



**ATTUALITÀ
NELLA TERAPIA INTEGRATA
LOCOREGIONALE DELLE NEOPLASIE
DELLE VIE AEREE DIGESTIVE SUPERIORI**

Taranto

12-14 Gennaio 2012



***Radioterapia:
dalla 3D alla I.M.R.T.***

***Mario Santarelli
Rieti***



Ruolo del chirurgo in ORL ...

Dati Rete Oncologica Regione Lazio 2011

Rieti 59 paz anno

Radioterapia

2008 IMRT 8 pazienti

2009 IMRT 26 pazienti

2010

2011

Press release October 2010: fighting cancer in 4 steps



- Early diagnosis
- Mini-invasive surgery
- “New” Radiotherapy
- Biological studies/smart drugs

1980

1990

2000

2010

RADIOTERAPIA
CONVENZIONALE

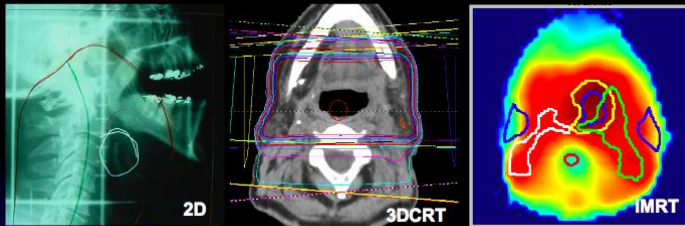
FRAZIONAMENTI
ALTERATI

CHEMIO +
RADIOTERAPIA 3D

RT+ TARGET
THERAPY

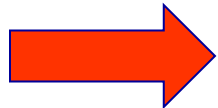
IMRT

From 2D to 3D to IMRT

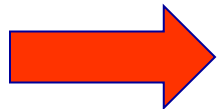
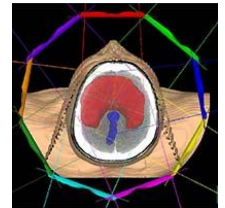


IL PROGRESSO TECNOLOGICO IN RADIOTERAPIA PROCEDE DI PARI PASSO CON L'EVOLUZIONE DELLA DIAGNOSTICA PER IMMAGINI

1970	Rx	COBALTO ROENTGEN	
1980	TAC	ACCELERATORI LINEARI	
1990	RMN	STEREOTASSI	
2000	PET	TECNICHE 3 D	IMRT
	IGRT	



**PROGRESSI TERAPEUTICI
DELLA CHIRURGIA, CHEMIOTERAPIA E
DELLA RADIOTERAPIA**



**MIGLIORE TOLLERANZA ALLE CURE CON
DIMINUZIONE DEGLI EFFETTI COLLATERALI**

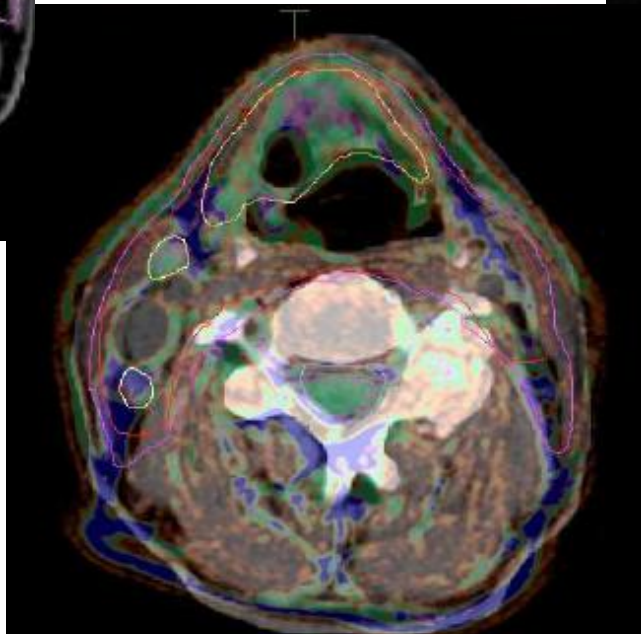
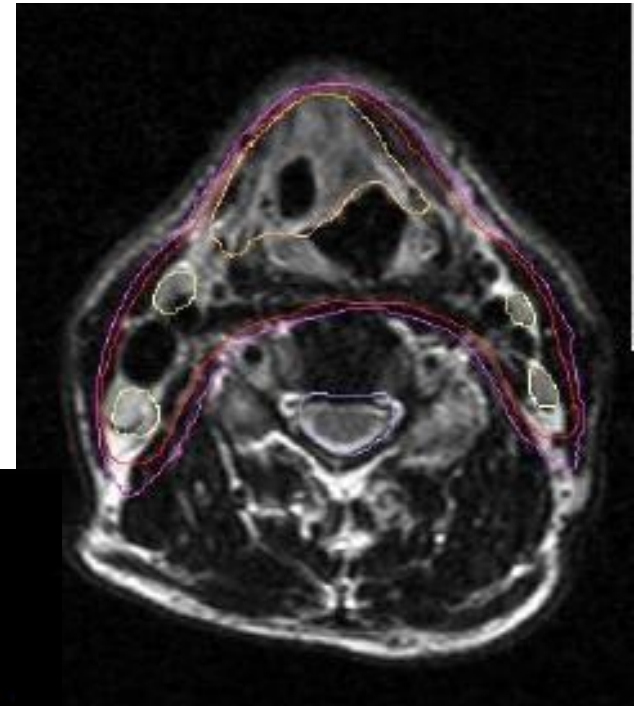
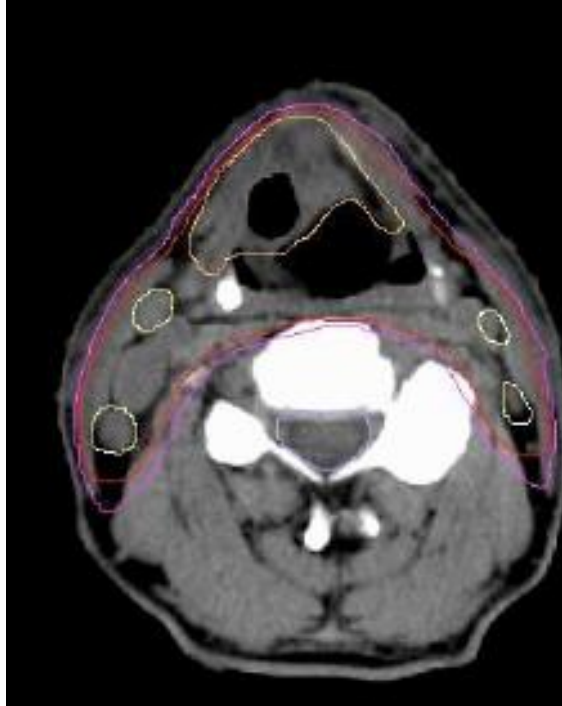


**SOPRATTUTTO *CT E MRI* PER DIAGNOSI E
FOLLOW UP... in RT ANCHE PER PLANNING E VERIFICA
DURANTE IL TRATTAMENTO**

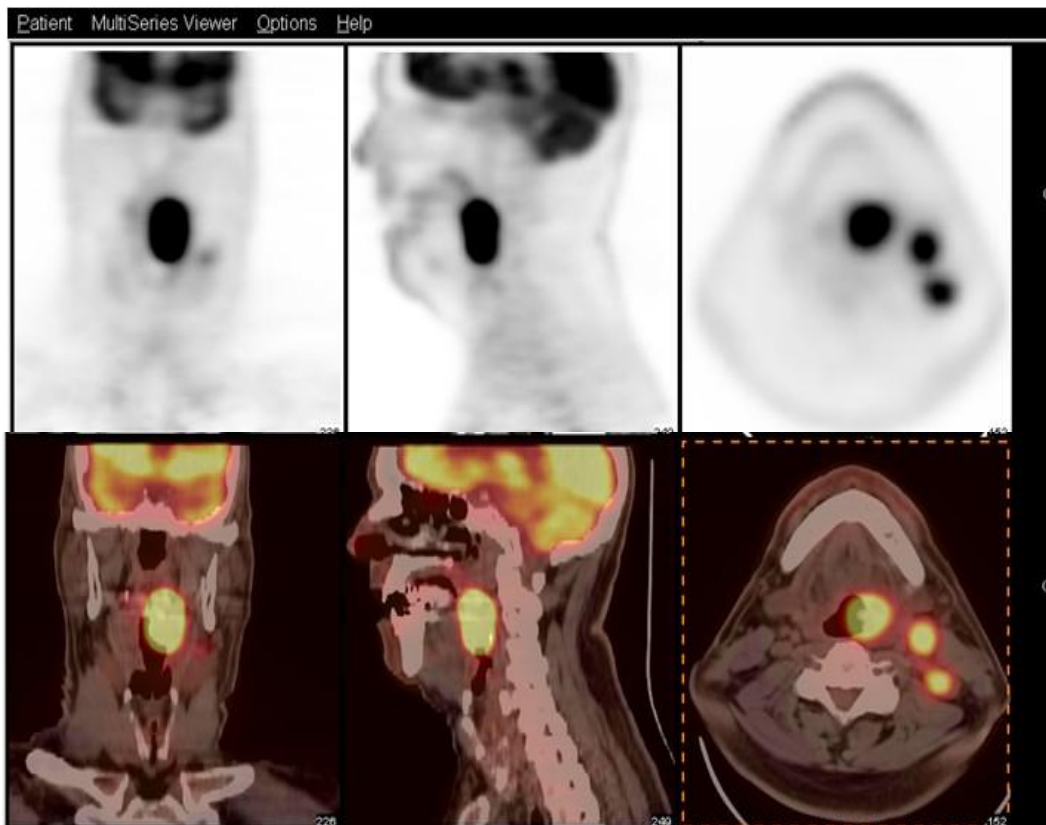


Processi di fusione TAC – RMN

Pianificazione



Radioterapia TAC-PET - guidata



Benefici:

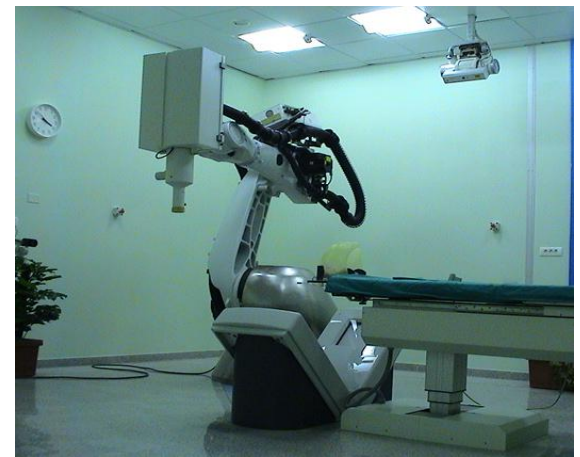
- Aiuto nella fase di staging
- selezione di **aree biologicamente aggressive** da essere pianificate con alta dose (Biological Target Volume-BTV)
- Pianificazione di tecnica RT unilaterale in casi selezionati.

Anni 80 e 90



Tecnologia avanzata

Tecnologia robotica



tomotherapy

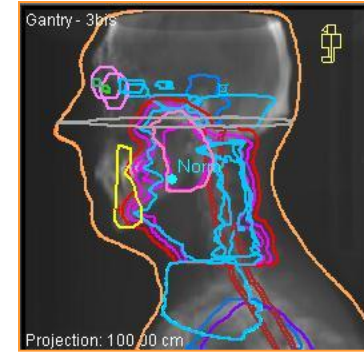
rapid arc

cyberknife

2D - 3-D-CRT: 3 D RADIOTERAPIA CONFORMAZIONALE

IMRT: RADIOTERAPIA AD INTENSITA' MODULATA

IGRT: RADIOTERAPIA GUIDATA DALLE IMMAGINI



1980

1990

2000

2010

miglioramento della precisione

2D

3D-CRT

IMRT-IGRT

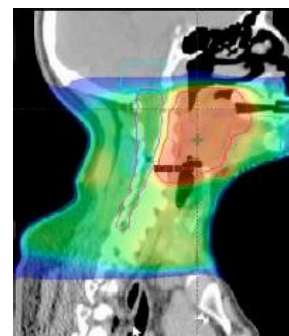
STEREOTASSI



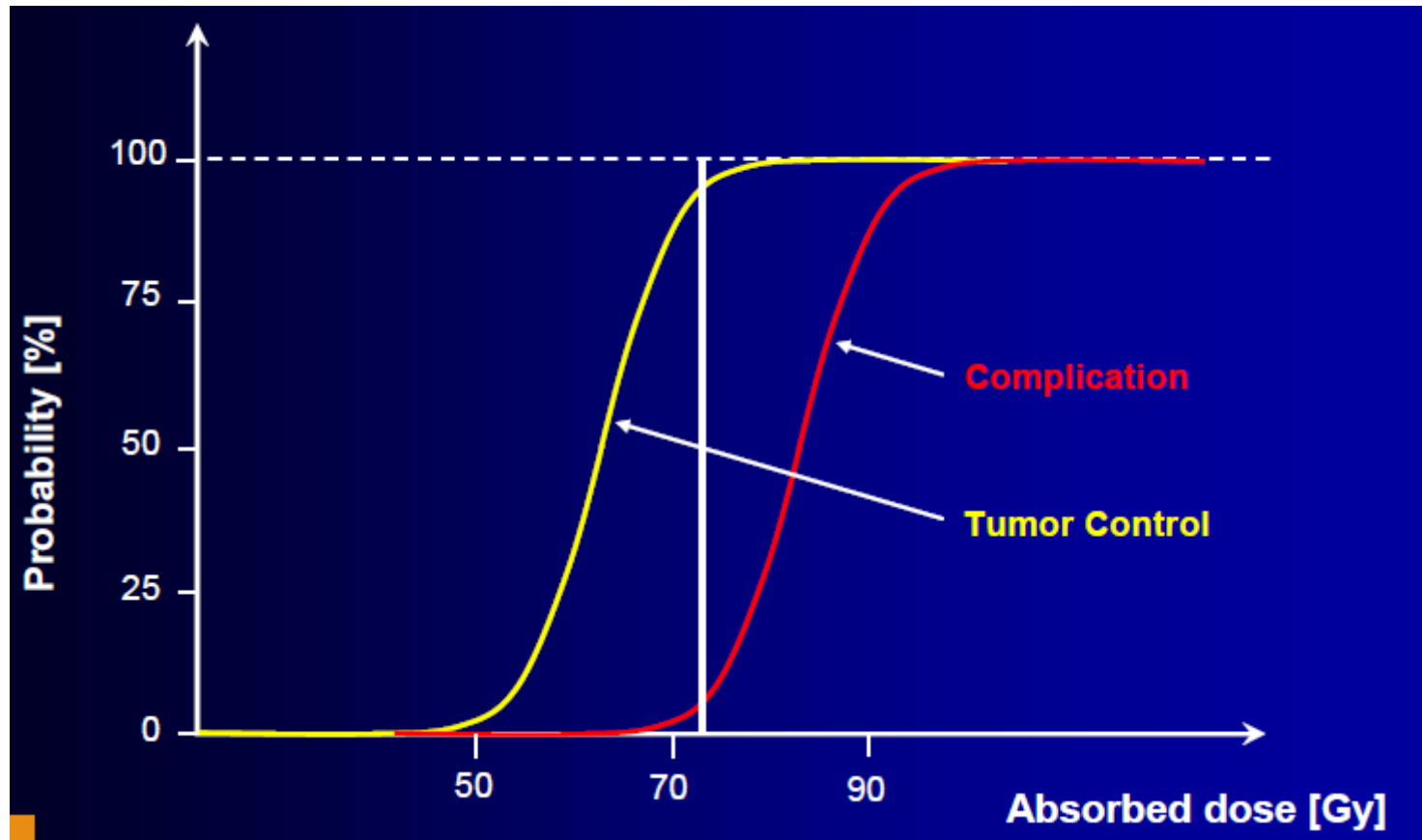
Radioterapia nei tumori testa-collo

Obiettivi del trattamento

1. Sopravvivenza
2. Controllo locale
3. Cura definitiva in paz con tumore limitato
3. Qualità di vita
4. Preservazione della funzione in paz con tumore resecabile o non resecabile



Radioterapia nei tumori testa collo



Tumori della testa e del collo

Variabili che possono interferire con la tolleranza degli organi sani

Individuo:

- risposta alle radiazioni
- Comorbidity (diabete, etilismo, malattie vascolari, collagenopatie ecc)
- Età

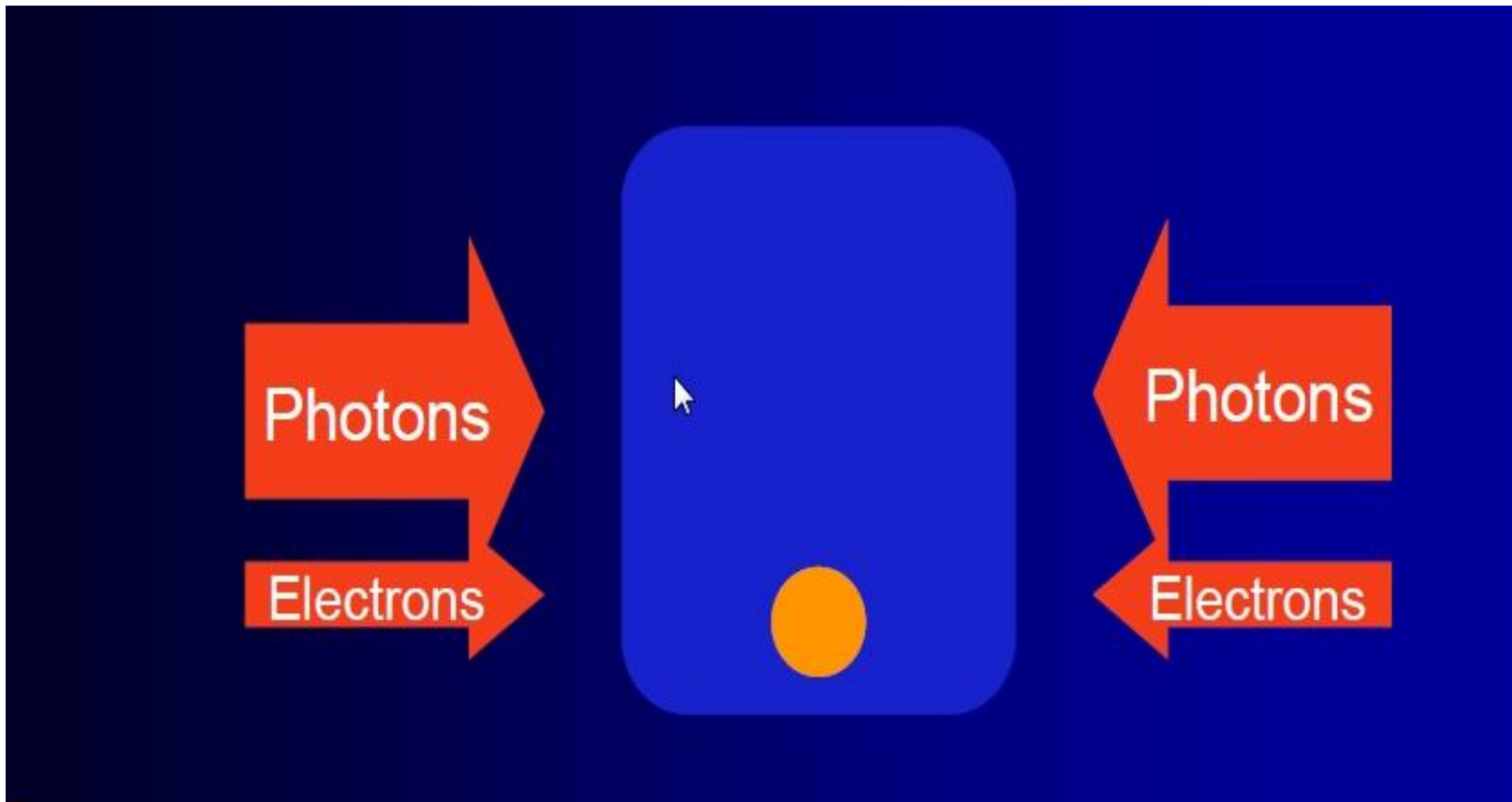
Legate al trattamento

- Dose/frazione, dose rate, tempo totale di trattamento , energia, volume,
- CHT concomitante, radioprotettori (amifostina..)

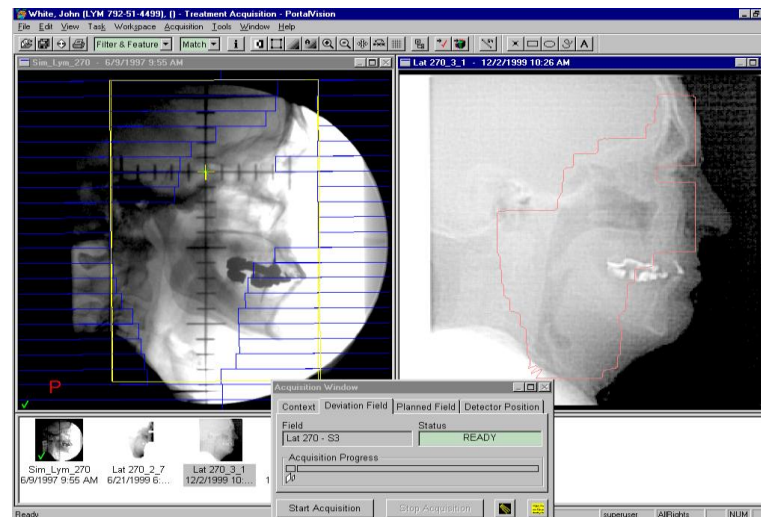
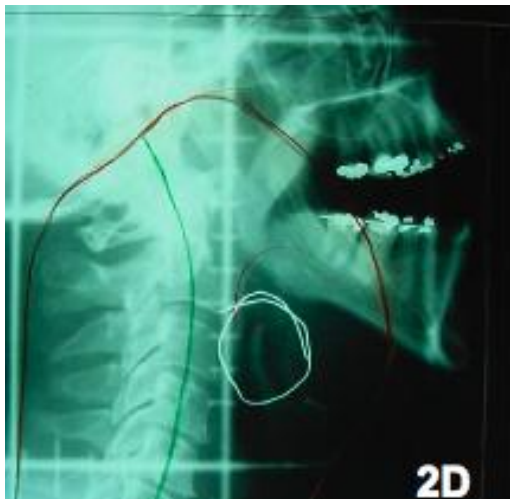
Organo

- Condizioni dell'organo pretrattamento
- Diversa o mutata radiosensibilità regionale nell'organo stesso (necrosi ecc)
- ***Sviluppo di tox acuta o cronica grave (con conseguenti effetti tardivi)***

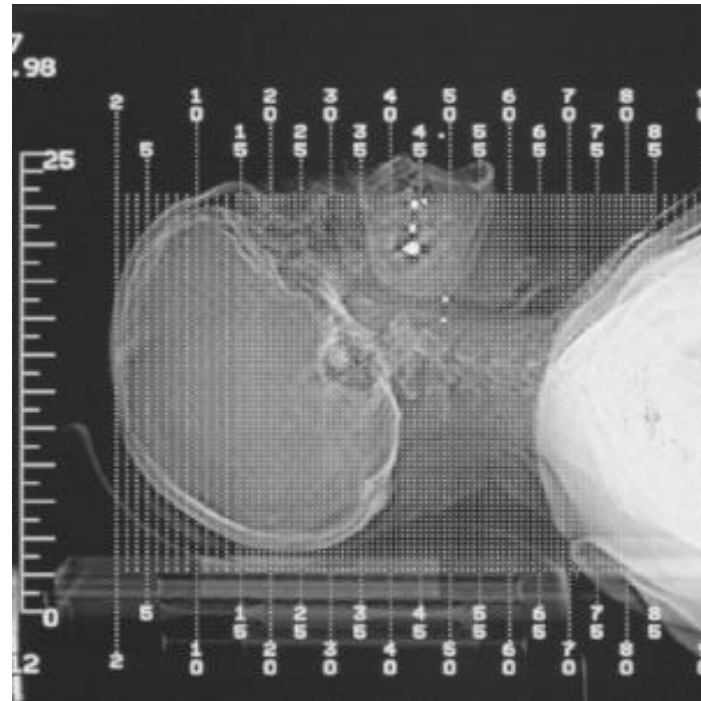
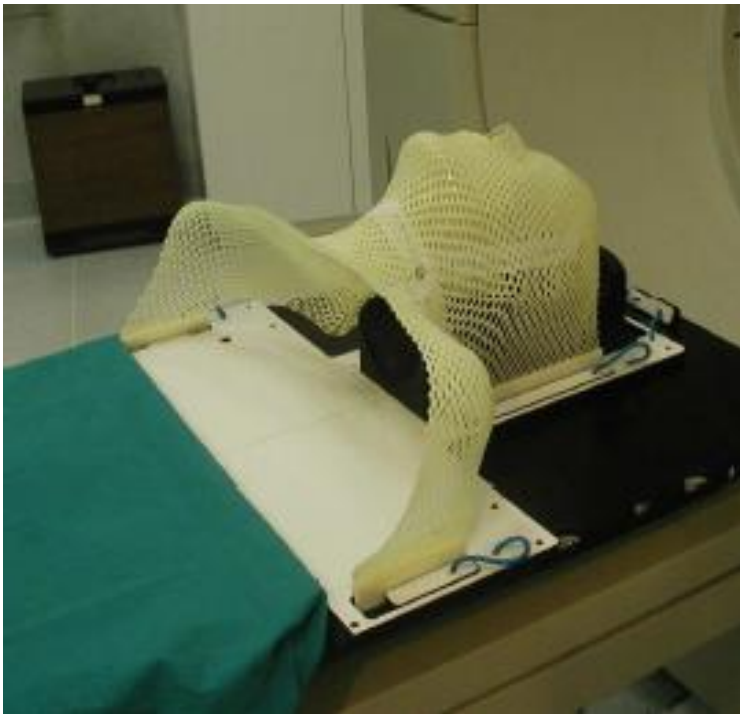
2-D Radioterapia anni 1980-2000 RT e planning basate senza uso di TAC :



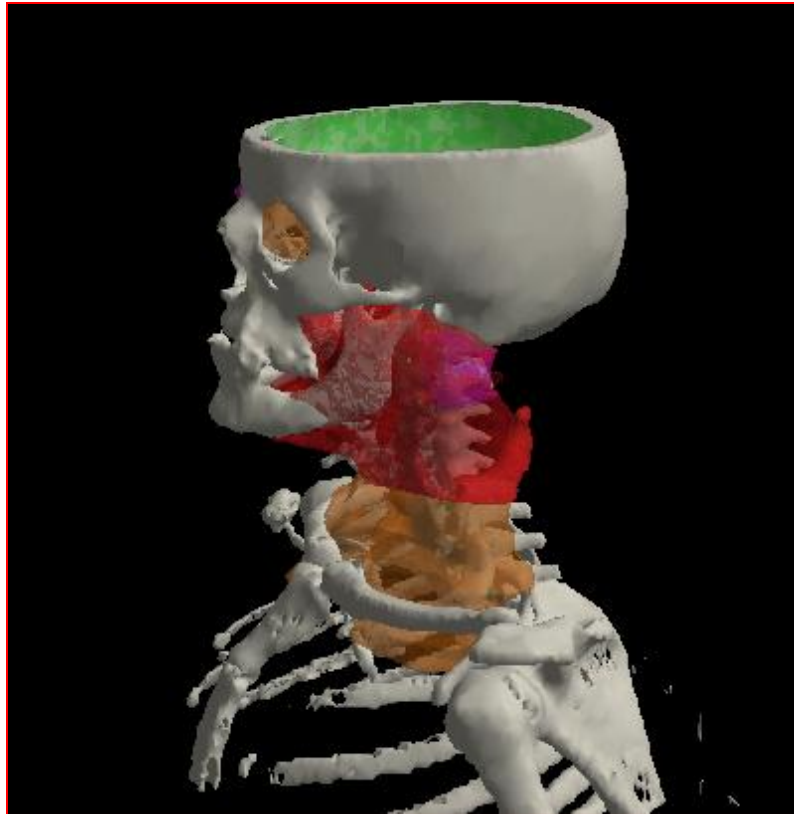
Processi di simulazione



Immobilizzazione con maschera testa collo



2-D Radioterapia anni 1980-2000
RT e planning basate senza uso di TAC :



3-D Radioterapia anni 2000
RT e planning basate sull'uso di TAC :

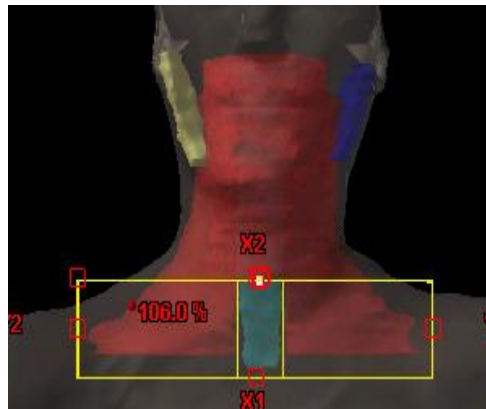
Descrizione della tecnica standard 3D



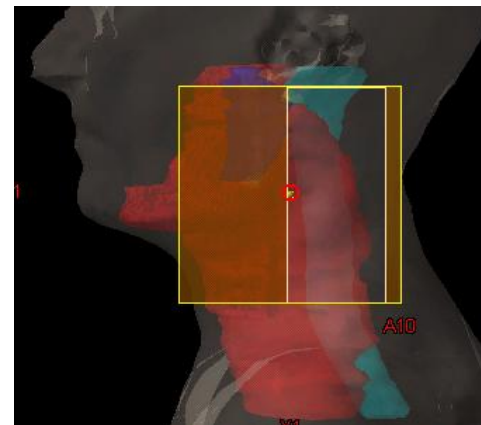
2 campi
latero laterali che
coprono la parte
superiore del PTV
(inclusi i linfonodi
spinali)



2 campi
latero laterali di
uguale altezza
chiusi
posteriormente sul
midollo



2 campi
antero-posteriori per
coprire la parte bassa
del collo evitando le
spalle



2 campi
latero-laterali di elettroni
per coprire i linfonodi
spinali

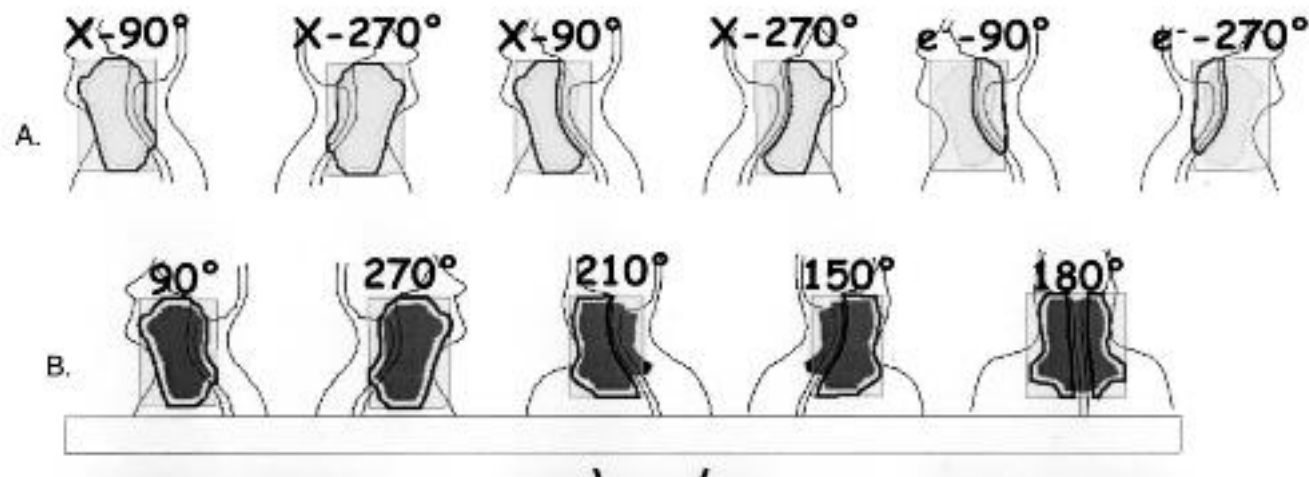
A treatment planning comparison of 3D conformal therapy, intensity modulated photon therapy and proton therapy for treatment of advanced head and neck tumours

Luca Cozzi^a, Antonella Fogliata^a, Antony Lomax^b, Alessandra Bolsi^a

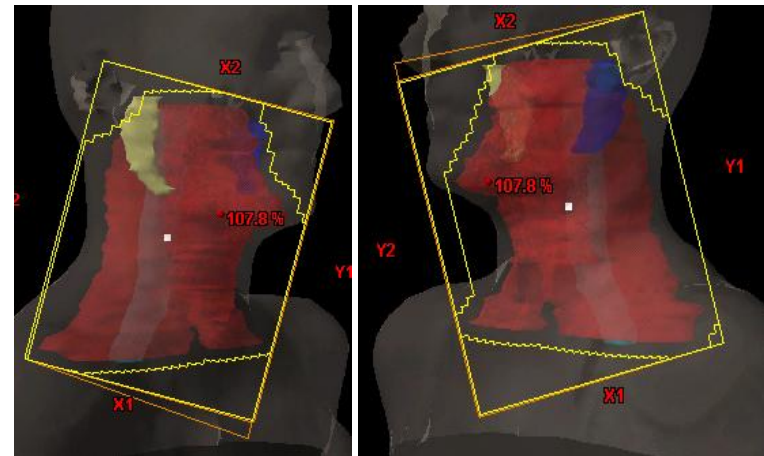
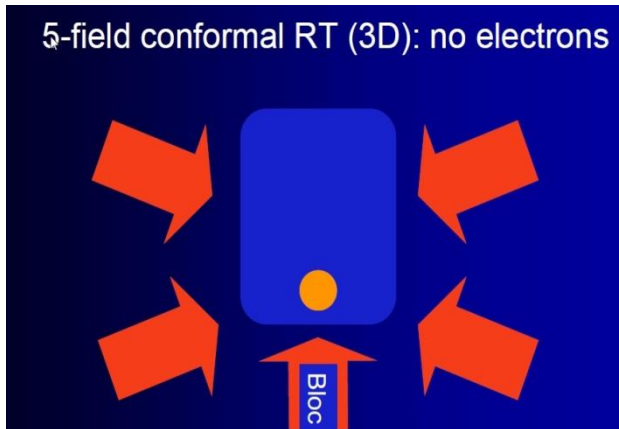
^aOncology Institute of Southern Switzerland, Medical Physics Unit, Bellinzona, Switzerland

^bDivision of Radiation medicine, Paul Scherrer Institute, Villigen-PSI, Switzerland

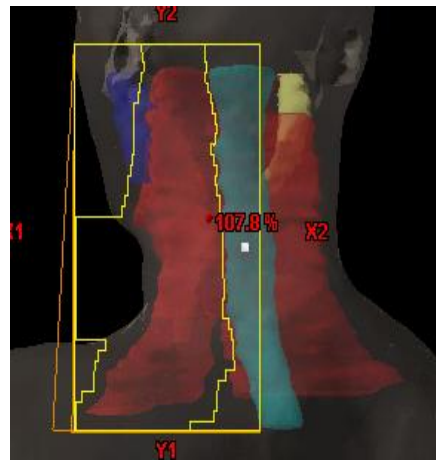
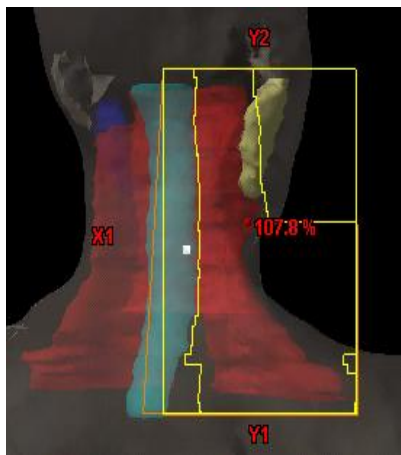
Received 2 January 2001; received in revised form 15 June 2001; accepted 18 June 2001



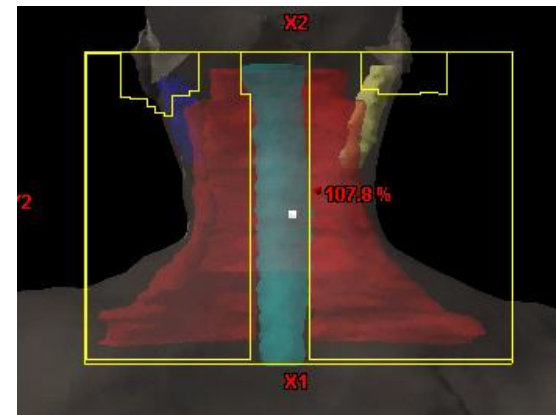
Descrizione della tecnica a 5 campi



2 campi anteriori che “vedono” tutto il PTV

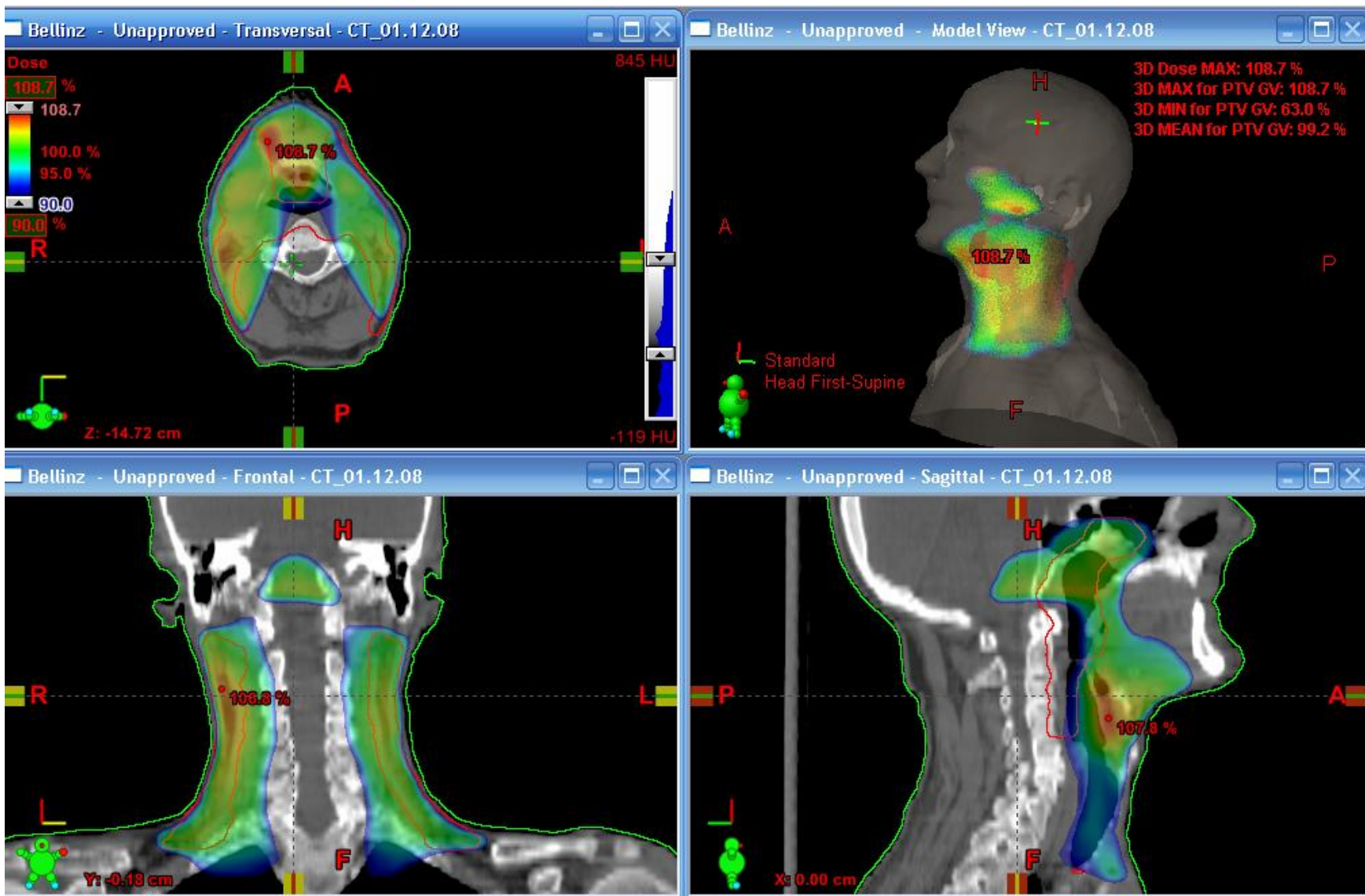


2 campi posteriori chiusi sul midollo

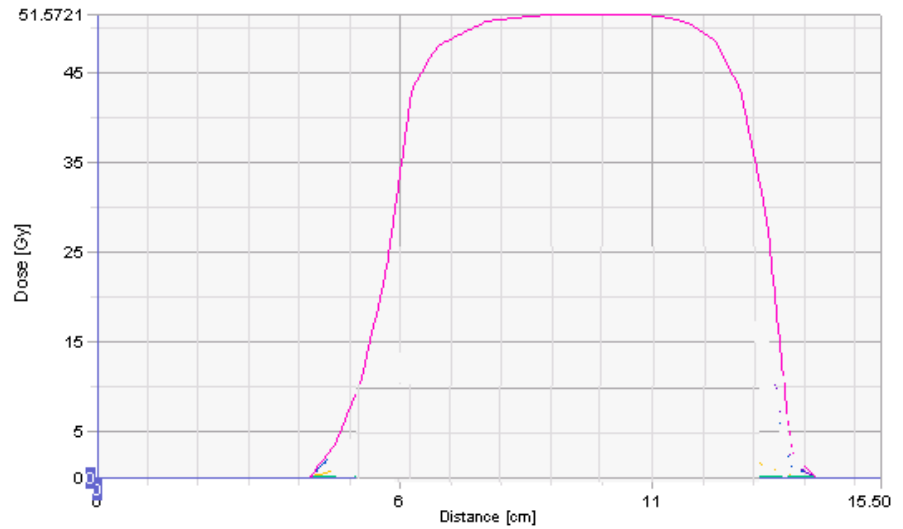
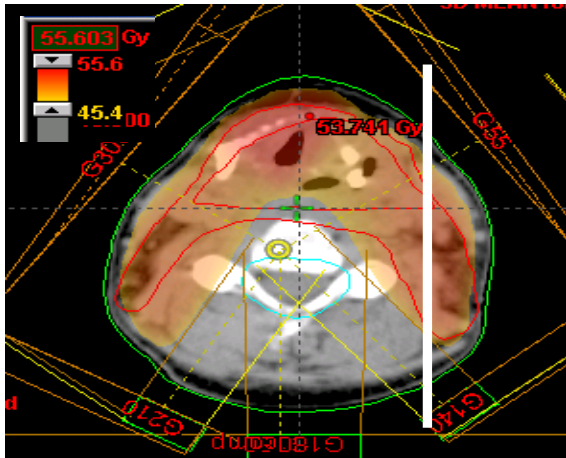


1 campo posteriore chiuso sul midollo

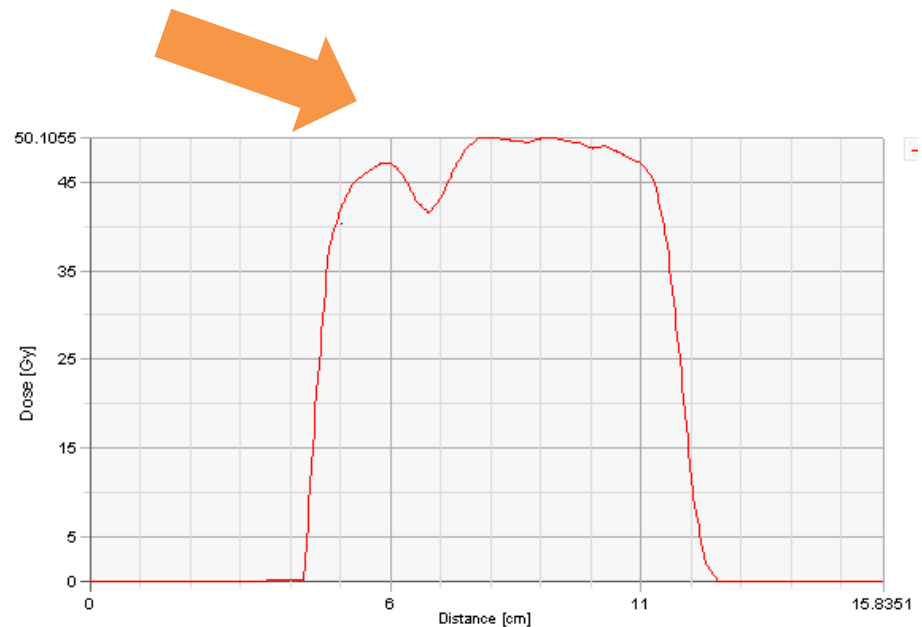
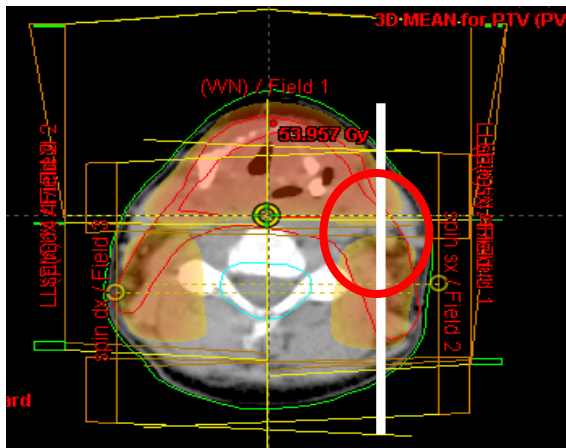
“bellinzona”



Confronto delle isodosi e dei profili lungo un piano passante per le catene spinali

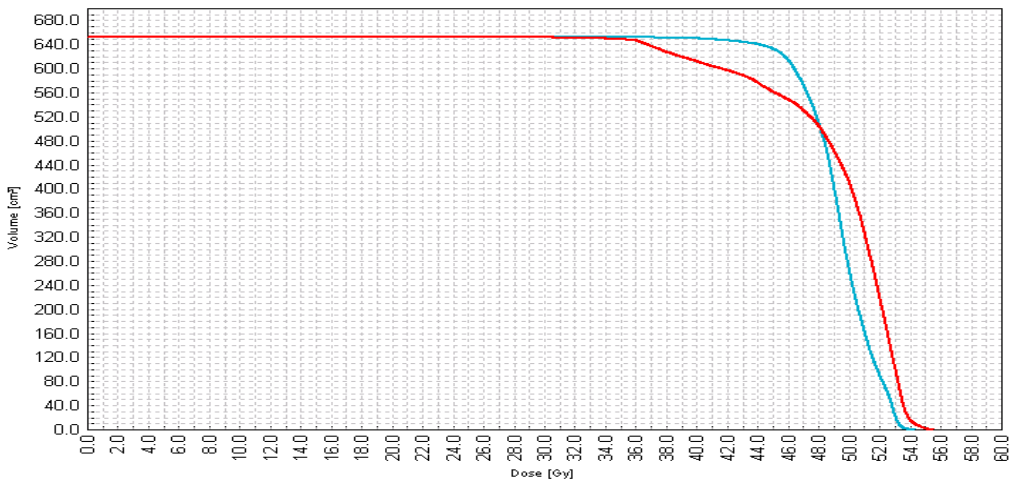


Tecnica a 5 campi



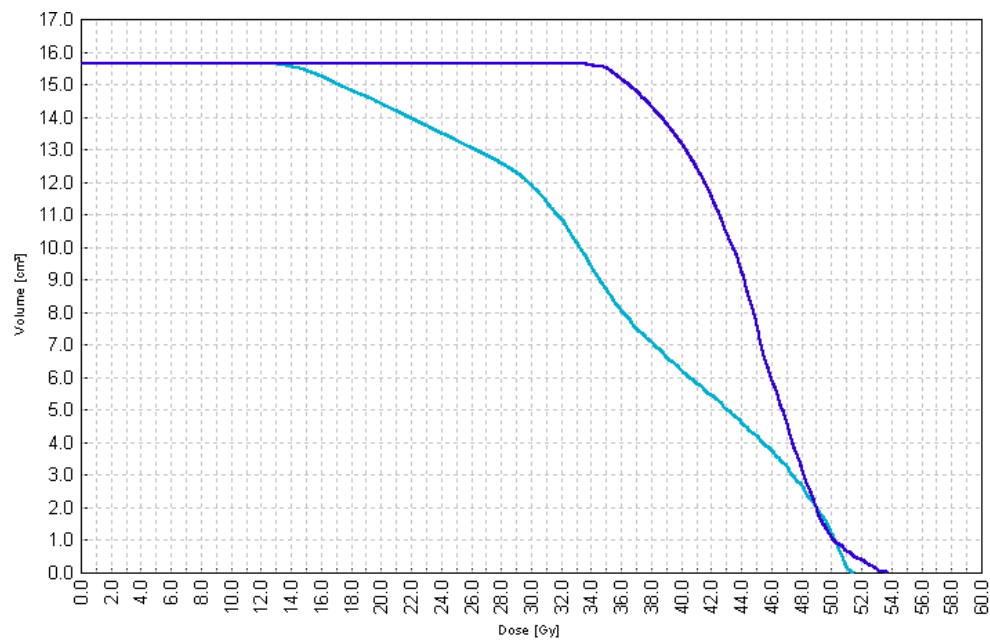
Tecnica standard (fotoni+elettroni)

Confronto dei parametri dosimetrici sul PTV e OAR



DVH PTV tecnica a 5 campi

DVH PTV tecnica standard



DVH parotide tecnica standard

DVH parotide tecnica a 5 campi

Tecniche convenzionali

Frazionamenti alterati

Hyperfractionated or accelerated radiotherapy in head and neck cancer: a meta-analysis



Jean Bourhis, Jens Overgaard, Hélène Audry, Kian K Ang, Michele Saunders, Jacques Bernier, Jean-Claude Horiot, Aurélie Le Maître, Thomas F Pajak, Michael G Poulsen, Brian O'Sullivan, Werner Dobrowsky, Andrzej Hliniak, Krzysztof Skladowski, John H Hay, Luiz H J Pinto, Carlo Fallai, Karen K Fu, Richard Sylvester, Jean-Pierre Pignon, on behalf of the Meta-Analysis of Radiotherapy in Carcinomas of Head and Neck (MARCH) Collaborative Group*

Lancet 2006; 368: 843-54

See [Comment](#) page 819

Published Online

August 17, 2006

DOI: 10.1016/S0140-

6736(06)69121-6

Ripopolazione interfrazione
Radioresistenza

Lancet 2006, 368: 843-854

Rays. 1993 Jul-Sep;18(3):320-9.

Mechanisms of radiation resistance.

[Article in English, Italian]

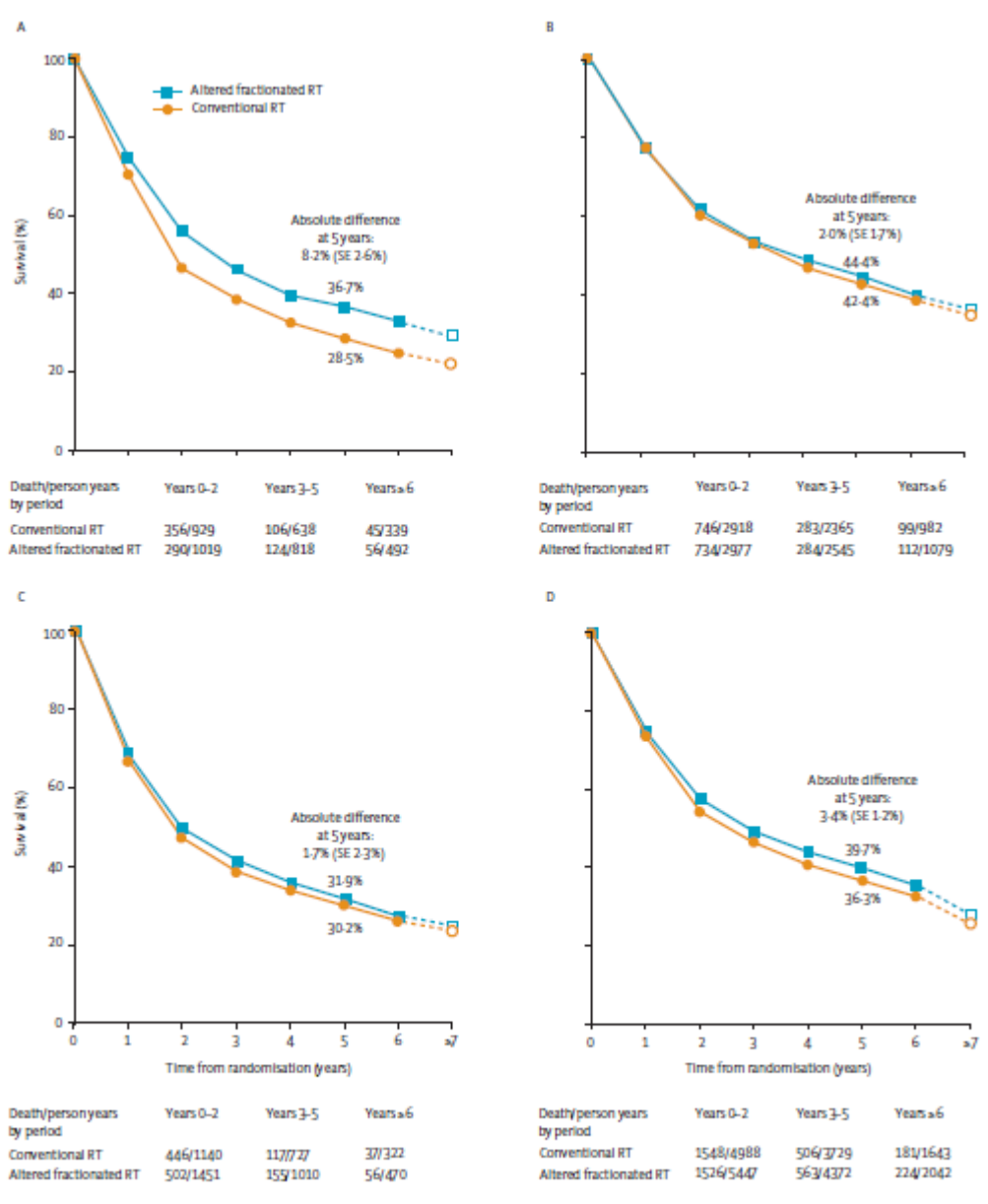
Biagini C, Enrici RM, Santarelli M.

Istituto di Radiologia, Università La Sapienza, Roma, Italy.

Meta-analisi	N° Trials	N° pazienti	Beneficio In OS	p value
<i>MARCH Bourhis et al, 2006</i>				
<i>RT fr. accelerato vs CFRT</i>				
Tutti i gruppi	15	6155	3.4% (5 anni)	0.0001
-Iperfrazionamento vs CFRT			(6.4% LRC → 8 % a 5 anni	0.003
RT Accelerata vs CFRT			1.7-2% a 5 anni	0.02

Iperfrazionamento

36% vs 28%



Frazionamento accelerato con riduzione della dose

Tutti i gruppi

39% vs 36%

Figure 2: Survival curves by treatment arm for all trials and for the three groups of trials according to the type of altered fractionated radiotherapy (A) Hyperfractionation. (B) Accelerated fractionation without total dose reduction. (C) Accelerated fractionation with total dose reduction. (D) All three groups together. The slopes of the broken lines from year 6 to year >7 are based on the overall death rates in the seventh and subsequent years. RT=radiotherapy.

Frazionamenti non convenzionali

Budach: metanalisi 2006

32 studi randomizzati periodo 1975-2003
Dosi totali 60 Gy

RT vs RT + CHT



- ❑ OS aumento del beneficio 12 mesi con CHT (vari frazionamenti) $p < 0.001$
- ❑ Significativo beneficio se si usa 5FU e cisplatino $p < 0.01$
- ❑ **Significativo aumento della OS con iperfrazionamento comparato con frazionamento convenzionale (senza CHT) $p < 0.001$**

Tossicità con la 3-D RT: OAR

RTOG

LENT SOMA

CTACE

Xerostomie gravi **82%**

↓ tasso di fluido parotideo stimolato

Disfonia circa **30%**

Disfagia cronica / aspirazione: **35-76%**

Perdita dell'udito sensoriale-neurale

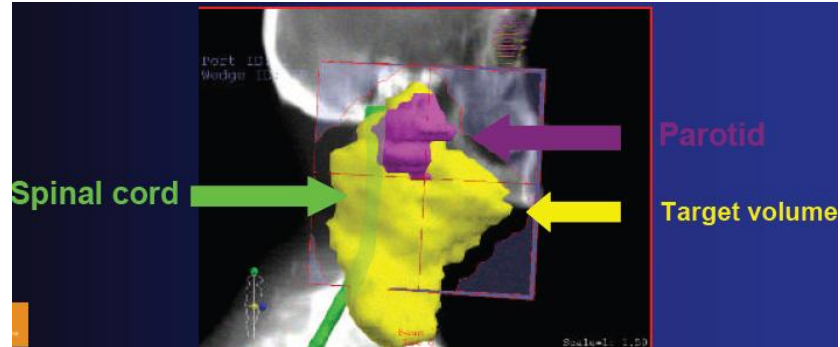
68% con dosi > 45 Gy

Sindrome dell'occhio secco **20%**

Perchè fare IMRT ?

Obiettivo : superare il 3D in modo da aumentare l'indice terapeutico

> 400 lavori



- Massimizzare la dose sulla neoplasia trattata

⇒ Incrementare le probabilità di controllo del tumore

- Minimizzare la dose ai tessuti sani

⇒ Ridurre gli effetti di tossicità indotti dalle radiazioni

Il problema è considerato in maniera inversa

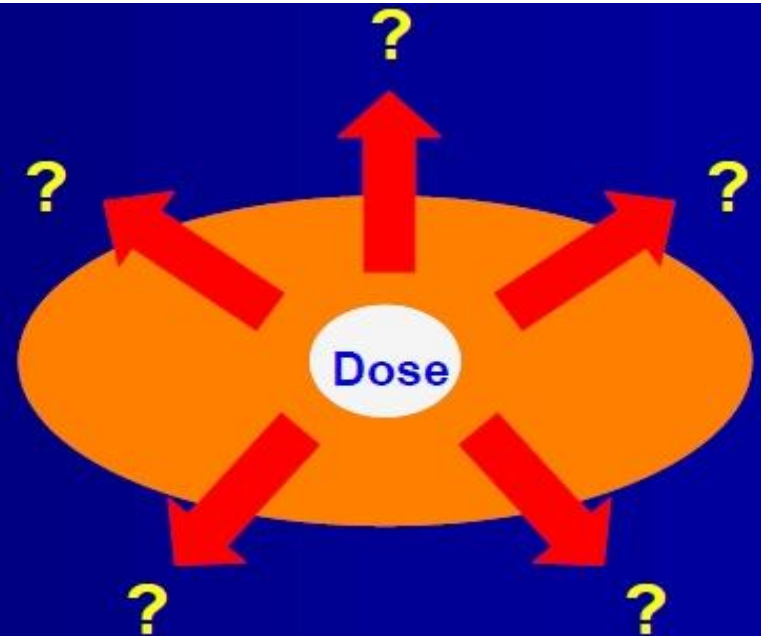
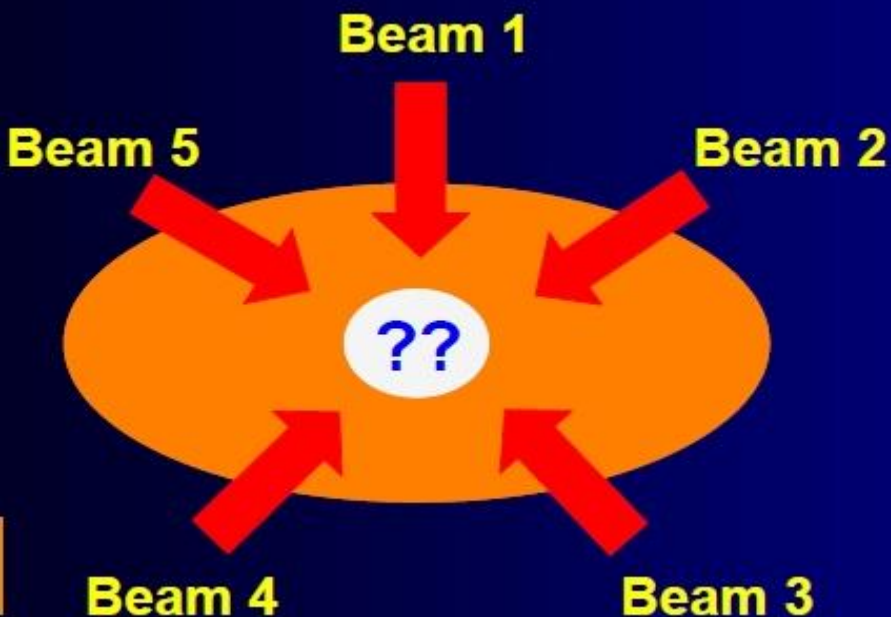
Gli obiettivi clinici sono tradotti matematicamente in forma di “constraints” e di “priorita” o “costo” o “score”.

Radioterapia convenzionale

Quale è la dose erogata al volume target per una data configurazione di fasci

IMRT

Quale è la migliore configurazione di fasci tali da ottenere una dose curativa per il volume prescelto

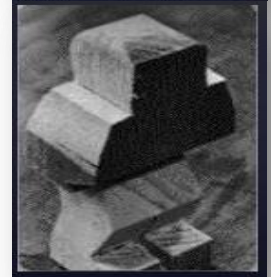
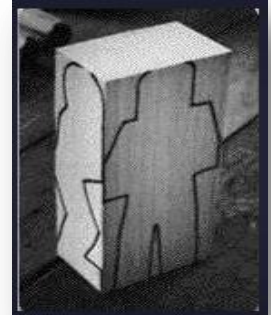


2D

Bianco e nero



3D



IMRT

Toni di grigio



Definizione di IMRT

Sistema per piani di trattamento dotato di due caratteristiche fondamentali:

- 1) Conformare la dose prescritta su un volume bersaglio in forma tridimensionale
- 2) L'intensità di dose all'interno del volume bersaglio è volutamente disomogenea

Ciò con l'ausilio di collimatori multilamellari con cui si creano fasci di radiazioni non uniformi



Forward planning



Inverse planning

- **Forward planning
(IMRT semplificata)**

Il fisico decide manualmente
la modalità di irradiazione
attraverso la creazione manuale
di segmenti all'interno dello
stesso campo in grado di creare la
modulazione del fascio radiante
La ottimizzazione dei pesi per
ogni segmento avviene
successivamente o in forma manuale
o automatica

Steep and shoot

Sliding windows



- **Inverse planning**

Gli obiettivi clinici sono tradotti matematicamente
sotto forma di “constraint” e di
priorità
Il computer cerca di ottimizzare
automaticamente il piano
proponendo tecnica e modalità
che più si avvicina a quanto
richiesto

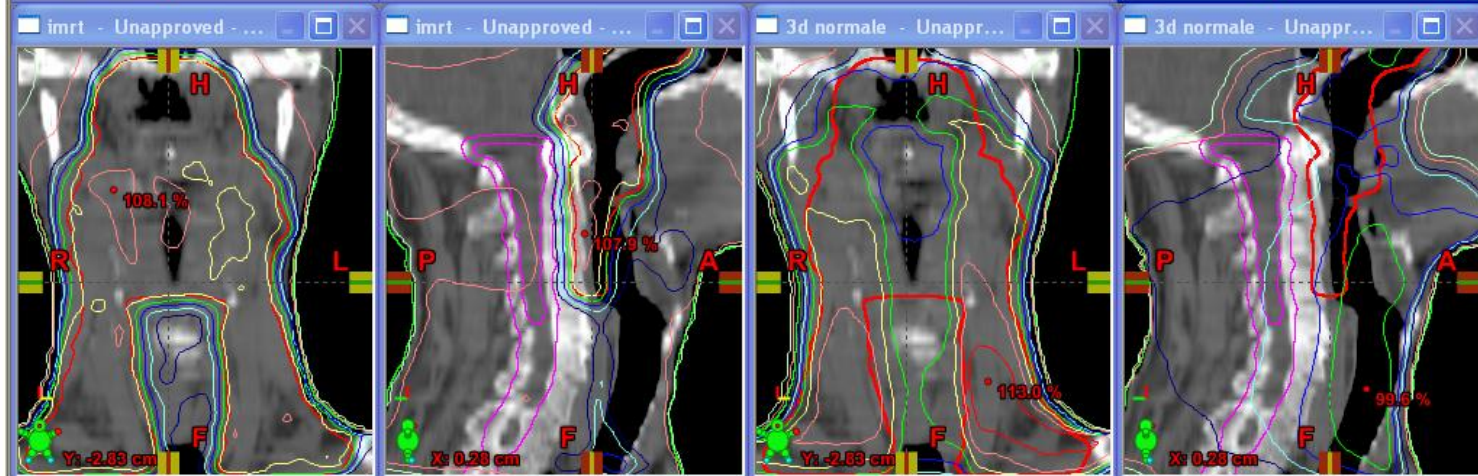
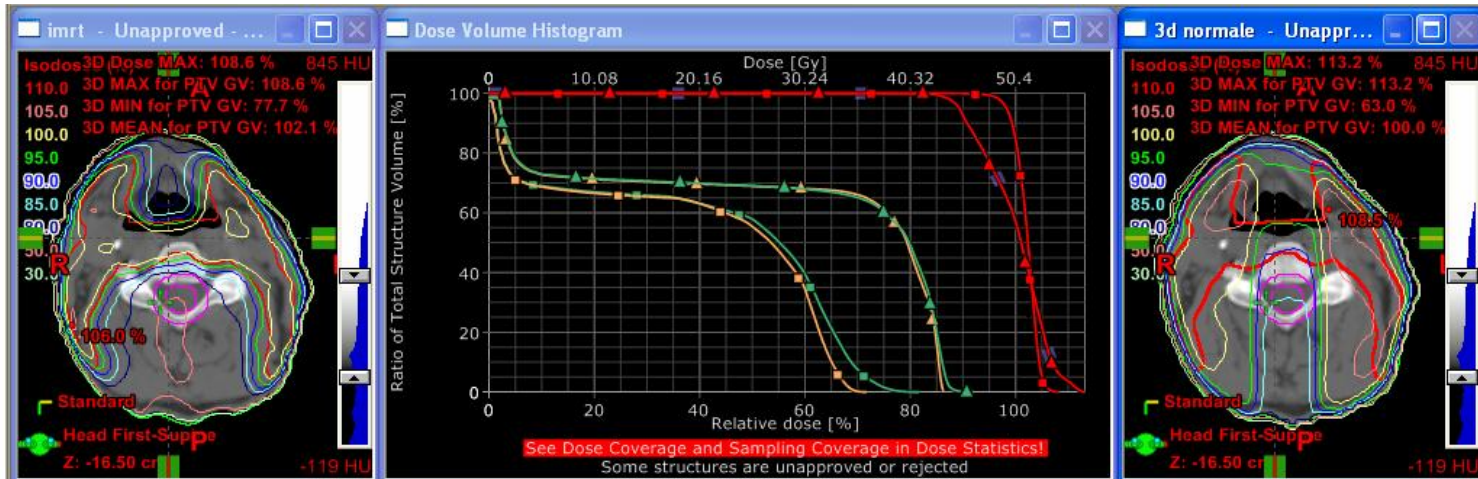
Tomoterapia seriale

Tomoterapia elicoidale

VMAT

Rapid arc

IMRT vs conformazionale 3D

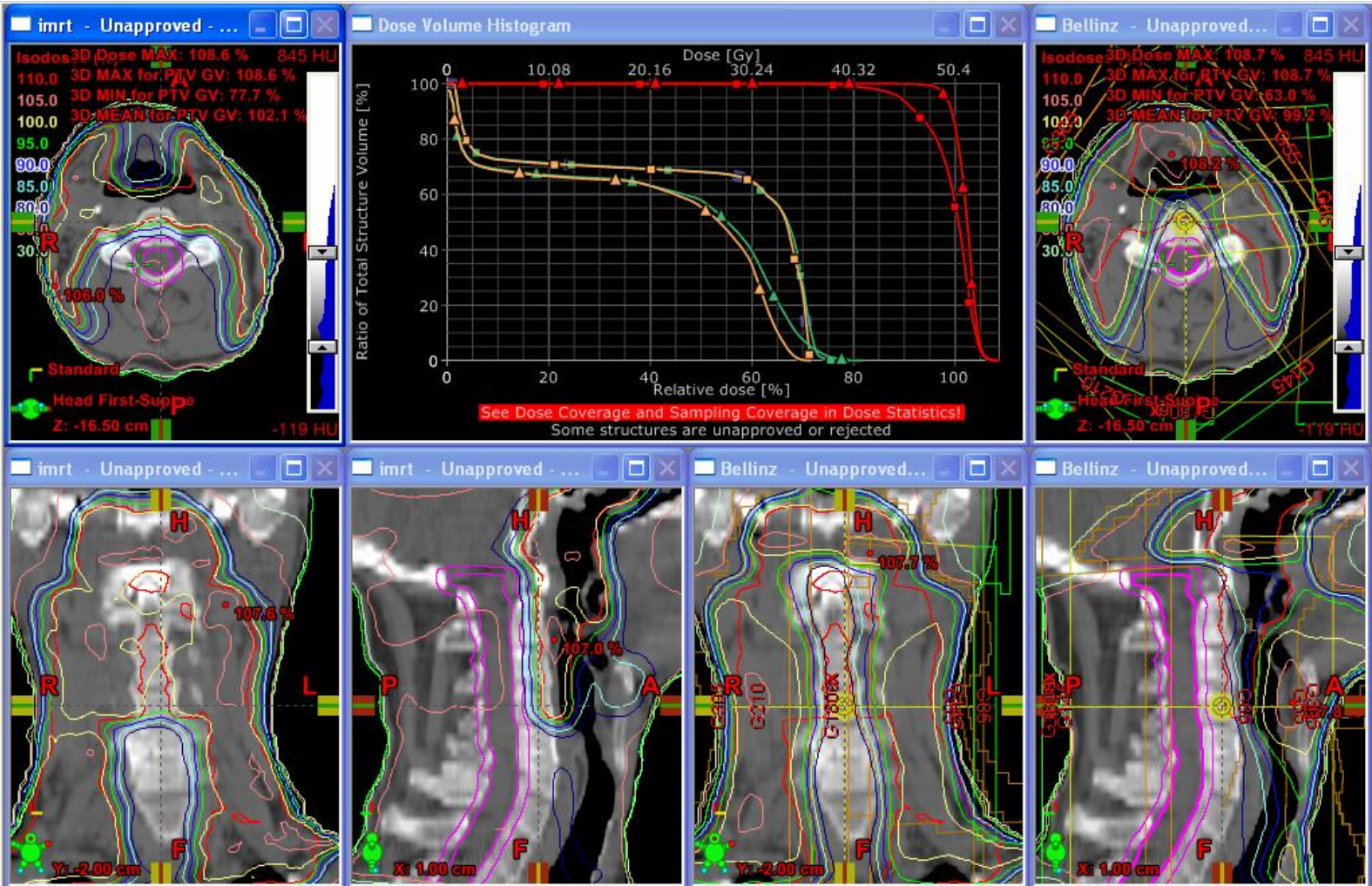


■	midollo spi	Unapproved	imrt	Testa collo	46.3	97.4	100.1	0.5	72.0	40.4
▲	midollo spi	Unapproved	3d normale	Testa collo	46.3	98.6	100.1	1.8	86.6	58.6
■	midollo spi.esp.	Unapproved	imrt	Testa collo	125.3	97.4	100.0	0.5	82.1	42.1
▲	midollo spi.esp.	Unapproved	3d normale	Testa collo	125.3	98.6	100.0	1.7	92.3	59.0
■	PTV GV	Unapproved	imrt	Testa collo	530.0	100.0	100.0	77.7	108.6	102.1
▲	PTV GV	Unapproved	3d normale	Testa collo	530.0	100.0	100.0	63.0	113.2	100.0

IMRT vs "Bellinzona"

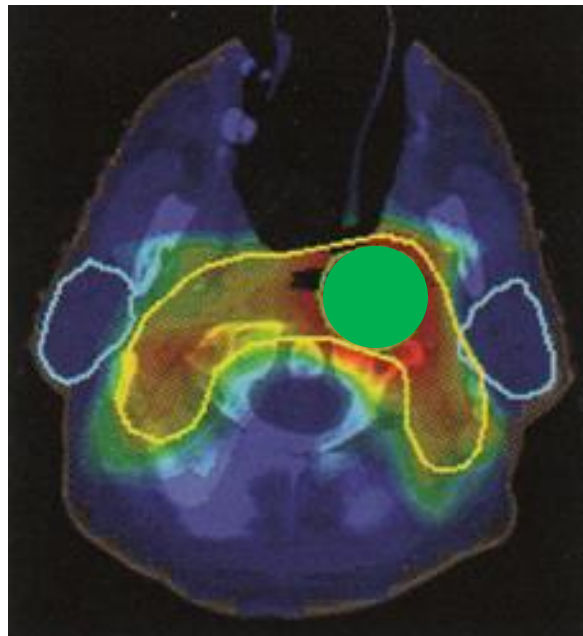
IMRT

BELL.



■	midollo spi	Unapproved	Bellinz	Testa collo	46.3	100.0	100.0	1.4	72.3	48.3
▲	midollo spi	Unapproved	imrt	Testa collo	46.3	97.4	100.1	0.5	72.0	40.4
■	midollo spi.esp.	Unapproved	Bellinz	Testa collo	125.3	100.0	100.0	1.4	79.4	48.7
▲	midollo spi.esp.	Unapproved	imrt	Testa collo	125.3	97.4	100.0	0.5	82.1	42.1
■	PTV GV	Unapproved	Bellinz	Testa collo	530.0	100.0	100.0	63.0	108.7	99.2
▲	PTV GV	Unapproved	imrt	Testa collo	530.0	100.0	100.0	77.7	108.6	102.1

Simultaneous (SIB -IMRT) Integrated Boost



SIB-IMRT : razionale

- Diminuire i tempi di trattamento
- Sostituire trattamenti multistep (sequenziale, concomitante, differito..) con un singolo piano di cura
- Utilizzare pienamente la capacità della IMRT di conformare contemporaneamente sia le regioni ad alto che a dosaggio inferiore
- Sfruttare il potenziale di dose escalation

iprofrazionamento: SIB -IMRT

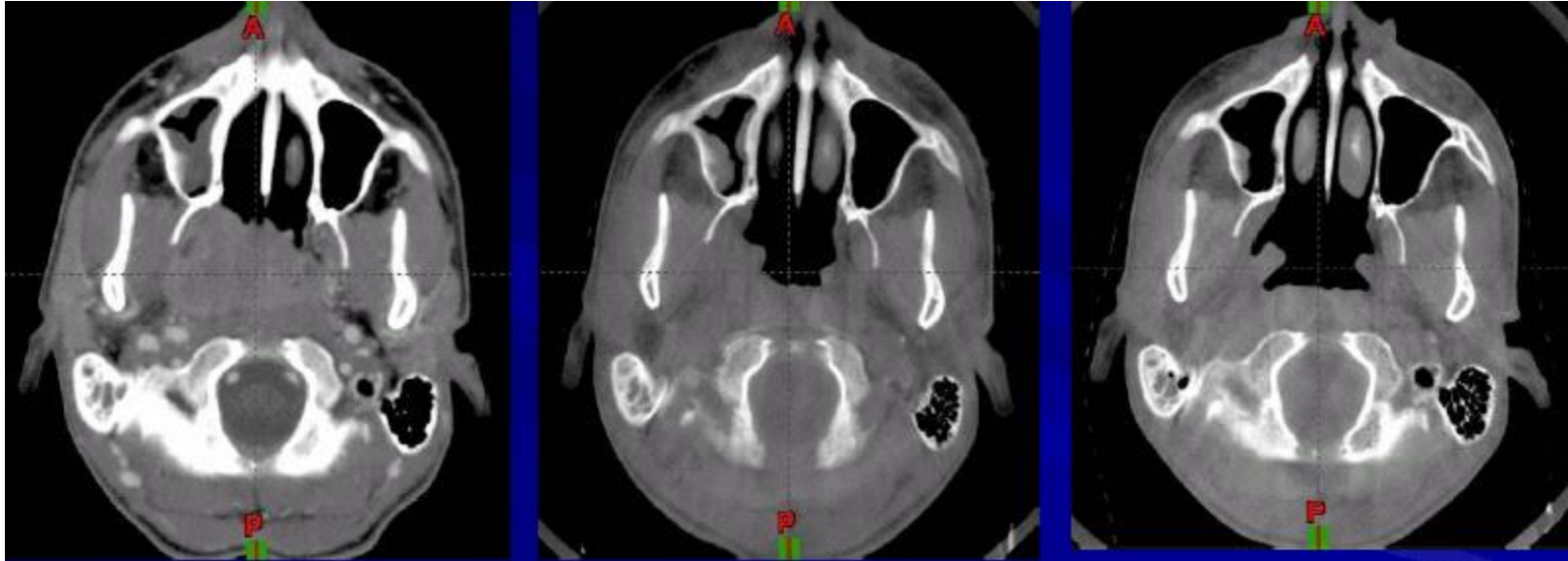
Vantaggi

- **Contrastare il ripopolamento cellulare tipico dei tumori in rapida crescita**
- Può essere usato anche con frazionamenti convenzionali. In tal caso viene ridotta la dose ai volumi precauzionali (utile in caso di attesa o certa tossicità su mucose ecc)
Rispetto al 3D minor dose alle porte di ingresso e quindi diminuzione del rischio di danno

Controversie

- La dose/frazione con SIB dovrebbe essere < 2.5 Gy
- Il SIB-IMRT nel faringe-laringe avanzato è ancora oggetto di indagine
- → **alto rischio di effetti tardivi se il SIB è associato a CHT**

SIB-IMRT: in caso di regressione veloce...



1 mese

Tecnica IMRT: considerazioni

- 1) **Fisica sanitaria adeguata**
- 2) **Ottima conoscenza della anatomia per la contornazione**
- 3) Necessità di imaging aggiuntivo (TAC in corso di terapia-RM-PET)
- 4) Consapevolezza di dover spendere più tempo per il calcolo
- 5) Necessario dover fare accurati e **personalizzati controlli di qualità**
- 6) Tempi e stress macchina superiori
- 7) Necessità di effettuare verifiche strette **(IGRT)**
- 8) Costo superiore del 30%

IMRT : Indicatori

Copertura del target

Controllo di malattia

Tossicità e qualità di vita

Tumori, 92: 503-510, 2006

TARGET COVERAGE IN HEAD AND NECK CANCER TREATED WITH INTENSITY-MODULATED RADIOTHERAPY: A COMPARISON BETWEEN CONVENTIONAL AND CONFORMAL TECHNIQUES

Mauro Palazzi¹, Ester Orlandi¹, Emanuele Pignoli², Manuela Lualdi², Giancarlo Zonca², Claudia Sangalli¹, Claudio Stucchi², and Patrizia Olmi¹

Target Coverage for Head and Neck Cancers Treated With IMRT: Review of Clinical Experiences

*Adam S. Garden, William I
and K. Kian Ang*

Acta Oncologica, 2007; 46: 214–220

informa
healthcare

ORIGINAL ARTICLE

Nasopharyngeal carcinoma. Treatment planning with IMRT and 3D conformal radiotherapy

CLAUS A. KRISTENSEN¹, FLEMMING KJÆR-KRISTOFFERSEN², WENDY SAPRU², ANNE K. BERTHELTSEN¹, ANNIKA LOFT³ & LENA SPECHT¹

I dati evidenziano una superiorità in termini di copertura del target con IMRT



ANTI TUMOUR TREATMENT

The current status of intensity-modulated radiation therapy in the treatment of nasopharyngeal carcinoma

Heming Lu ^{a,*}, Min Yao ^{b,c}**Table 1** Comparisons in IMRT versus non-IMRT techniques

Center	Sample size	Stage	Comparison arms			Target coverage	CNS dose sparing	Parotid dose sparing
			IMRT	2D-RT	3D-RT			
PWH ⁵	3	T1N0M0, T2N0M0, T4N0M0	Yes	Yes	Yes	Best with IMRT for T2N0M0 and T4N0M0	Best with IMRT for T2N0M0 and T4N0M0	Best with IMRT for T1N0M0
UCSF ⁶	1	Locally advanced	Yes ^a	Yes	Yes	Best with IMRT methods	Best with both IMRT methods	Best with fixed-field IMRT
WUMC ⁷	12	T2-4N1-3	Yes ^a	No	Yes	GTV _{LN} and CTV best with both IMRT methods	Best with both IMRT methods	Best with fixed-field IMRT
MSKCC ⁸	23	NA	Yes	Yes	Yes	PTV best with IMRT	Best with IMRT	Best with IMRT
CUH ⁹	11	All stages except stage I	Yes	No	Yes	Best with IMRT	Best with IMRT	Best with IMRT

Abbreviations: PWH, Prince of Wales Hospital, China; UCSF, University of California at San Francisco, USA; WUMC, Washington University Medical Center, USA; MSKCC, Memorial Sloan-Kettering Cancer Center, USA; CUH, Copenhagen University Hospital, Denmark.

^a Fixed-field IMRT and serial-field IMRT.

Migliore la IMRT rispetto a 3D

IMRT : Indicatori

Copertura del target

Controllo di malattia

Tossicità e qualità di vita



CLINICAL INVESTIGATION

QUALITY OF LIFE AND SURVIVAL OUTCOME FOR PATIENTS WITH NASOPHARYNGEAL CARCINOMA RECEIVING THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY VS. INTENSITY-MODULATED RADIOTHERAPY—A LONGITUDINAL STUDY

FU-MIN FANG, M.D., PH.D.,^{*†} CHIH-YEN CHIEN, M.D.,^{†‡} WEN-LING TSAI, PH.D.,^{***} HUI-CHUN CHEN, M.D.,^{*} HSUAN-CHIH HSU, M.D.,^{*} CHUN-CHUNG LUI, M.D.,[‡] TAI-LIN HUANG, M.D.,[§] AND HSUAN-YING HUANG, M.D.^{||}

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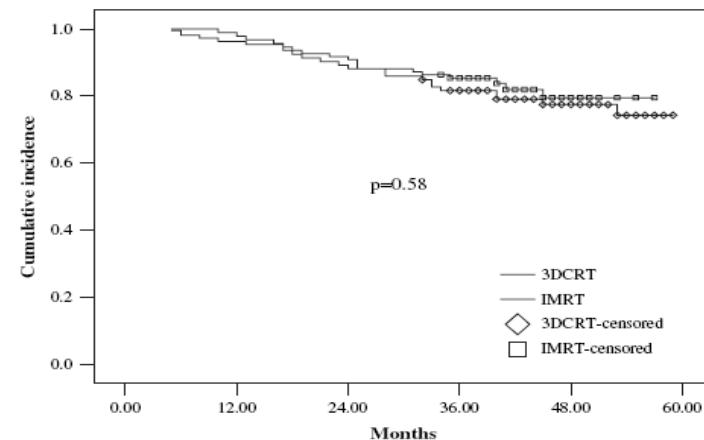
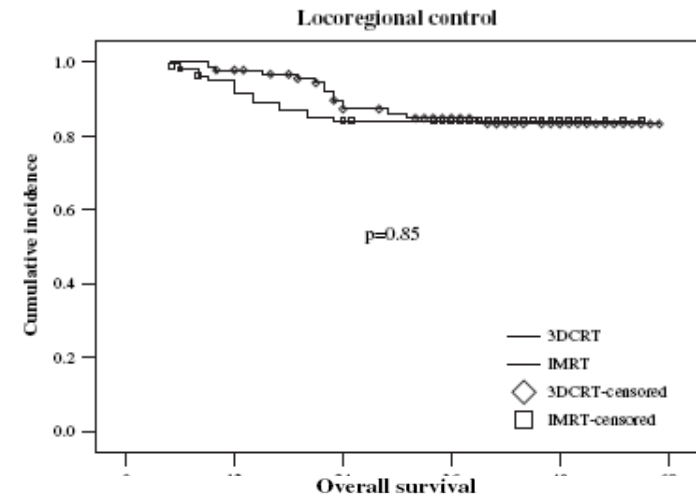
Published as: *Lancet Oncol.* 2011 February ; 12(2): 127-136.

Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer (PARSPORT): a phase 3 multicentre randomised controlled trial

Christopher M Nutting^{a,b,*}, James P Morden^b, Kevin J Harrington^{a,b}, Teresa Guerrero Urbano^c, Shreerang A Bhide^a, Catharine Clark^d, Elizabeth A Miles^e, Aisha B Miah^a, Kate Newbold^a, MaryAnne Tanay^a, Fawzi Adab^f, Sarah J Jefferies^g, Christopher Scrase^h, Beng



At 24 months, **no significant** differences were seen between randomised groups in non xerostomia, **locoregional control, or overall survival.**



IMRT: Indicatori

Copertura del target

Controllo di malattia

Tossicità e qualità di vita



ELSEVIER

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doi:10.1016/j.ijrobp.2009.09.040

INTRODUCTORY PAPER

QUANTITATIVE ANALYSES OF NORMAL TISSUE EFFECTS IN THE CLINIC (QUANTEC): AN INTRODUCTION TO THE SCIENTIFIC ISSUES

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AVI EISBRUCH, M.D.,§ ANDREW JACKSON, PH.D.,|| LAWRENCE B. MARKS, M.D.,¶
RANDALL K. TEN HAKEN, PH.D.,§ AND ELLEN D. YORKE, PH.D.||

From the *Departments of Human Oncology, Medical Physics, Biostatistics and Medical Informatics, University of Wisconsin School of Medicine and Public Health, Madison, WI; †Department of Radiation Oncology, University of Rochester Medical Center, Rochester, NY;

‡Department of Radiation Oncology, Washington University, St. Louis, MO; §Department of Radiation Oncology, University of Michigan, Ann Arbor, MI; ||Department of Medical Physics, Memorial Sloan Kettering Cancer Center, New York, NY; ¶Department of Radiation Oncology, University of North Carolina at Chapel Hill, NC

Advances in dose–volume/outcome (or normal tissue complication probability, NTCP) modeling since the seminal Emami paper from 1991 are reviewed. There has been some progress with an increasing number of studies on large patient samples with three-dimensional dosimetry. Nevertheless, NTCP models are not ideal. Issues related to the grading of side effects, selection of appropriate statistical methods, testing of internal and external model validity, and quantification of predictive power and statistical uncertainty, all limit the usefulness of much of the published literature. Synthesis (meta-analysis) of data from multiple studies is often impossible because of suboptimal primary analysis, insufficient reporting and variations in the models and predictors analyzed. Clinical limitations to the current knowledge base include the need for more data on the effect of patient-related cofactors, interactions between dose distribution and cytotoxic or molecular targeted agents, and the effect of dose fractions and overall treatment time in relation to nonuniform dose distributions. Research priorities for the next 5–10 years are proposed. © 2010 Elsevier Inc.

Tossicità: limiti di dose

Testa collo - Organi a rischio e tossicità

- Midollo spinale
- Chiasma – nervi ottici – ghiandole lacrimali
- Ghiandole salivari
- Strutture orofaringee
- Orecchio lobi temporali, massetere, cute atm

Tronco e midollo spinale)

- Asintomatico, lievi segni (Lhermitte... anche con dosi inferiori a quelle max, compare dopo diversi mesi)
- Debolezza , con o senza diminuzione del sensorio senza ripercussioni sulla qualità di vita
- Disabilità grave

Cause

- Demielinizzazione fino a necrosi della sostanza bianca (fino a 18 mesi dal termine del trattamento)
- Declino cerebrale dopo qualche anno
- Vasculopatia

Tronco e midollo spinale



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doi:10.1016/j.ijrobp.2009.04.095

QUANTEC: ORGAN SPECIFIC PAPER

Central Nervous System: Spinal Cord

RADIATION DOSE-VOLUME EFFECTS IN THE SPINAL CORD

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AND TIMOTHY E. SCHULTHEISS, PH.D.[‡]

From the *Department of Radiation Oncology, Duke University Medical Center, Durham, NC; †Department of Radiation Oncology, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands; and ‡Department of Radiation Physics, City of Hope Cancer Center, Duarte, CA

Dose-volume data for myelopathy in humans treated with radiotherapy (RT) to the spine is reviewed, along with pertinent preclinical data. Using conventional fractionation of 1.8-2 Gy/fraction to the full-thickness cord, the estimated risk of myelopathy is <1% and <10% at 54 Gy and 61 Gy, respectively, with a calculated strong dependence on dose/fraction ($\alpha/\beta = 0.87$ Gy). Reirradiation data in animals and humans suggest partial repair of RT-induced subclinical damage becoming evident about 6 months post-RT and increasing over the next 2 years. Reports of myelopathy from stereotactic radiosurgery to spinal lesions appear rare (<1%) when the maximum spinal cord dose is limited to the equivalent of 13 Gy in a single fraction or 20 Gy in three fractions. However, long-term data are insufficient to calculate a dose-volume relationship for myelopathy when the partial cord is treated with a hypofractionated regimen. © 2010 Elsevier Inc.

Fattori incidenti:

- Dose, volume, frazionamento
- CHT
- Età
- Diabete
- Vasculopatie ...



Effetti:

- Maggiori se dose > 250 cGy
- Frazionamento bigiornaliero
- Rischi di necrosi cerebrale se dose > 72Gy con fraz convenzionale
- Necrosi midollare se dose > 52Gy

**Radiochirurgia: rischi se dosi >12Gy
su volume > 5-10 cm³**

T.E.Merchant IJRBP 2010
MGH 1999



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doi:10.1016/j.ijrobp.2009.02.091

QUANTEC: ORGAN SPECIFIC PAPER

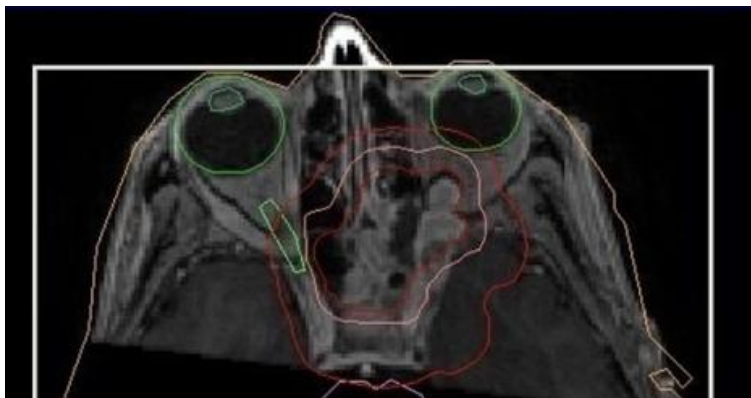
Central Nervous System: Brain

RADIATION DOSE-VOLUME EFFECTS IN THE BRAIN

YAACOV RICHARD LAWRENCE, M.R.C.P.,* X. ALLEN LI, PH.D.,[†] ISSAM EL NAQA, PH.D.,[‡]
CAROL A. HAHN, M.D.,[§] LAWRENCE B. MARKS, M.D.,[¶] THOMAS E. MERCHANT, D.O. PH.D.,^{||}
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Chiasma, nervi ottici



chiasma : neuropatia
nervi ottici : neuropatia ottica
occhi cataratta per dosi > 12 Gy
ghiandole lacrimali : occhio secco

- Dovuta ad ischemia del nervo ottico
- Si verifica per dosi comprese tra 45 e 65 Gy. **Dosi consigliate inferiori a 45 Gy**
- **Rischi maggiori quando si associano chemioterapici**
- Sindrome dell'occhio secco (iniziano a dosi di 30 Gy e sicura per dosi > 55 Gy)



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doi:10.1016/j.ijrobp.2009.07.1753

QUANTEC: ORGAN-SPECIFIC PAPER

Central Nervous System: Optic Nerve/Chiasm

RADIATION DOSE-VOLUME EFFECTS OF OPTIC NERVES AND CHIASM

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JOHN FLICKINGER, M.D.,§ JIHO NAM, M.D.,‡ AND JOHN KIRKPATRICK, M.D., PH.D.¶

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Ghiandole lacrimali



Radiotherapy and Oncology 64 (2002) 205–208

RADIOTHERAPY
& ONCOLOGY
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RADIATION THERAPEUTIC RADIOLOGY AND ONCOLOGY

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Short communication

Short term toxicity profile for 32 sinonasal cancer patients treated with IMRT. Can we avoid dry eye syndrome?

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Received 10 January 2002; received in revised form 1 July 2002; accepted 9 July 2002

Abstract

Intensity modulated radiation therapy (IMRT) was given for 32 patients with M0 sinonasal cancer, with a median follow-up of 15 months. Acute toxicity was mucositis grades 1–2 in 28 patients and grade 3 in four patients. No corneal injury was observed, except in one patient where it was present before the start of IMRT. Conjunctivitis and dry eye symptoms were mild (no grade 3–4 toxicity) and no evolution to dry eye syndrome was observed. We conclude that high dose conformality of IMRT results in mild acute toxicity and that IMRT allows avoiding dry eye syndrome by its ability to create concave dose distributions which avoid the main lacrimal glands. Follow-up is too short to evaluate local control, optic nerve or retinal toxicity. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Sinonasal; Radiotherapy; Intensity modulated radiation therapy; Acute toxicity; Dry eye

I disturbi compaiono alla dose di 30 Gy alla camera anteriore e sono sicuri con dosi di 55-60Gy

Million R, Parsons J. Radiation-induced eye injury from head and neck therapy. Front Radiat Ther Oncol Basel, Karger 1999;32:21–33.

F. Claus et al. / Radiotherap

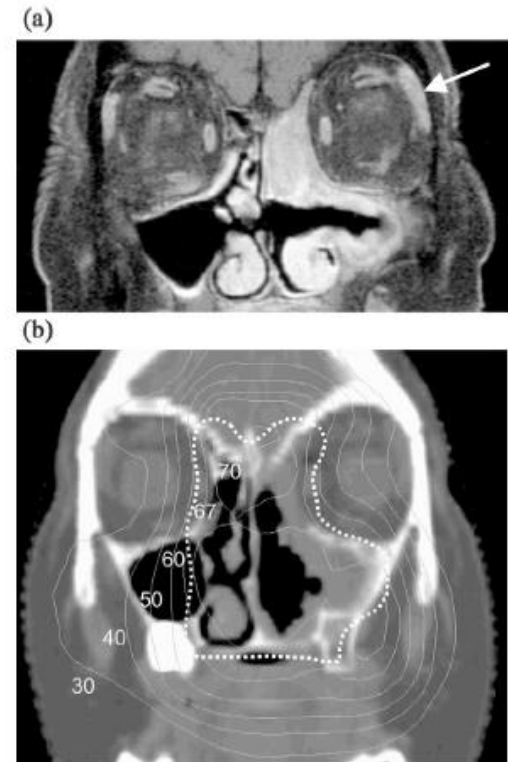


Fig. 1. (a) Location of the lacrimal gland (white arrow) on a coronal MRI scan. The patient was diagnosed with a melanoma originating in the left ethmoidal sinus cells. (b) Dose distribution display in a coronal plane of the IMRT plan for the case illustrated in Fig. 1a. The isodose lines are expressed in Gy. Both major lacrimal glands are excluded by the isodose line of 30 Gy.

Ghiandole salivari

Xerostomia

Sintomatica lieve (saliva densa o secchezza) senza significative alterazioni della dieta
Sintomatica severa con significativa alterazione dell'apporto di cibi (abbondante assunzione di acqua, lubrificanti, dieta limitata a cibi semisolidi o morbidi)

Parotide: 60% di cui 60% di saliva stimolata

Sottomandibolari e sottolinguali 40% di cui 70% di saliva non stimolata

PS: il risparmio delle parotidi da solo non è sufficiente per prevenire i sintomi di secchezza della bocca

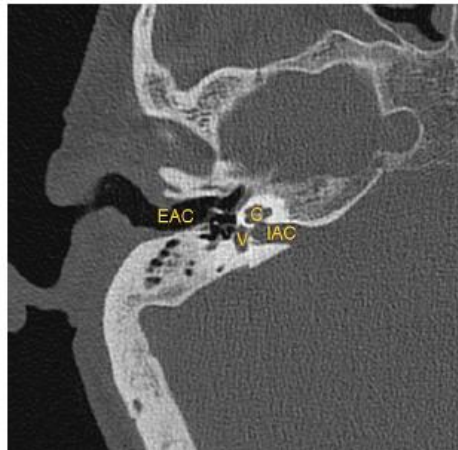
Strutture orofaringee

Disfagia

- I – Sintomatica . E' possibile però assumere una dieta regolarmente
- II – Sintomatica e alterata alimentazione- deglutizione (necessità di integratori alimentari, terapie di supporto e.v.)
- III – Sintomi che determinano alterazione severe della alimentazione e deglutizione
E' richiesta idratazione e posizionamento di sondino naso gastrico o PEG

Dosi ai muscoli costrittori

Orecchio Udito



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doi:10.1016/j.ijrobp.2009.04.096

QUANTEC: ORGAN-SPECIFIC PAPER

Central Nervous System: Ear

RADIATION THERAPY AND HEARING LOSS

NIRANJAN BHANDARE, M.S.,* ANDREW JACKSON, PH.D.,† AVRAHAM EISBRUCH, M.D.,‡
CHARLIE C. PAN, M.D.,‡ JOHN C. FLICKINGER, M.D.,§ PATRICK ANTONELLI, M.D.,||
AND WILLIAM M. MENDENHALL, M.D.*

lieve diminuzione dell'udito
perdita dell'udito che non richiede o richiede interventi o protesi
perdita marcata dell'udito bilaterale

Volume 0.13-0.56 Ha un volume troppo piccolo per definire un rapporto dose/volume

IMRT : Indicatori

Copertura del target

Controllo di malattia

Tossicità e qualità di vita

Cancer Treatment Reviews 37 (2011) 511–519



Contents lists available at ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevierhealth.com/journals/ctrv

Intensity-modulated radiotherapy versus conventional and 3D conformal radiotherapy in patients with head and neck cancer: Is there a worthwhile quality of life gain?

Silke Tribius^{a,*}, Corinna Bergelt^{b,c}

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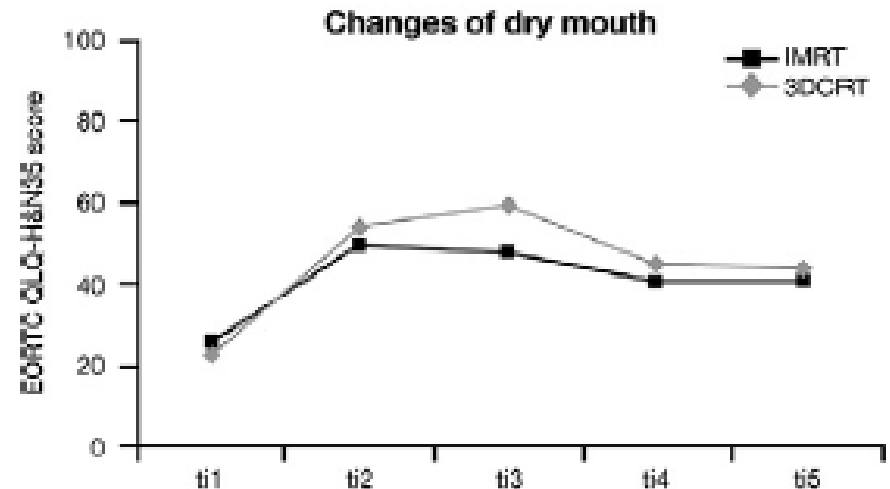
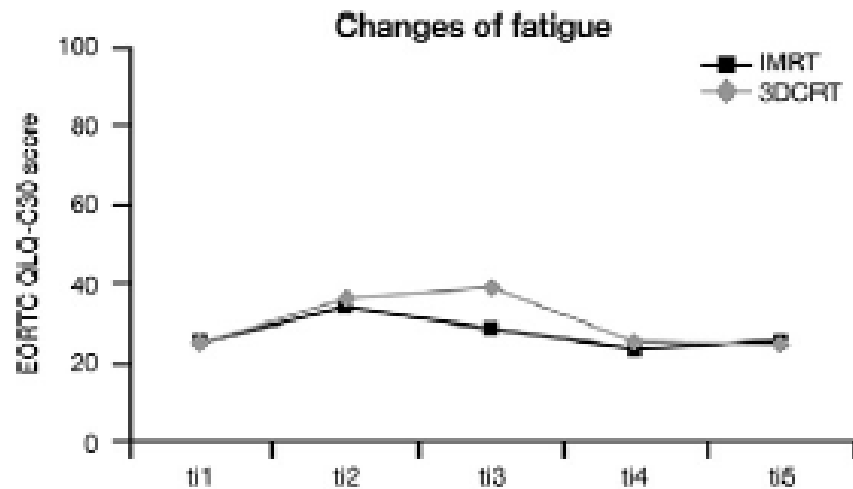
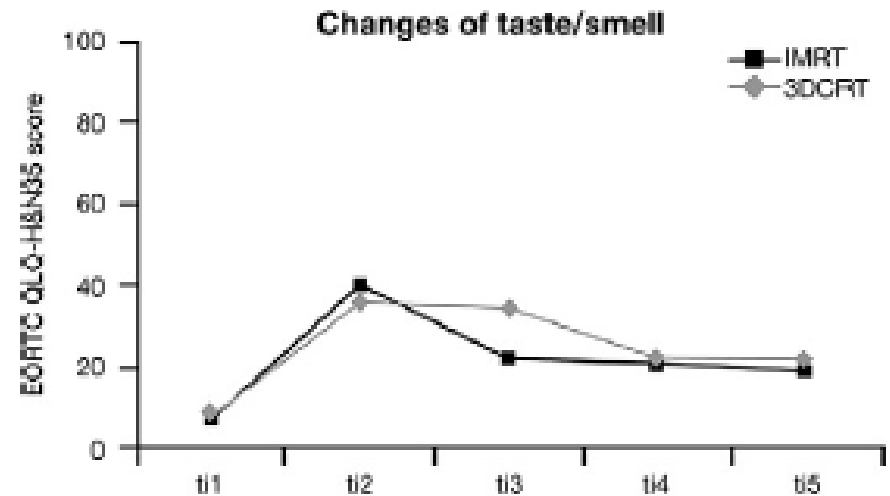
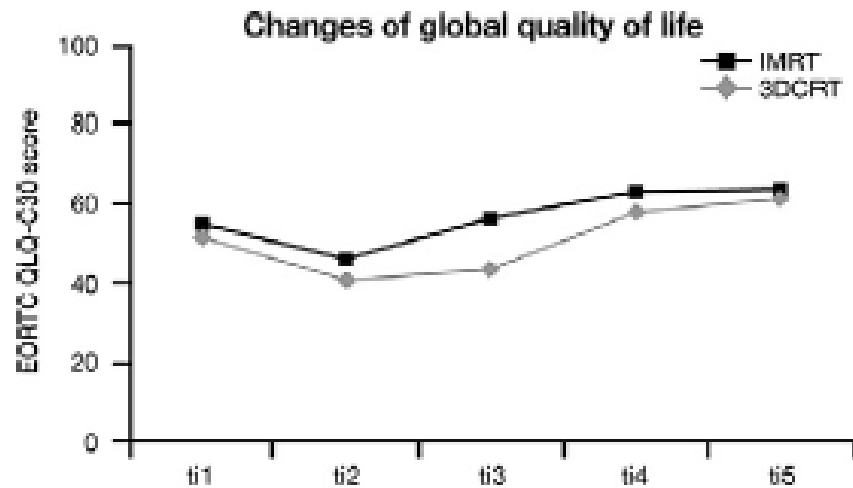
^bDepartment of Psychoanalytic Medicine, Institute for Medical Psychology, University Medical Center Hamburg-Eppendorf, Martinistrasse 52, 20246 Hamburg, Germany



Gennaio 2005 e l'Agosto 2010: 14 studi di confronto IMRT vs “
e 3D, **9 prospettici**, **5 retrospettivi**, **1 randomizzato**, per
valutare QoL

cancer only and mixed populations.

Results: The EORTC QLQ-C30 was the most widely used instrument, generally supplemented with the head and neck cancer module H&N35. IMRT was associated with statistically significant improvements in certain QoL domains versus 2DRT and 3DCRT, particularly those relating to xerostomia, including dry mouth, sticky saliva and eating-related domains. Improvements in global QoL were also observed in the IMRT groups in some studies.





2006

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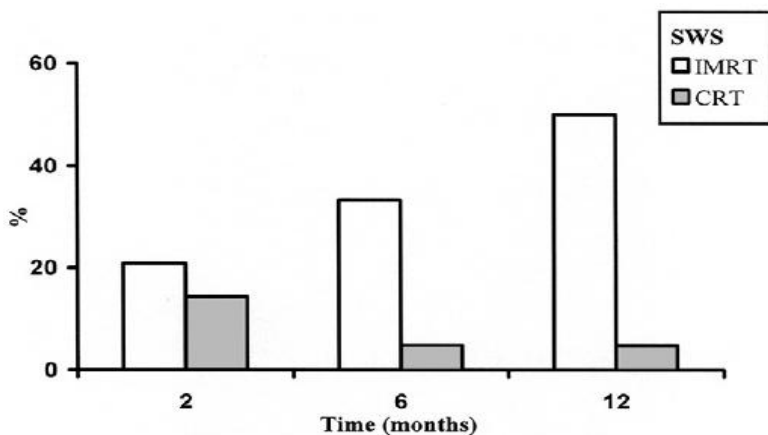
CLINICAL INVESTIGATION

Head and Neck

XEROSTOMIA AND QUALITY OF LIFE AFTER INTENSITY-MODULATED RADIOTHERAPY VS. CONVENTIONAL RADIOTHERAPY FOR EARLY-STAGE NASOPHARYNGEAL CARCINOMA: INITIAL REPORT ON A RANDOMIZED CONTROLLED CLINICAL TRIAL

EDMOND H. N. POW, M.D.S.,* DORA L. W. KWONG, M.B. B.S.,† ANNE S. McMILLAN, PH.D.,*
 MAY C. M. WONG, PH.D.,‡ JONATHAN S. T. SHAM, M.D.,† LUCULLUS H. T. LEUNG, PH.D.,†
 AND W. KEUNG LEUNG, PH.D.‡

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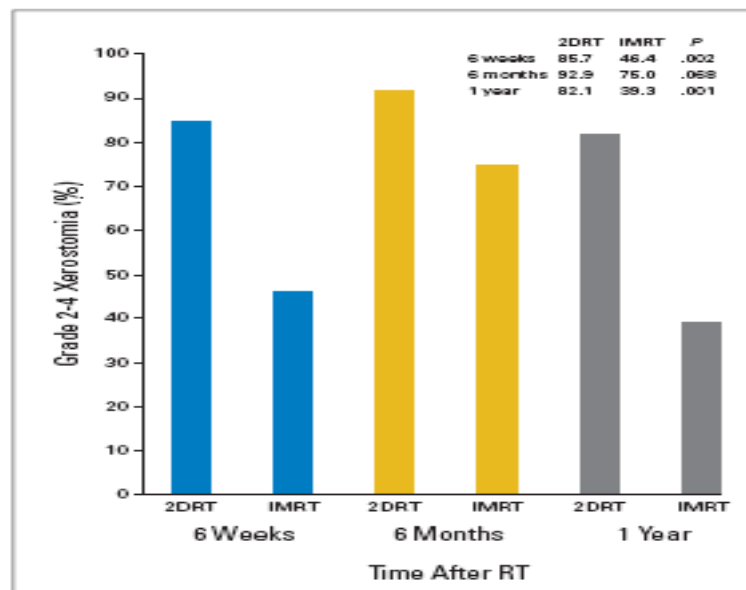


Meglio stimolato il flusso di saliva con IMRT

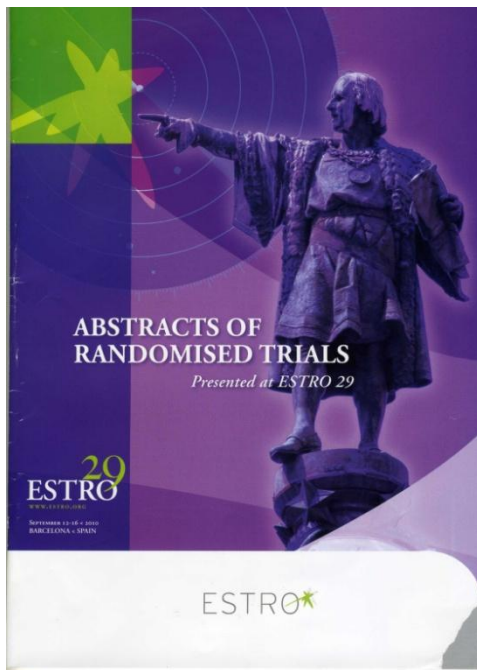
2007

Prospective Randomized Study of Intensity-Modulated Radiotherapy on Salivary Gland Function in Early-Stage Nasopharyngeal Carcinoma Patients

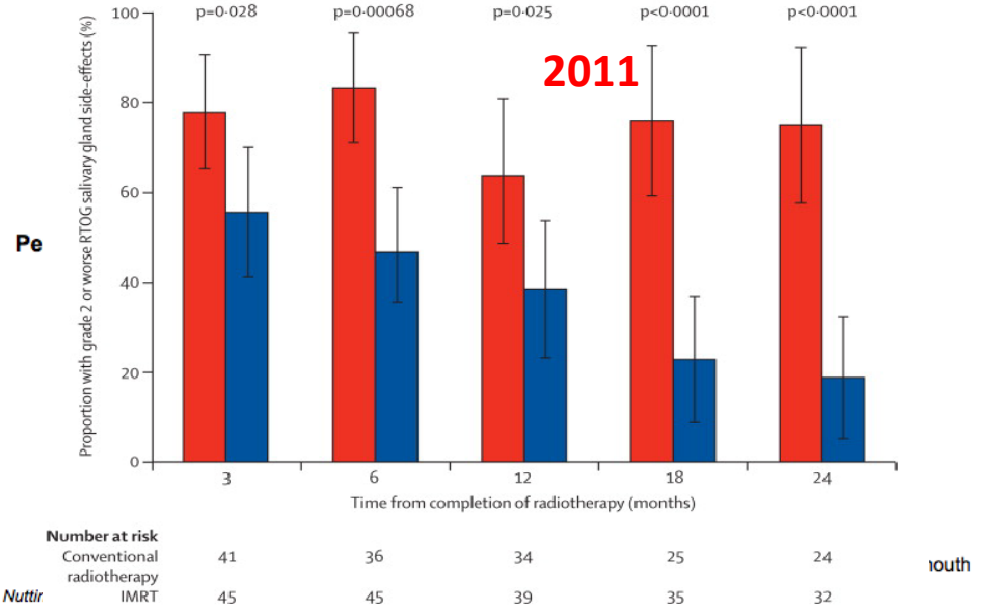
Michael K.M. Kam, Sing-Fai Leung, Benny Zee, Ricky M.C. Chau, Joyce J.S. Suen, Frankie Mo, Maria Lai, Rosalie Ho, Kin-yin Cheung, Brian K.H. Yu, Samuel K.W. Chiu, Peter H.K. Choi, Peter M.L. Teo, Wing-hong Kwan, and Anthony T.C. Chan



Minore incidenza di xerostomia con IMRT



RTOG Subjective Salivary Gland toxicity $\geq G2^*$



- 94 pts con ca faringeo T1-4, N0-3, M0
- 2003 → 2007

- 65 Gy/30 fr/6 w : 2-D vs parotid-sparing IMRT
- LENT-SOMA > G2 Xerostomia:

→ 12 mesi 74% con 2-D vs 39% con IMRT (p:0.002)

→ 24 mesi : 65% con 2-D vs 39% con IMRT (0.04)

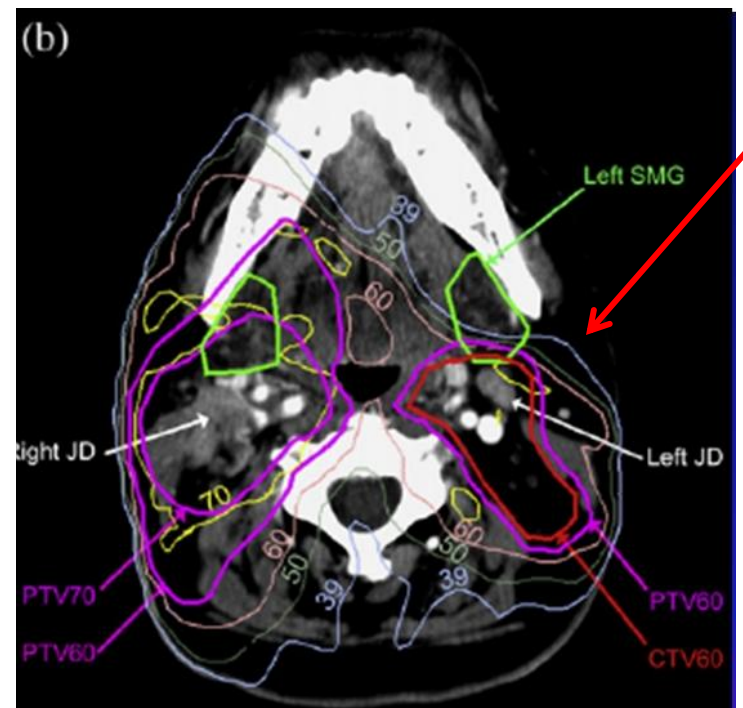
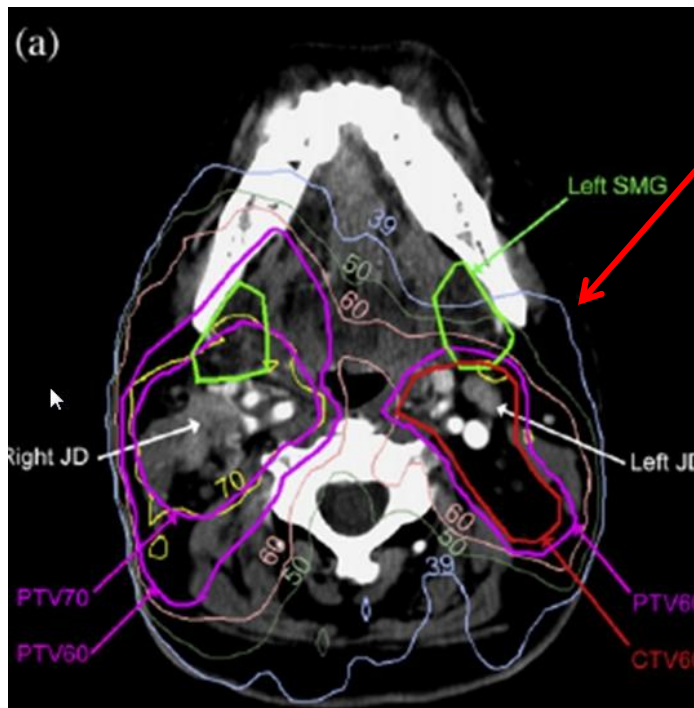
- Non differenze in termini di mucosite acuta OS, LRC

Nutting Estro 2009

Ghiandole sottomandibolari

La dose soglia stimata (per flusso salivare): 39Gy

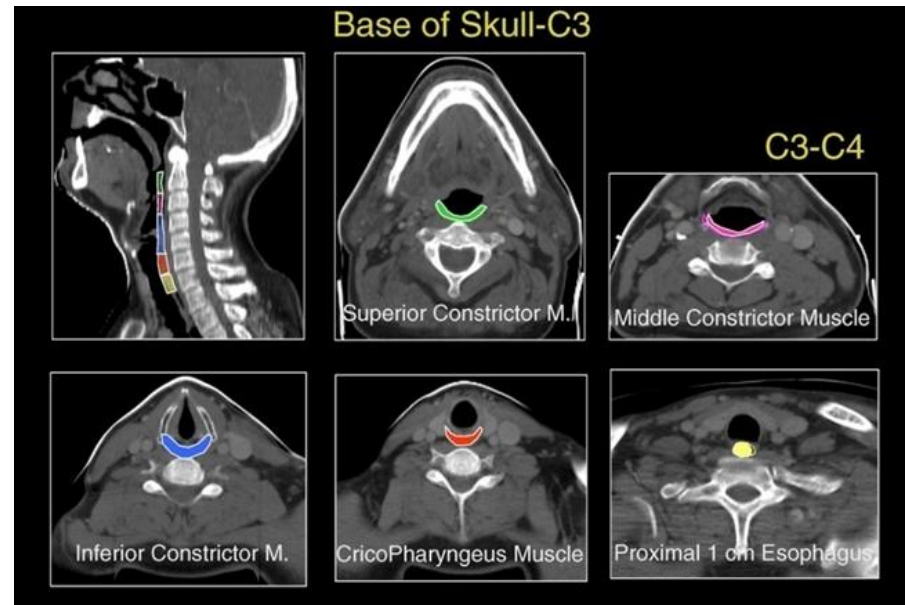
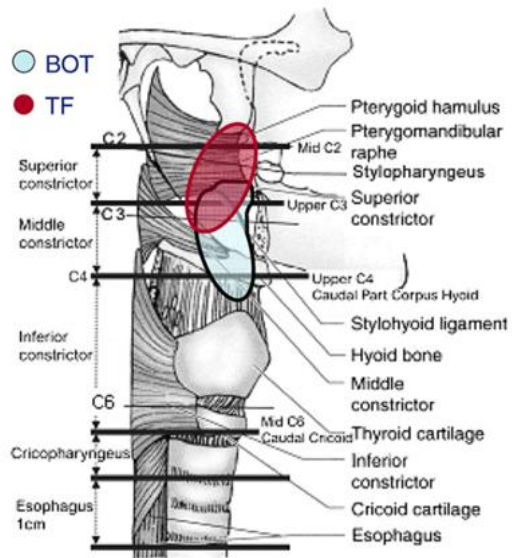
Valutare se possibile la fattibilità di riduzione di dose al disotto di tale valore alla ghiandola sottomandibolare senza sottodosare il target (utilizzo della funzione costo)



Dysphagia disorders in patients with cancer of the oropharynx are significantly affected by the radiation therapy dose to the superior and middle constrictor muscle:
A dose-effect relationship

Peter C. Levendag^{a,*}, David N. Teguh^a, Peter Voet^a, Henri van der Est^a, Inge Noever^c,
Wilhelmus J.M. de Kruijf^a, Inger-Karine Kolkman-Deurloo^a, Jean-Briac Prevost^a,
Johan Poll^a, Paul I.M. Schmitz^b, Ben J. Heijmen^a

^aDepartment of Radiation Oncology, ^bDepartment of Biostatistics, and ^cDepartment of Data management, Erasmus Medical Center – Daniel den Hoed, Rotterdam, The Netherlands



81paz trattati con 3D/IMRT per ca mesofaringe

La disfagia aumenta significamente per un aumento di dose ai muscoli costrittori superiori e medi
+19% per 10 Gy dopo i 55 Gy

Intensity-Modulated Chemoradiotherapy Aiming to Reduce Dysphagia in Patients With Oropharyngeal Cancer: Clinical and Functional Results

Felix Y. Feng, Hyungjin M. Kim, Teresa H. Lyden, Marc J. Haxer, Francis P. Worden, Mary Feng, Jeffrey S. Moyer, Mark E. Prince, Thomas E. Carey, Gregory T. Wolf, Carol R. Bradford, Douglas B. Chepeha, and Avraham Eisbruch

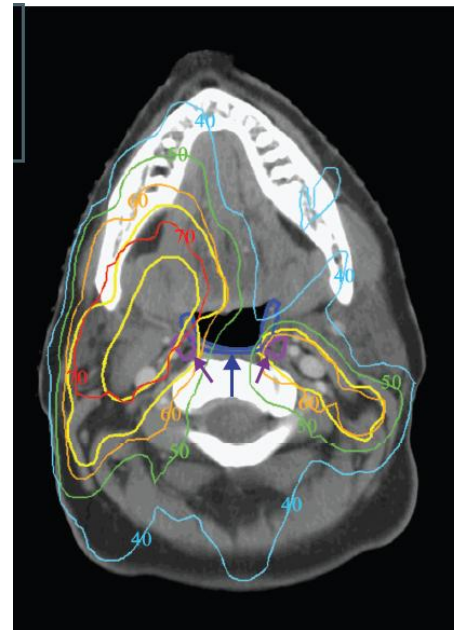
Table 2. Observer-Rated Dysphagia

Event Grade	Time Period (months)											
	Pre-therapy (n = 73)		3 (n = 72)		6 (n = 62)		12 (n = 68)		18 (n = 58)		24 (n = 51)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
0	71	97	36	50	32	52	39	58	36	62	30	59
1	1	2	25	35	22	35	25	37	19	33	19	37
2	1	2	6	8	4	6	3	4	2	3	1	2
3	0	0	5	7	4	6	1	1	1	2	1	2

Conclusion

Chemoradiotherapy with IMRT aiming to reduce dysphagia can be performed safely for OPC and has high locoregional tumor control rates. On average, long-term patient-reported, observer-rated, and objective measures of swallowing were only slightly worse than pretherapy measures, representing potential improvement compared with previous studies.

J Clin Oncol 28:2732-2738. © 2010 by American Society of Clinical Oncology



CLINICAL INVESTIGATION

Head and Neck

**SIMPLE CAROTID-SPARING INTENSITY-MODULATED RADIOTHERAPY
 TECHNIQUE AND PRELIMINARY EXPERIENCE FOR T1-2 GLOTTIC CANCER**

DAVID I. ROSENTHAL, M.D.,* CLIFTON D. FULLER, M.D.,† JERRY L. BARKER, JR., M.D.,‡
 BRYAN MASON, M.S.,* JOHN A. GARCIA, C.M.D.,* JAN S. LEWIN, PH.D.,§
 F. CHRISTOPHER HOLSINGER, M.D.,§ C. RICHARD STASNEY, M.D.,|| STEVEN J. FRANK, M.D.,*
 DAVID L. SCHWARTZ, M.D.,*¶ WILLIAM H. MORRISON, M.D.,* ADAM S. GARDEN, M.D.,*
 AND K. KIAN ANG, M.D., PH.D.*

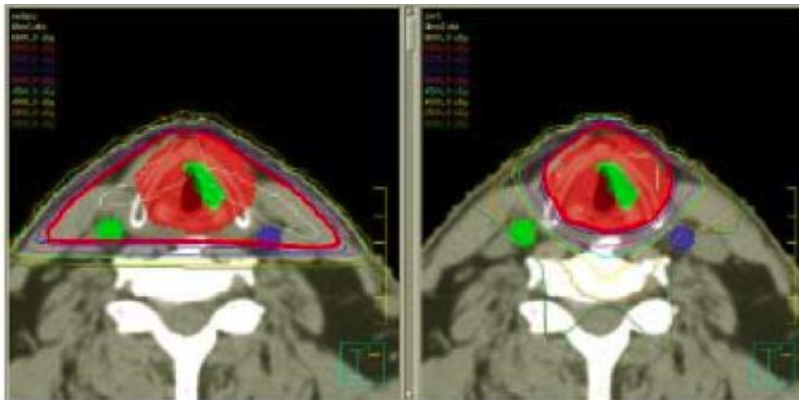
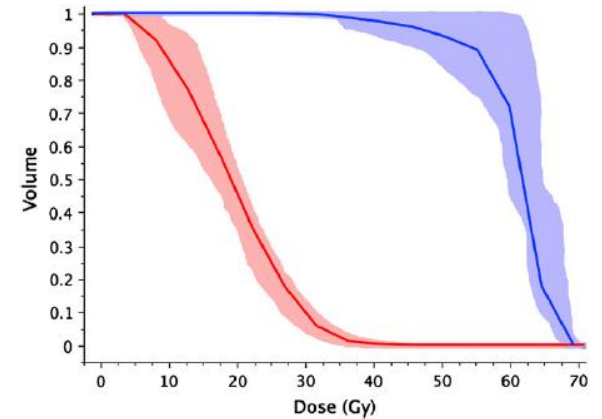


Fig. 2. Stereotactic isodose plans for (a) lateral field setup and (b) intensity-modulated radiotherapy

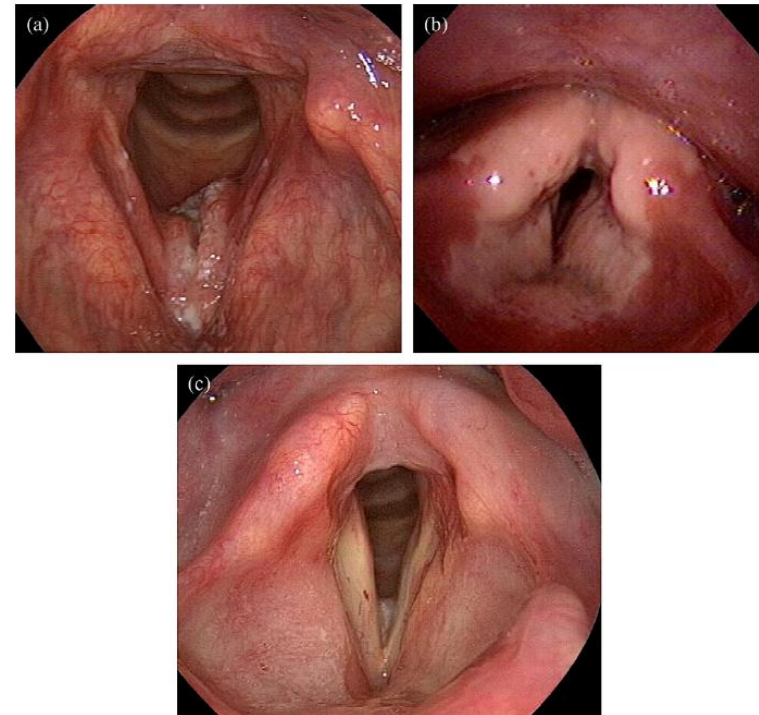


Fig. 3. (a), during (b), and post-intensity-modulated radiotherapy (c) laryngoscopic examination, showing resolution of circular mucositis, in a distribution similar to the expected isodose volumes.

Bassa incidenza di N+ (< 5%)
 Rischio di aterogenesi e incidenti vascolari
 Ridotta possibilità di future RT

IMRT: luci

- ❑ Alta conformazione della dose (target irregolare, zone critiche..)
- ❑ Possibilità di dose escalation
- ❑ Possibilità di SIB
- ❑ Possibilità di re-irradiazione in regioni già irradiate
- ❑ Risparmio organi critici (marginii stretti..)

IMRT: ombre

RECURRENCE IN REGION OF SPARED PAROTID GLAND AFTER DEFINITIVE INTENSITY-MODULATED RADIOTHERAPY FOR HEAD AND NECK CANCER

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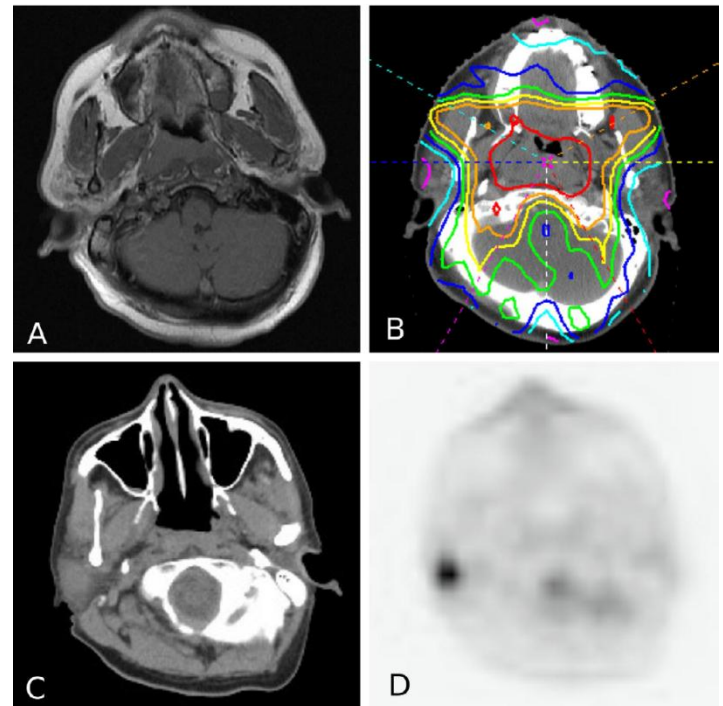
Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 3, pp. 660–665, 2008

- 1) Rischio di ***marginal missing*** dovuti ai ripidi gradienti di dose e dai movimenti intrafraction IMRT



IGRT

- 2) Maggior quota di tessuto sano esposta alle bassi dosi (effetti da valutare)



Conclusioni

IMRT: indicazioni

- **Certa:** tumori del nasofaringe , seni paranasali e della base del cranio e tumori recidivati.
- **Possibile:** orofaringe e cavità orale
- **Da valutare ancora:** ipofaringe e laringe

Conclusioni

- la **tecnica 3-D** è oggi lo standard minimo richiesto
- la **tecnica IMRT** deve essere adottata per la cura di selezionati tumori e selezionate condizioni cliniche
- Sono chiari i vantaggi in termini di dosimetria clinica, di riduzione degli effetti collaterali e della dose agli OAR, mentre sono ancora in corso di valutazione i dati sull'outcome complessivo

Grazie per l'attenzione

