

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliera Policlinico di
Modena

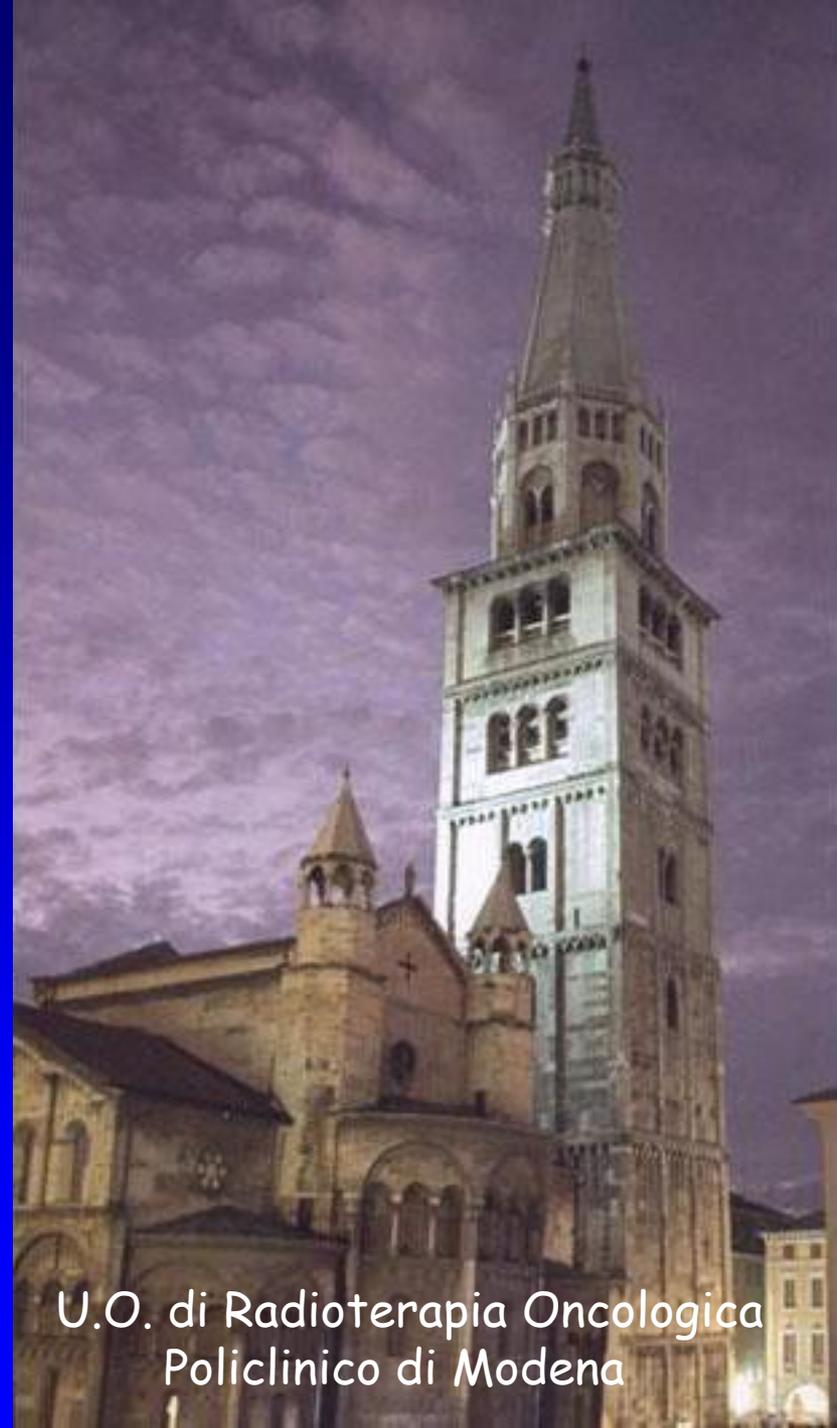


La TOMOTERAPIA in Italia: Esperienze a confronto

L'esperienza di Modena - Prostata

F. Bertoni

Bard 20 nov 2010



U.O. di Radioterapia Oncologica
Policlinico di Modena

**30 Aprile 2008: inizio installazione TomoTherapy presso
l'U.O. di Radioterapia del Policlinico di Modena.**



.....avvio attività clinica : 30/5/ 2008

2005:

....avvio del progetto cofinanziato di Technology Assessment....

La TomoTherapy nel 2010

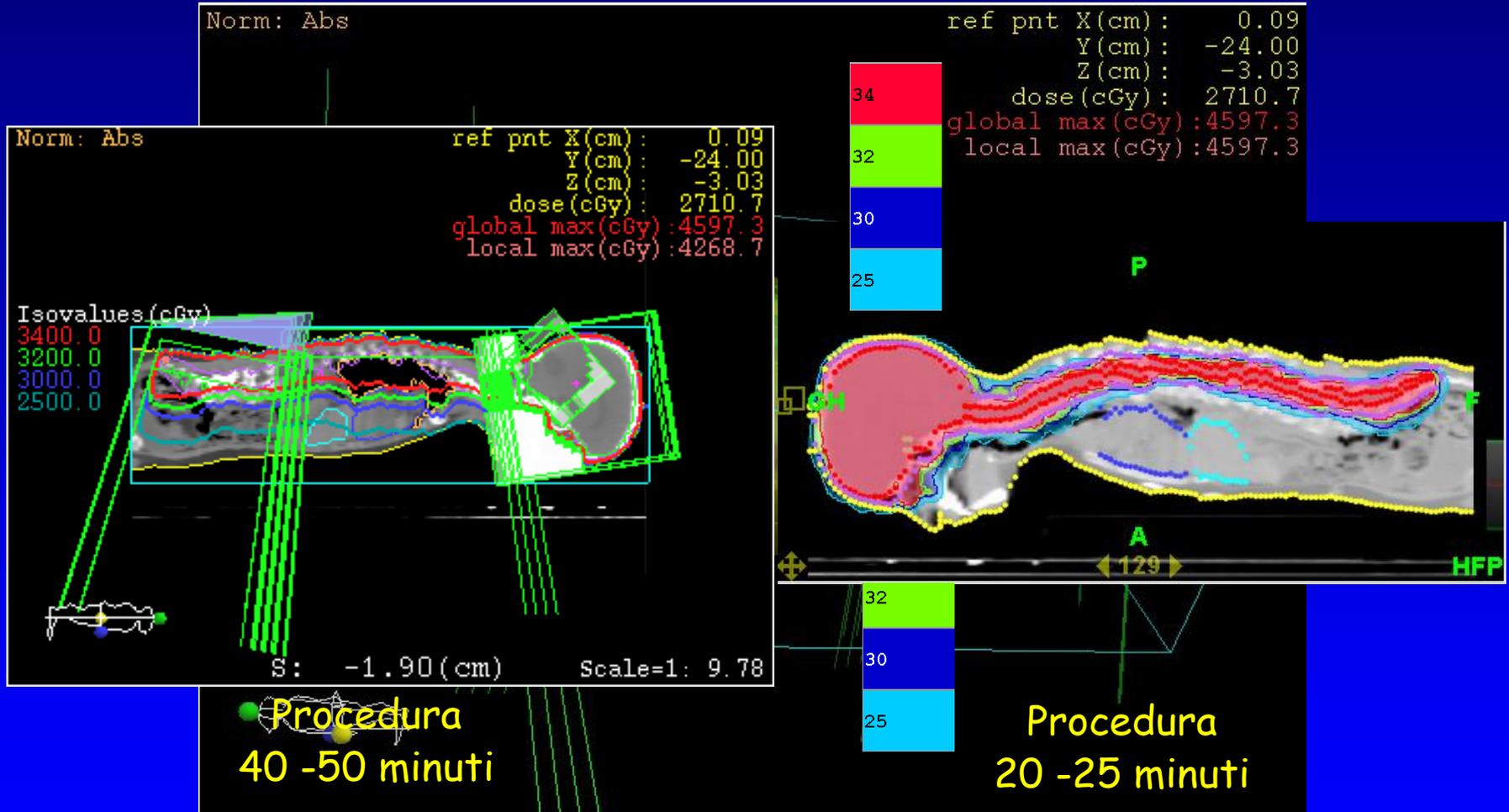


6 Clinical Research Program to acquire Tomotherapy

- 1. NSCLC** : Efficacy and tolerances of exclusive and post-surgery radiation therapy treatments with/without chemo association, using CT-PET and Dynamic IMRT. Patients survival and/or time to progression analysis. Procedures and cost-benefit evaluation. (Prof. L.Fabbri, Prof. U.Morandi, Prof. B.Bagni, Dr. F.Bertoni, Dr. C.Danielli)
- 2. H&N** : Radical treatments with concomitant chemotherapy using SIB, Dynamic IMRT, IGRT and Adaptive Radiation Therapy. Treatment conformity index, patients tolerance, efficacy and cost-benefit evaluation using Tomotherapy (Prof. P.E.Conte, Prof. A.Falchi, Dr. F.Bertoni, Dr. C.Danielli)
- 3. TBI** (National Health Research - PIO V): Clinical and dosimetric evaluation of Total Body Irradiation using Tomotherapy. Transplant procedure, adequacy and safety evaluations of the treatments using Tomotherapy. Problem solving, efficacy and efficiency. (Prof. G.Torelli, Dr. F.Bertoni, Dr. C.Danielli)
- 4. PAEDIATRIC** : Clinical evaluation of paediatric treatments. Paediatric patients management and performance assessment for high conformal and complex treatment using Tomotherapy. Clinical advantages and disadvantages. (Prof. P.Paolucci, Dr. F.Bertoni, Dr. C.Danielli)
- 5. BRAIN** : Clinical study for brain tumors using Tomotherapy. Clinical advantages and disadvantages, cost-benefit impact and patient management (Prof. G.Pinna, Dr. L.Mavilla, Prof. B.Bagni, Dr. F.Bertoni, Dr. C.Danielli)
- 6. TECHNOLOGY ASSESSMENT**: Technical, dosimetric and cost-benefit evaluation of a Tomotherapy Unit. Routine applicability in a Public Hospital of high conformal, IGRT and Adaptive Radiation Therapy treatments. Develop and optimization of treatment delivery, commissioning and Quality Assurance procedures. Time estimation and requirements to implement protocols and techniques (Dr. F.Bertoni, Dr. C.Danielli, Dr. Eng. M.Lugli)

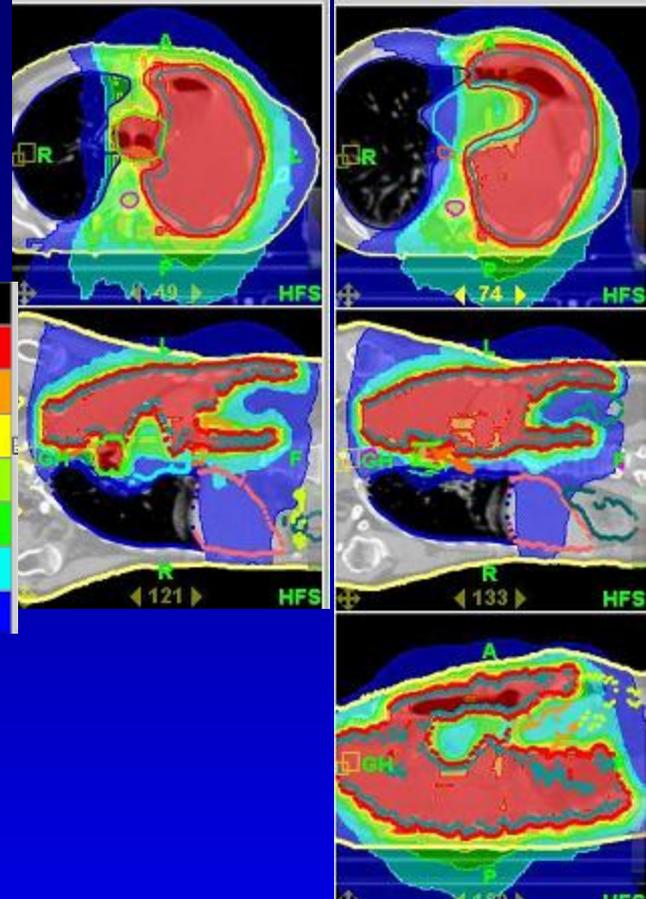
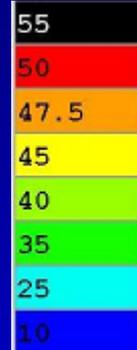
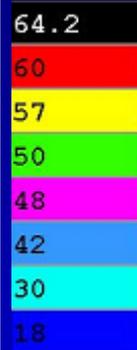
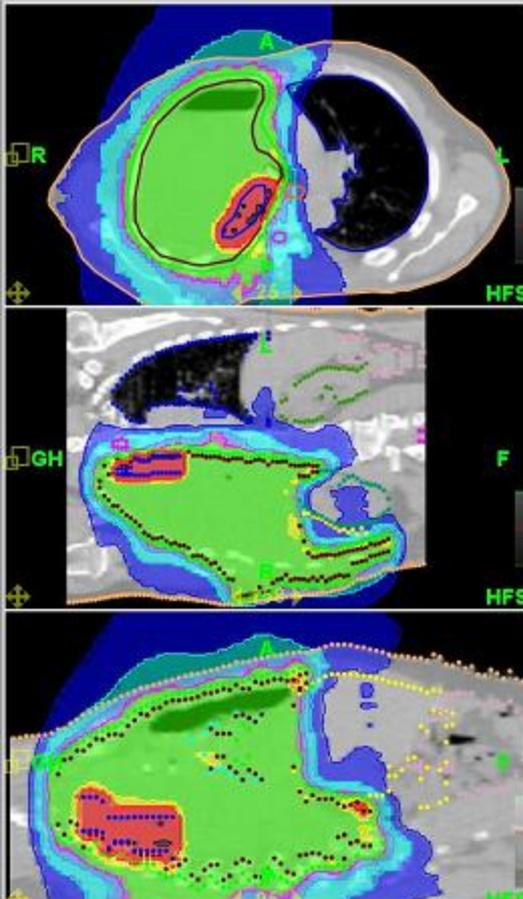
Modena

Progetto di Technology Assessment



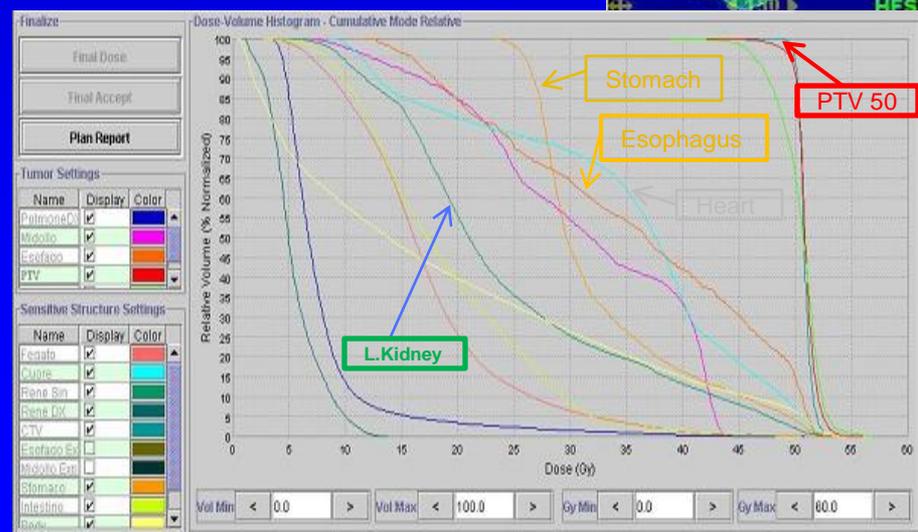
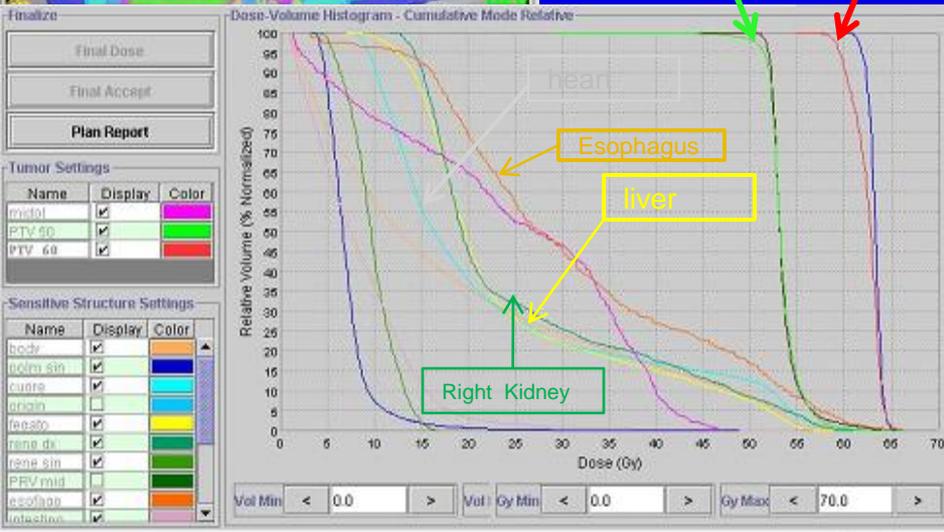
Trattamento cranio-spinale

Mesothelioma



PTV 50

PTV 60



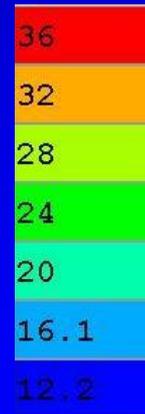
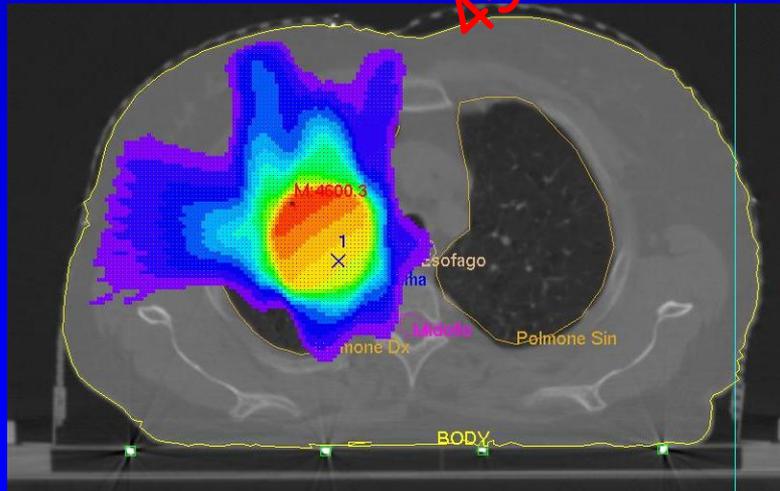
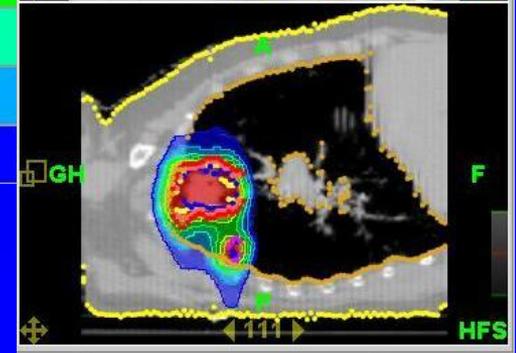
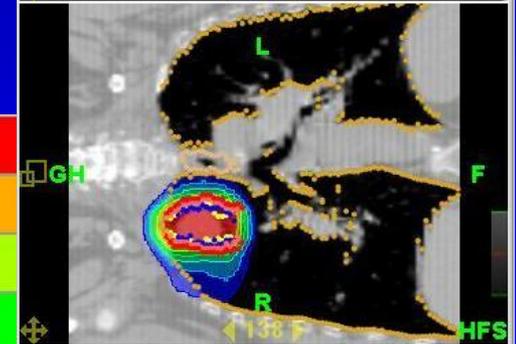
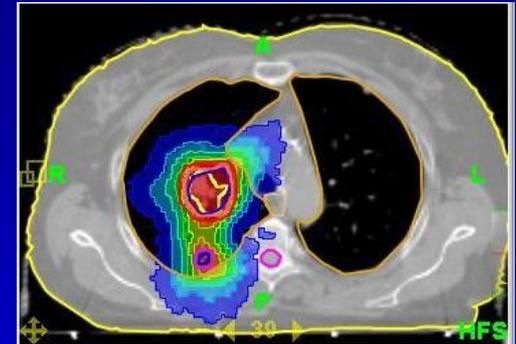
Progetto di Technology Assessment



45-60 minuti

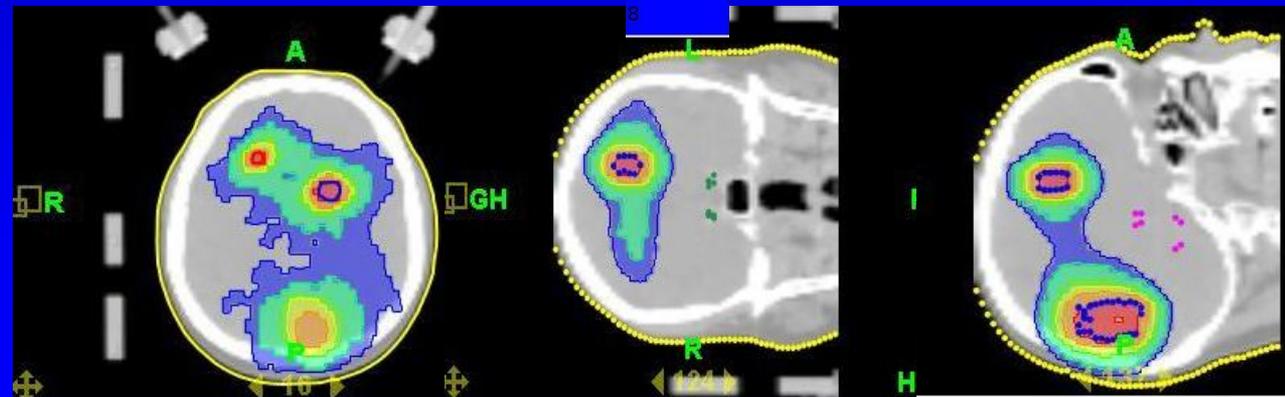
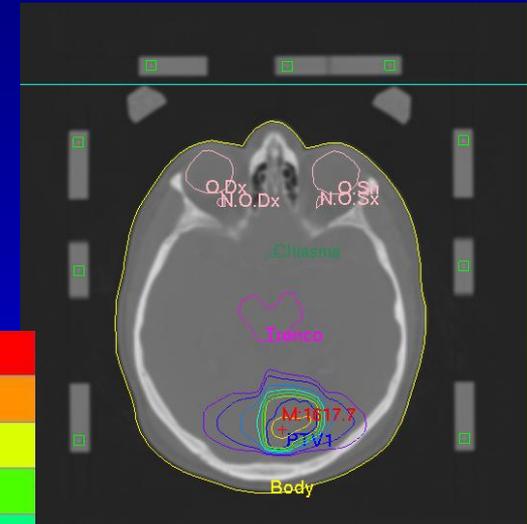
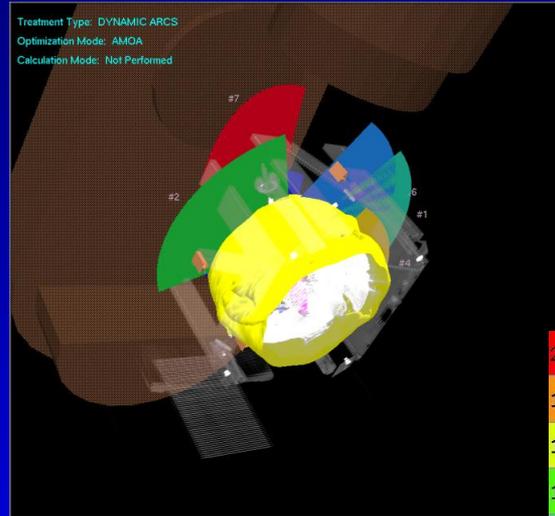
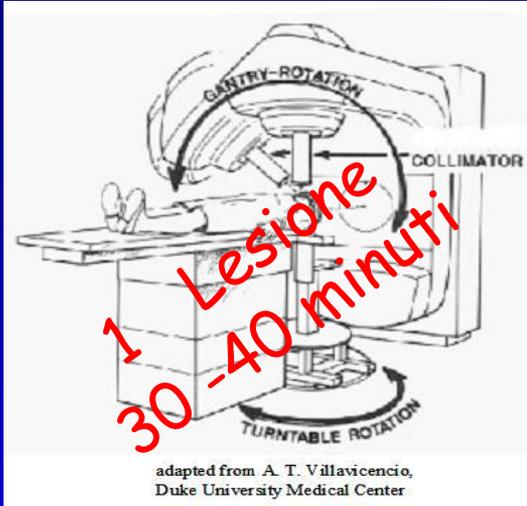


20 minuti



Trattamento stereotassico body

Progetto di Technology Assessment



Trattamento stereotassico cerebrale

6 Clinical Research Program to acquire Tomotherapy

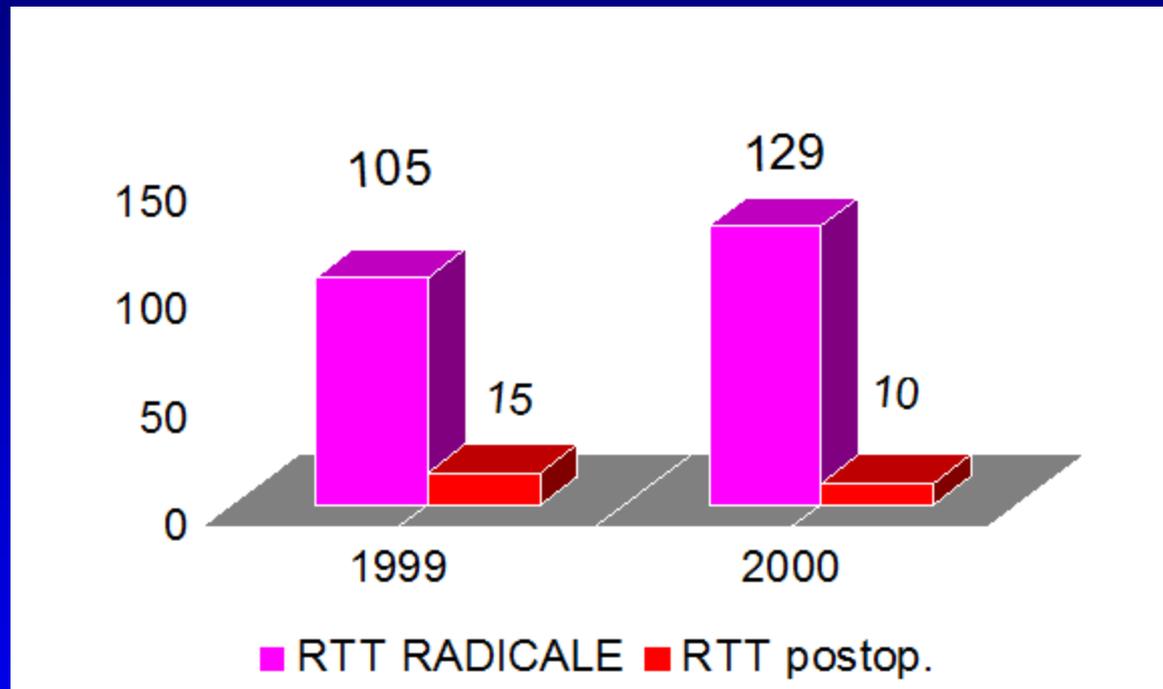
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PROSTATA ???

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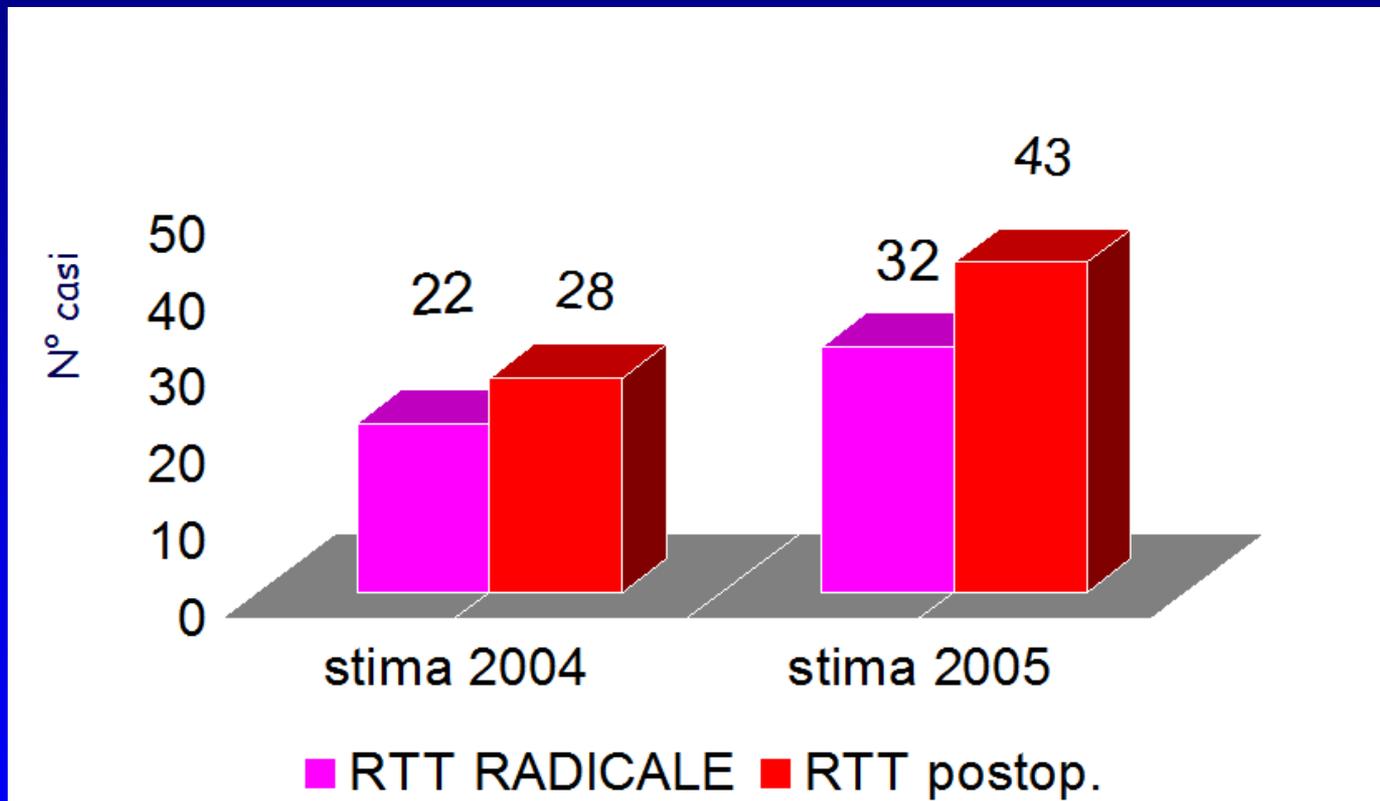
Neoplasie prostatiche

Caratteristiche della casistica italiana



Stime prospettiche AIRO (2002 - 2003) su 15 centri italiani
Post-operatoria in 16 paz. / anno per centro

Caratteristiche della casistica di.....



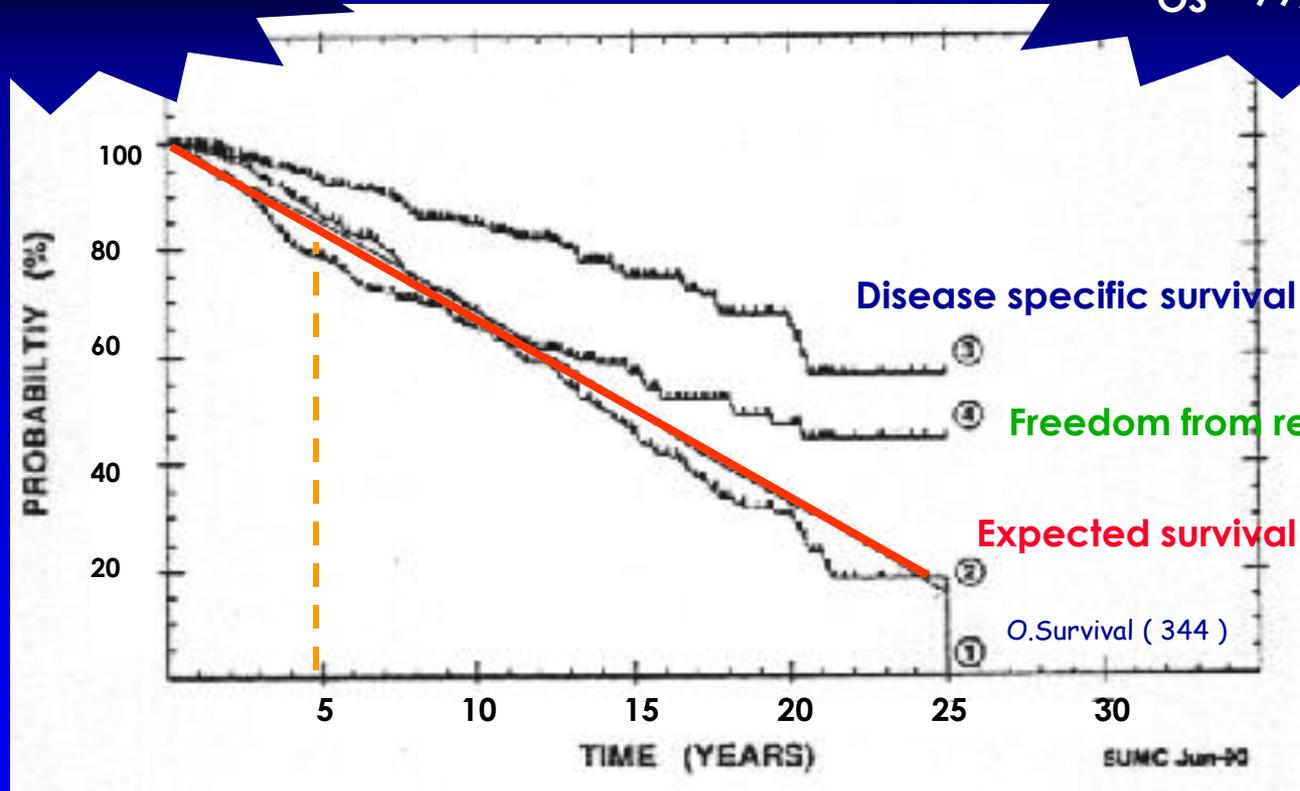
RISULTATI DELLA RTT RADICALE nei T1-2

Risultati Italiani
su 1110 paz. T1-2 Nx



a 5 a 8 aa

DSS	91%	84%
OS	79%	62%



Sopravvivenza cruda, determinata e libera da recidiva, a 25 aa. dalla RTT, in pazienti con Ca. prostatico T1abc e T2a , trattati a Stanford con RTT e che potevano essere candidati a prostatectomia radicale. (M. A. Bagshaw 1992)

SEQUELE TARDIVE DELLA RTT

	Review	RTOG
• Mortalità	0.2%	0%
• Complicazioni severe	1.9%	0%
• Incontinenza	0.9%	0.4%
• Stenosi uretrali	2%	1.2%
• Ematuria persist.		0.9%
• Rettorragie pers.		0.6%

L'incidenza di rettosigmoidite (G2- 3) : 10 % per RTT su pelvi in toto e 3% per RTT sulla sola prostata / Fistole e cistiti emorragiche : 0.4 - 0.2 %

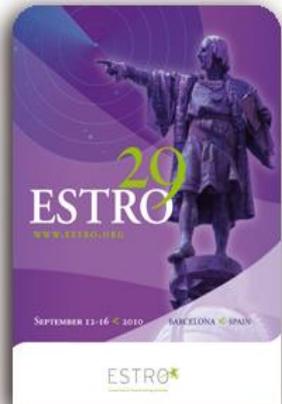
Potenza sessuale è mantenuta nel 33 - 60 % dei casi (sino al 90%)



Changing Patterns of Practice for prostate cancer in Italy. A survey by the prostate cancer study group of the Italian Radiation Oncology Society (A.I.R.O.)

Magrini S.M.(1), Pegurri L.(1), Girelli G.(2), Munoz F.(3), Panaia R.(4), Liwi L.(5), Bellavita R.(6), Bonetta A.(7), Krenkli M.(8), Cagna E.(9), Bunkheila F.(10), Borghesi S.(11), Signor, M.(12), Di Marco A.(13), Bertoni F.(14).

(1)Brescia University Radiotherapy Dept.; (2)Ivrea Radiotherapy Dept.; (3)Turin University Radiotherapy Dept.; (4)Candiolo Radiotherapy Dept.; (5) Florence University Radiotherapy Dept.; (6)Perugia University Radiotherapy Dept.; (7)Cremona Radiotherapy Dept.; (8)Novara University Radiotherapy Dept.; (9)Como Radiotherapy Dept.; (10)Bologna University Radiotherapy Dept.; (11)Arezzo Radiotherapy Dept.; (12) Udine Radiotherapy Dept.; (13)Mantua Radiotherapy Dept.; (14)Modena Radiotherapy Dept.



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PURPOSE: To describe the Patterns of Practice for prostate cancer and the results obtained in 14 Italian Radiation Oncology Centers: 1999 through 2003, in comparison with a previous survey covering the period 1995-1998 (Int. J. Radiation Oncology Biol. Phys., 52: 1309-19, 2002).

MATERIALS AND METHODS:

- The clinical and therapeutic features of 2923 pts were analyzed.
- Late toxicity (diarrhea and rectal) has been calculated as cumulative probability, according to the ITCCQED RTO scoring system.
- Overall, cause specific and disease free survival (OS, DSS, RFS and DFS) were calculated (Kaplan-Meier).
- Actuarial survival curves, cumulative toxicity and statistical comparisons were performed with the SPSS 17 statistical package.

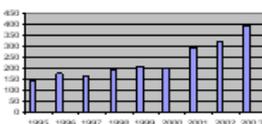


Fig. 1. Number of patients treated in 14 Italian Radiation Oncology Centers: 1999 through 2003.

RESULTS:

- 2923 patients were treated with radical radiotherapy from 1999 to 2003 and 1005 pts from 1995 to 1998.
- Median age was 70 years vs 69 years in the previous survey.
- Clinical, diagnostic, therapeutic features of the series accrued in the two periods are reported in the following Tables:

	1999-2003	1995-1998	P=
T1-T2	78%	88%	P<0.001
PSA < 10	38%	38%	P=1
T1c	74%	74%	P=1
RMN post/bi without (biobased coil)	9%	7%	P=0.001
Biobased coil	8%	12%	P=0.001
US	83%	88%	P=1
Dose tot. > 70 Gy	34%	23%	P<0.001
3D	8%	4%	P=0.007
DT	54%	33%	P<0.001

	1999-2003	1995-1998	P=
Prostatectomy	32.3%	7%	P<0.001
Prostatectomy + RT	17.2%	22%	P=0.002
RT	43.3%	67%	P<0.001
10-18 MV	88.1%	42%	P=0
> 18 MV	8.9%	52%	P=0
RT	77.3%	47%	P=0.001
RT+P	14.9%	49%	P=0.001
SB	22.3%	35%	P=0.001
SB+RT	32.7%	38%	P=0.001
No	7.3%	48%	P=0.001

The 5-year cumulative life expectancy and toxicity

	1999-2003	1995-1998
RTOG SCORE	34% ± 1%	37% ± 2%
G1-G3	1.4% ± 0.4%	0.7% ± 0.6%

The 5-year cumulative survival

	1999-2003	1995-1998
OS	47.3% ± 1.4%	7%
RFS	76.9% ± 0.7%	33%
DSS	99.2% ± 0.4%	98%

The 3-year cumulative biochemical RFS

	1999-2003	1995-1998
bioCR	47.3% ± 0.6%	38.3% ± 1.9%

CONCLUSIONS: In the present survey, the proportion of early stage pts, of those treated with 3DCRT and with doses > 70 Gy increased in comparison with the last period covered by the previous survey (1995-1998). Survival and toxicity data have been slightly better, even if such comparison should be considered very cautiously.

Results obtained in 14 Italian Radiation Oncology Centers 1999 through 2003

(2923 pts)

CONCLUSIONS:

- The proportion of early stage pts, of those treated with 3DCRT and with doses > 70 Gy increased in comparison with the last period covered by the previous survey (1995-1998).
- Survival and toxicity data have been slightly better, even if such comparison should be considered very cautiously.



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Confronto casistiche

	1999-2003	1995-1998
T1-T2	78%	68%
PSA < 10	36%	36%
TC	74%	74%
RMN	9% - 6%	7% - 12%
ECO transrettale	88%	88%
Dose totale > 70 Gy	44%	23%
3D	77.9% (IMRT 0.2%)	41%
OT	74%	80%



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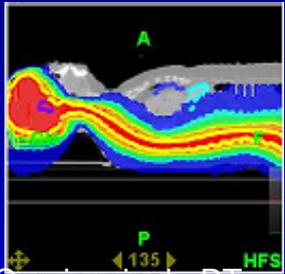
Sopravvivenze a 5 anni calcolate su 2550 paz/2923

- OS : 87.3% \pm 1% vs 79%
- RFS : 75.8% \pm 0.7% vs 67%
- DSS : 96.2% \pm 0.4% vs 90%
- bRFS : 79% \pm 1%
- RFS (locoregionale) : 95.9% \pm 0.5%

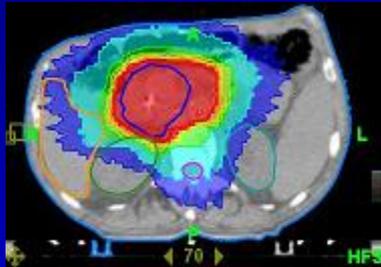
Tossicità a 5 anni:

- Tossicità tardiva cumulativa (rettale + vescicale) G1-G3 (RTOG) \rightarrow 34% \pm 1% (1999-2003) vs 37% \pm 2% (1995-1998)
- Tossicità tardiva (rettale + vescicale) solo G3 \rightarrow 1.4% \pm 0.3% (1999-2003) vs 5.1% (1995-1998)

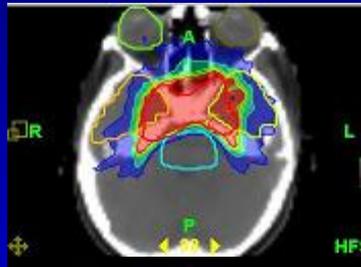
Present indications for routine clinical practice in Modena



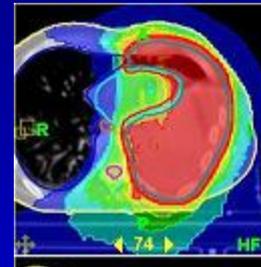
Cervicospinal - RT



Pancreas



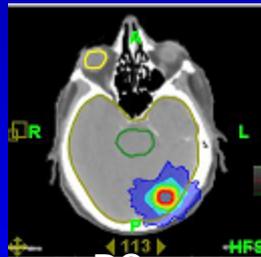
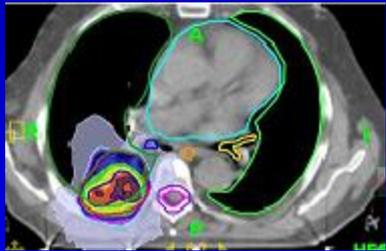
Reirradiation



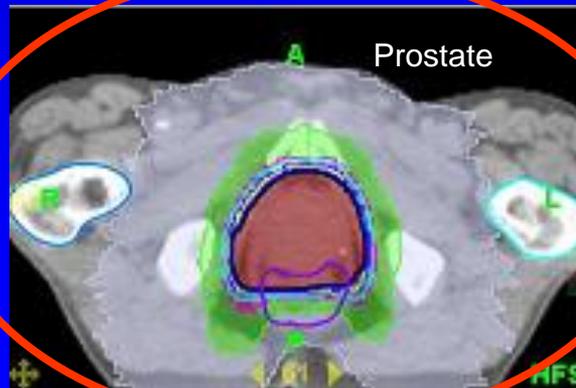
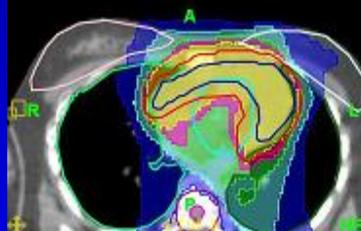
Mesothelioma



H-N



RS



Prostate

....non vi è alcun limite all'applicazione dell' Unità di terapia, tuttavia preferiamo un suo impiego quando sono necessari...

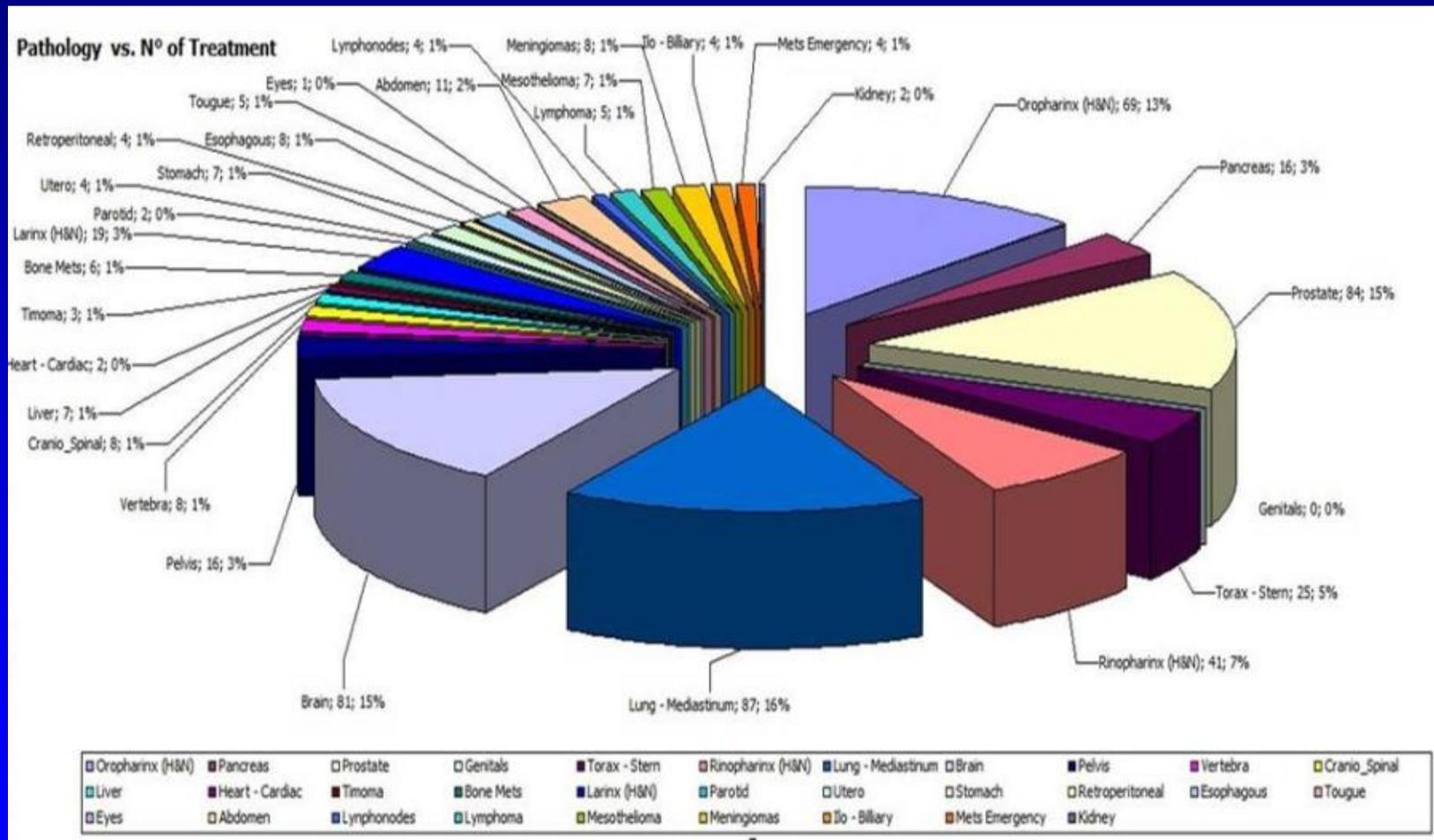
...elevata conformazione della dose,
con alti gradienti di dose fra la lesione e tessuti sani circostanti...

- Volumi che superano i 40 cm come max estensione longitudinale
- Lesioni multiple
- Volumi superficiali
- RT stereotassiche, RCS
- Ritrattamenti
- ...trattamenti per i quali è preferibile IMRT con IGRT volumetrica

.....4D-RT ? ART ? Tracking respiratorio.....

movimento d'organo e RT elicoidale.....?

N° PDT Tomo per Patologia



Tutte le lesioni della prostata ?

(..... soprattutto per la possibilità di IGRT volumetrica)

“L'outcome di RTT, Brachiterapia e Chirurgia è simile; l'evidenza di efficienza clinica per le terapie dei tumori localizzati è scarsa..”

European Urology 2003; 44: 40-46

SEER Medicare database 2002-2004

12598 paz. => 65 aa M0 (5845 IMRT , 6753 3D-CRT)

Tossicità GI (proctite, emorragia rettale) e GU (cistite, ematuria) a 24 mesi:

	IMRT	3D-CRT
GI globali	18,8%	22,2%
Rettali	3,5%	4,5%
GU	=	=
Disf. erettile	=	=

....IMRT is associated with fewer gastrointestinal problems after treatment...

RADIOTERAPIA TRANSCUTANEA

NCCN[®]

Practice Guidelines
in Oncology – v.1.2010

Prostate Cancer

PRINCIPLES OF RADIATION THERAPY

External Beam Radiotherapy:

- 3D conformal and IMRT (intensity modulated radiation therapy) techniques should be employed. Image guided radiation therapy (IGRT) is required if dose ≥ 78 Gy.
- Doses of 75.6-79 Gy in conventional 36-41 fractions to the prostate (\pm seminal vesicles for part of the therapy) are appropriate for patients with low-risk cancers. For patients with intermediate- or high-risk disease, doses between 78-80+ Gy provide improved PSA-assessed disease control.
- Patients with high-risk cancers are candidates for pelvic lymph node irradiation and the addition of neoadjuvant/concomitant/adjuvant ADT for a total of 2-3 y (category 1).
- Patients with intermediate risk cancer may be considered for pelvic lymph node irradiation and 4-6 mo-neoadjuvant/concomitant/adjuvant ADT.
- Patients with low risk cancer should not receive pelvic lymph node irradiation or ADT.
- The accuracy of treatment should be improved by attention to daily prostate localization, with techniques such as IGRT using CT, ultrasound implanted fiducials, electromagnetic targeting/tracking, or an endorectal balloon to improve oncologic cure rates and reduce side effects.
- Evidence supports offering adjuvant/salvage RT in all men with adverse pathologic features or detectable PSA and no evidence of disseminated disease.

Basso rischio : 74-75 Gy \rightarrow 78 - 79 Gy

Rischio intermedio/alto : 78 \rightarrow +80 Gy

IGRT se > 78 Gy

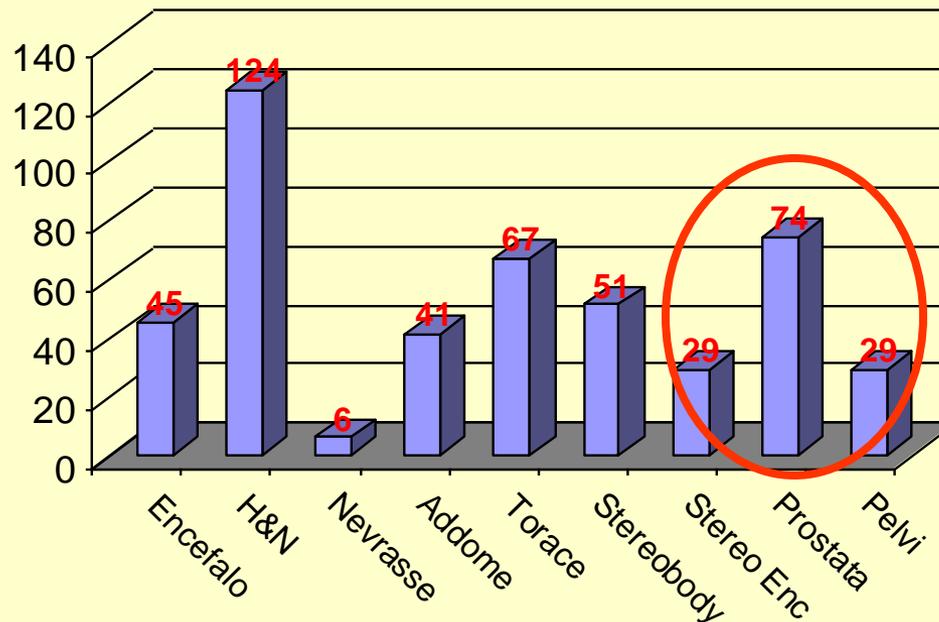
RTT su linfonodi pelvici e Ormono per rischio intermedio e alto

MODENA ESPERIENZA CLINICA CON TOMO

30/5/2008 - 14/11/2010

466 pazienti (10867 sedute)

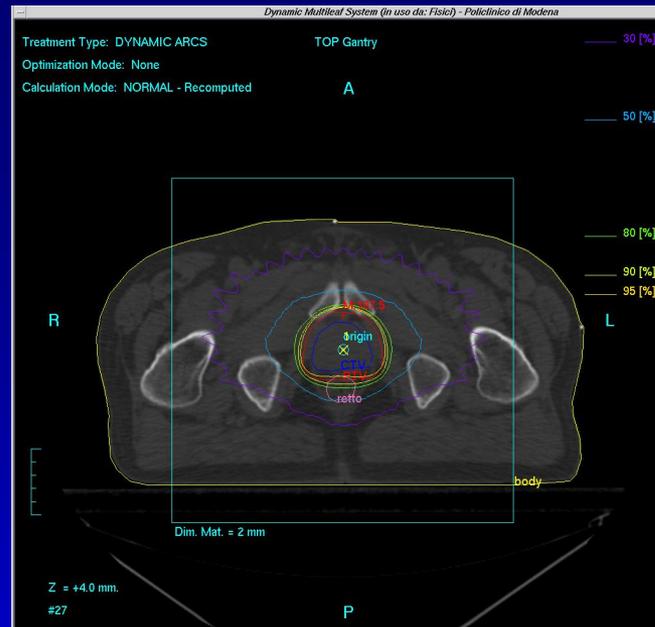
Nr. pazienti trattati con Tomo dal 30/05/2008 al 14/11/2010
466 pazienti



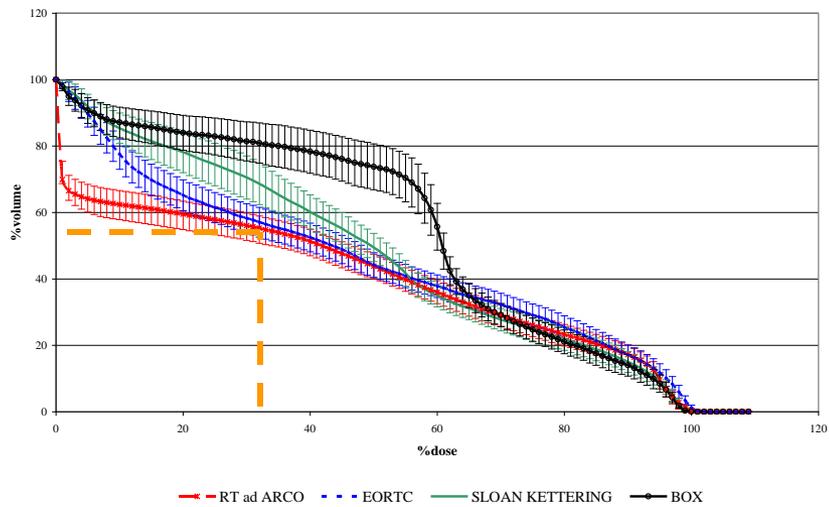
TOMOTERAPIA NELLE NEOPLASIE PROSTATICHE

Maggior consumo di risorse ? :

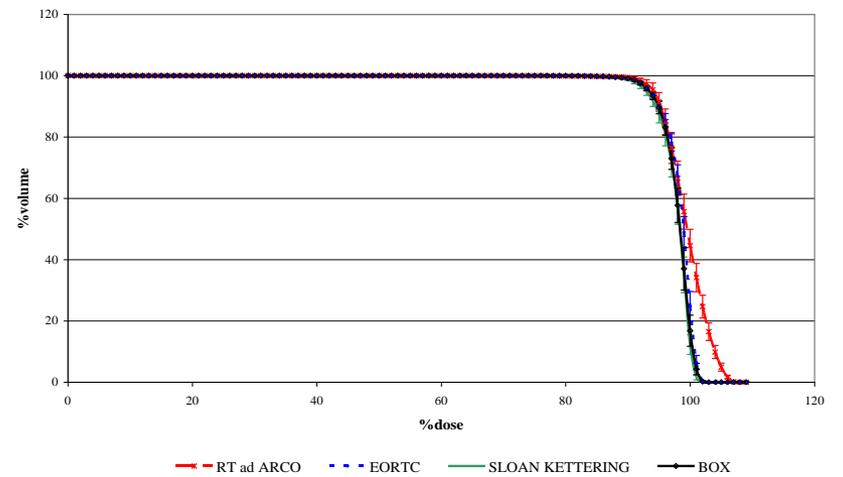
- Nella pianificazione: NO
- Nella contornazione: NO
- Nella elaborazione: dipende



DVH_{med} retto



DVH_{med} PTV

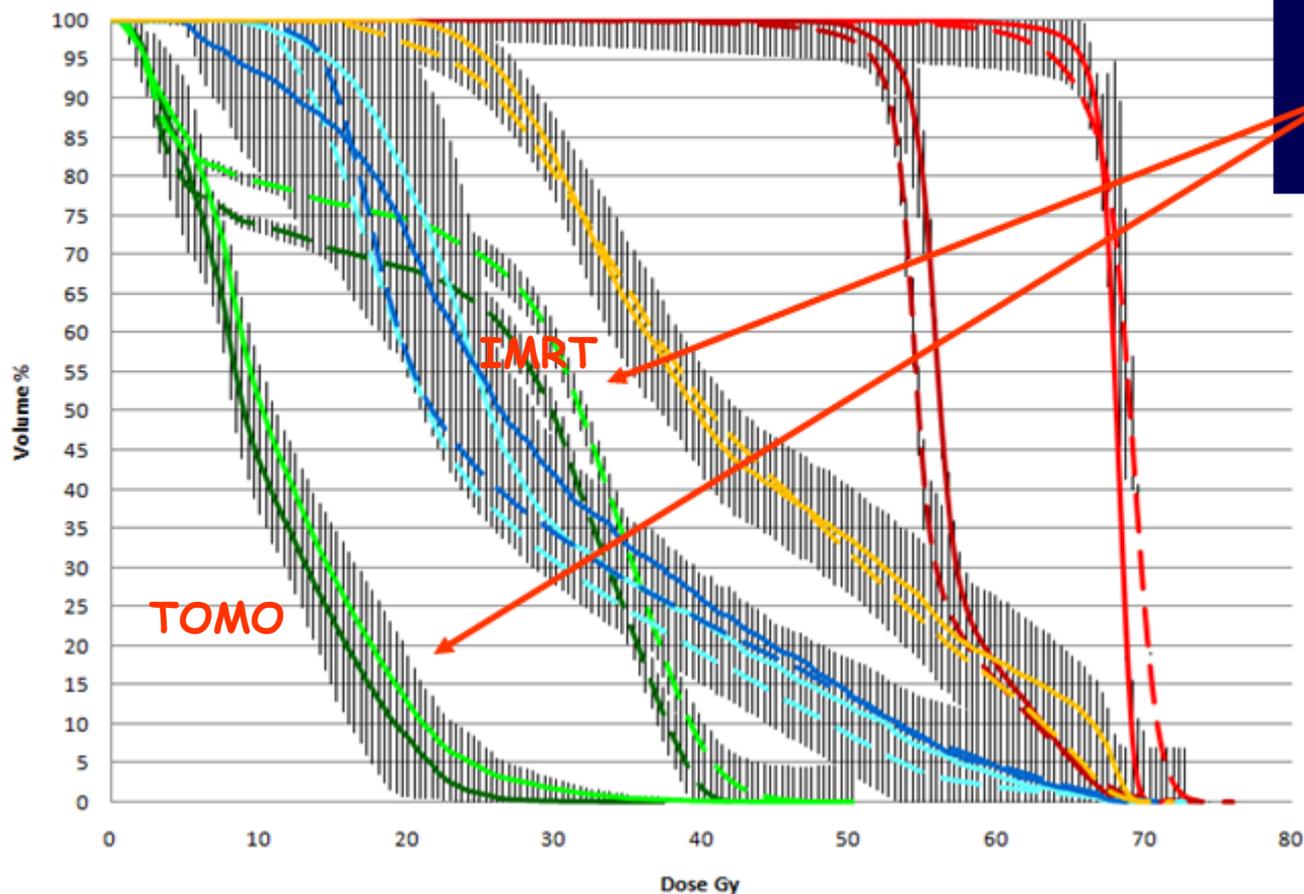


H-N: differenze tra IMRT S&S e TOMO

DVH medi

Limite di confidenza 95%

Midollo Spinale e
Midollo Spinale
Espanso



Adenoca prostatico con basso rischio di interessamento dei linfonodi pelvici
DF 2,5 Gy - DT 70 Gy x 28 frazioni (5,5 settimane di trattamento)
(equivalenti a circa 80 Gy con frazionamento standard di 2 Gy a frazione con LINAC, tempo di trattamento 8 settimane)

Prescription

% Vol For PTV 95.0 % will receive **70.5 Gy**

Field Width: 2.5 cm - Jaws(1.0,-1.0) Pitch: 0.287 Calc Grid: Normal Batch Beamlets

Tumor Constraints

Name	Display	Color	Blocked	Use?	Importa...	Max Dose [...]	Max Dose ...	DVH Vol [...]	DVH Dose [...]	Min Dose [...]	Min Dose P...
PTV	<input checked="" type="checkbox"/>	Red	None	<input checked="" type="checkbox"/>	1500	70.5	10	95.0	70.5	70.5	20

Sensitive Structure Constraints

Name	Display	Color	Blocked	Use?	Importance	Max Dose [...]	Max Dose ...	DVH Vol [%]	DVH Dose [...]	DVH Pt. Pen.
retto	<input checked="" type="checkbox"/>	Yellow	None	<input checked="" type="checkbox"/>	10	70.5	1	20.0	20.0	10
vescica	<input checked="" type="checkbox"/>	Green	None	<input checked="" type="checkbox"/>	20	70.5	1	25.0	50.0	100
testa femora	<input checked="" type="checkbox"/>	Blue	None	<input checked="" type="checkbox"/>	5	65.0	5	20.0	10.0	5
testa femora	<input checked="" type="checkbox"/>	Cyan	None	<input checked="" type="checkbox"/>	3	65.0	5	20.0	10.0	5

Density Image Viewer

Density Image

Optimize Mode: Beamlet Modulation Factor: 2.500

Initiate Full Dose after 20 iterations.

Start Pause Resume Get Full Dose Cancel

Dose Display

Isodose

77.55
70.5
 66.975
 63.45
 56
 50
 35
 20

Patient Images

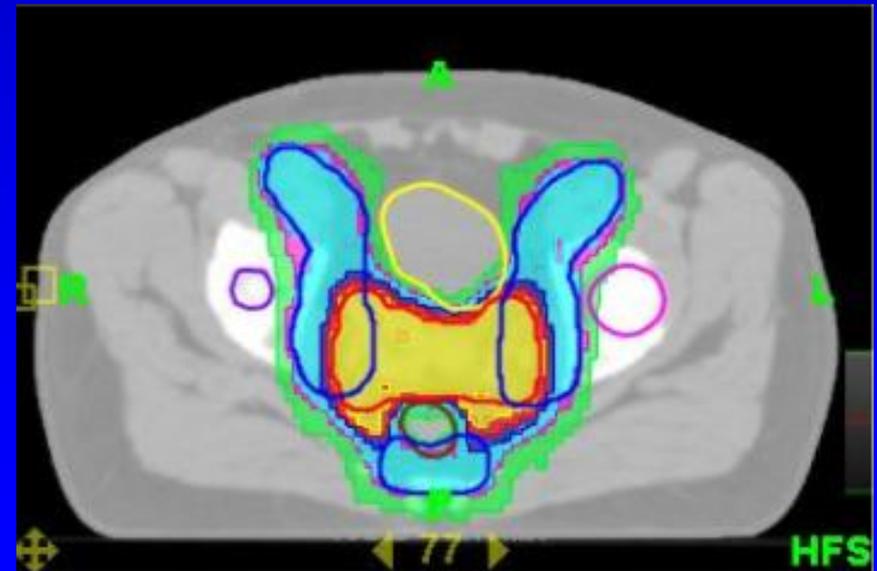
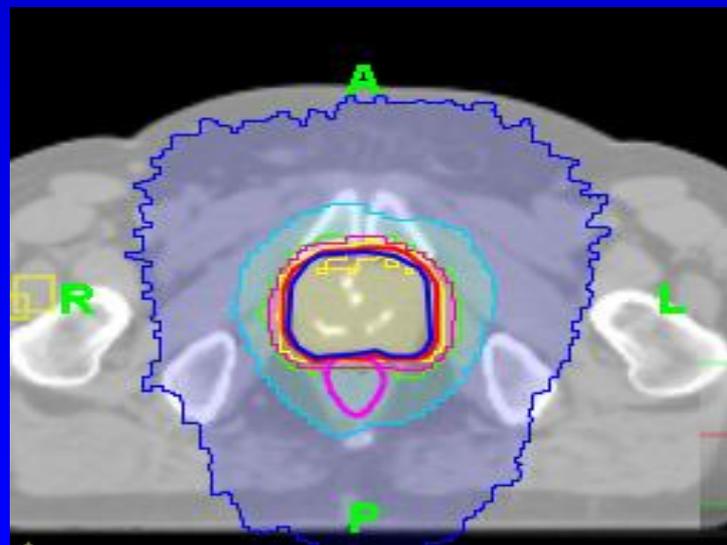
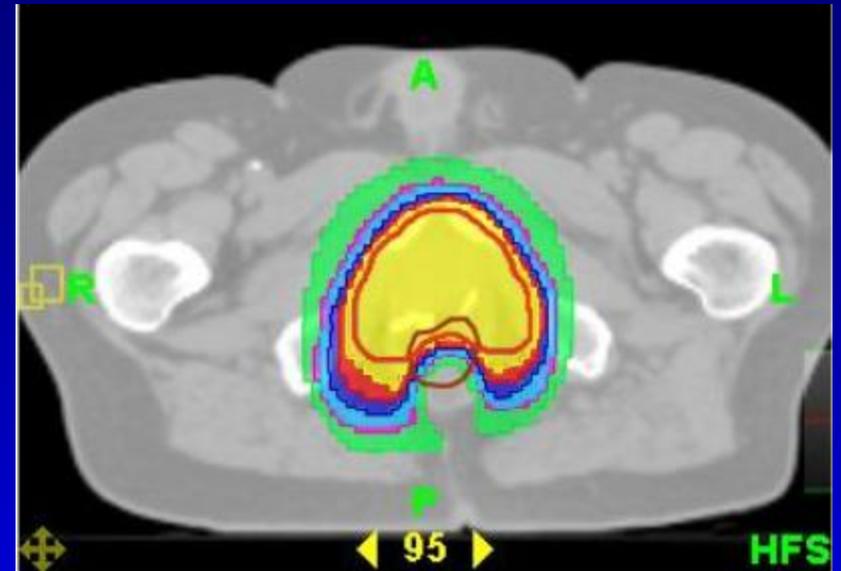
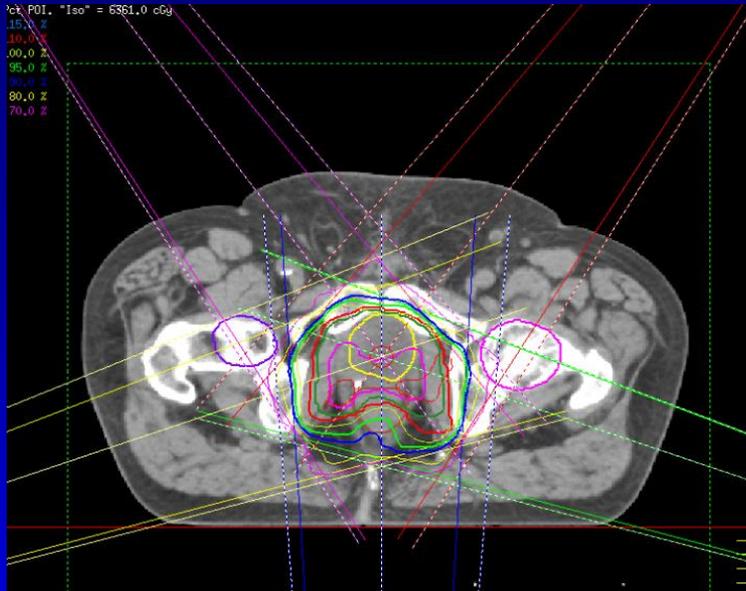
Dose-Volume Histogram - Cumulative Mode Relative

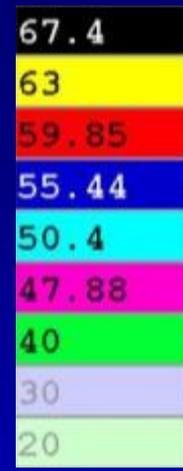
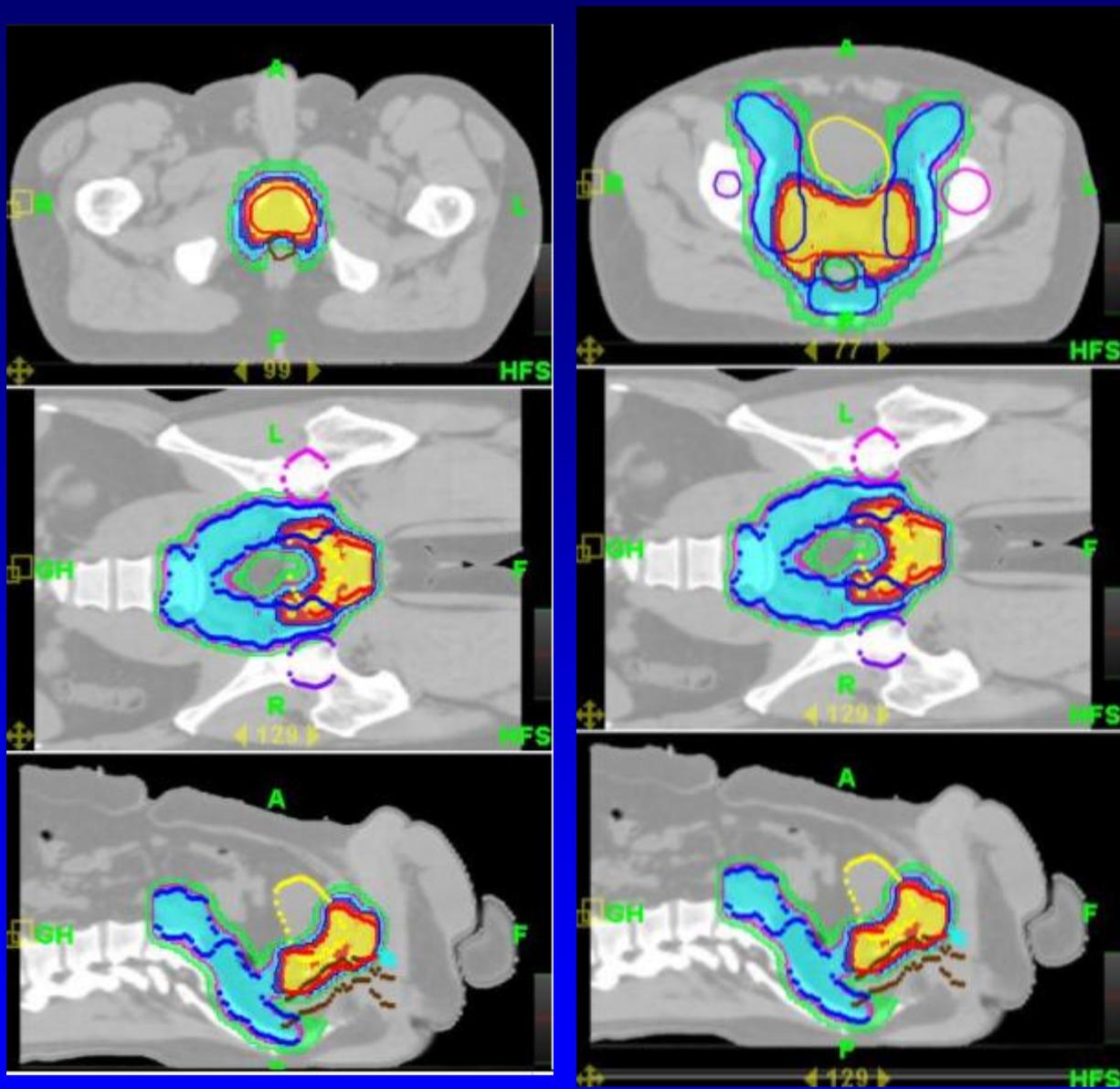
Relative Volume (% Normalized)

Dose (Gy)

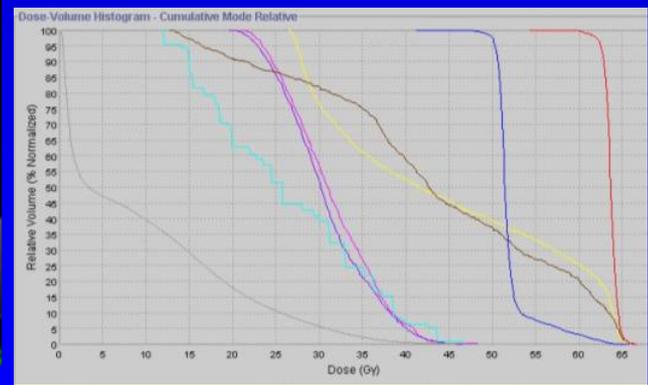
Vol Min < 0.0 > Vol Max < 100.0 0.0 > Gy Max < 77.5 >

IMRT - Tomotherapy





- 63 Gy al 95% del PTV 1
- 50,4 Gy al 95% del PTV2
- 28 frazione



TOMOTERAPIA NELLE NEOPLASIE PROSTATICHE

Maggior consumo di risorse ? :

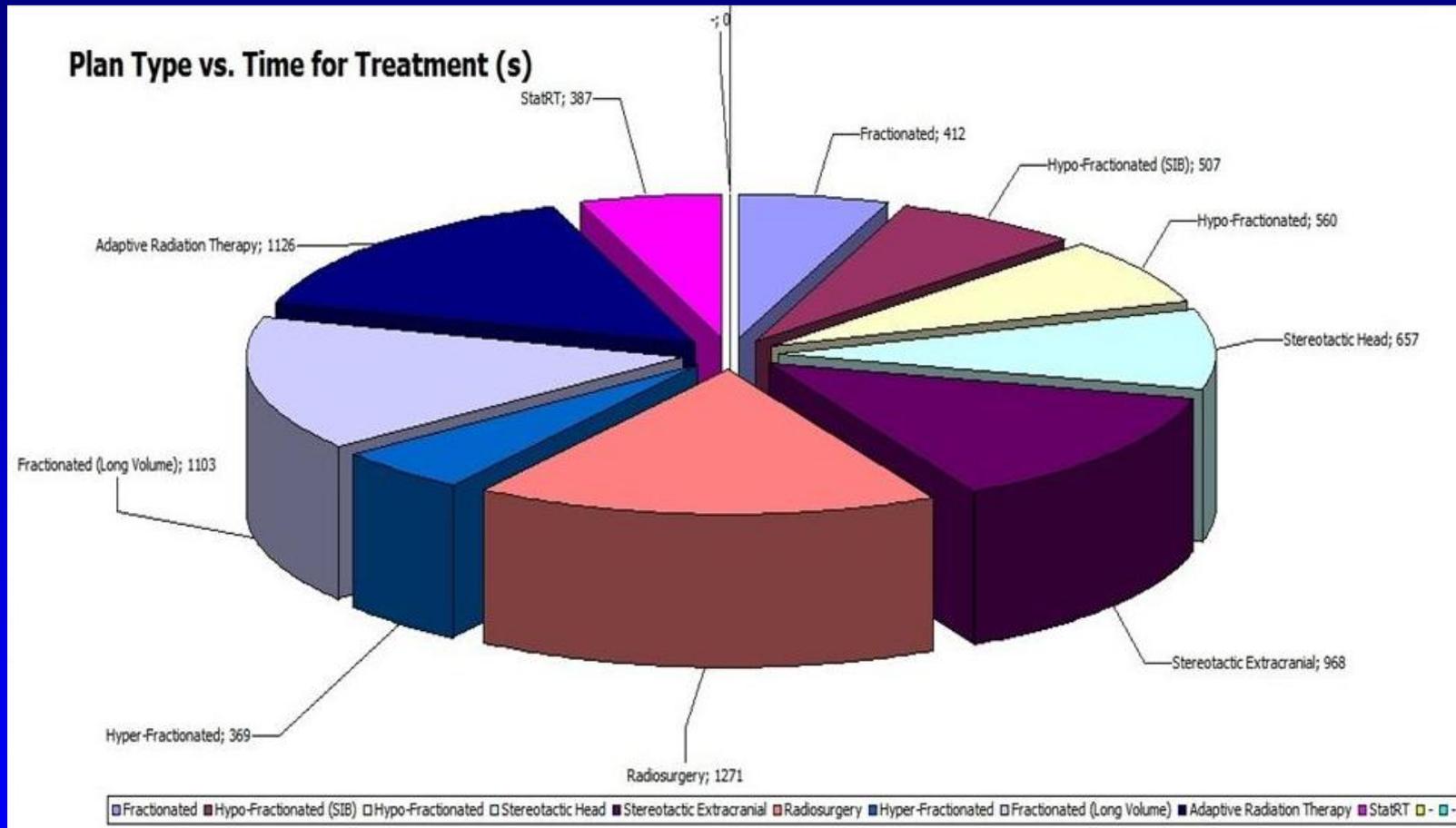
- Nella pianificazione: NO
- Nella contornazione: NO
- Nella elaborazione: dipende
- Nella esecuzione delle sedute: NO

Tempi di esecuzione

IGRT , scostamenti da correggere, erogazione:

- Automatica con TSRM ? Medico ?
- Valutazioni con Fine o course?

Tempi medi di beam-on in base al tipo di frazionamento utilizzato



.....varabili da 368 a 1271 sec.....

Tempi per trattamenti con Tomotherapy Hi-ART

Tumor	Number of patients	Number of fractions	Mean time on table	Mean radiation time
head-and-neck	19	413	23.2 min	8.5 min
prostate	14	441	20.7 min	6.2 min
gastrointestinal	13	260	24.9 min	8.0 min
breast	12	313	24.4 min	13.2 min
spinal reirradiation	7	127	19.1 min	6.1 min
total	100	2187	24.6 min	10.6 min

Su 207 sedute (1-10 sedute/paz.) : 25,6 +/- 8,7 min

SEDE	minTotale			min MV			min TE		
	media	min	max	media	min	max	media	min	max
H-N	26,2	13	53	3,2	1,4	6,7	8	3,4	14
Torace	35	23	50	3,5	2,5	6,2	11	7,6	15,6
Pelvi	23	13	40	2,3	1,3	5,3	8,2	3,2	14,8
Media globale 25,6 +/- 8,7 minuti									

IMRT prostata radicale

IGRT MODALITA' DI COREGISTRAZIONE

Differenze negli scostamenti (mm)

SEDE assi	Bone .vs B.+Tiss(2R) media +/-DS	B. vs B+T+ Med media +/-DS
<u>Prost.</u>		
- x	0,012 0,59	0,012 0,87
- y	-1,2 1,37	-0,437 0,7
- z	0,3 1,05	0,19 2,36
<u>H-N</u>		
- x	1,6 2,02	0,25 1,47
- y	0,15 2,10	0,92 1,53
- z	-0,03 1,09	-2,75 4,01

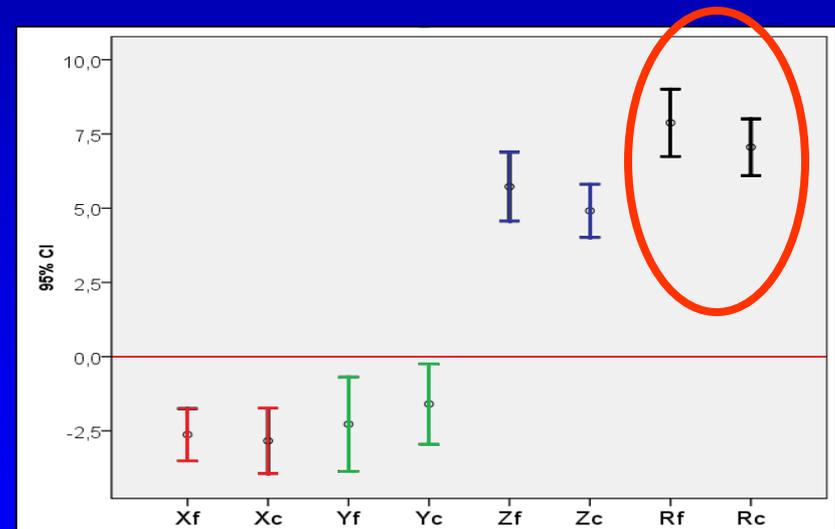
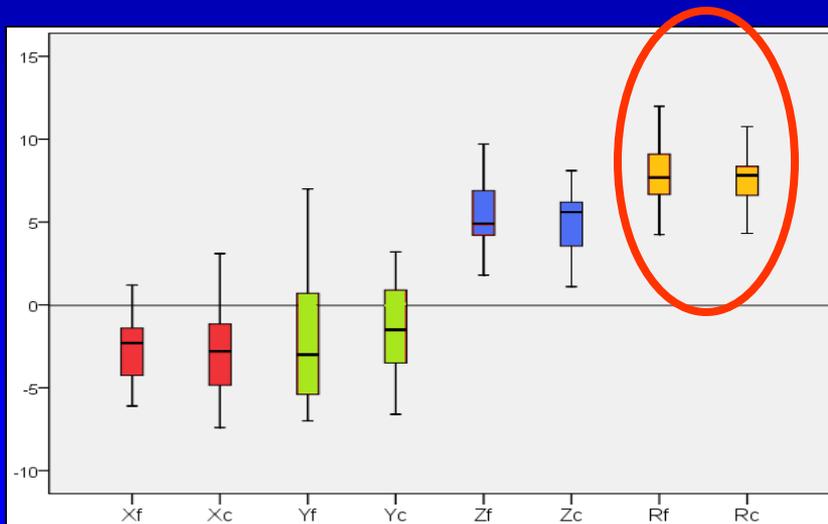
Fattore di correzione 3D : 2,0 +/- 1 mm SD vs 2,2 +/-1,2 mmSD

Fine o Course ?

Neoplasie prostatiche: 23 misure su 5 pazienti

		Valori delle medie			
		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Xf	-2,626	23	2,0296	0,4232
	Xc	-2,835	23	2,5485	0,5314
Pair 2	Yf	-2,274	23	3,6744	0,7662
	Yc	-1,596	23	3,1307	0,6528
Pair 3	Zf	5,726	23	2,6859	0,56
	Zc	4,913	23	2,0777	0,4332
Pair 4	Rf	7,88	23	2,62	0,55
	Rc	7,06	23	2,21	0,46

		differenze				
		Mean	Std. Deviation	Std. Error Mean	Lower	Upper
Xf - Xc		0,2087	2,6576	0,5541	-0,9405	1,3579
Yf - Yc		-0,6783	3,3507	0,6987	-2,1272	0,7707
Zf - Zc		0,813	2,8768	0,5998	-0,431	2,057
Rf - Rc		0,82	2,58	0,54	-0,29	1,94



... non differenze statisticamente significative.

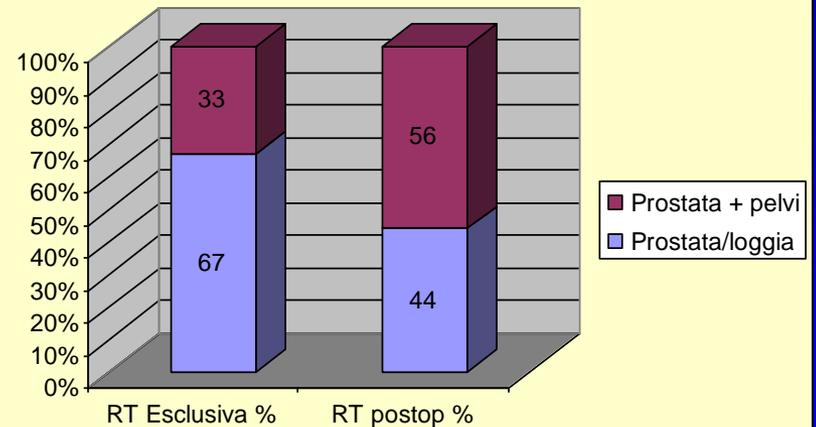
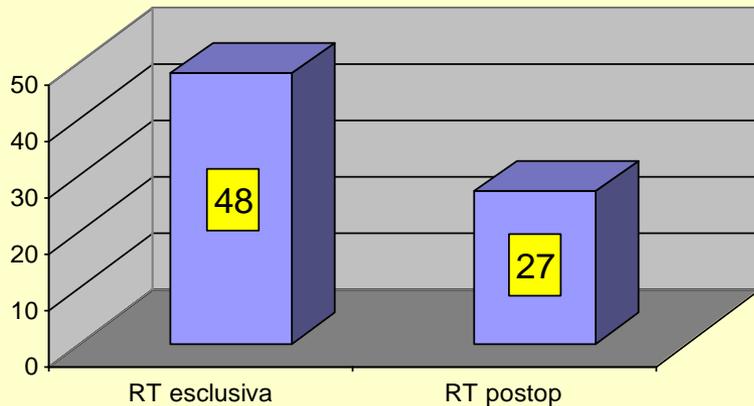
Casistica Modenese

..... esperienze con ipofrazionamento.....

(E.Turco , E. Mazzeo, P. Barbieri, B. Meduri, G. Guidi, E. Cenacchi)

75 pazienti con neoplasie prostatiche trattati con TOMO
dal 30/5/2008 al 8/11/2010

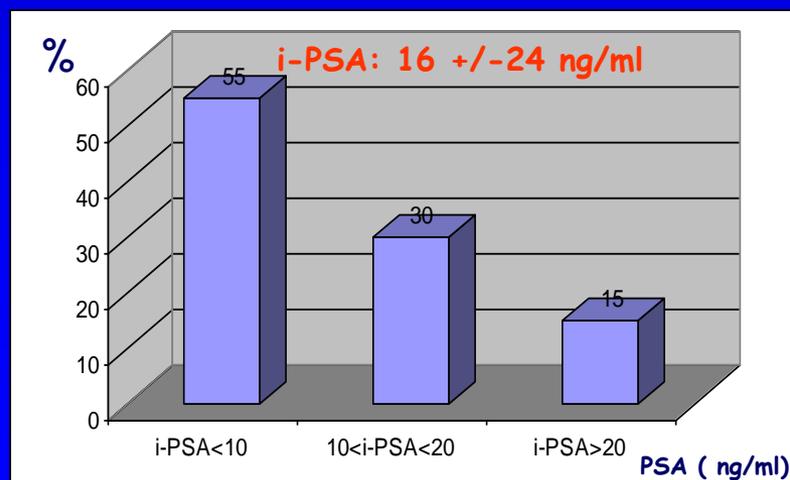
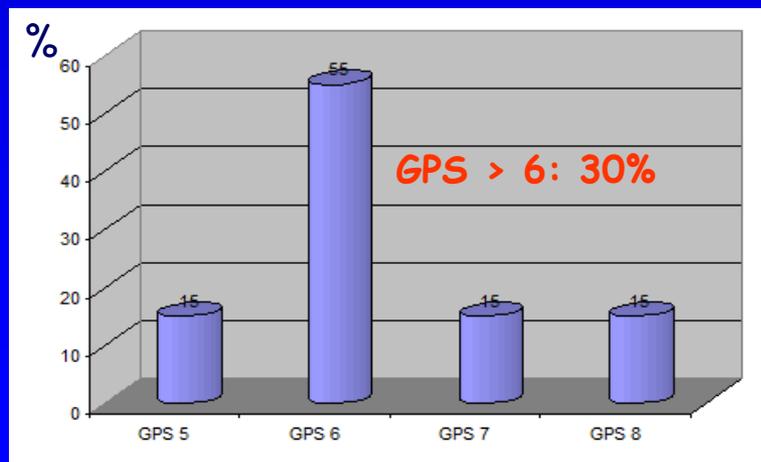
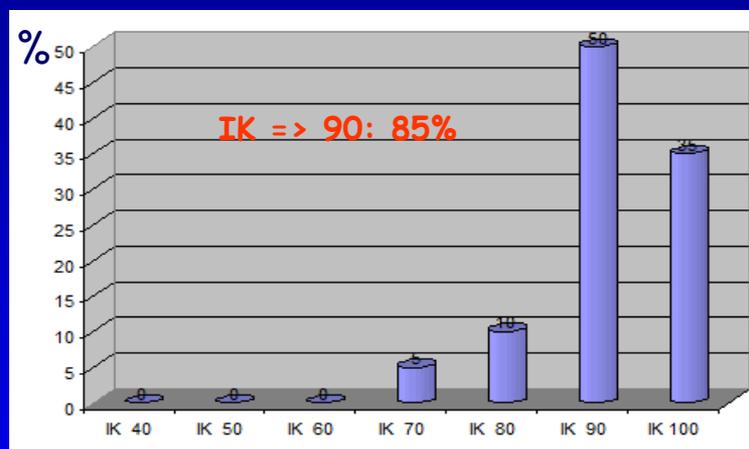
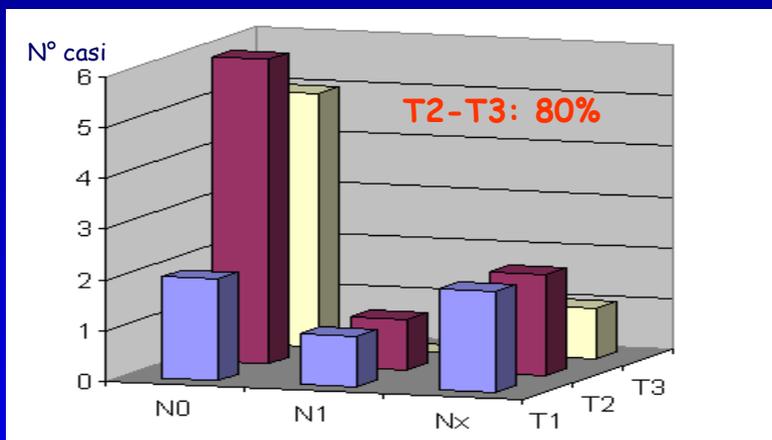
Pazienti Ca prostata trattati con tomo Maggio 08-Novembre 10



Ipofrazionamento con TOMO: 2,5 Gy/die fino a 70 Gy (10/20 SIB)

20 pazienti a rischio intermedio/alto, trattati nel 2009

T1-3/ N0-1 (riserva T3 per 3/9 paz. T2)
Età : 73 +/- 4 aa
Studio con RMN (bobina endorettale): 90%
Follow-up medio : 316 +/- 126 gg



Preparazione

- $\frac{1}{2}$ ora prima della TC e RT: urinae bere subito $\frac{1}{2}$ l di H₂O
- **Mantenere il retto libero da feci (eventuale peretta evacuativa)**

Sistema immobilizzazione Pro-STEP

Per classe di rischio intermedio –alto:

Con SIB

DF 2,5 Gy x 28 frazioni fino a 70 Gy per il CTV 1 (equivalenti a circa 79 Gy con frazionamento standard per il T e circa 77 Gy con frazionamento standard per OAR)

DF 2,1 Gy x 28 frazioni fino a 58,8 Gy per il CTV 2 (equivalenti a circa 60 Gy con frazionamento standard per T e OAR)

Teste Femorali: Dmax 45 Gy - **V 40 < 40 %**

Vescica: Dmax 70 Gy - V 62,5 < 18 % - **V 70 < 10 %**

Retto: Dmax 70 Gy - V 37,5 < 58 % - V 42,5 < 48 % - V 55 < 35 % - V 67,5 < 12 %
V 70 < 5 %

Bulbi penieni: Dmax 50 Gy

In tutti i casi l'espansione tra CTV - PTV è : 6 mm. tranne che a livello della parete anteriore del retto dove è di 4 mm

Se la probabilità di interessamento linfonodale subclinico calcolata sec. l'algoritmo predittivo di Roach (**$LN+ = 2/3 PSA + (GS - 6) \times 10$**) è **> 15 -20 %**, può essere presa in considerazione l'irradiazione dei linfonodi regionali (otturatori, presacrali, iliaci esterni, iliaci interni e iliaci comuni) che rappresenteranno il **CTV 3**, per il quale la DF è di 1,8 Gy x 28 frazioni fino a 50,4 Gy.

Prescrizioni previsionali

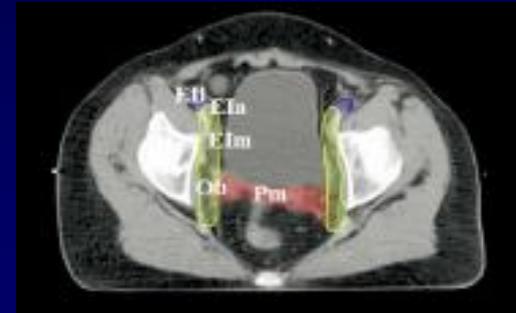
CTV : 100% della Dp al 100% del Vctv

PTV : 100% della Dp al 95% del Vptv

- Dmax puntuale: 107% della Dp

- Dmin al 100% del PTV: 95-98% Dp

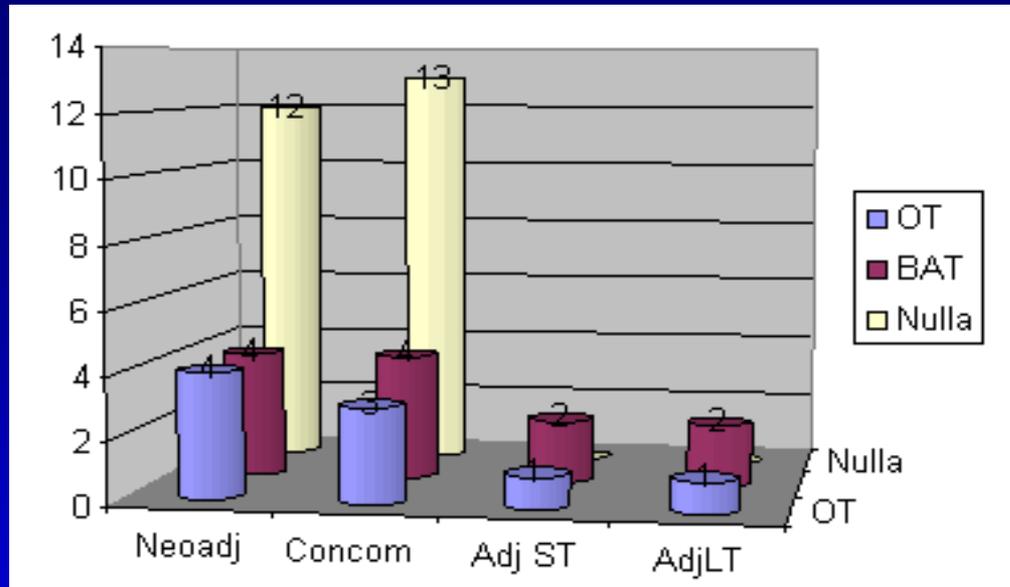
CTV per N pelvici (Taylor A. et al.)
IJROBP, vol.63 1604-1612,2005



Parametri per elaborazione:

_collimatore = 2.5 cm, Mod. Fact.= 2.2 -2.8 pitc= 0,285

TRATTAMENTO



TRATTAMENTO Radiante

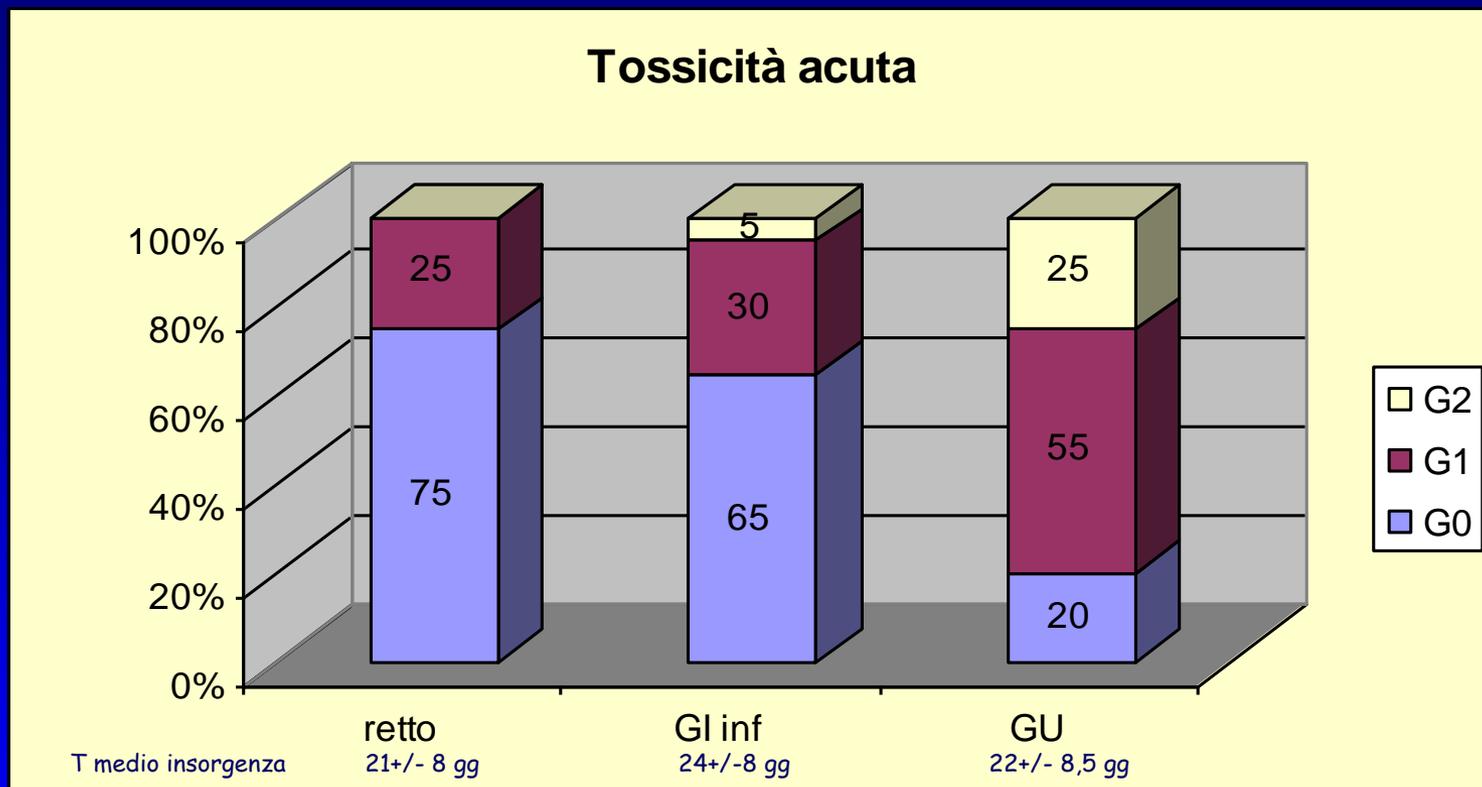
RT anche sulle stazioni linfonodali : 25%

- Durata RT : 41,4 +/- 3,9 gg
- Dosi PTV1: 2,5 Gy fino a 70 Gy in 28 fr
 - Dose min : 69,6 +/- 1,62 Gy
- Dosi PTV2: 1,8-2 Gy 54 - 60 Gy
 - Dose min : 56 +/- 5,9 Gy

VOLUMI E DOSI AGLI OAR

- PTV1 : 184,9 +/- 60,2 ml
- PTV2 : 306 +/- 152 (493 +/- 189) ml
- Dose media Retto : 31,2 +/- 6,8 Gy
- V70 retto: 5,9 +/- 2,8 ml
- V70 vescica: 13,1 +/- 8,8 ml

Tossicità Acuta



Retto (proctite) ; GI inf (transito intestinale) ; GU (Cistiti/uretriti)

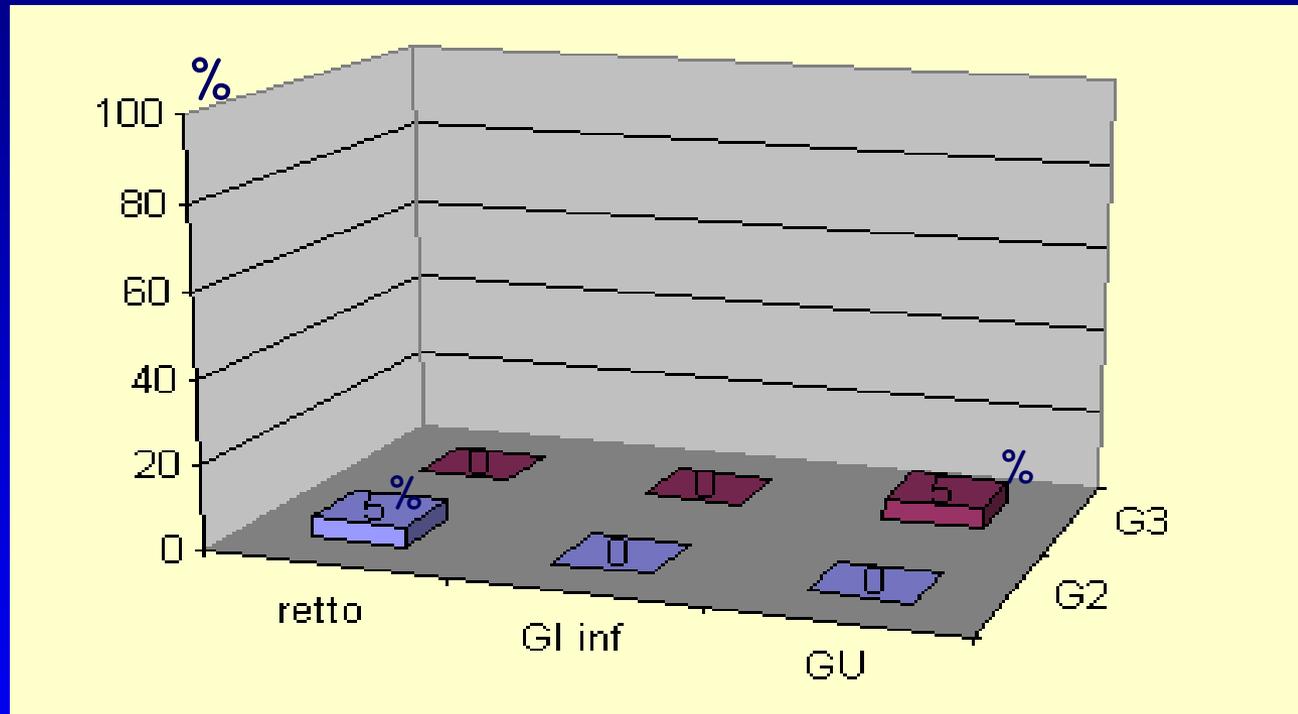
Nessuna tossicità acuta G3

Tossicità tardiva: dati preliminari

1/20 G2

1/20 G3

(9/20 G0)



Tutti i pazienti sono vivi, bNED:

(Media Ultimi PSA: 0,74 +/- 0,7 ng/ml (0,94 +/- 0,63 ng/ml, senza OT))

NUOVE TECNOLOGIE E CLINICA

III FASE dei PROGETTI MODENESI

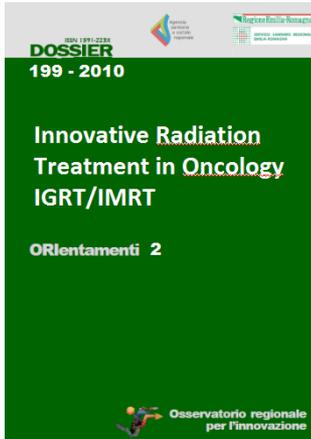
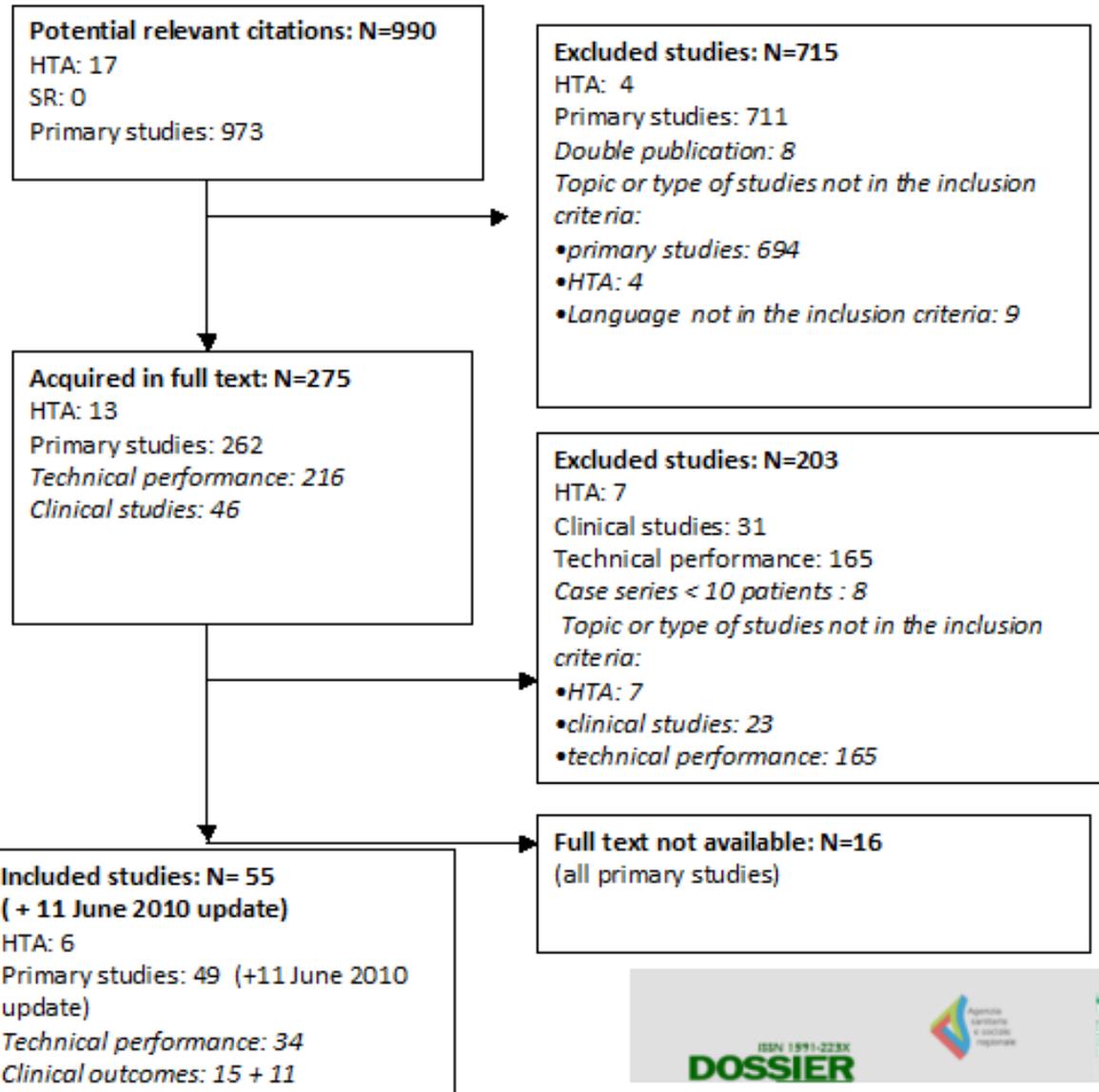
3D-CRT vs. IMRT / IGRT

Vantaggi clinici ?

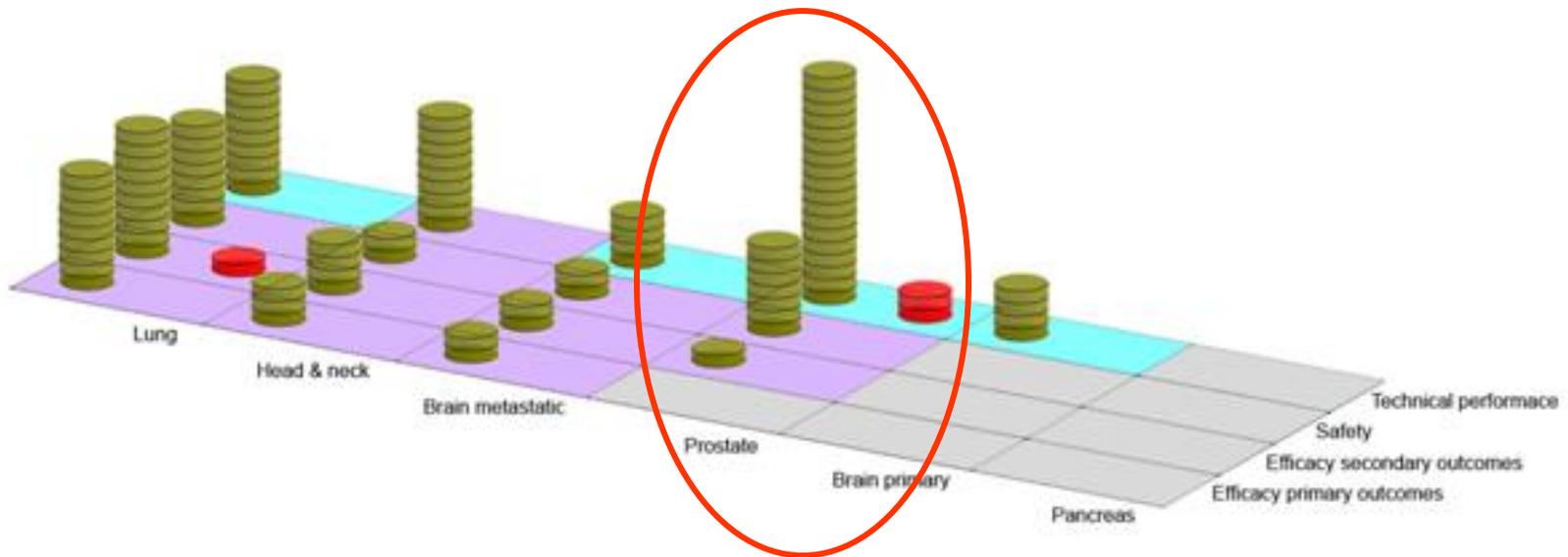
.....di valutazione e conferma
nell'ambito di studi cooperativi....

Systematic Review: up to June 2010

Flow chart of the search process



Systematic Review of literature: overall results



Levels of uncertainty

- Steady
- Plausible
- Uncertain
- Unknown

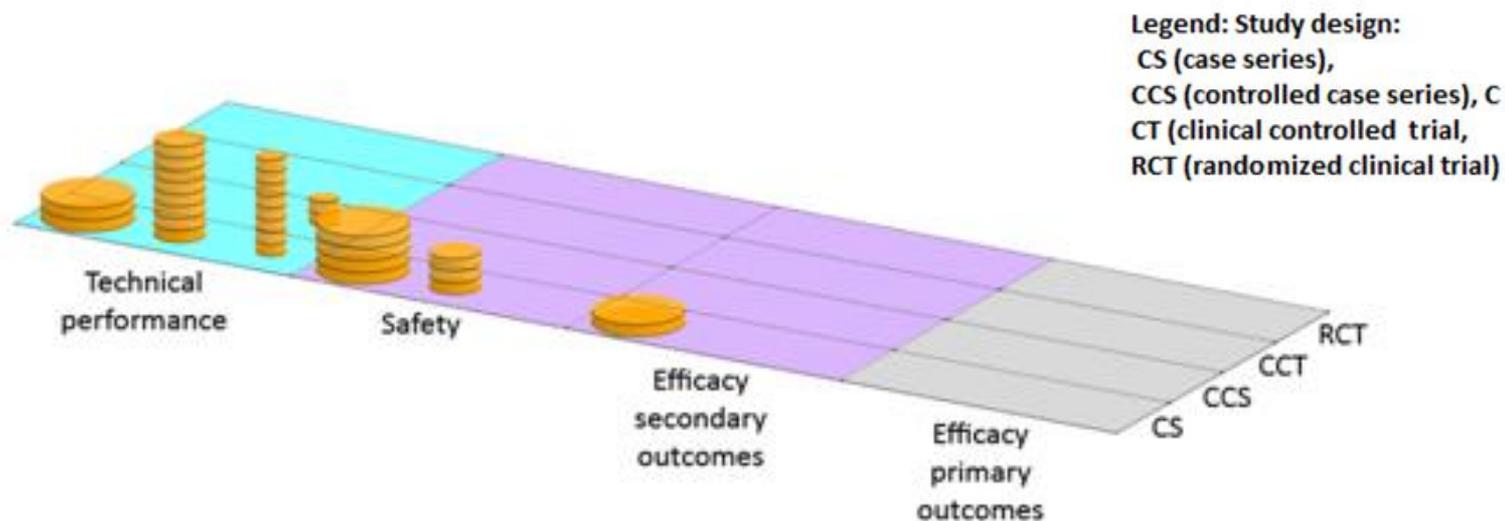
Type of studies

- Case series
- Controlled case series

I GAP CONOSCITIVI



RS DELLA LETTERATURA: prostate



Levels of uncertainty



Steady



Plausible



Uncertain



Unknown

Type of studies



Case series



Controlled case series

Number of patients



< 20



20 - 50



> 50

DOSSIER



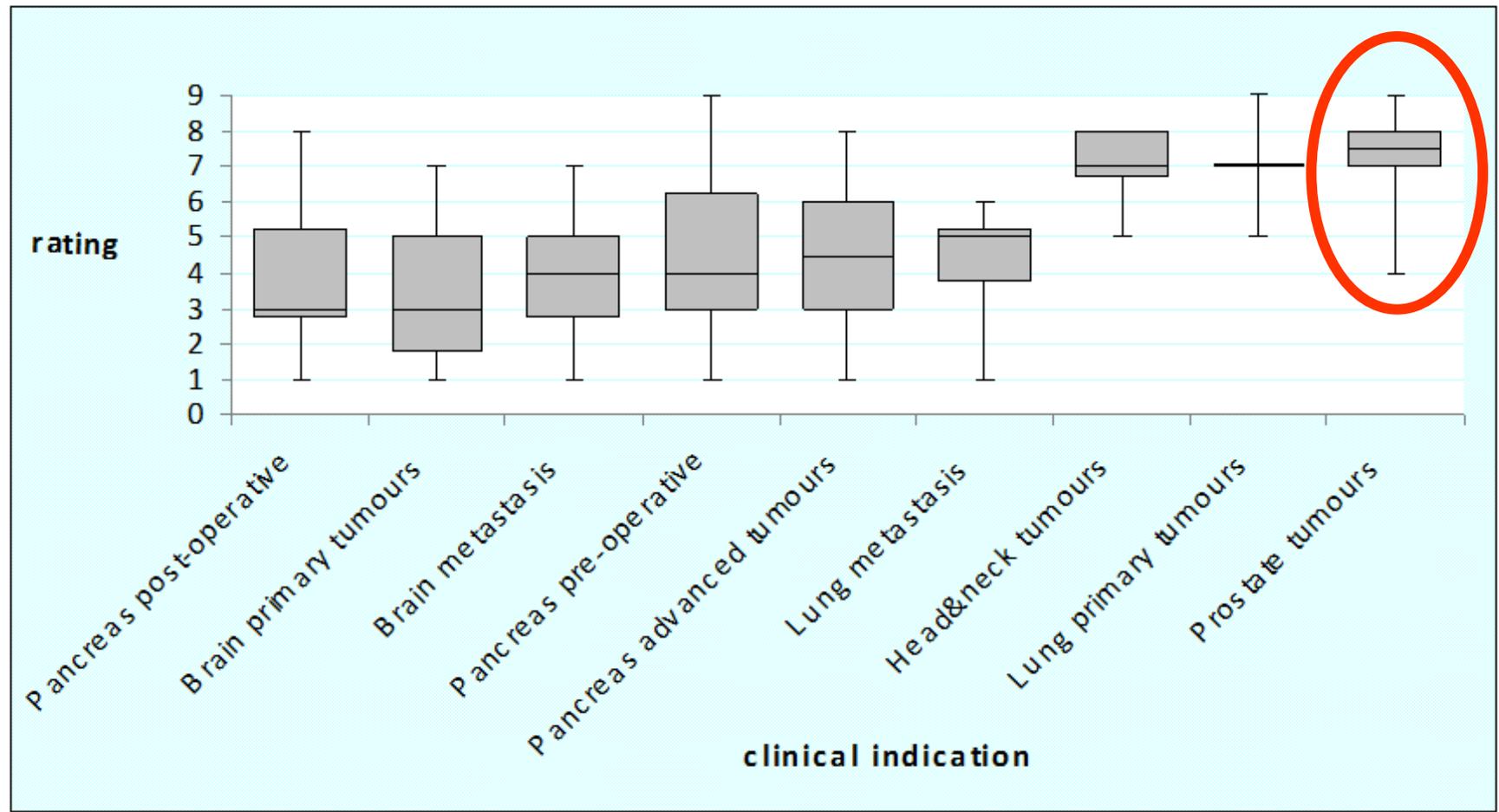


Vote on relevance of outcomes

Clinical condition	Outcome with highest median score for research relevance	Outcome with highest median score for clinical relevance
Prostate cancer	Disease specific survival	Disease specific survival, local control, recurrence, biochemical recurrence, late genito-urinary toxicity
Primary lung cancer	Local and loco-regional control	Disease free survival
Lung metastasis	Loco-regional control	Loco-regional control
Head & Neck cancer	Xerostomy	Xerostomy, Local control, Recurrence, Disease free survival



Vote on research priority



RECOMMENDATIONS FOR FUTURE RESEARCH

1. To assess whether radical radiation treatment with IGRT/IMRT with a higher biological dose in hypofraction regimen in patients with low and intermediate risk prostate cancer improves biochemical recurrence without increasing toxicity, compared to treatment with 3D-CRT/IMRT
2. To assess whether radical radiation treatment with IGRT/IMRT with a higher biological dose in hypofraction regimen in patients with primary lung cancer increases local and loco-regional control without increasing toxicity, compared to treatment with 3DCRT/IMRT
3. To assess whether radical radiation treatment with IGRT/IMRT with higher dose (not in hypofraction regimen) in patients with head & neck cancer increase local control without increasing toxicity, compared to treatment with 3D-CRT/IMRT

Prima Fase dello studio cooperativo

Project Leader: G. Frezza, Health Care Trust of Bologna

RICERCA FINALIZZATA 2009

Ministero della Salute – Direzione Generale della Ricerca Scientifica e Tecnologica

Application resume

Title: Assessment of the role of image guided hypofractionated intensity modulated radiotherapy in the treatment of prostate, lung and head and neck cancers

Code	RF-2009-1528879
Institution:	Emilia-Romagna
Type of research:	Clinical
Length (months)	36

.....to assess how the introduction of IGRT-IMRT radiotherapy could improve the efficacy and/or the efficiency of radiation treatment in cancer patients, starting from those for which the evidence retrieved is more promising. The works of the panel have been collected in a report (Dossier Innovative Radiation treatments in Oncology- ASSR-RER in press; <http://asr.regione.emilia-romagna.it/>).

The main feature of this study is to assess the impact of new radiation technologies not in a research institute, but within the frame of the oncological network of the Health Authority of the Emilia Romagna Region, that is in daily clinical practice.....

Radioterapia “image guided”
ipofrazionata e accelerata nel
trattamento dei tumori prostatici a
rischio basso e intermedio

Gruppo regionale AIRO
Emilia Romagna
(G. Frezza)

Courtesy of G. Frezza

.....oggi: le prove generali.....

- Pazienti a **rischio basso** (cT1T2a, PSA < 10ng/ml; GS uguale o < 6): 70Gy /28 fx vs 74 Gy/37 fx ; CTV prostata, no OT:
- Pazienti a **rischio intermedio** (almeno 1 fattore tra: cT2b T2c, PSA > 10ng/ml <20ng/ml; GS 7): 70.2 Gy/26 fx vs 78 Gy/39 fx; CTV: prostata + VS; OT (blocco androgenico totale) x 6 m.
- IMRT con imaging quotidiano per verifica set up e organ motion ed eventuale correzione

ENDPOINTS

Sopravvivenza libera da ricaduta biochimica a 3 aa
(criteri di Phoenix)

Tossicità rettale

Tossicità urinaria

Courtesy of G. Frezza

- The calculated BED in this study are:
- **Control arm, 74 Gy/37** fractions: BED10 88.8 Gy, BED3 123.3 Gy, BED1.5 172.6 Gy; **Experimental arm, 70 Gy/28** fractions BED10 87.5 Gy BED3 128.3 Gy, BED1.5 186.6 Gy.;
- **Control arm 78 Gy/39** fractions: BED10 93.6 Gy, BED3 130 Gy, BED1,5 182 Gy; **Experimental arm 70,2 Gy/26** fractions: BED10 89,1 Gy, BED3 133,4 Gy, BED 1,5 196.6 Gy.

Courtesy of G. Frezza

.....il futuro.....

ipofrazionamenti spinti ??

A PROSPECTIVE PHASE III RANDOMIZED TRIAL OF HYPOFRACTIONATION VERSUS CONVENTIONAL FRACTIONATION IN PATIENTS WITH HIGH-RISK PROSTATE CANCER

GIORGIO ARCANGELI, M.D.,* BIANCAMARIA SARACINO, M.D.,* SARA GOMELLINI, M.D.,*
MARIA GRAZIA PETRONGARI, M.D.,* STEFANO ARCANGELI, M.D.,* STENO SENTINELLI, M.D.,[†]
SIMONA MARZI, PH.D.,[†] VALERIA LANDONI, PH.D.,[†] JACK FOWLER, D.Sc., PH.D.,[§]
AND LIDIA STRIGARI, PH.D.[†]

*Department of Radiotherapy, [†]Laboratory of Medical Physics and Expert System, [‡]Department of Pathology, Regina Elena National Cancer Institute, Rome, Italy; and [§]Emeritus Departments of Human Oncology and Medical Physics, Medical School of the University of Wisconsin, Madison, WI

Purpose: To compare the toxicity and efficacy of hypofractionated (62 Gy/20 fractions/5 weeks, 4 fractions per week) vs. conventional fractionation radiotherapy (80 Gy/40 fractions/8 weeks) in patients with high-risk prostate cancer.

Methods and Materials: From January 2003 to December 2007, 168 patients were randomized to receive either hypofractionated or conventional fractionated schedules of three-dimensional conformal radiotherapy to the prostate and seminal vesicles. All patients received a 9-month course of total androgen deprivation (TAD), and radiotherapy started 2 months thereafter.

Results: The median (range) follow-up was 32 (8–66) and 35 (7–64) months in the hypofractionation and conventional fractionation arms, respectively. No difference was found for late toxicity between the two treatment groups, with 3-year Grade 2 rates of 17% and 16% for gastrointestinal and 14% and 11% for genitourinary in the hypofractionation and conventional fractionation groups, respectively. The 3-year freedom from biochemical failure (FFBF) rates were 87% and 79% in the hypofractionation and conventional fractionation groups, respectively ($p = 0.035$). The 3-year FFBF rates in patients at a very high risk (*i.e.*, pretreatment prostate-specific antigen (iPSA) >20 ng/mL, Gleason score ≥ 8 , or T $\geq 2c$), were 88% and 76% ($p = 0.014$) in the former and latter arm, respectively. The multivariate Cox analysis confirmed fractionation, iPSA, and Gleason score as significant prognostic factors.

Conclusions: Our findings suggest that late toxicity is equivalent between the two treatment groups and that the hypofractionated schedule used in this trial is superior to the conventional fractionation in terms of FFBF. © 2009 Elsevier Inc.

- 8 sett. vs. 5 sett. (62 Gy in 20 frazioni vs standard 80Gy in 40 frazioni)
- 3D-CRT

Tomotherapy

Soete 2009

Tomotherapy per 28 pz, 54 Gy in fr 1.8 Gy/die + SIB 70.5 su T
per 8 pz SIB su N+ fino a 60 Gy

RTOG	G2	G3	G4
Tossicità GI acuta	7 %	0%	0%
Tossicità GU acuta	14%	4%	0%

Ritter 2007

210 pts treated with Tomotherapy or Linac-based IMRT

110 pts 64.7 Gy\22 fx of 2.94 Gy

50 pts 58.08 Gy\16 fx of 3.63 Gy

50 pts 51.6 Gy\12 fx of 4.3 Gy

20-30 % with acute grade 2 GU toxicity

5-10 % with acute grade 2 GI toxicity



RT in 16 frazioni: risultati incoraggianti

