RE-IRRADIATION IN HEAD AND NECK CANCERS

Dr. Sarbani Ghosh Laska

e-Irradiation in HNC → What to ask yourself??

ho Require?? The need??

PRACTICAL CONSIDERATIONS IN THE RE-IRRADIATION OF RECUR
AND SECOND PRIMARY HEAD-AND-NECK CANCER: WHO, WHY, H
AND HOW MUCH?

hy to offer? Benefits??

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

hat to account for??

THE RADIATION DOSE–RESPONSE OF THE HUMAN SPINAL CO

RADIATION DOSE–VOLUME EFFECTS IN THE SPINAL CORD

hom to offer??

ACR APPROPRIATENESS CRITERIA® RETREATMENT OF RECURRENT
HEAD AND NECK CANCER AFTER PRIOR DEFINITIVE RADIATION

ow to deliver??

IMRT REIRRADIATION OF HEAD AND NECK CANCER—DISEASE
CONTROL AND MORBIDITY OUTCOMES

omplications?? Risks??

Complications Following Re-irradiation for Head and Neck Cancer

RISK OF CAROTID BLOWOUT AFTER REIRRADIATION OF
THE HEAD AND NECK: A SYSTEMATIC REVIEW

The need

R → 20-35% patients with locally advanced head and neck cancer develop LRR

M → occurs at an incidence of 17.9% at 5 years, and 23.1% at 10 years

current or second primary HNC in a previously irradiated field has a poor prognosis

rgical salvage → good results for resectable relapses → However only a small proportio
tients have resectable disease and adverse pathologic features like ECE or +ve margins
ten seen→ High risk of postop disease recurrence.

r unresectable disease, systemic therapy alone, the historical standard of care, results i
% 1-year OS and virtually no long-term survivors

r patients with recurrent or second primary HNC within a previously irradiated area, the
tentially curative option is a second course of radiation, with or without chemotherapy
rmed re-irradiation (RRT).

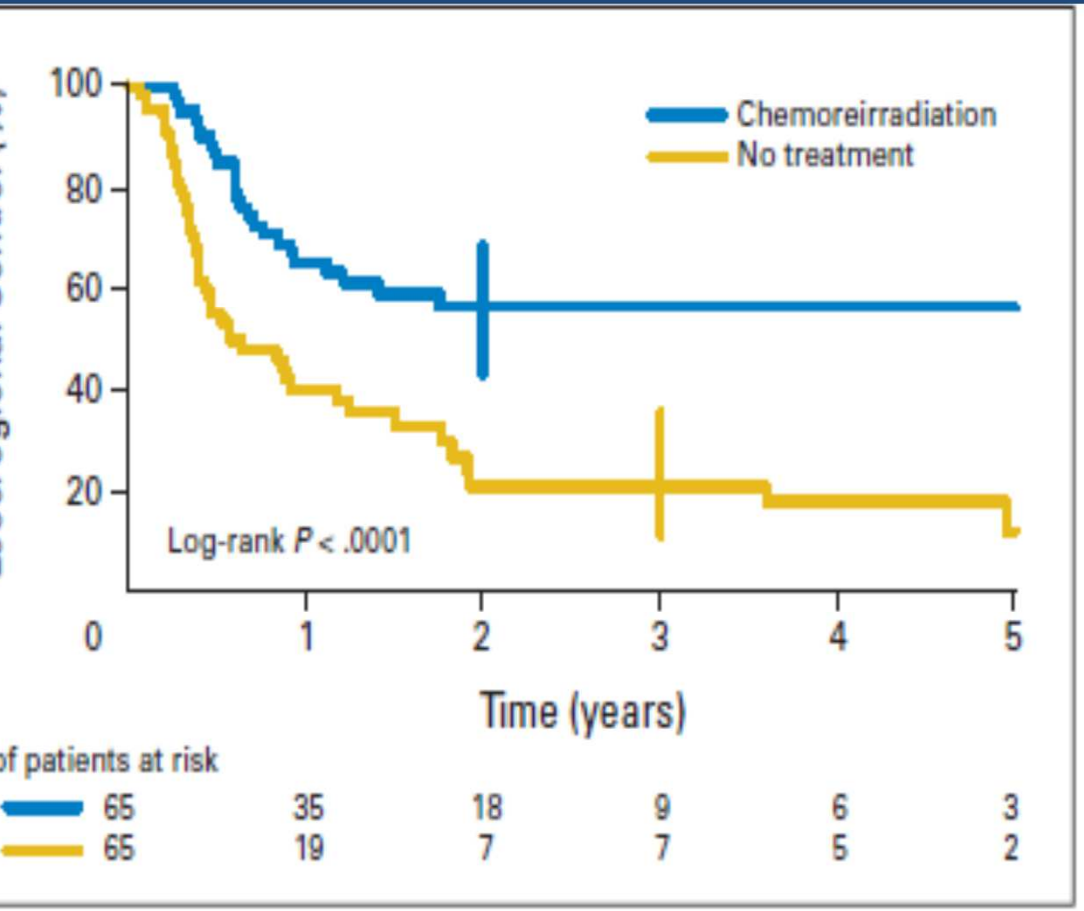
Benefits of Re-RT??

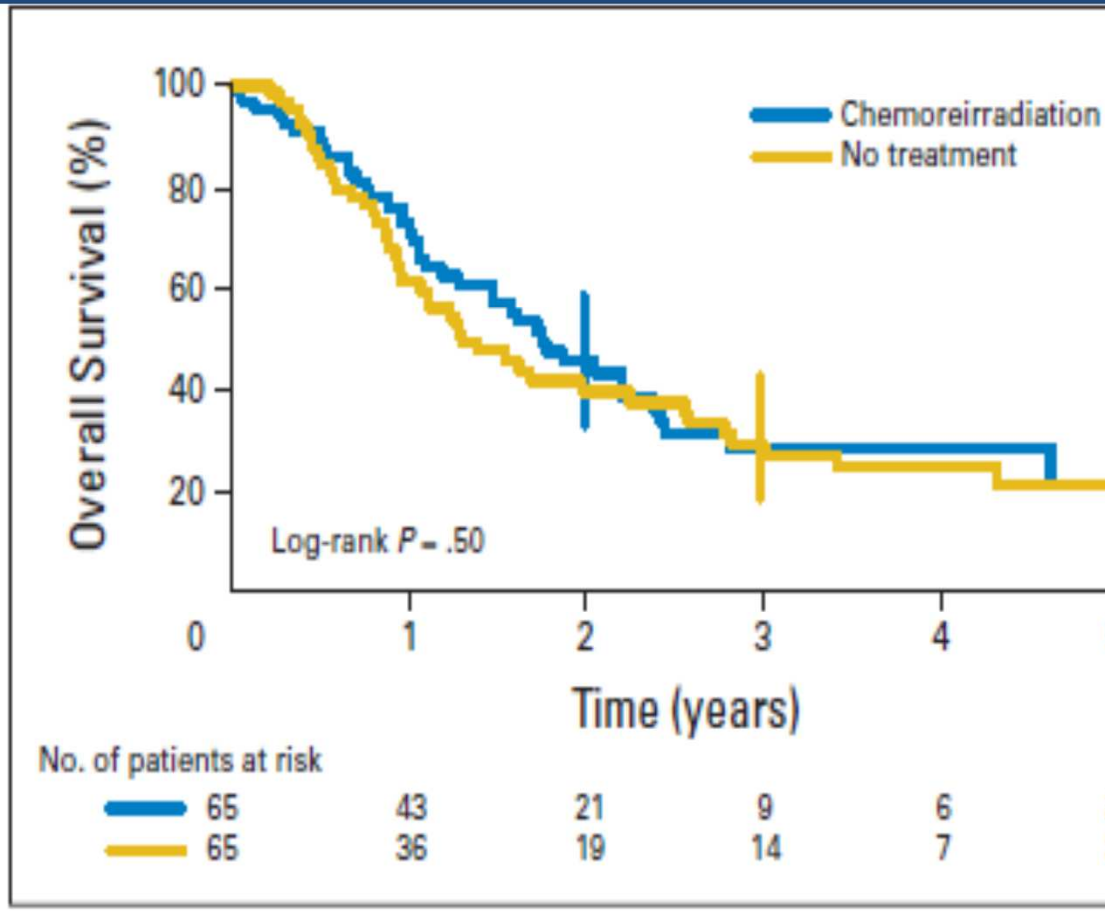
Table 1. Reirradiation following surgical salvage.

Study	Patient characteristics	Treatment		Results		Late toxicity
		Radiotherapy	*Chemotherapy*	*DFS (%)*	*OS (%)*	*(Grade 3–5)† (%)*
Level I evidence						
GORTEC (n = 130)	ECE 26% PSM 29%	60 Gy (2 Gy daily) every other week	5FU HU	2-year: 56†	2-year: 46†	ORN 17‡ Trismus 28‡ Fibrosis 6‡
Level II evidence						
Gustave–Roussy (Paris, France; n = 25)	ECE or PSM 100%	60 Gy (2 Gy daily) every other week	5FU HU	6-months: 64	4-year: 43	Fibrosis 44§ Necrosis 20 ORN 16
University of Pennsylvania (PA, USA; n = 16)	Stage III–IV recurrence	54–60 Gy (1.5 Gy b.i.d.) split course	5FU CDDP Amifostine	2-year: 100 3-year: 81	2-year: 81 3-year: 63	Vascular 12.5 Fibrosis 38 Pharynx 38
University of Chicago (IL, USA; n = 49)	R0–R2 resection	60–75 Gy (2 Gy daily and 1.5 Gy b.i.d.)	5FU HU Others¶	3-year: 68	3-year: 39	NR
The Netherlands (n = 39)	ECE or PSM 100%	60–66 Gy (2 Gy daily)	None	3-year: 74	3-year: 44	Fibrosis 39 Pharynx 36 Larynx 8 ORN 8

Randomized Trial of Postoperative Reirradiation Combine 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, J Clin Oncol 26:5518-5523. ©





lusion: Full-dose RE-RT combined with CT after salvage Sx significantly improved DFS without significant impact o

Benefits of Re-RT??

Table 2. Reirradiation for unresectable disease.

Study	Patient characteristics	Treatment		Results		Late toxicity
		Radiotherapy	*Chemotherapy*	*DFS (%)*	*OS (%)*	*(Grade 3–5)[†] (%)*
RTOG 96-10 (n = 79)	Recurrent 53%, OP 45%, prior CT 10%	60 Gy (1.5 Gy b.i.d.), every other week	5FU HU		1-year: 40.5 2-year: 15.2	Pharynx 12 Fibrosis 6 Necrosis 3
RTOG 99-11 (n = 99)	Recurrent 77%, OP 40%, prior CT 20%	60 Gy (1.5 Gy b.i.d.), every other week	CDDP Paclitaxel G-CSF	1-year: 35	1-year: 50.2 2-year: 25.9	Pharynx 18 Fibrosis 16 ORN 5 CAR 2
Gustave–Roussy (Paris, France; n = 139)	Recurrent 55%	60 Gy[‡] (2 Gy daily), every other week	5FU[‡] HU	2-year: 11 5-year: 6	2-year: 21 5-year: 9	ORN 8 CAR 4 Necrosis 21
Thomas Jefferson University (PA, USA; n = 38)	NR	42–60 Gy (1.5 Gy b.i.d.), every other week	CDDP Paclitaxel G-CSF	37	1-year: 50 2-year: 35	ORN 5 Brain necrosis 5 CAR 5 Fistula 5
University of Chicago (IL, USA; n = 85)	Recurrent 97%, OP 27%, prior CT 44%	60–75 Gy, (2 Gy daily and 1.5 Gy b.i.d.), every other week	5FU HU Others[§]	2-year: 19.9 5-year: 13.4	2-year: 24.8 5-year: 14.3	CAR 9 ORN 11 G-tube 56 Voice 4
The Netherlands (n = 34)	Recurrent 24%, OP 26%	60–66 Gy (2 Gy daily)	None	2-year: 27	2-year: 38	Pharynx 24 G-tube 12 ORN 3 Fibrosis 9

Gustave Roussy Institute 1998→ CTRT

Unresectable head and neck carcinoma

Median cumulative dose 120Gy

Median time interval- 33 months

3 Protocols

1. 65 Gy in 2-Gy fractions
2. 5-FU/hydroxyurea and 60Gy/30#/ 6 weeks
3. 5-FU/cisplatin/mitomycin with hyper fractionation @ 1.5Gy twice a day- 60Gy tota dose

Complete response rates -37%, 41%, and 25%, respectively

Overall survival at 2 years was 21%

Median survival of 11 months

RTOG 99-11 (2007)

- Phase II Study- 99 patients
- RT 1.5 Gy/fx BID x5 days every 2 weeks
- Cisplatin (15 mg/m^2) and paclitaxel (20 mg/m^2)
- Outcome: median OS 12 months
- 2-year OS 26%
- Grade 4-5 in 28%, treatment-related death 8%
- Conclusion: Despite high incidence of Grade 5 toxicity, results better than chemo alone

Zubrod performance status		
0	34	
1	65	
Recurrence type		
Second primary	23	
Locoregional recurrence	76	
Primary site at study entry		
Oral cavity	27	
Oropharynx	40	
Hypopharynx	12	
Larynx	10	
Other	10	
Months from prior RT		
Median		39.6
Range		6.1-317.9
< 36	48	
> 36	51	
Prior RT dose, Gy		
Median		65.4
Range		45.0-75.0
Prior chemotherapy		
None	79	
Lomustine	1	
Fluorouracil	3	
Platinum	2	
Procarbazine	1	
Carboplatin	2	
Multiple	9	
Administered, but drug unknown	2	

Chemotherapy alone

TABLE 1 Response rates and median survival for recurrent head and neck cancer patients treated with chemotherapy alone

Author	Chemotherapy	Median survival (mo)	Response rate (%)
Murphy *et al.* (7)	CP + 5-FU	8.0	22
	TAX + CP	8.0	28
Jacobs *et al.* (8)	CP	NR	18
	CP + MTX + LV	NR	33
Jacobs *et al.* (9)	CP	5.0	17
	5-FU	5.5	13
	CP + 5-FU	6.1	32
Vendahmane *et al.* (10)	DOC+5-FU	9.6	27 (PR)
Forastiere *et al.* (11)	MTX	5.6	10
	CP + 5-FU	6.6	32
	CARBO + 5-FU	5.0	21
Burtness *et al.* (12)	CP ± C225	6.7	13.7
Liverpool Head and Neck Oncology Group (13)	CP	NR	28
	MTX	NR	38
	CP+5-FU	NR	24
	CP+MTX	NR	22

Abbreviations: CARBO, carboplatin;CP, cisplatin; DOC, docetaxol; 5-FU, 5-fluorouracil; LV, leucovorin; MTX, methotrexate; NR, not reported; PR, partial responders; TAX, taxol.

Kao et al Cancer 2003

Randomized phase III trial (GORTEC 98-03) comparing re-irradiation plus chemotherapy versus methotrexate in patients with recurrent or a second primary head and neck squamous cell carcinoma, treated with a palliative inten

Radiotherapy and Oncology 100 (201

Jacques Tortochaux [a,1], Yungan Tao [b], Elodie Tournay [b], Michel Lapeyre [a], Francois Lesaunier [c],

Randomised phase III trial comparing palliative intent CTRT vs. Chemotherapy alone in unresectable disease

accrued only 57 out of planned 160 patients

only 43% of patients completed protocol directed CRRT.

More late toxicity was observed in the CRRT arm with 11 out of 23 patients developing RTOG grade 3+ toxicity

With limited statistical power, no difference was detected in 1-year OS, the primary end point, between groups (23 and 22%; p = 0.6).

Benefits of Re-RT

ummary

Resectable recurrences → salvage surgery followed by post op Re
RT offers chance of long term survival in good proportion of
patients

unresectable recurrences→ Re-RT with chemotherapy and pall
chemotherapy are the options available, Phase II studies have
shown incremental improvements in clinical outcomes with Re-RT
when compared with historical controls treated with pall CT

Whom to offer??

ACR APPROPRIATENESS CRITERIA® RETREATMENT OF RECURRENT HEAD AND NECK CANCER AFTER PRIOR DEFINITIVE RADIATION

EXPERT PANEL ON RADIATION ONCOLOGY–HEAD AND NECK CANCER

MARK W. MCDONALD, M.D.,* JOSHUA LAWSON, M.D.,† MADHUR KUMAR GARG, M.D.,‡

luation and re-irradiation for HNSCC be performed at a tertiary care nter with a head and neck oncology team that is equipped with the ources and experience to manage the complexities and toxicities of reatment

Whom to offer??

Selection Criteria → Ideal Candidate for Re-RT??

Patient Factors

S

ife expectancy

omorbidities

urrent speech & swallowing

unction

evere sequelae

(ORN, severe cervical fibrosis and severe dysphagia)

olerance to previous reatment

Treatment Factors

- **Surgically resectable**
- **Time interval (1yr or >)**
- **Chemo or not**
- **Previous volume treated**
- **Dose received (50Gy or <)**
- **OARs- which & what dose**
- **Technique used**

Disease Factors

- **Tumor size**
  - Smaller volumes (<30cc)- b
  - Chen et al <27 cm^3- 2yr LC 80%
  - Volumes >60 cm^3- very carefully considered
- **SPT vs. recurrence (SPT>>Rec)**
- **Location-Benefit more for laryr**

and nasopharynx LC & OS 60%

93% (Wang et al)

Reasons for poor outcomes with large volume

uboptimal dose distribution in advanced and extensive disease compromised by the rotection of critical, adjacent structures

oor blood supply and hypoxia associated with bulky tumors

issue fibrosis can lead to decreased radiation and/or chemotherapy sensitivity

ligh incidence of necrosis and/or massive hemorrhage

Whom to offer??

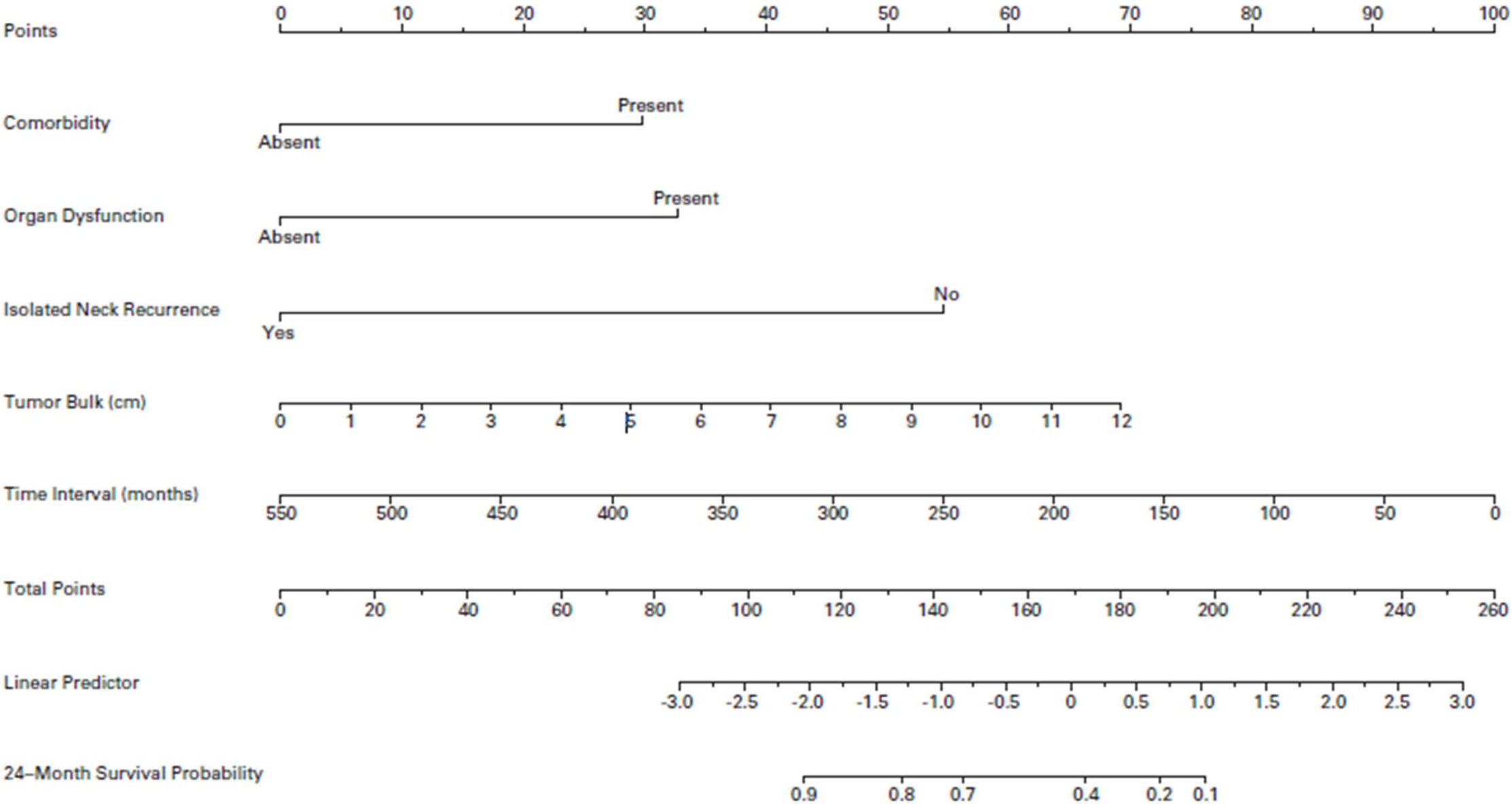
EIRRADIATION FOR HEAD-AND-NECK CANCER →DELICATE BALANCE BETWEEN EFFECTIVENESS AND OXICITY

Table 5. Suggested Factors to be considered with respect to risk of toxicity for re-irradiation to head and neck

Variable	Lower risk	Intermediate risk	Higher risk
Interval from previous RT	>3 y	1 y to 3 y	<1 y
KPS	90–100	70–80	<70
Tumor volume	<30 cm^3	30–60 cm^3	>60 cm^3
GT dependence	No	Somewhat	Entirely
Previous RT dose (Gy)	<50	50–60	>60

Abbreviations: KPS = Karnofsky performance status; GT = gastrostomy tube; RT = radiotherapy.

A. M. CHEN et al.IJROBP 2011


Points
0 10 20 30 40 50 60 70 80 90 100
Comorbidity
Absent
Present
Organ Dysfunction
Absent
Present
Isolated Neck Recurrence
Yes
No
Tumor Bulk (cm)
0 1 2 3 4 5 6 7 8 9 10 11 12
Time Interval (months)
550 500 450 400 350 300 250 200 150 100 50 0
Total Points
0 20 40 60 80 100 120 140 160 180 200 220 240 260
Linear Predictor
-3.0 -2.5 -2.0 -1.5 -1.0 -0.5 0 0.5 1.0 1.5 2.0 2.5 3.0
24–Month Survival Probability
0.9 0.8 0.7 0.4 0.2 0.1

How to deliver?? → Re-RT Techniques

Conventional RT with small fields Used traditionally → greater acute & late side effects

Unable to achieve tumoricidal dose- compromised local control

Total dose - important prognostic factor

Can be achieved with more conformal techniques

In recent years the utilization of IMRT and/or SBRT has improved healthy tissue tolerand

Lee et al. reported how IMRT has offered new possibilities for applying re-irradiation mo
safely with greater local control, compared to historical controls.

They reported a 2-year survival of 52% vs. 20% in patients who underwent IMRT and
patients who did not

How to deliver?? → Re-RT Techniques

Table 3. Intensity modulated radiotherapy reirradiation for unresectable disease.

Study	Patient characteristics (%)	Treatment		Results		Late toxicity
		Radiotherapy	*Concurrent chemotherapy (%)*	*DFS (%)*	*OS (%)*	*(Grade 3–5)[†] (%)*
MSKCC[‡] (n = 105)	Surgery 34	59.4 Gy (daily)	CDDP 24 Carbo-based 37 None 32	1-year: 48[§] 2-year: 42[§]	1-year: 56 2-year: 37	Brain necrosis 4 Pharynx 4 Trismus 3
MDACC (n = 67)	Surgery 27	63 Gy (1.8–2 Gy daily)	CDDP-based 46 None 53	2-year: 67[#] 4-year: 52[#]	2-year: 61 4-year: 46	ORN 5 Esophagus 4 Brain necrosis 1
Dana–Farber (MA, USA; n = 35)	Stage III–IV 83 Surgery 49	67.5 Gy (1.8–2 Gy daily)	CDDP-based 92 Cetuximab 42	1-year: 53 2-year: 45	1-year: 59 2-year: 48	Esophagus 49 Pulm 15 Trsimus 11 ORN 6
University of Miami (FL, USA; n = 41)	Surgery 41.5	59 Gy (2 Gy daily) every other week	CDDP-based 36 Carbo-based 63	2-year: 38	1-year: 77 2-year: 49	Esophagus 2 CAR 2 Fistula 5
Belgium (n = 84)	Stage III–IV 93 Surgery 23	69 Gy (2 Gy daily)	CDDP-based 14 None 86	2-year: 48 5-year: 40	2-year: 35 5-year: 20	Dysphagia 10 ORN 2 CAR 2
Wisconsin[§] (n = 38)	Surgery 34	68 Gy (2 Gy daily)	Carbo/taxol 100	2-year: 34 5-year: 29	3-year: 31 5-year: 20	44 for 3DCRT[¶] 7 for IMRT[¶]

How to deliver?? → Re-RT Techniques

Table 4. SBRT re-irradiation for unresectable disease.

Study	Median follow-up (months)	Treatment		Results		Late toxicity
		Radiotherapy	*Concurrent chemotherapy (%)*	*DFS (%)*	*OS (%)*	*(Grade 3–5)† (%)*
Turkey (n = 46)	7	30 Gy (5 fx)	None		1-year: 47 1-year: 41	CAR 17 Necrosis 2 ORN 2 Dysphagia 4
University of Pittsburgh (PA, USA; n = 98)	14.6	40 Gy (5 fx)	Cetuximab 35		2-year: 21‡ 2-year: 53§	Xerostomia 1 Dysphagia 1
Japan (n = 22)	24	33.7 Gy (2–5 fx)	Adjuvant 5FU 100		N1–3, 2-year OS: 12.5 N0, 2-year OS: 78.6	Xerostomia 22 ORN (Gr 2) 14
Korea (n = 36)	17.3	30 Gy (3–5 fx)	None	1-year: 61 2-year: 52	1-year: 52 2-year: 31	ORN 3 Necrosis 6
Henry Ford (n = 21)	NR	16–18 Gy (1 fx) 36–48 Gy (6–8 fx)	None	1-year: 61 2-year: 40	1-year: 38 2-year: 14	Dysphagia 5 Fistula 7 ORN 2
Georgetown (n = 65)	16	30 Gy (5 fx)	Cetuximab 17 Carbo 12 Other 22	2-year: 0	2-year: 41	Dysphagia 3 CAR 3 Fistula 1

How to deliver?? → Re-RT Techniques

parison between three different radiation modalities in treating recurrent HNSCC.

odality	Advantages	Disadvantages
)-Conformal Therapy	Rapid planning and delivery, larger volumes, coverage of microscopic disease	Limited sparing of normal tissue, greater elapsed days o treatment
IRT	Larger volumes, coverage of microscopic disease, sparing of previously irradiated tissues and normal tissues	Complex planning, potentially longer treatment time, gr elapsed days of treatment
BRT	Highly conformal, maximal sparing of normal tissues, higher BED (biological equivalent dose), less elapsed days	Complex planning, longer treatment time

How to deliver?? → Volume Delineation

Clinical target volume (CTV) is confined to the GTV plus a margin or to the high-risk area (surgical bed plus 1–2 cm) in the postoperative setting

Popovtzer et al. reported the appropriateness of limited field irradiation (G + margin) avoiding prophylactic treatment of the neck

In this series, despite limiting the re-irradiation volume to the gross diseas only 4% of the patients had a recurrence outside of the irradiated area.

Minimizing the amount of tissue re-irradiated →diminishes the probability side effects

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How to deliver?? → Volume Delineation

THE PATTERN OF FAILURE AFTER REIRRADIATION OF RECURRENT SQUAMOUS CELL HEAD AND NECK CANCER: IMPLICATIONS FOR DEFINING THE TARGETS

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THEODOROS N. TEKNOS, M.D.,† JEFFREY S. MOYER, M.D.,† MARK E. PRINCE, M.D.,†
CAROL R. BRADFORD, M.D.,† AND AVRAHAM EISBRUCH, M.D.*

Methods and Materials: This is a retrospective review of 66 patients who underwent curative-intent re-RT for non-resectable recurrent or second primary mucosal squamous cell HNC. Treatment was delivered with three-dimensional conformal (3D) RT or intensity-modulated RT (IMRT). The targets in all patients consisted of the rGTVs with tight (0.5-cm) margins, with no intent to treat prophylactically lymph nodes or subclinical disease in the vicinity of the rGTVs. The sites of locoregional failures (LRFs) were determined using imaging at the time of failure and were compared with the rGTVs.

Results: Median re-RT dose was 68 Gy. Forty-seven patients (71%) received concomitant chemotherapy, and 31 (47%) received hyperfractionated, accelerated RT. At a median follow-up of 42 months, 16 (23%) were alive and disease-free. Fifty patients (77%) had a third recurrence or persistent disease, including 47 LRFs. All LRFs occurred within the rGTVs except for two (4%) (95% confidence interval, 0–11%). Nineteen patients (29%) had Grade ≥ 3 late complications, mostly dysphagia (12 patients).

Conclusions: Almost all LRFs occurred within the reirradiated rGTVs despite avoiding prophylactic RT of tissue at risk of subclinical disease. These results support confining the re-RT targets to the rGTVs to reduce reirradiated tissue volumes.

How to deliver?? → Dose and fractionation

Re-treatment doses are frequently decided on purely empirical bases

Several studies have suggested that disease control is superior when doses of approximately 50–60Gy or higher are used

Salama et al. reported that the radiation dose administered was an independent prognostic factor for overall survival, progression-free survival and local control

Patients receiving >58Gy had a 3-year overall survival rate of 30%, compared to a 3-yea overall survival rate of 6% in patients receiving <58Gy

Hyperfractionation does not seem to benefit over conventional # for OS and shows comparable toxicities.

ndidate/major considerations

vere no severe sequelae in previous radiation treatments and no significant medical comorbidities [7,28,30,41]
is suggested for accurate staging [7,42–46]
s undergoing previous surgery have better prognoses [6,21,28,31,47–49]
liation with an interval of at least 6 months after the previous course of radiation has been described. However, a longer interval is preferred (1 year or
,30,53,59]
ng tumor size, small volumes are preferable (<30 cm^3). Re-irradiation of bulky tumors must be very cautiously evaluated (>60 cm^3) [22,30,55]
cond primary tumors have better prognoses than recurrences [23,59–61]
arising in the nasopharynx and larynx are good candidates, compared to other tumor locations (hypopharynx) [62–64]
an exhaustive analysis of the previous treatment portals and dose distribution. Patients with previous doses (in the recurrence area) ⩽50 Gy are pref
ner risk if ⩾60–70 Gy) [67]
ical target volume is confined to the GTV plus a margin [25,31,70–72]
f ⩾60 Gy (approximately) are recommended to achieve greater local control [23–25]
ord: do not exceed 50 Gy (total accumulative dose) whenever possible [18,19]
s of myelopathy have been reported for cumulative doses ⩽60 Gy in 2 Gy equivalent doses (i.e., a BED of 120 Gy_2) [25,35]
herapy is an interesting option for small recurrences in the oral cavity and oropharynx. Additionally, it is recommended in some cases of neck recurre
30–85]
r SBRT techniques are preferable for reducing treatment-related toxicity (alone or in combination with chemotherapy or cetuximab) [7,31,47,70,72,10
ns about treatment should always been considered by a multidisciplinary team [7,30,39]
e the possibility of including the patient in a trial

Accounting for normal tissue repair

OAR→ Treatment time interval- depends upon doses to OARs and type of tissue damage epair

ypes of OARS-

- Neurological- spinal cord, brainstem, temporal lobe, optic apparatus
- Bones
- Soft tissue
- Mucosa

arly radiation damage recovery (skin or oral mucosa)- 12 to 90 days (Dorr W et al, IJROB 003)

ate radiation damage tissue recovery- almost 5- 6 months

Min 6 months gap between re-RT, Gap >1 year- lower toxicities

lowever, no consensus about cumulative maximum tolerance doses and minimum tim f recovery

Skin and mucosa

e Crevoisier et al. 1998

Median cumulative dose of 130 Gy

1 and 8% incidences of mucosal necrosis and osteoradionecrosis

iologically effective dose (BED) of the first radiation course affects risk of late injury gnificantly

MP- Mesenchymal tissues recover from radiation injury less than rapidly reacting tissues ke the epidermis and mucosa

Recovery- spinal cord

g et al – Rhesus Monkey

- Recovery -76%, 85% and 101% of initial dose after 1, 2 and 3 years respectively
- Under conservative assumptions, an estimated overall recovery of 26Gy (61%) was calculated
- Time interval of 1, 2 and 3 years between the treatment courses, cumulative doses of 150, 156 and 167% of the first-line setting's tolerance dose appear possible

mans- for initial dose of 45Gy @ 2Gy/#, additional 23–24Gy in 2Gy/# (50% of the tolerance dos n be delivered 1 or 2 years later (Schiff et al. 1995; Grosu et al.2002)

eder at al 2006-

- Risks-
  - time interval
  - cumulative dose
  - highest BED of all treatment series in a particular individual
- Risk of RM small after < or =135.5Gy when the interval is not shorter than 6 months and the d of each course is < or =98Gy

Organ	Dose- Volume (QUANTEC)	Time Interval	Re-RT Evidence
Brain Necrosis	-SRS V_{12} <5-10ccm ->60Gy 1-5% risk at 5 years (not in Re-RT)	3-55 months	-Lee 2007- 3% grade 4 toxicity (62Gy+59.4Gy) @ 38 months median -Dose < 100Gy- no risk found @ 3-55mo interval (Mayer et al 2008)
Brainstem Necrosis	1-10cc upto 59Gy Entire brainstem- 54Gy	-	None
Optic apparatus- Radiation Induced Optic Neuropathy	Threshold Dmax <55 -55- 60Gy- 3-7% > 60Gy- 7-20%	7.5 year Interval	-Lee 2007- 0.9% Blindness to CD- 58-148Gy @ 5-380months -Flickinger et al 1989 1/10 pt RION with 40+46G
Bones- Osteoradionecrosis	60Gy without extraction		Salama et al- 11% ORN wit CD 131Gy De Crevoisier et al- 8% (CD 130Gy)
Soft tissue	Can tolerate as high as 90% of original dose		

Accounting for normal tissue repair→ Re-Irradiation tolerance

e constraints.

ecommendations

linical toxicity data analyzing the dose response relationship is limited. In general, toxicity is underscored in most studies, and there is a lack of quantitative evide based dose volume constraints [74]

linical studies have shown that acute skin and mucosal reactions after re-irradiation were within the range observed after the first course of radiotherapy [78]. Th tissues present an almost complete recovery within a few months [22,25]

Vith regard to re-irradiation of late responding tissue (epithelial and mesenchymal), tolerance is depending on the specific organ at risk [76,78]

steoradionecrosis is a possible late-responding tissue complication. However, no clear dose and volume effect has been reported [78]. Salama et al. reported an osteoradionecrosis rate of the mandible after a median lifetime radiation dose of 135 Gy [21]. De Crevoisier et al. reported an 8% osteoradionecrosis rate in pati treated to a total cumulative dose of 130 Gy with conventional radiotherapy [22]

he tolerance of the carotid artery is uncertain. Patients treated with accelerated fractionations, prior neck dissection and tumor adherent to the carotid fascia ar particular risk of this complication [33,79]

pinal cord: No cases of myelopathy have been reported for cumulative doses $\leqslant$60 Gy in 2 Gy equivalent doses (i.e., a BED of 120 Gy_2) [25,35]. Some authors ha suggested a cumulative total BED of 135.5 Gy_2 (nBED = 68 $Gy_{2/2}$) as safe, provided that the interval between courses is not shorter than 6 months and the dos each course is $\leqslant$98 Gy_2 (nBED = 49 $Gy_{2/2}$) [77]. However, most clinical trials have recommended limiting the cumulative spinal cord dose to 50 Gy [23,24]

case of re-irradiation to the spinal cord with hypofractionated stereotactic radiation therapy, the SBRT-course should not exceed 25 Gy (2 Gy-fractionated equiva dose, $\alpha/\beta = 2$ (EQD 2/2)), the dose to the initial course did not exceed 50 Gy (EQD 2/2) and the interval between the two courses should not be shorter than 5 mo [76]

he influence of very steep dose gradients from stereotactic and intensity-modulated approaches (i.e., a more complex volume-effect) requires further evaluation opulation constraints are very important in this context but can obviously not stand alone. It has been recognized that other factors such as multimodal therapies use of concomitant chemotherapy or previous surgery), patient's age or comorbidity (diabetes mellitus, hypertension) can confound the risk assessment [75,

COMPLICATIONS & TOXICITIES

Life threatening

- **Carotid blow out- infrequent—**lower in conventional or hyperfractionated schedules c/w accelerated (Mc Donald et al)
- **Brain/ brainstem necrosis**
- **Sepsis**
- **Pulmonary embolism**

Morbid affecting QOL

- **Myelitis- L'Hermitte's syndrome**
- **ORN**
- **Severe Xerostomia**
- **Disfigurement**
- **Blindness**
- **NGT feeding**
- **Soft tissue necrosis**
- **Fistula formation**

Table 7. Grade 4–5 complications*

Complication	*n*
Carotid hemorrhage	6
Osteoradionecrosis	13
Brain necrosis	0
Myelopathy	1
Peripheral neuropathy	1

* Using common terminology criteria for adverse events.

J. K. SALAMA *et al IJROBP 2006*-Full dose CTRT for recurrent head and neck cancer

Re-irradiation toxicity

Acute (almost always resolves)	Late (slow recov never recovers)
Mucositis	Temporal lobe ne optic neuropathy
Pigmentation of skin/ desquamation	Osteoradionecros chondroradionecr
Dysphagia	Pharyngeal steno dysphagia
Acute toxicity can sometimes translate into consequential late toxicity*	Severe trismus
	Soft tissue necro fistulae and carot

RISK OF CAROTID BLOWOUT AFTER REIRRADIATION OF THE HEAD AND NECK: A SYSTEMATIC REVIEW

MARK W. MCDONALD, M.D.,*‡ MICHAEL G. MOORE, M.D.,† AND

mong 1554 patients receiving salvage H&N reirradiation, there were 41 reported CBs, f
ate of 2.6% → 76% were fatal.

here was no statistically significant difference in the rate of CB between patients treate
ith or without concurrent chemotherapy, or between patients treated with or without
alvage surgery before reirradiation.

clusion:

arotid blowout is an infrequent but serious complication of salvage reirradiation for H&
ancer.

he rate of CB was lower among patients treated with conventional or hyperfractionated
chedules compared with regimens of accelerated hyperfractionation

Proton Beam Re-Irradiation for Recurrent Head and Neck Cancer: Multi-Institutional Report on Feasibility and Early Outcomes

Paul B. Romesser, MD[1], Oren Cahlon, MD[1,2], Eli D. Scher, BA[1], Eugen B. Hug, MD[2], Kevin Sine, CMD[2], Carl DeSelm, MD, PhD[1], Jana L. Fox, MD[3], Dennis Mah, PhD[2], Madhur K. Garg, MD[3], John Han-Chih Chang, MD[4], and Nancy Y. Lee, MD[1]*

2 patients were treated with curative intent re-RT with PBRT between 2011 and 2014
Median PBRT dose was 60.6Gy (RBE). 39% had salvage surgery prior to re-RT

he cumulative incidence of loco regional failure at 12-months was 25.1%.
ctuarial 12-month FFDM and OS were 84.0% and 65.2%, respectively.

cute grade ≥3 toxicities included mucositis (9.9%), dysphagia (9.1%),esophagitis (9.1%) & dermatitis (3.3
rade 3 or > late skin and dysphagia toxicity were noted in 6 (8.7%) and 4 (7.1%) of patients.
patients had grade 5 toxicity secondary to treatment-related bleeding

clusions: Proton beam re-irradiation of the head and neck can provide effective tumour control with
ptable acute and late toxicity profiles likely secondary to the decreased dose to the surrounding normal,
t previously irradiated tissue

Conclusions

Patient selection is the cornerstone to successful outcome

Ascertain details of previous RT
Optimal treatment of localized recc: Combined modality whenever feasible

Issues with ReRT:

- Longer time intervals: Superior outcomes
- Target volumes: No Elective volumes, use of functional imaging
- OAR doses: To be respected, as low as achievable
- Fractionation: Conventional or altered
- Technique: Conformal
- Dose: 50 – 60Gy

Attention to supportive care & QOL issues

Diligent documentation & reporting