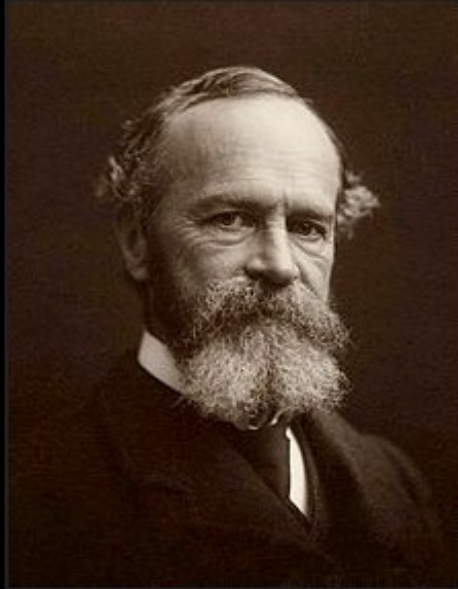


HDR Brachytherapy: Practice for Localized High Risk Prostate Cancer

Nikolaos Zamboglou and Nikolaos Tselis
Strahlenklinik
Klinikum Offenbach - Germany

*Prostate Brachytherapy
UK & Ireland Conference 2013*



It is our attitude at the beginning of a
difficult task which, more than anything else,
will affect its successful outcome.

(William James)

American philosopher and physician (1842 –1910)

The crux of defining high risk patients

Memorial Sloan Kettering criteria

VS

National Comprehensive Cancer Network criteria

VS

D'Amico criteria

High risk prostate cancer meeting criteria by all classification definitions

- **PSA +20**
- **Gleason Score 8-10**
 - **T2c +**

**Standard Therapy with
HDR-Brachytherapy in High Risk:**

HDR-Brachytherapy as Boost to EBRT

Randomized Study

HDR Boost to EBRT vs EBRT



ELSEVIER

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Phase III randomised trial

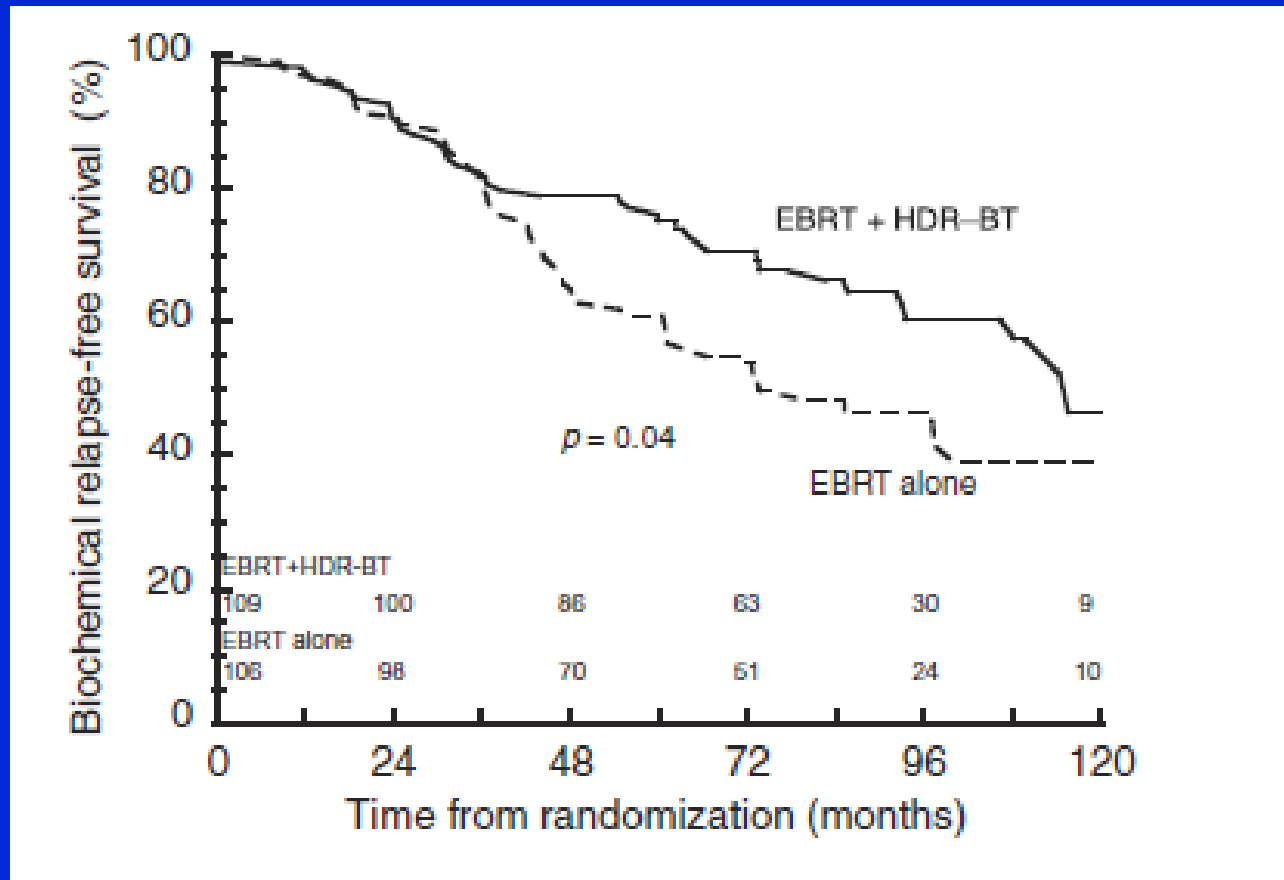
Randomised trial of external beam radiotherapy alone or combined with high-dose-rate brachytherapy boost for localised prostate cancer

Peter J. Hoskin^a, Ana M. Rojas^{a,*}, Peter J. Bownes^b, Gerry J. Lowe^a, Peter J. Ostler^a, Linda Bryant^a

^aCancer Centre, Mount Vernon Hospital, Northwood, UK; ^bSt. James's Institute of Oncology, St. James's University Hospital, Leeds, UK

Risk Group ^a	Low	7 (7)	2 (2)
	Intermediate	43 (40)	48 (44)
	High	56 (53)	60 (54)

EBRT 55 Gy vs 35.75 Gy EBRT plus 2x8.5 Gy HDR-BRT



Phase III randomised trial

High dose rate brachytherapy in combination with external beam radiotherapy in the radical treatment of prostate cancer: initial results of a randomised phase three trial

Peter J. Hoskin*, Kate Motohashi, Peter Bownes, Linda Bryant, Peter Ostler

Mount Vernon Cancer Centre, Northwood, UK

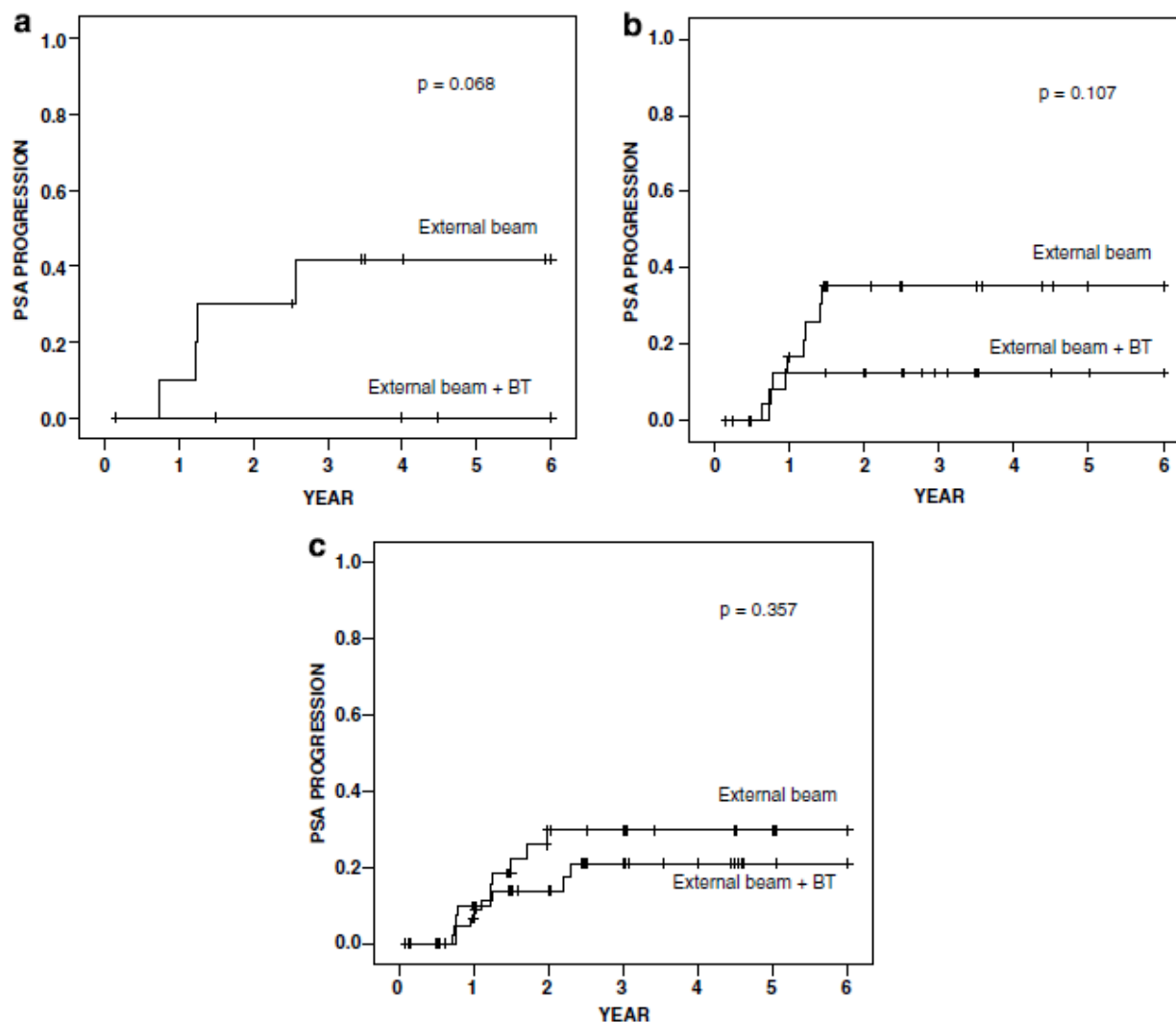


Fig. 3. Biochemical response by risk group. (a) Risk Group 1, PSA <10 ng/ml, Gleason 6 or less and Stage T2b or less. (b) Risk Group 2, neither Group 1 or 3. (c) Group 3, PSA >10 ng/ml, Gleason >6 and Stage T2c or higher.

**HDR Boost to EBRT vs EBRT
in unfavorable prostate cancer**

**Less Failure and Less Toxicity
after Combined Treatment**

HDR Boost to EBRT - Overview

Author	No. of patients	Median FU (months)	bNED (%)	Grade 3 Tox. (%)
Borghede (1997)	50	45	78	8
Galalae (2002)	144	96	73	6
Martinez (2003)	207	56	74	8
Eulau (2000)	104	78	77	N.S.
Pellizzon (2003)	119	41	75	0
Rodriguez (2001)	36	57	92	4
Zamboglou (2006)	543	86	77	5

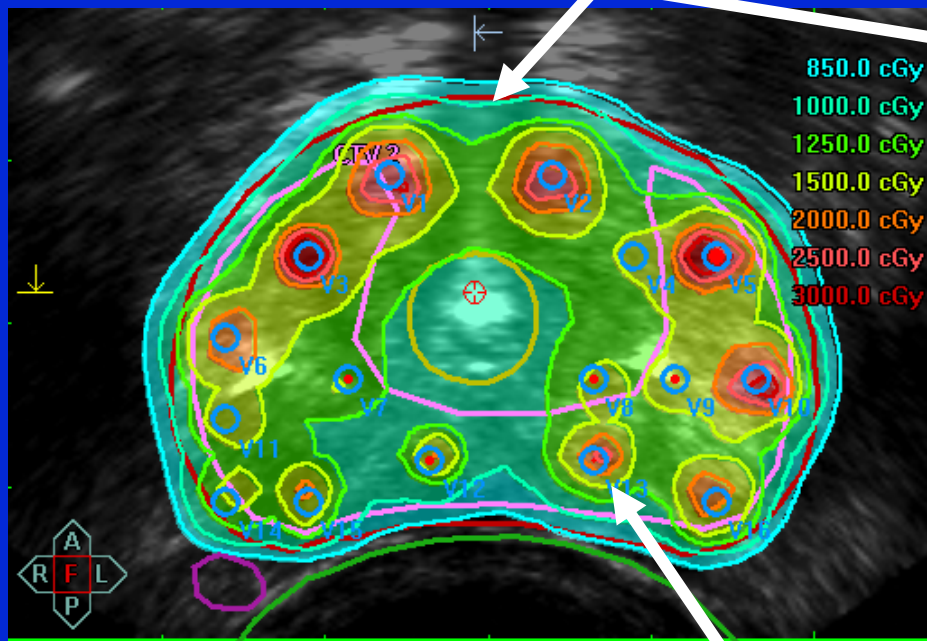
Some more Aspects ...

HDR-Boost to EBRT Studies

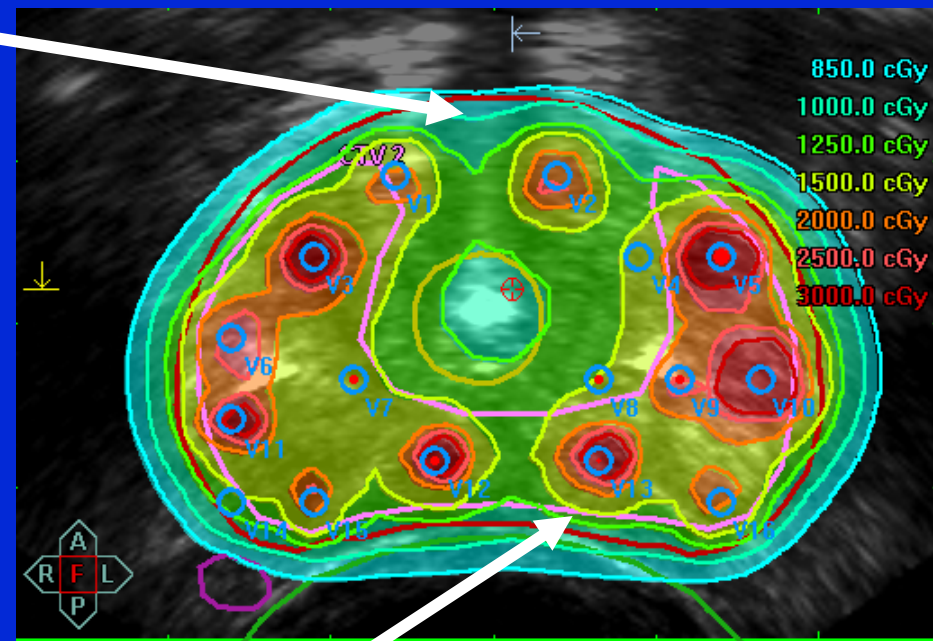
	<u>EBRT</u>	<u>BTfx</u>	<u>Gy/fx</u>	<u>Target</u>	
Borghede et. al.	50	2	15	Tumor volume	CTV3
Dinges et. al.	45	2	10	Prostate capsule	CTV1
Kovács et. al.	40/50	2	15	Peripheral zone	CTV2
Martinez et. al.	45	3	5.5-10.5	Prostate capsule	CTV1
Mate et. al.	50.4	4	3-4	Prostate capsule	CTV1
Offenbach	45	2	10.5	Prostate capsule	CTV1
Offenbach	39.6	4	7	Prostate capsule	CTV1

Dose Specification and Inverse Planning on CTV 1 *versus* CTV 2

CTV 1: 10 Gy



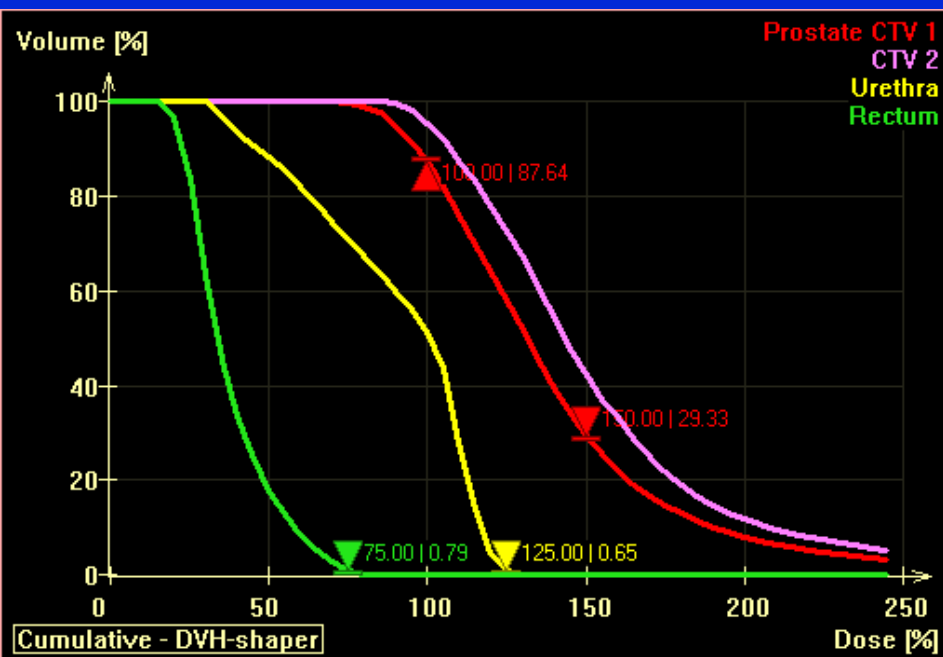
CTV 2: 15 Gy



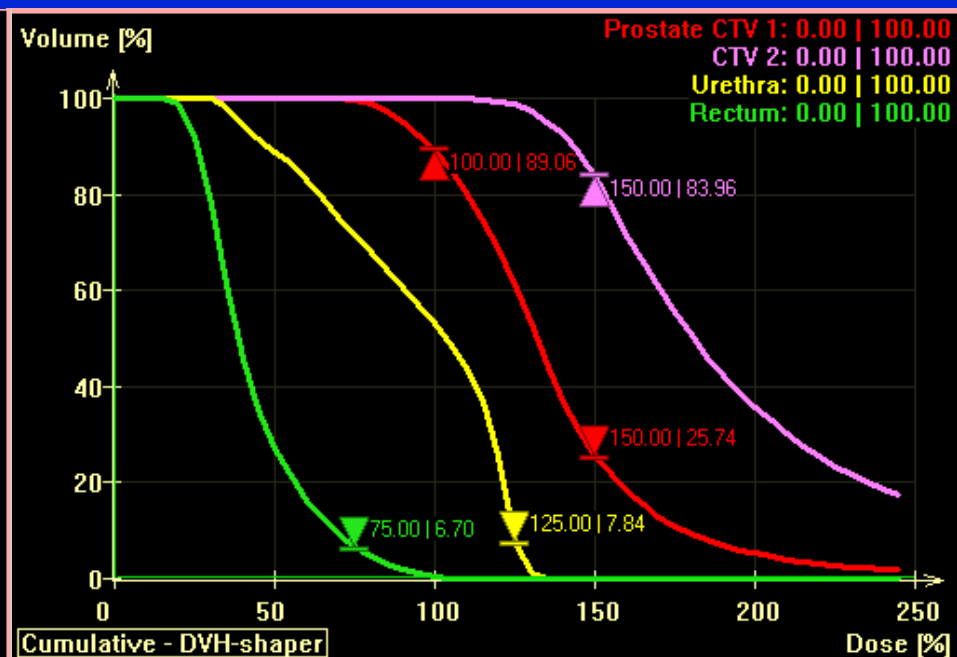
15.0 Gy

Dose Specification and Inverse Planning on CTV 1 *versus* CTV 2

CTV 1: 10 Gy



CTV 2: 15 Gy



HDR Boost to EBRT Protocols

1 fraction per implant:

Dinges:	2 implants (9 Gy per implant)	+ 45 Gy EBRT
Borghede:	2 implants (10 Gy per implant)	+ 50 Gy EBRT
Martinez:	2 implants (11.5 Gy per implant)	+ 46 Gy EBRT
Galalae:	2 implants (15 Gy per implant)	+ 50 Gy EBRT
Offenbach:	4 implants (7 Gy per implant)	+ 39.6 Gy EBRT
	2 implants (10.5 Gy per Implant)	+ 45.0 Gy EBRT

HDR Boost to EBRT Protocols

Multiple fractions per implant:

Rodriguez: 2 implants (2 x 6 Gy per implant) + 36 Gy EBRT

Pellizzon: 2 implants (2 x 6 Gy per implant) + 45 Gy EBRT

Linares: 1 implant (4 x 5.5 Gy per implant) + 45 Gy EBRT

Mate: 1 implant (3 x 6 Gy per implant) + 45 Gy EBRT

HDR Boost to EBRT Protocols - Summary

No. of implants:	1 - 4
No. of fractions per implant:	1 - 4
HDR dose per fraction:	5.5 – 15 Gy
HDR total dose:	18 – 30 Gy
Scheme:	HDR before/after/during EBRT
EBRT total dose:	36-50 Gy
	IMRT- 3D conformal
	(with/without pelvic LN)
BRT Dose Specification:	CTV 1 / CTV 2 / CTV 3
BED of HDR + EBRT:	78 – 163 Gy

HDR Boost to EBRT

simplex sigillum veri **Role of BED**

BED OF EBRT+HDR BOOST

	DOSE LEVEL	# PTS	MEAN FU YEARS	$\alpha/\beta = 10$	BED* - Gy $\alpha/\beta = 1.2$
low	5.50 Gy x 3	19	10.4	67.1	80.2
	6.00 Gy x 3	15	10.	70.0	86.1
	6.50 Gy x 3	35	8.2	72.6	92.5
	8.25 Gy x 2	36	73	72.0	94.2
high	8.75 Gy x 2	25	6.1	74.2	99.9
	9.50 Gy x 2	38	5.9	78.0	108.9
	10.50 Gy x 2	86	5.1	82.9	122.0
	11.50 Gy x 2	69	3.9	87.0	136.3

* BIOLOGICAL EQUIVALENT DOSE TO EXTERNAL BEAM

Courtesy Alvaro Martinez

5-year outcome by BED-dose group (n=197)

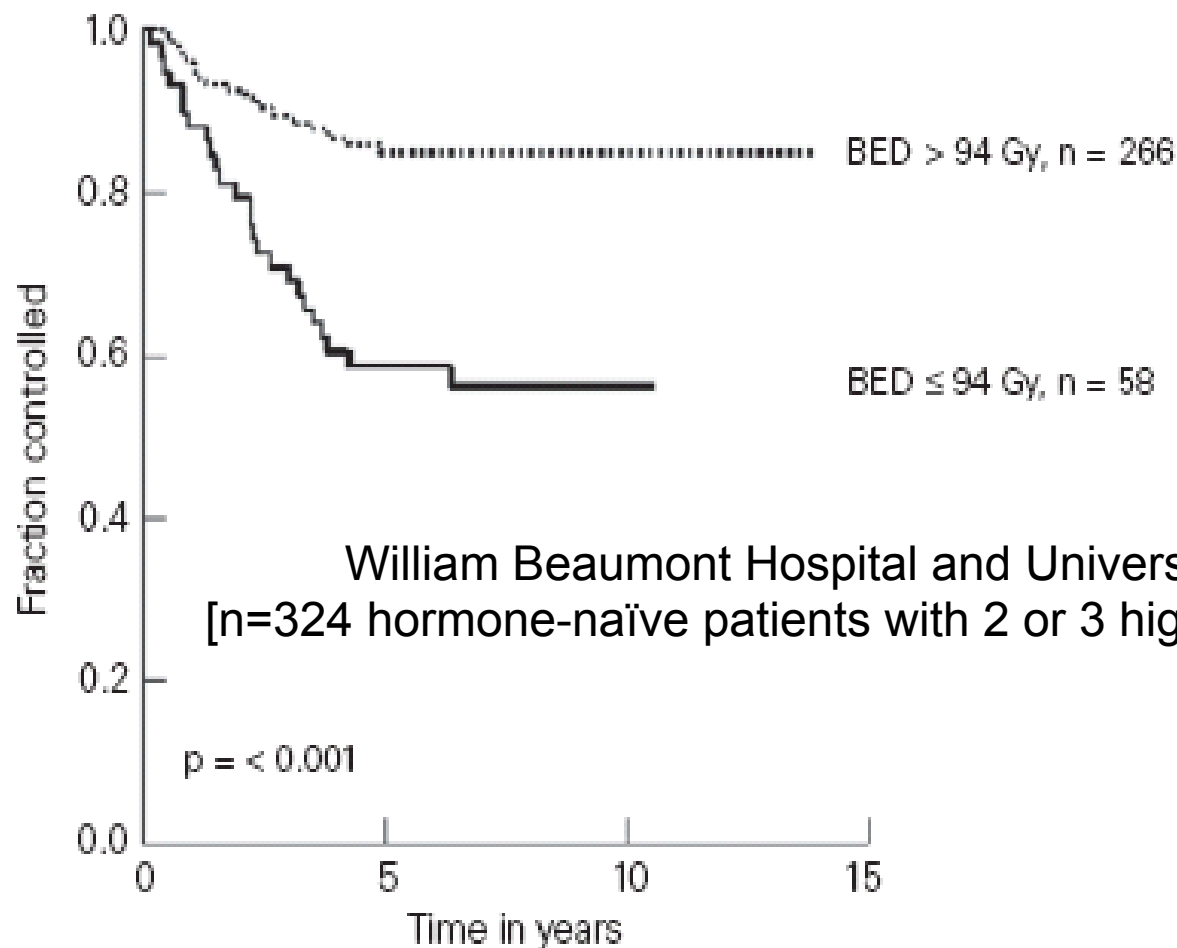
Dose Group	n	Biochemical Control (ASTRO)	Local failure	Distant metastasis	Clinical Failure	Clinical DFS	CSS	OS
Low dose	67	68.7%	8.6%	9.1%	15.6%	75.5%	95.4%	86.2%
High dose	130	90.0%	3.5%	2.7%	6.1%	91.7%	100%	97.8%
p-value		0.001	0.3	0.05	0.04	0.003	0.02	0.002
All cases	197	81.4%	4.8%	5%	9.8%	84.8%	98.3%	92.9%

Courtesy Alvaro Martinez

Effectiveness of HDR-Boost

- Cumulative BED at least 100 Gy D_2
- HDR-BRT component of BED at least 60%

BED common denominator in HDR+EBRT regimes



Offenbach protocol for High Risk **HDR Boost to EBRT**

- PTV = CTV 1 (in cT3: CTV 1+ 5.0 mm)
- BRT Boost: 2 x 10.5 Gy = 21.0 Gy upfront
- EBRT of Prostate+SV = 45.0 Gy after BRT
- Androgen deprivation for 9 months

Offenbach protocol for High Risk

Dose characteristics

α/β of 1.2 Gy: EQD2 = 119 Gy

BED=317 Gy (65 % by BRT Boost)

α/β of 1.5 Gy : EQD2 = 108 Gy

BED=267 Gy (63 % by BRT Boost)

α/β of 2.0 Gy : EQD2 = 114 Gy

BED=216 Gy (61 % by BRT Boost)

..... **Role of BED**

concordia cum veritate 100 % of BED by BRT
.... HDR-Monotherapy

2002-2009: 718 consecutive patients with localized prostate cancer

Transperineal Implantation under TRUS-guidance

2002-2004 (A): 1 Implant (4 x 9.5 Gy)	CT- Plan (n=141)
2004-2008 (B): 2 Implants (2 x 9.5 Gy/Implant)	TRUS-Plan (n=351)
2008-2009 (C): 3 Implants of 11,5 Gy	TRUS-Plan (n=226)

	Group A (n = 141)	Group B (n = 351)	Group C (n = 226)
Median follow-up (months)	91.9 (45.5.-113.4)	59.3 (16.5-82.6)	25.4 (5.8-35.5)
Median Gland volume (cc)	40 (20-90)	39 (16-107)	36 (11-90)
Risk group (MSKCC) Low Intermediate High	Low risk: n= 395 (55 %) Intermediate: n= 177 (25 %) High risk: n= 146 (20 %)		

High risk with temporary hormonal therapy 87 (60 %)
High risk without temporary hormonal therapy 59 (40 %)

