SBRT prostate: clinical data

Aifm Associazione Italiana di Fisica Medica
UNIVERSITÀ DEGLI STUDI DI MILANO
24/25 OTTOBRE 2014
Università degli studi di Milano
STEREOTACTIC BODY RADIATION THERAPY
Implementazione, Sostenibilità, Avanzamento Tecnologico e Risultati a Confronto

Patrocinio
Associazione Italiana Radioterapia Oncologica

S. Arcangeli

Background of SBRT for PCa

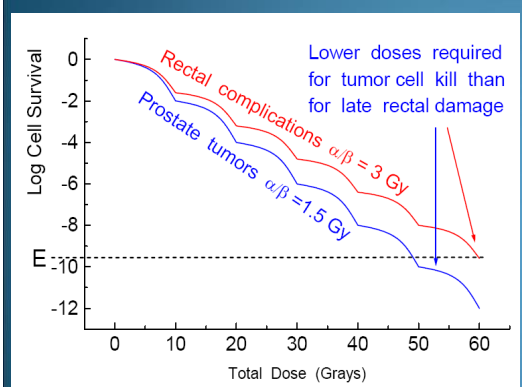
- **BIOLOGICAL**: unusual radiobiology of PCa
- **PHYSICAL**: accurate targeting and delivering
- **CLINICAL**: phase III trials of moderate hypofractionation

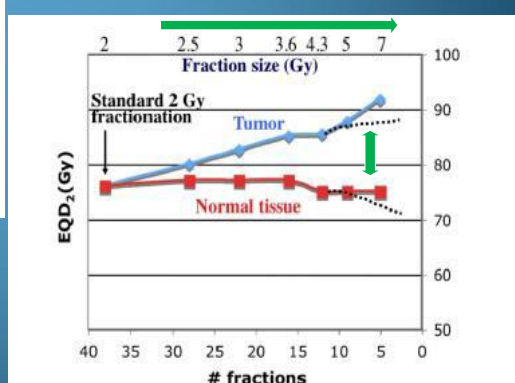
Unusual Radiobiology of PCa

Tumour type	T_{pot} (days)	T_d (days)	Radiobiological/clinical properties	Treatment indication
Head and neck	4.5 (1.8–5.9) Rew et al. [6]	45 Rew et al. [6]	– Rapid regrowth during treatment – High hypoxic content	Hyperfractionation Accelerated radiotherapy
Prostate	28 (16–61) Haustermans et al. [7]	1100 Lee et al. [8]	– Slow proliferation – Very low α/β ratio	Hypofractionation
Glioblastoma	3.9–7.5 Hlatky et al. [9] 2.3–13.3 Nakajima et al. [10]	3.3–29.2 Nakajima et al. [10]	– High hypoxic content – Poor differentiation; radioresistance – High proliferation	Hyperfractionation Accelerated radiotherapy Hyperfractionation
Breast	10.4 (8.2–12.5) Rew et al. [6]	82 Spratt et al. [11] 44–295 Peer et al. [12]	– Age-dependent proliferation – α/β ratio similar to the normal tissue one	Hypofractionation Accelerated radiotherapy
Lung (non-small cell lung cancer – NSCLC)	7.1 Shimomatsuya et al. [13] 8.2 Shibamoto et al. [14]	46 Sharouni et al. [15] 67.5 Arai et al. [16] 81 Lindell et al. [17]	– Small volume doubling time – Rapid regrowth during treatment – NCSLC higher radioresistance than other histologic types	Hyperfractionation Accelerated radiotherapy

Cancer Treatment Reviews 36 (2010)

Hypofractionation & Therapeutic Ratio





Ritter et al Cancer J 2009

How Best Can Hypofractionation Be Explored in a Clinical Setting?

Two approaches:

1) Normal tissue de-escalation of total dose while maintaining constant predicted tumour control.

2) Tumour biological dose escalation with constant predicted normal tissue late effects.

Ritter, Sem Rad Onc 2008

NCCN National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2014
Prostate Cancer

NCCN Guidelines Index
Prostate Table of Contents
Discussion

Moderately hypofractionated image-guided IMRT regimens (2.4–4 Gy per fraction over 4-6 weeks) have been tested in randomized trials and efficacy and toxicity have been similar to conventionally fractionated IMRT.[106,107] These RT techniques can be considered as an alternative to conventionally fractionated regimens when clinically indicated.

106. Pollack A, Walker G, Horwitz EM, et al. Randomized trial of hypofractionated external-beam radiotherapy for prostate cancer. J Clin Oncol 2013;31:3860-3868. Available at: http://www.ncbi.nlm.nih.gov/pubmed/24101042.

107. Arcangeli S, Strigari L, Gomellini S, et al. Updated results and patterns of failure in a randomized hypofractionation trial for high-risk prostate cancer. Int J Radiat Oncol Biol Phys 2012;84:1172-1178. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22537541.

"MODERN" Randomized Trials

Explicit assumptions about the α/β ratio of PCa

Trial	Pts	Schedule	RT	NTD2 1.5 (Gy)	NTD2 3 (Gy)	Median FUP	% 5y-bRFS	%GI	%GU
USA *IJROBP 2014*	102 LI 102 LI	75.6 Gy/1.8 Gy/42 f 72 Gy/2.4 Gy/30 f	I MR T	71.3 80.2	72.6 77.8	72 mo	92 96	≥ G2 5.1 ≥ G2 10	≥ G2 16.5 ≥ G2 15.8
ITALY *IJROBP 2012*	85 H 83 H	80 Gy/2Gy/40 f 62 Gy/3.1 Gy/20 f	3D	80 81.5	80 74	70 mo	74 85	≥ G2 17 ≥ G2 16	≥ G2 14 ≥ G2 11
USA *JCO 2013*	152 LIH 151 LIH	76 Gy/2 Gy/38 f 70.2 Gy/2.7 Gy/26 f	I MR T	76 84.2	76 80	68.4 mo	78.6 76.7	≥ G2 22.5 ≥ G2 18.1	≥ G2 13.4 ≥ G2 21.5

"MODERN" Randomized Trials

Assumption of α/β ratio of PCa = 1.5 Gy

Trial	Pts	Schedule	RT	NTD2 1.5 (Gy)	NTD2 3 (Gy)	Median FUP	% 5y-bRFS	%GI	%GU
USA *IJROBP 2014*	102 LI 102 LI	75.6 Gy/1.8 Gy/42 f 72 Gy/2.4 Gy/30 f	I MR T	71.3 80.2	72.6 ! 77.8	72 mo	92 96	≥ G2 5.1 ≥ G2 10	≥ G2 16.5 ≥ G2 15.8

+ 9 Gy *+ 5 Gy*

P = 0.23 P = 0.11 P = 0.97

REJECTED

HYPOTHESIS

t[illegible] difference in biochemical failure at 5 –y

in [illegible] of hypo arm

"MODERN" Randomized Trials

Assumption of α/β ratio of PCa = 1.5 Gy

Trial	Pts	Schedule	RT	NTD2 1.5 (Gy)	NTD2 3 (Gy)	Median FUP	% 5y-bRFS	%GI	%GU
USA *JCO 2013*	152 LIH 151 LIH	76 Gy/2 Gy/38 f 70.2 Gy/2.7 Gy/26 f	I MR T	76 84.2	76 80	68.4 mo	78.6 76.7	≥ G2 22.5 ≥ G2 18.1	≥ G2 13.4 ≥ G2 21.5
				+ 8 Gy	*+ 4 Gy*				

!

P = 0.745 P = 0.39 P = 0.15

REJECTED

HYPOTHESIS

t… hypofx would improve FFBF from 70% to 85%

5 –… out increasing late complic's

"MODERN" Randomized Trials

Assumption of α/β ratio of PCa = 1.5 Gy

Trial	Pts	Schedule	RT	NTD2 1.5 (Gy)	NTD2 3 (Gy)	Median FUP	% 5y-bRFS	%GI	%GU
ITALY *IJROBP 2012*	85 H 83 H	80 Gy/2Gy/40 f 62 Gy/3.1 Gy/20 f	3D	80 81.5	80 74	70 mo	79 85	≥ G2 17 ≥ G2 16	≥ G2 14 ≥ G2 11
					- 6 Gy				

P = 0.065 P = 0.571 P = 0.098

REJECTED

HYPOTHESIS

h… result in similar disease control and

fe… s than a half) late complications

"MODERN" Randomized Trials

Moderate Hypofractionation: Contemporary Superiority Trials

Study (Author)	Sample Size	ADT (%)	Median Follow-up	Randomization Arms	Toxicity	Efficacy
Regina Elena (Arcangeli)	168	100	5.8 years	80 Gy/2 Gy 62 Gy/3.1 Gy	NS	NS
FCCC (Pollack)	303	45	5.5 years	76 Gy/2 Gy 70.2 Gy/2.7 Gy	Hypofractionation: worse GU effects **if IPSS ≥ 12**	NS
MDACC (Kuban)	204	21	4.7 years	75.6 Gy/1.8 Gy 72 Gy/2.4 Gy	NS	NS

Abbreviations: ADT, androgen deprivation therapy; FCCC, Fox Chase Cancer Center; GU, genitourinary; MDACC, MD Anderson Cancer Center; NS, no significant difference.

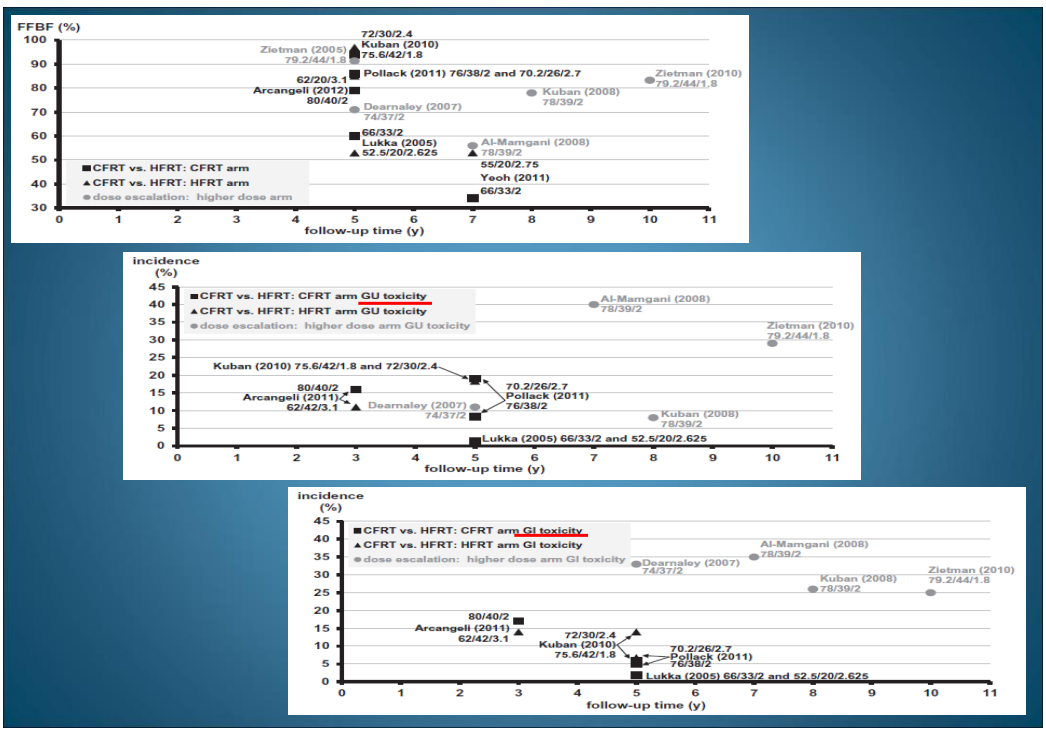
Statistical insignificance in a superiority study does not imply that treatments are equivalent, only that the data are insufficient to conclude that the treatments are different

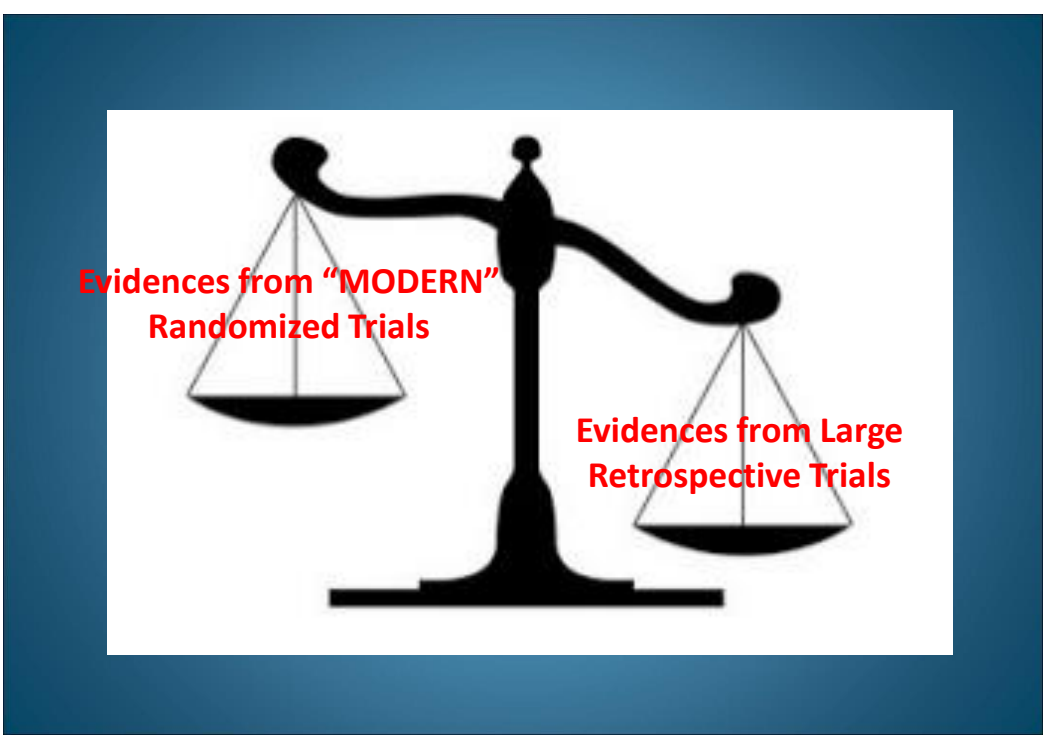
"MODERN" Randomized Trials

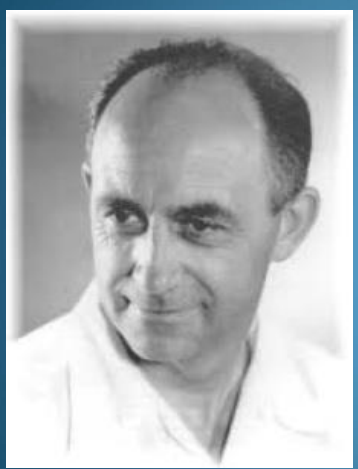
statistically significant

OR

clinically relevant ?


FFBF (%)
follow-up time (y)
CFRT vs. HFRT: CFRT arm
CFRT vs. HFRT: HFRT arm
dose escalation: higher dose arm
72/30/2.4
Kuban (2010)
75.6/42/1.8
Zietman (2005)
79.2/44/1.8
Pollack (2011) 76/38/2 and 70.2/26/2.7
62/20/3.1
Arcangeli (2012)
80/40/2
Dearnaley (2007)
74/37/2
Kuban (2008)
78/39/2
Zietman (2010)
79.2/44/1,8
66/33/2
Lukka (2005)
52.5/20/2.625
Al-Mamgani (2008)
78/39/2
55/20/2.75
Yeoh (2011)
66/33/2
incidence (%)
CFRT vs. HFRT: CFRT arm GU toxicity
CFRT vs. HFRT: HFRT arm GU toxicity
dose escalation: higher dose arm GU toxicity
Kuban (2010) 75.6/42/1.8 and 72/30/2.4
80/40/2
Arcangeli (2011)
62/42/3.1
70.2/26/2.7
Pollack (2011)
76/38/2
Lukka (2005) 66/33/2 and 52.5/20/2.625
incidence (%)
CFRT vs. HFRT: CFRT arm GI toxicity
CFRT vs. HFRT: HFRT arm GI toxicity
dose escalation: higher dose arm GI toxicity


Evidences from "MODERN" Randomized Trials
Evidences from Large Retrospective Trials



"Ci sono soltanto due possibili conclusioni: se il risultato conferma le ipotesi, allora hai appena fatto una misura; se il risultato è contrario alle ipotesi, allora hai fatto una scoperta".

E. Fermi

Multi-institutional Non-Inferiority Trials

Moderate Hypofractionation: Ongoing Noninferiority Trials

Study (Group)	Sample Size	Risk Group	Randomization Arms
CHHiP (MRC)	3216	Intermediate/ low	74 Gy/2 Gy 57 Gy/3 Gy 60 Gy/3 Gy
0415 (RTOG)	1067	Low	73.8 Gy/1.8 Gy 70 Gy/2.5 Gy
PROFIT (OCOG)	1204	Intermediate	78 Gy/2 Gy 60 Gy/3 Gy

Abbreviations: CHHiP, conventional or hypofractionated high-dose intensity-modulated radiotherapy in prostate cancer; MRC, Medical Research Council; OCOG, Ontario Clinical Oncology Group; PROFIT, Prostate Fractionated Irradiation Trial; RTOG, Radiation Therapy Oncology Group.

EXPERT REVIEWS

From radiobiology to technology: what is changing in radiotherapy for prostate cancer

Expert Rev. Anticancer Ther. 14(5), 553–564 (2014)

Review — De Bari, Fiorentino, Arcangeli, Franco, D'Angelillo & Alongi

↓

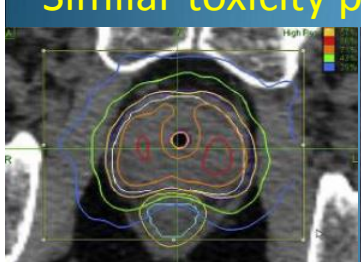
Clinical view: from moderate hypofractionation to extreme hypofractionation

↓

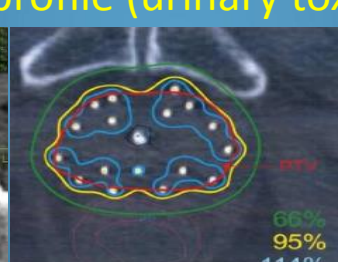
Extreme hypofractionation & SBRT

SBRT for PCa = Virtual Prostate Brachytherapy

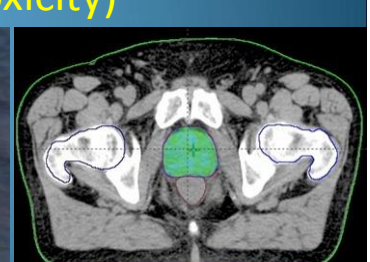
- Non-invasive procedure
- Similar dose distributions "peripheral loading"
- Similar toxicity profile (urinary toxicity)



SBRT: 4 x 9.5 Gy = 38 Gy
Cyberknife®: 45-90min/fx
Fuller et al.: IJROBP; 70, 2008



EBRT+HDR-BT46Gy + 2 x 9.5Gy
Zwahlen et al.:
Brachytherapy; 9, 2009



SBRT-10X FFF: 5 x 7Gy = 35 Gy
TrueBeam®: 2 min/fx
Alongi et al.: RO, 2013

SBRT for PCa: Features

- Very large dose per fractions
- Highly focused RT beams
- Image Guidance (allowing minimal CTV–PTV margin)
- Additional devices to minimize toxicity (spacer hydrogel)

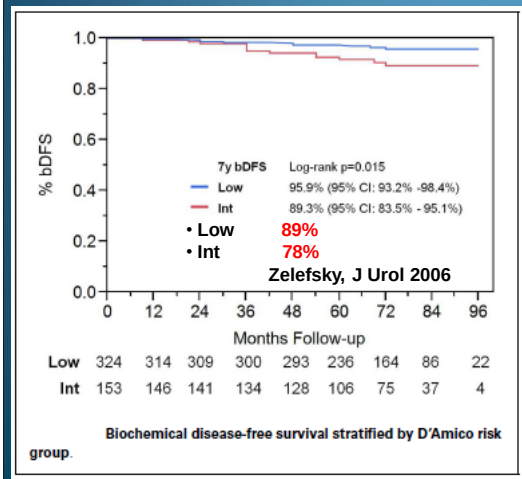
Study	Schedule	# of patients	Risk class	Median F/U (mos)	Late Grade 3 GU Toxicity	Late Grade 3 GI Toxicity	FFBF
CyberKnife							
Katz et al. 2010	35 – 36.25 Gy in 5 fx	304	L-I-H	48	2%	-	97, 93, 75% at 4 y
Freeman, King. 2011	7-7.25 Gy in 5 fx	41	L	60	< 1%	-	93% at 5 y
Kang et al. 2011	32-36 Gy in 4 fx	44	L-I-H	40	-	-	100%, 100%, 90.9% at 5 y
McBride et al. 2012	36.25-37.5 Gy in 5 fx	45	L	44.5	< 1%	-	97.7% at 3 y
Fuller et al. 2012	38 Gy in 4 fx	54	L-I	36	4%	-	96% at 3 y
King et al. 2012	36.25 Gy in 5 fx	67	L	32.4	3.5%	-	94% at 4 y
Bolzicco et al. 2013	35 Gy in 5 fx	100	L-I-H	36	1%	-	96%
Oliai et al. 2013	37,5Gy vs 35-36,25Gy in 5 fx	70	L-I-H	27-37	4%	-	100%, 95%, 77.1% at 3 y
Gantry-based Systems							
Madsen et al. 2007	33.5 Gy in 5 fx	40	L	41	-	-	90% at 4 y
Boike et al. 2011	45-50 Gy in 5 fx	45	L-I	30, 18, 12	4%	2% plus 1 Grade 4	100% at 1-2.5 y
Loblaw et al. 2013	35 Gy in 5 fx (once a week)	84	L	55	1%	-	98% at 5 y

frontiers in ONCOLOGY
ORIGINAL RESEARCH ARTICLE
published: 02 September 2014
doi: 10.3389/fonc.2014.00240

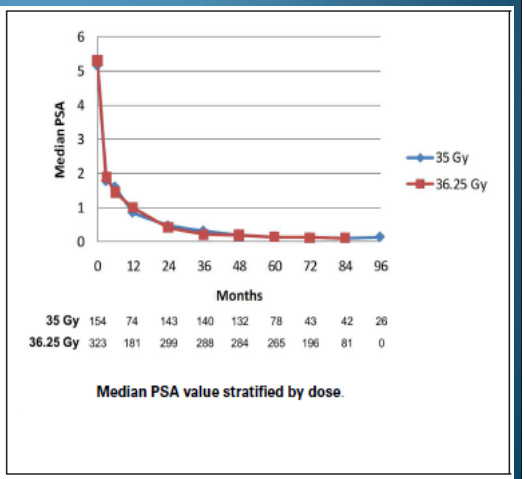
Stereotactic body radiotherapy as treatment for organ confined low- and intermediate-risk prostate carcinoma, a 7-year study

Alan Jay Katz[1] and Josephine Kang[1,2]*

2014



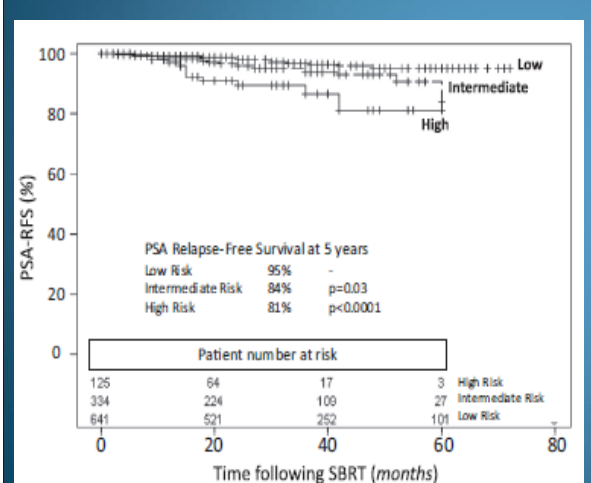
Biochemical disease-free survival stratified by D'Amico risk group.



Median PSA value stratified by dose.

Phase II trial

Stereotactic body radiotherapy for localized prostate cancer: Pooled analysis from a multi-institutional consortium of prospective phase II trials ☆,☆☆



1100 patients

5-year Kaplan–Meier PSA relapse-free survival rates as a function of risk group, use of ADT and dose.

	5-yr bRFS	p-Value
Low Risk	95.2%	-
Intermediate Risk	84.1%	$p = 0.03$
High Risk	81.2%	$p < 0.0001$
ADT use	92.6%	-
No ADT	91.3%	$p = 0.71$
Dose 35 Gy	92.5%	-
Dose 36.25 Gy	90.7%	$p = 0.08$
Dose 38–40 G y	95.8%	$p = 0.83$

CLINICAL INVESTIGATION — **Genitourinary Cancer**

LONG-TERM OUTCOMES FROM A PROSPECTIVE TRIAL OF STEREOTACTIC BODY RADIOTHERAPY FOR LOW-RISK PROSTATE CANCER

CHRISTOPHER R. KING, PH.D., M.D.,* JAMES D. BROOKS, M.D.,† HARCHARAN GILL, M.D.,† AND JOSEPH C. PRESTI, JR., M.D.†

Late urinary (GU) and rectal (GI) toxicity on the RTOG scale after prostate stereotactic body radiotherapy

Grade	GU	GI
0	68% (39/57 pts)	84% (48/57 pts)
1	23% (13/57 pts)	14% (8/57 pts)
2	5% (3/57 pts)	2% (1/57 pts)
3	3.5% (2/57 pts)	0
4	0	0

Comparison of late urinary (GU) and late rectal (GI) RTOG toxicity between consecutive daily treatments (QD) vs. those delivered three times a week on alternating days (QOD)

GU toxicity	QD	QOD	*p* value*
RTOG Gr. 0	37% (6/16 pts)	80% (33/41 pts)	0.003
RTOG Gr. 1	50% (8/16 pts)	12% (5/41 pts)	0.004
RTOG Gr. 2	6% (1/16 pts)	5% (2/41 pts)	1
RTOG Gr. 3	6% (1/16 pts)	2% (1/41 pts)	0.48
RTOG Gr. 1–2	56% (9/16 pts)	17% (7/41 pts)	0.007
GI toxicity	**QD**	**QOD**	
RTOG Gr. 0	56% (9/16 pts)	95% (39/41 pts)	0.001
RTOG Gr. 1	37% (6/16 pts)	5% (2/41 pts)	0.0004
RTOG Gr. 2	6% (1/16 pts)	0% (0/41 pts)	0.28
RTOG Gr. 1–2	44% (7/16 pts)	5% (2/41 pts)	0.001

RESEARCH — **Open Access**

Hypofractionated SBRT versus conventionally fractionated EBRT for prostate cancer: comparison of PSA slope and nadir

Mekhail Anwar*, Vivian Weinberg, Albert J Chang, I-Chow Hsu, Mack Roach III and Alexander Gottschalk

2014

Results (all patients)

		SBRT	CF-EBRT	p-value
	Through year			
PSA Measurements #				
Mean (range)	1	3.9 (2 – 6)	4.1 (3 – 11)	
	2	5.8 (4 – 9)	5.6 (3 – 15)	
	3	7.6 (5 – 11)	7.3 (3 – 21)	
Nadir PSA (ng/mL)				
Median (range)	1	0.70 (0 – 2.5)	1.00 (0 – 8.5)	
	2	0.40 (0 – 1.4)	0.72 (0 – 2.7)	p = 0.0005*
	3	0.24 (0.1 – 1.4)	0.60 (0 – 2.2)	p = 0.002*
Time to Nadir PSA (mos.)				
Median (range)	1	12.0 (2.7 – 15.0)	11.5 (1.2 – 15.0)	
	2	21.0 (2.7 – 26.9)	18.0 (1.2 – 26.9)	
	3	32.3 (2.7 – 41.6)	28.6 (1.0 – 41.1)	p = 0.004^
Rate of PSA change: ng/mL/month				
Median slope (range)	1	−0.09 (−0.88, 0.04)	−0.09 (−0.60, 0.06)	
	2	−0.06 (−0.38, 0.01)	−0.04 (−0.65, 0.05)	p = 0.04*
	3	−0.05 (−0.19, 0.00)	−0.02 (−0.38, 0.04)	p = 0.006*

Prostate radiotherapy

Prostate stereotactic ablative body radiotherapy using a standard linear accelerator: Toxicity, biochemical, and pathological outcomes

Andrew Loblaw [a,b,d,*,1], Patrick Cheung [a,b,1], Laura D'Alimonte [a,d], Andrea Deabreu [d], Alexandre Mamedov [d], Liying Zhang [a], Colin Tang [e], Harvey Quon [f], Suneil Jain [g], Geordi Pang [a,d], Robert Nam [c,d]

A B S T R A C T

Background and purpose: Biological dose escalation through stereotactic ablative radiotherapy (SABR) holds promise of improved patient convenience, system capacity and tumor control with decreased cost and side effects. The objectives are to report the toxicities, biochemical and pathologic outcomes of this prospective study.

Materials and methods: A phase I/II study was performed where low risk localized prostate cancer received SABR 35 Gy in 5 fractions, once weekly on standard linear accelerators. Common Terminology Criteria for Adverse Events v3.0 and Radiation Therapy Oncology Group late morbidity scores were used to assess acute and late toxicities, respectively. Biochemical control (BC) was defined by the Phoenix definition.

Results: As of May 2012, 84 patients have completed treatment with a median follow-up of 55 months (range 13–68 months). Median age was 67 years and median PSA was 5.3 ng/ml. The following toxicities were observed: acute grade 3+: 0% gastrointestinal (GI), 1% genitourinary (GU), 0% fatigue; late grade 3+: 1% GI, 1% GU. Ninety-six percent were biopsy negative post-treatment. The 5-year BC was 98%.

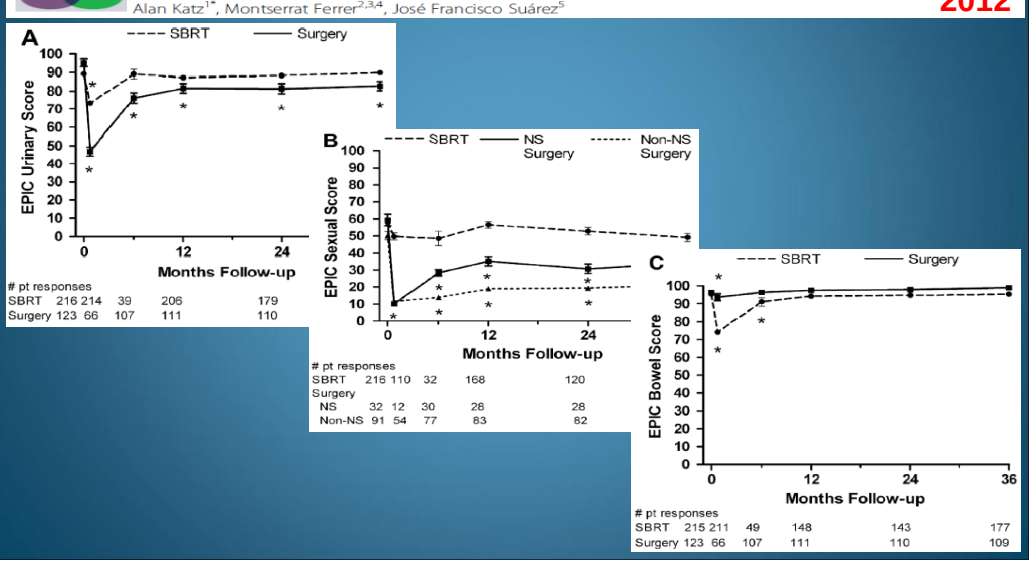
Conclusions: This novel technique employing standard linear accelerators to deliver an extreme hypofractionated schedule of radiotherapy is feasible, well tolerated and shows excellent pathologic and biochemical control.

RADIATION ONCOLOGY
RESEARCH Open Access

Comparison of quality of life after stereotactic body radiotherapy and surgery for early-stage prostate cancer

Alan Katz[1*], Montserrat Ferrer[2,3,4], José Francisco Suárez[5]

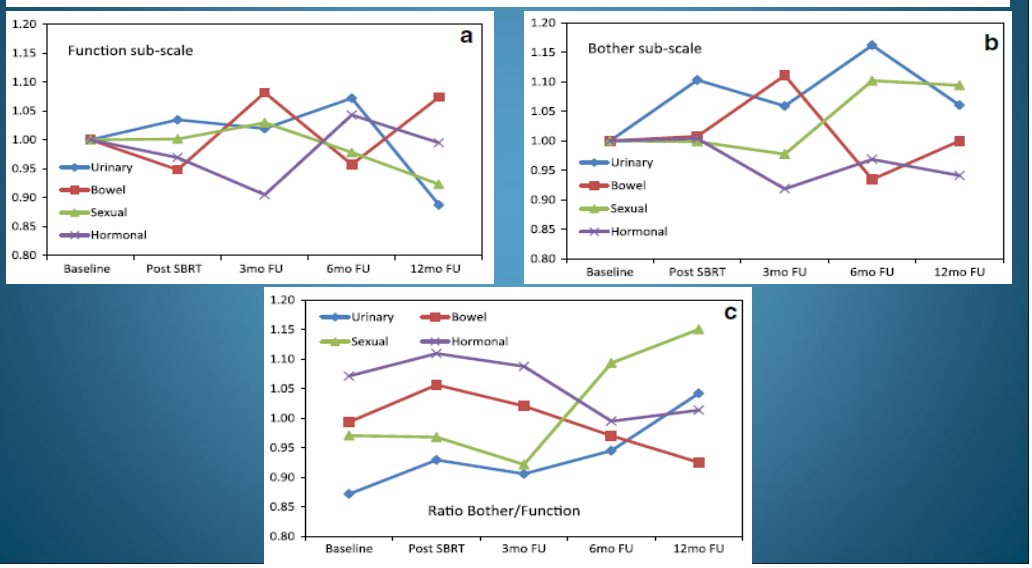
2012



Stereotactic body radiotherapy with flattening filter-free beams for prostate cancer: assessment of patient-reported quality of life

Marta Scorsetti · Filippo Alongi · Elena Clerici · Tiziana Comito · Antonella Fogliata · Cristina Iftode · Pietro Mancosu · Piera Navarria · Giacomo Reggiori · Stefano Tomatis · Elisa Villa · Luca Cozzi

J Cancer Res Clin Oncol 2014



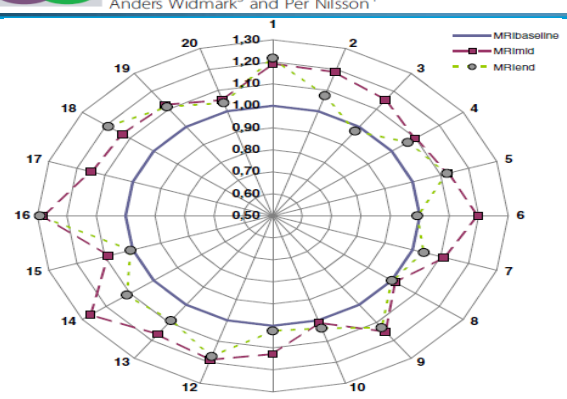
RADIATION ONCOLOGY

RESEARCH Open Access

Change in prostate volume during extreme hypo-fractionation analysed with MRI

Adalsteinn Gunnlaugsson[1*], Elisabeth Kjellén[1], Oskar Hagberg[2], Camilla Thellenberg-Karlsson[3], Anders Widmark[3] and Per Nilsson[4]

2014

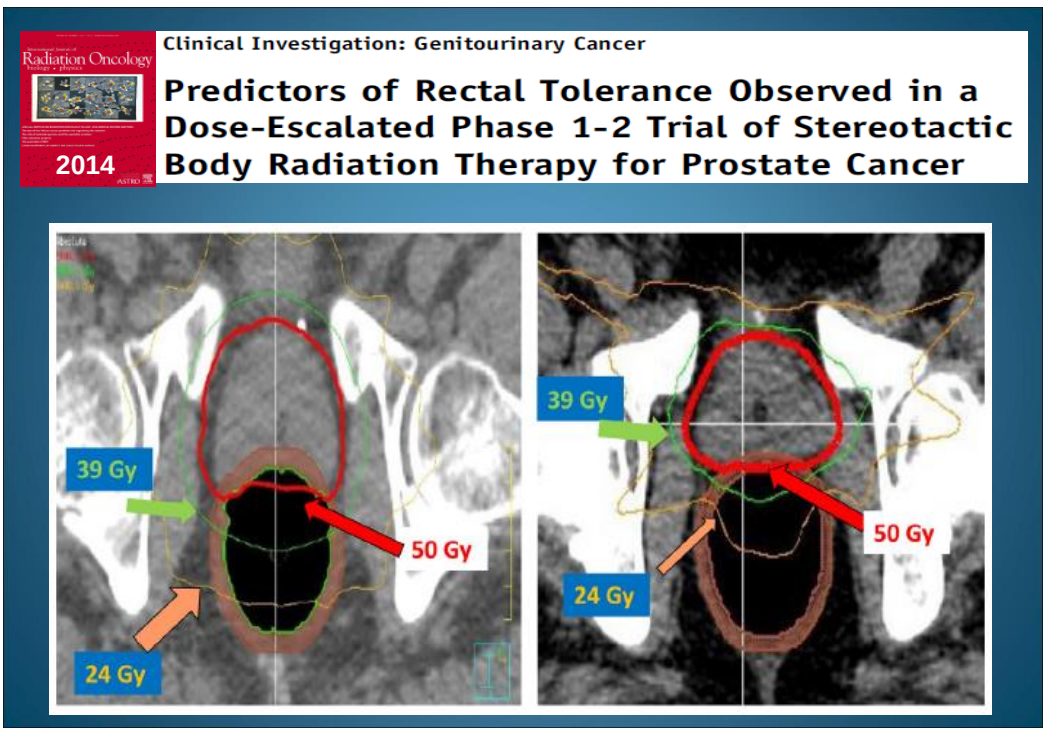


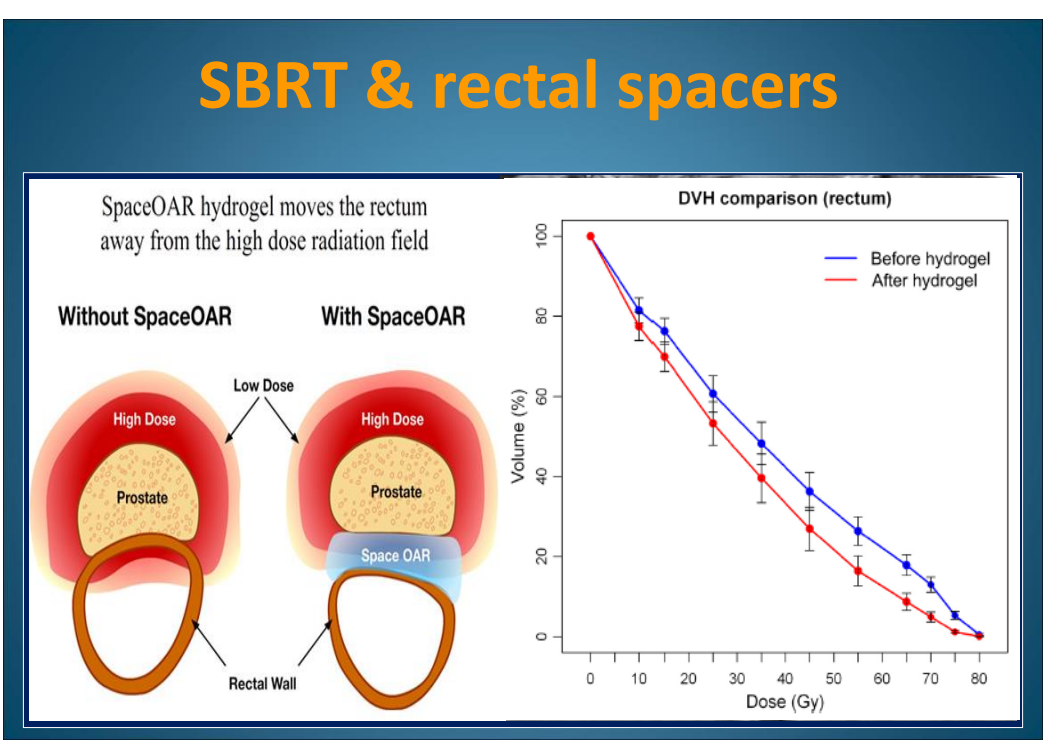
Relative prostate volume compared to baseline

- At MRI_{mid}: **+16%**
- At MRI_{end}: **+ 9%**

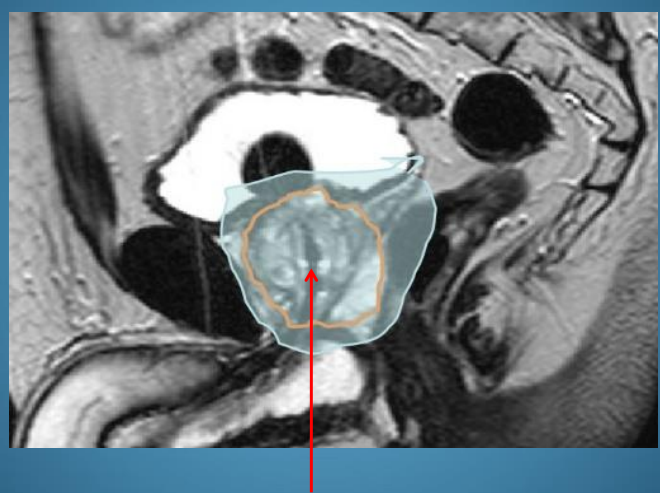
Average change in maximum prostate extension in lateral (Δx_{max}), anterior–posterior (Δy_{max}) and cranial–caudal (Δz_{max}) direction (mean values and 95% CI)

	Δx_{max} (mm)	P	Δy_{max} (mm)	p	Δz_{max} (mm)	p
MR_{mid}–$MR_{baseline}$	0.2 (−1.1–1.5)	0.72	3.3 (1.8–4.8)	0.0002	2.5 (1.0–3.9)	0.0019
MR_{end}–$MR_{baseline}$	0.3 (−0.9–1.4)	0.60	2.0 (0.5–3.4)	0.010	2.0 (0.8–3.1)	0.0029
MR_{end}–MR_{mid}	0.1 (−0.8–0.9)	0.89	−1.4 (−2.7–−0.1)	0.036	−0.6 (−1.7–0.6)	0.32


Radiation Oncology
2014
Clinical Investigation: Genitourinary Cancer
Predictors of Rectal Tolerance Observed in a Dose-Escalated Phase 1-2 Trial of Stereotactic Body Radiation Therapy for Prostate Cancer
39 Gy
50 Gy
24 Gy
39 Gy
50 Gy
24 Gy


SBRT & rectal spacers
SpaceOAR hydrogel moves the rectum away from the high dose radiation field
Without SpaceOAR
With SpaceOAR
Low Dose
High Dose
Prostate
High Dose
Prostate
Space OAR
Rectal Wall
DVH comparison (rectum)
Before hydrogel
After hydrogel
Volume (%)
Dose (Gy)
0
20
40
60
80
100
0
10
20
30
40
50
60
70
80

SBRT: notes of caution



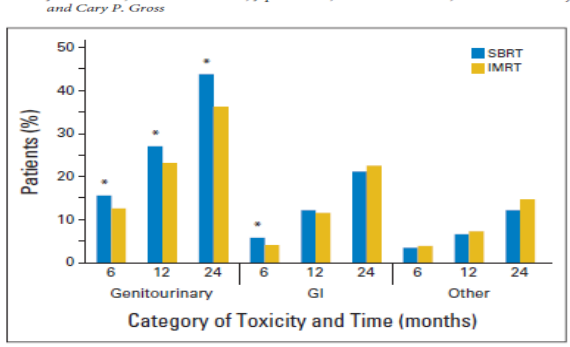
GU Toxicity ?

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

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

James B. Yu, Laura D. Cramer, Jeph Herrin, Pamela R. Soulos, Arnold L. Potosky, and Cary P. Gross

2014



Adjusted Random Effects Logit Model of Subcategories of Genitourinary Toxicity

Toxicity	Duration of Follow-Up: 6 Months OR*	6 Months Pt	12 Months OR*	12 Months Pt	24 Months OR*	24 Months Pt
Diagnostic procedures to investigate incontinence or obstruction	**1.80**	**< .001**	**1.64**	**< .001**	**2.23**	**< .001**
Urethritis, urethral strictures, and bladder outlet obstruction	1.25	.14	**1.45**	**.002**	**1.78**	**< .001**
Therapeutic procedures to correct urinary incontinence	0.71	.22	1.00	1.00	1.33	.09
Other genitourinary toxicity	0.77	.45	1.14	.58	0.73	.23
Infections	1.01	.99	2.30	.11	2.42	.15
Erectile dysfunction	1.46	.03	1.15	.28	1.13	.35

JOURNAL OF CLINICAL ONCOLOGY | CORRESPONDENCE

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

Stefano Arcangeli
San Camillo Forlanini Hospital, Rome, Italy
Berardino De Bari
Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland
Filippo Alongi
Ospedale Sacro Cuore-Don Calabria–Negrar, Verona, Italy

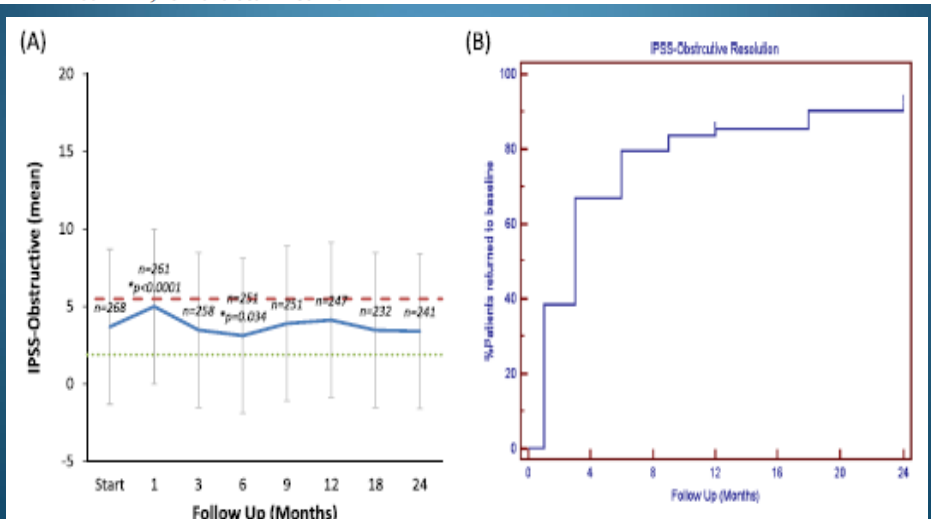
- Scale and grade of GU toxicity?
  Not reported!
  - Diagnostic procedures as surrogate of treatment related effects
    Unreliable!
    - Dose, fields, constraints?
      Ignored!

RADIATION ONCOLOGY
RESEARCH Open Access

Obstructive voiding symptoms following stereotactic body radiation therapy for prostate cancer

W Tristram Arscott[1†], Leonard N Chen[1†], Nathan Wilson[1], Aditi Bhagat[1], Joy S Kim[1], Rudy A Moures[1], Thomas M Yung[1], Siyuan Lei[1], Brian T Collins[1], Keith Kowalczyk[2], Simeng Suy[1], Anatoly Dritschilo[1], John H Lynch[2] and Sean P Collins[1*]

2014



SBRT for PCa
Open Issues

- **Optimal duration of treatment**
  Every day/Every other day?
- **Late toxicicy**
  Accurate evaluation of long term tolerance and toxicity, >of the urethra, an unavoidable organ at risk in the irradiation of prostate cancer
- **Patients selection**
  Mostly low and intermediate risk patients

SBRT ongoing randomized trials

ClinicalTrials.gov

Prostate Accurately Targeted Radiotherapy Investigation of Overall Treatment Time (PATRIOT)

Arms	Assigned Interventions
Experimental: Short treatment time (11 days)	Radiation: Image-guided radiotherapy 40 Gy / 5 fractions / 11 days
Experimental: Long treatment time (29 days)	Radiation: Image-guided radiotherapy 40 Gy / 5 fractions / 29 days

RADIATION THERAPY ONCOLOGY GROUP

RTOG 0938

A RANDOMIZED PHASE II TRIAL OF HYPOFRACTIONATED RADIOTHERAPY FOR FAVORABLE RISK PROSTATE CANCER

Arms	Assigned Interventions
Experimental: Arm I Patients undergo intensity-modulated radiation therapy (IMRT) twice a week for approximately 2½ weeks (36.25 Gy total).	Radiation: hypofractionated radiation therapy Given twice a week for 2½ weeks (36.25 fractions)
Experimental: Arm II Patients undergo IMRT once a day, 5 days a week, for approximately 2½ weeks (51.6 Gy total).	Radiation: hypofractionated radiation therapy Given twice a week for 2½ weeks (36.25 fractions)

SBRT ongoing randomized trials

ClinicalTrials.gov

Prostate Advances in Comparative Evidence (PACE)

Arms	Assigned Interventions
Active Comparator: Laparoscopic prostatectomy vs CyberKnife prostate SBRT Patients for whom surgery is considered will be randomized to laparoscopic prostatectomy (manual laparoscopic prostatectomy or da Vinci prostatectomy) or CyberKnife prostate SBRT.	Other: CyberKnife prostate SBRT delivered by the CyberKnife in 36.25Gy in 5 fractions or 38Gy in 4 fractions CyberKnife prostate SBRT delivered by the CyberKnife in 36.25Gy in 5 fractions or 38Gy in 4 fractions.
Active Comparator: Conventionally fractionated RT vs CyberKnife prostate SBRT Patients for whom surgery is not considered or who refuse surgery will be randomized to either conventionally fractionated radiotherapy or CyberKnife SBRT.	Other: CyberKnife prostate SBRT delivered by the CyberKnife in 36.25Gy in 5 fractions or 38Gy in 4 fractions CyberKnife prostate SBRT delivered by the CyberKnife in 36.25Gy in 5 fractions or 38Gy in 4 fractions.

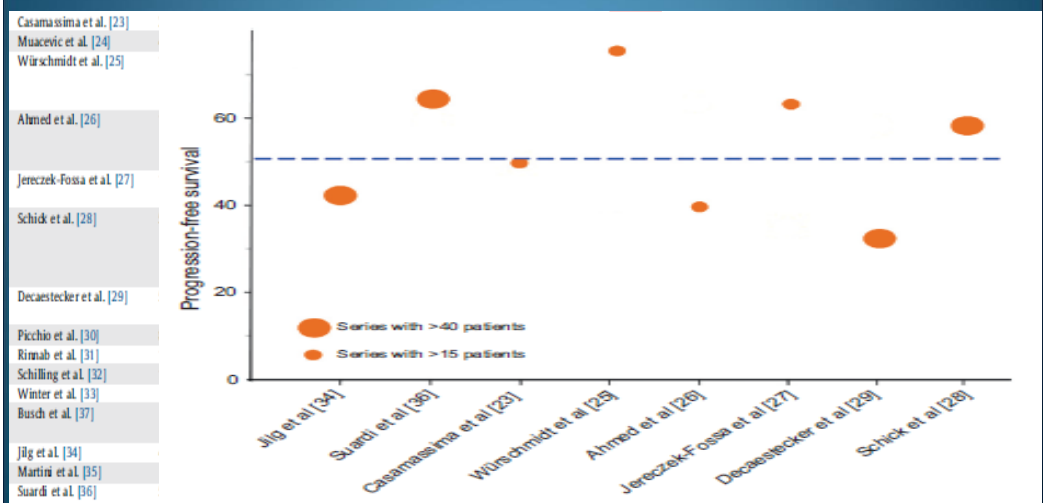
Phase III study of HYPOfractionated RadioTherapy of intermediate risk localised Prostate Cancer

Interventions	Fractionation schedule and treatment durations: Conventional arm: radiotherapy is given daily (5 days/week) with 39 fractions of 2.0 Gy, i.e. total 78.0 Gy. The total treatment time is 53 - 55 days. Maximum allowed treatment days are 65. Hypofractionated arm: radiotherapy is given working-days with 7 fractions of 6.1 Gy, i.e. total 42.7 Gy. The total treatment time is 15 - 19 days. Treatment is given every other weekday, always including two weekends.

SBRT for PCa: emerging scenarios

Metastasis-directed Therapy of Regional and Distant Recurrences After Curative Treatment of Prostate Cancer: A Systematic Review of the Literature

Piet Ost[a,], Alberto Bossi[b], Karel Decaestecker[c], Gert De Meerleer[a], Gianluca Giannarini[d], R. Jeffrey Karnes[e], Mack Roach III[f], Alberto Briganti[g]*



Retreatment for prostate cancer with Stereotactic Body Radiation Therapy (SBRT): feasible or foolhardy?

Stefano Arcangeli*^ MD, Linda Agolli° MD, Vittorio Donato* MD

- About 92% of patients who previously received RT are usually managed with androgen deprivation therapy (ADT) alone as secondary treatment on PSA progression, or with no salvage procedure
- **Patients with radio-recurrent PCa may still be selected for curative treatment, especially those in good clinical conditions and long life expectancy**

Delivering affordable cancer care in high-income countries

Lancet Oncol 2011; 12: 933–80

- Improved tumour control, less toxicity, and reduced treatment courses decrease the indirect costs of cancer care, including lost time and economic productivity secondary to treatment-related and cancer-related illness and death
- **Advances in radiation therapy can potentially result in substantial direct and indirect cost savings**

Treatment	Mean Cancer-Related Cost ($)*	95% CI ($)	Mean Radiation Cost ($)*	95% CI ($)
SBRT	16,608	15,878 to 17,338	13,645	13,370 to 13,921
IMRT	23,000	22,505 to 23,496	21,023	20,780 to 21,265

SBRT for PCa

Will SBRT replace conventional radiotherapy in patients with low-intermediate risk prostate cancer? A review

Stefano Arcangeli *, Marta Scorsetti, Filippo Alongi

Radiotherapy and Radiosurgery department, Istituto Clinico Humanitas, Humanitas Cancer Center, Rozzano, Milano, Italy

Could single-high-dose radiotherapy be considered the new frontier of stereotactic ablative radiation therapy?

Filippo Alongi[1], Berardino De Bari[2], and Marta Scorsetti[3]