



Linee Guida AIRO di tecnica RT

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Pavia

Pisa

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Milano

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Vicenza

Bergamo

Parma

Novara

Treviso

Bergamo

LA RADIOTERAPIA DEI TUMORI DELLA TESTA E DEL COLLO

Indicazioni e Criteri Guida

GIUGNO 2007

Linee Guida AIOM-AIRO 2008

I Tumori della Testa e del Collo

DICEMBRE 2008

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Estensori AIOM: M. Benasso
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2009

Coordinatore AIOM: Adriano Paccagnella

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TUMORI DELLA TESTA E DEL COLLO



Associazione
Italiana
Radioterapia
Oncologica



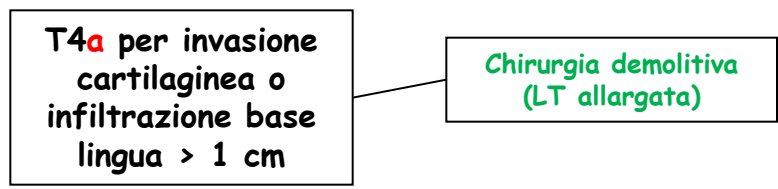
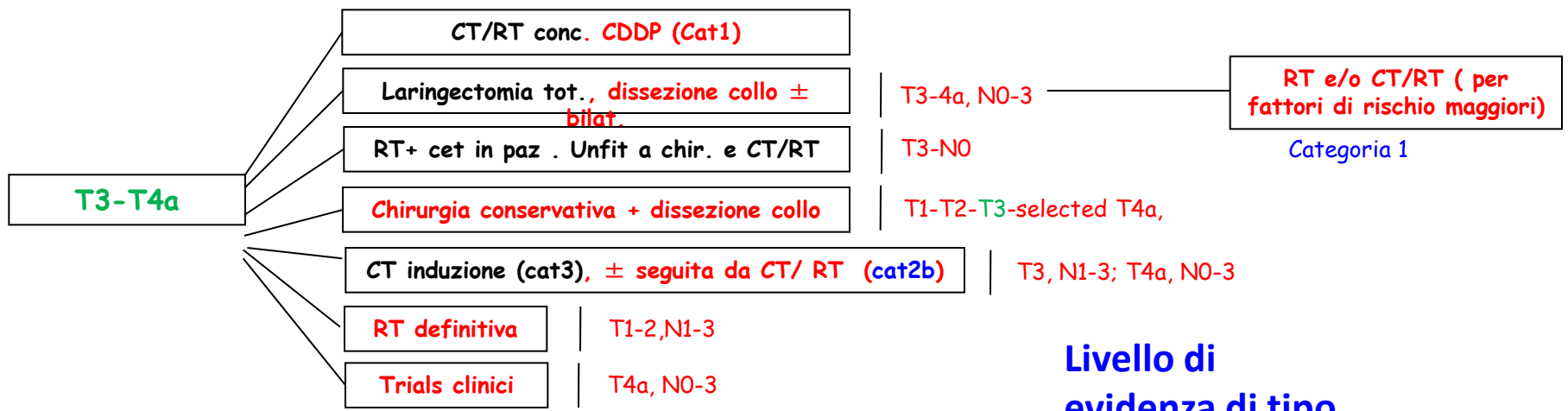
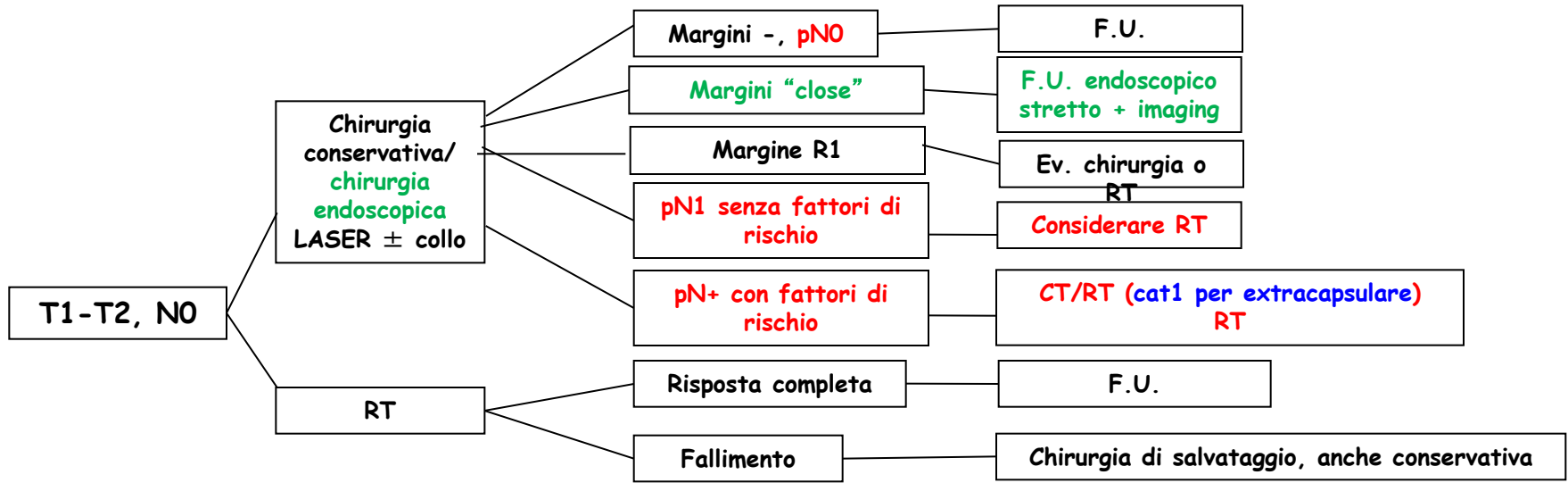
***Linee guida AIRO-AIOM
revisionate dai chirurghi in ambito AIOCC FEBBRAIO
2012***

TUMORI DELLA TESTA E COLLO.

Algoritmi diagnostico-terapeutici del testo 2008

- in nero: gli algoritmi delle Linee Guida AIRO-AIOM 2008
- in rosso: le integrazioni con linee guida NCCN H&N 2010
- in azzurro: i livelli di evidenza
- in verde: le integrazioni

CARCINOMA DELLA LARINGE SOVRA-GLOTTICA



Livello di evidenza di tipo Ib
Forza di raccomandazione A

Laringe sovra-glottica



2012-13

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Linee guida

TUMORI DELLA TESTA E DEL COLLO

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6.3.1 Preservazione laringea

Obiettivo complesso che si è evoluto nel tempo e nel corso degli studi clinici da semplice preservazione dell'organo a preservazione delle sue funzioni, fonazione e deglutizione. Prima di proporre un trattamento di preservazione laringeo vanno sempre considerati alcuni fattori come l'età del paziente (>70 aa), sottosede e estensione della malattia. Si dovrebbe considerare di escludere i pazienti con laringe non funzionante prima dell'avvio delle cure dai programmi di preservazione (presenza di tracheotomia; alimentazione attraverso SNG o gastrostomia; episodi ricorrenti di polmoniti nei 12 mese precedenti).

6.4 Note di tecnica radioterapica

Definizione del bersaglio, organi a rischio, dosi e frazionamento e tecnica di trattamento si rimanda alla linee guida AIRO su www.radioterapiaitalia.it.

6.5 Trattamento

6.5.1 Tumori limitati della laringe sovraglottica stadio I-II)

I tumori sopraglottici in stadio iniziale possono essere trattati con una sola modalità terapeutica, chirurgia conservativa (con tecnica aperta o endoscopica) o chirurgia conservativa o con radioterapia esclusiva. Le casistiche non sono uniformi e i risultati sembrano sovrapponibili con controllo locale variabile dal 90 al 100% per lo stadio T1 e risultati inferiori nei casi T2 (40 – 70%). Nei casi di insuccesso del trattamento radiante è possibile un recupero chirurgico, a volte anche conservativo. La scelta chirurgica ha senso quando l'intervento ha ottime probabilità di ottenere un'exeresi radicale della malattia. Qualora dopo chirurgia conservativa si rilevassero fattori di rischio, in particolare margini R1, è preferibile una radicalizzazione chirurgica.

Nei margini "close", è invece consigliata la radioterapia post-operatoria anche se potrebbe comportare una riduzione della funzionalità laringea con conseguente rischio di "ab ingestis", edema irreversibile e quindi la necessità di una tracheotomia permanente.

Linee guida di tecnica RT

(progetto di ampliamento delle Linee guida AIRO H&N)

**I stesura completata il 12/09/2011 Coordinamento
Prof. R. Corvò**

- 1) Luciana Lastrucci (Arezzo) METASTASI LINFONODALI DA PRIMITIVO IGNOTO
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Linee guida di tecnica RT

(progetto di ampliamento delle Linee guida AIRO H&N)

Il stesura terminata 2013, in inglese, finalizzata ad una successiva pubblicazione.

Coordinamento Prof. G. Sanguineti

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Technical Guidelines of IMRT for Head and Neck Cancer on behalf of the task group of the Italian Association of Radiation Oncology

Anna Merlotti¹, Daniela Alterio², Riccardo Vigna Taglianti³, Alessandro Muraglia⁴, Luciana Lastrucci⁵, Roberto Manzo⁶, Giuseppina Gambaro⁷, Orietta Caspiani⁸, Francesco Miccicchè⁹,
Francesco Deodato¹⁰, Renzo Corvò¹¹, Elvio Russi³, Giuseppe Sanguineti¹²

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NASOPHARYNX

Target definition remarks

- CTV-HD or high dose volume that **encompasses the GTV with a margin**; both CT and MRI should be used to identify the primary tumor location;
- CTV-HR that typically includes the tissue around the gross tumor volume and/or the neck nodal stations that have high risk of cancer involvement and/or lymph nodes that look suspicious on imaging; given the high rate of subclinical disease in the nasopharynx **the whole nasopharynx should be included within this volume** (N. Lee et al. 2009)(Orlandi et al. 2013)
- CTV-LR includes the lymph nodal stations which have relatively lower **risk (5-15%) of cancer involvement** (i.e. the lower neck) and do not look suspicious at imaging. Standard treatment of nasopharyngeal carcinoma is definitive radiotherapy + chemotherapy.

Dose/fractionation remarks

Commonly used fractionation regimens:

	D (Gy)	d (Gy)	fxs	OTT (wks)	Comment
CTV-HD	70	2	35	7	
	69.96	2.12	33	6.5	RTOG0225(N. Lee et al. 2009)
	67.5	2.25	30	6	(K. Kim et al. 2009)
	66-69.63	2.2-2.11	30-33		(Peponi et al. 2010)
CTV-HR	63	1.8	35	7	
	54-60	1.8-2	30	6	(K. Kim et al. 2009)
	59.4	1.8	33	6.5	(N. Lee et al. 2009)RTOG0225
CTV-LR	58.1	1.66	35	7	
	56.1	1.7	33		
	48	1.6	30	6	(K. Kim et al. 2009)
	50.4	1.8	28		(N. Lee et al. 2009)RTOG0225
	51	1.7	30		(Peponi et al. 2010)

Primary tumor contour

- **CTV HD = GTV+5-10 mm margin** (2 mm if lies behind neural structures)
- **CTV HR = Standard anatomic limits:**
 - a. Anterior: 1/3 post nasal cavity – 1/3 post maxillar sinuses- pterygoid fossae
 - b. Posterior: anterior third of clivus (entire clivus if macroscopic infiltration), retrostyloid space
 - c. Lateral: lateral parts styloid processes (parapharyngeal space)
 - d. Cranial: inferior half sphenoid sinus – anterior half clivus (entire clivus and top sphenoid sinus if macroscopic infiltration or in T4 cases). For lesions confined to the nasopharynx, the pituitary fossa can be excluded from the irradiated volume(Sham et al. 1994)
 - e. Caudal: soft palate
- Induction chemotherapy is sometimes used for dosimetric purposes to shrink and downsize the tumor especially when it is abutting OARs whose tolerance is inferior to the prescribed GTV dose (i.e. brainstem)(Kong et al. 2010). In this case, the dose to the original site of disease is often limited to the tolerance of surrounding OAR (i.e. 60 Gy, optic pathways) while the residual tumor is prescribed/delivered a full dose.

Lymph node stations

The following table provides some guidelines for contouring bilateral neck levels that are negative on imaging:

Side	Level	Risk	Remarks
Bilateral	IB	Very Low	Omit or include only in case of neck node positivity
	Retropharyngeal, II, III, Va	High	
	IV, Vb	Low	Higher risk when level III is clinically involved

5. Retropharyngeal nodes (top of C1 to bottom of C2, sometimes C3) are to be included always in the CTV-HR.
6. Note #1: Spare ≥ 3 mm dermal tissues if no skin involvement.
7. Note #2: few studies have investigated the option to withhold elective treatment for cN0 patients. One of them found a high regional salvage rate with either surgery or radiotherapy (Lee et al, 1989). It should be noted, however, that patients with residual persistent disease in the neck or who fail in the neck have a higher risk of distant metastases than patients who do not fail in the neck. Therefore, comprehensive neck irradiation is always advocated for NPC.

Perché linee guida di tecnica?

- As with any precision technique, it is possible to be highly precise and precisely inaccurate.
- With historical techniques, for example, **parallel opposed lateral fields matched with a supraclavicular field, the probability of missing the tumor was low**, although the technique was not as precise in limiting dose to normal structures.
- The success of such a highly conformal planning process is highly sensitive to two major factors:
 - delineation of tumor/target volume in 3 dimensions by the clinician around which the high-dose distribution is developed through conformal planning
 - day-to-day variations in setup that could result in the tumor “sneaking” outside of the high-dose distribution of the conformal plan, thus missing the intended treatment dose altogether.

Variazioni nell'interpretazione delle linee guida

- Consensus guidelines are available for delineating regional lymphatics, but **not for the high-risk regions that immediately surround the gross tumor.**
- Besides, the infinite subtle anatomical variations between patients preclude replication of contours based on modal cases that are depicted in guidelines, and **clinical judgment is required more often than not.**
- Eisbruch et al. reported that **despite clear and well-written guidelines** that were formalized by many clinicians and physicists after considerable debate, overall **not a single case was judged to be according to protocol without any variation** in the RTOG 0022 study.

(A. Eisbruch, J. Harris, A. S. Garden et al., “Multi-Institutional trial of accelerated hypofractionated intensity-modulated radiation therapy for early-stage oropharyngeal cancer (RTOG 00-22),” International Journal of Radiation Oncology Biology Physics, vol. 76, no. 5, pp. 1333–1338, 2010)

Anche tra esperti...

- Contouring of target volumes can vary even among expert radiation oncologists. Cooper et al. reported the discrepancies in contouring of supraglottic carcinomas based on CT images between 8 leading experts in head and neck cancer management including 4 radiation oncologists and 4 neuroradiologists. **The average proportion of overlap (i.e., the degree of agreement) was approximately 50%.**
- They concluded that **“the estimation of tumor shape currently is imprecise, even for experienced physicians”.**

J. S. Cooper, S. K. Mukherji, A. Y. Toledano et al., “An evaluation of the variability of tumor-shape definition derived by experienced observers from CT images of supraglottic carcinomas (ACRIN protocol 6658),” *International Journal of Radiation Oncology Biology Physics*, vol. 67, no. 4, pp. 972–975, 2007

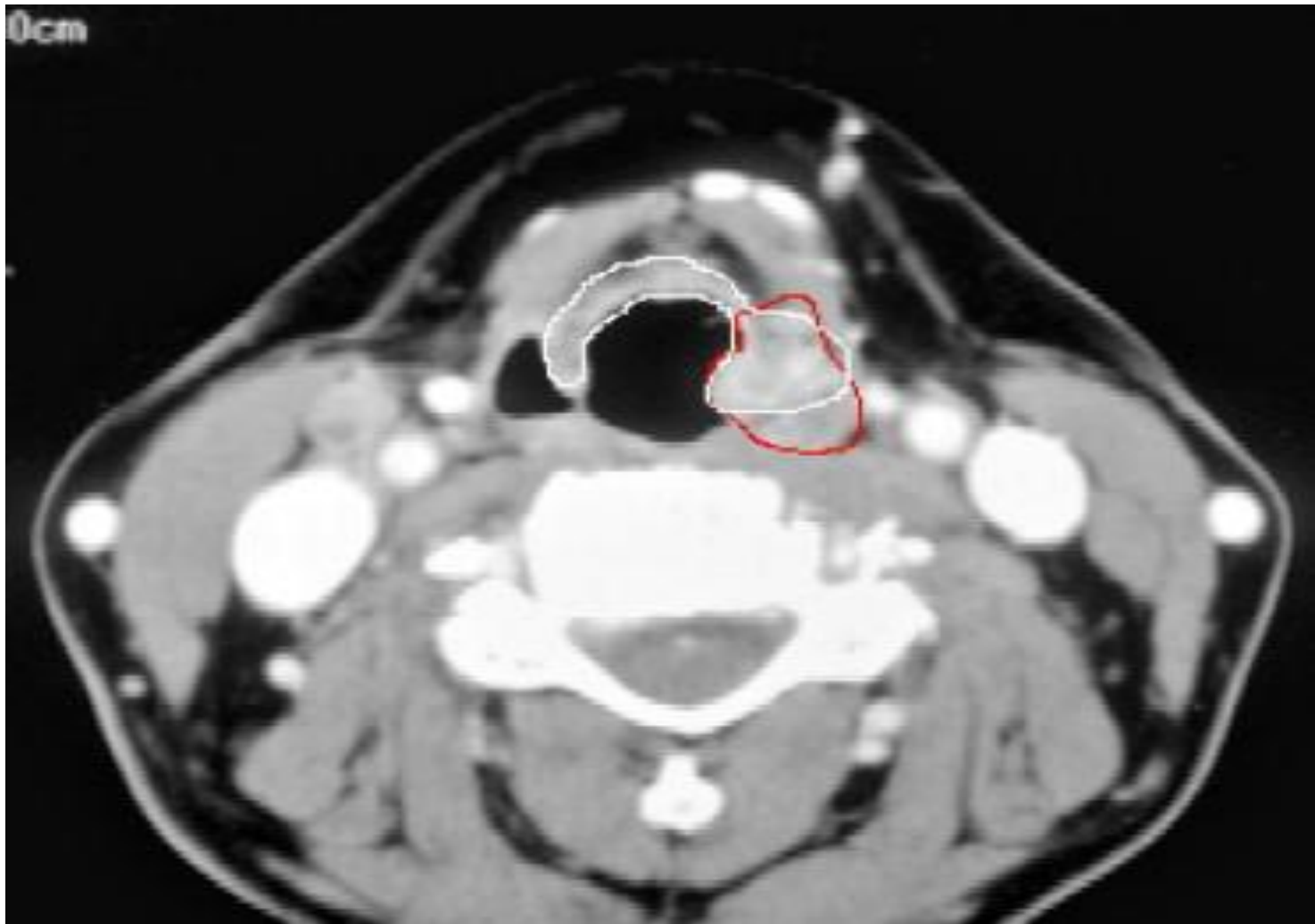


Fig. 2 Example of relatively poor concordance of shape estimates by two physicians.

Jay S. Cooper , et al. **An evaluation of the variability of tumor-shape definition derived by experienced observers from CT images of supraglottic carcinomas (ACRIN protocol 6658)**. International Journal of Radiation Oncology*Biophysics Volume 67, Issue 4 2007 972 - 975

Fidarsi dell' "agreement"?

- The presence of overlapping volumes does not ensure correctness. As there is no gold standard measure of a tumor's shape while it remains *in situ*, we recognize that **two physicians can draw GTVs that have perfect overlap in the wrong location**, or no overlap with each including only part of the tumor, and we could not measure the difference from "absolute truth."



The Gross Tumor volume (GTV)



Radiology

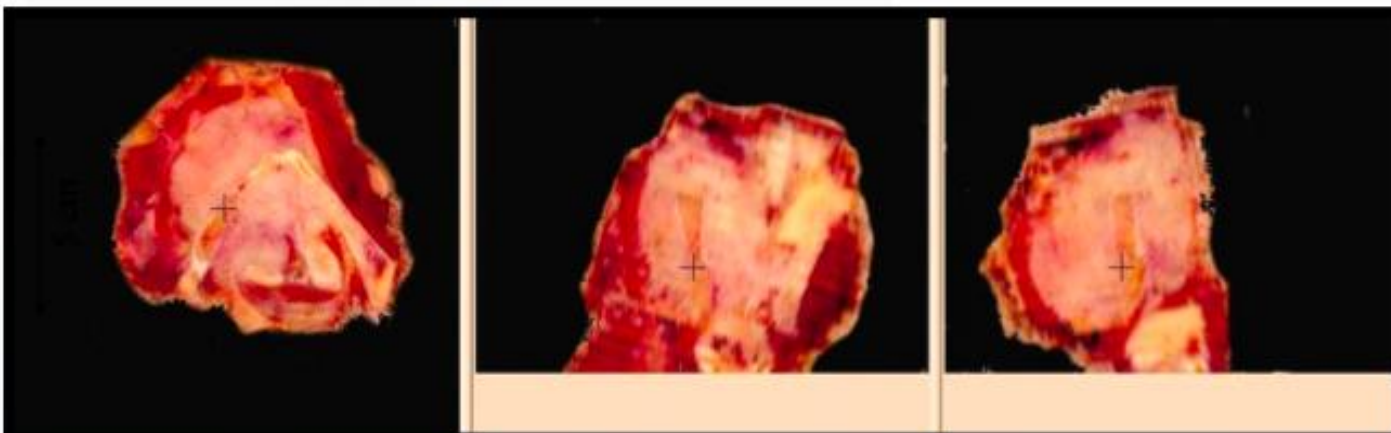
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Index terms:
Head and neck neoplasms, CT,
26.1211, 27.1211
Head and neck neoplasms, MR,

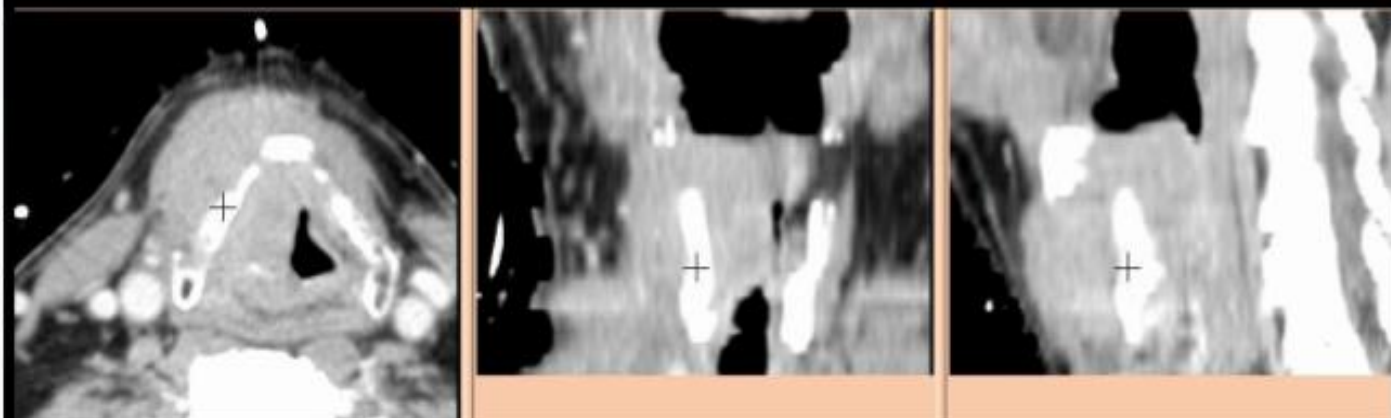
Tumor Volume in Pharyngolaryngeal Squamous Cell Carcinoma: Comparison at CT, MR Imaging, and FDG PET and Validation with Surgical Specimen¹



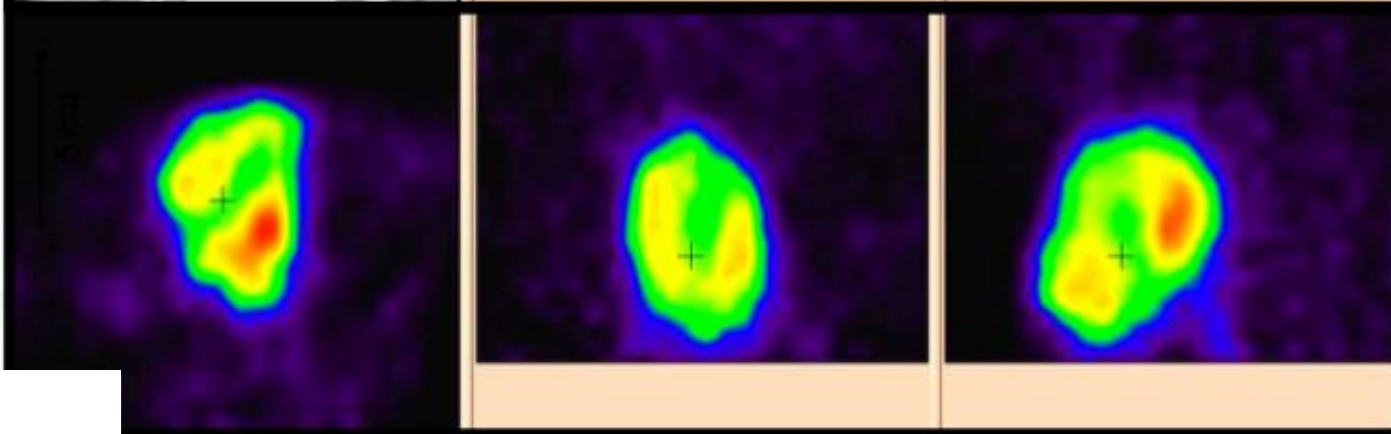
Macroscopy



CAT Scan



^{18}F -FDG
PET



Daisne *et al*, 2004



The “ground truth” GTV



	Vol (ml)	Mismatch _x /CT	Mismatch _x /MR	Mismatch _x /PET	Mismatch _x /macro
CT	20.8	-	26%	48%	81%
MR	23.8	45%	?	67%	107%
FDG-PET	16.3*	17%	15%	-	47%
Macro	12.6*	10%	9%	13%	-

*p<0.05 (Wilcoxon rank test)



A.I.R.O. GRUPPO DI STUDIO TESTA COLLO

27 maggio 2013, Isola Tiberina

**CONFRONTO DELLE CONTORNAZIONI DI GTV, CTVS E
OARS PRIMA E DOPO L'UTILIZZO DELLE LINEE GUIDA
DI TECNICA E ATLANTE OARS**

*Courtesy
Angelo Di Pilla*

STRUMENTI PER LA CONTORNAZIONE DEL CTV

CT-based delineation of lymph node levels in the N0 neck: DAIANCA, EORTC, GORTEC, RTOG consensus guidelines.

Vincent Grégoire, Radiation Oncology
Peter Levendag*, Radiation Oncology

UCT, St-Luc University Hospital, Brussels, Belgium
and *Erasmus Medical Center, Rotterdam, The Netherlands

2004

Nasopharynx

(da Bozza Gruppo di lavoro AIRO testa collo)

Target definition remarks

CTV-HD or high dose volume that encompasses the GTV with a margin; both CT and MRI should be used to identify the primary tumor location;

CTV-HR that typically includes the tissue around the gross tumor volume and/or the neck nodal stations that have high risk of cancer involvement and/or lymph nodes that look suspicious on imaging; given the high rate of subclinical disease in the nasopharynx the whole nasopharynx should be included within this volume (N. Lee et al. 2009)(Orlandi et al. 2013)

CTV-LR includes the lymph nodal stations which have relatively lower risk (5-15%) of cancer involvement (i.e. the lower neck) and do not look suspicious at imaging.

Standard treatment of nasopharyngeal carcinoma is definitive radiotherapy ± chemotherapy.

Pathology remarks

Histological subtypes: the old WHO classification of nasopharyngeal carcinomas (Shanmugaratnam and Sobin 1978), yet widely used in literature, should be replaced by the new one (J. Chan et al. 2005) for not generating confounding factors:

- WHO type 1= keratinizing carcinoma
- WHO type 2.1= non keratinizing differentiated carcinoma
- WHO type 2.2= non keratinizing undifferentiated carcinoma (with lymphoepithelioma variants)
- WHO type 3= basaloid squamous cell carcinoma (a rarity)

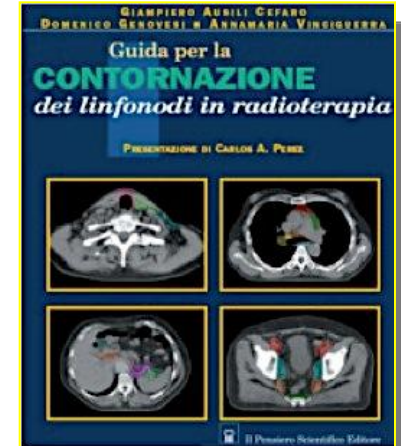
While subsite per se is not a predictor of treatment outcome, histological subtypes are strongly variables by race and strongly influence prognosis:

- a) Asians have a greater proportion of non keratinizing tumors up to 90% (Tse et al. 2006) while white caucasian race have a 60-70% of non keratinizing tumours (Ruckenstein 2004) (Pathmanathan et al. 1995). WHO Type I, II differentiated, and II undifferentiated lesions have 41%, 56.1% and 68.5% 5-year survival rates, respectively (J. T. Lee and Ko 2005).
- b) Also, WHO subtypes influence risk of nodal and distant metastases: Type 1 and 2 have 60% and 90% N+ respectively at diagnosis; Type 1 and 2 have 5-8% and 30-40% distant metastases respectively at diagnosis (Reddy et al. 1995).
- c) Of note, the same radiation dose is prescribed for all variants.

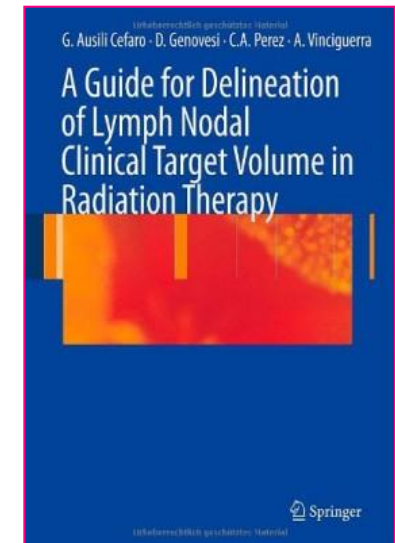
Dose/fractionation remarks

Commonly used fractionation regimens:

In press

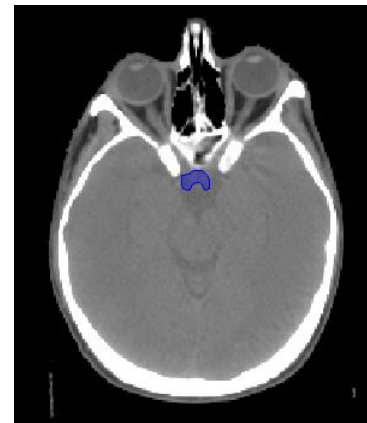
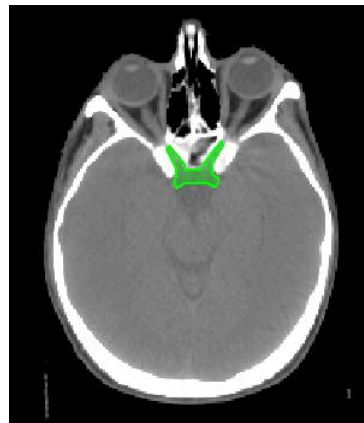
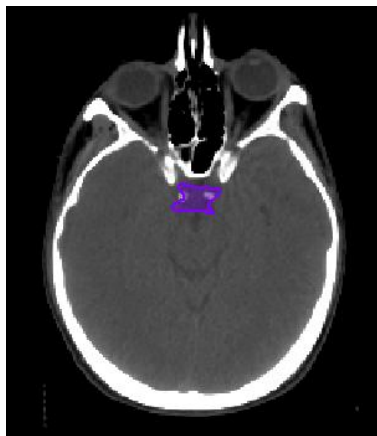


2006



2009

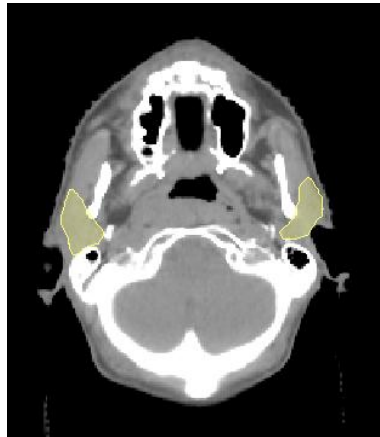
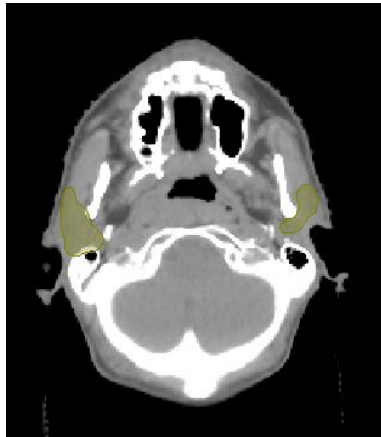
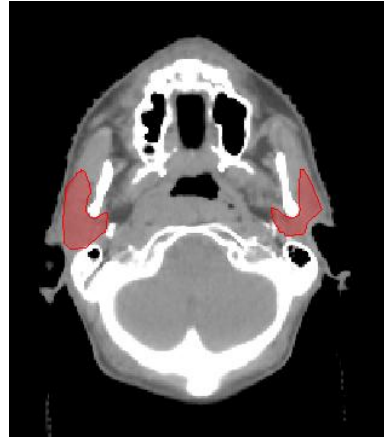
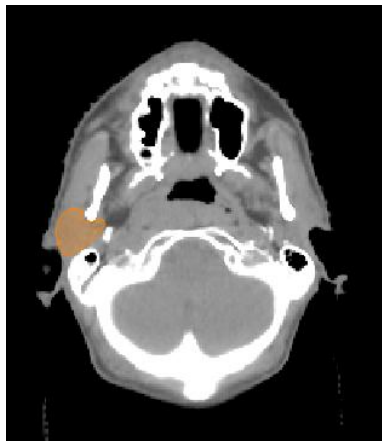
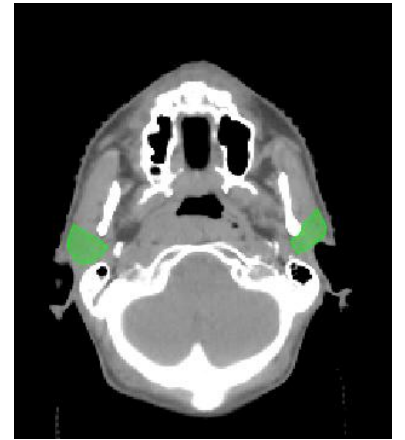
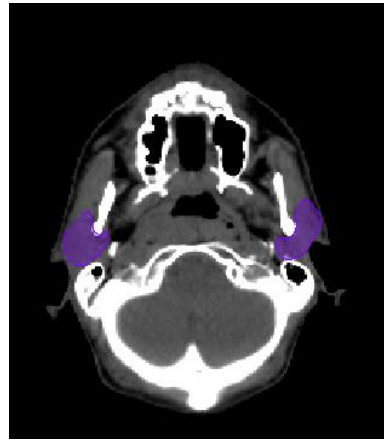
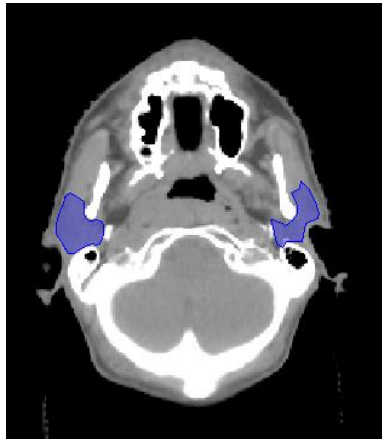
CHIASMA

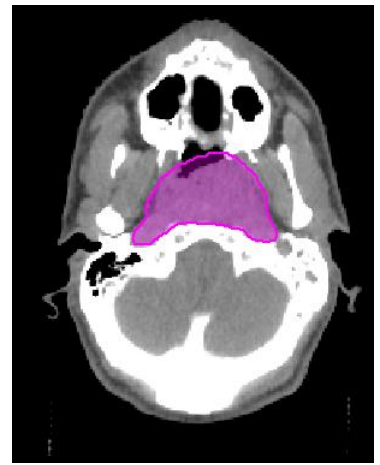
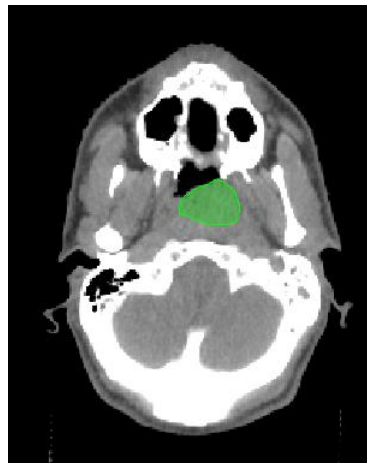
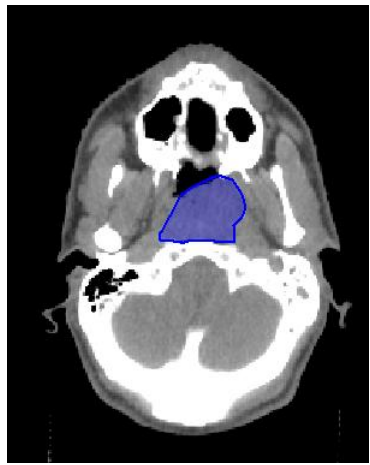


SLICES DIVERSE



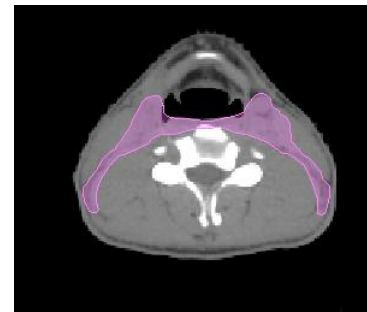
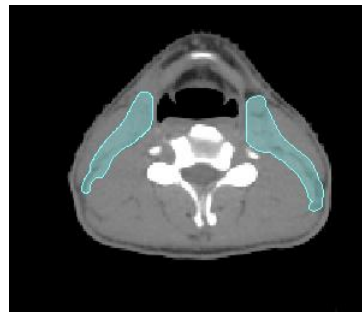
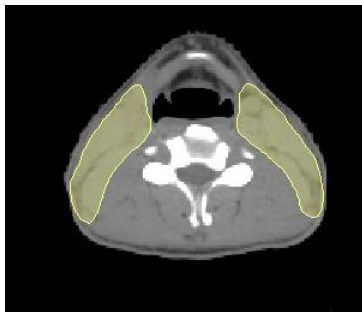
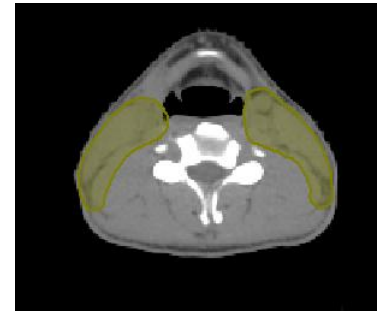
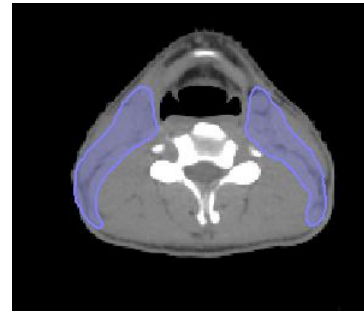
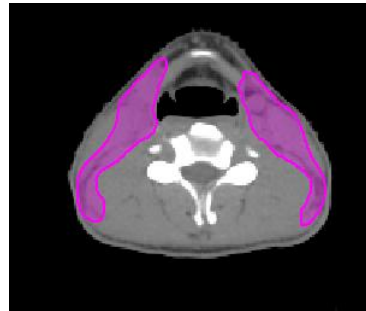
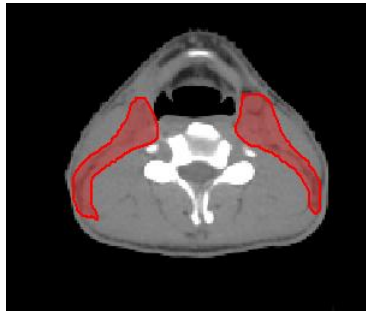
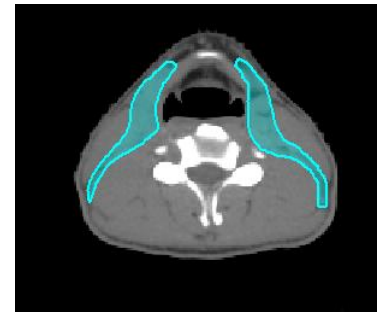
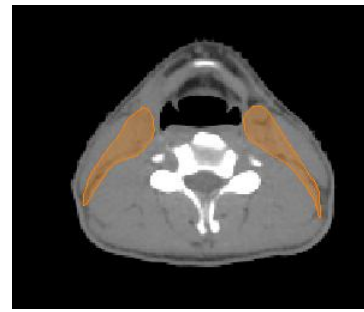
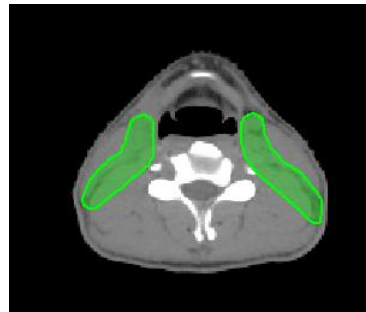
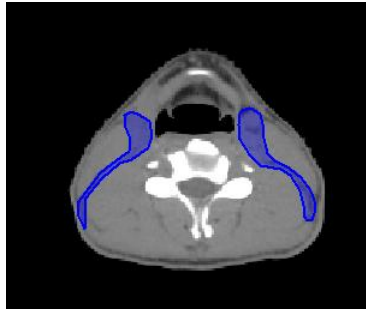
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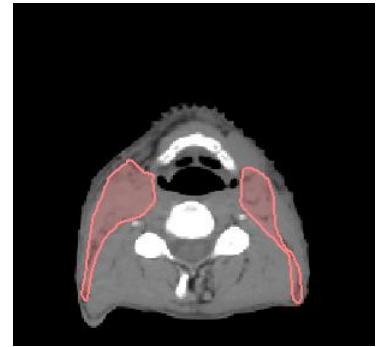
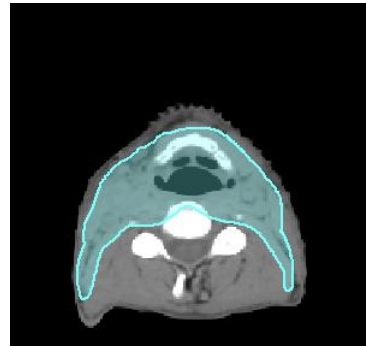
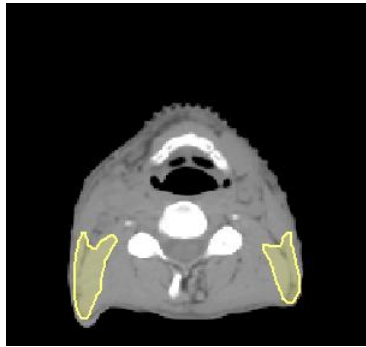
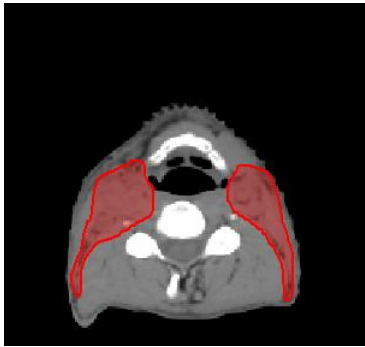
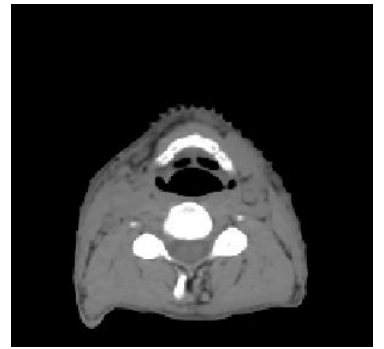
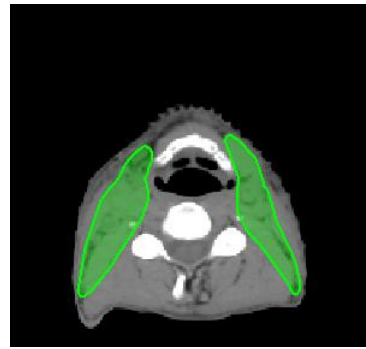
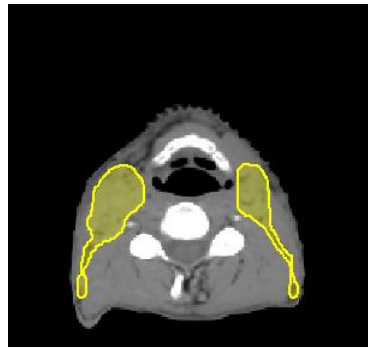
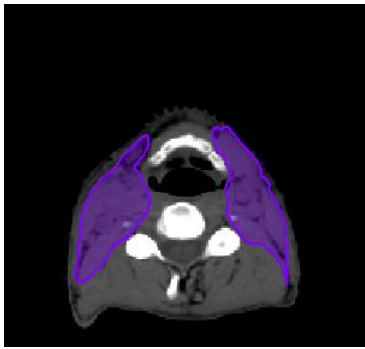


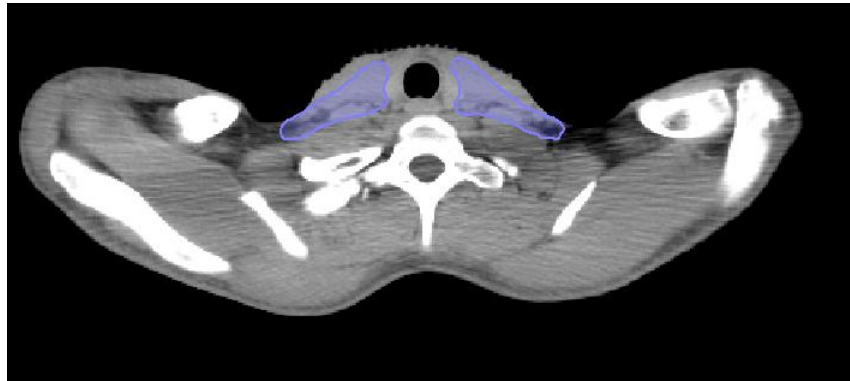
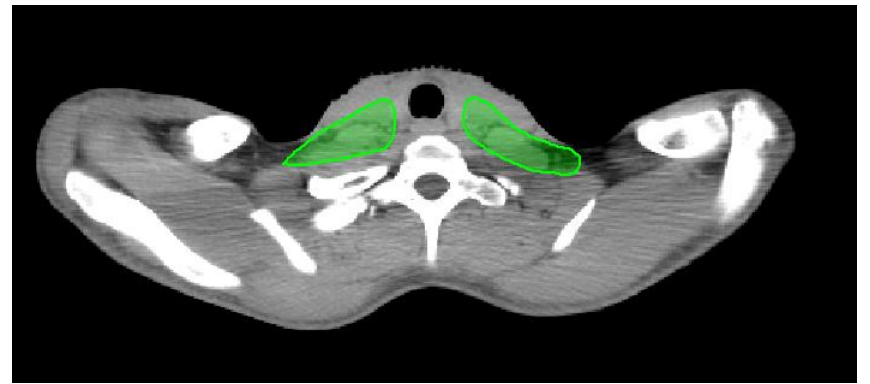
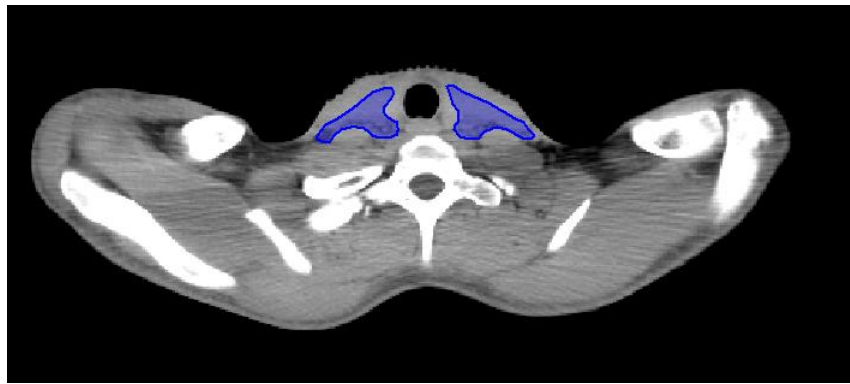


CTV HD

CTV LR



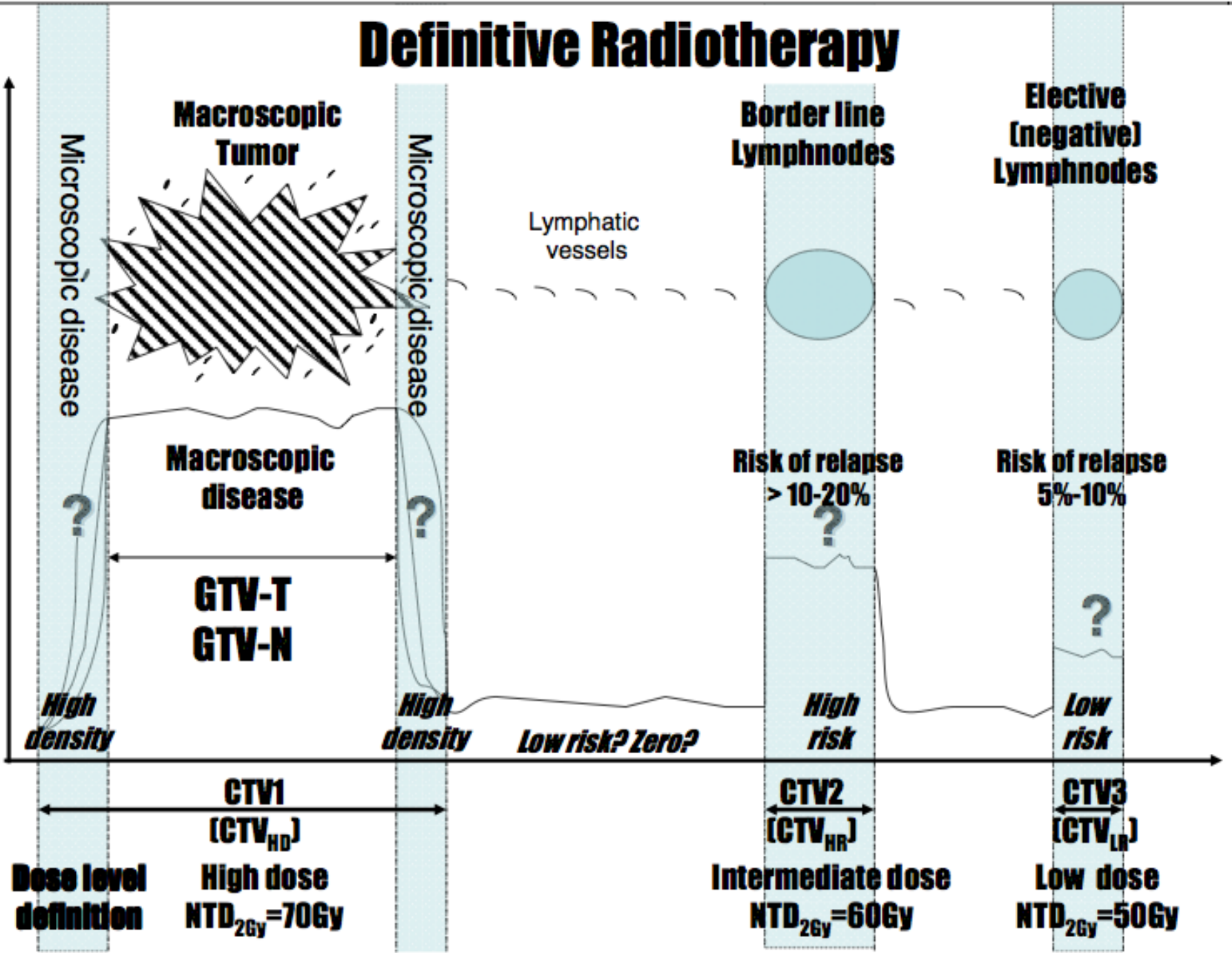




Burden of Disease	Description	ICRU definition	Adopted Definition	Finality	T - level	N - level	Dose level definition	Dose level NTD
Macroscopic	Known gross disease	GTV	GTV	Definitive	Primary tumor	Each Positive-nodes		
High risk of microscopic disease	Risk of relapse > 10-20% ⁵	CTV	CTV1 (CTV _{HD} [^])	Definitive	Peri-GTV areas considered to contain potential microscopic disease ⁶ (T+3/10 mm) ^{7*}	Positive Nodes + 5 ⁸ -10 ⁹ mm.	High Dose	70 Gy
				Post-S	Surgical bed with soft tissue involvement (Positive or close margins): PTB+0.5-1cm according to anatomical barriers ⁸ .	Nodal region with extracapsular extension ⁸ : PTB plus 1 cm up to the skin ⁷ .		66-70 Gy
			CTV2 (CTV _{HR})	Definitive	Preferential areas of diffusion.(Optional) ⁷	Border-line lymph-nodes ^{12,13}	Intermediate Dose	60 Gy
				Post-S	Surgical bed without soft tissue involvement ⁸	Nodal region without extracapsular extension		66§ Gy
Low risk of microscopic disease	Risk of relapse 5-10% ⁸	CTV	CTV3 (CTV _{LR})	Definitive	Structure or compartment adjacent to tumor ⁷	Elective nodal regions, defined for each primary-tumor subsite	Low dose	50 Gy
				Post-S				50 Gy

Depending from anatomic barrier;§ though one prospective study failed to show a benefit for 66 Gy over 60 Gy in the high risk post-operative region¹⁰, this is the dose recommended by some cooperative groups (EORTC¹¹); PTB: postoperative tumour bed; ^ definition of the high-risk region is controversial¹; D= Definitive Radiotherapy; Post-S= postoperative. CTV_{HD}: High Disease; CTV_{HR}= High Risk; LR=Low risk

Definitive Radiotherapy



Conclusioni

- Tecniche altamente conformate richiedono alta expertise
- Linee guida
- Anatomia radiologica (OARs)
- Formazione permanente
- Conoscenza diffusione microscopica di malattia
- **RAGIONAMENTO CLINICO**

Di tutte le malattie,
l'ignoranza e'
la piu' pericolosa.



noopy forever