Radioterapia ipofrazionata con localizzazione stereotassica nelle neoplasie toraciche ed addominali

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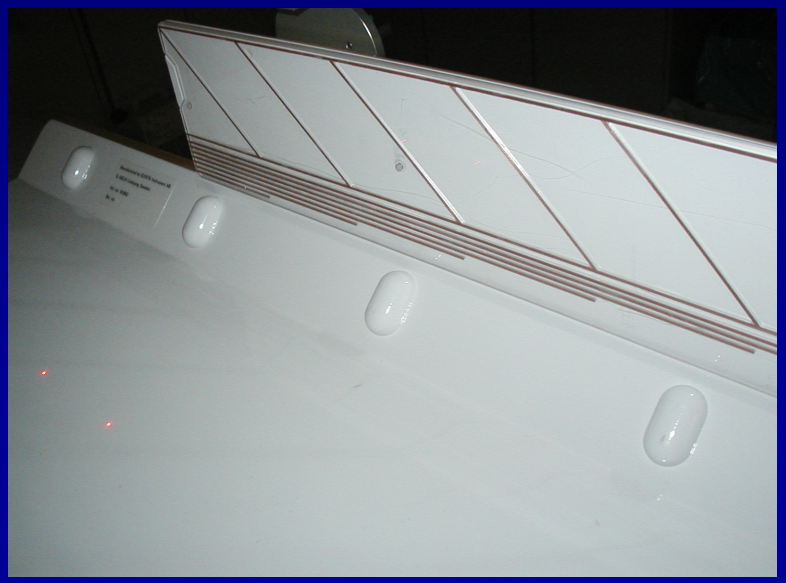
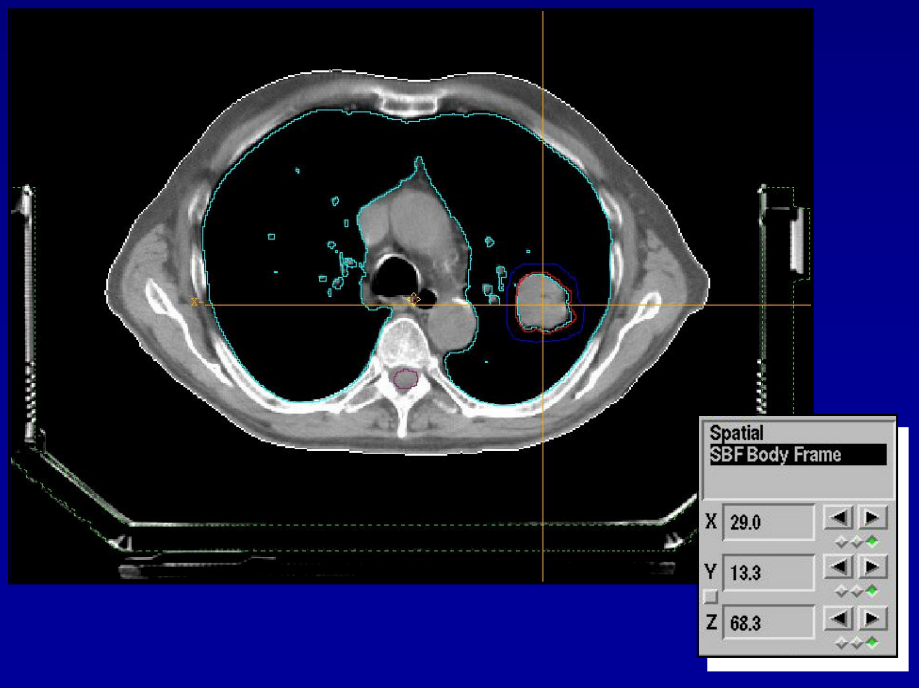
Radioterapia ipofrazionata con localizzazione stereotassica nelle neoplasie toraciche ed addominali

- ✓ Somministrazione in poche frazioni di dosi elevate di radioterapia con l'obiettivo di eradicare un "focus" neoplastico localizzato mediante l'uso di frame stereotassici





Radioterapia ipofrazionata con localizzazione stereotassica nelle neoplasie toraciche ed addominali

- ✓ Ipofrazionamento
- ✓ Accuratezza nella definizione del volume bersaglio (imaging: CT, MR, PET)
- ✓ Elevata conformazione della dose al volume bersaglio con elevato gradiente di dose nei confronti degli organi adiacenti (tecniche di precisione: 3D CRT non coplanare, IMRT, Cyberknife, Tomotherapy)
- ✓ Controllo del trattamento prima (IGRT) e durante l'irradiazione (tecniche per il controllo dell'organ motion)

Ipofrazionamento

RADIOBIOLOGIA E FRAZIONAMENTO DELLA DOSE

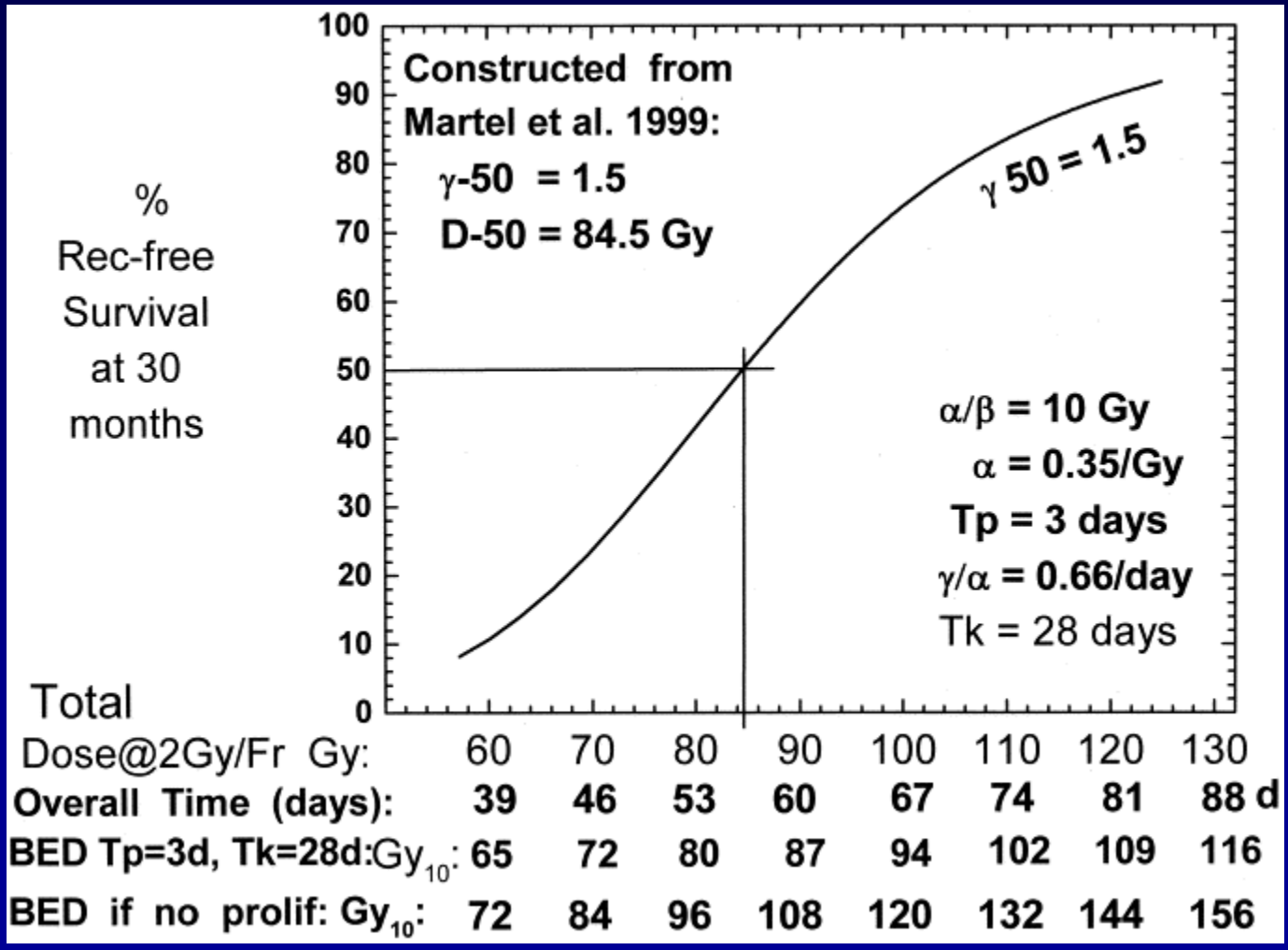
L'esempio delle neoplasie polmonari

Estimated LPFS for isocenter dose > 70 Gy and < 70 Gy

Isocenter dose	N. Pts.	12 months LPFS%	24 months LPFS%	36 months LPFS%
> 70 Gy group, mean = 75 Gy	52	81	61	38
<70 Gy group, mean = 65 Gy	24	53	26	26
Dose at 50 % LPFS	-	64	72	84,5
Standard deviation	-	7	2,5	8

Martel, Lung Cancer, 1999

Razionale dell'ipofrazionamento della dose:
L'esempio delle neoplasie polmonari



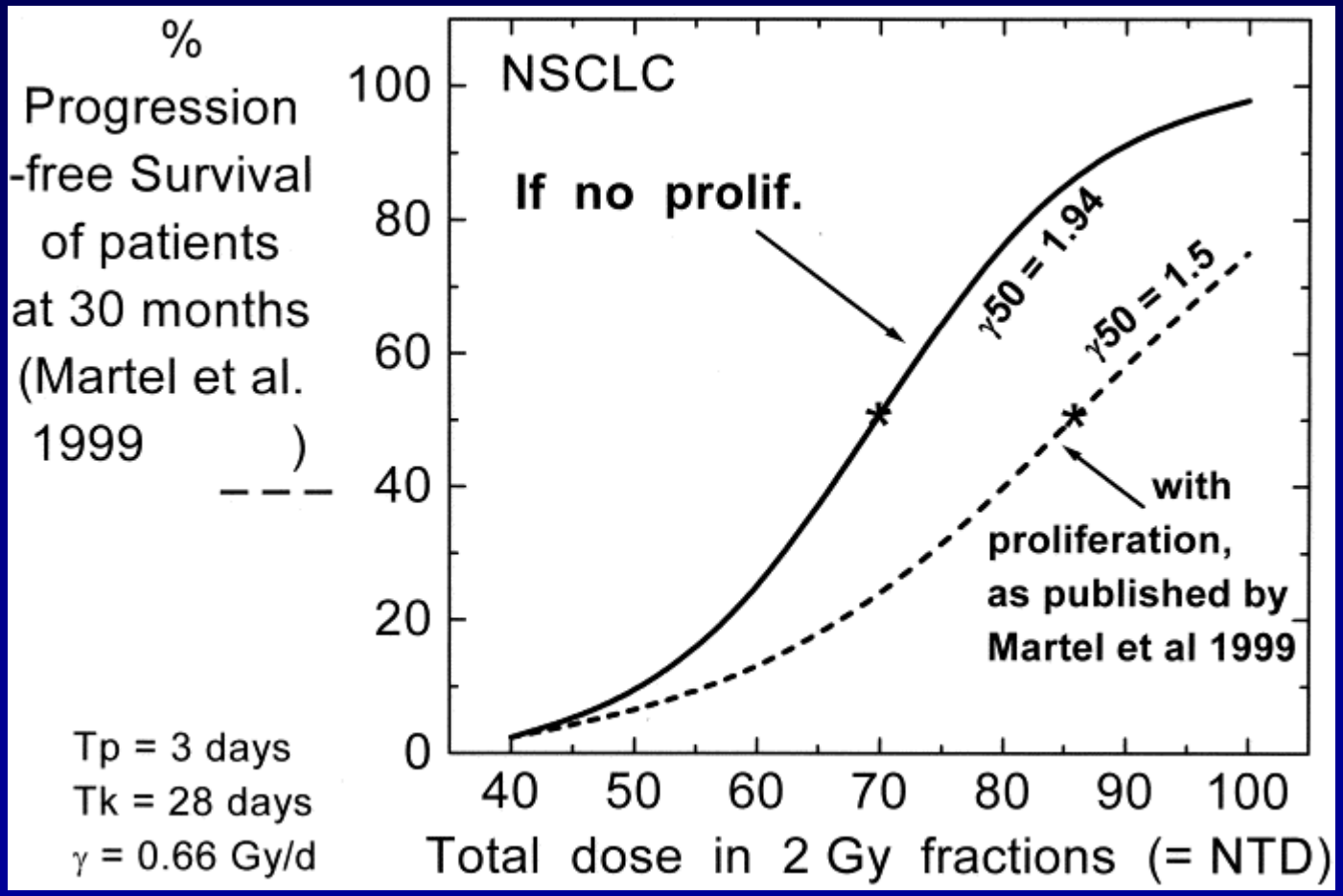
Total Dose@2Gy/Fr Gy:	60	70	80	90	100	110	120	130
Overall Time (days):	**39**	**46**	**53**	**60**	**67**	**74**	**81**	**88 d**
BED Tp=3d, Tk=28d:Gy_{10}:	**65**	**72**	**80**	**87**	**94**	**102**	**109**	**116**
BED if no prolif: Gy_{10}:	**72**	**84**	**96**	**108**	**120**	**132**	**144**	**156**

Mehta, IJROBP, 2001

RADIOBIOLOGIA E FRAZIONAMENTO DELLA DOSE

L'esempio delle neoplasie polmonari

Modellizzazione radiobiologica di trattamenti ipofrazionati



Fowller,IJROBP, 2004

STEREOTACTIC RADIATION THERAPY IN EARLY STAGE LUNG TUMORS

LOCAL FAILURE RATE AFTER HYPOFRACTIONATED IF RT (CT based plans): T1-T2 N0 pts

Author	Pts	Dose/ N.Fx	BED acute	Local control
• Uematsu	50	50 Gy/5 *	100,0	96%
• Nagata	33	48 Gy/4 ^	104,8	92%
• Arimoto	24	60 Gy/8 ^	105,6	94%
• Wulf	17	45 Gy/3 *	112,5	94%

* Prescribed to reference isodose
^ Prescribed to isocenter

BED acute = nd (1 + d/ alfa/beta) Time factor not relevant

RADIOBIOLOGIA E FRAZIONAMENTO DELLA DOSE

Modellizzazione radiobiologica di trattamenti ipofrazionati

L'esempio delle neoplasie polmonari

- ✓ Analisi secondo il modello lineare quadratico (Fowler, Br J Radiol 1989)
- ✓ Il modello lineare quadratico appare in grado di descrivere in maniera affidabile la risposta dei tessuti epiteliali alle radiazioni fino ad una dose per frazione di 23 Gy (Fowler, IJROBP 2004)
- ✓ Il modello lineare quadratico è in grado di predire in maniera affidabile la BED necessaria ad ottenere un determinato log kill in tumori epiteliali trattati con vari schemi di frazionamento (Fowler, Radiother Oncol 2003)

Modellizzazione radiobiologica di trattamenti ipofrazionati
L'esempio delle neoplasie polmonari
Fowler, Radiother Oncol 2003

Schema	Dose	BED early	NTD 2 Gy	Log 10 Cell Kill	PFS a 30 mos. (Martel)
35 x 2 Gy	70 Gy	84	70	11.0*	26%
4 x 12 Gy	48 Gy	105.6	88	16.1	82%
3 x 15 Gy	45 Gy	112.5	94	17.1	95%
3 x 20 Gy	60 Gy	180	150	27.4	> 99%
3 x 23 Gy	69 Gy	228	150	34.7	>99%

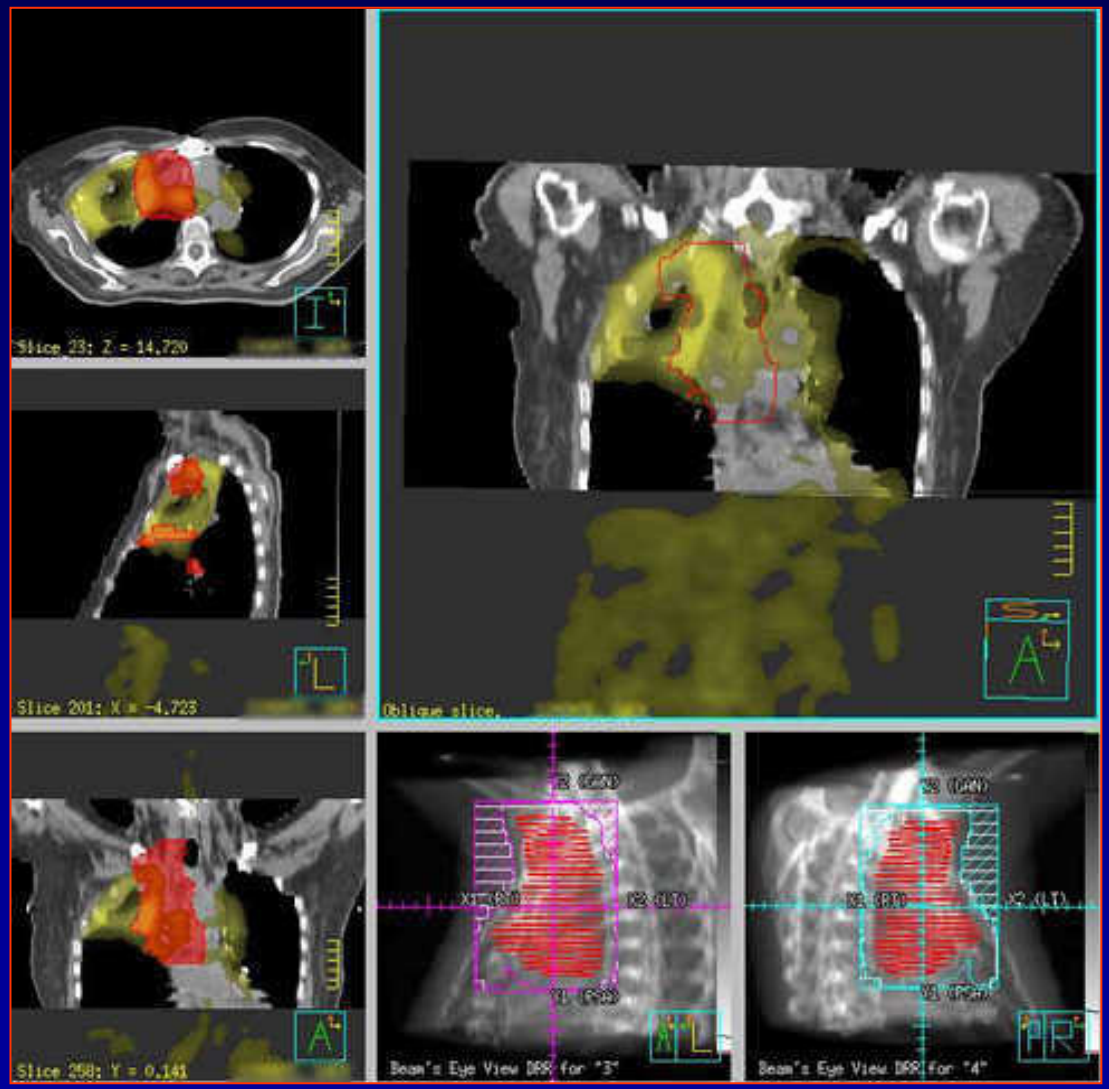
* **proliferazione**

✓Loge survival = - α x BED + λ x (T – Tk)
✓Log10 cell kill = (Loge survival) / 2,303

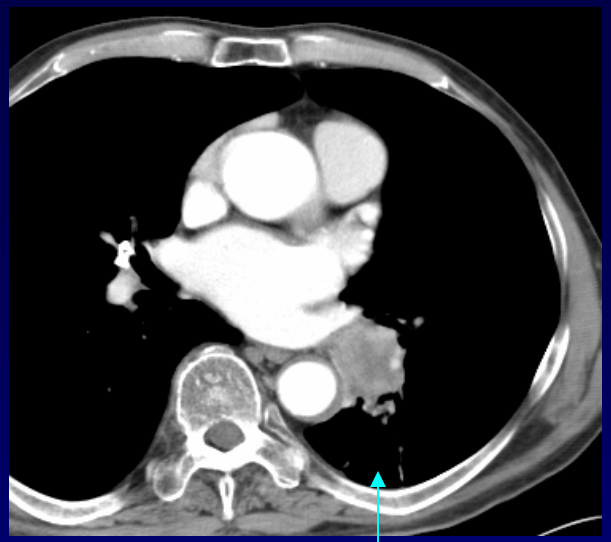
λ = 0.693 / Tpot; α = 0.35 loge Gy;
Tpot = 3 gg. ; Tk = 28 gg.

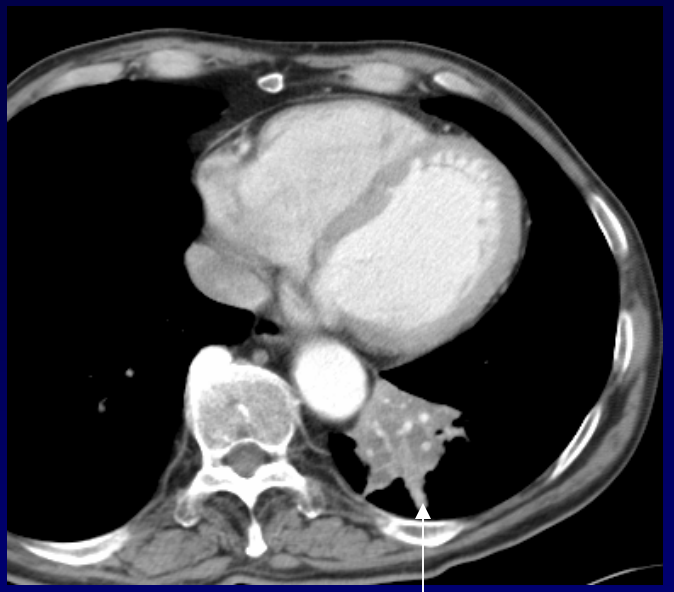
Accuratezza nella definizione del volume bersaglio (imaging: CT, MR, PET)

Estensioni parenchimatose
Nestle et al, IJROBP 1999



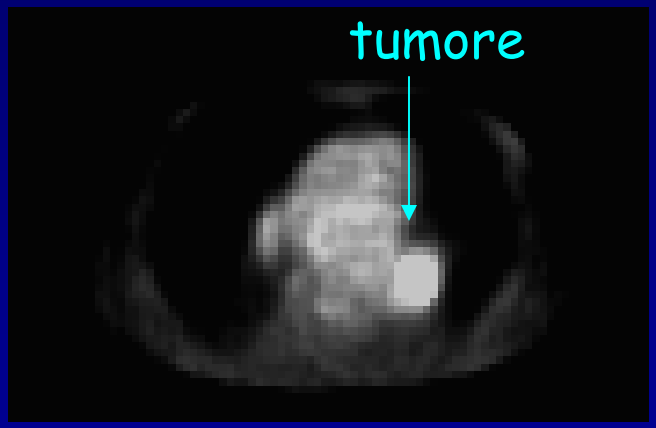
In questa analisi retrospettiva le informazioni apportate dalla FDG-PET hanno determinato una sostanziale riduzione del volume bersaglio. In particolare nei Pazienti con tumore associato ad importante atelettasia.

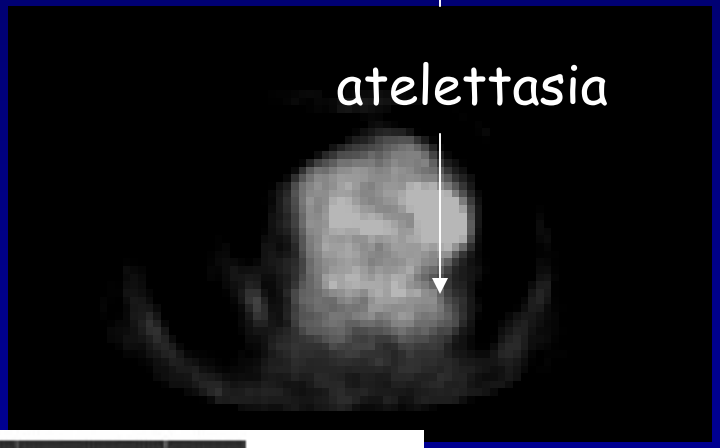




tumore

atelettasia





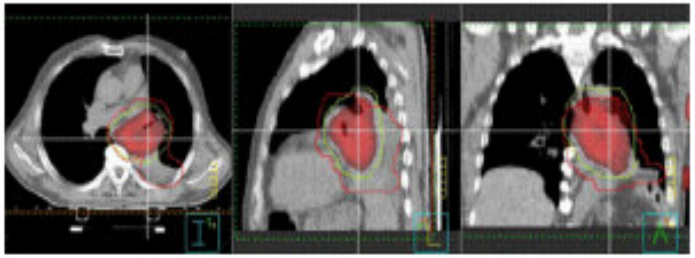
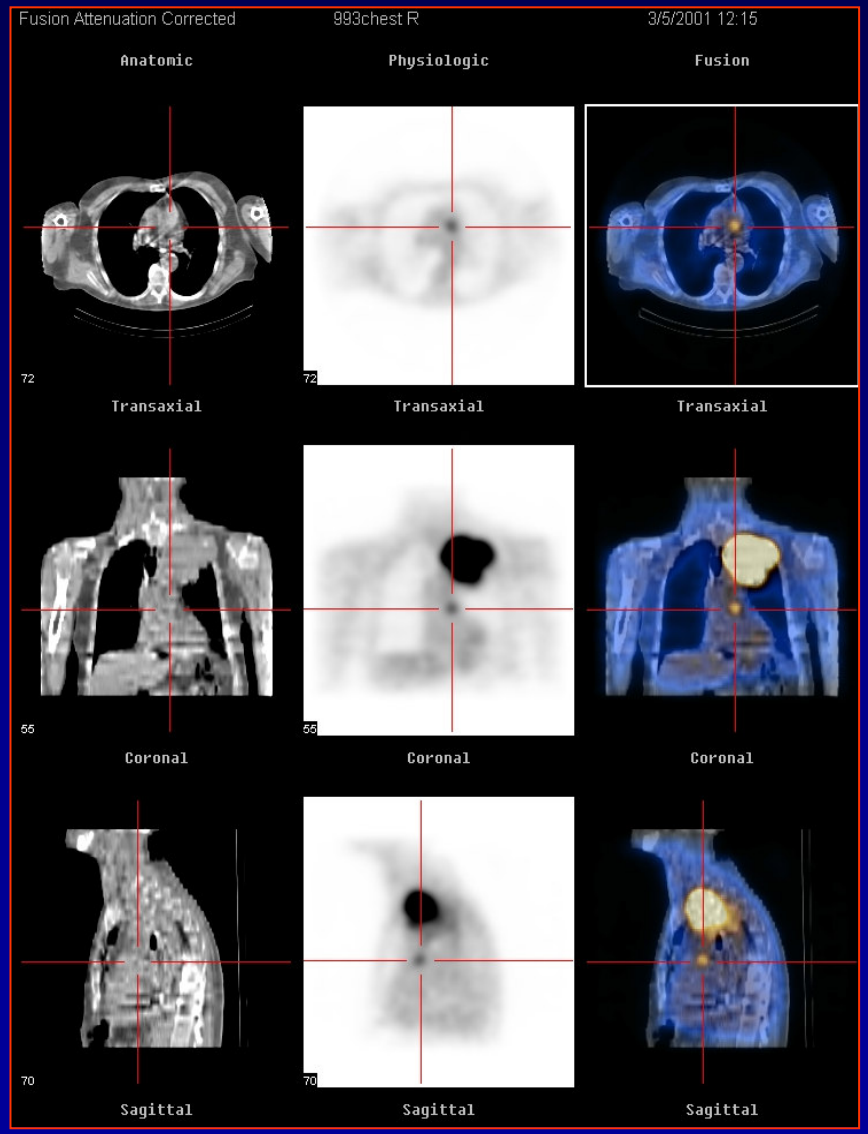
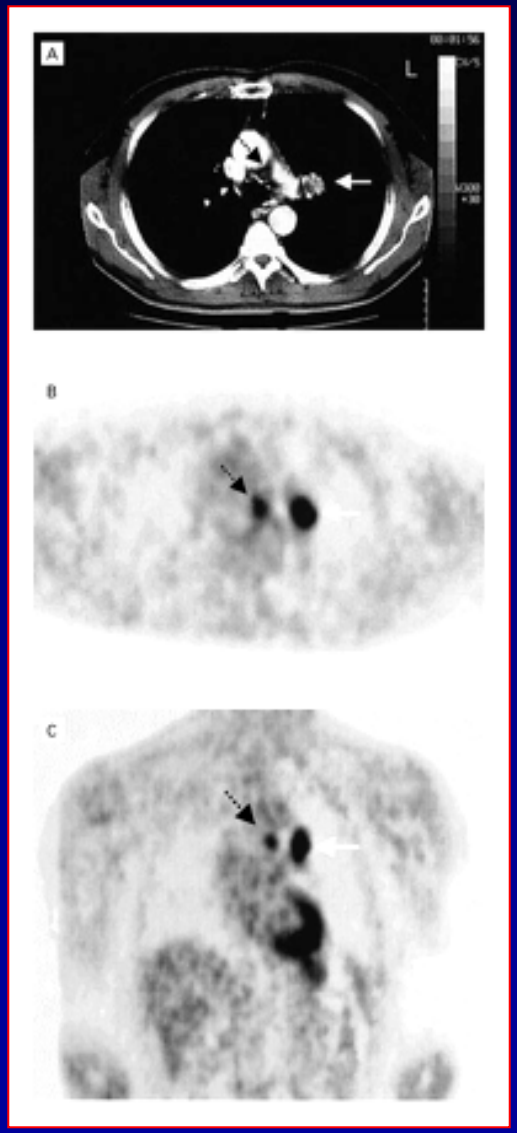
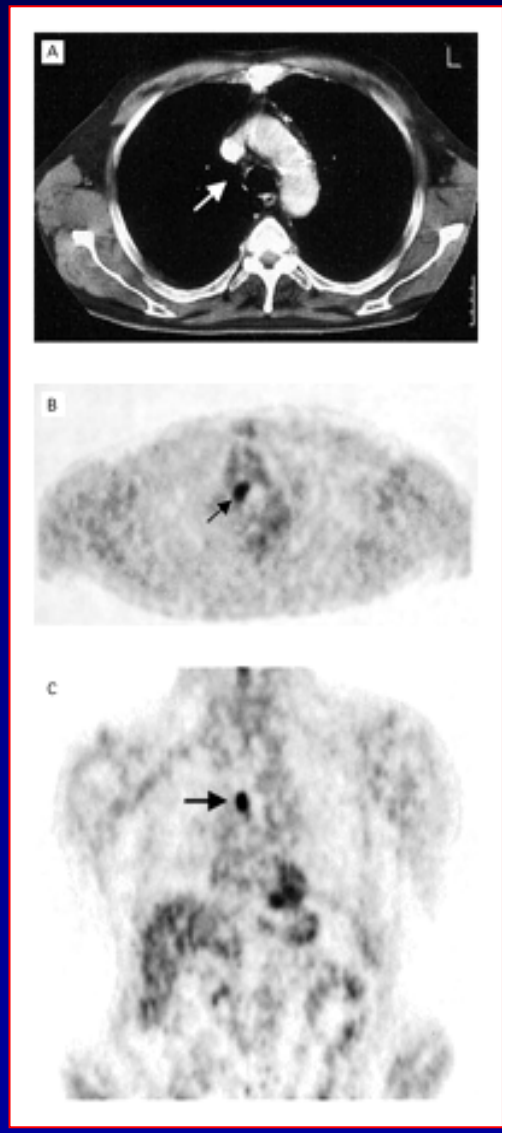


Fig. 6. FDG-PET-CT fusion images of patient with [^{18}F]-FDG-negative atelectasis. Pink structure: GTV derived from PET (source-background algorithm). Red contour: GTV derived from CT.

Staging mediastinico
Interesse della FDG-PET

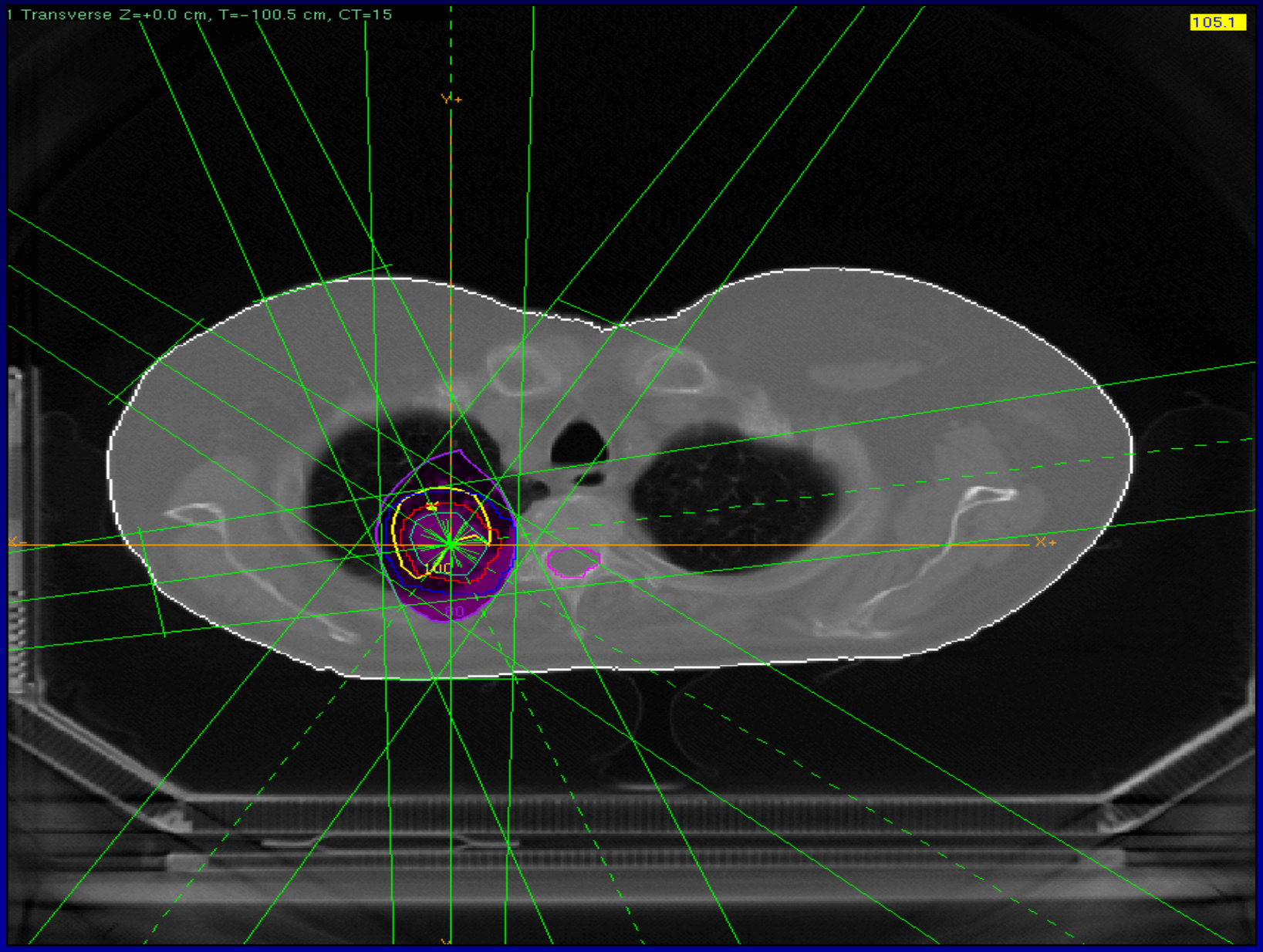






Elevata conformazione della dose al volume bersaglio con elevato gradiente di dose nei confronti degli organi adiacenti (tecniche di precisione: 3D CRT non coplanare, IMRT, Cyberknife, Tomotherapy)

PLANNING



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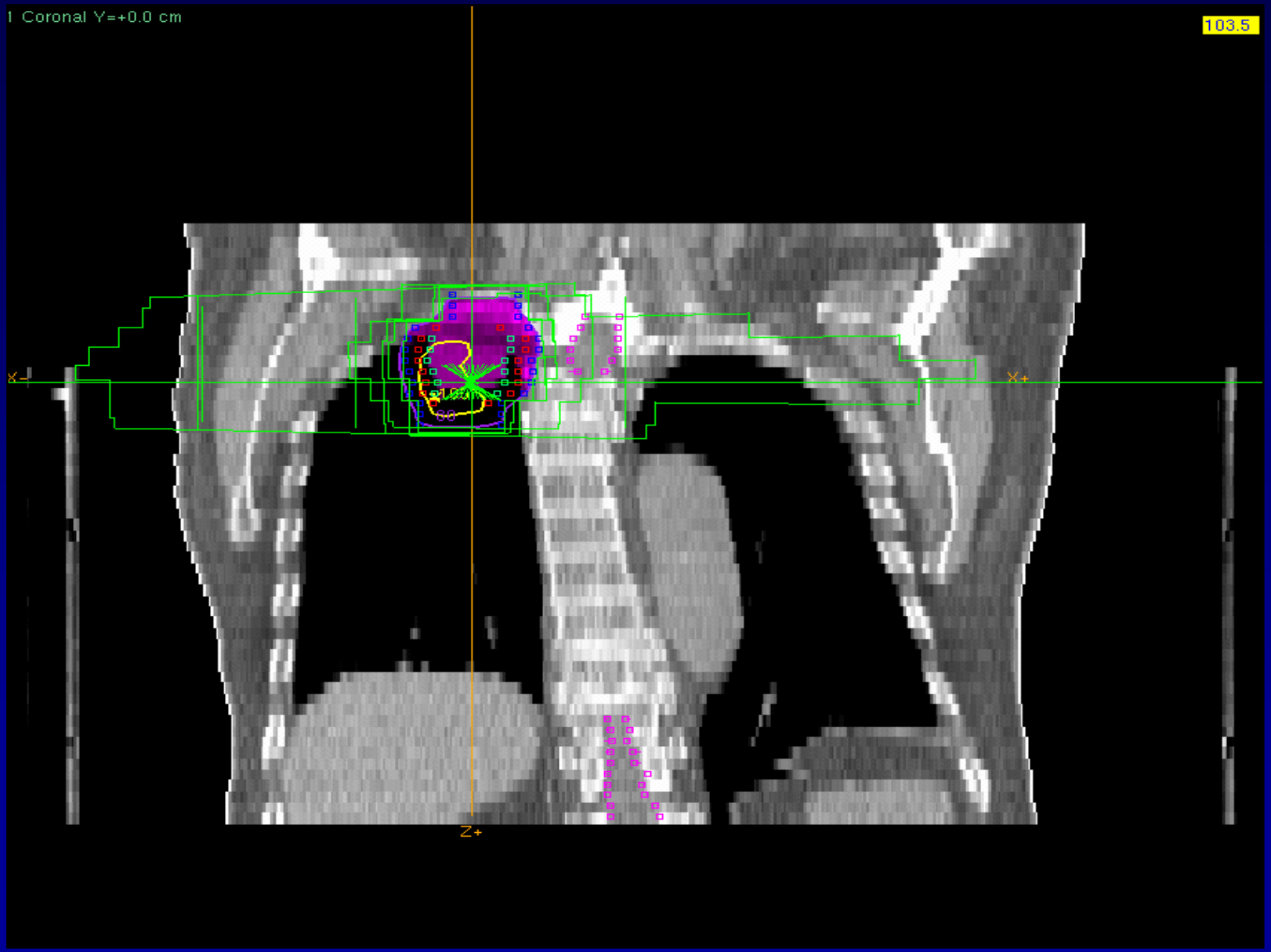

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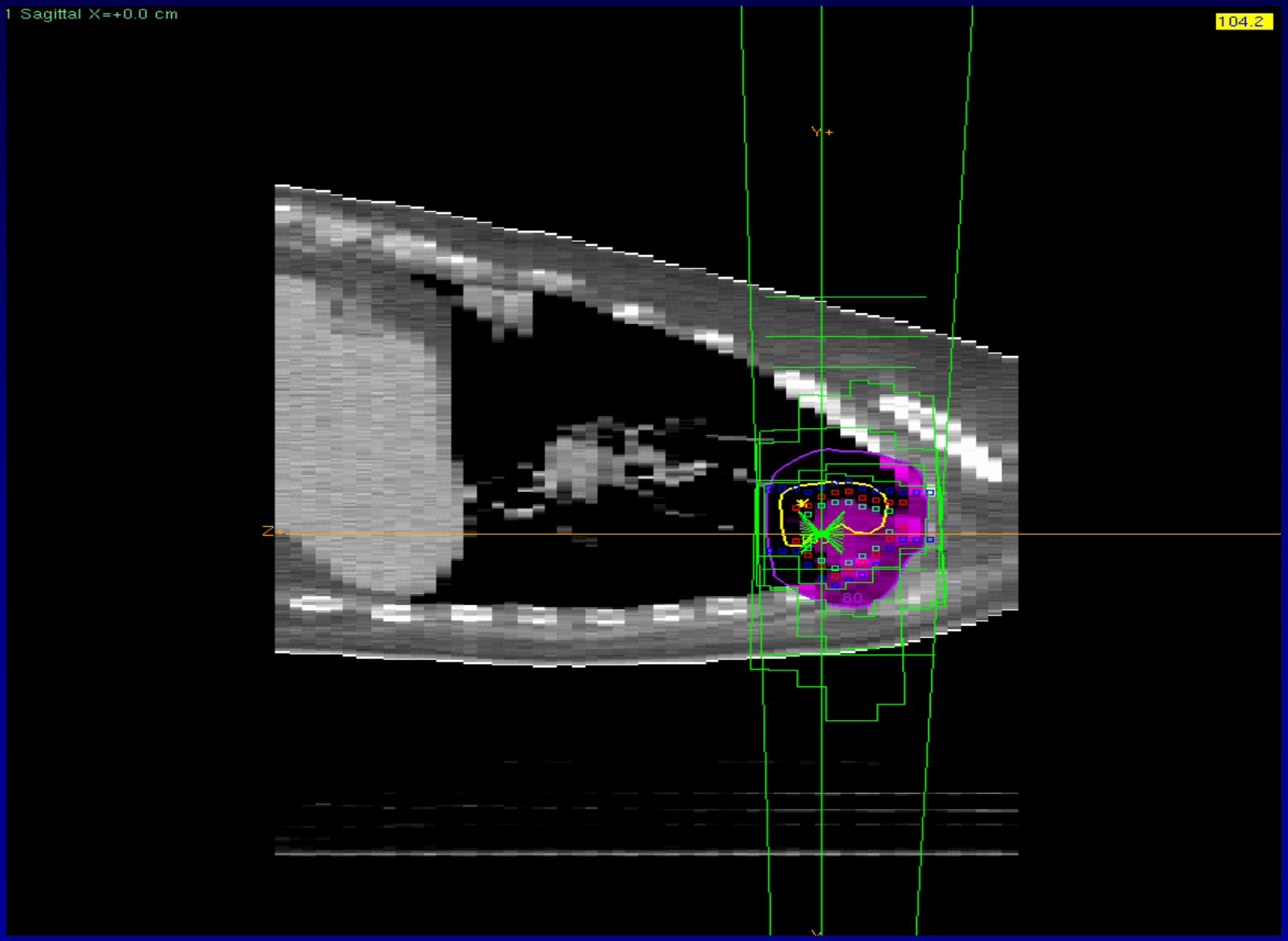
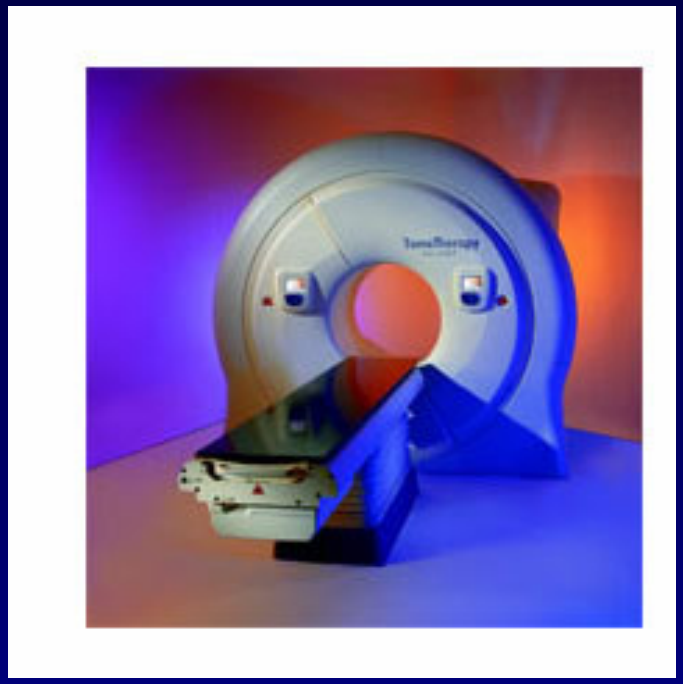
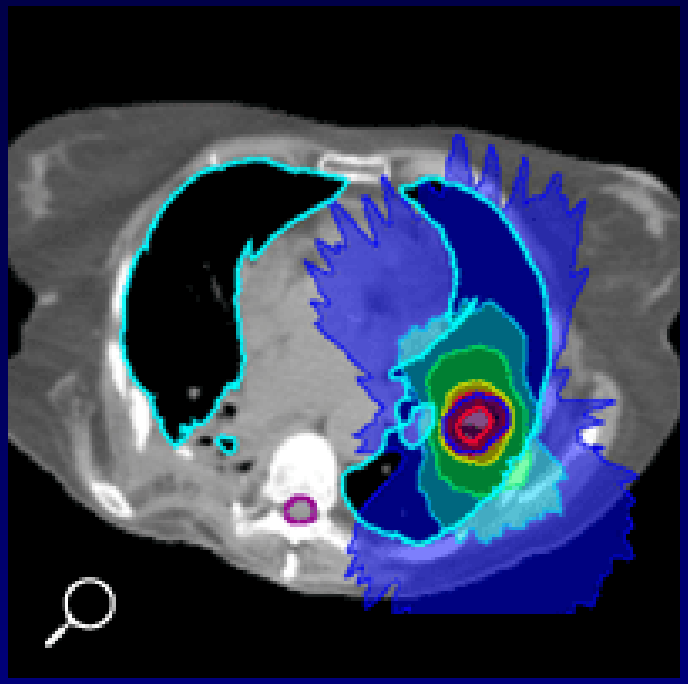
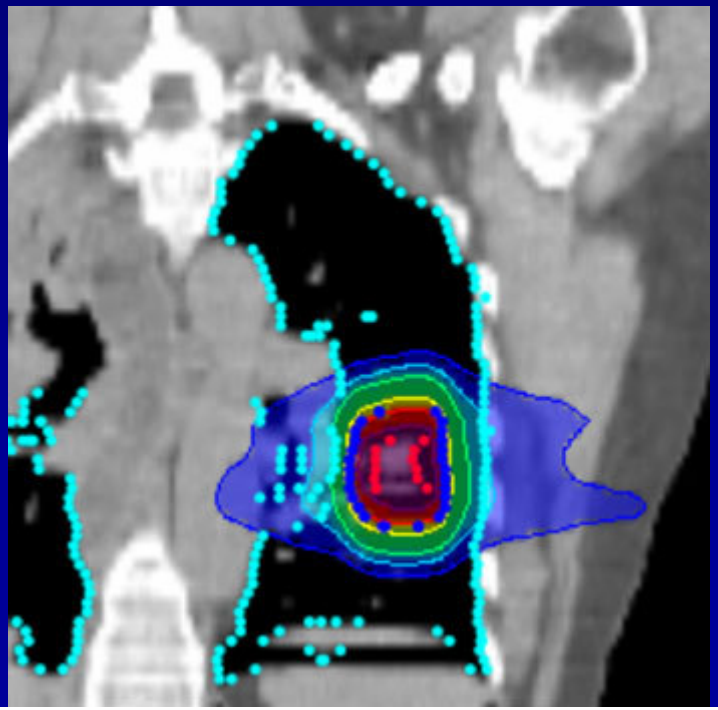
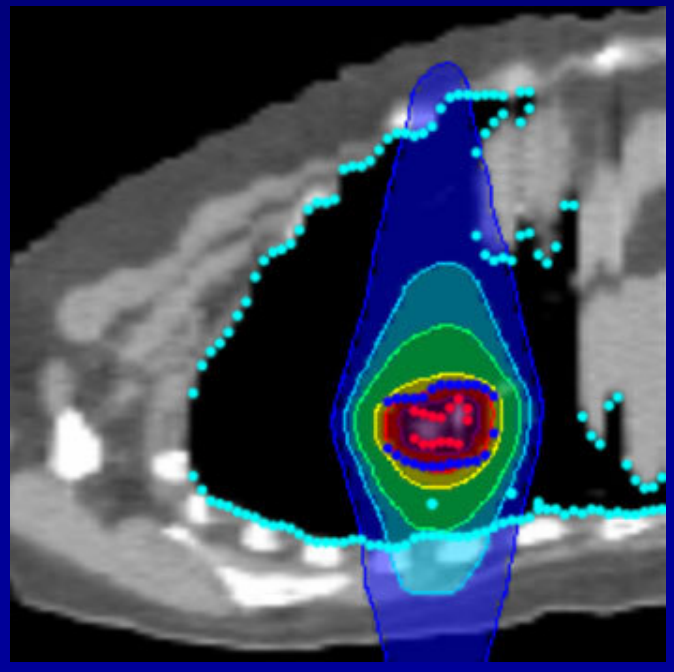
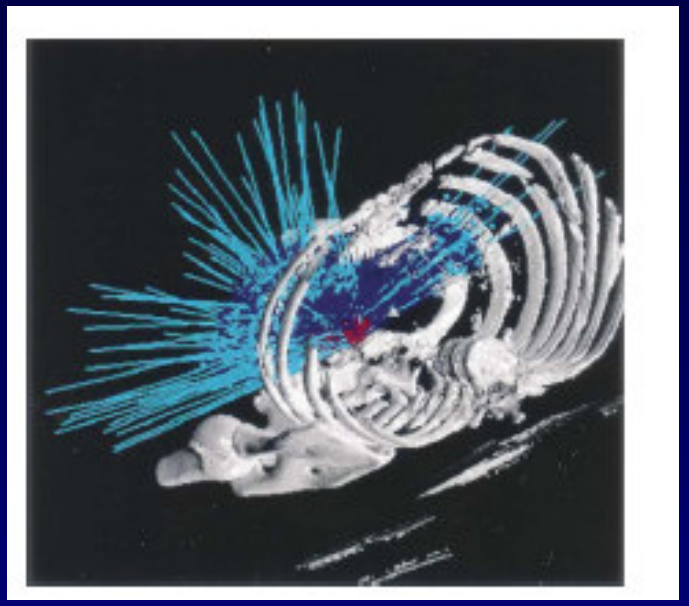


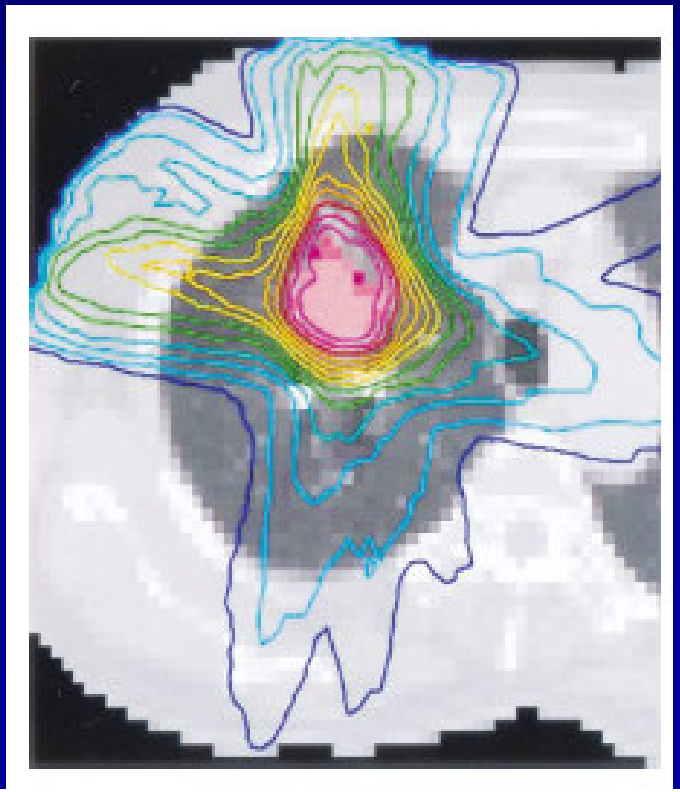






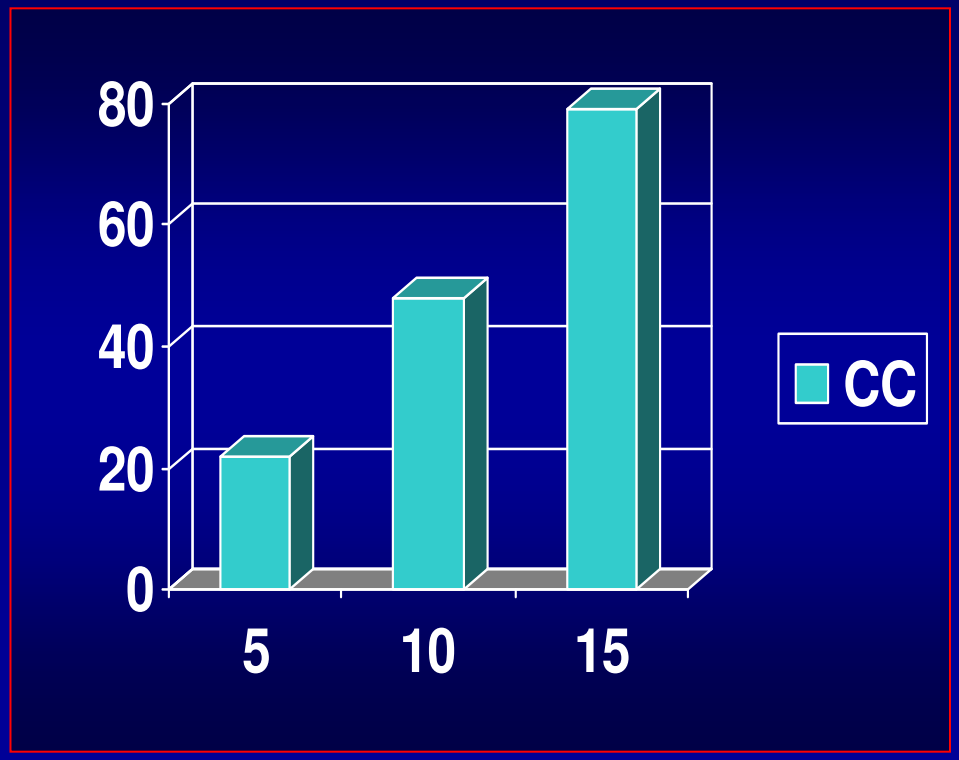






Controllo del trattamento prima (IGRT) e durante l'irradiazione (tecniche per il controllo dell'organ motion)

Nell'espansione da GTV a PTV,
ogni millimetro di margine ha un impatto significativo sul volume di polmone sano irradiato !

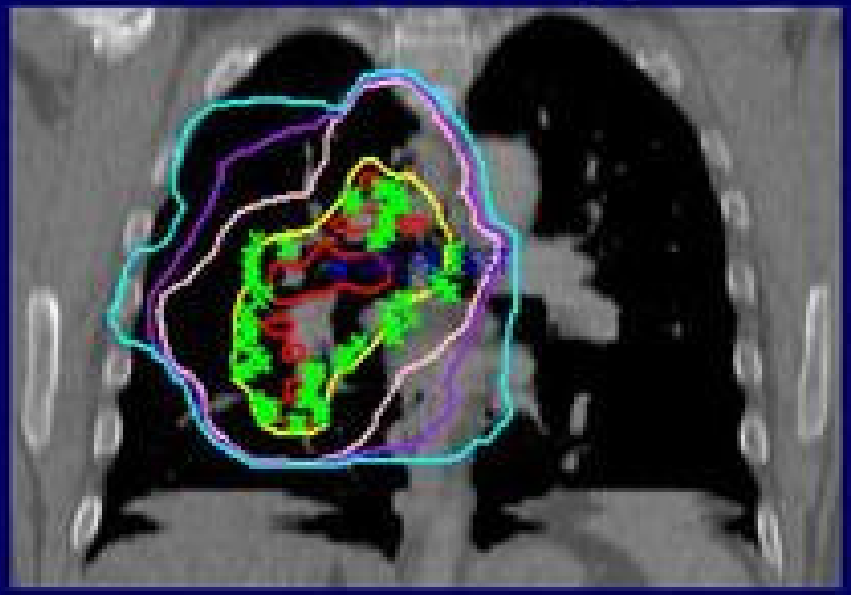


Diametro	Volume Polmone sano
50 mm	65 cc
+ 5 mm	87 cc (+22 cc)
+ 10 mm	113 cc (+48 cc)
+ 15 mm	144 cc (+79 cc)

Institut S. Catherine- Avignone

Comparison of Free Breathing and Respiratory Gated Treatment Plans

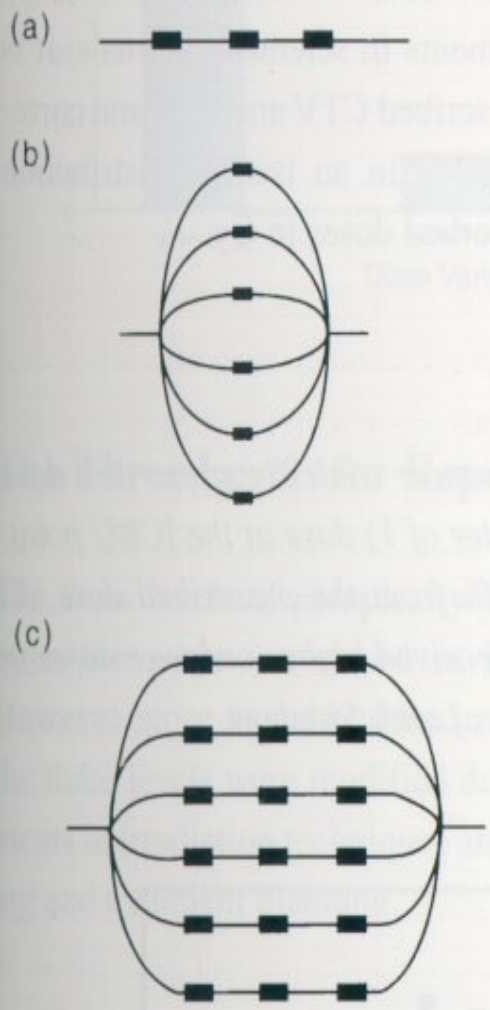
Free breathing

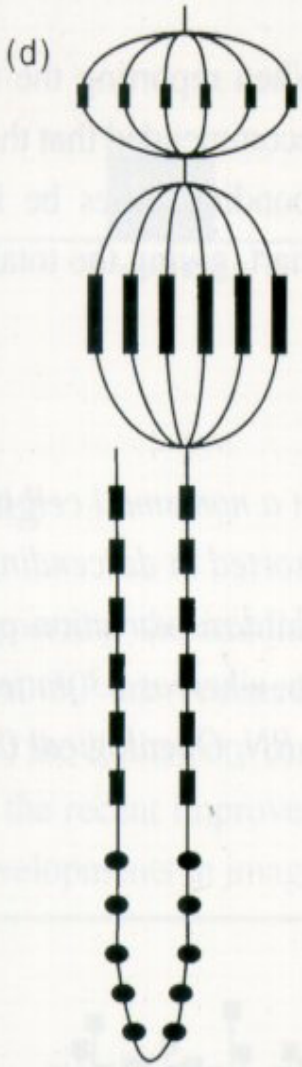


Gated - inspiration

- Less lung within the radiation field with gating on inspiration
- NTCP decreased from 30% to 19% with gating technique

Figure 4. *Schematic examples of tissue organization structures in the parallel-serial model.*





a) a serial string of subunits (*e.g.*, the spinal cord),

b) a parallel string of subunits (*e.g.*, the lungs),

c) a serial-parallel string of subunits (*e.g.*, the heart),

d) a combination of parallel and serial structures (*e.g.*, a nephron)

(Modified from Withers et al., (1988) and Källman et al., (1992))

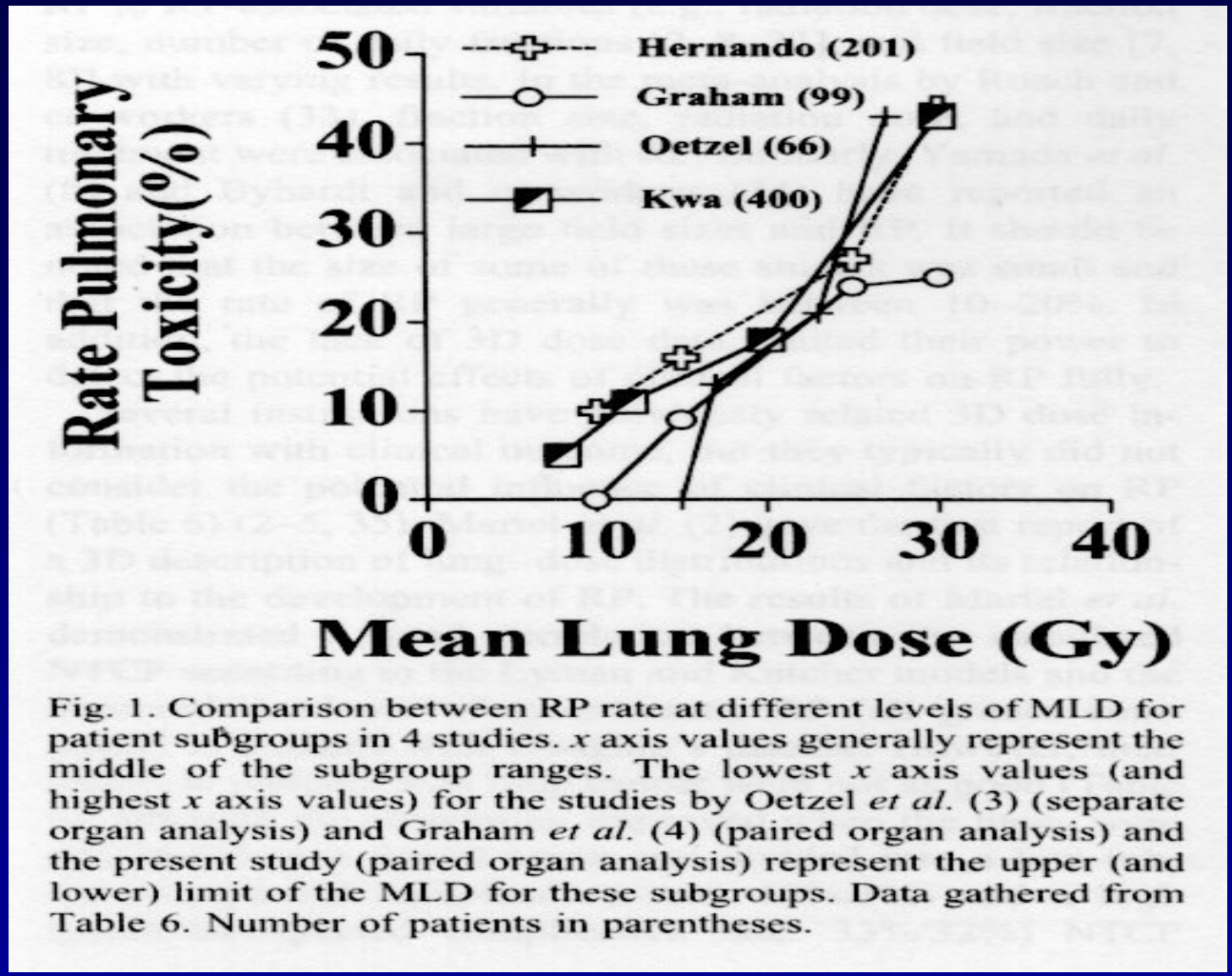
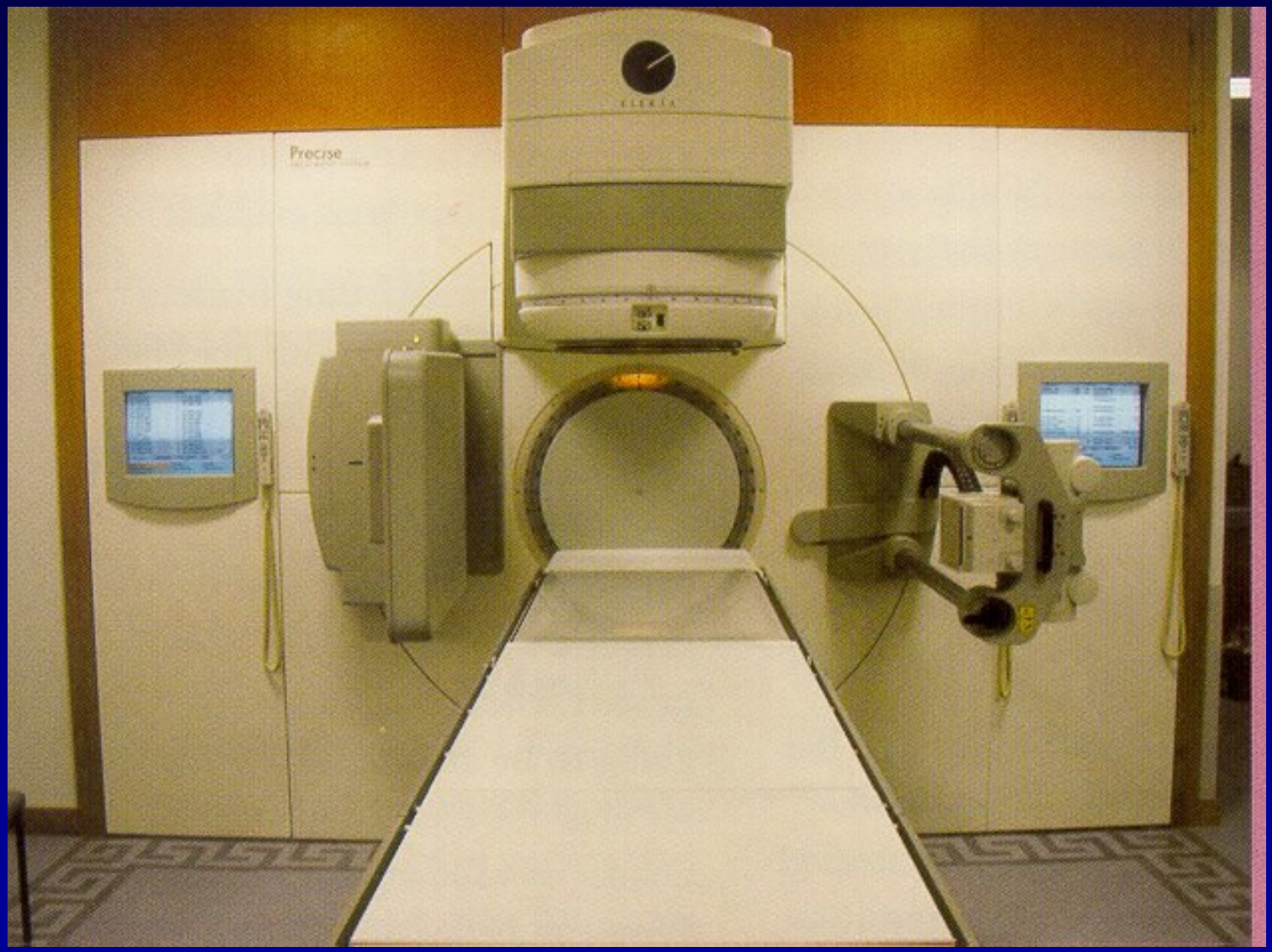
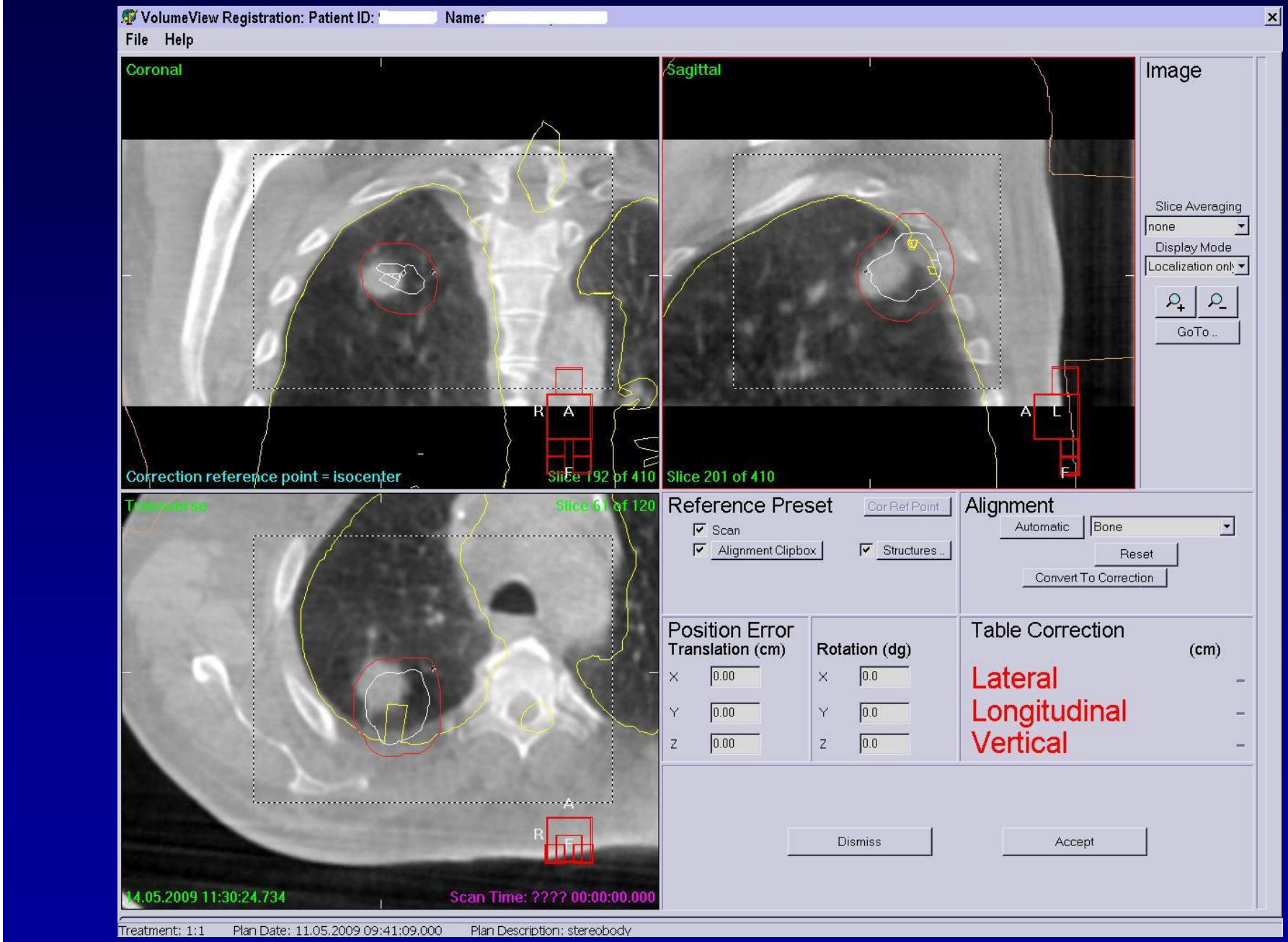


Fig. 1. Comparison between RP rate at different levels of MLD for patient subgroups in 4 studies. *x* axis values generally represent the middle of the subgroup ranges. The lowest *x* axis values (and highest *x* axis values) for the studies by Oetzel *et al.* (3) (separate organ analysis) and Graham *et al.* (4) (paired organ analysis) and the present study (paired organ analysis) represent the upper (and lower) limit of the MLD for these subgroups. Data gathered from Table 6. Number of patients in parentheses.

From: Hernando, M.L., IJROBP, 2001


Precise


VolumeView Registration: Patient ID:
Name:
File
Help
Coronal
Correction reference point = isocenter
Slice 192 of 410
Sagittal
Slice 201 of 410
Image
Slice Averaging
none
Display Mode
Localization onl
GoTo ..
Transverse
Slice 61 of 120
14.05.2009 11:30:24.734
Scan Time: ???? 00:00:00.000
Reference Preset
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Scan
Alignment Clipbox
Structures ..
Alignment
Automatic
Bone
Reset
Convert To Correction
Position Error
Translation (cm)
Rotation (dg)
X 0.00
Y 0.00
Z 0.00
X 0.0
Y 0.0
Z 0.0
Table Correction
(cm)
Lateral
Longitudinal
Vertical
Dismiss
Accept
Treatment: 1:1
Plan Date: 11.05.2009 09:41:09.000
Plan Description: stereobody


VolumeView Registration: Patient ID:
Name:
File
Help
Coronal
Sagittal
Image
Slice Averaging
none
Display Mode
Localization onl
GoTo ..
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A
Correction reference point = isocenter
Slice 192 of 410
Slice 201 of 410
Transverse
Slice 61 of 120
Reference Preset
Cor Ref Point..
Scan
Alignment Clipbox
Structures ..
Alignment
Automatic
Manual
Reset
Convert To Correction
Position Error
Translation (cm)
Rotation (dg)
X
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359.6
Y
-0.05
1.3
Z
0.88
358.9
Table Correction
(cm)
Lateral
Longitudinal
Vertical
Dismiss
Accept
14.05.2009 11:30:24.734
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Treatment: 1:1
Plan Date: 11.05.2009 09:41:09.000
Plan Description: stereobody

Active breath control

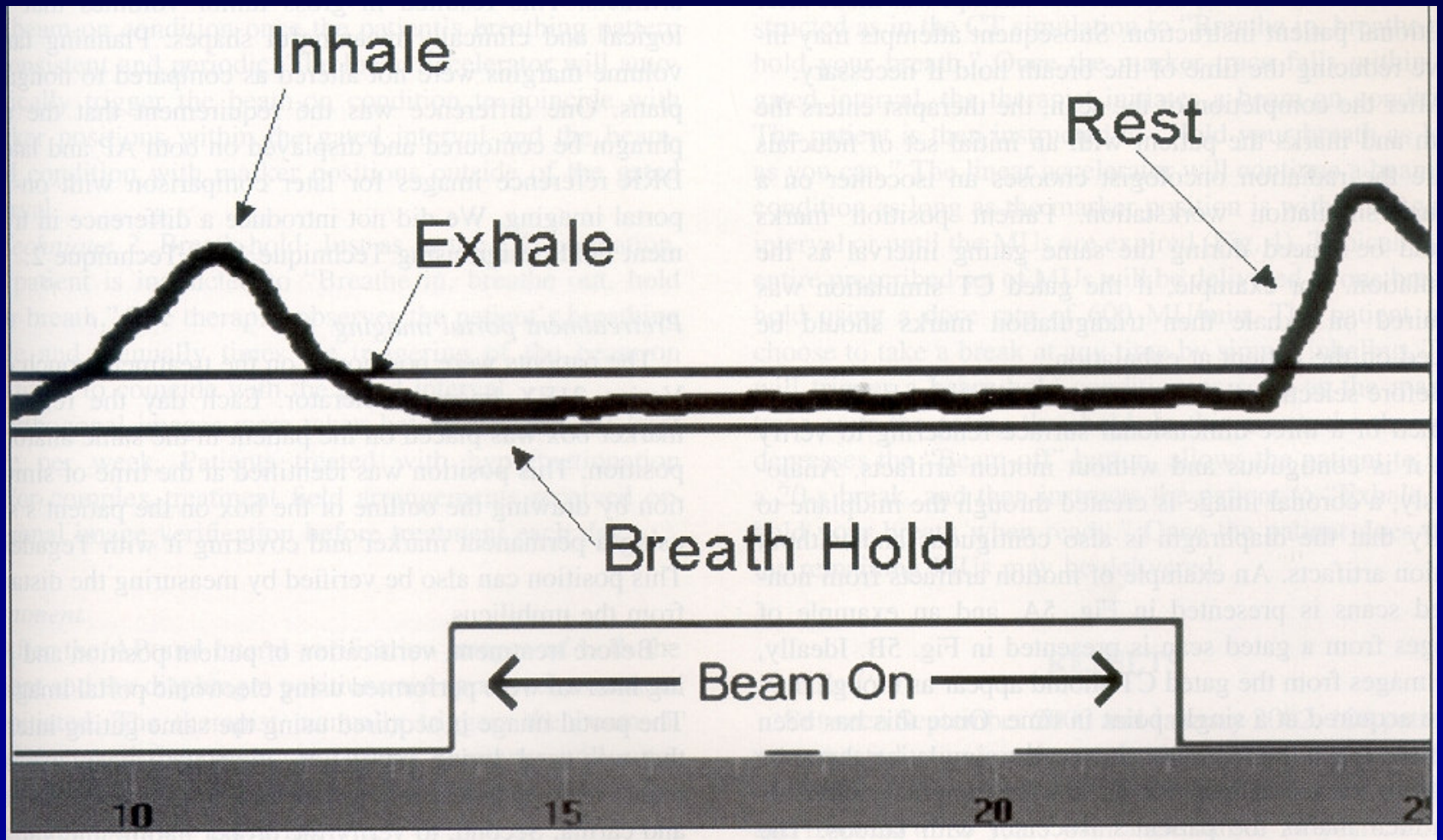


Fig. 4. Part of the respiratory gating software user interface. The wave represents the patient's respiration during a breath hold on exhalation. The beam-on condition corresponds to the amplitude-gated exhalation.

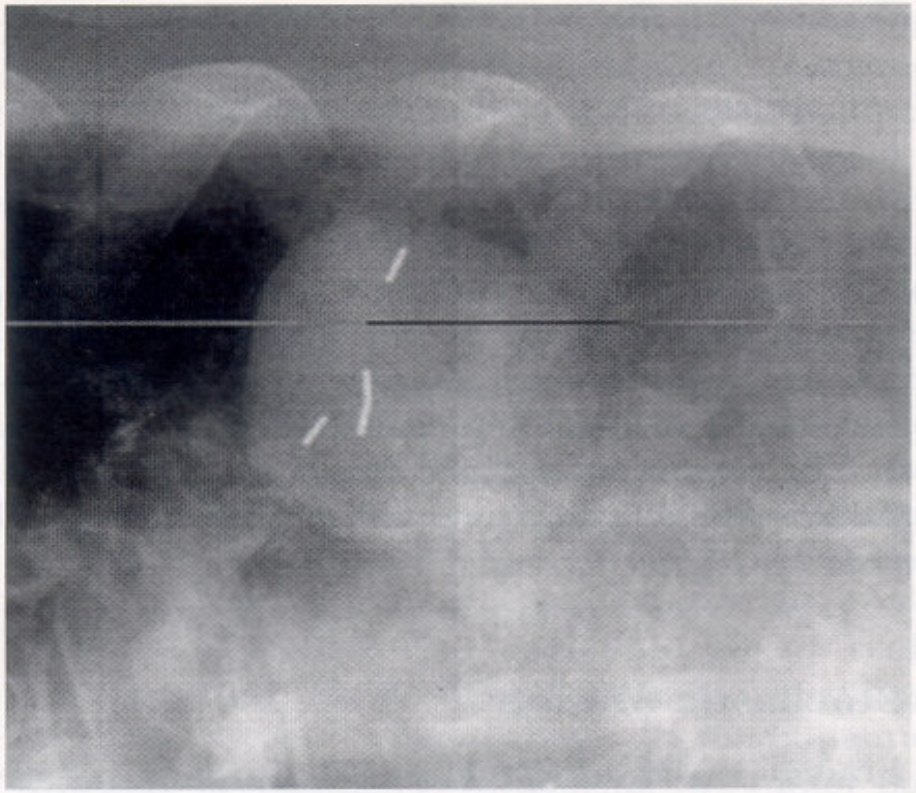


Figure 1. A radiographic image of a lung tumor containing 4 gold fiducials, taken with a real-time amorphous silicon imaging system during a CyberKnife lung radiosurgery treatment.

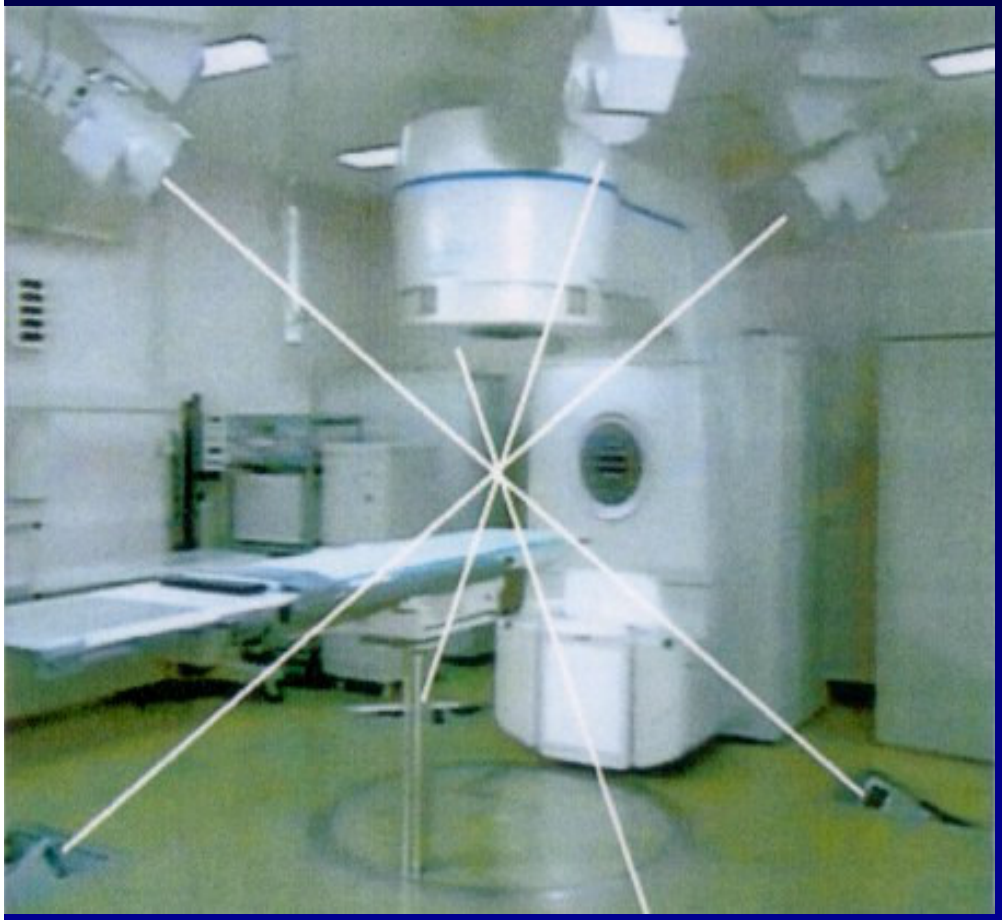
4 ways to locate the target:

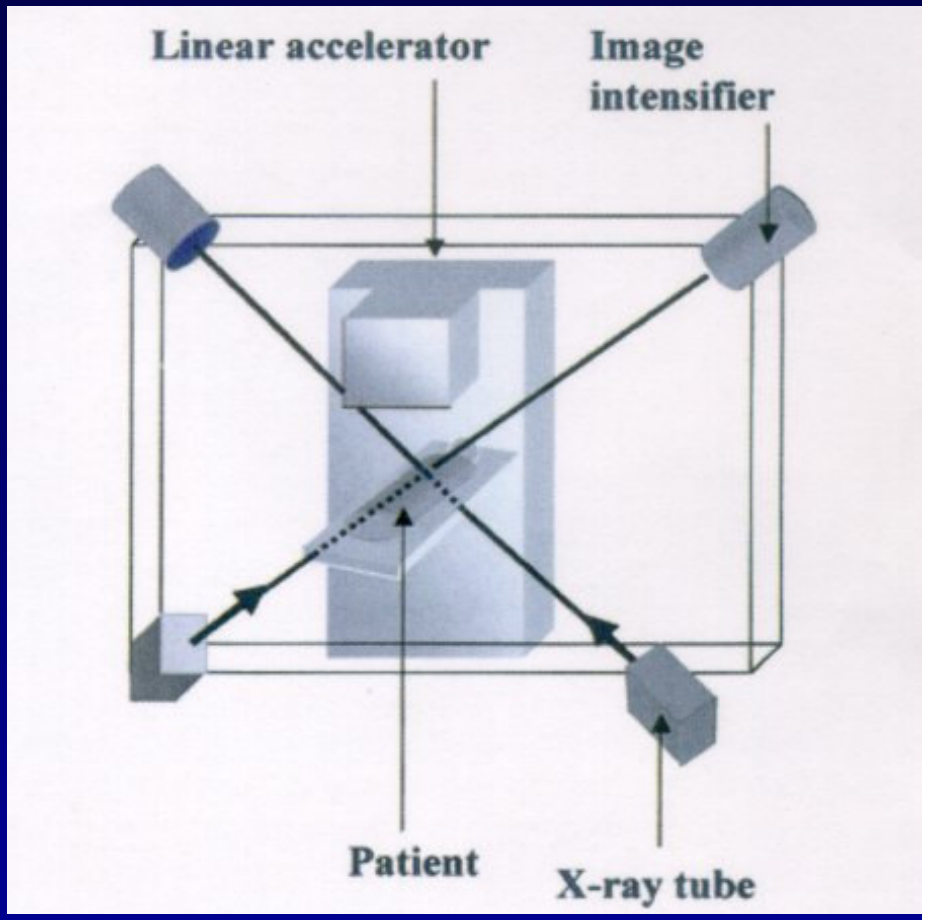
- Image the tumor
- Image anatomical structures rigidly connected to the tumor
- Detect artificial fiducials implanted in the tumor
- Track surrogate organs that move in synchrony with the tumor

Tumor motion measured via radiographic imaging

Measure the target position on a time scale faster than the motion itself

Fiducial based guidance has the advantage that the fiducials are easily located with automatic image processing tools and the time needed to make a position determination is short (50 msec)





Determination of 3D coordinates of tumor markers by mean of fluoroscopic digitized images

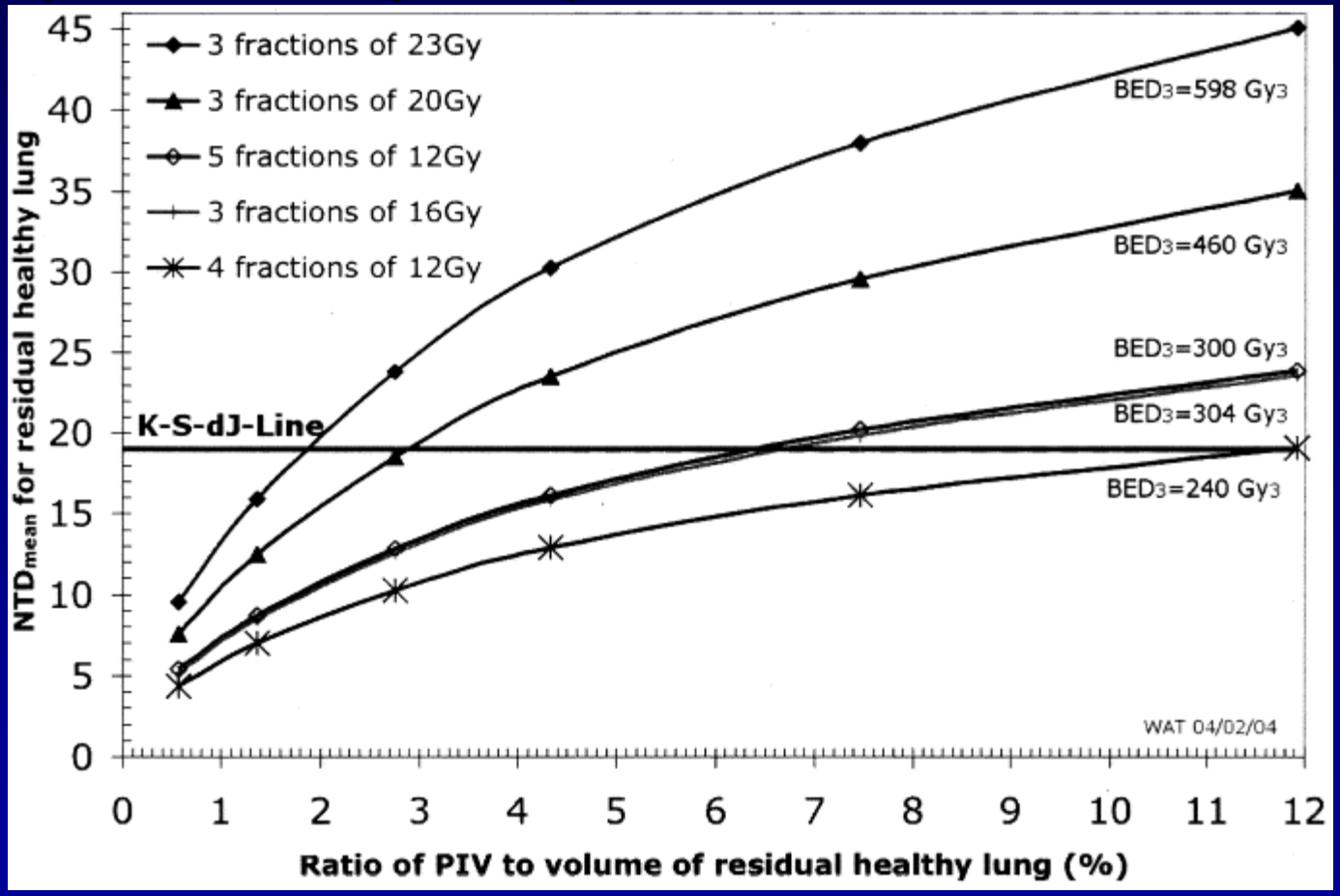
Radioterapia ipofrazionata con localizzazione stereotassica nelle neoplasie toraciche ed addominali

- ✓ Volumi irradiati di piccole dimensioni posti all'interno di organi con architettura funzionale "in parallelo"
- ✓ Dose per frazione elevata
- ✓ Distribuzione di dose non uniforme con risparmio degli organi adiacenti
- ✓ Riduzione del set up e internal margin: controllo della riproducibilità (IGRT) e del movimento d'organo (gating)

RADIOBIOLOGIA E FRAZIONAMENTO DELLA DOSE

Modellizzazione radiobiologica di trattamenti ipofrazionati

L'esempio delle neoplasie polmonari



Fowler, IJROBP 2004

RADIOTERAPIA IPOFRAZIONATA CON LOCALIZZAZIONE STEREOTASSICA DELLE NEOPLASIE POLMONARI (NSCLC) IN STADIO INIZIALE (T1-T2 N0):PROBLEMATICHE TECNICHE E RISULTATI CLINICI

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INTRODUZIONE

- **L'escissione chirurgica rappresenta ancora lo standard terapeutico in pz affetti da NCSLC in stadio iniziale (I-II).**
- **La radioterapia esclusiva rappresenta una alternativa terapeutica nei pz giudicati inoperabili per comorbidità o che rifiutino l'intervento**
- **La RT con finalità radicale nel NSCLC in stadio I-II continua tuttavia ad essere una sfida a causa:**
  - **della immediata prossimità di organi critici a tolleranza limitata (polmoni, esofago, midollo, cuore)**
  - **della mobilità degli organi intratoracici**

RADIOBIOLOGIA E FRAZIONAMENTO DELLA DOSE
L'esempio delle neoplasie polmonari

Author	N. Pts.	Stage	Mean dose (Gy)	Loc. Rec. (%)	OS (5ys)
Jeremic (1999)	67	T1-2 N0-1	69.6	58	30%
Cheung (2000)	102	T1-2 N0-1	52.5	53	16%
Krol (1996)	108	T1-T2 N0	65.0	71	16%
Sandler (1990)	77	T1-T2 N0	60.0	56	17%
Morita (1997)	149	T1-T2 N0	64.7	44	22%

STEREOTACTIC RADIATION THERAPY IN EARLY STAGE LUNG TUMORS

LOCAL FAILURE RATE AFTER HYPOFRACTIONATED IF RT (CT based plans): T1-T2 N0 pts

Author	Pts	Dose/ N.Fx	BED acute	Local control
• Uematsu	50	50 Gy/5 *	100,0	96%
• Nagata	33	48 Gy/4 ^	104,8	92%
• Arimoto	24	60 Gy/8 ^	105,6	94%
• Wulf	17	45 Gy/3 *	112,5	94%

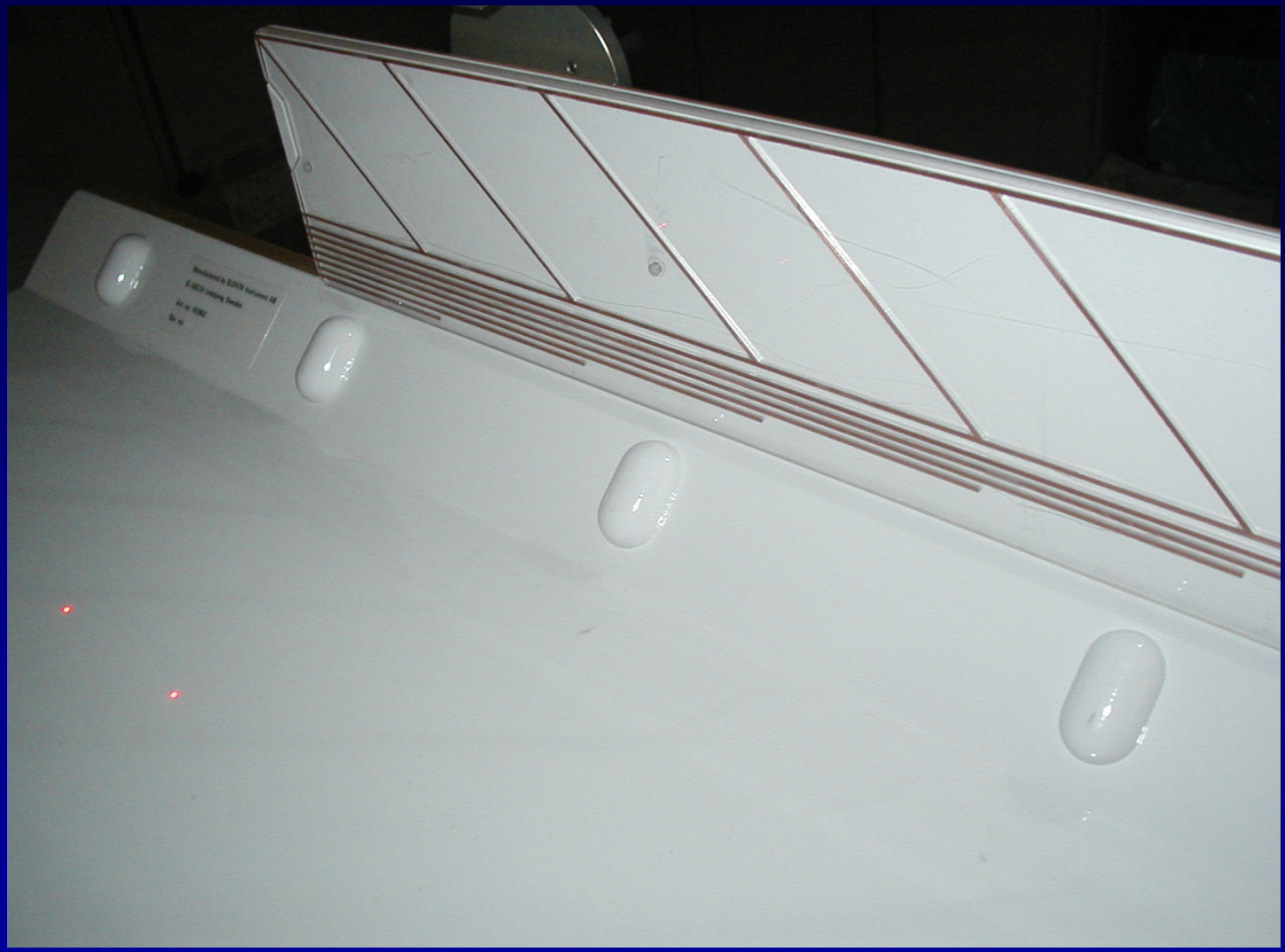
* Prescribed to reference isodose
^ Prescribed to isocenter

BED acute = nd (1 + d/ alfa/beta) Time factor not relevant

RADIOTERAPIA STEREOTASSICA: L'ESPERIENZA DELL'OSPEDALE BELLARIA

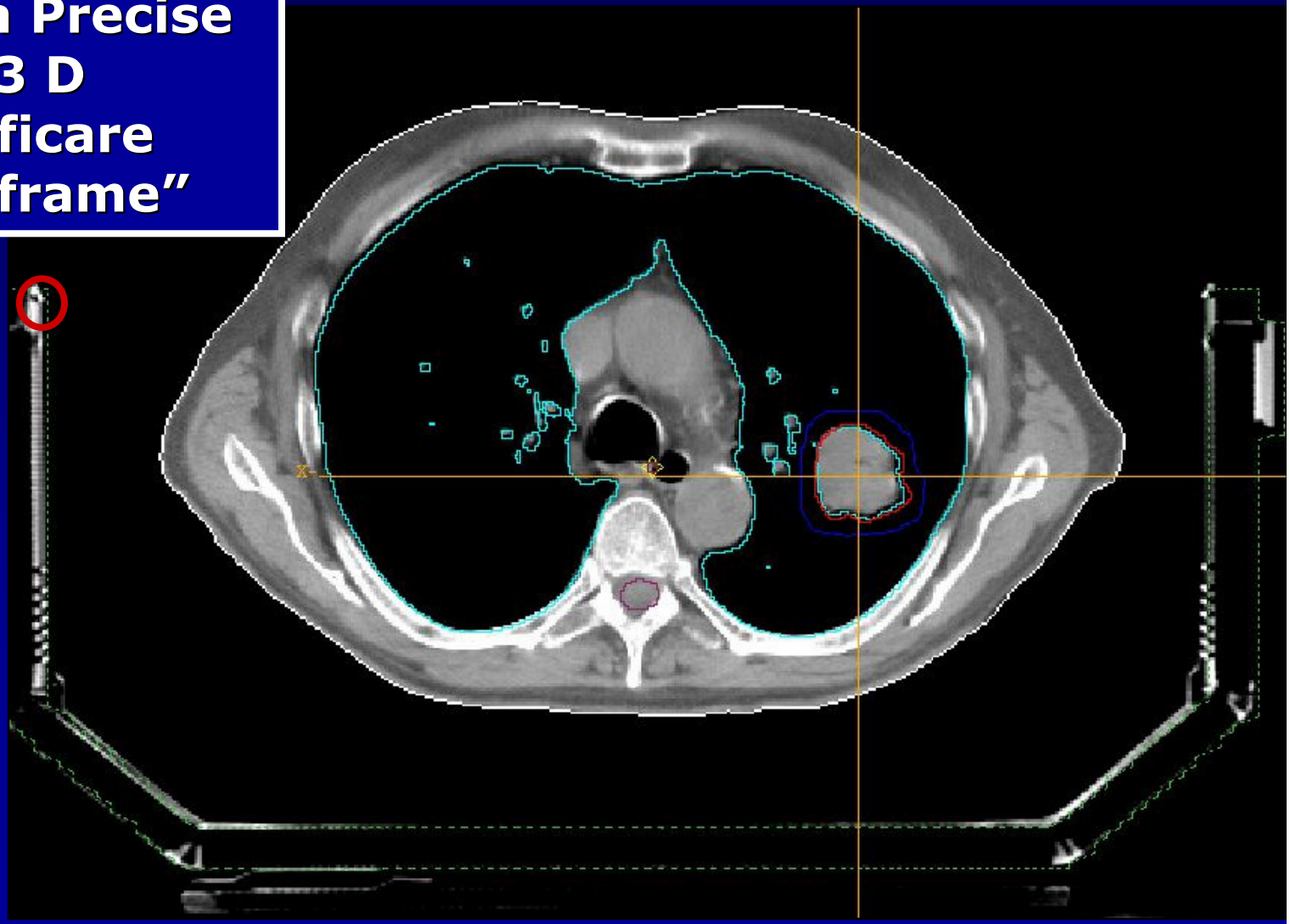
- GIUGNO 2002- FEBBRAIO 2007
- 57 pazienti (10 femmine and 47 maschi)
- Età media: 73,3 anni (59-86 aa)
- Esami di staging: TC e PET
- NSCLC T1 N0: 49 pz
  T2 N0: 8 pz
- Sede lesione: periferica
- Intervento chirurgico controindicato per comorbidità

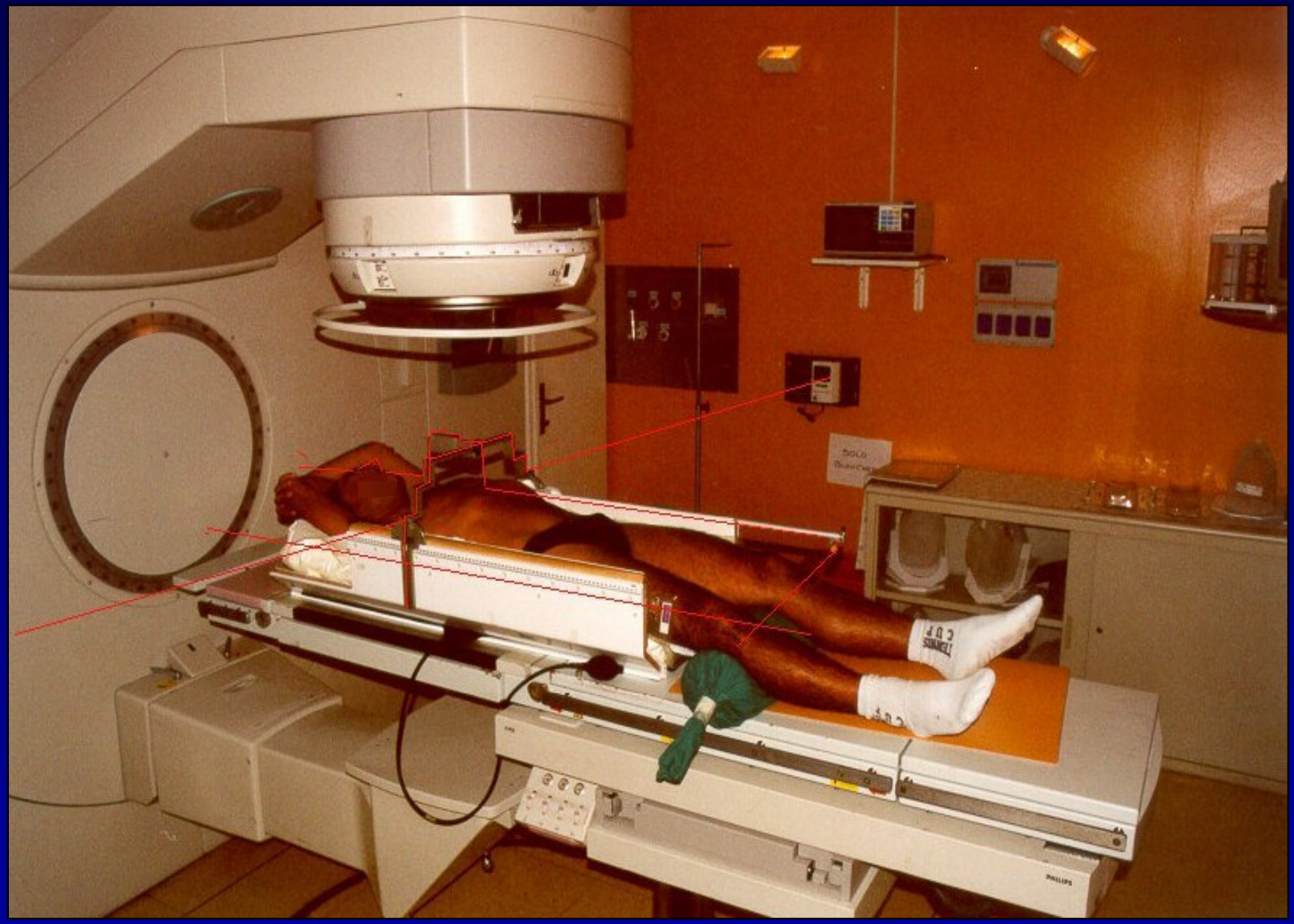
IMMOBILIZZAZIONE



AUTOMATICA IDENTIFICAZIONE DEL "FRAME"

L' identificazione di un singolo marker permette a Precise Plan 3 D d'identificare l'intero "frame"





Viene utilizzata una compressione controllata diaframmatica solo quando in fluoroscopia si osserva una mobilità del target è > +/- 7 mm (lesioni del lobo polmonare inferiore o dell'addome superiore)

TC DI CENTRATURA: definizione di GTV e OAR

Il contorno del GTV e degli OAR (polmone, midollo spinale, cuore) è stato tracciato su sezioni TAC acquisite ogni 3 mm, con tecnica spirale "slow" (3 sec/rot).

Si assume che venga catturata la posizione media del target. TAC spirale rapida potrebbe generare errori di posizione (distribuzione di dose pianificata non corrispondente a quella reale).

"SLOW" O "FAST" CT SCANS DEL TORACE POSSONO DARE UNA DIVERSA RAPPRESENTAZIONE DELLA FORMA E DIMENSIONE DEL GTV

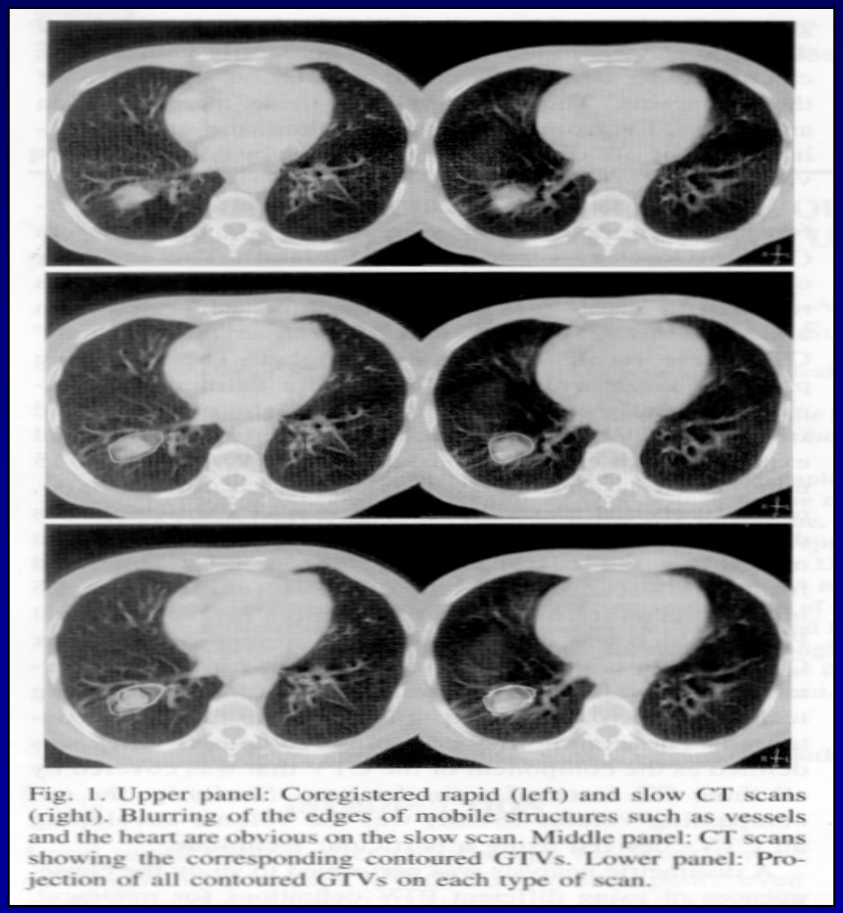
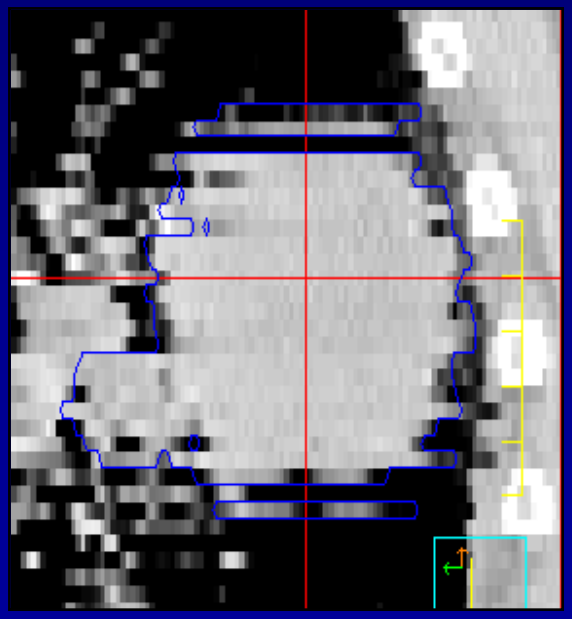


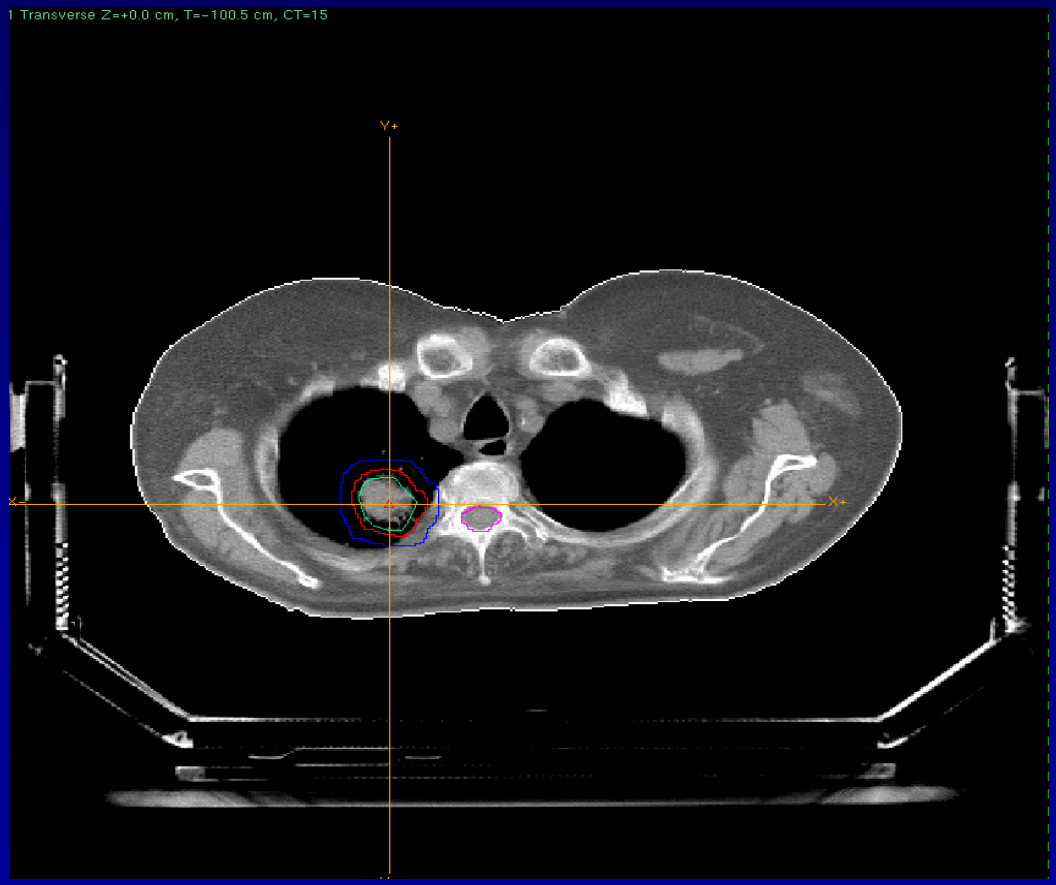
Fig. 1. Upper panel: Coregistered rapid (left) and slow CT scans (right). Blurring of the edges of mobile structures such as vessels and the heart are obvious on the slow scan. Middle panel: CT scans showing the corresponding contoured GTVs. Lower panel: Projection of all contoured GTVs on each type of scan.

DIFFICOLTÀ DI CONTOURING

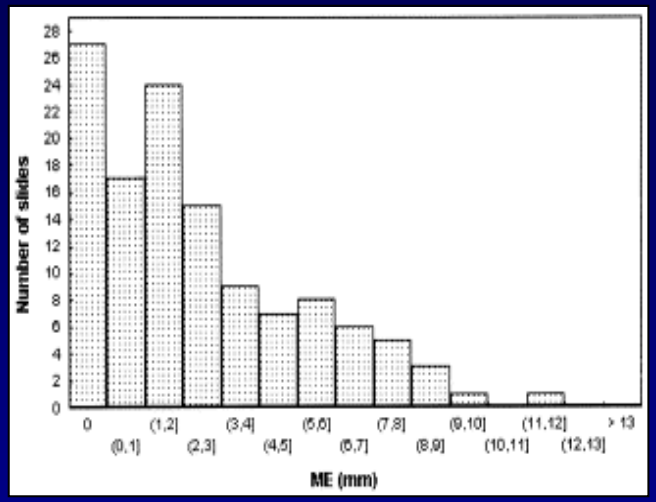


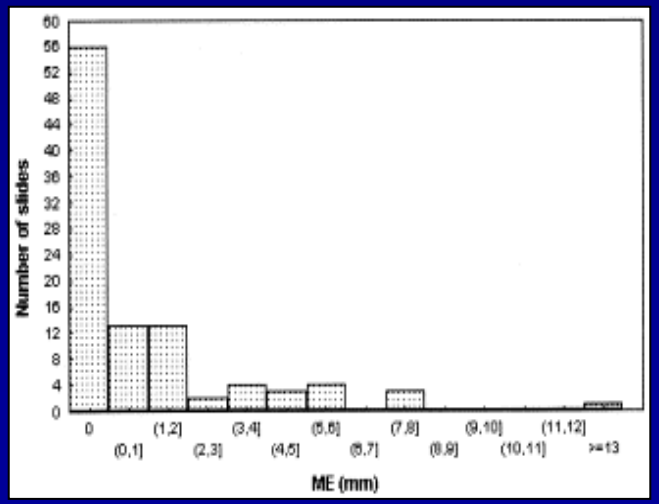
RADIOTERAPIA STEREOTASSICA NEI TUMORI POLMONARI

- **CTV è ottenuto mediante espansione isotropica di 5 mm del GTV**
- **PTV è ottenuto espandendo il CTV di 5 mm nel piano assiale e 10 mm in direzione longitudinale**

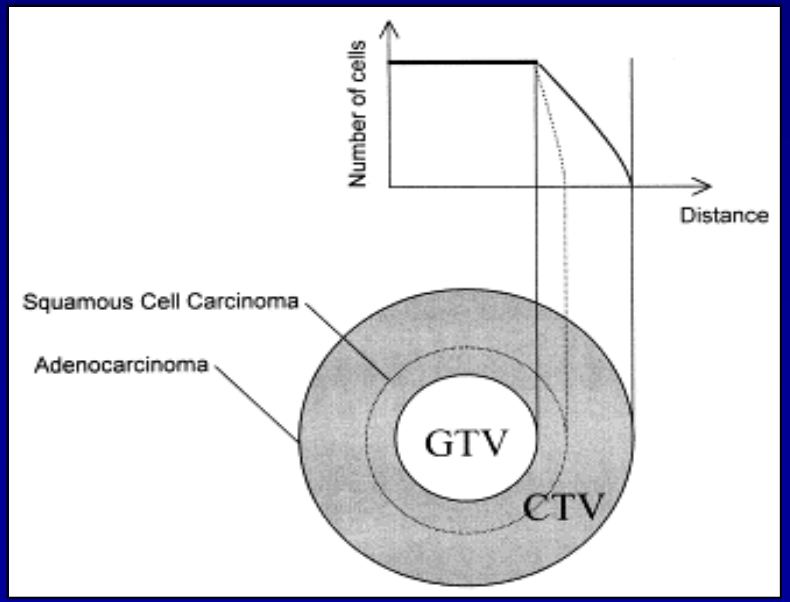


Estensioni infracliniche
Giraud et al, IJROBP 2000





Microscopic extension in adenocarcinoma and in squamous cell carcinoma.



Definizione GTV-CTV (Tumore Primitivo)

Per coprire il 95% dell'estensione microscopica nel parenchima polmonare si raccomanda l'aggiunta di un margine di:

8 mm se Adenocarcinoma

6 mm se Ca. squamoso.

Giraud IJROBP 2000 48, 4 pp 1015-1024

CTV = GTV

Recidive locali = 8/31 (26%)

CTV = GTV+ 6-8 mm

NO recidive locali

RTRT for Lung Tumors"

Fujino et al, IJROBP 57, 2, S 415-2003

Tecnica di trattamento:

6-9 campi statici

Fotoni X 6-10 MV

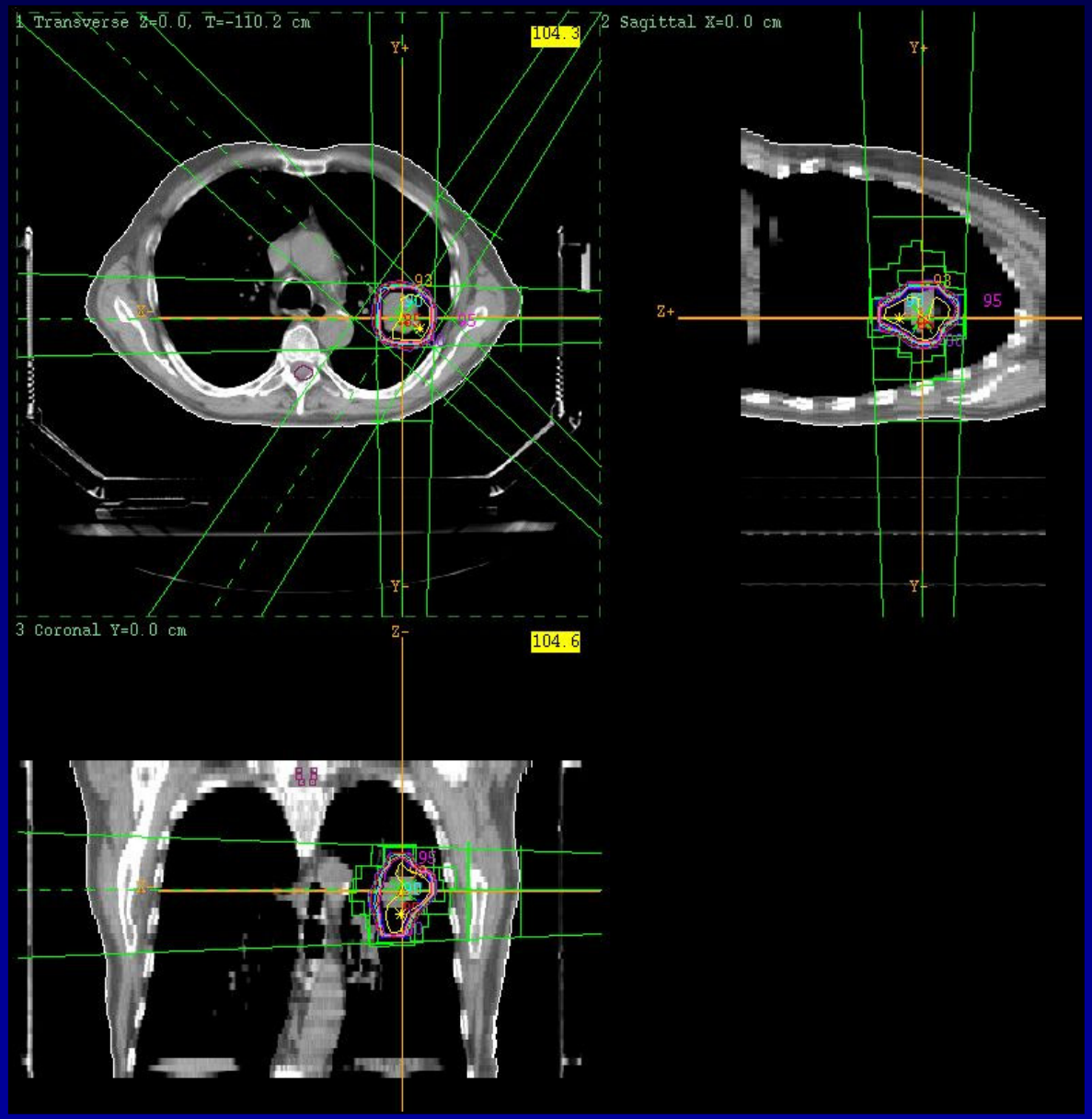
Campi conformati con MLC

Campi coplanari e non coplanari distribuiti su un ampio angolo solido

Non utilizzati campi contrapposti

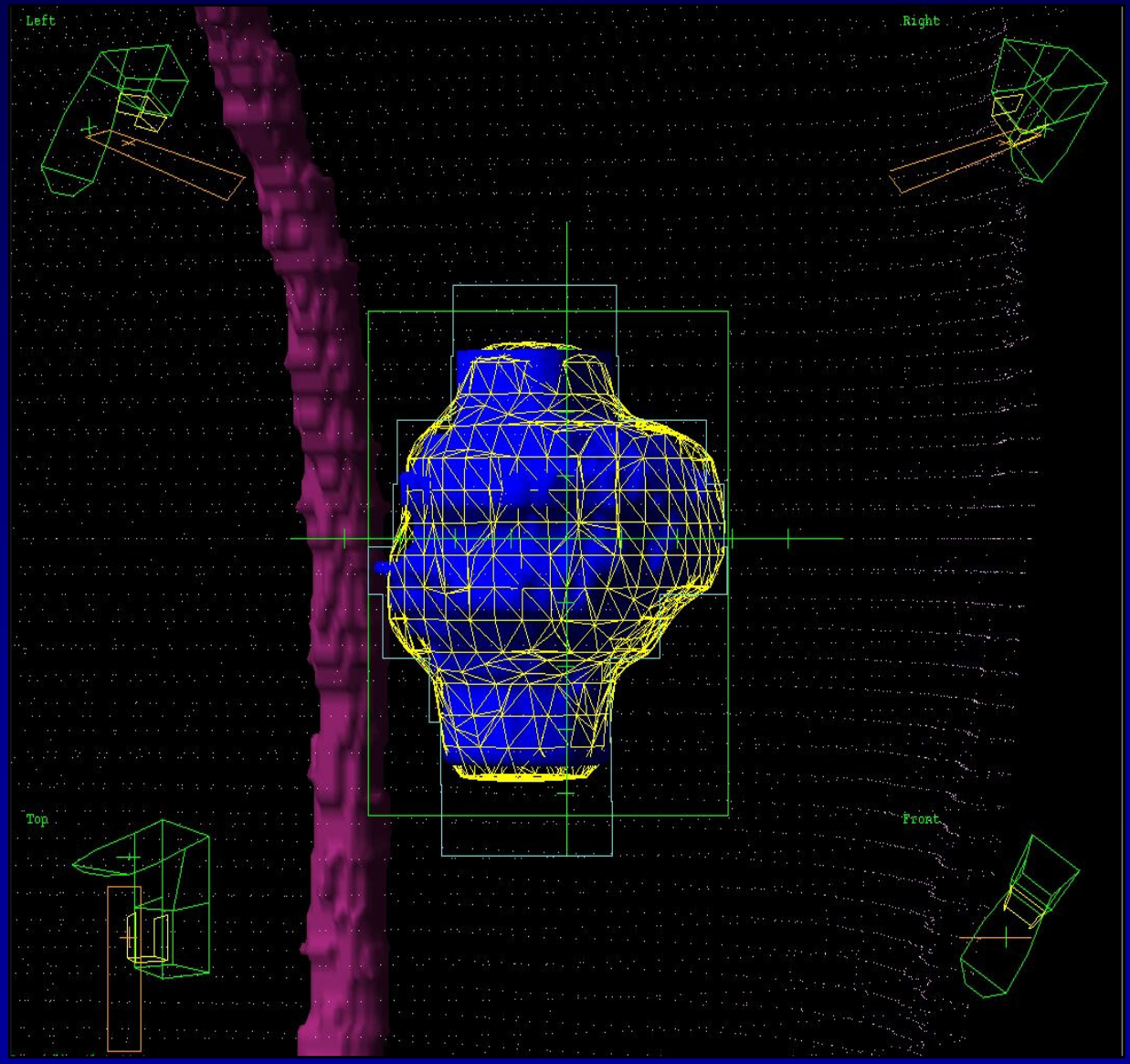
Graphical representation of the Stereotactic Body Frame.

DOSE PRESCRIPTION



- Isocentro = punto di normalizzazione della dose
- Copertura completa del PTV con l'isodose 80% (Minima dose al PTV)
- Disomogeneità programmata della dose al PTV: 20-30% (110-80% della dose all'isocentro)

FRAZIONAMENTO



Tumori primitivi:

5 frazioni

10 -12 Gy / frazione all'isocentro

8-10 Gy / frazione all'isodose 80%

- **Dose "costraints" agli OAR sono i seguenti:**

Polmoni: V12 < 20% Vol

Cuore: < 3 Gy/fraction

Midollo spinale: < 3 Gy/fraction

STEREOTACTIC RADIATION THERAPY IN THE TREATMENT OF LUNG TUMORS

- CTV volume ranged from 10,3 to 82,9 cc (mean: 36.2 cc)
- PTV volume ranged from 35,9 to 161,7 cc (mean 86 cc)
- Mean dose to PTV ranged from 4780 cGy to 5060 cGy (mean 4919 cGy)

STEREOTACTIC RADIATION THERAPY IN THE TREATMENT OF LUNG TUMORS

- ✓V12 to lung ranged from 5,0% to 19,2% of volume (mean 11,4%)
- ✓Mean dose to lung ranged from 190 cGy to 760 cGy (mean 448 cGy)
- ✓Total lung volume ranged from 1859 to 7660 cc (mean 4208 cc).

RISULTATI

Valutazione risposta: TC a 3 mesi e PET e PFR a sei mesi

Follow-up medio: 38 mesi (24-64 mos)

Controllo locale (no progressione nel torace): 89% (51/57 pz)

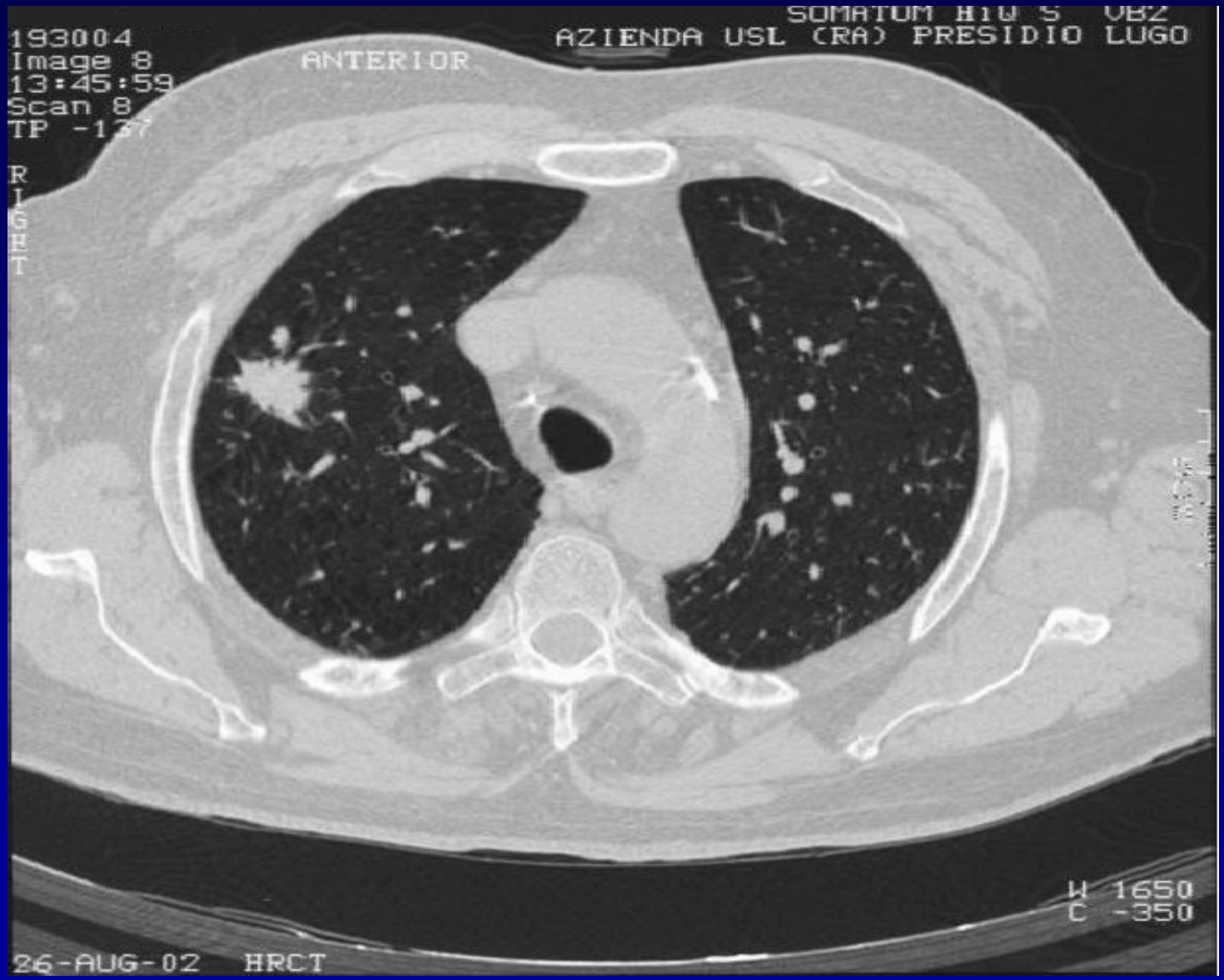
32 pz (56,1%) viventi , 25 liberi da malattia (43,8%)

23 pz deceduti: 8 per progressione della malattia

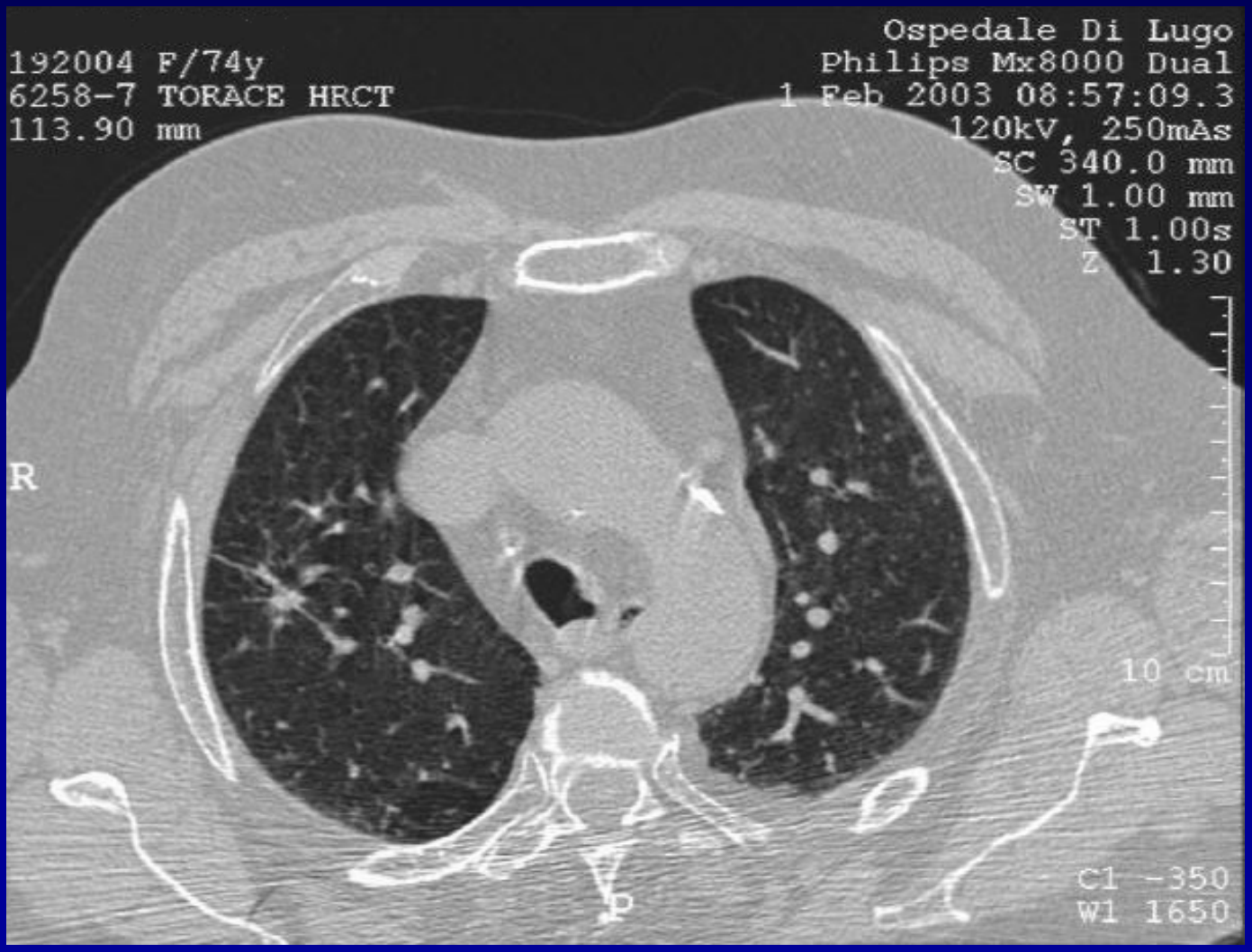
6 pz ricadute toraciche : 3 ln. Mediastinici
2 N+ meta associate
1 relapse sul T

Complicanze respiratorie >grado 1: 1 paziente

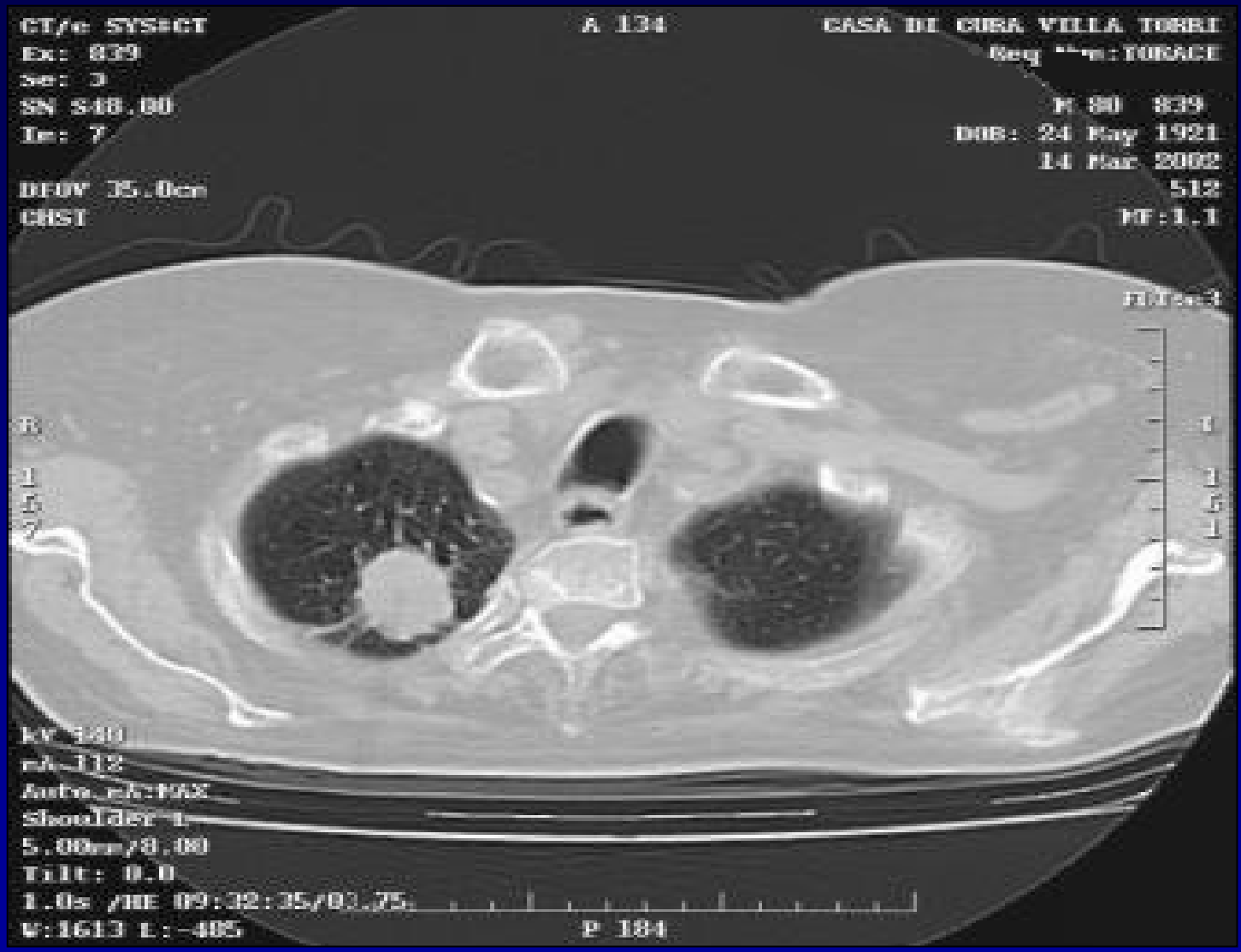
Pre-stereotassi



Post-stereotassi



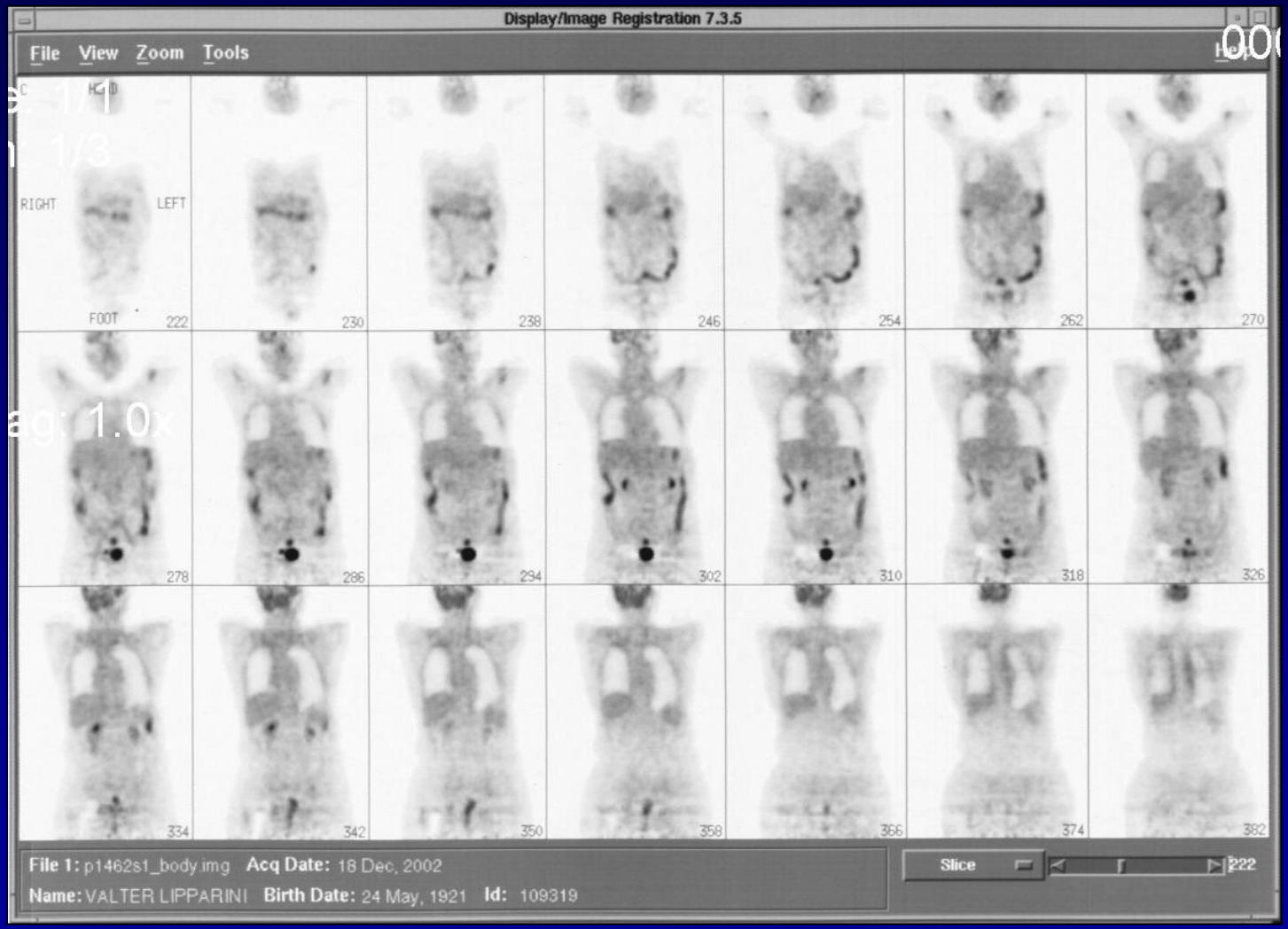
TC DI STAGING

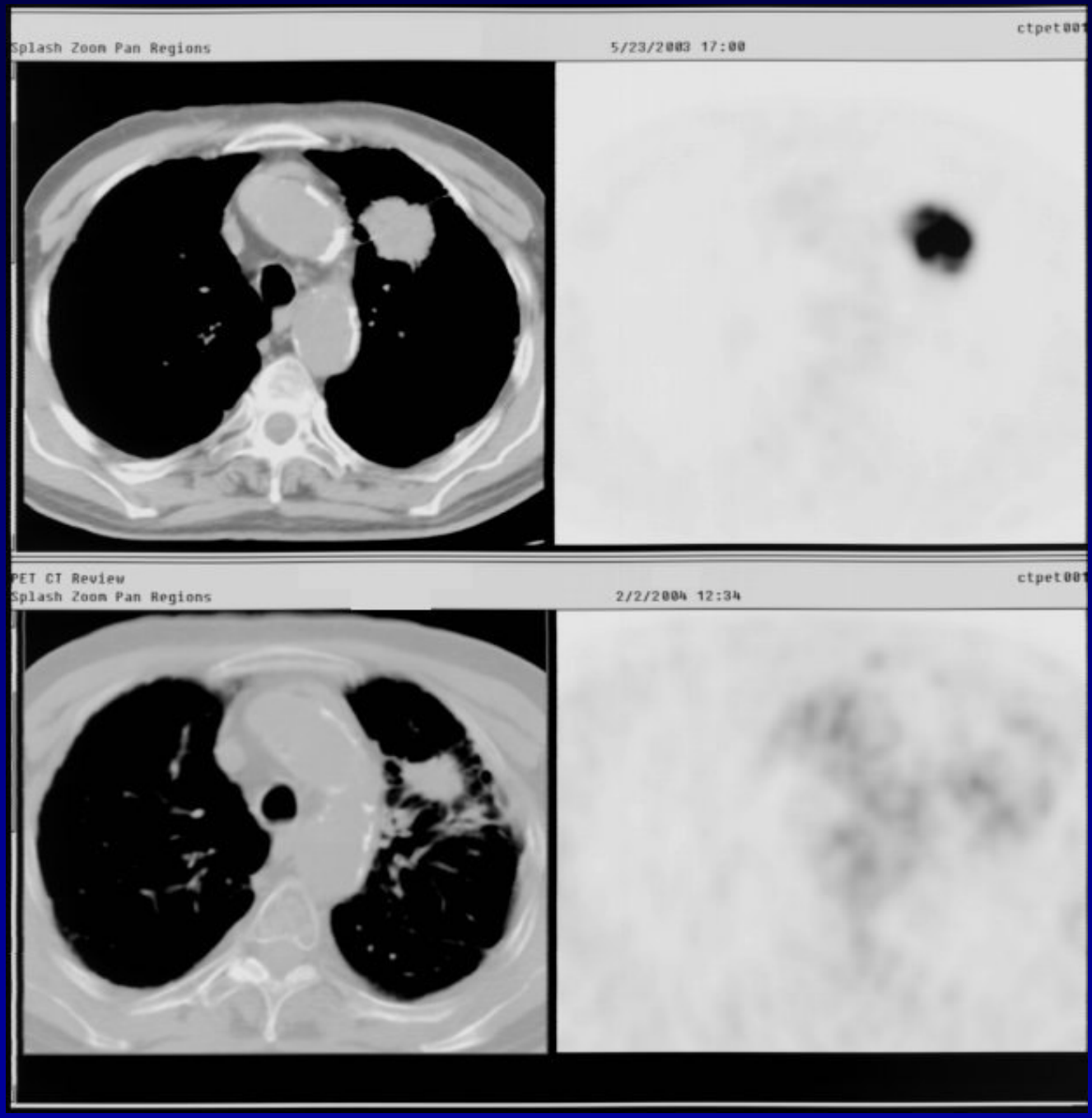


PET DI STAGING

TC RESTAGING A 3 MESI

PET RESTAGING A 6 MESI




Splash Zoom Pan Regions
5/23/2003 17:00
PET CT Review
Splash Zoom Pan Regions
2/2/2004 12:34

CONCLUSIONI

- La RT ipofrazionata con localizzazione stereotattica negli stadi iniziali del NSCLC è un trattamento ben tollerato
- Al fine di ottenere un buon controllo locale è necessario somministrare una dose elevata (BED_{10}: 100 Gy)
- Rispettando i constraints di dose suddetti, non è stata osservata alcuna tossicità significativa alle dosi somministrate

Table 1
Summary of the results on SBRT for primary lung cancer

Author (Refs.)	Year	Number of patients	Median follow-up (months)	Prescribed dose	Reference point	Isocenter dose (Gy)	BED[a] (Gy)	Overall survival rate (%)	Local control rate (%)
Uematsu et al. [14]	2001	50	36	50–60 Gy/5–10 fr.	Isocenter	50–60	96–100	66 (3 years)	94
Fukumoto et al. [3]	2002	22	24	48–60 Gy/8 fr.	Isocenter	48–60	76.8–105	NA	94
Hof et al. [4]	2003	10	15	19–26 Gy/1 fr.	Isocenter	19–26	55.1–93.6	64	80
Wulf et al. [15]	2004	20	11	30–37.5 Gy/3 fr.	Periphery	45–56.25	113–162	32	92
Onishi et al. [11]	2004	35	13	60 Gy/10 fr.	Periphery	70–75	119–131	58	94
McGarry et al. [6]	2005	47	27 (T1), 19 (T2)	24–72 Gy/3 fr.	Periphery	30–90	60–360	NA	79
Zimmermann et al. [17]	2005	30	18	37.5 Gy/3 fr.	Periphery	62.5	193	75	87
Nagata et al. [7]	2005	45	30	48 Gy/4 fr.	Isocenter	48	106	83 (T1), 72 (T2)	98
Nyman et al. [9]	2006	45	43	45 Gy/3 fr.	Periphery	63	195	71	80
Beitler et al. [2]	2006	75	17	40 Gy/5 fr.	Periphery	47	91.2	45	NA

[a] Biologically effective dose at the isocenter with α/β ratio of 10.

Recommendations for implementing stereotactic radiotherapy in peripheral stage IA non-small cell lung cancer: report from the Quality Assurance Working Party of the randomised phase III ROSEL study

Coen W Hurkmans*[1], Johan P Cuijpers[2], Frank J Lagerwaard[2], Joachim Widder[3], Uulke A van der Heide[4], Danny Schuring[1] and Suresh Senan[2]

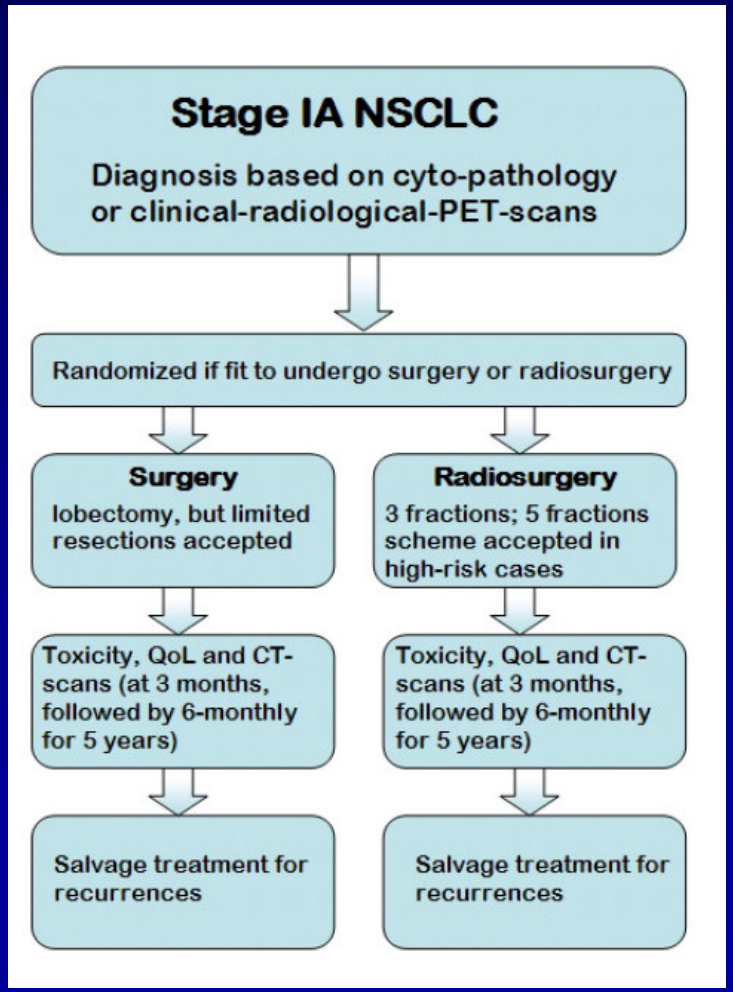


Table 1: Dose conformity requirements and definition of protocol deviations. $R_{100\%}$ and $R_{50\%}$ = ratio of respectively the 100% and 50% Prescription Isodose Volume to the PTV. $D_{2\ cm}$ = dose maximum at 2 cm from the PTV as percentage of the prescribed dose. $V_{20\ Gy}$ = Percent of lung receiving 20 Gy or more (both lungs minus GTV).

Type A models (standard algorithms)								
$R_{100\%}$		$R_{50\%}$		$D_{2\ cm}$ (%)		$V_{20\ Gy}$ (%)		PTV (cc)
Deviation		Deviation		Deviation		Deviation		
None	Minor	None	Minor	None	Minor	None	Minor	
<1.15	1.15–1.25	<8	8–10	<55	55–60	<4	4–6	0–20
<1.15	1.15–1.25	<7	7–8	<65	65–70	<6	6–8	20–40
<1.10	1.10–1.20	<6	6–6.5	<65	65–75	<8	8–10	>40
Type B models (more advanced algorithms)								
$R_{100\%}$		$R_{50\%}$		$D_{2\ cm}$ (%)		$V_{20\ Gy}$ (%)		PTV (cc)
Deviation		Deviation		Deviation		Deviation		
None	Minor	None	Minor	None	Minor	None	Minor	
<1.25	1.25–1.40	<12	12–14	<65	65–75	<5	5–8	0–20
<1.15	1.15–1.25	<9	9–11	<70	70–80	<6	6–10	20–40
<1.10	1.10–1.20	<6	6–8	<70	70–80	<10	10–15	>40

Table 2: Dose constraints for organs at risk and definition of protocol deviations.

Organ	Volume (cc)	Deviation given as cumulative absolute dose (Gy)			
		3 fraction scheme		5 fraction scheme	
		None	Minor	None	Minor
Spinal Cord	Any point	18	> 18 to 22	25	> 25 to 28
Oesophagus	1	24	> 24 to 27	27	> 27 to 28.5
Ipsilateral Brachial Plexus	1	24	> 24 to 26	27	> 27 to 29
Heart	1	24	> 24 to 26	27	> 27 to 29
Trachea and main stem bronchus	1	30	> 30 to 32	32	> 32 to 35

CONCLUSIONI

- **Problemi limitanti un'ulteriore escalation di dose:**

  Una definizione del GTV più accurata(ottimizzazione tecniche di imaging anatomico-funzionale)

  Un miglioramento della riproducibilità del trattamento e del controllo dell'attività respiratoria (image guided RT, dispositivi di controllo del respiro)

- **Non vi è ancora evidenza riguardo la modalità ottimale di frazionamento della dose. ulteriori studi sono necessari per definire il ruolo delle tecniche ipofrazionate**

HYPOFRACTIONATED RADIOTHERAPY WITH STEREOTACTIC LOCALIZATION IN THORACIC METASTASES

G. Frezza.
U.O. di Radioterapia
Ospedale Bellaria
Bologna

Introduction

- Standard local treatment for solitary lung metastases from selected primaries is surgical resection.

- In pts considered medically or functionally inoperable hypofractionated stereotactic radiotherapy is a alternative treatment.

CLINICAL EXPERIENCE AT OSPEDALE BELLARIA

STEREOTACTIC RADIATION THERAPY IN THE TREATMENT OF THORACIC METASTASES OR RECURRENT THORACIC TUMORS AT OSPEDALE BELLARIA

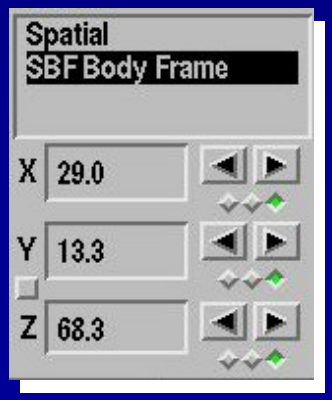
- **August 2004 - December 2007**
- **33 pts, 12 females and 21 males**
- **Age: 38 - 80 years (mean age 60,6)**
- **41 lesions:**

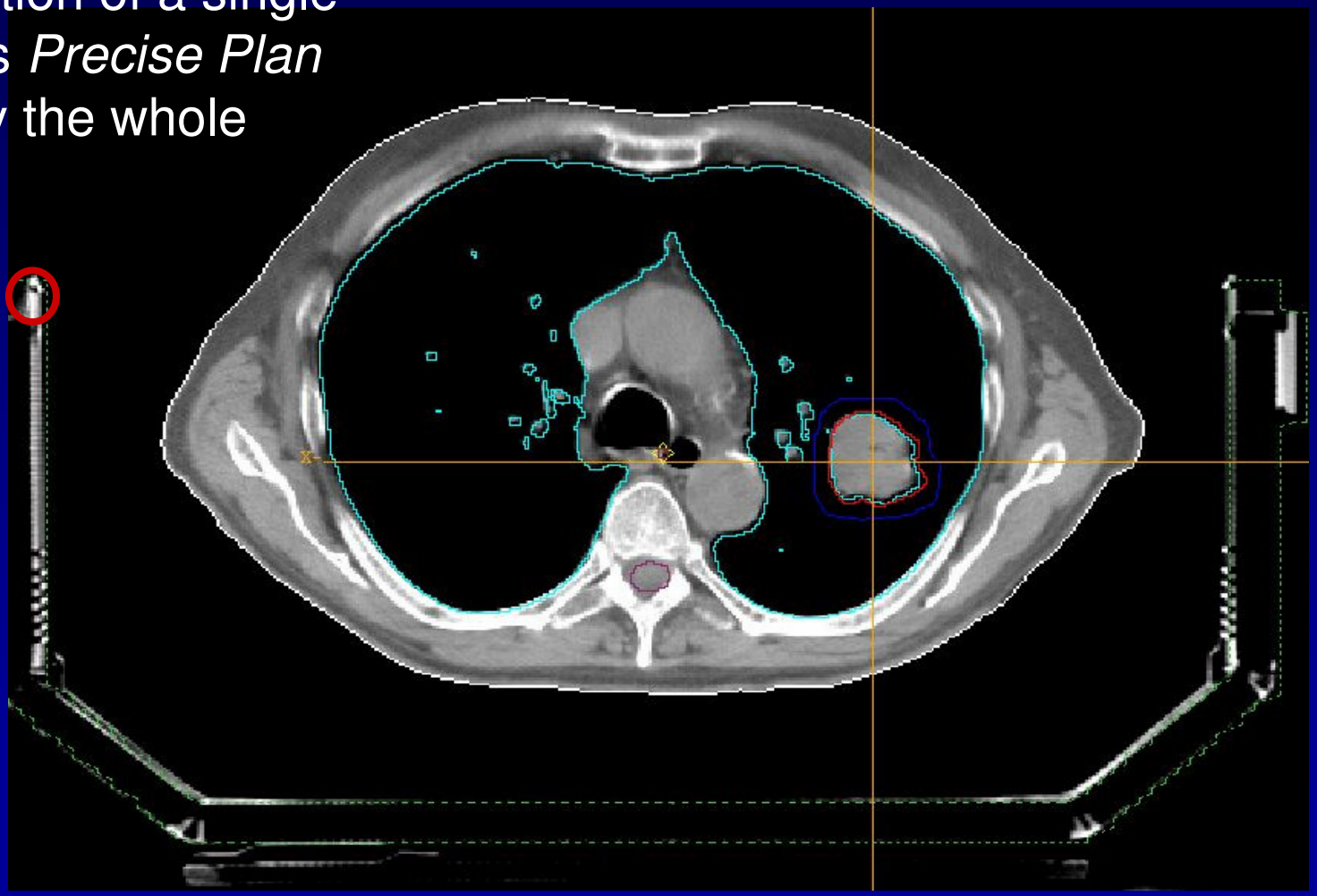
  - 7 local recurrence of lung cancer

  - 34 lung metastases of various cancer (10 colon rectum; 7 breast; 1 kidney; 10 lung; 1 ureter; 1 ovary; 3 mesothelioma, 1 thyroid)

AUTOMATED IDENTIFICATION OF THE FRAME

The identification of a single marker allows *Precise Plan 3 D* to identify the whole frame

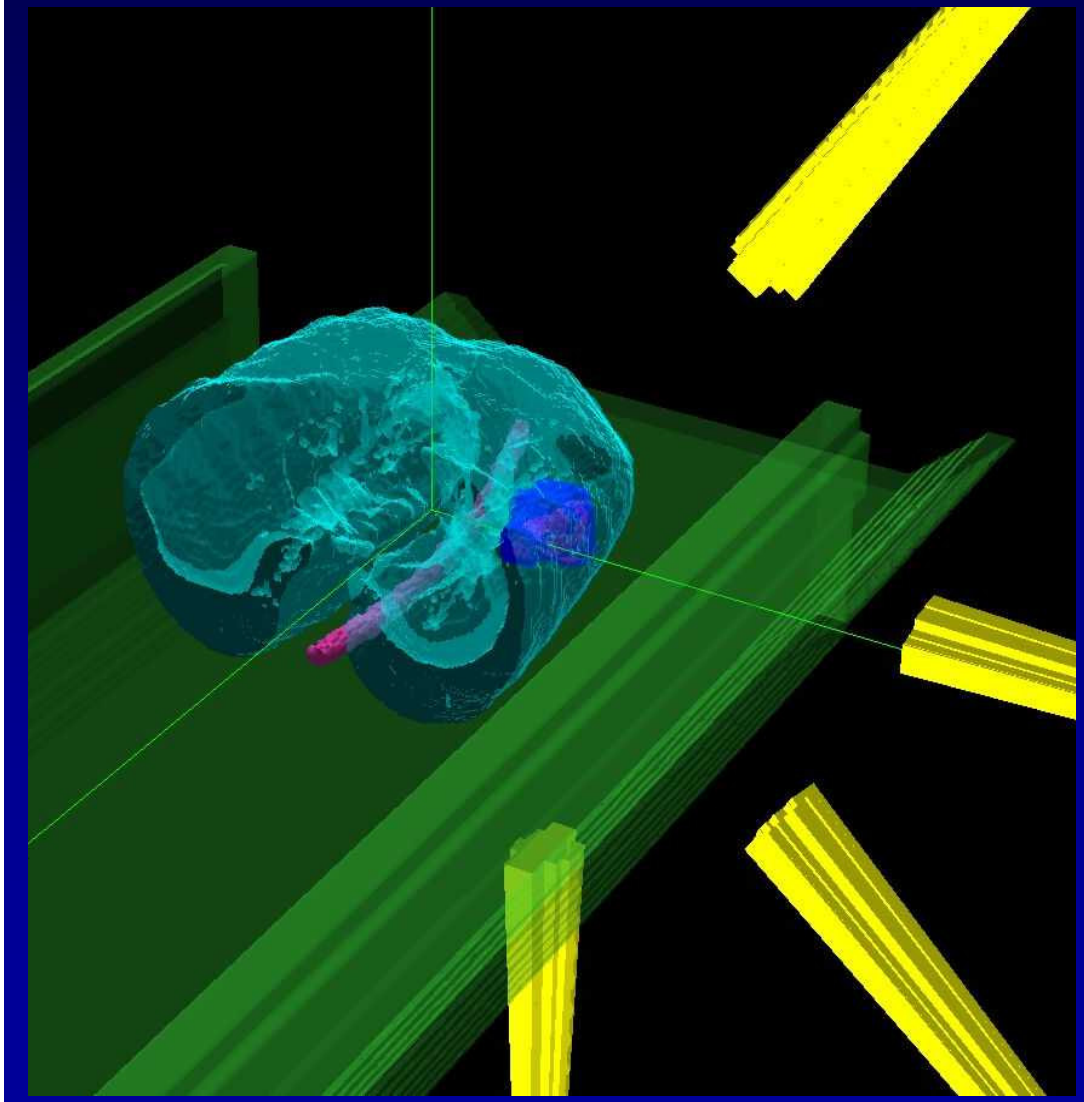




STEREOTACTIC RADIATION THERAPY IN THE TREATMENT OF THORACIC METASTASES OR RECURRENT THORACIC TUMORS AT OSPEDALE BELLARIA

- **GTV and OAR were delineated on CT scan acquired for treatment planning (3 mm spaced sections)**
- **CTV was obtained with a 5 mm isotropic expansion of GTV**
- **PTV was obtained adding to CTV a 5 mm margin on transversal plane and a 10 mm margin in cranio-caudal direction**

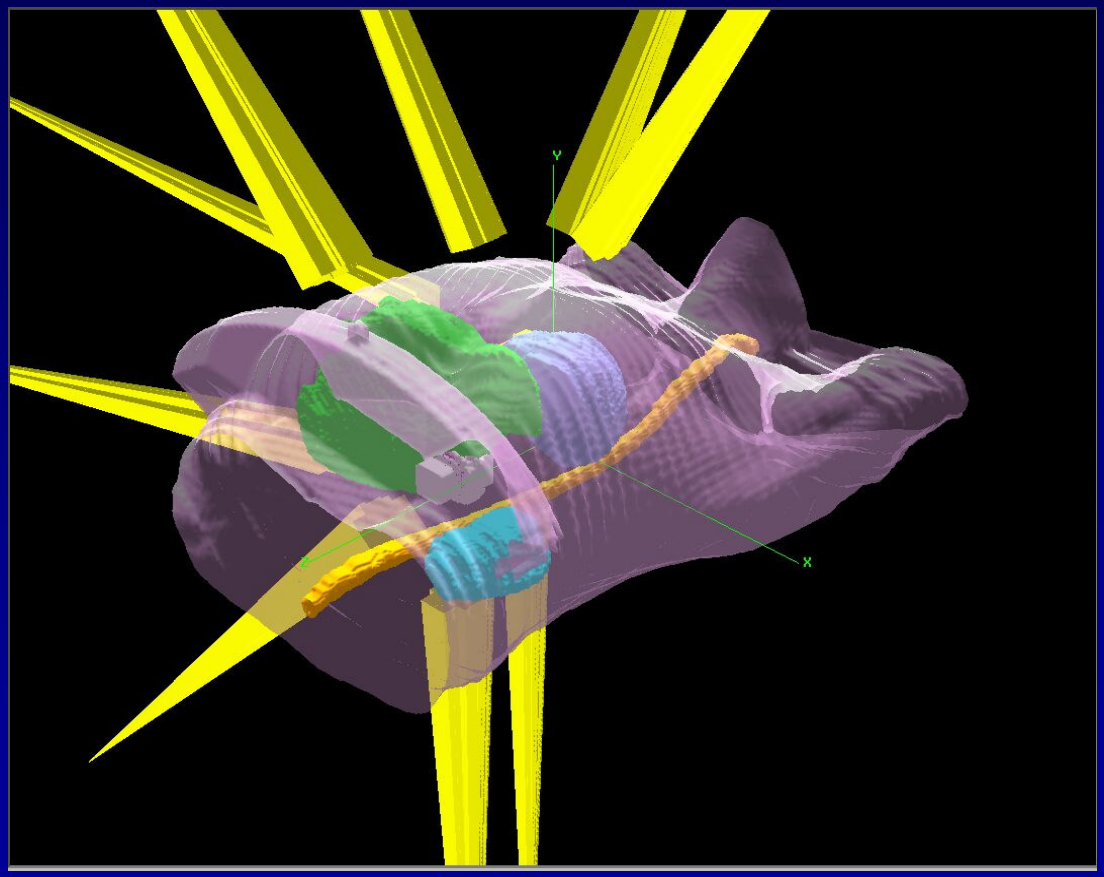
TREATMENT PLANNING



Treatment technique

- 6-9 static fields, 6-10 MV
- Conformation with MLC
- Not coplanar fields distributed over a wide solid angle
- No opposed fields

DOSE PRESCRIPTION AND FRACTIONATION



- Isocenter = point of dose normalization
- Minimal dose to PTV: 80%
- 3 - 5 fractions
- 10-12 Gy/fx to isocenter

- **Dose costraints to OAR were the following:**

Lung: V12 < 20% Vol

Heart: V15 Gy < 10% Vol

Cord: < 15Gy (5 fx); <13,5 Gy (3 fx)

Esophagus: < 4 Gy/fraction

- Total dose to isocenter was 30 Gy/3 fractions in 9 lesions, 36 Gy/3 fractions in 8 lesions and 50 Gy/5 fractions in the remaining lesions (according to performance status, number of lesions, respect of OAR costraints). Treatments was performed on 3-5 consecutive daily fraction (3-8 days:mean 4,5 days).

- In all pts with more than one lesion treatment was performed in different courses (dose distribution was however calculated as the sum of all treatments)

- V12 to lung ranged from 0,5% to 21,1% of volume (mean 11,1 %)

- Mean dose to lung ranged from 43 cGy to 777 cGy (mean 426 cGy)

STEREOTACTIC RADIATION THERAPY IN THE TREATMENT OF THORACIC METASTASES OR RECURRENT THORACIC TUMORS AT OSPEDALE BELLARIA

- **CTV volume ranged from 6,9 to 108,5 cc (mean: 28,73)**
- **PTV volume ranged from 26,9 to 246,9 cc (mean 76,2)**
- **10-12 Gy per fraction were prescribed at isocenter, ensuring that 80% isodose encompassed the PTV (minimal dose to PTV)**

STEREOTACTIC RADIATION THERAPY IN THE TREATMENT OF THORACIC METASTASES OR RECURRENT THORACIC TUMORS AT OSPEDALE BELLARIA

FOLLOW UP in 19 pts. (25 lesions) alive > 6 mos.

range: 7 to 37 months (median : 17,8 months)

RESULTS *

Dose	Lesions	RC (%)	RP (%)
30 Gy / 3 fx.	9	6/9 (66,6%)	3/9 (33,3%)
36 Gy / 3 fx.	8	6/8 (75,0%)**	2/8 (25,0%)
50 Gy / 5 fx	8	8/8 (100,0%)	-

*** Response evaluated with CT scan (19/19 pts) and PET scan (9/19pts) after 6 months**

**** 2 lesions are in RP according CT but in RC according to PET.**

STEREOTACTIC RADIATION THERAPY IN THE TREATMENT OF THORACIC METASTASES OR RECURRENT THORACIC TUMORS AT OSPEDALE BELLARIA

10/19 (52,6%) pts. relapsed in distant sites (min 3 - max 18 months: mean 8 months)

Lung: 2 pts

Brain: 2 pts

Abdomen:1 pt

Adrenal gland: 2 pts

Bone: 1 pt

Pleura: 1 pt

Liver: 1 pt

Radioterapia ipofrazionata con localizzazione stereotassica nelle metastasi addominali e nelle recidive di tumori dell'addome

Giovanni Frezza
U. O. Radioterapia Ospedale Bellaria
Bologna

La radioterapia stereotassica extracranica rappresenta una tecnica sempre più utilizzata nel trattamento di metastasi e lesioni primitive di dimensioni contenute, localizzate in più organi (es. polmone, fegato, e altre sedi in addome e pelvi).

Table 2 Overview of Selected Clinical Results Using SBRT

Treatment Site	Total Dose and Fractionation	Local Control (percent)	References
Spine	6-30 Gy in 1-5 fractions (many with previous CFRT)	>95%	10, 11, 29
Lung – Primary Lung Cancer	15-66 Gy in 1-5 fractions	80-95%	2-4, 6-9
Lung – Metastatic	36-60 Gy in 3-5 fractions	60-90%	2,4,6
Liver – Primary and Metastatic	20-45 Gy in 1-3 fractions	75-95%	2,4,5
Retroperitoneal (kidney)	30-40 Gy in 2-4 fractions	Not reported	30
Pelvic (prostate)	33.5 in 5 fractions	Not reported	31-32

Semin Radiat Oncol 15:202-207 © 2005

Table 5b. Comparison of published treatment results of stereotactic irradiation for targets in the liver. Data with * have been recalculated from the data of the original publication of Blomgren et al [2] for easier comparison of results. The median of the follow-up for the targets of Blomgren et al could not be re-calculated because the f/u data are not published in detail. HCC: hepatocellular carcinoma; CCC: cholangiocellular carcinoma.

Tabelle 5b. Vergleich der bisher veröffentlichten Behandlungsergebnisse der stereotaktischen Bestrahlung von Zielvolumina in der Leber. Die mit * versehenen Daten wurden aus den Angaben der Publikation von Blomgren et al. [2] nachträglich berechnet, um die Ergebnisse besser vergleichen zu können. HCC: hepatozelluläres Karzinom; CCC: cholangiozelluläres Karzinom.

Author	Indication	No of cases	Dose/fractionation/normalization	Volume of CTV (median) (cm^3)	Median f/u (min-max) (months)	Local control (crude)	Local control (actuarial)
Blomgren et al [2]	HCC, CCC	n = 20	3 × 10 to 2 × 15 Gy/ 65%-isodose	3–622 (22)*	12 (mean) (1.5–38)	20/20 (100%)	Not reported
Blomgren et al [2]	Metastases	n = 21	3 × 10 to 2 × 15 Gy/ 65%-isodose	2–263 (24)*	9.6 (mean) (1.5–28)	20/21 (95%)	Not reported
Herfarth et al [6]	Metastases	n = 60	1 × 14 to 1 × 24 Gy/ isocenter	1–132 (10)	5.7 (1–26) (78%)	47/60	All targets: 71% (12 months) 67% (18 months) After dose escalation: 81% (18 months)
Wulf et al (presented study)	Metastases CCC	n = 23 n = 1	3 × 10 Gy/65%-isodose	9–516 (50)	9 (2–28)	19/23 (83%)	76% (12 months) 61% (24 months)

OBIETTIVI

Valutare efficacia e tossicità del trattamento radiante con tecnica ipofrazionata in pazienti affetti da lesioni secondarie o recidive addominali, mediante l'utilizzo di un frame stereotassico.

Casistica Ospedale Bellaria

- Da Maggio 2003 a Gennaio 2008 sono stati trattati 22 pazienti non suscettibili di chirurgia o di altri trattamenti locali (26 lesioni)
- 12 M, 10 F
- Età media 64,2 (min 39, max 75)

Staging

- TC torace addome (22 pazienti)
- 18FDG-PET (13 pazienti)

TIPOLOGIA LESIONI

16	Metastasi epatiche
7	Metastasi surrenaliche
1	Metastasi linfonodale lomboaortica
1	Metastasi renale
1	Recidiva pancreatica

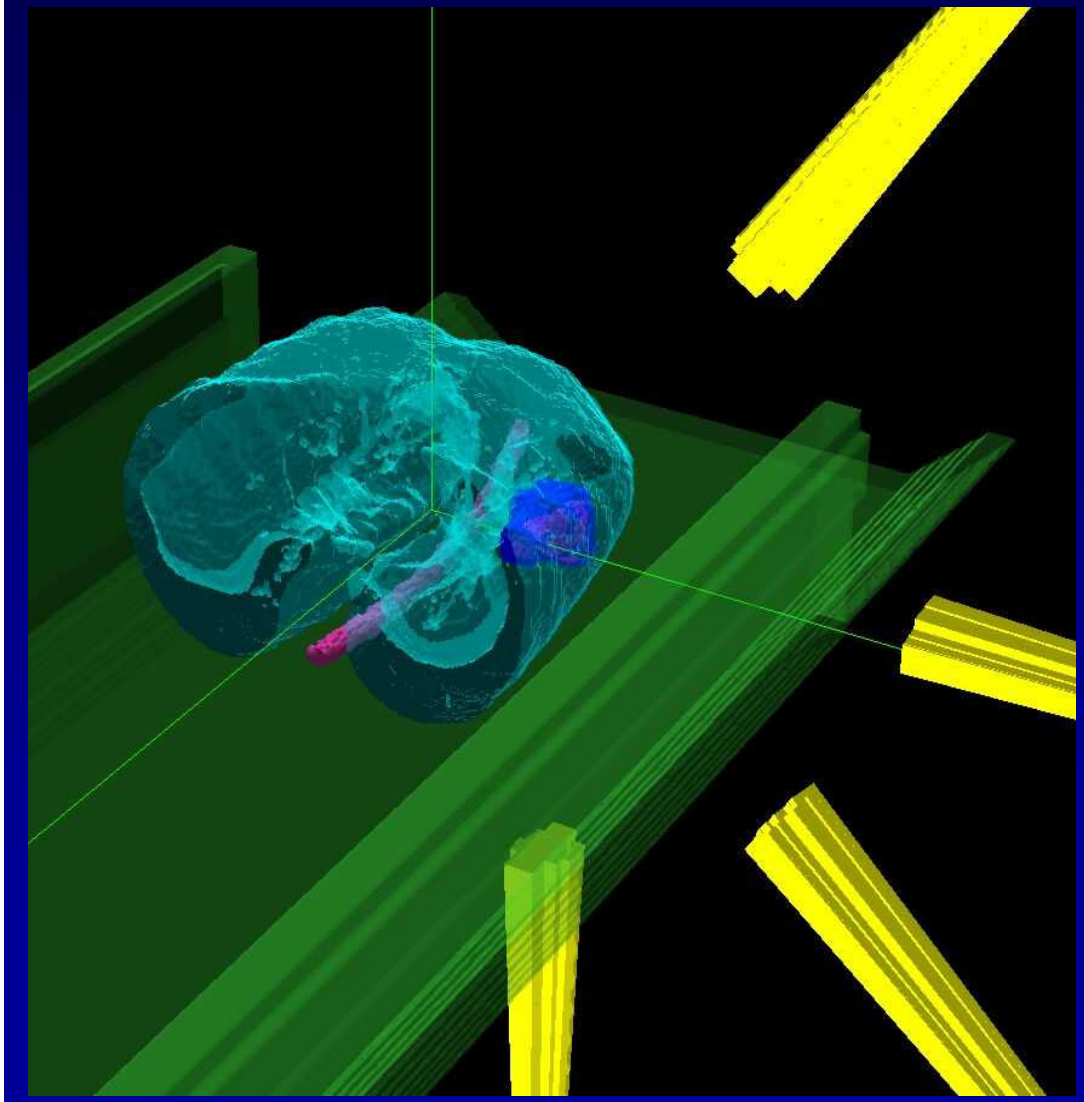
SEDE TUMORE PRIMITIVO

mammella	5
polmone	5
colon	3
fegato	2
colecisti	1
ghiandole salivari	1
ovaio	1
retto	1
stomaco	1
pancreas	1

Tutti i pazienti sono stati posizionati in un frame dedicato (Elekta) ed è stato utilizzato un dispositivo meccanico di compressione addominale per ridurre i movimenti del diaframma.

E' stata eseguita una TC di centratura spirale slow (3sec/rot) con slice ogni 3 mm.

TREATMENT PLANNING



Treatment technique

- 6-9 static fields, 6-10 MV
- Conformation with MLC
- Not coplanar fields distributed over a wide solid angle
- No opposed fields

Definizione dei Volumi

- GTV (Gross Tumor Volume)
- CTV (Clinical Target Volume): GTV+ 5mm di espansione isotropica; medio 39.5 cc (range 2.96-147.3 cc)
- PTV (Planning Target Volume): CTV+ espansione assiale di 5 mm e longitudinale di 10 mm; medio 91.5 cc (range 14.4-359.2 cc)
- OAR (Organi A Rischio): fegato, reni, midollo spinale

DOSE PRESCRITTA

1 lesione	27 Gy
15 lesioni	30 Gy
9 lesioni	36 Gy
1 lesione	37.5 Gy

La dose è stata somministrata in 3 frazioni (1/die) mediante 4/6 fasci coplanari e non coplanari conformati mediante MLC, in modo che il PTV sia racchiuso dall'isodose 80%.

CONSTRAINTS DI DOSE AGLI OAR

MIDOLLO	< 13.5 Gy
FEGATO	V10 < 33% Vol. V15 < 700 cc
RENI	V12 < 33% Vol.

FOLLOW-UP

Esami di restaging: TC con mdc e/o 18FDG-PET

Durata follow-up da 9 a 33 mesi (mediano: 16 mesi)

RISULTATI

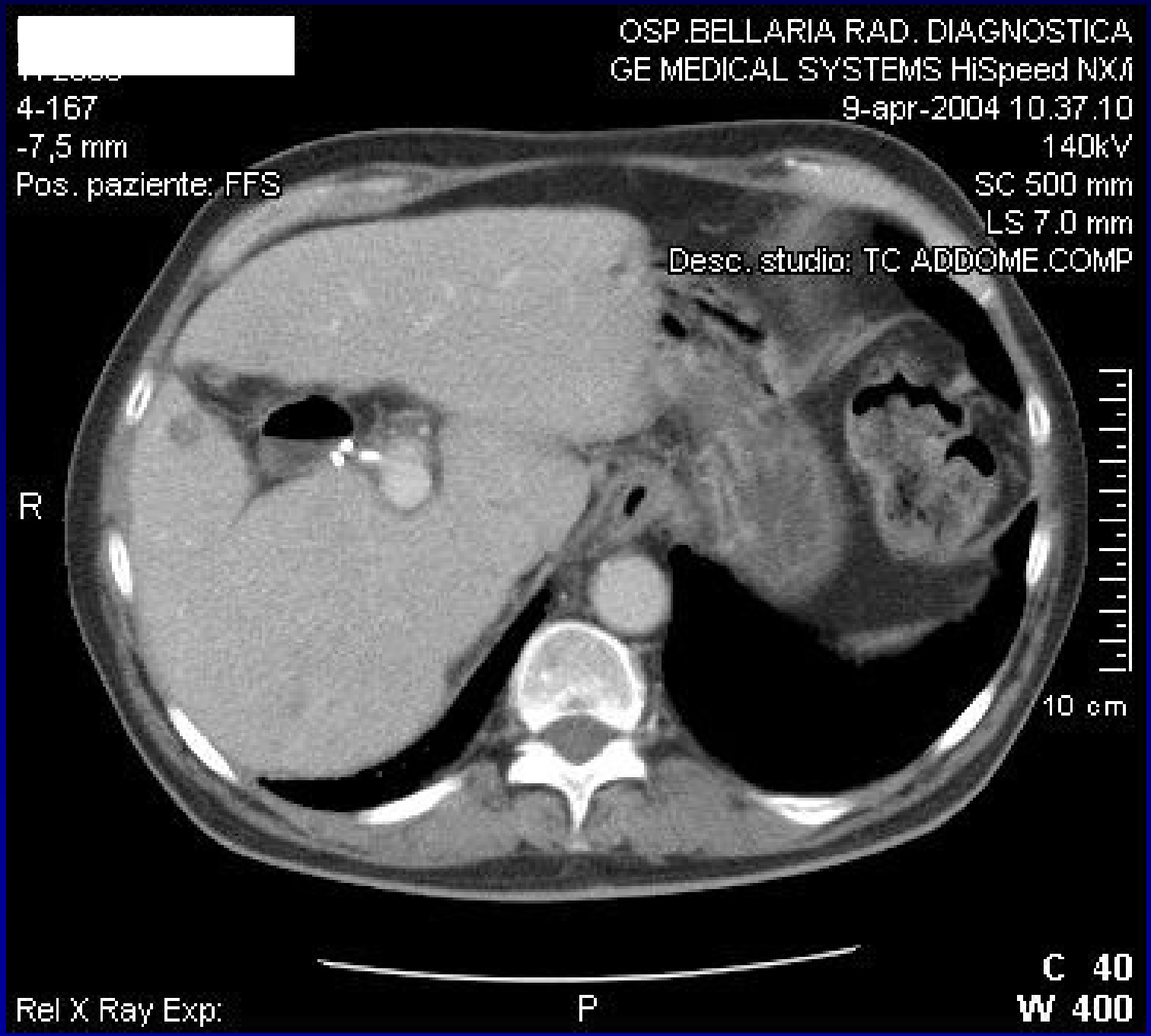
Risposta completa	12/26 lesioni (46%)
Risposta parziale	14/26 lesioni (54%)
Progressione di malattia nella sede trattata	0 (0%)

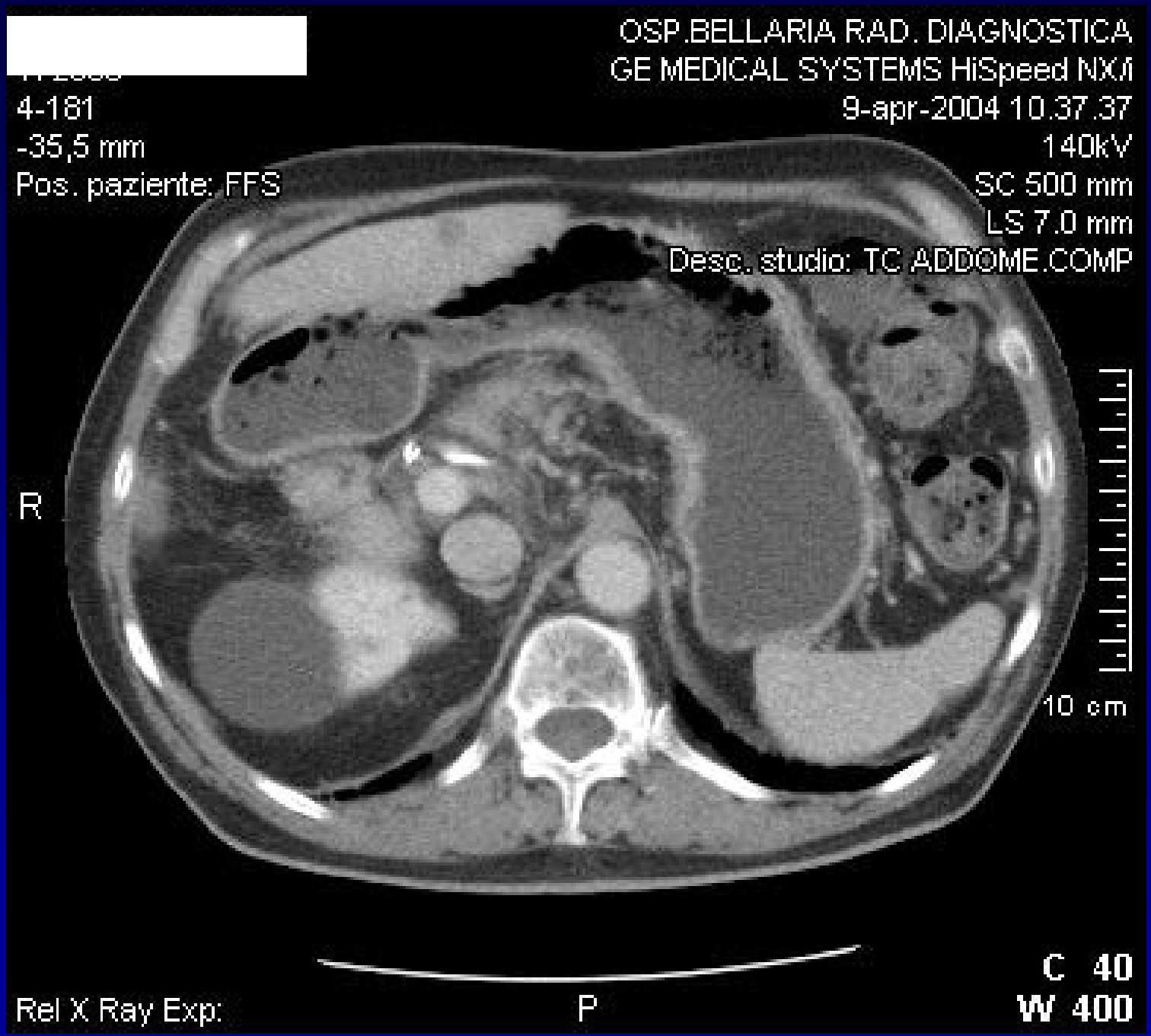
RISULTATI

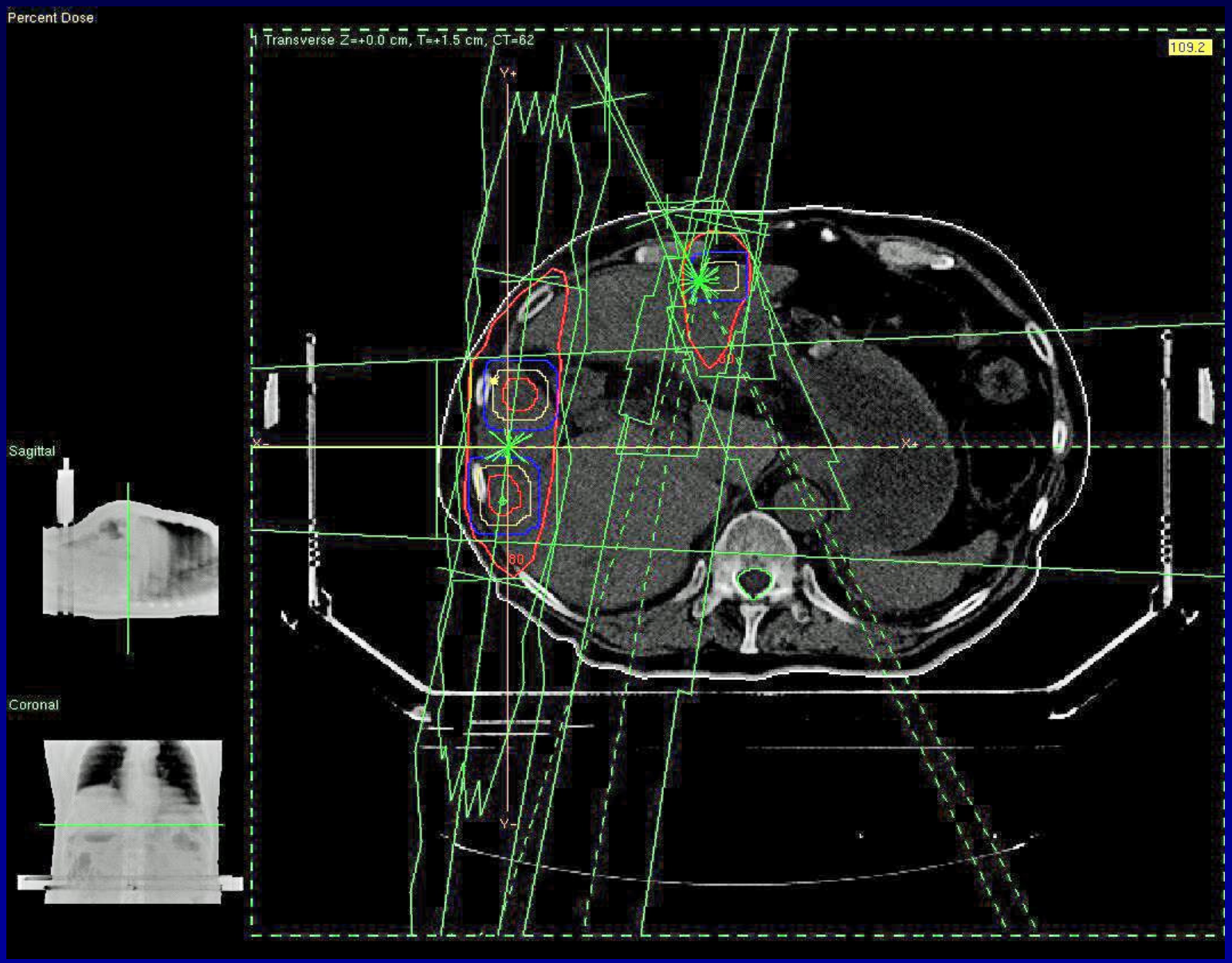
Nessun paziente ha sviluppato tossicità acuta o tardiva di Gr.> 2 (sec. Criteri RTOG).

15/22 pazienti hanno sviluppato metastasi a distanza

Pazienti deceduti: 8/22

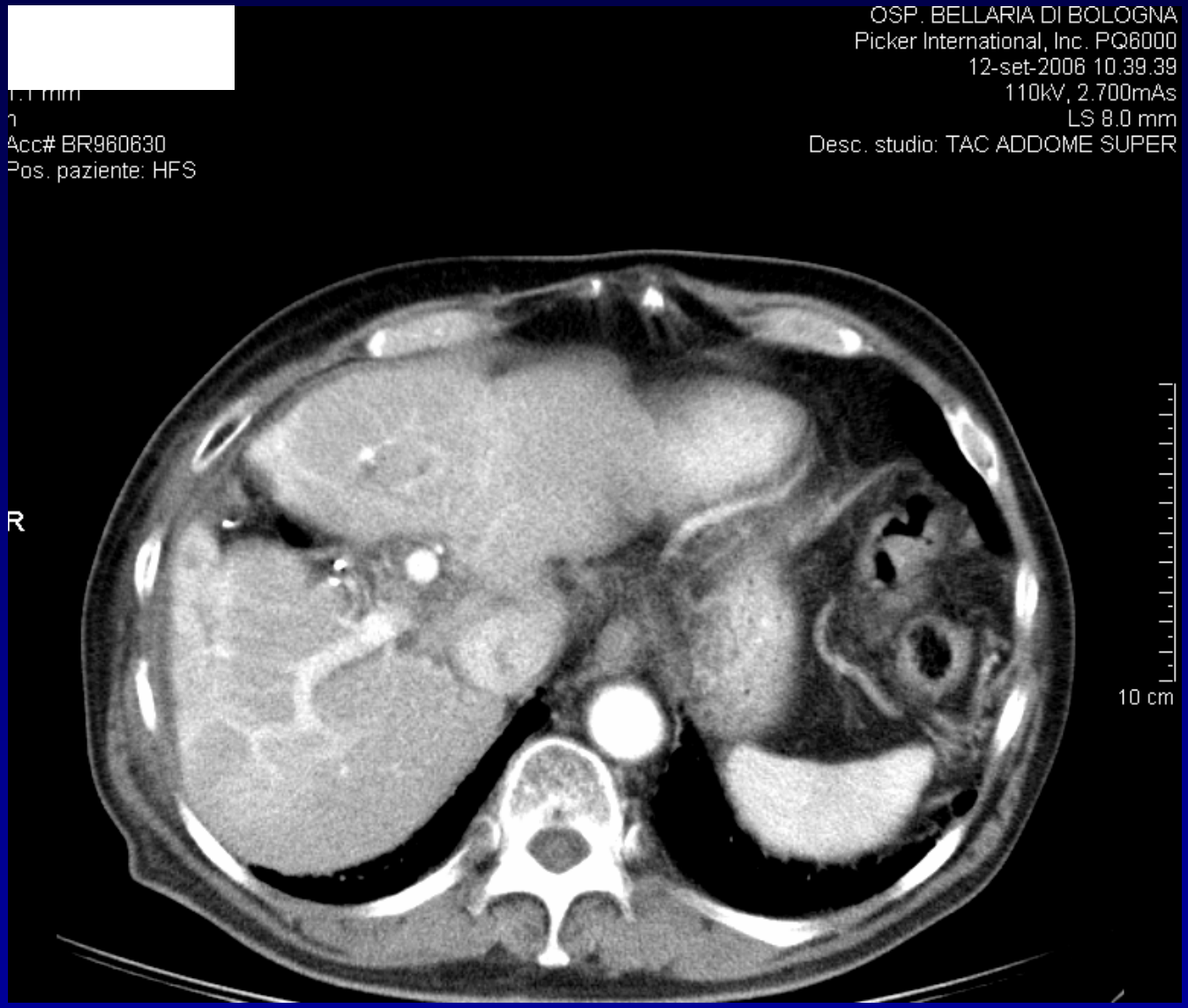

OSP.BELLARIA RAD. DIAGNOSTICA
GE MEDICAL SYSTEMS HiSpeed NX/i
4-167
9-apr-2004 10.37.10
-7,5 mm
140kV
Pos. paziente: FFS
SC 500 mm
LS 7.0 mm
Desc. studio: TC ADDOME.COMP
R
10 cm
Rel X Ray Exp:
P
C 40
W 400

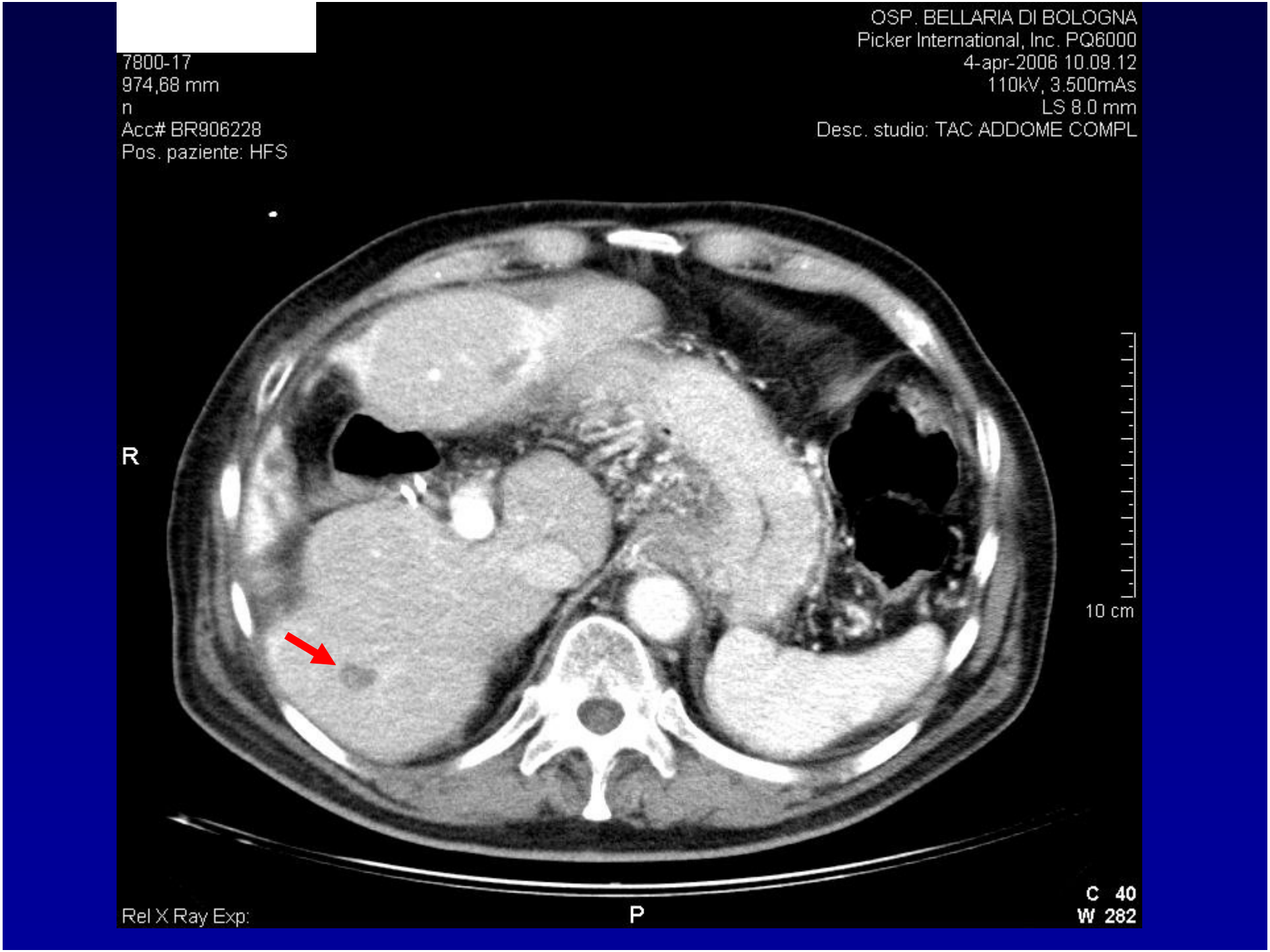

OSP.BELLARIA RAD. DIAGNOSTICA
GE MEDICAL SYSTEMS HiSpeed NX/i
4-181
9-apr-2004 10.37.37
-35,5 mm
140kV
Pos. paziente: FFS
SC 500 mm
LS 7.0 mm
Desc. studio: TC ADDOME.COMP
R
10 cm
C 40
W 400
Rel X Ray Exp:
P

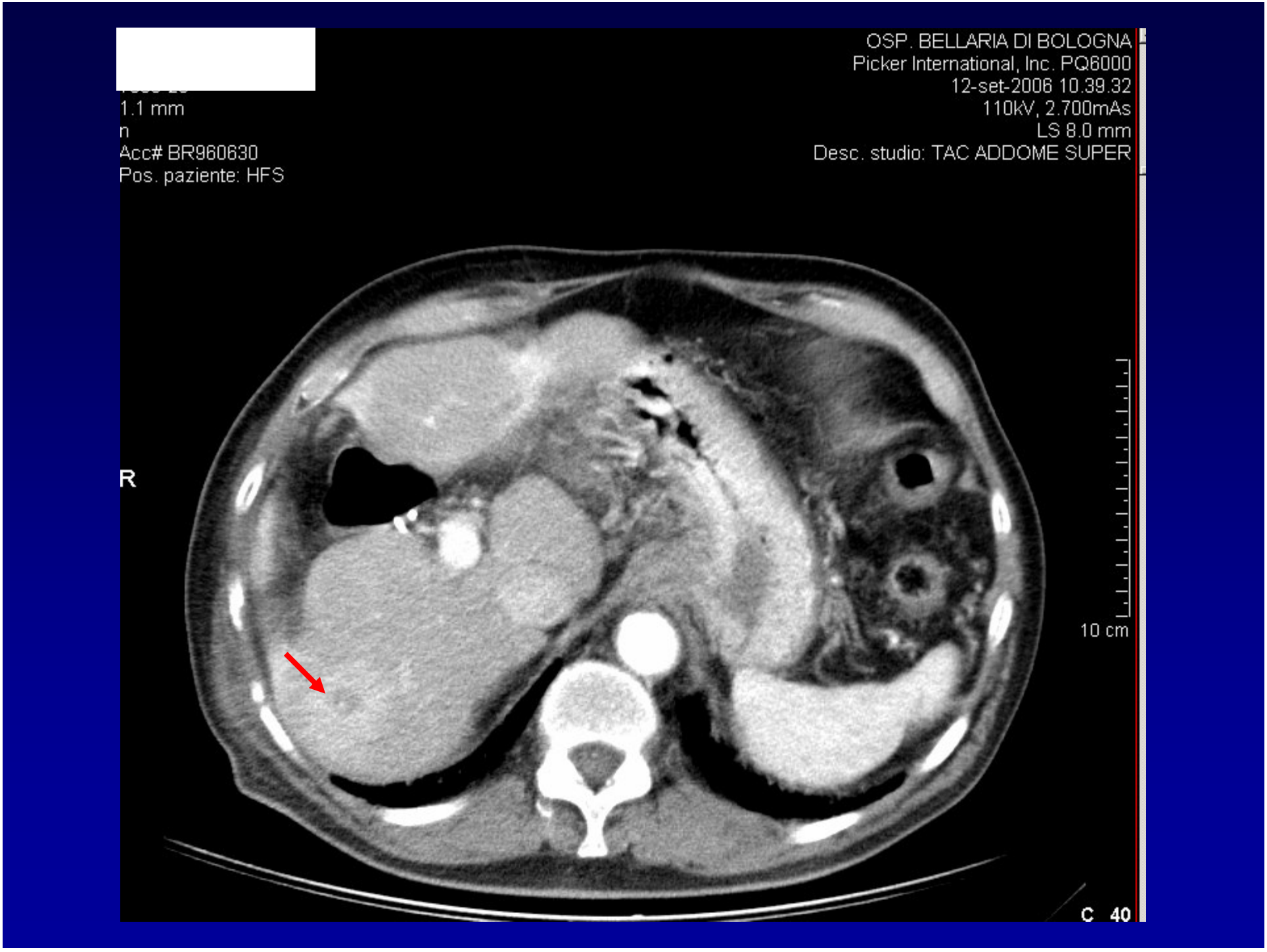

Percent Dose
Transverse Z=+0.0 cm, T=+1.5 cm, CT=62
109.2
Y+
X-
X+
80
Y-
Sagittal
Coronal

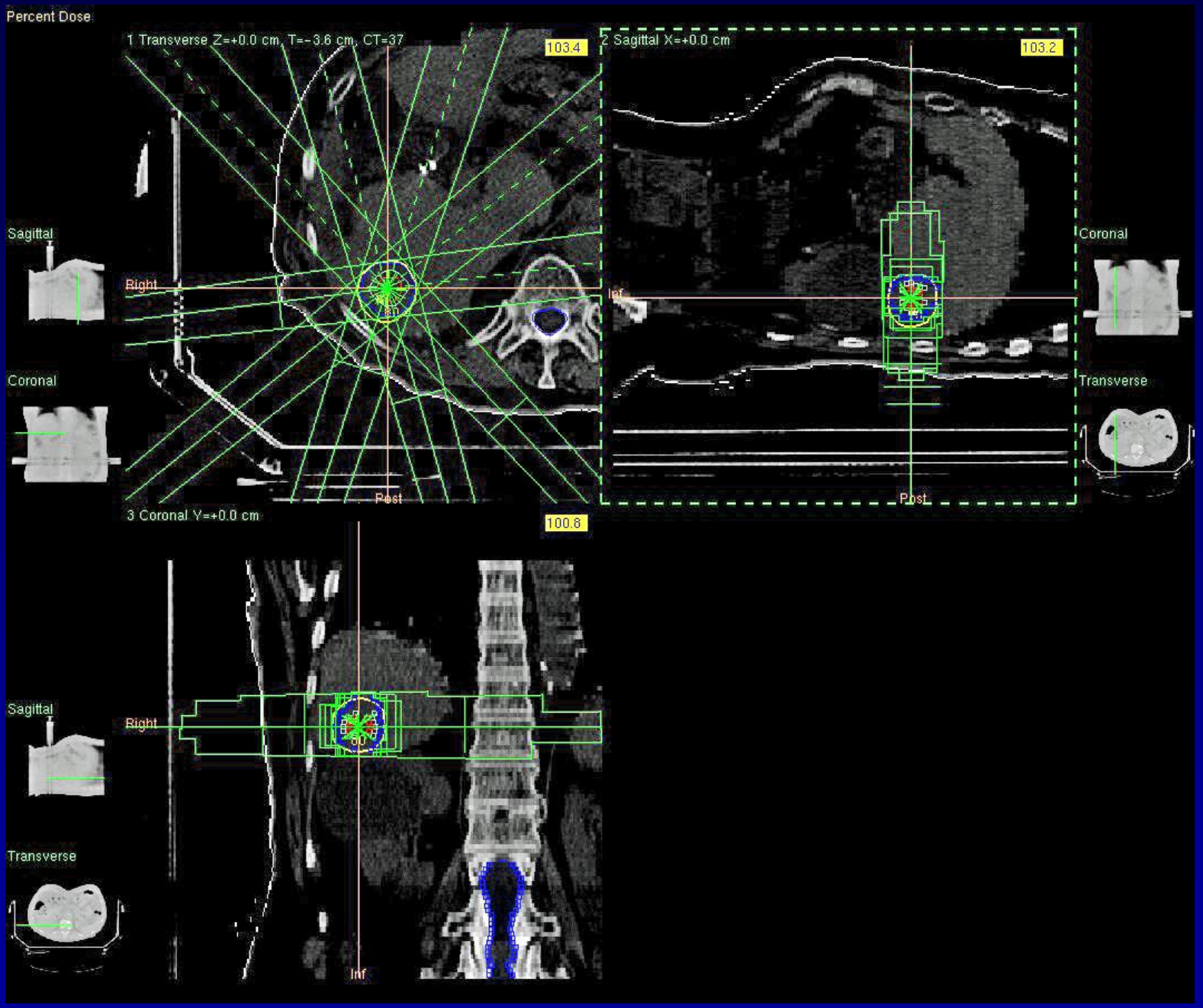

OSP. BELLARIA DI BOLOGNA
Picker International, Inc. PQ6000
4-apr-2006 10.09.09
110kV, 3.500mAs
LS 8.0 mm
Desc. studio: TAC ADDOME COMPL
7800-16
968,68 mm
n
Acc# BR906228
Pos. paziente: HFS
R
10 cm
Rel X Ray Exp:
P
C 40
W 300


OSP. BELLARIA DI BOLOGNA
Picker International, Inc. PQ6000
4-apr-2006 10.09.06
110kV, 3.500mAs
LS 8.0 mm
Desc. studio: TAC ADDOME COMPL
962,68 mm
n
Acc# BR906228
Pos. paziente: HFS
R
10 cm
Rel X Ray Exp:
P
C 40
W 300


OSP. BELLARIA DI BOLOGNA
Picker International, Inc. PQ6000
12-set-2006 10.39.39
110kV, 2.700mAs
LS 8.0 mm
Desc. studio: TAC ADDOME SUPER
Acc# BR960630
Pos. paziente: HFS
R
10 cm


OSP. BELLARIA DI BOLOGNA
Picker International, Inc. PQ6000
4-apr-2006 10.09.12
110kV, 3.500mAs
LS 8.0 mm
Desc. studio: TAC ADDOME COMPL
7800-17
974,68 mm
n
Acc# BR906228
Pos. paziente: HFS
R
10 cm
C 40
W 282
Rel X Ray Exp:
P


OSP. BELLARIA DI BOLOGNA
Picker International, Inc. PQ6000
12-set-2006 10.39.32
110kV, 2.700mAs
LS 8.0 mm
Desc. studio: TAC ADDOME SUPER
1.1 mm
n
Acc# BR960630
Pos. paziente: HFS
R
10 cm
C 40


Percent Dose
1 Transverse Z=+0.0 cm, T=-3.6 cm, CT=37
103.4
Sagittal
Right
Coronal
Post
2 Sagittal X=+0.0 cm
103.2
Inf
Coronal
Post
Transverse
3 Coronal Y=+0.0 cm
100.8
Sagittal
Right
Transverse
Inf

CONCLUSIONI

La radioterapia stereotassica, nelle metastasi addominali e nelle recidive di tumori dell'addome, consente di ottenere un ottimo controllo locale di malattia a prezzo di una modesta tossicità.

Un follow-up più lungo è però necessario al fine di valutare se tale risultato positivo si traduca in un effettivo miglioramento della durata della sopravvivenza.