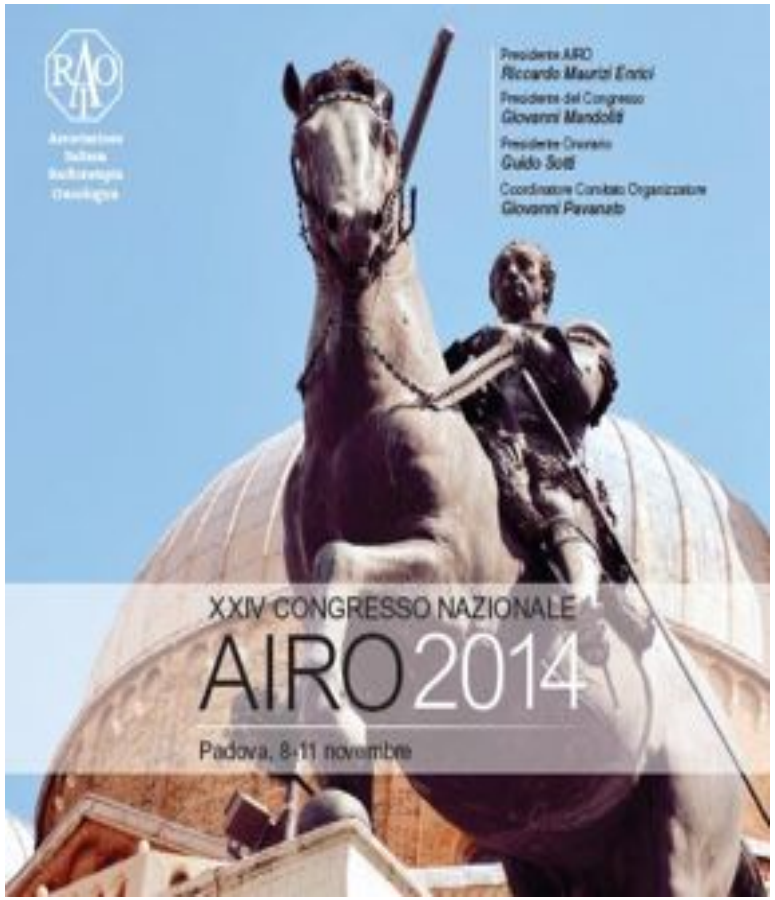
VALUTAZIONE DOSIMETRICA DEI PIANI DI CURA IN IMRT CON BOOST SIMULTANEO INTEGRATO PER IL TRATTAMENTO DI NEOPLASIE DEL RINOFARINGE LOCALMENTE AVANZATE

^A.Errico, **^^R.D'Agostino**, ^A. Natuno, ^D.Di Cosmo, ^G.Squeo,^ S.Carbone, ^^A.De Zio,^^ C.M.Malcangi, ^^A. Lamacchia, ^^A.M. Cicoria, ^^A. Favia, ^S. Bambace

U.O.C.Radioterapia - Osp. Dimiccoli,Barletta



NEOPLASIE DEL RINOFARINGE

INCIDENZA

- **BASSA**:USA, Europa (0,2-0,5 casi/100.000 abitanti)
- **ALTA**: Cina meridionale, Hong Kong (25-50 casi/ 100.000abitanti)

Africa settentrionale (8-12 casi /100.000 abitanti)

EZIOLOGIA

- Abitudini voluttuarie:fumo di tabacco, consumo di alcool
- Abitudini alimentari
- Infezioni virali: EBV

ISTOLOGIA

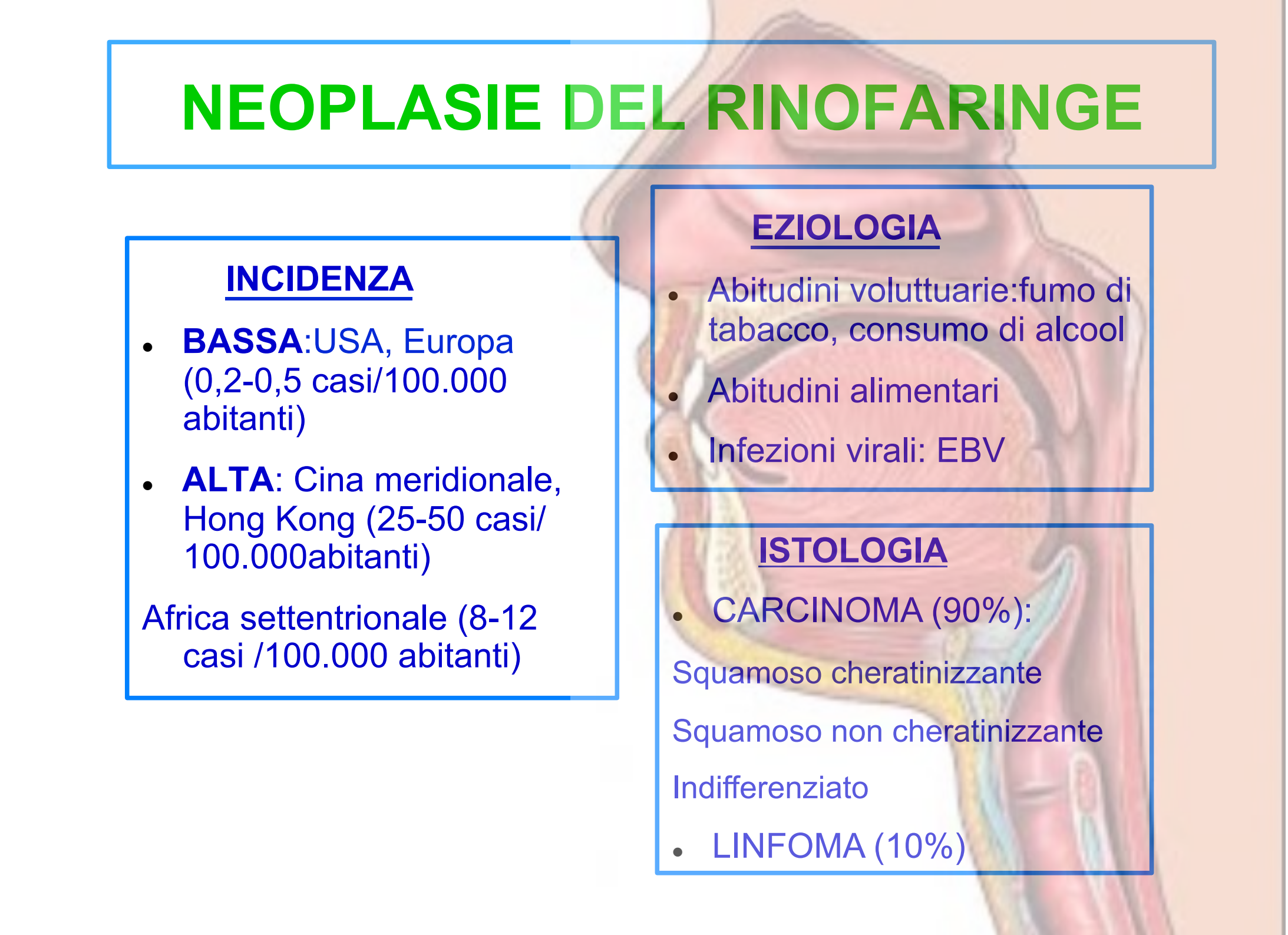
- CARCINOMA (90%):

Squamoso cheratinizzante

Squamoso non cheratinizzante

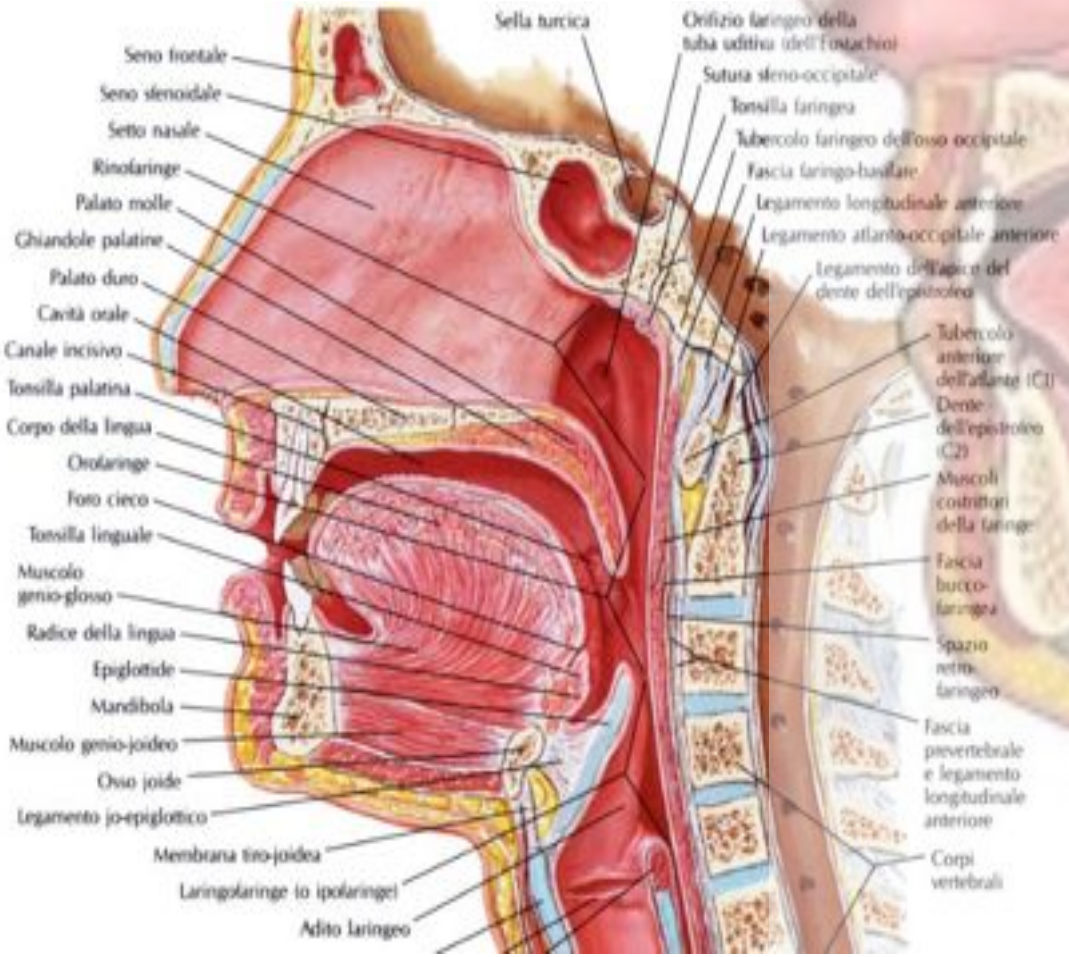
Indifferenziato

- LINFOMA (10%)



NEOPLASIE DEL RINOFARINGE

ANATOMIA E VIE DI DIFFUSIONE



Per contiguità

IN ALTO — osso sfenoide, base cranio

LATERALMENTE — tube uditive, nervi cranici

IN AVANTI — a. carotide, cavità nasale, v. giugulare int.

Per via linfatica

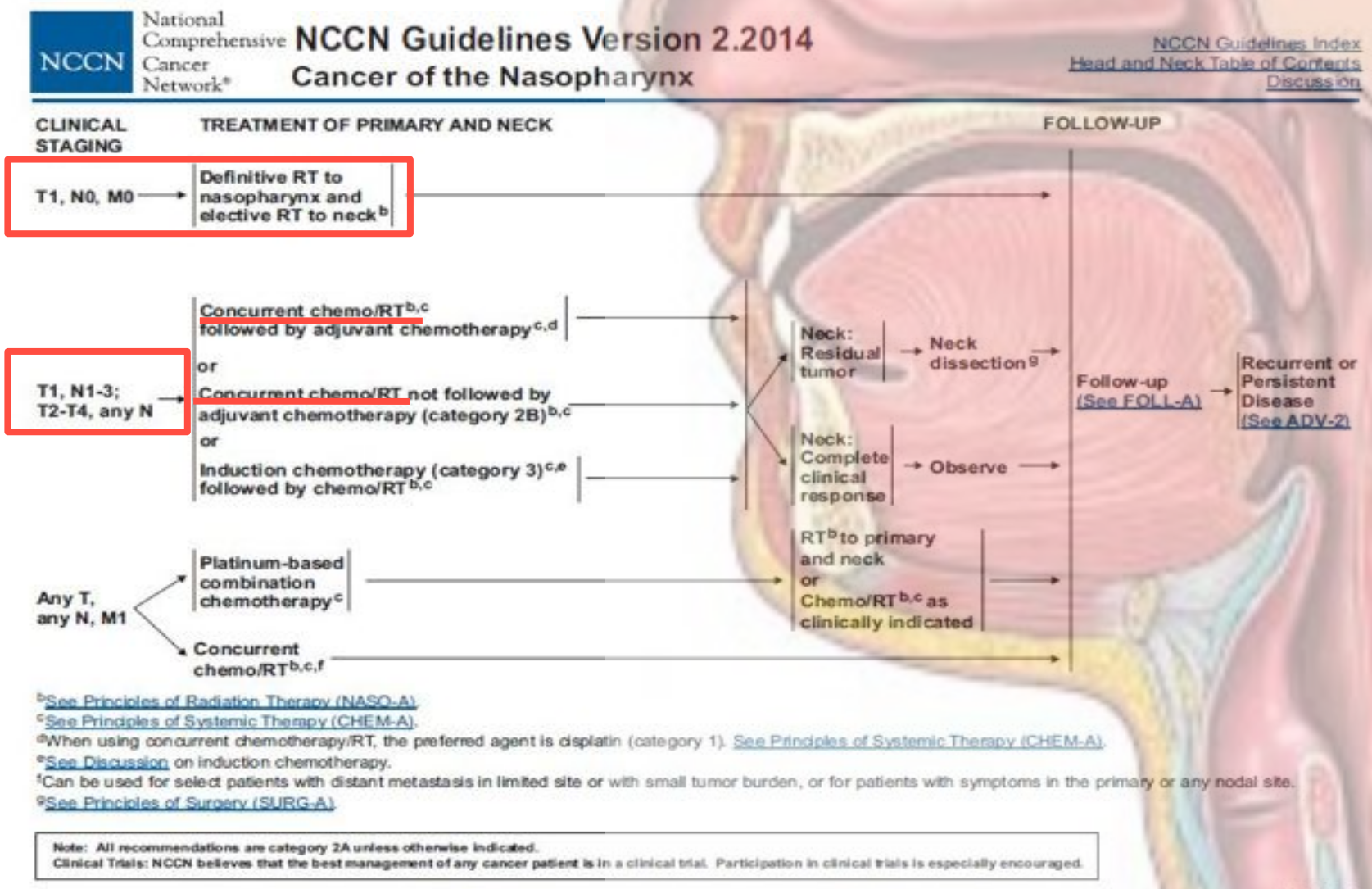
linfonodi laterocervicali

NEOPLASIE DEL RINOFARINGE

SINTOMI

- EPISTASSI
- OTALGIA
- OSTRUZIONE NASALE
- DEFICIT NERVI CRANICI
- TURBE OLFATTIVE

NEOPLASIE DEL RINOFARINGE: TRATTAMENTO



NEOPLASIE DEL RINOFARINGE

L'IMRT rappresenta il *gold standard* nel trattamento delle neoplasie del rinofaringe

ottimizzare la distribuzione di dose al target

minimizzare la dose agli organi a rischio

NEOPLASIE DEL RINOFARINGE

Int. J. Radiation Oncology Biol. Phys., Vol. 69, No. 2, Supplement, pp. S115–S117, 2007

0360-3016/07/$–see front matter

ELSEVIER

HEAD AND NECK CANCER SYMPOSIUM

NASOPHARYNGEAL CANCER: ADVANCES IN RADIOTHERAPY

ANNE W. M. LEE, F.R.C.R.

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Nasopharyngeal cancer (NPC) is one of the greatest challenges for oncologists. Because of the deep-seated anatomic location and the proximity to critical structures, radical surgical resection is most difficult. This highly malignant cancer was invariably lethal until the advent of radiotherapy (RT). The first reports of long survivors (25% at 5 years) in the mid-1960s marked the first major breakthrough. Megavoltage RT has since become the mainstay of treatment, but the therapeutic margin is notoriously narrow.

Meticulous attention to every single step in the RT process is important, particularly when using an increasingly conformal technique. The first fundamental step is accurate delineation of the gross tumor extent. Fusion of magnetic resonance images with planning computed tomography is indicated. Positron emission tomography is being increasingly used, not only for better detection of distant metastases, but also for depiction of locoregional tumor metabolic activity for supplementary information.

Optimization of dose fractionation is crucial. Although NPC is radiosensitive, a significant dose response has been suggested by retrospective data. The general consensus is that a total dose of 70 Gy or above is needed for the gross tumor and 50–60 Gy for elective treatment of potential at-risk sites. One method of achieving dose escalation is to give

Table 1. Intensity-modulated radiotherapy for nasopharyngeal carcinoma: methods and results from different centers

Variable	Study				
	UCSF (10, 11)	MSKCC (12)	PWH (13)	QMH (14)	QMH (15)
Patients (*n*)	118	74	63	50	50
T stage	All	All	All	T1-T2	T3-T4
Median follow-up (mo)	30	35	29	14	25
RT regimen					
PTV-G (margin around GTV; mm)		5–10	2		
Total dose (Gy)	70	70.2	66	68–70	76
Dose/fraction (Gy)	2.12	2.34	2	2–2.06	2.17
Additional treatment (%)					
Accelerated fractionation	—	80	—	—	—
Boost	22		56		—
Chemotherapy	90	93	30	0	68
Tumor control					
Time point (y)	4	3	3	2	2
Local control (%)	96	91	92	100	96
Nodal control (%)	98	93	98	94	
Distant control (%)	72	78	79	94	94
Overall survival (%)	74	83	90	NR	92
Late toxicities (%)					
Xerostomia (Grade ≥2)	2* (2 y)	32 (1 y)	23 (2 y)		
Deafness (Grade >2)	7%*	>15%	15		42
Fibrosis (Grade >2)			11		14
Dysphagia (Grade >2)	1*		5		
Hypopituitarism			23		
Osteonecrosis	0.8		2		
Temporal lobe necrosis	0.8		3		4
Torrential epistaxis	0.8*				4

Abbreviations: UCSF = University of California, San Francisco; MSKCC = Memorial Sloan-Kettering Cancer Center; PWH = Prince of Wales Hospital (Hong Kong); QMH = Queen Mary Hospital (Hong Kong); PTV-G = planning target volume for gross tumor; GTV = gross tumor volume.

* According to data reported by Lee *et al.* (10) in 2002.

NEOPLASIE DEL RINOFARINGE

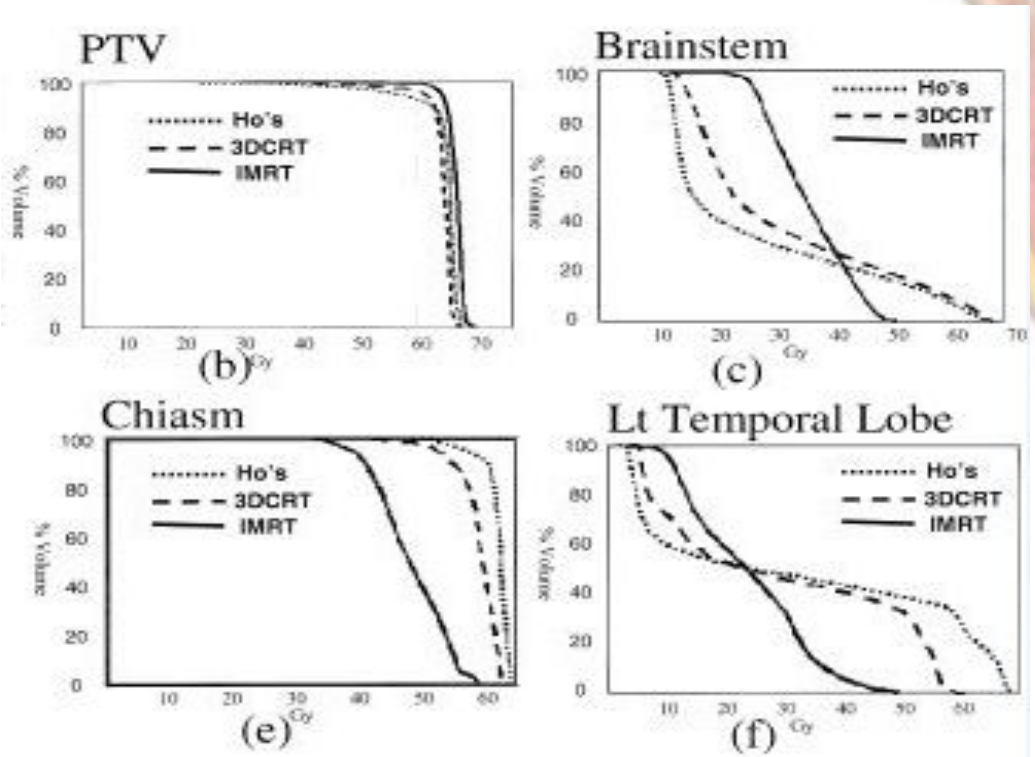
Int. J. Radiation Oncology Biol. Phys., Vol. 56, No. 1, pp. 145–157, 2003

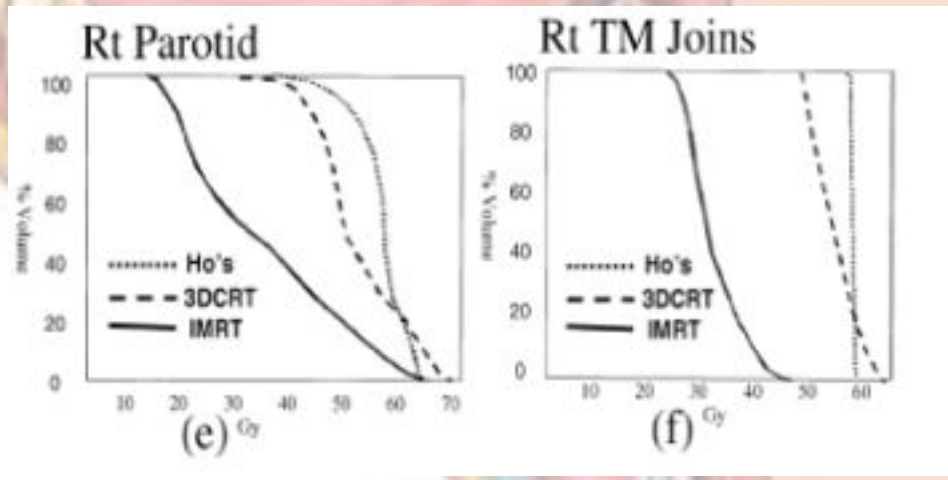
3D-CRT

INTENSITY-MODULATED RADIOTHERAPY IN NASOPHARYNGEAL CARCINOMA: DOSIMETRIC ADVANTAGE OVER CONVENTIONAL PLANS AND FEASIBILITY OF DOSE ESCALATION

MICHAEL K. M. KAM, F.R.C.R., RICKY M. C. CHAU, M.Sc., JOYCE SUEN, M.B.Ch.B., PETER H. K. CHOI, F.R.C.R., AND PETER M. L. TEO, M.D., F.R.C.R.

Department of Clinical Oncology, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR, China





NEOPLASIE DEL RINOFARINGE

Int. J. Radiation Oncology Biol. Phys., Vol. 75, No. 5, pp. 1481–1486, 2009

0360-3016/09/$–see front matter

CLINICAL INVESTIGATION **Head and Neck**

TREATMENT OF NASOPHARYNGEAL CARCINOMA USING INTENSITY-MODULATED RADIOTHERAPY—THE NATIONAL CANCER CENTRE SINGAPORE EXPERIENCE

IVAN WENG-KEONG THAM, FRCR.,*† SIEW WAN HEE, MSc.,† RICHARD MING-CHERT YEO, FRCR.,* PATEMAH BTE SALLEH, CMD.,* JAMES LEE, PHD.,* TERENCE WEE-KIAT TAN, FRCR.,* KAM WENG FONG, FRCR.,* EU TIONG CHUA, FRCR.,* AND JOSEPH TIEN-SENG WEE, FRCR.*†

* Department of Radiation Oncology, and † Division of Clinical Trials and Epidemiological Sciences, National Cancer Centre, Singapore

Table 3. One- and three-year survival rates

Type	Events/*N*	1-year rate %	1-year rate SE	3-year rate %	3-year rate SE
All patients					
Overall survival	14/195	98.4	0.009	94.3	0.018
Local recurrence-free survival	19/195	96.8	0.013	89.6	0.024
Distant relapse-free survival	19/195	96.8	0.013	89.2	0.024
Disease-free survival	41/195	93.7	0.018	79	0.031
Patients with complete response					
Overall survival	10/188	98.9	0.008	96.5	0.014
Local recurrence-free survival	12/188	NE	NE	93.1	0.021
Distant relapse-free survival	16/188	97.8	0.011	90.6	0.023
Disease-free survival	34/188	96.7	0.013	82.1	0.029

Table 4. Frequency (%) of acute toxicity

Toxicity	Chemotherapy Grade 0–2	Chemotherapy Grade 3	Chemotherapy Grade 4	No chemotherapy Grade 0–2	No chemotherapy Grade 3	No chemotherapy Grade 4
Dermatitis	192 (98)	2 (2)	0	77 (100)	0	0
Mucositis	75 (71)	30 (29)	0	63 (80)	15 (20)	0
Dysphagia	83 (79)	22 (21)	0	73 (92)	6 (8)	0
Xerostomia	101 (97)	3 (3)	—	77 (100)	0	—
Hemoglobin nadir	105 (95)	5 (5)	0			
Total white count nadir	69 (63)	37 (34)	4 (4)			
Neutrophil count nadir	73 (66)	33 (30)	4 (4)			
Platelet count nadir	107 (97)	3 (3)	0			

NEOPLASIE DEL RINOFARINGE: TRATTAMENTO

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2014
Cancer of the Nasopharynx

NCCN Guidelines Index
Head and Neck Table of Contents
Discussion

PRINCIPLES OF RADIATION THERAPY[1]

DEFINITIVE
RT Alone (preferred if no chemotherapy is being used)
- **PTV**
  - **High risk: Primary tumor and involved lymph nodes (this includes possible local subclinical infiltration at the primary site and at the high-risk level lymph node(s))**
    - **66 Gy (2.2 Gy/fraction) to 70 Gy(2.0 Gy/fraction); daily Monday-Friday in 6-7 weeks**
- **Intermediate and low risk: Sites of suspected subclinical spread**
  - **44 Gy (2.0 Gy/fraction) to 60 Gy (1.6 Gy/fraction)**[2]

CONCURRENT CHEMORADIATION:[3]
(preferred for patients eligible for chemotherapy)
- **PTV**
  - **High risk: typically 70 Gy (2.0 Gy/fraction)**
  - **Intermediate and low risk: 44 Gy (2.0 Gy/fraction) to 60 Gy (1.6 Gy/fraction)**[2]

IMRT is preferred over 3D conformal RT in cancer of the nasopharynx to minimize dose to critical structures.

[1] See Radiation Techniques (RAD-A) and Discussion.
[2] Suggest 44-54 Gy in 3D conformal RT and 54-60 Gy in IMRT due to dose painting (dependent upon dose per fraction).
[3] See Principles of Systemic Therapy (CHEM-A).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

NASO-A

IL NOSTRO STUDIO

SCOPO: valutare la qualità dosimetrica dei piani di trattamento in modalità SIB-IMRT di neoplasie rinofaringee localmente avanzate eseguiti c/o l'U.O.Radioterapia dell'Osp. Dimiccoli di Barletta

MATERIALI E METODI: da Febbraio 2010 a Febbraio 2014 sono stati trattati 10 pz mediante radioterapia SIB-IMRT, associata a chemio concomitante a base di CDDP.

3 volumi target

PTV1:T,N+ → 66/69,96Gy

PTV2:N ad alto rischio di malattia subclinica → 60Gy

PTV3 :N a basso rischio di malattia subclinica → 54Gy

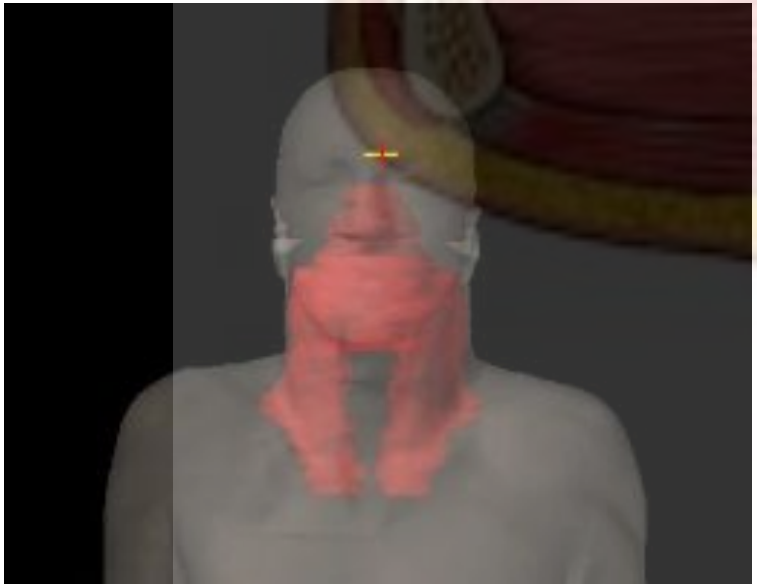
Organi a rischio

Midollo spinale,tronco encefalico,parotidi,coclee,laringe, chiasma ottico

IL NOSTRO STUDIO

PTV 69,96

PTV 60

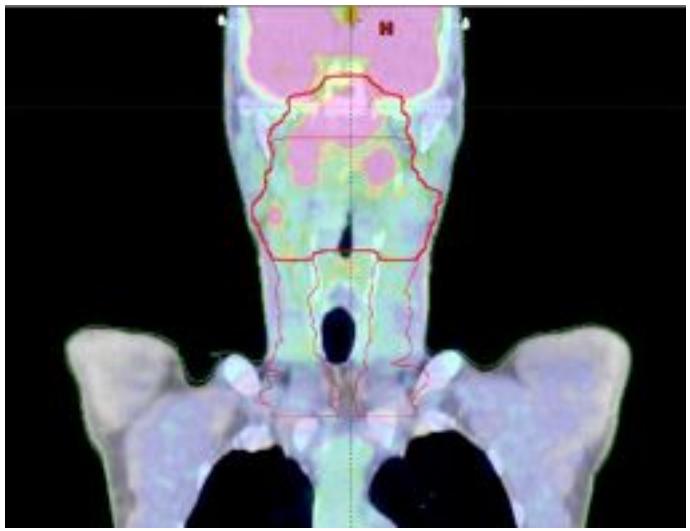


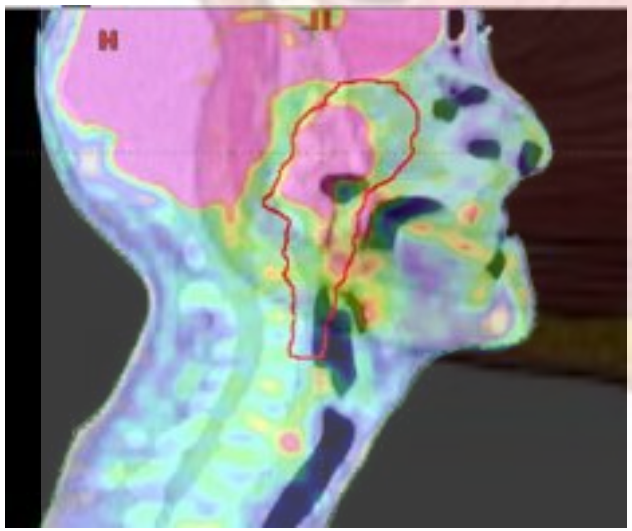
PTV 54

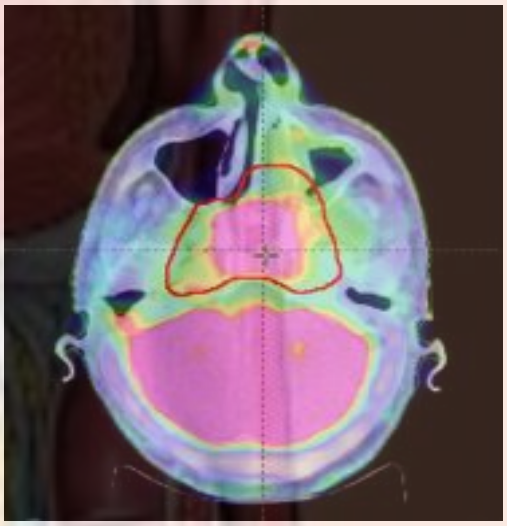
IL NOSTRO STUDIO

STRATEGIE RT

Tutti i pazienti sono stati sottoposti a TC PET di fusione per la delineazione dei volumi bersaglio



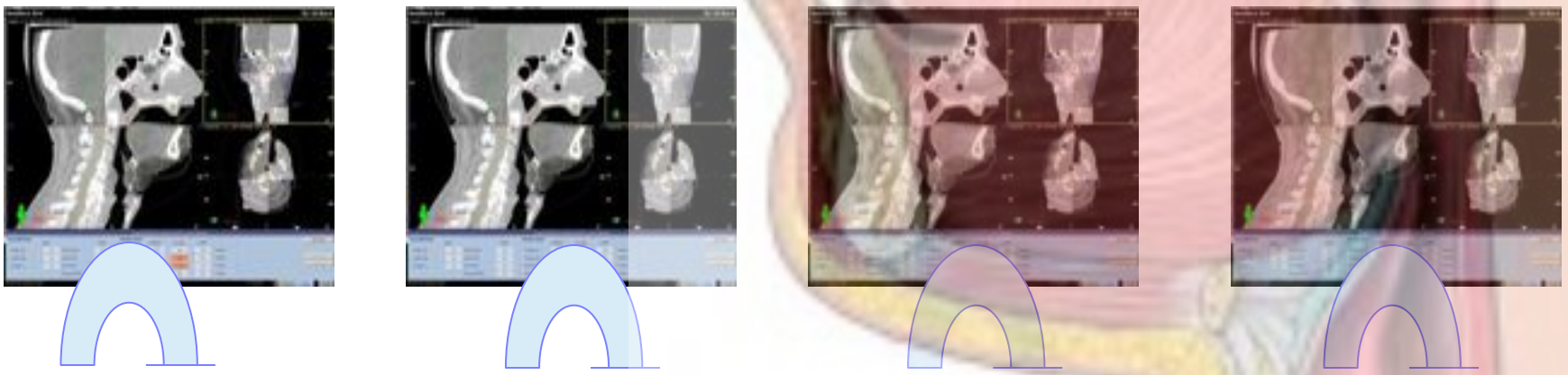


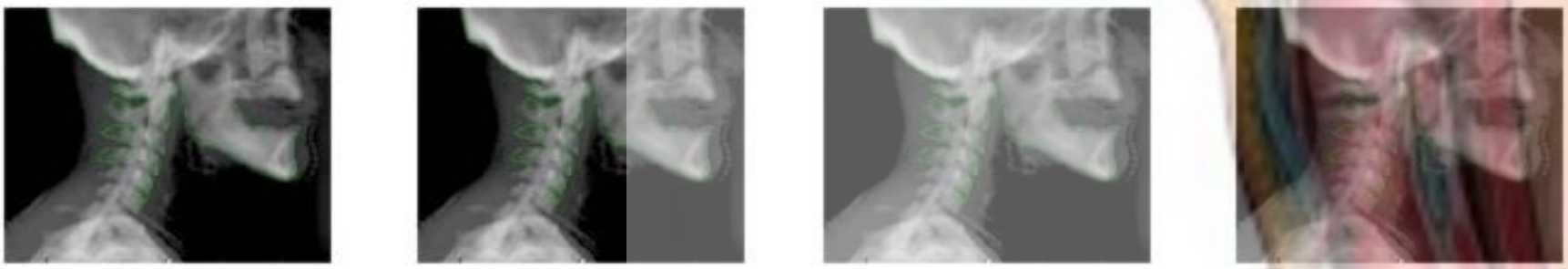


IL NOSTRO STUDIO

CONTROLLI IGRT

Tutti i pazienti sono stati sottoposti a controlli di *setup* mediante *imaging* a kV giornaliero e *cone-beam* una volta a settimana

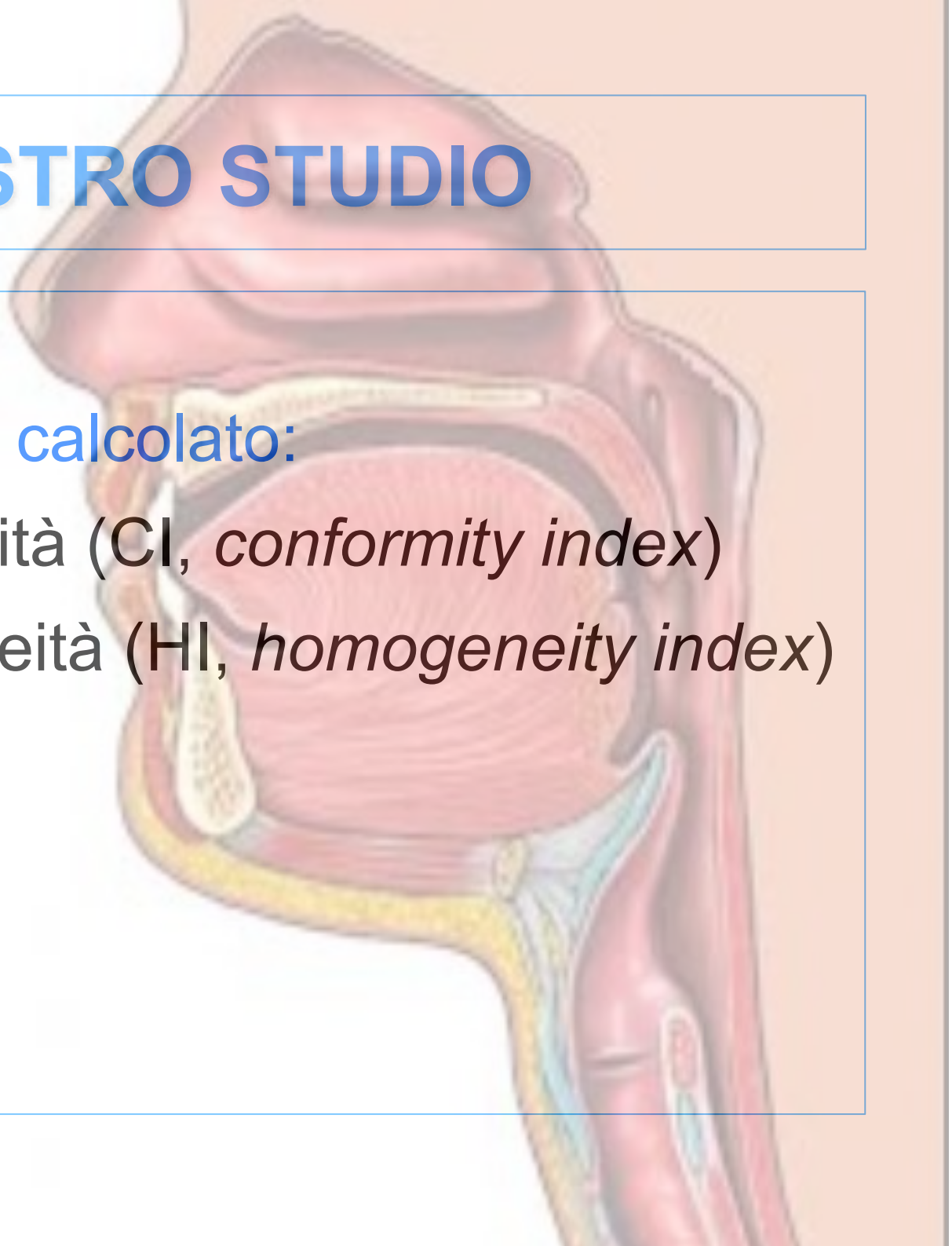




IL NOSTRO STUDIO

Di ogni piano è stato calcolato:

- L'indice di conformità (CI, *conformity index*)
- L'indice di omogeneità (HI, *homogeneity index*)



IL NOSTRO STUDIO

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 64, No. 2, pp. 333–348, 2006

0360-3016/06/$–see front matter

CRITICAL REVIEW

CONFORMITY INDEX: A REVIEW

LOÏC FEUVRET, M.D.,* GEORGES NOËL, M.D.,* JEAN-JACQUES MAZERON, M.D., PH.D.,*† AND PIERRE BEY, M.D.*‡

*Institut Curie, Orsay, France; †Pitié Salpêtrière Hospital, Paris, France; ‡Institut Curie, Paris, France

$$Conformity\ Index_{RTOG} = \frac{V_{RI}}{TV} \quad (1c)$$

where V_{RI} = reference isodose volume, and TV = target volume.

The RTOG "conformity index" (Eq.1c) is easy to interpret. A conformity index equal to 1 corresponds to ideal conformation. A conformity index greater than 1 indicates that the irradiated volume is greater than the target volume and includes healthy tissues. If the conformity index is less than 1, the target volume is only partially irradiated. According to RTOG guidelines, ranges of conformity index values have been defined to determine the quality of conformation, because a value of 1 is rarely obtained. If the

Int. J. Radiation Oncology Biol. Phys., Vol. 56, No. 2, pp. 573–585, 2003

0360-3016/03/$–see front matter

PHYSICS CONTRIBUTION

SIMULTANEOUS INTEGRATED BOOST INTENSITY-MODULATED RADIOTHERAPY FOR LOCALLY ADVANCED HEAD-AND-NECK SQUAMOUS CELL CARCINOMAS. I: DOSIMETRIC RESULTS

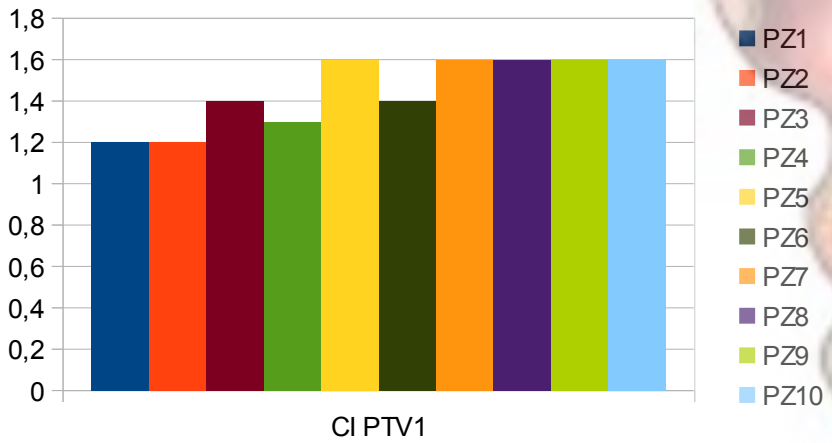
QIUWEN WU, PH.D., RADHE MOHAN, PH.D., MONICA MORRIS, M.D., ANDREW LAUVE, M.D., AND RUPERT SCHMIDT-ULLRICH, M.D.

Department of Radiation Oncology, Virginia Commonwealth University, Richmond, VA

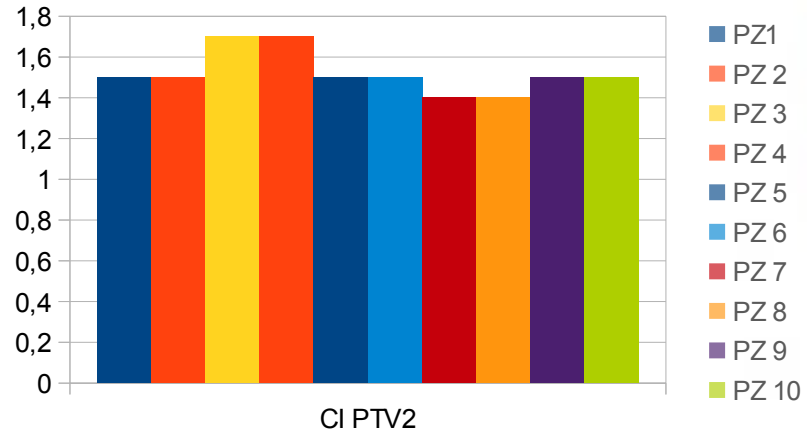
$$HI = \frac{D_2 - D_{98}}{D_{prescription}} \times 100\% \quad (1)$$

Lower HI values are indicative of a more homogeneous target dose.

IL NOSTRO STUDIO

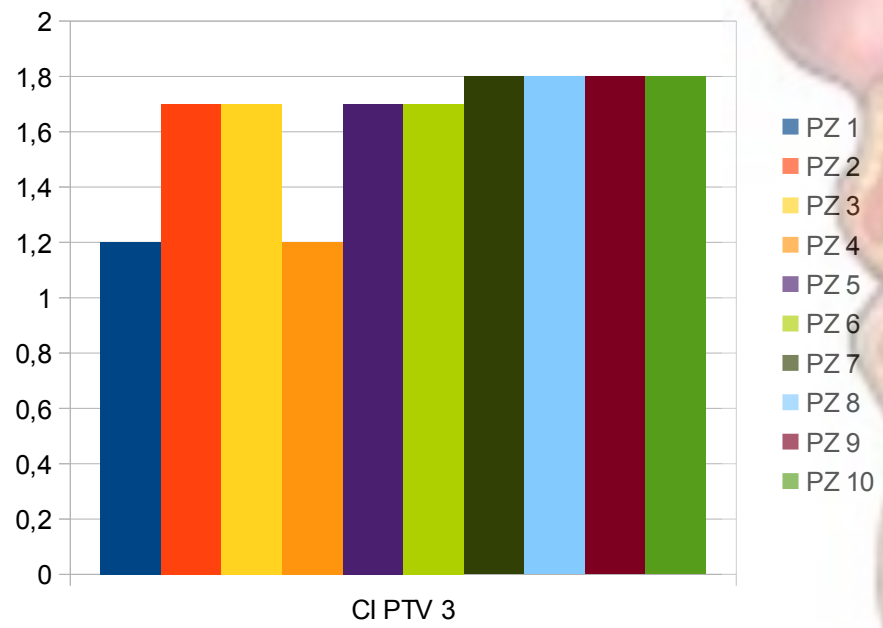


CI mediano per il PTV1 è 1,40 (range 1,20- 1,60)



Il CI mediano per il PTV2 è 1,50 (range1,40- 1,70)

IL NOSTRO STUDIO



Il CI mediano per il PTV3 è 1,50 (range 1,20- 1,80)

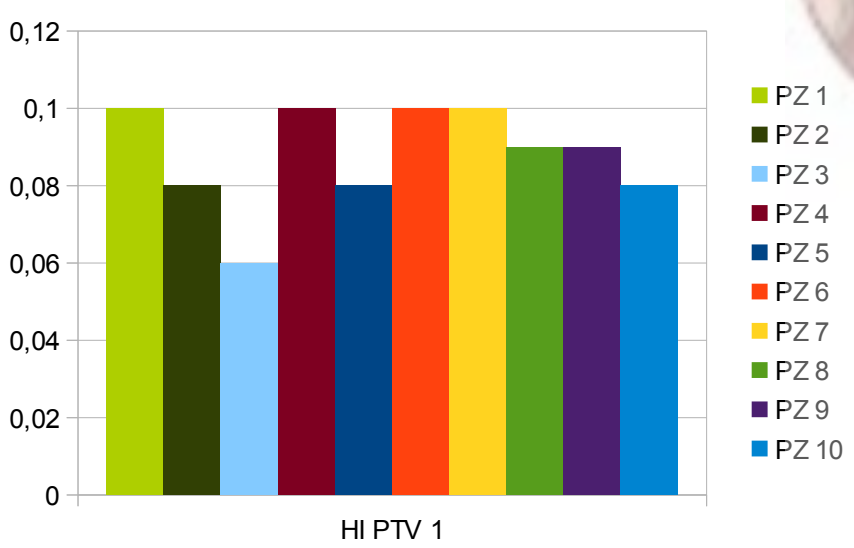
Per tutti i PTV considerati l'indice di conformità mediano è compreso in tali limiti

Int. J. Radiation Oncology Biol. Phys., Vol. 64, No. 2, pp. 333–342, 2006

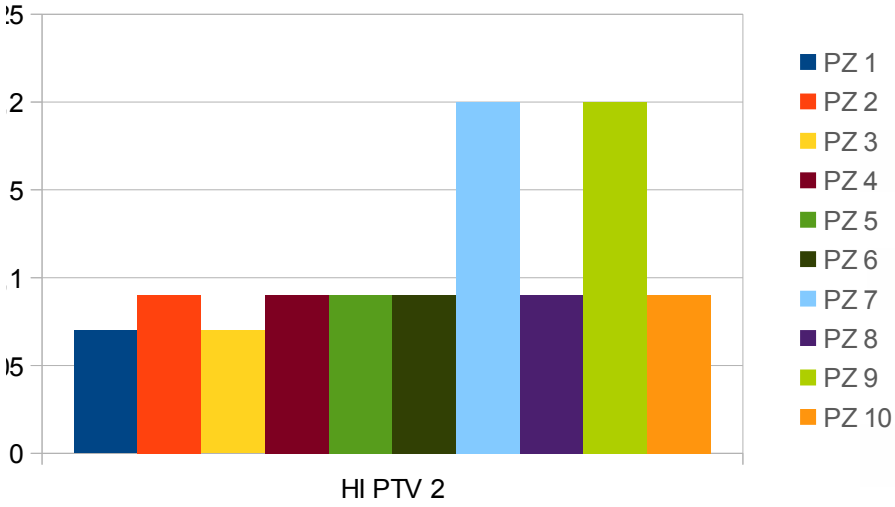
0360-3016/06/$–see front matter

formation, because a value of 1 is rarely obtained. If the conformity index is situated between 1 and 2, treatment is considered to comply with the treatment plan; an index between 2 and 2.5, or 0.9 and 1, is considered to be a minor violation, and an index less than 0.9 or more than 2.5 is considered to be a major violation. However, this index

IL NOSTRO STUDIO

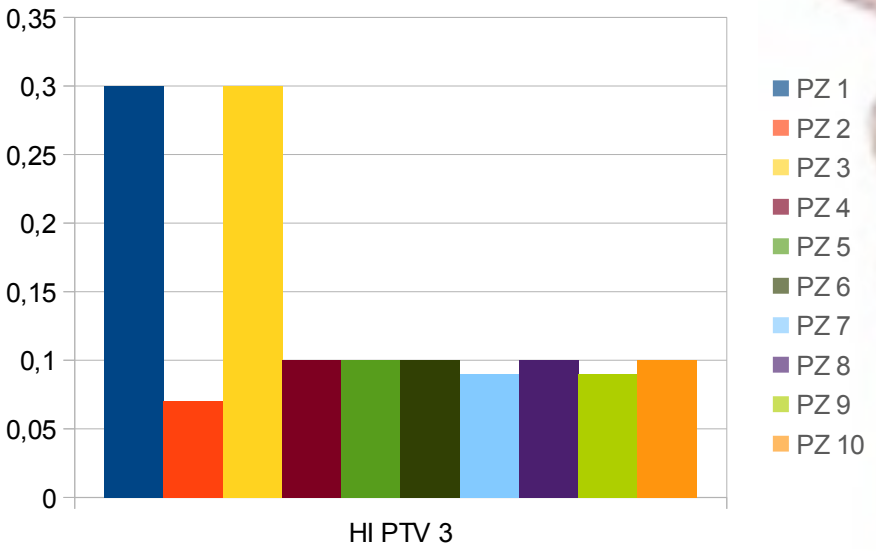


L'HI mediano per il PTV1 è 0,08 (range 0,06- 0,10)



L'HI mediano per il PTV2 è 0,14 (range 0,07- 0,20)

IL NOSTRO STUDIO



L'HI mediano per il PTV 3 è 0,19 (range 0,07- 0,30)

IL NOSTRO STUDIO

RISULTATI

USE OF NORMAL TISSUE COMPLICATION PROBABILITY MODELS IN THE CLINIC

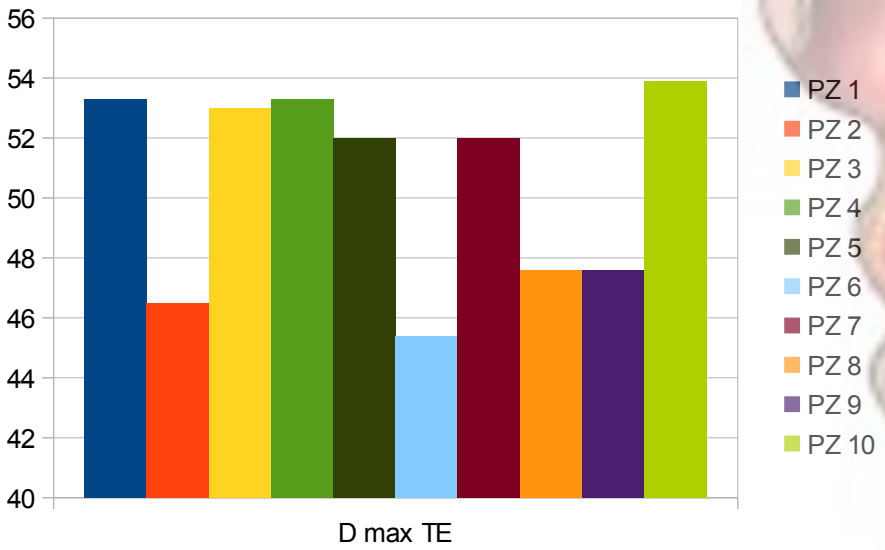
LAWRENCE B. MARKS, M.D.,* ELLEN D. YORKE, PH.D.,† ANDREW JACKSON, PH.D.,†
RANDALL K. TEN HAKEN, PH.D.,† LOUIS S. CONSTINE, M.D.,‡ AVRAHAM EISBRUCH, M.D.,†
SØREN M. BENTZEN, PH.D.,§ JIHO NAM, M.D.,* AND JOSEPH O. DEASY, PH.D.¶

Table 1. QUANTEC Summary: Approximate Dose/Volume/Outcome Data for Several Organs Following Conventional Fractionation (Unless Otherwise Noted)*

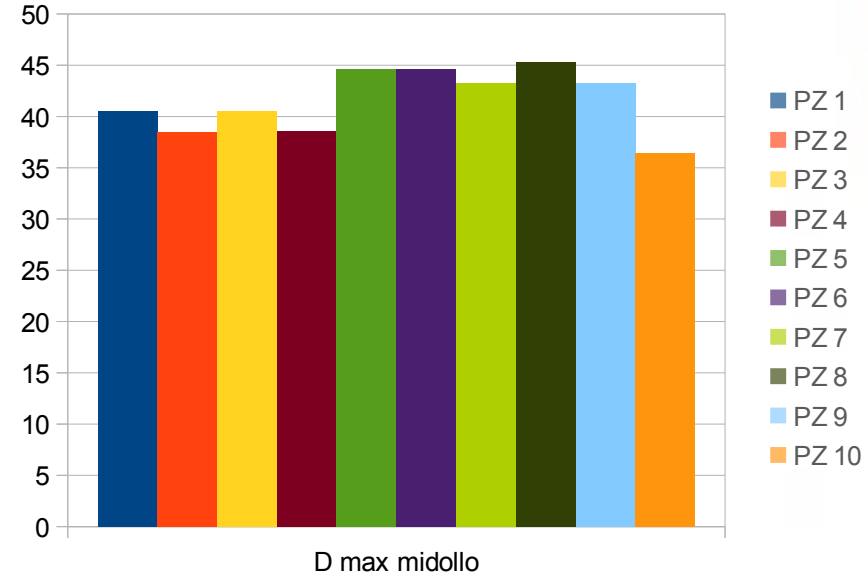
Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated)†	Endpoint	Dose (Gy), or dose/volume parameters†	Rate (%)	Notes on dose/volume parameters
Brain stem	Whole organ	Whole organ	Permanent cranial neuropathy or necrosis	Dmax <54	<5	
	Whole organ	3D-CRT	Permanent cranial neuropathy or necrosis	D1–10 cc‖ ≤59	<5	
	Whole organ	3D-CRT	Permanent cranial neuropathy or necrosis	Dmax <64	<5	Point dose <<1 cc
	Whole organ	SRS (single fraction)	Permanent cranial neuropathy or necrosis	Dmax <12.5	<5	For patients with acoustic tumors
Spinal cord	Partial organ	3D-CRT	Myelopathy	Dmax = 50	0.2	Including full cord cross-section
	Partial organ	3D-CRT	Myelopathy	Dmax = 60	6	
	Partial organ	3D-CRT	Myelopathy	Dmax = 69	50	
	Partial organ	SRS (single fraction)	Myelopathy	Dmax = 13	1	Partial cord cross-section irradiated
	Partial organ	SRS (hypofraction)	Myelopathy	Dmax = 20	1	3 fractions, partial cord cross-section irradiated

IL NOSTRO STUDIO

RISULTATI



La mediana della D max al tronco encefalico è 49,6 Gy (range 45,4 Gy - 53,9 Gy)

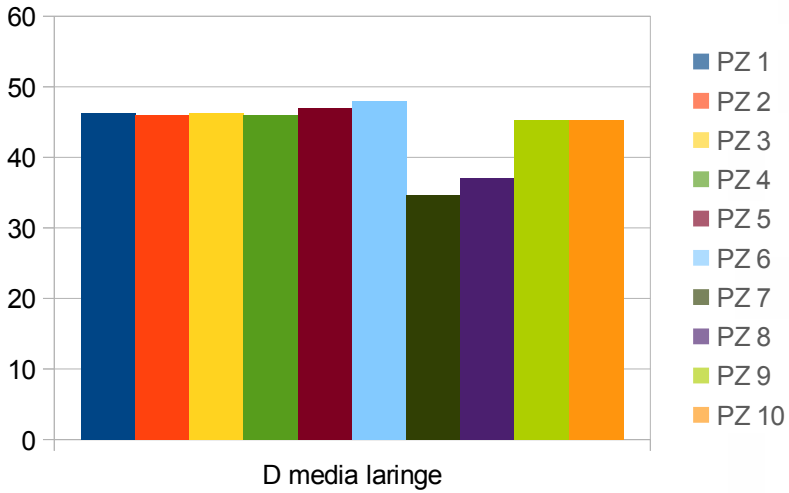


La mediana della D max al midollo spinale è 41,9 Gy (range 38,5 Gy - 45,3 Gy)

IL NOSTRO STUDIO

Table 1. QUANTEC Summary: Approximate Dose/Volume/Outcome Data for Several Organs Following Conventional Fractionation (Unless Otherwise Noted)*

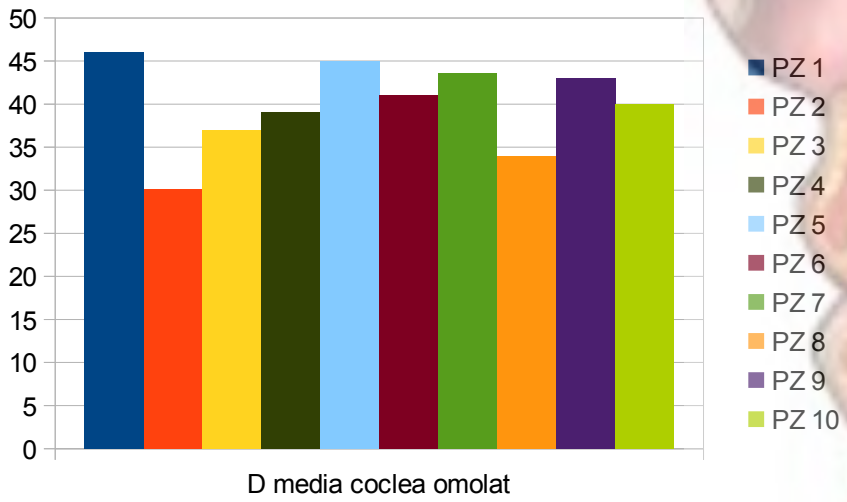
Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated)†	Endpoint	Dose (Gy), or dose/volume parameters†	Rate (%)	Notes on dose/volume parameters
Larynx	Whole organ	3D-CRT	Vocal dysfunction	Dmax <66	<20	With chemotherapy, based on single study (see Section A4.2 in paper)
	Whole organ	3D-CRT	Aspiration	Mean dose <50	<30	With chemotherapy, based on single study (see Fig. 1 in paper)
	Whole organ	3D-CRT	Edema	Mean dose <44	<20	Without chemotherapy, based on single study in patients without larynx cancer**
	Whole organ	3D-CRT	Edema	V50 <27%	<20	
Cochlea	Whole organ	3D-CRT	Sensory neural hearing loss	Mean dose ≤45	<30	Mean dose to cochlear, hearing at 4 kHz
	Whole organ	SRS (single fraction)	Sensory neural hearing loss	Prescription dose ≤14	<25	Serviceable hearing



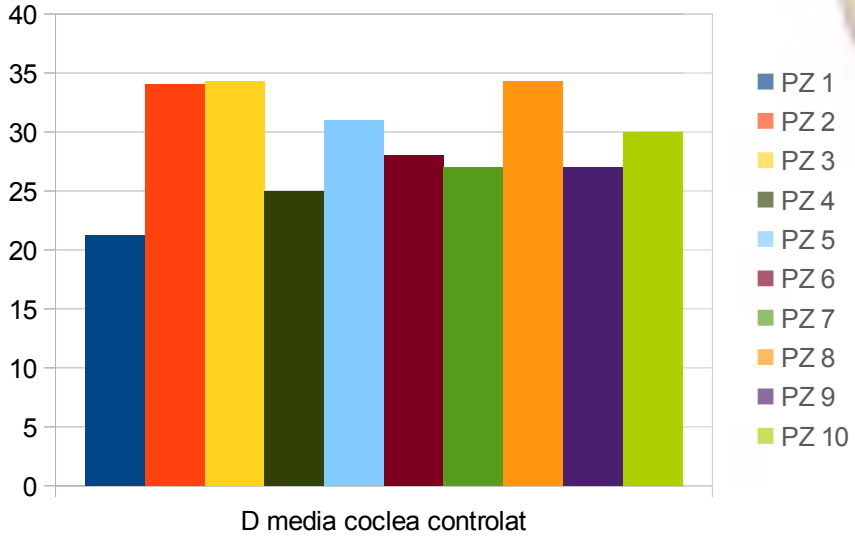
La mediana della D media al laringe è 41,3 Gy (range 34,6 Gy- 48,0 Gy)

IL NOSTRO STUDIO

RISULTATI



La mediana della D media alla coclea omolaterale è 38,1 Gy (range 30,1 Gy - 46,0 Gy)



La mediana della D media alla coclea controlaterale è 27,8 Gy (range 21,2 Gy - 34,3 Gy)

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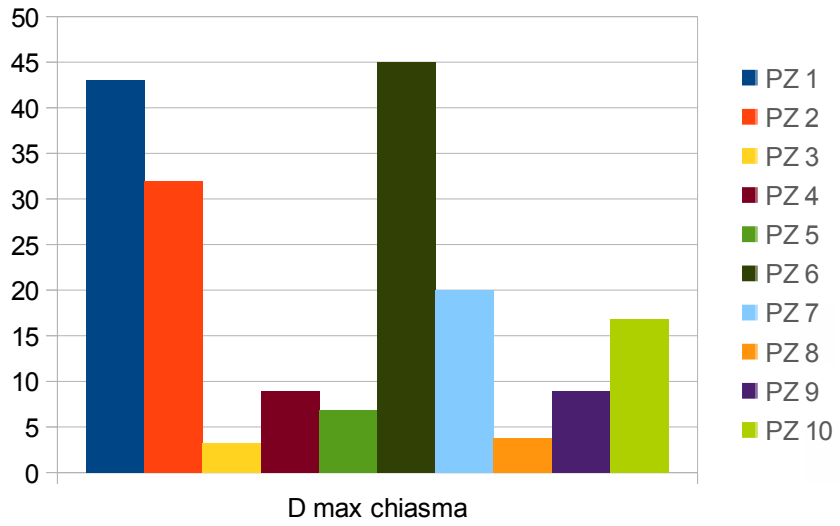
Table 1. QUANTEC Summary: Approximate Dose/Volume/Outcome Data for Several Organs Following Conventional Fractionation (Unless Otherwise Noted)*

Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated)†	Endpoint	Dose (Gy), or dose/volume parameters‡	Rate (%)	Notes on dose/volume parameters
Optic nerve / chiasm	Whole organ	3D-CRT	Optic neuropathy	Dmax <55	<3	Given the small size, 3D-CRT is often whole organ††
	Whole organ	3D-CRT	Optic neuropathy	Dmax 55–60	3–7	
	Whole organ	3D-CRT	Optic neuropathy	Dmax >60	>7–20	
	Whole organ	SRS (single fraction)	Optic neuropathy	Dmax <12	<10	



La mediana della D max al chiasma ottico è 24,1 Gy (range 3,2 Gy – 45,0 Gy)

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Table 1. QUANTEC Summary: Approximate Dose/Volume/Outcome Data for Several Organs Following Conventional Fractionation (Unless Otherwise Noted)*

Organ	Volume segmented	Irradiation type (partial organ unless otherwise stated)†	Endpoint	Dose (Gy), or dose/volume parameters†	Rate (%)	Notes on dose/volume parameters
Parotid	Bilateral whole parotid glands	3D-CRT	Long term parotid salivary function reduced to <25% of pre-RT level	Mean dose <25	<20	For combined parotid glands¶
	Unilateral whole parotid gland	3D-CRT	Long term parotid salivary function reduced to <25% of pre-RT level	Mean dose <20	<20	For single parotid gland. At least one parotid gland spared to <20 Gy¶

La mediana della D media alla parotide omolaterale è 28,2 Gy (range 22,4 Gy - 34 Gy)
La mediana alla parotide controlaterale è 22,7Gy (range18,5 Gy - 26,9 Gy)

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CONCLUSIONI

I risultati della nostra analisi dimostrano l'adeguatezza del piano di trattamento IMRT-SIB nell'assicurare la corretta e omogenea distribuzione di dose ai volumi irradiati simultaneamente e nel minimizzare l'estensione delle alte dosi nei tessuti sani circostanti.