

Head and Neck Cancer

Radio Oncology

L. Plasswilm

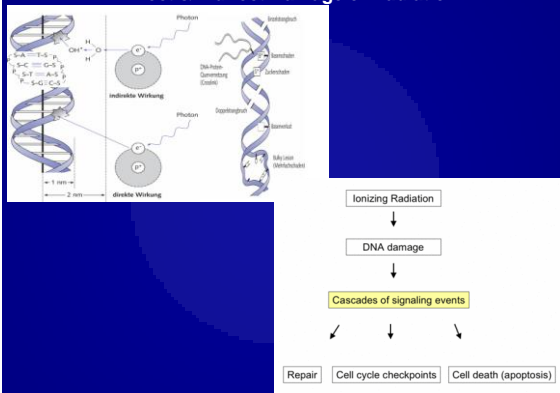
Kantonsspital St.Gallen – ein Unternehmen, drei Spitäler: St.Gallen Rorschach Flawil

- Basics
- Technique
- Indication
- Treatment Results
- Toxicity

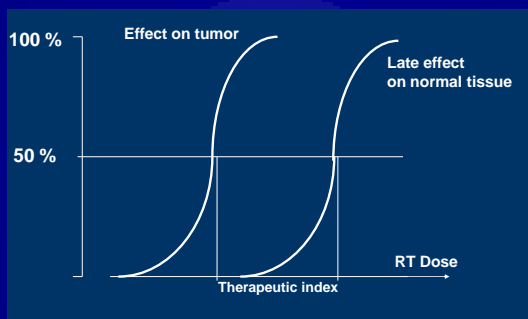
BASICS



Direct & Indirect Damage of Radiation

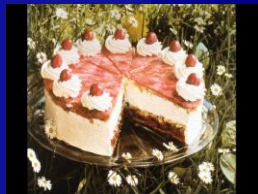


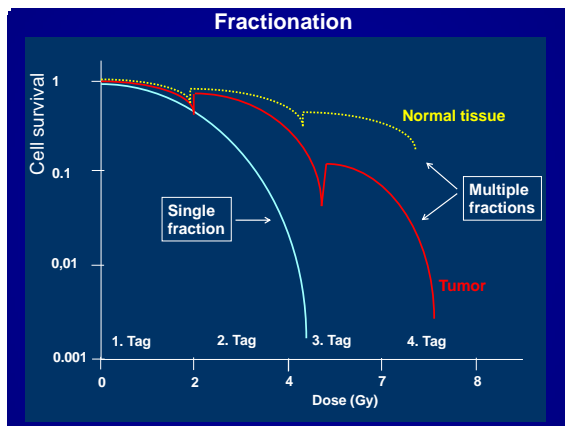
Effect on tumor vs late toxicity

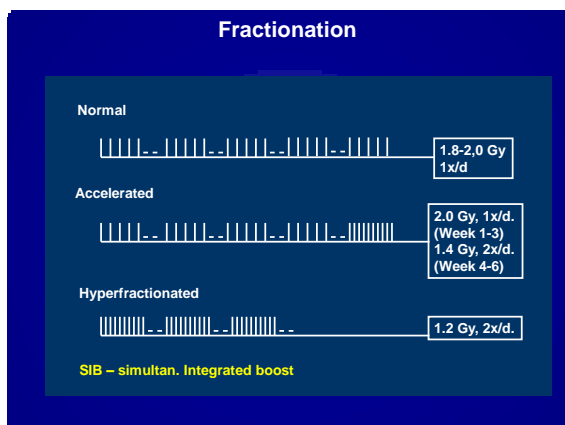


Dosage / Schedule

- Total Dose
- Fractionation

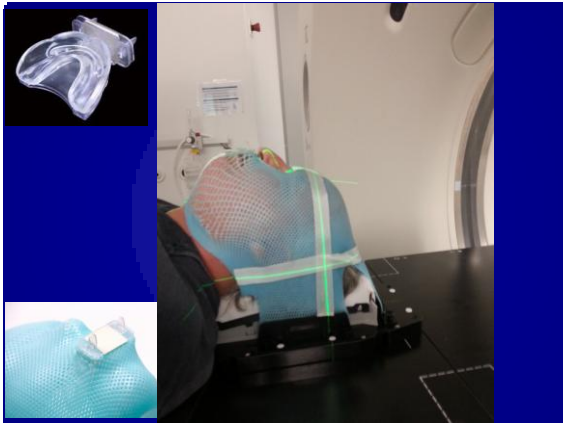


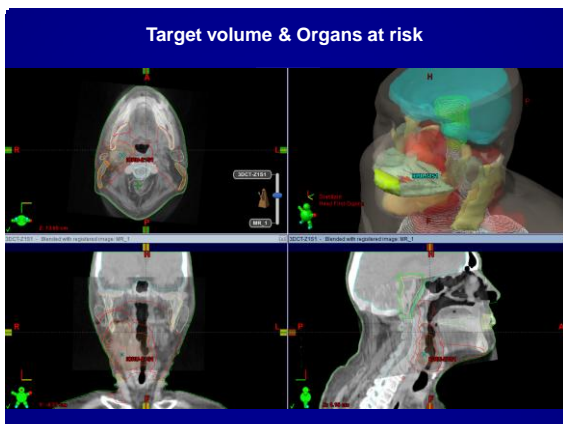


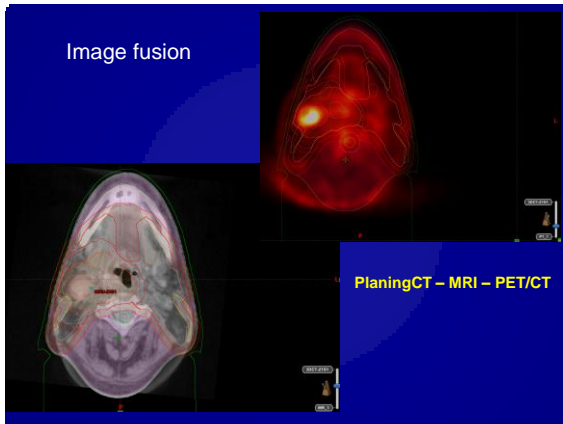


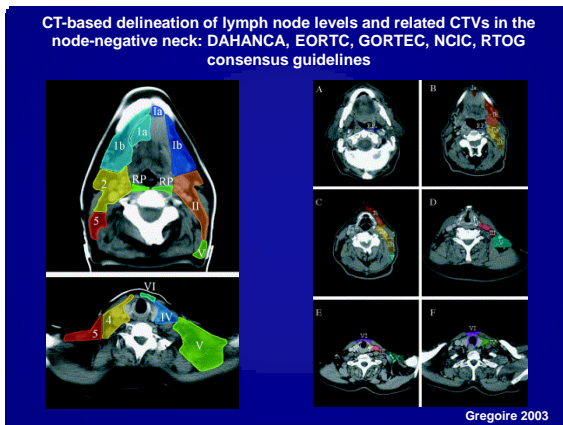


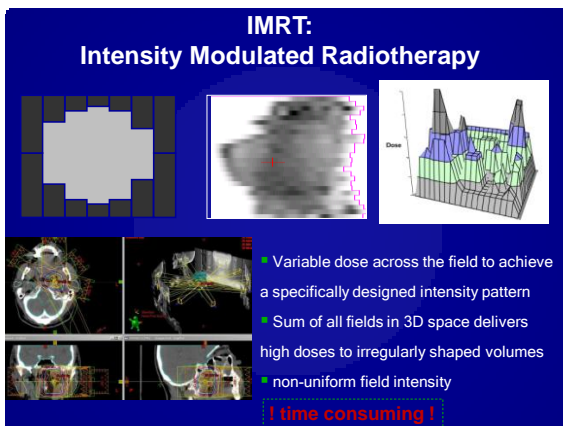




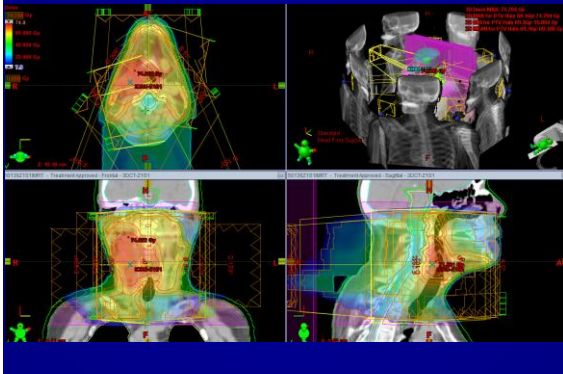






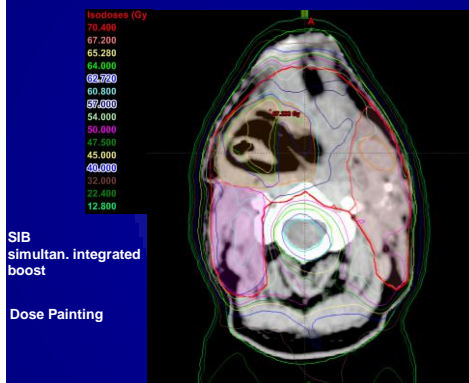


Treatment plan



IMRT

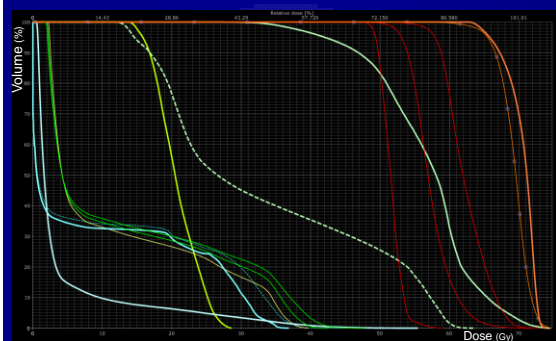
post-OP



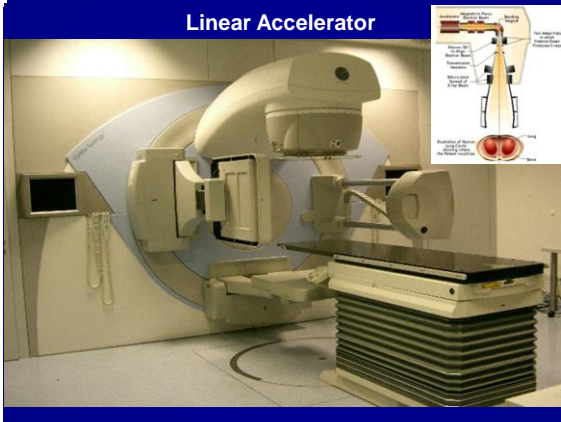
SIB
simultan. integrated
boost

Dose Painting

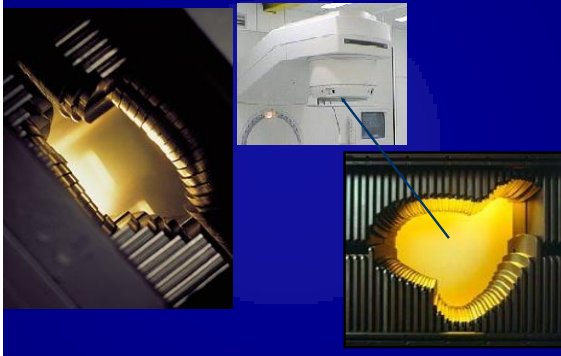
Dose Volume Histogram



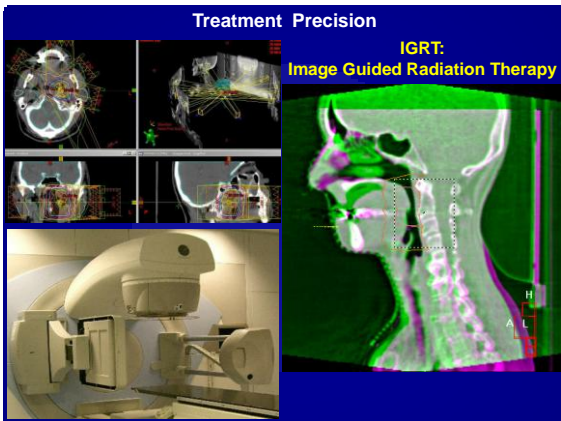
Linear Accelerator



Multi Leaf Collimator (MLC)



Treatment Precision



Indication

RT / RCT

Primary operated



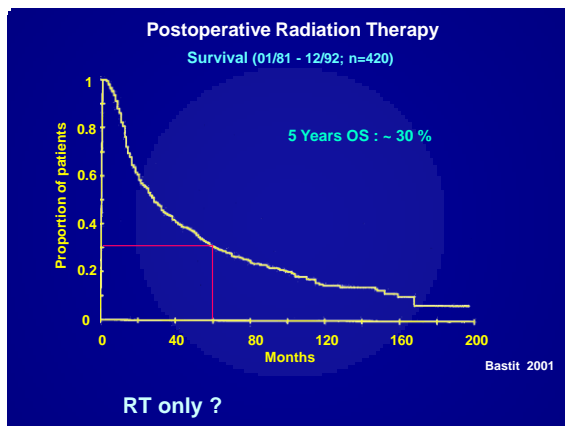
Post Operative RT / RCT ? !

Post Operative RT / RCT

Primary tumor: - R1 / R2
- pT3 / pT4

Lymphnodes: - R1 / R2
- N involvement

but: 1-2 involved nodes ?



Radiotherapy vs. Radiochemotherapy post-OP

Postoperative Irradiation with or without Concomitant Chemotherapy for Locally Advanced Head and Neck Cancer (EORTC)

"Postoperative concurrent administration of high-dose cisplatin with radiotherapy is more efficacious than radiotherapy alone"

Bernier 2004

Postoperative Concurrent Radiotherapy and Chemotherapy for High-Risk Squamous-Cell Carcinoma of the Head and Neck (RTOG)

"Among high-risk patients with resected head and neck cancer, concurrent postoperative chemotherapy and radiotherapy significantly improve the rates of local and regional control and disease-free survival. However, the combined treatment is associated with a substantial increase in adverse effects"

Cooper 2004

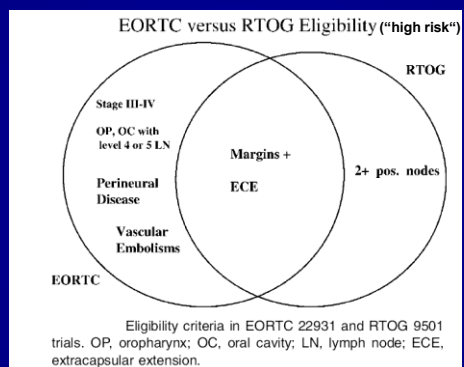
Locoregional Control

	<u>OP + RT</u>	<u>OP + RCT</u>	
EORTC 22931	69%**	82%**	p=0.007
RTOG 9501	72%*	82%*	p=0.01
*2years	**5years		

Progression-Free Survival

	<u>OP + RT</u>	<u>OP + RCT</u>	
EORTC 22931	36%	47%	p=0.04
RTOG 9501	25%	35%	p=0.04

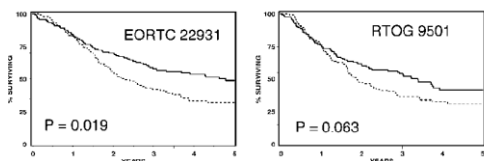
Radiotherapy vs. Radiochemotherapy post-OP



A COMPARATIVE ANALYSIS OF CONCURRENT POSTOPERATIVE RADIATION PLUS CHEMOTHERAPY TRIALS OF THE EORTC (#22931) AND RTOG (#9501)

Overall Survival

Patients with positive margin and/or ECE



at Risk

Year	0	2	5	0	2	5
RCT	122	82	31	130	80	16
RT	111	59	16	116	55	11

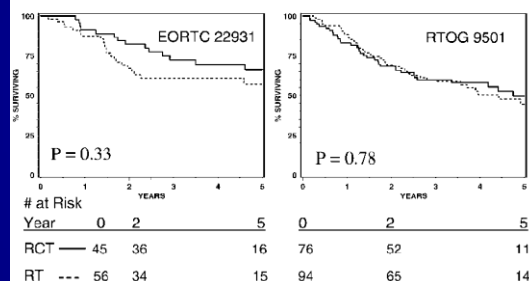
Impact of adjuvant chemoradiation on overall survival according to the presence of extracapsular extension (ECE) and/or positive surgical margins in the EORTC and RTOG trials

Bernier & Cooper 2005

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Impact of adjuvant chemoradiation on overall survival according to the presence of extracapsular extension (ECE) and/or positive surgical margins in the EORTC and RTOG trials
Bernier & Cooper 2005

Primary not operated

Radiotherapy

Radiochemotherapy (see also B. Gay)

Radiotherapy

Standard fractionation:

2 Gy/fract., 70 Gy / 35 fract. / 7weeks

Hyperfractionation:

1.2 Gy/fract., twice daily, 81.6 Gy / 68 fract. / 7weeks

Accelerated fractionation with split:

1.6 Gy/fract., twice daily, 67.2 Gy / 42 fract. / 6weeks

2-week rest after 38.4 Gy

Accelerated fractionation with concomitant boost:

1.8 Gy/fract./day to large field

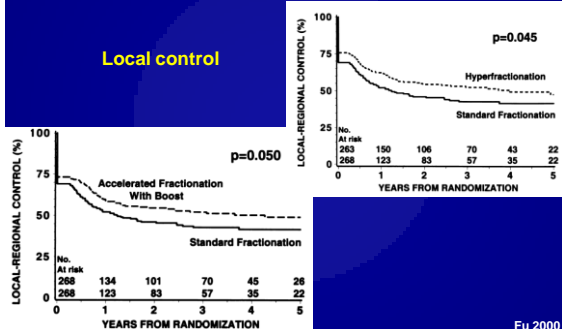
+ 1.5 Gy/fract./day to boost for the last 12 treatment days

72 Gy / 42 fract. / 6 weeks

RTOG 9003

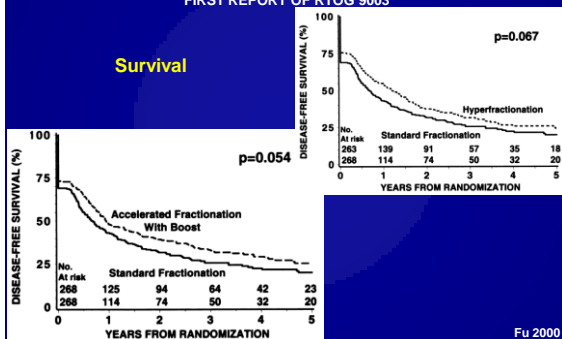
A RADIATION THERAPY ONCOLOGY GROUP (RTOG) PHASE III RANDOMIZED STUDY TO COMPARE HYPERFRACTIONATION AND TWO VARIANTS OF ACCELERATED FRACTIONATION TO STANDARD FRACTIONATION RADIOTHERAPY FOR HEAD AND NECK SQUAMOUS CELL CARCINOMAS: FIRST REPORT OF RTOG 9003

Local control

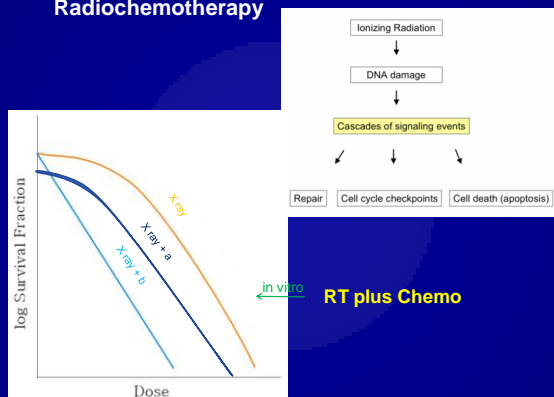


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Survival



Radiochemotherapy



Chemotherapy Added to Locoregional Treatment for Head and Neck Squamous-cell Carcinoma: Meta-Analyses of Updated Individual Data (n=10741)

Meta-analysis of locoregional treatment with and without chemotherapy: effects on survival

Trial category	Hazard ratio (95% CI)	Chemotherapy effect (p)	Heterogeneity	benefit	
				At 2 years*	At 5 years*
Adjuvant	0.98 (0.85-1.19)	0.74	0.35	1%	1%
Neoadjuvant	0.95 (0.88-1.01)	0.10	0.38	2%	2%
Concomitant	0.81 (0.76-0.88)	<0.0001	<0.0001	7%	8%
Total	0.90 (0.85-0.94)	<0.0001	<0.0001	4%	4%

* Assuming survival rates of 50% at 2 years and 32% at 5 years in control groups

Pignon 2000

Adverse effects

Scin	Inflammation, Fibrosis
Mucosa	Mucositis
Salivary gland	Xerostomia
Larynx	Edema, Necrosis
Thyroid gland	Hormon. dysfunction
Ear	Ototoxicity
Spinal cord	Paralysis
Bone	Osteonecrosis

RT: Adverse effects

Incidence (%) of grade 3 or worse

	acute adverse effects	late adverse effects
Standard fractionation	35	28
Hyperfractionation	55	28
Accel. fract. with split	51	28
Accel. fract. with boost	59	38

RTOG 9003

➡ Supportive treatment !!!

RCT: Acute adverse effects

Merlano et al. 1996	Ø	(RT-Dose at RCT ₁)
Al Sarraf et al. 1998	↑	
Calais et al. 1999	↑	
Adelstein et al. 2000	↑	
Wendt et al. 1998	↑	
Brizel et al. 1998	Ø	
Jeremic et al. 1999	↑	
Dobrowsky et al.	↑	
Staer et al. 2000	Ø	
Budach et al. 2005	Ø	

➡ Supportive treatment !!!

RCT: Late adverse effects

Merlano et al. 1996	↑	(RT-Dose at RCT ₁)
Calais et al. 1999	↑	
Adelstein et al. 2000	Ø	
Wendt et al. 1998	Ø	
Brizel et al. 1998	Ø	
Jeremic et al. 1999	Ø	
Budach et al. 2005	Ø	

Concomitant Chemoradiotherapy as Primary Therapy for Locoregionally Advanced Head and Neck Cancer

Quality of life before, during and after treatment*

QOL domainst*	before	during	after
Emotional	15.93	16.89	16.53
Social	22.94	22.31	23.70
Functional	18.37	14.82	16.12
Physical	22.32	18.30	21.79
Overall QOL	86.27	80.53	84.68

Abbreviation: QOL, quality of life

* Higher scores indicate better QOL.

* Pretreatment/ on-treatment comparisons are based on n of 30 to 33; pretreatment/ 12-month comparisons are based on n of 33 to 34

Vokes 2000

„take home“**Indication:**

No OP: Radiochemo., EGFR-I, altered fractionated RT
Post OP: low risk of recurrence — no RT
intermediate risk of recurrence — RT
high risk of recurrence — RCT

Technique:

IMRT (CT-Planing, MRI, PET); IGRT

Dose:

TD: 50 – 56 – 64 - > 70 Gy; SD: 1.2 – 2.0 / > 2,0 Gy

Treatment duration:

5½ - 7½ weeks

Treatment results:

curative intention, 5 years OS : 25 - 65 %

Adverse effects:

Inflammation (mucosa, skin), Xerostomia, Edema, Fibrosis, Necrosis
