FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

IMPOSTAZIONE RADIOTERAPICA NEI TUMORI DEL RINOFARINGE

Volumi bersaglio tumorali

Dott.ssa Ester Orlandi **Dott.ssa Eva Iannacone**

27 Maggio 2013, Roma Isola Tiberina

Background

L'IMRT è attualmete la tecnica radioterapica di elezione per il trattamento del carcinoma rinofaringeo.

IMRT vs 2DRT

• Nella malattia in **stadio iniziale** (T1/T2N0-N1) migliora significativamente il LRC, la xerostomia e la QOL

• Nella malattia **localmente avanzata** migliora il LRC e alcuni profili di tossicità (xerostomia, ipoacusia)

Pow E.H.N., Int J Radiat Oncol Biol Phys , 2006
Lee AW, Int J Radiat Oncol Biol Phys, 2009
Kam MK, JCO, 2007

Table 1 Results from series treating NPC with IMRT with or without chemotherapy

18 Studi+1 (INT)

Study	Year	Stage	No.	Median follow-up (months)	Time point (years)	Local control rate (%)	Regional control rate (%)	Distant met-free rate (%)	OS (%)
Lee et al. [19] (UCSF)	2002	All	67	31	4	97	98	66	88
Kwong et al. [20] (Hong Kong)	2004	T1 N0–1[a]	33	24	3	100	92	100	100
Kam [21] (Hong Kong)	2004	All	63	29	3	92	98	79	90
Wolden et al. [22] (MSKCC)	2006	All	74	35	3	91	93	78	83
Kwong et al. [23] (Hong Kong)	2006	III–IVB[a]	50	25	2	96	NA	94	92
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Tham et al. [32] (Singapore)	2009	All	195	37	3	90	NA	89	94
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Su et al. [31] (China)	2012	I–IIB[b]	198	51	5	97	98	98	NA
Orlandi et al. (INT, Italy)	2013	80%IIII-IV	106	43	5	88	88	NA	82

Wang T.J.C. J Radiat Oncol , 2012

Background

• Recentemente, lo studio di fase II **RTOG 0225** ha dimostrato la fattibilità della IMRT per il trattamento del carcinoma rinofaringeo in un setting multististuzionale

• **Mancanza di consenso**
relativamente a tutte le fasi del *treatment planning*

➢ definizione e contornazione dei **volumi bersaglio tumorali** (GTV; High Risk CTV)

➢ **prescrizioni di dose**

Fleury B, Cancer Radiother, 2010
Wang T.J.C. J Radiat Oncol , 2012

Background

- GTV (T e N)
- HR-CTV : High Risk CTV
- IR–CTV: Intermediate Risk CTV
- LR-CTV : Low Risk CTV

- PTVs

GTV

- **Esame clinico/endoscopico**

- **MRI con mdc:** imaging di riferimento per valutare invasione locale e linfonodi retrofaringei (RPN)

- **FDG-PET:** accuratezza diagnostica simile a MRI per il nodal staging, eccetto per RPN

- **TC centratura** con o senza mdc, pz con capo lievemente iperesteso, pilot da vertice a metà corpo sternale, spessore - 3 mm

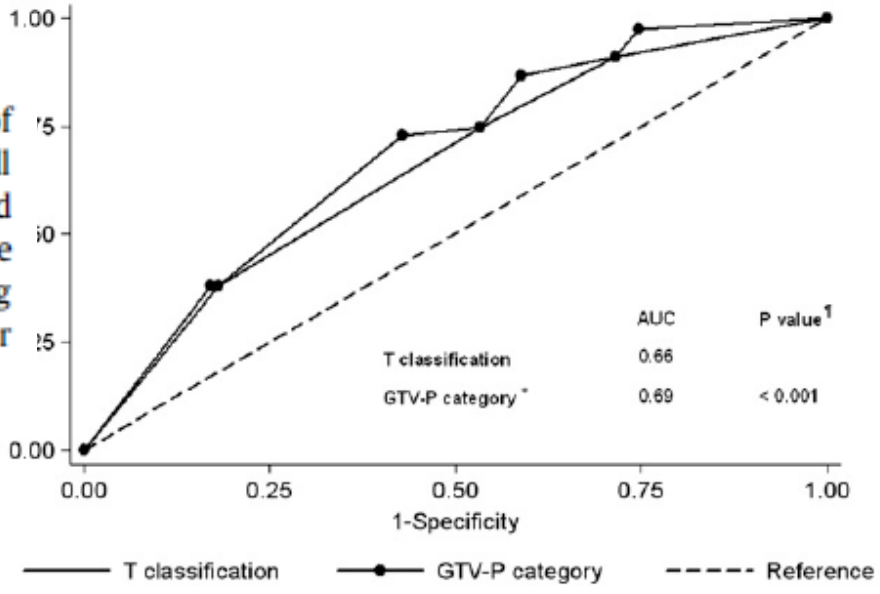
- **Fusione/Coregistazione** TC-MRI/TC-PET

Manavis J, 2005
King AD, Br J Radiol, 2008
Nishioka T , Int J Rad Oncol Biol Phys, 2002
Ng SH, Eur J Nucl Med Mol Imaging, 2004

Is primary tumor volume still a prognostic factor in intensity modulated radiation therapy for nasopharyngeal carcinoma?

Endpoint	Variable	HR	HR (95% CI)	*P*-value
*Early T1-T2 patients**				
Disease-free survival	GTV-P (⩾19 ml vs.<19 ml)	7.678	3.735–15.785	<0.001
	N classification* (N1–3 vs. N0)	2.562	0.884–7.429	0.083
Overall survival	GTV-P (⩾19 ml vs.<19 ml)	8.714	3.613–21. 016	<0.001
	N classification* (N1–3 vs. N0)	3.866	0.894–16.721	0. 070
Local relapse-free survival	GTV-P (⩾19 ml vs.<19 ml)	NS		
Distant metastasis-free survival	GTV-P (⩾19 ml vs.<19 ml)	9.636	4.071–22.812	<0.001
*Advanced T3-T4 patients**				
Disease-free survival	GTV-P (⩾19 ml vs.<19 ml)	7.256	2.284–23.057	0.001
	Age (⩾45 vs.<45 years)	1.613	1.118–2.328	0.011
	N classification* (N1–3 vs. N0)	1.877	1.049–3.359	0.034
Overall survival	GTV-P (⩾19 ml vs.<19 ml)	5.725	1.804–18.172	0.003
	Age (⩾45 vs.<45 years)	2.146	1.378–3.342	0.001
Local relapse-free survival	GTV-P (⩾19 ml vs.<19 ml)	NS		
Distant metastasis-free survival	GTV-P (⩾19 ml vs.<19 ml)	6.961	1.692–28.634	0.007
	N classification* (N1–3 vs. N0)	2.208	1.014–4.811	0.046

ROC curves were used to compare the prognostic validity of adding GTV-P to the T classification of TNM staging system. In all patients ($n = 694$), the AUC was 0.66 for T classification alone and 0.69 ($P < 0.001$) when GTV-P (<19 and ⩾19 ml) was added to the T classification (Fig. 2). The results revealed that, in predicting outcomes, the addition of GTV-P to T classification was superior to T classification alone.



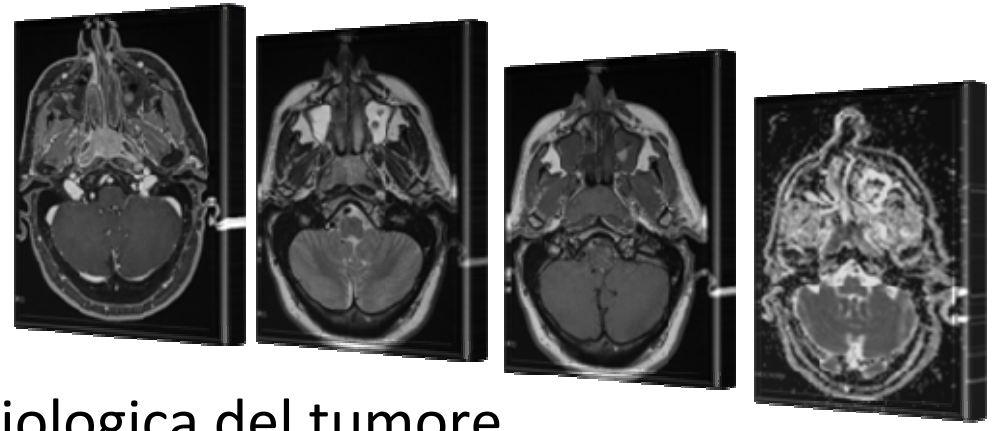
Guo R, RadiotOncol , 2012

GTV –T/MRI

Sequenze:

- **T1 e T2** basali e dopo mdc

  3D ultra fast gradient echo- fat-sat (es. VIBE , THRIVE …)



Studi preliminari

- **Diffusion (DWI)**

- caratterizzazione biologica del tumore
- diagnosi differenziale con altre neoplasie in aree endemiche
- valutazione della risposta e tossicità dopo RT

Manavis J, Clin Imaging, 2005

GTV –N/MRI

Criteri diagnostici per metastasi linfonodali:

- **Linfonodi retrofaringei (RPN)**

- Diametro assiale minimo (MID) ≥ 5 mm per i RPN laterali
- Qualsiasi dimensione per i RPN mediali

- **Linfonodi Cervicali**

- MID ≥ 11 mm al II-III livello o ≥ 10 mm se altri livelli
- Qualsiasi dimensione con necrosi centrale
- Raggruppamento linfonodale con presenza di 3 o più LNs contigui o confluenti, ognuno con MID di 8-10 mm
- Qualsiasi dimensione con estensione extracapsulare (ECS)

Tang L, 2008
Van den Brekel MW, 1990

GTV T-N/PET

- Esistenza di correlazione SUV max e prognosi

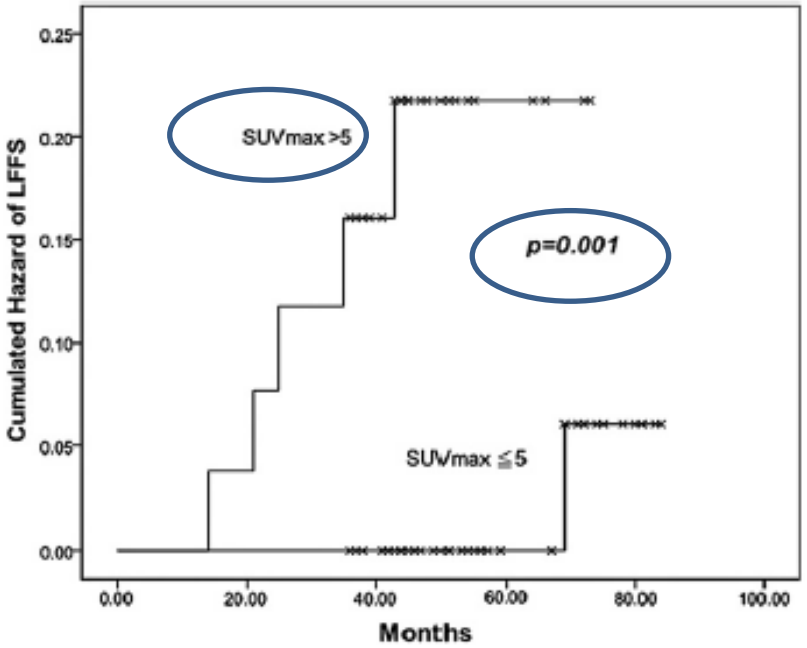


Fig. 2. The cumulative hazards of 5-year local failure-free survival (LFFS) for maximum standardized uptake value (SUVmax) ≤5 and >5 ($p = 0.001$).

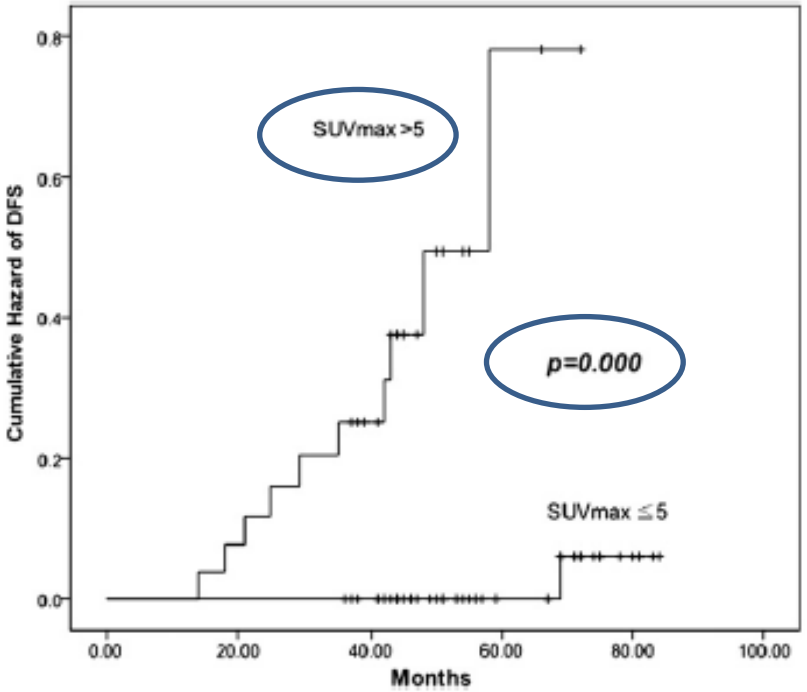


Fig. 3. The cumulative hazards of 5-year disease-free survival (DFS) for maximum standardized uptake value (SUVmax) ≤5 and >5 ($p = 0.000$).

- Identificati cut-off di SUV max variabili (2.5-10), piu elevati per T rispetto a N

Liu WS, Int j Rad Oncol Biol Phys, 2012

GTV, High Risk-CTV, Intermediate Risk-CTV

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Wang T.J.C. J Radiat Oncol , 2012

GTV / MR-PET

- **Metodiche di immagine utilizzate per la definizione del GTV**

➢ Tutti gli autori utilizzano la **RM** pretrattamento
(14 /19 in più del 95% dei pazienti)

➢ La **PET** è stata utilizzata in 8 studi ➡ **7** **+ 1 (INT)**

➢ Le immagini di PET o RM sono state **coregistrate o fuse** con la CT di centratura solo in 11 studi ➡ **10** **+ 1 (INT)**

"The use of MRI is mandatory"

Wang TJC, J Radiat Oncol , 2012

GTV / MR-PET

- **Definizione e contornamento del GTV**

Kwong et al.

- GTV = "macroscopic tumor and the whole nasopharynx, including bilateral Eustachian cushions and prevertebral muscles" *Cancer , 2004*

- GTV = "whole nasopharynx, tumor extending outside the nasopharynx, any skull base erosion, and intracranial disease as well as enlarged neck nodes" *Int J Radiat Oncol Biol Phys,* 2006

➢ Ogni **N** di dmax **> 1 cm** o con **centro necrotico** ➡ **4/19**

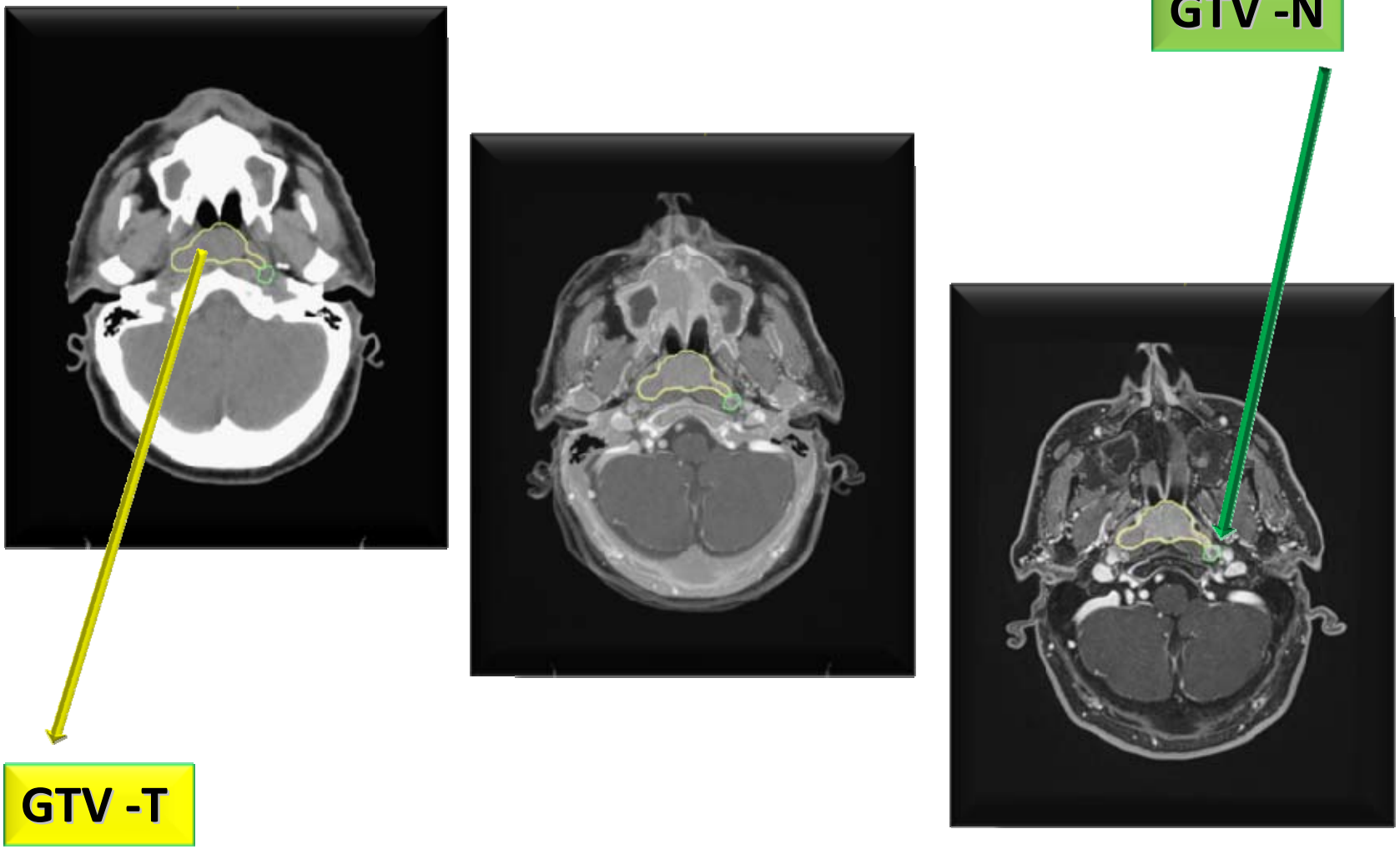
➢ Ogni **N coinvolto** (criterio non specificato) ➡ **14** **+1 (INT)**

(non distinzione tra GTV-T e GTV- N)

"In general, all lymph nodes that are PET positive or greater than 1 cm in short axis should receive definitive treatment"

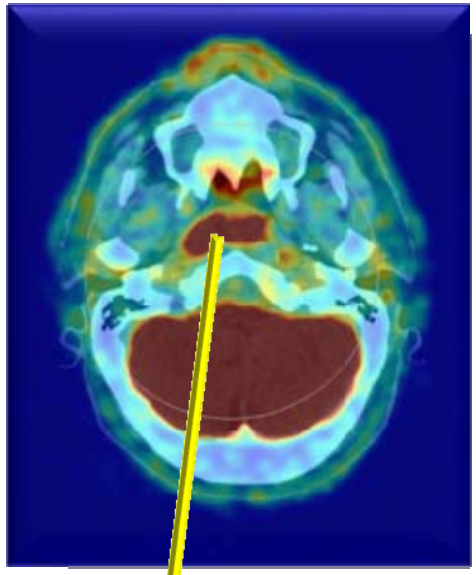
Wang TJC, J Radiat Oncol , 2012

GTV / MR

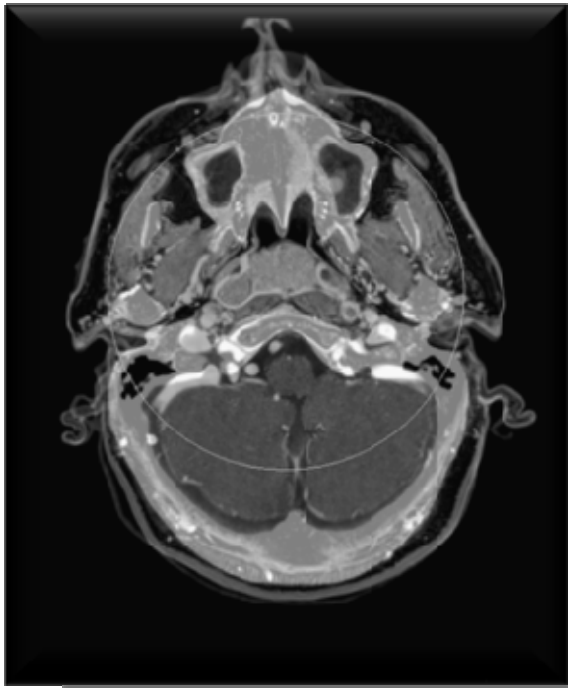


INT

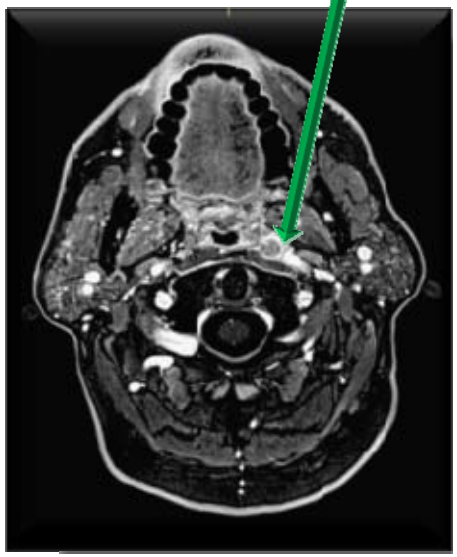
GTV /RMN/PET



GTV -T



GTV -N



INT

High Risk CTV (≥70 Gy)

- **La definizione dell'HR-CTV varia ancor più del GTV:**

➢ **HR-CTV = GTV + margine anatomico:**

1cm (3/19, ≥ 0.5 cm (8/19), ≥ 0,2cm (1/19)

➢ **HR-CTV = nasofaringe** (3/19)

➢ ~~**HR-CTV**~~ **= PTV = GTV + 1cm** (2/19)

➢ In 7 Studi il margine GTV-CTV è stato **ridotto posteriormente** fino a **1mm** quando il CTV risultava vicino alle strutture critiche (es. trono encefalico).

"A margin of 0,5-1 cm around GTV is generally adopted and recommended with an optional posterior margin reduction of 0,1-0,5cm"

Wang TJC, J Radiat Oncol , 2012

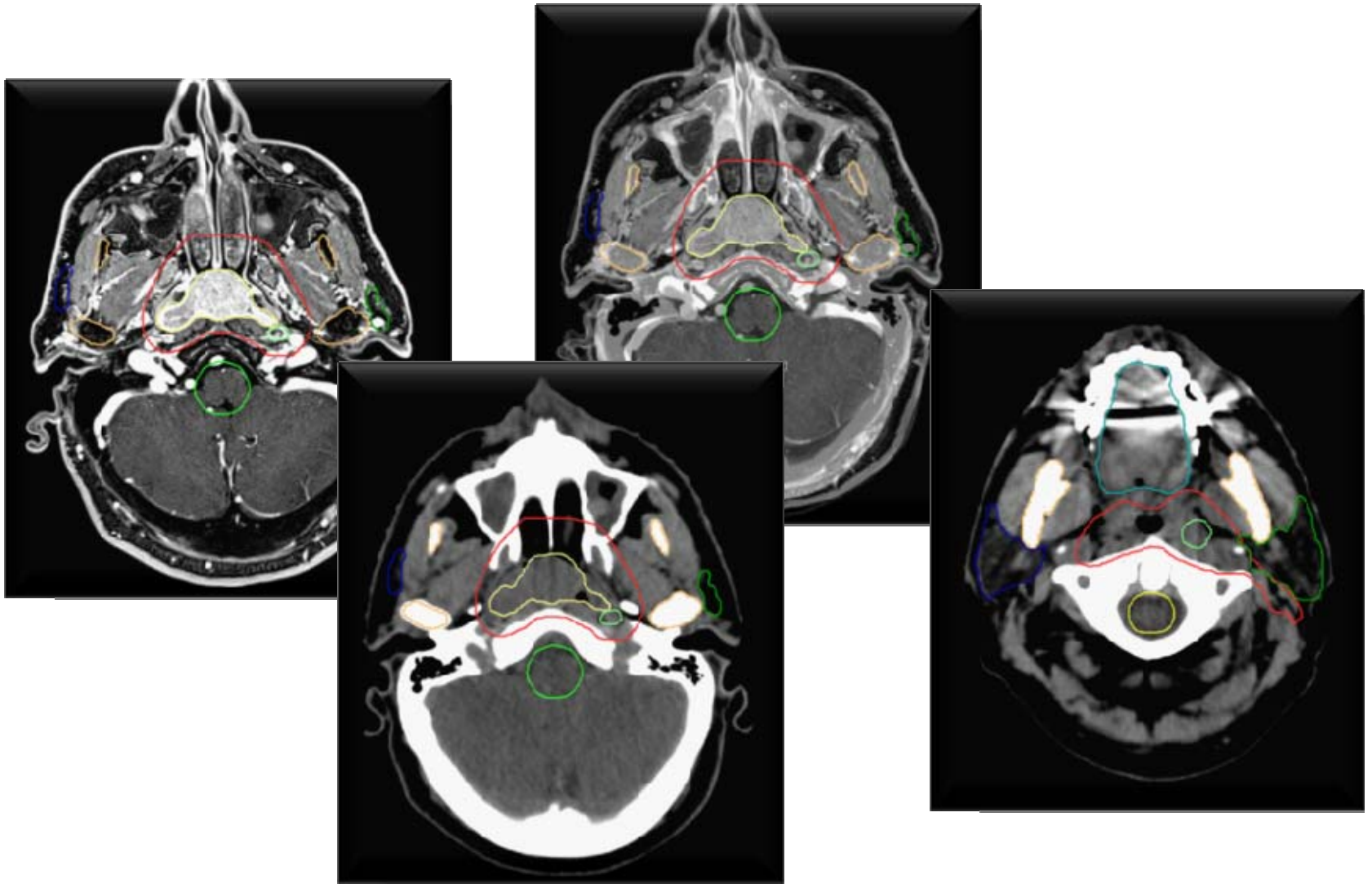
High Risk CTV (≥70 Gy)

In INT l' HR-CTV comprende:

- **GTV T /N** più una espansione volumetrica ed anatomica da **0.5 a 2.5 cm**
  (In molti casi l'intero Rinofaringe e i livelli linfonodali negativi adiacenti ai livelli coinvolti)

- **Nei pazienti T3/T4:**
  clivus, base cranica, forami, seno sfenoidale e cavernoso, muscoli paravertebrali.

High Risk CTV (≥70 Gy)



INT

Intermediate Risk CTV (60-68 Gy)

- **In generale nell'IR- CTV vengono inclusi:**

il clivus, il basicranio, il seno sfenoidale inferiore, il seno cavernoso, la fossa pterigoidea, lo spazio parafaringeo, la parte posteriore della cavità nasale e del seno mascellare, i linf. retrofaringei, e i linf. dal II al V livello.

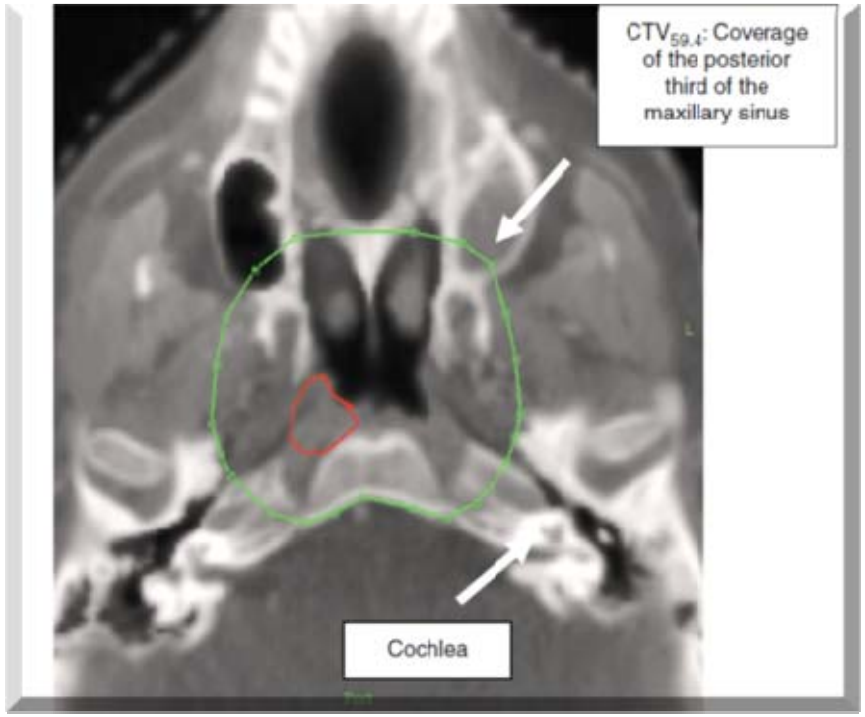
- **CLIVUS** (terzo o la metà anteriore se non coinvolto, intero se coinvolto) 8/18
- **BASE CRANICA:**

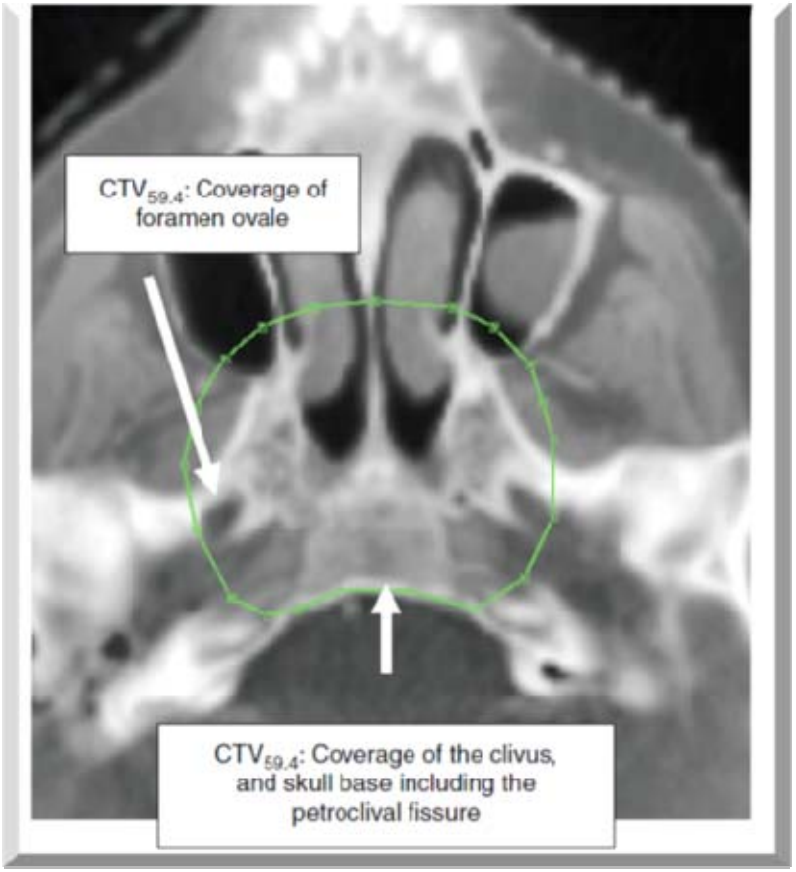
rocca petrosa e/o il forame ovale 6/18.
forame rotondo (1/18)
forame spinoso (2/18)

- **FESSURA ORBITARIA INFERIORE** (2/18)
- **ARCO ANTERIORE DELL'ATLANTE** (un terzo anteriore o la metà anteriore) (4/18)

Wang TJC, J Radiat Oncol , 2012

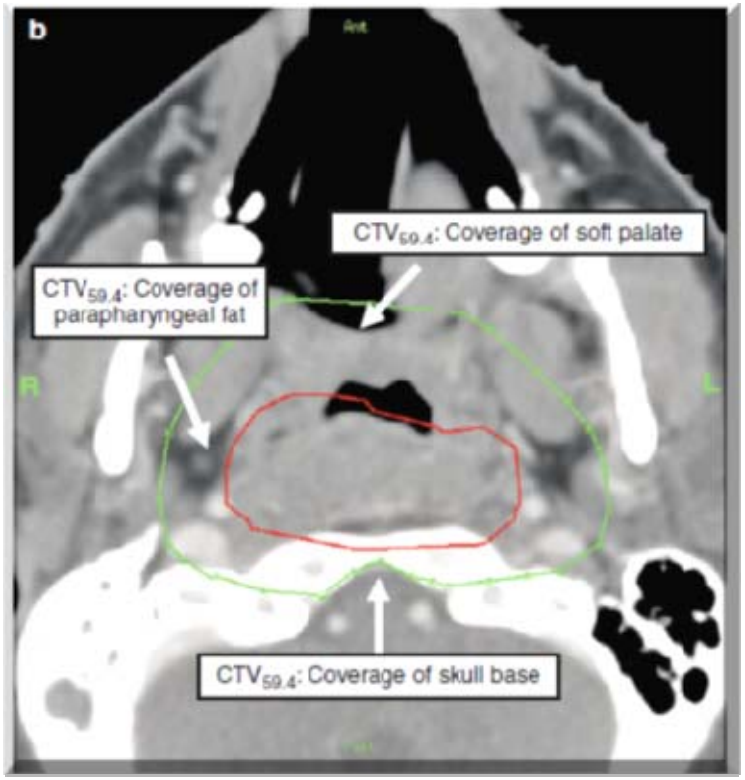
Intermediate Risk CTV (60-68 Gy)

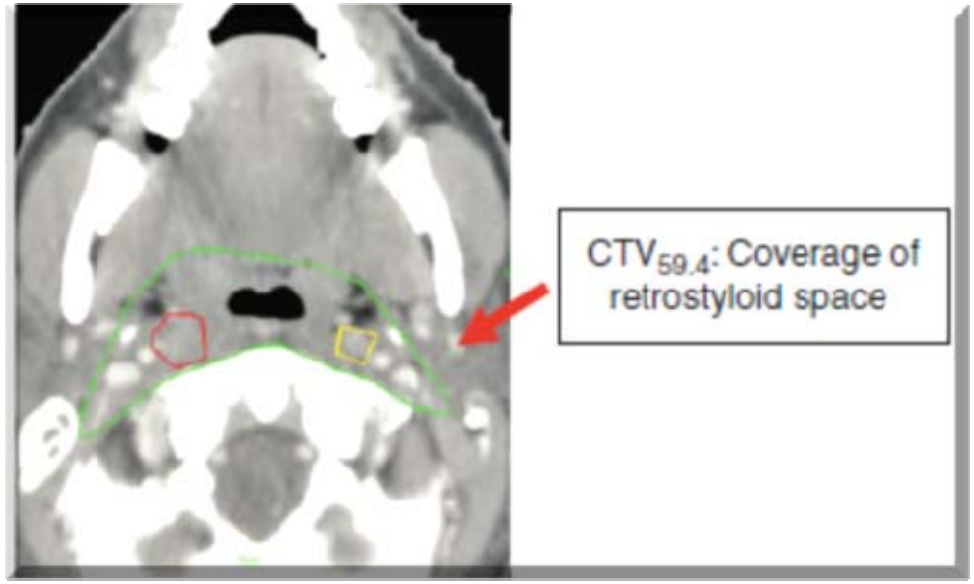




Nancy J. lee, Jade J. Lu 2013
Lee N et al. RTOG 0225, J Clin Oncol. 2009

Intermediate Risk CTV (60-68 Gy)





Nancy J. lee, Jade J. Lu 2013
Lee N et al. RTOG 0225, J Clin Oncol. 2009

Intermediate Risk CTV (60-68 Gy)

In INT l'IR-CTV viene definito solo in casi selezionati e comprende:

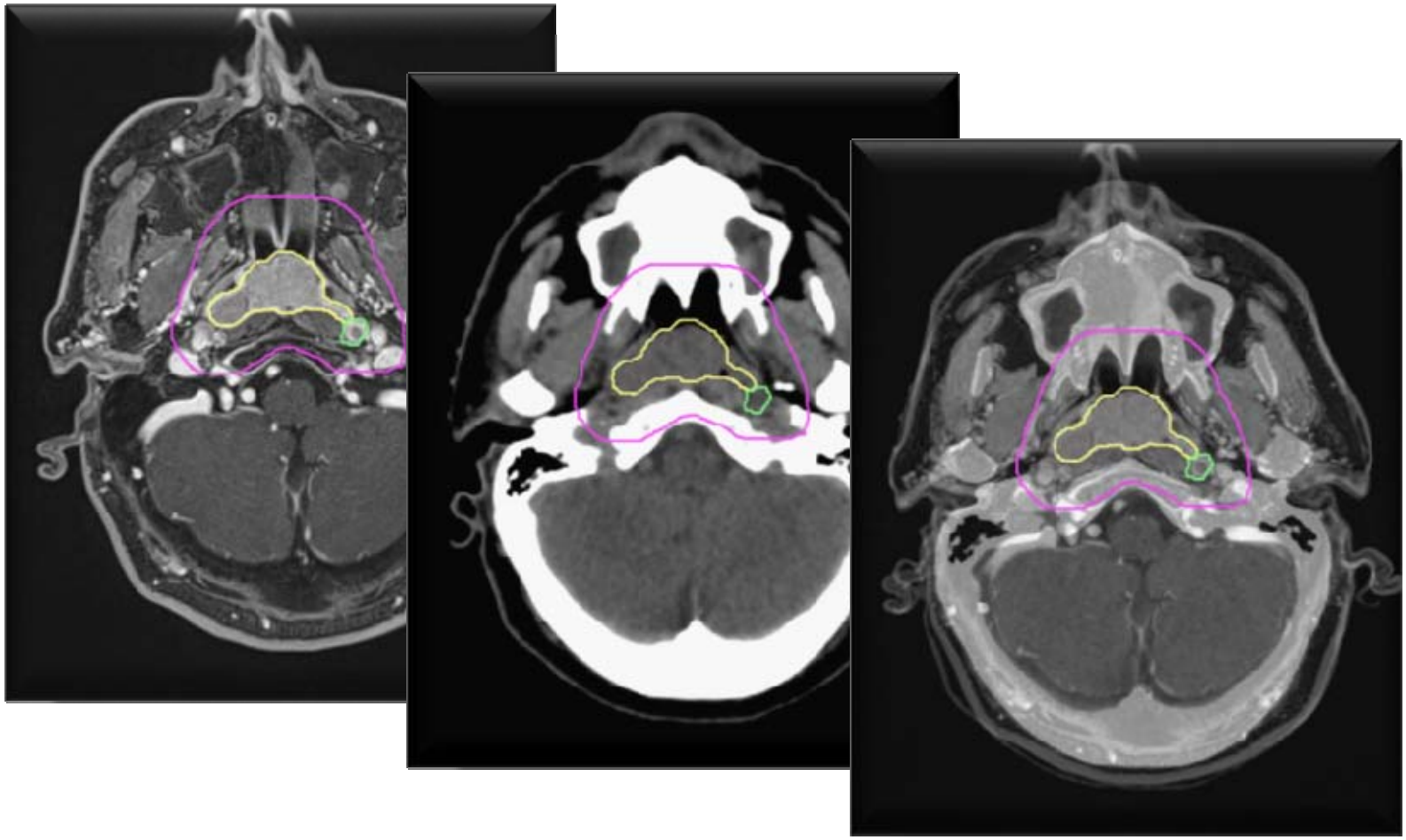
- **HR-CTV** più un margine di **0,3 cm**

- I livelli linfonodali non coinvolti nel **collo violato** o nel collo in cui vi è un **massiccio coinvolgimento linfonodale**.

- Le intere **stazioni linfonodali retrofaringee**, quando sono interessati i retrofaringei alti.

- Tutti i **linfonodi sospetti in RM,** anche se clinicamente negativi e non captanti alla PET.

Intermediate Risk CTV (60-68 Gy)



INT

CT di induzione e Volumi

- RT- CT (platino basata): trattamento standard per malattie in stadio avanzato

- Ruolo CT induzione: attualmente non disponibili studi di fase III

CT di induzione e Volumi

ClinicalTrials.gov Identifier: NCT01245959

Cinese

Prospective Randomized Trial Comparing Induction Chemotherapy (TPF) Plus Concurrent Chemoradiotherapy With Concurrent Chemoradiotherapy in Patients With Locoregionally Advanced Nasopharyngeal Carcinoma

ClinicalTrials.gov Identifier: NCT00828386

Gortec

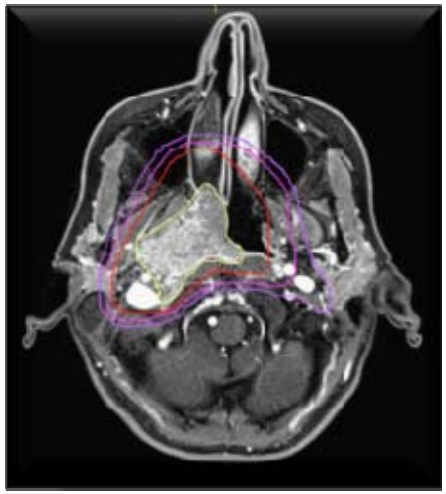
A Randomized, Multicenter, Phase III Trial Comparing Induction Chemotherapy With Docetaxel, Cisplatin and 5-Fluorouracil (TPF) Followed by Concurrent Chemoradiotherapy to Concurrent Chemoradiotherapy Alone, in Nasopharyngeal Cancers Staged as T2b, T3, T4 and/or With Lymph Node Involvement (>N1)

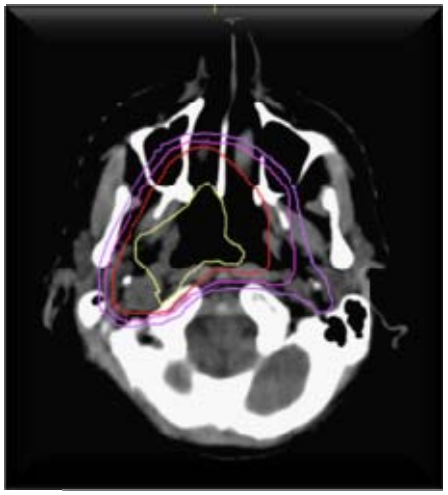
ClinicalTrials.gov Identifier: NCT00201396

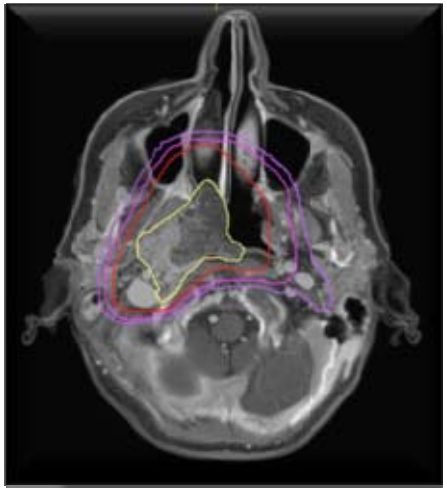
ClinicalTrials.gov Identifier: NCT00180973

CT di induzione e Volumi

- **E' in genere raccomandato definire il GTV pre-CT e quindi prescrivere ad HR-PTV pre-CT**







- **E' possibile ridurre il volume dopo CT di induzione?**

CT di induzione e Volumi

25 PZ (II B-IV)
CT Induzione: PF o TPF
Follow up medio: 29 mesi

INTENSITY-MODULATED RADIATION THERAPY WITH SIMULTANEOUS INTEGRATED BOOST TECHNIQUE FOLLOWING NEOADJUVANT CHEMOTHERAPY FOR LOCOREGIONALLY ADVANCED NASOPHARYNGEAL CARCINOMA

CTV1: **"GTV T e N post-CT"** + 5mm.
CTV2: rinofaringe, muscoli prevertebrali, fossa pterigopalatina, spazio parafaringeo, terzo post. cavità nasali e seno mascellare, seno sfenoidale inferiore, clivus, base cranica, N+ , linfonodi retrofaringei e II livello, estensione della malattia pre-CT.
CTV3: III- IV V livello non coinvolti
PTV: CTV + 3mm

PTV1 (**67,5Gy** , 2,25Gy/fx) *Normalized total dose of 74 Gy.8*
PTV2 (**54Gy** ; 1,8/fx, in 4 casi 60 Gy, 2Gy/fx)
PTV3 (**48 Gy**; 1,6Gy/fx)

" 3 locoregional recurrences within the 67.5-Gy volume
1 in the 60-Gy (where it was free of tumor the initial imaging work-up)
1 in the 48-Gy volume "

Kim K et al, Head and Neck 2009

Staging linfonodi: AJCC 7ª edizione

Regional Lymph Nodes (N)

- **NX**: Regional lymph nodes cannot be assessed.
- **N0**: No regional lymph node metastasis.
- **N1**: Unilateral metastasis in cervical lymph node(s), ≤6 cm in greatest dimension, above the supraclavicular fossa, and/or unilateral or bilateral, retropharyngeal lymph nodes, ≤6 cm in greatest dimension.
- **N2**: Bilateral metastasis in cervical lymph node(s), ≤6 cm in greatest dimension, above the supraclavicular fossa.
- **N3**: Metastasis in a lymph node(s) >6 cm and/or to supraclavicular fossa. N3a >6 cm in dimension. N3b Extension to the supaclavicular fossa.

Proposed Lymph Node Staging System Using the International Consensus Guidelines for Lymph Node Levels Is Predictive for Nasopharyngeal Carcinoma Patients From Endemic Areas Treated With Intensity Modulated Radiation Therapy

Wen-Fei Li, MD,* Ying Sun, MD, PhD,* Yan-Ping Mao, MD,* Lei Chen, MD,* Yuan-Yuan Chen, MD,* Mo Chen, MD,* Li-Zhi Liu, MD,† Ai-Hua Lin, MD, PhD,‡ Li Li, MD, PhD,† and Jun Ma, MD*

Results: Nodal level and laterality were the only independent prognostic factors for distant failure and disease failure in multivariate analysis. Compared with unilateral levels Ib, II, III, and/or Va involvement (hazard ratio [HR] 1), retropharyngeal lymph node involvement alone had a similar prognostic value (HR 0.71; 95% confidence interval [CI] 0.43-1.17; $P=.17$), whereas bilateral levels Ib, II, III, and/or Va involvement (HR 1.65; 95% CI 1.06-2.58; $P=.03$) and levels IV, Vb, and/or supraclavicular fossa involvement (HR 3.47; 95% CI 1.92-6.29; $P<.01$) both significantly increased the HR for distant failure. Thus we propose that the N category criteria could be revised as follows: N0, no regional LN metastasis; N1, retropharyngeal lymph node involvement, and/or unilateral levels Ib, II, III, and/or Va involvement; N2, bilateral levels Ib, II, III, and/or Va involvement; N3, levels IV, Vb, and/or supraclavicular fossa involvement. Compared with the 7th edition of the UICC/AJCC criteria, the proposed N staging system provides a more satisfactory distinction between the HRs for regional failure, distant failure, and disease failure in each N category.

Int J Radiat Oncol Biol Phys 2013

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Regional Lymph Nodes (N)

- **N0**: No regional lymph node metastasis (RLN).
- **N1**: RLN involvement and/or unilateral levels Ib, II, III, and or Va
- **N2**: Bilateral levels Ib, II, III and/or Va
- **N3**: Metastasis in levels IV, Vb and/or SCF

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"Lymph node metastasis in NPC follows a predictable and orderly pattern".

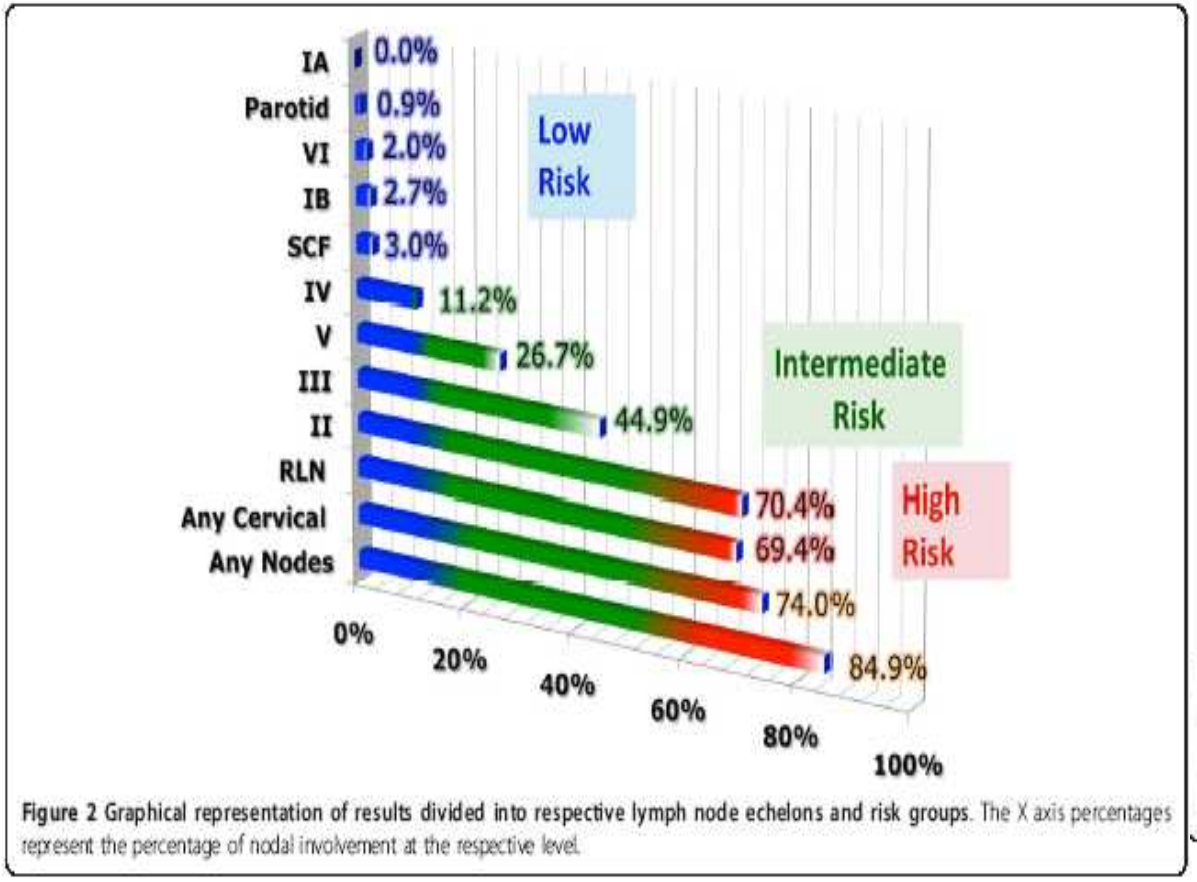


Figure 2 Graphical representation of results divided into respective lymph node echelons and risk groups. The X axis percentages represent the percentage of nodal involvement at the respective level.

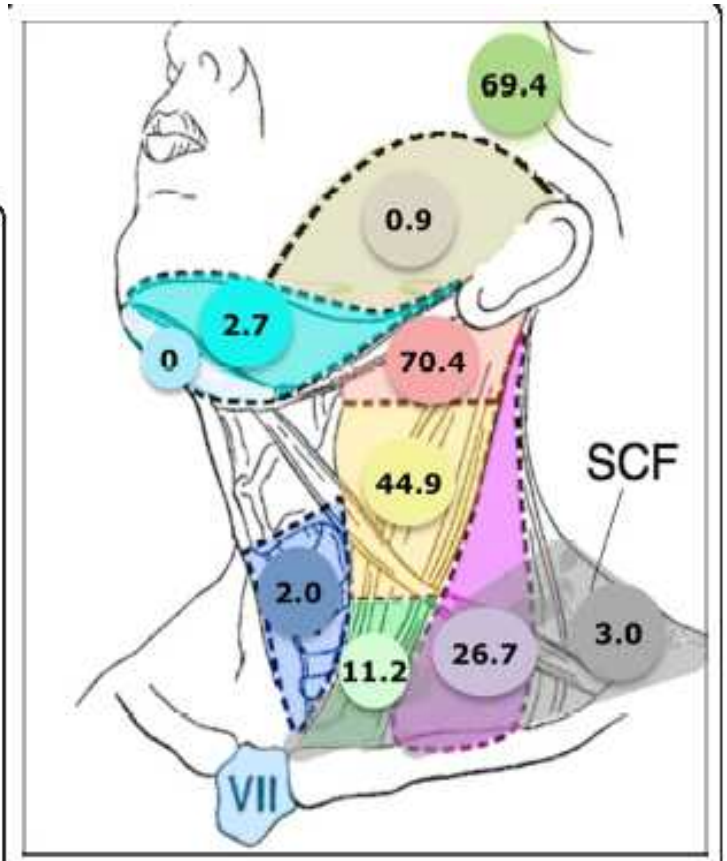


Figure 14 Pictorial summary of incidence of LN metastasis in NPC. This is a pictorial representation of the neck. The respective numbers represent the overall percentage of NPC patients presenting with positive LN metastasis at the particular nodal station.

Ho FCH, BMC Cancer , 2012

Low Risk-CTV

18 Studi+1 (INT)

Table 1 Results from series treating NPC with IMRT with or without chemotherapy

Study	Year	Stage	No.	Median follow-up (months)	Time point (years)	Local control rate (%)	Regional control rate (%)	Distant met-free rate (%)	OS (%)
Lee et al. [19] (UCSF)	2002	All	67	31	4	97	98	66	88
Kwong et al. [20] (Hong Kong)	2004	T1 N0–1[a]	33	24	3	100	92	100	100
Kam [21] (Hong Kong)	2004	All	63	29	3	92	98	79	90
Wolden et al. [22] (MSKCC)	2006	All	74	35	3	91	93	78	83
Kwong et al. [23] (Hong Kong)	2006	III–IVB[a]	50	25	2	96	NA	94	92
RTOG 0225 [5]	2009	All	68	31	2	93	91	85	80
Tham et al. [32] (Singapore)	2009	All	195	37	3	90	NA	89	94
Lin et al. [29] (China)	2009	II–IV[a]	323	30	3	95	98	90	90
Wong et al. [33] (China)	2010	All	175	34	3	94	93	87	87
Lin et al. [28] (China)	2010	IIB–IVB[a]	370	31	3	95	97	86	89
Kam et al. [57] (Hong Kong)	2010	All	231	59	6	82	91	75	66
Ng et al. [30] (Hong Kong)	2011	All	193	30	2	95	96	90	92
Xiao et al. [34] (China)	2011	III–IVA[a]	81	54	5	95	NA	NA	75
Bakst et al [35] (MSKCC)	2011	II–IVB[a]	25	33	3	91	91	91	89
Xiayun et al. [37] (China)	2011	IIB–IVB[b]	54	30	3	95	98	86	88
Ma et al. [36] (Hong Kong)	2011	III–IVB[b]	30	32	2	93	93	93	90
RTOG 0615 [27]	2012	IIB–IVB[c]	42	30	2	NA	NA	91	91
Su et al. [31] (China)	2012	I–IIB[b]	198	51	5	97	98	98	NA
Orlandi et al. (INT, Italy)	2013	80%IIII-IV	106	43	5	88	88	NA	82

Wang TJC, J Radiat Oncol , 2012

Low Risk CTV

La maggiore variabilità è nell'inclusione del livello I:

- In 2 Studi, il livello IA è coperto elettivamente solo se interessato il livello IB o la cavità orale.
- In 3 studi il livello IB viene sempre incluso.
- In 3 studi il livello IB viene risparmiato solo negli N0.
- In 2 studi il livello IB non viene incluso (il LRC è stato superiore al 95%).

Non è raccomandabile includere il livello IA, il livello IB può essere risparmiato anche in caso di N+

Per i RPNs, il bordo inferiore è:

- In 2 Studi a livello del margine craniale del corpo dell'**osso ioide**
- In 2 studi a livello del margine craniale della **seconda vertebra cervicale**

Wang T.J.C. J Radiat Oncol , 2012

Low Risk CTV

In INT LR-CTV comprende:

- **HR-CTV** più un margine di **0,5 cm**
- Tutti i livelli linfonodali del collo non coinvolti **dal II al V**.
- Il Livello IB è incluso solo in caso di coinvolgimento del IIA o IIB-bulky

LR-CTV: questioni aperte

E’ perseguibile un’irradiazione linfonodale selettiva in determinati stadi di malattia?

IS ELECTIVE IRRADIATION TO THE LOWER NECK NECESSARY FOR N0 NASOPHARYNGEAL CARCINOMA?

YUNSHENG GAO, M.D.,* GUOPEI ZHU, M.D.,* JIADE LU, M.D., M.B.A.,*† HONGMEI YING, M.D.,* LING KONG, M.D.,* YONGRU WU, M.D.,* AND CHAOSU HU, M.D.*

Purpose: To summarize our experience and treatment results in lymph node–negative nasopharyngeal carcinoma treated in a single institution.

Methods and Materials: From January 2000 to December 2003, 410 patients with lymph node–negative nasopharyngeal carcinoma were retrospectively analyzed. The T-stage distribution was 18.8% in T1, 54.6% in T2 (T2a, 41 patients; T2b, 183 patients), 13.2% in T3, and 13.4% in T4. All patients received radiotherapy to the nasopharynx, skull base, and upper neck drainage areas, including levels II, III, and VA. The dose was 64–74 Gy, 1. 8–2.0 Gy per fraction over 6.5–7.5 weeks to the primary tumor with ^{60}Co or 6-MV X-rays, and 50–56 Gy to levels II, III, and VA. Residual disease was boosted with either ^{192}Ir afterloading brachytherapy or small external beam fields.

Results: The median follow-up time was 54 months (range, 3–90 months). Four patients developed neck recurrence, and only 1 patient (0.2%) experienced relapse outside the irradiation fields. The 5-year overall survival rate was 84.2%. The 5-year relapse-free survival rate, distant metastasis-free survival rate, and disease-free survival rate were 88.6%, 90.6% and 80.1%, respectively. Both univariate and multivariate analyses demonstrated that T classification was the only significant prognostic factor for predicting overall survival. The observed serious late toxicities were radiation-induced brain damage (7 cases), cranial nerve palsy (16 cases), and severe trismus (13 cases; the distance between the incisors was ≤1 cm).

Conclusion: Elective levels II, III, and VA irradiation is suitable for nasopharyngeal carcinoma without neck lymph node metastasis.

Escludendo i livelli IV, VB, SCF
4 recidive linfonodali: solo 1 out-field!

AJCC 1997, RPNs non valutati

Int J Rad Oncol Biol Phys, 2010

Treatment outcome of nasopharyngeal carcinoma with retropharyngeal lymph nodes metastasis only and the feasibility of elective neck irradiation

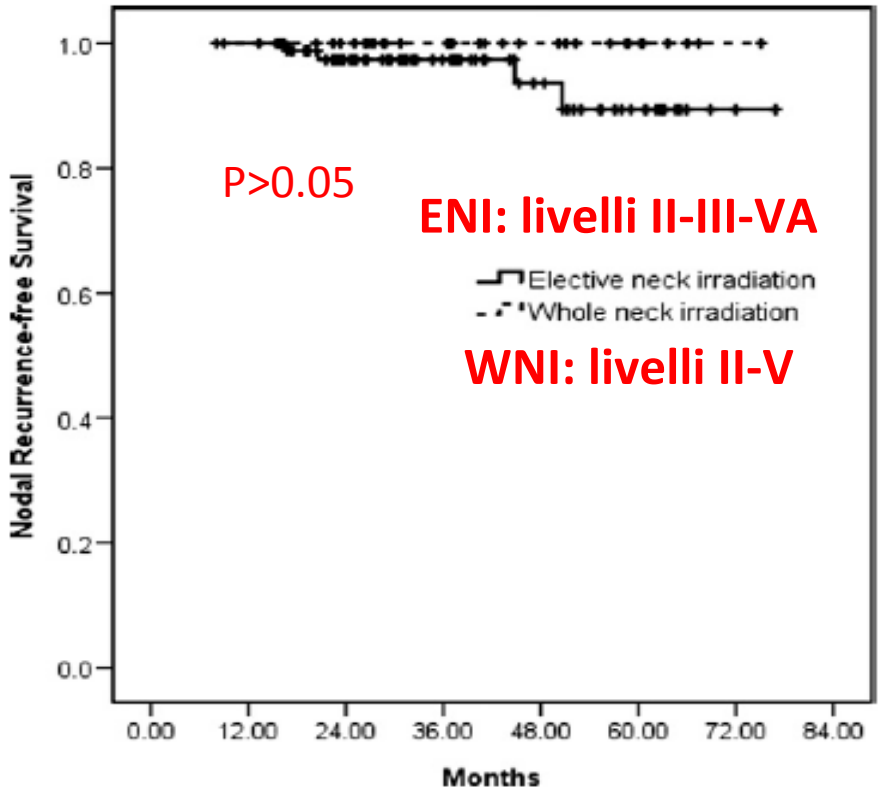


Fig. 1 Nodal recurrence-free survival between the two groups: elective neck irradiation and whole neck irradiation. There wasn't significant difference between the two groups ($p > 0.05$). The 95% of confidence interval of nodal recurrence-free survival was 69.4–76.7 months in the group of elective neck irradiation. Since there was no nodal recurrence in the group of whole neck irradiation, the 95% CI was not reached.

AJCC 2002, RPNs inclusi nel GTV -T

- Studio retrospettivo
- IMRT-3DRT/2DCRT
- 119 PZ, ~50% Stadio II
- **89 ENI; 30 WNI**
- Follow-up mediano: 36.6 mesi

- CTV1: 66-70.4 Gy
- CTV2: 60Gy
- CTV3: 50-62 Gy

Ou X, Oral Oncology, 2012

Lei Zeng MD, Xue-Ming Sun MD, Chun-Yan Chen MD et al.
A comparative study on prophylactic irradiation to the whole neck and to the upper neck for neck lymph node-negative nasopharyngeal carcinoma patients.
Head & Neck In press.

- Studio retrospettivo
- 270 PZ
- IMRT/2DCRT
- FU:65,1 m

AJCC 2002, RPNs inclusi nel GTV -T

- CTV1: 68Gy
- CTV2: 60Gy
- CTV3: 50 Gy

		171 pz PROPHYLACTIC UPPER NECK IRRADIATION: II-III-VA		**99 pz PROPHYLACTIC WHOLE NECK IRRADIATION**
5- year	**OS**	93,6%		90,9%
	NRFS	99,4%	***ns***	99%
	DMFS	98,8%		94,9%

HR-PTV, IR-PTV, LR-PTV

PTVs

Il PTV è un concetto puramente geometrico.

- Deve tenere conto degli errori sistematici e random che si hanno in ciascun Istituto.

Non vi è consenso nei vari studi nel definire un margine standard per il PTV.

Nelle diverse casistiche sono stati utilizzati margini che vanno da 0,2 cm a 0,5 cm. (anche meno di 1mm in prossimità delle strutture critiche: brainsteam, cord)

Wang TJC, J Radiat Oncol , 2012

PTVs

Molti autori hanno proposto dei metodi per calcolare i margini CTV-PTV in base agli errori sistematici e random.

van Herk (2000): $2{,}5\,\Sigma + 0.7\,\sigma$

Σ=deviazione standard errori sistematici

σ= deviazione standard errori random

PTVs

Table 4.4. Summary of various published recommendations for margins around target volumes (CTV) and OAR (modified from van Herk, 2004).

Author	Region	Recipe	Comments
Bel *et al.* (1996)	PTV	0.7σ	Statistical uncertainties only (linear approximation)—Monte Carlo.
Antolak and Rosen (1999)	PTV	1.65σ	Statistical uncertainties only, block margin?
Stroom *et al.* (1999a)	PTV	$2\Sigma + 0.7\sigma$	95 % absorbed dose to on average 99 % of CTV tested in realistic plans.
van Herk *et al.* (2000)	PTV	$2.5\,\Sigma + 0.7\,\sigma$ (or more correctly): $2.5\Sigma + 1.64(\sigma - \sigma_a)$	Minimum absorbed dose to CTV is 95 % for 90% of patients. Analytical solution for perfect conformation.
McKenzie (2000)	PTV	$2.5\,\Sigma + \beta + (\sigma - \sigma_a)$	Extension of van Herk *et al.* (2000) for fringe dose due to limited number of beams. The factor β depends on the beam organization.
Parker *et al.* (2002)	PTV	$\Sigma + \sqrt{(\sigma^2 + \Sigma^2)}$	95 % minimum absorbed dose and 100 % absorbed dose for 95 % of volume. Probability levels not specified.
van Herk *et al.* (2002)	PTV	$2.5 + \Sigma + 0.7\sigma + 3$ mm (or more correctly): $\sqrt{2.7^2\Sigma^2 + 1.6^2\sigma^2} - 2.8$ mm	Monte Carlo based test of 1 % TCP loss due to geometrical errors for prostate patients, fitted for various σ and Σ.
Ten Haken *et al.* (1997), Engelsman *et al.* (2001a, 2001b)	PRV (liver and lung)	0	No margin for respiration, but compensation by absorbed-dose escalation to iso-NTCP, reducing target-dose homogeneity constraints.
McKenzie *et al.* (2000)	PRV	A	Margin for respiration on top of other margins when respiration dominates other uncertainties.
van Herk *et al.* (2003)	PRV (lung)	0.25 A (caudally); 0.45 A (cranially)	Margin for (random) respiration combined with random setup error of 3 mm SD, when respiration dominates other uncertainties ($A > 1$ cm).
McKenzie *et al.* (2002)	PRV	$1.3\,\Sigma \pm 0.5\,\sigma$	Margins for small and/or serial organs at risk in low (+) or high (−) absorbed-dose region.

Symbols: Σ, standard deviation of systematic uncertainties; σ, standard deviation of statistical (random) uncertainties; σ_a, describes width of beam penumbra fitted with a Gaussian function; A, peak-to-peak amplitude of respiration.

PTVs

Acta Oncologica, 2011; 50: 61–71

informa
healthcare

ORIGINAL ARTICLE

Set-up errors analyses in IMRT treatments for nasopharyngeal carcinoma to evaluate time trends, PTV and PRV margins

VALERIA MONGIOJ[1], ESTER ORLANDI[2], MAURO PALAZZI[2,3], ELENA DEPONTI[4], FRANCESCHINI MARZIA[1], CLAUDIO STUCCHI[1], CLAUDIA SANGALLI[2], CARLO FALLAI[2], GIANCARLO ZONCA[1], PATRIZIA OLMI[2] & EMANUELE PIGNOLI[1]

[1]*Department of Medical Physics, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy,* [2]*Department of Radiotherapy, Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy,* [3]*Department of Radiotherapy, A.O. Niguarda Ca'Granda and* [4]*Department of Medical Physics A.O. San Gerardo, Monza, Italy*

FONDAZIONE IRCCS
ISTITUTO NAZIONALE
DEI TUMORI

PTV

S-I: 3 mm

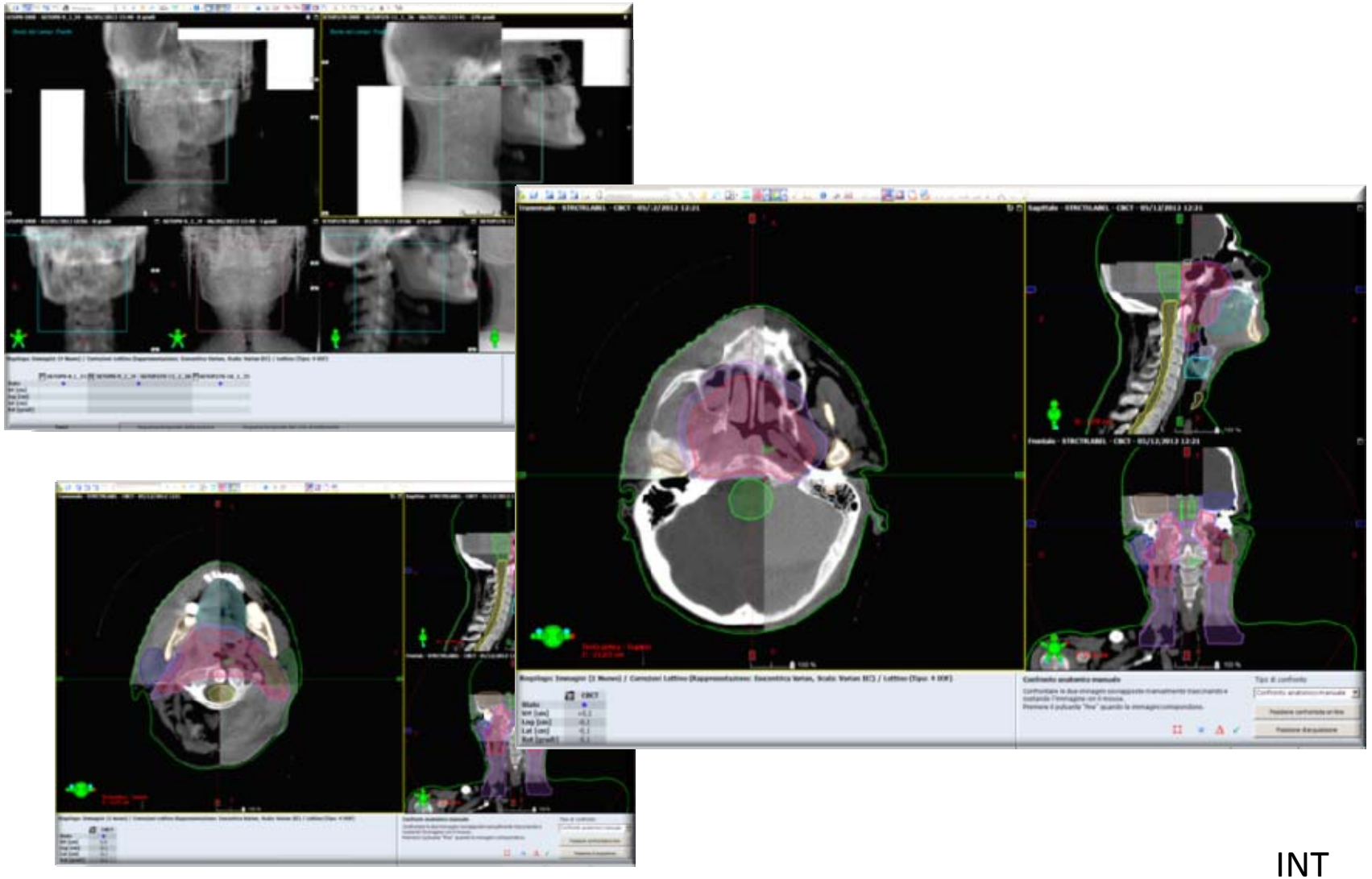
L-R: 3.4 mm

A-P: 3.2 mm

Retrospective evaluation of PTV and PRV margins

The results obtained for population systematic and random error allowed margins estimation for our treatment protocol. Margin from CTV to PTV should be at least 3.4 mm in the L-R direction, 3.0 mm in the S-I direction and 3.2 mm in the A-P direction, respectively. PRV margins obtained for brainstem were 2 mm, 2.3 mm and 2.1 mm in S-I, L-R and A-P directions, respectively, while for spinal cord were 3.8 mm, 3.5 mm and 3.2 mm in L-R, A-P and S-I directions, respectively.

PTVs



INT

PTVs

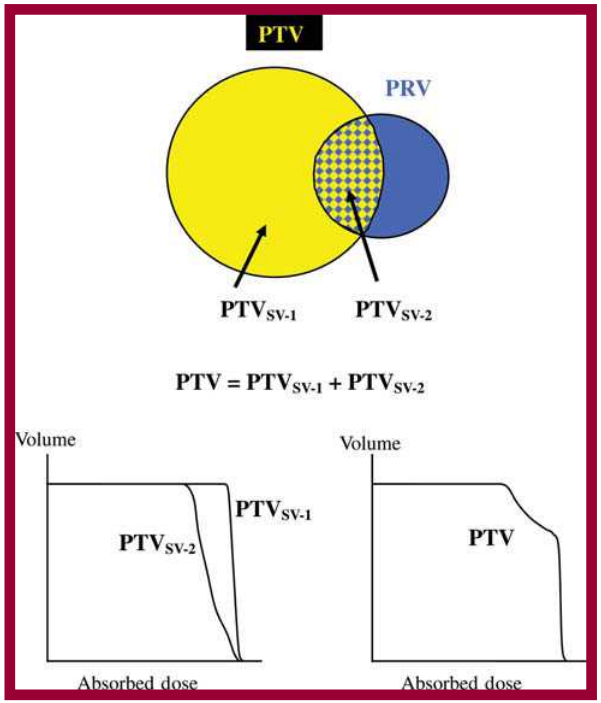
Se c'è sovrapposizione tra PTV e PRV, cosa fare?

l'ICRU 83 raccomanda di <u>non modificare il PTV.</u>

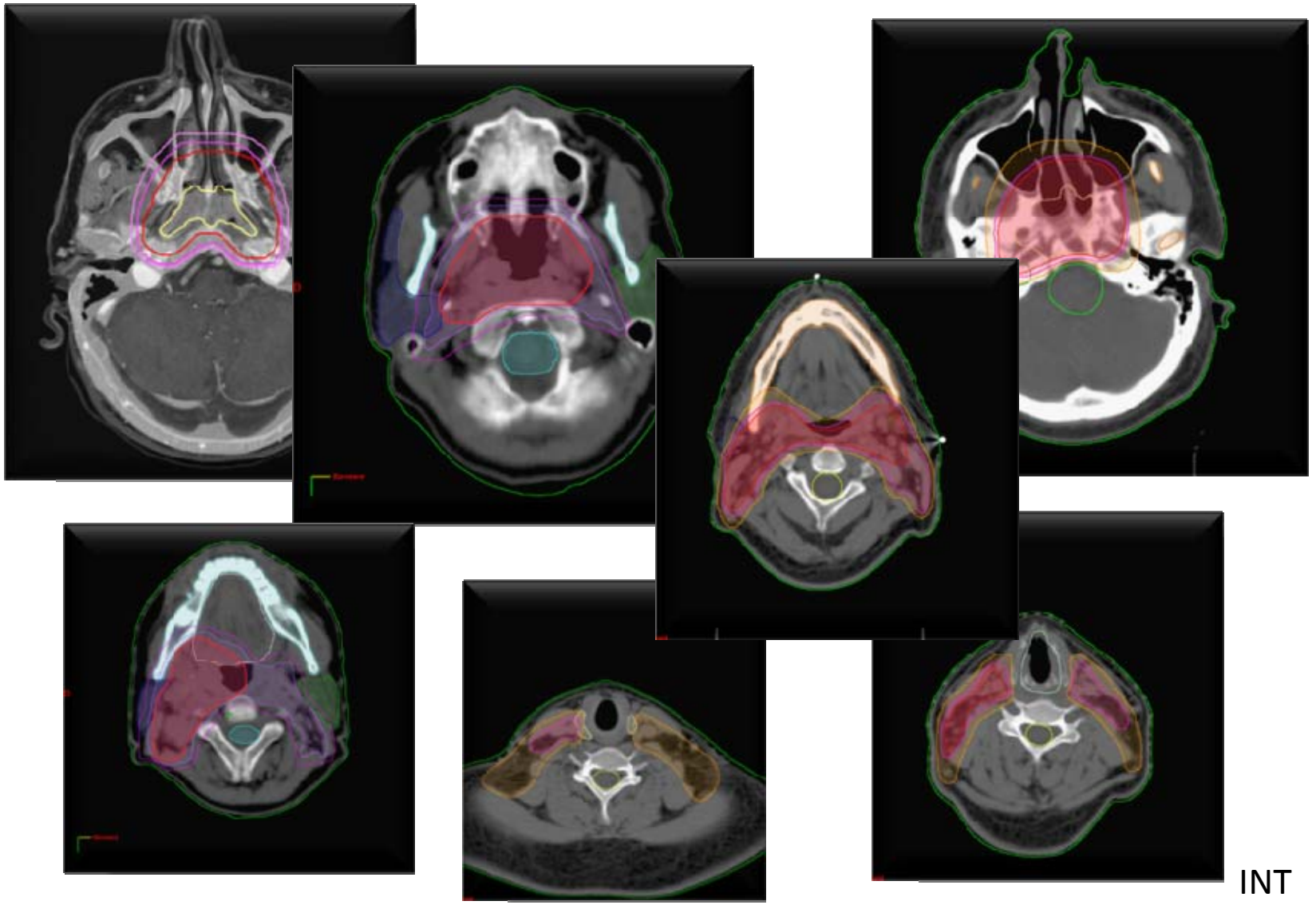
I nuovi software permettono di ottenere un risparmio sufficiente degli organi a rischio attraverso le "priorità".

In alternativa si può suddividere il PTV in regioni a diversa prescrizione di dose

PTVsv = PTV subvolumi.



PTVs



INT

Conclusioni

- ✓ Accuratezza nella selezione e delineazione del GTV (coregistrazione con RMN, margini GTV-CTV adeguati)
- ✓ Dopo CT di induzione delineare il volume del GTV pre-CT
- ✓ La “whole neck irradiation” rimane lo standard anche nella malattia N0
- ✓ PTV: valutare gli errori di set-up in ciascun centro

Diamoci una linea guida!