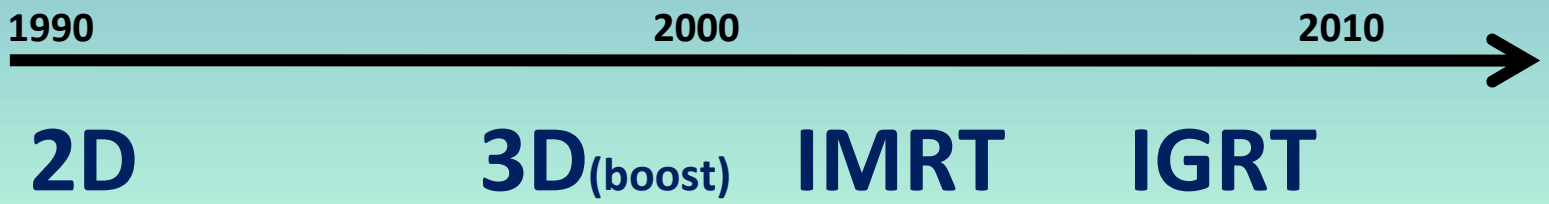
Importanza del Contouring nell'Outcome Clinico

Giuseppe Sanguineti

Radioterapia, Negrar (VR)

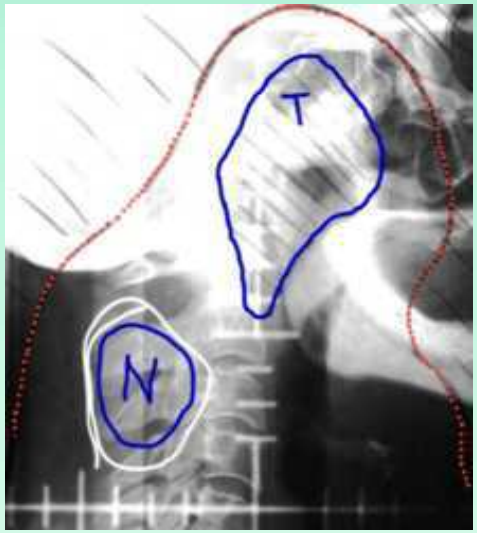
Historical Perspective



Historical Perspective

1990 2000 2010

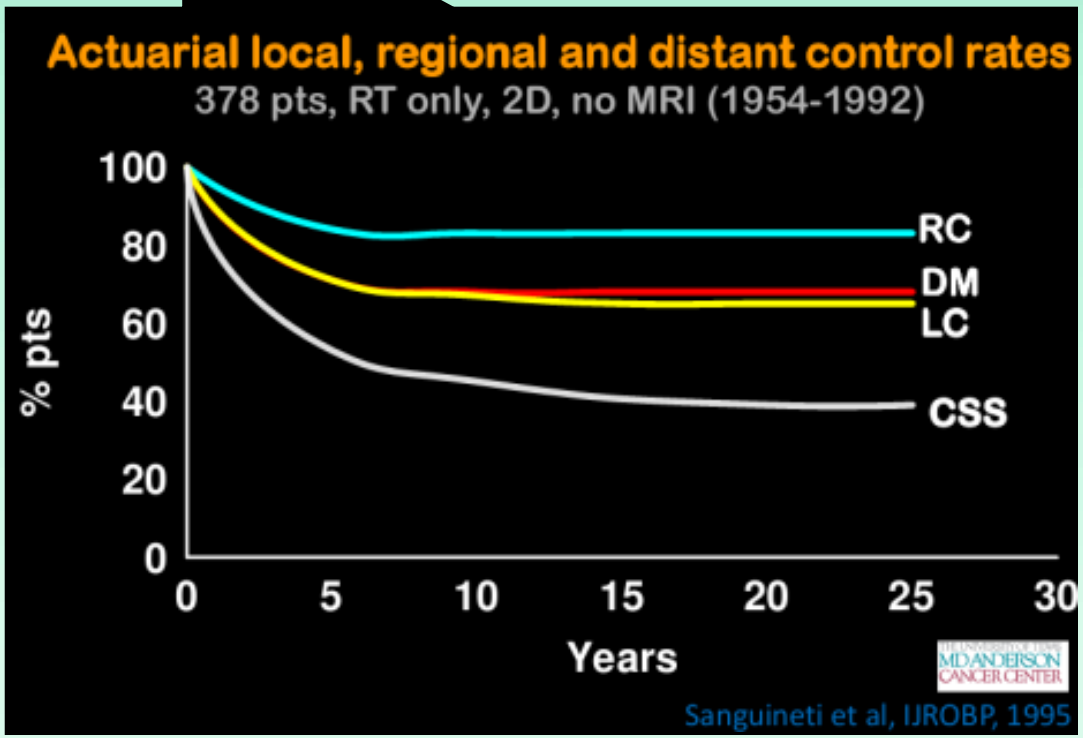
2D **3D(boost)** **IMRT** **IGRT**



Historical Perspective

1950 — 1990 — 2000 — 2010

2D — 3D(boost) — IMRT — IGRT



Historical Perspective

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JOHNS HOPKINS MEDICINE

1950 1990 2000 2010

3D(boost) IMRT IGRT

Historical Perspective

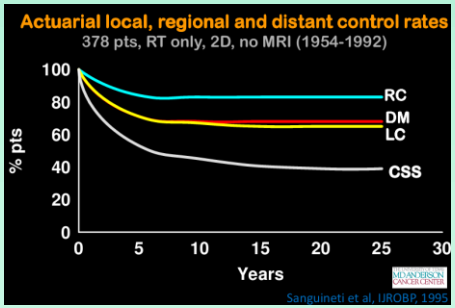
1950 — 1990 — 2000 — 2010

2D

3D(boost)
MRI
CHT

IMRT

IGRT

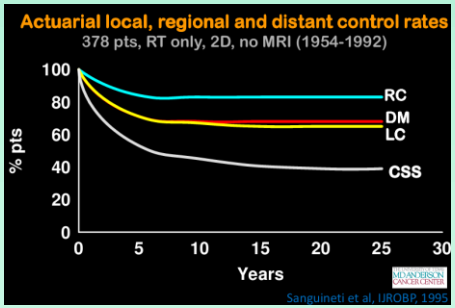


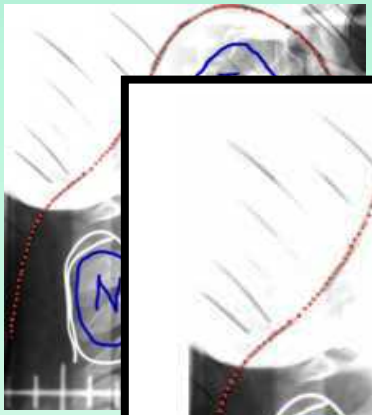
Historical Perspective

1950 — 1990 — 2000 — 2010

2D — 3D(boost) — IMRT — IGRT

MRI





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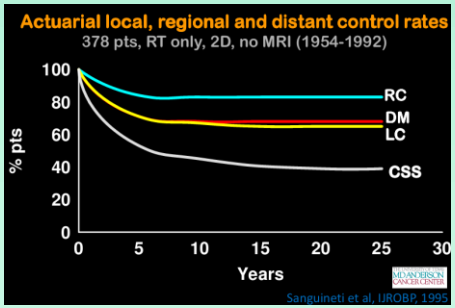

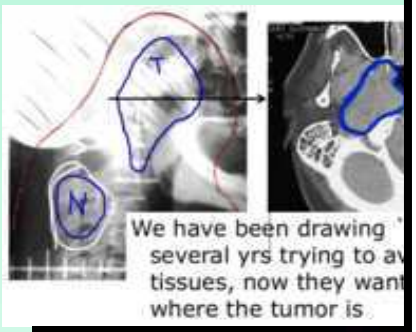

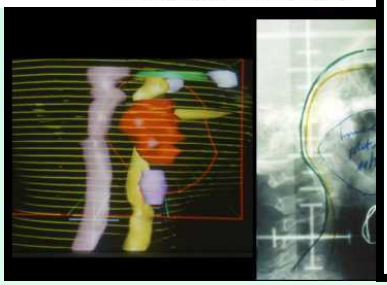

T Classification and Clivus Margin as Risk Factors for Determining Locoregional Control by Radiotherapy of Nasopharyngeal Carcinoma

- meticolous planning w MRI
- 2D-RT

Jian et al, Cancer, 1998

Historical Perspective

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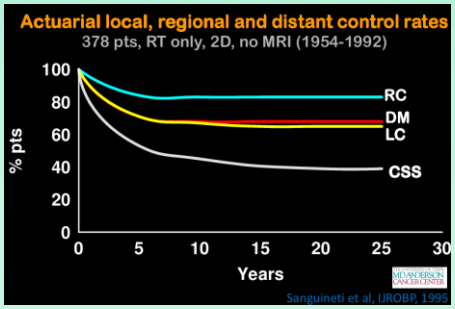

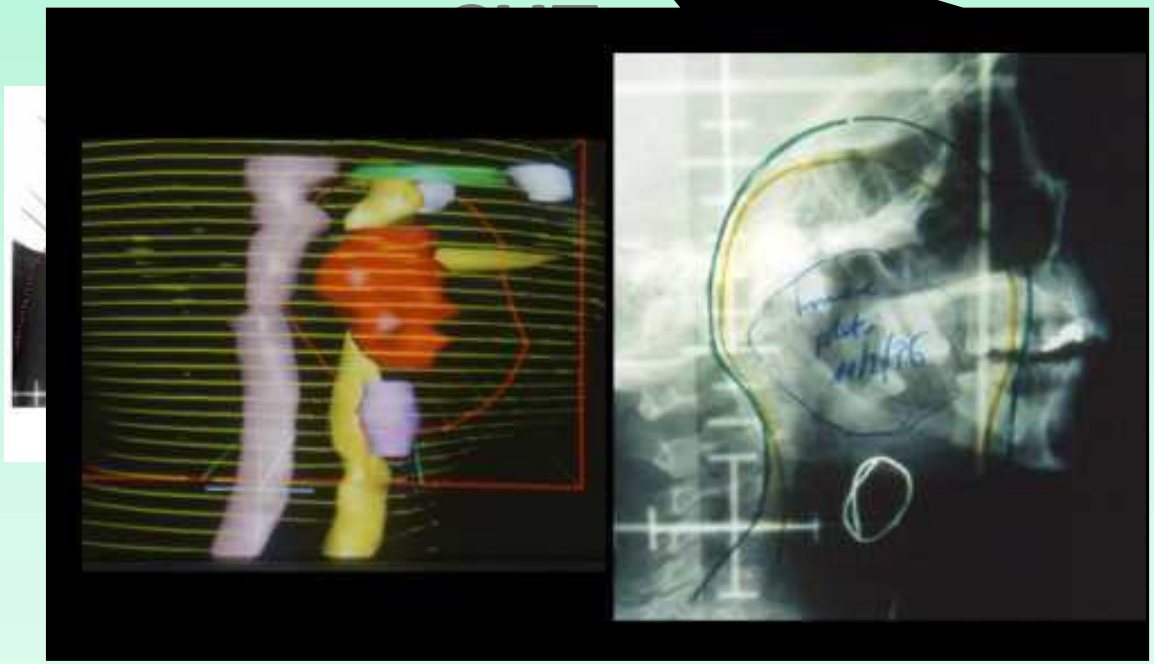

Historical Perspective

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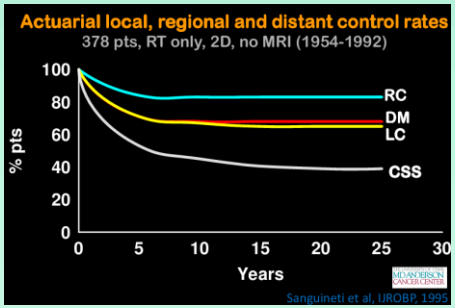
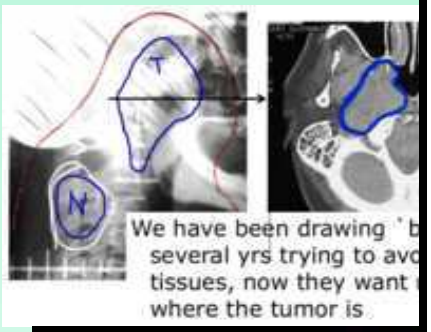
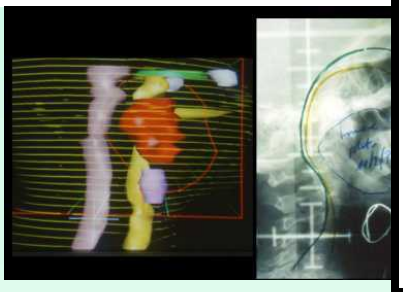






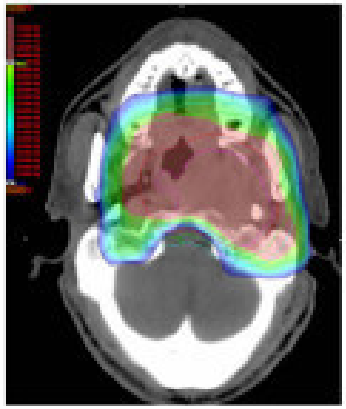
CLINICAL INVESTIGATION — Head and Neck

PARAPHARYNGEAL EXTENSION OF NASOPHARYNGEAL CARCINOMA: STILL A SIGNIFICANT FACTOR IN ERA OF MODERN RADIOTHERAPY? **NO**

Wai T. Ng, F.R.C.R.,* Siu H. Chan, F.R.C.R.,* Anne W. M. Lee, F.R.C.R.,* Kam Y. Lau, F.R.C.R.,† Tze K. Yau, F.R.C.R.,* Wai M. Hung, C.M.D., M.Sc.,* Michael C. H. Lee, Ph.D.,† and Cheuk W. Choi, M.Sc.*

Departments of *Clinical Oncology, †Diagnostic Radiology, and ‡Physics, Pamela Youde Nethersole Eastern Hospital, Hong Kong, People's Republic of China

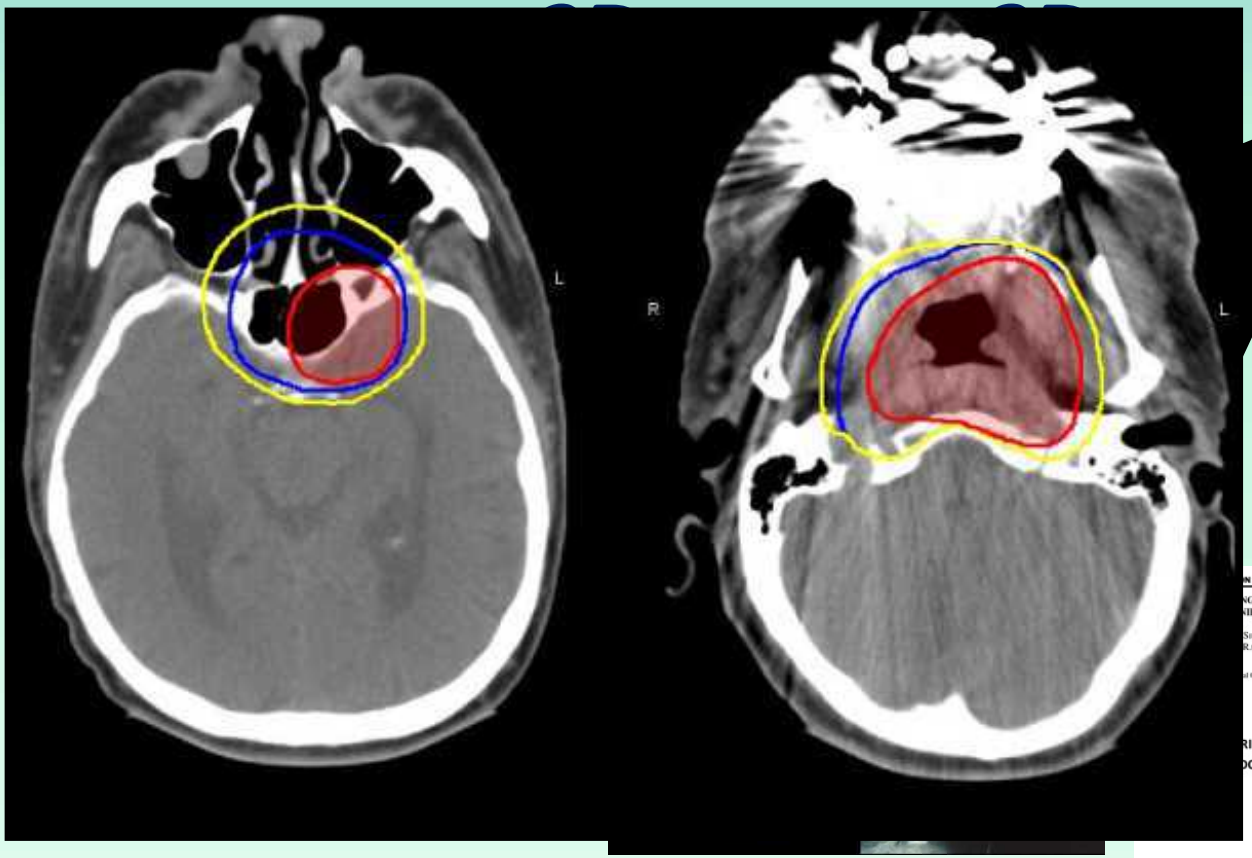
- 700 pts,
- all staged w MRI and
- treated with 3DCRT



IJROBP, 2008

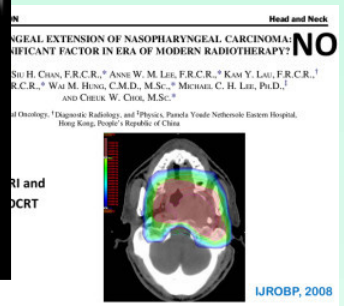
Historical Perspective

1950 1990 2000 2010



IMRT

- More conformal
- More concavity
- Sharper dose gradients
- SIB
- Avoid junctions
- More D control to OARs



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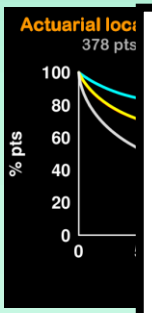


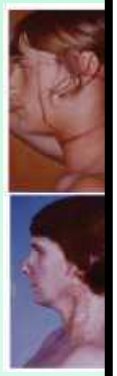
Contemporary outcome of NPC (IMRT series)

Table 3. The various published single institution reports of outcomes and toxicity using intensity-modulated radiotherapy for radiation delivery in nasopharyngeal cancers

Author	Patients, *n*	Stage	CRT	LRC	OS	Incidence >grade 2 xerostomia (late)
Sultanem et al [19]	35	I–IV	91%	100% (4 years)	94% (4 years)	0%
Lee et al [88]	67	I–IV	74%	98% (4 years)	88% (4 years)	0.3%
Kam et al [89]	63	I–IV	30%	92% (3 years)	90% (3 years)	23%
Wolden et al [90]	74	I–IV	93%	91% (3 years)	83% (3 years)	32%
Lai et al [91]	512	I–IV	82%	93% (5 years)	76% (5 years)	NR
Han et al [92]	305	I–IV	85%	98% (3 years)	89% (3 years)	7%
Lin S [93]	323	II–IV	90%	98% (3 years)	90% (3 years)	8%

CRT, concomitant radiotherapy; LRC, locoregional control; NR, not reported; OS, overall survival.

Bhide et al, 2012



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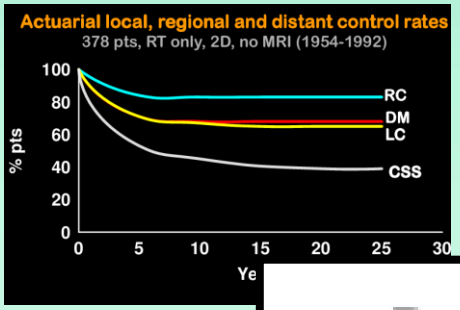
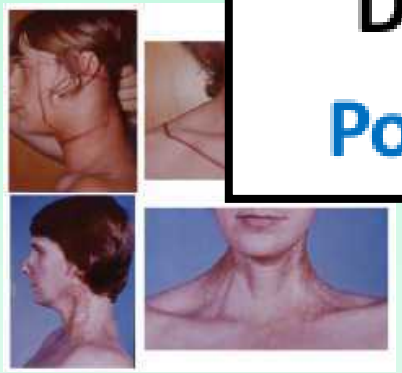
MRI

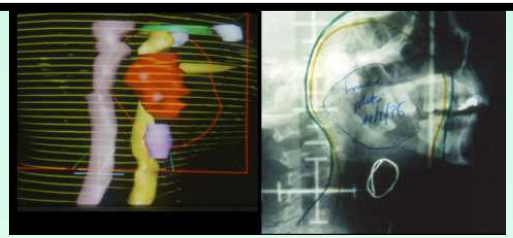
CHT

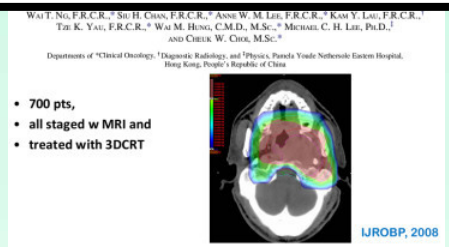


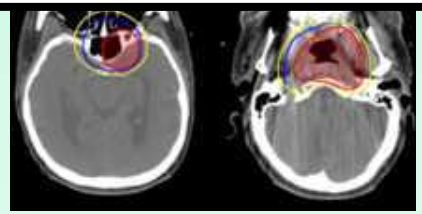
Decreased toxicity w IMRT over 3DCRT

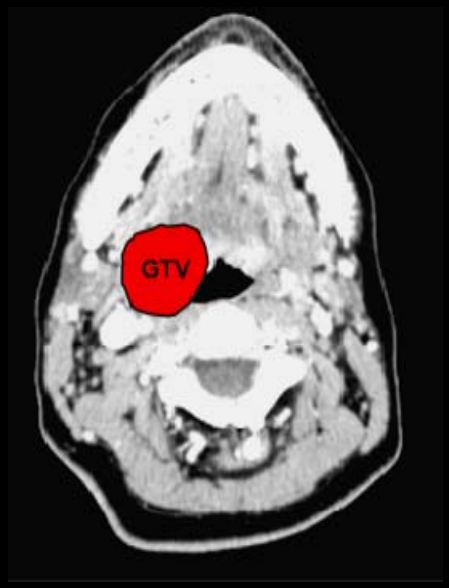
Pow et al, IJROBP, 2006; Kam et al, JCO, 2007

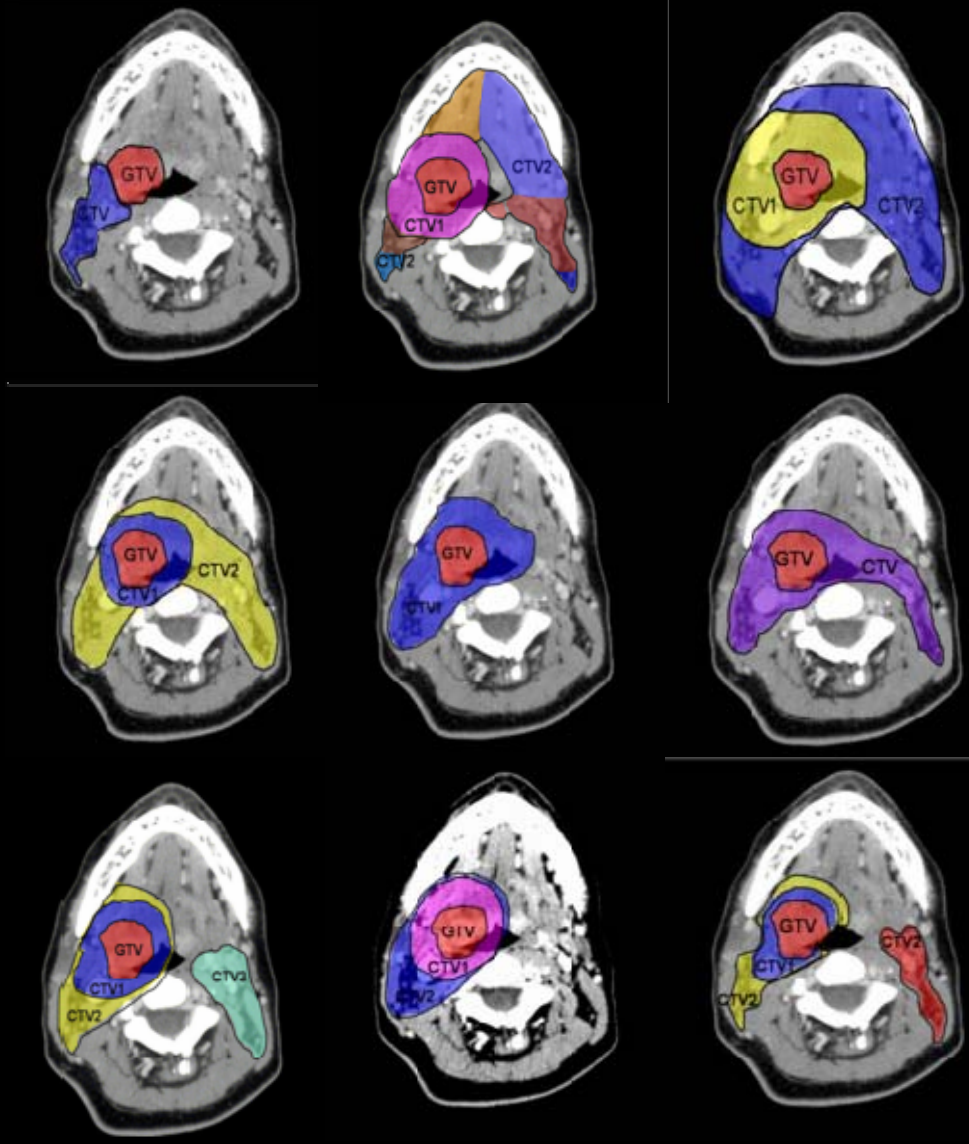






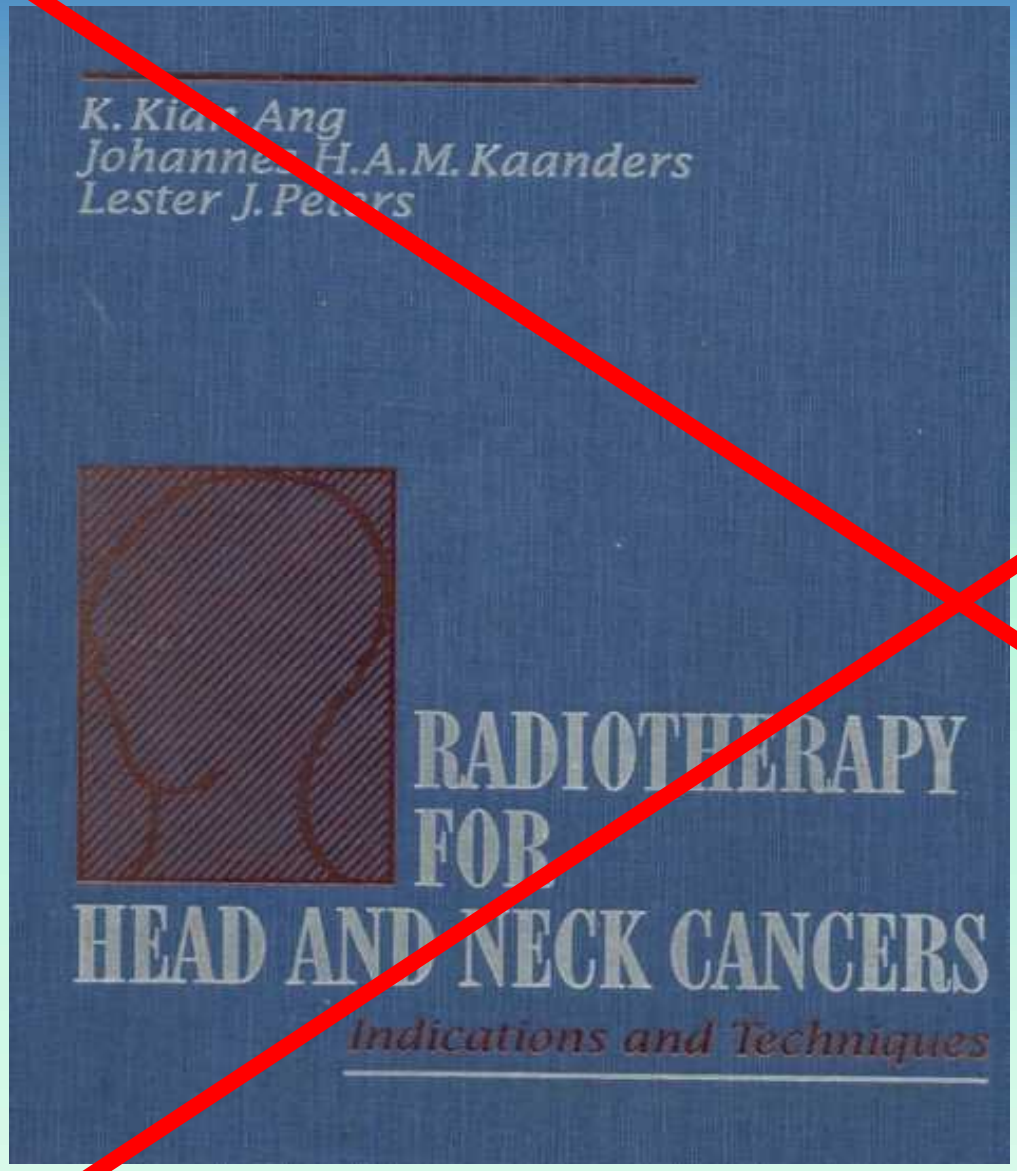


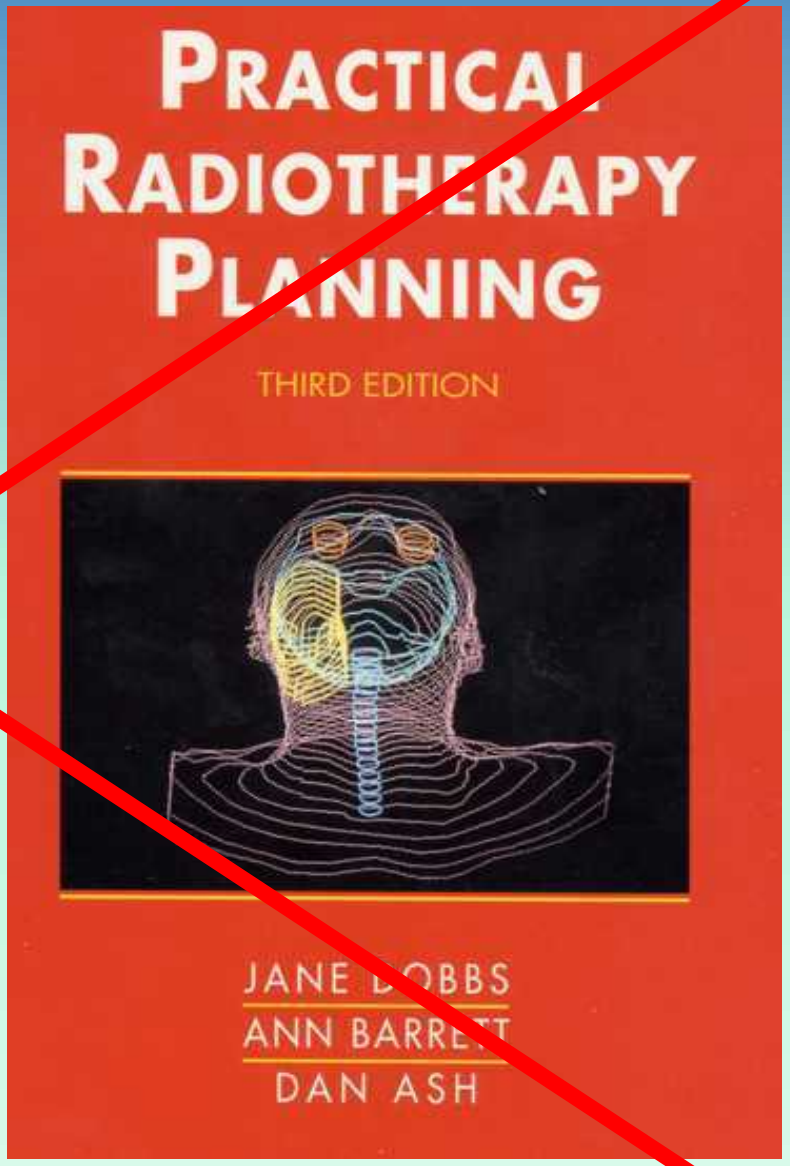


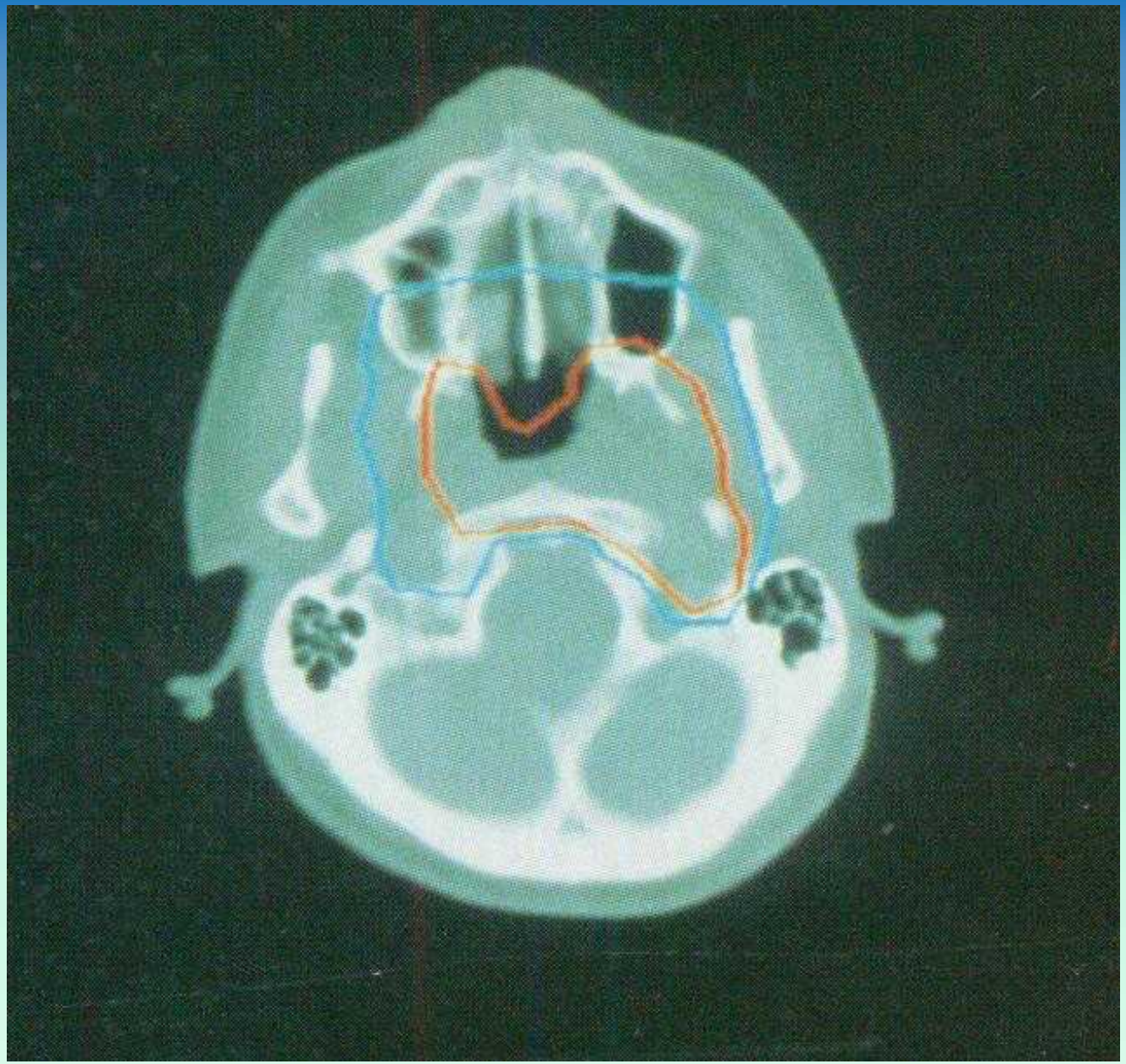


Harari et al., 2005

Courtesy of V. Gregoire


K. Kian Ang
Johannes H.A.M. Kaanders
Lester J. Peters
RADIOTHERAPY FOR HEAD AND NECK CANCERS
Indications and Techniques


PRACTICAL RADIOTHERAPY PLANNING
THIRD EDITION
JANE DOBBS
ANN BARRETT
DAN ASH



Kutcher et al, 1991

VOLUME 27 · NUMBER 22 · AUGUST 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Intensity-Modulated Radiation Therapy With or Without Chemotherapy for Nasopharyngeal Carcinoma: Radiation Therapy Oncology Group Phase II Trial 0225

Nancy Lee, Jonathan Harris, Adam S. Garden, William Straube, Bonnie Glisson, Ping Xia, Walter Bosch, William H. Morrison, Jeanne Quivey, Wade Thorstad, Christopher Jones, and K. Kian Ang

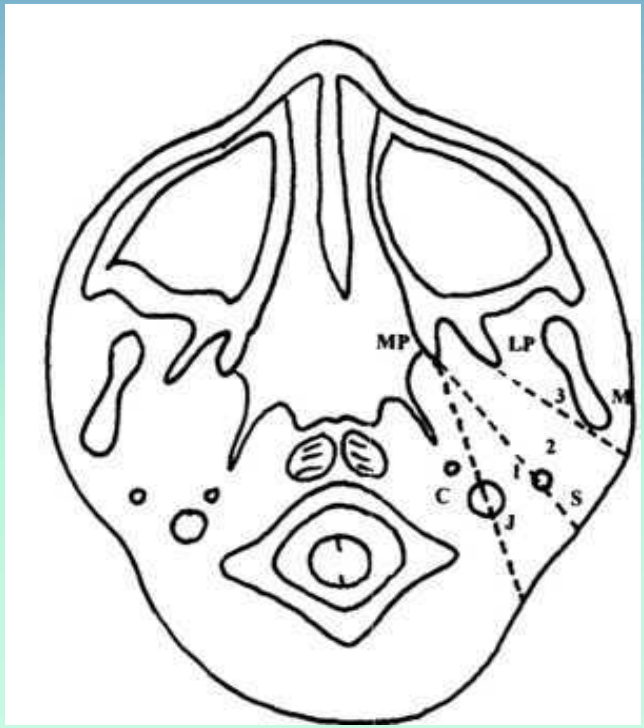
Disclosures

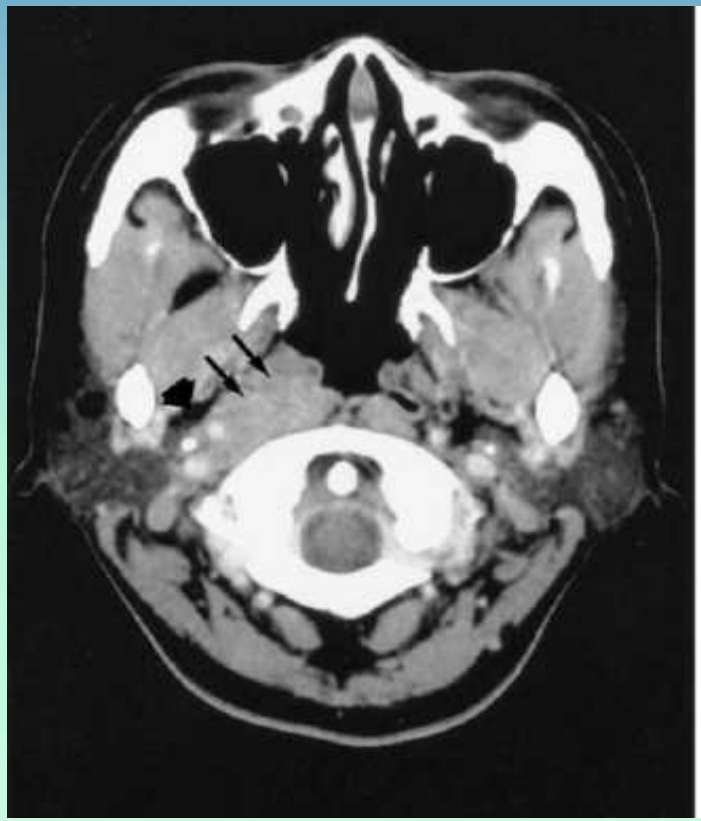
- Chemotherapy often part of tmt (less effect of underdosing)
- Impossibility to have path confirmation of image findings, i.e. RP nodes
- Most evidence comes from ‘oriental’ studies on type II and III cancer where technical shortage was common
- Staging & Techniques continuously evolving

Evolution of AJCC/UICC systems for T stage

Version	4th	5th	6th	7th
Year	1992	1997	2002	2010
T1	1 site within NPX	Confined to NPX		Confined to NPX or ext to nasal cavity/oro w/o PP ext
T2	>1 site	Nasal fossa, oropharynx	a: w/o PP ext b: w PP ext	PP ext
T3	Nasal fossa, oropharynx	Bony erosion, paranasal sinuses		
T4	Bony erosion, CN	CN, intracranial, orbit, infratemporal, hypopharynx...	...and masticator space	same

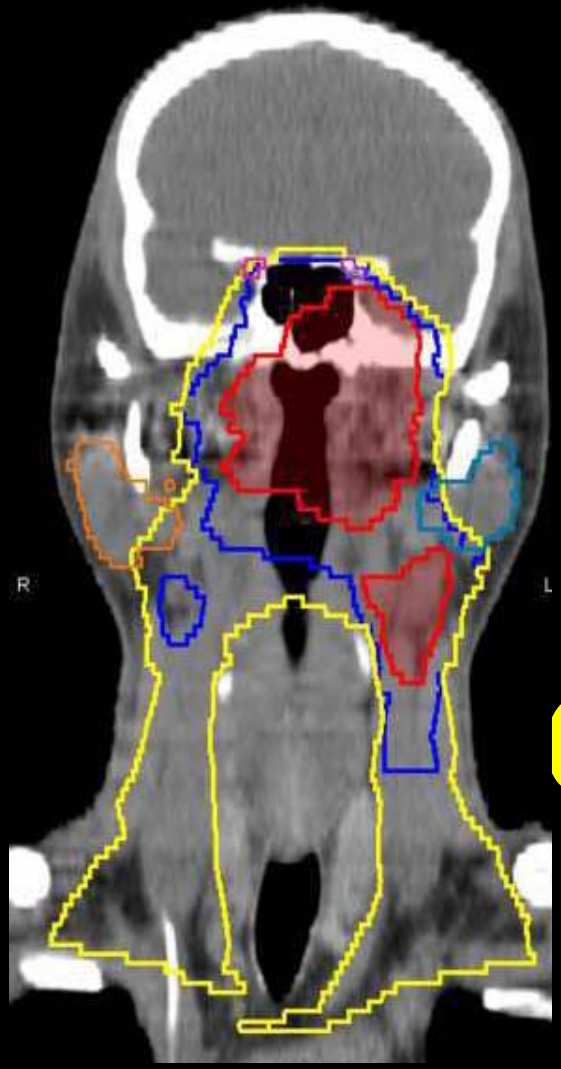
PP ext according to CT and MRI





Chua et al, Cancer 1996

King et al, Clin Oncol 2000

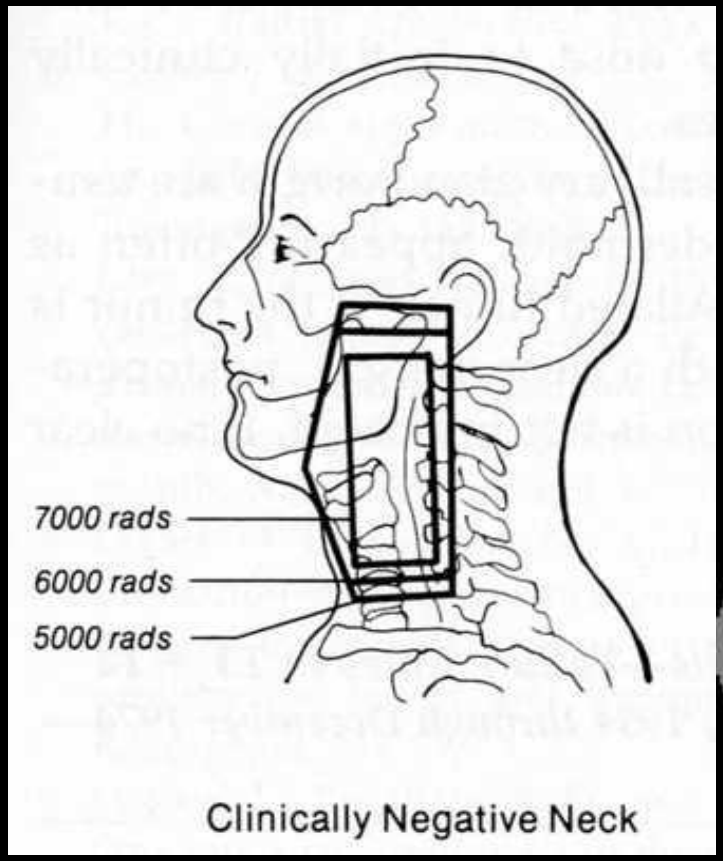


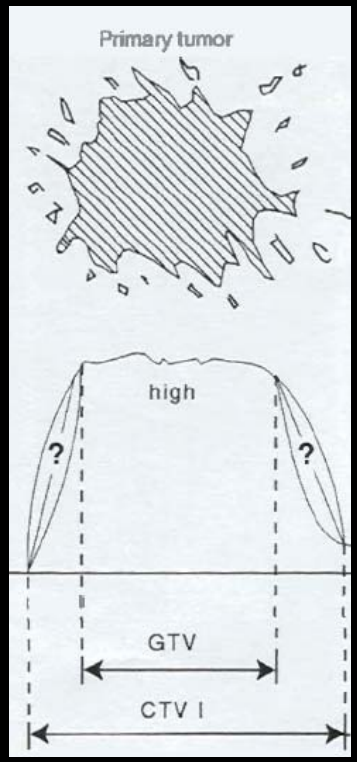
Gross Tumor Volume

Clinical Target Volume

Planning Target Volume

3 target-concept





Fletcher et al, 1978

....CTV1, CTV2, CTV3

PE, fibro, MRI, CT, PET

To allow for uncertainties to 'see' the tumor

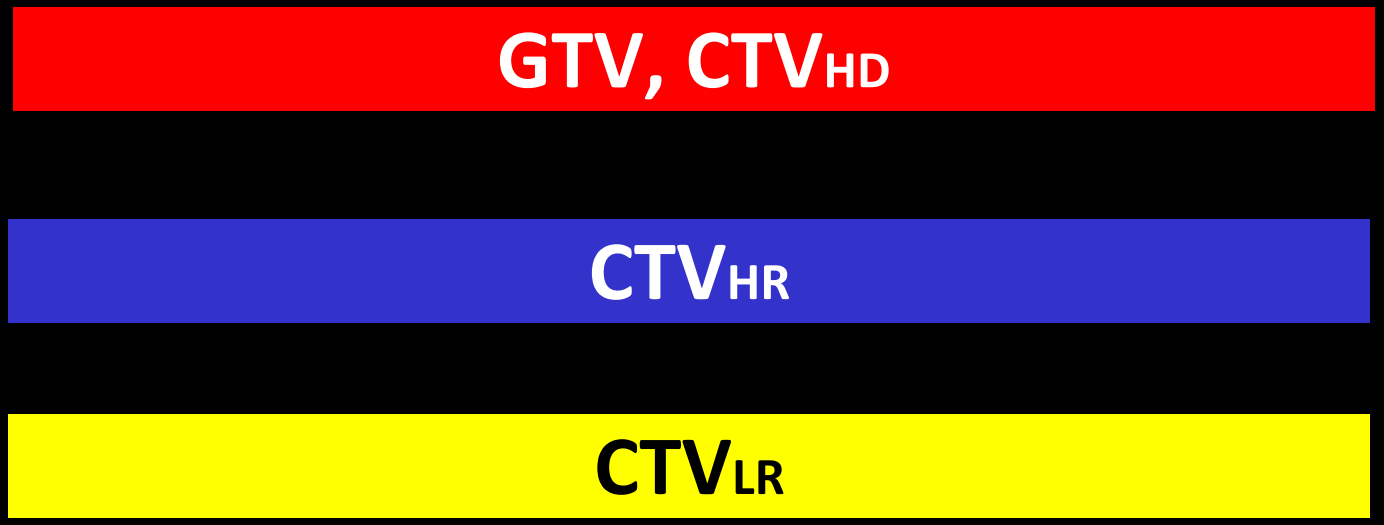
GTV → CTV_{HD} — **70 Gy @ 2 Gy**

CTV_{HR} → High risk of subclinical diz — **60 Gy @ 2 Gy**

CTV_{LR} — **50 Gy @ 2 Gy**

Low risk of subclinical diz

Primary Tumor



GTV, CTV_{HD}-T

- **The Gross Tumor Volume (GTV) is defined as all known gross disease determined from CT, MRI, clinical information, and endoscopic findings**

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GTV, CTV_{HD}-T

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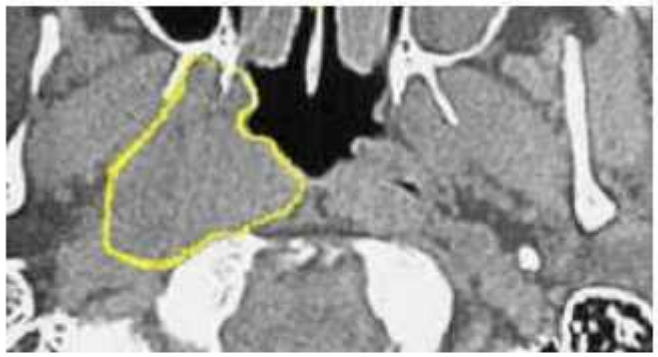

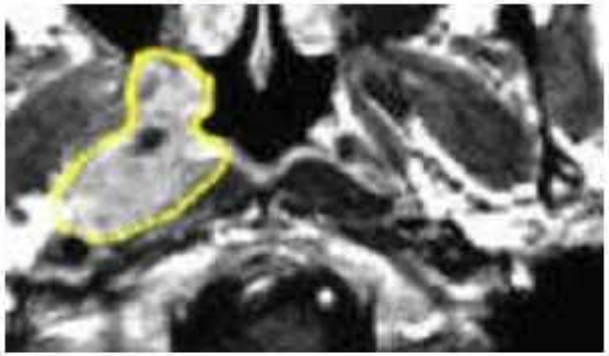

CT MRI

GTV by MRI is *smaller* and has less interobserver variability

Rasch et al, 1997

GTV, CTV_{HD}-T

- The Gross Tumor Volume (GTV) is defined as all known gross disease determined from CT, MRI, clinical information, and endoscopic findings
- **It is strongly encouraged that the radiation oncologist outlines the radiologic extent of the primary tumor along with a neuro-radiologist (→ *uncertainty*)**
- **It is recommended that the diagnostic images be fused to the planning CT scan image dataset to more accurately define the GTV (→ *uncertainty*)**
- **A margin of ≥ 5 mm should be given circumferentially around the GTV and this volume will be called the CTV70… (but can be 0-1 mm when anatomical barriers are present)**

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CTV_{HR}-T

- For regions deemed to be at high risk for microscopic disease, all potential routes of spread for primary GTV should be delineated. This is known as CTV for high risk subclinical disease

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Pattern of submucosal spread of NPC @ fibroscopy

- **247 pts, multiple NPX biopsies**
- **56% T1-2, 11% T3, 33% T4**
- **only 7% had involvement of one subsite;**
- **submucosal spread correlated with PP ext and #/size/level of N+**

Sham et al, 1991

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Version	4th	5th	6th	7th
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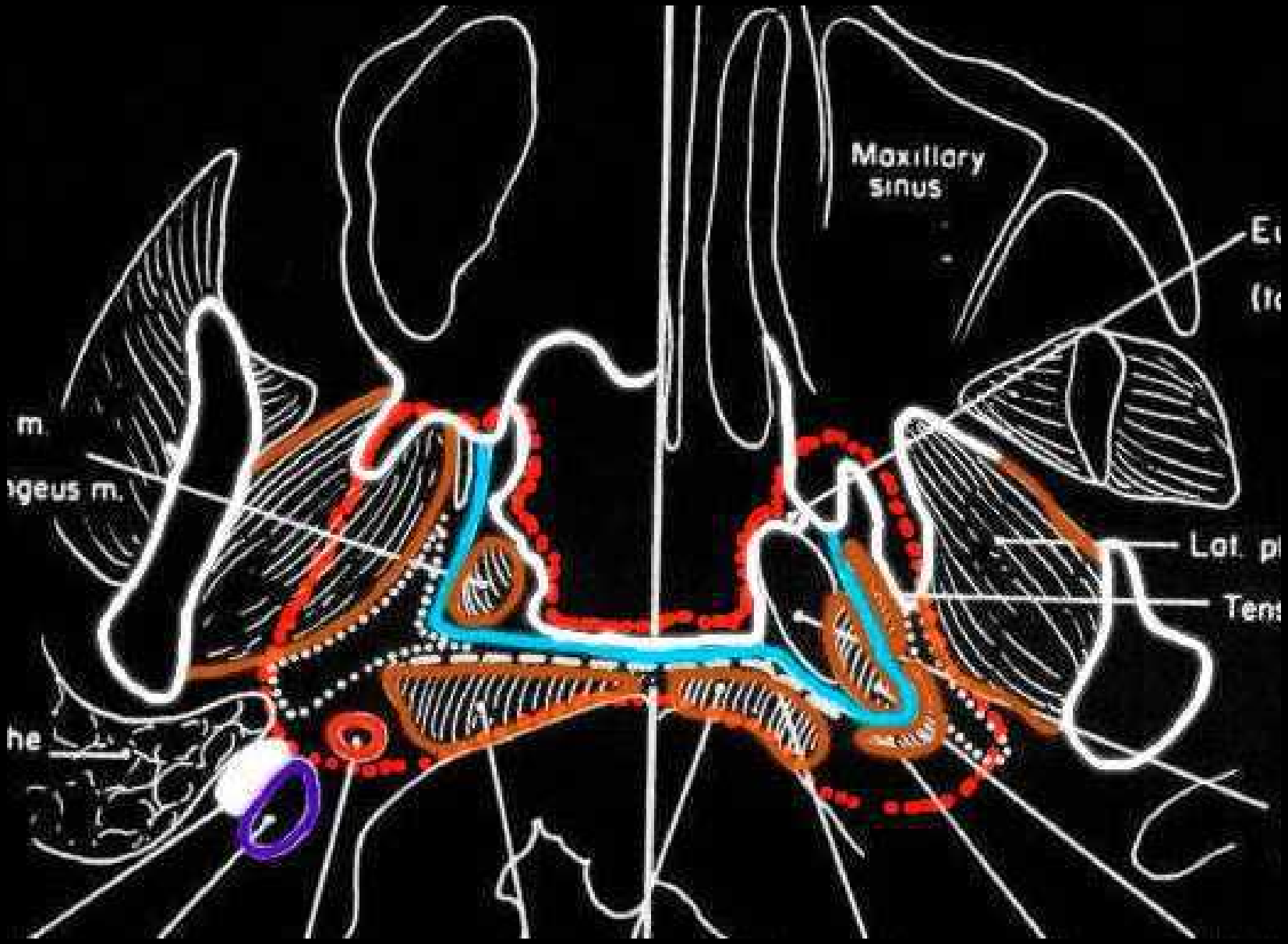
- 56% T1-2, 11% T3, 33% T4
- only 7% had involvement of one subsite;
- submucosal spread correlated with PP ext and #/size/level of N+

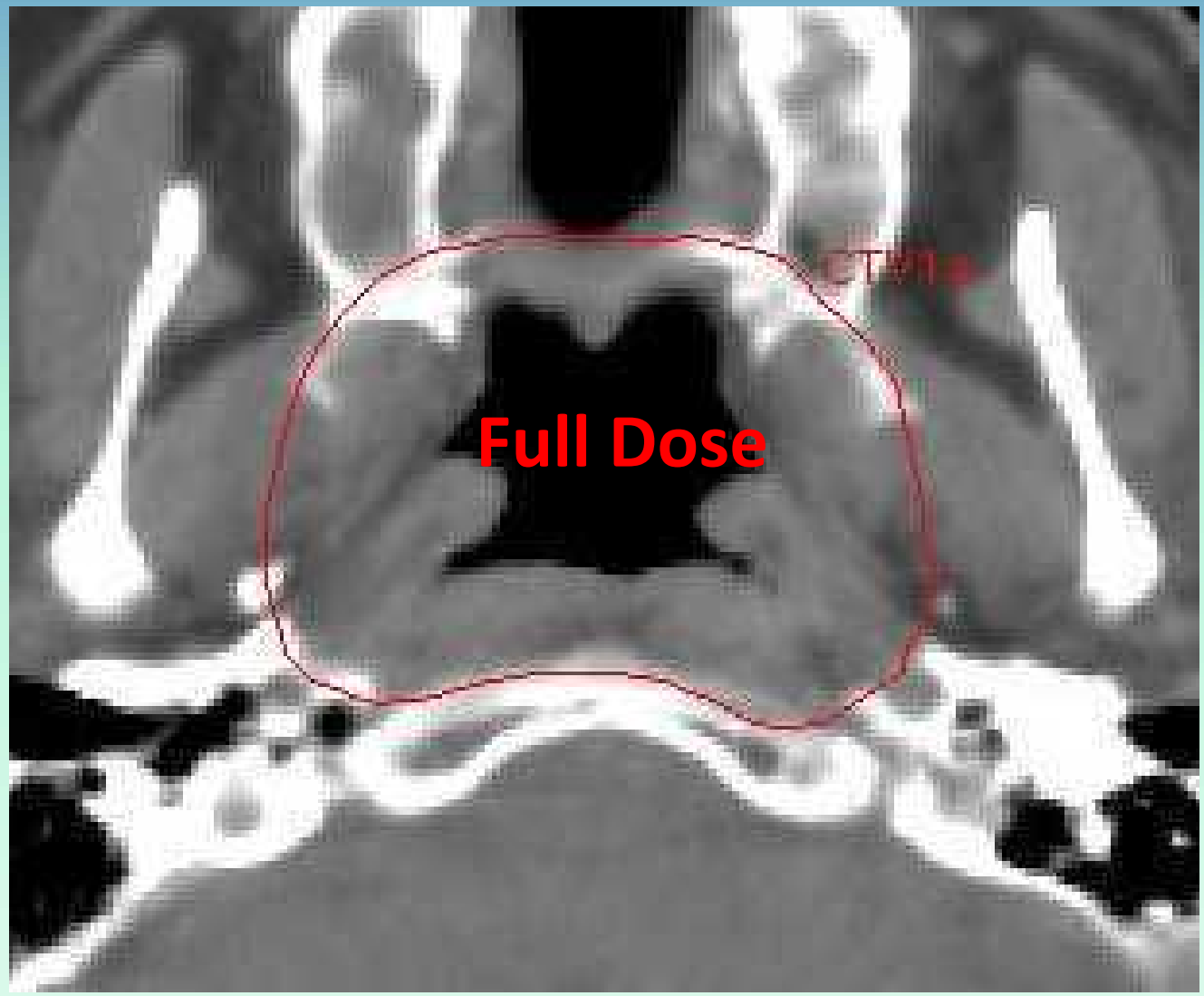
→Whole NPX at high risk regardless T site
→Whole NPX used to be included within the HD

Sham et al, 1991

NPX



NPC – Primary T volume



CTV_{HR}-T

- For regions deemed to be at high risk for microscopic disease, all potential routes of spread for primary GTV should be delineated. This is known as CTV for high risk subclinical disease
- The high risk subclinical region includes the entire NPX, anterior 1/2 to 2/3 of the clivus (entire clivus, if involved), skull base (foramen ovale and rotundum bilaterally must be included for all cases), pterygoid fossae, parapharyngeal space, inferior sphenoid sinus (in T3-T4 disease, the entire sphenoid sinus) and posterior fourth to third of the nasal cavity and maxillary sinuses (to ensure pterygopalatine fossae coverage). The cavernous sinus should be included in high risk patients (T3, T4, bulky disease involving the roof of the nasopharynx)
- The outer most boundary of CTV-HR should be at least 10 mm from the GTV

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CTV_{HR}-T

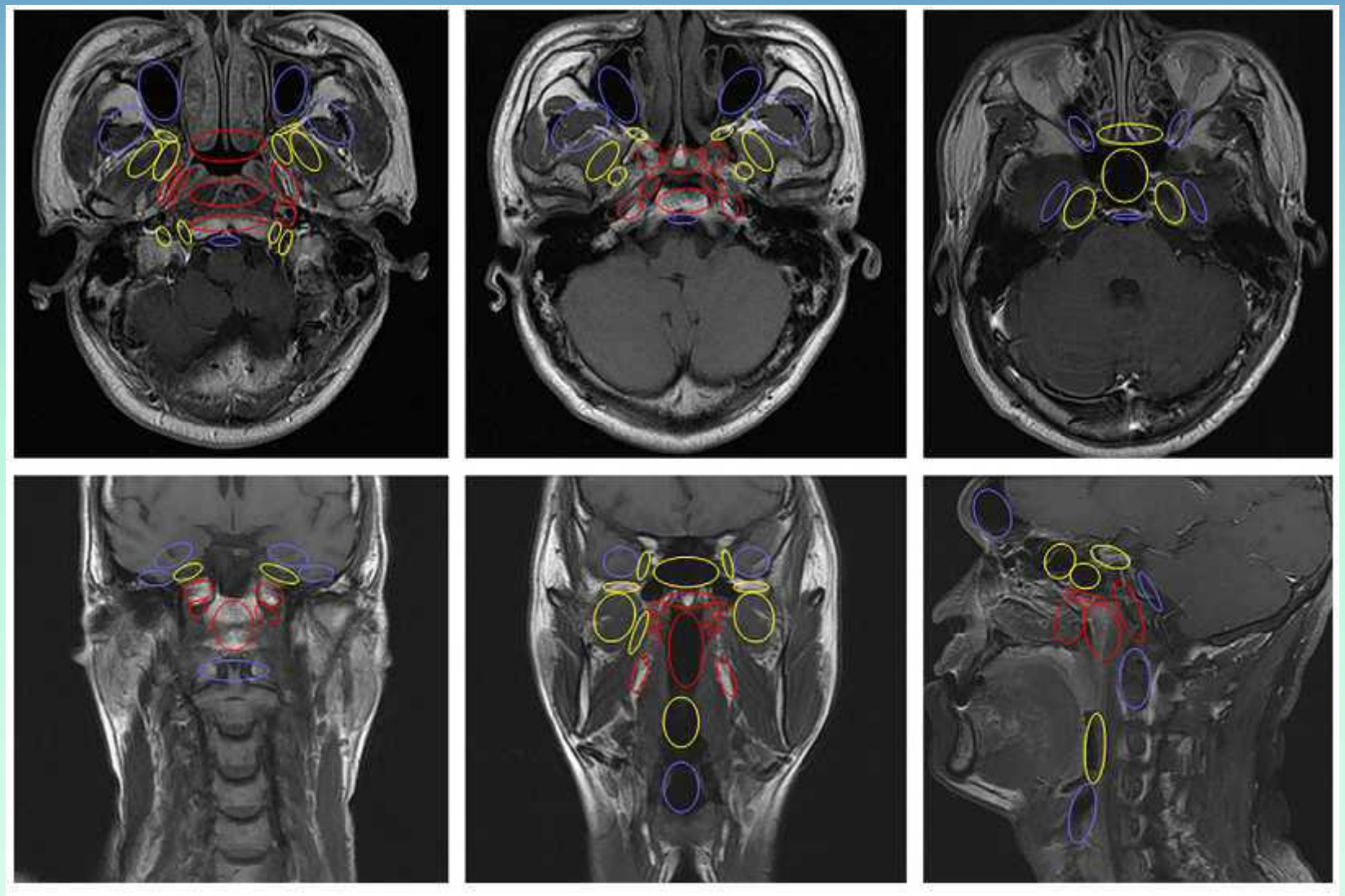
- For regions deemed to be at high risk for mic isease, all potential routes of spread for primary C be delineated. This is known as CTV for hi clinical disease
- The high risk subclinical region inc entire NPX, anterior 1/2 to 2/3 of the clivus vus, if involved), skull base (foramen ovale and ro laterally must be included for all cases), pterygoid f rapharyngeal space, inferior sphenoid sinus (in T3 se, the entire sphenoid sinus) and posterior fourth the nasal cavity and maxillary sinuses (to e ygopalatine fossae coverage). The cavernou ould be included in high risk patients (T3, T4, bulky involving the roof of the nasopharynx)
- T most boundary of CTV-HR should be at least 10 mm fr e GTV

NO CTV_{LR} AT PRIMARY SITE

RTOG®
RADIATION THERAPY ONCOLOGY GROUP

CTV_{HR}-T

Pattern of local spread of NPC @ MRI



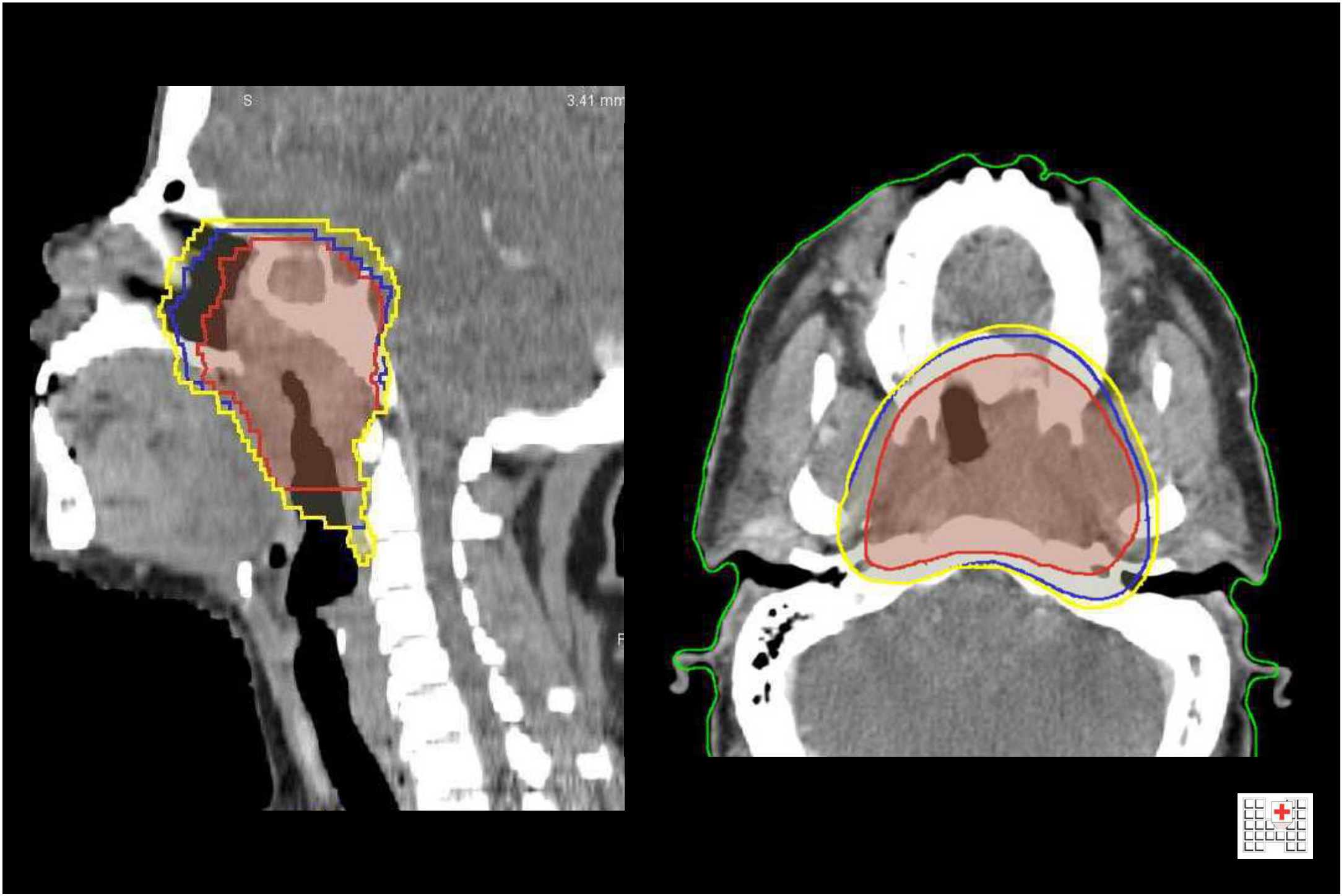
High, >35%

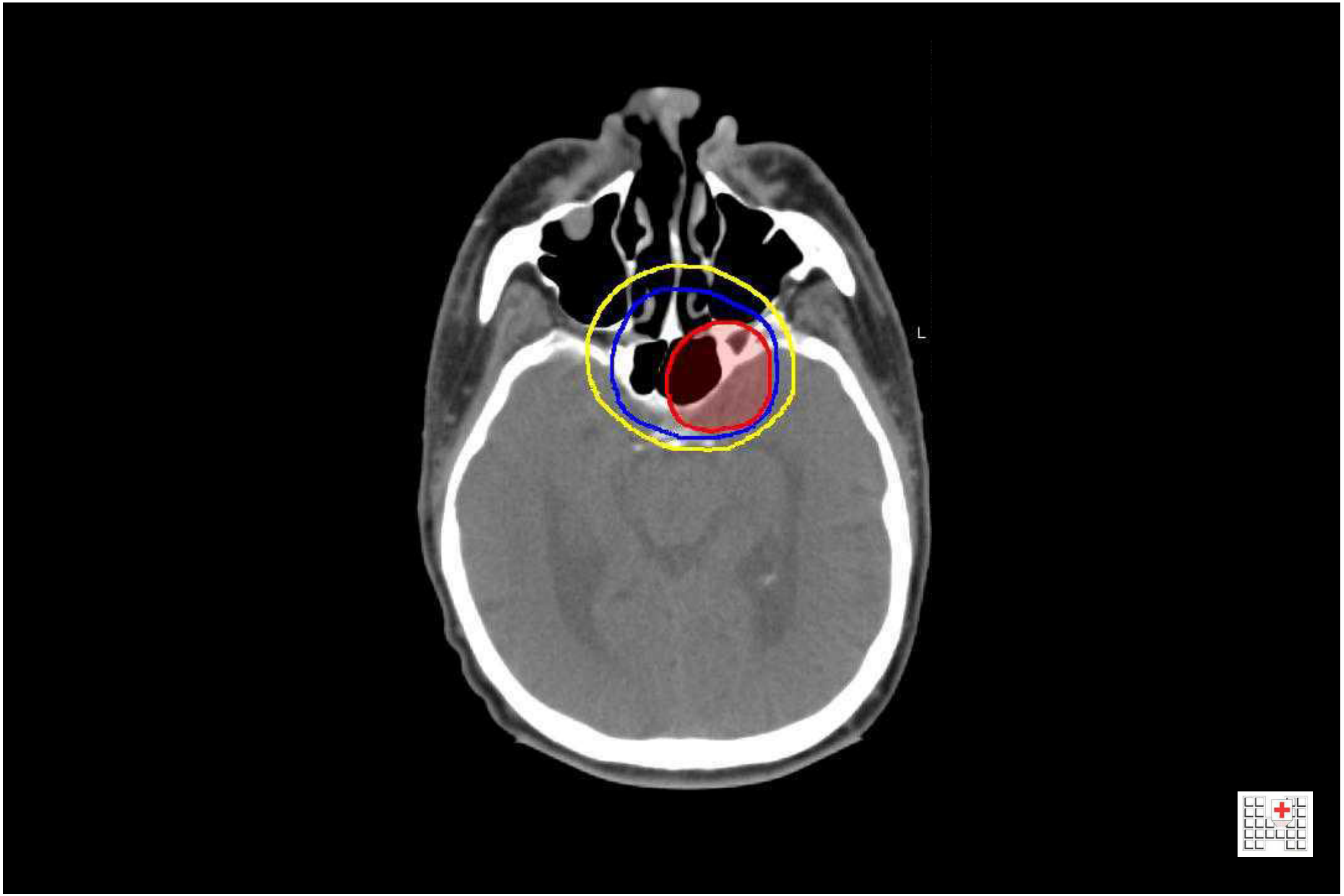
Int, 5-35%

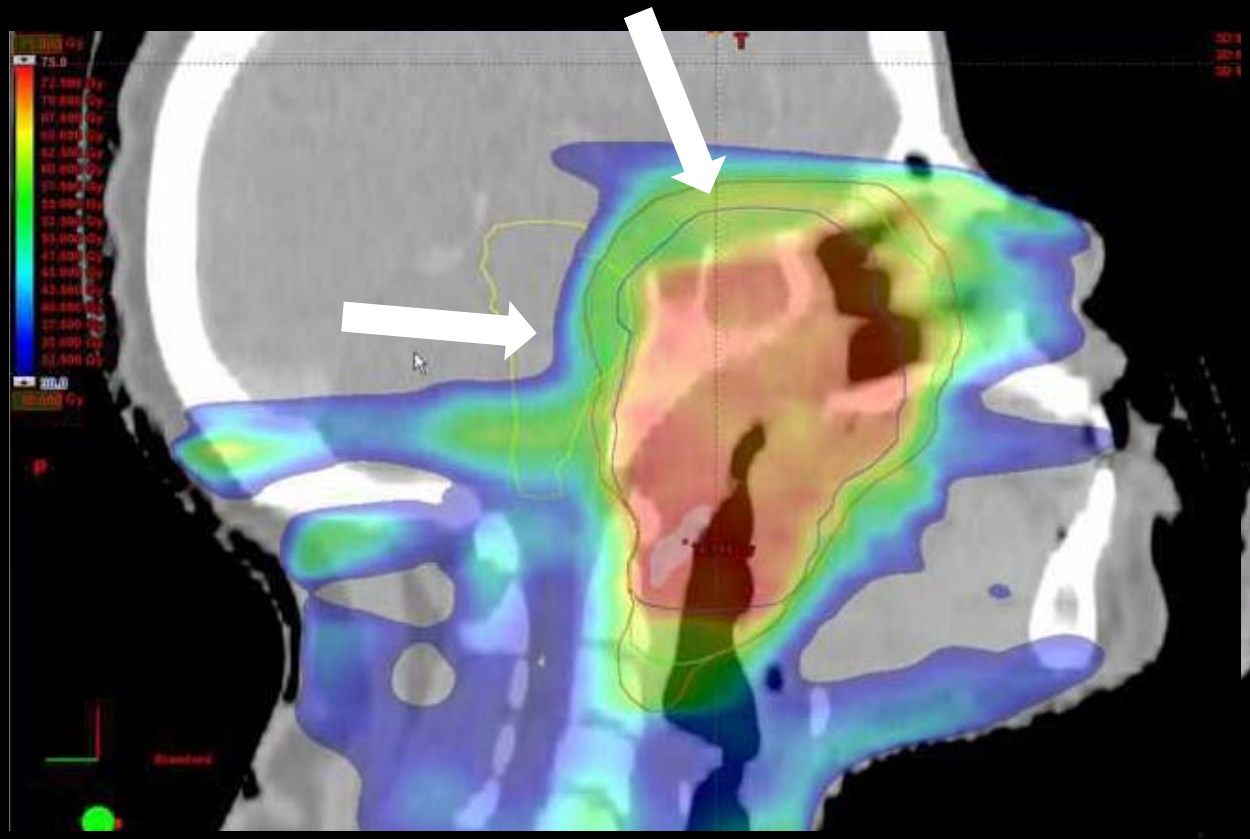
Low, <5%

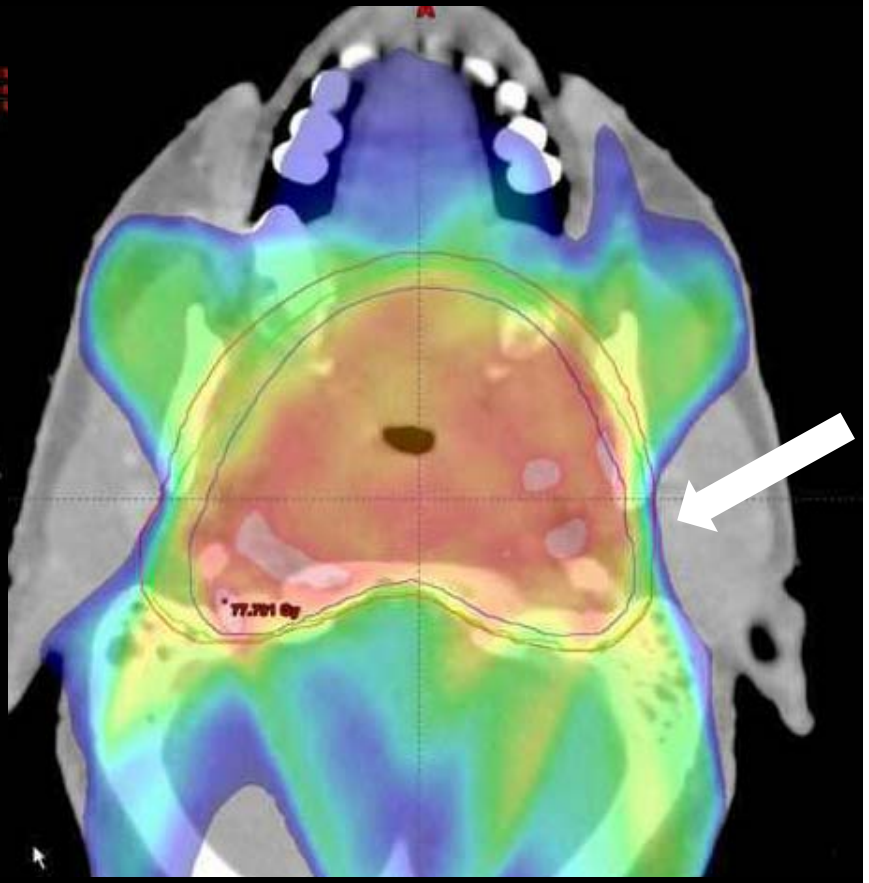
943 consecutive pts

Liang et al, IJROBP, 2009


S
3.41 mm


L





CTV_{HR}-T

No need to cover the pituitary fossa in T1

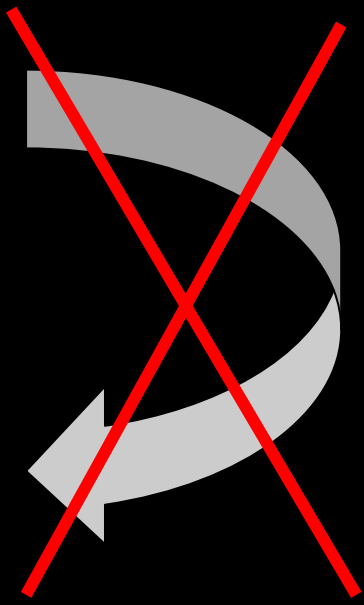
- 152 pts w/o erosion of base of skull and sphenoid sinus (CT), no extention to the nasal fossa or ethmoid sinus
- Random: w or without shielding of the pituitary fossa (sphenoid sinus)
- no difference in tumor control (p=0.39), but in neuroendocrine complications (p=0.006)

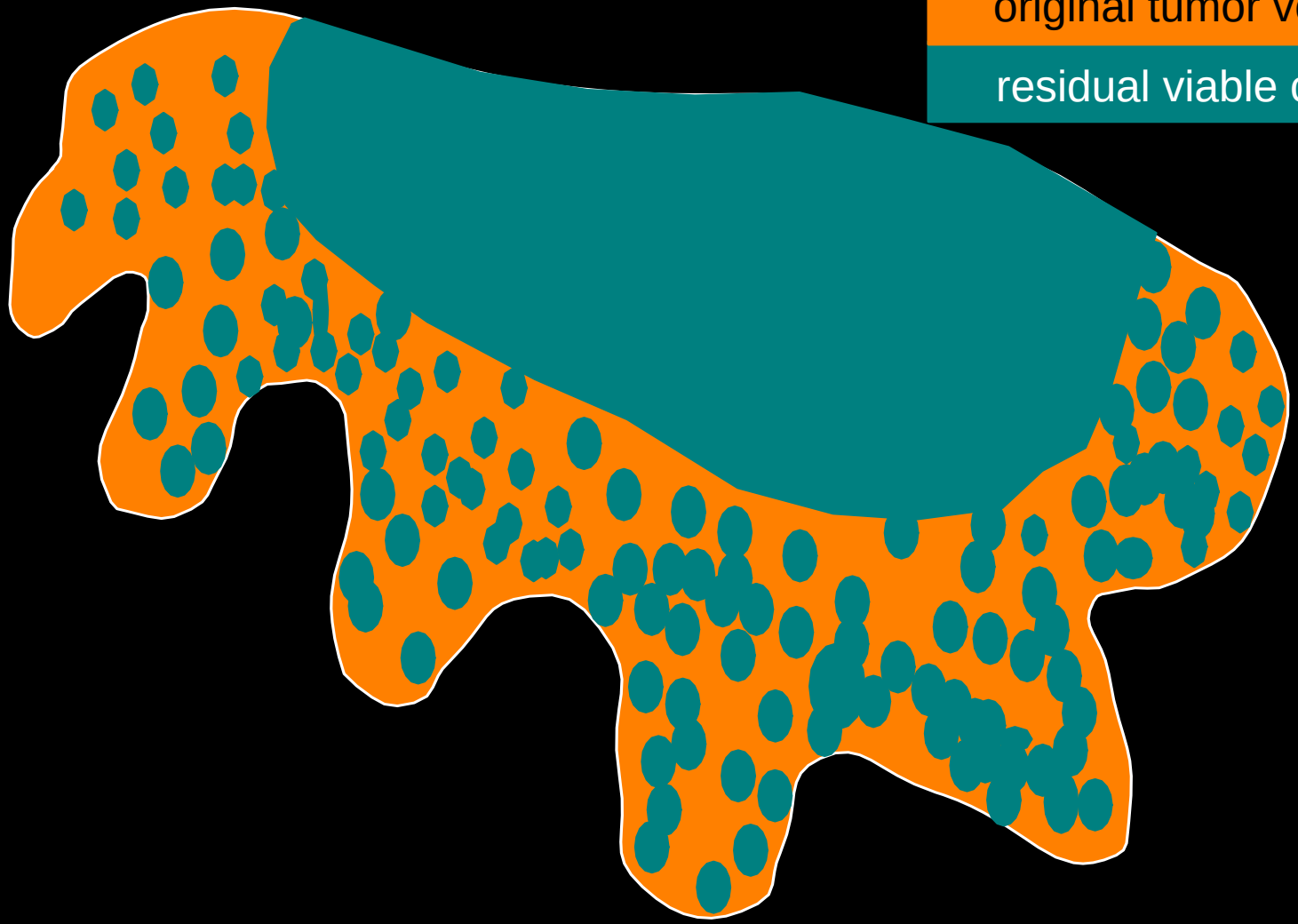
Sham et al, IJROBP 1994

Induction chemotherapy and dosimetric advantages at T

GTV→ CTV_{HD}

CTV_{HR}





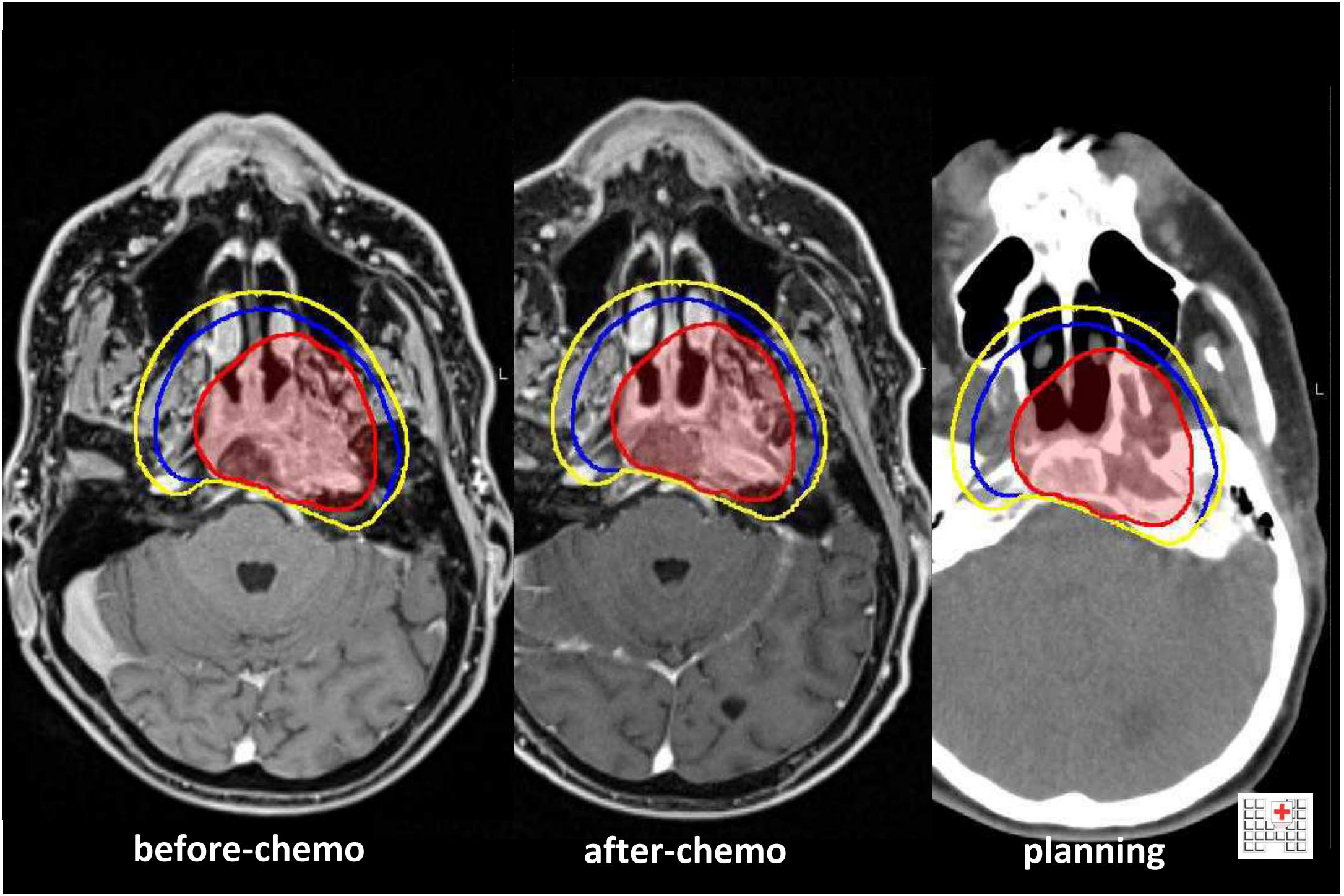
Osaki et al, 1994

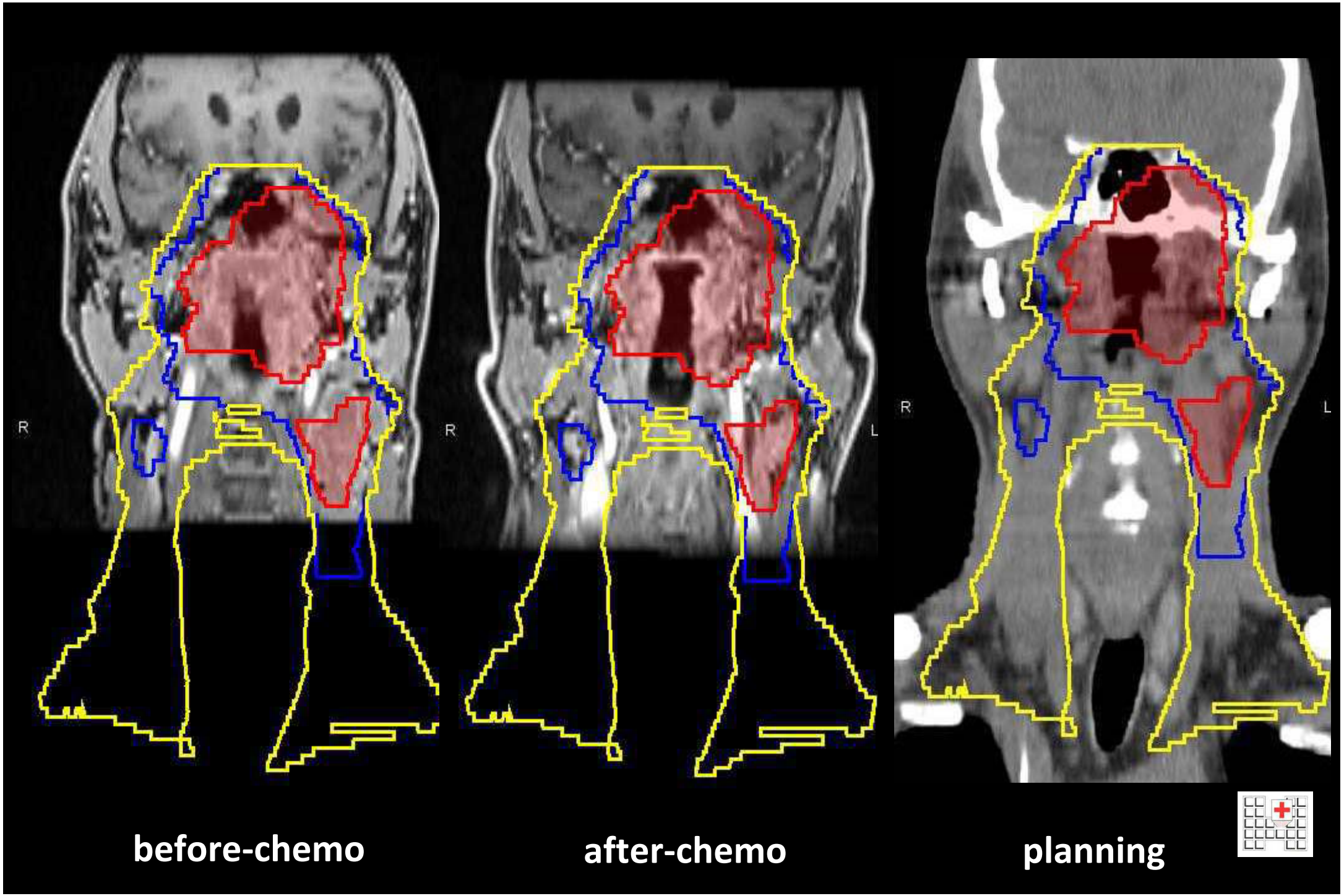
CLINICAL PRACTICE GUIDANCE FOR RADIOTHERAPY PLANNING AFTER INDUCTION CHEMOTHERAPY IN LOCOREGIONALLY ADVANCED HEAD-AND-NECK CANCER

JOSEPH K. SALAMA, M.D.,* ROBERT I. HADDAD, M.D.,† MERRIL S. KIES, M.D.,‡ PAUL M. BUSSE, M.D., PH.D.,§ LEI DONG, PH.D.,‡ DAVID M. BRIZEL, M.D.,¶ AVRAHAM EISBRUCH, M.D.,‖ ROY B. TISHLER, M.D., PH.D.,† ANDY M. TROTTI, M.D.,# AND ADAM S. GARDEN, M.D.‡

Results: Recommendations and guidelines emerged that emphasize up-front evaluation by all members of the head-and-neck management team, high-quality baseline and postinduction planning scans with the patient in the treatment position, the use of preinduction target volumes, and the use of full-dose RT, even in the face of a complete response.

Int. J. Radiation Oncology Biol. Phys., Vol. 75, No. 3, pp. 725–733, 2009


before-chemo
after-chemo
planning

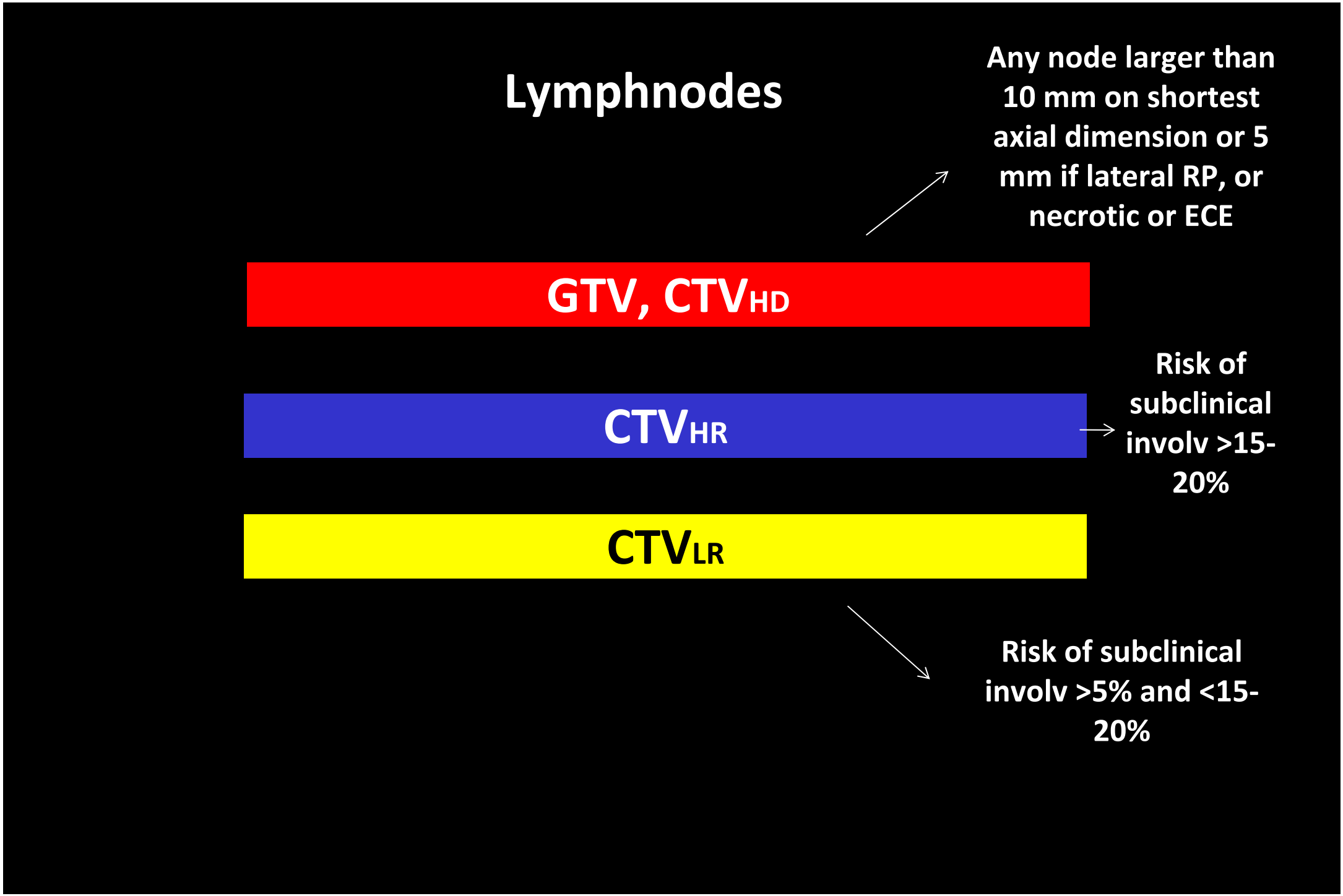

R
R
L
R
L
before-chemo
after-chemo
planning

Lymphnodes

GTV, CTV_{HD}

CTV_{HR}

CTV_{LR}

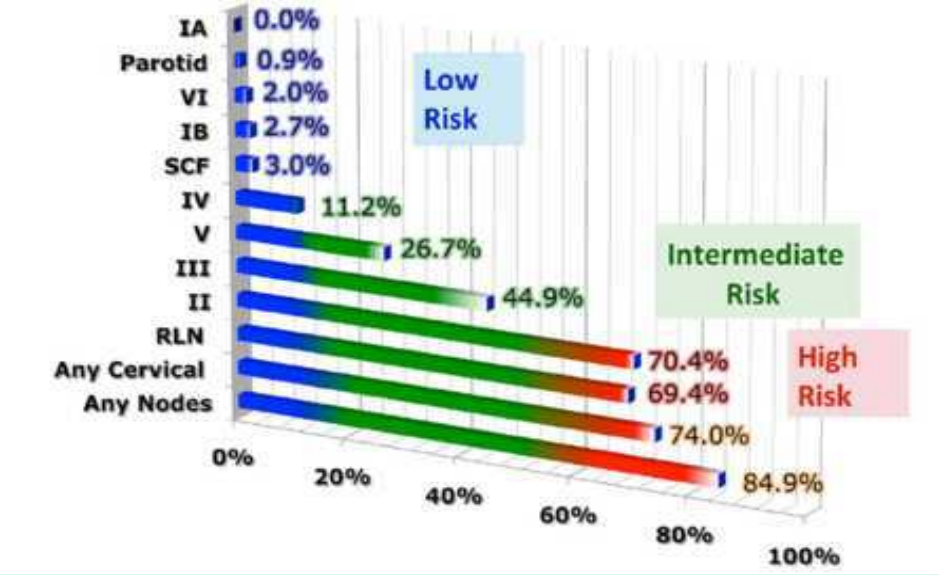

Lymphnodes
Any node larger than 10 mm on shortest axial dimension or 5 mm if lateral RP, or necrotic or ECE
GTV, CTVHD
CTVHR
Risk of subclinical involv >15-20%
CTVLR
Risk of subclinical involv >5% and <15-20%

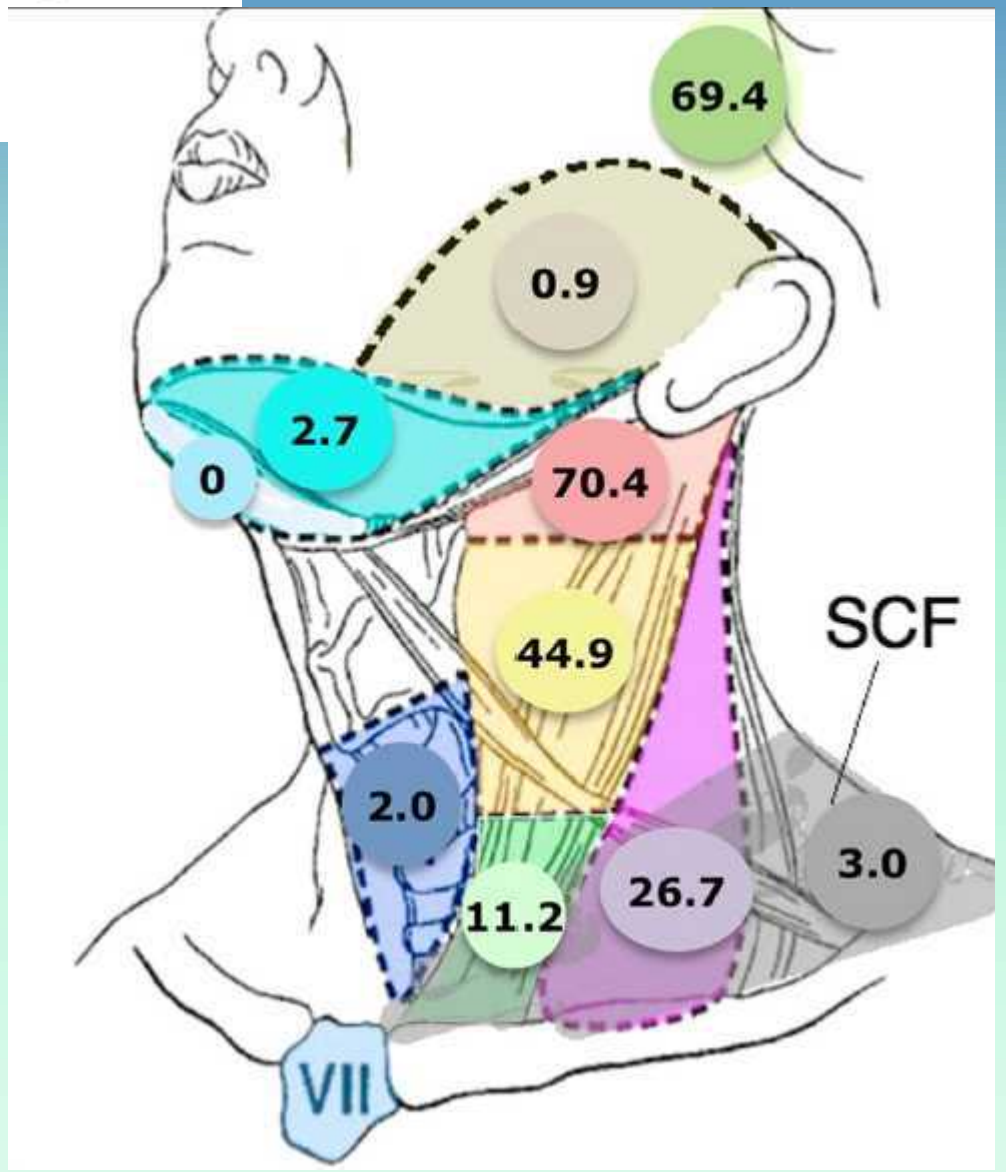
The risk of positive lymph nodes at diagnosis is NOT correlated to T stage

Patterns of regional lymph node metastasis of nasopharyngeal carcinoma: A meta-analysis of clinical evidence

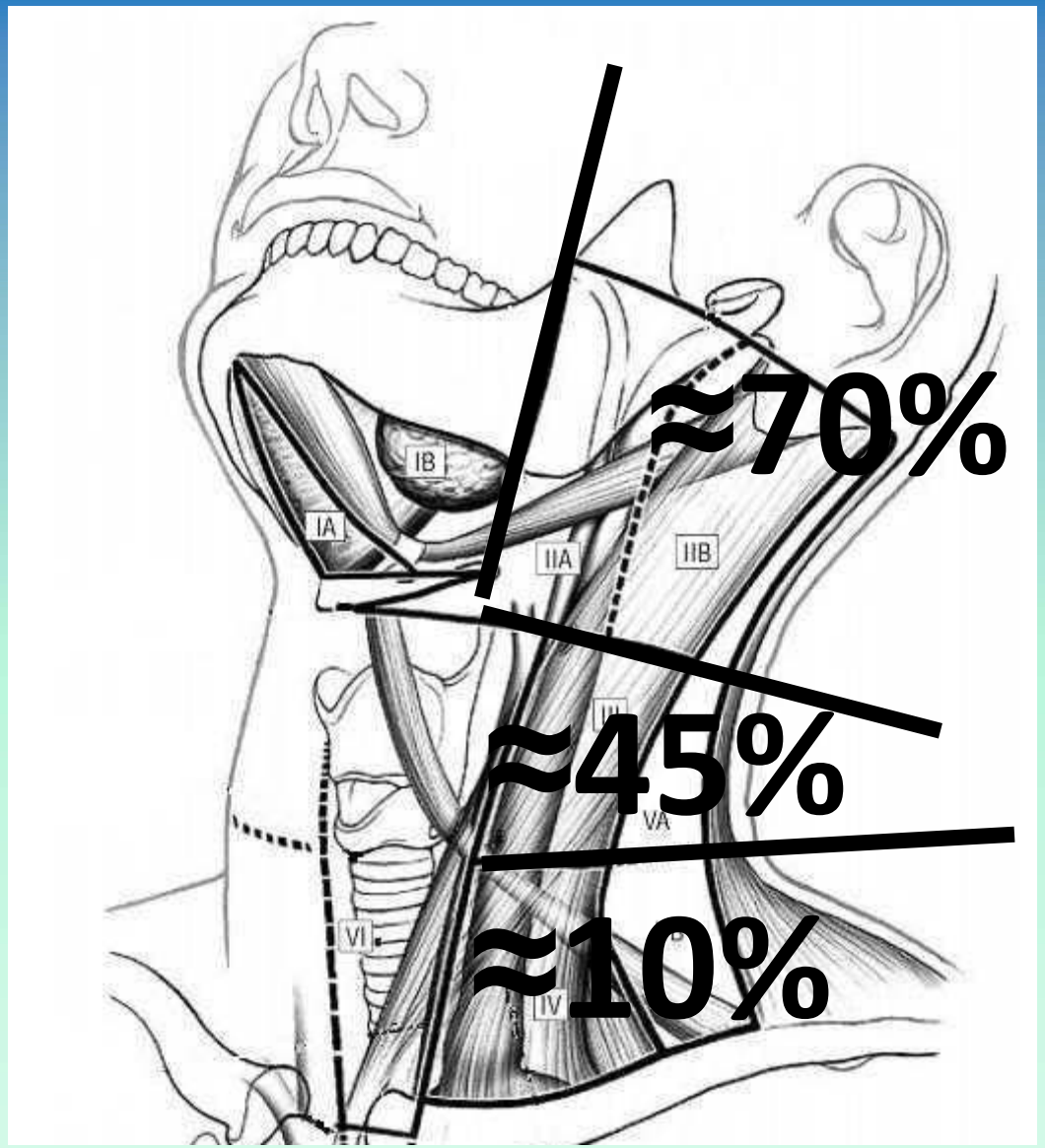
Francis CH Ho[1*], Ivan WK Tham[1], Arul Earnest[2], Khai Mun Lee[1] and Jiade J Lu[1*]

- **2920 pts staged w MRI**
- **85% were cN+ at dx**
- **lymphatic spread follows an orderly fashion:**





BMC Cancer 2012



out: PAROTID*, IA, VI

CTV$_{HR}$

CTV$_{LR}$

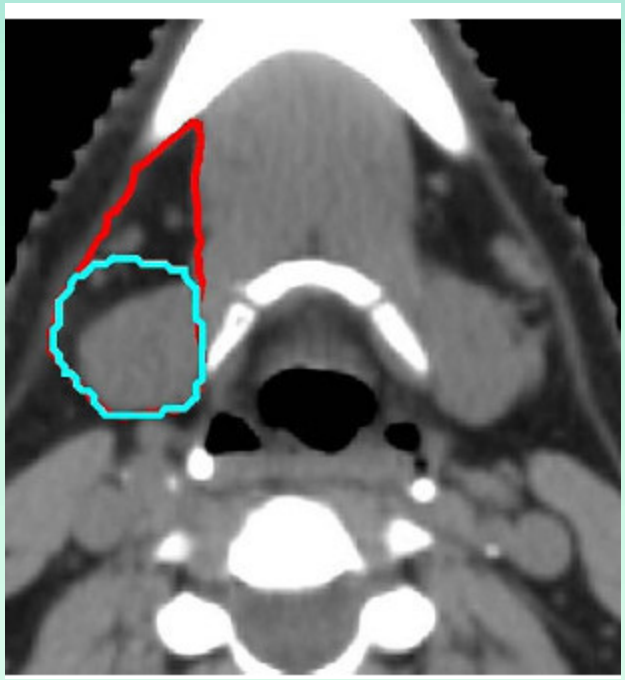
RTOG®
RADIATION THERAPY ONCOLOGY GROUP

Level IB

IB: used to be included (most of it)

RTOG: can be spared if patient is node negative. Level IB may also be spared or limited to the anterior border of the SMG in low risk cN+. Patients presenting with isolated RP nodes or isolated level IV nodes are considered low risk for level IB involvement. Treatment of level IB should be considered in cN0 patients with extensive involv of the hard palate, nasal cavity or maxillary antrum.

CTV_{LR}



Sanguineti et al, IJROBP 2009

Retropharyngeal nodes, RP

CTV$_{HR}$

- N1 in the current AJCC classification
- Need MRI
- never medial, lateral if 5 mm or larger in shortest axial
- Prevalence at dx:

		pts	Overall Prev	Prev in cN+	Skip	RP only in cN+
King et al, HN 2000	Prince of Wales, HK	150	72%	94%	6%	24%
Wang et al, IJROBP 2009	Fudan Un, Shanghai	618	63.4%	72%	28%	6.5%
Liu et al, IJROBP 2006	Sun Yat-sen Un Guangzhou	275	63.6%	81.4%	18.6%	18.6%
Tang et al, Cancer 2009	Sun Yat-sen Un Guangzhou	924	73.5%	86.4%	13.6%	24.7%

Retropharyngeal nodes, RP

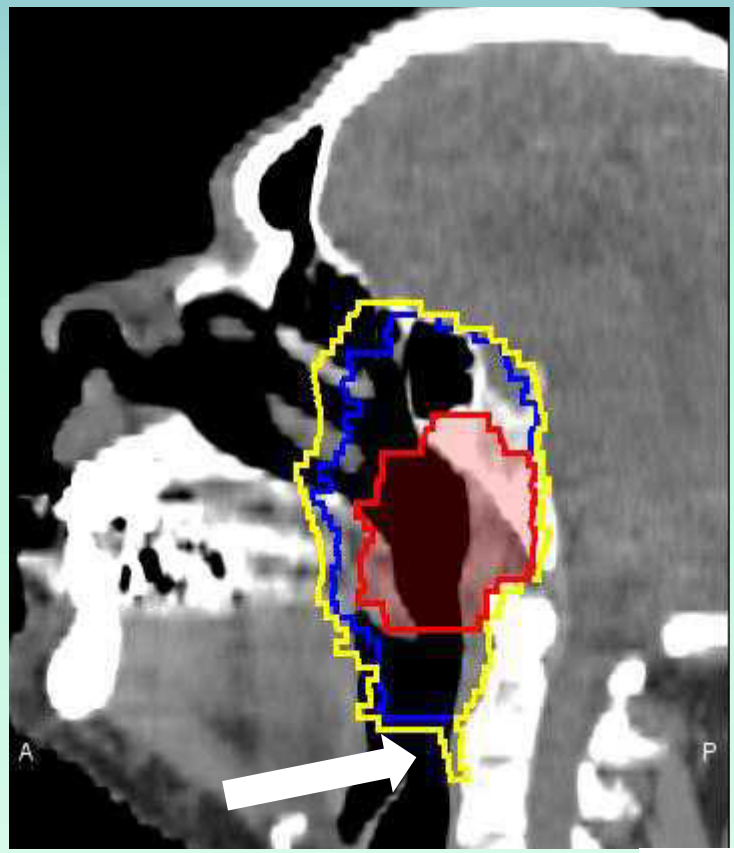
- **Location – INFERIOR/CAUDAL extent on MRI**

	King et al	Wang et al
Body C2	63%	35.7%
C2-C3	18.5%	
Body C3	5.5%	5%

Retropharyngeal nodes, RP

- Location – INFERIOR/CAUDAL extent on MRI

	King et al	Wang et al
Body C2	63%	35.7%
C2-C3	18.5%	
Body C3	5.5%	5%



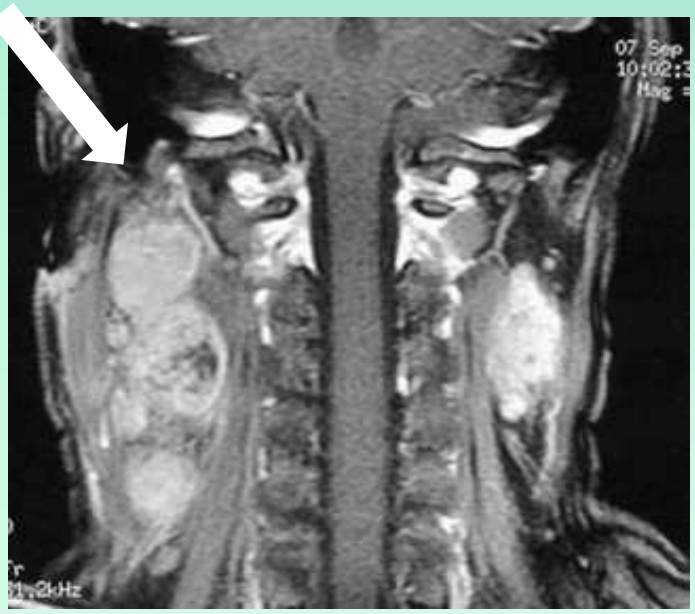
Level II nodes

CTV$_{HR}$

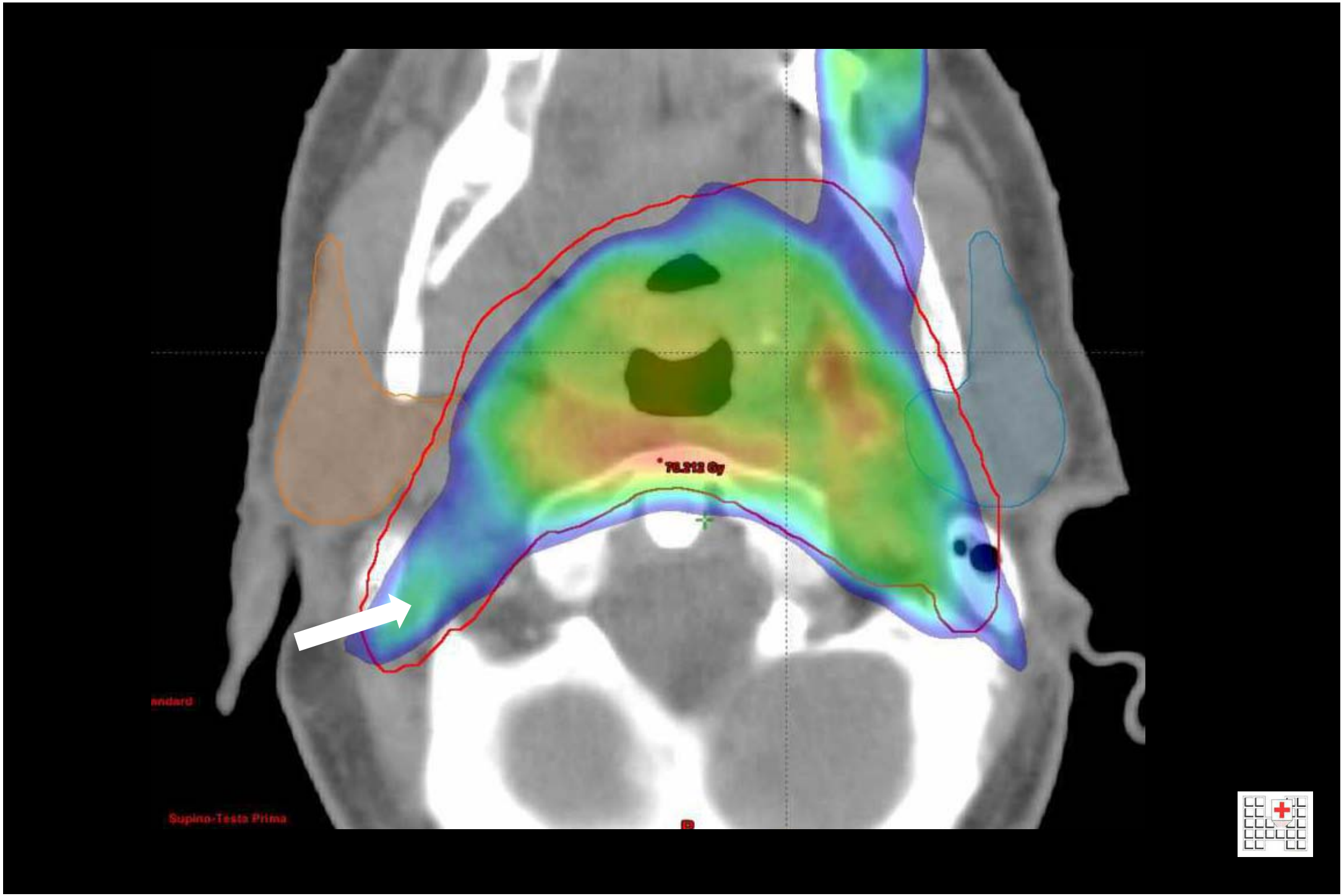
- **IIb most frequently involved nodes at dx**
- **not correlated to T ext or stage**
- **location – CRANIAL BORDER**

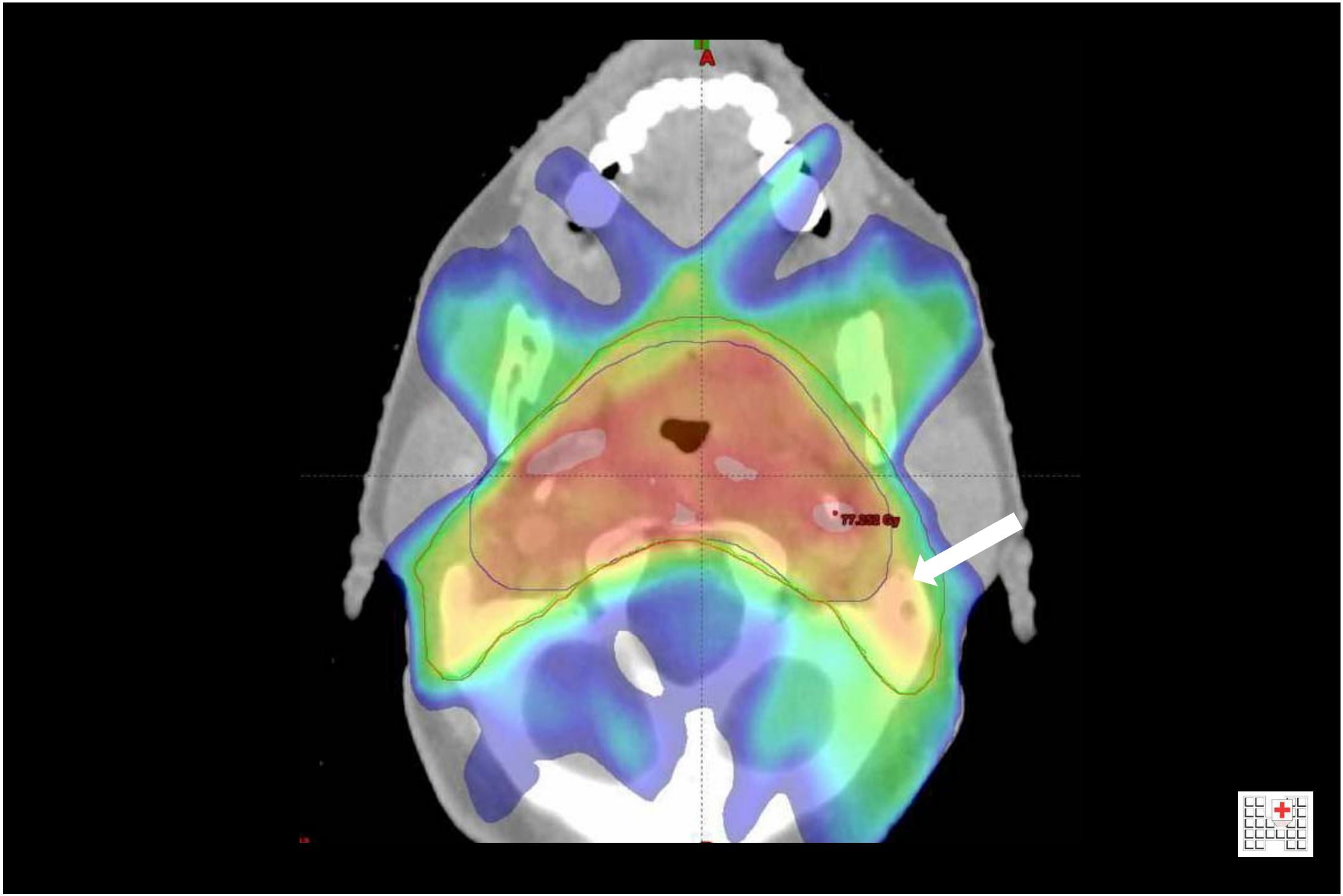
The cranial borders of metastatic level II node on MR imaging

Location on MR	Cranial border	
	Level IIb	Level IIa
Skull base	24 (5.1%)	0
1/2 of C1	112 (23.8%)	0
Caudal edge of C1	334 (71.1%)	326 (100%)

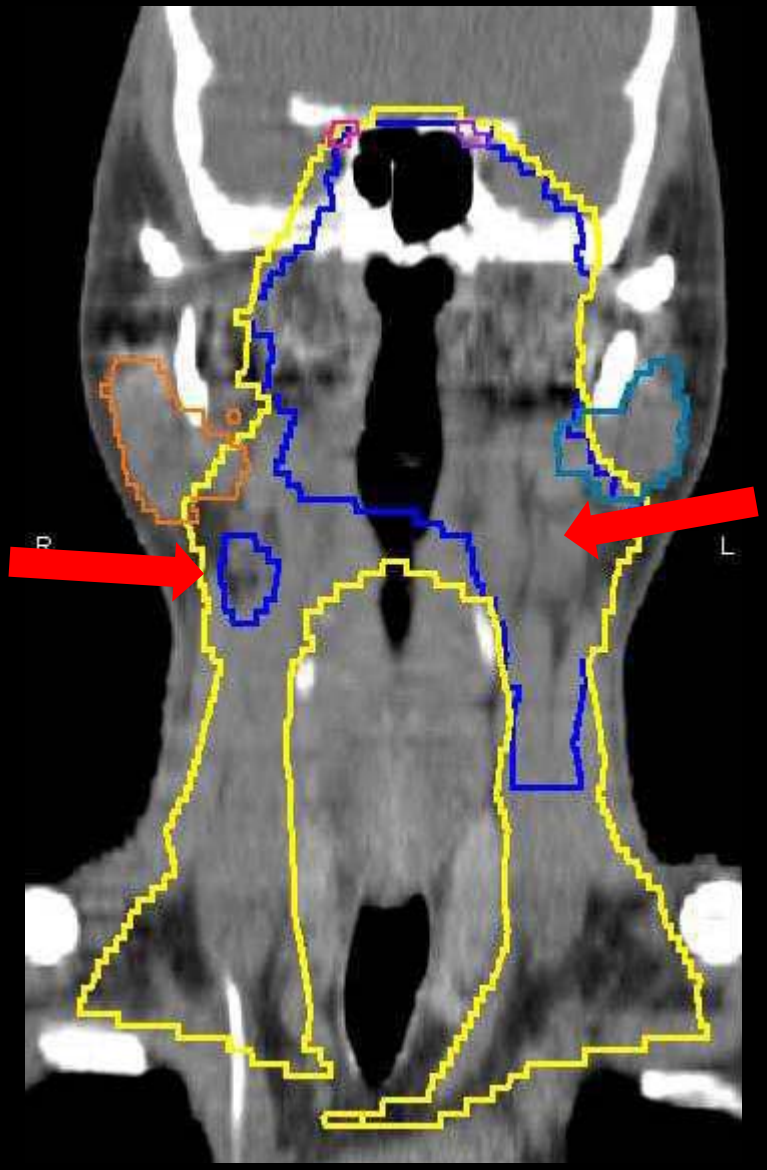


Wang et al, RO 2008

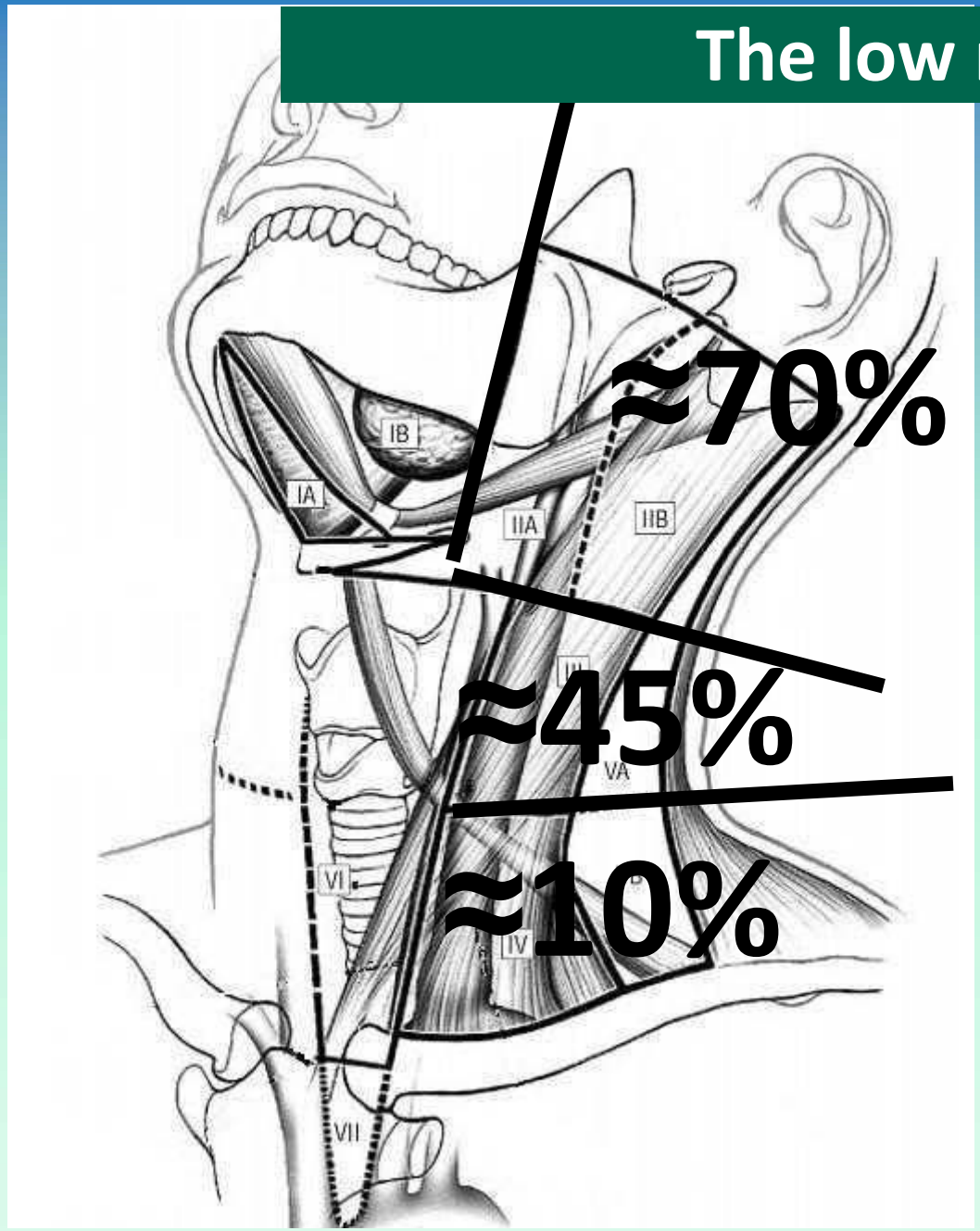

78.212 Gy
Supino-Testa Prima

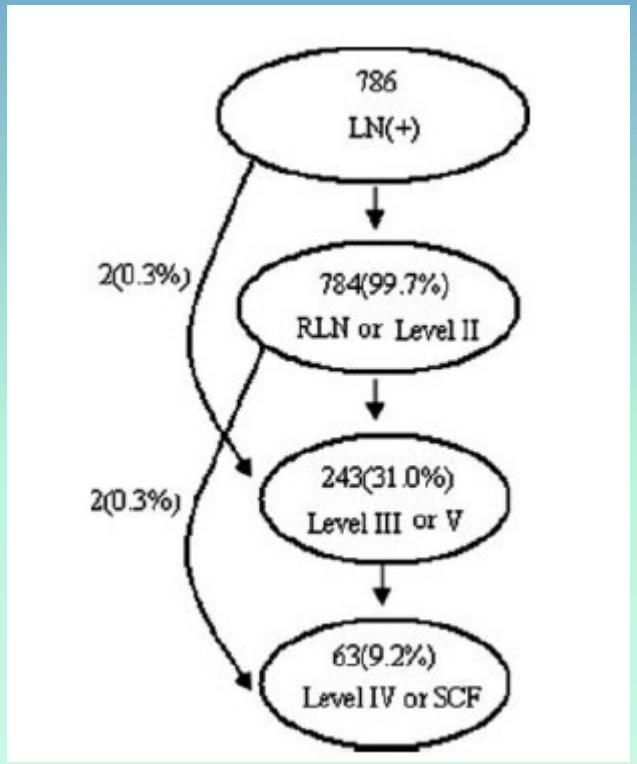

A
77.333 Gy

Which is the extension of CTV_{HR}?



The low neck

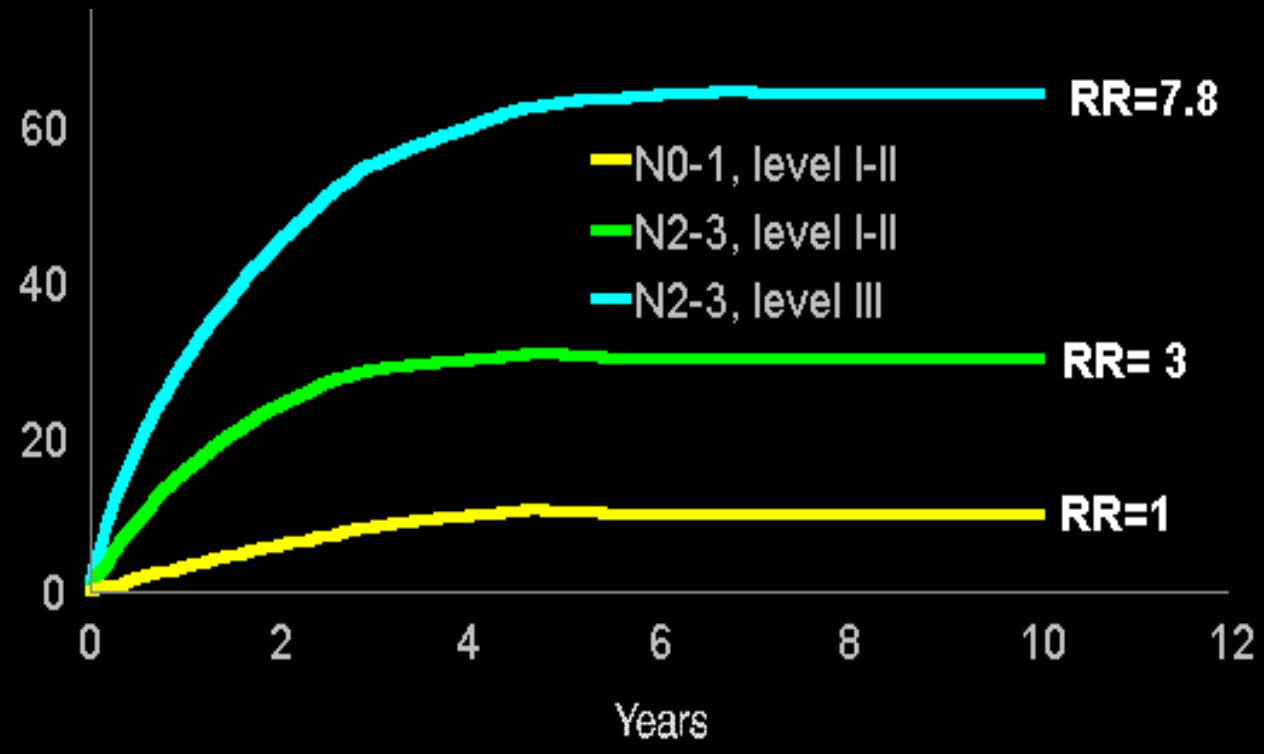


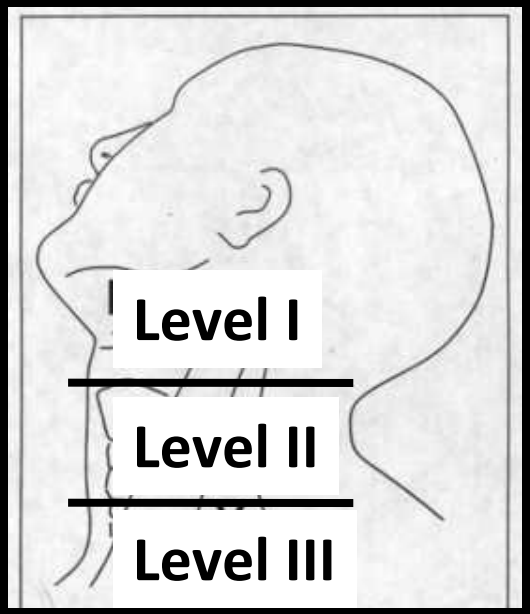


CTV$_{LR}$

Tang et al, Cancer 2009

Prognosis - DM rate by N stage and level





THE UNIVERSITY OF TEXAS MD ANDERSON CANCER CENTER

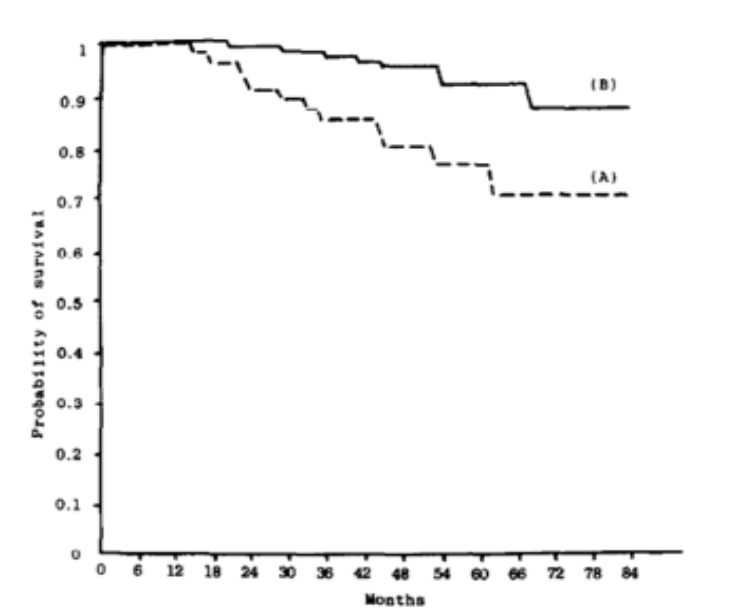
Geara et al, 1997

TREATMENT OF STAGE I NASOPHARYNGEAL CARCINOMA: ANALYSIS OF THE PATTERNS OF RELAPSE AND THE RESULTS OF WITHHOLDING ELECTIVE NECK IRRADIATION

ANNE W. M. LEE, F.R.C.R., JONATHAN S. T. SHAM, F.R.C.R., Y. F. POON, F.R.C.R. AND JOHN H. C. HO, M.D., D.SC., F.R.C.P., F.R.C.R. (D & T), F.R.C.R.A., F.A.C.R.

Institute of Radiology and Oncology, Medical and Health Department, Queen Elizabeth Hospital, Wylie Road, Kowloon, Hong Kong

- outcome of 196 pts w stage I NPC not electively in the neck;
- 53 pts (27%) subsequently failed in the neck, mostly upper neck
- nodal salvage rate was 81%
- however, OS was lower fr pts wh failed compared to pts who did nt fail in the neck due to a higher incidence of DM (20% vs 3%)

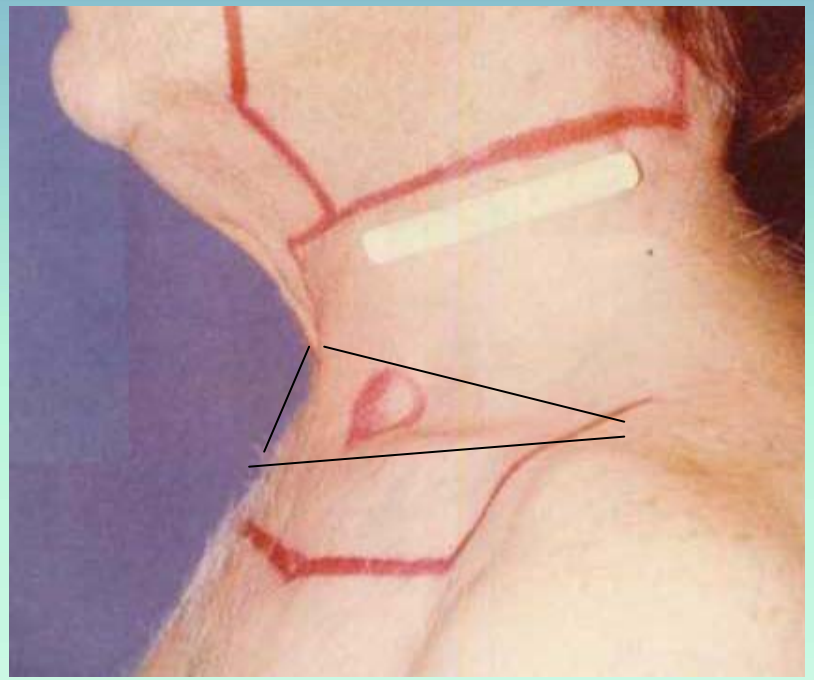


IJROBP, 1989

Supraclavicular Nodes

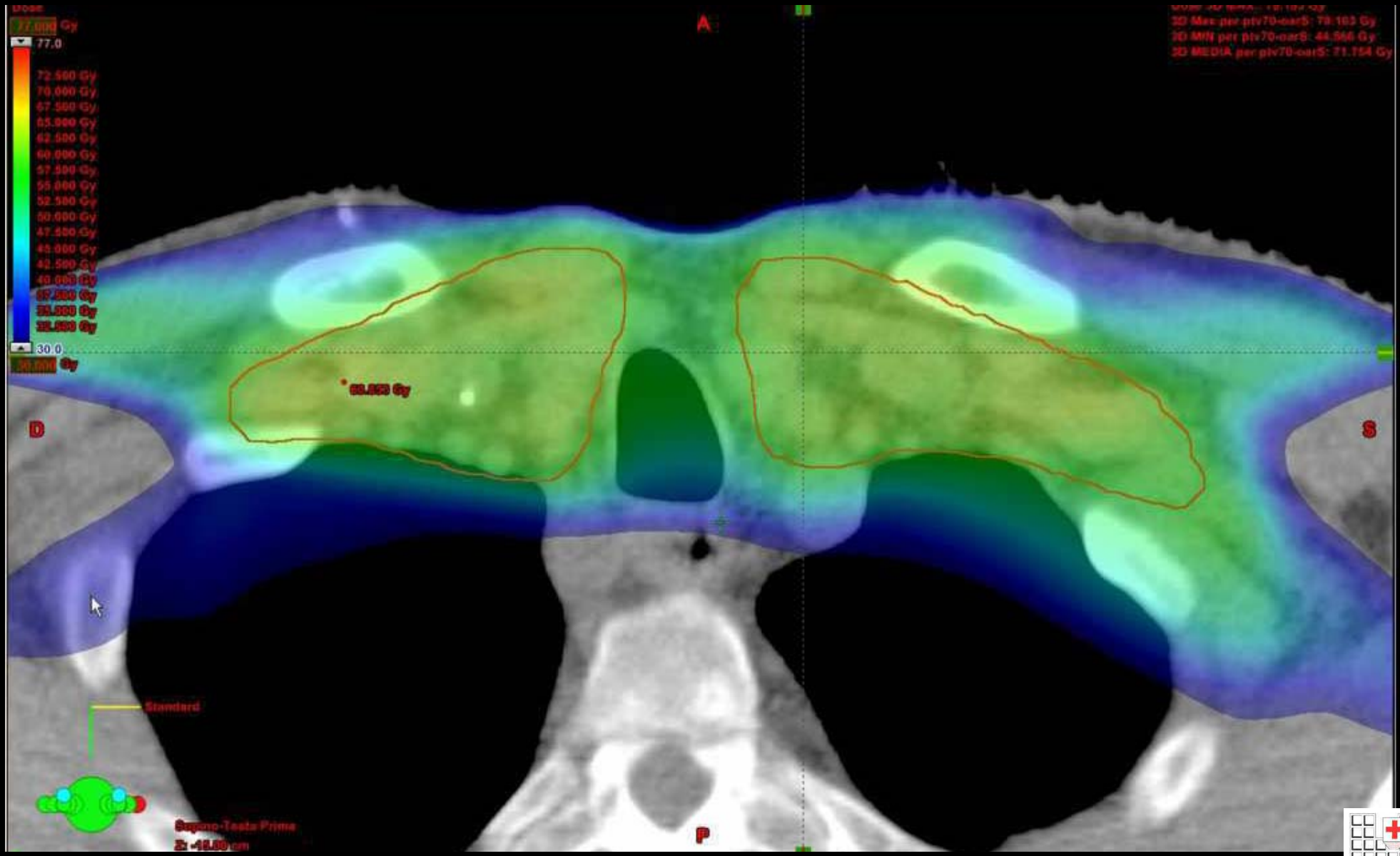
CTV$_{LR}$

- **Not in the ASTRO/ESTRO consensus atlas;**
- **'natural' caudal extension of both lvs IV and V;**
- **Ho's level III is defined by 3 points: 1. superior margin of the sternal end of the clavicle; 2. the superior margin of the lateral end of the clavicle; 3. the point where the neck meets the shoulder (AJCC, 2010).**
- **In the atlas for N+:**



Space	Cranial	Caudal	Anterior	Posterior	Lateral	Medial
Supraclavicular fossa	Lower border of level IV/Vb	Sterno-clavicular joint	SCM m.; skin; clavicle	Anterior edge of posterior scalenus m.	Lateral edge of posterior scalenus m.	Thyroid gland/ trachea

Gregoire et al, 2006


A
D
S
P
77.0
72.500 Gy
70.000 Gy
67.500 Gy
65.000 Gy
62.500 Gy
60.000 Gy
57.500 Gy
55.000 Gy
52.500 Gy
50.000 Gy
47.500 Gy
45.000 Gy
42.500 Gy
30.0
Standard

Conclusions

- Contouring has been an issue for >15 yrs, but standardization is doable (following guidelines);
- MRI is mandatory for T(N) staging and contouring;
- Careful (& multiD) evaluation of diagnostic imaging is essential;
- Distinction of targets according to their risk of containing disease helps to maximize the therapeutic index