

CONVEGNO DEL GRUPPO REGIONALE PIEMONTE-LIGURIA-VALLE D'AOSTA



Associazione
Italiana
Radioterapia
Oncologica

Radiochirurgia e Radioterapia stereotassica: *non solo tecnica*



Genova
25 MARZO
2017

E.O. Ospedali Galliera

**RADIOCHIRURGIA E RADIOTERAPIA
STEREOTASSICA BODY: ESPERIENZE CLINICHE
E INTEGRAZIONI CON TERAPIE SISTEMICHE**

Prostata: letteratura ed esperienza clinica



CONVEGNO DEL GRUPPO REGIONALE PIEMONTE-LIGURIA-VALLE D'AOSTA



Risultati clinici

Aspetti radiobiologici

Aspetti tecnologici

Esperienza clinica multicentrica **Genova-Torino-Brescia**





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Esperienza clinica multicentrica **Genova-Torino-Brescia**

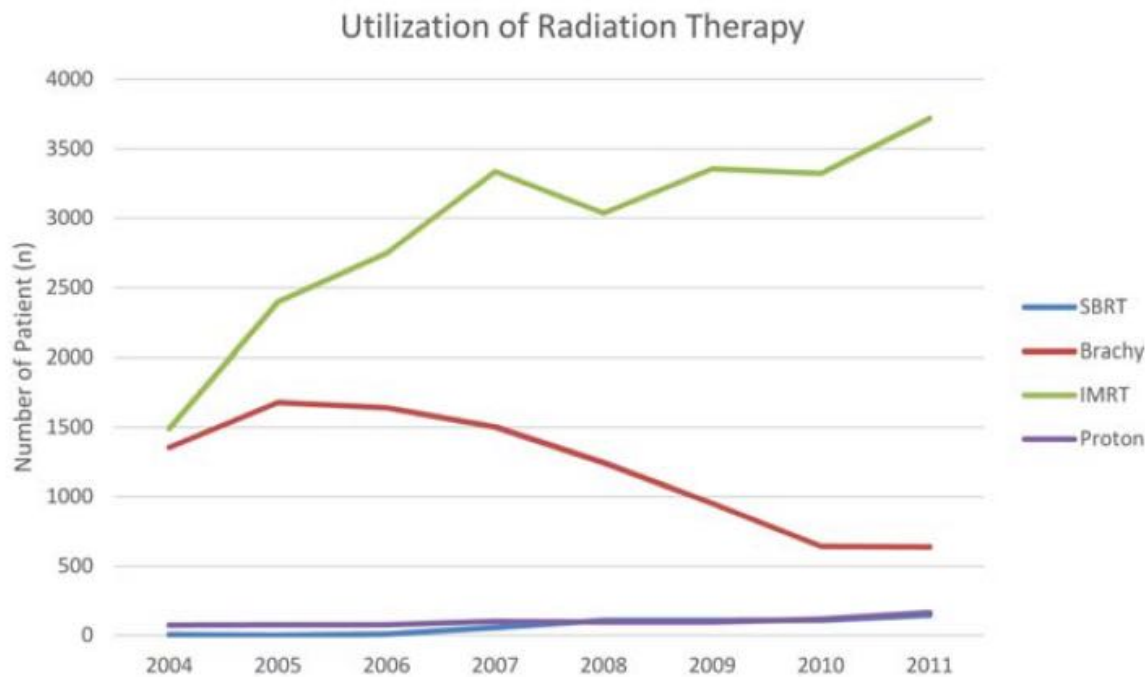




Use, Complications, and Costs of Stereotactic Body Radiotherapy for Localized Prostate Cancer

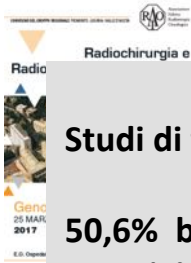
Cancer August 15, 2016

2004 and 2011 from Surveillance Epidemiology and End Results Program (SEER)-Medicare linked data



From 2004 to 2011, a total of 542 patients underwent SBRT, 9647 patients received brachytherapy, 23,408 patients received IMRT and 800 patients received proton. There was an increase in SBRT use from <math><0.4\%</math> to 2.7% among all radiotherapies.





Studi di fase I/II retrospettivi prospettici

- 50,6% basso rischio**
- 39,6% intermedio rischio**
- 9,7% alto rischio**

R

In 20 lavori pubblicati 15 trattati con Cyberknife , 5 Linac e/o Tomo

Follow-up mediano range 55 - 18 mesi

(RPCR registry)

99 % low risk
97-85 % interm.
87 % high

Tossicità

GU range

- G2 5-15%**
- G3 0-5%**

GI range

- G2 7-10%**
- G3 0-2%**

disuria, nicturia, raro sanguinamento rettale, rara emospermia, conservazione della capacità erettile nell'80 % dei pazienti di età ≤ 70 anni.



[49]

Oliai et al. [50] 70 37

FFBF
100 %/95 %/77 %

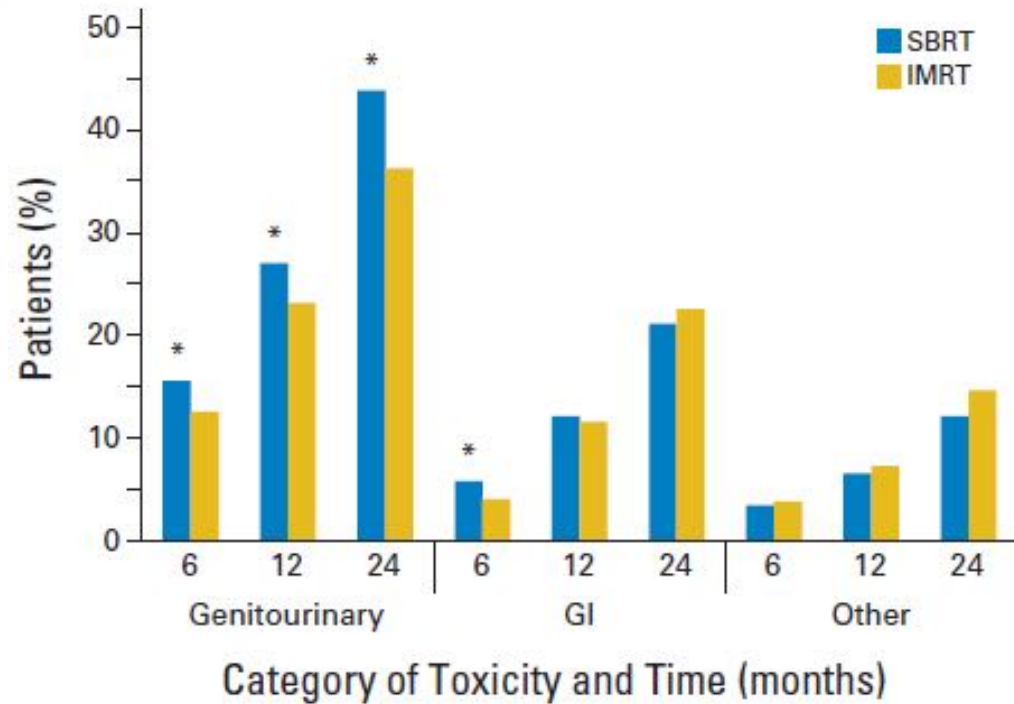
Quon et al. [51] 84 18

BRFS 99 % @ 3y



Stereotactic Body Radiation Therapy Versus Intensity-Modulated Radiation Therapy for Prostate Cancer: Comparison of Toxicity

1.335 SBRT and 2.670 IMRT patients





NCCN

National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 2.2017 Prostate Cancer

- **Extremely hypofractionated image-guided IMRT/SBRT regimens (6.5 Gy per fraction or greater) are an emerging treatment modality with single institutional and pooled reports of similar efficacy and toxicity to conventionally fractionated regimens. They can be considered as an alternative to conventionally fractionated regimens at clinics with appropriate technology, physics, and clinical expertise.**





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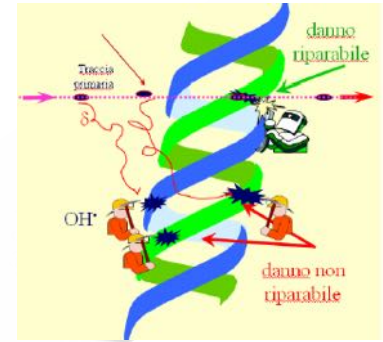
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Principali modelli Radiobiologici



LQ:

1. La perdita della capacità riproduttiva può avvenire sia per un singolo evento in un singolo target che per più eventi nello stesso target
2. La prima modalità di danno ha un andamento lineare con la dose (α)
3. La seconda un andamento con il quadrato della dose (β)
4. La curva dose effetto è priva di un tratto retto
5. La prevalenza della componente α o della componente β determina la forma della curva

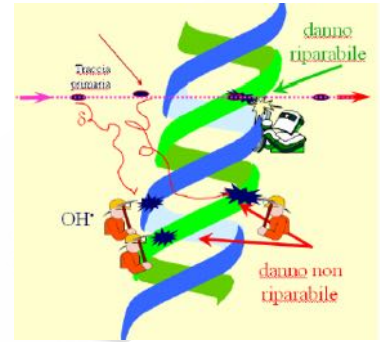
Multi-target

1. In ogni cellula esistono più n bersagli sensibili in ognuno dei quali devono verificarsi almeno un evento per avere la perdita della capacità riproduttiva
2. La curva ha una spalla iniziale e una parte esponenziale
3. La larghezza della spalla dipende dal numero di bersagli che devono essere colpiti per determinare la morte cellulare.
4. N è il numero di estrapolazione che definiscono il numero dei bersagli
5. D_q è la dose dopo la quale la curva assume un andamento esponenziale
6. D° esprime la pendenza del tratto esponenziale
7. Le cellule che sono state colpite da un numero inferiore a n possono riparare il danno





Is the Linear-Quadratic Model appropriate to model high dose for fraction affects in SBRT/SRS?



The Linear-Quadratic Model Is an Appropriate Methodology for Determining Isoeffective Doses at Large Doses Per Fraction

David J. Brenner, PhD, DSc

Seminars in
**RADIATION
ONCOLOGY**

2008



Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 3, pp. 847-852, 2008
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0360-3016/08/\$-see front matter

doi:10.1016/j.ijrobp.2007.10.059

BIOLOGY CONTRIBUTION

UNIVERSAL SURVIVAL CURVE AND SINGLE FRACTION EQUIVALENT DOSE: USEFUL TOOLS IN UNDERSTANDING POTENCY OF ABLATIVE RADIOTHERAPY

CLINT PARK, M.D. M.S., LECH PAPIEZ, PH.D., SHICHUAN ZHANG, M.D., PH.D.,
MICHAEL STORY, PH.D., AND ROBERT D. TIMMERMAN, M.D.

Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX



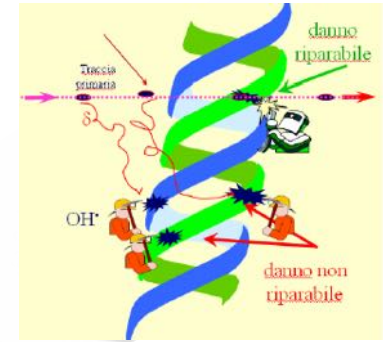


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Biologically effective dose (BED) when expressed through linear quadratic (LQ) model parameters overestimates actual biologically effective dose as determined through empirical survival curve

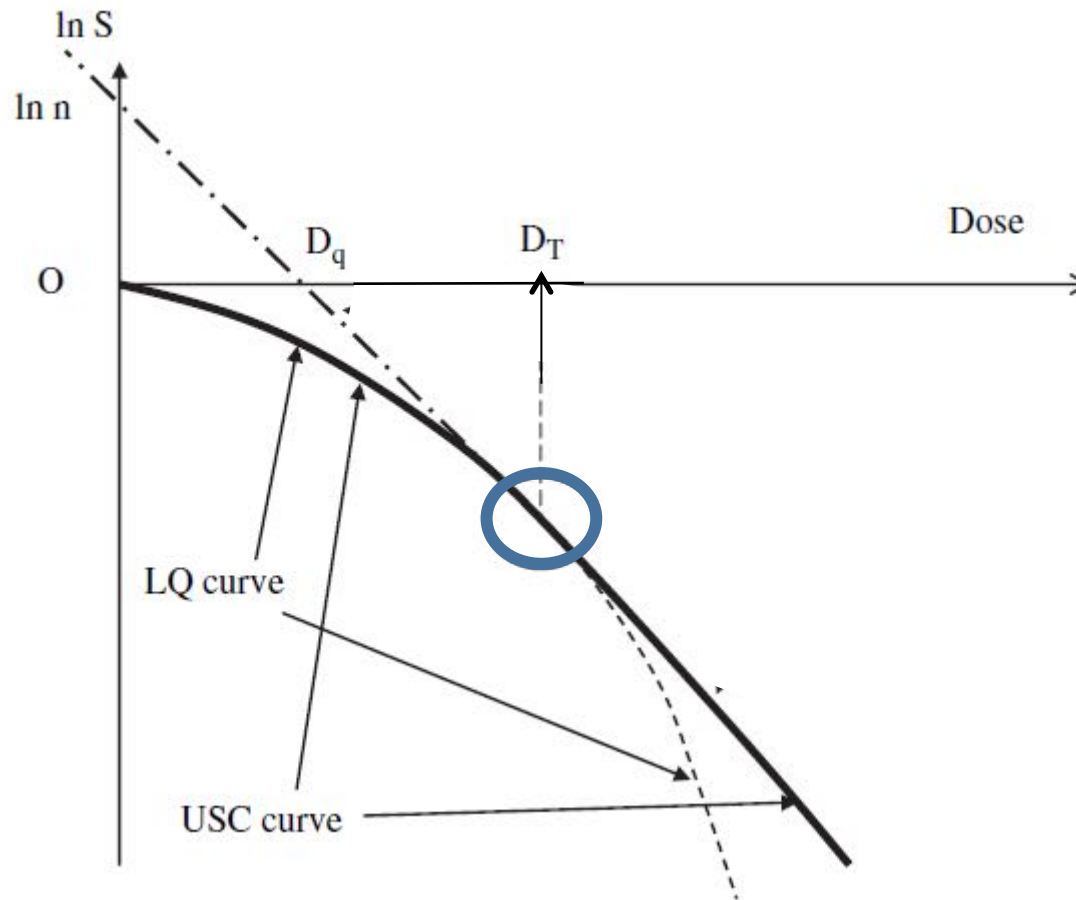
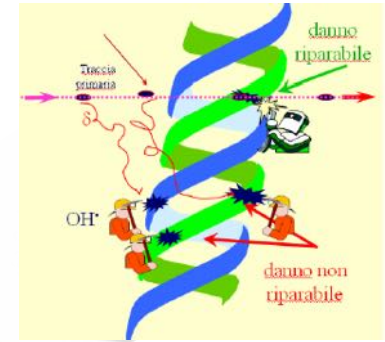


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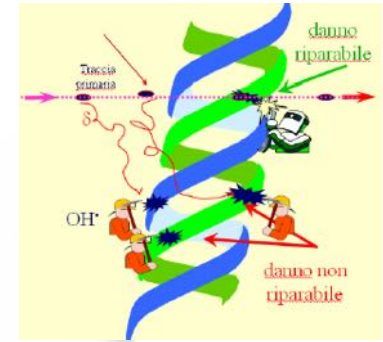




Prostate radiotherapy

The role of overall treatment time in the outcome of radiotherapy of prostate cancer: An analysis of biochemical failure in 4839 men treated between 1987 and 1995

_____ OT ≥ 52 days - - - - - OT ≤ 52 days



Published estimates of dose equivalent of proliferation (Gy/day).

Tumor	D_{prolif} (95% CI)
Present results	0.24 (0.03,0.44)
Various head and neck ²³	0.8 (0.5,1.1)
Tonsil ²⁴	0.73 (-,-)
Various ²⁵	0.64 (0.42,0.86)
Nonsmall cell lung ²⁶	0.45 (-,-)
Larynx ²⁷	0.74 (0.30,1.2)
Medulloblastoma ²⁸	0.52 (0.29,0.75)
Esophagus ²⁹	0.59 (0.18,0.99)

Modified from Bentzen and Joiner.²⁰

These effects were quantified as a relative increase after 5 years follow-up of 6% in biochemical failure for a 1-week increase in OT, a relative decrease of 15% in BFs for a 6-Gy increase in dose, and a dose equivalent of proliferation of 0.24 Gy/day.





Contents lists available at ScienceDirect

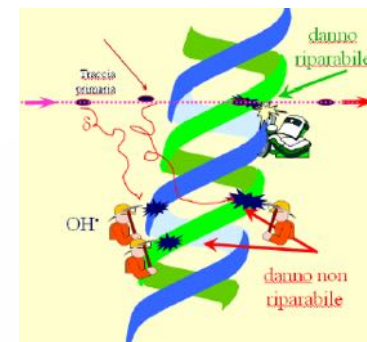
Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Prostate radiotherapy

The role of overall treatment time in the outcome of radiotherapy of prostate cancer: An analysis of biochemical failure in 4839 men treated between 1987 and 1995



challenges the widespread view of a negligible time factor for prostate cancer, and leads to the hypothesis that meaningful improvements in outcome may be targeted by modest increases in total dose and decreases in OT. Treatment interruptions leading to prolonged overall treatment times can have negative consequences and have to be adequately compensated.





Critical Review

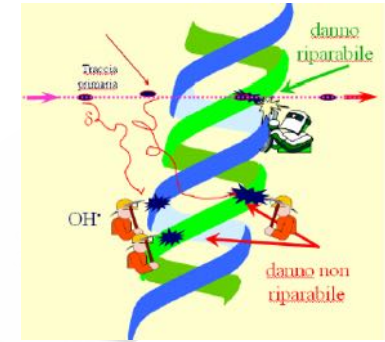
The Tumor Radiobiology of SRS and SBRT: Are More Than the 5 Rs Involved?

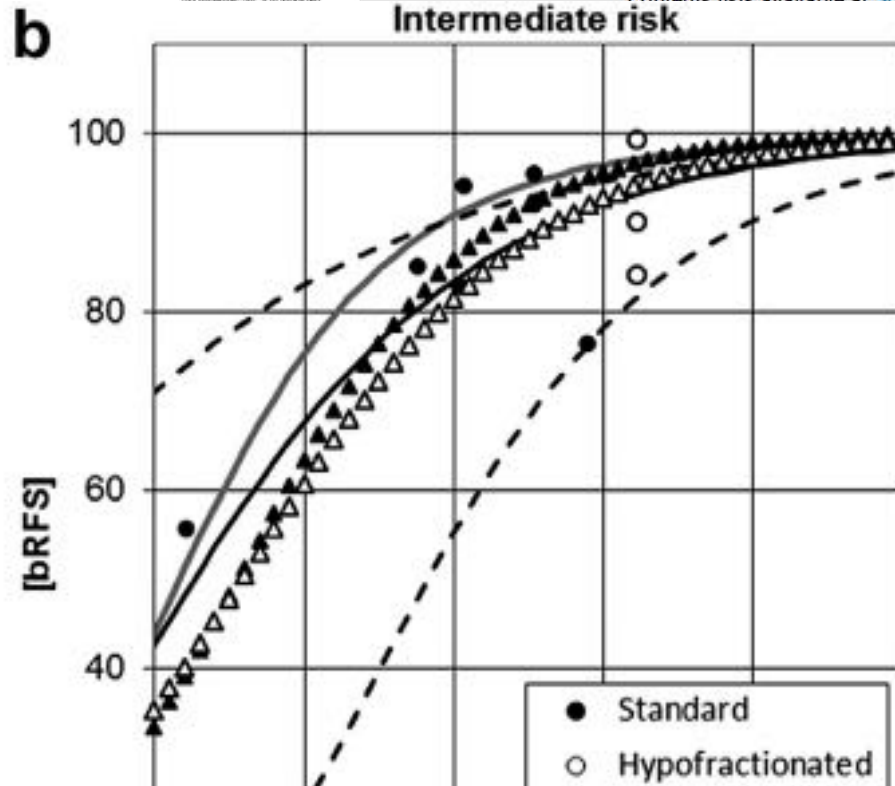
In addition to objections to the LQ model, the possibility of additional biological effects resulting from endothelial cell damage, enhanced tumor immunity, or both have been raised to account for the success of SRS and SBRT.



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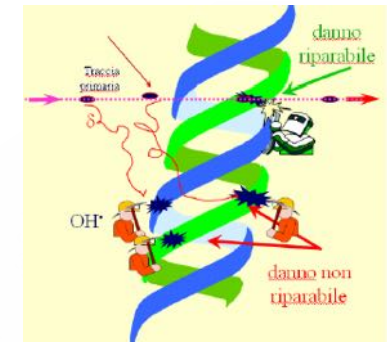
number of models for patients treated with to test these models were included.

ed from large series of the purpose of this study was pofractionated radiotherapy

The data reviewed show consistency between the various radiobiological model predictions and the currently observed data.

Conclusion: Current radiobiological models provide accurate predictions of biochemical relapse-free survival, even when profoundly hypofractionated patients are included in the analysis

CONVEGNO DEL



Aspetti radiobiologici:

1. Il modello LQ sovrastima , per dosi singole alte, l'effetto sulla sopravvivenza cellulare
2. Nuovi modelli per ottenere curve predittive di sopravvivenza cellulare più accurate rispetto al modello LQ quando si utilizzano dosi singole elevate: Universal Survival Curve (USC)
3. Il fattore tempo può giocare un ruolo importante sulla risposta biologica.
4. il tempo ristretto nei protocolli di ipofrazionamento può in parte spiegare l'efficacia clinica



Queste considerazioni possono spiegare

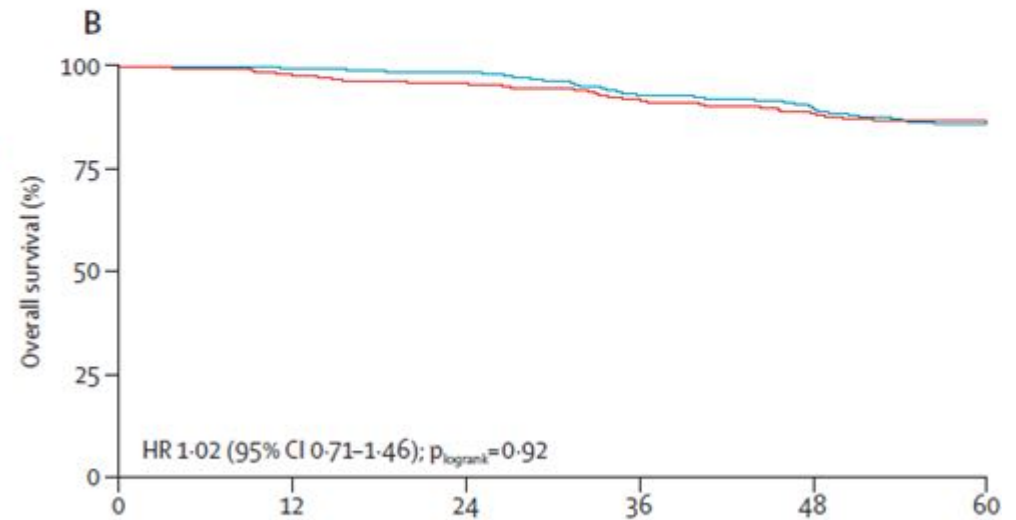
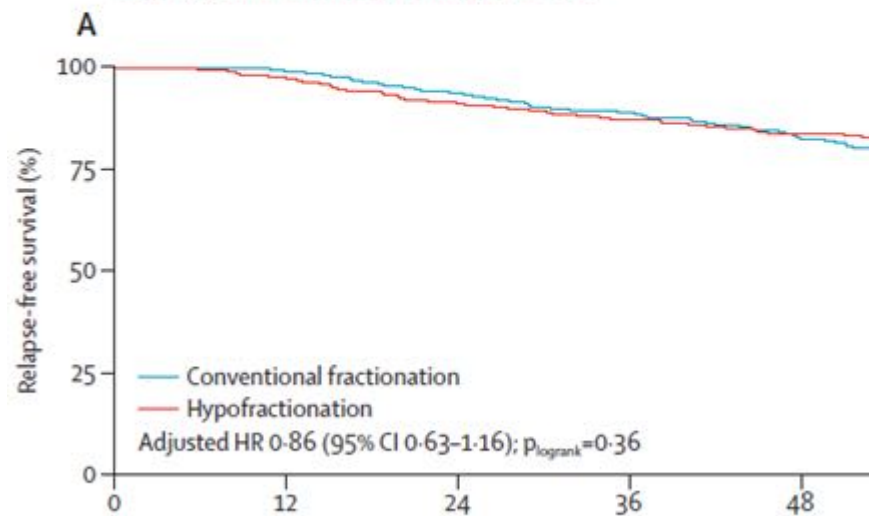


Hypofractionated versus conventionally fractionated radiotherapy for patients with localised prostate cancer (HYPRO): final efficacy results from a randomised, multicentre, open-label, phase 3 trial



Lancet Onco 2016; 17: 1061-69

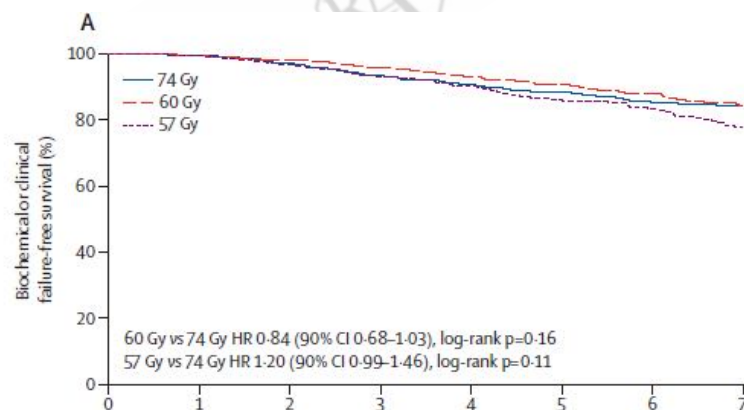
Luca Incrocci*, Ruud C Wortel*, Wendimagegn Ghidye Alemayehu, Shafak Aluwini, Erik Schimmel, Stijn Krol, Peter-Paul van der Toorn, Hanja de Jager, Wilma Heemsbergen, Ben Heijmen, Floris Pos



CONVEGNI

Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial

Lancet Oncol 2016; 17: 1047-60

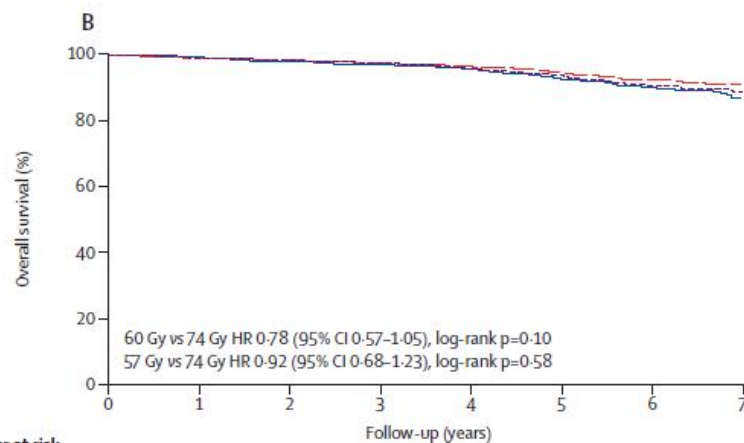


Number at risk (events)

74 Gy	1065 (4)	1037 (24)	991 (39)	926 (24)	795 (20)	495 (11)	284 (3)	167 (11*)
60 Gy	1074 (4)	1042 (15)	1011 (23)	965 (28)	816 (18)	533 (10)	280 (10)	176 (10*)
57 Gy	1077 (5)	1044 (30)	1004 (35)	944 (31)	798 (31)	492 (9)	262 (13)	151 (9*)

Number censored

74 Gy	0	24	22	26	107	280	200	114
60 Gy	0	28	16	23	121	265	243	94
57 Gy	0	28	10	25	115	275	221	98



Number at risk

Follow-up (years)



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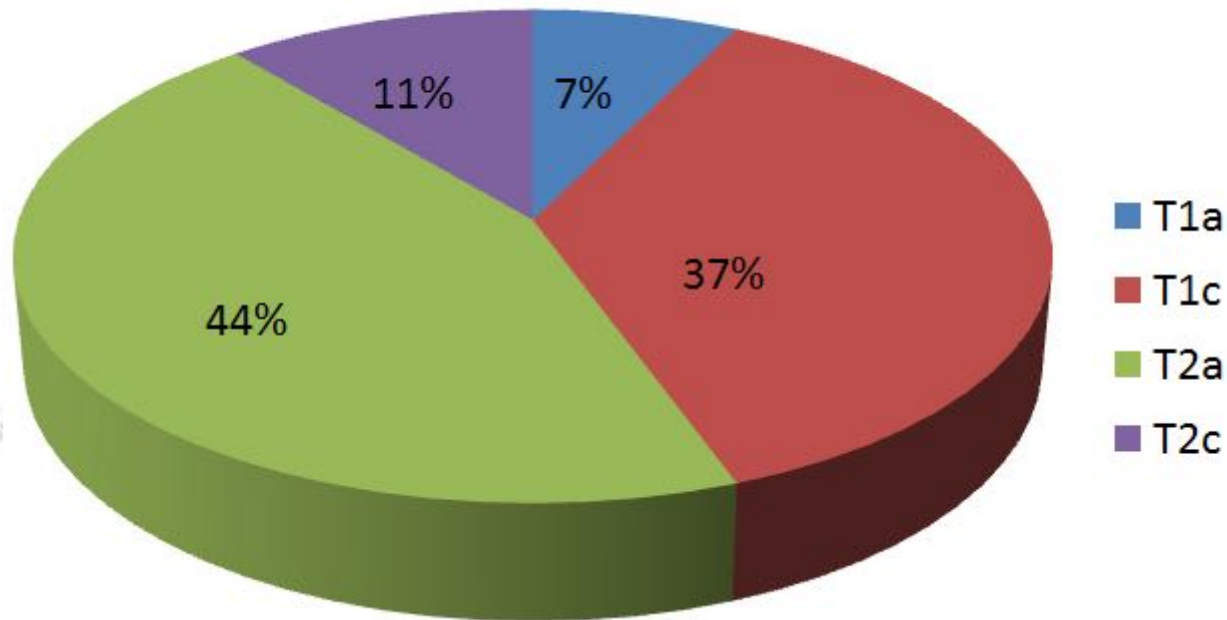


Aspetti tecnologici



multiple non-coplanar fields
intensity modulated
arc-therapy
image-guided RT (IGRT)
flattening filter-free beam technology
intraprostatic fiducial markers
Spacers and endorectal balloons





28 pazienti inseriti follow-up mediano 28 mesi

Tox acuta urinaria 7,1 % G2

Tox tardiva urinari 28,5 % G1

Tox acuta rettale 3,1 G2

Tox tardiva rettale 10,7 G1

Nessuna ricaduta biochimica

- . **Ottima fattibilità**
- . **Buona compliance del paziente**
- . **Risultati di tossicità in linea con i dati pubblicati**
- . **Risultati preliminari sulla qualità di vita promettenti**



REVIEW ARTICLE

Hypofractionated radiotherapy for localized prostate cancer

Cancer Treatment Reviews 50 (2016) 48–60

Contents lists available at ScienceDirect



Cancer Treatment Reviews

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



extreme hypofractionat
RS is delivered with few
there is strong evidence

Gratie

follow-up for most studies has been relatively short
cost-effectiveness RS/IMRT
Randomized clinical trials ongoing
long-term follow-up is needed to evaluate biological endpoints such: disease-free survival,
metastasis-free and overall survival.



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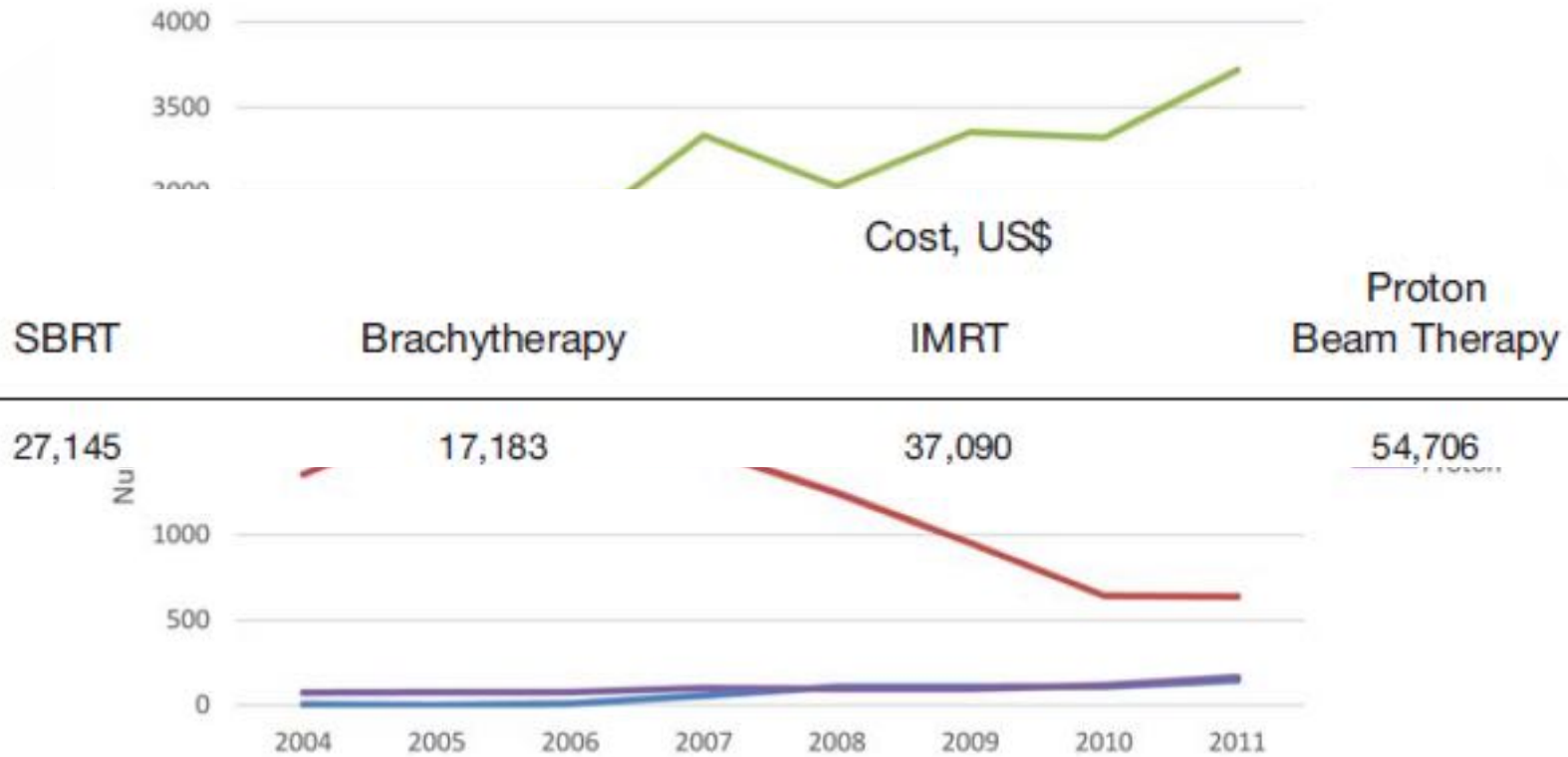
grazie

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Utilization of Radiation Therapy



CONVEGNO DEL GRUPPO REGIONALE

Cancer August 15, 2016



Variation BED in a dose escalation 0-27 Gy for cells DU145

