive techniques (e.g., transoral robotic surgery or transoral laser microsurgery) in selected patients may be feasible, well-tolerated, and effective

Therapy for the Neck

There is a high risk of occult neck metastases in association with radiotherapy alone or systemic therapy concurrent with radiotherapy, even in the clinically node-negative neck; consider elective nodal therapy (i.e., bilateral radiotherapy to the neck for midline tumors or ipsilateral radiotherapy to the neck)

There is a high risk of occult neck metastases in association with radiotherapy alone or systemic therapy concurrent with radiotherapy, even in the clinically node-negative neck; consider selective or elective ipsilateral neck dissection, or consider bilateral neck dissection for midline primary tumors (radiotherapy can less commonly be

References

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THE NEW ENGLAND JOURNAL OF MEDICINE

REVIEW ARTICLE

David L. Longo, M.D., Editor
Head and Neck Cancer
 Laura Q. M. Chow, M.D.

Oslo universitetssykehus



Tonsillecancer

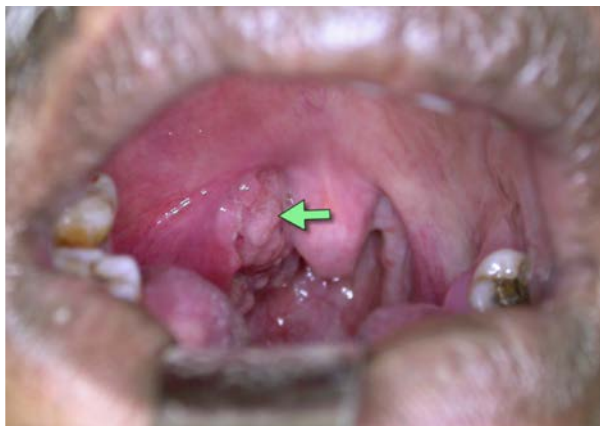


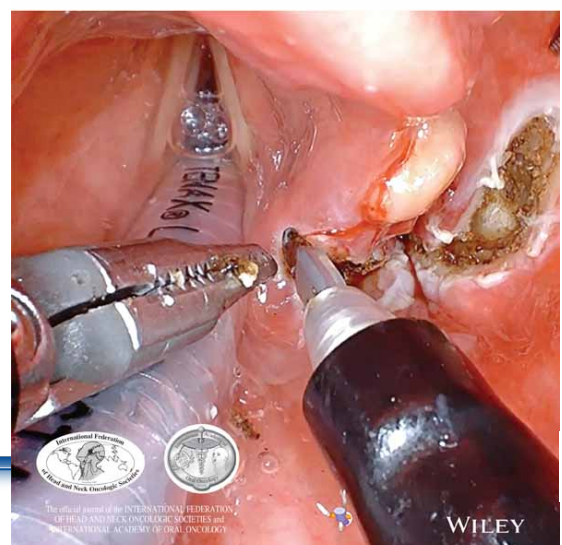
Foto: T. Osnes Presentasjon: Krefit i hodet og hals 2018

Oslo universitetssykehus

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HEAD&NECK

JOURNAL FOR THE SCIENCES AND SPECIALTIES OF THE HEAD AND NECK



Hypopharynx

Treatment Options for Squamous-Cell Carcinoma of the Head and Neck

TUMOR SITES

- ① Lip (mucosa)
- ② Oral Cavity
- ③ Oropharynx
- ④ Larynx
- **Hypopharynx**
- ⑤ Paranasal Sinuses

EARLY STAGE

LOCALLY ADVANCED STAGE

Description

Includes the pyriform sinuses, posterior surface of the larynx and postcricoid area, and inferior posterior and inferolateral pharyngeal walls

Stage III or IV

T2 or T3, N0-N3, if amenable to pharyngectomy with partial or total laryngectomy

or

Very locally advanced stage T4a, N0-N3

Initial Treatment of the Primary Tumor

Multidisciplinary assessment with goals of preservation of organ function and survival free of laryngopharyngeal dysfunction (speech, swallowing, and airway patency)

OPTION 1

Perform definitive radiotherapy alone if patient is medically unfit for chemotherapy

or

Perform sequential chemotherapy and then radiotherapy if concurrent therapy would be associated with an unacceptable adverse-events profile; however, this treatment is associated with a lower rate of larynx preservation and a higher risk of local recurrence

OPTION 2

Surgery with partial laryngectomy or endoscopic or open partial resection if indicated for small primary (T1 or T2) tumors if laryngeal conservation is feasible, tumor exposure is adequate, and negative margins can be achieved

or

Surgery: total laryngopharyngectomy plus neck dissection plus hemithyroidectomy or total thyroidectomy for extensive T3 or large T4a lesions and poor pretreatment laryngeal function

OPTION 3

Consider induction chemotherapy followed by radiotherapy alone or sequential therapy with induction chemotherapy followed by concurrent chemoradiotherapy for large bulky tumors with individualization for site, response, toxic effects, and locoregional control requirements

NEW ENGLAND JOURNAL of MEDICINE

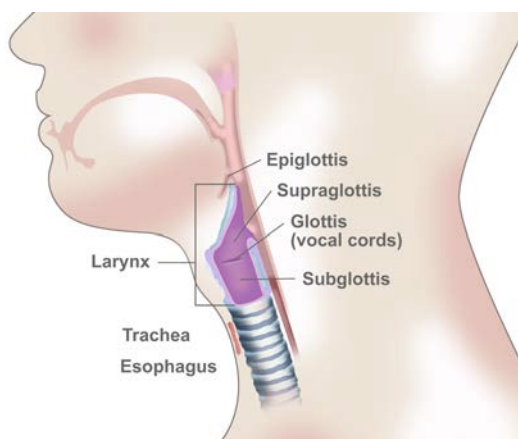
REVIEW ARTICLE

Dan L. Longo, M.D., Editor

Head and Neck Cancer

Laura Q.M. Chow, M.D.

Larynx



- Primær kirurgi
 - T1a glottis cancer
 - T4a glottis cancer
 - Selekterte T1-2 øvrige
- Primær (C)RT

Larynx – glottis T1a



Foto: T. Osnes Presentasjon: Kreft i hovud og hals 2018



Larynx - laryngectomy

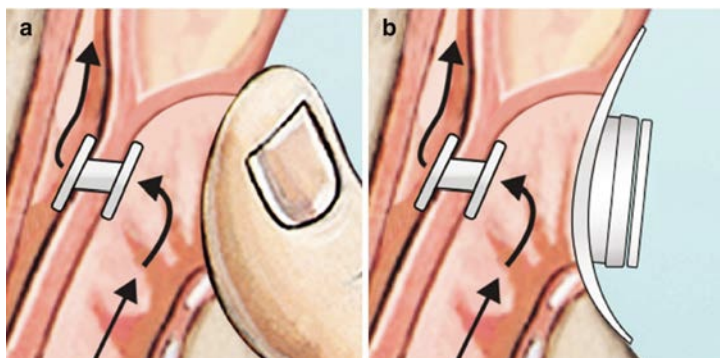


Jatin Shah's Head and Neck Surgery and Oncology 4th ed.



Larynx – laryngectomy, talerehabilitering

- Taleprotese Provox ©
- (Talevibrator)
- (Øsofagusstemme)



Shout at Cancer Choir

Nese, bihuler

Lokalisering

- Hud
- Cavum nasi
- Bihuler
 - Maxillaris
 - Ethmoidal
 - Sphenoid
- Skallebasis

Histologi

- SCC
- Adenocarcinom
- Adenoid cystisk carcinom
- Mucoepidermoid carcinom
- Melanom
- Sinonasalt udifferensiert carcinom SNUC
- Esthesionevroblastom
- ++



Nese, bihuler, skallebasis

- Behandling særlig avhengig av histologi og operabilitet
- Tilganger: Endoskopisk, åpne, kombinasjoner, kraniofacial (NKIR)

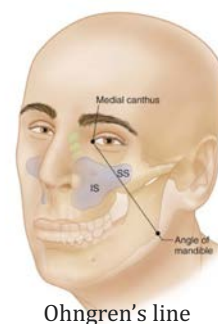
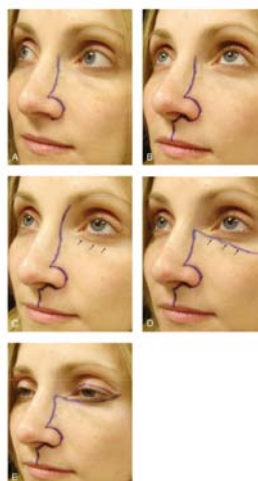


Foto: T. Osnes Presentasjon: Kreft i hovud og hals 2018



Thyroidea

○ KIRURGI

- Hemithyroidektomi
- Total thyroidektomi
- Halsglandeldisseksjon
 - Sentralt (VI)
 - Lateralt (II-IV)

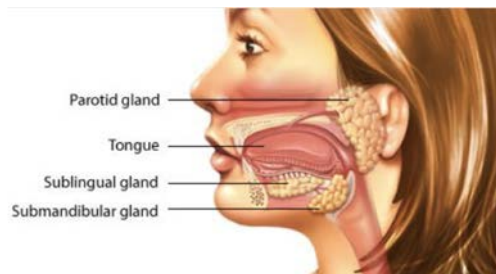
○ Øvrig behandling

- Suppresjonsbehandling
- RAI
- Etanol
- Øvrig medikamentell behandling
- (Stråleterapi)



Spyttkjertel

- Mucoepidermoid
- Acinærcelecarcinom
- Adenoidcystisk
- +++



Forekomst		Andel malign
80%	Gl. Parotis	30%
10%	Gl. Submandibularis	50%
10%	Små spyttkjertler	50%
1%	Gl. Sublingualis	90%

Spyttkjertel

- Parotis
 - Parotidectomi +/- HLD.
 - Reseksjon av n. Facialis dersom tegn til innvekst **pre-** el. peri-operativt. Statisk og dynamisk rekonstruksjon
- Submandibularis
 - HLD
- Små spyttkjertler - individualisert
- Postoperativ stråleterapi dersom høygradig malign eller ufrie reseksjonsrender

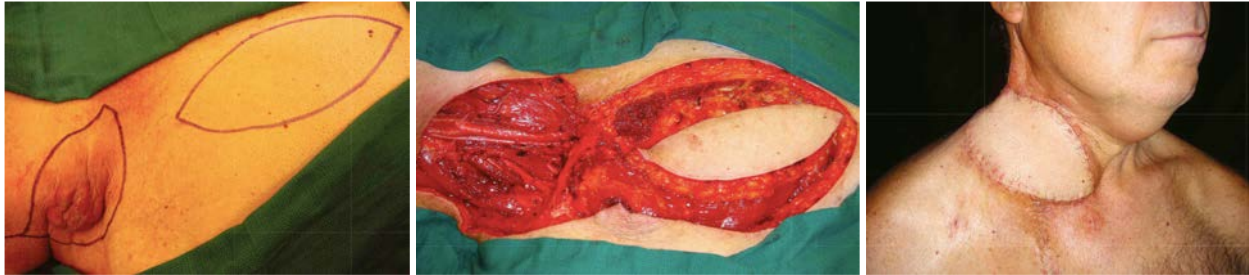
Rekonstruksjon

- Rekonstruksjon
 - Primær lukning
 - Sekundærtilheling
 - Hud tx
 - Lokal lapp
 - Regional lapp
 - Fri mikrovaskulær lapp
 - Protese

Lokal lapp



Regional lapp



Jatin Shah's Head and Neck Surgery and Oncology 4th ed.

Fri mikrovaskulær lapp

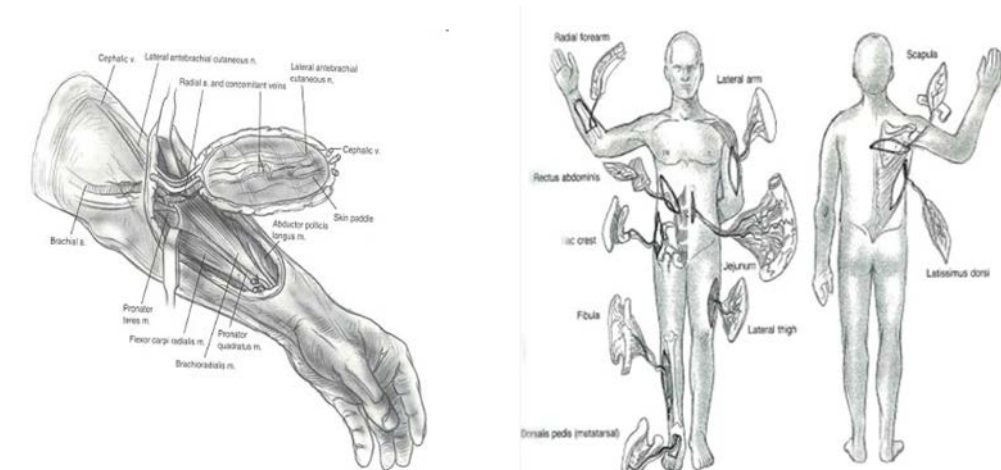


Foto: T. Osnes Presentasjon: Krefte i hode og hals 2018

Ektoprotese

OPPFØLGING

- Primære operasjonspasienter
 - Patologisvar - MDT – stillingstakning behov for adjuvant terapi
 - Avhengig av stadium, render, LK-status (ekstranodal ekstensjon)
- Primære (C)RT pasienter
 - 6 ukers kontroll – smerter, ernæring, progresjon?
 - 12 ukers kontroll - Responsevaluering

Responsevaluering

- PET CT
 - N+
 - Avansert T-stadium
 - (PET CT planlagt)
- CT el. MR
 - N0



Responsevaluering



OPPFØLGING

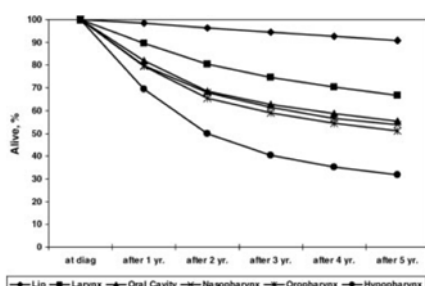
- 1-2 år hver 3 mnd.
- 3-4 år hver 4 mnd.
- 5 år hver 6 mnd.
- Rehabilitering
- Restpotensiale for kirurgi/ salvage
- Samtale
- Klinisk undersøkelse
- UL hals
- Øvrig radiologi kun på indikasjon

OPPFØLGING – Sekveler/morbiditet

- Svelgfunksjon og ernæring
 - Spyttproduksjon nedsatt, tørre slimhinner/seigt slim
 - Stivt arrvev
 - Aspirasjon
- Tale
 - Etter laryngektomi
- Tannproblem
- Kosmetisk
- Lymfødem, utvendig og innvendig
- Osteoradionekrose
- Hørsel (strålefelt)
- Fatigue

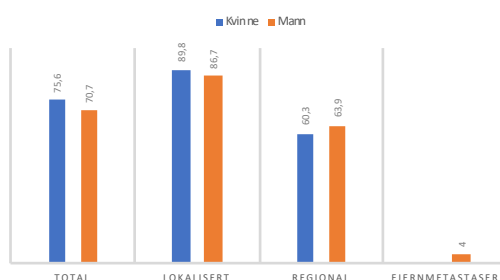
PROGNOSE

Avhengig av: TNM-stadium,
lokalisasjon, HPV, komorbiditeter



Cancer Registry of Norway. Cancer in Norway 2020.
Cooper et al. Head Neck 2009

5 ÅRS OVERLEVELSE C00-14



FREMTIDEN?

- Organbevarende behandling
- Individualisert behandling
- Eskalering og De-eskalering*
- TOS
- Immunoterapi
- Protonbestråling**

*Mehanna et al. Lancet 2019

*Gillison et al. Lancet 2019

** Blanchard et al. Semin Radiat Oncol 2018

FREMTIDEN?

Prospective phase II Open-Label Randomized Controlled Trial to Compare Mandibular Preservation in Upfront Surgery With Neoadjuvant Chemotherapy Followed by Surgery in Operable Oral Cavity Cancer

cT2-T4 and N0/N+ (AJCC 7th ed.)

Surgery with segmental resection followed by adjuvant treatment

vs

Two cycles of neoadjuvant chemotherapy followed by surgery dictated by postchemotherapy disease extent.

Mandibular preservation 16/34 in intervention group. Similar DFS and OS after 3,6 years.

Chaukar et al. JCO 2021

FREMTIDEN?

- Mayo Clinic - Phase 2 - Oropharynx HPV +
 - Primary surgery (TOS) and neck dissection followed by dose de-escalated RT (30 Gy or 36 Gy) were compared with a cohort of patients who received standard adjuvant therapy (60 Gy).

TABLE 2 Summary of survival rates for standard and de-escalation cohorts

Outcome	Rate (95% CI; number still at risk)	
	Standard, N = 115	De-escalation, N = 79
Local recurrence-free survival		
1 year	99 (97-100; 99)	97 (94-100; 75)
2 year	99 (97-100; 95)	97 (94-100; 72)
3 year	99 (97-100; 84)	96 (92-100; 34)
Regional recurrence-free survival		
1 year	98 (96-100; 99)	99 (96-100; 75)
2 year	98 (96-100; 94)	99 (96-100; 72)
3 year	98 (96-100; 84)	99 (96-100; 34)
Distant metastases-free survival		
1 year	96 (93-100; 98)	99 (96-100; 75)
2 year	92 (87-98; 90)	95 (90-100; 72)
3 year	91 (86-97; 81)	91 (85-98; 34)
PFS		
1 year	94 (89-98; 96)	95 (90-100; 75)
2 year	90 (84-96; 89)	91 (85-98; 72)
3 year	90 (84-96; 81)	87 (79-95; 34)

Moore et al. Head Neck 2021

FREMTIDEN?

ECOG-ACRIN E3311 – Phase 2 RCT

- Reduced vs. standard dose PO(C)RT for resected (TOS) stage III-IVa (AJCC 7th ed.) HPV + OPC

○ A low risk	PFS 96,9%
○ B intermediate risk 50 Gy	PFS 94,9%
○ C intermediate risk 60 Gy	PFS 96,0%
○ D high risk 66 Gy + cisplatin	PFS 90,7%

- *Primary TOS and reduced postoperative RT result in outstanding oncologic outcome and favorable functional outcomes in intermediate risk HPV + OPC*

Ferris et al. JCO 2021

FREMTIDEN?

- Keynote 689 trial – RCT Phase 3 – *“Study of pembrolizumab given prior to surgery and in combination with radiotherapy given post-surgery for advanced head and neck cell carcinoma”*

- Keynote-412 trial – RCT Phase 3 – *Evaluating efficacy and safety of pembrolizumab or placebo given concomitantly with CRT followed by maintenance pembrolizumab therapy or placebo in patients with LA HNSCC*

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