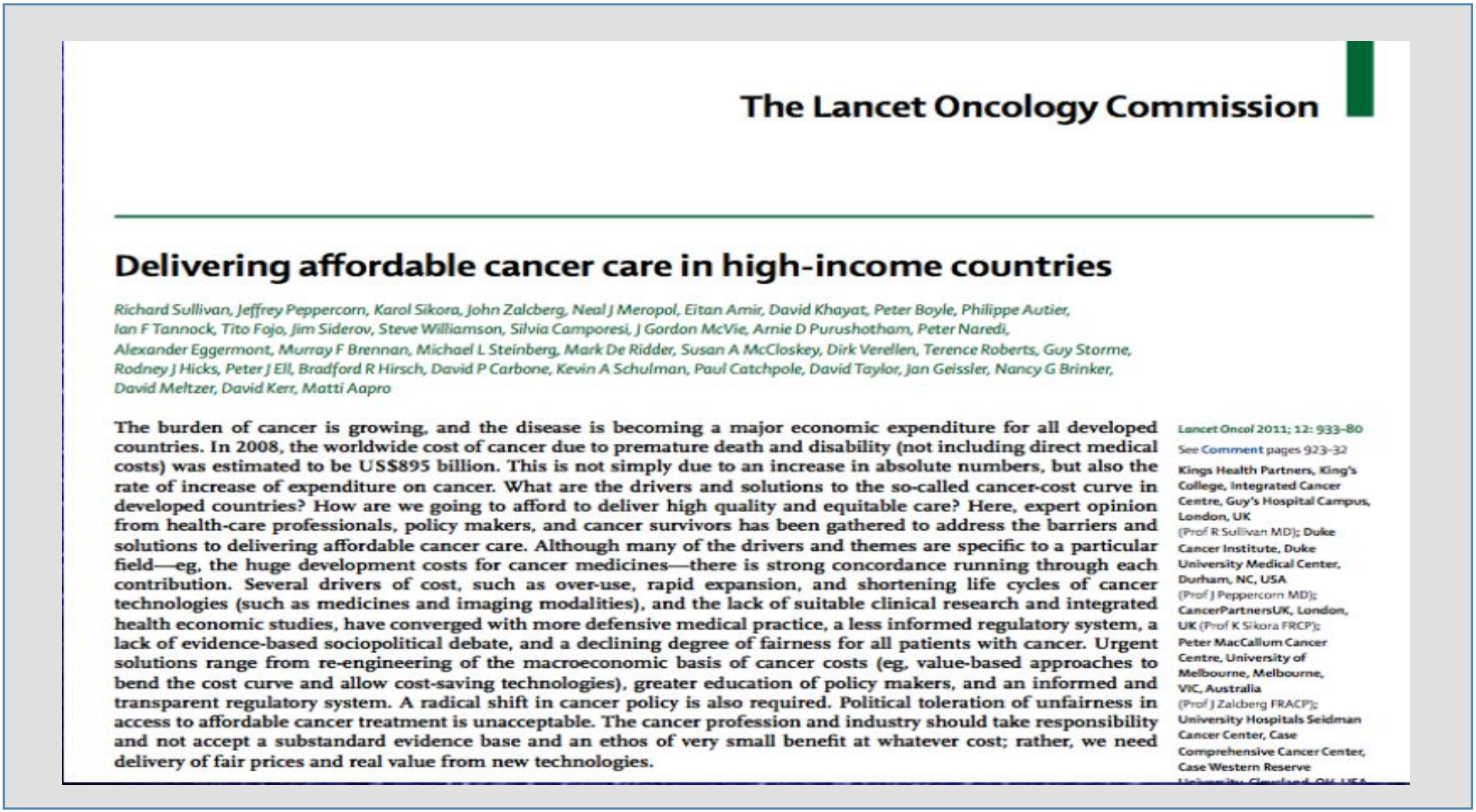

ciet'a Italiana di Radiobiologia
Associazion
Italiana
Radioterapi
Oncologica
Dr. Alessio Bruni
UO Radioterapia di Modena
BRT in Prostate cancer
XXIX Congresso Nazionale AIRB
meeting congiunto con
VII Congresso Nazionale AIRO Giovani
Firenze 13-14 Giugno 2014

Why and When SBRT???



The Lancet Oncology Commission

Delivering affordable cancer care in high-income countries

Richard Sullivan, Jeffrey Peppercorn, Karol Sikora, John Zalcberg, Neal J Meropol, Eitan Amir, David Khayat, Peter Boyle, Philippe Autier, Ian F Tannock, Tito Fojo, Jim Siderov, Steve Williamson, Silvia Camporesi, J Gordon McVie, Arnie D Purushotham, Peter Naredi, Alexander Eggermont, Murray F Brennan, Michael L Steinberg, Mark De Ridder, Susan A McCloskey, Dirk Verellen, Terence Roberts, Guy Storme, Rodney J Hicks, Peter J Ell, Bradford R Hirsch, David P Carbone, Kevin A Schulman, Paul Catchpole, David Taylor, Jan Geissler, Nancy G Brinker, David Meltzer, David Kerr, Matti Aapro

The burden of cancer is growing, and the disease is becoming a major economic expenditure for all developed countries. In 2008, the worldwide cost of cancer due to premature death and disability (not including direct medical costs) was estimated to be US$895 billion. This is not simply due to an increase in absolute numbers, but also the rate of increase of expenditure on cancer. What are the drivers and solutions to the so-called cancer-cost curve in developed countries? How are we going to afford to deliver high quality and equitable care? Here, expert opinion from health-care professionals, policy makers, and cancer survivors has been gathered to address the barriers and solutions to delivering affordable cancer care. Although many of the drivers and themes are specific to a particular field—eg, the huge development costs for cancer medicines—there is strong concordance running through each contribution. Several drivers of cost, such as over-use, rapid expansion, and shortening life cycles of cancer technologies (such as medicines and imaging modalities), and the lack of suitable clinical research and integrated health economic studies, have converged with more defensive medical practice, a less informed regulatory system, a lack of evidence-based sociopolitical debate, and a declining degree of fairness for all patients with cancer. Urgent solutions range from re-engineering of the macroeconomic basis of cancer costs (eg, value-based approaches to bend the cost curve and allow cost-saving technologies), greater education of policy makers, and an informed and transparent regulatory system. A radical shift in cancer policy is also required. Political toleration of unfairness in access to affordable cancer treatment is unacceptable. The cancer profession and industry should take responsibility and not accept a substandard evidence base and an ethos of very small benefit at whatever cost; rather, we need delivery of fair prices and real value from new technologies.

Lancet Oncol 2011; 12: 933–80

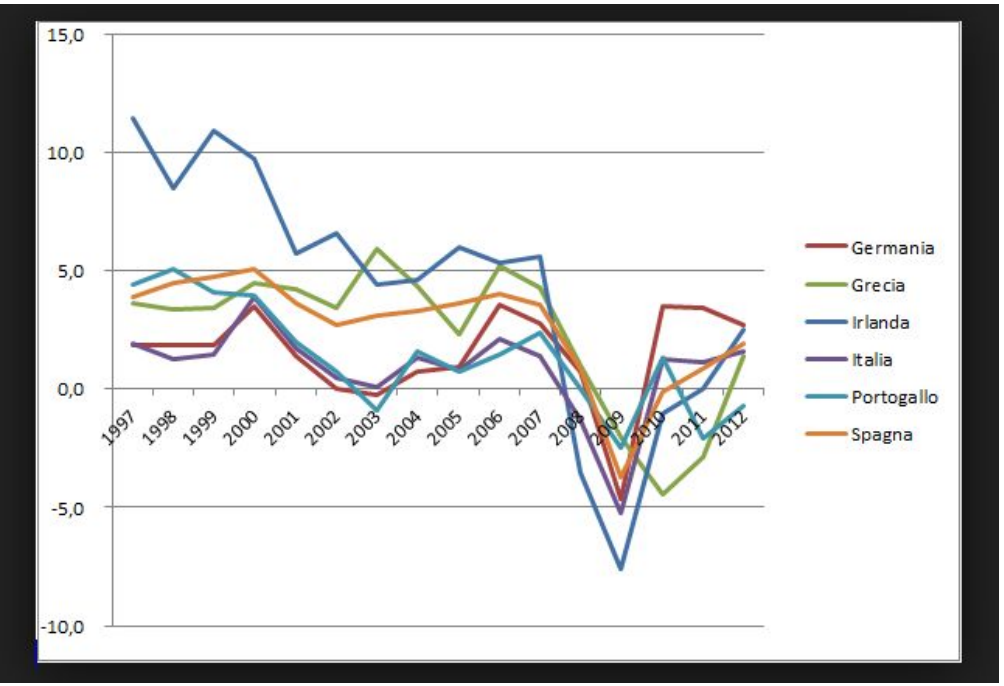
See Comment pages 923–32

Kings Health Partners, King's College, Integrated Cancer Centre, Guy's Hospital Campus, London, UK (Prof R Sullivan MD); Duke Cancer Institute, Duke University Medical Center, Durham, NC, USA (Prof J Peppercorn MD); CancerPartnersUK, London, UK (Prof K Sikora FRCP); Peter MacCallum Cancer Centre, University of Melbourne, Melbourne, VIC, Australia (Prof J Zalcberg FRACP); University Hospitals Seidman Cancer Center, Case Comprehensive Cancer Center, Case Western Reserve

Sullivan R et al. - Lancet Oncology - 2011

Why and When SBRT???

Cancer **is becoming a** ***major economic expenditure*** **for all developed countries. In 2008, the worldwide cost of cancer due to premature death and disability was estimated to be** ***US $ 895 billion*****.**



The cancer ***profession and indust*** **should** take responsibility and ***not acce*** a **substandard evidence base** and ***ethos of very small benefit at whatev*** ***cost*** : rather, we need delivery of f prices and real value from n technologies [..]

Sullivan R et al. - Lancet Oncology - 2011

Why SBRT in Prostate Cancer ?????

From 2008…
To……
NOW!!!!!

Why to threat Prostate Cancer ?????

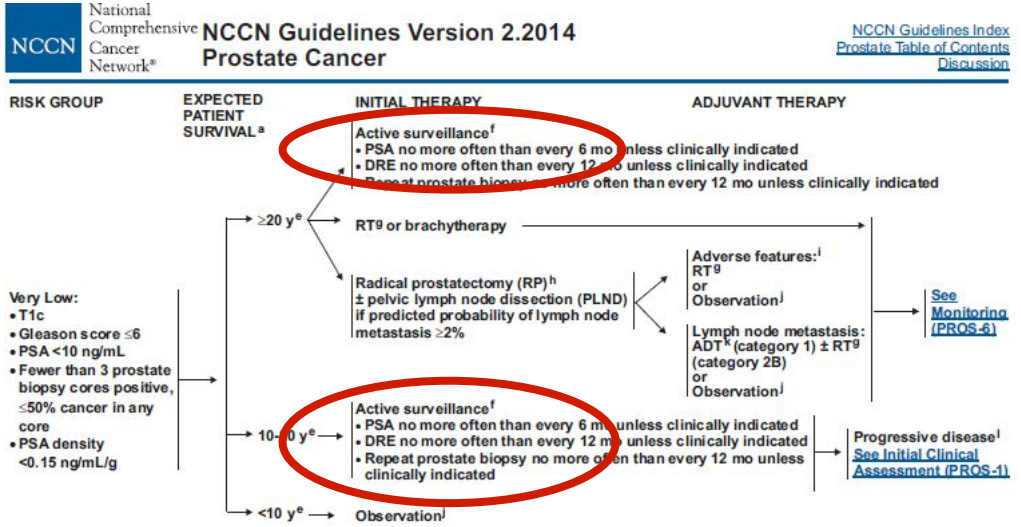
8. TREATMENT: DEFERRED TREATMENT (WATCHFUL WAITING/ACTIVE MONITORING)

8.1 Introduction

There is a great difference between the incidence of PCa and deaths from PCa. In 2007, in the USA, there were 240,890 new cases with only 33,720 deaths (1). Several autopsy studies of people dying from different causes have shown that while 60-70% of older men have histological PCa (2), a large proportion of these tumours will not progress. Prostate cancer is diagnosed in only 15-20% of men during their lifetime, with a 3% lifetime risk of death (3).

The incidence of small, localised, well-differentiated PCa is increasing, mainly as a result of prostate-specific antigen (PSA) screening and 'multicore' schemes of prostate biopsy. These data suggest that many men with localised PCa would not actually benefit from definitive treatment. With the aim of reducing the risk of overtreatment in this subgroup of patients, two conservative management strategies of 'watchful waiting' and 'active surveillance' have been proposed.

EAU 2013

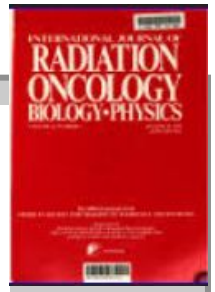


AIOM 2013

La sopravvivenza dei pazienti con carcinoma prostatico, non considerando la mortalità per altre cause, è attualmente attestata all'88% a 5 anni dalla diagnosi, in costante e sensibile crescita [3]. Il principale fattore correlato a questa tendenza temporale è dato dall'anticipazione diagnostica e dalla progressiva diffusione dello screening opportunistico, comportante evidentemente una quota di sovradiagnosi, peraltro con distribuzione disomogenea sul territorio nazionale.

Why SBRT in Prostate Cancer ?????

BACKGROUND



ELSEVIER

2012

Int. J. Radiation Oncology Biol. Phys., Vol. 82, No. 1, pp. e17–e24, 2012

0360-3016/$ - see front matter

doi:10.1016/j.ijrobp.2010.10.075

CLINICAL INVESTIGATION Genitourinary Cancer

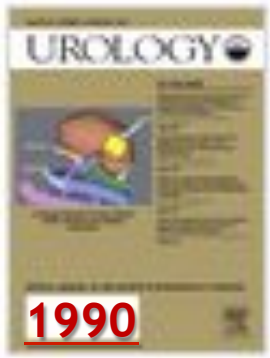
DOSE-FRACTIONATION SENSITIVITY OF PROSTATE CANCER DEDUCED FROM RADIOTHERAPY OUTCOMES OF 5,969 PATIENTS IN SEVEN INTERNATIONAL INSTITUTIONAL DATASETS: α/β = 1.4 (0.9–2.2) GY

RAYMOND MIRALBELL, M.D.,*† STEPHEN A. ROBERTS, PH.D.,‡ EDUARDO ZUBIZARRETA, M.D.,§ AND JOLYON H. HENDRY, PH.D.‖

*University Hospital, Geneva, Switzerland; †Institut Oncològic Teknon, Barcelona, Spain, ‡Health Sciences—Methodology, Manchester Academic Health Sciences Centre, University of Manchester, Manchester, United Kingdom; §International Atomic Energy Agency, Vienna, Austria; and ‖Adlington, Macclesfield, United Kingdom

ch ***a low α/β value (=1.5)*** , related to a long doubling time of PCa cells and t
ffective repair capacity of sublethal RT damage at low dose per fraction, suppo
hypofractionation as an optimal RT option particularly for localized PCa

History……



Carcinoma of prostate treated by radical external beam radiotherapy using hypofractionation twenty-two years' experience (1962—1984)

M.S., F.R.C.S. R.W. Lloyd-Davies, M.B., B.S., F.R.C.R. C.D. Collins, M.Sc., PH.D. A.V. Swan

In the 1960s-1980s, **209** pts were treated with 36 Gy in 6 fx over 18 days

68% 5 year survival in a mixed risk cohort

....More Recent Years

	Stats	LE	Nr pts	Class Risk	iPSA	Dose/Fractionatio
2007	P	2b	44	Low Intermediate High		32 (4x8) 36 (4 x 9)
land 2009	P	2b	112	Low, Intermediate	5.2	35 (5x7)
ride 2011	P	2b	45	Low	4,9	36.25 (5x7.25) 37.5 (5x7.5)
2011	P	1b	82	Low, Intermediate	5.35	35 (5x7) 36.25 (5x7.25)
2012	P	2b	67	Low	<10	36.25 (5x7.25)
2013	P	2b	304	Low, Intermediate, High	5.8	35 (5x7) 36.25(5x7.25)
cco 2013	P	2b	100	Low, Intermediate	8.07	35 (5 X 7)
2013	P	2b	100	Low Intermediate High	6.9	35 (5x7) 36.25 (5x7.25)
gi 2013	P	2b	40	Low, Intermediate	6,25	35(5x7)

VOLUME 29 · NUMBER 15 · MAY 20 2011

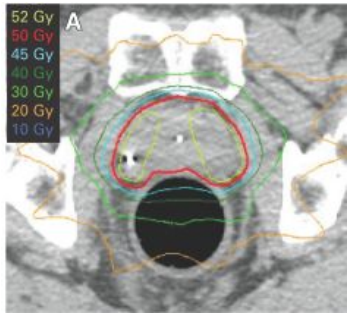
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Phase I Dose-Escalation Study of Stereotactic Body Radiation Therapy for Low- and Intermediate-Risk Prostate Cancer

Thomas P. Boike, Yair Lotan, L. Chinsoo Cho, Jeffrey Brindle, Paul DeRose, Xian-Jin Xie, Jingsheng Yan, Ryan Foster, David Pistenmaa, Alida Perkins, Susan Cooley, and Robert Timmerman

Phase I Dose Escalation Study **2006-2009**

t has been shown that ***SBRT can mimic*** these ***highly conformal brachytherapy*** dose distributions



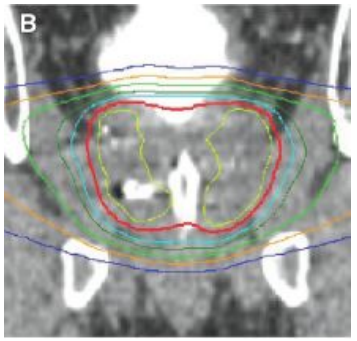
48 patients enrolled

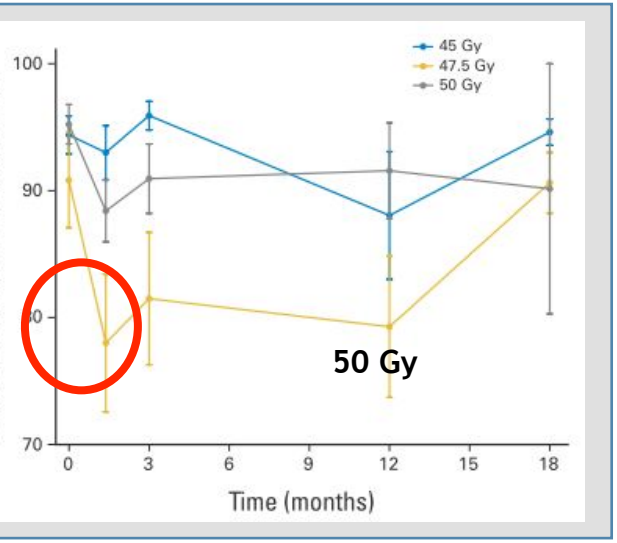
9Gy/36Hrs up to 45 Gy

TOMO

9,5Gy/36Hrs to 47.5 Gy

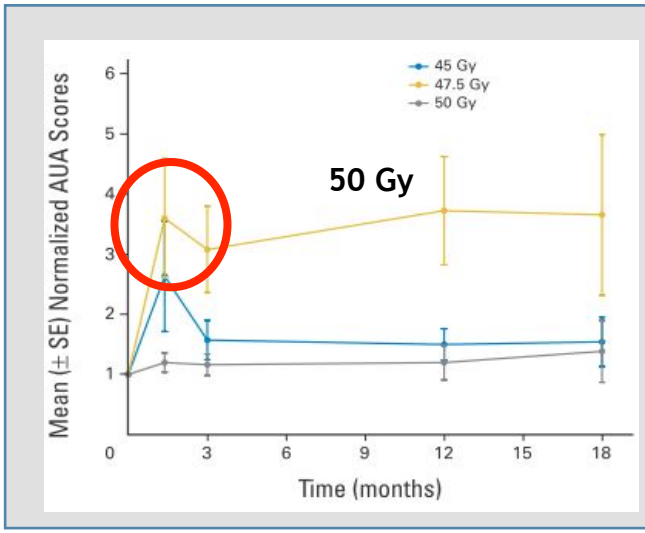
10Gy/36Hrs up to 50 Gy





No DLT was seen within 90 days from the start of treatment

The **47.5-50Gy** dose level **had significantly worse QOL Scores** for bowel and increase in AUA scores at early time points



Alongi et al. Radiation Oncology 2013, 8:171
http://www.ro-journal.com/content/8/1/171

Published on June 2013

RADIATION ONCOLOGY

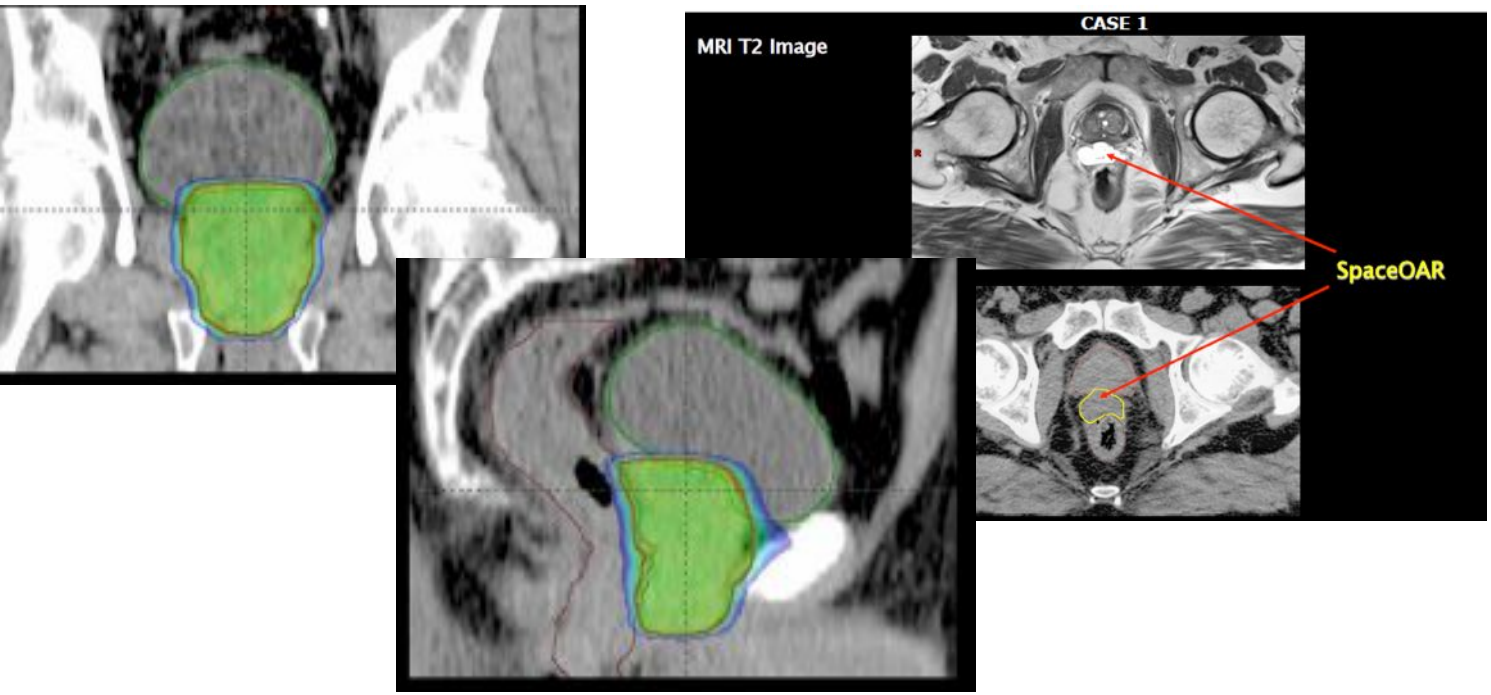
RESEARCH Open Access

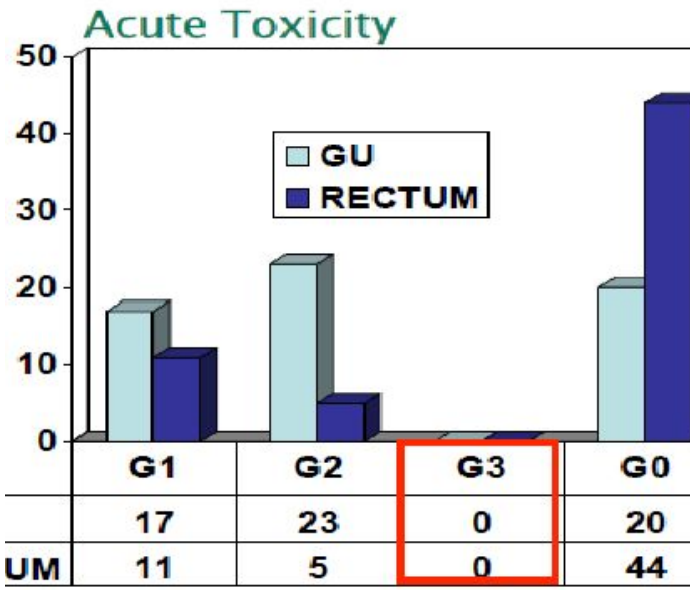
Linac based SBRT for prostate cancer in 5 fractions with VMAT and flattening filter free beams: preliminary report of a phase II study

Filippo Alongi[1,4*], Luca Cozzi[2], Stefano Arcangeli[1], Cristina Iftode[1], Tiziana Comito[1], Elisa Villa[1], Francesca Lobefalo[1], Pierina Navarria[1], Giacomo Reggiori[1], Pietro Mancosu[1], Elena Clerici[1], Antonella Fogliata[2], Stefano Tomatis[1], Gianluigi Taverna[3], Pierpaolo Graziotti[3] and Marta Scorsetti[1]

40 PTS
T1-T2 N0
PSA <20ng/ml

- Dose: 35 Gy in 5 fractions
- Median follow-up: 11 months
- SpaceOAR: 8 pts





	G1	G2	G3	G0
	17	23	0	20
UM	11	5	0	44

RESEARCH ARTICLE Open Access

A single-center study of 100 consecutive patients with localized prostate cancer treated with stereotactic body radiotherapy

2013

BMC Urology

Giampaolo Bolzicco[1*†], Maria Silvia Favretto[1†], Ninfa Satariano[3†], Enrico Scremin[2†], Carmelo Tambone[2†] and Andrea Tasca[2†]

A prospective protocol-based study for the treatment of **100 pts** with localized prostate cancer treated with **CyberKnife Robotic Radiosurgery** System

Table 1 Cyberknife®-SBRT: dinical characteristics of 100 patients

T Stage	Patients
T1c	44 (44%)
T2a-b	29 (29%)
(T2a, 10 pts)	
(T2b, 19 pts)	
T2c	27 (27%)
Gleason score	
<6 (2+2, 2+3, 3+2)	8 (8%)
6 (3+3)	76 (76%)
>7 (3+4 11 pts, 4+3 4 pts, 5+5 1 pt)	16 (16%)
PSA	
at diagnosis	**ng/ml**
All patients	7.72 ng/ml
SBRT (71 pts)	6.48 ng/ml
SBRT+ADT (29 pts)	10.77 ng/ml
Pre-treatment	**ng/ml**
All patients	5.03 ng/ml
SBRT (71 pts)	6.31 ng/ml
SBRT+ADT (29 pts)	1.90 ng/ml
Risk category	**Patients**
Low (PSA <10, GS 6, T1c, T2a)	41 (41%)
Intermediate (PSA >10, GS 7 or T2b-c)	42 (42%)
High (PSA >20, GS 8–10, 2 Int. risk features)	17 (17%)
Prostate volume (medium 33 cc)	
≤ 33 cc.	51 (51%)
> 33 cc.	49 (49%)

35 Gy was in 5 fractions of 7 Gy over 5 consecutive days

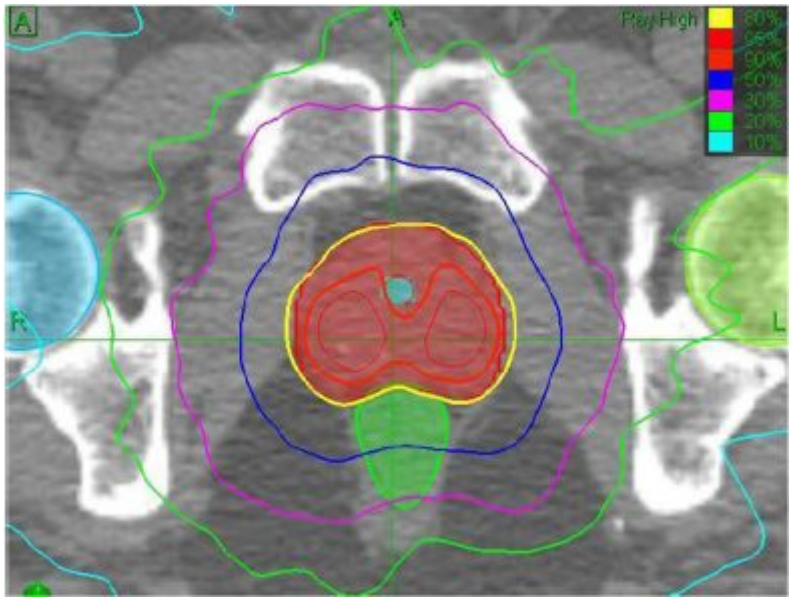
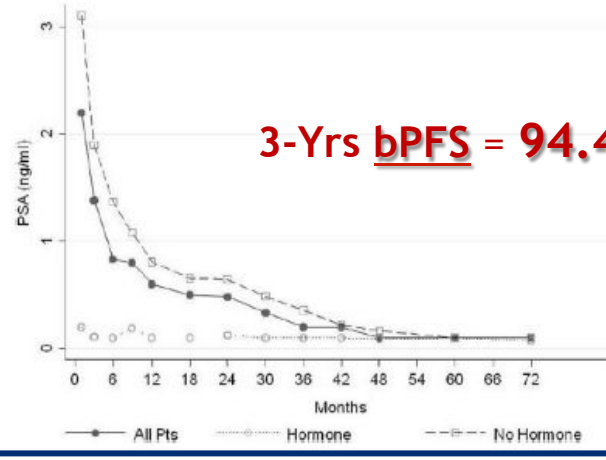


Table 2 Cyberknife®-SBRT: toxicity in 100 patients

	RTOG grade		
Acute (62 pts)	I	II	III
Urinary	34%	12%	-
Rectal	27%	18%	
Late (9 pts)			
Urinary	4%	3%	1%
Rectal	2%	1%	-



3-Yrs bPFS = 94.4

RESEARCH Open Access

Stereotactic body radiotherapy for localized prostate cancer: disease control and quality of life at 6 years

Alan J Katz[1*], Michael Santoro[1], Fred Diblasio[2] and Richard Ashley[3]

2013

RADIATION ONCOLOGY

"…..A **6-year** update of treatment results from **304** low-, intermediate-, and high-risk prostate cancer patients who received **CyberKnife SBRT**……."

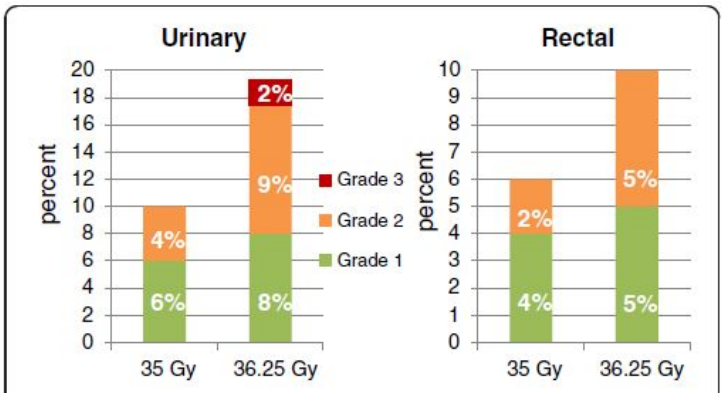
50 pts → 35 Gy - 7 Gy/die
254 pts → 36.25 Gy - 7,25 Gy/die

+ Amifostina

Table 2 Acute bladder/rectal toxicity using RTOG scoring after prostate treatment using the 35 and 36.25 Gy doses

		RTOG grade% (number) of patients			
	Total dose	0	I	II	III & IV
Acute urinary	35 Gy	24% (12)	72% (36)	4% (2)	–
	36.25 Gy	20.5% (52)	74.8% (190)	4.7% (12)	–
Acute rectal	35.00 Gy	20% (10)	76% (38)	4% (2)	–
	36.25 Gy	22.% (56)	74.4% (189)	3.5% (9)	–

Late Tox



"…. Actuarial **5-year biochemical recurrence-f** survival was **97%** for low-risk, **90.7%** for intermedi risk, and **74.1%** for high-risk patients»

RESEARCH Open ess

Stereotactic body radiotherapy with or wit external beam radiation as treatment for confined high-risk prostate carcinoma study

Alan Katz[1,2*] and Josephine Kang[2,3]

ION
OLOGY

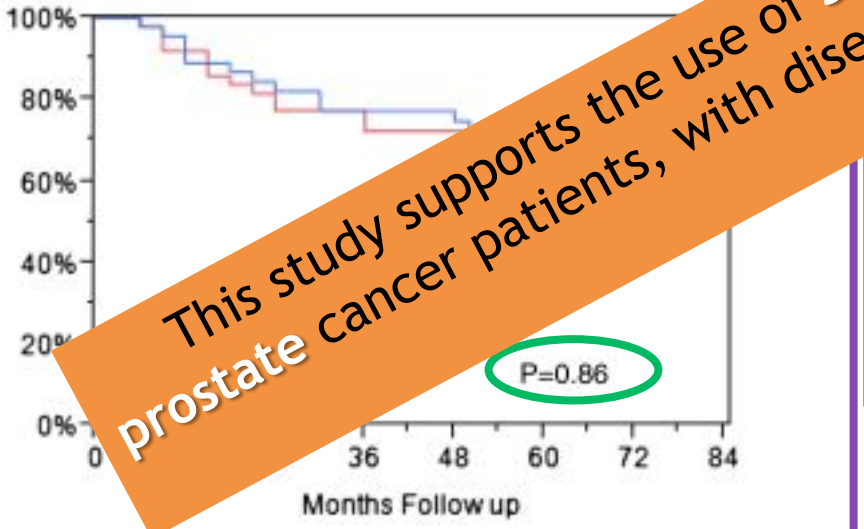
2014

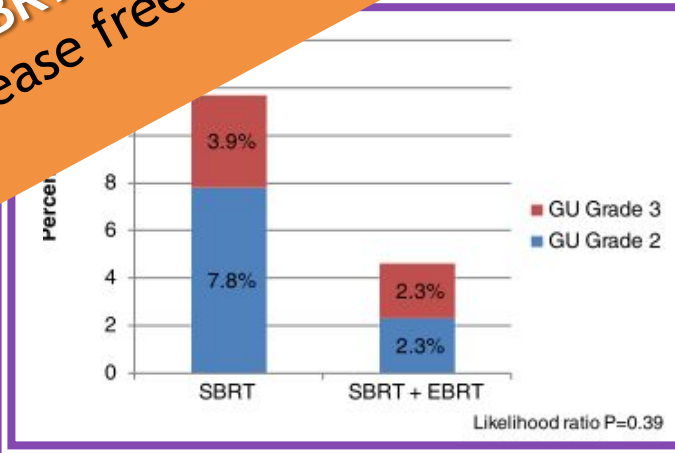
Retrospective study on 97 pts with Hi

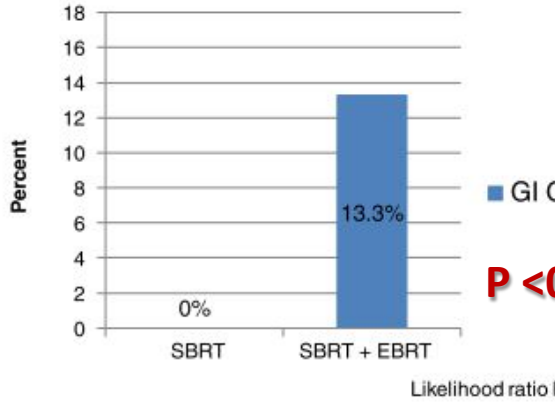
45Gy in 25 fx,
to prostate-pelvic nodes
SBRT 18-21 Gy in 3 fx

M alone
.25 Gy in 5 fxs

This study supports the use of SBRT as a single-modality treatment for high-risk prostate cancer patients, with disease free survival comparable to HDR brachy and IMRT.







5-year DFS of 68%

instead of standard RT is **huge in terms of cost and time** that patients must commit to their therapy. SI
vantageous as compared to HDR as it **is done non-invasively**, without need for anesthesia

Radiother Oncol. 2013 Nov;109(2):217-21. doi: 10.1016/j.radonc.2013.08.030. Epub 2013 Sep 20.

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

King CR[1], Freeman D, Kaplan I, Fuller D, Bolzicco G, Collins S, Meier R, Wang J, Kupelian P, Steinberg M, Katz A.

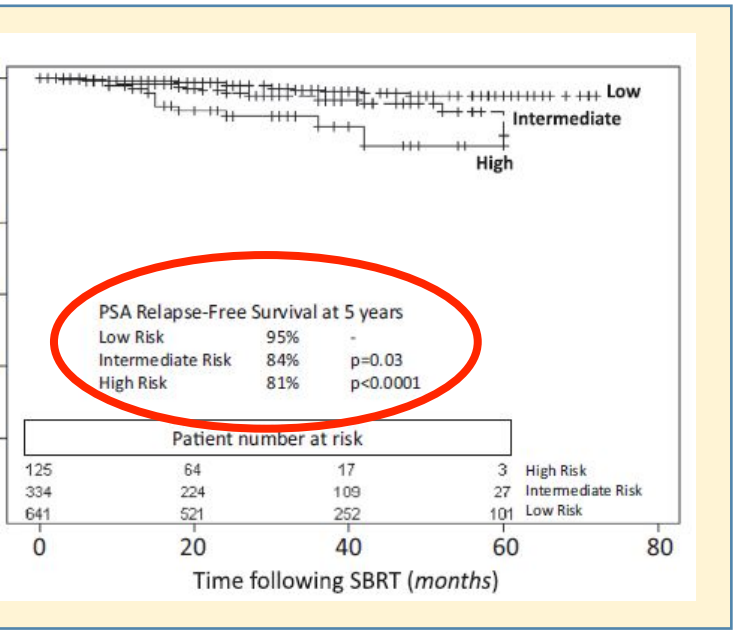
2013

A consortium of 8 centres for prostate SBRT founded in 2011

group	N (%)	35 Gy	36.25 Gy	38–40 Gy
rmediate	641 (58%)		(50%)	68 (11%)
	334 (30%)		(56%)	38 (11%)
l	125 (11%)		66%)	20 (16%)
	1100	385 (35%)	589 (54%)	126 (11%)

1100 pts

RT ± OT
35-40 Gy in
5 fx



	Low risk		Intermediate risk		
	5-yr bRFS	*p*-Value			
ADT use	96.8%				80.2%
No ADT					NE
		0.77	87.2%	0.73	74.1%
	94.4%	0.41	96.7%	0.58	NE

No Difference in bRFS due to total RT dose

SBRT with a Total RT dose of ***35-40 Gy is safe*** and ***sufficient*** to obtain satisfactory clinical outcome in low/intermediate PCa

ubMed.gov
National Library of Medicine
onal Institutes of Health

Abstract

Send to:

nin Radiat Oncol. 2014 Jan;24(1):35-42. doi: 10.1016/j.semradonc.2013.08.004.

omparative effectiveness research in radiation oncology: stereotactic radiosurgery, hypofractionation, and achytherapy.

eja S[1], Yu JB.

2014

ROs

cute/Late Toxicity appears ***acceptable*** though the numbers of pts/duration of FUP has been very limited

RS is delivered with ***fewer visits*** (4-5 in 1 or 2 weeks)

ere is strong evidence it is ***less expensive*** than IMRT and consequently more cost effective.

ONTRAs

cause both IMRT and SRS have already disseminated into clinical practice,it may be ***difficult*** for prospectiv domized clinical trials ***to enroll patients***.

n ***prospective and observational studies are necessary*** to better understand differences between erent treatment modalities

ng-term follow-up is needed to evaluate biological end-points, such as disease-free survival, metastasis- survival and overall survival

,,,,,,Some Concerns!!!!!

THE LANCET Oncology
The Lancet Oncology Commission

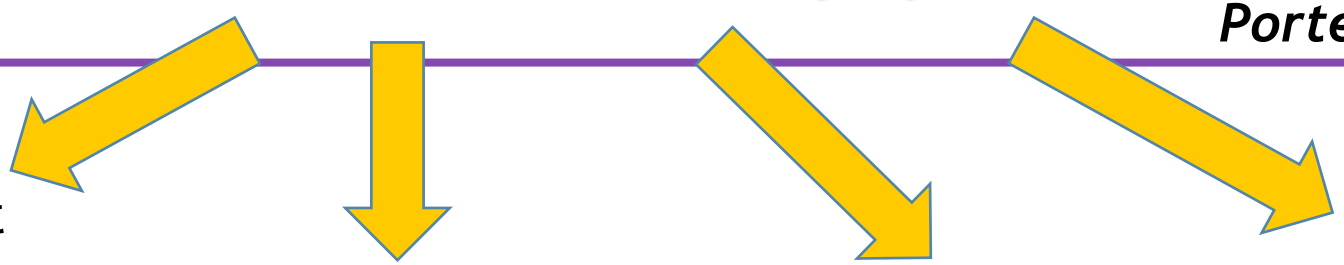
Delivering affordable cancer care in high-income countries

Richard Sullivan, Jeffrey Peppercorn, Karol Sikora, John Zalcberg, Neal J Meropol, Eitan Amir, David Khayat, Peter Boyle, Philippe Autier, Ian F Tannock, Tito Fojo, Jim Siderov, Steve Williamson, Silvia Camporesi, J Gordon McVie, Arnie D Purushotham, Peter Naredi, Alexander Eggermont, Murray F Brennan, Michael L Steinberg, Mark De Ridder, Susan A McCloskey, Dirk Verellen, Terence Roberts, Guy Storme, Rodney J Hicks, Peter J Ell, Bradford R Hirsch, David P Carbone, Kevin A Schulman, Paul Catchpole, David Taylor, Jan Geissler, Nancy G Brinker, David Meltzer, David Kerr, Matti Aapro

Notably, different societies set different thresholds for what is considered good value or ***cost effective***.

.....not only the traditional outcome measure of survival, but also **endpoints** uch as ***recovery time***, ***time to resumption of normal activities***, disutility of care and ***sustainability of health*****.....**

Porter, Health Care 2009



horten treatment time (e.g. PBI)

Fewer recurrences or long-term complications (e.g. SBRT in Lung)

Less toxicity (e.g. IMRT)

Effective palliation

…Thoughts….

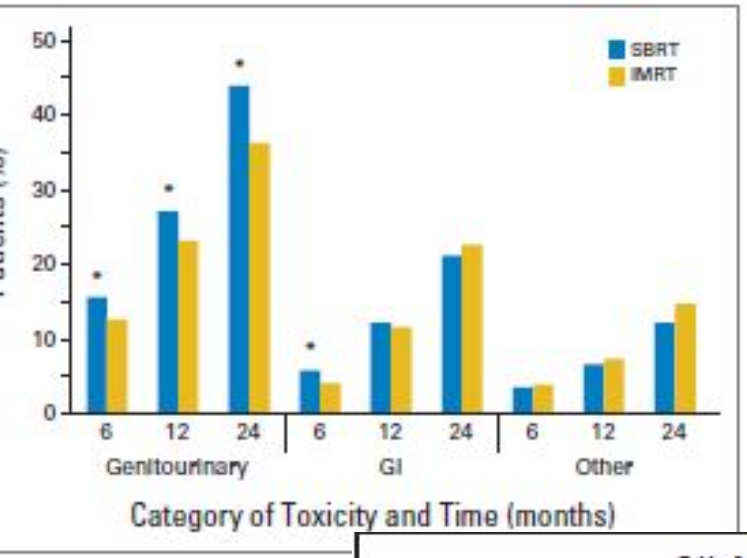
JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

2014

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

"From MEDICARE fee-for-service database we identified **53,841** patients who received **IMRT** and **1,335** patients who received **SBRT**…"



« More GU Toxicity in SBRT group»

Table 2. Adjusted Random Effects Logit Model of Categories of Toxicity

Toxicity Type and Follow-Up Interval (months)	Adjusted Random Effects Logit Model* OR†	95% CI	*P*
GU			
6	1.29	1.05 to 1.53	.009
12	1.23	1.03 to 1.43	.01
24	1.38	1.12 to 1.63	.001
GI			
6	1.42	1.00 to 1.85	.02
12	1.06	0.82 to 1.29	.62
24	0.92	0.71 to 1.12	.49
Other			
6	0.89	0.57 to 1.20	.51
12	0.89	0.63 to 1.15	.44
24	0.80	0.58 to 1.02	.11
Any			
6	1.22	1.02 to 1.41	.02
12	1.12	0.96 to 1.29	.13
24	1.16	0.94 to 1.37	.12

Abbreviations: GU, genitourinary; OR, odds ratio.
*Random effects logit model specified the match group (stereotactic body radiation therapy or intensity-modulated radiation therapy) as a random effect and adjusted for age, comorbidity, and use of androgen deprivation therapy.
†Odds of radiation therapy compared with intensity-

Table 3. Adjusted Random Effects Logit Model of Subcategories of Genitourinary Toxicity

Toxicity	Duration of Follow-Up: 6 Months OR*	6 Months *P*†	12 Months OR*	12 Months *P*†	24 Months OR*	24 Months *P*†
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

...Thoughts....

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

2014

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

"SBRT patients were more likely to be white, younger, healthier, from higher income areas, and less likely to undergo ADT, which may indicate less aggressive disease..."

Table 4. Cancer-Related, Radiation, Nonradiation Cancer-Related, and Complication Costs ($)

Treatment	Mean Cancer-Related Cost ($)*	95% CI ($)	Mean Radiation Cost ($)*	95% CI ($)	Mean Nonradiation Cancer-Related Cost ($)*	95% CI ($)	Mean Complication Cost ($)*	95% CI ($)
SBRT	16,608	15,878 to 17,338	13,645	13,370 to 13,921	2,963	2,295 to 3,630	145	69 to 221
IMRT	23,000	22,505 to 23,496	21,023	20,780 to 21,265	1,978	1,535 to 2,420	69	44 to 95

Abbreviations: IMRT, intensity-modulated radiation therapy; SBRT, stereotactic body radiation therapy.
*Wilcoxon Mann-Whitney U test $P < .001$.

-6300

....SBRT is less expensive....

Contents lists available at SciVerse ScienceDirect

Clinical Oncology

Clinical Oncology 25 (2013) 483–498

Overview

Biological Dose Escalation and Hypofractionation: What is There to be Gained and How Will it Best be Done?

A.C. Tree *‡, E.J. Alexander †‡, N.J. Van As *, D.P. Dearnaley †, V. Khoo *†

2013

Although results are encouraging (***5Yrs bDFS=97%***) they ***do not prove that SBRT*** to standard fractionation in localised PCa

Comparison of the biologically effective dose (BED) of the standard fraction compared with [illegible] stereotactic body radiotherapy

	BED if alpha/beta ratio = 10 Gy	BED if alpha/beta ratio = 5 Gy	BED if alpha/beta ratio = 3 Gy	[illegible]/beta ratio = 1.5 Gy	BED if alpha/beta ratio = 1.0 Gy
78 Gy in 39 fractions	94 Gy	109 Gy	130 Gy	182 Gy	234 Gy
42.7 Gy in 7 fractions	69 Gy	95 Gy	12[illegible]	216 Gy	303 Gy
36.25 Gy in 5 fractions	63 Gy	88 Gy	[illegible]	211 Gy	299 Gy

On going RCTs will help us to understand whether biological dose escalation by exploiting the low alpha/beta ratio of Pca really translates into a clinical benefit for patients

Several factors ne[illegible]ted for in the treatment delivery

[illegible]mage Guidance
[illegible] Fiducial M[illegible]
[illegible]CT
MV-CT
Calypso
EXACTRACT

[illegible]TV margins
3 mm
5 mm
8 mm

Strategies to account for prostate motion
Electromagnetic tracking
Stereoscopic kV X-rays
Fluoroscopic photon imaging
Endorectal Ballon (gas/no Gas)

Focal dose escalation
More heterogeinity
Focal boost
Hydrocolloid gel
Adaptive RT

Future Perspectives

www.current-trials.com

Started in ***2005***.....

HYPO-RT-PC Study

RCT - ISRCTN45905321

Hypofractionated RT of intermediate risk localised Pca
Phase III,randomised, open, multicentre trial

592 patients needed

.....Still On

Going!!!!

Inclusion Criteria

Pts with intermediate risk (T1c - T3a)
with one or two of the following risk factors:
- < 75 years
- T3a or Gleason greater than 7
- PSA greater than 10
- PSA less than 20 µg/L

R

Conventional arm: 5 days/week , 2.0 Gy up to78.0 Gy.
Maximum allowed TTT days are 65.

HypoRT arm: working-days, ***7 fractions of 6.1 Gy,total 42.7Gy***
The total treatment time is 15 - 19 days.

AIMS

To demonstrate a ***10%*** unit increase (70% to 80%) in ***freedom from failure*** (PSA or any clinical test) in the HYPO-RT arm at ***5 years*** after the end of treatment

RESEARCH Open Access

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

2014

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

RADIATION ONCOLOGY

Prostate swelling is known to occur during *brachytherapy*

Table 2 Prostate volumes in descending order as segmented on the treatment planning CT and on the MR images before radiotherapy ($MRI_{baseline}$), in the middle of the treatment (MRI_{mid}) and at the end of treatment (MRI_{end})

Pat #	CT		$MRI_{baseline}$	MRI_{mid}		MRI_{end}	
	Abs. vol. (cm^3)	Rel. vol.	Abs. vol. (cm^3)	Abs. vol. (cm^3)	Rel. vol.	Abs. vol. (cm^3)	Rel. vol.
1	35.3	1.579	22.4	26.7	1.191	27.2	1.217
2	44.5	1.369	32.5	38.6	1.187	34.9	1.074
3	33.8	0.999	33.9	39.0	1.151	33.1	0.976
4	47.8	1.105	43.3	47.5	1.098	46.2	1.067
5	45.8	1.054	43.4	48.9	1.126	48.7	1.122
6	64.8	1.455	44.5	53.3	1.198	44.1	0.991
7	71.6	1.597	44.8	49.8	1.112	46.6	1.040
8	43.5	0.906	48.0	48.7	1.015	48.0	1.000
9	79.4	1.648	48.2	55.5	1.152	54.4	1.129
10	73.0	1.511	48.4	48.9	1.011	50.1	1.037
11	59.4	1.102	53.9	60.8	1.128	55.2	1.023
12	57.0	1.037	54.9	65.3	1.189	64.4	1.172
13	–*	–*	57.2	66.6	1.166	62.2	1.089
14	83.8	1.196	70.1	88.7	1.265	78.0	1.112
15	99.0	1.347	73.5	80.0	1.088	74.1	1.008
16	79.4	1.066	74.5	95.5	1.282	96.2	1.291
17	96.5	1.145	84.3	96.8	1.148	–†	–†
18	105.8	1.242	85.2	96.3	1.131	101.4	1.190
19	106.2	1.021	104.0	116.8	1.123	115.6	1.112
20	153.7	1.045	147.1	155.0	1.054	152.9	1.040
Mean	**72.7**	**1.233**	**60.7**	**68.9**	**1.141**	**64.9**	**1.089**
SD	30.4	0.233	28.7	31.3	0.070	31.9	0.084
p-value†	**0.0001**	**0.0004**	—	**<0.0001**	**<0.0001**	**0.0008**	**0.0002**

0 pts selected by
HYPO-RT-PC
Phase II Study

fractions of 6.1 Gy,total 42.7Gy

Mean volume Differen
(MRI base vs MRI Mid)
23%

CTV is **larger** than that kn
for conventional RT

CTV stays enlarged
during the whole RT cour

RESEARCH Open Access

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

2014

RADIATION ONCOLOGY

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

….the prostate seemed ***to swell most profoundly in the anterior-posterior and cranial-caudal*** directions. This might indicate that a **margin reduction towards the rectum should be applied with caution**, especially during extreme hypo-fractionation….

..No lateral direction on the other hand could be due to the pelvic side wall acting as an anatomic barrier….

Daily IGRT correction usually involves 3 markers implanted centrally in the gland, it is probably adequate for prostate motion but less adequate for taking changes in the outer boundaries of the gland into consideration.

Re-contouring followed by re-planning before each fraction could be needed when using narrow margins (≤ 3 mm).

Great care has to be taken to compensate for prostate swelling if the segmentation and treatment planning process is performed with MR-only

Up to 2 mm extra margin could be needed if prostate segmentation is based only on MRI.

Adaptive radiotherapy with **re-planning** before each fraction, which would also take changes in prostate shape into consideration, **would be optimal**.

Future Perspectives

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

RTOG0938 Multicenter Study- NCT01434290

rted in 2011 – still On Going

TIONALE : RT uses high-energy x-rays to kill tumor cells.
Specialized RT that delivers a high dose of radiation directly to the tumor may kill mo
tumor cells and cause less damage to normal tissue.
Given radiation therapy in different ways may kill more tumor cells.

ROLLEMENT : ***240*** patients

RPOSE: ***Randomized Phase II trial*** studies RT to see how well it works in treating patients with Pca

perimental Arm I : IMRT twice a week for approximately 2½ weeks (**36.25 Gy** total, **7,25 Gy/die**)
perimental Arm II : IMRT once a day, 5 days a week, for approximately 2½ weeks (***51.6 Gy*** total, **4.3Gy/die**)

JECTIVE: 1-year health-related quality of life (HRQOL) for at least one hypofractionated arm is not significantly lower than basel
as measured by the the Bowel and Urinary domains of EPIC instrument

Future Perspectives

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

Prostate Advances in Comparative Evidence (PACE)

NCT01584258

Started in 2012 - still On Going

PURPOSE: ***International multicenter Phase III Randomized study*** for low/intermediate risk PC

Estimated Enrollment : ***1036*** *patients*

SURGERY

YES

- **Laparoscopic RPP**
- **Da Vinci RPP**
- **Cyberknife SBRT**

R

36.25 Gy in 5 Fx
or
38 Gy in 4 Fx

NO

R

- **Conventional RT**
- **Cyberknife SBRT**

Datas in APRIL 2025

OBJECTIVES : ***Five Years Biochemical disease-free survival***

Future Perspectives

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

T01045148	Phase II	**3800 cGy** in **4fx** Vs **3400** cGy in **5fx** in Localized Pca T1b-T2c	2006	***Open**, Recruiting*
T00643617	Phase II	**3800 cGy** delivered in 4Fx for Localized Pca with Ciberknife RadioSurgery	2008	***Open**, Not Recruiting*
T00851916	Phase II	Virtual **HDR Cyberknife** RadioSurgery for Locally recurrent PCa	2009	***Open**, Recruiting*
T01226004	Observational	Overview of pts with low/intermediate Pca treated by Radiosurgery	2010	***Open***
T01655836	Phase I	**HDR Brachytx** Combined With SBRT for Intermediate Risk PCa	2012	***Open**, Recruiting*
T01923506	Phase I	To find MTD with upper limit **45 Gy in 5** Fx in delivering SBRT to **prostate fossa**	2013	***Open**, Recruiting*
T01737151	Randomized Phase II	**4Fx Split-Course SART** for Pts with Low/ Intermediate Risk PCa	2013	***Open**, Recruiting*

Conclusions

SBRT, as an ***alternative to surgery***, provides ***high biochemical control***, low risk of complications, minimal duration of treatment, and outpatient treatment opportunity

Further escalation of SBRT ***doses above 38-40 Gy is not warranted*** at this time and would not be prudent given the potential for higher rates of grade 3 GI and GU

"Several *technologies in radiation oncology* may provide *cost savings* not only in terms of dollars saved, but also reduced human costs by shortening treatment courses.
In addition,these *technologies may allow more pts to have access to necessary treatments*"

On going RCTs will help us to understand whether biological dose escalation by exploiting the low alpha/beta ratio of Pca translates into a clinical benefit for pts

THANKS and……

.have a rest!!!!!!!