IS THERE ANY ACHIEVEMENT IN INCREASING THE THERAPEUTIC RATIO IN H&N,PROSTATE &CERVICAL CANCER

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THERAPEUTIC RATIO

CURE CANCER WITHOUT INCURRING SIDE EFFECT

$$\frac{\text{TUMOR CONTROL PROBABILITY}}{\text{NORMAL TISSUE TOXICITY}} > 1$$

THERAPEUTIC RATIO:- FACTORS

IMPROVING THE TUMOR CONTROL

- ***CONCURRENT CHEMORADIATION***
- ***INCREASE RT DOSE***
- ***INDUCTION CHEMOTHERAPY***
- ***ADDN OF BIOLOGICAL THERAPY***

TARGETED THERAPY

DECREASING TOXICITY

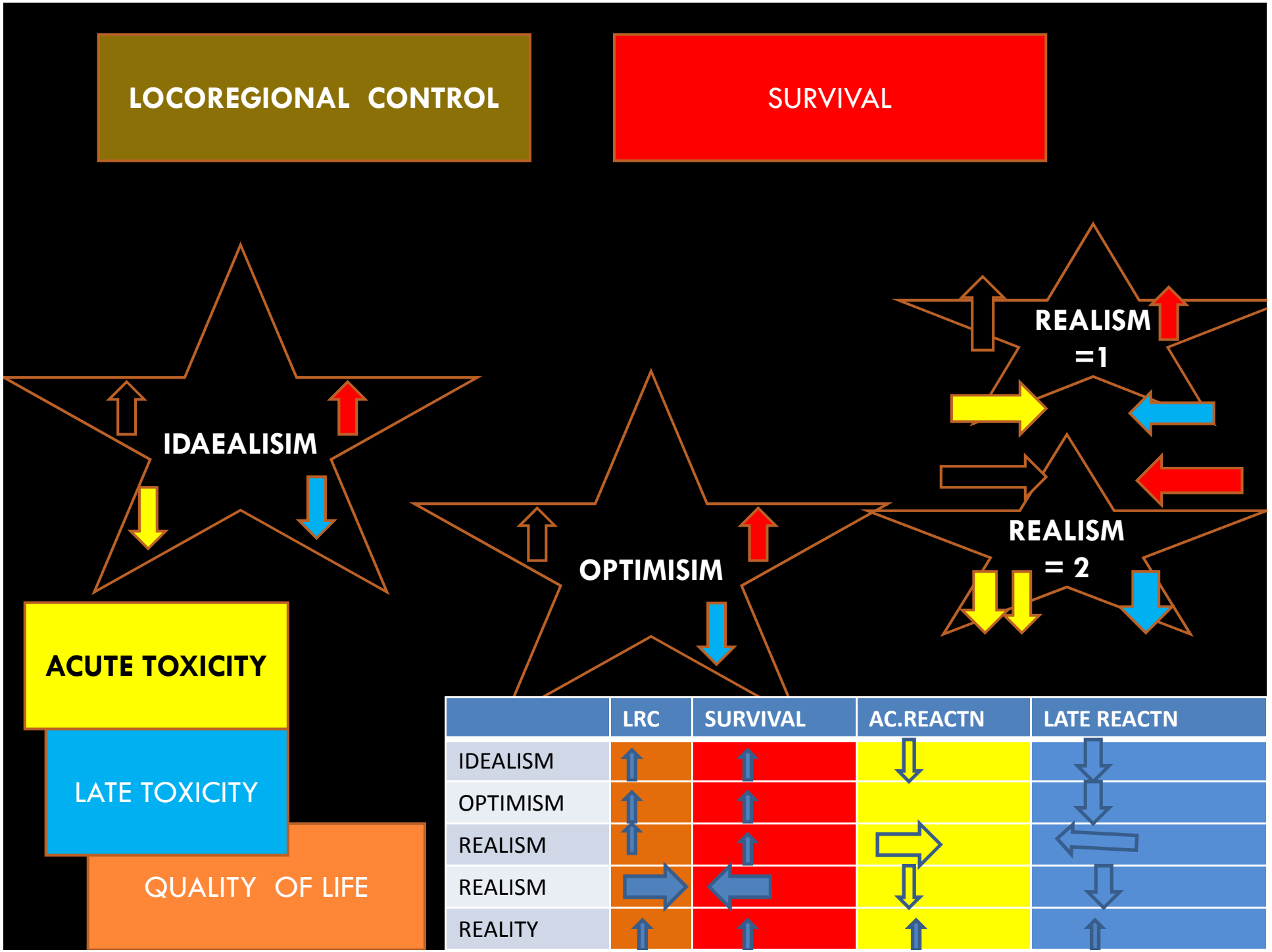
- **IMPROVE RT TECHNOLOGY**
- **CHEMO-RADIO PROTECTOR**

INTERRUPTION OF TREATMENT
EXTENDING THE TREATMENT PERIOD,REDUCE THE TOTAL DOSE ,
FAILED TO COMPLETE PLANED TREATMENT

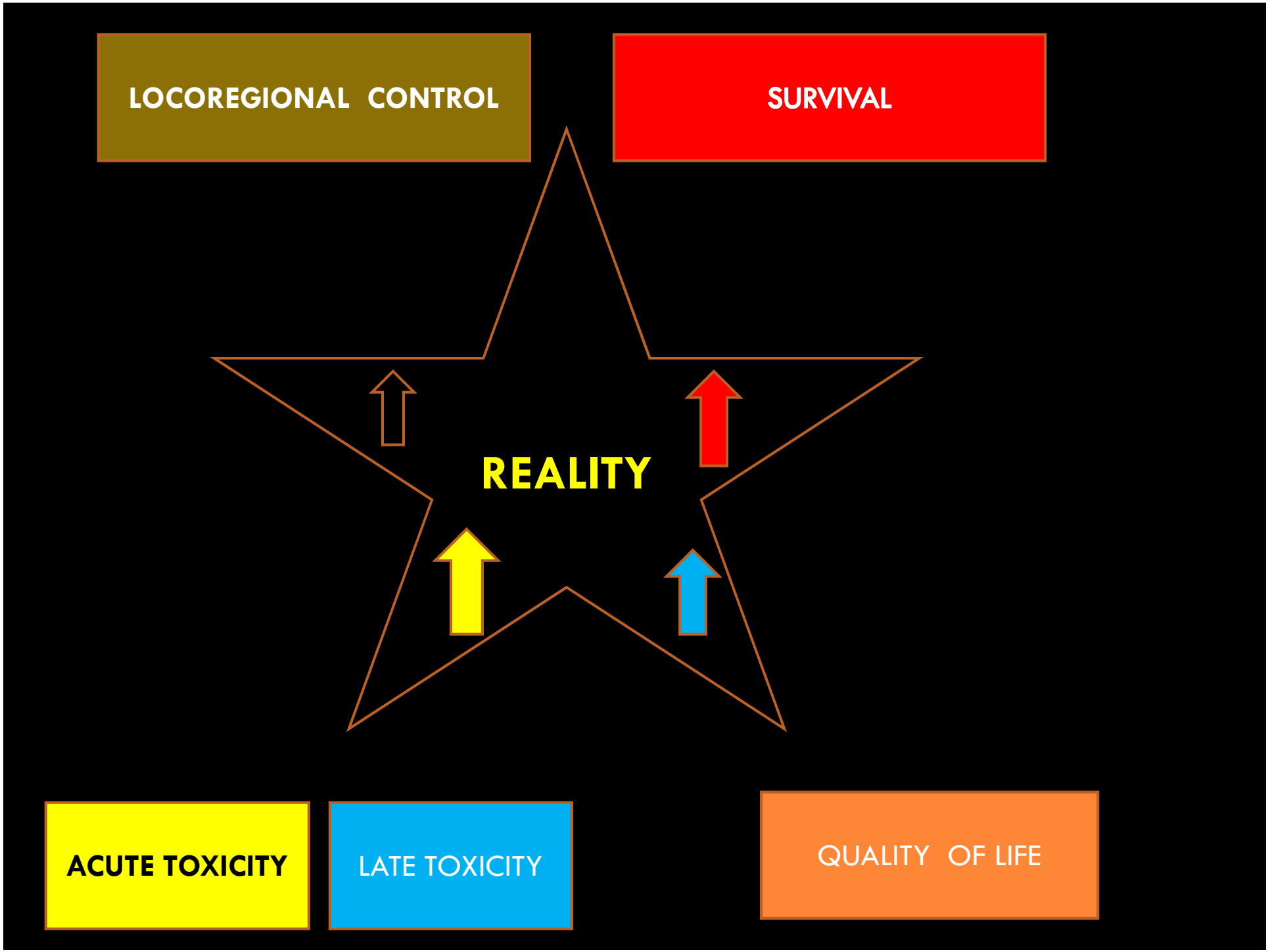
Negative impact and toxicity on survival

- Treatment inturruption of 1 day decrease disease control 1.4%
- Treatment inturruption of 1 wk decreases disease control by 10%

Hariot JC.IJROBP 60,2004
Fowler J,IJROBP 23,1992
Robertson C,IJROBP40,1998



	LRC	SURVIVAL	AC.REACTN	LATE REACTN
IDEALISM	↑	↑	↓	↓
OPTIMISM	↑	↑		↓
REALISM	↑	↑	→	←
REALISM	→	←	↓	↓
REALITY	↑	↑	↑	↑


LOCOREGIONAL CONTROL
SURVIVAL
REALITY
ACUTE TOXICITY
LATE TOXICITY
QUALITY OF LIFE

INNOVATIONS

OPTION	CONTROL	INNOVATION 1	INNOVATION 2	INNOVATION 3
RT DOSE INTENSITY	STD DOSE	INCREASE TOTAL RT DOSE	DECREASE TOTAL TREATMENT TIME	INCREASE # SIZE
CONCURRENT CT RT	NIL	CDDP &/ 5FU	TAXANE COMBN	
ANTITUMOR BIOLOGICS	NIL	CETUXIMAB	ERLOTONIB	
PHYSICS	2D/3DCRT	IMRT(ORGAN SPARING)	IMRT (DOSE ESCALATION)	SRT BOOST
RADIOPROTECTOR	NIL	AMIFOSTIN	Rh-KGF	

INNOVATIONS AND METHODS TO IMPROVE THERAPEUTIC RATIO

HEAD AND NECK CANCER

CHEMORADIATION

ALTERED FRACTIONATION

TARGETED THERAPY

IMRT

DRUGS

PROSTATE

IMRT

DOSE ESCALATION

CERVIX

CHEMORADIATION

HEAD AND NECK CANCER

General guidelines for selecting a treatment modality:

- Stage I / II disease- Single modality (Surgery or RT)

- Stage III & IV disease -- Combined modality
  Surgery + Radiotherapy (In most patients),
  Chemotherapy + radiotherapy (In selected patients)

When different modalities are available, the modality that gives *maximum chance of cure* should be used.
When different modalities have similar results, a modality that gives *better quality of life, with organ / voice preservation,Functional and cosmetic results is preferred*

SURGERY VS RADIOTHERAPY

Surgery is preferred over radiotherapy as a single modality in

1. Young patients -due to high incidence of second primary

2. Sub mucous fibrosis

3. Lesions involving or close to bone - to prevent radionecrosis.

4. Sites where surgery is not morbid (cosmetically and functionally)

RT is preferred over surgery as a single modality, where

1. Severe impairment of function / cosmesis with surgery.
2. Surgery has high morbidity and poor results e.g. nasopharyngeal carcinoma.
3. Patient refuses surgery / high risk of surgery

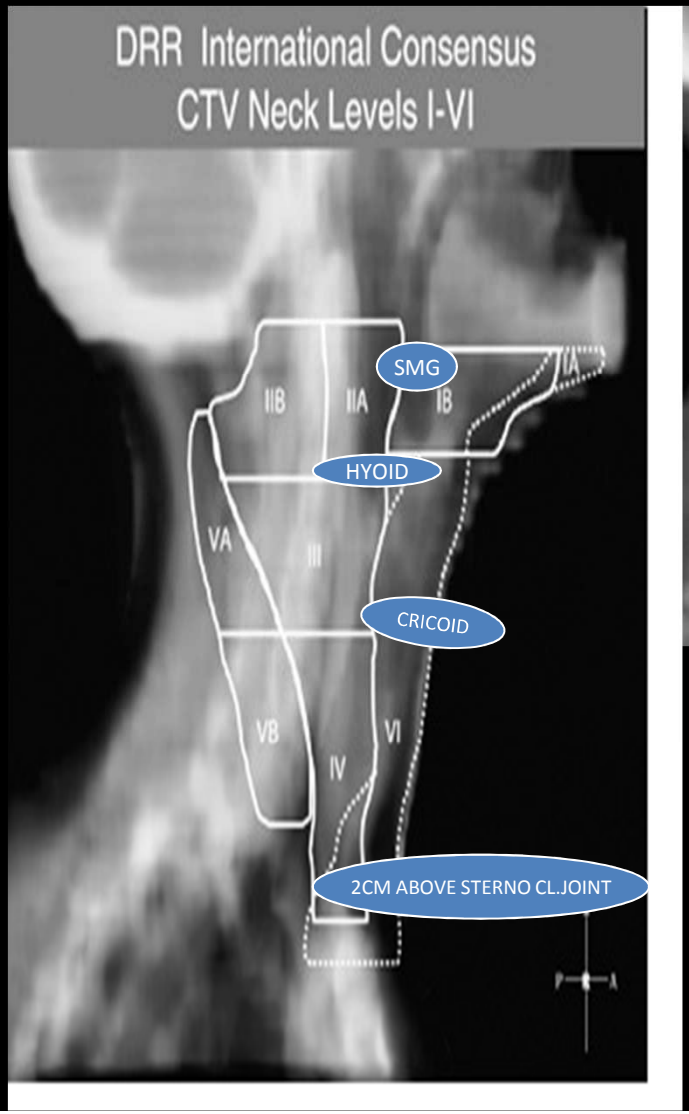
Tumour suitable for brachytherapy

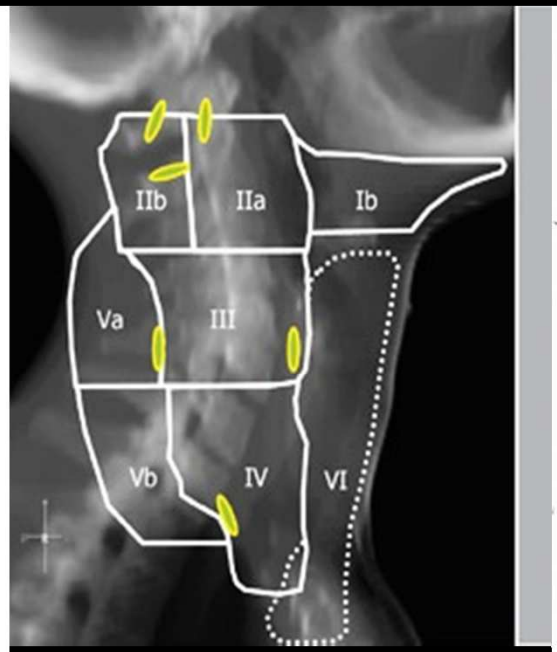
- **T1-2 N0: Radical BRT: 60-70Gy Low Dose Rate 192Iridium Or equivalent doses with fractionated high dose rate.**
- **T1-3 N0-1: External RT: 56-60Gy/ 28-30#/ 6 wks Boost BRT: Low dose rate 192Iridium: 15-20Gy or High Dose Rate: 14Gy in 4 fractions over 2 days (4-3-3-4 Gy)**

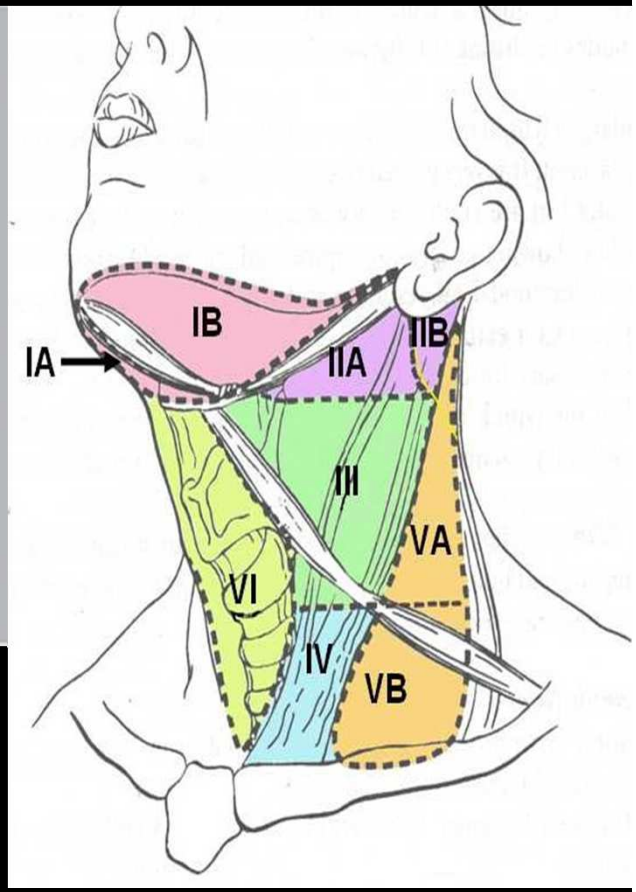
Tumours not suitable for brachytherapy:

- **T1-4 N0-2: Concomitant Chemoradiation: 66-70Gy/33-35# /6-7 wks + concomitant weekly Cisplatinum, 30mg/m2 for 6-7 wks Or**
- **External RT: 66-70Gy/33-35# /6-7 wks (reducing fields)**

Digital reconstructed radiograph (DRR) levels I–V NECK NODES.







Neck Treatment Based on Risk of Metastasis

Distribution of Pathologically Positive Nodes

Levels Involved (%)

Tumor Site	I	II	III	IV	V
Oral Cavity	48	39	31	15	4
Oropharynx	15	71	42	27	9
Hypopharynx	10	75	72	45	11
Larynx	6	61	54	30	6
Nasopharynx	13	95	60	21	44

Levendag, ASTRO 2002

PATIENT IN WHOM THE PRIMARY LESION TO BE TREATED BY RADIATION ,WHO HAVE CLINICALLY –VE NODES AND WHOM THE RISK OF SUBCLINICAL DISEASE IS 20% OR GREATER,USUALLY RECEIVE ELECTIVE NECK RT OF 45-50Gy

Table 46.2 DEFINITION OF RISK GROUPS

Group	Estimated Risk of Subclinical Neck Disease %	Stage	Site
I Low risk	<20	T1	Floor of mouth, retromolar trigone, gingiva, hard palate, buccal mucosa
II Intermediate risk	20–30	T1	Oral tongue, soft palate, pharyngeal wall, supraglottic larynx, tonsil
		T2	Floor of mouth, oral tongue, retromolar trigone, gingiva, hard palate, buccal mucosa
III High risk	>30	T1–4	Nasopharynx, pyriform sinus, base of tongue
		T2–4	Soft palate, pharyngeal wall, supraglottic larynx, tonsil
		T3–4	Floor of mouth, oral tongue, retromolar trigone, gingiva, hard palate, buccal mucosa

From Mendenhall WM, Million RR. Elective neck irradiation for squamous cell carcinoma of the head and neck: analysis of time–dose factors and causes of failure. *Int J Radiat Oncol Biol Phys* 1986;12:741–746, with permission.

OROPHARYNX,NASOPHARYNX,SUPRAGLOTTIC LARYNX AND HYPOPHARYNX

LOWER NECK NODE WITH SINGLE ANT FIELD

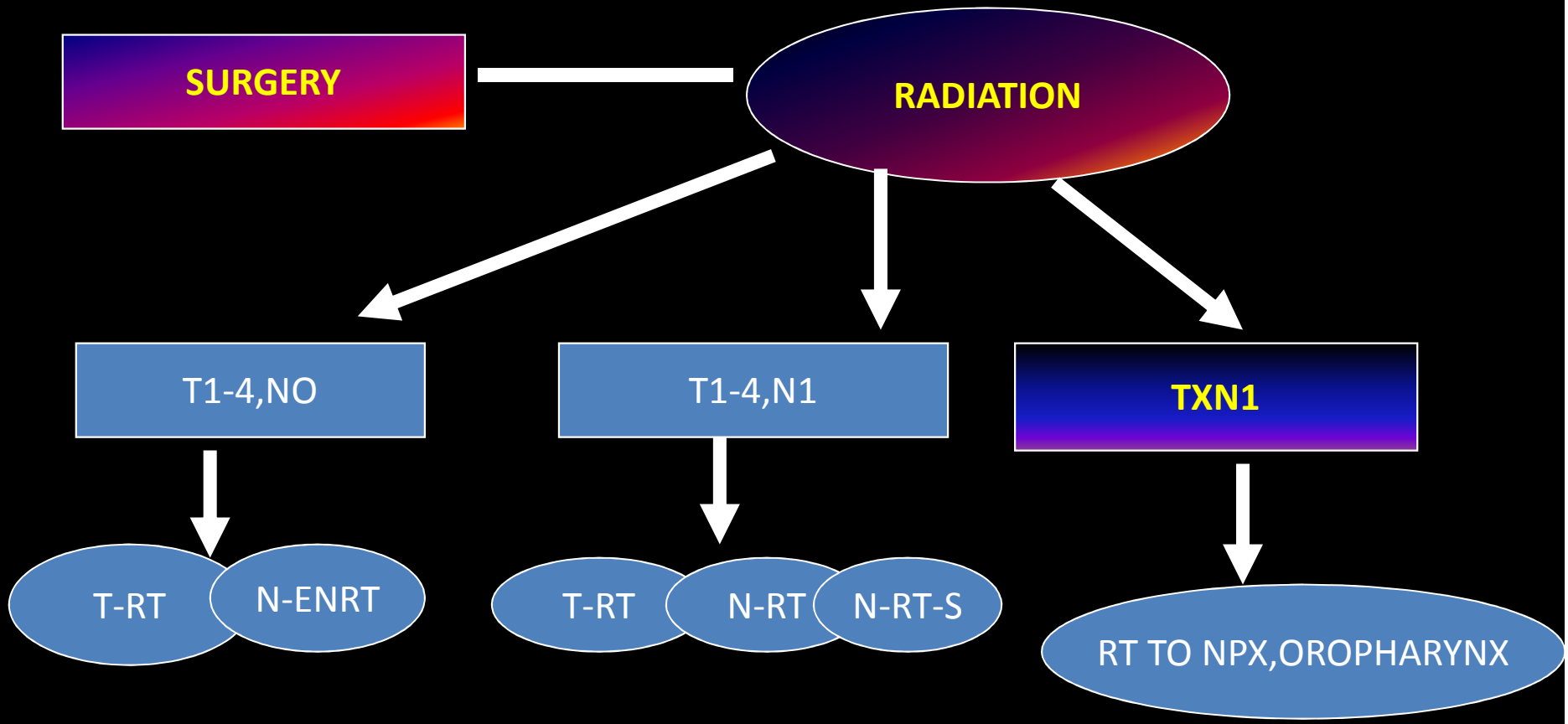
- ON LYMPH NODE EXAMINATION OBSERVE ANATOMICAL LOCATION,SIZE,CONSISTANCY AND MOBILITY
- MOST COMMON INVOLVE LYMPH NODE-SUBDIGASTRIC L.N
- INCIDENCE OF POSITIVE L.N VS CAPSULAR INVN VS L.N SIZE

Table 46.4 RELATIONSHIP BETWEEN NODE SIZE, THE PRESENCE OF TUMOR IN THE NODE, AND CAPSULAR PENETRATION IN 519 NODES[a]

	Size of Node (cm)				
	1	2	3	4	≥5
Number of nodes	177	183	84	17	58
Percent positive	33	62	81	88	100
Percent positive with capsular penetration	14	26	49	71	76

[a]Data from the Institut Gustave-Roussy, Villejuif, France.
Modified from Richard JM, Sancho-Garnier H, Micheau C. Prognostic factors in cervical lymph node metastasis in upper respiratory and digestive tract carcinoma: study of 1713 cases during a 15-year period. *Laryngoscope* 1987;97:97–101, with permission.

MANAGEMENT OF NECK NODE



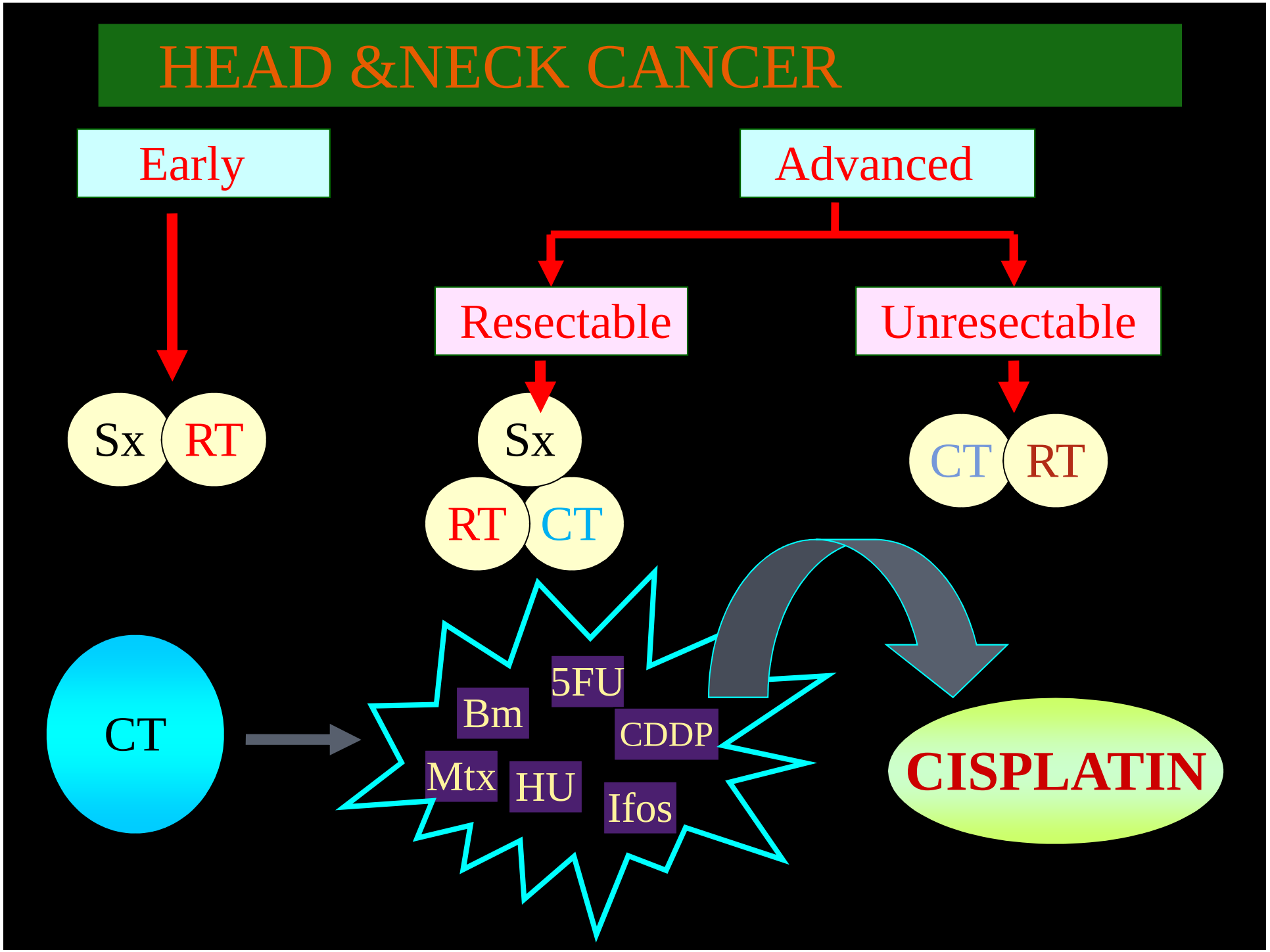
IN +VE NECK NODE

- ADVANCED DISEASE HAS BETTER CHANCE OF CURE WITH ALTERED # /CONCOMITTANT RT
- +VE NODE RECEIVE 70 TO 74Gy OF RT

NODE SIZE AND DOSE OF RADIATION BEFORE SURGERY

NODE SIZE	DOSE OF RT
3-4 cm,MOBILE	50GY
5-6CM,FIXED	60GY
7-8 CM	70-75GY

TIME OF SURGERY:-4-6 WKS AFTER RT.INITIAL REGRESSION IS SLOW. MUCH REGRESSION AT 4-6 WKS


HEAD &NECK CANCER
Early
Advanced
Resectable
Unresectable
Sx
RT
Sx
RT
CT
CT
RT
5FU
Bm
CDDP
Mtx
HU
Ifos
CISPLATIN

SURGERY Vs S+RT

Treatment	Ipsilat neck failure (No –N_3b)	Contralat neck failure (No –N_3b)
Surgery	51/199 (25.6%)	35/130(27%)
Radiation	54/292(18.5%)	7/172(4%)
Combined	8/105 (7.8%)	3/85(3%)

Barkley et al A.J.Surg 124 : 462-467,1972

(***Post operative RT eleminated subclinical disease after surgery in both Ipsilat neck as well as Contralat neck)***

But no comment on survival.

Resectable Head & Neck Cancer
Pre Vs Post op RT
RTOG 73 - 03

Estimated 4 yr Locoregional control percentage hy Rx & Region

Site	Pre op (%)	Post op (%)	Total (%)
Oral cavity	40	44	42
Oropharynx	47	61	54
Supraglottic Larynx	53	77	64
Hypopharynx	50	61	55
All Regions	48	65	57
For 194 pts who competed planned t/t	56	74	

POST OF RADIATION IS THE STANDARD OF CARE

Huang et al. (medical college of Virginia)

	SURGERY	S +RT	P
3 yrs DFS	25%	45%	0.0001
ECE +3yr Local control	31%	66%	0.03
RPM 3yr local control	41%	49%	=0.04
ECE +RPM 3yr local control	0%	68%	0.0003
3yr overall survival	41%	72%	0.0003

Risk stratification in post op setting in H&N Cancer

HIGH RISK FACTORS :

Extracapsular Extension Of Nodal Disease

≥2 of the following factors

- Oral cavity site
- Microscopicaly positive mucosal margins
- Nerve invasion
- ≥ 2 involved neck nodes
- > 1 positive nodal group
- Node size>3 cm

INTERMEDIATE RISK FACTOR:

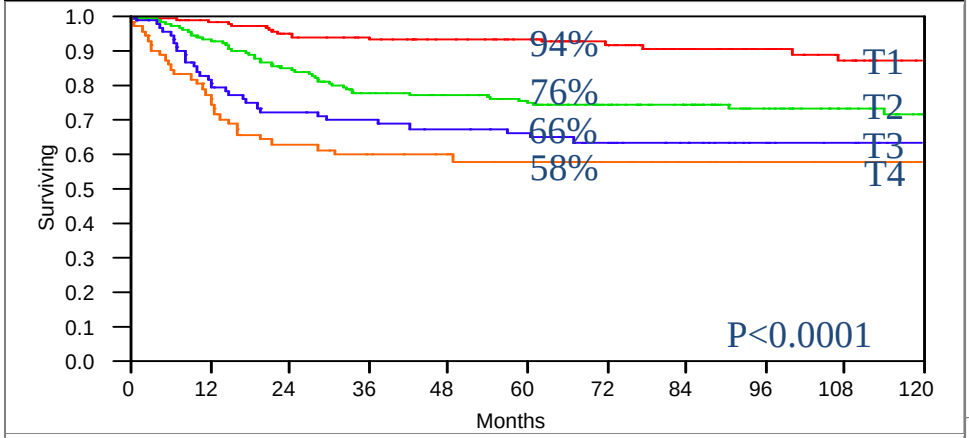
No ECE

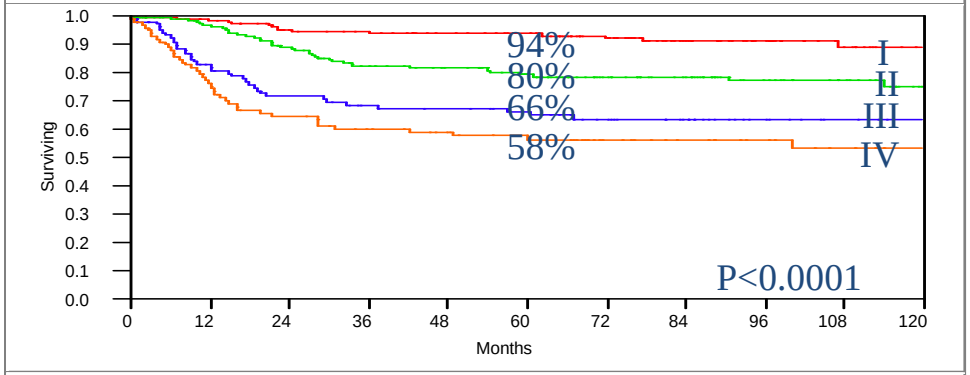
One of the above risk factor

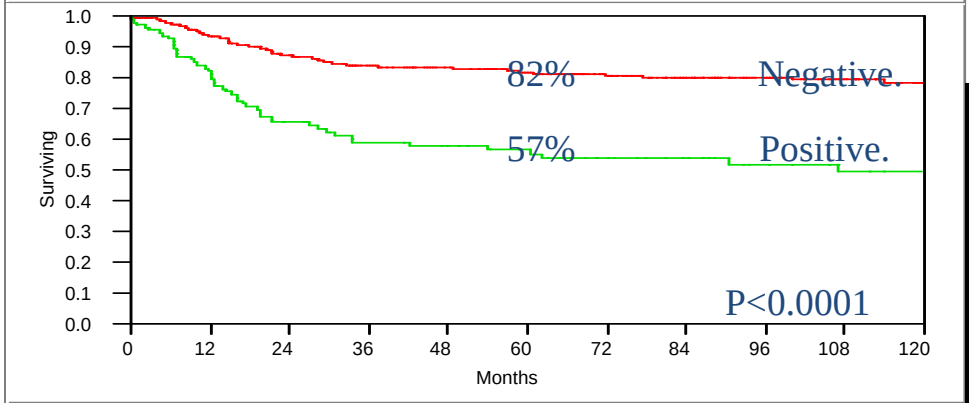
***LOW RISK FACTOR*:**

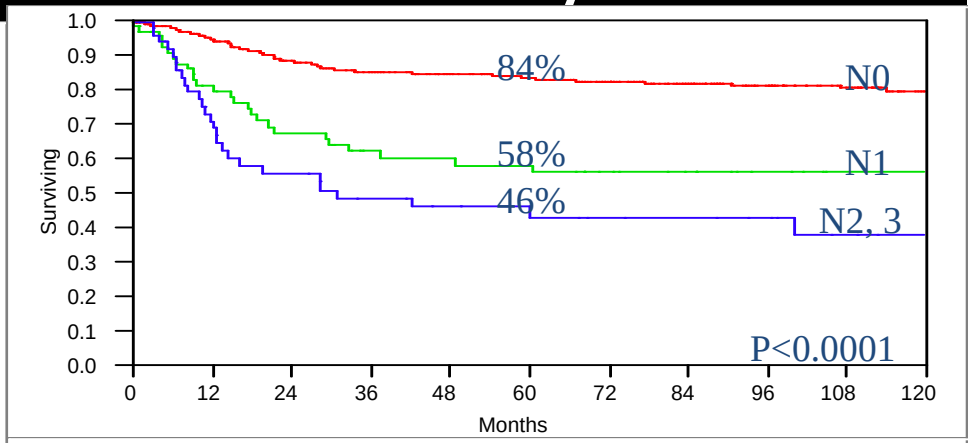
None of the above factor

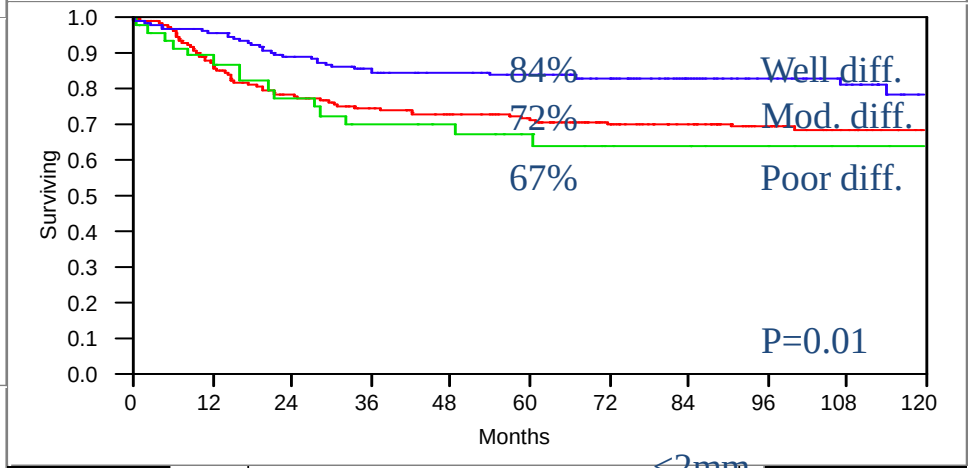
Disease-Specific Survival Vs Risk factors in Ca. Oral cavity

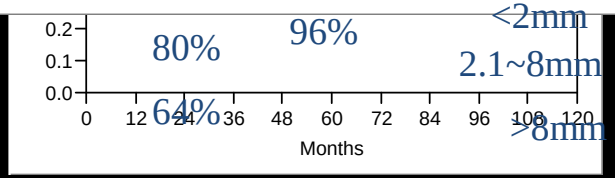








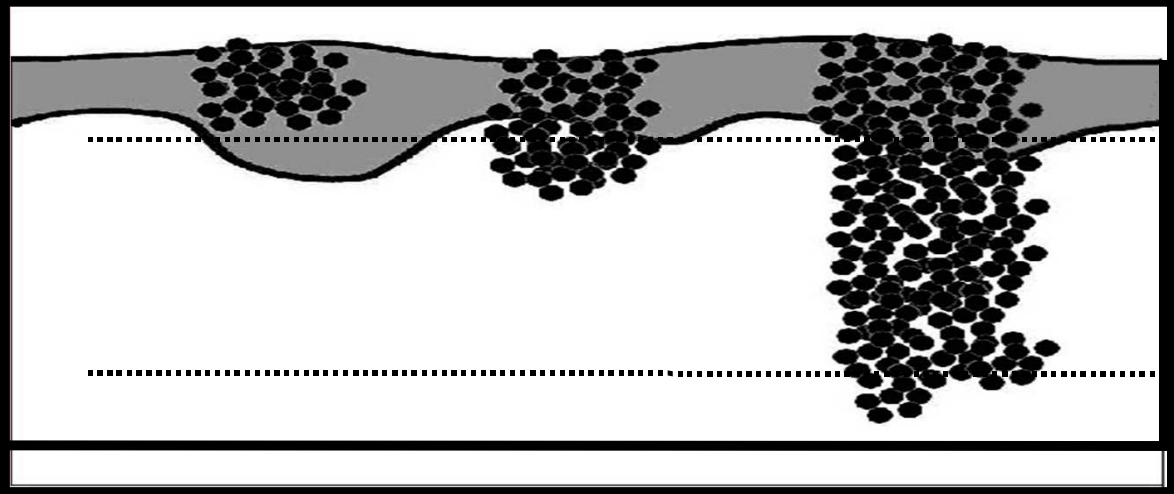




P<0.0001

Depth of Invasion

	<2 mm	2.1-8 mm	>8 mm
	n=60	n=190	n=187



Risk of Occult Metastasis	2%	15%	19%
Overall pN+	5%	27%	45%

- **Early Disease (Stage I, II) - Monotherapy**

  Surgery or Radio-therapy

  NOOOOOOOOOOOOOO

CONCURRENT CT RT IN HIGH RISK PATIENTS

	#pt	F/U	LC	LRC (CTRT Vs RT)	DFS (CTRT Vs RT)	Survival (CTRT Vs RT)
RTOG 9501 [31]	459	46 month median	Not reported	80% vs 68% P = 0.003	54% vs 45% p =0.04	42% vs 36% P = 0.19
EORTC 22931 [30]	334	60 month median	Not reported	82% vs 69% P = 0.007	47% vs 36% P =0.04	53% vs 40% P = 0.02
Bachaud (1996) [29]	83	5 year minimum	84% vs 59% P=0.05	Not reported	68% vs 44% P<0.02	72% vs 46% P <0.01

CDDP-100MG/M2 AT 3 WEEKS INTERVAL
EBRT:-66Gy

Results

Outcome end points	EORTC Trial 2931 (5yr estimates)	RTOG Trial 9501 2-year Estimates
Loco-regional failure rates	**17% versus 31% (p=0.007)**	**18% Vs 28% (p=0.01)**
Grade 3 + acute toxicity	Functional 41% Vs 21% (p=.008)	**77% Vs 34% (p<0.0001)**
Late toxicity	38% Vs 41% (p=0.25)	21% Vs 17% (p=0.29)
Impact on Distant metastases	p=0.61(21% vs. 25%)	p=0.46(20% Vs 20%)

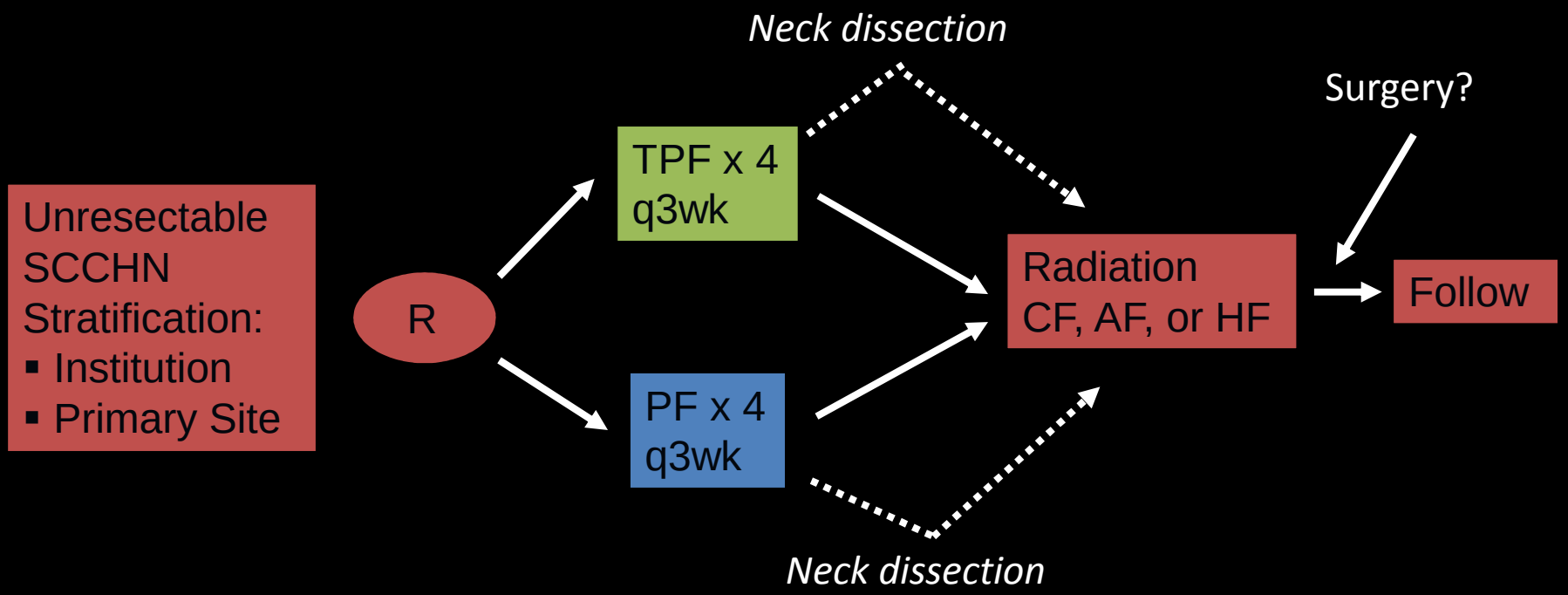
Treatment strategy in post op Head & Neck Cancer

- Low Risk → No adv. Factor – Obs
- Int Risk → One risk factor
  No ECI – RT
- High Risk → 2 risk factor
  & ECI – CT+RT. Alt#

Randomized Trials of PF ± Taxane Induction Therapy Trials

Study	Eligibility	N	T + PF CR/PR, n/N (%)	PF CR/PR, n/N (%)	TPF/PF PFS, Mos	TPF/PF OS, Mos	*P* Value (HR)
Hitt JCO 2005	Stage III-IV	382	33/47 (80)	14/54 (68)	20 12	43 37 2 yrs: 66%/61%	.035 (0.67)
TAX 323 ASCO 2006	Unresectable	358	(68)	(54)	11 8	18.6 14.2 3 yrs: 24%/18%	.005 (0.71)
Gortec ASCO 2006	L/HP II-IV	205	43/39 (82)	30/30 (60)	LP: 63%/41%		.036
TAX 324 ASCO 2006	III-IV	501	17/55 (72)	15/49 (64)	2-yr PFS: 53%/42%	70 30 3 yrs: 62%/48%	.006 (0.7)

Cisplatin/5-FU vs Docetaxel + Cisplatin/ 5-FU in SCCHN: Study Design

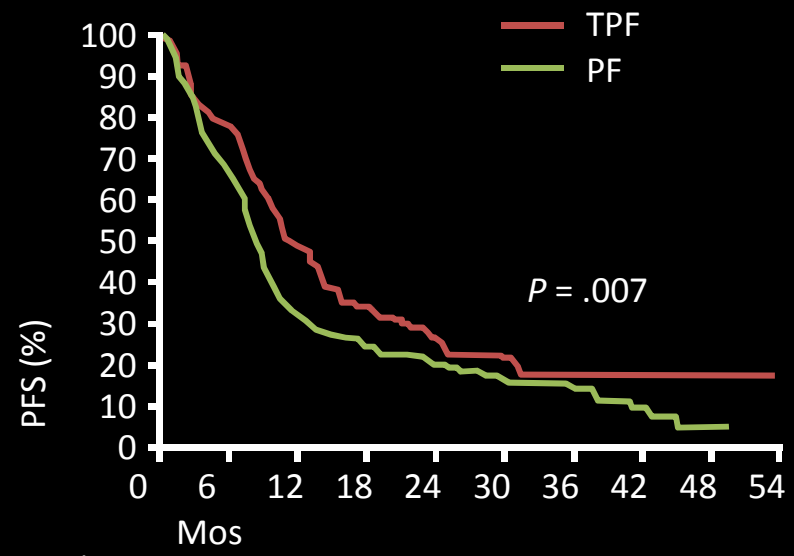


Planned sample size: 358 patients

Number of events: 260 progression events needed to show 50% increase in PFS (10-15 months; HR: 0.67)

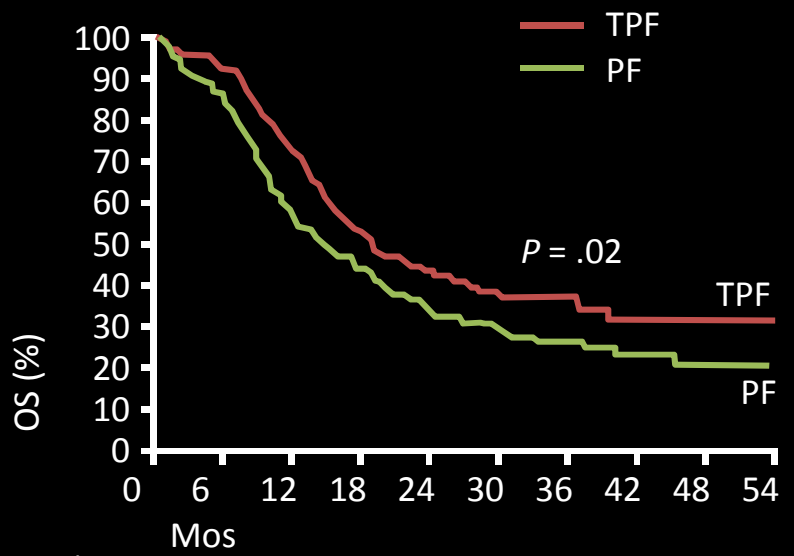
Vermorken JB, et al. N Engl J Med. 2007;357:1695-1704.

PFS and OS



Pts at Risk, n

PF	181	112	52	37	25	19	11	5	1
TPF	177	129	79	48	23	16	5	3	1



Pts at Risk, n

PF	181	149	97	72	49	32	20	13	4
TPF	177	163	127	89	57	36	21	9	1

Efficacy of radiation therapy and concurrent chemotherapy in Head & Neck cancer

	French Trial (n = 226)	P	German Trial (n = 270)	P	Nasopharynx Intergroup Trial (n = 193)	P	Duke University Trial (= 116)	P
Local control rate %	66 v 42	--	35 v 17	<.004	NR	-	70 v 44	.006
Disease-free survival rate,%	42 v 19	.002	NR	-	69 v 24	<.001	60 v 40	.07
Survival rate %	51 v 31	.003	49 v 24	<.0003	78 v 47	.005	42 v 28	.05
Mucositis rate%	67 v 36	-	38 v 16	<.001	NR	-	77 v 75	-

Concurrent CTRT

- RT+CT(concurrent) :- ↑LRC, ↑ DFS, ↑OS
- MONOCHEMOTHERAPY using Cisplatinum seems give better overall result
- No consensus regarding optimal radiation –dose fractionation
- Acute toxicities with use of concurrent CT & RT is high,so can considered IMRT
- Recommended as standard of care in Locally advanced H&N cancer.

Meta-Analysis of Chemotherapy in H&N Cancer (MACH-NC)

- Analyzed 63 randomized trials, 1965 - 1993
- Locoregional Rx +/- chemotherapy
- Updated individual patient data
- Total of 10,741 patients

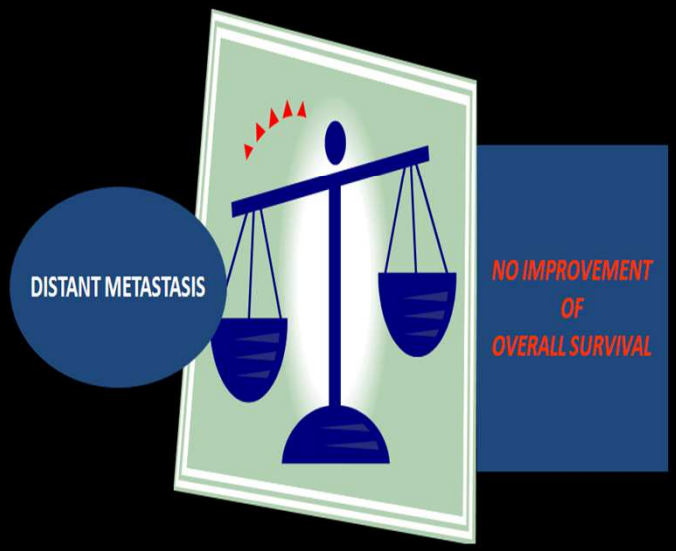
Lancet 355:949-955, 2000

Meta-analysis of loco-regional treatment with and without chemotherapy : effect on survival (MACH-NC Collaborative Group)

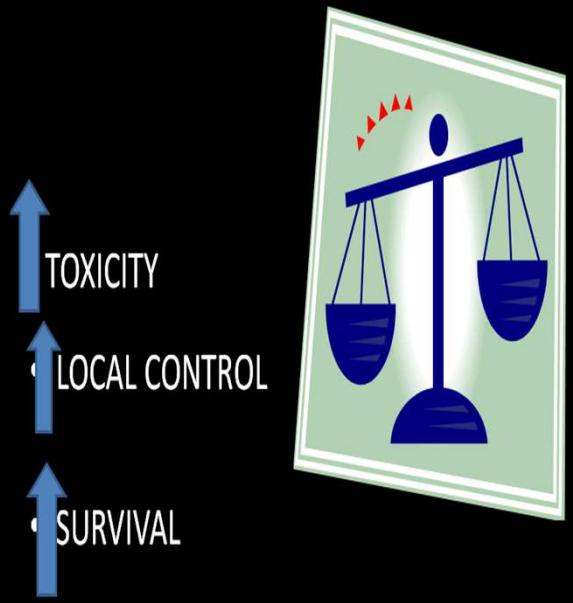
Trial category	Hazard ratio	Effect of chemotherapy (p)	Absolute benefit At 2 yrs	At 5 yrs
Adjuvant	0.98 (0.85-1.19)	0.74	1%	1%
Neoadjuvant	0.95 (0.88-1.01)	0.10	2%	2%
Concomitant	0.81 (0.76-0.88)	< 0.0001	7%	8%
Total	0.90 (0.85-0.94)	< 0.0001	4%	4%

* Assuming survival rates of 50% at 2yrs and 32% at 5yrs in control groups receiving loco-regional treatments

NEOADJUVANT CT

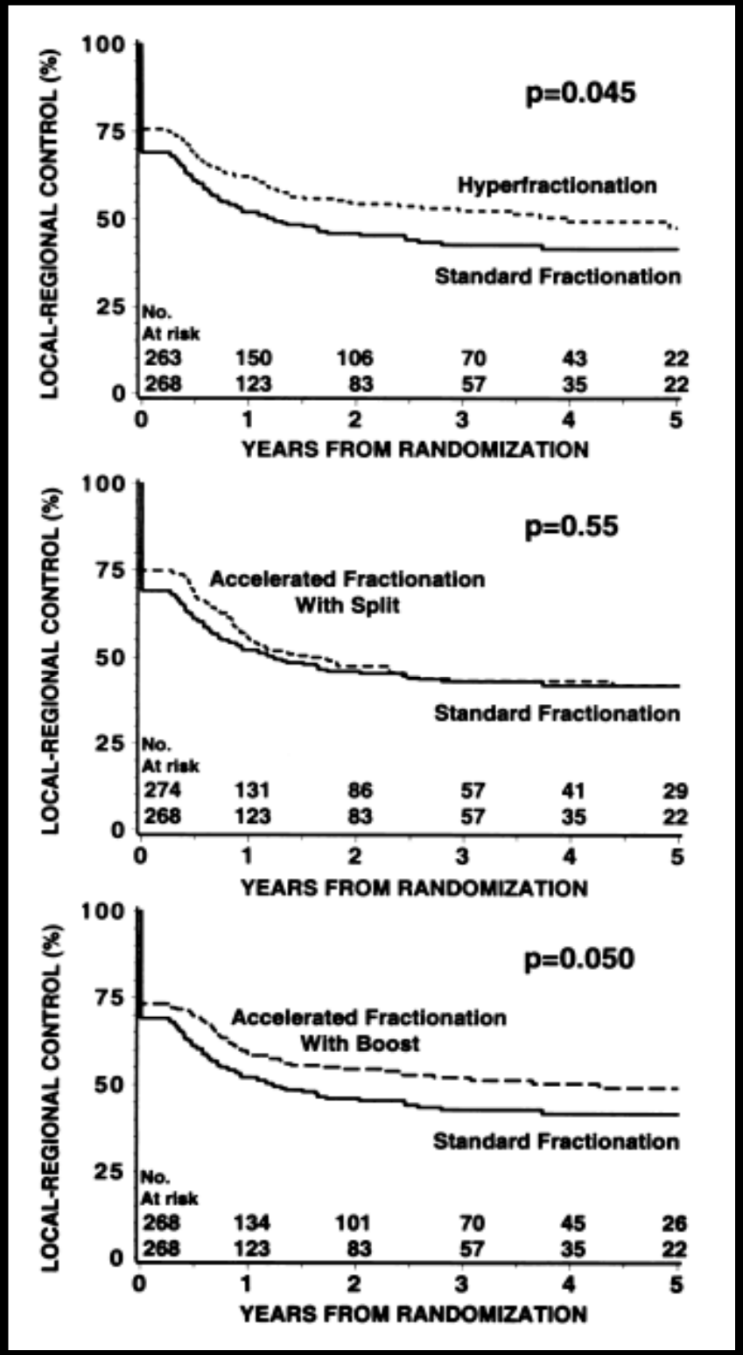


OUTCOME VERSUS TOXICITY(CONCURRENT CTRT)



RTOG 90-03 : 5-YEAR DATA

	LOCOREGIONAL CONTROL	DFS	OS
STANDARD RT	41%	20%	30 %
Hfx RT	49% (p = .08)	26%(p =.08)	37%
AFX-SPLIT RT	42%	23%	29%
AFX-CONC.BOOST RT	49%(p=0.4)	25% (p=.06)	34%



RTOG 90-03

- Improved local control (expected) with hyperfractionation and accelerated fractionation *without* split.
- Increased acute effects (expected).
- No increase in late effects (expected).

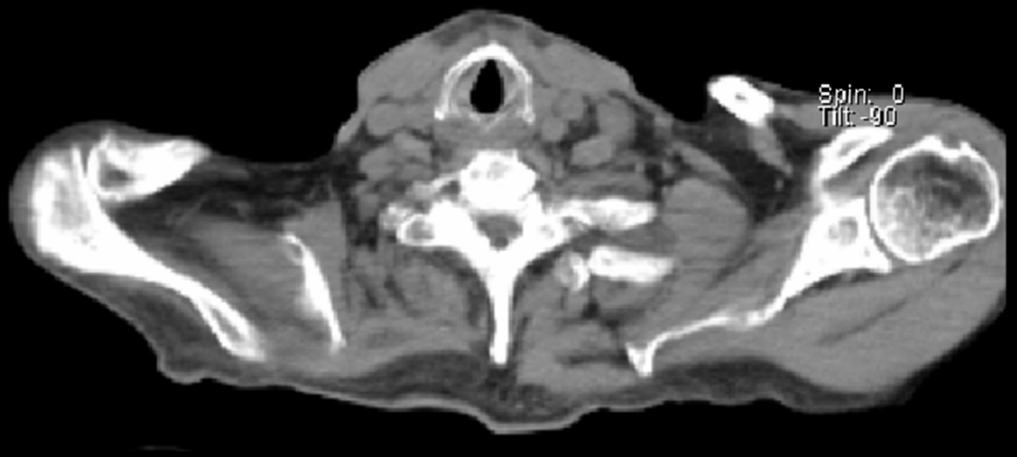
Rationale of IMRT in H & N Cancer

- **Anatomically complex H&N region - *an ideal option - IMRT.***
- **Lack of organ motion in the H&N region - *an ideal region for IMRT.***
- **Allows for dose escalation - *concomitant boost – ideal for H&N***

IMRT IN HEAD & NECK CANCERS :

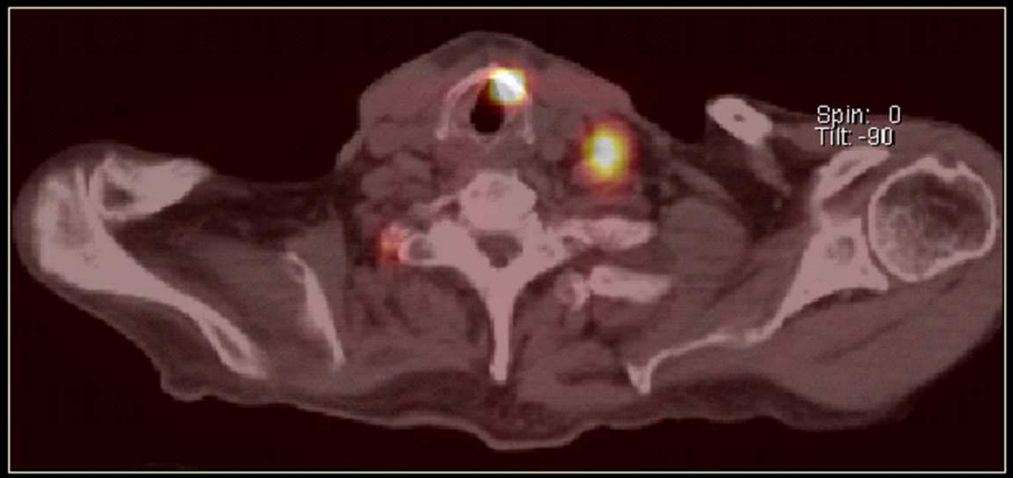
SITE	RADIATION DOSE
Gross tumour volume (GTV)	66Gy / 30 #s
Subclinical disease	60Gy / 30#s
Un involved lymph nodes	54 Gy / 30 #s
Parotids	< 26 Gy
Brain Steam	< 45 Gy
Optic N .Chiasma	< 50 Gy

PET Scores over others!



CT, MRI

Anatomical imaging



PET

is functional imaging

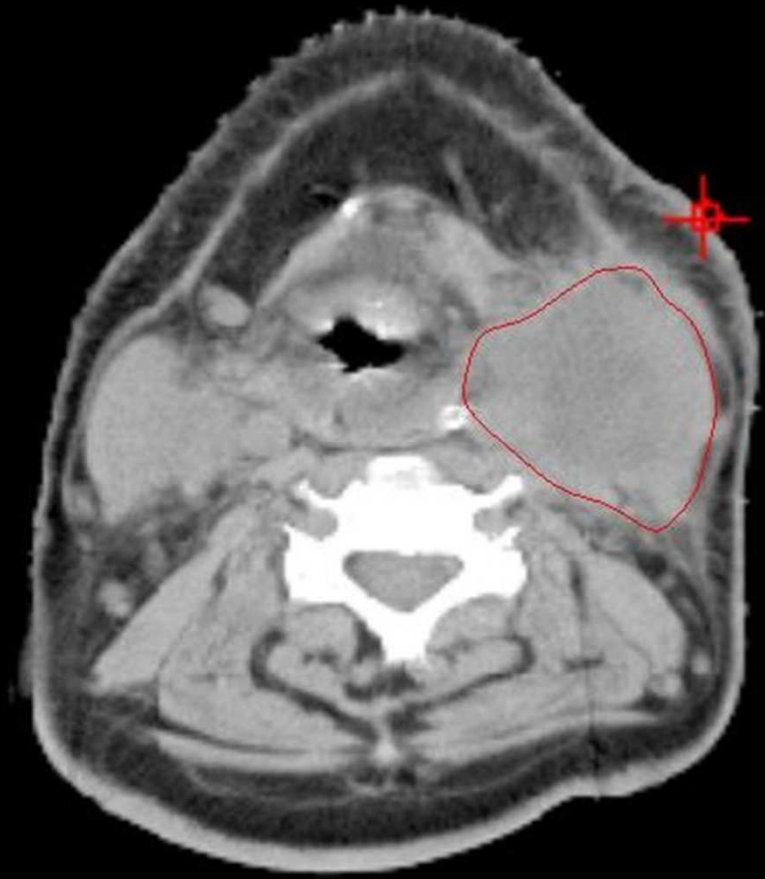
Active viable tumor

Impact of PET-CT in H & N Cancer

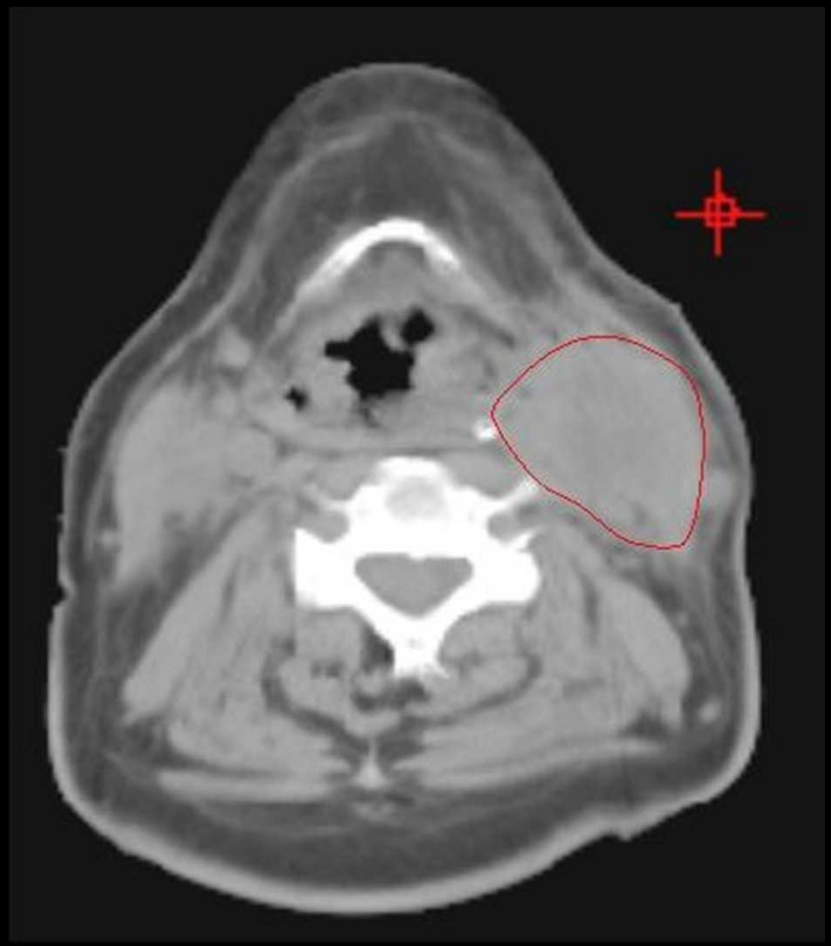
Author	Patients using PET	Change of GTV	Increase in GTV	Decrease in GTV	Remarks
Rahn, 1998	22(prim)	41%	41%	0%	No image fusion
	12(recur)	58%	58%	0%	
Nishioka, 2002 fusion	21	71%	0%	71%	PET/CT/MRI
Ciernik, 2003	12	50%	17%	33%	Integrated PET-CT
Daisne, 2004	29	93%	18%	75%	CT-PET image fusion
Paulino, 2005 image fusion	40	100%	-	-	PET/CT/MRI and surgical specimen

Changes in Anatomy during course of Rx

Planning CT

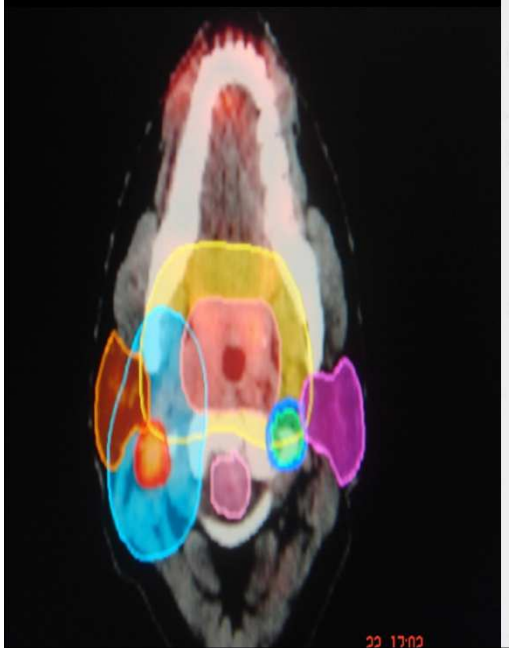


Three Weeks into RT



Barker et al. *IJROBP* 59:960, 2004 & Lei Dong et al. (MDACC)

Anatomical modifications during radiotherapy



Author	No. of Patients	Per-Treatment Imaging	Image Registration	Volume Analysis	Shape and Positional Analysis
Barker et al (2004)[6]	14	In-room CT-on-rail 3 times/wk; no iv contrast	Rigid	Reduction of: • GTV: 1.8% per treatment day • PGs: 0.6%/treatment day	• GTV: COM displacement: 3.3 mm (asymmetric shrinkage) • PG: COM shift medially by 3.1 mm
Geets et al (2007)[50]	10	CT scan at mean doses of 14, 25, 35, and 45 Gy; iv contrast	Rigid	After a mean dose of 45 Gy: • GTV_T: mean decrease of 65.5% • High dose CTV_T: mean decrease of 50.9% • High dose PTV_T: mean decrease of 47.9%	NA
Han et al (2008)[43]	5	Daily helical MVCT	Rigid	At the end of treatment: PGs had decreased from 20.5 to 13.2 cm^3, ie, an average decrease of 0.21 cm^3/treatment day or 1.1%/treatment day	NA
Vasquez Osorio et al (2008)[51]	10	CT scan at 46 Gy; iv contrast	Deformable	Reduction after 46 Gy: • GTV: 25 15% • Homolat PG: 17 7% • Heterolat PG: 5 4% • Homolat SMG: 20 10% • Heterolat SMG: 11 7%	After 46 Gy: • Lateral and inferior regions of homolat PG: medial and posterior shift (3 mm) • Homolat SMG: medial, cranial, and posterior shift (4 mm)
Hansen et al (2006)[52]	13	CT scan after a mean dose of 38 Gy	Rigid	Reduction: • GTV: no change • Right PG: 15.6% • Left PG: 21.5%	NA
Robar et al (2007)[53]	15	Weekly CT scans; no iv constrast	Rigid	Reduction of supercial regions of both PGs: 4.9%/wk	Supercial regions show medial translation of: left PGs: medial shift of 0.91 0.9 mm/wk right PGs: medial shift of 0.78 0.13 mm/wk
Castadot et al (2008)	10	CT scan at mean doses of 14, 25, 35, and 45 Gy; iv contrast	Deformable	Reduction of • GTV_T: 3.2%/treatment day • GTV_N: 2.1%/treatment day • Homolateral PG: 0.9%/treatment day • Heterolat PG: 1.0%/treatment day • Low dose homolat CTV_N: 0.5%/treatment day • low dose heterolat CTV_N: 0.4%/treatment day	After 5 treatment wks: • Homolat PG: medial shift of 3.4 mm • GTV_T: lateral shift of 1.3 mm • GTV_N: medial shift of 0.9 mm • Low dose homolat CTV_N: medial shift of 1.8 mm No shift for the heterolat PG and heterolat low dose CTV_N.

CT, computerized tomography; GTV, gross tumor volume; CTV, clinical target volume; PTV, planning target volume; PG, parotid gland; COM,

Dosimetric effect of Anotomical modifications during radiation therapy

Author	No. of Patients	Per-Treatment Imaging	Image Registration	Results	Comments
O'Daniel et al (2007)[44]	11	In-room CT-on-rail scans twice/wk; no iv contrast	Deformable	Cumulative PG dose greater than planned; median dose increase: 1 Gy No impact on tumor dose coverage	If no image-guidance for daily setup error correction, cumulative PG dose greater than planned; median dose increase: 3 Gy for homolat PG and 1 Gy for heterolat PG
Hansen et al (2006)[52]	13	CT scan after a mean dose of 38 Gy	Rigid	• High dose PTV D_{99}, D_{95}, $V_{93\%}$ decreased by 12.1, 12.2 Gy, and 7%, respectively • Low dose PTV D_{99}, D_{95}, $V_{93\%}$ decreased by 12.6, 11.3 Gy, and 8.2%, respectively • Right PG V_{26Gy} increased by 10.9% • Mandible V_{60Gy} increased by 7.2%	If replanning; signicant improvement of: • Low and high dose PTVs D_{99} D_{95} and $V_{93\%}$ • Spinal cord D_{max}, D_{1cc} • Brainstem D_{max} • Right parotid PG D_{mean}, D_{50}, and V_{26Gy} • Mandible D_{max} and V_{60Gy}
Robar et al (2007)[53]	15	Weekly CT scan; no iv contrast	NA	Left PG D_{mean} increased by 2.6 ± 4.3%, V_{26Gy} increased by 3.5 ± 5.2% Right PG D_{mean} increased by 0.2 ± 4.0%, V_{26Gy} increased by 0.3 ± 4.7%	
Han et al (2008)[43]	5	Daily helical MVCT	Rigid	PG D_{median} increased from 0.83 to 1.42 Gy with an average increase rate of 0.17 Gy/treatment day corresponding to an average increase of 2.2%/treatment day	Strong correlation between the volume and the median parotid dose during the treatment (correlation coefcient, − 0.95)
Lee et al (2008)[56]	10	Daily helical MVCT	Deformable	• PG daily D_{mean} differed from the planned dose by an average of 15% • PG cumulative D_{mean}: planned: 29.7 Gy actual: 32.7 Gy (110% of planned dose)	• Changes in the distance between the COMs of the left and right PGs correlated strongly with the mean parotid dose changes (R^2= 0.88) • Correlation between the relative weight loss and higher parotid mean doses (R^2 0.58)
Castadot et al (2009)	10	CT scan at mean doses of 14, 25, 35, and 45 Gy; iv contrast	Deformable	• PGs D_{mean}: planned: 17.9 Gy, actual 18.7 Gy • SMGs D_{mean}: planned 51.9 Gy, actual: 52.8 Gy • OC D_{mean}: planned 26.0 Gy, actual 26.7 Gy • SC D_2: planned 40.1 Gy, actual: 41.0 Gy • Skin V_{60}: planned 17.2 Gy, actual 18.3 Gy • No difference in PTV or CTV coverage	

OC, oral cavity; SC, spinal cord; D_x, dose to x% of the volume; D_{max}, maximum dose; D_{1cc}, dose to 1 cc.; D_{mean}, mean dose; D_{median}, dose to 50% of the volume; V_x, volume receiving a dose of x Gy or x% of the prescribed dose.

Table 1. Locoregional Control After IMRT for Head and Neck Cancer

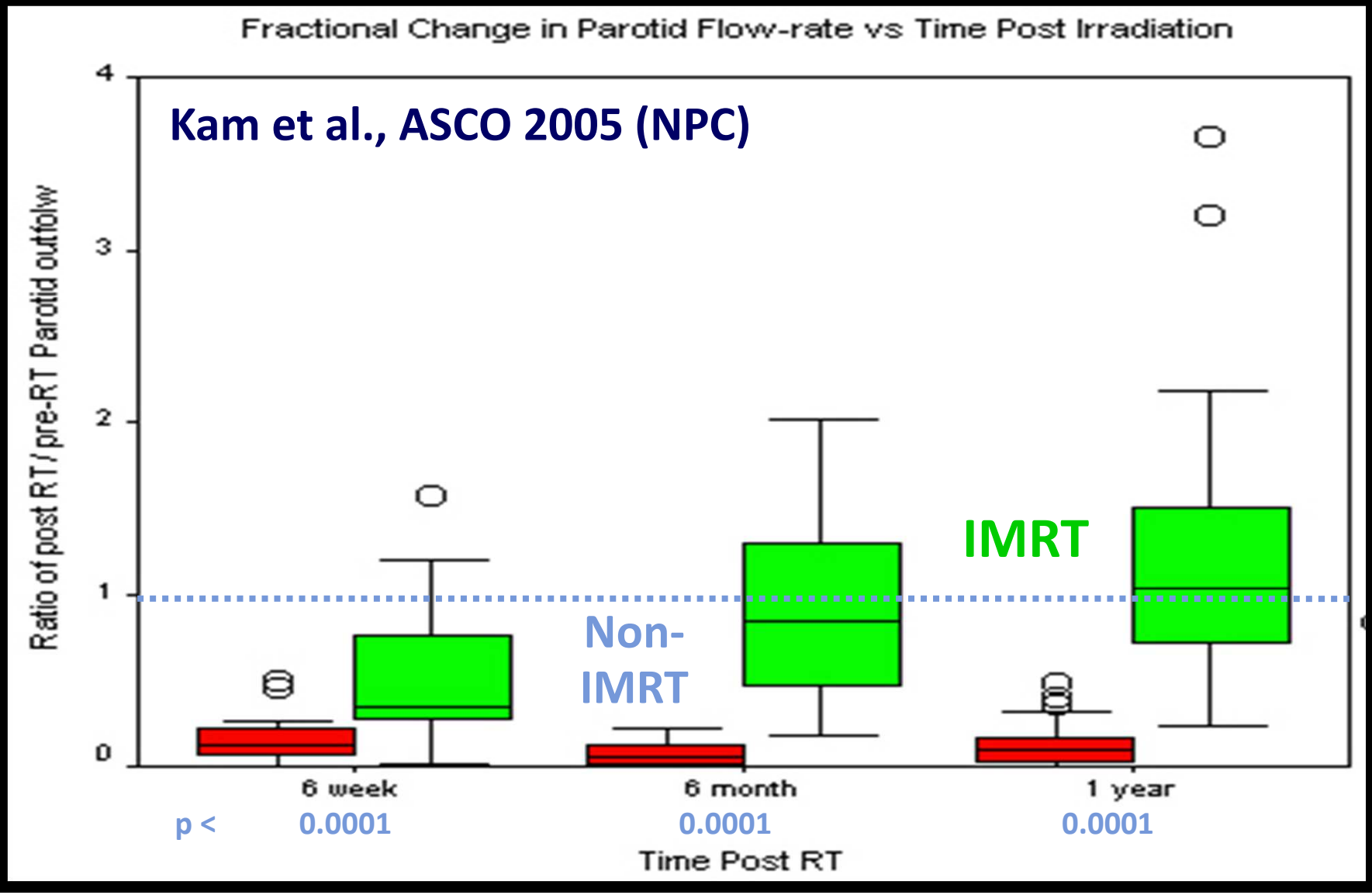
Study	No. of Patients	Primary Site	RT		Follow-Up (months)		Control		
			Definitive	Postoperative	Median	Range	Local (%)	Regional (%)	Interval (years)
Chao et al[19]	126	Various	52	74	26	12-55		85	2
Lee et al[5]	67	NPX	67	0	31	7-72		98	4
Chao et al[20]	74	OPX	31	43	33	9-60		87	4
Eisbruch et al*[21]	133	Various, non-NPX	60	73	32	6-107		82	3
Kam et al[33]	63	NPX	63	0	29	8-45	92	98	3
Kwong et al[34]	33	NPX	33	0	29	11-42	100	92	3

Abbreviations: IMRT, intensity-modulated radiotherapy; RT, radiotherapy; NPX, nasopharynx; OPX, oropharynx.

*Patients treated from 1994 to 2002; three-dimensional conformal radiotherapy was used before 1996, and IMRT thereafter.

JCO, 2006

Saliva Flow


Fractional Change in Parotid Flow-rate vs Time Post Irradiation
Kam et al., ASCO 2005 (NPC)
Ratio of post RT / pre-RT Parotid outflow
4
3
2
1
0
IMRT
Non-IMRT
6 week
6 month
1 year
p <
0.0001
0.0001
0.0001
Time Post RT

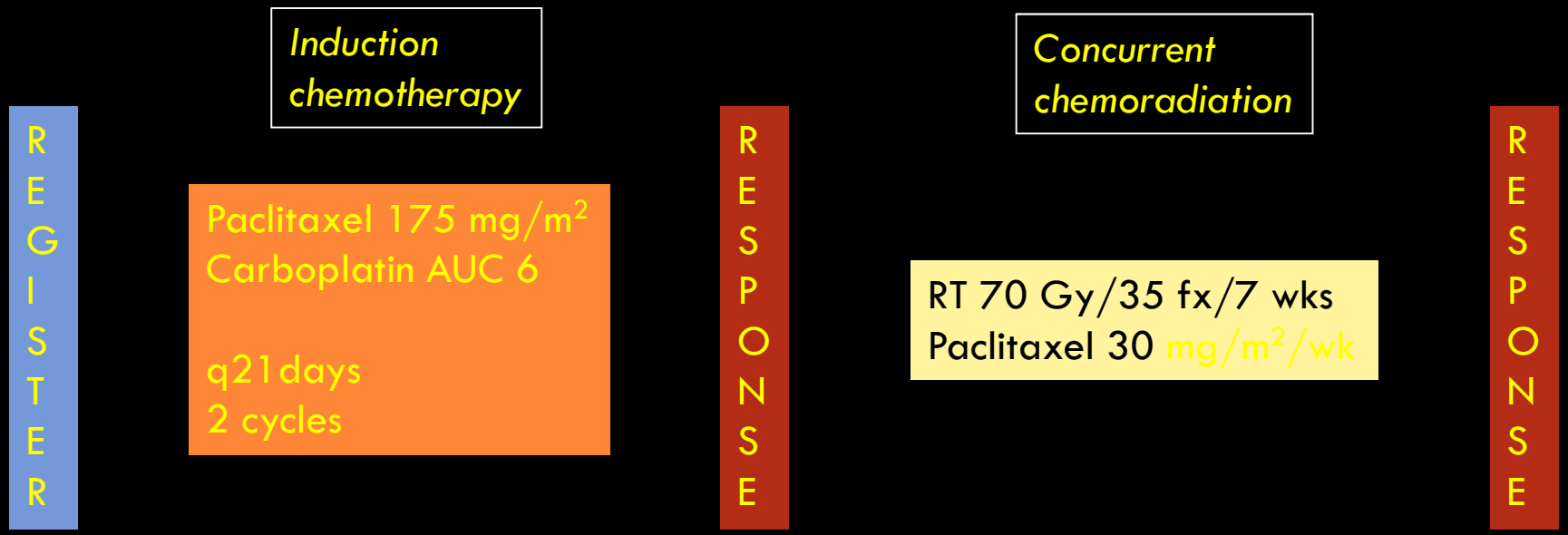
IMRT:- WHAT HAS BEEN LEARNT

- IMRT IS FEASIBLE
- IMRT HAS GOOD LOCOREGIONAL CONTROL
- IMRT CAN BE COMBINED WITH CHEMO
- IMRT DOES NOT IMPROVE ACUTE TOXICITY
- IMRT ALLOWS PRESERVATION OF SALIVA,ESPECIALLY WITH MEAN DOSE </= 25 Gy

Emerging Influence of HPV in HNC

Characteristic	HPV Positive	HPV Negative
Anatomic site	OP: tonsil, base of tongue	Larynx, OC, hypopharynx
Age	Younger	Older
Male:female	1:1	3:1
Risk factors	Sexual	Tobacco/Etoh
Cofactors	Marijuana	Diet/hygiene
Clinical presentation	Unknown or cystic primary	Classical
Incidence	Increasing	Decreasing
Comorbidities	Fewer	Greater
Prognosis	Better	Worse

ECOG 2399: Study Design

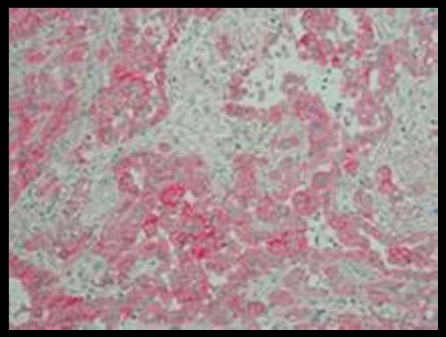


Fakhry C, et al. J Natl Cancer Inst. 2008;100:261-269.

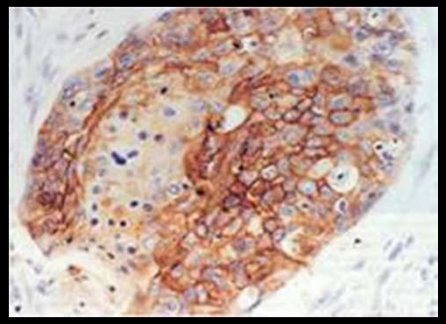
ECOG 2399: Efficacy by HPV Status

	HPV Positive, % (n = 38; 40%)	HPV Negative, % (n = 58; 60%)	*P* Value
Response ▪ Induction ▪ Protocol	 82 84	 55 57	 .01 .07
2-yr PFS	86	53	.02
2-yr OS	95	62	.005
Survival, OP cancers ▪ 2-yr PFS ▪ 2-yr OS	 85 94	 50 58	 .05 .004

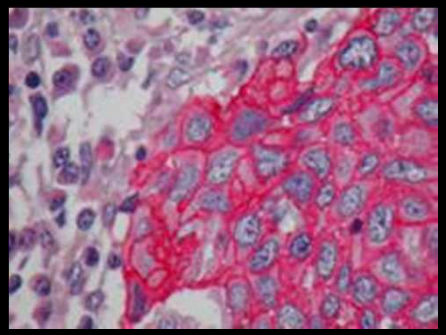
EGFR Expression in Solid Tumors



Colorectal



Lung
(NSCLC)



Head and neck
(SCCHN)

EGFR is expressed in a variety of solid tumors

Tumor Target	%
Head and neck cancer	95–100
Colorectal cancer	72–89
Pancreas	upto 95 %
Lung cancer (NSCLC)	40–80
Breast cancer	14–91
Ovarian cancer	35–70
Renal cell cancer	50–90

nningham et al. *N Engl J Med* 2004;351:337–345; Grandis et al. *Cancer* 1996;78:1284–1292; Salomon et al. *Crit Rev Oncol Hematol* 1995;19:183–232; Walker & Dearing. *Breast Cancer Res Treat* 1999;53:167–176; Folprecht et al. ASCO 2004 (Abstract #283).

Tumor EGFR Expression as a Prognostic Factor

- EGFR expression correlates with poor prognosis.

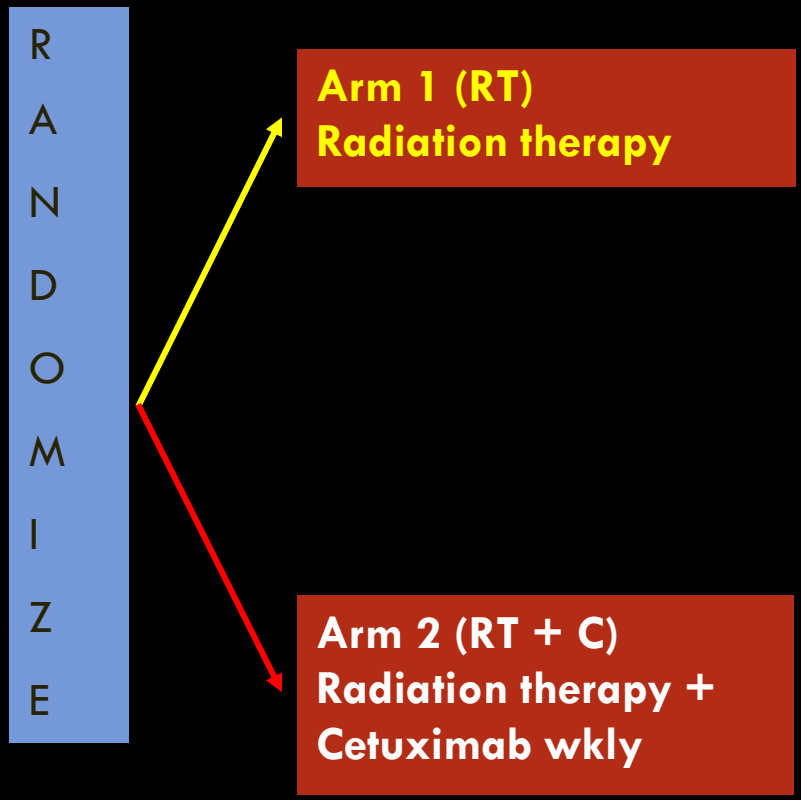
Tumor type	Prognosis	Survival	Risk of metastasis	References
Colorectal	Poor	-	Increased	Hemming (1992)
Lung	Poor	Decreased OS	-	Ohsaki (2000)
(NSCLC)	Poor	-	Increased	Pavelic (1993)
Head & neck (SCCHN	Poor	Decreased DFS	-	Grandis (1998)
		Decreased OS		Maurizi (1996)

- EGFR expression also linked to reduced response, and/or increased resistance to chemotherapy

Phase III Study Design

Stratified by

- Karnofsky score: 90-100 vs 60-80
- Regional nodes: negative vs positive
- Tumor stage: AJCC T1-3 vs T4
- RT fractionation: concomitant boost vs once daily vs twice daily



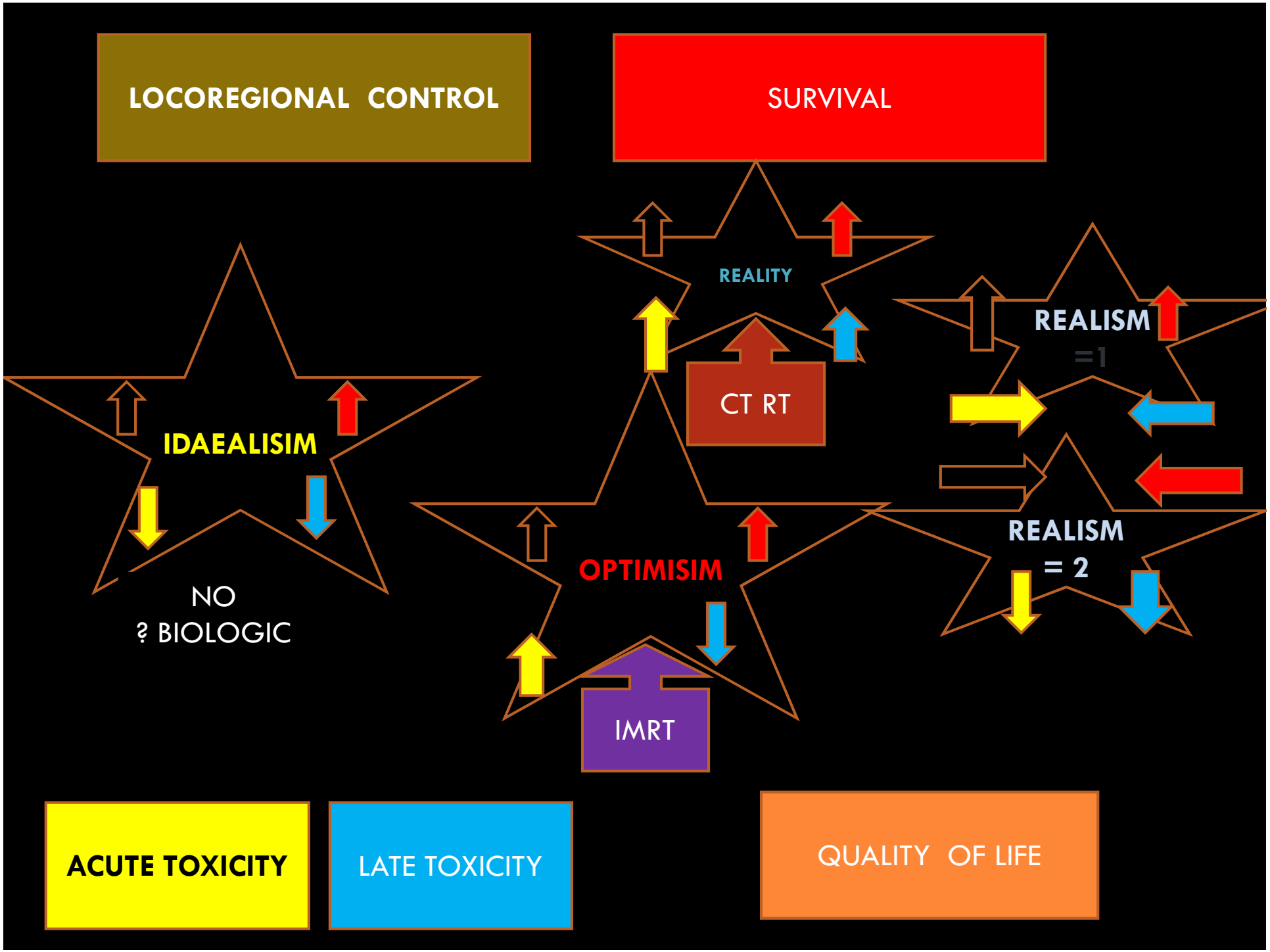
Overall Survival

	RT (n = 213)	RT + C (N=211)
Median survival,* mos	29.3	49
▪ 95% confidence limits	21-38	36-58+
2 yrs, %	55	62
3 yrs, %	44	57
5 yrs, %	36.4	45.6
Log rank *P* value	.018	
HR (95% CI)	0.71 (0.54-0.95)	

Bonner JA , et al. Lancet Oncol. 2009 Nov 6;[Epub ahead of print].

CONCURRENT CHEMORT OR CONCURRENT C-225 RT

	CDDP + RT	C-225 RT
ABS.SURV.ADV OVER RT(2 YRS)	8%	7%
POTENTIAL SURV.ADV.OVER XRT(best data)	21%	13%
GRADE 3 + MUCOSITIS	80%	56%


LOCOREGIONAL CONTROL
SURVIVAL
REALITY
CT RT
IDAEALISIM
NO
? BIOLOGIC
OPTIMISIM
IMRT
REALISM
=1
REALISM
= 2
ACUTE TOXICITY
LATE TOXICITY
QUALITY OF LIFE

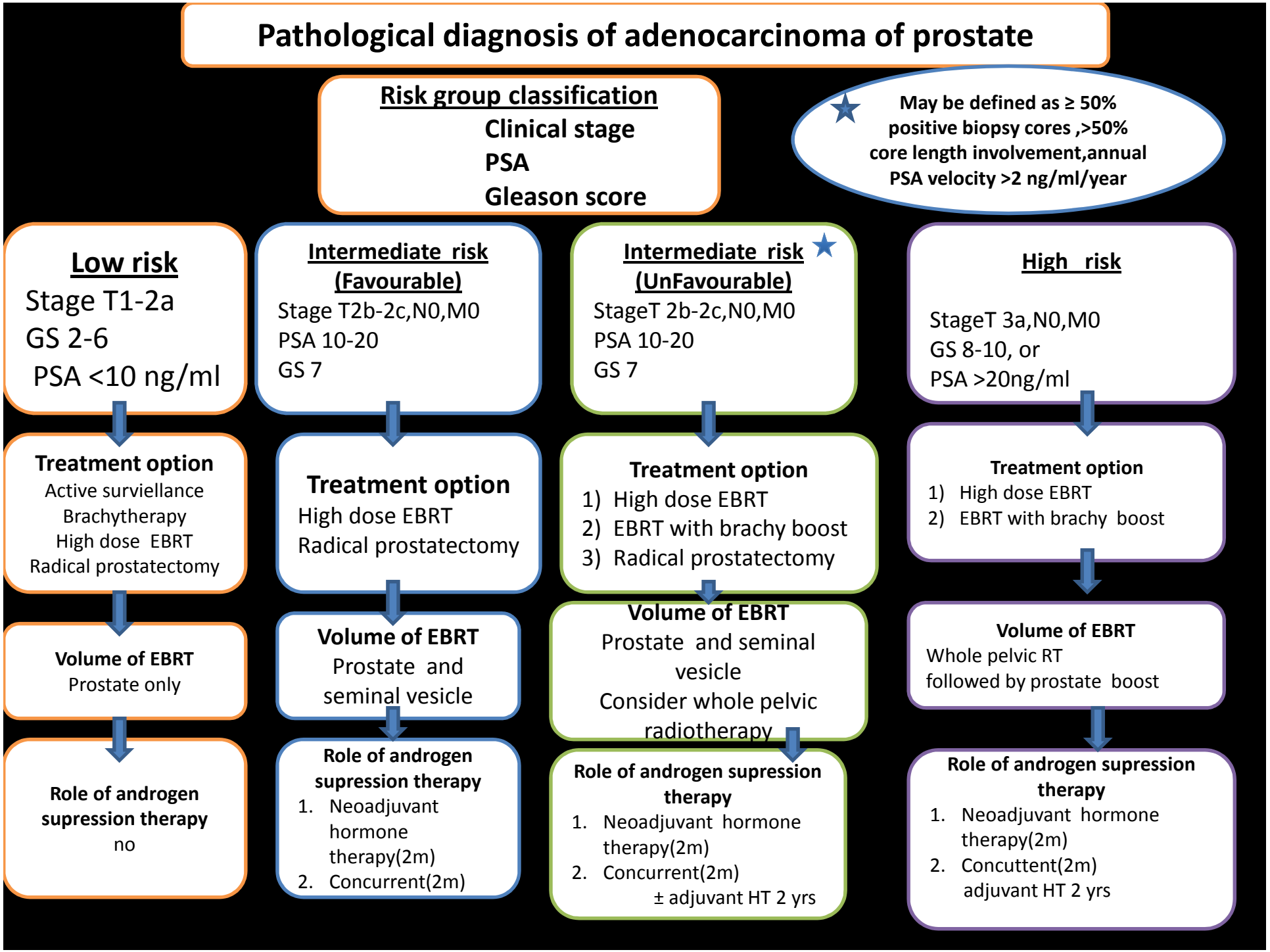
CONCLUSION

- TREATMENT BASED ON RISK FACTORS
- ECE IS ONE OF THE MOST IMPORTANT FACTOR
- INT.RISK:- RADIATION,HIGH RISK :-CT+RT
- ALT FRACTIONATION:- (HPX,ALT FX+BOOST) INCREASED LRC,OS BUT INCREASED ACUTE TOXICITY,NOT LATE TOXICITY
- IMRT:- INCRESED LRC,DECREASED LATE COMPLICATION LIKE XEROSTOMIA
- CAN WE USE LESS TOXIC BIOLOGIC RADIOSENSITIZERS.

CARCINOMA PROSTATE

Disease characteristics

		Stage	Gleason score	PSA (ng/ml)
Risk group	Low risk	T1-2a	2-6,and	<10
	Intermediate risk	T2b-2c, or	7,or	10-20
	High risk	T3a, or	8-10	>20
	Locally advanced	T3b-T4	any	Any
	metastatic	N1 and/or M1	any	any


Pathological diagnosis of adenocarcinoma of prostate
Risk group classification
Clinical stage
PSA
Gleason score
May be defined as ≥ 50% positive biopsy cores ,>50% core length involvement,annual PSA velocity >2 ng/ml/year
Low risk
Stage T1-2a
GS 2-6
PSA <10 ng/ml
Treatment option
Active surviellance
Brachytherapy
High dose EBRT
Radical prostatectomy
Volume of EBRT
Prostate only
Role of androgen supression therapy
no
Intermediate risk (Favourable)
Stage T2b-2c,N0,M0
PSA 10-20
GS 7
Treatment option
High dose EBRT
Radical prostatectomy
Volume of EBRT
Prostate and seminal vesicle
Role of androgen supression therapy
1. Neoadjuvant hormone therapy(2m)
2. Concurrent(2m)
Intermediate risk (UnFavourable)
StageT 2b-2c,N0,M0
PSA 10-20
GS 7
Treatment option
1) High dose EBRT
2) EBRT with brachy boost
3) Radical prostatectomy
Volume of EBRT
Prostate and seminal vesicle
Consider whole pelvic radiotherapy
Role of androgen supression therapy
1. Neoadjuvant hormone therapy(2m)
2. Concurrent(2m)
± adjuvant HT 2 yrs
High risk
StageT 3a,N0,M0
GS 8-10, or
PSA >20ng/ml
Treatment option
1) High dose EBRT
2) EBRT with brachy boost
Volume of EBRT
Whole pelvic RT
followed by prostate boost
Role of androgen supression therapy
1. Neoadjuvant hormone therapy(2m)
2. Concuttent(2m)
adjuvant HT 2 yrs

Treatment volume

Prostate alone

T1c-T2a,Gleason score <6,PSA <10 ng/ml

Prostate + SV

If seminal vesicle involvement >15%
= PSA + (GS - 6) ×10

Whole pelvis

Pelvis LN risk >15% (pertins table / Roach's formula
Patient with suspisious pelvic LN

BRA CHYTHERAPY IN CARCINOMA PROSTATE

INDICATION
BRACHYTHERAPY AS MONOTHERAPY

Stage T1-2a
GS 2-6
PSA <10 ng/ml

INDICATION
BRACHYTHERAPY AS BOOST

Stage T2b-c
GS 8-10
PSA >20 ng/ml

DOSE MONOTHERAPY

Iodine 125	100 -110 Gy
Paladium 103	90-100 Gy

CONTRA INDICATION

Life expectation <5 yrs
Large TURP defect
Unacceptable operative risk
Distant metastasis

RELATIVE CONTRAINDICATION

large median lobe
Previous pelvic RT
High IPSS score >15
Gleason score >60 cc
Positive seminal vesicle

ADJUVANT RT

- INDICATION:

  Extracapsular extension.

  +ve surgically margin.

  seminal vesicle invasion.
- Risk of late toxicity is more.

			Dist Mets	PSA RFS	Local Failure	Complication
SWOG	+ve margin ECE SVI	PORT Vs Obs	35% vs 43.1%	HR 0.43%	8% 22%	Stricture 17.80 %Vs 9.5 % Incont 6.5% Vs 2.8% Rectal compl 3.3% Vs 0%
BOLLA et	pT3a-b,	PORT vs Obs		74% vs	5.4%	Severe Late

EBRT + BRACHY :- INDICATION

- Risk of Extra-capsular extension.
- Seminal vesicle invasion.
- Brachytherapy alone may not be able to encompass the disease.
- Sub-optimal Brachytherapy dose distribution.
- Brachy boost is (American Brachytherapy Society recomendation): T2b-c, GS=8-10, PSA >20ng/ml.

ANDREGEN SUPPRESION THERAPY

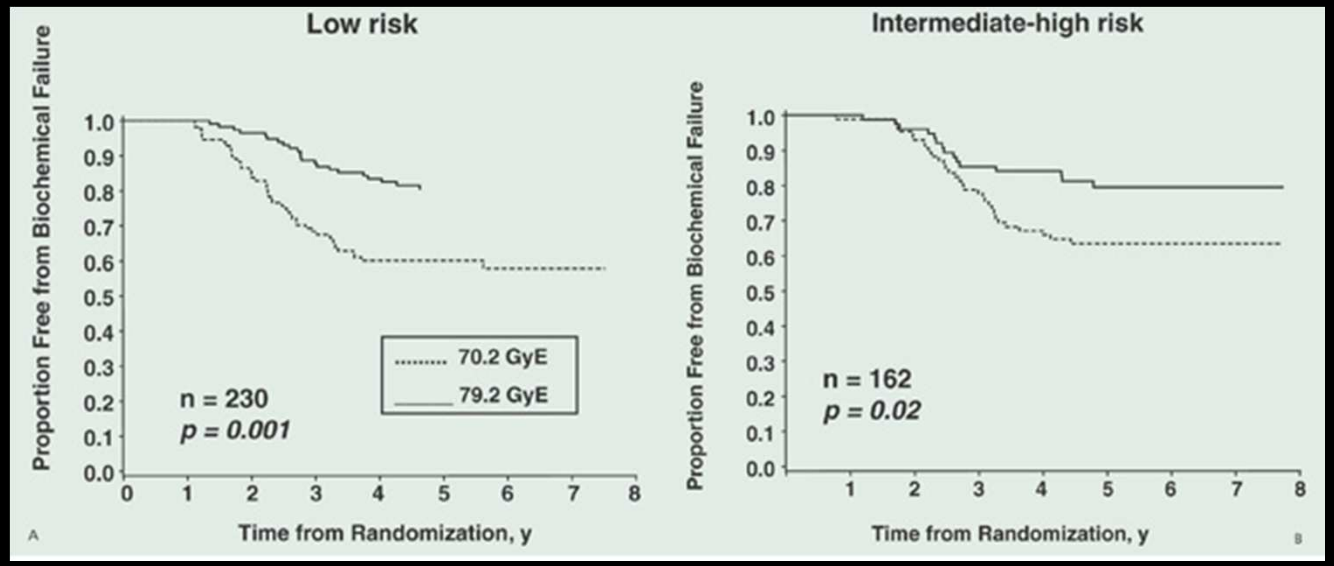
- LHRH agonist: Goserelin, Leuprolide.
- Anti Androgen: Flutamide, Bicalutamide.
- EBRT doses 70Gy/ Less.
- Not recommended in low risk Ca. prostate.
- In intermediate risk recommended: (Grade A)
  2mo. neoadjuvant then concurrent HT.
- In high risk recommendation: (Grade A)
  2mo neoadjuvant, concurent & 2-3yr adjuvant HT.

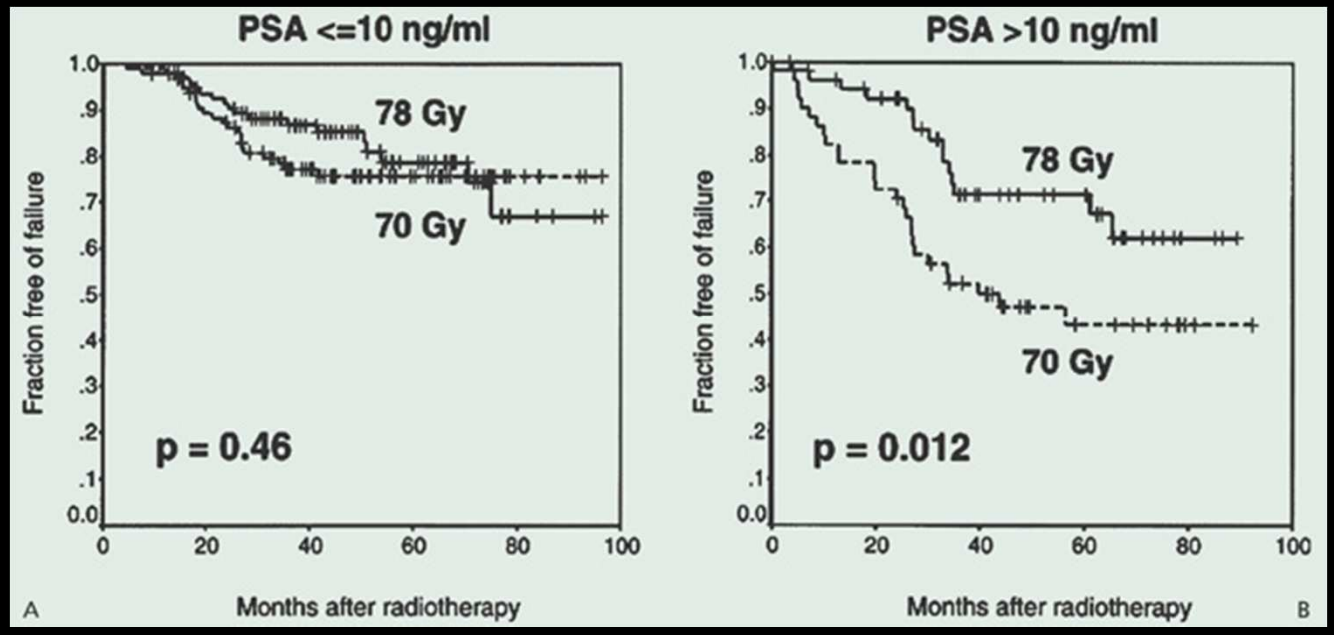
WHY DOSE ESCALATION

- With dose 70Gy of conv. EBRT alone T2c-T4, 30-50% of patient develop local recurrence within 10yrs & majority will develop distant mets.
- Standard dose of RT doesn’t have the capacity to completely eradicate the prostate disease in majority.
- Thus dose escalation is needed.

auther	stage	dose	outcome	P value	Side effects	Comments
Pollack et al 2002 Kuban et al 2008	T1-3	70(C) vs 78 Gy(C+ 3DCRT)	8 yr PSA 59% vs 78%	0.004		Benefit is patient has PSA > 10 ng/ml
Zeitman et al 2005 JAMA 294(10): 2005	T1b-2b PSA<15ng/ml	70.2 Gy vs 79.2Gy	5 yr PSA control 61.4% vs 80.4%	<0.001		Benefit in both low and intermediate risk
Peeter et al 2006	T1-4	68 Gy vs 78 Gy	5 yr freedom of failure 54% vs 64%	0.02		No benefit in low risk. Benefit in intermediate and high risk
MRC RT01 Zel	cT1b-3N0	64Gy vs 74 Gy	5 yr PSA control 71% vs 60%	0.007	More late grade 2 or 3 bowel toxicities, not bowel toxicities	No difference in OS and distant mets

auther	stage	Dose(Gy)	outcome				Side effects		
RTOG 9406	All N0 M0 except T1a ,T1b- T2b PSA < 70 ng/ml	68.4 73.8 79.2 74 78		78			79.2		
					LR	IR		LR	IR
				Gr II	38 %	33 %	Gr II	13 %	9 %
				Gr III	5%	7 %	Gr III	2%	1 %


Low risk
Intermediate-high risk
Proportion Free from Biochemical Failure
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
0 1 2 3 4 5 6 7 8
Time from Randomization, y
70.2 GyE
79.2 GyE
n = 230
p = 0.001
n = 162
p = 0.02
A
B


PSA <=10 ng/ml
PSA >10 ng/ml
Fraction free of failure
1.0
.9
.8
.7
.6
.5
.4
.3
.2
.1
0.0
0 20 40 60 80 100
Months after radiotherapy
78 Gy
70 Gy
p = 0.46
p = 0.012
A
B

TOXICITY Conventional EBRT

60% Pts developGr II rectal/ urinary complication who requires medication

Toxicity 3D Conformal RT

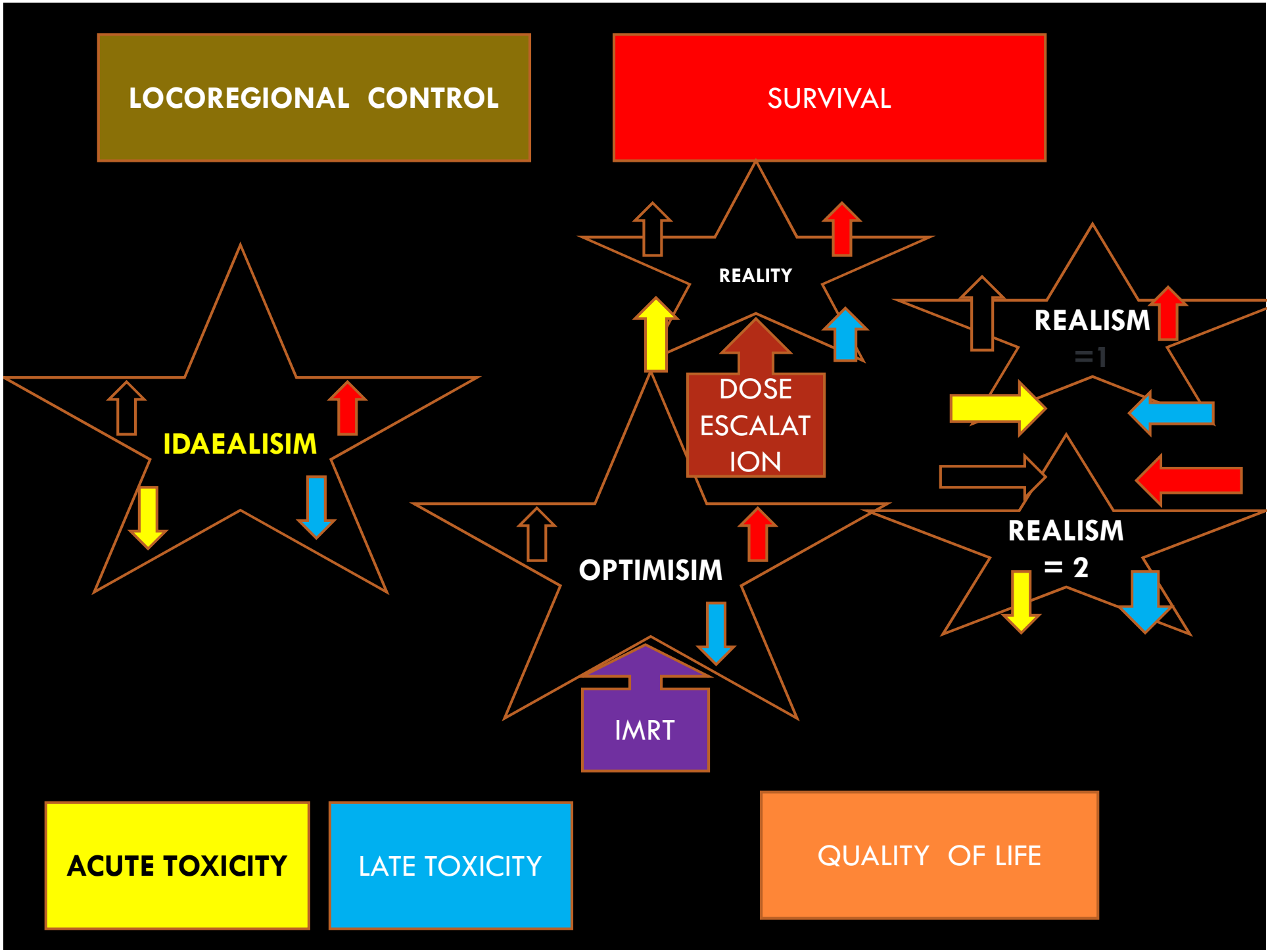
RG 9406	**68.4 vs 78 Gy**	**Gr II A rectal Gr II L RECTAL Gr III L RECTAL**	**16% 22% 2%**	
STOREY et. al	70 Gy vs 78Gy	Late Gr II/ III	14% vs 21%	% reaction ICREASES beyond 70Gy % of rectal tissue
ZELEFSKY et.al	64.8 – 70.2Gy vs 75.6Gy	Late Gr II	6% vs 17%	Dose >75.6Gy DM, acute GI symptom
PEETERS et.al	68 – 78Gy	Gr II LGI Gr III Gr II Urinary	23% vs 26.5% 2% vs 10% 28.5% vs 30%	Pre Gi/urinary symp Neo adj HT Prior TURP

3 D CRT Vs IMRT

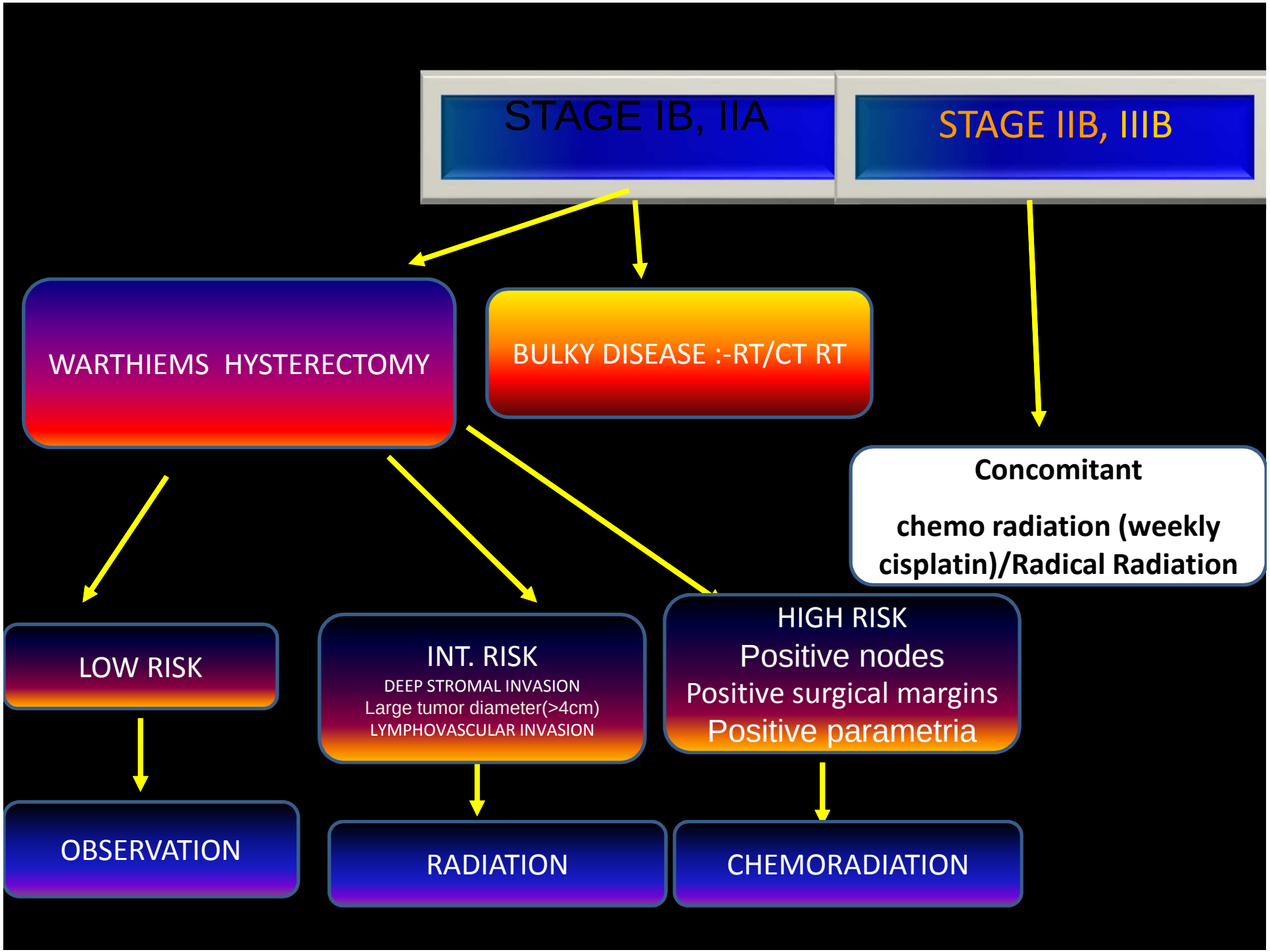
ZELEFSKY et.al	**3 D CRT Vs IMRT**	**Gr II L RECTAL**	**10% Vs 2% p <.001**

TOXICITIES

- Conventional EBRT:- Grade 2/ higher rectal/ bladder morbidity; needs medication in 60%.
- The risk of complication increases when RT dose exceeds 70Gy.
- Rectal complication depends on % of rectum treated to 70Gy/ higher dose.
- Rectal complication increases with increased dose of radiation.
- IMRT reduces the incidence of acute & late rectal effect compared to 3DCRT but not acute & late urinary complication.
- At present time IMRT doesn't appear to significantly reduce the urinary symptoms compared to 3DCRT.
- With EBRT + Brachytherapy, the complication rates are high.


LOCOREGIONAL CONTROL
SURVIVAL
REALITY
IDAEALISIM
DOSE ESCALAT ION
REALISM =1
OPTIMISIM
REALISM = 2
IMRT
ACUTE TOXICITY
LATE TOXICITY
QUALITY OF LIFE

CARCINOMA CERVIX


STAGE IB, IIA
STAGE IIB, IIIB
WARTHIEMS HYSTERECTOMY
BULKY DISEASE :-RT/CT RT
Concomitant
chemo radiation (weekly cisplatin)/Radical Radiation
LOW RISK
INT. RISK
DEEP STROMAL INVASION
Large tumor diameter(>4cm)
LYMPHOVASCULAR INVASION
HIGH RISK
Positive nodes
Positive surgical margins
Positive parametria
OBSERVATION
RADIATION
CHEMORADIATION

STAGE Ib & IIa TREATMENT

Wertheim's Hysterectomy

Or

Radical radiation therapy

(Ext + Brachy)

Choice of treatment determined by age, menopausal status, ovarian preservation, co-morbid conditions, patient's wish & availability of expertise in surgery & RT

1NIH Guidelines 997)

Risk Stratification (GOG Guidelines)

Deep stromal invasion
Large tumor diameter(>4cm)
LVSI

Intermediate risk (Any two)

Positive nodes
Positive surgical margins
Positive parametria

High risk (Any one)

Stage Ib/IIa
Impact of Lymph node Metastases

	Survival(%)	Relapse(%)
L.N –Ve	95.8 %	
L.N +Ve		
Pelvis	63.5%	32%
P.A	40.8%	57%
Pelvis+PA	18.4%	73.7%

Early Stage Carcinoma Cervix

Intermediate Risk : Role of Adjuvant therapy

GOG 92 : RCT (*Gynae Oncol 73 ;177-183: 1999*)

Outcome	No Adj RT N = 140	Adj RT N = 137	p value
2 yr RFS	79%	88%	.008
2 yr OAS	79%	87%	.008
Pelvic rec	21%	13%	
Dist mets	7%	2%	

Risk of Recurrence reduced by 44% (RR 0.56.p=0.019).

Mortality reduced by 36%(p=.005).

"Grade A"

ADJUVANT PELVIC RT IS BENEFICIAL

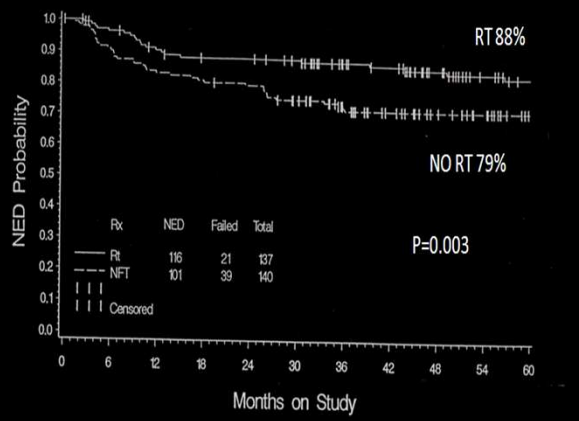
Early Stage Carcinoma Cervix

High Risk : Role of Adjuvant Therapy

Intergroup 0107 RCT Trial (*Gynae Oncol 73 ;177-183: 1999)*

Outcome	PORT N = 116	POSTOPCT+RT N = 127	p value
4yr RFS	63%	80%	0.01
4yr OAS	71%	81%	0.01
Pelvic rec	17%	6%	
Distant mets	11%	7%	
Pelvic+ distant	4%	3%	

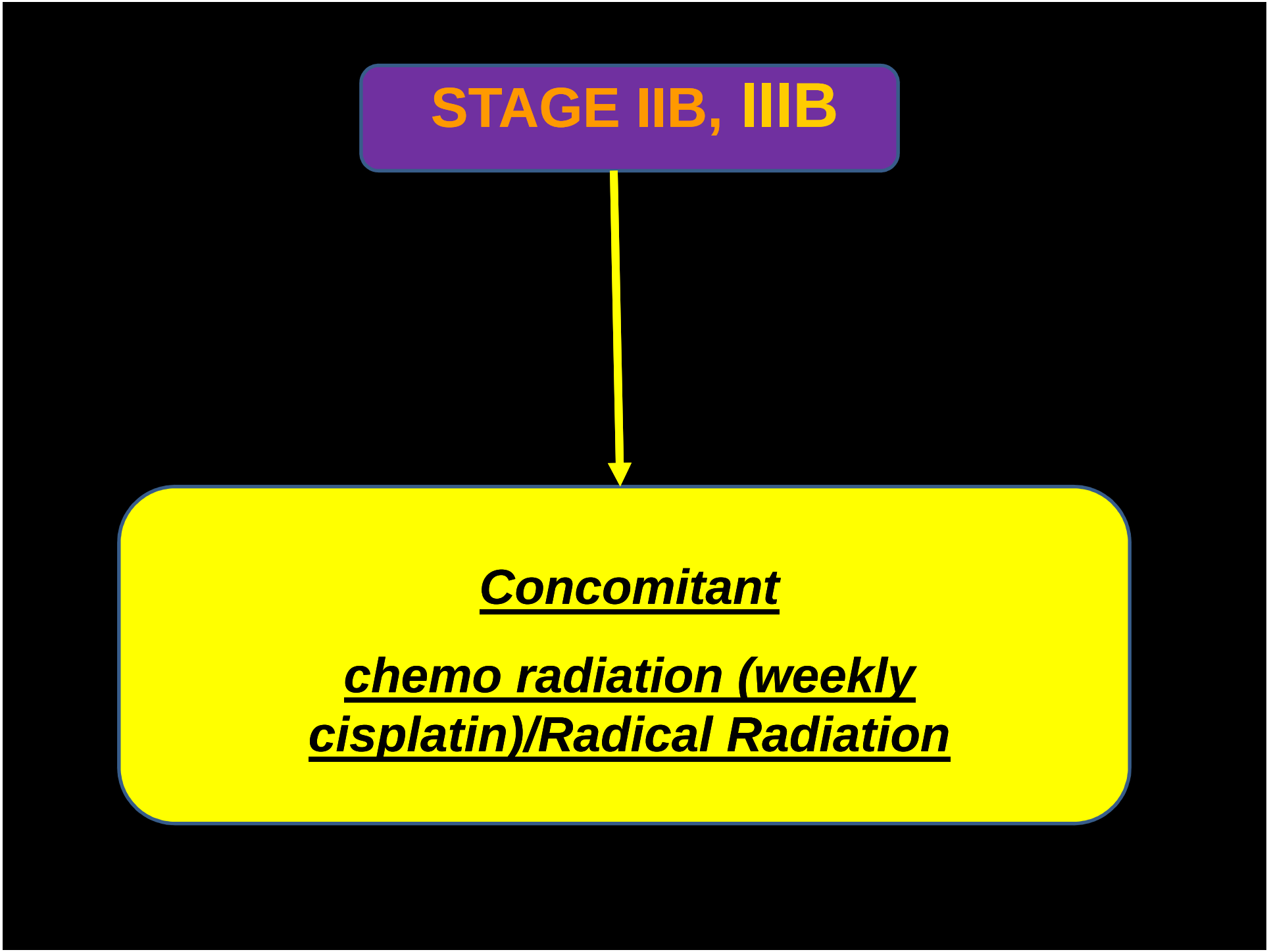
High Risk* Node Negative Stage IB Ca Cx: RH + PLND vs. RH + PLND + RT
(Sedlis et al, Gyn Onc 73, '99)



Defined a specific subgroup of patients with intermediate risk factors who are benefited from pelvic RT though at cost of increased toxicity

CHEMO-RADIATION SHOULD BE STANDARD OF CARE

"Grade A"


STAGE IIB, IIIB
Concomitant
chemo radiation (weekly cisplatin)/Radical Radiation

NATIONAL CANCER INSTITUTE CLINICAL ANNOUNCEMENT

'CONCURRENT CHEMORADIATION FOR CERVICAL CANCER'

in February 1999

"Five major randomized phase III trials show that platinum based chemo when given concurrently with RT prolongs survival in women with locally advanced cervical cancer stages Ib2 - IVa as well as in women with stage I / IIa found to have metastatic pelvic lymph nodes, positive parametrial disease and positive surgical margins at the time of primary surgery

LOCALLY ADVANCED CARCINOMA CERVIX CONCURRENT CHEMORADIATION

AUTHOR	CT	SURV CT-RT	% RT	P
MORRIS	PF	73	58	.004
KEYS	P	84	68	.008
PETERS	PF	81	63	.01
WHITNEY	PF	50.8	-	018
	H	39.8	-	-
ROSE	P	64	-	0.02
	H	39	-	
	PHF	66	-	0.58

Acute toxicity grades for each trial specified in standard versus chemoradiation status

	Chemoradiation				Radiotherapy			
	1 and 2		3 and 4		1 and 2		3 and 4	
	Number	%	Number	%	Number	%	Number	%
Haemoglobin [21,28,32,42,44,45]	448/1141	39.3	78/1201	6.5	231/796	29.0	35/858	4.1
WCC [15,21,28,31,32,42,44,45]	656/1328	49.4	227/1388	16.4	393/982	40	82/1044	7.9
Platelets [15,21,28,31,32,42,44,45]	251/1223	20.5	22/1283	1.7	87/874	10	4/936	0.4
Haematology' NOS [17,20,23]	104/195	53.3	112/378	27.6	34/198	17.2	5/379	1.3
Genitourinary [17,23,28,32,42]	198/1133	17.5	21/1358	1.5	165/966	17.1	19/1191	1.6
Gastrointestinal [17,23,28,32,42]	530/1172	45.2	112/1397	8	404/991	40.8	51/1216	4.2
Neurological [23,28,32,42]	52/836	6.2	5/836	0.6	18/670	2.7	3/670	0.5
Skin [17,23,28,32,42]	161/1028	15.7	23/1223	1.9	113/858	13.2	13/1051	1.2

RESULTS OF LATE TOXICITY

Chemoradiation in cervical cancer: comparison of long-term toxicity across trials specified

Trial	Chronic toxicity	Genitourinary	Gastrointestinal	Neurological	Fistula	Other	Overall	Comments	Follow-up		
									Minimum	Maximum	Median
Keys [17]	Yes	–	–	–	–	–	No diff	Same number of fistula and bowel	11*	61*	36
Morris [23]	Yes	Bladder/ureters	Small/large bowel and rectum	–	–	34	No diff	–	0*	86	43[a]
Peters [28]	Yes	1234	1234	–	–	–	–	–	12[a]	72[a]	42
Pras	No	–	–	–	–	–	–	–	–	–	–
Rose [32]	No	–	–	–	–	–	–	–	5[a]	65[a]	35
Tseng [39]	Yes	Radical cystitis	Radical proctitis	3 + 4	3 + 4	Intestinal obstruction	3 + 4	CRT 23.3% RT 12.9%	12	69	46.8
Whitney [42]	Yes	–	–	–	–	–	No diff	CRT 16.2% RT 16.5%	2[b]	66[b]	–
Pearcey [27]	No	–	–	–	–	–	–	CRT6% RT 12%	6.6	102.8	65
Hongwei [15]	Yes	3	2 + 3	–	–	–	No diff	–	–	–	–
Wong 89 [44]	No	–	–	–	–	–	–	–	42	72	–
Lira Puerto [20]	No	–	–	–	–	–	–	–	–	–	–
Fernandez [10]	No	–	–	–	–	–	–	–	17	48	25
Hernandez [14]	No	–	–	–	–	–	–	–	2	49	27
Lorvidhaya [21]	No	–	–	–	–	–	–	–	15	59	25
Roberts [31]	No	–	–	–	–	–	–	–	-	–	–
Singh [35]	No	–	–	–	–	–	–	–	12?	?	?
Thomas [37]	Yes	–	–	–	–	–	No diff	–	?	?	59
Wong 99 [45]	Yes	–	–	2	1234	–	No diff	–	12	130	66/96
Leborgne	Yes	–	–	–	–	–	No diff	–	3	51	27

- It is not yet possible to make firm conclusions on the additive effect of chemotherapy on late toxicities of radiotherapy.
- Based on the current available data the late gastrointestinal and urologic toxicity seem to be comparable in patients treated with or without concomitant Chemotherapy.

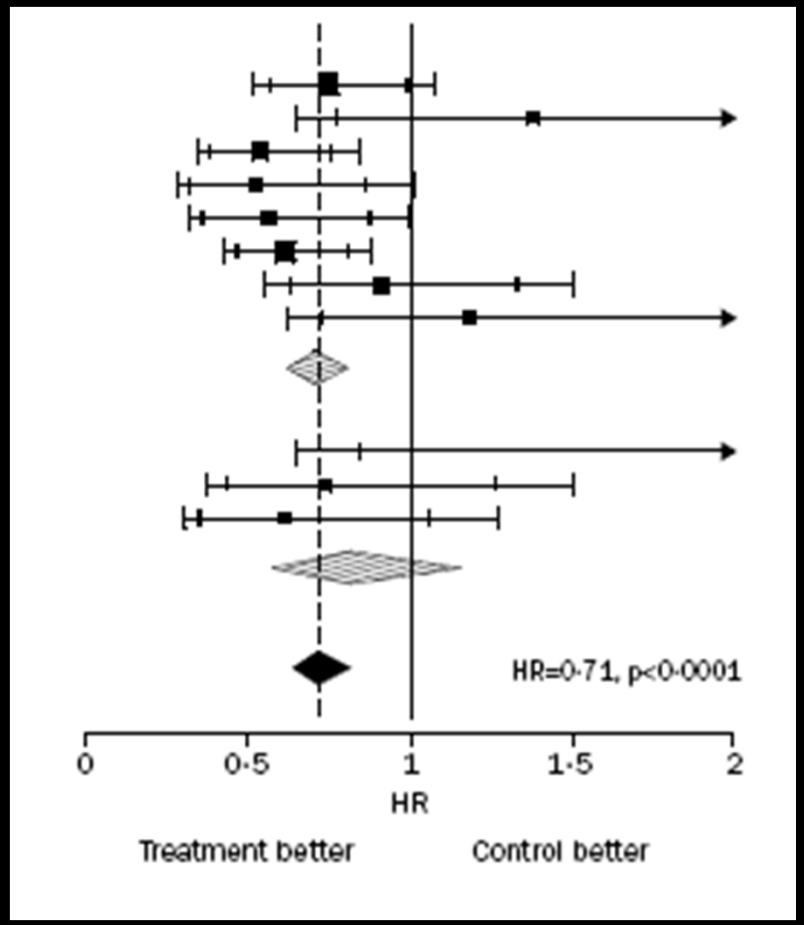
Concurrent Chemoradiation
Results of Meta-analyses

"Grade A"

Cochrane Collaborative Group (19 Trials) (4580 patients)

Green JA et al Lancet 358;781 (Sept. 2001)

- **19 RCTs between 1981 and 2000 : 4580 randomized patients**
- **Increase in OAS by 12% & RFS by 16% (absolute benefit) (p=0.0001)**
- **Greater benefit in patients in stages IB2 and IIB**
- **Decrease in local and systemic recurrence (p=0.0001)**



Update in July 2005: 21 trials and 4921 pts

- Similar findings (absolute benefit: 10%)
- Test for Heterogeneity : Positive
- No data on late toxicities

Cochrane Database Syst Rev. 2005 Jul 20;(3):CD002225.

Green et al meta-analysis on concurrent chemoradiation: *update*

Review strongly suggests that concomitant chemoradiation improves OS and DFS whether or not platinum was used with absolute benefits of 10% and 13% respectively.

Cochrane Database Syst Rev, 2005;Jul 20: (3)

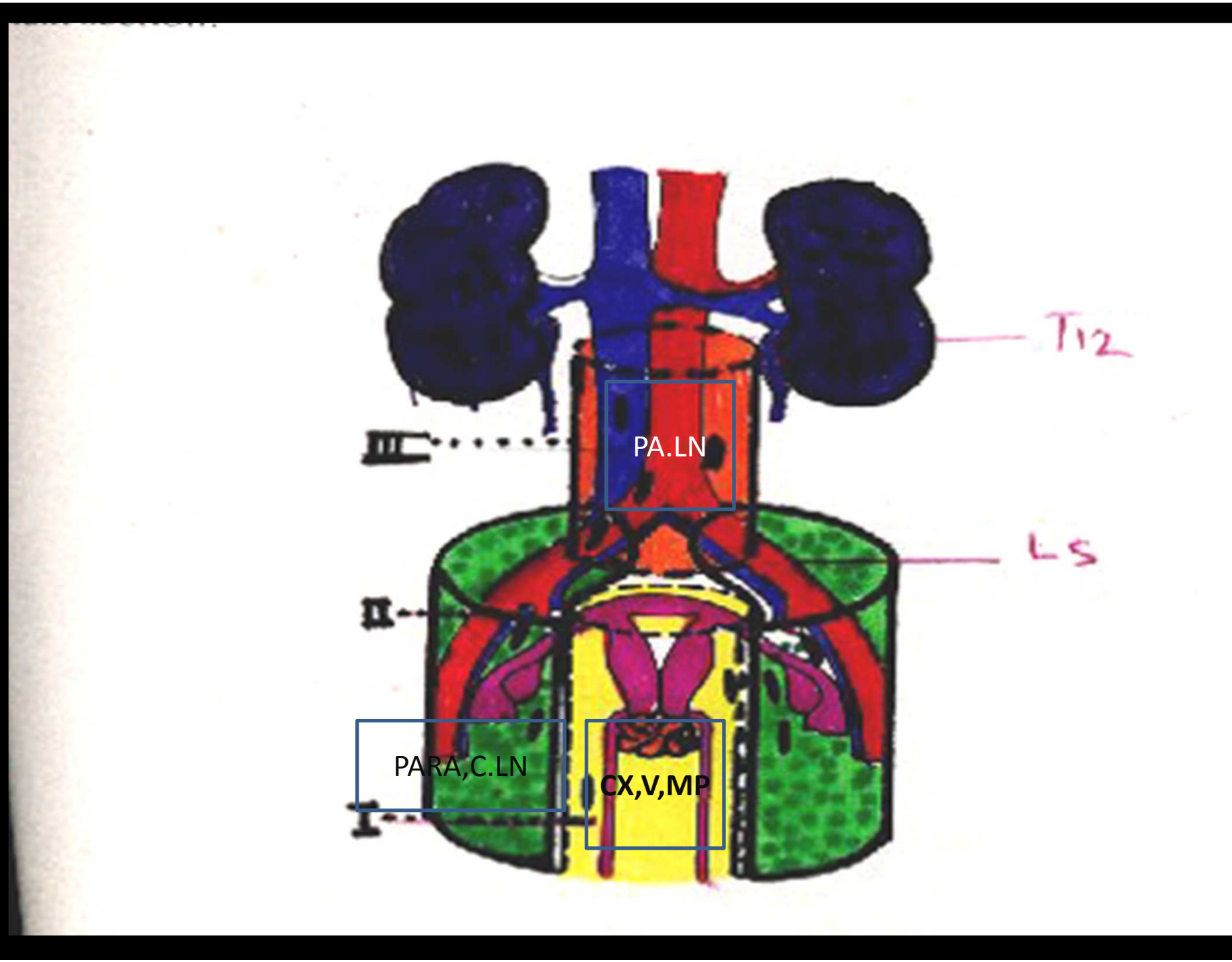
Chemoradiation in Advanced Carcinoma Cx
Results of Meta-analyses

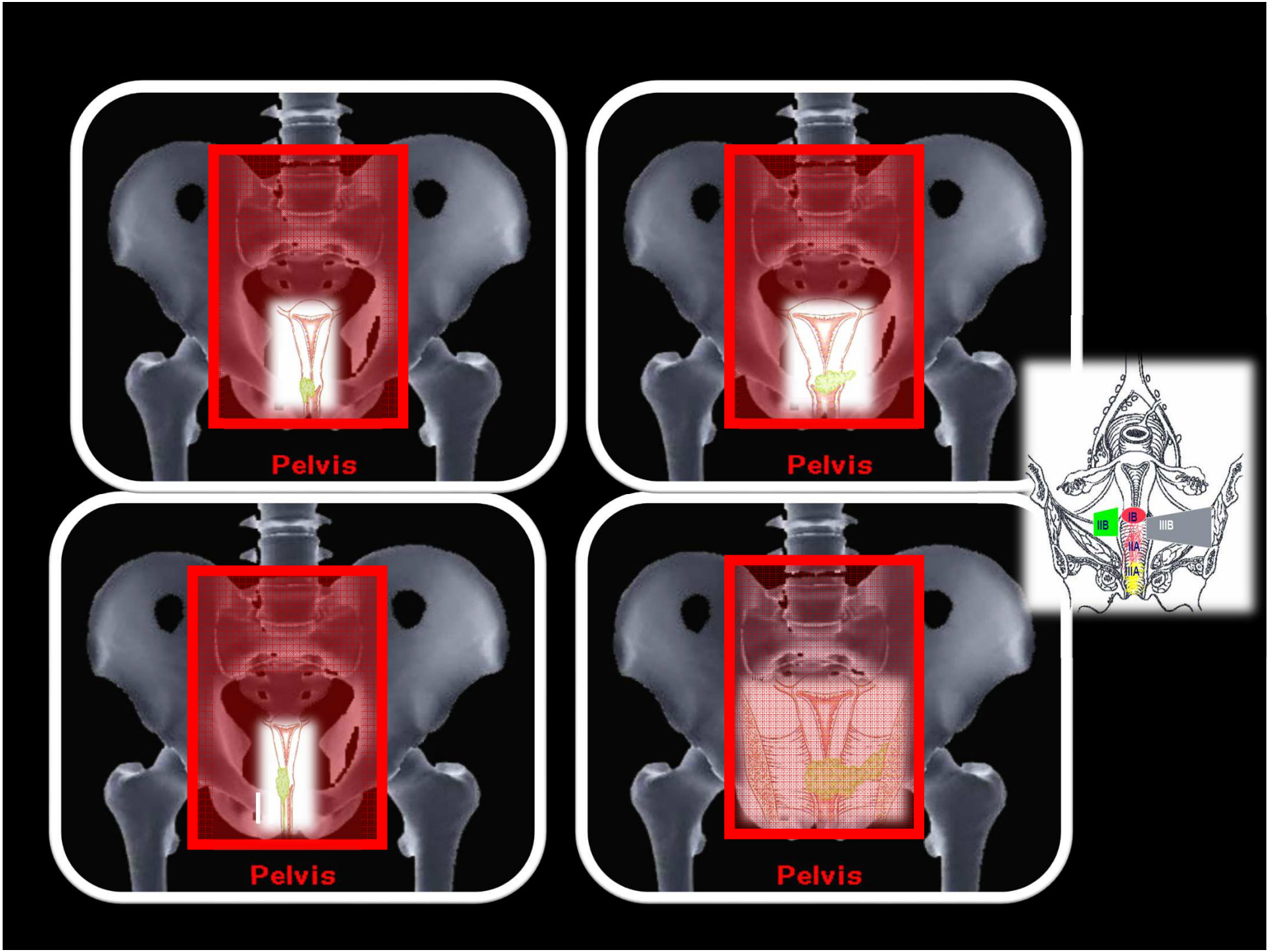
Canadian Group(9 Trials) - 4 year survival data

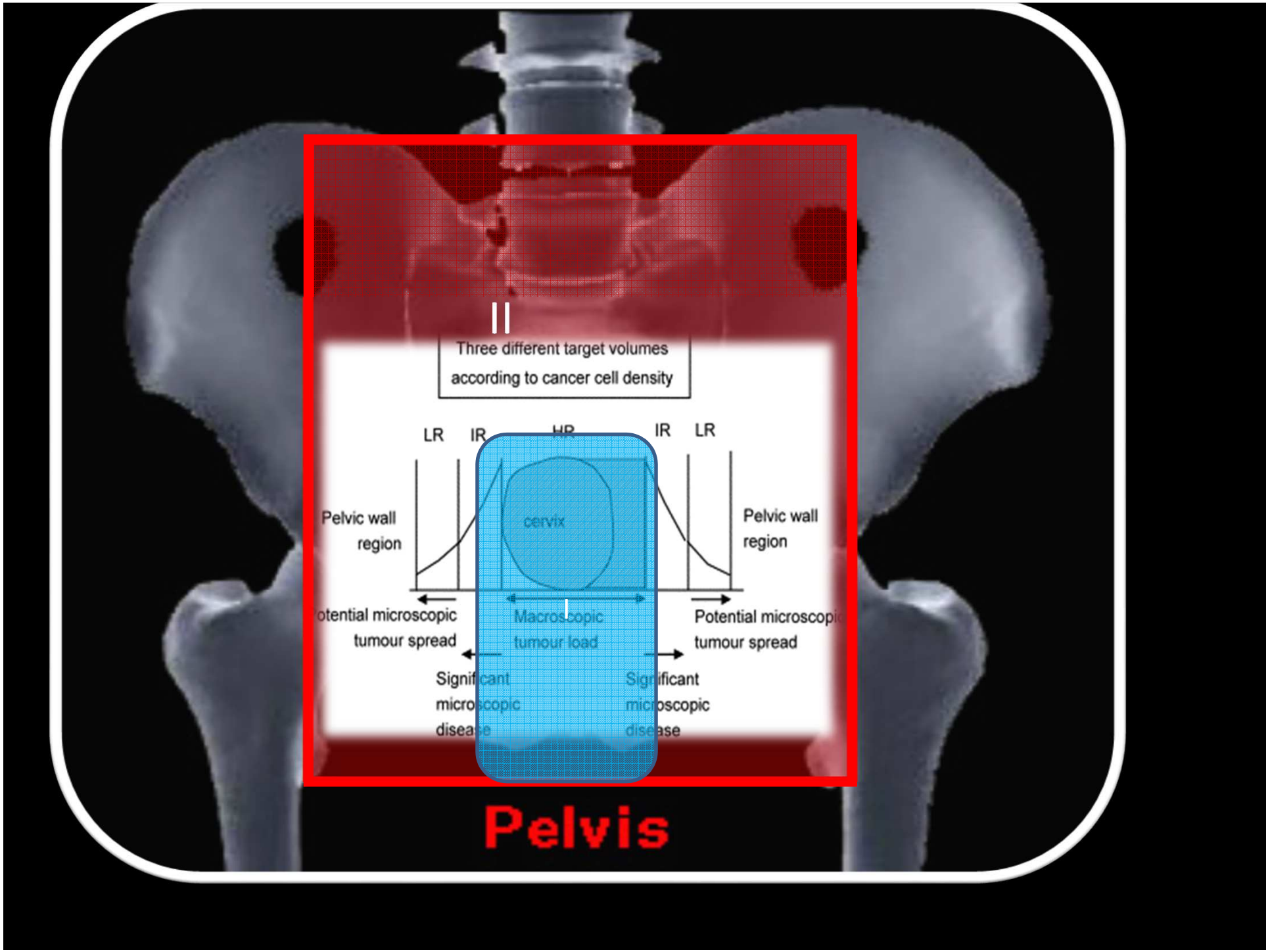
Lukka et al, Clinical Oncology 14;203(June 2002)

- **Cisplatin based Concomitant Chemo-radiation**
- **Significant improvement in Overall Survival**
  - Advanced Stages (Only 30% tumors)
  - Bulky IB tumors (prior to surgery)
  - High risk early disease (post-surgery)
- **Toxicites** Acute Grade 3/4 Hematological and G.I significantly higher : all short lived
  - 2 deaths due to the toxicities
  - No significant late toxicities seen

"Grade A"


T12
L5
PA.LN
PARA,C.LN
CX,V,MP

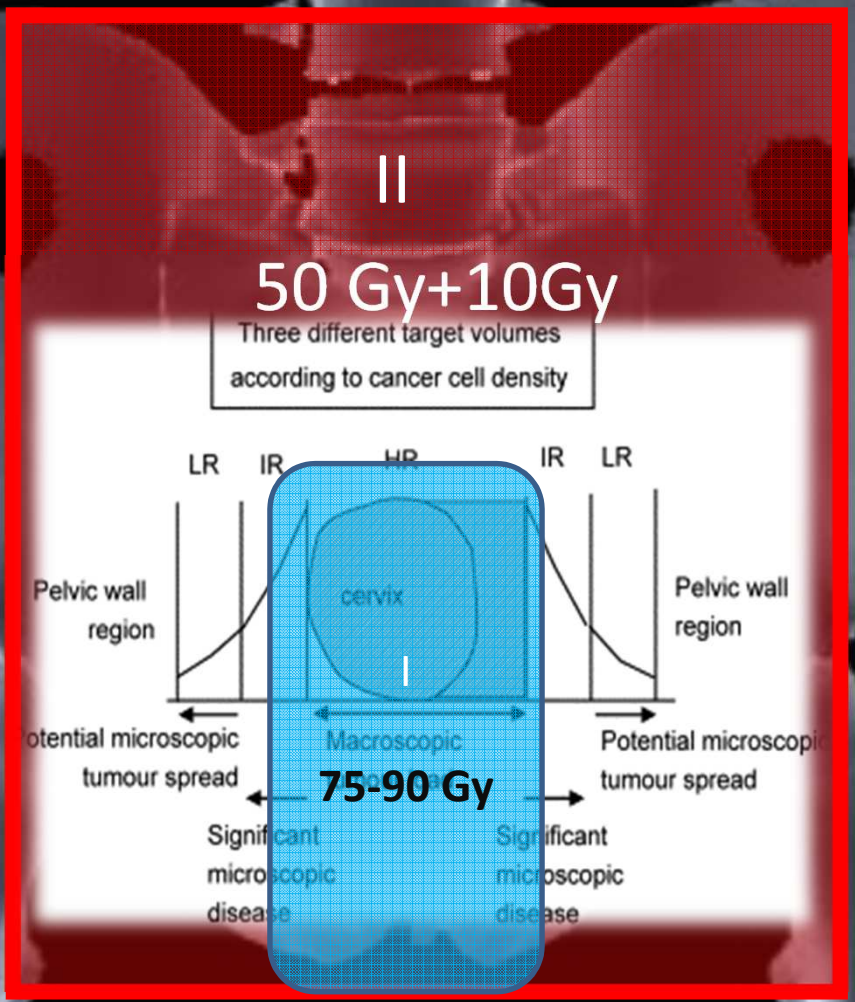

Pelvis
Pelvis
Pelvis
Pelvis
IIB
IB
IIIB
IIA
IIIA


II
Three different target volumes
according to cancer cell density
LR
IR
HR
IR
LR
Pelvic wall
region
cervix
Pelvic wall
region
otential microscopic
tumour spread
Macroscopic
tumour load
Potential microscopic
tumour spread
Significant
microscopic
disease
Significant
microscopic
disease
Pelvis

45-50 Gy+
5-10Gy III

II

50 Gy+10Gy



PROBABILITY OF TUMOR CONTROL
SUBCLINICAL:-45-50Gy
MICROSCOPIC:-50-60Gy
GROSS DISEASE:-75-85Gy

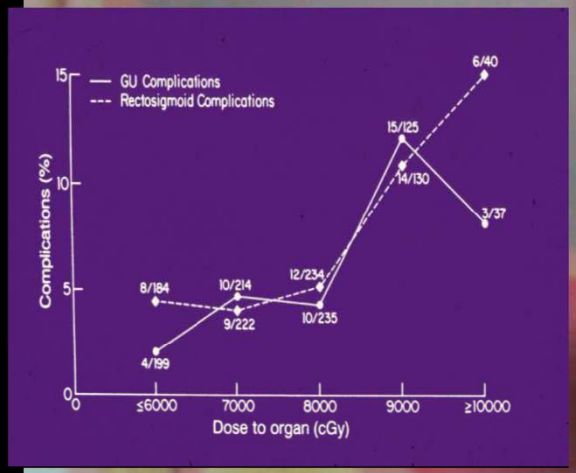
Pelvis

RECTAL COMPLICATION COMMON THAN BLADDER COMPLICATION

DOSE TO BLADDER & RECTUM SHOULD BE 80% OF DOSE TO POINT A

BLADDER -65-70Gy.RECTUM-60-65 GY,SMALL BOWEL 60GY(Perez etal)

< 45 Gy



75-90

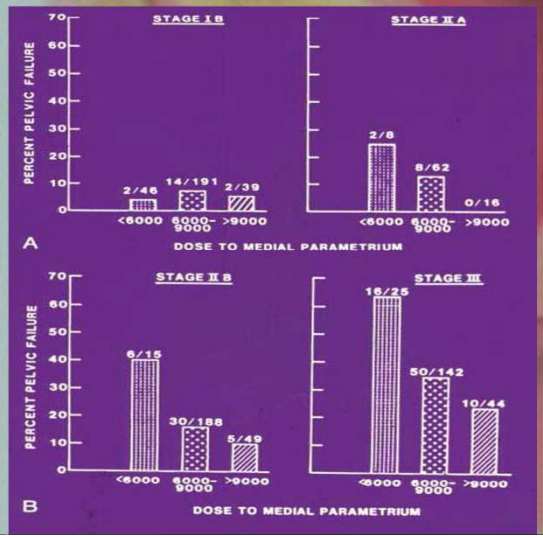
65-70Gy

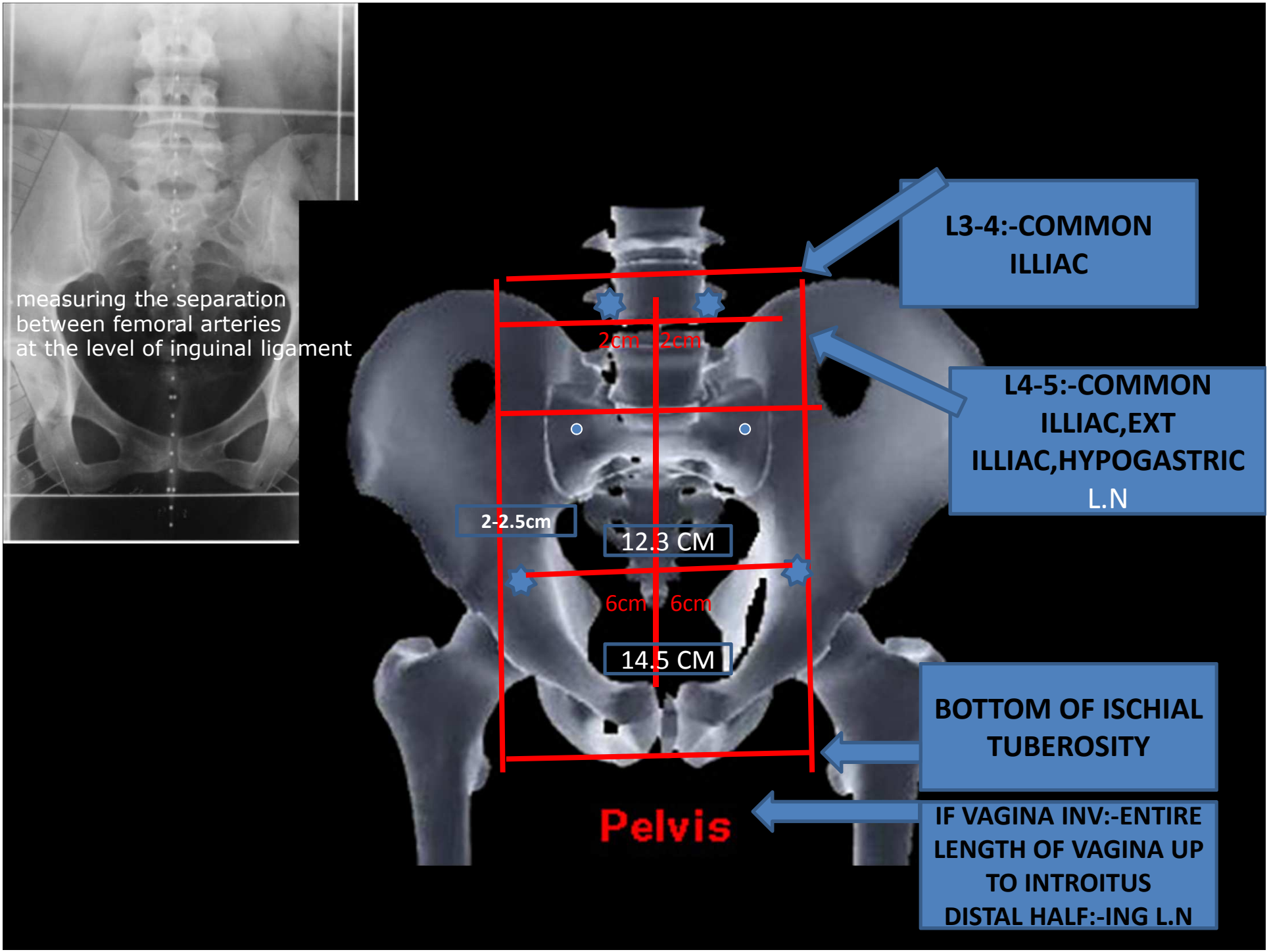
60-65Gy

120Gy

60-65Gy

80-90Gy




measuring the separation between femoral arteries at the level of inguinal ligament
L3-4:-COMMON ILLIAC
2cm
2cm
L4-5:-COMMON ILLIAC,EXT ILLIAC,HYPOGASTRIC L.N
2-2.5cm
12.3 CM
6cm
6cm
14.5 CM
BOTTOM OF ISCHIAL TUBEROSITY
Pelvis
IF VAGINA INV:-ENTIRE LENGTH OF VAGINA UP TO INTROITUS
DISTAL HALF:-ING L.N

shield posterior rectal wall. shield reg
for microscopic diseases in presacral
and external iliac nodes , uterosacral ligament

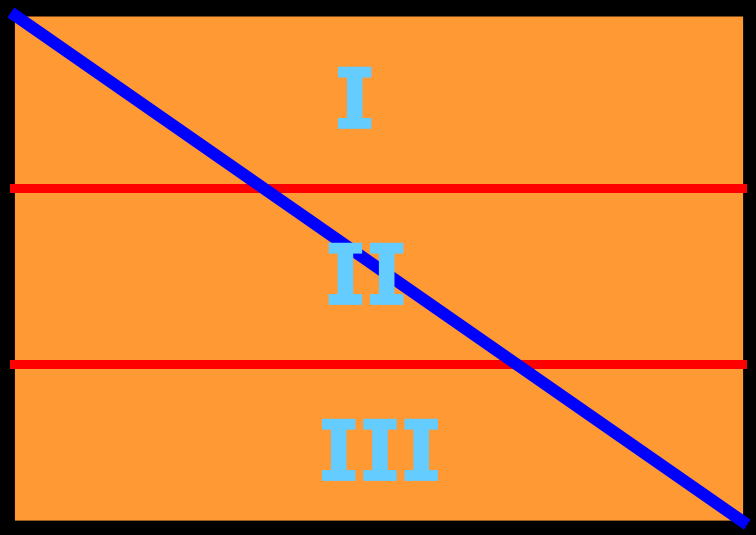
For AP/PA Portal

Superior: L4 - L5 inter space.
Inferior: Inferior border of obturator foramen (if no vaginal extension).
If Vagina inv- Up to Introitus
Lateral borders: 2 cm margin lateral to bony pelvis.

LATERAL PORTAL

- Anterior margin:- In front of Pubic symphisis .
- Posterior margin:- traversing S2/S3 inter space
- Advanced stage :-Sacral Hollow

EBRT : BRACHYTHERAPY



EBRT

Brachy

Ratio of EBRT dose to Brachy dose depends on volume & stage of the disease

CA CERVIX

IS THERE ANY NEED OF BRACHYTHERAPY IN CA CERVIX

Brachytherapy is Necessary

"Tumor control probability correlated with RT dose and cancer volume"

(Fletcher, Shukovsky J Radiol Electrol 56:383400,1975)

	Externalbeam only	External Beam +brachytherapy
4 y LC	**45%**	**67%**
4 y Survival	**19%**	**46%**
Lanciano IJROBP 20:95, 1991		
Local Control	**40%**	**52%**
Montana Cancer 57:148, 1986		

Cont..

PATTERN OF CARE STUDIES

Results of 2nd National Survey

Coia L,Cancer'90(12)2451-56

- **Pattern of care study of 565 pts. treated in 1978**
- **Use of ICRT sig. improved survival & reduced local failure**
- **No. of ICRT applications were important**


Brachytherapy must be included as a component of the definitive radiation for cervical carcinoma.
[ABS Recommendations for HDR Brachytherapy in cancer cervix, IJROBP'00(48):201-11]

LDR vs HDR

Dose Rates

LDR - 0.4 – 2 Gy/hr

MDR- 2 – 12 Gy/hr

HDR ->12 Gy/hr

[ICRU Report 38]

(More standard ranges of LDR – 40 – 100cGy/hr
HDR – 20 -250cGy/min
i.e – 12Gy to 150 Gy/hr)

	L	D	R			H	D	R			
AUTHORS	n	Local control	RFS	complic ation	n	Local control	p	RFS	p	complic ation	p
Teshima et al	**171**	**73%**	**I-93 II-78 III-47**	**BI-0 Rct-3**	**259**	**76**	**ns**	**I-85 II-73 III-53**	**ns**	**BI-3 Rct-4**	ns
Hareyama et al	**61**	**I-100% III-70%**	**II-87% III-60%**	**13%**	**71**	**II-89% III-73%**	**ns**	**II-69% III-51%**	**ns**	**10%**	ns
Lerstanguanstncgai	**109**	**89%**	**69.9%**	**2.8%**	**112**	**71**	**ns**	**69.9%**	**ns**	**7.8**	**n.s**
Patel et al	**246**	**79.7%**	**I-73 II-62 III-50**	**BI-3.7 Rct-2.4 19.9**	**236**	**75.8**	**ns**	**I-78 II-64 III-43**	**ns**	**BI-3.8 Rct-4 6.4%**	ns
TMH	**400**		**I/II-83% III-87%**	**I/II-3% III-2.7**	**400**			**II-78% III-94%**	**ns**	**I/II-2.8% III-2.7%**	ns

HDR Brachytherapy in Carcinoma Cervix

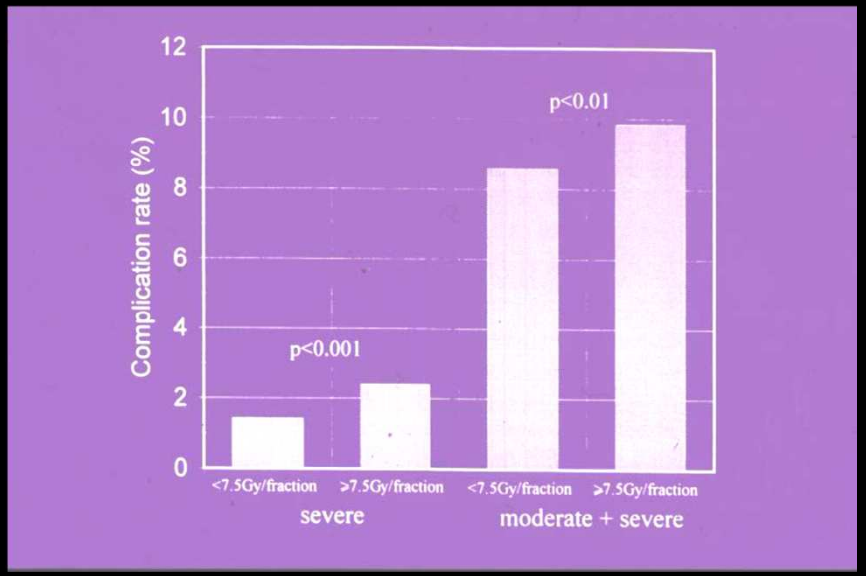
- **ABS RECOMMENDATIONS**

HDR dose per fraction should be kept to < 7.5 Gy. due to reports of higher toxicity with larger fractions sizes.

(Orton 1991 & 1998)

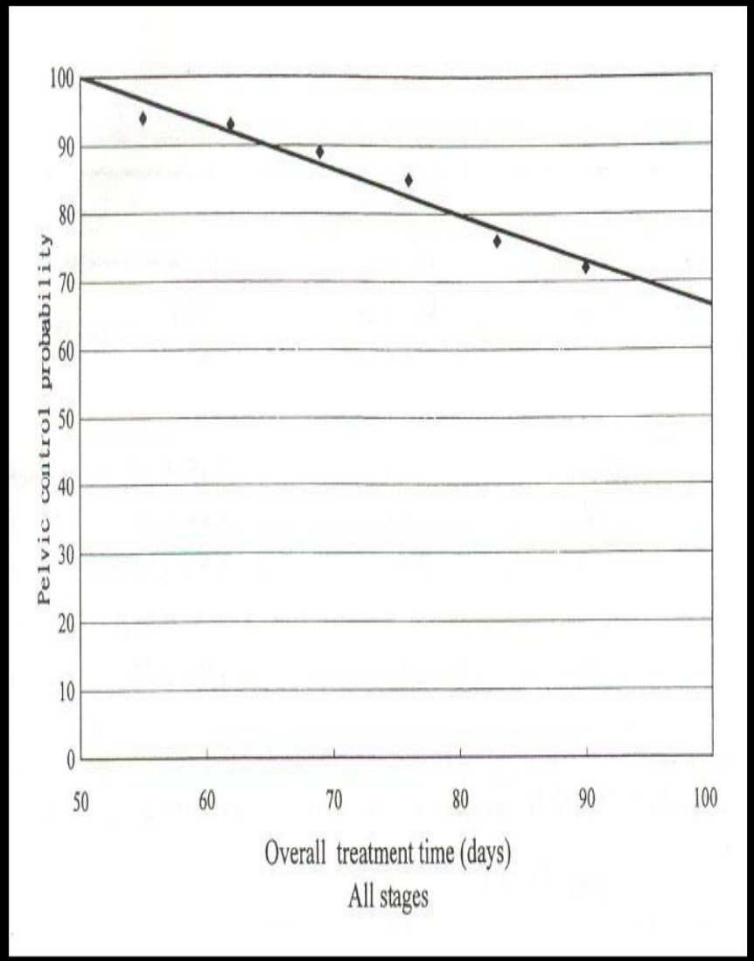
- Number of HDR fractions range from 4 to 8 – caution

was included "it should be noted that these schedules have not been thoroughly tested clinically".



Orton; Acta Oncologia 37:1998

Cervical Cancer
Treatment duration is important



SURVIVAL DECREASES BY <1%/DAY WITH PROLONGATION OF RADIATION BEYOND 7-8 WKS.

Overall treatment time (0TT)
<63 vs > 63 days
was statistically significant in Multivariate analysis for both cause specific survival and pelvic control

Chen et al Radiother Oncol 67:6976, 2003

TAKE HOME MESSAGE

Early stages

Post op RT – Inermediate risk group

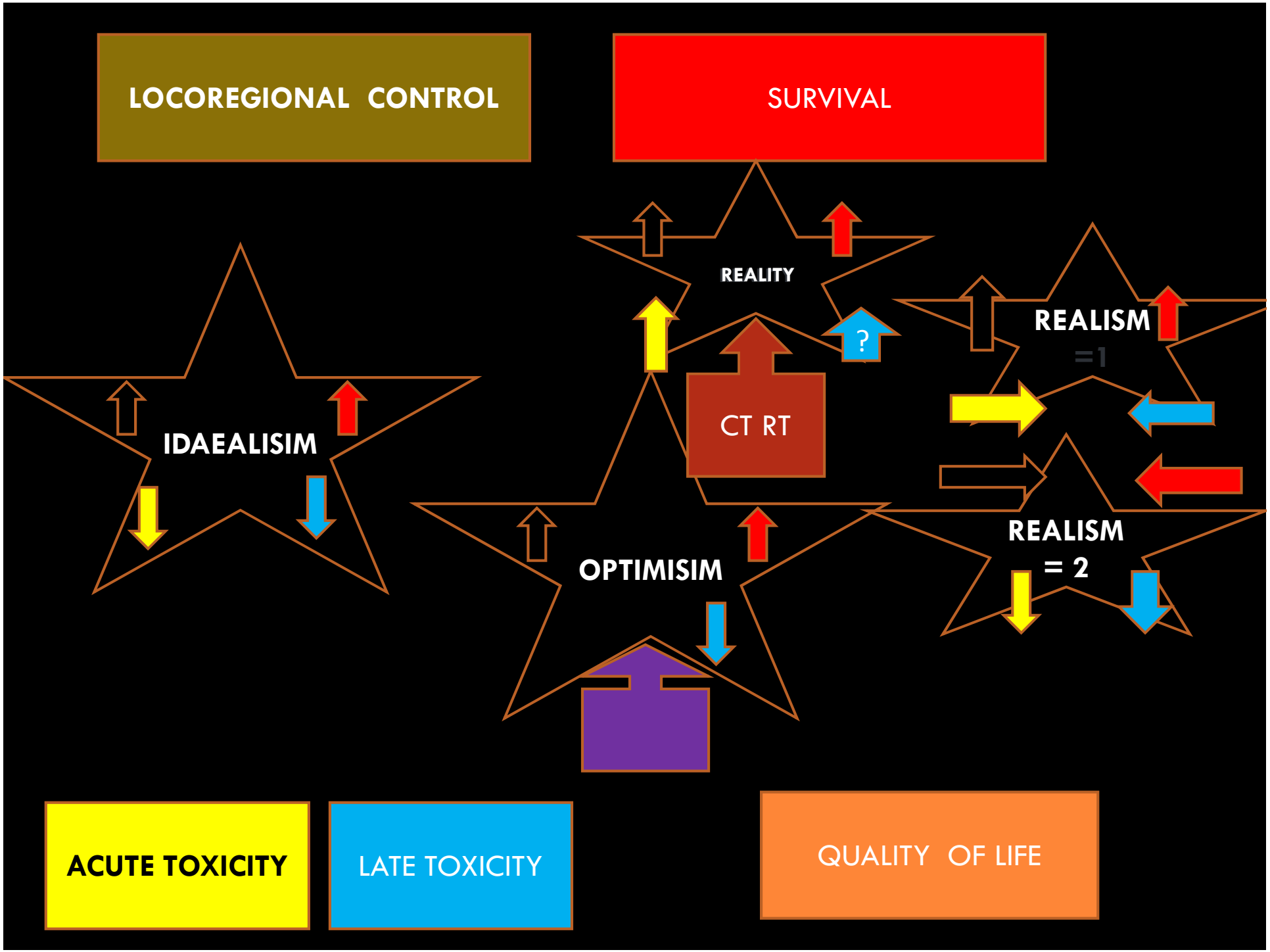
Post op CT+RT :- High risk group

Concurrent chemoradiation – Bulky stage Ib/IIa

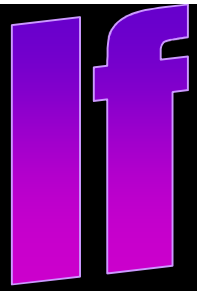
Neoadjuvant CT+ Surgery + RT- Still investigational

Locally Advanced

Concurrent chemoradiation


LOCOREGIONAL CONTROL
SURVIVAL
REALITY
?
IDAEALISIM
CT RT
REALISM
=1
OPTIMISIM
REALISM
= 2
ACUTE TOXICITY
LATE TOXICITY
QUALITY OF LIFE

A SMALL TRUTH TO MAKE LIFE 100%



A B C D E F G H I J K L M N O P Q R S T U V W X Y Z

is equal to

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26

Hard Work

H+A+R+D+W+O+R+K

8+1+18+4+23+15+18+11 = 98%

Knowledge

K+N+O+W+L+E+D+G+E

11+14+15+23+12+5+4+7+5 = 96%

Love

L+O+V+E

12+15+22+5 = 54%

Luck

L+U+C+K

12+21+3+11 = 47%

(don't most of us think this is the most important ???)

Then what makes 100% ?

Is it Money ? ... NO ! ! !

M+O+N+E+Y

13+15+14+5+25 = 72%

Leadership ? ... NO ! ! !

L+E+A+D+E+R+S+H+I+P

12+5+1+4+5+18+19+9+16 = 89%

Every problem has a solution, only if we perhaps change our attitude.

To go to the top,

to that 100% ,

what we really need to go further... a bit more...

ATTITUDE

A+T+T+I+T+U+D+E

1+20+20+9+20+21+4+5 = 100%

It is OUR ATTITUDE towards Life and Work that makes OUR Life 100% ! ! !

ATTITUDE IS EVERYTHING

Change Your Attitude ...

And You Change Your Life ! ! !


Keep the Candle Going
Thank You
This is not the end...