REIRRADIATION OF HEAD & NECK TARGETS

WORKSHOP-Current challenges of patient re-irradiation

6-7 september 2018, Stockholm, Sweden

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STOCKHOLM

KAROLINSKA UNIVERSITY HOSPITAL

Outline of Presentation

1. Primary tumour: Basic treatment principles

2. Reirradiation: Interpretation of published data

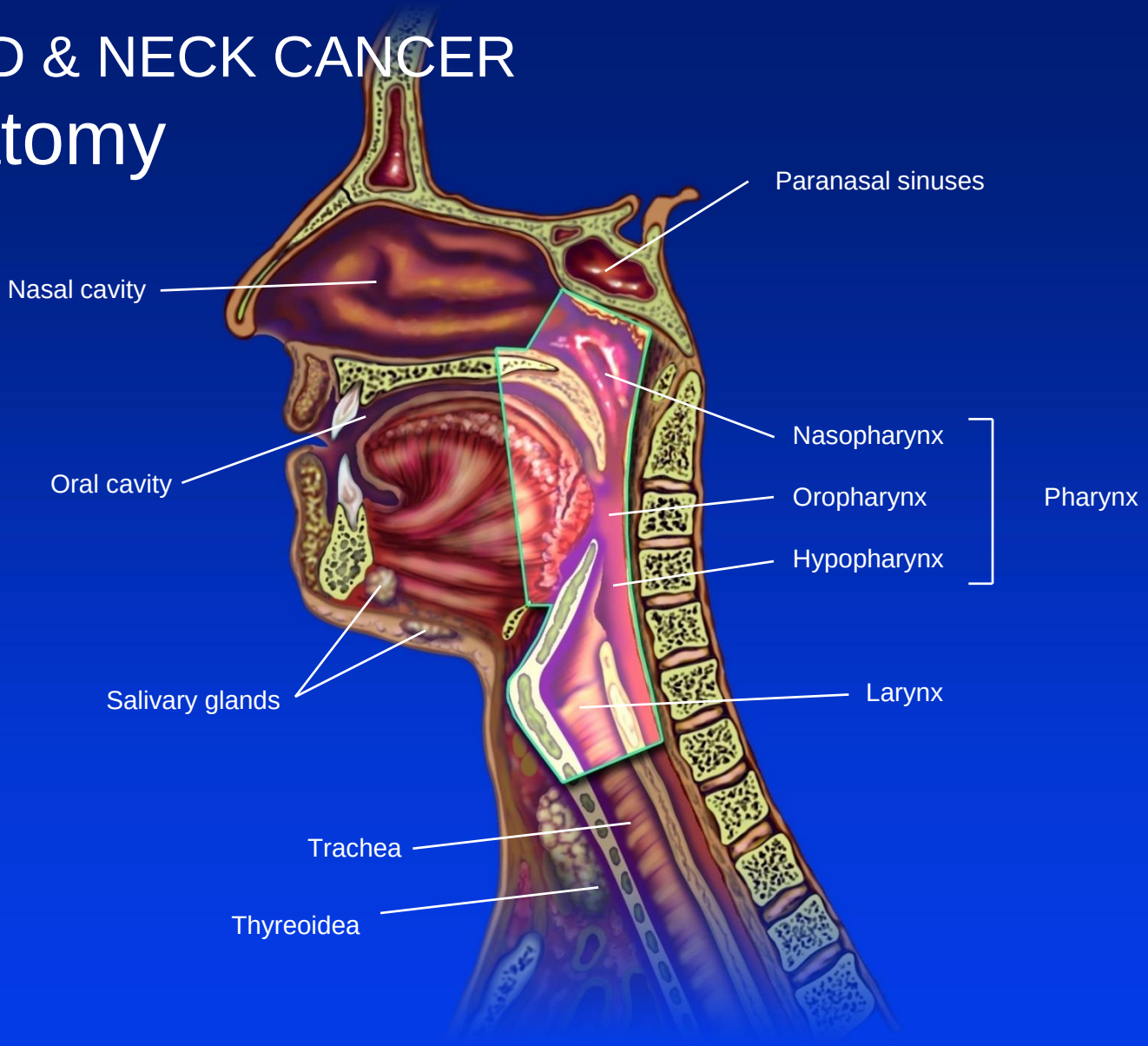
Conclusions; potential guidelines for the clinic

HEAD AND NECK CANCER

- ~ 6% of all malignancies
- ~ (50-)75% are locally advanced, not resectable

HEAD & NECK CANCER

Anatomy



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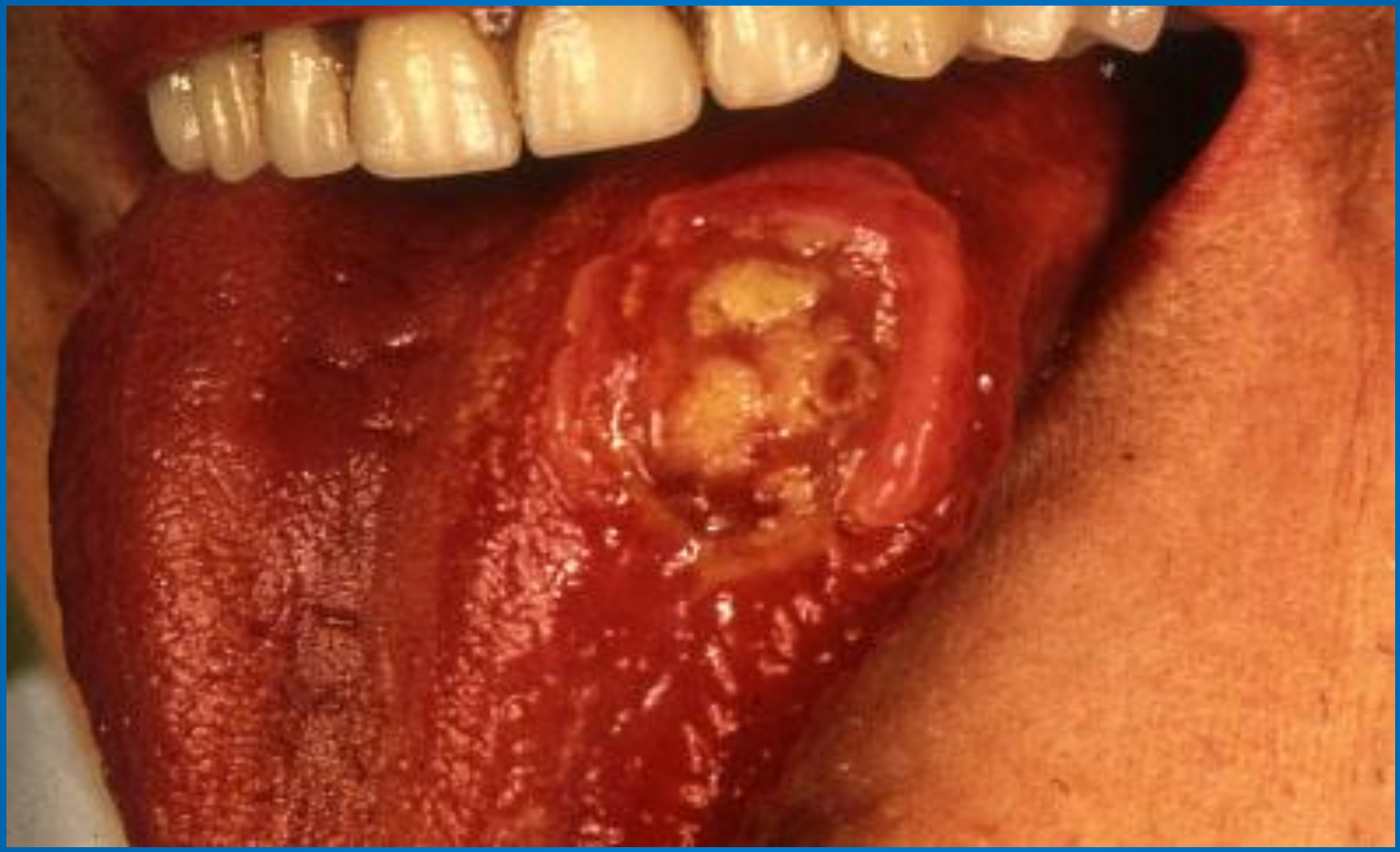
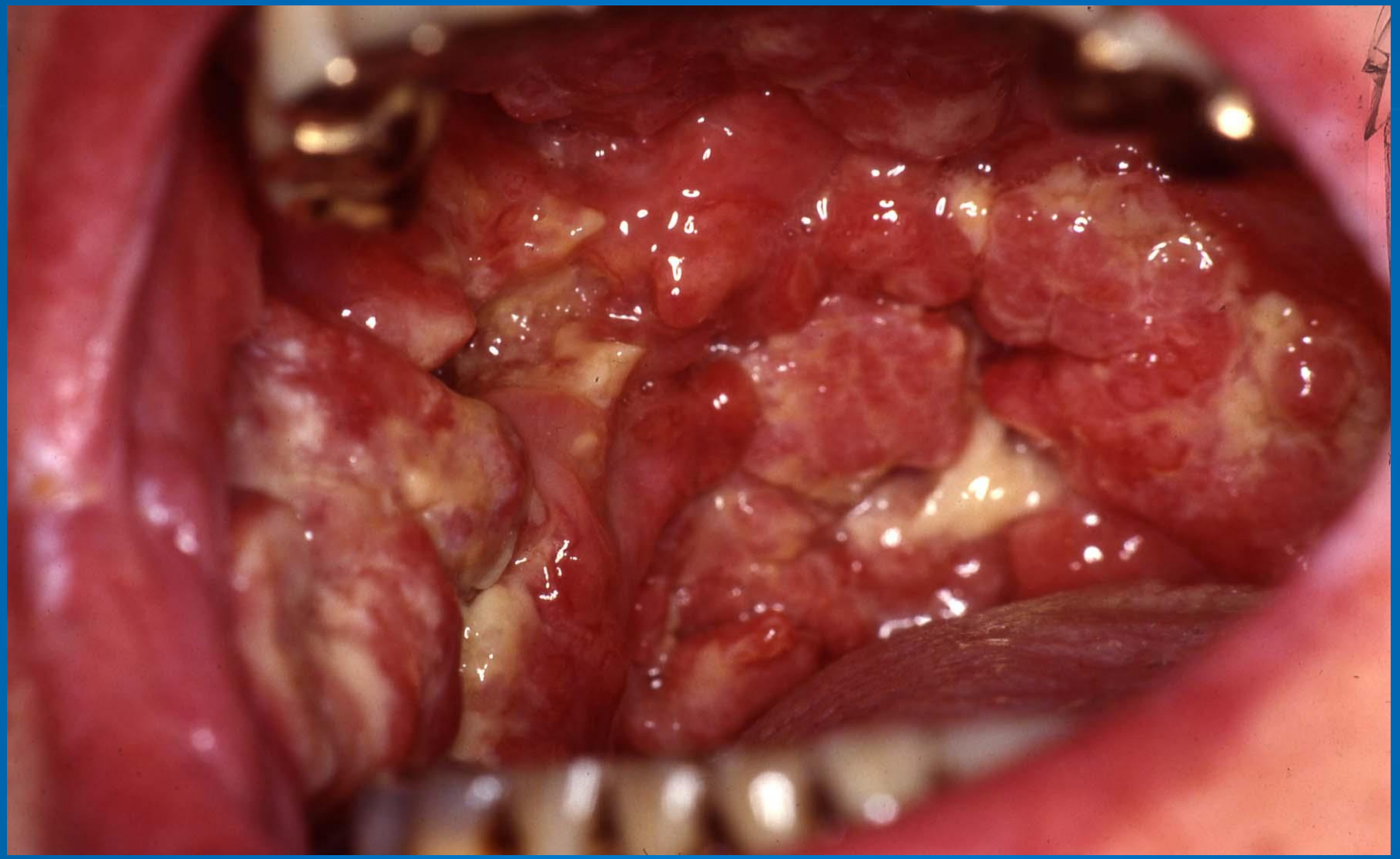
IMPORTANT ORGAN/TISSUE PRESERVATION IN HEAD&NECK CANCER

Larynx	-	Speach
Mandible	-	Mastication
		Contour of face
Tongue	-	Speach
		Swallowing
Pharynx	-	Swallowing
Facial nerve	-	Contour of face
Salivary glands	-	Salivation
Eyes, ear (cochlea)		Vision, hearing





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Standard Treatment options for Patients with Locoregionally Advanced Disease

	EVIDENCE	RECOMMEND.
Surgery → RT or CCRT	**I**	**A**
Concomitant CT and RT*	**I**	**A**
Cetuximab plus RT	II	B
CCRT or ICT → RT for organ preservation	II	A
ICT → CCRT (sequential therapy)	Still under evaluation	

in case of mutilating surgery and in nonresectable disease ;* ***Cisplatin dose: 100 mg/m² x3 during CF-RT*
Gregoire V et al, Ann Oncol 2010: 21 (suppl 5): VI84-VI86

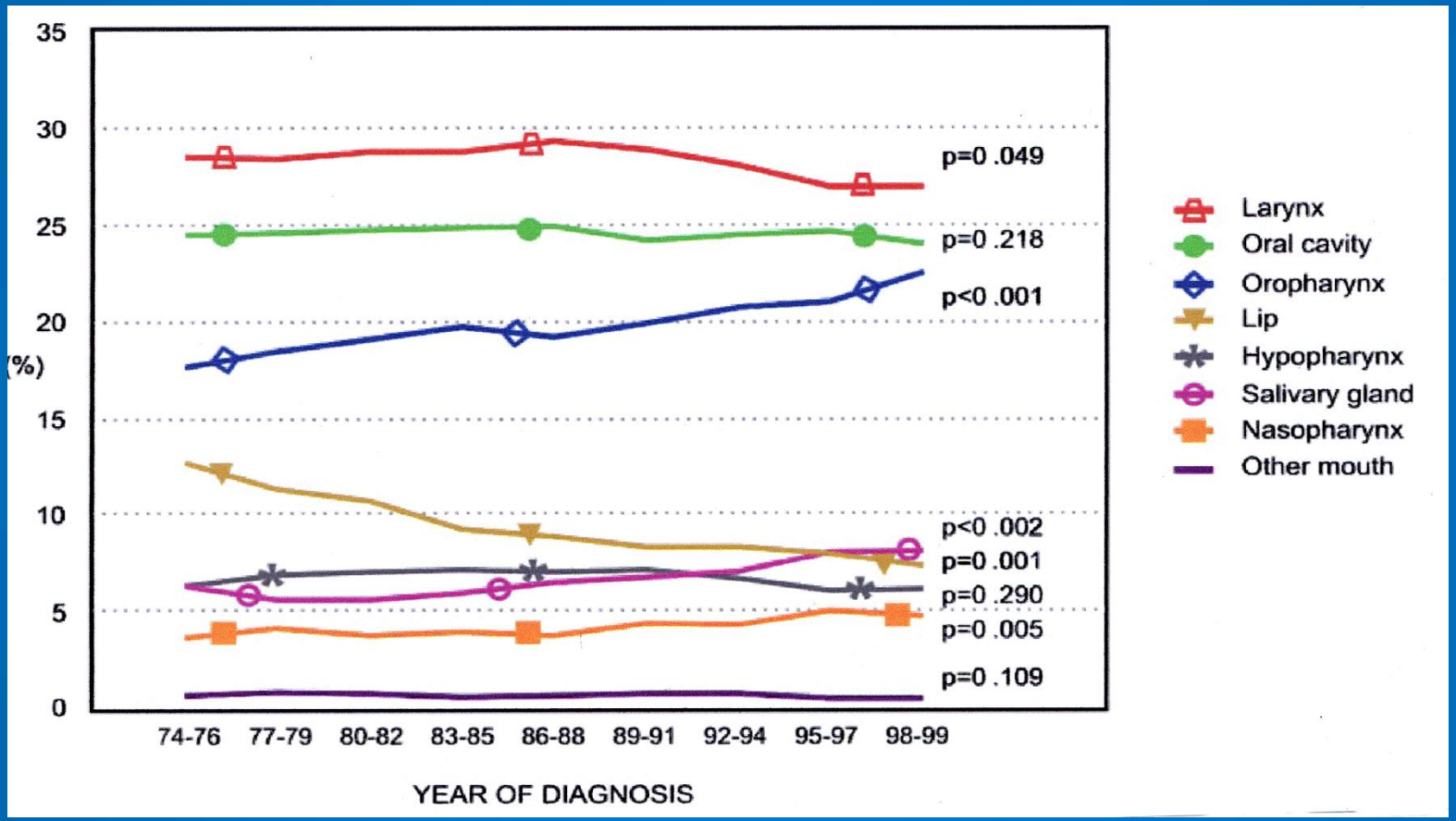
FUNCTIONAL GENOMICS IN RELATION TO TUMOUR ETIOLOGY

- ETIOLOGY
  - *Smoking*
  - Virus*: HPV*, EBV….
- Cause different diseases with respect to characteristics such as
  - Proliferation
  - DNA repair
  - Apoptosis

TRENDS IN INCIDENCE AND PROGNOSIS FOR HEAD AND NECK CANCER IN THE UNITED STATES: A SITE-SPECIFIC ANALYSIS OF THE SEER DATABASE (2005):

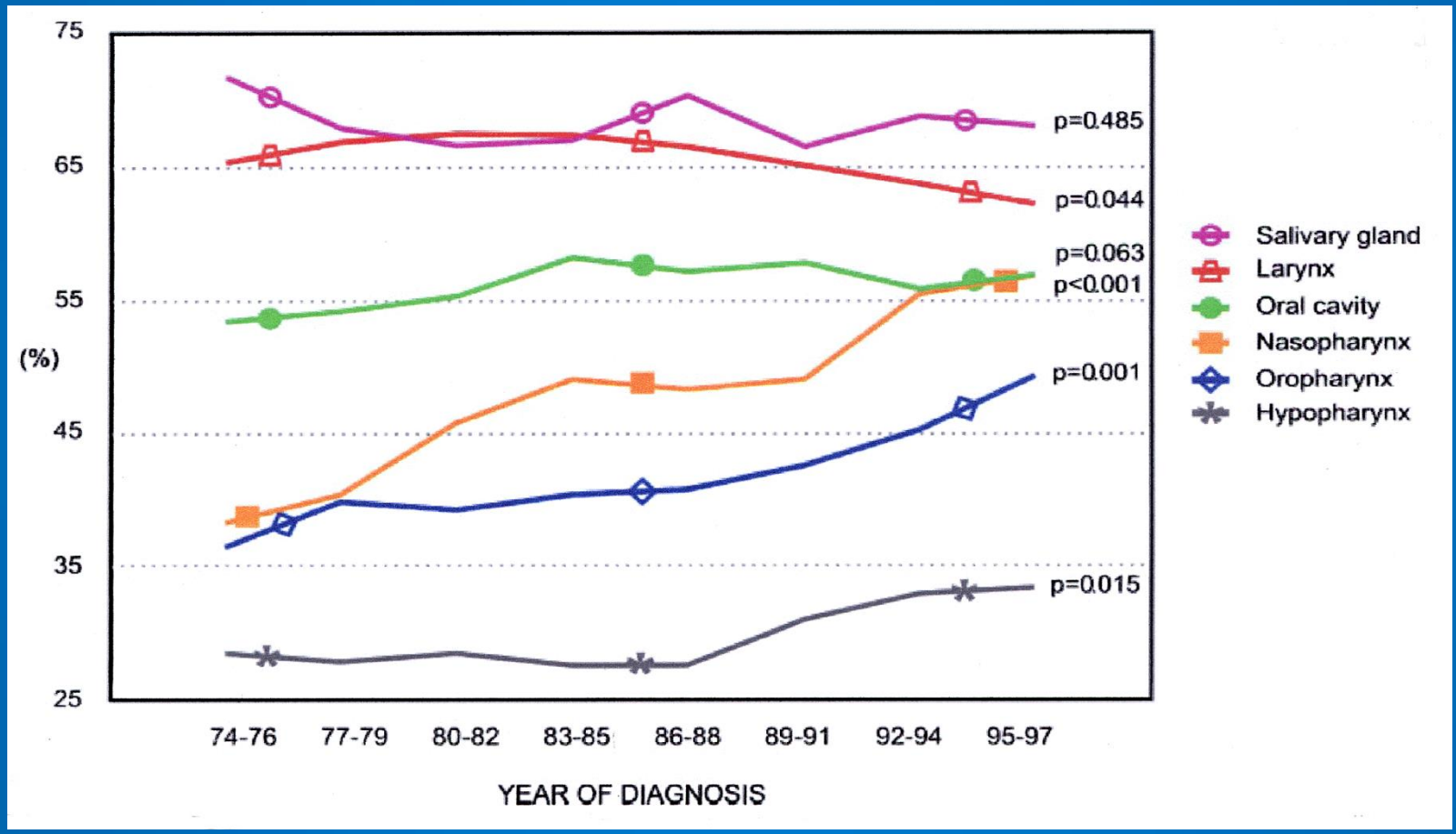
”Overall, the prognosis for HNC has improved in the last decade compared to the 2 decades before, and this improvement is most significant in the last. Most notably, all pharynx cancer patients (naso, oro and hypo) demonstrated an improvement in prognosis, while larynx cancer patients showed a decrease in their survival rates.”

Incidence of Head and Neck Cancer According to Tumor Site, United States SEER Database (2005)



Trends in 5-Year Survival (%)According to Tumor Site

United States SEER Database (2005)



Contents lists available at ScienceDirect

Oral Oncology

journal homepage: www.elsevier.com/locate/oraloncology

Differential survival trends for patients with tonsillar, base of tongue and tongue cancer in Sweden

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ARTICLE INFO

Article history:
Received 10 November 2010
Received in revised form 18 April 2011
Accepted 19 April 2011
Available online 17 May 2011

Keywords:
Tonsillar cancer
Base of tongue cancer
Tongue cancer
Prognosis
Relative survival rate

SUMMARY

Tonsillar, base of tongue and tongue cancer have similar anatomical and histopathological appearances but present differences in prognosis. Human papillomavirus (HPV) is a known risk factor for tonsillar and base of tongue cancer, and a survival benefit has been shown for these tumors; however, HPV prevalence in tongue cancer is low. Tonsillar, base of tongue and tongue cancer patients registered in the Swedish Cancer Registry between 1960 and 2004 were followed from the date of cancer diagnosis until death, emigration out of Sweden, or the end of a follow-up (5 years since cancer diagnosis), whichever occurred first. The relative survival rate was computed as the ratio of the observed to the expected survival rate, in which the latter was inferred from the survival of the entire Swedish population in the same age, sex and calendar year stratum. The relative survival rate has improved significantly over time for patients with tonsillar and base of tongue cancer although delineated by different patterns. However, the relative survival rate in tongue cancer patients exhibited only a very modest improvement during the same time period. Contrary to the overall improved survival for patients with tonsillar and base of tongue cancer, the patients with tongue cancer show a very modest improvement in Sweden since 1960. Further studies are warranted to elucidate more effective treatment options for tongue cancer patients.

WHY HAVE RESULTS IMPROVED (TUMOUR CONTROL,SURVIVAL)?

A. Implementation of clinical radiation biology
   - Altered fractionation — ALL
   - ”Chemoradiation” — BASED ON RANDOMISED
   - ”Bioradiation” — STUDIES

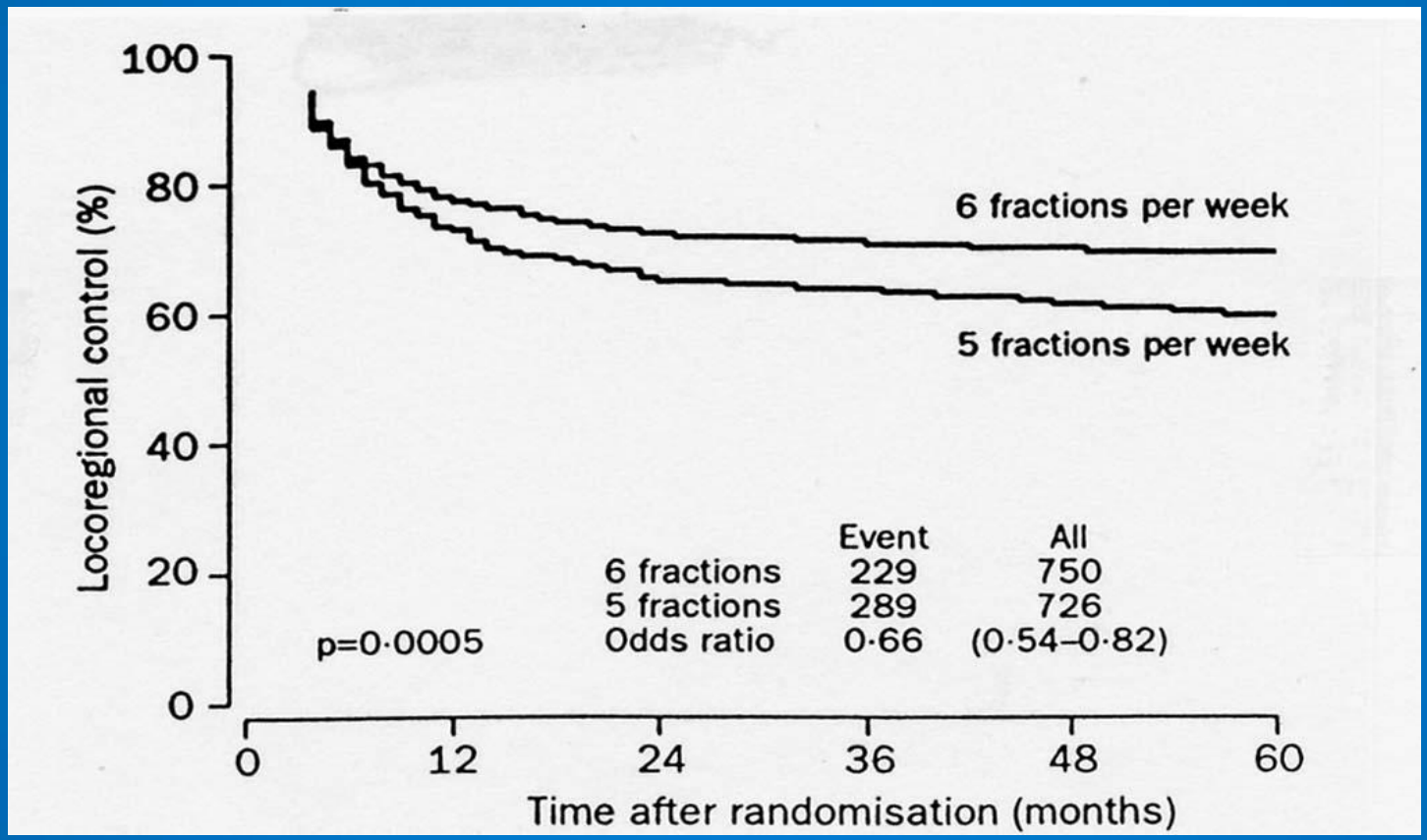
B. Dose escalation (64 to 72 Gy; No randomised studies)

   More conformal radiotherapy, 3D dose planning, IMRT, VMAT,SBRT?, BT)

C. Less aggressive tumours (HPV +)

D. Improved diagnostic radiology, MRI, PET/CT

Advanced Head & Neck cancer
Loco-regional tumour control
as a function of number of fractions per week



Dahanca, Lancet 2003, 362

SURVIVAL BENEFIT WITH CHEMORT VS RT FOR LOCOREGIONALLY ADVANCED NON-RESECT. DISEASE

Metaanalysis of randomised trials with *concomittant* CRT :

8% at 5 years (El-Sayed&Nelson 1996, Pignon 2000)

14-25% at 5 years (Brizel 1998, Adelstein 2003)

4.5% at 5 years, 6.5% for concomittant therapy, 2.4% for induction chemotherapy (Pignon 2009 : 93 randomised trials and 17346 pts)

5-year absolute survival benefits with concomitant chemotherapy is for

Oral cavity = 8.9%

Oropharynx = 8.1% **Metananalysis, Pignon et al 2011**

Larynx = 5.4%

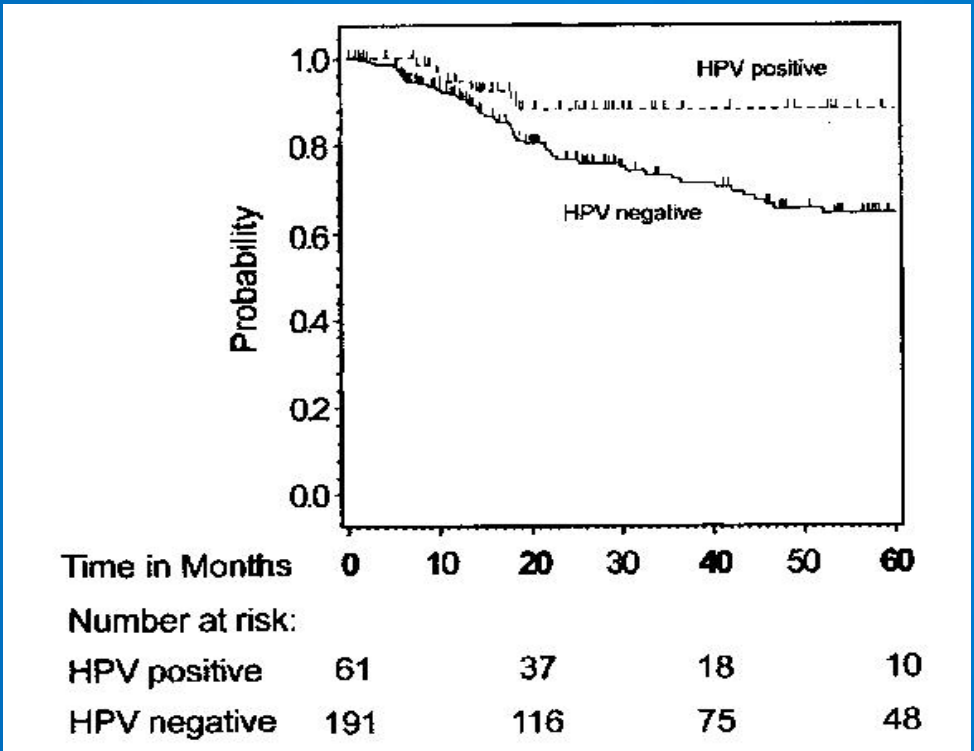
Hypopharynx = 4%

TREATMENT OF HEAD AND NECK CANCER IN 2018

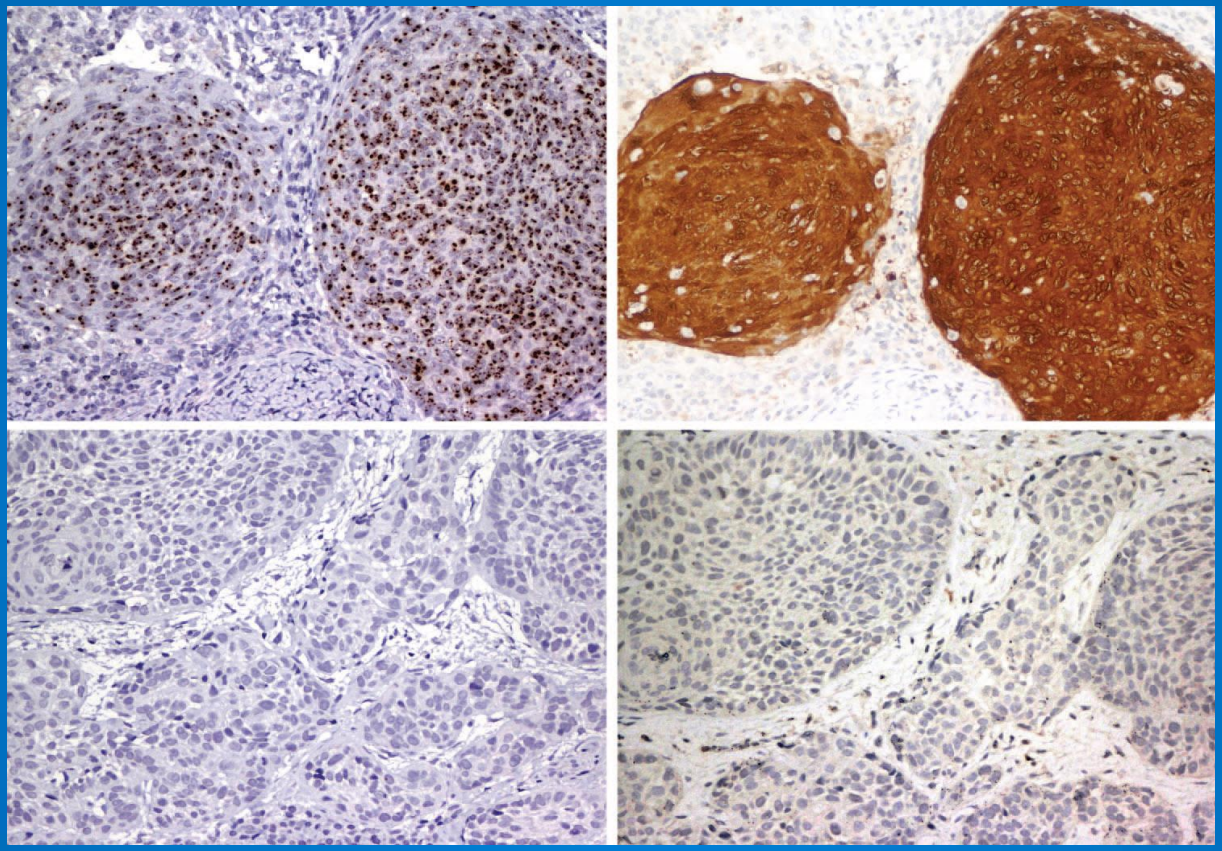
- Concomittant chemoradiotherapy (with cisplatin) or bioradiotherapy (with Cetuximab) is the standard of care for locally advanced tumours

- (Chemo)radiotherapy is being increasingly used also for less advanced, resectable tumours

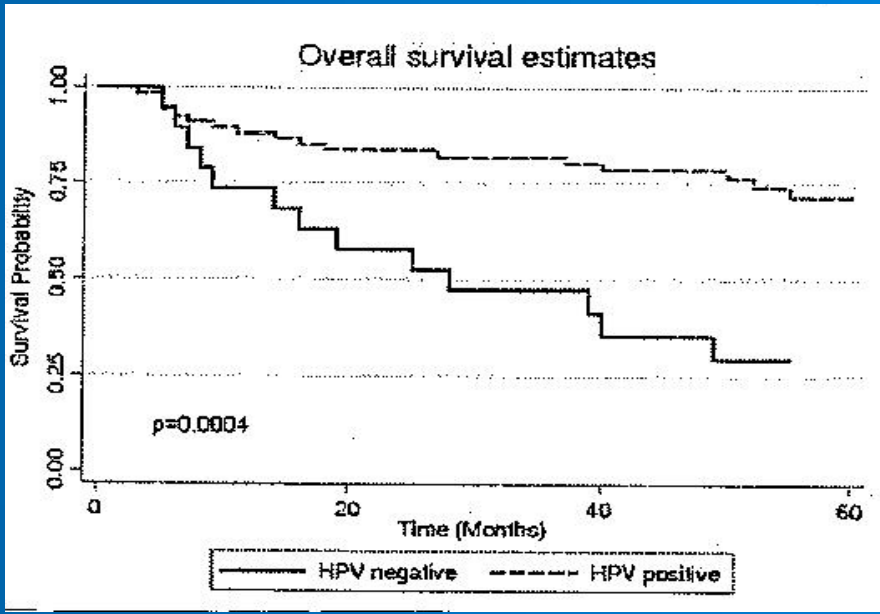
HPV STATUS AND OUTCOME OF TREATMENT OF HEAD & NECK CANCER (SURVIVAL-IRRESPECTIVE OF TREATMENT)

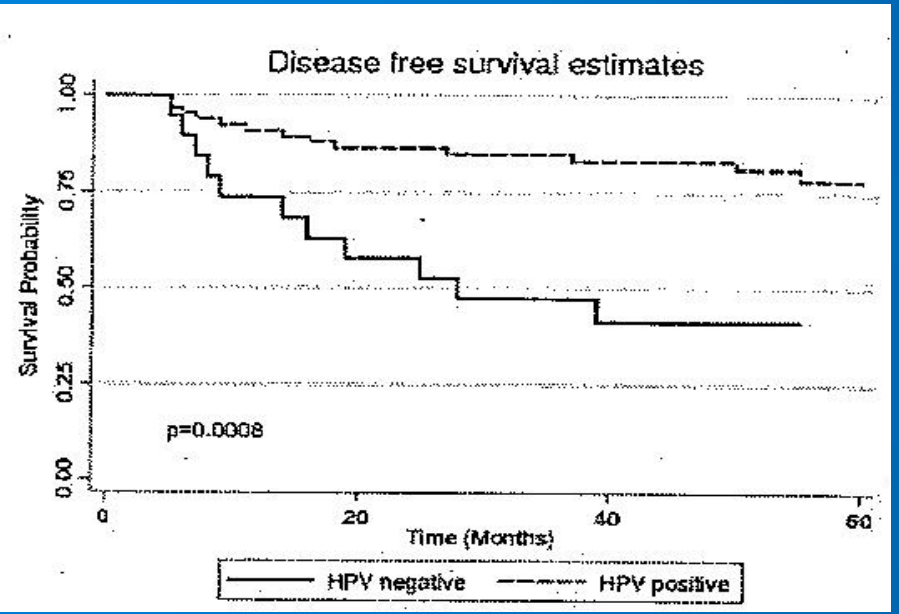


Gillison, M. et al 2000Gillison,GGgi



BASE OF TONGUE CANCER RADIOTHERAPY ± CHEMOTHERAPY (Stockholm 1998-2007; 89 PTS)





Attner, P. et al 2012

DEESCALATION OF TREATMENT INTENSITY FOR PATIENTS WITH HPV + TUMOURS?

Decrease radiation dose to targets of different potential clonogenic infestations ?

De-escalation studies are ongoing with interesting results, supporting the hypothesis that some/several patients can be cured with lower radiation doses. 54 Gy to the target for manifest tumour instead of 70 Gy?

How Do we find them? Implications for a future reiradiation?

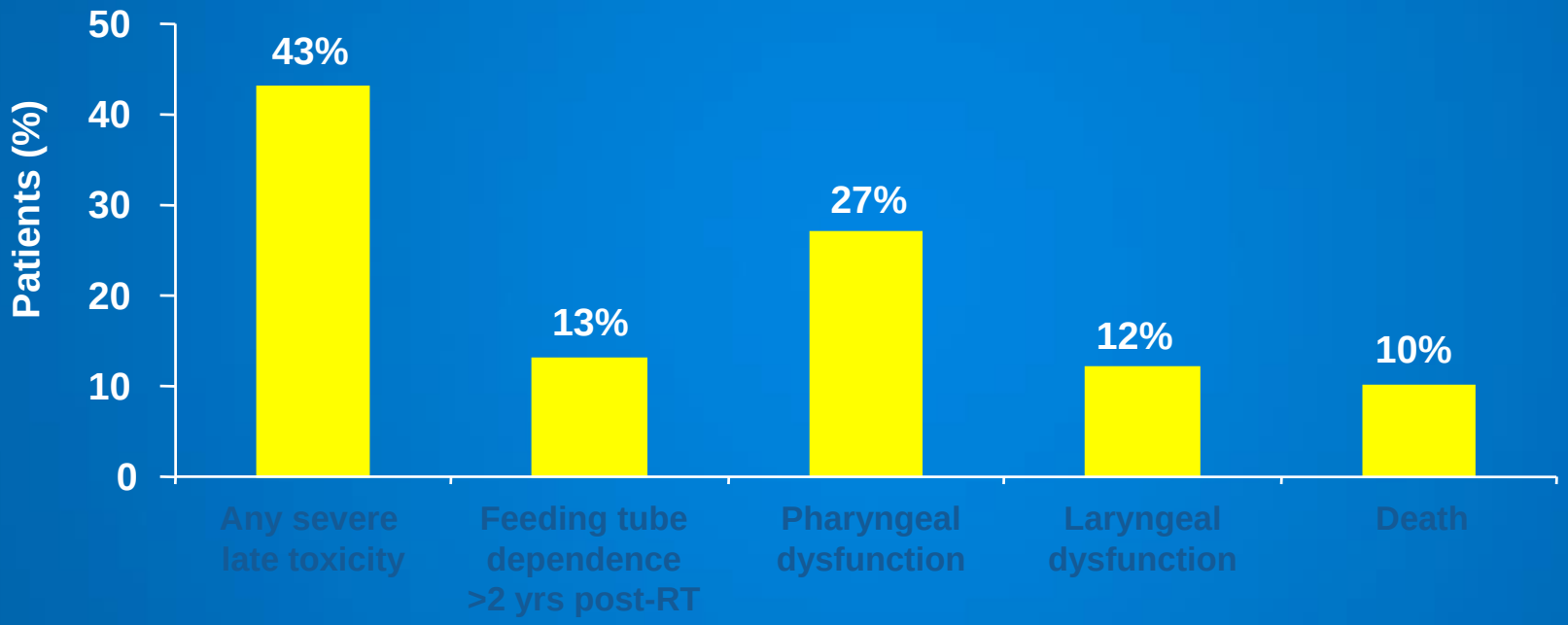
Tumour control of head and neck cancer patients has increased substantially, mostly during the last decade

but……..

At the expense of increased toxicity

CRT: High rate of late toxicity[a]

- Analysis of 230 patients receiving CRT in 3 studies (RTOG 91-11, 97-03, 99-14)



[a] Chronic grade 3-4 pharyngeal/laryngeal toxicity and/or requirement for feeding tube >2 years after registration and/or potential treatment-related death within 3 years

Machtay M, et al. J Clin Oncol 2008;26:3582-3589

HEAD AND NECK CANCER
POTENTIAL TREATMENT SIDE-EFFECTS

Surgery

- Loss of function (speech, swallowing etc.)
- Disfigurement

Radiotherapy (± chemotherapy)

- *Xerostomia*
- Trismus
- Soft tissue fibrosis/necrosis
- *Dysphagia*
- *Osteonecrosis*
- Hematological

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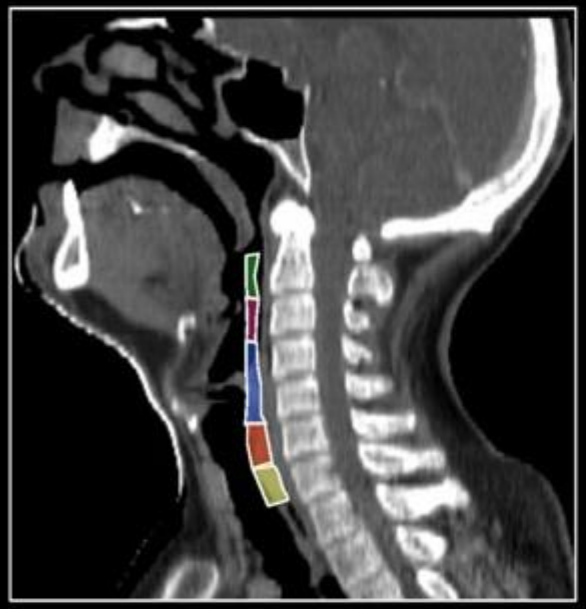
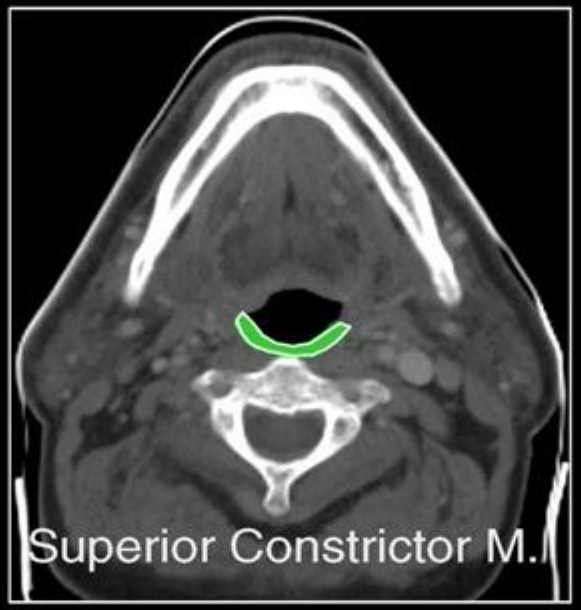
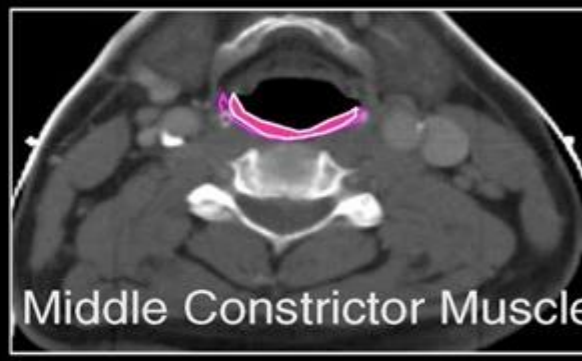
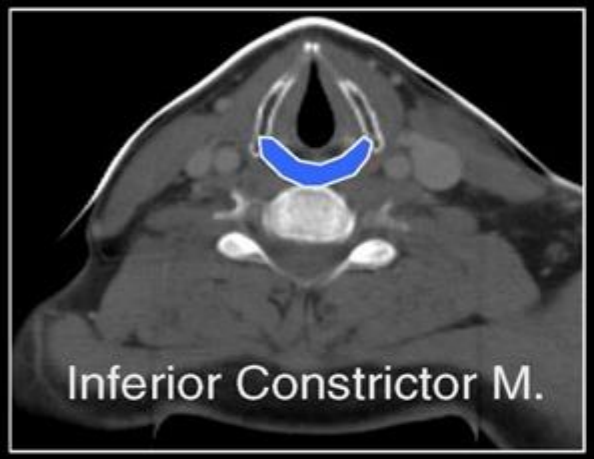
Base of Skull-C3

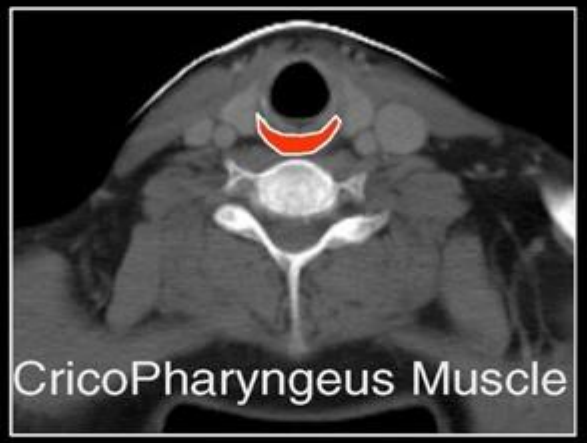


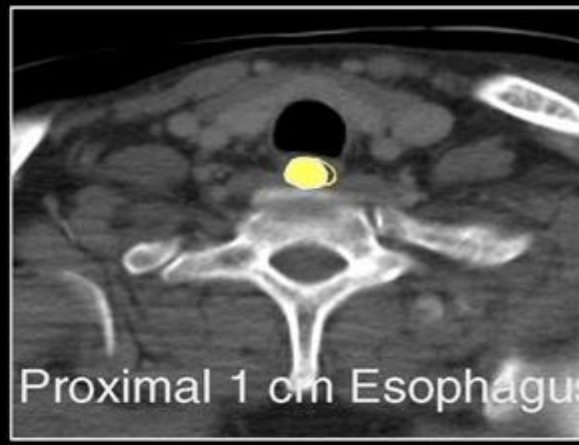


C3-C4









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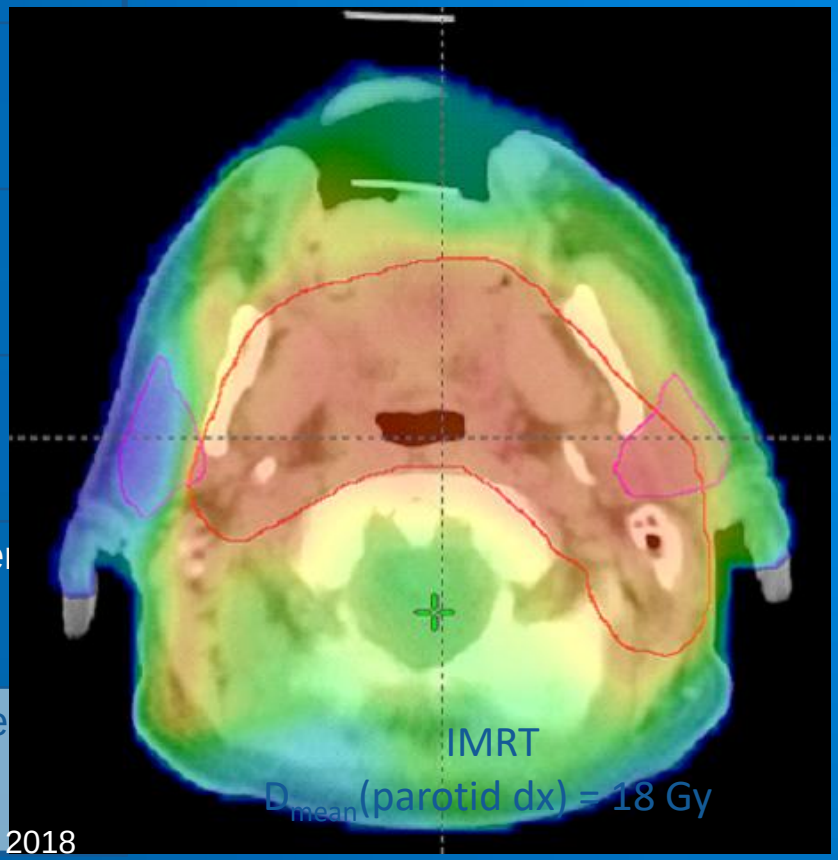
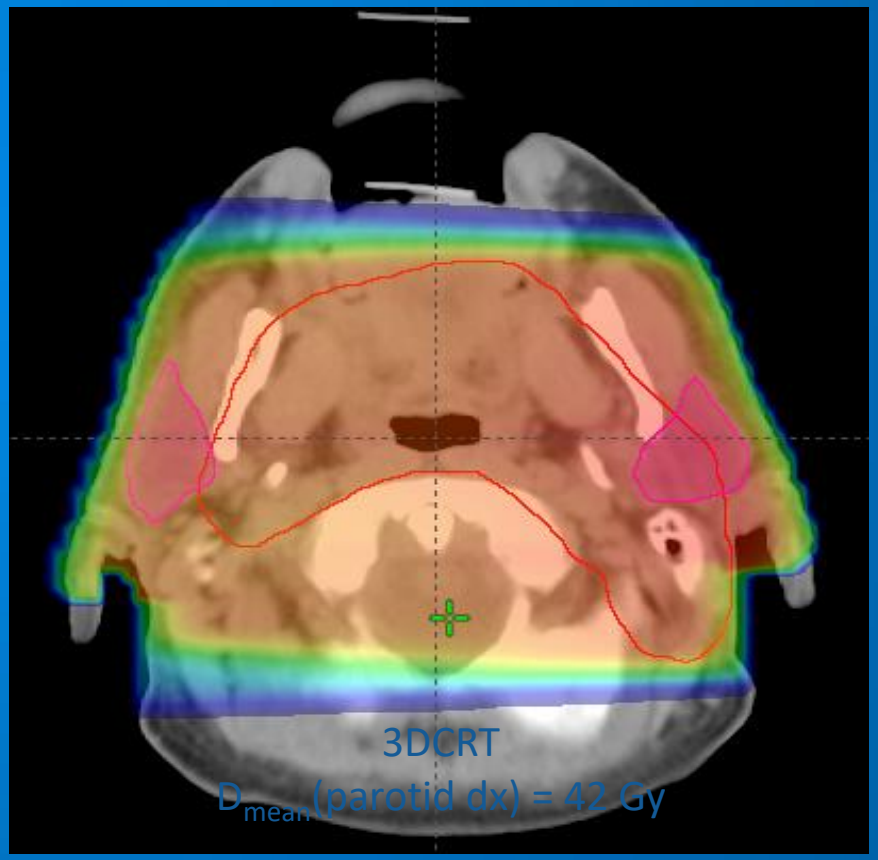
RADIOTHERAPY TECHNIQUES
IMRT

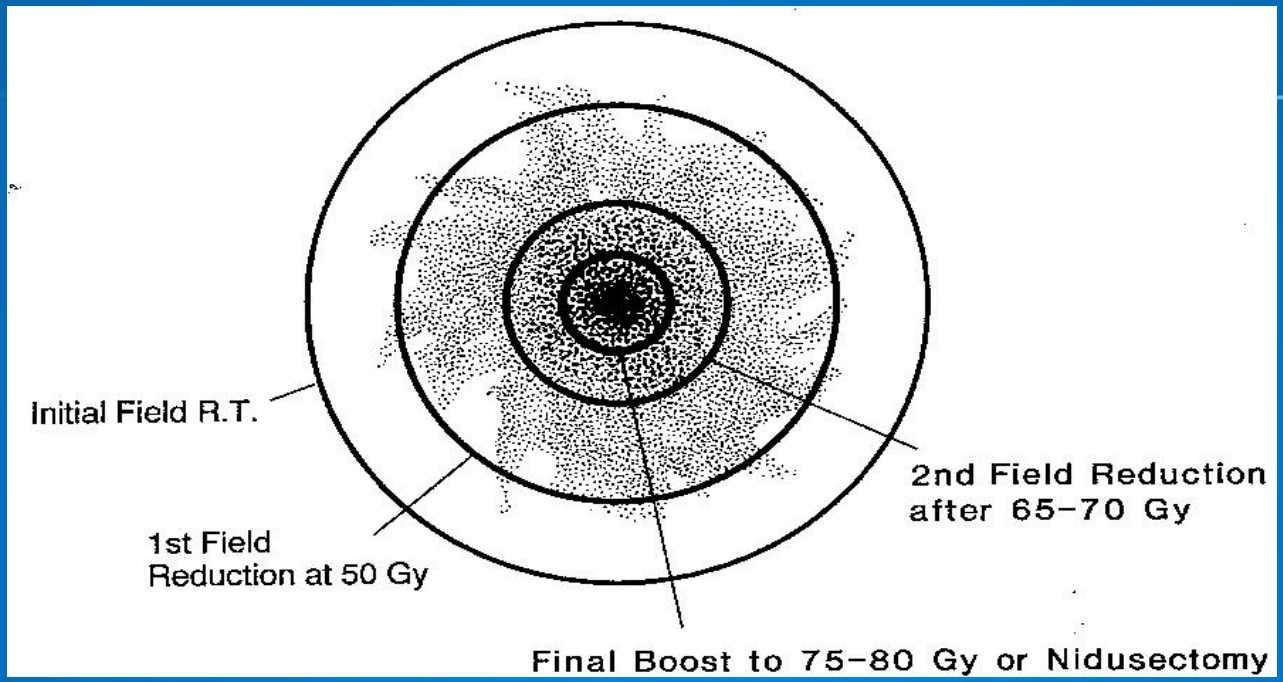
1. Can reduce xerostomia (also in one prospective, randomised phase 3 study, the PARSPORT study)
2. Can improve swallowing (ameliorate dysphagia)
3. Can potentially escalate tumor dose (e.g.”SIB”)

Intro
Agenda
Svårigheter
3DCRT
IMRT
Brachy
Protoner
Jämföre

Comparison: dose to parotid glands (IMRT vs. 3DCRT)







From C.C. Wang:
”Radiation therapy for head and neck neoplasms” 1984

CONFORMAL (HIGHLY) RADIOTHERAPY TECHNIQUES AVAILABLE FOR HEAD AND NECK CANCER PATIENTS IN STOCKHOLM

- IMRT, VMAT
- Brachytherapy, BT
- SBRT (ongoing project)

CONSTRAINTS FOR IMPORTANT ORGAN FUNCTIONS

Priority	Organ/Tissue	Dose (Gy)	Consequence
1	Medulla Spinalis	46, max $\leq$ 50 Gy	Myelitis necrosis
2	PTV 2 (all stages)	46	Tumour control
	PTV 1 (stages T1-T2)	66-76	Tumour control
	PTV 1 (stages T3-T4)	76-85	Tumour control
		$V_{95} \geq 95\%$	
		$V_{105} \leq 5\%$	
3 a	Contralateral parotid	Mean dose $\leq$ 26 Gy	Xerostomia (Dry mouth)
b	Larynx	Mean dose $\leq$ 44 Gy	Hoarseness, voice exhaustion, swallowing problems
c	Swallowing constrictors	Mean dose $\leq$ 45 Gy	Swallowing problems
d	Mandible/mandibular joints	68, max $\leq$ 74 Gy	Osteoradionecrosis, "fracture"
e	Oral cavity	Minimize	"Acute mucositis", Xerostomia
f	Inner ear	Mean dose $\leq$ 50 Gy	Reduced hearing
4 a	Ipsilateral parotid	Minimize	Xerostomia
b	Submandibularis	Minimize	Xerostomia
c	Auditory meatus	Mean dose $\leq$ 50 Gy	External otitis, affected hearing
d	Trachea	Minimize, mean dose $\leq$ 44 Gy	Sensitivity to infections

Dose-volume constraints for critical organs/tissues and their order of priority

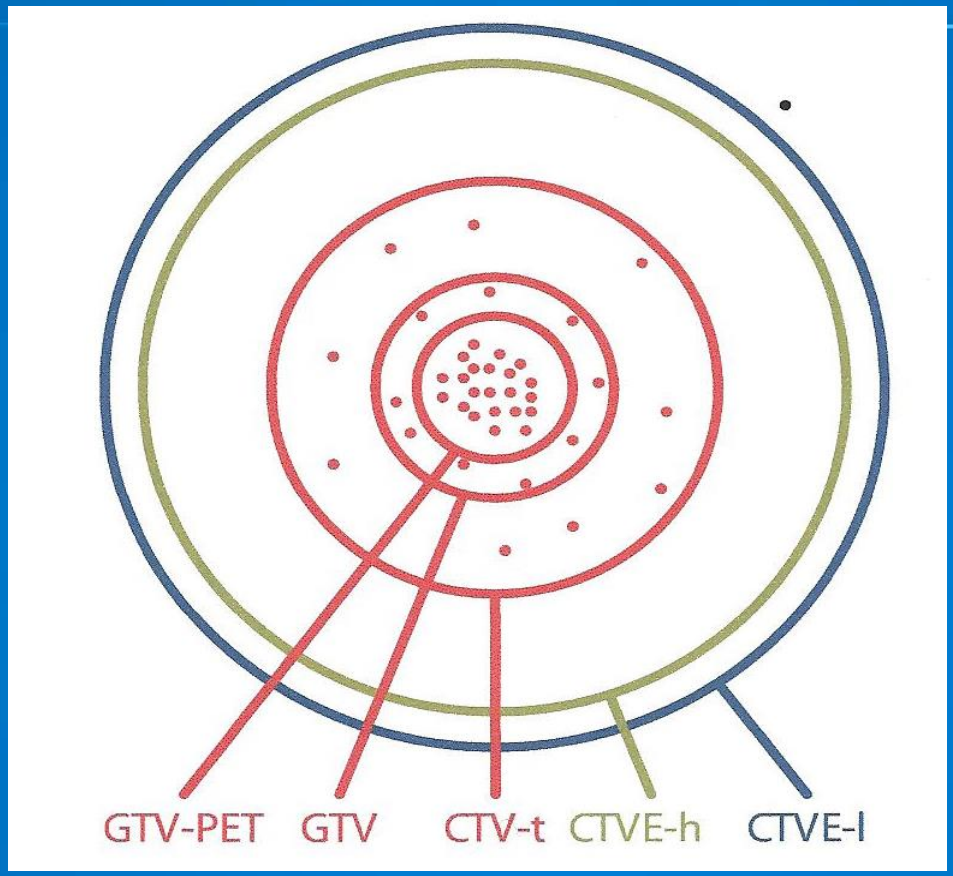
(ongoing project)

RECURRENT TUMOUR IN PREVIOUSLY IRRADIATED VOLUME

1. DESPITE BEST EFFORTS: About 30-40% of patients have a locoregional recurrence, most often isolated, sometimes with distant metastases

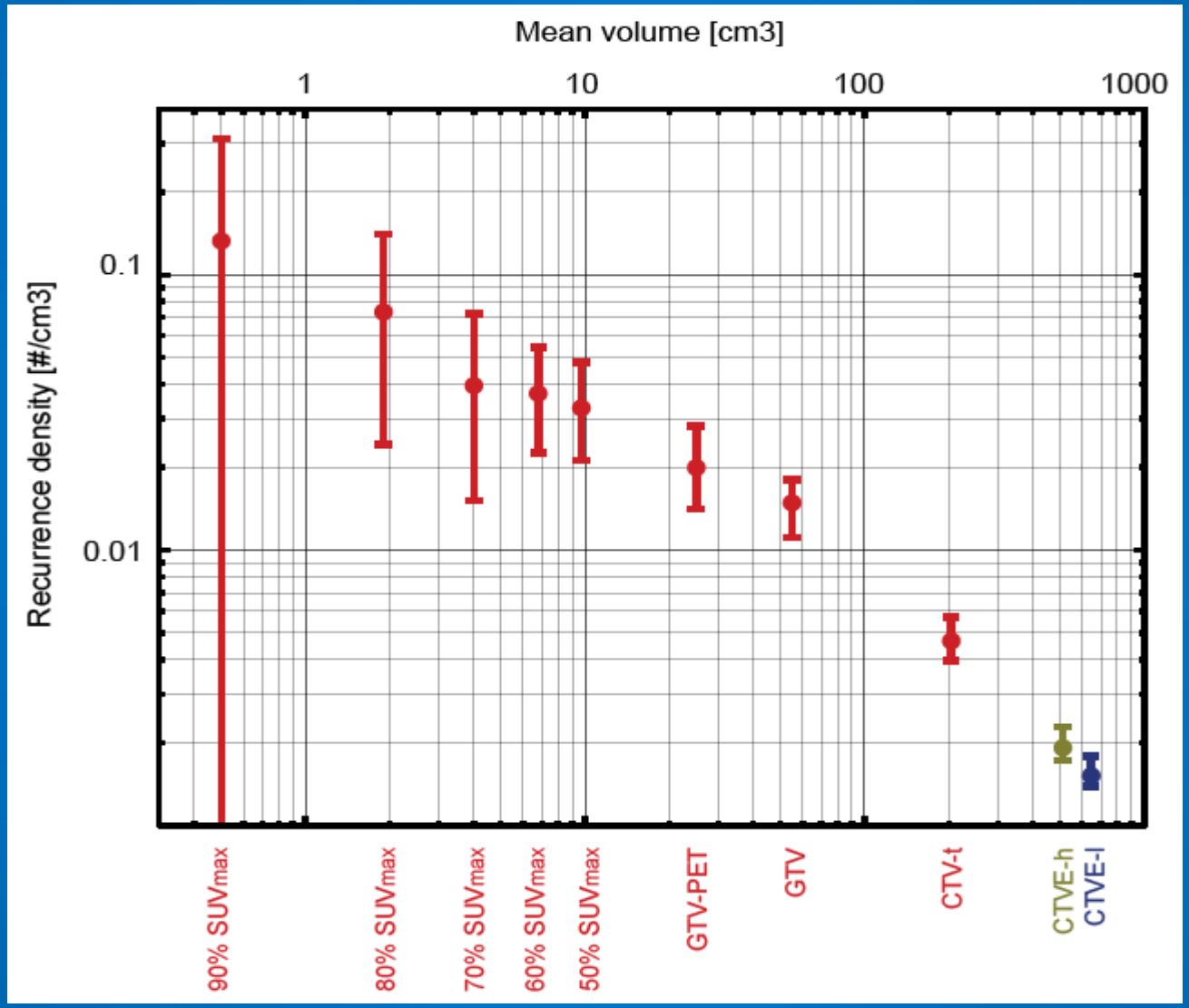
2. WHERE DO THEY APPEAR?

Recurrences in irradiated target volume



Thesis: Kirkebjerg Due, A. (Specht, L., Copenhagen 2012)

Recurrence density increased with increasing FDG-avidity in high dose region



TREATMENT OPTIONS IN PATIENTS WITH RECURRENT DISEASE 2018

1. SURGERY: For resectable disease; surgery if possible with postop RT or CCRT (if not complete)

2. RADIOTHERAPY OR CHEMORADIOTHERAPY: For non-resectable disease

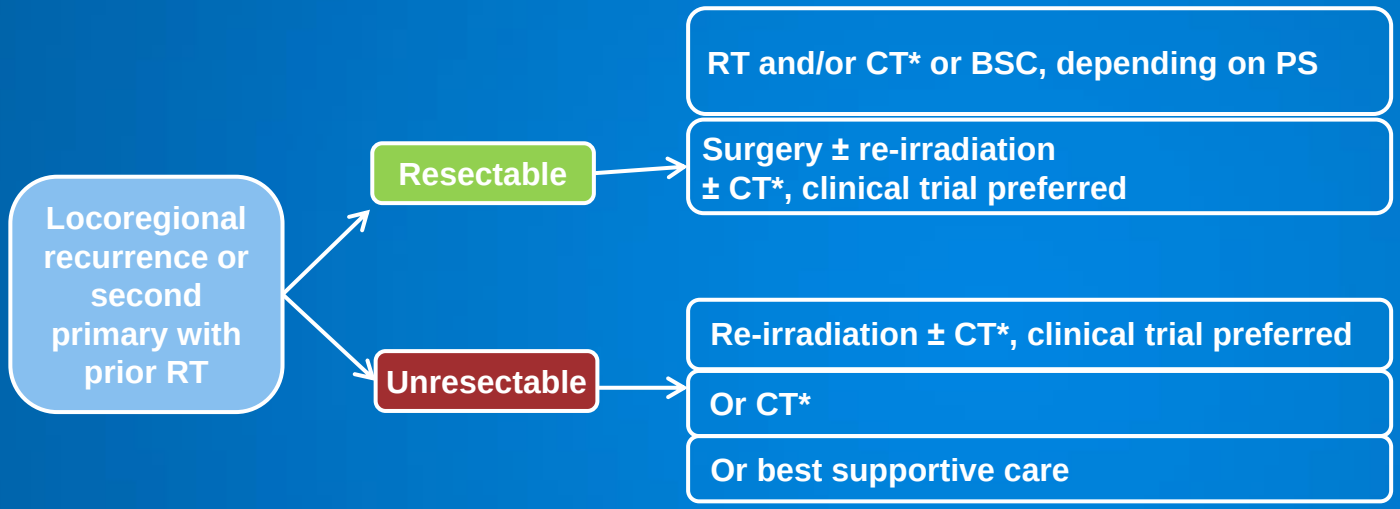
3. CHEMOTHERAPY (CYTOSTATICS): Palliative (e.g. pain)

4. CHEMOTHERAPY (”TARGETED”): Mostly palliative?

5. CHEMOTHERAPY (IMMUNE CHECKPOINT INHIBITORS): Mostly palliative?

6. BEST SUPPORTIVE CARE

NCCN guidelines for treatment of locoregional recurrence of SCCHN

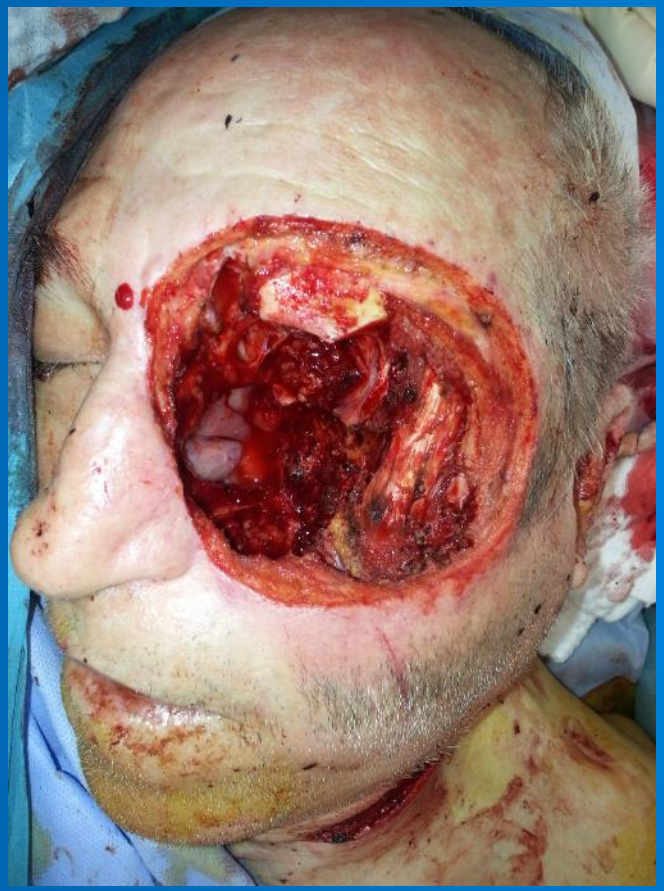


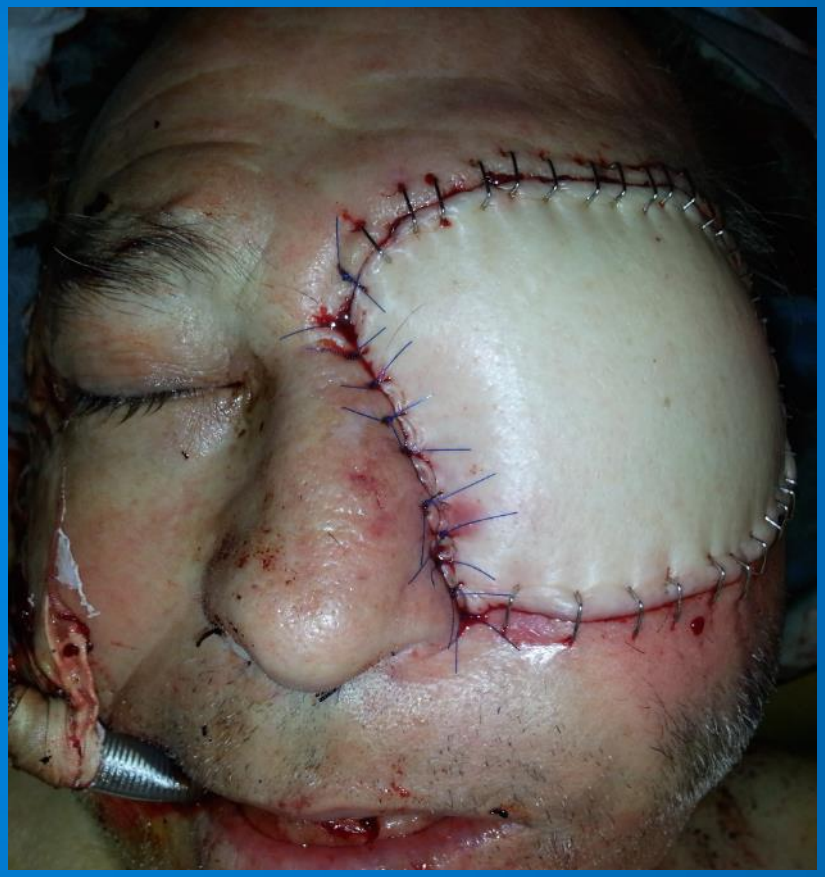
Treatment should be dictated largely by PS. Patients should be fully informed about goals of treatment and potential for added toxicity

Regimens with category 1 evidence: cisplatin + RT or carboplatin + 5-FU + RT or cetuximab + RT
*May be single-agent or combination therapy CT or cetuximab
BSC, best supportive care; NCCN, National Comprehensive Cancer Network; PS, performance status; RT, radiotherapy

NCCN Clinical Practice Guidelines in Oncology: Head and Neck Cancers V2.2014

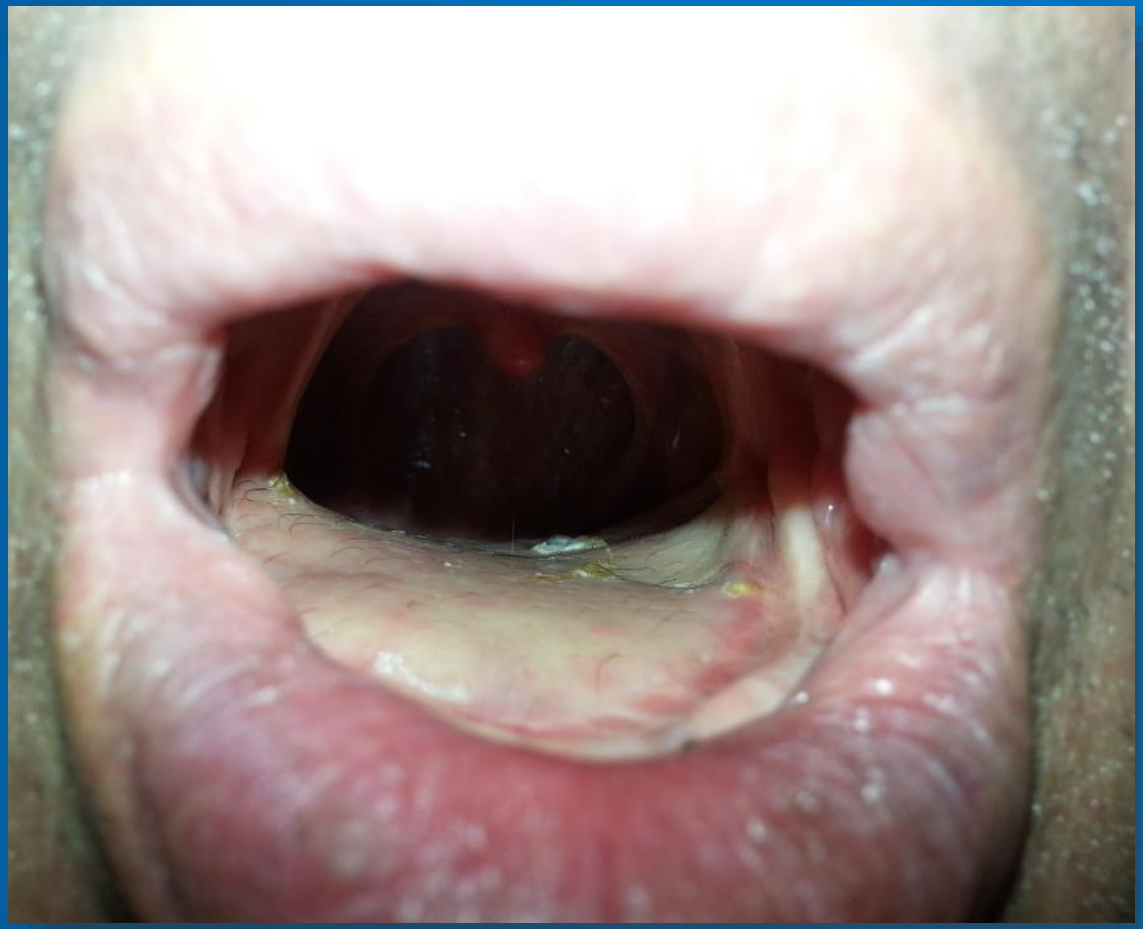
Do we have to advocate salvage surgery?

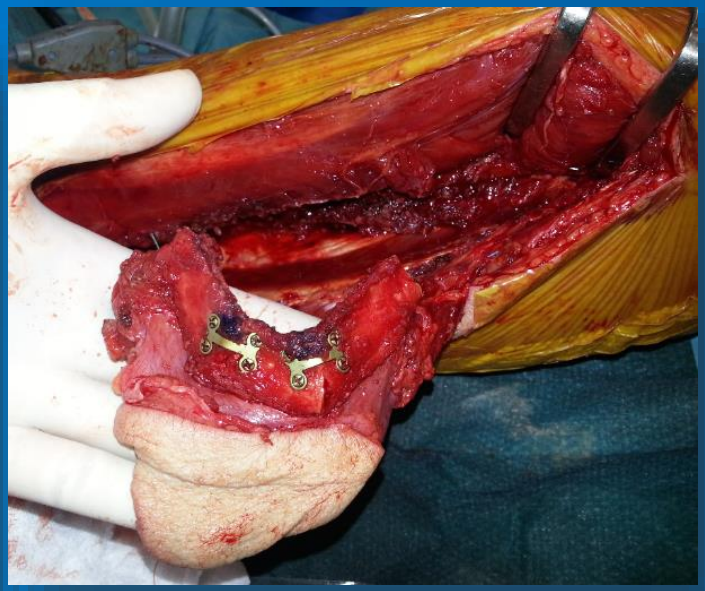


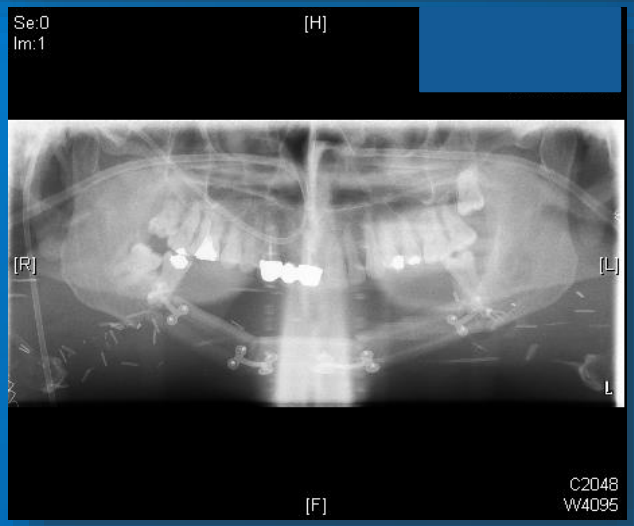


Images provided by Professor Céruse

Do we have to advocate salvage surgery?







Images provided by Professor Céruse

Salvage surgery may be associated with a range of postoperative complications

Post-operative complications experienced by 124 patients treated with en-bloc salvage surgery for SCCHN (retrospective study)

Variable	
Post-operative complications	58 (46.8%)
Minor complications, number of events*	n=85
Major complications, number of events*	n=27
Death	3.2%
Length of hospital stay, days, mean (range)	11.2 (1–90)
Tracheotomy, with no intent of removal	21.1%
Feeding tube at death or last follow-up	27.4%

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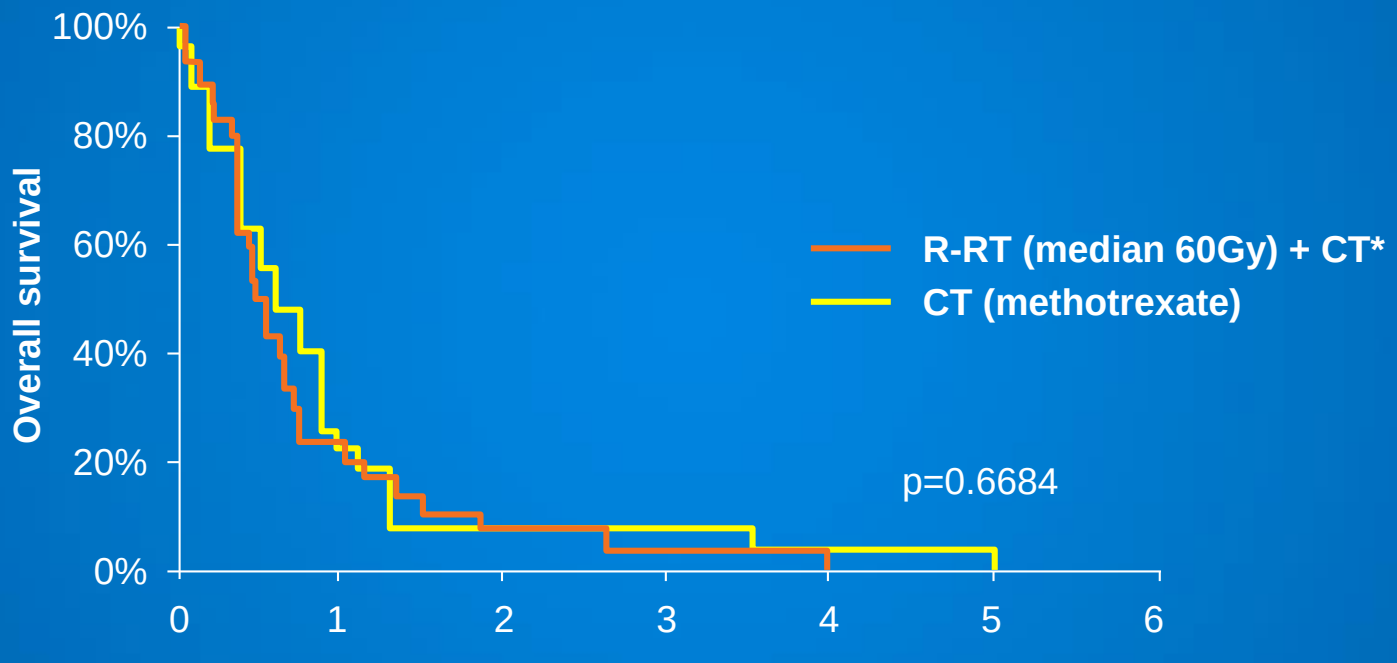
*Patients may have had >1 event

Agra IM, et al. Arch Otolaryngol Head Neck Surg 2003;129:1317–1321

Do we have to advocate re-irradiation?

57 patients accrued to a Phase III trial treated for recurrent or second primary SCCHN



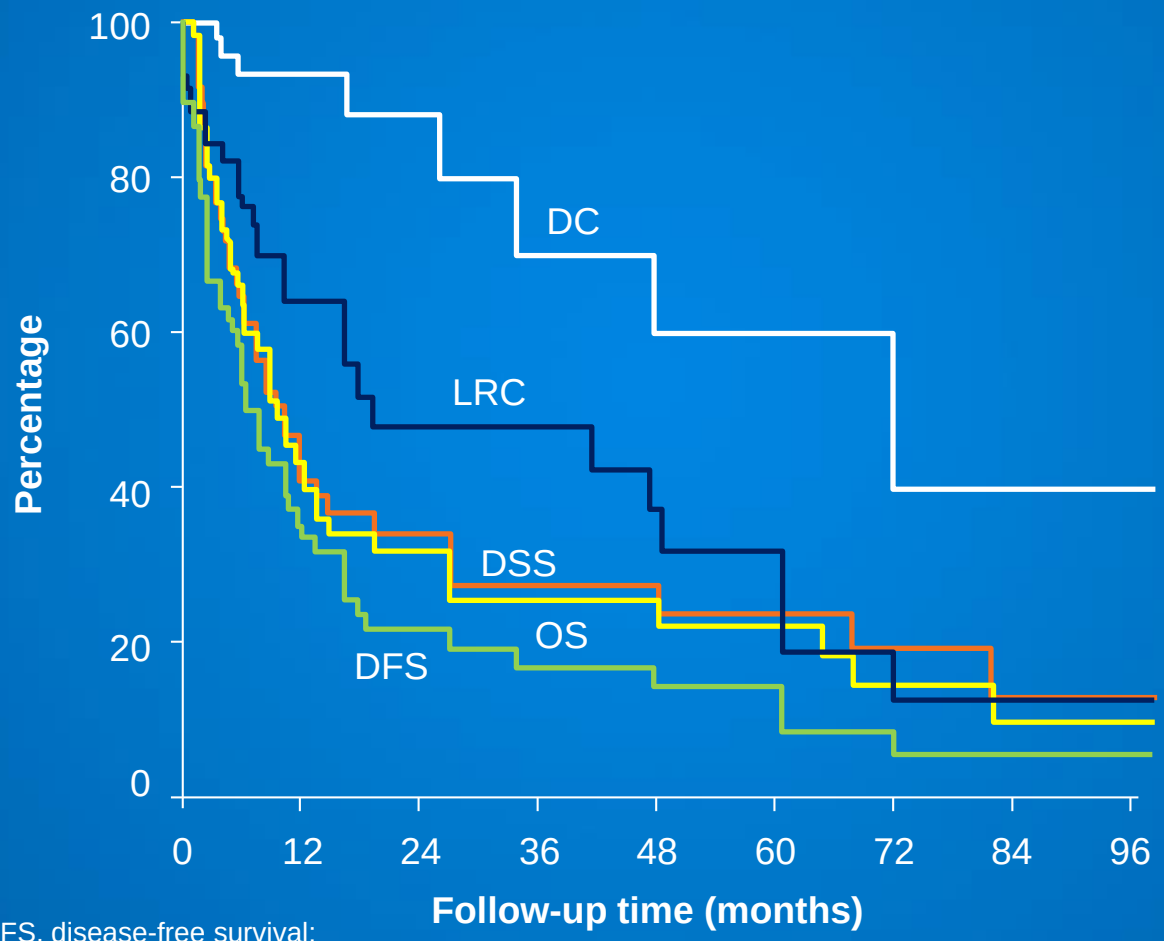
At risk						
R-RT	30	7	2	1		
CT	27	6	2	2	1	1

R-RT, re-irradiation
*Hydroxyurea & 5-FU

Tortochaux J, et al. Radiother Oncol 2011;100:70–75

Do we have to advocate re-irradiation?

Retrospective study of 60 consecutive patients re-irradiated using IMRT (66Gy) for recurrent SCCHN

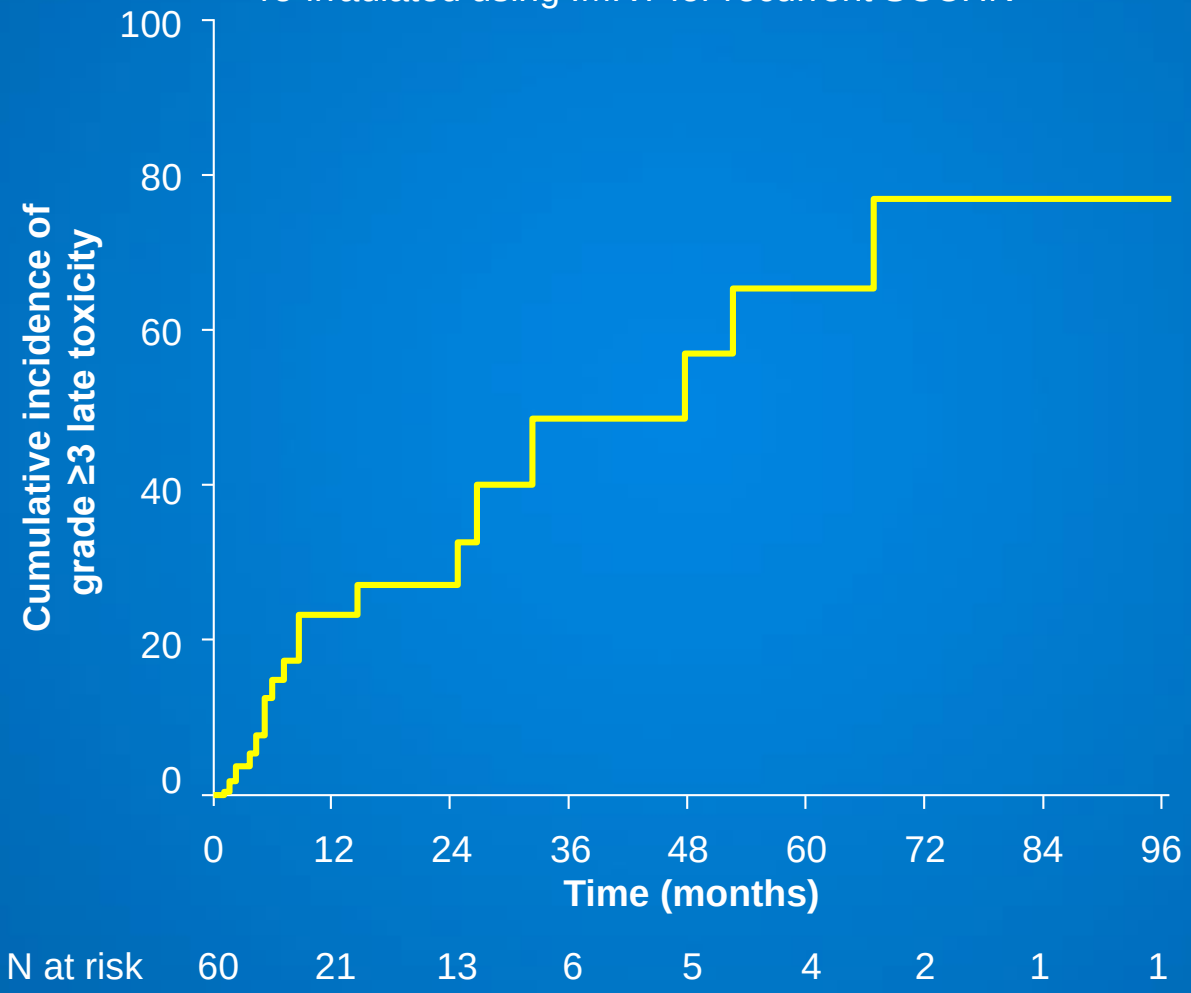


DC, distant control; DFS, disease-free survival;
DSS, disease-specific survival;
LRC, locoregional control

Duprez F, et al. Radiother Oncol 2014;111:388–392

Do we have to advocate re-irradiation?

Cumulative incidence of grade ≥3 late toxicity among 60 consecutive patients re-irradiated using IMRT for recurrent SCCHN



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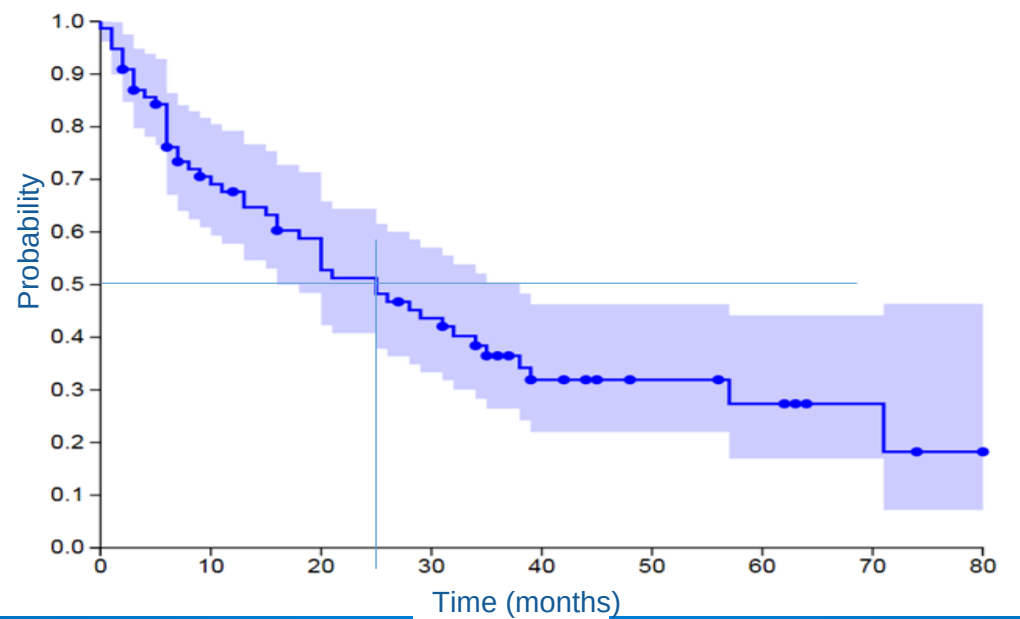
Duprez F, et al. Radiother Oncol 2014;111:388–392

Reirradiated patients Karolinska University Hospital: Overall Survival



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PUBLICATION OF REIRRADIATION STUDIES HAVE INCREASED SUBSTANTIALLY DURING THE LAST DECADE!

Interpretation of data is difficult with respect to description of:

A. Treatment of primary tumour:

Dose distribution, doses to OARs, tumour site (oral cavity, oropharynx etc.), patient general status (Charlson scales), RT techniques, HPV status etc.

B. Reirradiation:

Dose distribution: OVERLAPPING VOLUMES: how big? where in the tissues?

WHAT IS ”REIRRADIATION”?

”Patients treated with overlapping field borders to a dose >40Gy”

REIRRADIATION WITH BRACHYTHERAPY FOR CARCINOMAS OF OROPHARYNX AND TONGUE

Nancy, France, 1972-1984 (retrospective study)

- 1.Technique/Dose: Afterloading 192Ir implants, the Nancy technique, the Paris system for dose calculation, first treatment dose was 36-140 Gy, average 69 Gy, reirradiation dose was 31-80 Gy, average 62 Gy, dose rate less than 8 Gy/day in 23 pts 8-16 Gy/day in 76, more than 16 Gy/day in 23 patients.

- 2. Patients: 123 patients were recorded, 111 treated with curative intent. Site of first irradiation: oropharynx 56, pharyngolarynx 35, oral cavity 32. Site of reirradiation: tonsil 43, base of tongue 32, mobile tongue 26, soft palate 22. Size of reirradiated tumor: T1 35, T2 49, T3 38 and T4 1. 71 tumors were smaller than 3 cm and 52 larger than 3 cm.

- 3. Results: Actuarial survival rates at 2 and 5 years were 48 and 24%. Survival was correlated with size (3cm or larger), new primary tumor and not relapse of earlier tumor, reirradiation dose above 60 Gy, Site of tumor correlated with 2-year tumor control (78, 69 and 48% resp. for oral cavity, pharyngolarynx and oropharynx)

MILESTONE STUDY 1996: ” Re-irradiation with concomitant chemotherapy of unresectable head and neck cancer: A potentially curable disease"

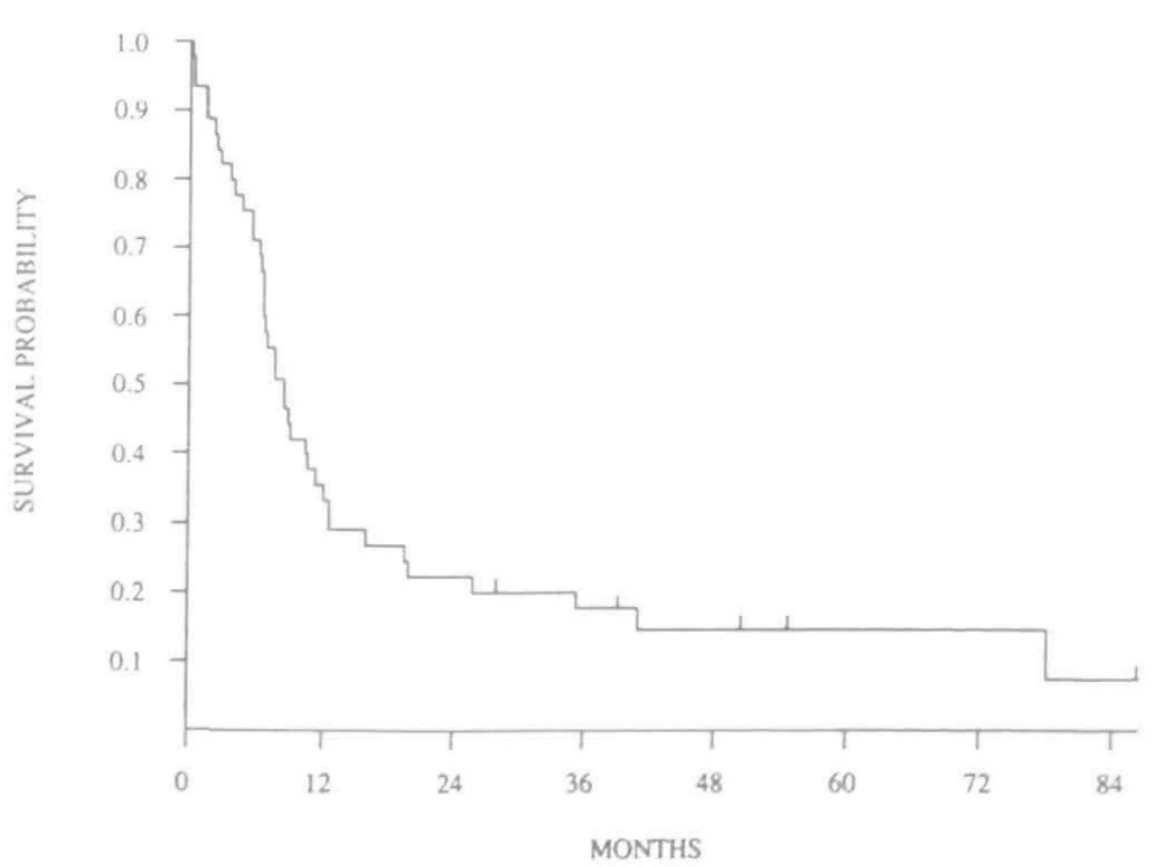

Figure 2. Overall survival.

Haraf DJ, Weichselbaum RR and Vokes EE: Ann Oncol 7(9):913-918

MILESTONE STUDY 1996: ” Re-irradiation with concomitant chemotherapy of unresectable head and neck cancer: A potentially curable disease"

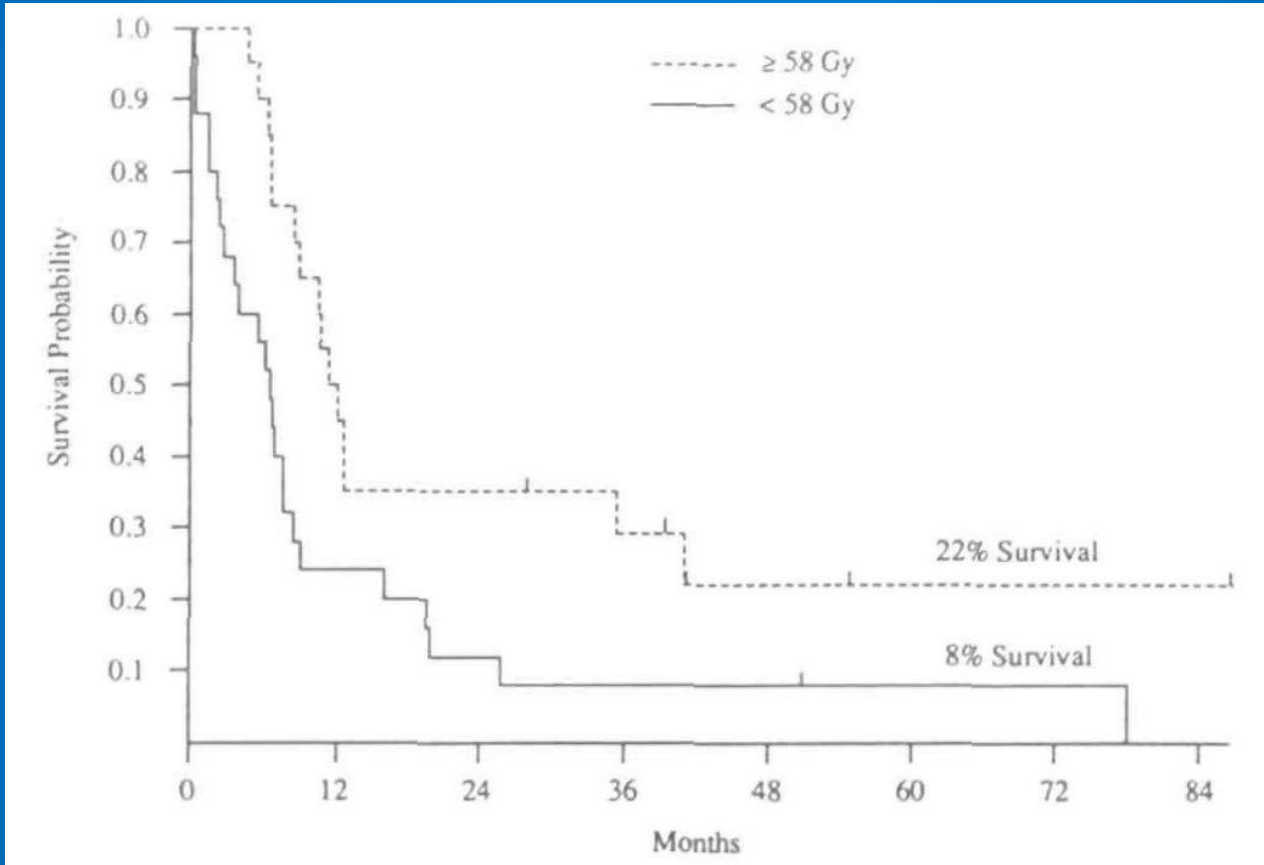

Figure 3. Overall survival according to radiation dose.

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Haraf DJ, Weichselbaum RR and Vokes EE: Ann Oncol 7(9):913-918

MILESTONE STUDY 1996: ” Re-irradiation with concomitant chemotherapy of unresectable head and neck cancer: A potentially curable disease"

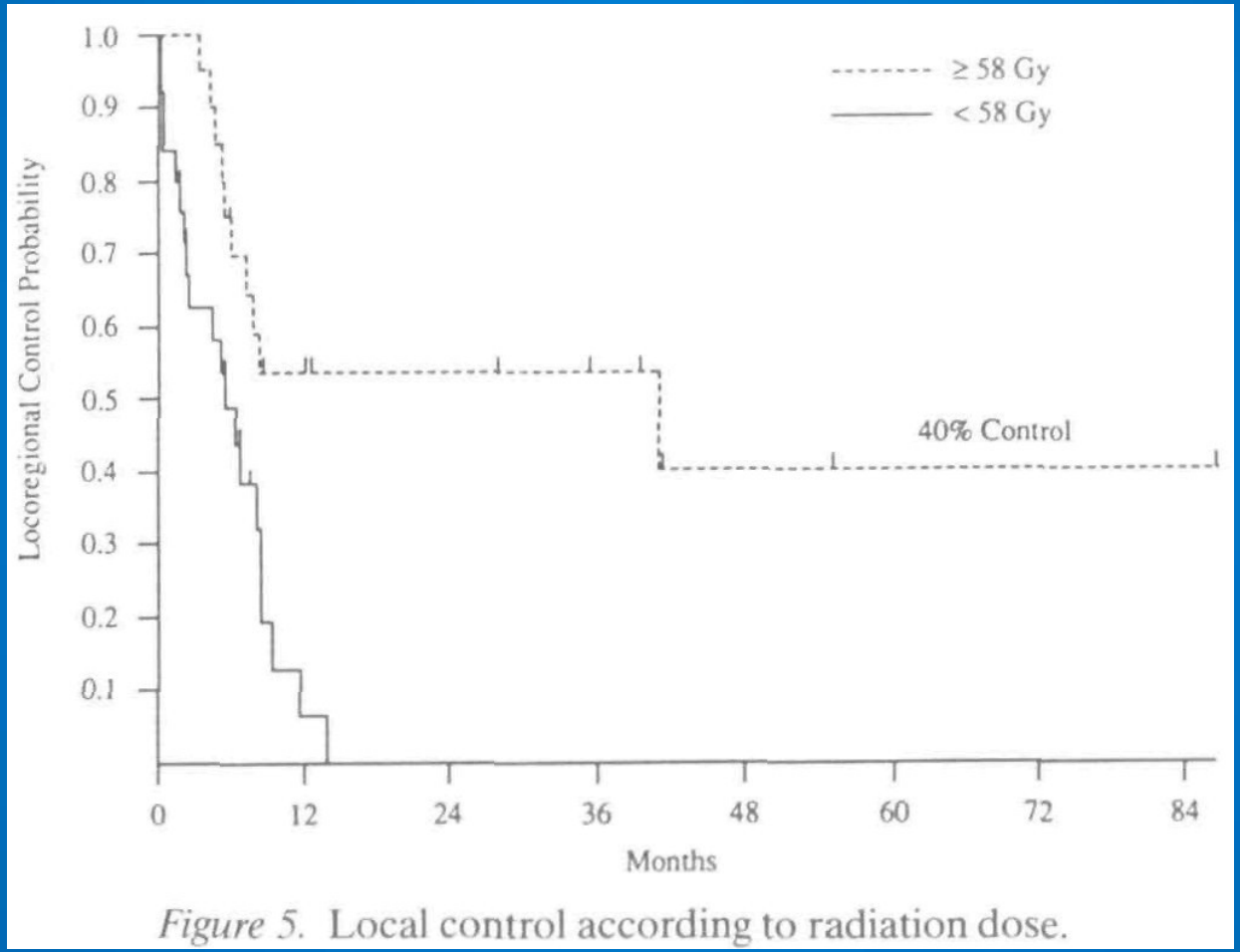

Figure 5. Local control according to radiation dose.

Haraf DJ, Weichselbaum RR and Vokes EE: Ann Oncol 7(9):913-918

Actuarial Local Control Rate: All Patients

2 years = 26%

3 years = 26%

5 years = 20%

Haraf DJ, Weichselbaum RR and Vokes EE: Ann Oncol 1996; 7(9):913-918

VOLUME 26 · NUMBER 34 · DECEMBER 1 2008

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Randomized Trial of Postoperative Reirradiation Combined With Chemotherapy After Salvage Surgery Compared With Salvage Surgery Alone in Head and Neck Carcinoma

François Janot, Dominique de Raucourt, Ellen Benhamou, Christophe Ferron, Gilles Dolivet, René-Jean Bensadoun, Marc Hamoir, Bernard Géry, Morbize Julieron, Marine Castaing, Etienne Bardet, Vincent Grégoire, and Jean Bourhis

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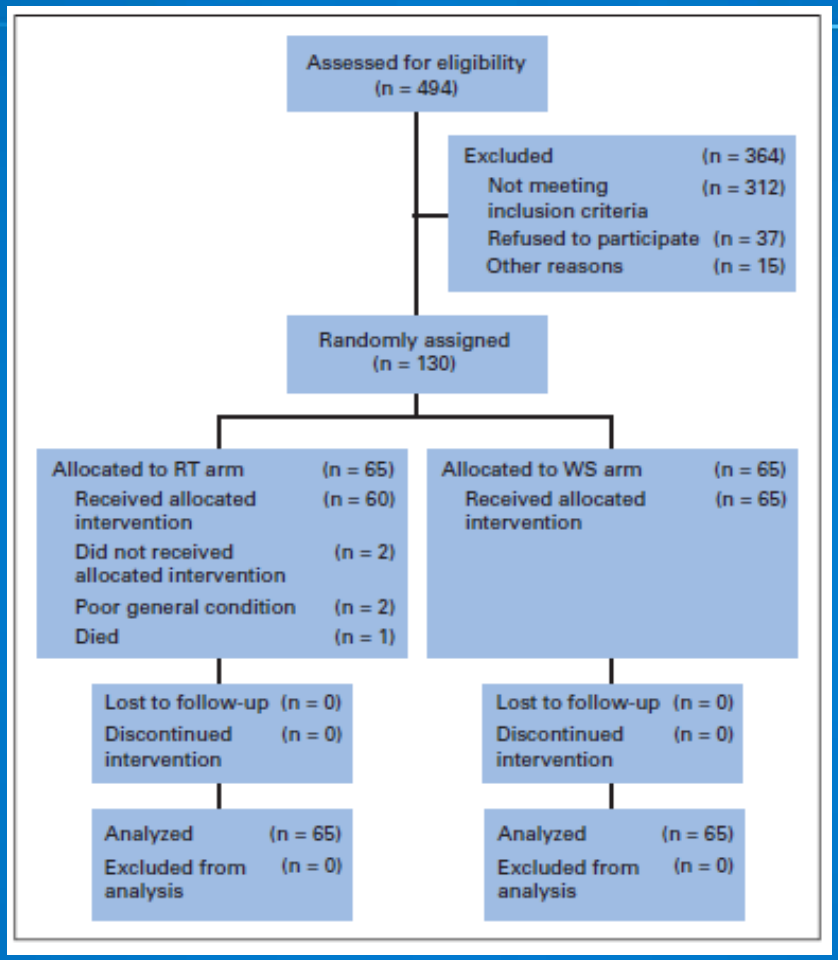
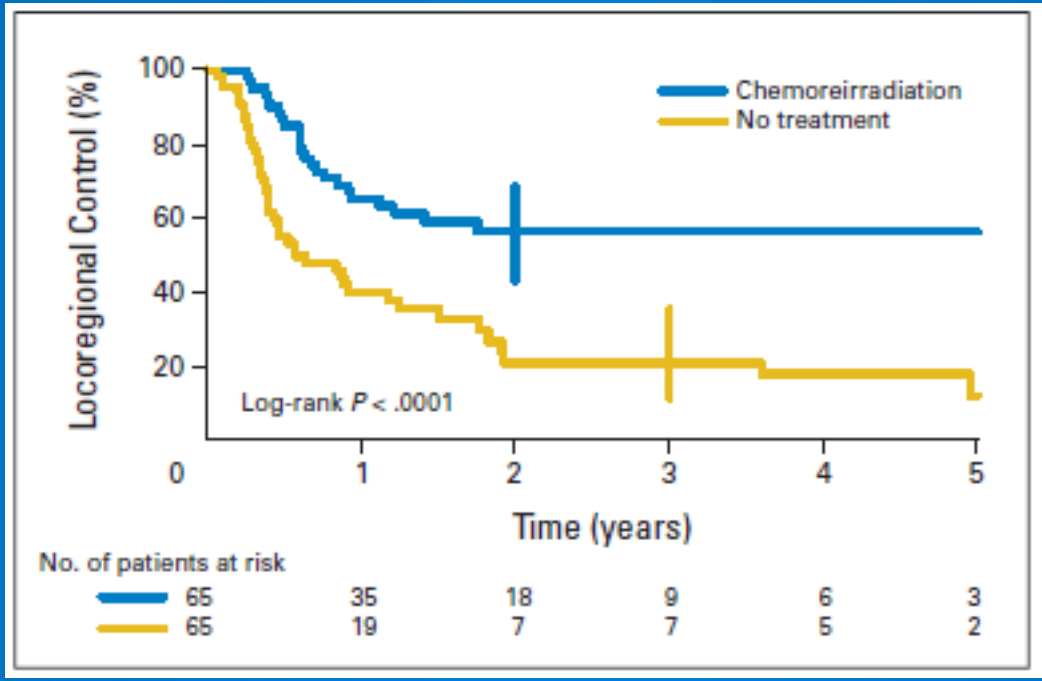


Janot F, de Raucourt D, Benhamou E et al.
J Clin Oncol 2008; 26: 5518-5523

LOCOREGIONAL CONTROL



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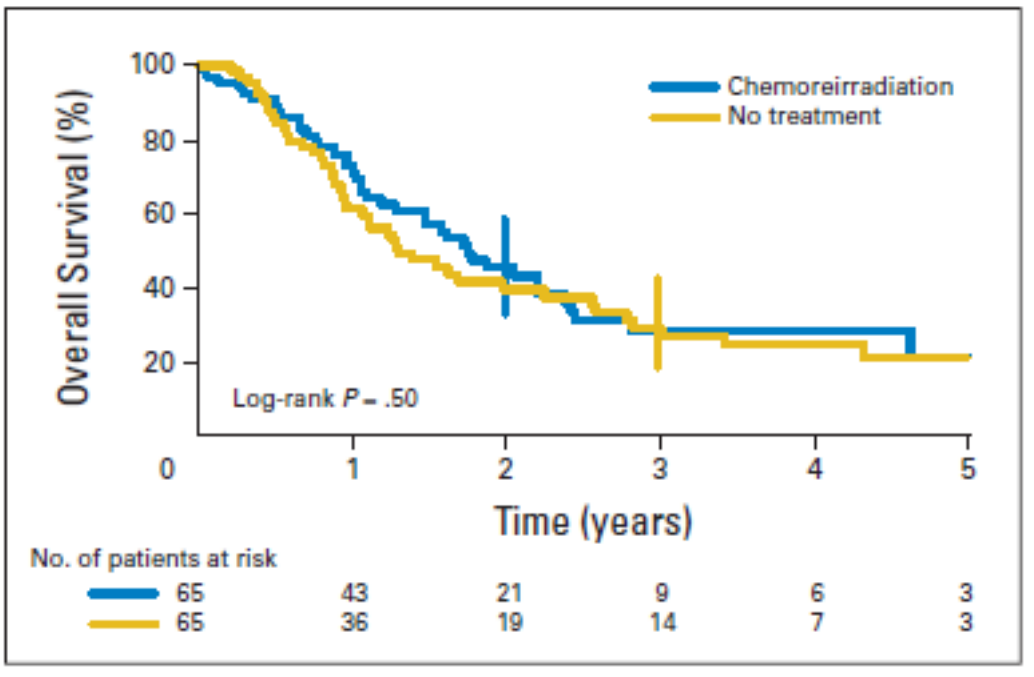
OVERALL SURVIVAL

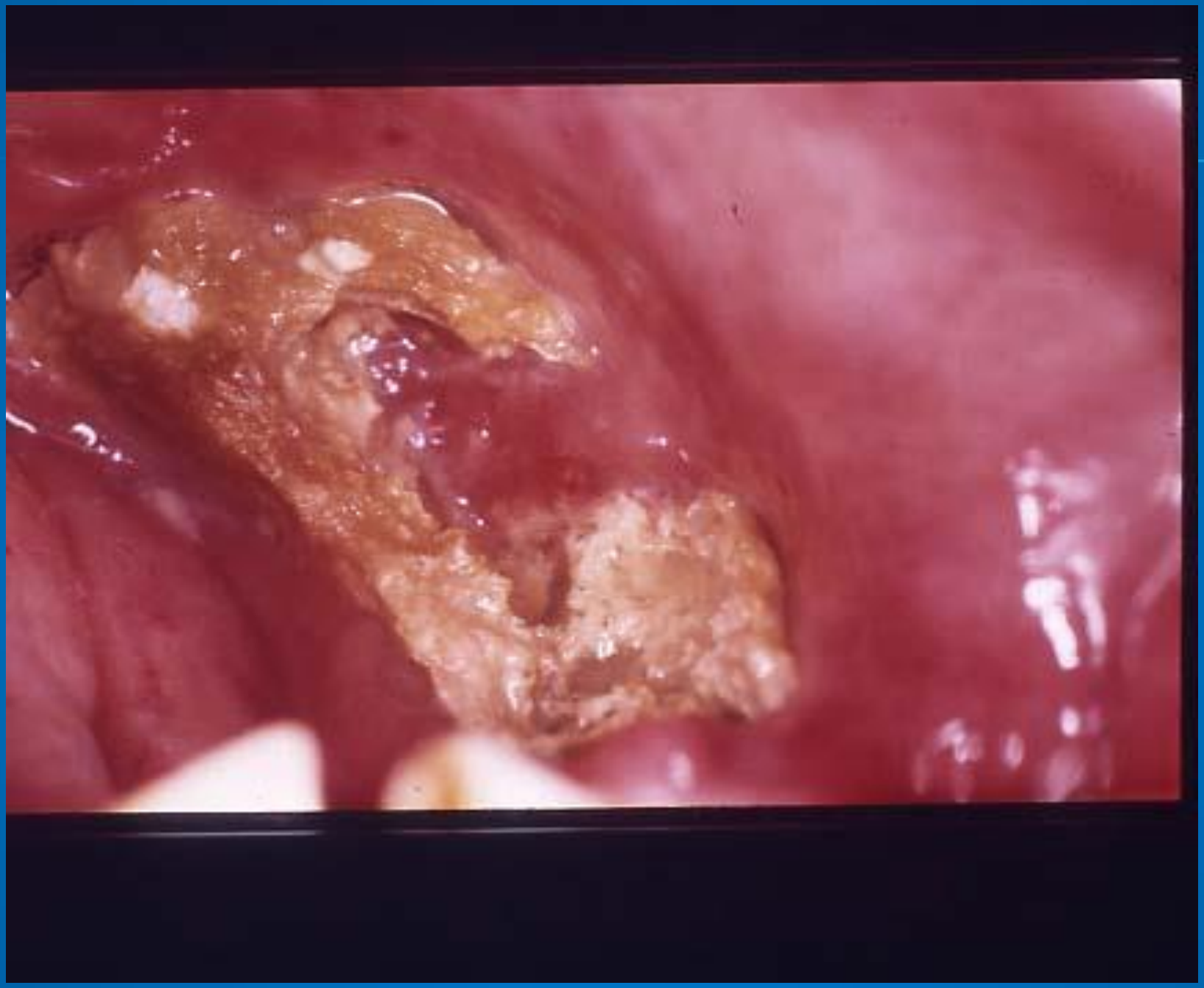


Janot F, de Raucourt D, Benhamou E et al. J Clin Oncol 2008; 26: 5518-5523

TOXICITY (GRADE 3,4)

		RT	Wait/See
Acute	2 years	28%	0%
Late	2 years	39%	10%

Janot F, de Raucourt D, Benhamou E et al. J Clin Oncol 2008; 26: 5518-5523



Refining patient selection for reirradiation of head and neck squamous carcinoma in the IMRT era: A multi-institution cohort study by the MIRI collaborative

Ward MC et al. Int J Rad Oncol Biol Phys;100(3): 586-594

THE MULTI-INSTITUTION REIRRADIATION COLLABORATIVE (MIRI)
7 CENTERS IN USA ; 412 PATIENTS

INCLUSION CRITERIA :

a) ”Patients irradiated to the head and neck to doses > 40 Gy,

with recurrent tumour or secondary primary in previously irradiated field”

Patients were retrospectively identified

b) ”Patients treated with overlapping field borders to a dose >40 Gy,

using conformal techniques, IMRT or VMAT; patients treated with SRT >5 Gy per fraction were not included

Ward MC et al. Int J Rad Oncol Biol Phys 2018;100(3): 586-594

WHAT IS ”REIRRADIATION”?

”Patients treated with overlapping field borders to a dose >40Gy”

PATIENTS´PERFORMANCE STATUS

a) Comorbidity was evaluated at the time of retreatment with Charlson Index

b) Pretreatment organ dysfunction: feeding tube and/or tracheostomy dependence was recorded

Ward MC et al. Int J Rad Oncol Biol Phys 2018;100(3): 586-594

IDENTIFICATION OF 3 PROGNOSTIC SUBGROUPS

Class I : Patients > 2 years from first radiotherapy course with resected tumours (2 year overall survival = 61.9%)

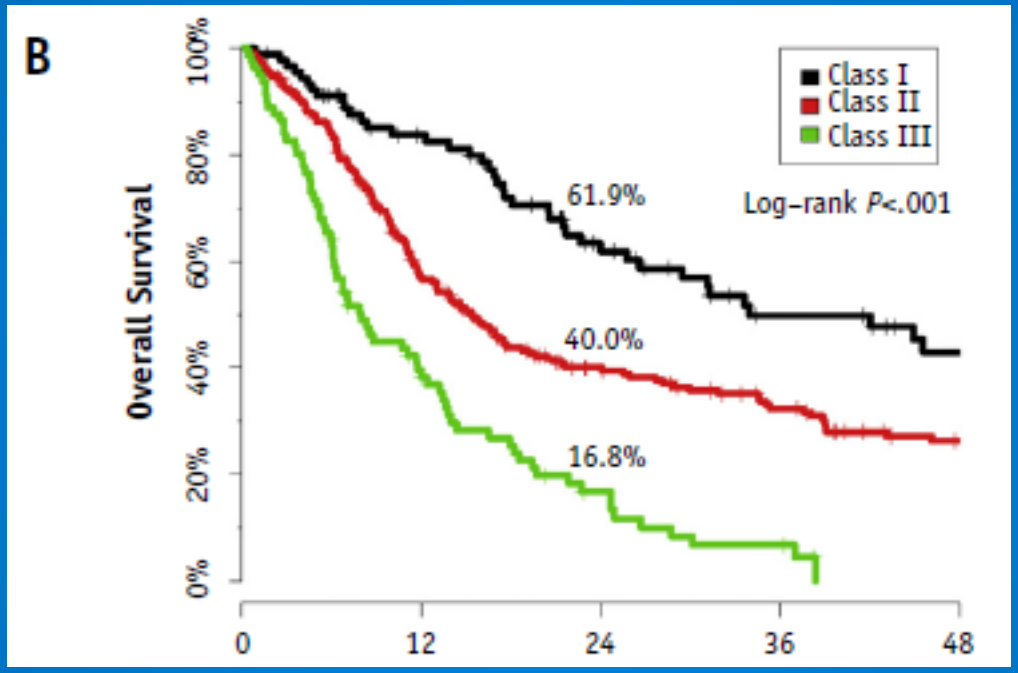
Class II : Patients > 2 years from first radiotherapy course and with no feeding tube or tracheostomy (2 year overall survival = 40%)

Class III: Remaining patients (2 year overall survival = 16.8%)

(“Refining patient selection for reirradiation of head and neck squamous carcinoma in the IMRT era: A multi-institution cohort study by the MIRI collaborative”)

Ward MC et al. Int J Rad Oncol Biol Phys 2018;100(3): 586-594

OVERALL SURVIVAL DIFFERENT CLASSES



Ward MC et al. Int J Rad Oncol Biol Phys 2018;100(3): 586-594

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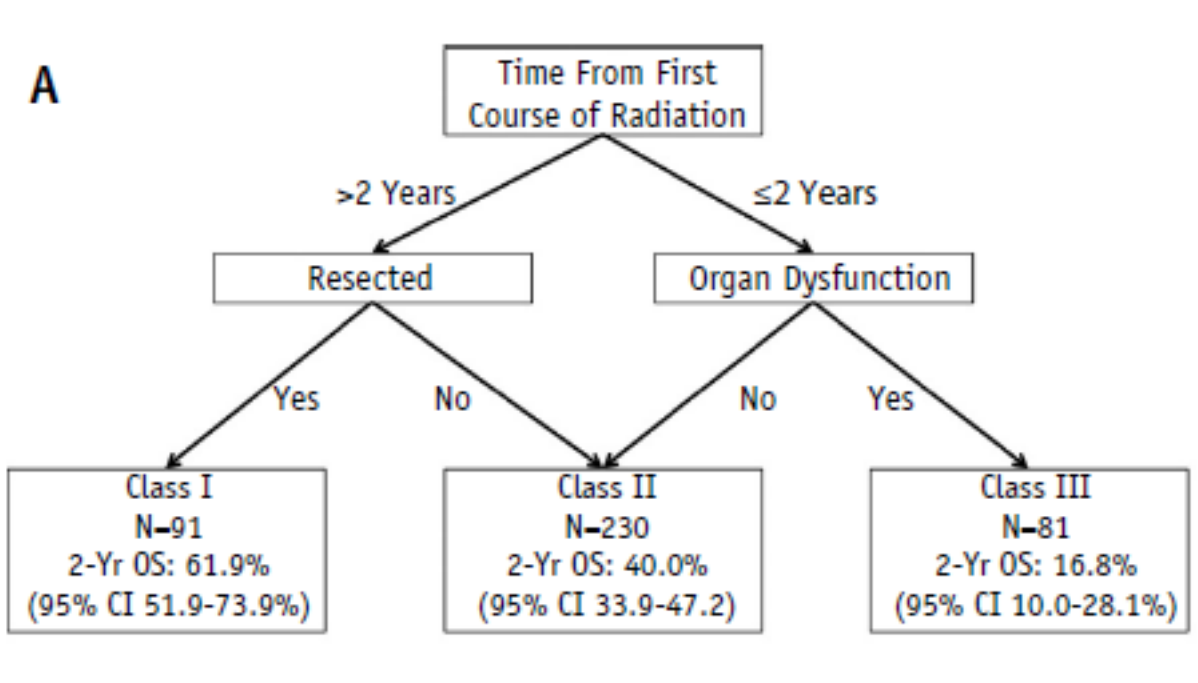
RECURSIVE PARTITIONING ANALYSIS FOR OVERALL SURVIVAL



Ward MC et al. Int J Rad Oncol Biol Phys 2018;100(3): 586-594

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IMPACT OF QUALITY OF SURGERY

2 year overall survival

Gross disease at time of reirradiation : 33.2 %

No gross disease at time of reirradiation : 50 %

Ward MC et al. Int J Rad Oncol Biol Phys;100(3): 586-594

FACTORS ASSOCIATED WITH OVERALL SURVIVAL

1. Site : Nasopharynx, base of skull tumours
2. Performance Status : Better/improved KPS
3. Organ function : Good/bad before reirradiation
4. Use of surgery
5. Interval between radiotherapy courses

CAUSES OF DEATH

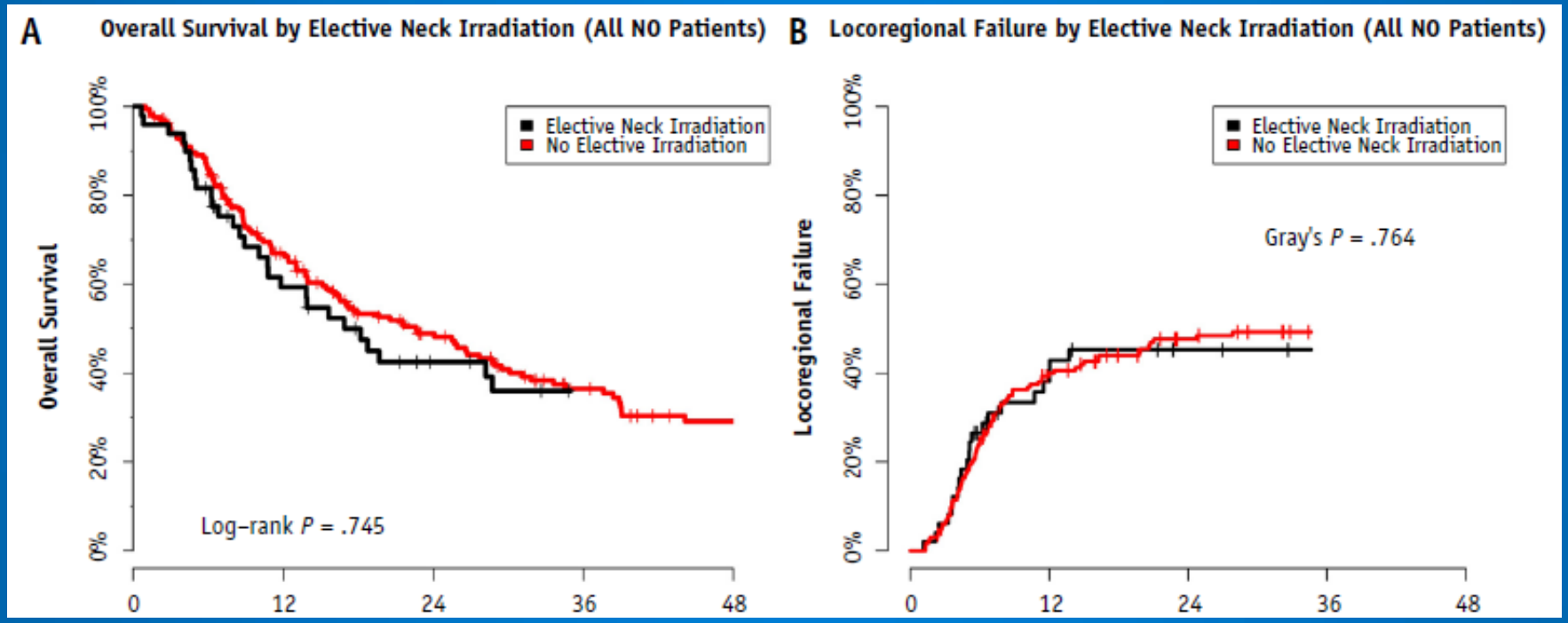
Locoregional progression only: 43%

Locoregional progression with DM: 12%

Incidence of carotid blow ot syndrome: 1.2% (5/412 patients)

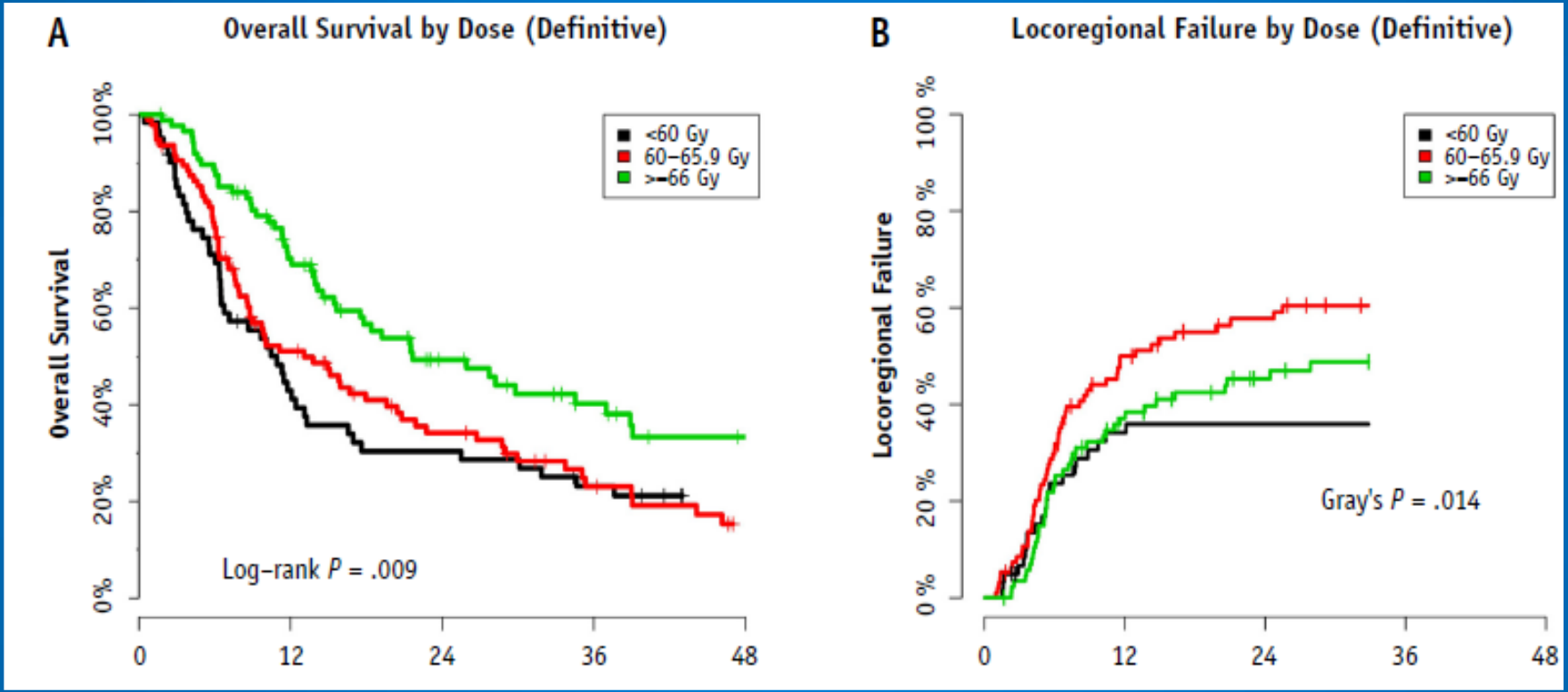
Ward MC et al. Int J Rad Oncol Biol Phys;100(3): 586-594

OVERALL SURVIVAL BY ELECTIVE NECK IRRADITION (All NO patients)



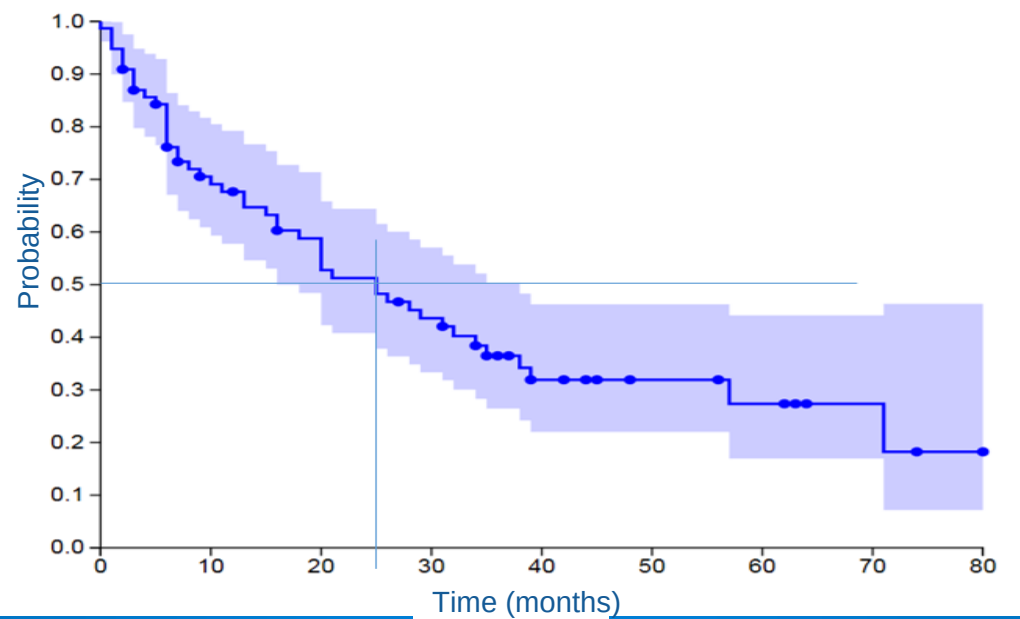
Caudell JJ: Int J Radat Oncol Biol Phys 2018; 100(3):606-617

OVERALL SURVIVAL BY DOSE
(”Definitive” treatment – no surgery)



Caudell JJ: Int J Radat Oncol Biol Phys 2018; 100(3):606-617

Reirradiated patients Karolinska University Hospital: Overall Survival



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CONCLUSIONS

1. Surgery is recommended for resectable disease
2. Cytostatic chemoherapy is palliative
3. Reirradiation is potentially curative for patients with recurrent unresectable head and neck cancer in previously irradiated volumes
4. Reirradiation can be dramatically toxic; treatment related deaths are reported.
5. No randomized studies exist, nor do level I or II data, only observational studies

6. The definition of "reirradiation" in publications is often not clear: volumes, doses, dose distributions, doses to OAR, fractionation etc.

7. Patient selection is of utmost important: reference to the 3 classes according to the MIRI Group

8. Important evaluation of life expectancy, assessment of comorbidities, performance status, prior radiotherapy sequelae, e.g. carotid stenosis, soft-tissue fibrosis, osteonecrosis

9. The chance of tumour control is higher with doses of at least 60 Gy

10. The longer the interval to prior radiotherapy, the better the prognosis; an interval of at least 1 year could be advantageous

11. Advanced radiotherapy techniques should be used, such as IMRT, VMAT, brachytherapy, or protons
12. No certain data exist to stipulate that the addition of chemotherapy improves tumour control or has an impact on severe toxicity
13. Second primaries have better prognosis than "true recurrences"
14. Primary constraints related to: carotid artery, brain tissue, mandible; Relative constraints related to: larynx, temporo-mandibular joint, soft tissues in the neck.

IMPORTANT – AND DIFFICULT: PATIENT INFORMATION !

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REIRRADIATION WITH SBRT AND CETUXIMAB multiinstitutional french prospective study 2007-2010

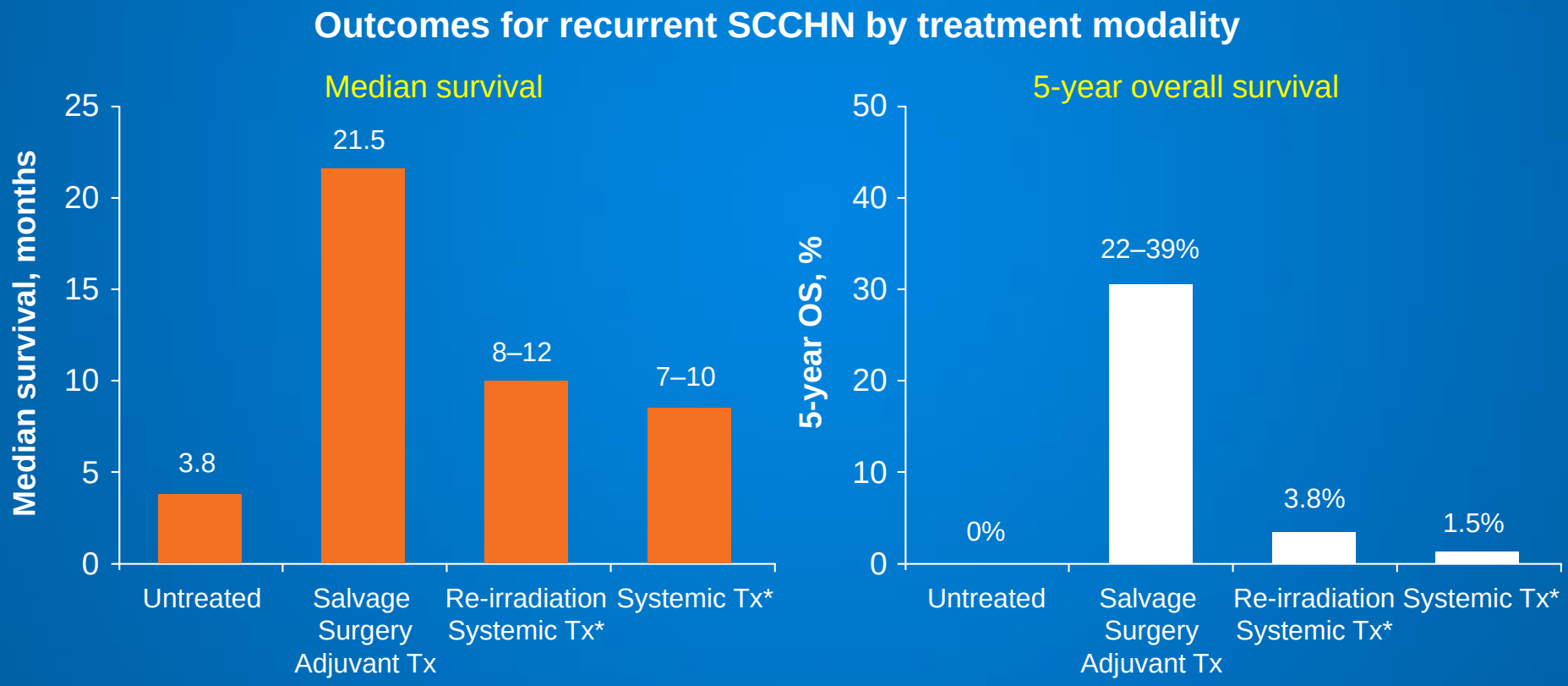
1. Technique/Dose: SBRT/ Dose was 36 Gy in 6 fractions to the 85% isodose lining covering 95% of the PTV.

2. Patients: Inoperable recurrent or new primary tumor in previously irradiated area; all had previous radiotherapy, 85% had previous surgery and 48% previous chemotherapy;mean time between previous radiotherapy and start of SBRT was 38 months

3. Results: 60 patients were included, 56 had all therapy; all 56 had squamous cell carcinoma; mean time between between previous radiotherapy and SBRT was 38 months; one toxic death; at 3 months response rate was 58.4% and disease control rate was 91.7%; 1-year OS rate was 47.5% (95% CI: 30.8-62.4)

What treatments are available in our armentarium?

- Surgery
- Re-irradiation
- Chemotherapy

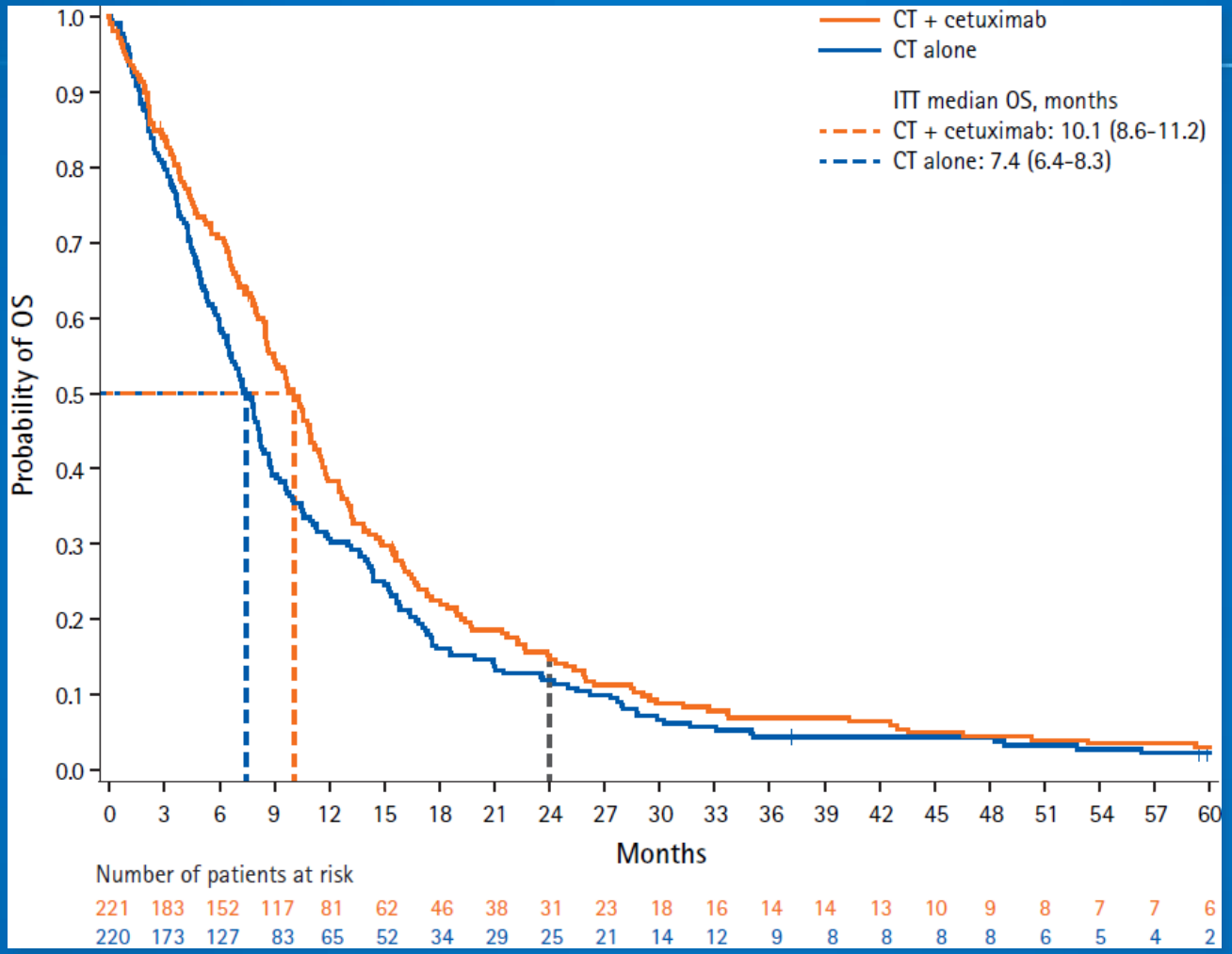


*Largely palliative population

CT, chemotherapy

Ho AS, et al. Head Neck 2014; 36:144–151

EXTREME – Overall Survival



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SURGERY

TECHNICALLY DIFFICULT:

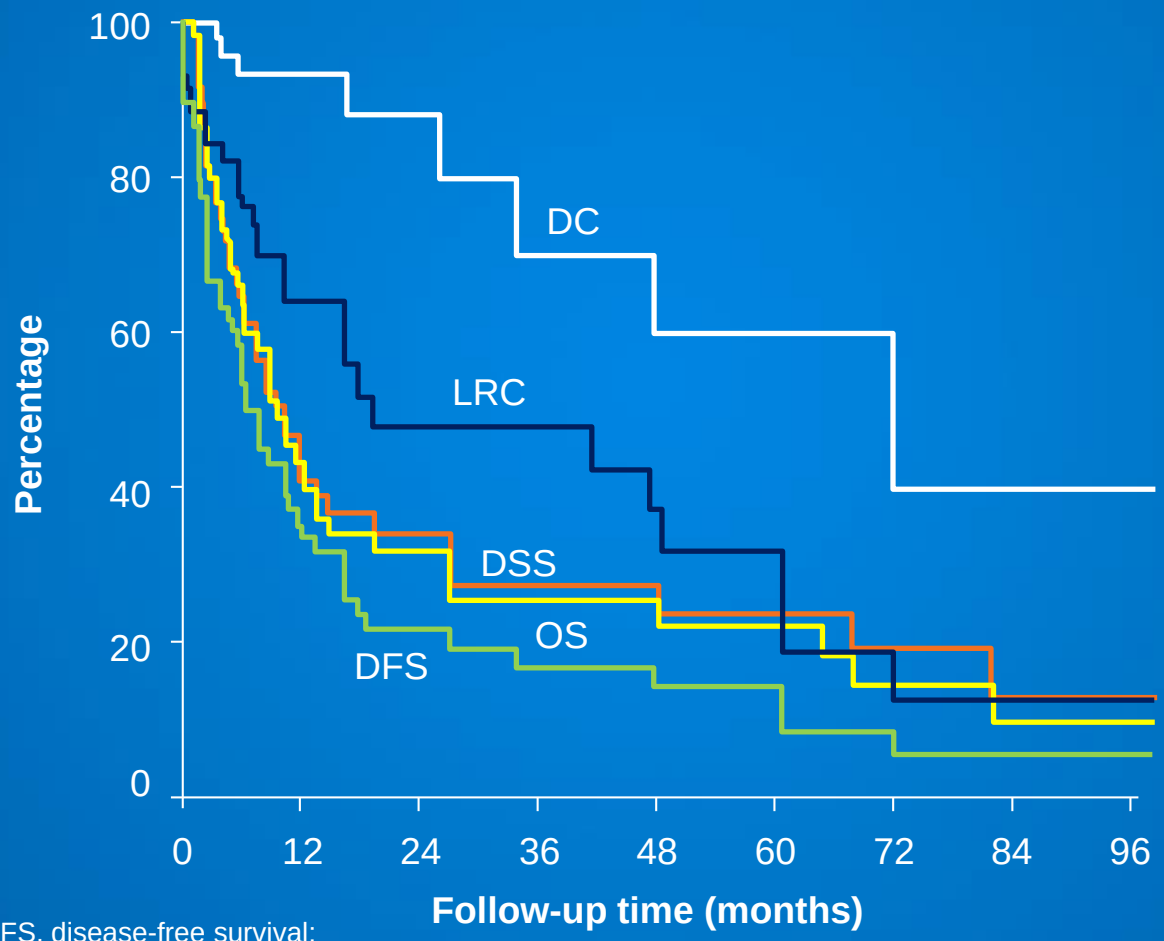
1. SURGICAL PROCEDURE IN PREVIOUSLY IRRADIATED AREA/VOLUME

2. CLOSE VICINITY TO IMPORTANT STRUCTURES, CAROTID ARTERY, SKULL BASE ETC.

3. COMPLICATIONS CAN BE IMPORTANT.....

Do we have to advocate re-irradiation?

Retrospective study of 60 consecutive patients re-irradiated using IMRT (66Gy) for recurrent SCCHN



DC, distant control; DFS, disease-free survival;
DSS, disease-specific survival;
LRC, locoregional control

Duprez F, et al. Radiother Oncol 2014;111:388–392

MILESTONE STUDY 1996: ” Re-irradiation with concomitant chemotherapy of unresectable head and neck cancer: A potentially curable disease"

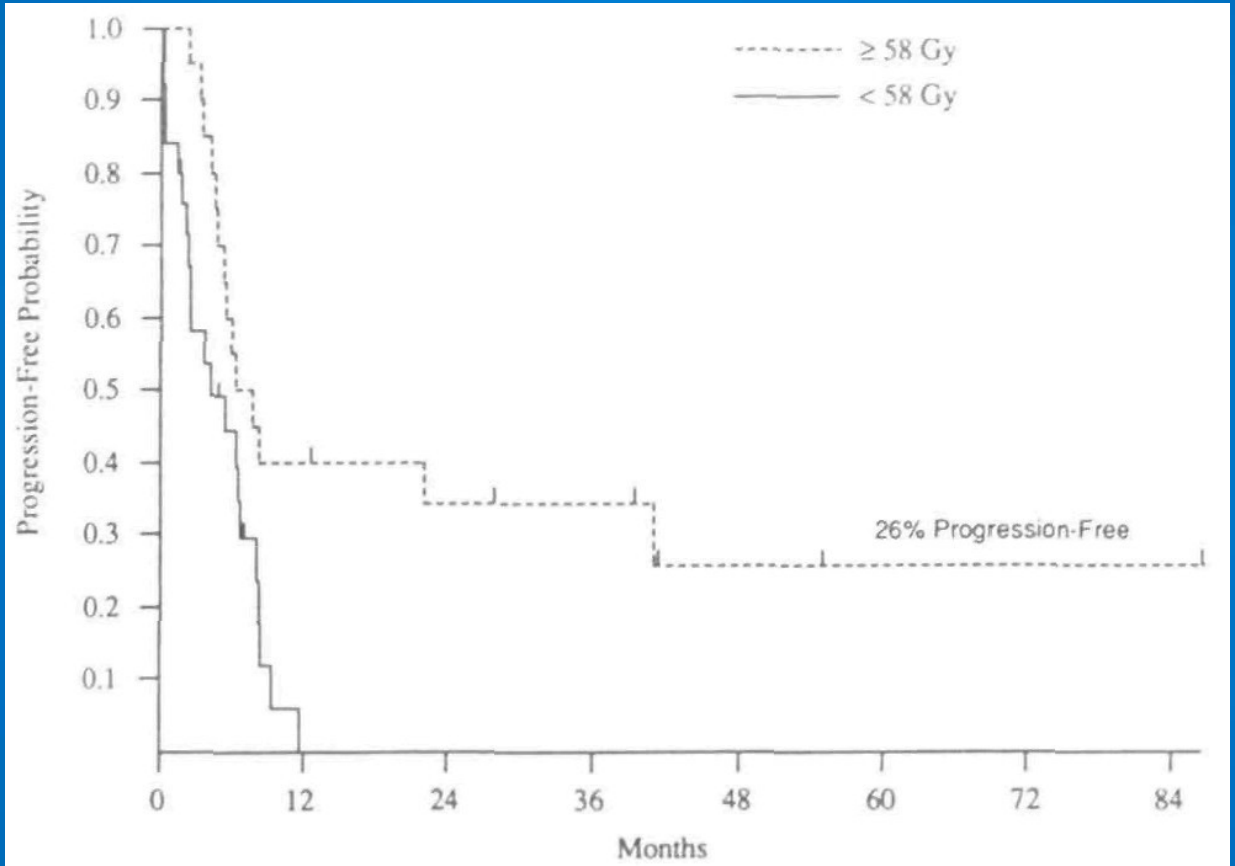


Figure 4. Time to progression according to radiation dose.

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Haraf DJ, Weichselbaum RR and Vokes EE: Ann Oncol 7(9):913-918

DOSE (PRIMARY TUMOUR)

What determines dose level for the primary tumour target?

Why 68 – 70 Gy as a standard dose?

DOSE TO TARGET OF PRIMARY TUMOUR

All constraints are looked at, but in clinical practice dose distribution with respect to following organs/tissues (OARs) representing major functions rule:

Salivary glands – xerostomia

Swallowing muscles – dysphagia

Mandible – osteoradionecrosis

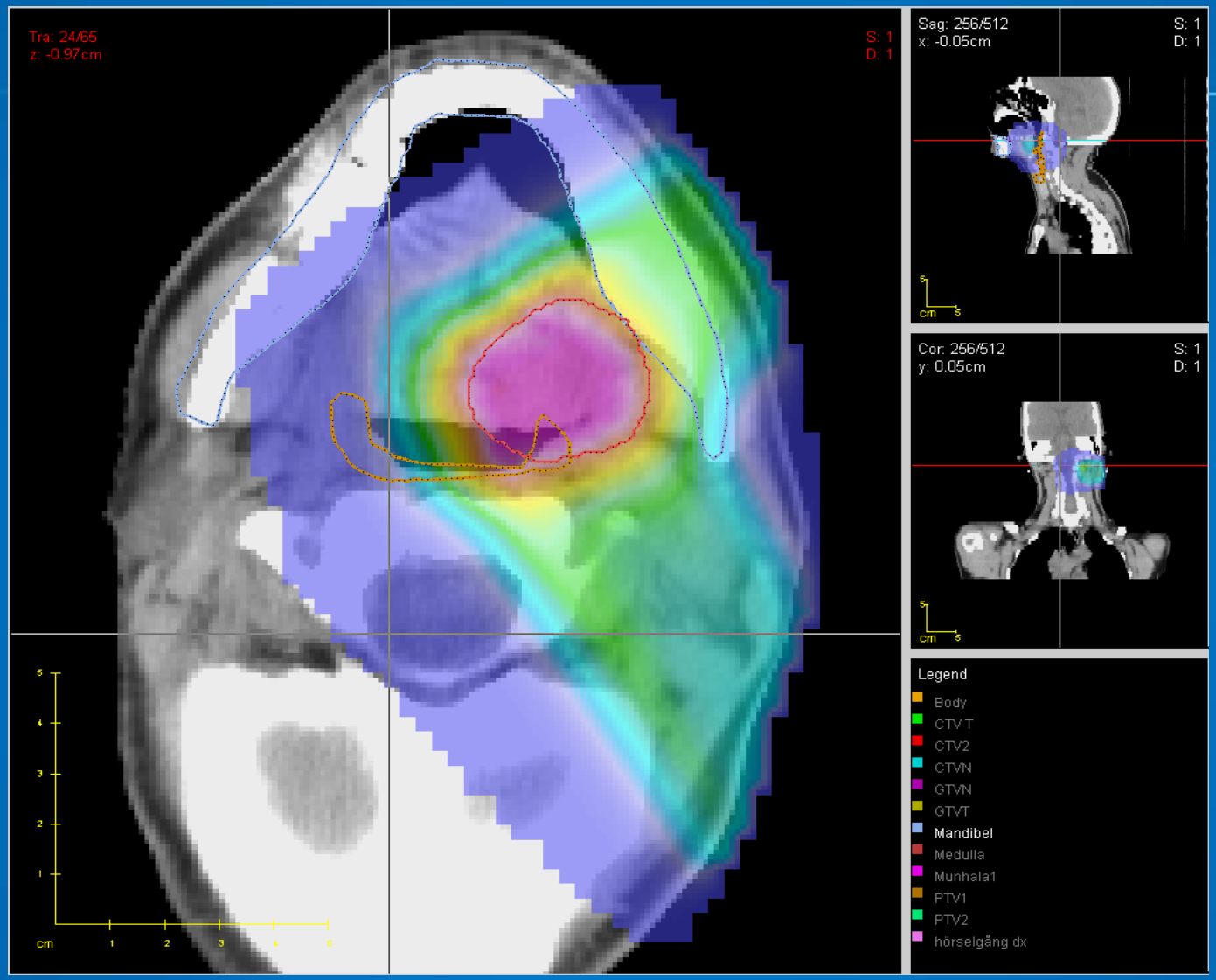
Larynx – speech, voice exhaustion, necrosis

Necrosis of soft tissues or vessels: VERY SELDOM impact on final dose distribution/dose level

DOSE ESCALATION IN HEAD AND NECK CANCER-ARE THERE DATA?

1. Hyperfractionation studies (EORTC, RTOG) are good supporters for the hypothesis of potential improvement (80.5 Gy)
2. Doses over 80 Gy, often administered with brachytherapy (boost) represent the best data published (not randomised studies)
3. Model studies with redistribution of doses to different targets with IMRT (Copenhagen, Belgium etc.)

Protons


Tra: 24/65
z: -0.97cm
S: 1
D: 1
Sag: 256/512
x: -0.05cm
S: 1
D: 1
Cor: 256/512
y: 0.05cm
S: 1
D: 1
cm
Legend
Body
CTV T
CTV2
CTVN
GTVN
GTVT
Mandibel
Medulla
Munhala1
PTV1
PTV2
hörselgång dx

Intro

Agenda

Svårigh

3DCRT

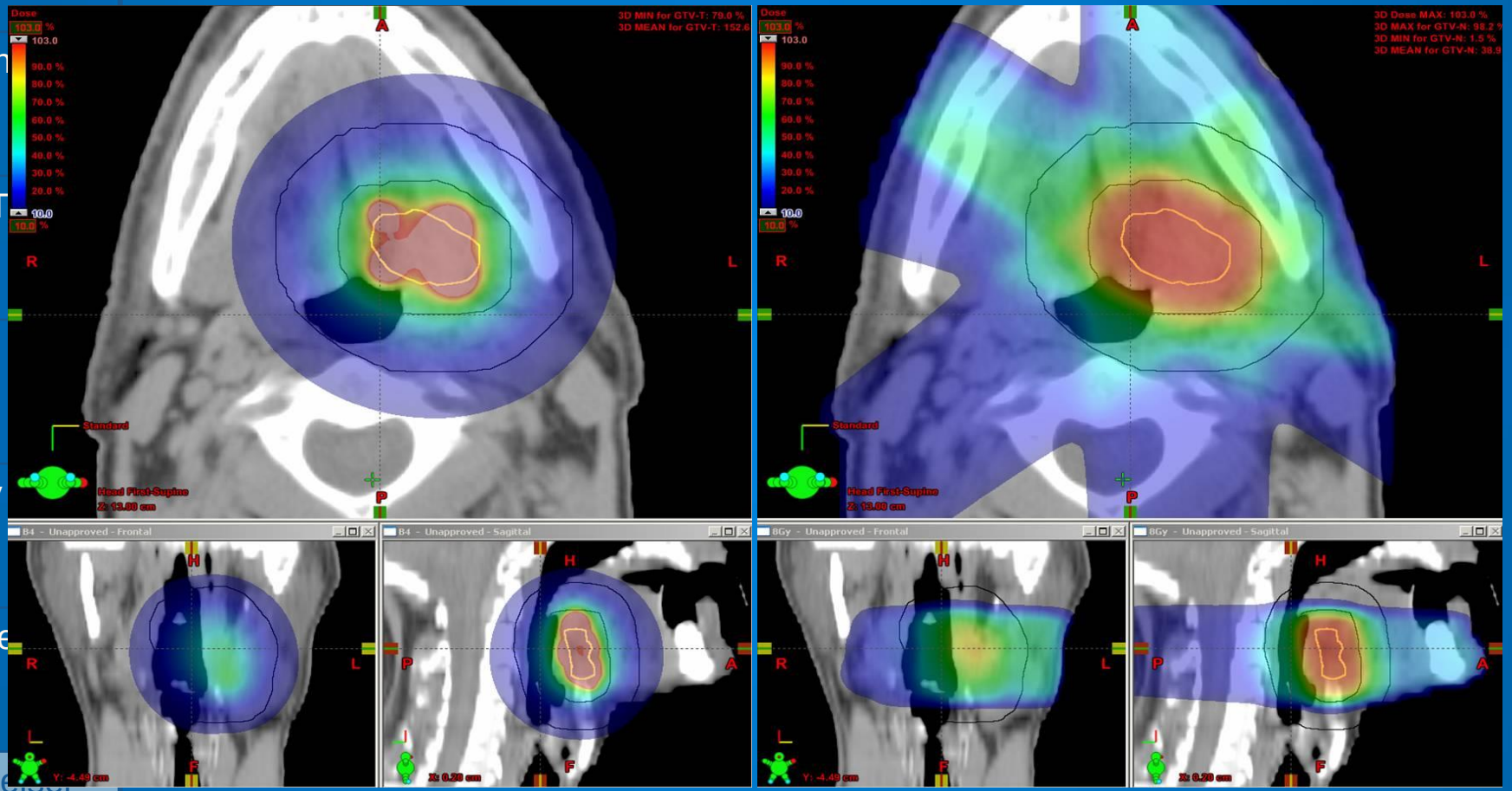
IMRT

Brachy

Protone

Jämförelse

Comparison (boost with BT or IMRT for base tongue ca)

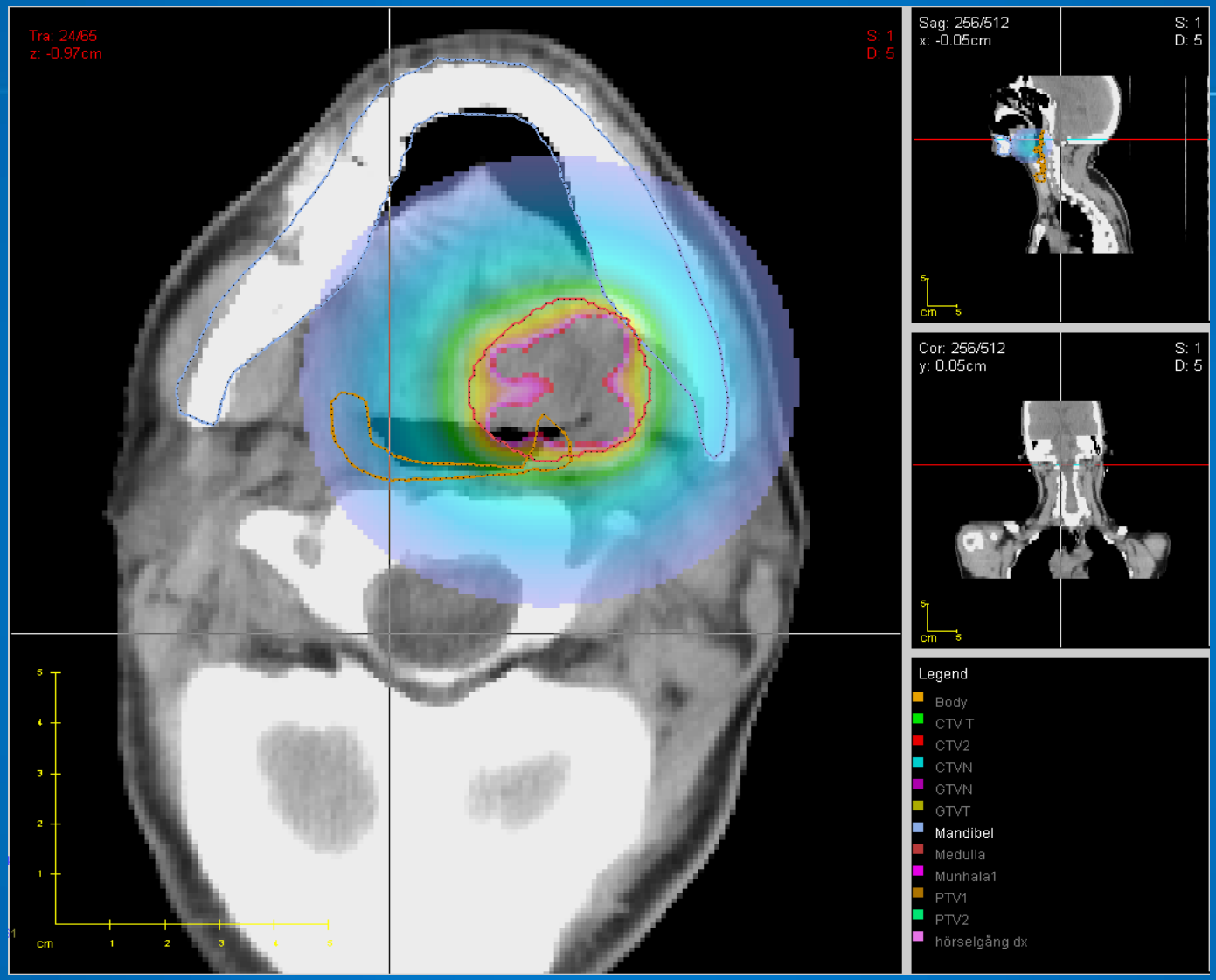


Brachy

IMRT

17 feb 2009 Solna

Brachy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x: -0.05cm
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Legend
Body
CTV T
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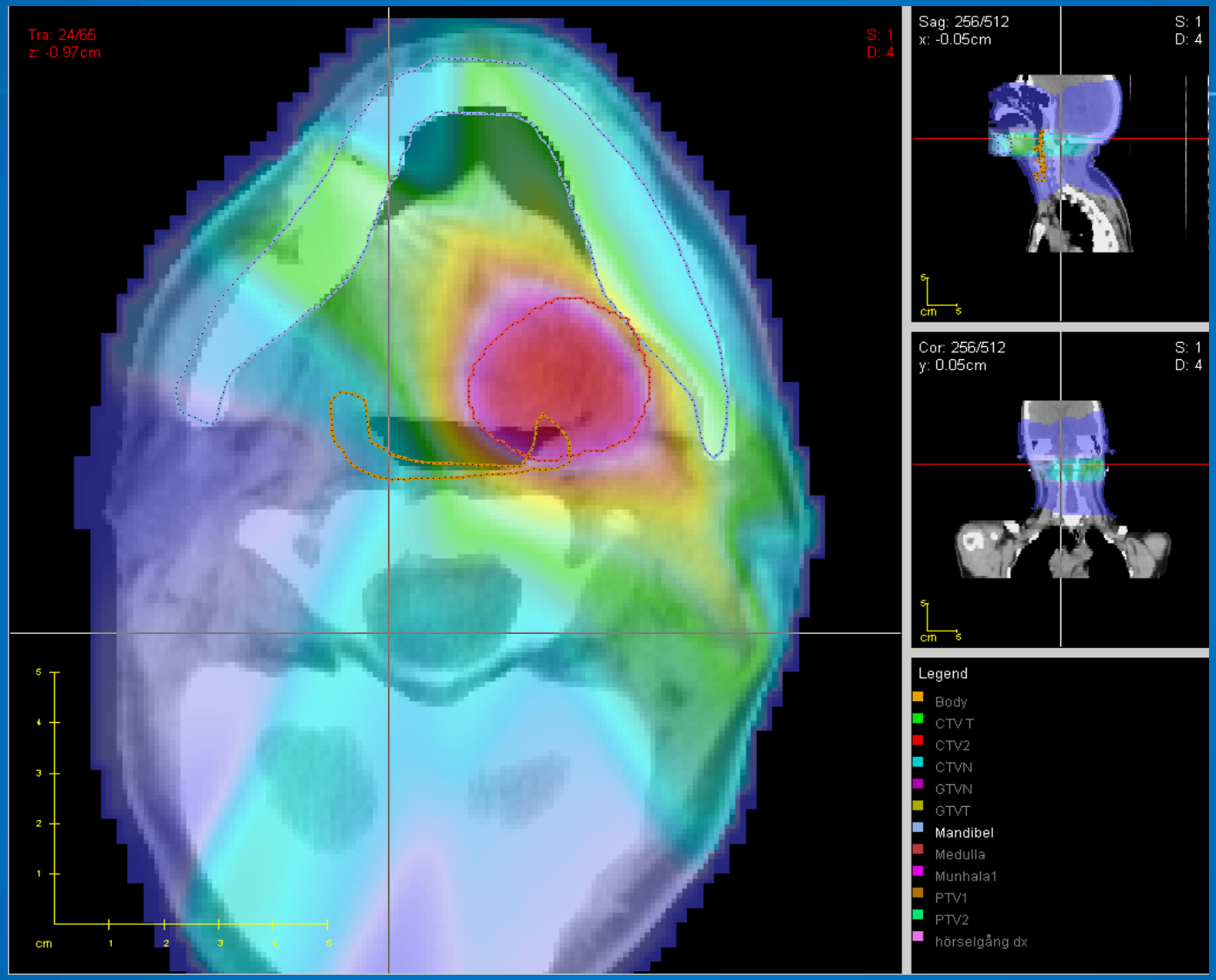
GTVT
Mandibel
Medulla
Munhala1
PTV1
PTV2
hörselgång dx

IMRT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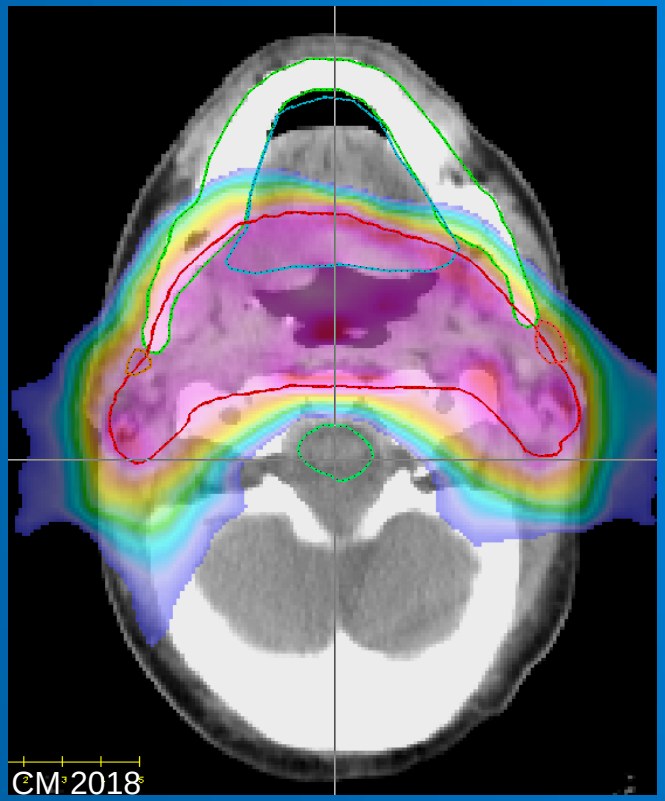
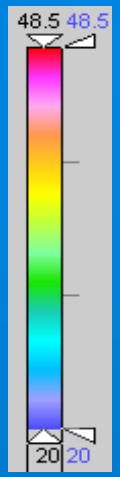
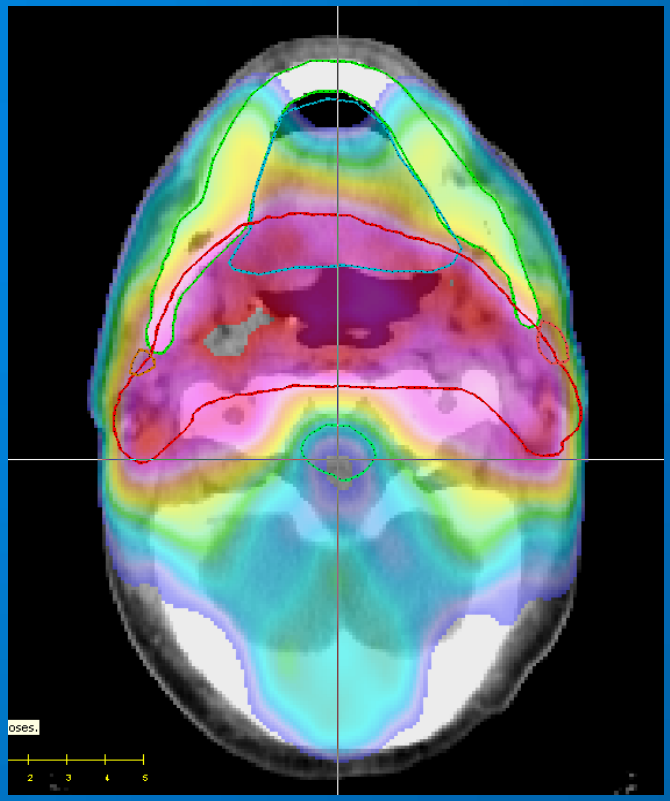
D: 4
Cor: 256/512
y: 0.05cm
S: 1
D: 4
cm
Legend
Body
CTV T
CTV2
CTVN
GTVN
GTVT
Mandibel
Medulla
Munhala1
PTV1
PTV2
hörselgång dx

IMPT (protons) 46 Gy for PTV2)





IMRT (photons) 46 Gy for PTV2



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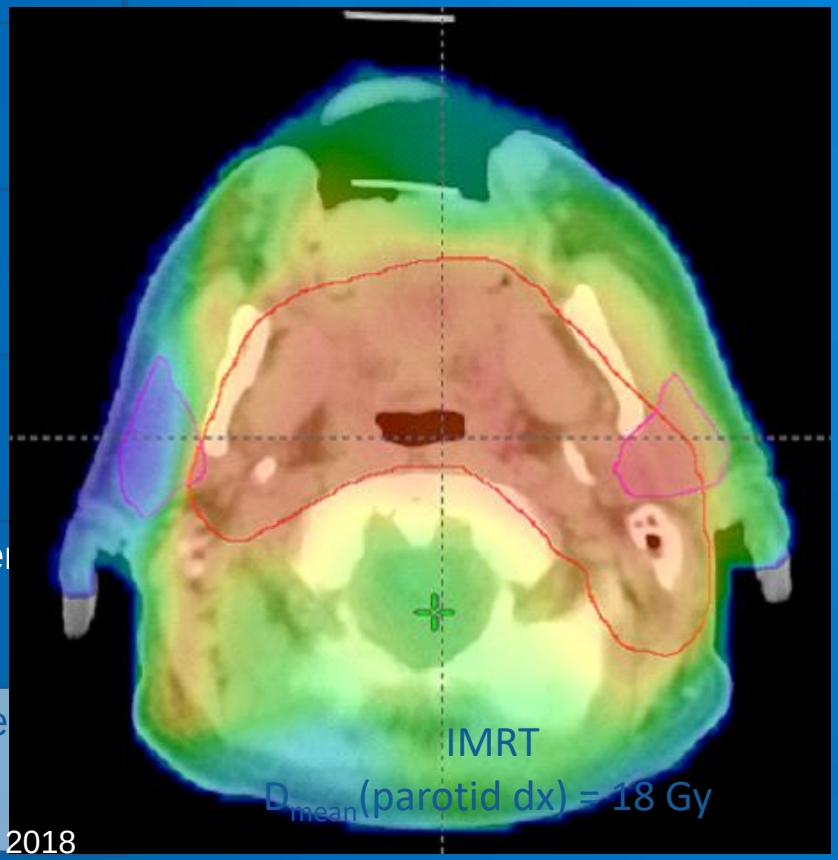
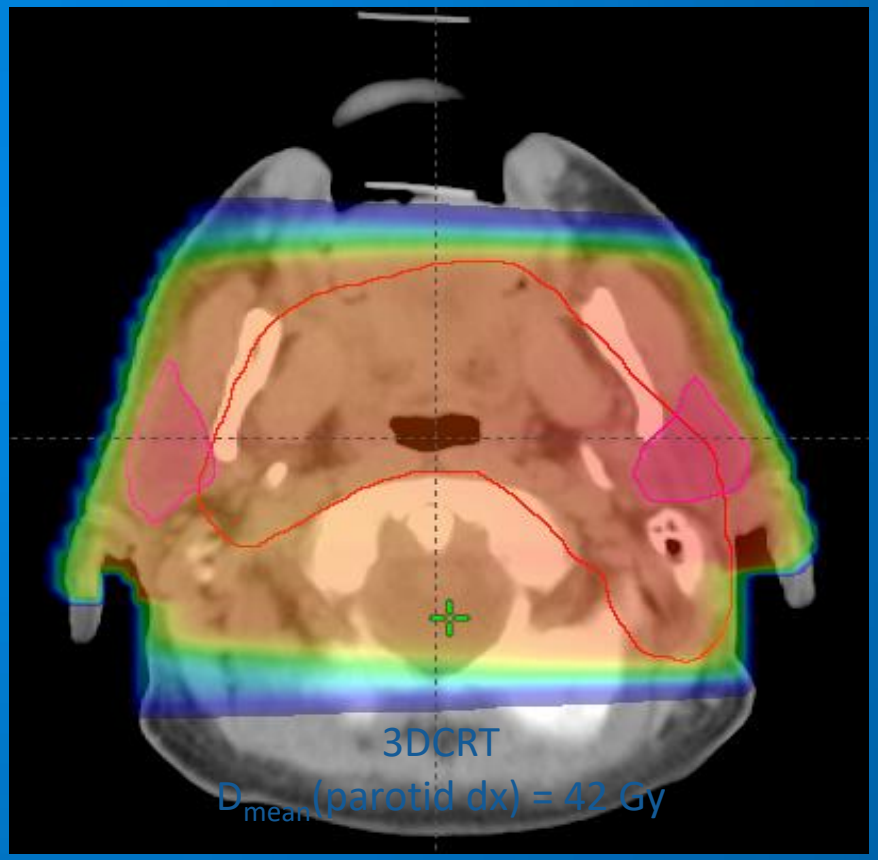
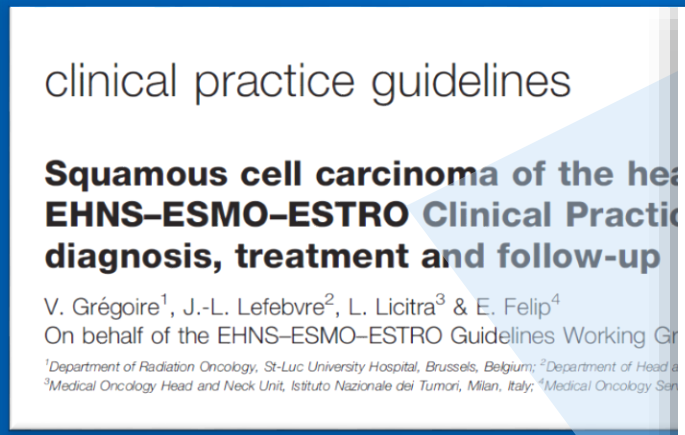
Intro
Agenda
Svårigheter
3DCRT
IMRT
Brachy
Protoner
Jämföre

Comparison: dose to parotid glands (IMRT vs. 3DCRT)





EHNS–ESMO–ESTRO guidelines for 1st line treatment of recurrent and/or metastatic SCCHN



clinical practice guidelines

Squamous cell carcinoma of the hea
EHNS–ESMO–ESTRO Clinical Practi
diagnosis, treatment and follow-up

V. Grégoire[1], J.-L. Lefebvre[2], L. Licitra[3] & E. Felip[4]
On behalf of the EHNS–ESMO–ESTRO Guidelines Working Gr
[1]Department of Radiation Oncology, St-Luc University Hospital, Brussels, Belgium; [2]Department of Head a
[3]Medical Oncology Head and Neck Unit, Istituto Nazionale dei Tumori, Milan, Italy; [4]Medical Oncology Ser

local, regional and metastatic recurrence

In selected cases of localized recurrence, surgery (if operable) or re-irradiation can be considered. For most patients palliative chemotherapy is the standard option. First-line option for fit patients should include the combination of cetuximab with cisplatin or carboplatin plus 5-fluorouracil (PF). It resulted in longer survival than PF alone [II, A]. In patients for which

EHNS, European Head and Neck Society;
ESMO, European Society for Medical Oncology;
ESTRO, European Society for Radiotherapy and Oncology

Grégoire V, et al. Ann Oncol 2010;21(Suppl 5):184–186

REIRRADIATION WITH SBRT AND CETUXIMAB multiinstitutional french prospective study 2007-2010

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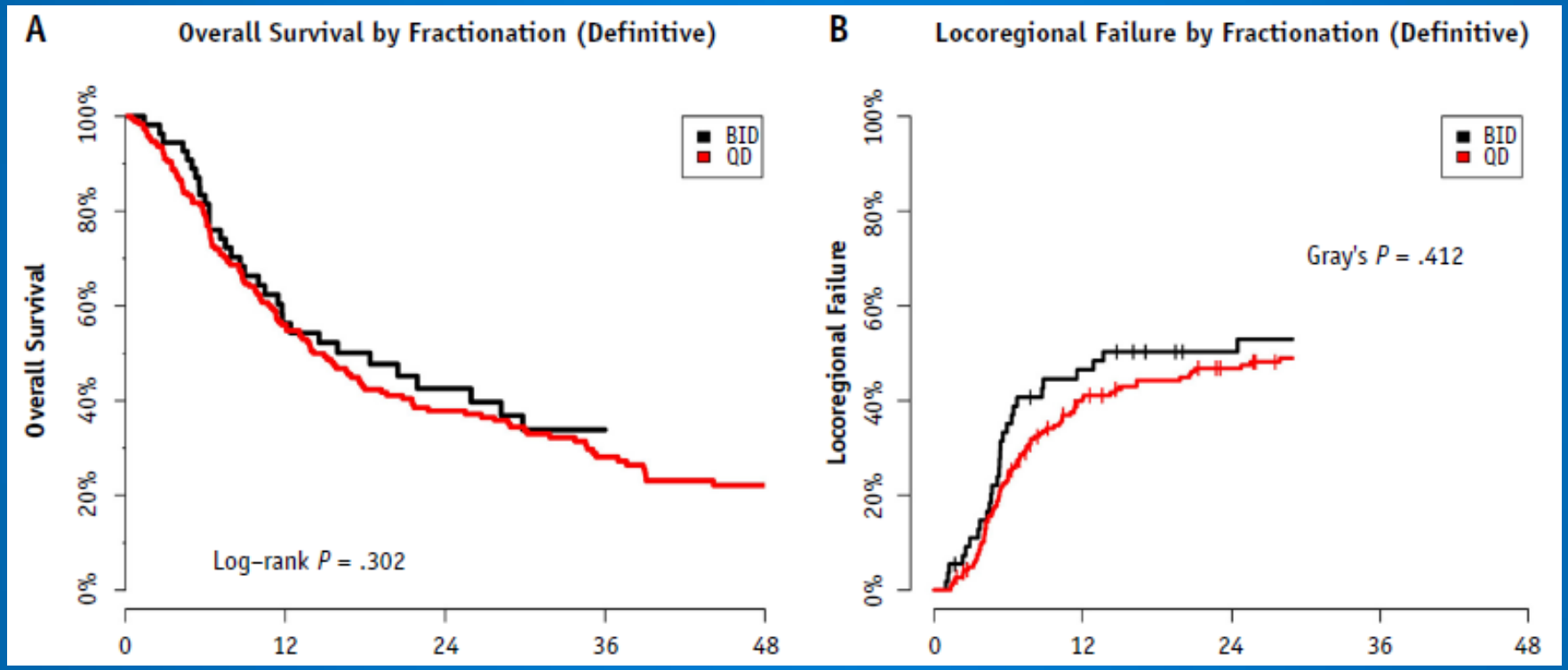
4. Reirradiation can be dramatically toxic; treatment related deaths are reported.
5. No randomized studies exist, nor do level I or II data, only observational studies

VOLUME (PRIMARY TUMOUR)

What decides volume to the primary tumour target?

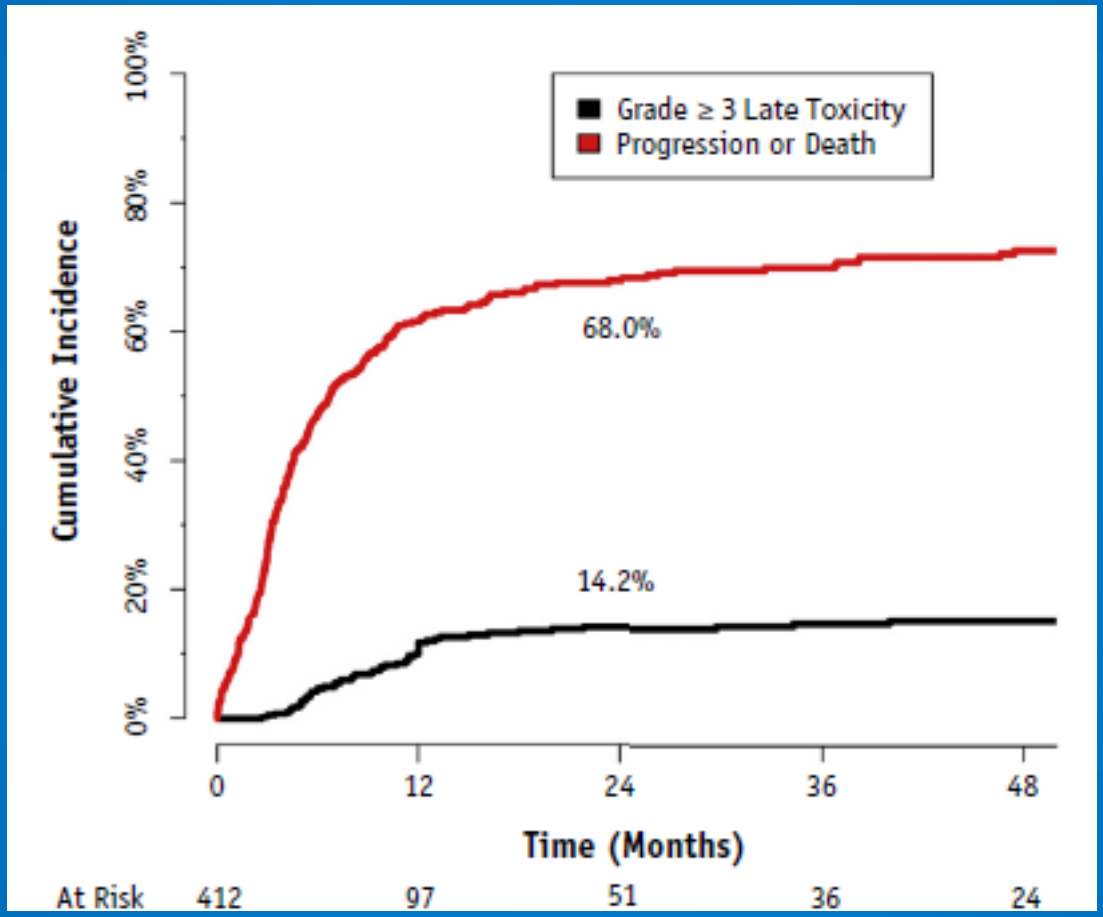
1. GTV-T: Representing the volume with the highest infestation of clonogenic cells
2. GTV-N: Representing a volume with a high infestation of clonogenic cells
3. Elective volumes: No malignant cells identified with present diagnostic methods but ”at risk”

OVERALL SURVIVAL BY FRACTIONATION (”Definitive” treatment – no surgery)



Caudell JJ: Int J Radat Oncol Biol Phys 2018; 100(3):606-617

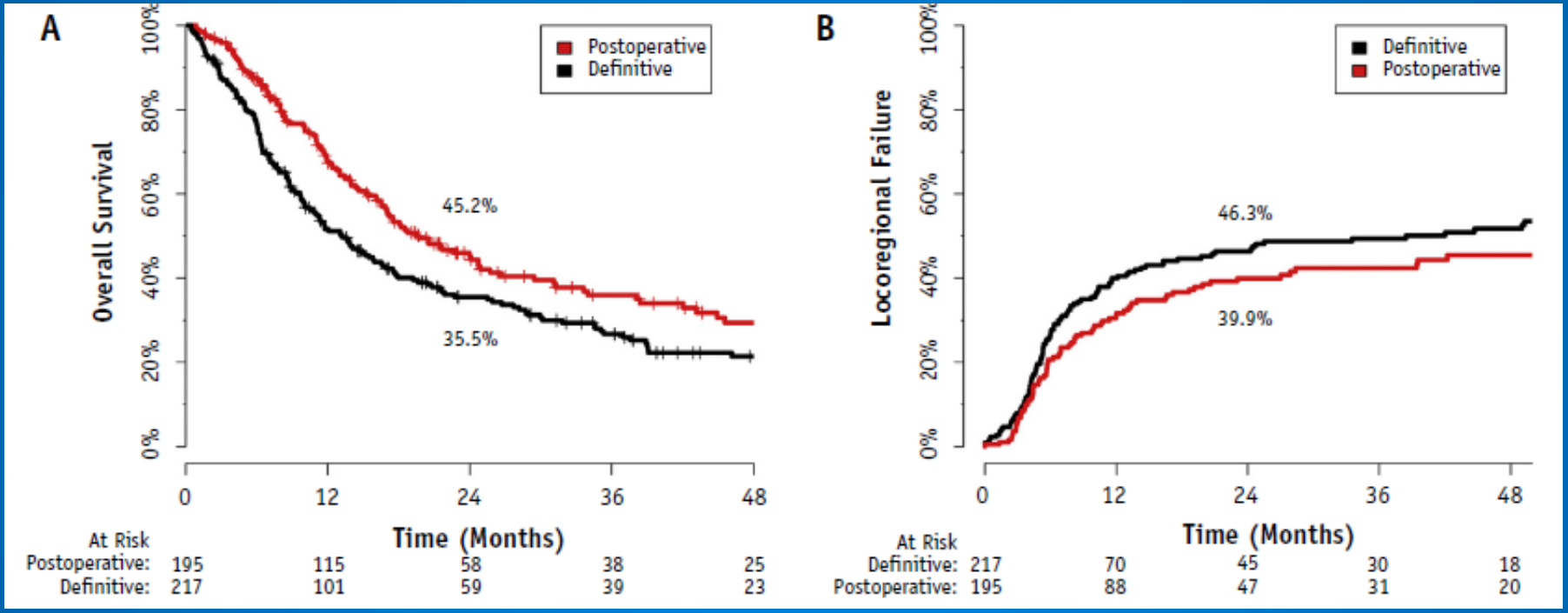
INFLUENCE OF GRADE >= 3 TOXICITY



Ward MC et al. Int J Rad Oncol Biol Phys 2018;100(3): 586-594

CM 2018

OVERALL SURVIVAL 412 PATIENTS

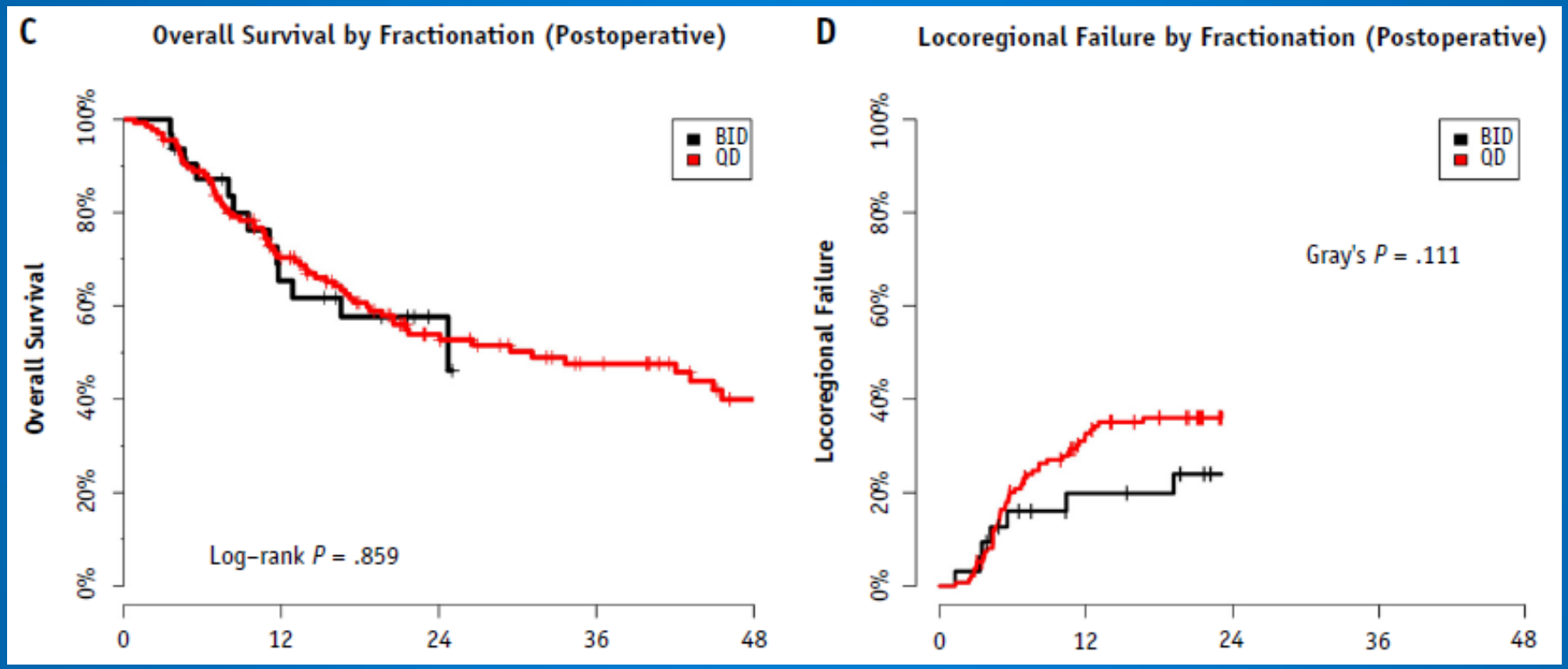


Ward MC et al. Int J Rad Oncol Biol Phys 2018;100(3): 586-594

ASSESSED PARAMETERS WITH POTENTIAL IMPACT ON SURVIVAL, LOCOREGIONAL CONTROL AND TOXICITY

a) Elective nodal treatment
b) Dose
c) Fractionation

OVERALL SURVIVAL BY FRACTIONATION (Postoperative)



Caudell JJ: Int J Radat Oncol Biol Phys 2018; 100(3):606-617

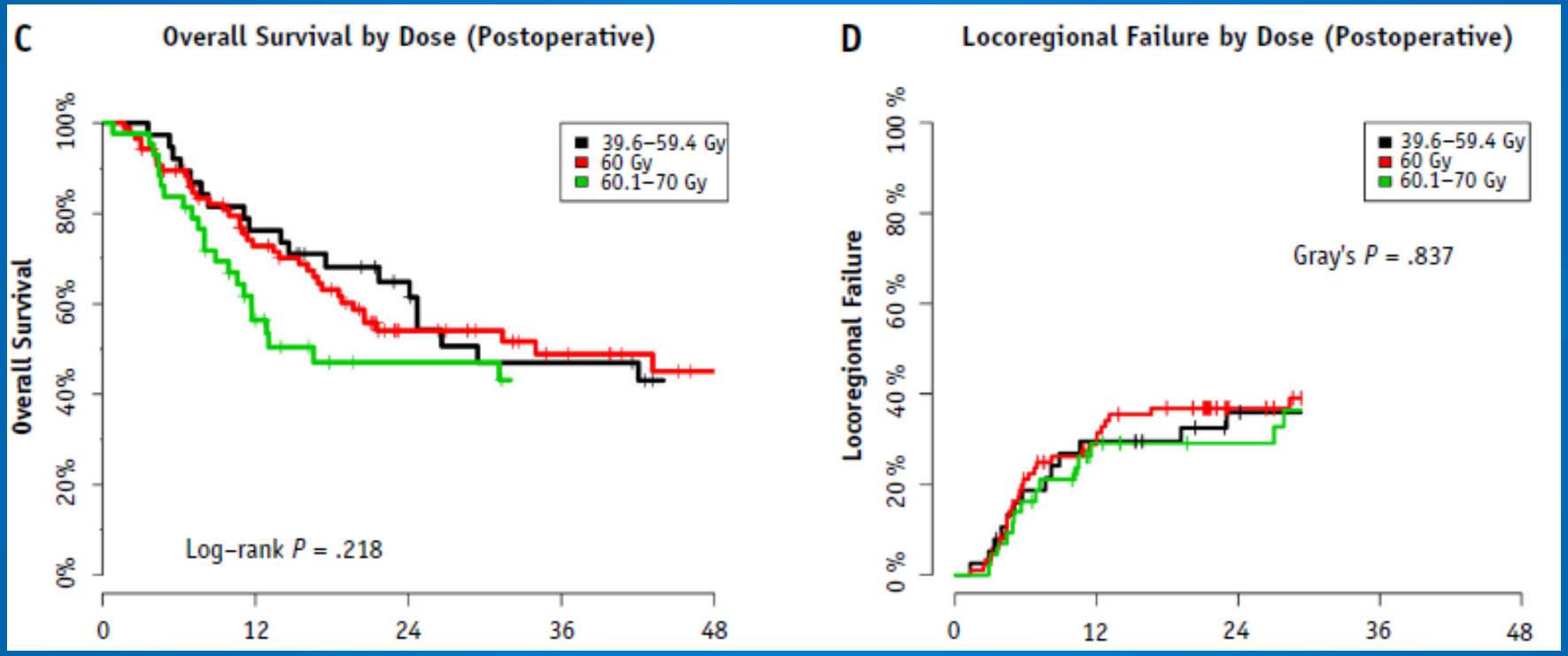
REIRRADIATION WITH SBRT AND CETUXIMAB multiinstitutional french prospective study 2007-2010

1. Technique/Dose: SBRT/ Dose was 36 Gy in 6 fractions to the 85% isodose lining covering 95% of the PTV.

2. Patients: Inoperable recurrent or new primary tumor in previously irradiated area; all had previous radiotherapy, 85% had previous surgery and 48% previous chemotherapy;mean time between previous radiotherapy and start of SBRT was 38 months

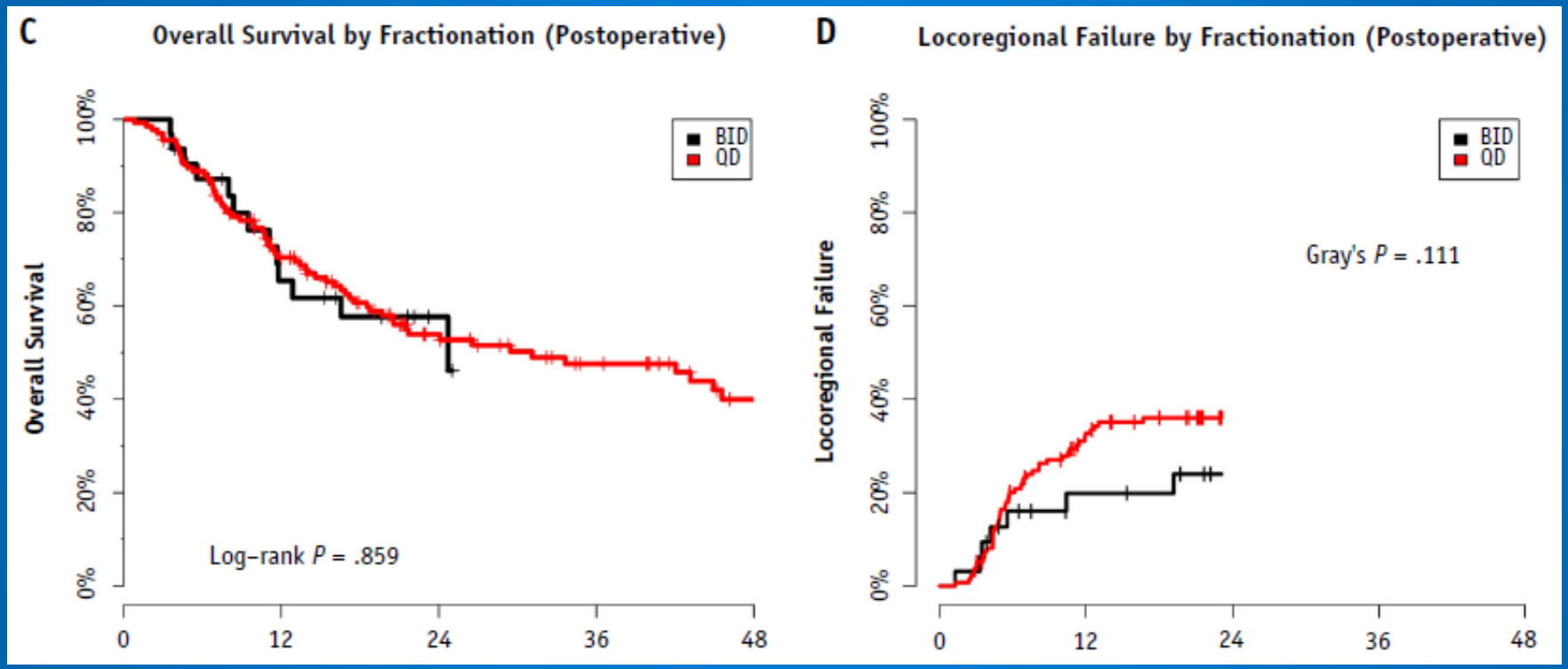
3. Results: 60 patients were included, 56 had all therapy; all 56 had squamous cell carcinoma; mean time between between previous radiotherapy and SBRT was 38 months; one toxic death; at 3 months response rate was 58.4% and disease control rate was 91.7%; 1-year OS rate was 47.5% (95% CI: 30.8-62.4)

OVERALL SURVIVAL BY DOSE (Postoperative)



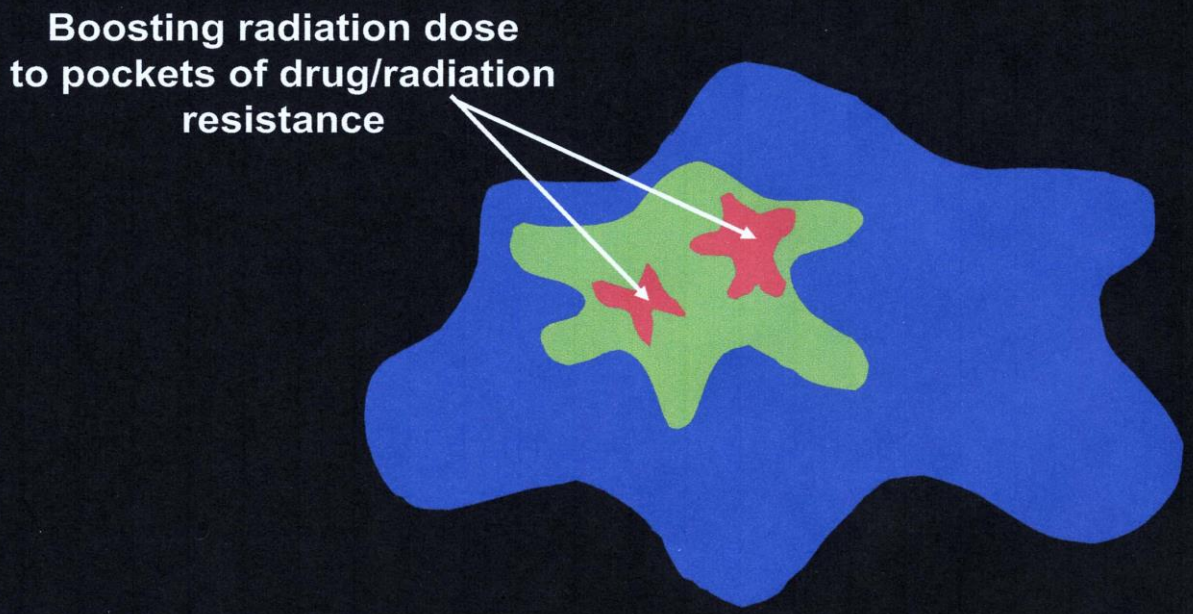
Caudell JJ: Int J Radat Oncol Biol Phys 2018; 100(3):606-617

OVERALL SURVIVAL BY FRACTIONATION (Postoperative)



Caudell JJ: Int J Radat Oncol Biol Phys 2018; 100(3):606-617

Spatial modulation of RT



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