



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

# **IGRT Radioterapia Guidata dalle Immagini**

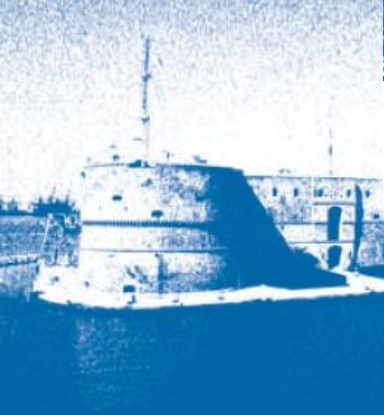


**Taranto, 12-14 gennaio 2012  
Grand Hotel Delfino**

**Mauro Palazzi**

**SC Radioterapia**

**Ospedale Niguarda, Milano**



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- 14.30 IV SESSIONE – Attualità in Radioterapia Oncologica**  
Moderatori: V. Fusco, S. Bambace
- 14.40 Dalla 3D alla IMRT  
M. Santarelli
- 15.00 La IGRT  
M. Palazzi
- 15.20 Tomoterapia e Cyberknife  
C. Iotti
- 15.40 Radiochemioterapia, farmaci biologici e Radioprotezione  
G. Silvano, M. Soloperto
- 16.00 I ritrattamenti  
A. Bacigalupo

# 3 “rivoluzioni” tecnologiche recenti in Radioterapia

1. inizio anni '90- pianificazione ( RT 3D )
2. fine anni '90- erogazione ( IMRT )
3. >2000- verifica ( IGRT )

**PIANIFICAZIONE 3D**

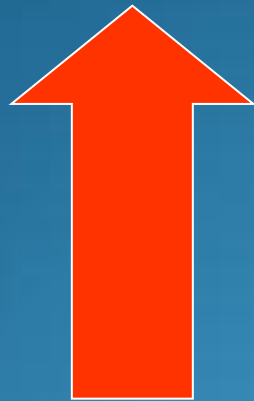


**EROGAZIONE  
(IMRT)**

**VERIFICA (IGRT)**



**RI-PIANIFICAZIONE 3D**



**VERIFICA (IGRT)**



**EROGAZIONE  
(IMRT)**



# **In un futuro non lontano:**

**verifica in tempo reale con TC  
della anatomia “del giorno”**

**ri-pianificazione in tempo reale  
per l'erogazione “del giorno”**

**(adaptive radiotherapy)**

# PROBLEMA 1:

**Quanto costa la tecnologia in RT?**

- **RT 3D = 80 euro**
- **IMRT = +70 = 150 euro**
- **IGRT = +70 = 220 euro**



## **RISPOSTA 1:**

**I costi della RT tendono ad  
aumentare significativamente**



## **PROBLEMA 2:**

**Quanto “rende” la tecnologia in RT?**

- **e' quasi impossibile fare studi randomizzati sulle nuove tecnologie (IMRT, IGRT)**
- **?**



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

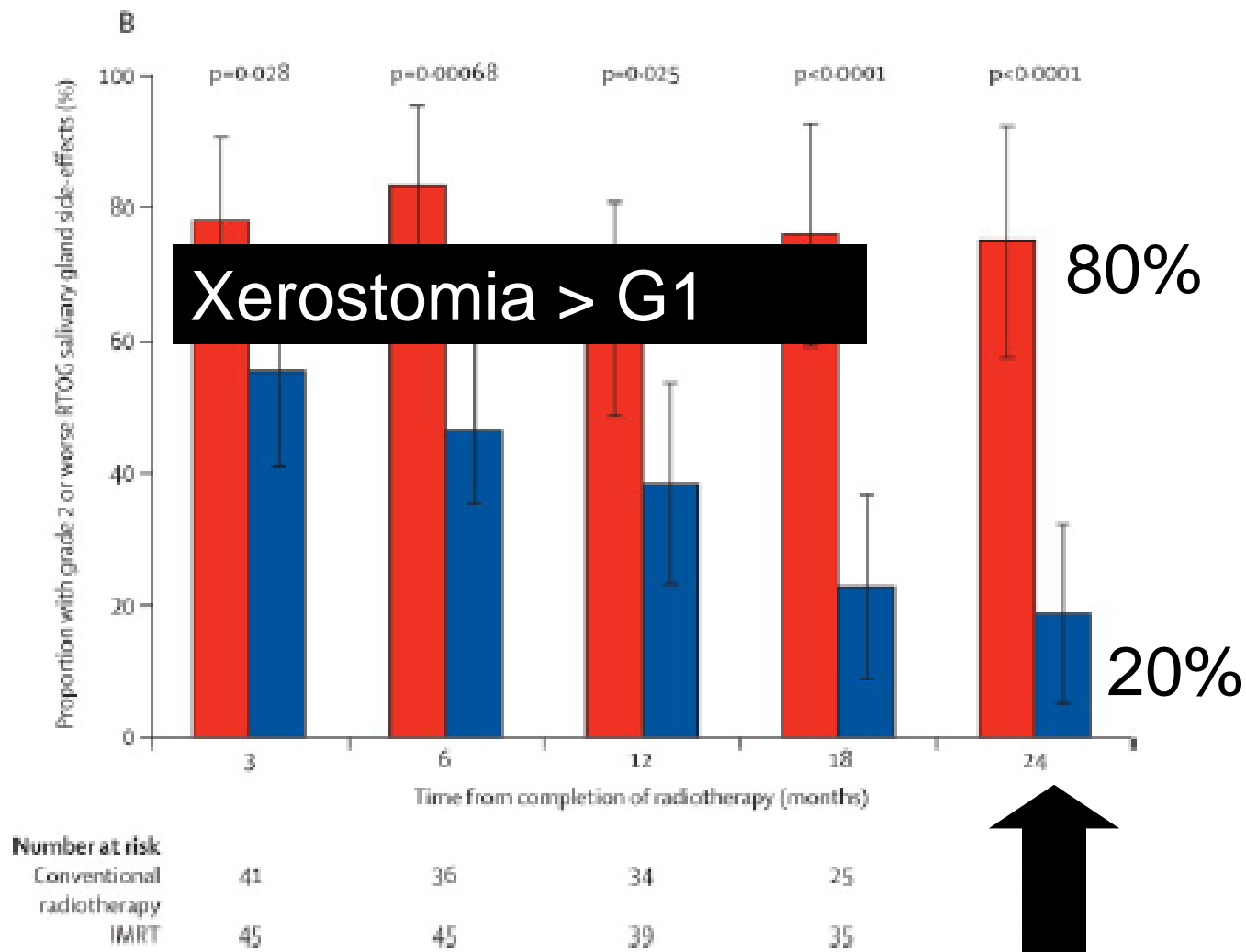
Christopher M Nutting<sup>a,b,\*</sup>, James P Morden<sup>b</sup>, Kevin J Harrington<sup>a,b</sup>, Teresa Guerrero Urbano<sup>c</sup>, Shreerang A Bhide<sup>a</sup>, Catharine Clark<sup>d</sup>, Elizabeth A Miles<sup>e</sup>, Aisha B Miah<sup>a</sup>, Kate Newbold<sup>a</sup>, MaryAnne Tanay<sup>a</sup>, Fawzi Adab<sup>f</sup>, Sarah J Jefferies<sup>g</sup>, Christopher Scrase<sup>h</sup>, Beng K Yap<sup>i</sup>, Roger P A'Hern<sup>b</sup>, Mark A Sydenham<sup>b</sup>, Marie Emson<sup>b</sup>, Emma Hall<sup>b</sup>, and on behalf of the PARSPORT trial management group<sup>†</sup>

<sup>a</sup>Head and Neck Unit, Royal Marsden Hospitals NHS Foundation Trust, London, UK

**2003-2007, UK**

**94 pazienti con ca faringe randomizzati a: 3DRT vs IMRT (60-65 Gy/30 frazioni)**

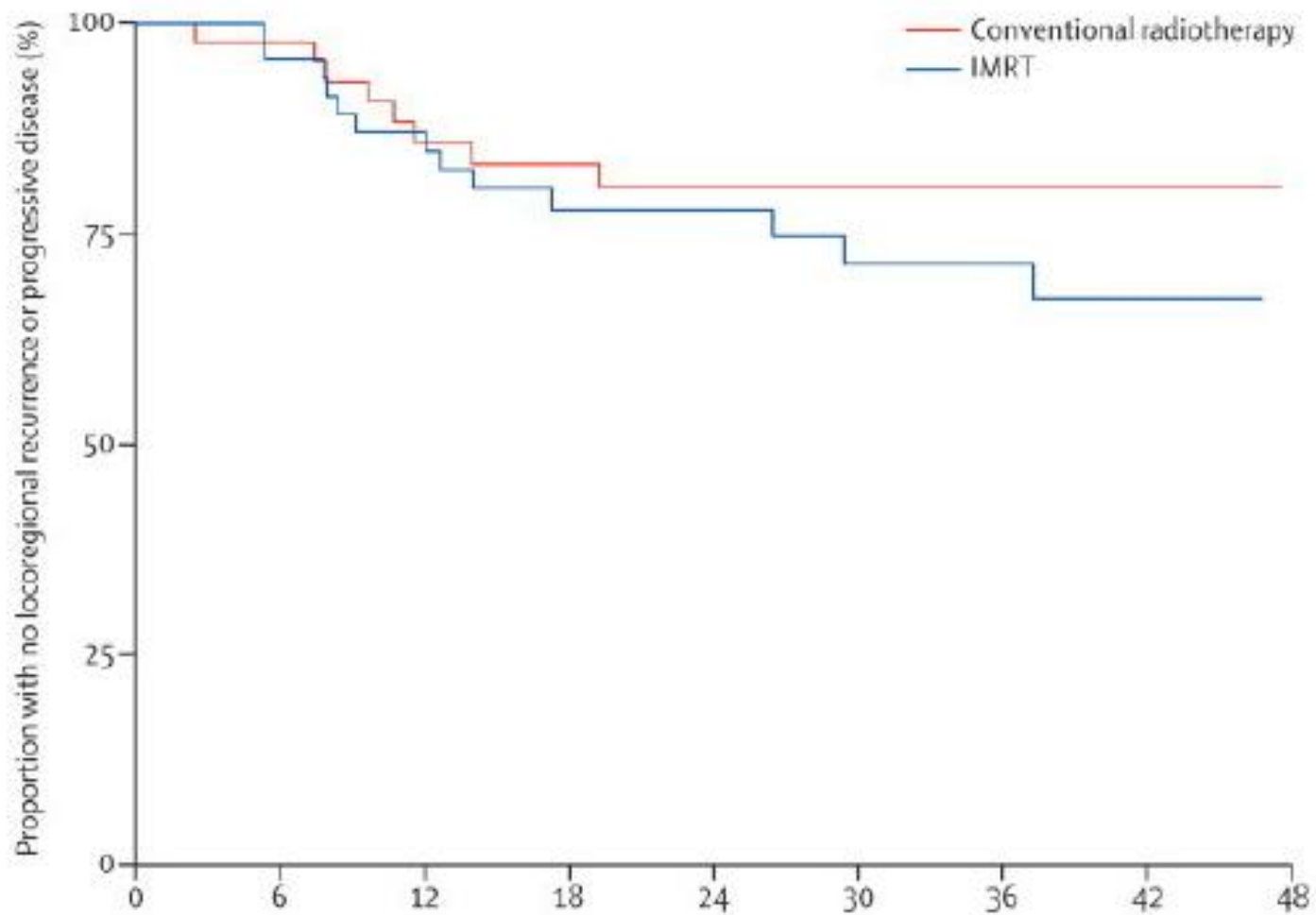
**Endpoint primario: xerostomia  $\geq$  G2**



**Figure 2.**

Proportion of patients reporting grade 2 or worse LENT SOMA subjective xerostomia and RTOG salivary gland side-effects

$p$  values quoted compare proportions with grade 2 or worse side-effects in each group with a  $\chi^2$  test. Error bars represent 95% CIs. IMRT=intensity-modulated radiotherapy. LENT SOMA=Late Effects of Normal Tissues Subjective-Objective Management Analytic. RTOG=Radiation Therapy Oncology Group.



**Number of events/at risk**

Conventional radiotherapy

IMRT

0/47

1/42

5/34

1/30

1/29

0/23

0/19

0/15

0/8

0/47

2/44

4/39

4/31

0/28

2/22

0/18

1/15

0/11

## **DIGRESSIONE 1:**

**E' possibile ipotizzare che un  
“miglioramento terapeutico”  
comporti un rischio di  
peggioramento del risultato?**

**SI !!!!**

## **DIGRESSIONE 2:**

**Siamo pronti a misurare un  
miglioramento in termini di qualità  
di vita dei nostri  
“miglioramenti terapeutici” ?**

**NO !!!!**

## **PROBLEMA 2:**

**Quanto rende la tecnologia in RT?**

- **e' quasi impossibile fare studi randomizzati sulle nuove tecnologie (IMRT),**
- **IGRT ?**

## **PROBLEMA 2:**

**Quanto rende la tecnologia in RT?**

- e' ~~quasi~~ impossibile fare studi randomizzati sulle nuove tecnologie (IGRT)



**IGRT = image-guided  
radiotherapy**

**(radioterapia guidata  
dalle immagini)**



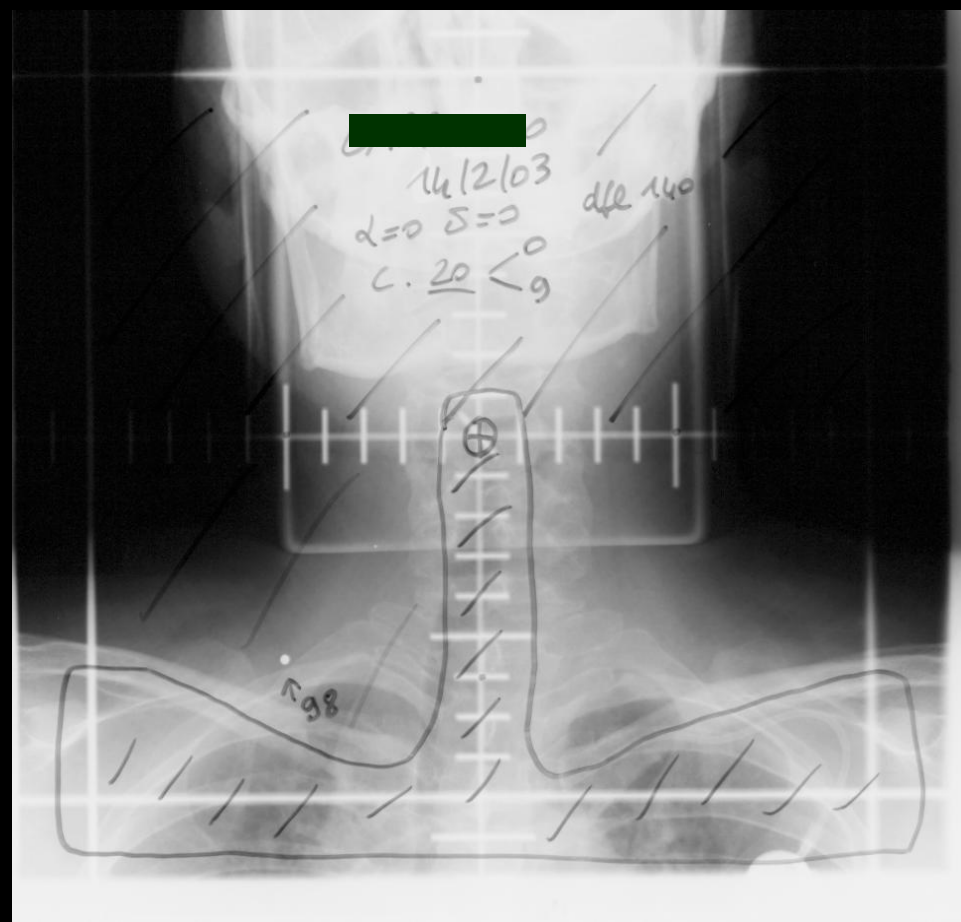
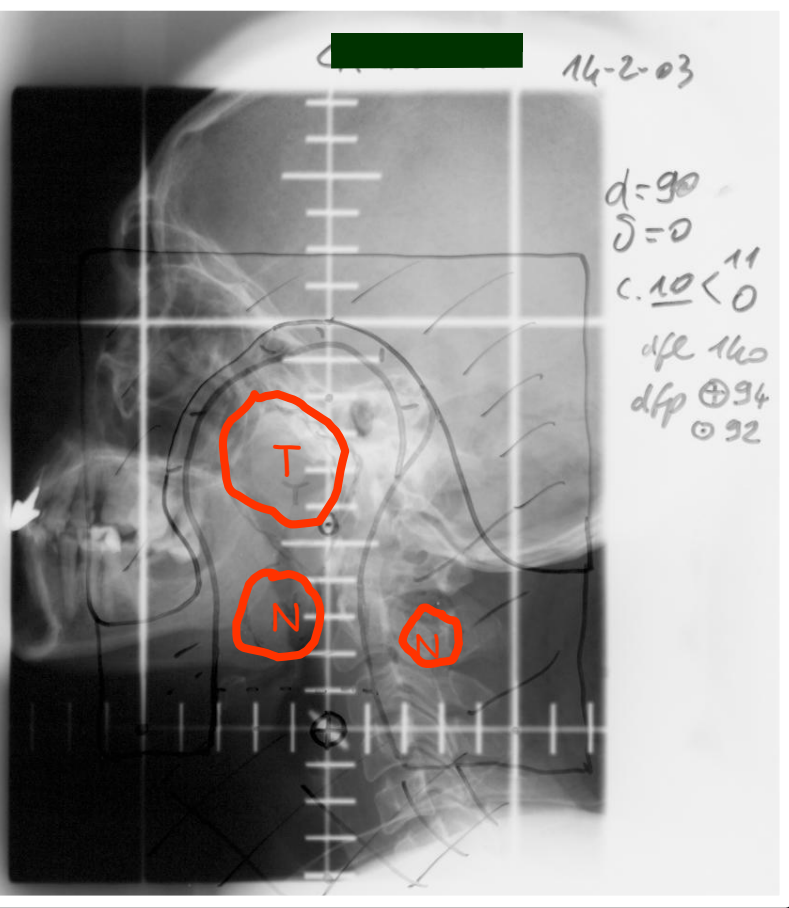
doi:10.1016/j.meddos.2005.12.004

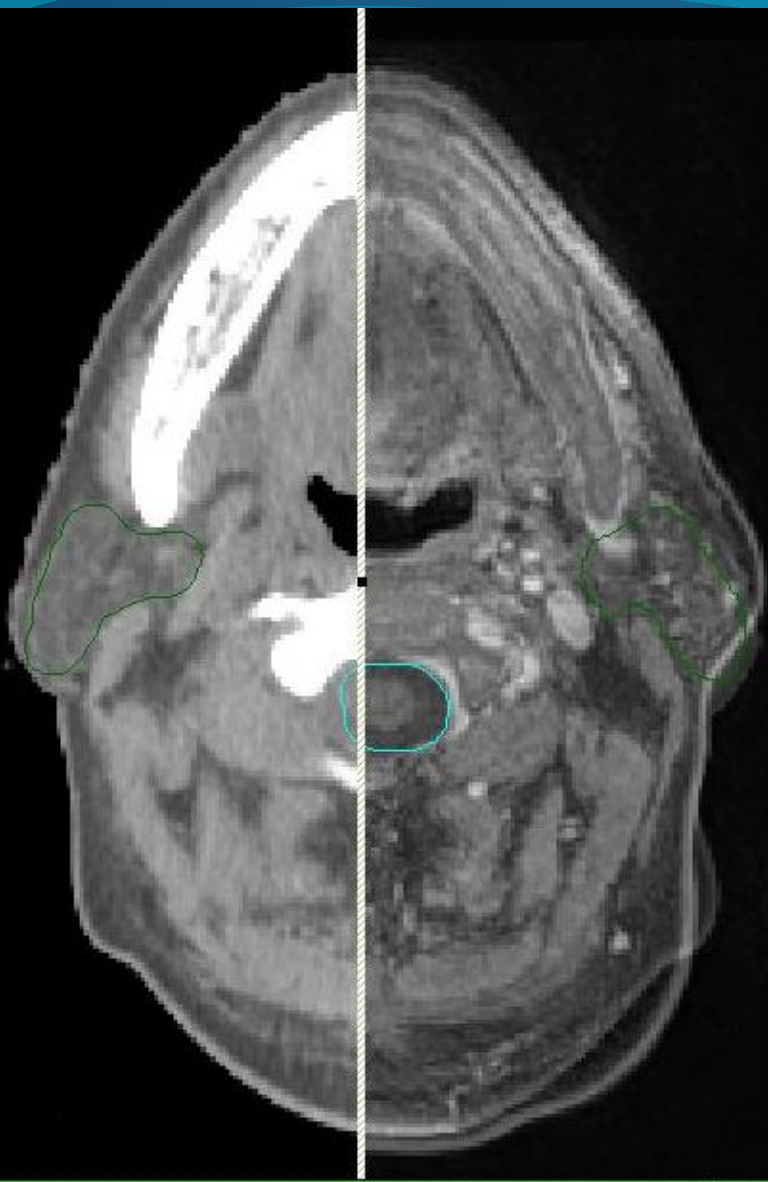
## OVERVIEW OF IMAGE-GUIDED RADIATION THERAPY

LEI XING, PH.D., BRIAN THORNDYKE, PH.D., EDUARD SCHREIBMANN, PH.D.,  
YONG YANG, PH.D., TIAN-FANG LI, PH.D., GWE-YA KIM, PH.D., GARY LUXTON, PH.D.,  
and ALBERT KOONG, M.D.

Department of Radiation Oncology, Stanford University School of Medicine, Stanford, CA

1. Tumor target volume definition
2. Intra-fraction organ movement
3. Inter-fraction organ movement
4. Rigid and deformable image registration





AL



Sagittal

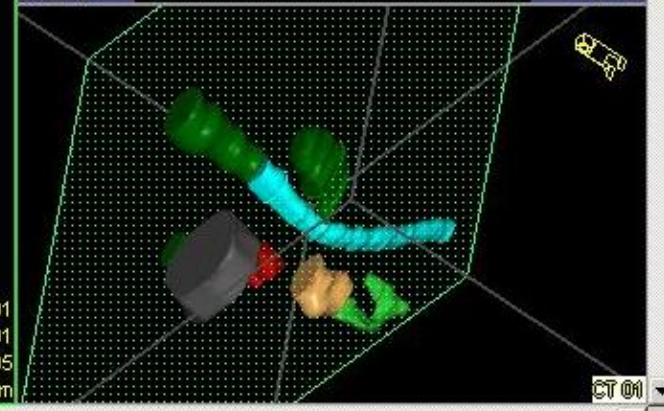
CT 01

AL



Coronal

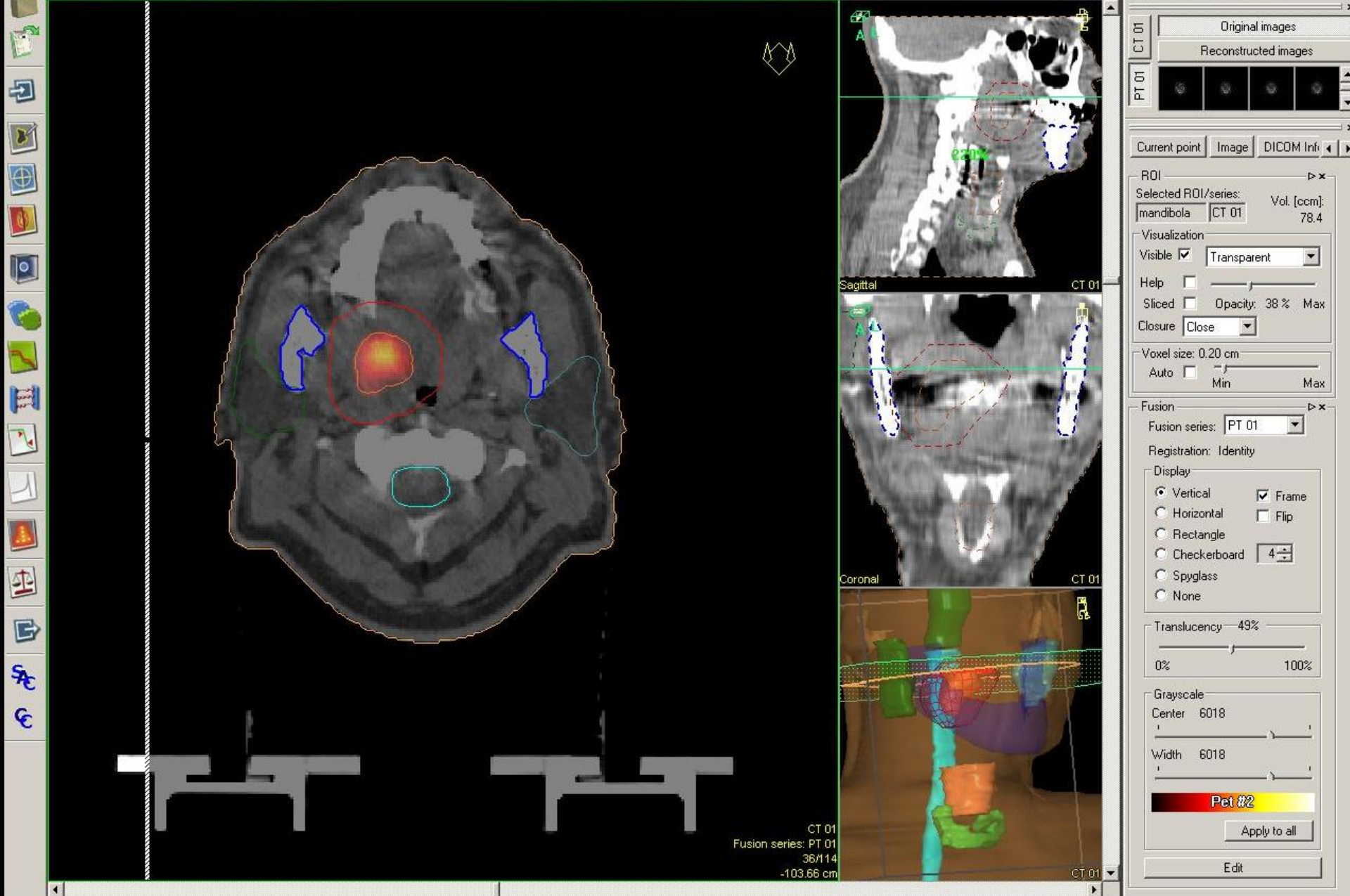
CT 01



CT 01  
Fusion series: MR 01  
33/95  
80.70 cm

CT 01





ORIGINAL ARTICLE

**An overview of volumetric imaging technologies and their quality assurance for IGRT**

D. VERELLEN, M. DE RIDDER, K. TOURNEL, M. DUCHATEAU, T. REYNDERS,  
T. GEVAERT, N. LINTHOUT & G. STORME

*Radiotherapie, Oncologisch Centrum, UZ Brussel, Brussels, Belgium*

IGRT = Frequente acquisizione di immagini  
**nel bunker di terapia**, durante un ciclo di  
trattamento, con decisioni prese sulla base  
di queste informazioni

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IGRT = **Frequente** acquisizione di immagini nel bunker di terapia, durante un ciclo di trattamento, con decisioni prese sulla base di queste informazioni

Perché è importante verificare  
**FREQUENTEMENTE** il trattamento erogato?

Perché rispetto alla situazione di riferimento  
(piano di cura) si possono verificare, lungo  
**TUTTO** l'arco del trattamento, importanti  
variazioni che tendono a peggiorare la  
qualità del trattamento stesso



# VARIAZIONI =

**1. Variazioni di tipo geometrico ( errori di riposizionamento) inter-frazionali**

**2. Cambiamenti fisiologici degli organi interni (e del bersaglio)  
(intra-) e inter-frazionali**

**3. Variazioni dimensionali del tumore e degli organi in seguito al trattamento  
inter-frazionali**

**Un altro fattore importante,  
nella verifica del trattamento, è  
la **qualità** delle informazioni  
fornite dalla verifica**

**Idealmente, vorremmo disporre di uno strumento che ci consenta di verificare il trattamento effettivamente erogato:**

- 1. frequentemente (tutte le frazioni?)**
- 2. sulla base di un imaging di alta qualità (reperi ossei vs strutture anatomiche )**

# le tecniche protagoniste della “rivoluzione” IGRT

## 1. tecniche planari

- EPID (electronic portal imaging devices)
- cyberknife

## 2. tecniche volumetriche

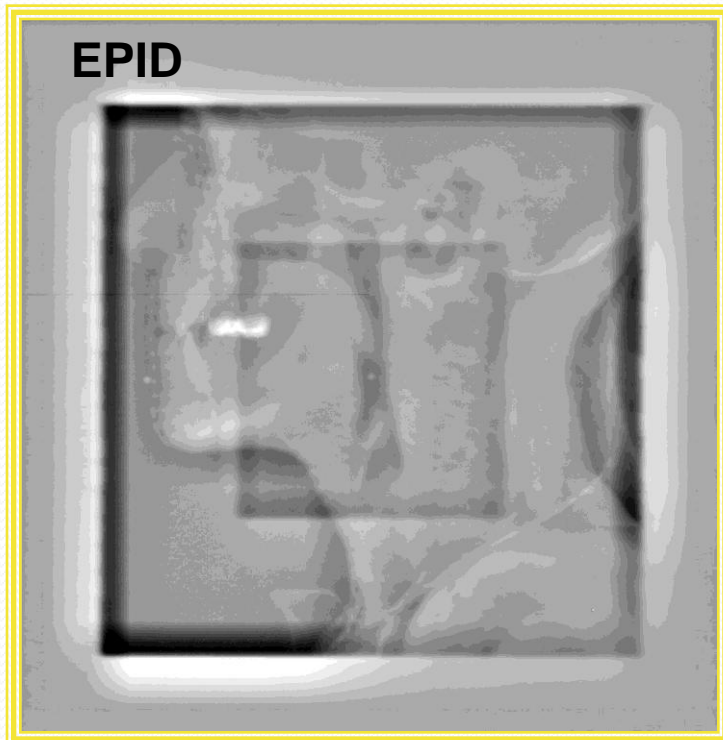
- in-room CT scanner “on rails”
- cone-beam CT (kV, MV)
- Tomoterapia

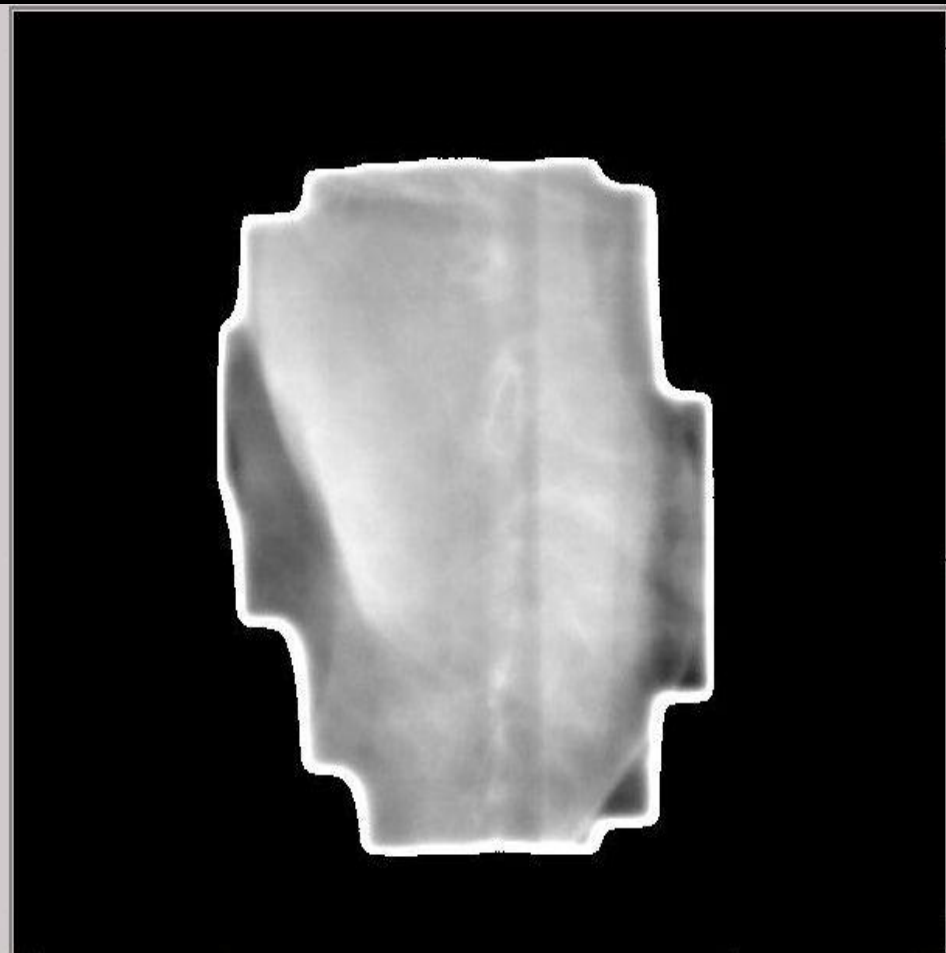
## 3. tecniche non radiografiche

- ecografia
- on-board RM

Prima fase dell'epoca IGRT:

Impiego dell'EPID  
(Electronic Portal Imaging Device)





L'impiego dell'EPID ha dato origine all' "era IGRT":

## Vantaggi:

- 1- possibile alta frequenza di rilevazioni
- 2- possibilità di utilizzo on-line
- 3- software per facilitare il confronto manuale con DRR (immagine di riferimento prodotta dal piano di cura)

## Svantaggi:

- 1- qualità relativamente bassa
- 2- esposizione addizionale a Rx significativa
- 3- limitate possibilità di registrazione automatica
- 4- no possibilità di ri-pianificazione

# le tecniche protagoniste della “rivoluzione” IGRT

## 1. tecniche planari

- EPID
- cyberknife

## 2. tecniche volumetriche

- in-room CT scanner “on rails”
- cone-beam CT (MV, KV)
- tomoterapia



## 3. tecniche non radiografiche

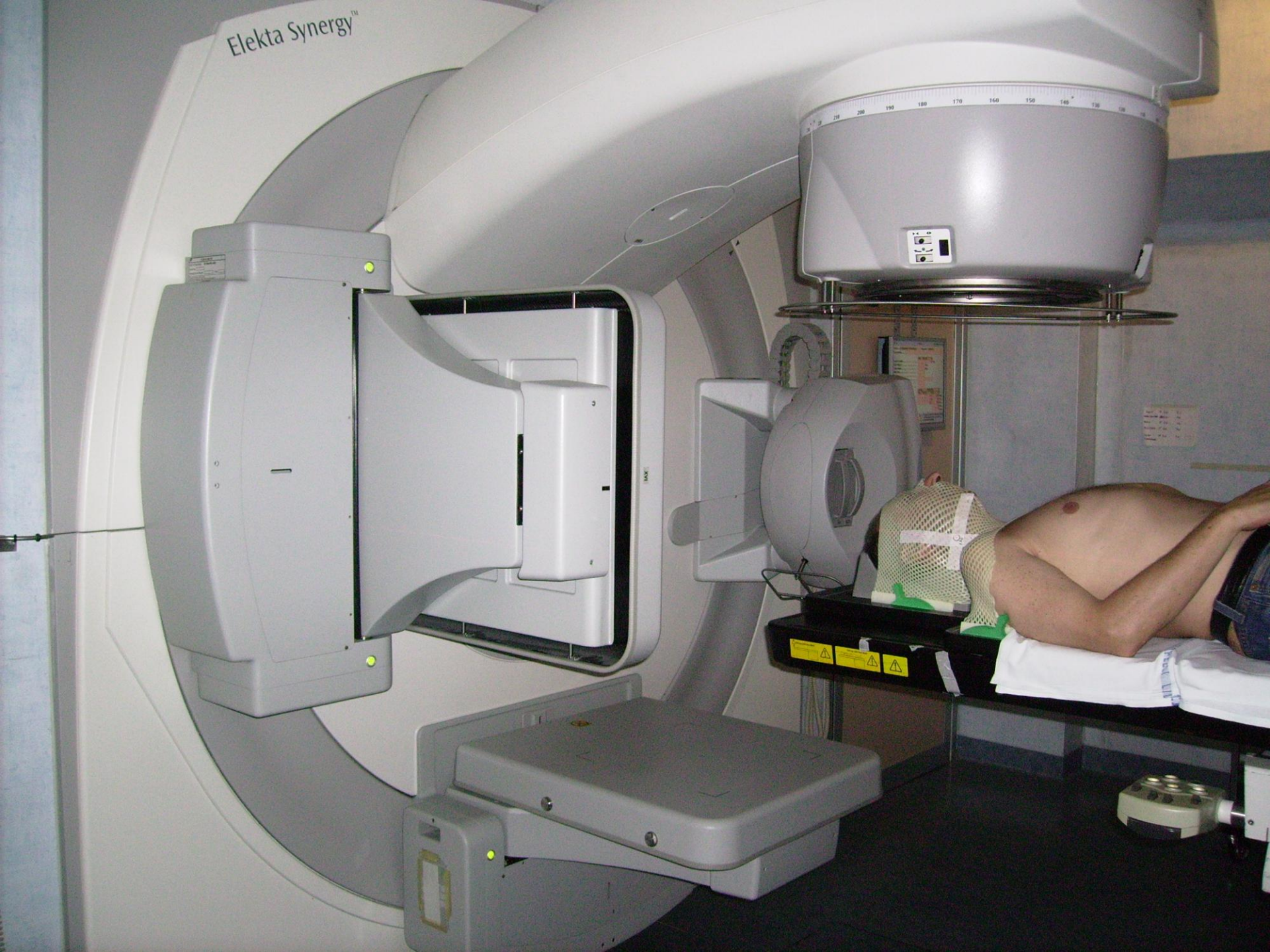
- ecografia
- on-board RM



# CONE BEAM CT

- Accessorio montato su Linac
- Consente la acquisizione in tempo reale di immagini TC volumetriche con una singola rotazione (parziale o completa) del gantry
- Possibilità di registrazione delle immagini **TC di localizzazione con quelle di pianificazione** con algoritmi automatici (bone, grey) o manualmente

Elekta Synergy™







CARTELLE - FINE TERAPIA -

INIZIO PZ.

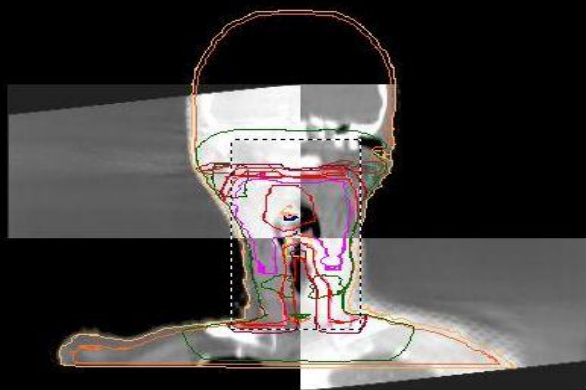
IBM

User XYZ

TEMA



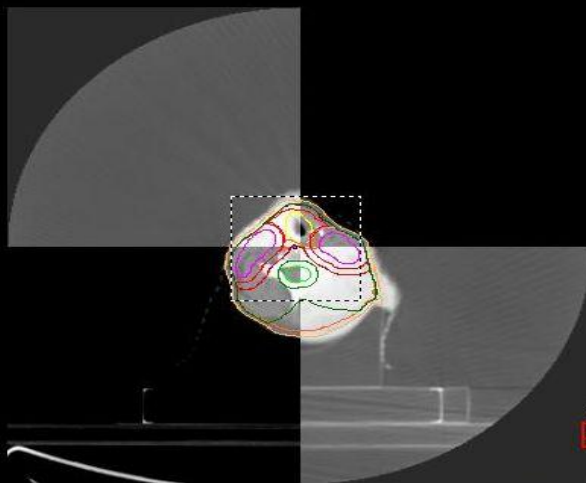
Coronal



Slice 195 of 410

Correction reference point = isocenter

Transverse

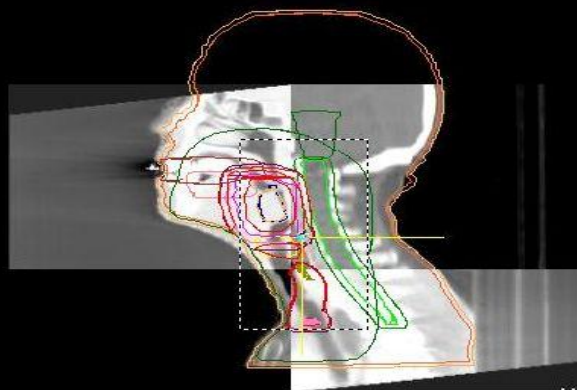


Slice 140 of 264

08.06.2009 09:14:00.156

Scan Time: 19.05.2009 12:51:44.000

Sagittal



Slice 203 of 410

Image

Slice Averaging  
 7 slices  
 Display Mode  
 Cut  
 + -  
 GoTo ..

Reference Preset

Cor Ref Point...

- Scan
- Alignment Clipbox
- Structures...

Alignment

Automatic Grey value

Reset

Convert To Correction

Position Error  
Translation (cm)

X	-0.16
Y	0.07
Z	0.01

Rotation (dg)

X	359.5
Y	0.2
Z	0.3

Table Correction

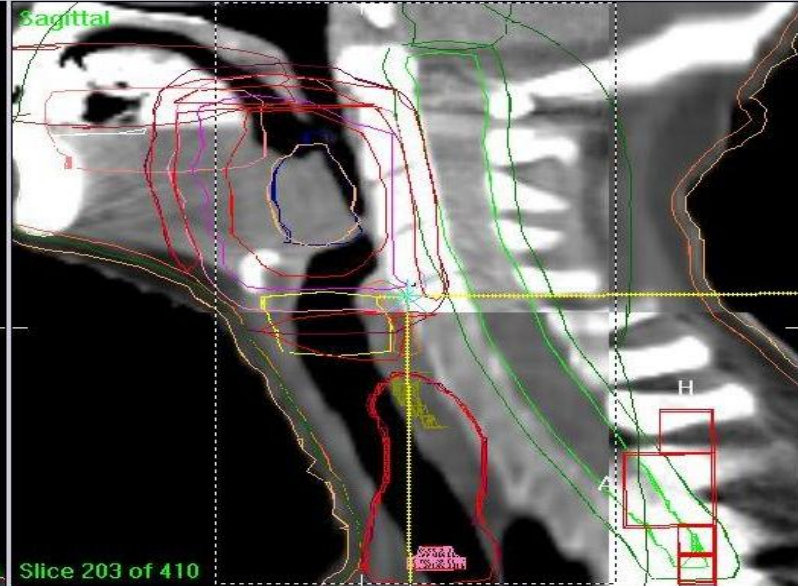
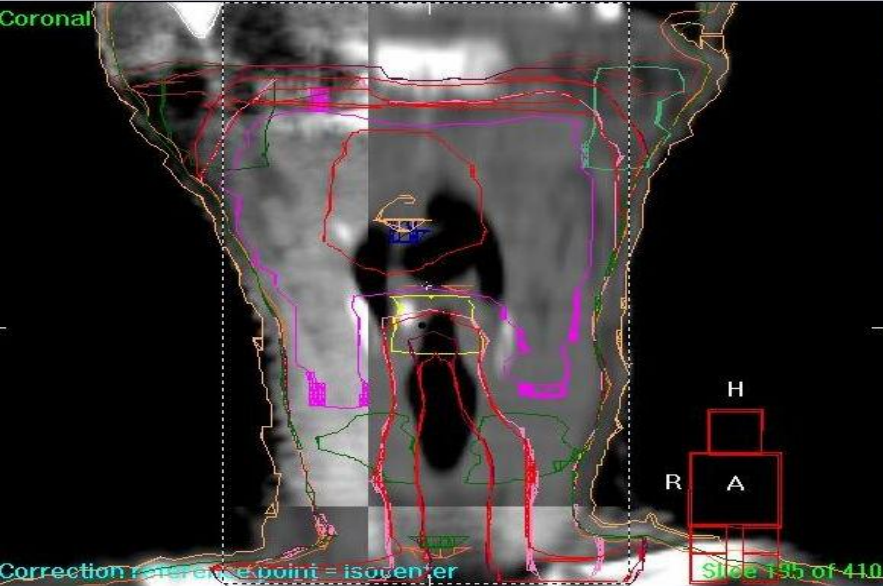
(cm)

Lateral  
Longitudinal  
Vertical

-  
-  
-

Dismiss

Accept

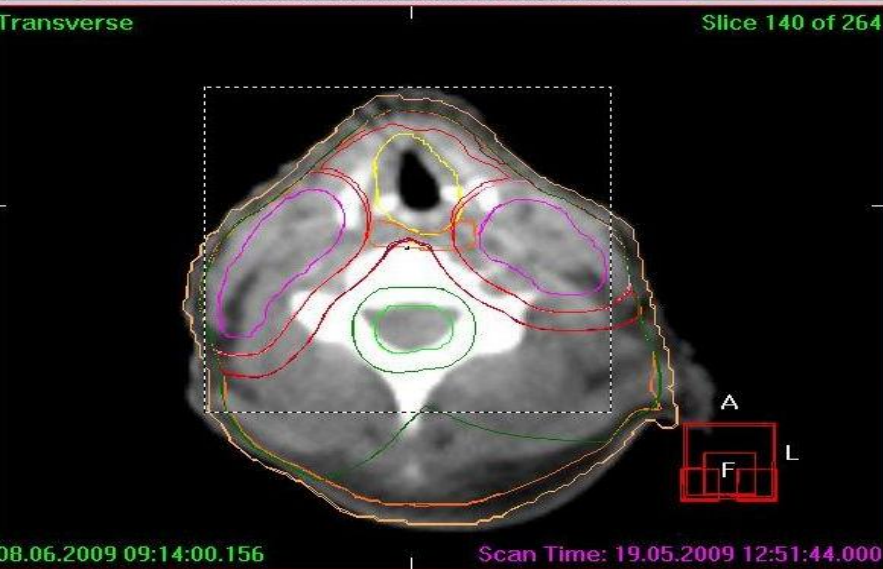


Image

Slice Averaging  
7 slices

Display Mode  
Cut

GoTo ..



Reference Preset

Cor Ref Point ..

Scan  
 Alignment Clipboard  
 Structures ..

Alignment

Automatic Grey value

Reset

Convert To Correction

Position Error

Translation (cm)		Rotation (dg)	
X	-0.16	X	359.5
Y	0.07	Y	0.2
Z	0.01	Z	0.3

Table Correction (cm)

Lateral	-
Longitudinal	-
Vertical	-

Dismiss

Accept

Con l'impiego della CBCT l'era IGRT è entrata nel vivo:

## Vantaggi:

- 1- possibile alta frequenza di rilevazioni, on-line
- 2- buona qualità delle immagini (kV, MV)
- 3- software per registrazione automatica
- 4- possibilità di ri-pianificazione
- 5- correzioni anche rotazionali (lettino 6 gradi libertà?)

## Svantaggi:

- 1- qualità non ottimale
- 2- esposizione addizionale a Rx significativa?



## Nonrigid Patient Setup Errors in the Head-and-Neck Region

Buelent Polat, Juergen Wilbert, Kurt Baier, Michael Flentje, Matthias Guckenberger<sup>1</sup>

**Purpose:** To investigate the magnitude and clinical relevance of relative motion/nonrigid setup errors in the head-and-neck (H&N) region.

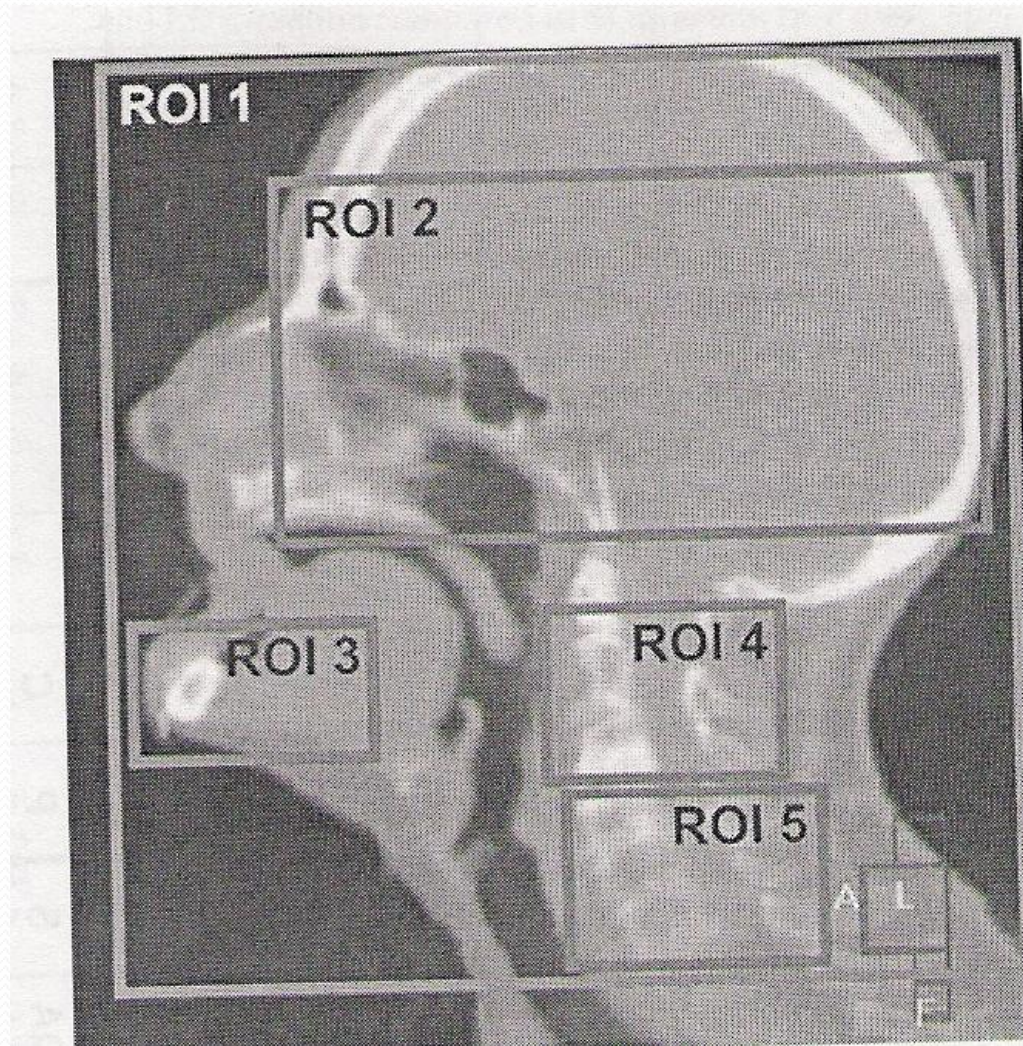
**Material and Methods:** Eleven patients with tumors in the H&N region were immobilized in thermoplastic head masks. Patient positioning was verified using a kilovoltage cone-beam CT (kv CBCT) prior to 100 treatment fractions. Five different regions of interest (ROIs) were selected for automatic image registration of planning CT and verification CBCT: (1) the whole volume covering planning CT and CBCT, (2) the skull, (3) the mandible, (4) C1–C3, and (5) C4–C6. Differences were calculated describing relative motion between the ROIs.

**Results:** The 3-D patient setup error was  $3.2 \text{ mm} \pm 1.7 \text{ mm}$  based on registration of the whole volume. No systematic relative motion (group mean errors  $< 0.5 \text{ mm}$  and  $< 0.5^\circ$ ) between planning and treatment for any ROI was observed. Mobility was largest for the skull and the mandible relative to C4–C6 with 3-D displacements of  $4.7 \text{ mm} \pm 2.5 \text{ mm}$  and  $4.4 \text{ mm} \pm 2.5 \text{ mm}$ . Relative rotations were largest around the left-right axis (nodding) between C1–C3 and C4–C6 with maximum  $11^\circ$ . No time trend of relative motion was observed. Margins for compensation of relative motion ranged between 5 mm and 10 mm.

**Conclusion:** The simplification of the patient as a rigid body was shown to result in significant errors due to relative motion in the H&N region. Margins for compensation of relative motion exceeded margins for compensation of patient positioning errors.

**Key Words:** Nonrigid setup errors · Cone-beam CT · Automatic image registration · Safety margin · Head and neck tumors

# IL PROBLEMA DELLA NON-RIGIDITA' DEL PAZIENTE





## Nonrigid Patient Setup Errors in the Head-and-Neck Region

Buelent Polat, Juergen Wilbert, Kurt Baier, Michael Flentje, Matthias Guckenberger<sup>1</sup>

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## 1- aspetti logistici (extra-time) I

L'acquisizione delle immagini (singola rotazione parziale o completa della testata) dura (**minuti**):

	tonsilla	prostata
<b>Elekta (kVCBCT)</b>	<b>2</b>	<b>3</b>
<b>Siemens (MVCBCT)</b>	<b>2.5</b>	<b>2</b>
<b>Tomoterapia (MVFBCT)5</b>		<b>4.5</b>
<b>Varian (kVCBCT)</b>	<b>2.5</b>	<b>3</b>

## 1- aspetti logistici (extra-time) II

La ricostruzione/registrazione/correzione dura  
(**minuti**):

	tonsilla	prostata
<b>Elekta (kVCBCT)</b>	<b>2</b>	<b>2.5</b>
<b>Siemens (MVCBCT)</b>	<b>3</b>	<b>3.5</b>
<b>Tomoterapia (MVFBCT)</b>	<b>4.5</b>	<b>5</b>
<b>Varian (kVCBCT)</b>	<b>1.5</b>	<b>4</b>

ESTRO report on 3D CT-based IGRT (Radiother Oncol 94:129,2010)

## 1- aspetti logistici (extra-time) III

L'intera fase dura (**minuti**):

	<b>tonsilla</b>	<b>prostata</b>
<b>Elekta (kVCBCT)</b>	<b>4.5</b>	<b>5.5</b>
<b>Siemens (MVCBCT)</b>	<b>7.5</b>	<b>5.5</b>
<b>Tomoterapia (MVFBCT)11</b>		<b>10</b>
<b>Varian (kVCBCT)</b>	<b>4.5</b>	<b>7</b>

ESTRO report on 3D CT-based IGRT (Radiother Oncol 94:129,2010)

**2- aspetti operativi: quale protocollo di IGRT?  
(frequenza di imaging)?**

### **Bilancio costi-benefici**

**Costi: occorre tener conto sia dei fattori logistici  
che di quelli radioprotezionistici**

**Benefici: errori residui nei “giorni non-IGRT”**

**Correlazione frequenza IGRT : errori residui**



ELSEVIER

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0360-3016/07/\$—see front matter

doi:10.1016/j.ijrobp.2006.09.040

**CLINICAL INVESTIGATION**

**Head and Neck**

**EVALUATION OF IMAGE-GUIDANCE PROTOCOLS IN THE TREATMENT  
OF HEAD AND NECK CANCERS**

OMAR A. ZEIDAN, PH.D., KATJA M. LANGEN, PH.D., SANFORD L. MEEKS, PH.D.,  
RAFAEL R. MANON, M.D., THOMAS H. WAGNER, PH.D., TWYLA R. WILLOUGHBY, M.S.,  
D. WAYNE JENKINS, M.D., AND PATRICK A. KUPELIAN, M.D.

Department of Radiation Oncology, M. D. Anderson Cancer Center Orlando, Orlando, FL

**24 pazienti con T distretto testa-collo, IGRT (tomo) tutte le frazioni (802)**

**A posteriori, calcolo dell'errore residuo nei giorni non-IGRT / tutti i giorni  
utilizzando 8 protocolli diversi (% = % fraz IGRT/ fraz totali):**

**no IGRT (0%), prime 1, 3, 5, 7 frazioni (3, 9, 15, 21%),**

**settimanale (20%), prime 5 poi sett. (31%), giorni alterni (50%)**



**CLINICAL INVESTIGATION**

**Head and Neck**

**EVALUATION OF IMAGE-GUIDANCE PROTOCOLS IN THE TREATMENT OF HEAD AND NECK CANCERS**

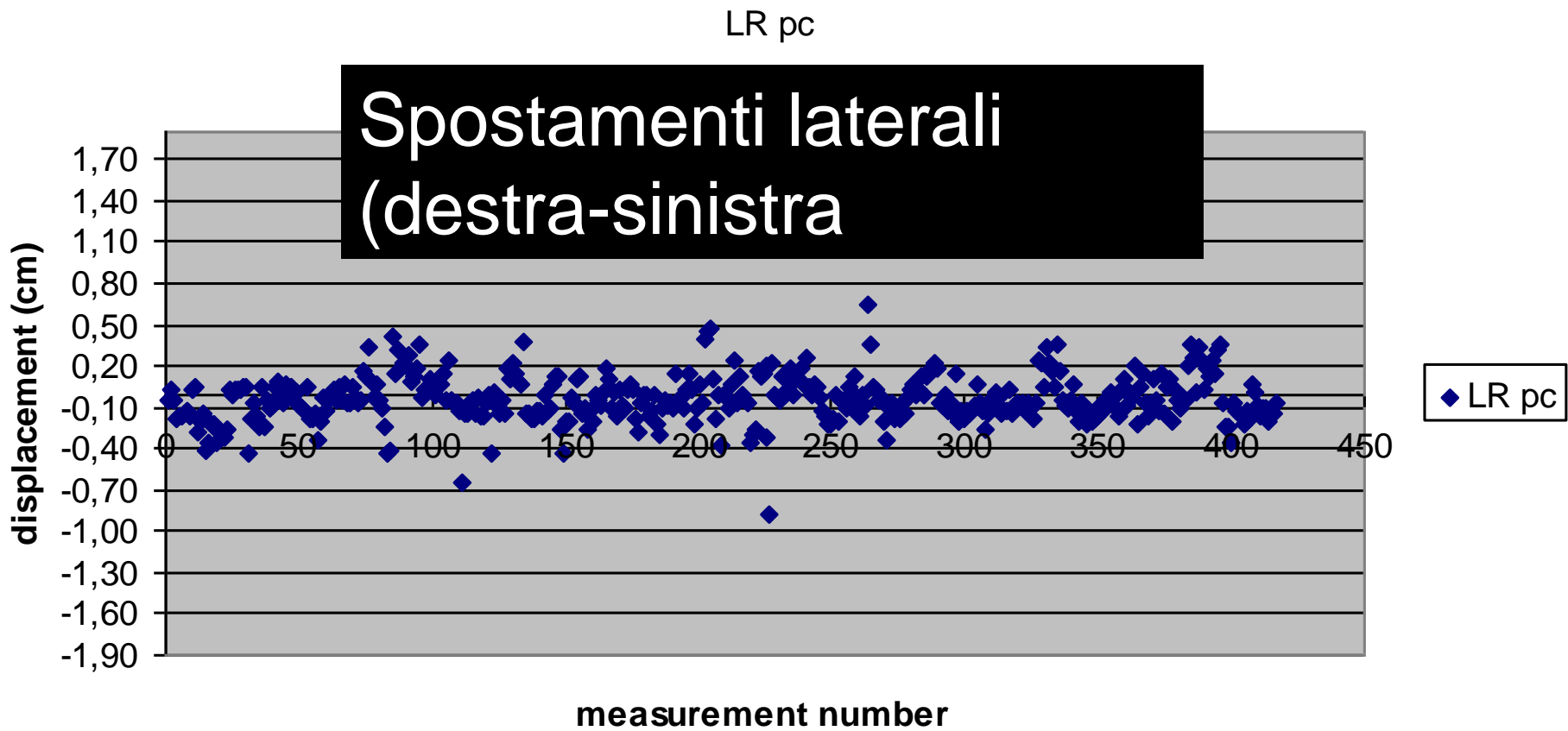
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 RAFAEL R. MANON, M.D., THOMAS H. WAGNER, PH.D., TWYLA R. WILLOUGHBY, M.S.,  
 D. WAYNE JENKINS, M.D., AND PATRICK A. KUPELIAN, M.D.

Department of Radiation Oncology, M. D. Anderson Cancer Center Orlando, Orlando, FL

Table 2. Frequencies of residual errors observed with different protocols exceeding 3, 5, and 10 mm

Protocol	IG%	Error >3 mm	Errors >5 mm	Errors >10 mm
A: No imaging	0%	72% ± 3%	37% ± 2%	4% ± 1%
B1: Initial fraction only	3%	79% ± 3%	47% ± 2%	5% ± 1%
B3: Mean of initial three fractions	9%	63% ± 3%	31% ± 2%	1% ± 0.5%
B5: Mean of initial five fractions	15%	58% ± 3%	26% ± 2%	1% ± 0.5%
B7: Mean of initial seven fractions	21%	53% ± 3%	26% ± 2%	1% ± 0.5%
C: Weekly imaging, 3-mm threshold	20%	60% ± 3%	31% ± 2%	2% ± 0.5%
D: First five fractions + weekly imaging, patient-specific threshold	31%	50% ± 2%	27% ± 2%	4% ± 1%
E: Imaging every other fraction, running mean	50%	29% ± 2%	11% ± 1%	0.5% ± 0.3%

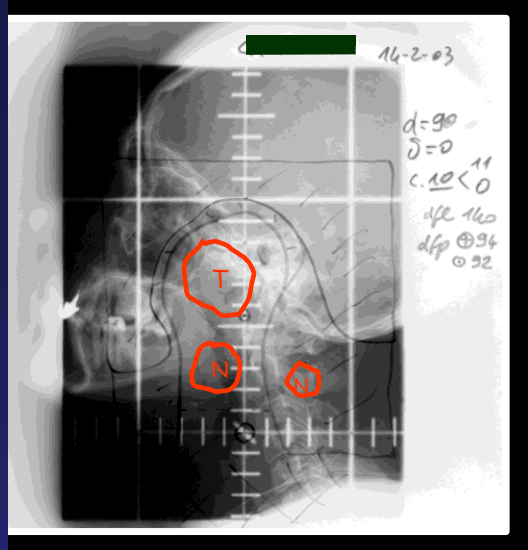
The three-dimensional setup error is the vector calculated from the remaining setup errors in the three directions. Data in this table are calculated for all (*i.e.*, image-guided as well as nonimage-guided, treatments). The uncertainty in the results was estimated by using the square root of  $N$ , where  $N$  is the number of observations. The percentage of fractions that are image guided (IG%) according to each protocol is also shown.



Dati Niguarda, in press 2012

**Meno spostamenti > riduzione dei margini!**



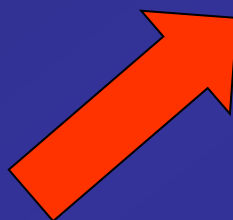


**2D**



**3D**

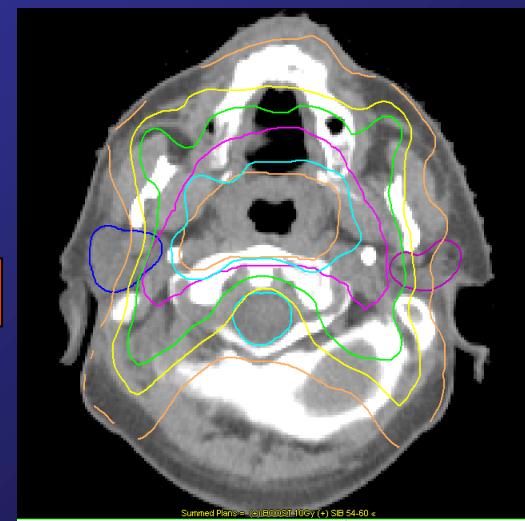
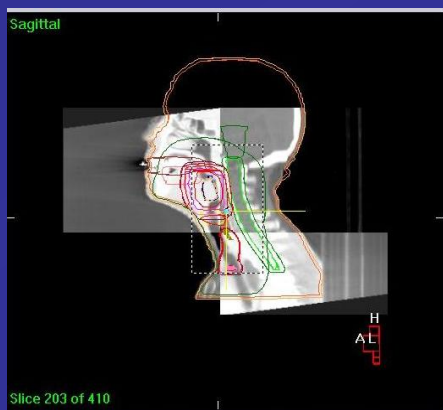
**ART**



**IMRT**

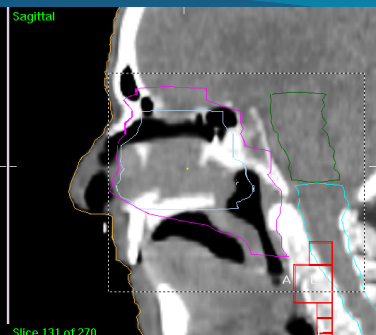
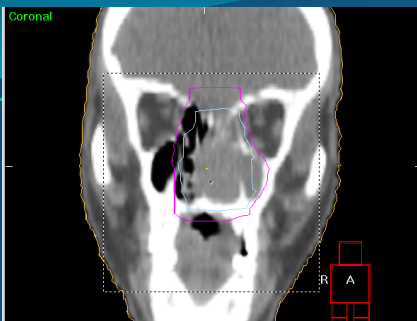


**IGRT**

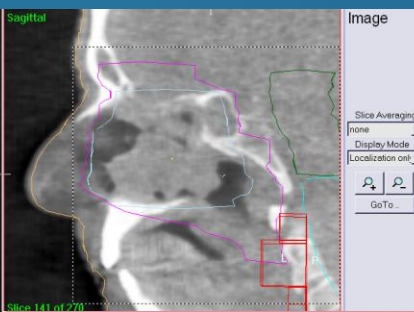
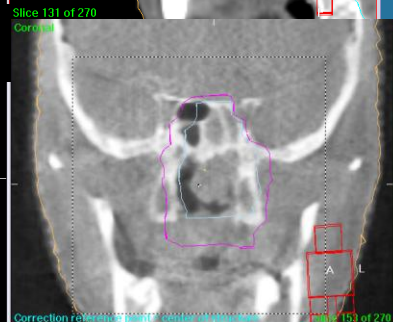
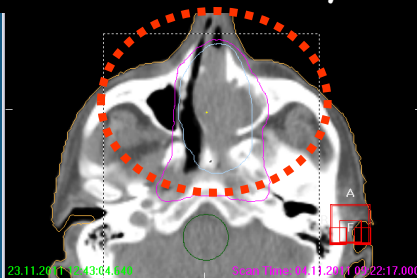


# IGRT >> ART (1)

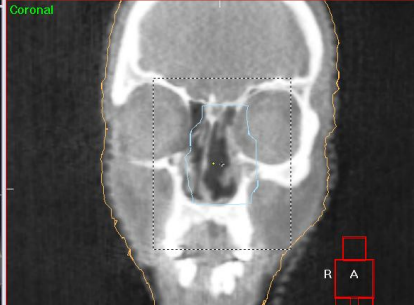
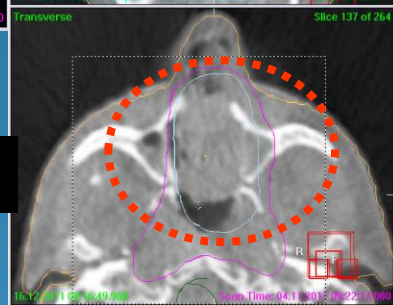
77 aa ♂, ca squamocelleulare G3  
fossa nasale T3N0, in corso RT  
esclusiva a scopo curativo



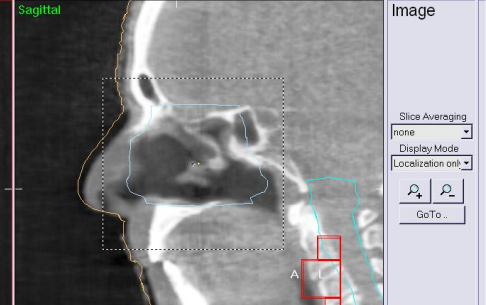
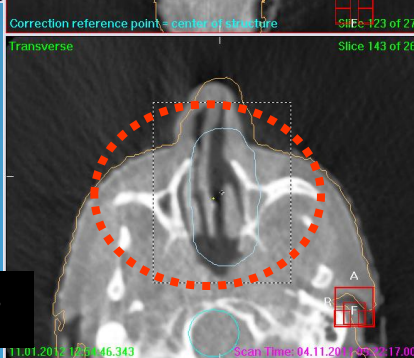
TC centratura 0 Gy



CBCT 30 Gy



CBCT 62 Gy



Image

Slice Averaging: none  
Display Mode: Localization only  
Go To...

Reference Preset: Cor Ref Point  
 Scan  
 Alignment Clipbox  
 Structures

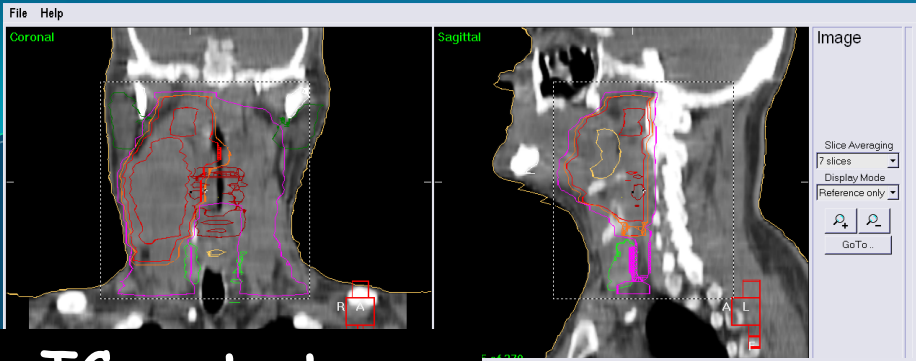
Alignment: Automatic  
Manual  
Reset  
Convert To Correction

Position Error Translation (cm)	Rotation (dg)	Table Correction (cm)
X: 0.04	X: 0.0	Lateral: -
Y: 0.26	Y: 0.0	Longitudinal: -
Z: 0.07	Z: 0.0	Vertical: -

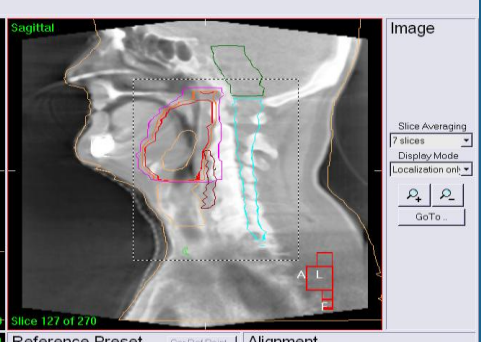
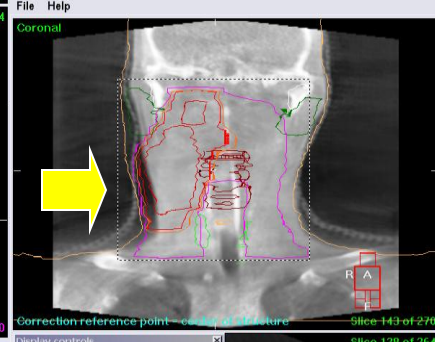
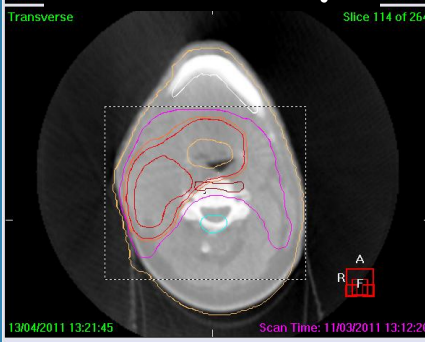
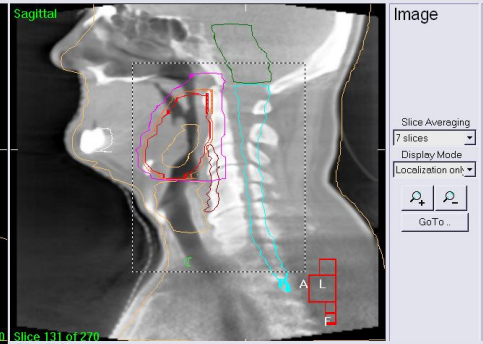
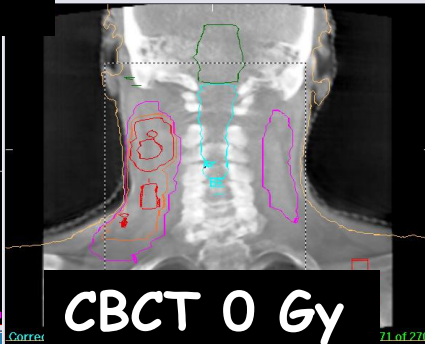
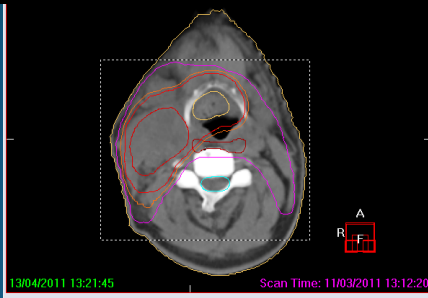
Dismiss Accept

# IGRT >> ART (2)

56 aa, ♂ ca squamoso orofaringe G2 T2N3

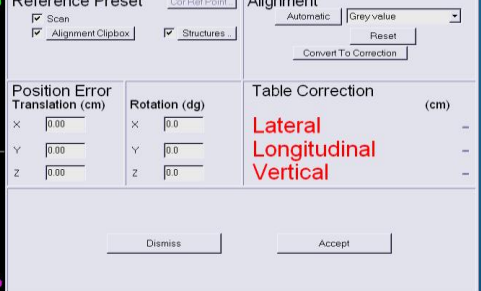
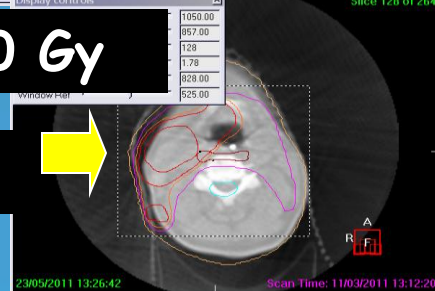


TC centratura



CBCT 50 Gy

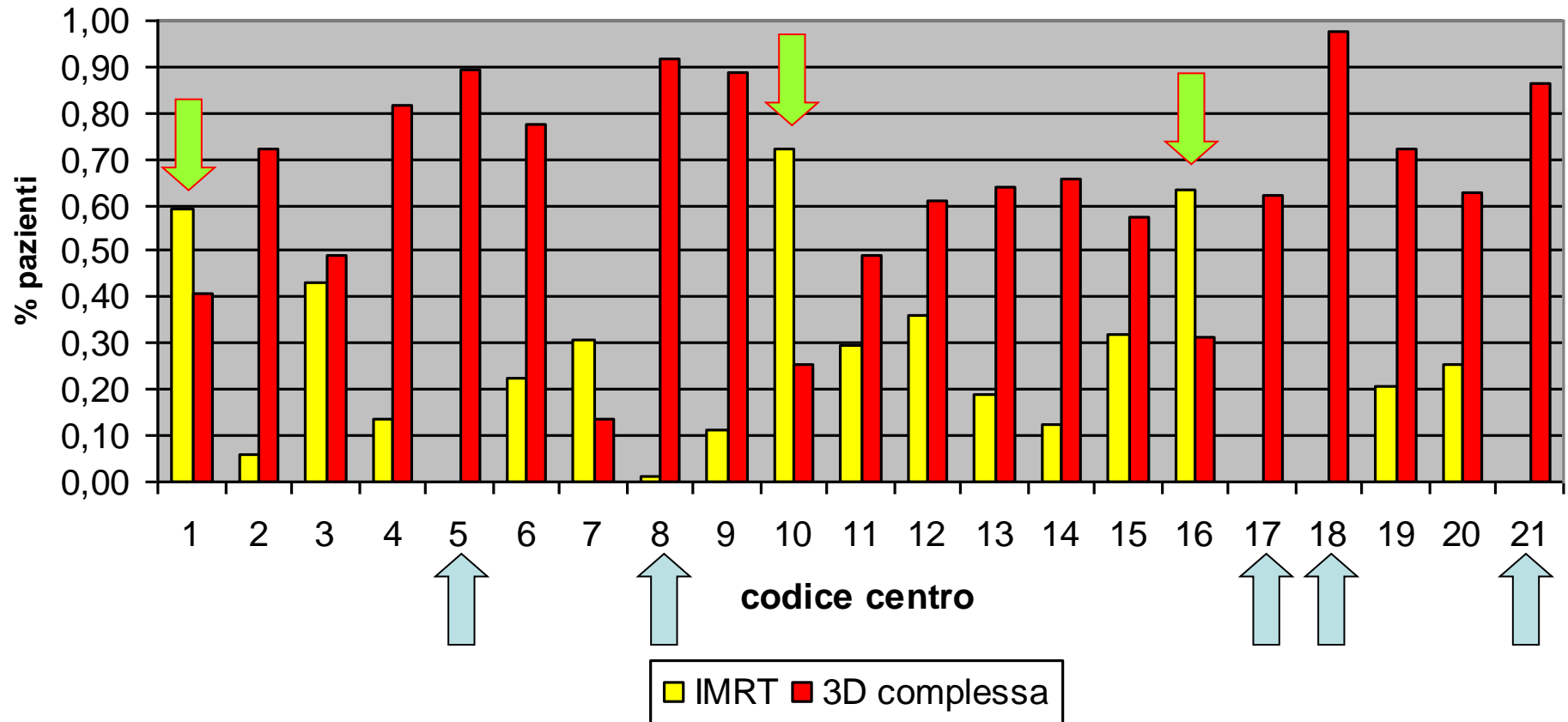
replanning



## **PROBLEMA 3:**

**La tecnologia, in RT,  
è una scelta ?**

## ripartizione per tecnica RT



## CONCLUSIONI

- **IGRT = avanzamento tecnologico dalle potenzialità straordinarie**
- **aumenta i costi, impossibile misurare i benefici e quindi i criteri di appropriatezza**
- **attualmente nettamente sotto-utilizzato, essenzialmente per carenza di risorse**
- **occorre fare ogni sforzo, a tutti i livelli, per portare questa tecnologia a disposizione del maggior numero possibile di pazienti**