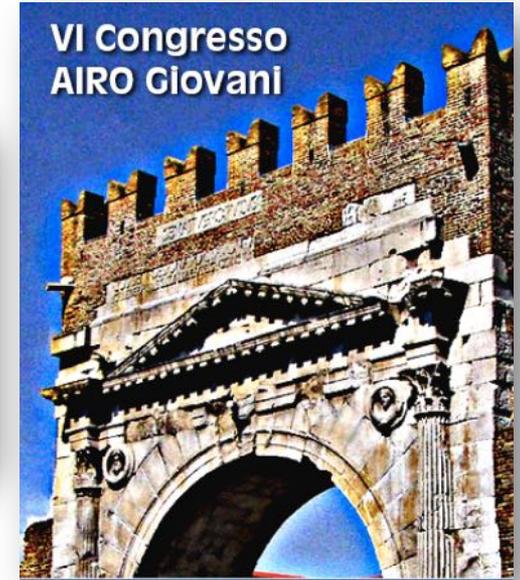


# Adenocarcinoma della prostata: il radio-oncologo e la gestione terapeutica tra evidenze e nuove prospettive

VI Congresso  
AIRO Giovani



## Brachiterapia vs. EBRT? Il dilemma

*U.O. di Radioterapia Oncologica  
Direttore: Dott. Vincenzo Fusco*



**IRCCS CROB**

Istituto di Ricovero e Cura  
a Carattere Scientifico



# Brachiterapia vs. EBRT?

## Il dilemma

### Di chi parliamo?

**NCCN** National Comprehensive Cancer Network® **NCCN Guidelines Version 2.2013**  
**Prostate Cancer**

RECURRENCE RISK

EXPECTED  
PATIENT  
SURVIVAL<sup>a</sup>

INITIAL THERAPY

**Low:**

- T1-T2a
- Gleason score  $\leq 6$
- PSA  $< 10$  ng/mL

$< 10$  y<sup>d</sup>

Active surveillance<sup>e</sup>

- PSA at least as often as every 6 mo
- DRE at least as often as every 12 mo

Active surveillance<sup>e</sup>

- PSA at least as often as every 6 mo
- DRE at least as often as every 12 mo
- Repeat prostate biopsy as often as every 12 mo

$\geq 10$  y

**RT<sup>f</sup> (Daily IGRT with IMRT/3D-CRT) or brachytherapy**

Radical prostatectomy (RP)<sup>g</sup>

± pelvic lymph node dissection (PLND) if predicted probability of lymph node metastasis  $\geq 2\%$





# Brachiterapia vs. EBRT?

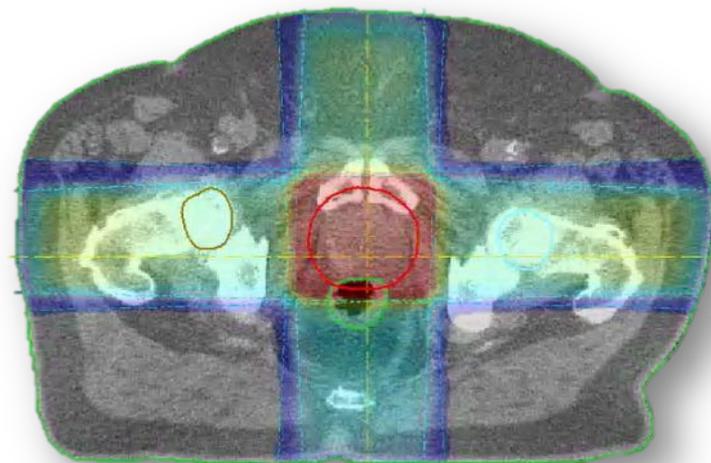
## Il dilemma

### Conosciamo gli sfidanti!

#### EBRT: Radioterapia a fasci esterni

La radioterapia è disciplina clinica che si serve delle radiazioni ionizzanti per la cura dei tumori.

La radioterapia a fasci esterni utilizza delle apparecchiature (Linac, Tomotherapy, etc) che producono fotoni e elettroni.

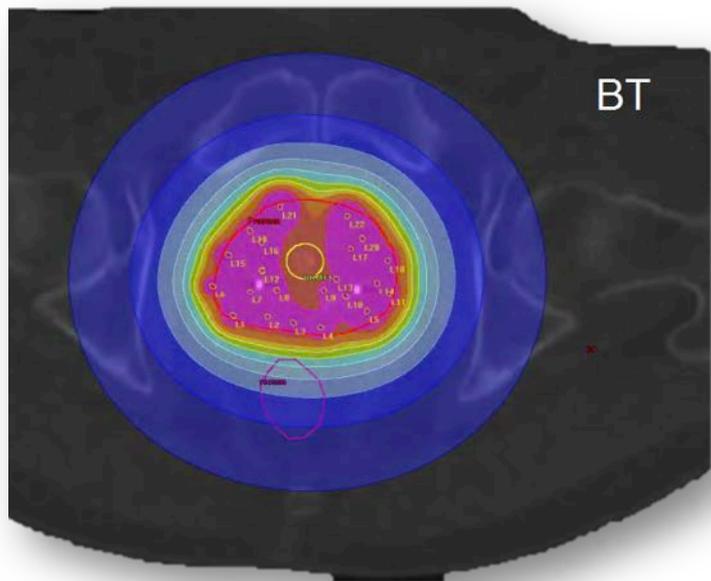




# Brachiterapia vs. EBRT?

## Il dilemma

### Conosciamo gli sfidanti!



### Brachiterapia

E' una **tecnica radioterapica** conformazionale che consiste nel **posizionare sorgenti radioattive all'interno del tumore** o a contatto con esso per un tempo prestabilito!

La caratteristica fondamentale è un rapido **“gradiente di dose”** che consente di adattarsi al volume da irradiare, **risparmiando i tessuti sani** circostanti!





# Brachiterapia vs. EBRT?

## Il dilemma

### Confronto diretto?



**NON esistono studi randomizzati che confrontano le due metodiche**

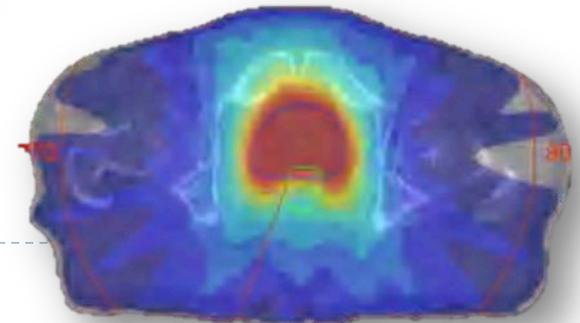
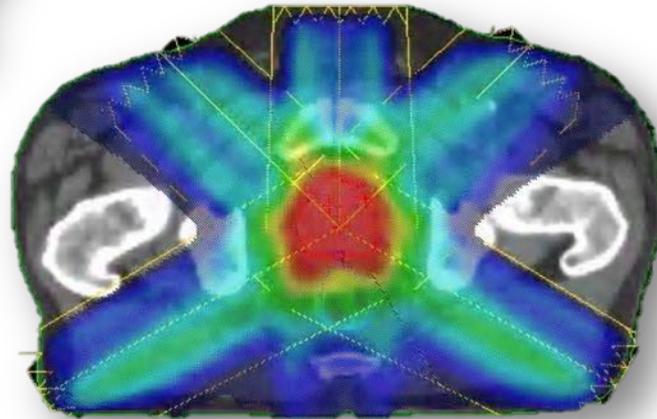
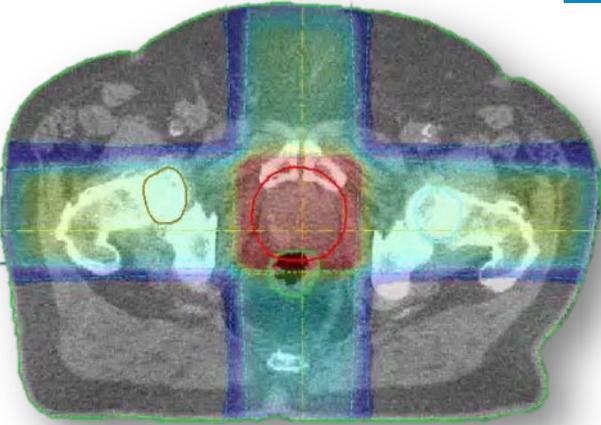




# Brachiterapia vs. EBRT? Il dilemma

Difficile il confronto diretto!

EBRT: Radioterapia a fasci esterni



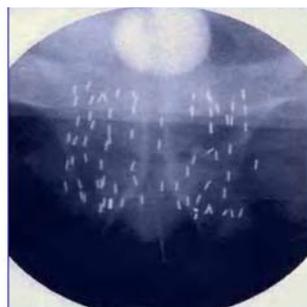


# Brachiterapia vs. EBRT?

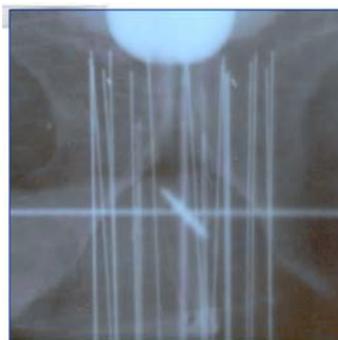
## Il dilemma

### Difficile il confronto diretto!

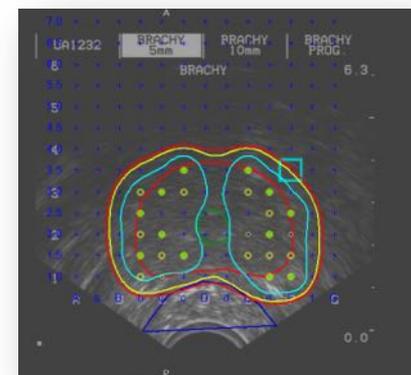
Impianto permanente  
**LDR** (125 I , 103 Pd) erogazione  
continua della dose (mesi)



Impianto temporaneo  
**HDR** (192 Ir) erogazione frazionata  
della dose (minuti)



### Brachiterapia

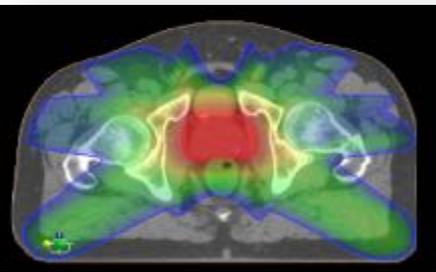




# Brachiterapia vs. EBRT?

## Il dilemma

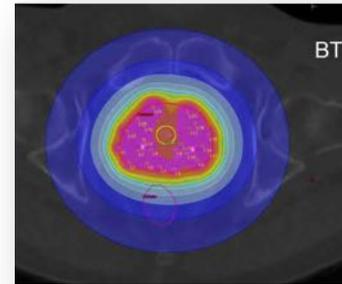
### Conosciamo gli sfidanti!



EBRT:

vs

Brachiterapia



1. Outcome (SVV, Biochemical failure)

2. Toxicity

3. Costs



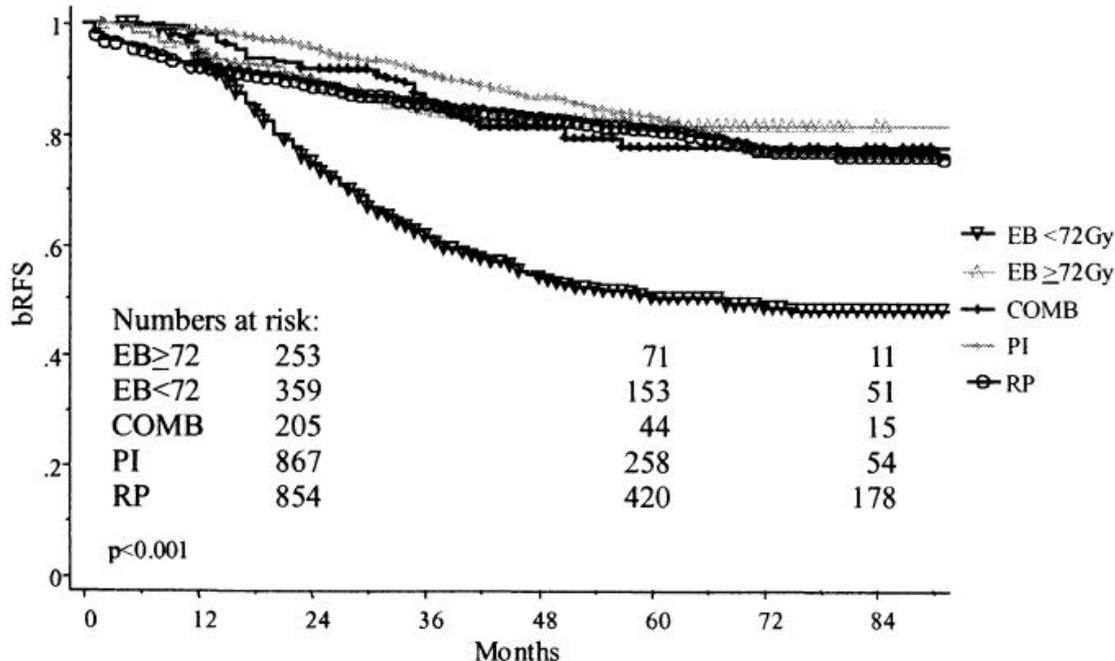


# Brachiterapia vs. EBRT?

## Il dilemma

Table 1. Patient characteristics

Characteristic	All (n = 2991; 100%)	RP (n = 1034; 35%)	EBRT <72 Gy (n = 484; 16%)	EBRT ≥72 Gy (n = 301; 10%)	COMB (n = 222; 74%)	PI (n = 950; 32%)
Mean age (y)	67	63	70	68	69	70
Age (y)						
<65	1191 (40%)	689 (67%)	133 (27%)	93 (31%)	72 (32%)	204 (21%)
≥65	1800 (60%)	345 (33%)	351 (73%)	208 (69%)	150 (68%)	746 (79%)
Race						
White	2687 (90%)	932 (90%)	368 (76%)	228 (76%)	221 (90%)	938 (90%)
Black	304 (10%)	102 (10%)	116 (24%)	73 (24%)	1 (1%)	12 (1%)
Stage						



5-YRS BRFS

RP 81%

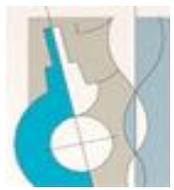
ERT ≥ 72Gy 81%

BRT 83%

Chirurgia, RTE ≥72 Gy e BRT hanno mostrato risultati di sopravvivenza libera da fallimento a 5 anni sovrapponibili

Abbreviations: RP = radical prostatectomy; EBRT = external beam radiotherapy; COMB = combined seeds and EBRT; PI = permanent seed implantation; iPSA = pretreatment prostate-specific antigen (level).

Data presented as the number of patients, with the percentage in parentheses, unless otherwise/noted.



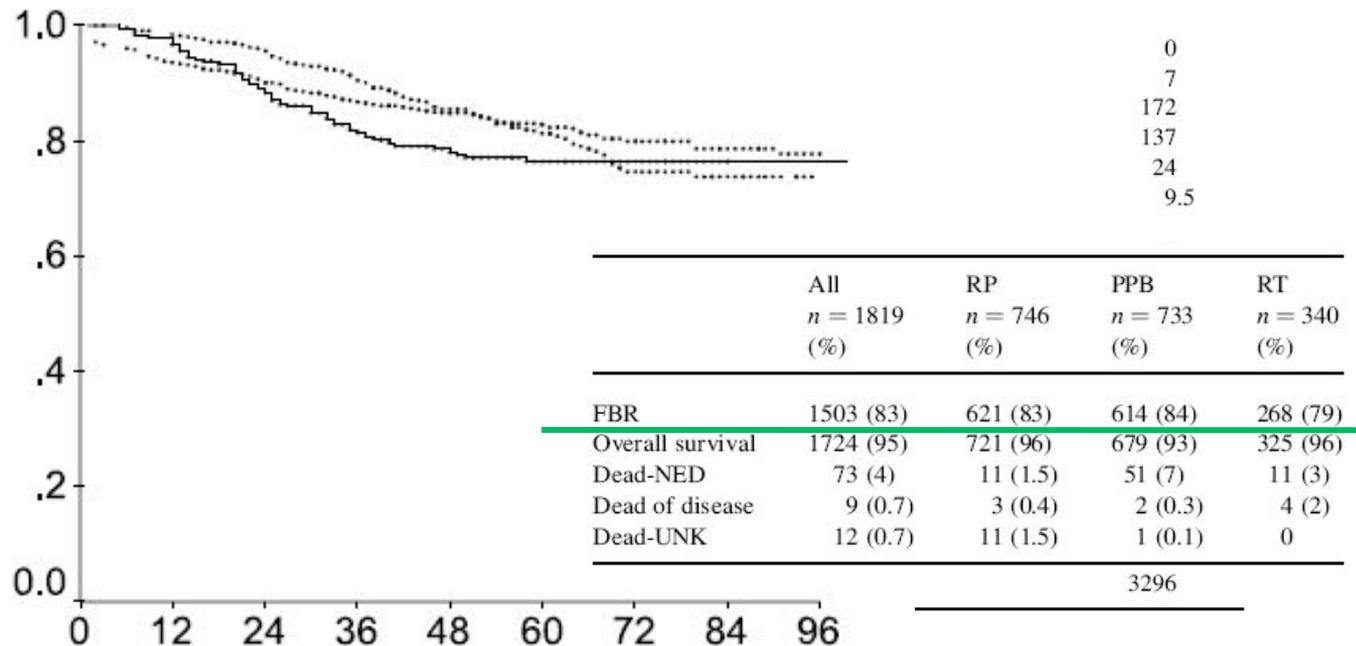
# Brachiterapia vs. EBRT?

## Il dilemma

### 1. OUTCOME

Table 1  
Patient characteristics for all 1819 patients

Characteristic	All	RP	PPB	EBRT
Mean age (range)	65.9	61.8	69.4	68.0
Race (%)				
White	1654	670	724	260
AA				80
Stage (%)				
T1a				0
T1b				7
				172
				137
				24
				9.5
Treatment dates				
Median F/U up in months				
Mean F/U PSA values (range)				
Total F/U PSA values				3296



Chirurgia, RTE e BRT hanno mostrato risultati di sopravvivenza libera da fallimento a 5 anni sovrapponibili





# Brachiterapia vs. EBRT?

## Il dilemma

### 1. OUTCOME

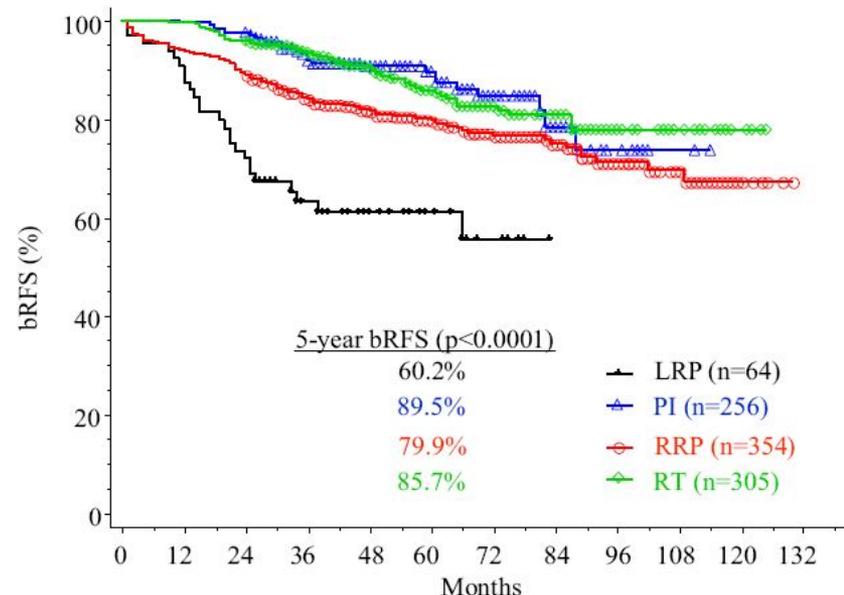
## Five Year Biochemical Recurrence Free Survival for Intermediate Risk Prostate Cancer After Radical Prostatectomy, External Beam Radiation Therapy or Permanent Seed Implantation

Andrew D. Vassil, Erin S. Murphy, Chandana A. Reddy, Kenneth W. Angermeier, Andrew Altman, Nabil Chehade, James Ulchaker, Eric A. Klein, and Jay P. Ciezki

UROLOGY 76:  
1251-1257, 2010.

**Table 2.** Univariate analysis of biochemical relapse-free survival

Factor	Hazard Ratio	95% Confidence Interval	P Value
Treatment			
LAP vs. RT	4.080	2.502-6.655	<.0001
PI vs. RT	0.875	0.550-1.392	.5738
RRP vs. RT	1.531	1.070-2.193	.0200
LAP vs. PI	4.662	2.728-7.966	<.0001
RRP vs. PI	1.750	1.142-2.680	.0101
LAP vs. RRP	2.664	1.692-4.195	<.0001





# Brachiterapia vs. EBRT?

## Il dilemma

### 1. OUTCOME

#### Prostate Cancer: Alternative Therapies

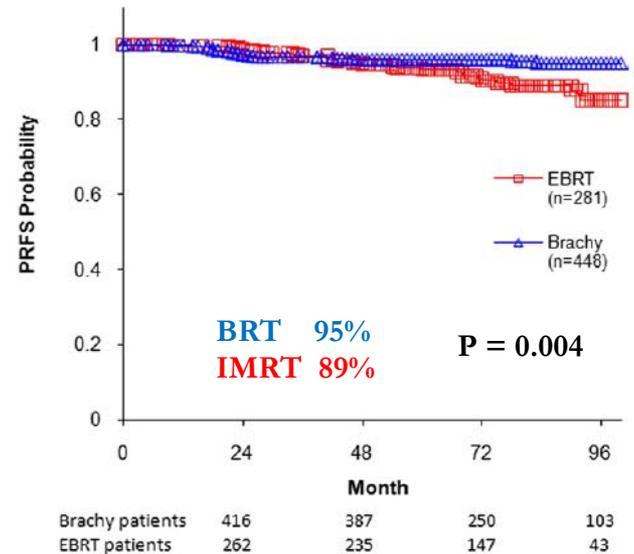
### Comparison of Tumor Control and Toxicity Outcomes of High-dose Intensity-modulated Radiotherapy and Brachytherapy for Patients With Favorable Risk Prostate Cancer

Michael J. Zelefsky, Yoshiya Yamada, Xin Pei, Margie Hunt, Gilad Cohen, Zhigang Zhang, and Marco Zaider

UROLOGY 77: 986–993, 2011.

**Table 1.** Patient characteristics

Characteristic	Brachytherapy (n = 448)*	EBRT (n = 281)†
Age (y)		
<65	188 (42.0)	86 (30.6)
≥65	260 (58.0)	195 (69.4)
Pretreatment PSA (ng/mL)		
<4	93 (20.8)	43 (15.3)
≥4	355 (79.2)	238 (84.7)
T stage		
T1c	365 (81.5)	197 (70.1)
T2a	83 (18.5)	84 (29.9)
Neoadjuvant hormonal therapy		
No	310 (69.2)	192 (68.3)
Yes	138 (30.8)	89 (31.7)



IGRT?



# Brachiterapia vs. EBRT?

## Il dilemma

### 2. TOXICITY

#### Prostate Cancer: Alternative Therapies

#### Comparison of Tumor Control and Toxicity Outcomes of High-dose Intensity-modulated Radiotherapy and Brachytherapy for Patients With Favorable Risk Prostate Cancer

UROLOGY 77: 986–993, 2011.

Michael J. Zelefsky, Yoshiya Yamada, Xin Pei, Margie Hunt, Gilad Cohen, Zhigang Zhang, and Marco Zaider



**Table 3.** Late toxicity outcomes

Toxicity	Brachytherapy (n = 448)	EBRT (n = 281)	P Value
Gastrointestinal late toxicity (n)			
Grade 2	23 (5.1)	4 (1.4)	.018
Grade 3	5 (1.1)	0 (0.0)	.19
Genitourinary late toxicity (n)			
Grade 2	70 (15.6)	12 (4.3)	<.0001
Grade 3	10 (2.2)	4 (1.4)	.62

Impotenza: BRT 33% vs. IMRT 44 % (p=0.004)



# Brachiterapia vs. EBRT?

## Il dilemma

## 2. TOXICITY

### CLINICAL INVESTIGATION

Int. J. Radiation Oncology Biol. Phys., Vol. 82, No. 1, pp. 204–212, 2012

### COMPARISON OF ACUTE AND LATE TOXICITIES FOR THREE MODERN HIGH-DOSE RADIATION TREATMENT TECHNIQUES FOR LOCALIZED PROSTATE CANCER

NASIRUDDIN MOHAMMED, M.D., M.B.A., LARRY KESTIN, M.D., MIHAI GHILEZAN, M.D., PH.D., DANIEL KRAUSS, M.D., FRANK VICINI, M.D., DONALD BRABBINS, M.D., GARY GUSTAFSON, M.D., HONG YE, M.S., AND ALAVARO MARTINEZ, M.D.

EB-IGRT (n = 1039)      EBRT+HDR (n = 447)      BT (n = 417; n = 210 HDR; n = 207 LDR)

Table 3. Acute genitourinary (GU) and gastrointestinal (GI) toxicity  $\geq$  Grade 2

	EB-IGRT (%)	EBRT + HDR (%)	BT (%)	p
Acute GU				
Dysuria	8	25	9	<0.001
Frequency	39	38	27	<0.001
Retention	6	6	13	<0.001
Hematuria	3	0.6	0	0.04
Incontinence	2	1	2	0.65
Any acute GU	43	50	35	<0.001
Acute GI				
Diarrhea	9	21	2	<0.001
Tenesmus	16	21	1	<0.001
Bleeding	3	1	0	0.004
Any acute GI	16	26	2	<0.001
Any acute toxicity	49	55	35	<0.001

Table 5. Late genitourinary (GU) toxicity  $\geq$  Grade 2

	EB-IGRT (%)	EBRT + HDR (%)	BT (%)	p	Median time to toxicity (y)
Late GU					
Dysuria	0.5	3	4	<0.001	0.9
Frequency/urgency	14	17	18	0.26	0.8
Retention	3	12	9	<0.001	1.5
Hematuria	7	4	5	0.12	1.3
Incontinence	3	5	2	0.17	1.6
Urethral stricture	2	11	4	<0.001	1.9
Any late GU	21	28	22	0.01	1.3



# Brachiterapia vs. EBRT?

## Il dilemma

## 2. TOXICITY

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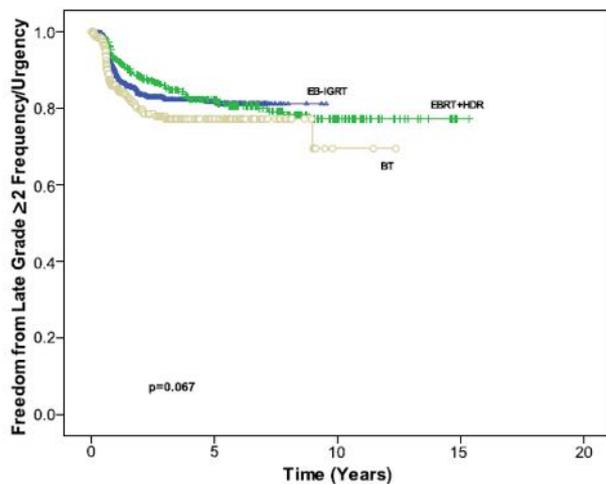


Fig. 1. Kaplan-Meier plot for late Grade  $\geq 2$  frequency/urgency ( $p = 0.07$ ).

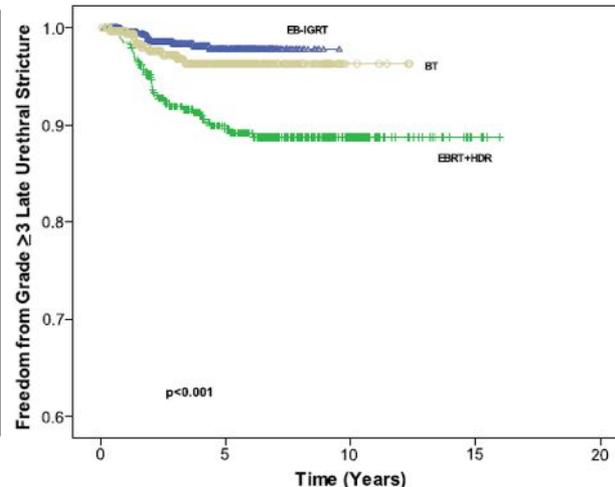


Fig. 2. Kaplan-Meier plot for late Grade  $\geq 3$  urethral stricture ( $p = 0.001$ ).

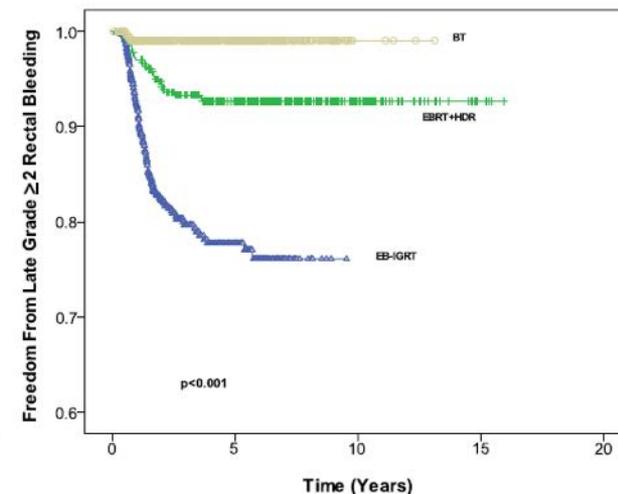


Fig. 3. Kaplan-Meier plot for late Grade  $\geq 2$  rectal bleeding ( $p < 0.001$ ).



# Brachiterapia vs. EBRT?

## Il dilemma

### 2. TOXICITY

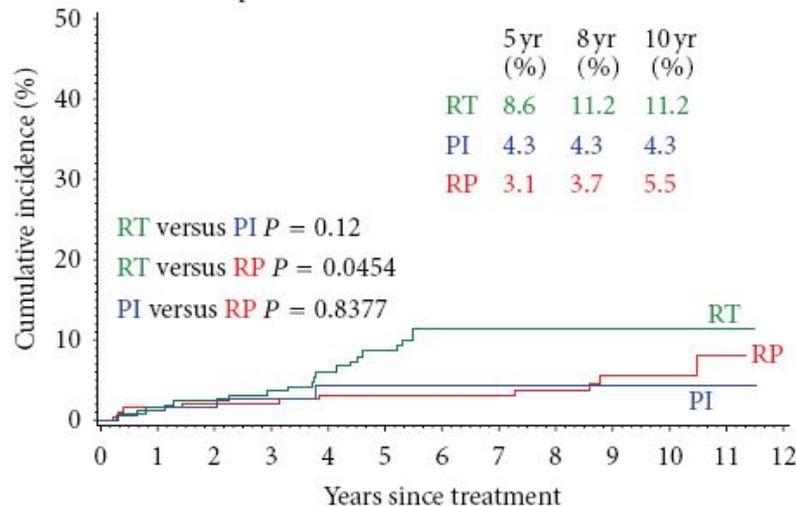
*Clinical Study*

### Long-Term (10-Year) Gastrointestinal and Genitourinary Toxicity after Treatment with External Beam Radiotherapy, Radical Prostatectomy, or Brachytherapy for Prostate Cancer

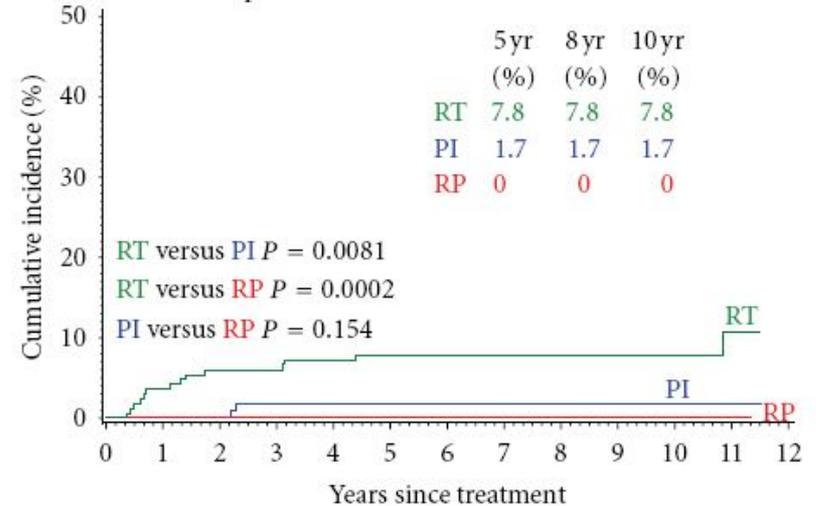
Prostate Cancer

Volume 2012, Article ID 853487, 7 pages

Cumulative incidence for late GU toxicity ( $\geq 2$ ) by treatment for patients treated in 1999



Cumulative incidence for late GI toxicity ( $\geq 2$ ) by treatment for patients treated in 1999



CRITICITA': pazienti trattati nel 1999; EBRT (no IGRT; 3D:78Gy, IMRT:70Gy solo 11pz)



# Brachiterapia vs. EBRT? Il dilemma

2012 BJUI INTERNATIONAL | 110, 221-225

## BJUI Long-term potency preservation following brachytherapy for prostate cancer

Kurt M. Snyder, Richard G. Stock, Michael Buckstein and Nelson N. Stone\*

### OBJECTIVES

- To assess potency preservation in men following brachytherapy for prostate cancer with or without external beam radiation therapy (EBRT) and/or androgen deprivation therapy (ADT).
- To evaluate the factors that significantly impact this rate.

### Mount Sinai Erectile Function Score (MSEFS)

59.7% LDR I<sup>125</sup> seeds implant  
40.3% LDR Pd<sup>103</sup> seeds implant

Characteristic	No. (%)
Clinical stage	
≤T2a	773 (72.7)
T2b	190 (17.9)
≥T2c	100 (9.4)
Gleason score	
2-6	759 (71.4)
7	214 (20.6)
8-10	85 (8.0)
PSA	
<10	838 (78.8)
10-20	180 (16.9)
>20	45 (4.2)
MSEFS	
2	294 (27.7)
3	769 (72.3)
Age	
<60	271 (25.5)
60-70	590 (55.5)
>70	202 (19.0)
EBRT	
No	740 (69.6)
Yes	323 (30.4)
ADT	
No	541 (50.9)
Yes	522 (49.1)
Treatment	
Brachytherapy alone	480 (45.2)
Brachytherapy + ADT	260 (24.5)
Brachytherapy + EBRT	61 (5.7)
Brachytherapy + ADT + EBRT	262 (24.6)



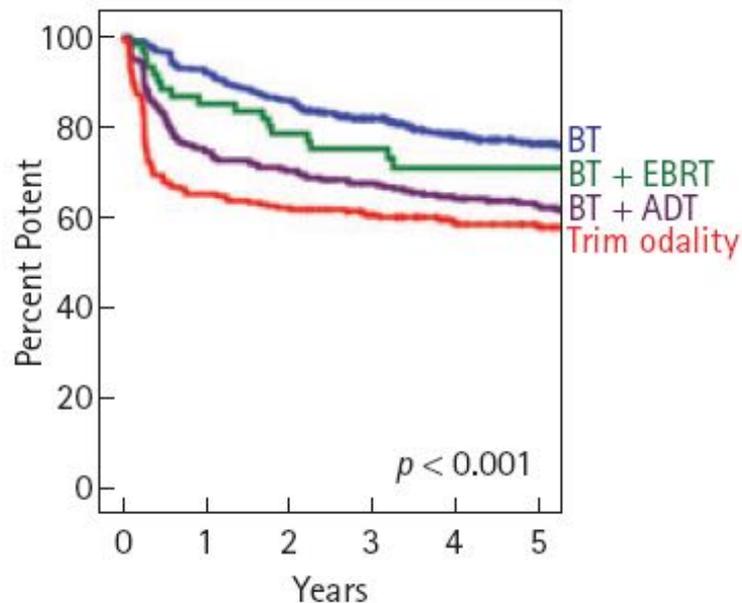
# Brachiterapia vs. EBRT? Il dilemma

## 2. TOXICITY

2012 BJU INTERNATIONAL | 110, 221-225

### BJUI Long-term potency preservation following brachytherapy for prostate cancer

Kurt M. Snyder, Richard G. Stock, Michael Buckstein and Nelson N. Stone\*



Factor	<i>P</i>	Exp <i>B</i> (95% CI)
Age	<0.001	2.09 (1.77-2.46)
MSEFS pretreatment potency	<0.001	1.79 (1.44-2.22)
Addition of EBRT	0.007	1.39 (1.09-1.77)
ADT	0.009	1.36 (1.08-1.71)



# Brachiterapia vs. EBRT?

## Il dilemma

## 2. TOXICITY

Radiol med (2012) 117:

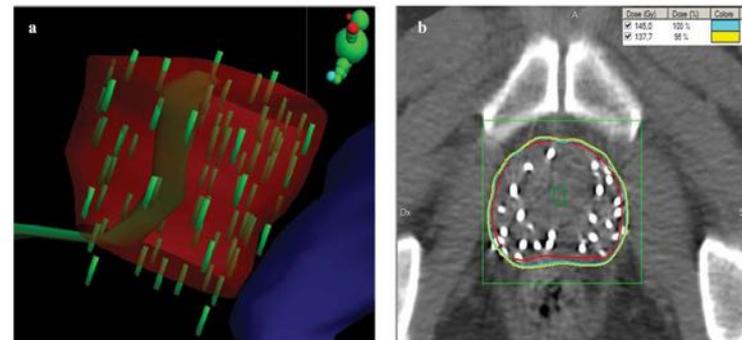
URO-GENITAL RADIOLOGY  
RADIOLOGIA URO-GENITALE

### Low-dose rate brachytherapy of the prostate in elderly patients

#### *Brachiterapia prostatica low-dose rate nel paziente anziano*

C. Chiumento • A. Fiorentino • R. Caivano • S. Clemente • V. Fusco

Age	≤75	> 75	<i>p</i> value
Patients, n	43	37	
GU toxicity, n (%)			
G0	4 (9)	5 (13)	0.6
G1	28 (65)	22 (60)	
G2	11 (26)	10 (27)	
GI toxicity, n (%)			
G0	22 (51)	20 (54)	0.9
G1	16 (37)	10 (27)	
G2	5 (12)	7 (19)	



Tumori, 97: 335-340, 2011

### A retrospective analysis after low-dose-rate prostate brachytherapy with permanent <sup>125</sup>I seed implant: clinical and dosimetric results in 70 patients

Costanza Chiumento, Antonietta Montagna, Stefania Clemente, Mariella Cozzolino, and Vincenzo Fusco





# Brachiterapia vs. EBRT?

## Il dilemma

## 2. TOXICITY

F. Alongi<sup>1</sup> · A. Fogliata<sup>2</sup> · P. Navarria<sup>1</sup> · A. Tozzi<sup>1</sup> · P. Mancosu<sup>1</sup> · F. Lobefalo<sup>1</sup> ·  
G. Reggiori<sup>1</sup> · A. Clivio<sup>2</sup> · L. Cozzi<sup>2</sup> · M. Scorsetti<sup>1</sup>

<sup>1</sup> Department of Radiotherapy, Humanitas Cancer Center, Istituto Clinico Humanitas, Rozzano, Milan

<sup>2</sup> Medical Physics Unit, Oncology Institute of Southern Switzerland, Bellinzona

## Moderate hypofractionation and simultaneous integrated boost with volumetric modulated arc therapy (RapidArc) for prostate cancer

### Report of feasibility and acute toxicity

Strahlenther Onkol 2012 · 188:990–996

DOI 10.1007/s00066-012-0171-7

Received: 05 April 2012

Accepted: 13 June 2012

Published online: 29 September 2012

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		Low risk	Intermediate risk	High risk	All
Age (years)	Median (range)	75 (60–79)	75 (60–84)	74 (62–82)	75 (60–84)
Stage	Patients (n)	25	34	11	70
Gleason score	Median (range)	6 (4–8)	7 (4–9)	8 (6–10)	7 (4–10)
Initial PSA	Median (range)	6.3 (3–10)	5.8 (3–44)	23.6 (7–40)	6.8 (3–44)
<b>Rectal toxicity</b>					
Patients, n (%)	Grade 0	18/25 (72%)	22/34 (65%)	6/11 (55%)	46/70 (66%)
	Grade 1	2/25 (8%)	7/34 (21%)	3/11 (27%)	12/70 (17%)
	Grade 2	5/25 (20%)	5/34 (15%)	2/11 (18%)	12/70 (17%)
	Grade 3	0/25 (0%)	0/34 (0%)	0/11 (0%)	0/70 (0%)
<b>GU toxicity</b>					
Patients, n (%)	Grade 0	10/25 (40%)	17/34 (50%)	4/11 (36%)	31/70 (44%)
	Grade 1	7/25 (28%)	11/34 (32%)	4/11 (36%)	22/70 (31%)
	Grade 2	7/25 (28%)	6/34 (18%)	3/11 (27%)	16/70 (23%)
	Grade 3	1/25 (4%)	0/34 (0%)	0/11 (0%)	1/70 (1%)
<b>Upper GI toxicity</b>					
Patients, n (%)	Grade 0	22/25 (88%)	26/34 (76%)	6/10 (60%)	54/69 (78%)
	Grade 1	2/25 (8%)	6/34 (18%)	3/10 (30%)	11/69 (16%)
	Grade 2	1/25 (4%)	2/34 (6%)	1/10 (10%)	4/69 (6%)
	Grade 3	0/25 (0%)	0/34 (0%)	0/10 (0%)	0/69 (0%)

PSA prostate-specific antigen, GU genitourinary, GI gastrointestinal.



# Brachiterapia vs. EBRT?

## Il dilemma

## 2. TOXICITY

Rectal spacing in prostate RT

Radiotherapy and Oncology 106 (2013) 215–219

Low rectal toxicity after dose escalated IMRT treatment of prostate cancer using an absorbable hydrogel for increasing and maintaining space between the rectum and prostate: Results of a multi-institutional phase II trial

Matthias Uhl<sup>a,\*</sup>, Baukelien van Triest<sup>b</sup>, Michael J. Eble<sup>c</sup>, Damien C. Weber<sup>d</sup>, Klaus Herfarth<sup>a</sup>, Theodore L. De Weese<sup>e</sup>

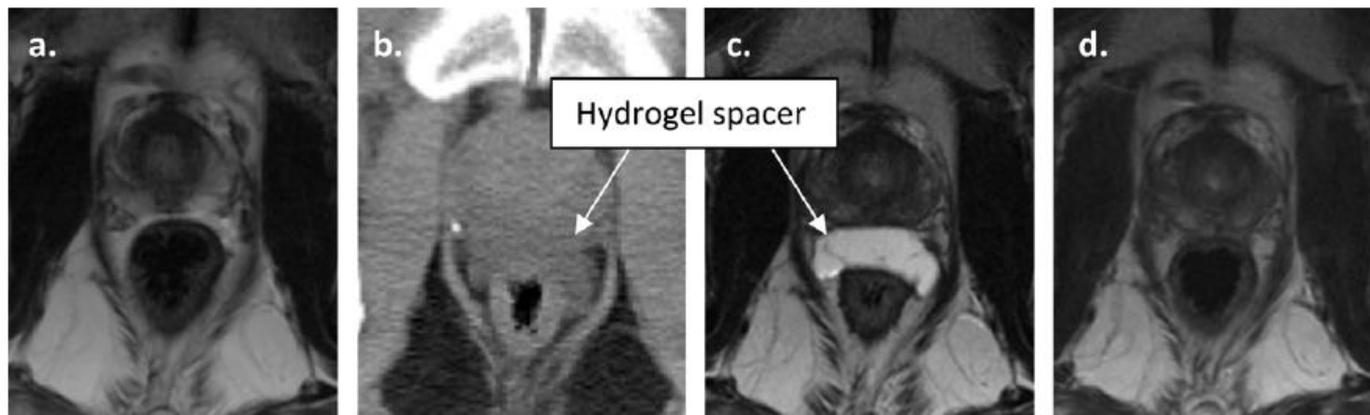


Fig. 2. Axial images from the same patient at (a) pre implant baseline (T2w MRI), (b) post implant/pre IMRT (CT), (c) post IMRT (T2w MRI), and (d) 6 months post-implant showing hydrogel absorption (T2w MRI).



# Brachiterapia vs. EBRT?

## Il dilemma

## 2. TOXICITY

*Acta Oncologica*, 2013; 52: 463–469

**Urinary functional outcomes and toxicity five years after proton therapy for low- and intermediate-risk prostate cancer: Results of two prospective trials**

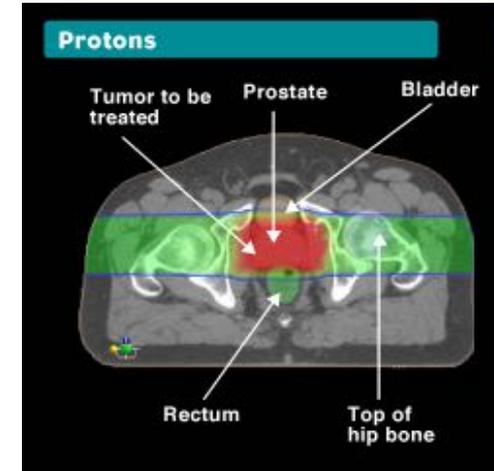


Table I. Median IPSS at six-month intervals.

Pretreatment IPSS	N	Median Pretreatment IPSS (range)	Median post-treatment IPSS (range)					
			6M	12M	24M	36M	48M	60M
< 15	137	6 (0–14)	5 (0–35) 130 pts.	7 (0–25) 117 pts.	6 (0–25) 112 pts.	6 (0–23) 95 pts.	6 (0–20) 92 pts.	6 (0–23) 50 pts.
≥ 15	34	18 (15–25)	11 (1–21) 30 pts.	14.5 (2–27) 30 pts.	13.5 (3–28) 26 pts.	12 (3–30) 20 pts.	12 (3–27) 10 pts.	10 (3–21) 12 pts.
<b>Total</b>	<b>171*</b>	<b>8 (0–25)</b>	<b>7 (0–35) 160 pts.</b>	<b>7 (0–27) 147 pts.</b>	<b>7 (0–28) 138 pts.</b>	<b>6 (0–30) 115 pts.</b>	<b>7 (0–27) 111 pts.</b>	<b>7 (0–23) 62 pts.</b>

IPSS, International Prostate Symptom Score; M, month; N, number of patients.

\*171 patients available for analysis of pretreatment data.





# Brachiterapia vs. EBRT?

## Il dilemma

### 3. COSTS

Brachytherapy provides comparable outcomes and improved cost-effectiveness in the treatment of low/intermediate prostate cancer

Chirag Shah, Thomas B. Lanni Jr.  , Mihai I. Ghilezan, Gary S. Gustafson, Kimberly S. Marvin, Hong Ye, Frank A. Vicini, Alvaro A. Martinez

Brachytherapy

Volume 11, Issue 6, November–December 2012, Pages 441–445

CARATTERISTICHE DELLA CASISTICA  
1328 (92-08)

LDR

207 (Palladium, 120 Gy)

HDR (4 frazioni)

252 (38.0 Gy)

IMRT

869 (dose mediana 75.6 Gy in 42-44 fr)

\$ 9,938

\$ 17,514

\$ 29,356

Le tre modalità di terapia hanno outcomes comparabili, ma l'IMRT ha costi significativamente più alti della brachiterapia



# Brachiterapia vs. EBRT?

## Il dilemma

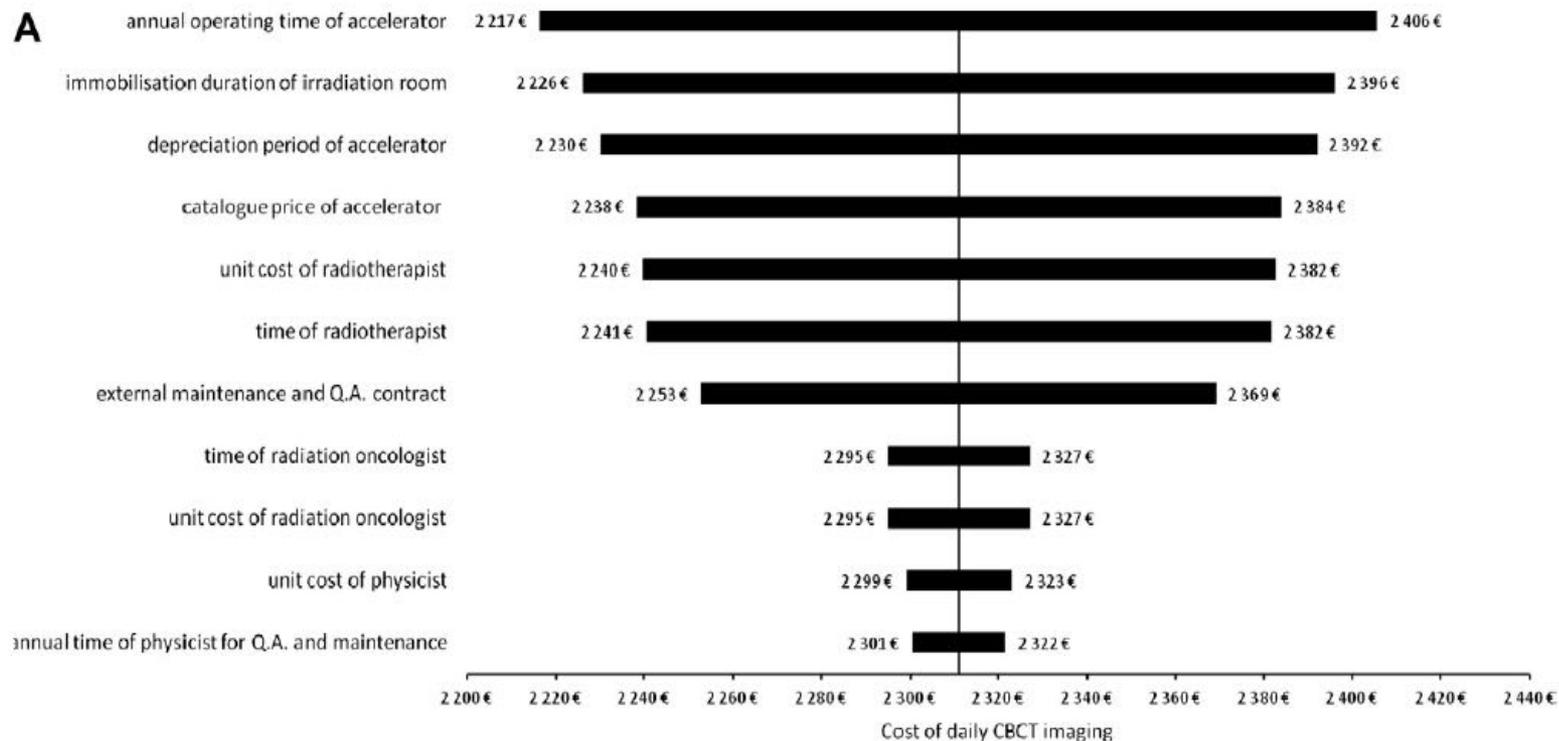
### 3. COSTS

Phase III randomised trial

Radiotherapy and Oncology 106 (2013) 50–58

#### Cost of prostate image-guided radiation therapy: Results of a randomized trial

Lionel Perrier<sup>a</sup>, Magali Morelle<sup>a</sup>, Pascal Pommier<sup>a</sup>, Jean-Léon Lagrange<sup>b</sup>, Agnès Laplanche<sup>c</sup>, Philippe Dudouet<sup>d</sup>, Stéphane Supiot<sup>e</sup>, Bruno Chauvet<sup>f</sup>, Tan-Dat Nguyen<sup>g</sup>, Gilles Crehange<sup>h</sup>, Véronique Beckendorf<sup>i</sup>, Françoise Pene<sup>j</sup>, Xavier Muracciole<sup>k</sup>, Jean-Marc Bachaud<sup>l</sup>, Elisabeth Le Prisé<sup>m</sup>, Renaud de Crevoisier<sup>m,n,\*</sup>





# Brachiterapia vs. EBRT?

## Il dilemma

### And the winner is?

RTE e BRT hanno  
mostrato risultati di  
sopravvivenza libera da  
fallimento a 5 anni  
**sovrapponibili**

RTE-IGRT e BRT  
tossicità acute e tardive  
**sovrapponibili**

Costi a favore  
della BRT LDR

Compliance del  
paziente





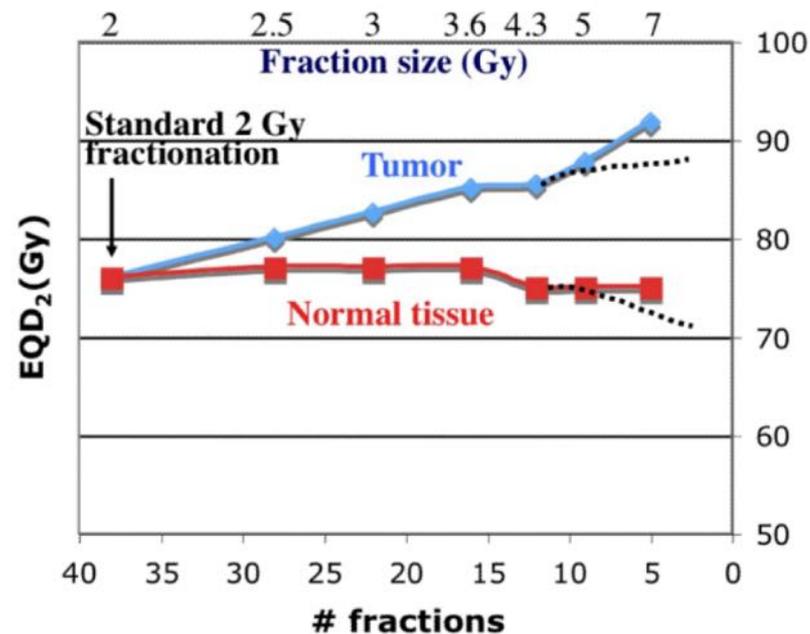
# Brachiterapia vs. EBRT?

## Il dilemma

### And the FUTURE ?

$\alpha/\beta$  Ratio for Prostate Cancer

Author	Ref	# pts	$\alpha/\beta$	Conf inter
Brenner	IJROBP 43(5):1095	367	<b>1.5</b>	0.8 - 2.2
Brenner	IJROBP 52(1):6	192	<b>1.2</b>	0.03 - 4.1
Wang	IJROBP 57(4):1101	192	<b>3.1</b>	1.5 - 5.7
Fowler	IJROBP 50(4):1021	1471	<b>1.49</b>	1.25 - 1.76
Kal	IJROBP 57(4):1116	1471	<b>3.5</b>	3.1 - 3.9
Bentzen	Rad&Oncol 75:1-3	936	<b>1.12</b>	-3.3 - 5.6
		330	<b>8.3</b>	0.7 - 16
Williams	IJROBP 68(1):24	3756	<b>2.6</b>	0.9 - 4.8
			<b>4.5</b>	1.6 - 8.7



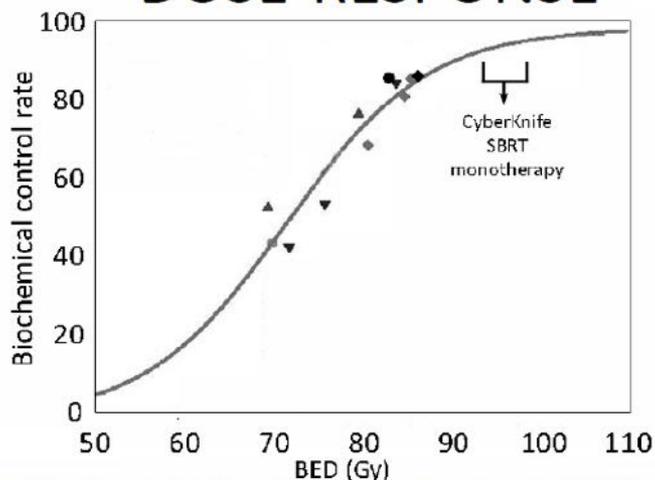


# Brachiterapia vs. EBRT?

## Il dilemma

### And the FUTURE ?

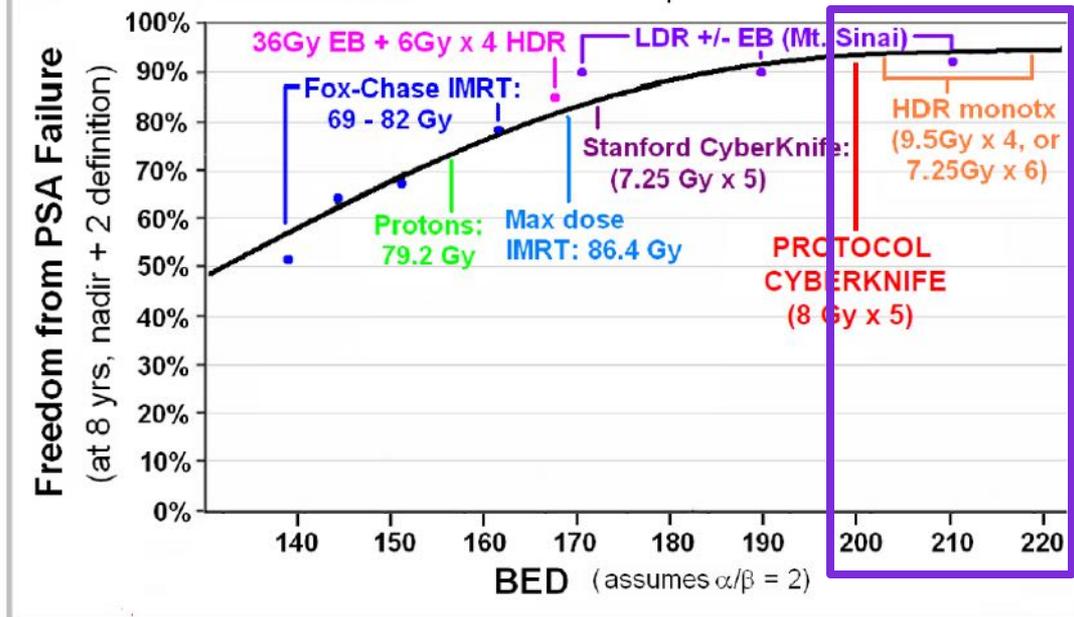
### DOSE-RESPONSE



Dose-response curve highlighting biochemical control as a function of biologically equivalent dose (BED) of 1.8 Gy per fraction for an  $\alpha/\beta$  ratio of 1.5. ◆ Cahlon et al. *Int J Radiat Oncol Biol Phys* 71, 330-337 (2008), ● Kupelian et al. *Int J Radiat Oncol Biol Phys* 63, 1463-1468 (2005), ▼ Pollack (50), ▲ Zelefsky et al. *Int J Radiat Oncol Biol Phys* 41, 491-500 (1998), ◆ Hanks et al. *Int J Radiat Oncol Biol Phys* 46, 823-832 (2000). Adapted from Fowler et al. *Acta Oncol* 44, 265-276 (2005).

### BED & bDFS FOR VARIOUS RT MODALITIES

#### Estimated Dose-Response Curve





# Brachiterapia vs. EBRT?

## Il dilemma

### And the FUTURE ?

#### A comparative dosimetric analysis of virtual stereotactic body radiotherapy to high-dose-rate monotherapy for intermediate-risk prostate cancer

Daniel E. Spratt<sup>1</sup>, Lawrence M. Scala<sup>1</sup>, Michael Folkert<sup>1</sup>, Laszlo Voros<sup>2</sup>, Gil'ad N. Cohen<sup>2</sup>, Laura Happersett<sup>2</sup>, Evangelia Katsoulakis<sup>1</sup>, Michael J. Zelefsky<sup>1</sup>, Marisa A. Kollmeier<sup>1</sup>, Yoshiya Yamada<sup>1</sup>

Brachytherapy

Available online 23 April 2013

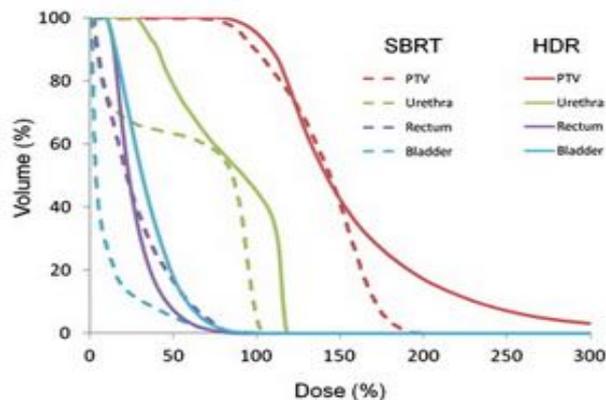
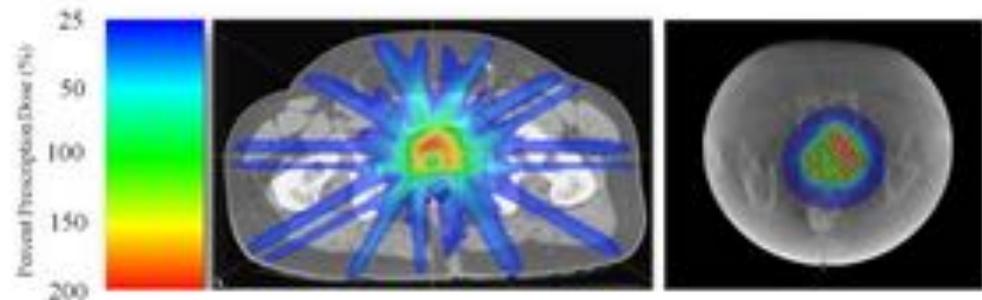


Fig. 2. Representative dose–volume histogram for the normal tissue–prioritized plan. SBRT = stereotactic body radiotherapy; HDR = high-dose rate; PTV = planning target volume.





# Brachiterapia vs. EBRT? Il dilemma

## And the FUTURE ?

Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 5, pp. 1588–1597, 2008

### PHYSICS CONTRIBUTION

#### VIRTUAL HDR<sup>SM</sup> CYBERKNIFE TREATMENT FOR LOCALIZED PROSTATIC CARCINOMA: DOSIMETRY COMPARISON WITH HDR BRACHYTHERAPY AND PRELIMINARY CLINICAL OBSERVATIONS

DONALD B. FULLER, M.D.,\* JOHN NAITOH, M.D.,† CHARLES LEE, PH.D.,\* STEVEN HARDY, C.M.D.,\* AND HAORAN JIN, PH.D.\*

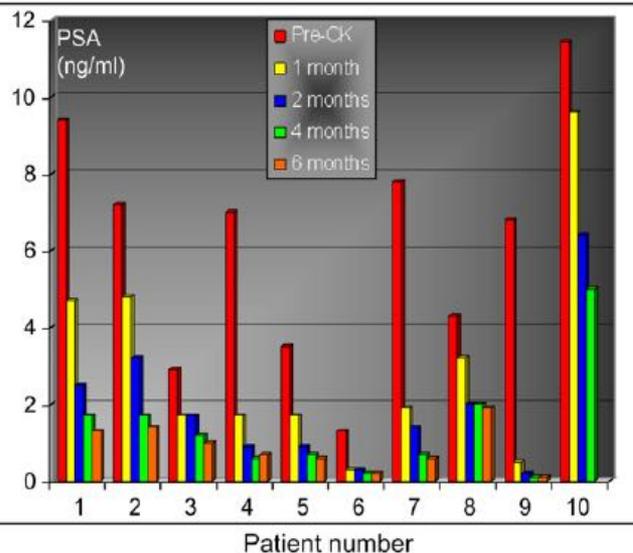


Table 3. Rectal wall and mucosa statistics

	CyberKnife actual	High-dose-rate simulated	<i>p</i> (paired <i>t</i> -test)
Rectal wall V80 (ml)	1.3 (0.3–4.0)	2.4 (0.6–6.0)	0.06
Rectal wall Dmax (Gy)	37.3 (34.7–38.0)	37.5 (34.6–43.3)	Not significant
Rectal wall D1 (Gy)	33.3 (29.6–34.7)	34.7 (30.5–37.2)	0.02
Rectal wall D10 (Gy)	23.2 (20.0–25.6)	25.7 (20.7–30.7)	0.002
Rectal wall D25 (Gy)	15.8 (13–18.7)	19.4 (13.7–24.5)	<0.001
Rectal mucosa V80 (ml)	0.0 (0.0–0.7)	0.1 (0.0–2.3)	Not significant
Rectal mucosa Dmax (Gy)	29.0 (25.3–33.5)	31.4 (27.4–35.0)	0.04
Rectal mucosa D1 (Gy)	25.9 Gy (22.1–30.2)	29.0 Gy (24.8–33.6)	0.001
Rectal mucosa D10	19.5 (16.3–22.7)	23.8 (18.5–28.9)	<0.001
Rectal mucosa D25 (Gy)	14.2 (11.7–17.3)	19.4 (13.6–23.8)	<0.001

# Brachiterapia vs. EBRT?

## Il dilemma

### And the FUTURE ?

Critical Reviews in Oncology/Hematology 84 (2012) 101–108

Overview of SBRT schedules and toxicity outcomes for localized prostate cancer.

Reference	No of patients	Risk classification	Target	Total dose (Gy)	Fraction size (Gy)	Duration of treatment	Median Follow up (months)	Grade $\geq 3$ late GI toxicity	Grade $\geq 3$ late GU toxicity
Collins 1991	232	NS	Little pelvis	36.0	6	Three weeks	$\geq 24$	-	-
Choi 2007	44	All risk categories	Prostate only	36.0	9	NS	13	0	0
Madsen 2007	40	Low risk	Prostate only	33.5	6.7	5 Consecutive days	41	0	0
Tang 2008	30	Low risk	Prostate only	35	5	Once a week over 29 days.	6	0	0
Friedland 2009	112	Low risk	Prostate and the proximal seminal vesicles	35	5	5 Consecutive days	24	0	0
Bolzicco 2010	45	Low-intermediate-risk	N.S.	35	5	5 Consecutive days	20	2.2%	0
Katz 2010	304	All risk categories	Prostate and the proximal seminal vesicles <sup>a</sup>	35/36.25	7/7.25	5 Consecutive days	36	0	0
King 2011	41	Low risk	Prostate only	36.25	7.25	5 Consecutive days/5 non consecutive days	33	0	3%
Freeman 2011	41	Low risk	Prostate and the proximal 1 cm of the seminal vesicles	36.25	7.25	5 Consecutive days	60	0	2.5%



# Brachiterapia vs. EBRT? Il dilemma

## And the FUTURE ?

### In Regard to Miralbell et al

*To the Editor:* In a recent analysis of 7 international institutional datasets, Miralbell et al (1) contributed to the well-known debate on how low is the  $\alpha/\beta$  value of prostate cancer (2-4). Based on the multiple primary datasets collected for analysis, the authors deduced the dose fractionation sensitivity of prostate cancer as  $\alpha/\beta = 1.4$  Gy. Moreover, when the  $\alpha/\beta$  ratio was allowed to vary among risk groups, the values of 0.6, 1.7, and 1.6 Gy for low-, intermediate-, and high-risk groups were obtained.

International Journal of Radiation Oncology • Biology • Physics

Volume 85 • Number 1 • 2013

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### Biology Contribution

## Estimation of a Self-Consistent Set of Radiobiological Parameters From Hypofractionated Versus Standard Radiation Therapy of Prostate Cancer

Piernicola Pedicini, PhD,\* Lidia Strigari, PhD,<sup>†</sup> and Marcello Benassi, PhD<sup>‡</sup>

Int J Radiation Oncol Biol Phys, Vol. 85, No. 5, pp. e231–e237, 2013





# Brachiterapia vs. EBRT?

## Il dilemma

### And the FUTURE ?

Biology Contribution

Int J Radiation Oncol Biol Phys, Vol. 85, No. 5, pp. e231–e237, 2013

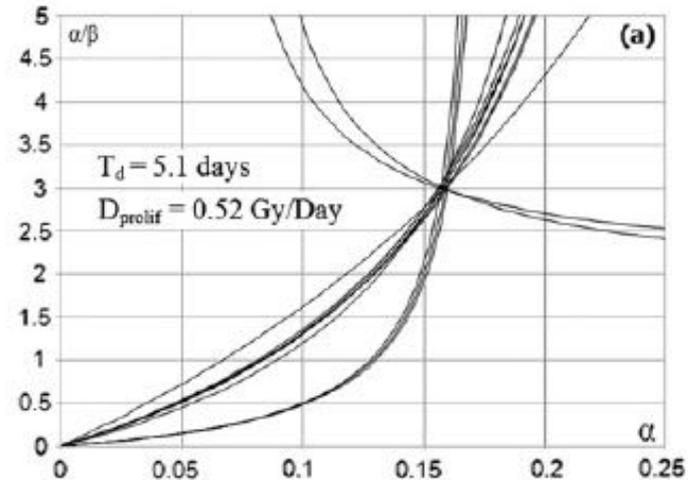
## Estimation of a Self-Consistent Set of Radiobiological Parameters From Hypofractionated Versus Standard Radiation Therapy of Prostate Cancer

Piernicola Pedicini, PhD,\* Lidia Strigari, PhD,<sup>†</sup> and Marcello Benassi, PhD<sup>‡</sup>

**Table 1** Clinical data of the external beam treatment of prostatic cancer (biochemical relapse-free survival) used to estimate the radiobiological parameters and to verify the results

Author (reference)	Study size (n)	Dose/fraction (Gy)	No. fractions	Total dose (Gy)	OTT	ADT	Low-risk	Intern-risk	High-risk	All risks
Data used to estimate the parameters										
Kupelian (7)	189	2.0	39	78	53	No	0.95	0.83	1.00	-
	310	2.5	28	70	38		0.95	0.84	0.64	-
Lukka (8)	470	2.0	33	66	45	No	0.66	0.38	0.28	-
	466	2.62	20	52.4	26		0.59	0.47	0.29	-
Yeoh (9)	109	2.0	32	64	44	No	0.76	0.57	0.42	-
	108	2.75	20	55	26		0.73	0.67	0.64	-
Zelevsky (10)	116	1.8	38	68.4	52	No	-	0.54	-	-
	94	1.8	44	79.2	60		-	0.79	-	-
Arcangeli (11)	85	2.0	40	80	54	Yes	-	-	0.79	-
	83	3.1	20	62	28		-	-	0.85	-
Pollack 1 (12)	150	2.0	35	70	49	No	-	-	-	0.64
	151	2.0	37	78	53		-	-	-	0.74
Pollack 2 (13)	152	2.0	38	76	52	Yes	-	-	-	0.85
	151	2.7	26	70.2	36		-	-	-	0.86
Data used to verify the results										
Miralbell (1)	225	2.0	37	74	49	No	0.87	0.67	0.32	-
	71	4.0	14	56	44		0.90	0.72	0.74	-
Valdagni (14)	179	2.0	37	74	52	Mixed	-	-	-	0.70
	151	1.2	66	79.2	46		-	-	-	0.83

Abbreviations: ADT = androgen deprivation therapy; OTT = overall treatment time.



$$S = e^{-E}, \quad E = D \cdot (\alpha + \beta \cdot d) + \gamma(T - T_k), \quad \text{bRFS} = e^{-N \cdot S}, \quad \ln\left(\frac{\ln \text{bRFS}_a}{\ln \text{bRFS}_b}\right) = \alpha(D_b - D_a) + \beta(d_b D_b - d_a D_a) - \frac{\ln 2}{T_d}(T_b - T_a),$$

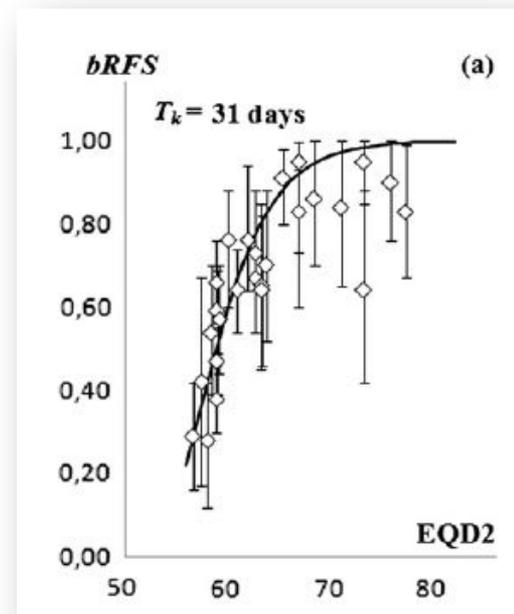
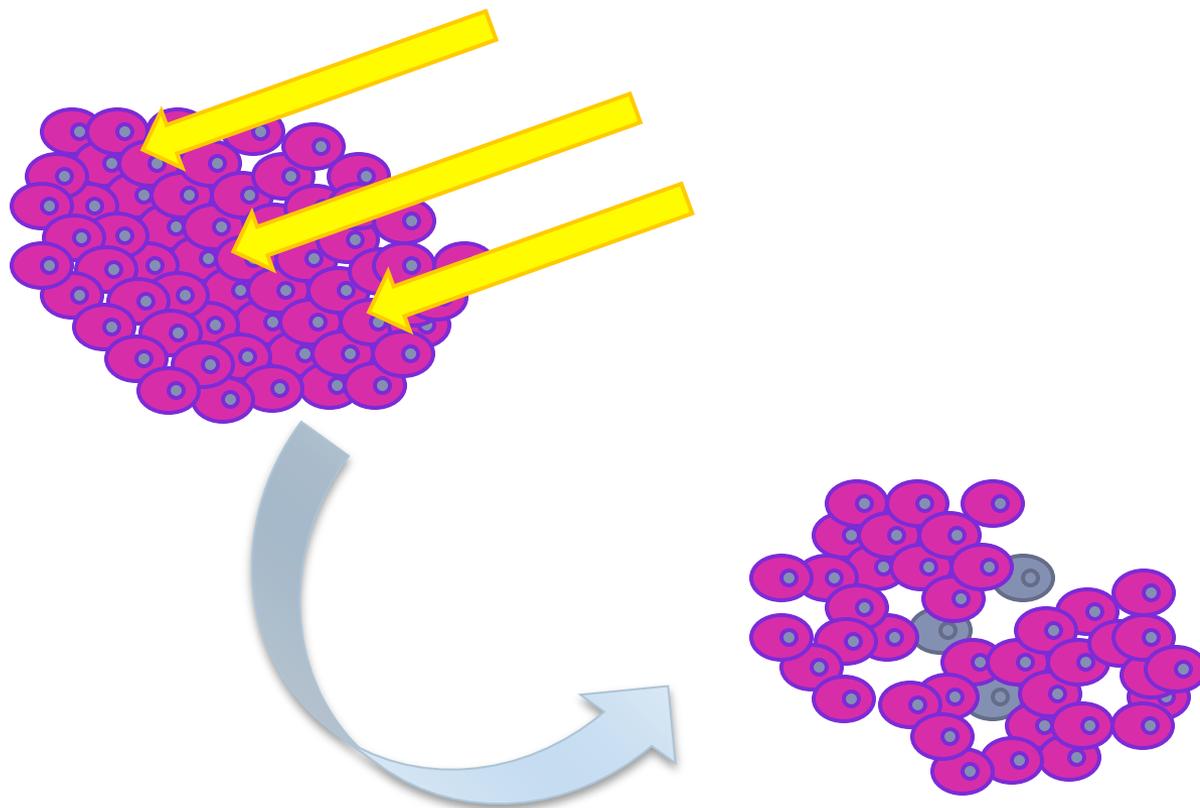


# Brachiterapia vs. EBRT?

## Il dilemma

### And the FUTURE ?

Int J Radiation Oncol Biol Phys, Vol. 85, No. 5, pp. e231–e237, 2013



$T_d = 5.1$  days  
 $D_{prolif} = 0.52$  Gy/Day

**Radiobiologia: Nuove schedule di RT**



# Brachiterapia vs. EBRT? Il dilemma

## And the FUTURE ?

Lancet Oncol 2005; 6: 112-17

### Theragnostic imaging for radiation oncology: dose-painting by numbers

Søren M Bentzen

### Molecular Imaging–Based Dose Painting: A Novel Paradigm for Radiation Therapy Prescription

Søren M. Bentzen, PhD, DSc,<sup>\*,†</sup> and Vincent Gregoire, MD, PhD, FRCR<sup>\*,†</sup>

Semin Radiat Oncol 21:101-110 © 2011

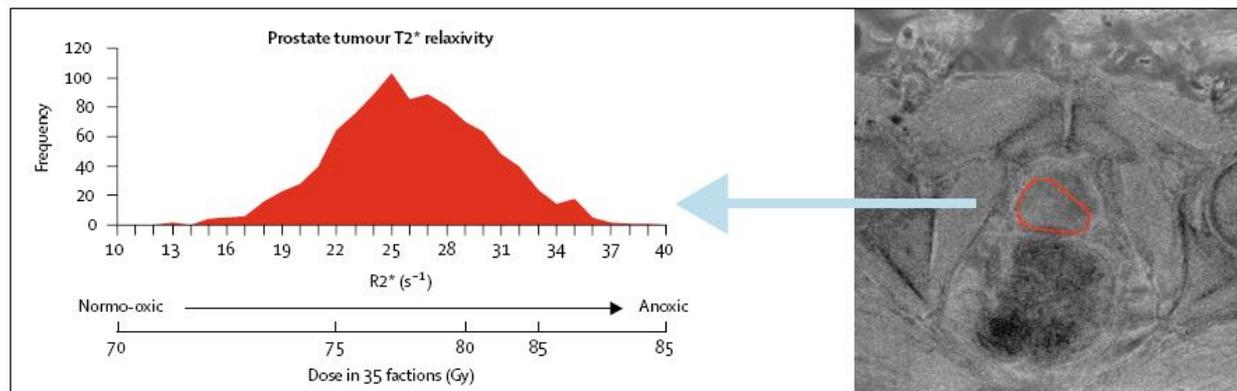
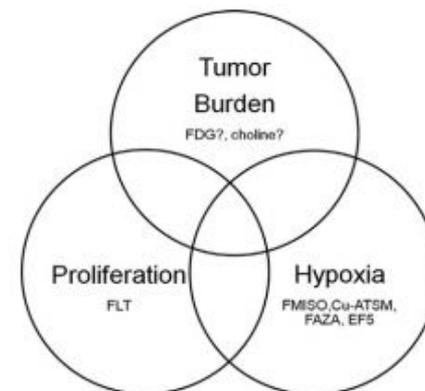


Figure 2: BOLD MR image of a patient with prostate cancer

The region of interest was defined from haematoxylin-eosin staining of the prostate sections and transferred to the MR image. The distribution of  $R2^*$  values in the region of interest covers the range of oxygenation status from normal to anoxic. Dose-painting by numbers involves the prescription of a specific, physically absorbed dose of radiation on a voxel-by-voxel basis according to a defined prescription function as indicated by the non-linear scale below the histogram.



Courtesy of N Taylor, D Camell, and A Padhani, Mount Vernon Hospital, UK



# Brachiterapia vs. EBRT?

## Il dilemma

Thanks for your attentions

