Current status of HDR Brachytherapy for prostate cancer (in the UK)

Paul Evans Memorial lecture

Peter Hoskin
Mount Vernon Cancer Centre

ELSEVIER

Brachytherapy 11 (2012) 20–32

BRACHYTHERAPY

American Brachytherapy Society consensus guidelines for high-dose-rate prostate brachytherapy

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ABSTRACT **PURPOSE:** A well-established body of literature supports the use of high-dose-rate (HDR) brachytherapy as definitive treatment for localized prostate cancer. Most of the articles describe HDR as a boost with adjuvant external beam radiation, but there is a growing experience with HDR monotherapy.

Healthcare Improvement Scotland

evidence | note

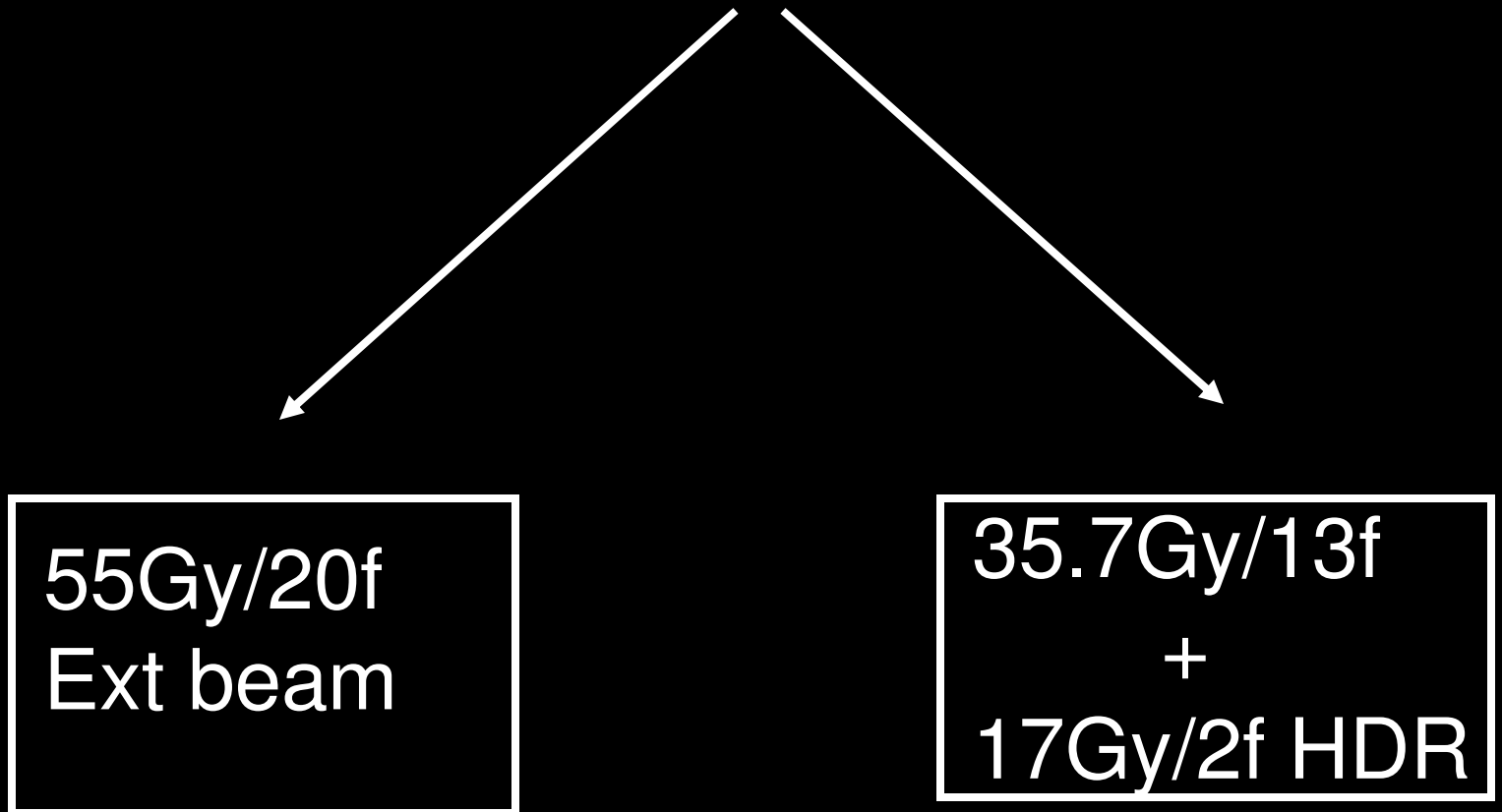
In response to an enquiry from the Scottish Radiotherapy Advisory Group | Number 37 June 2011

The clinical and cost effectiveness of the use of brachytherapy to treat localised prostate cancer

Key points

- Evidence from low-level observational studies suggests that high dose rate (HDR) brachytherapy in combination with EBRT may improve outcomes in patients with localised prostate cancer. Two randomised trials support this conclusion, although it should be noted that in both of these the dose of EBRT used in the control arm was relatively low.

MVH RCT



Closed 08/05: 220 patients randomised

HDR implant: biological advantage

	α/β 1.5	α/β 3.5	α/β 10
• Ext beam			
74Gy/40f	165.2	113.1	87.7
55Gy/20f	155.8	98.2	70.1
• HDR Boost after 35.7Gy/13f			
17Gy/2f	214.5	122.0	77.0

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

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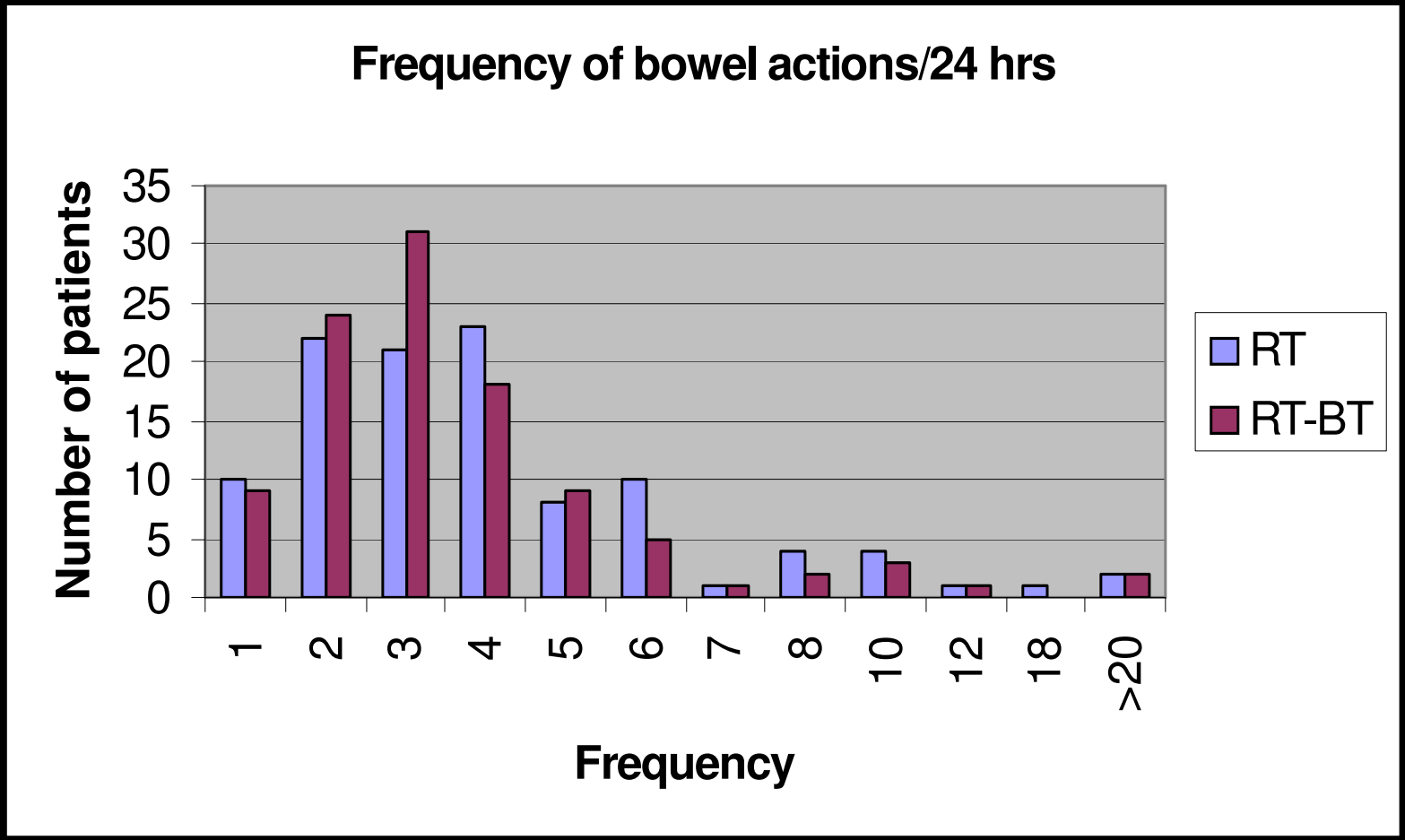
Radiotherapy and Oncology xxx (2012) xxx–xxx

Demographic details of patients given external beam radiotherapy alone (arm 1) or with a boost of high-dose-rate brachytherapy (arm 2).

Variable	Category	Arm 1 (n = 106) n (%)	Arm 2 (n = 110) n (%)
Age	Median	70	70
	Range	47–80	47–80
Follow-up time (months)	Median	85	85
	Mean	88	86
	Range	9–147	8–144
T stage	T_1	27 (25)	29 (26)
	T_2	55 (52)	47 (43)
	T_3	24 (23)	34 (31)
Gleason	<7	48 (45)	46 (42)
	7	40 (38)	44 (40)
	⩾8	18 (17)	20 (18)
PSA (μg/l)	<10	36 (34)	35 (32)
	10–20	43 (41)	45 (41)
	>20	27 (25)	30 (27)
Risk Group[a]	Low	7 (7)	2 (2)
	Intermediate	43 (40)	48 (44)
	High	56 (53)	60 (54)
ADT	No	26 (25)	25 (23)
	Yes	80 (75)	85 (77)
ADT (duration)			
6 months	Low	2 (29)	1 (50)
6 months	Intermediate	26 (60)	29 (60)
⩽3 years	High	52 (93)	55 (92)

Median follow up 7 yrs

Acute toxicity: bowel frequency



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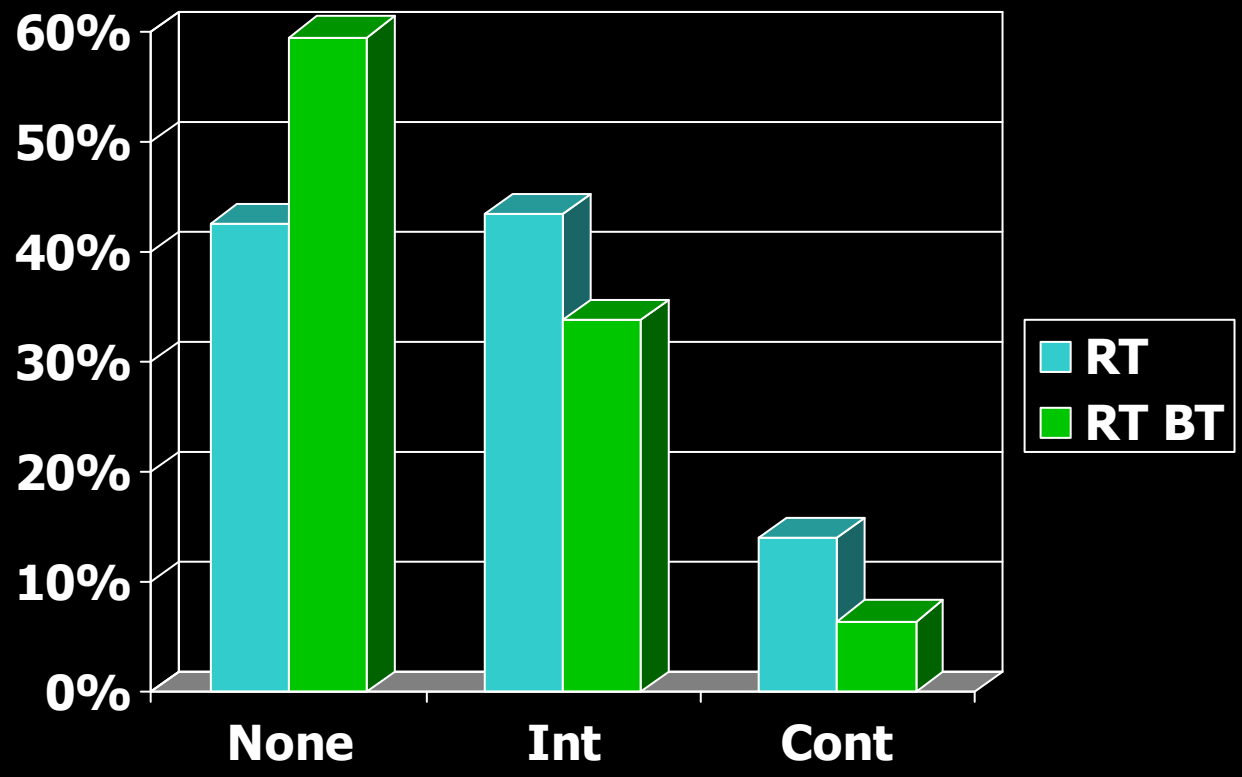
Acute toxicity: rectal discharge



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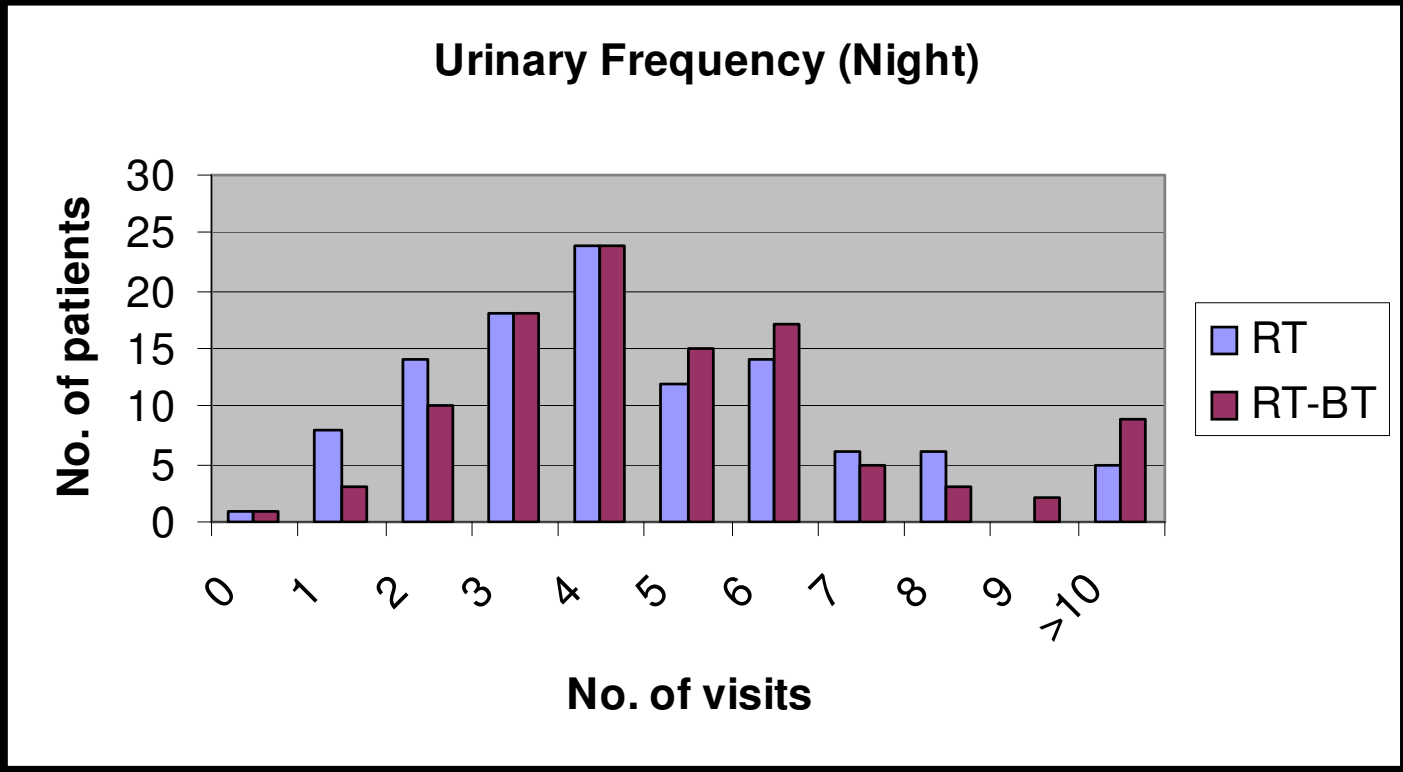
Acute toxicity: urinary frequency



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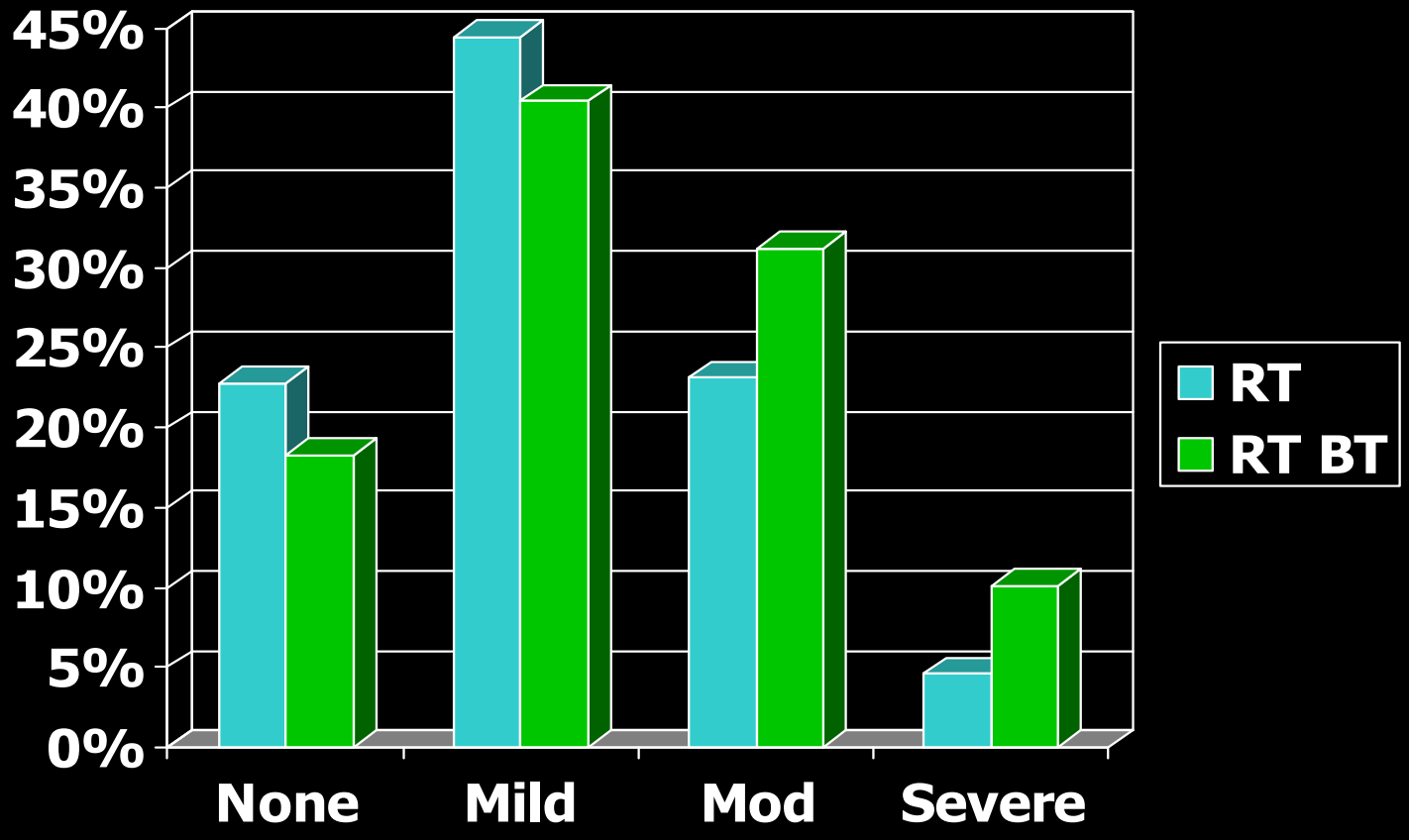
Acute toxicity:dysuria



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Current issues in HDR prostate brachytherapy

- Optimal dose for boost
- Relative efficacy vs modern high dose IMRT

- Role of monotherapy
- Optimal dose for monotherapy
- Monotherapy as focal treatment

- HDR salvage

Current dose fractionation schedules

Institution	Dose fractionation	Bladder	Urethra	Rectum
MSKCC	Boost 7Gyx3 Mono 9.5Gyx4 Salvage 8Gyx4		<120% prescription	$D_{2\ cc} < 70\%$
UCSF	Boost 15Gyx1 Mono 10.5Gyx3 Salvage 8Gyx4*	$V_{75} < 1$ cc	$V_{125} < 1$ cc, $V_{150} = 0$ cc *(dose tunnel whenever possible)	$V_{75} < 1$ cc
WBH	Boost 10.5Gyx2 Mono 4 × 9.5 Gy (historical) 12–13.5Gyx2 (current) Salvage 7Gyx4 combined with hyperthermia	No constraint (intra-op TRUS-based dosi)	$V_{100} < 90\%$ of prescription $V_{115} < 1\%$ of prescription	$V_{75} < 1\%$ of prescription
TCC	Boost 6Gyx2 ×2 implants	<80% of Rx	<125% of prescription	<80% of Rx to outer wall
GW	Boost 6.5Gyx3 Mono two sessions of 6.5Gyx3	<100% prescription	<110% prescription	mucosa <60%, outer wall <100%
Toronto	Boost 15Gyx1	n/a	$D_{10} < 118\%$ Max < 125%	$V_{80} < 0.5$ cc
UCLA-CET	Boost 6Gyx4 Mono7.25Gyx6	90–100% wall 80% balloon	120% combo 105% any TUR 110% mono	Rectal wall 80% Rectal wall 80–85%

Grade 3 late GU complications

Author	*N*	Followup (mo)	Dose	Type of treatment	Comments
Astrom (60)	214	48	10Gyx2	Boost	13 patients experienced urethral strictures
Demanes (17)	209	86	5.5 Gy−6.0Gyx4	Boost	6.7% late Grade 3 and 1% Grade 4 GU toxicity (TUR related)
Hsu (7)	112	30	9.5Gyx2	Boost	Less than 3% Grade 3 toxicity at 18 mo
Phan (49)	309	59	6Gyx4	Boost	4% late Grade 3 GU
Deger (50)	442	60	9−10 Gyx2	Boost	9% late Grade 3 GU toxicity
Martinez (77)	207	66	5.5−11Gyx2	Boost	8% late Grade 3 GU toxicity
Sullivan (52)	425	41	4−5Gyx46.5 Gyx3	Boost	8% late Grade 3 GU toxicity
Zwahlen (73)	587	66	5Gyx4−6Gyx3	Boost	7% late Grade 3 GU toxicity
Demanes (57)	298	62	7Gyx6 9.5Gyx4	Mono	3% late Grade 3 GU toxicity
Ghilizan (51)	173	17	12−13.5Gyx2	Mono	1% late GU Grade 3 toxicity
Hoskin (78)	197	37	8.5Gyx4 9Gyx4 10.5Gyx3 13Gyx2	Mono	3−7% strictures

SINGLE-FRACTION HIGH-DOSE-RATE BRACHYTHERAPY AND HYPOFRACTIONATED EXTERNAL BEAM RADIOTHERAPY FOR MEN WITH INTERMEDIATE-RISK PROSTATE CANCER: ANALYSIS OF SHORT- AND MEDIUM-TERM TOXICITY AND QUALITY OF LIFE

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IJROB 2009

HEALTH-RELATED QUALITY OF LIFE AFTER SINGLE-FRACTION HIGH-DOSE-RATE BRACHYTHERAPY AND HYPOFRACTIONATED EXTERNAL BEAM RADIOTHERAPY FOR PROSTATE CANCER

Gerard C. Morton, M.B., F.R.C.P.C.,* D. Andrew Loblaw, M.D., M.Sc., F.R.C.P.C.,* Hans Chung, M.D., F.R.C.P.C.,* Gail Tsang, M.D., F.R.A.N.Z.C.R.,† Raxa Sankreacha, M.Sc.,‡ Andrea Deabreu,§ Liying Zhang, Ph.D.,§ Alexandre Mamedov,§ Patrick Cheung, M.D., F.R.C.P.C.,* Deidre Batchelar, Ph.D.,‡ Cyril Danjoux, M.D., F.R.C.P.C.,* and Ewa Szumacher, M.D., M.Ed., F.R.C.P.C.*

IJROB 2011

Brachytherapy

Is single fraction 15 Gy the preferred high dose-rate brachytherapy boost dose for prostate cancer?

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RT & O 2011

UK national protocol for high dose rate brachytherapy boost in prostate cancer

- Christie Hospital
- Exeter
- Lincoln
- Mount Vernon
- Northampton
- Southend
- St James Leeds

HDR single dose boost study

Small volume	Pelvic nodes
35.7Gy in 15 fractions	46Gy in 23 fractions IMRT Boost 50.4Gy in 23 fractions
HDR 15Gy: D90 ≥ 15Gy V100 >95%	HDR 15Gy: D90 ≥ 15Gy V100 >95%
91.4Gy EQD2	96Gy EQD2

HDR single dose boost study

- Urethral tolerance

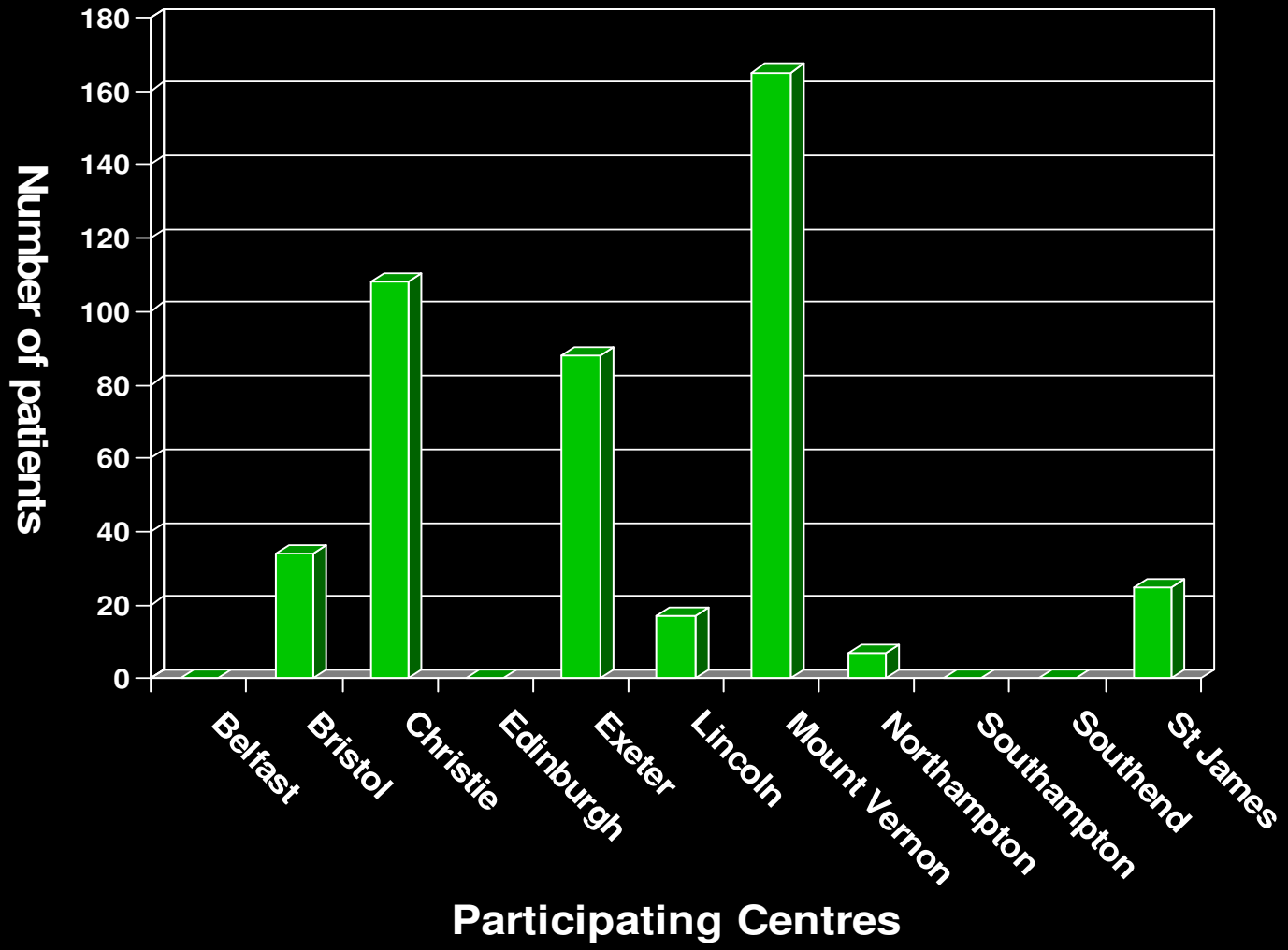
D10	<17.5Gy
D30	<16.5Gy
D150	zero

- Rectal tolerance

D2cc	<12Gy
EQD2 $\alpha\beta$3.5 = 74.7Gy	
V100	<15Gy

Recruitment to Date

Total number = 444



Age Distribution

	Range	Median
• Bristol	53 – 82	67
• Christie	55 – 79	68
• Exeter	56 – 78	69
• Lincoln	52 – 78	68
• Mount Vernon	48 – 81	70
• Northampton	58 – 71	65
• St James	52 – 78	68

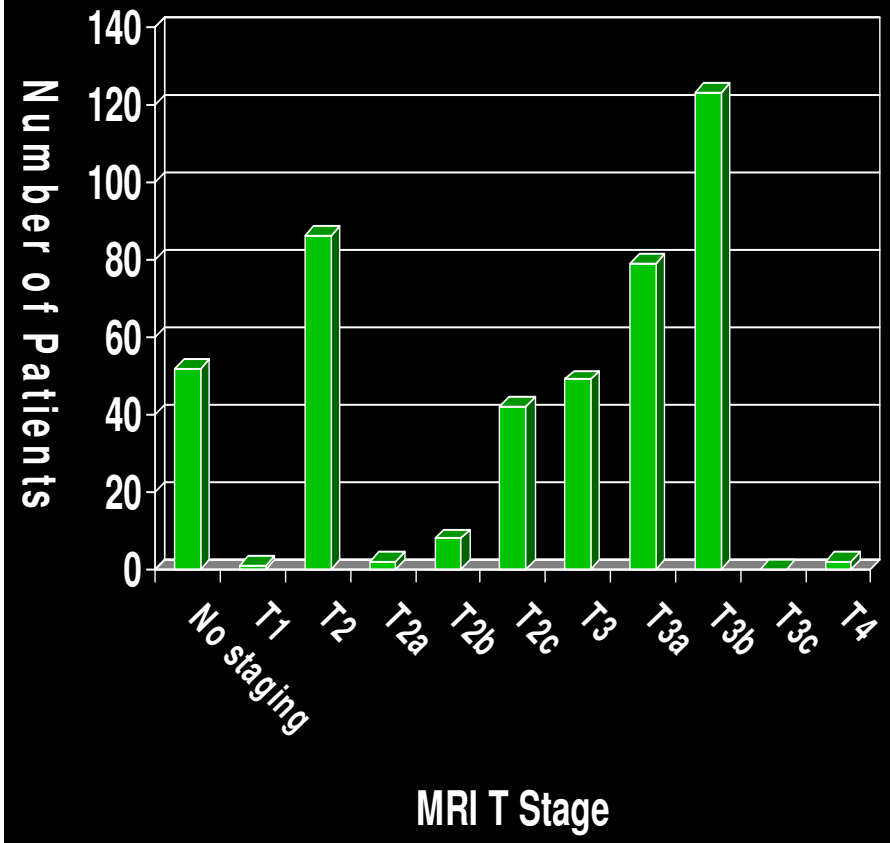
PSA at presentation

	Range	Median
• Bristol	4.60 – 113.00	19.40
• Christie	3.40 – 102.00	17.30
• Exeter	2.30 – 188.00	19.00
• Lincoln	5.80 – 99.00	19.60
• Mount Vernon	4.10 – 240.00	19.20
• Northampton	5.30 - 16.00	12.05
• St James	3.90 – 108.00	10.60

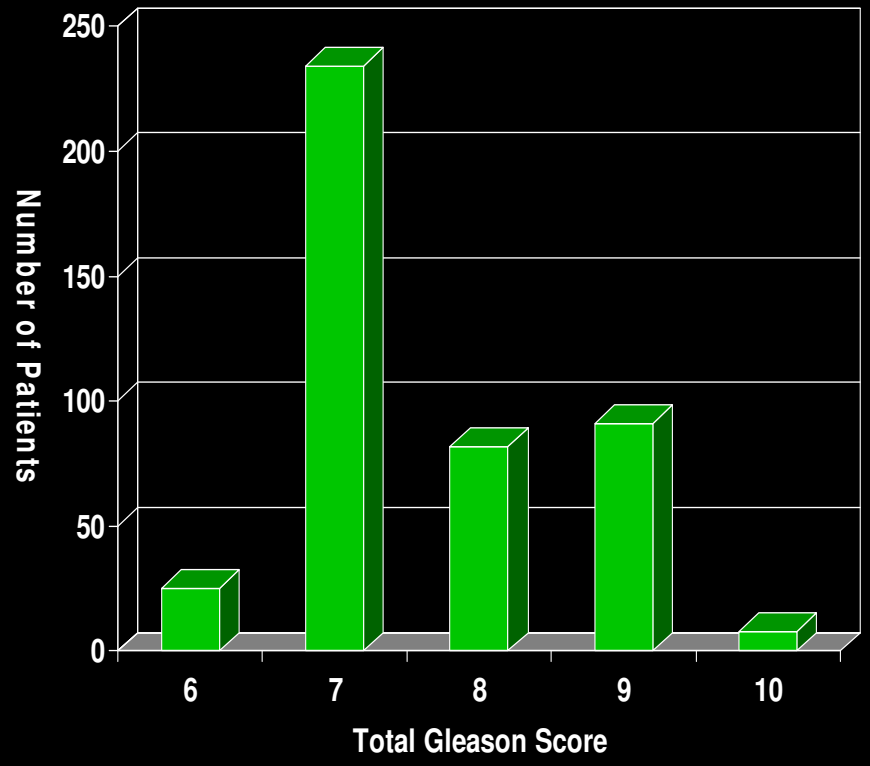
PSA at RT

	Range	Median	Data Recorded
• Bristol	0.10 - 6.10	0.60	All patients
• Christie			No Data
• Exeter	0.10 - 82.0	4.60	19/88
• Lincoln	0.20 - 23.8	0.80	All
• Mount Vernon	0.10 - 22.0	0.40	132/165
• Northampton	5.30 - 16.0	12.05	All
• St James	0.60 -131.0	3.90	7/25

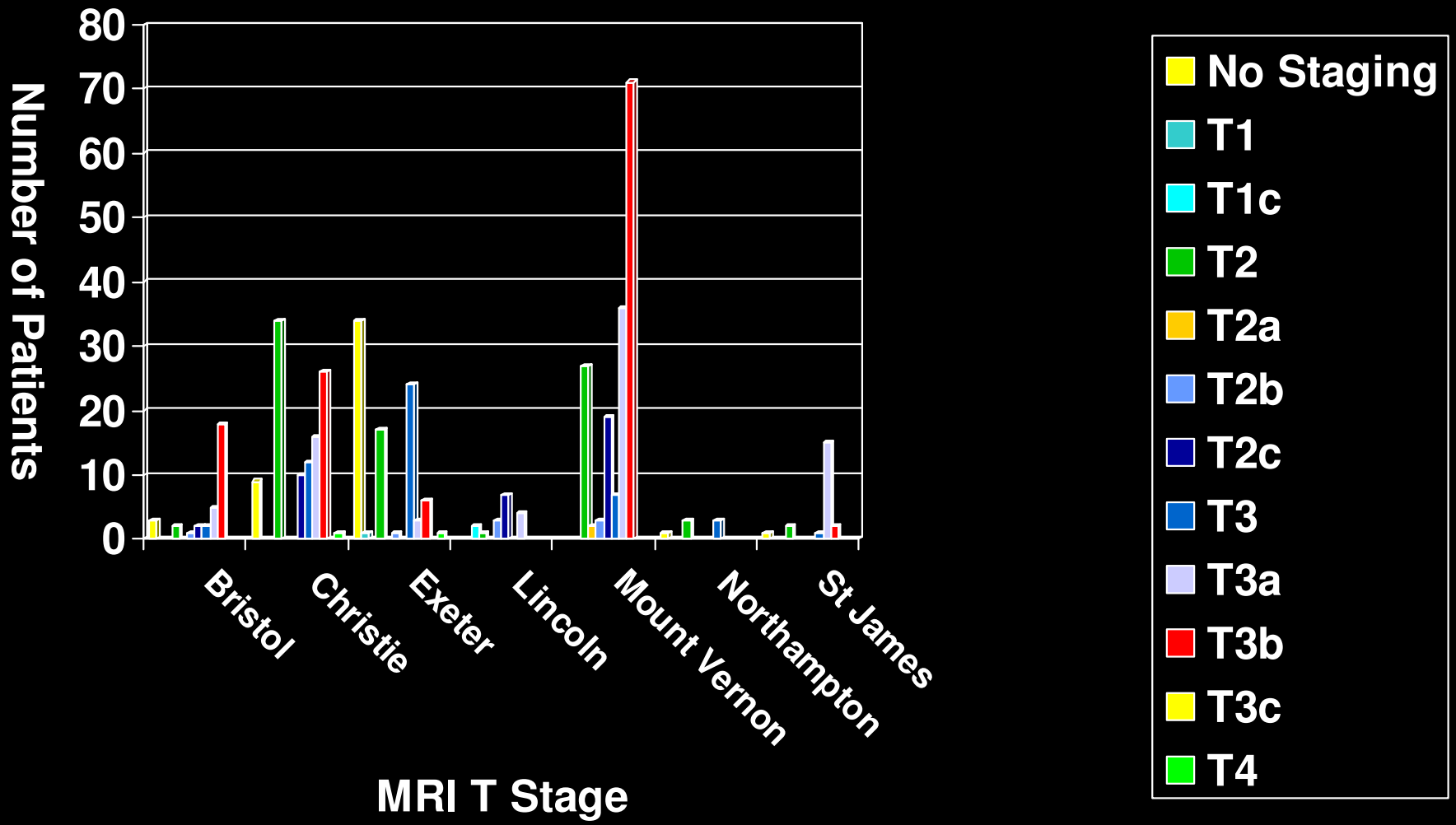
T Stage



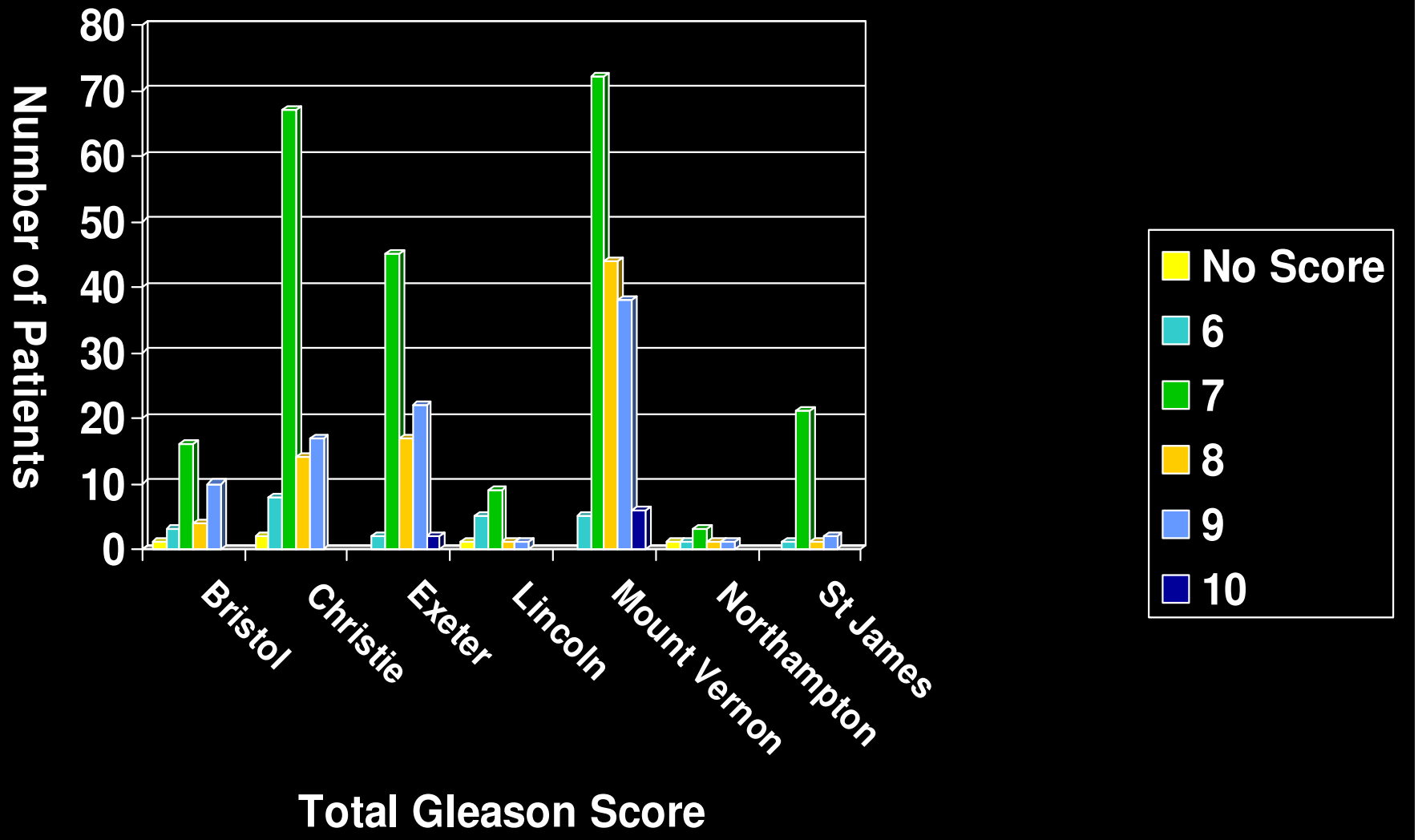
Gleason



MRI T Stage by Centre



Total Gleason Score by Centre



Dose by centre

Centre	37.5Gy	46Gy	Other	No Data
Bristol		33		1
Christie	63			45
Exeter	42	4	2	40
Lincoln	16	1		
Mount Vernon	1	149	3	12
Northampton	4			2
St James	25			
Total	**151**	**187**	**5**	**100**

PTV dose delivered

- D90: ≥15Gy = 391
  Treated outside protocol ≤ 15Gy = 24
  No Data = 53

- V100: ≥95% = 255
  Treated outside protocol ≤95% =130
  No Data = 59

Dose Tolerances

- Rectum D2cc <12Gy = 283
  Median = 46.1Gy
  No Data = 161

- Urethra D10 <17.5Gy = 384
  Treated outside protocol >17.5Gy = 2
  No Data = 58

- Urethra D30 <16.5Gy = 257
  Treated outside protocol >16.5Gy = 129
  No Data = 58

Current issues in HDR prostate brachytherapy

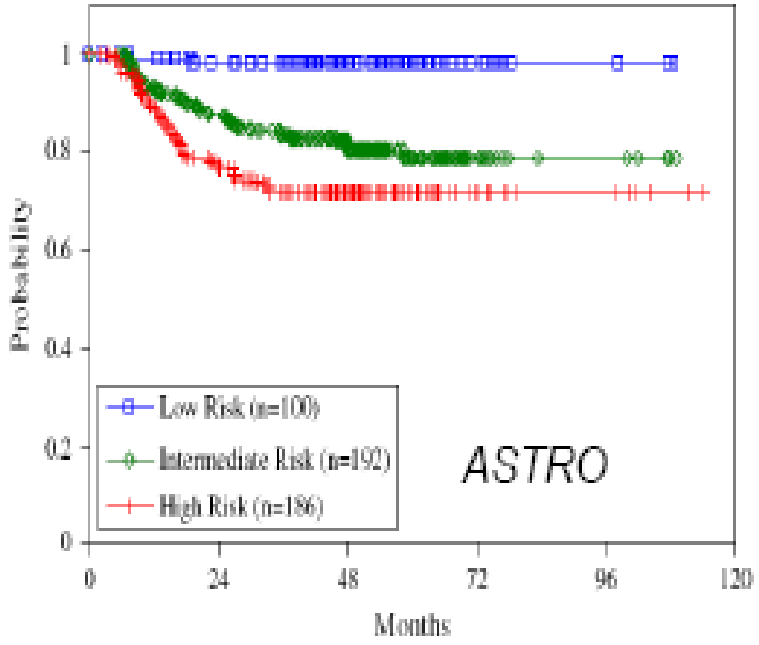
- Optimal dose for boost
- Relative efficacy vs modern high dose IMRT

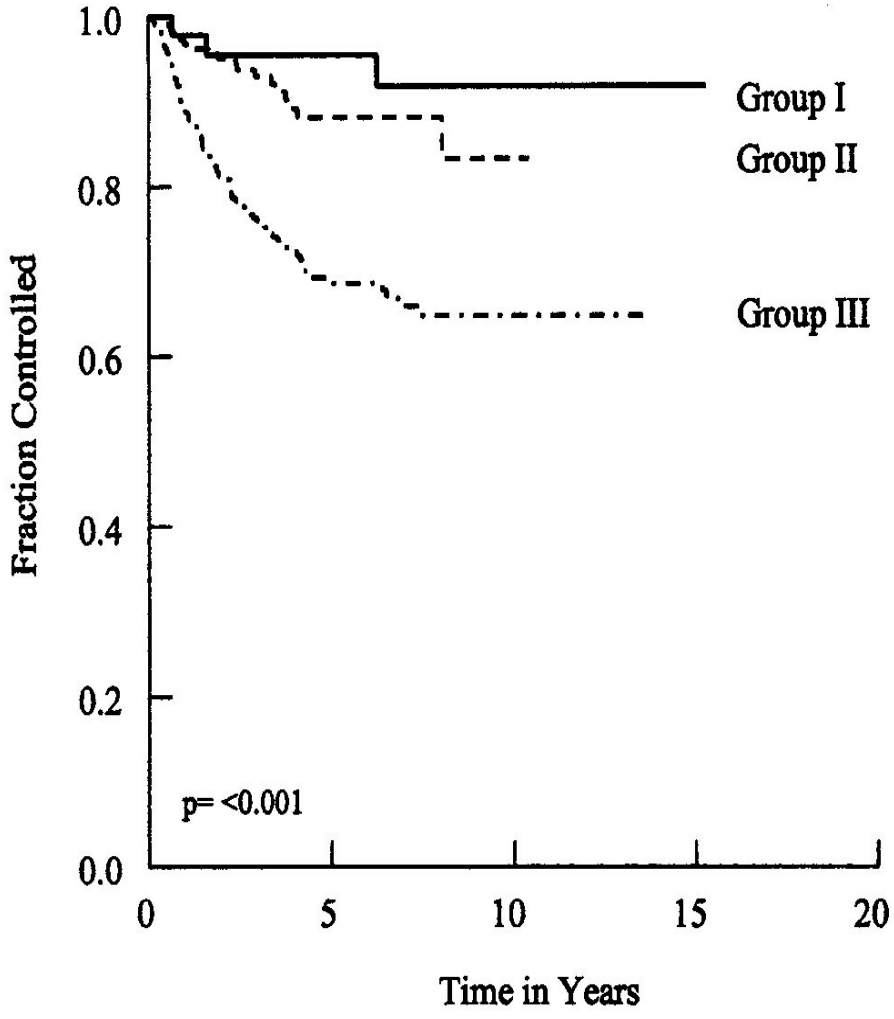
- Role of monotherapy
- Optimal dose for monotherapy
- Monotherapy as focal treatment

- HDR salvage

Long term outcome of prostate HDR boost brachytherapy
Kiel: Michigan: Seattle [Galalae et al 2004] n=611

Zelefsky IMRT





Comparison of PSA relapse-free survival in patients treated with ultra-high-dose IMRT versus combination HDR brachytherapy and IMRT

Israel Deutsch[1], Michael J. Zelefsky[1], Zhigang Zhang[2], Qianxing Mo[2], Marco Zaider[3], Gil'ad Cohen[3], Oren Cahlon[1], Yoshiya Yamada[1,*]

[1]*Department of Radiation Oncology, Memorial Sloan-Kettering Cancer Center New York, New York, NY*
[2]*Department of Biostatistics, Memorial Sloan-Kettering Cancer Center New York, New York, NY*
[3]*Department of Medical Physics, Memorial Sloan-Kettering Cancer Center New York, New York, NY*

Brachytherapy 2010

160 patients: HDR 3 x 5.5-7Gy + 50.4Gy XRT
470 patients: IMRT 86.4Gy

	IMRT	HDR
Low risk	21%	14%
Inter risk	40%	71%
High risk	39%	15%

Comparison of PSA relapse-free survival in patients treated with ultra-high-dose IMRT versus combination HDR brachytherapy and IMRT

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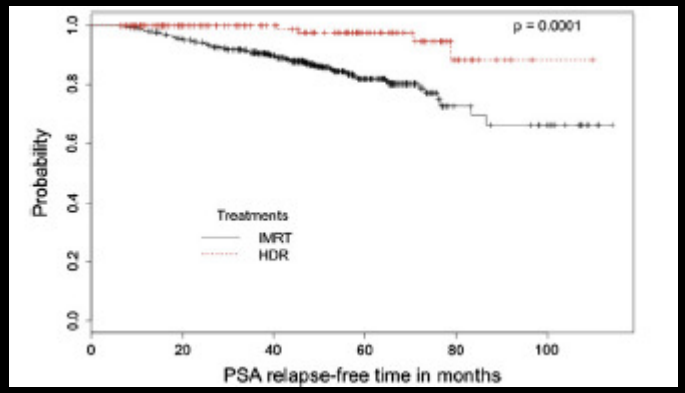
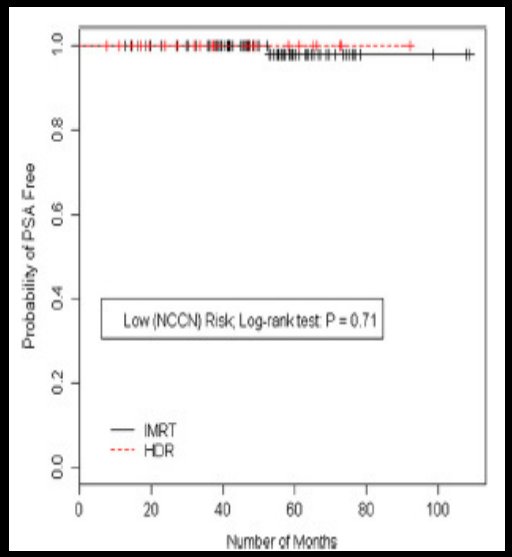
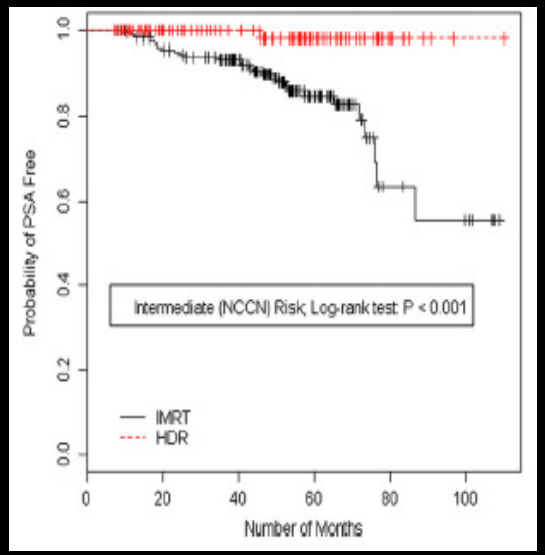
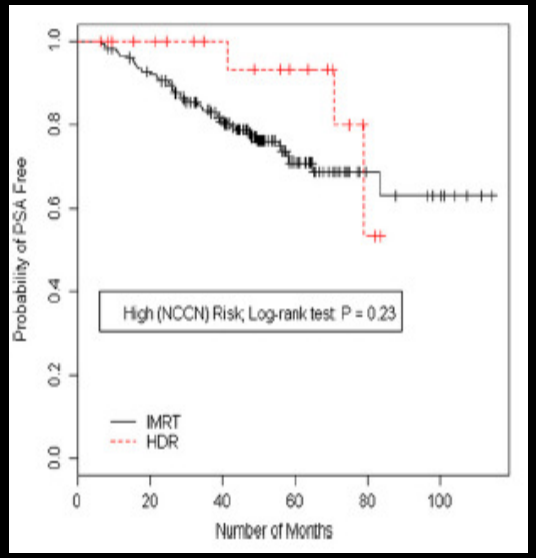
Brachytherapy 2010









Where is the next RCT????

Current issues in HDR prostate brachytherapy

- Optimal dose for boost
- Relative efficacy vs modern high dose IMRT

- Role of monotherapy
- Optimal dose for monotherapy
- Monotherapy as focal treatment

- HDR salvage

Current dose fractionation schedules

Institution	Dose fractionation	Bladder	Urethra	Rectum
MSKCC	Boost 7Gyx3		<120% prescription	$D_{2\ cc} < 70\%$
→	Mono 9.5Gyx4			
	Salvage 8Gyx4			
UCSF	Boost 15Gyx1	$V_{75} < 1$ cc	$V_{125} < 1$ cc, $V_{150} = 0$ cc	$V_{75} < 1$ cc
→	Mono 10.5Gyx3			
	Salvage 8Gyx4*		*(dose tunnel whenever possible)	
WBH	Boost 10.5Gyx2	No constraint	$V_{100} < 90\%$ of prescription	$V_{75} < 1\%$ of prescription
→	Mono 4 × 9.5 Gy (historical)	(intra-op TRUS-based dosi)	$V_{115} < 1\%$ of prescription	
	12–13.5Gyx2 (current)			
	Salvage 7Gyx4 combined with hyperthermia			
TCC	Boost 6Gyx2	<80% of Rx	<125% of prescription	<80% of Rx to outer wall
	×2 implants			
GW	Boost 6.5Gyx3	<100% prescription	<110% prescription	mucosa <60%, outer wall <100%
→	Mono two sessions of 6.5Gyx3			
Toronto	Boost 15Gyx1	n/a	$D_{10} < 118\%$	$V_{80} < 0.5$ cc
			Max < 125%	
UCLA-CET	Boost 6Gyx4	90–100% wall	120% combo	Rectal wall 80%
→	Mono7.25Gyx6	80% balloon	105% any TUR	Rectal wall 80–85%
			110% mono	

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Results of HDR: monotherapy

Study	*N*	HDR dose (Gy)			Median follow-up (y)	PSA–PFS (risk group)
		Gy/Fx	Fxs	Total		
Yoshioka *et al.*, 2006 (14)	111	6	9	54 Gy	2.3	100% low 89% intermediate 70% high
Corner *et al.*, 2008 (15)	110	8.5–9 10.5	4 3	36 Gy 31.5 Gy	1–2.5	100% All
Ghadjar *et al.*, 2008 (16)	36	9.5	4	38 Gy	3	100% Low and intermediate
Rogers *et al.*, 2010 (17)	284	6	6	36 Gy	3	94% Intermediate
Mark *et al.*, 2010 (18)	301	7.5	6	45 Gy	8	88% all Median Gleason 7
Present study CET WBH, 2010	298	7 9.5	6 4	42 Gy 38 Gy	5.2	97% Low and intermediate

HIGH-DOSE-RATE BRACHYTHERAPY AS MONOTHERAPY DELIVERED IN TWO FRACTIONS WITHIN ONE DAY FOR FAVORABLE/INTERMEDIATE-RISK PROSTATE CANCER: PRELIMINARY TOXICITY DATA

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doi:10.1016/j.ijrobp.2011.05.001

173 patients: low/intermeduiate risk
Median follow up 17 months
50: 12Gy x 2
123: 13.5Gy x 2

		Toxicity grade				
Toxicity	Total	0	1	2	3	4
Gastrointestinal						
Diarrhea	99	77 (91.7)	7 (8.3)	0	0	0
Rectal bleeding	99	84 (100)	0	0	0	0
Proctitis	99	83 (100)	0	0	0	0
Rectal pain/tenesmus	99	52 (100)	0	0	0	0
Rectal fistula	99	92 (100)	0	0	0	0
Anal fissure	99	84 (100)	0	0	0	0
Genitourinary						
Dysuria	99	67 (77.9)	15 (17.4)	4 (4.7)	0	0
Frequency/urgency	99	39 (45.9)	34 (40)	11 (12.9)	1 (1.2)	0
Retention	99	75 (88.2)	9 (10.6)	1 (1.2)	0	0
Incontinence	99	85 (100)	0	0	0	0
Hematuria	99	81 (96.4)	1 (1.2)	2 (2.4)	0	0
Urethral stricture	99	80 (96.4)	3 (3.6)	0	0	0

HIGH-DOSE-RATE BRACHYTHERAPY ALONE FOR LOCALIZED PROSTATE CANCER IN PATIENTS AT MODERATE OR HIGH RISK OF BIOCHEMICAL RECURRENCE

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Cancer Centre, Mount Vernon Hospital, Northwood, Middlesex, United Kingdom

doi:10.1016/j.ijrobp.2011.04.031

Variable	Category	26 Gy $n = 33$	31.5 Gy $n = 109$	34 Gy $n = 30$	36 Gy $n = 25$	All $n = 197$
Age (y)	Median	73	69	68	67	69
	Range	61–80	55–81	60–77	57–77	55–81
Follow-up (months)	Median	6	34	54	60	37
	Range	2–13	16–50	42–58	37–72	2–72
T stage	T1–2a	10 (30)	24 (22)	17 (57)	10 (40)	61 (31)
	T2b–2c	15 (46)	66 (61)	6 (20)	7 (28)	94 (48)
	≥T3	8 (24)	19 (17)	7 (23)	8 (32)	42 (21)
Gleason	<7	5 (15)	30 (27)	11 (37)	6 (24)	52 (26)
	7	21 (64)	73 (67)	15 (50)	16 (64)	125 (64)
	≥8	7 (21)	6 (6)	4 (13)	3 (12)	20 (10)
PSA μg/l	<10	13 (39.4)	43 (39)	11 (37)	10 (40)	77 (39)
	10–20	13 (39.4)	38 (35)	12 (40)	8 (32)	71 (36)
	>20	7 (21.2)	28 (26)	7 (23)	7 (28)	49 (25)
Risk group	Low	0	2 (2)	5 (17)	1 (4)	8 (4)
	Intermediate	19 (58)	61 (56)	14 (47)	9 (36)	103 (52)
	High	14 (42)	46 (42)	11 (37)	15 (60)	86 (44)
ADT duration (months)	N	25	96	17	19	157
	Median	6	6	17.3	19	6.3
	Range	3–36	1–37	3–36	1–40	1–40
IPSS ($n = 177$)	Median	6	6.5	5	3	6
	Range	0–24	0–27	0–22	0–21	0–27

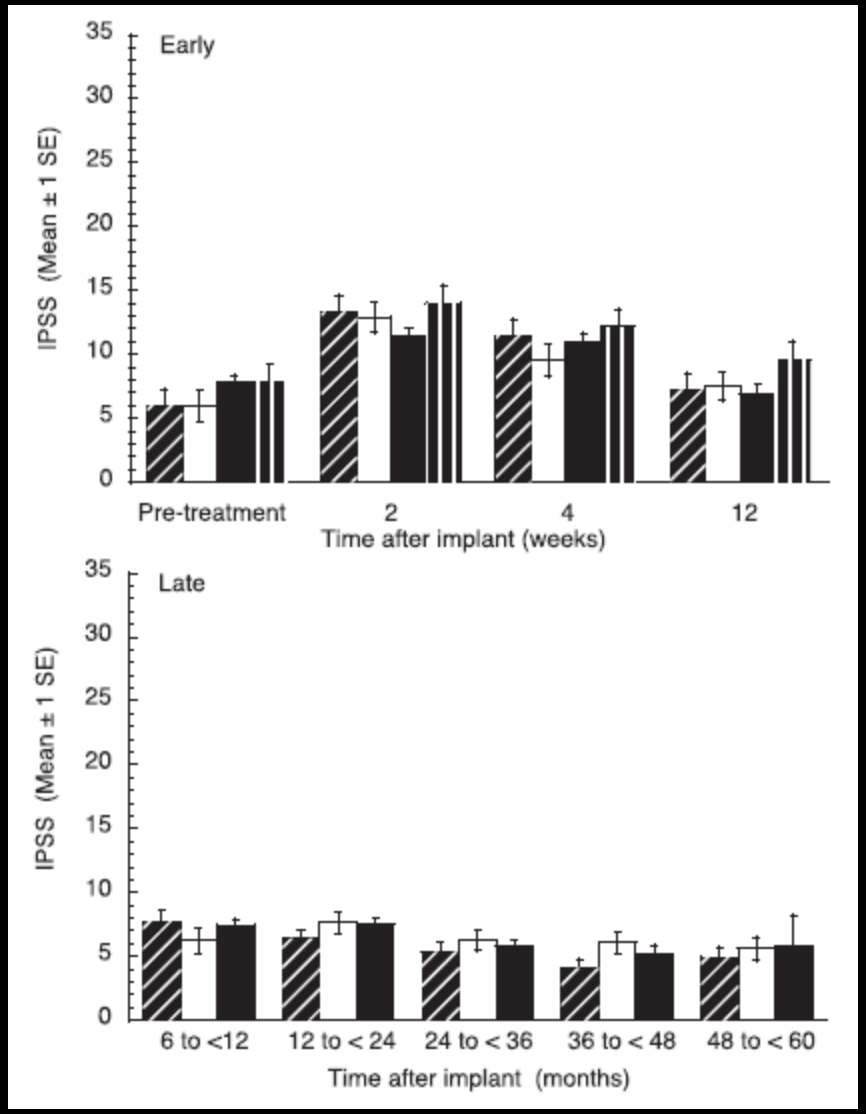
HDR implant: biological advantage 2Gy EQD

	α/β 1.5	α/β 3.5	α/β 10
• Ext beam 74Gy/37f	74	74	74
• HDR mono			
34Gy/4f	96.9	74.2	52.4
36Gy/4f	108	81.8	57.0
31.5Gy/3f	108	80.2	53.8
26Gy/2f	108	78.0	49.8

HIGH-DOSE-RATE BRACHYTHERAPY ALONE FOR LOCALIZED PROSTATE CANCER IN PATIENTS AT MODERATE OR HIGH RISK OF BIOCHEMICAL RECURRENCE

doi:10.1016/j.ijrobp.2011.04.031

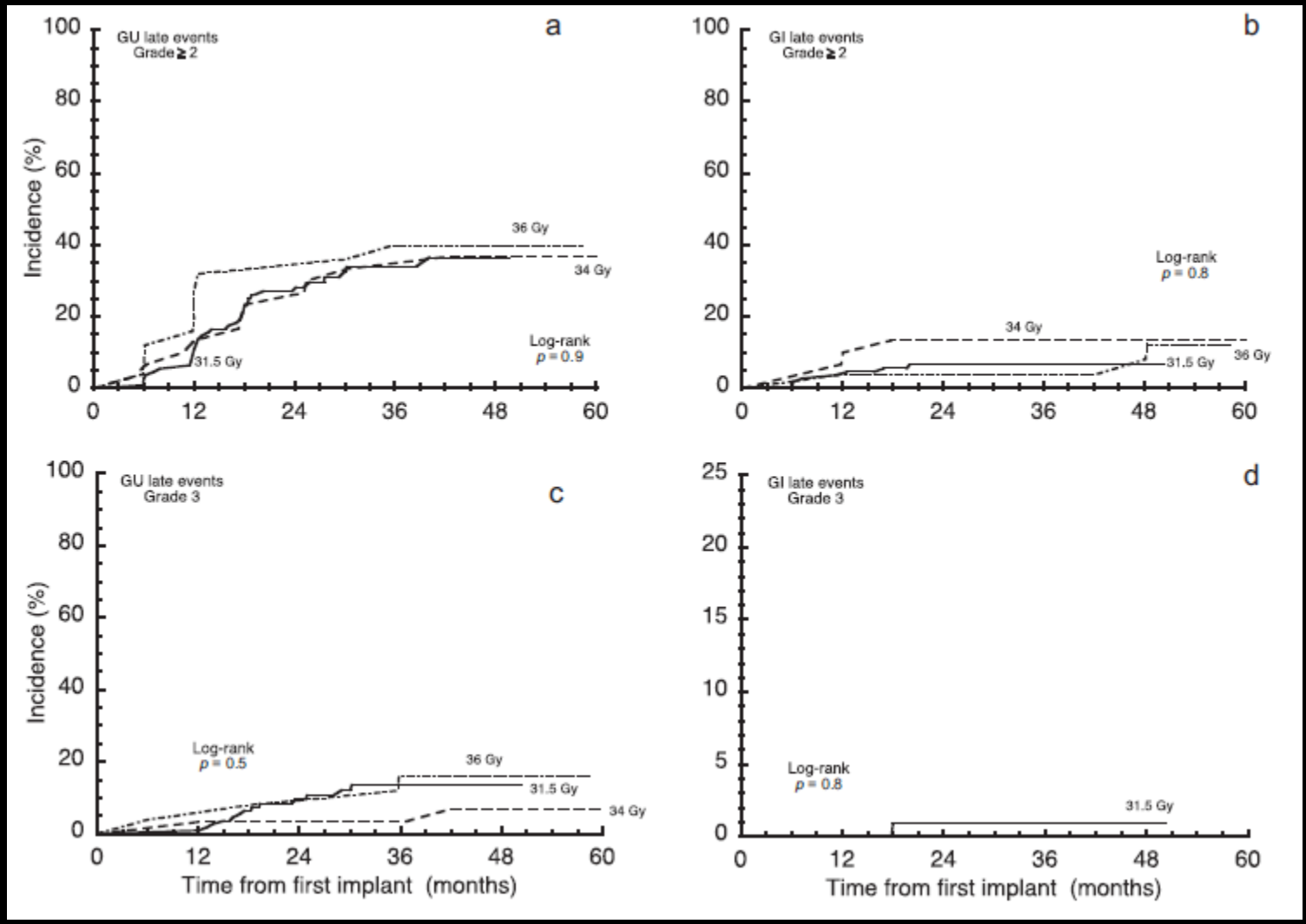
Urinary symptom scores



HIGH-DOSE-RATE BRACHYTHERAPY ALONE FOR LOCALIZED PROSTATE CANCER IN PATIENTS AT MODERATE OR HIGH RISK OF BIOCHEMICAL RECURRENCE

doi:10.1016/j.ijrobp.2011.04.031

Late toxicity (>6 months)



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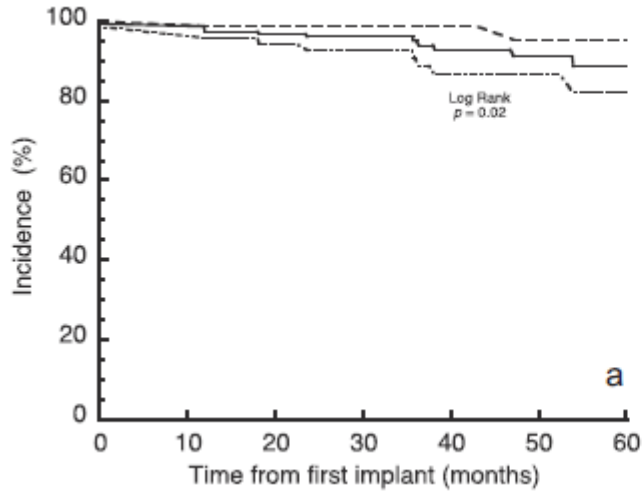
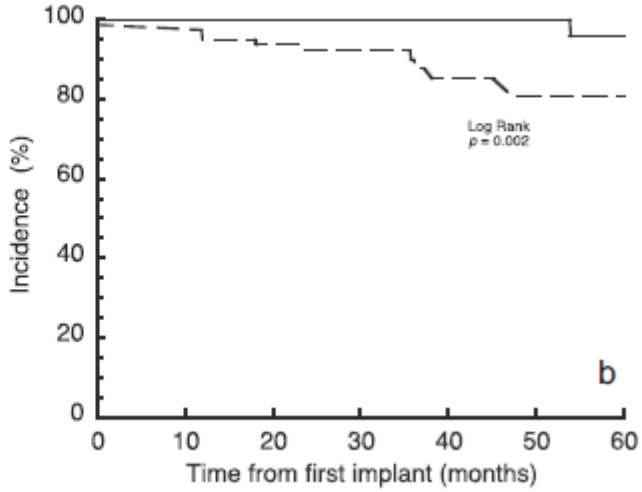
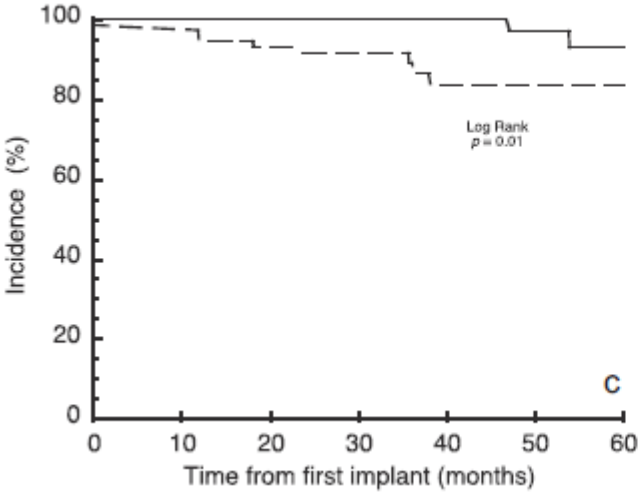
Freedom from biochemical failure







d

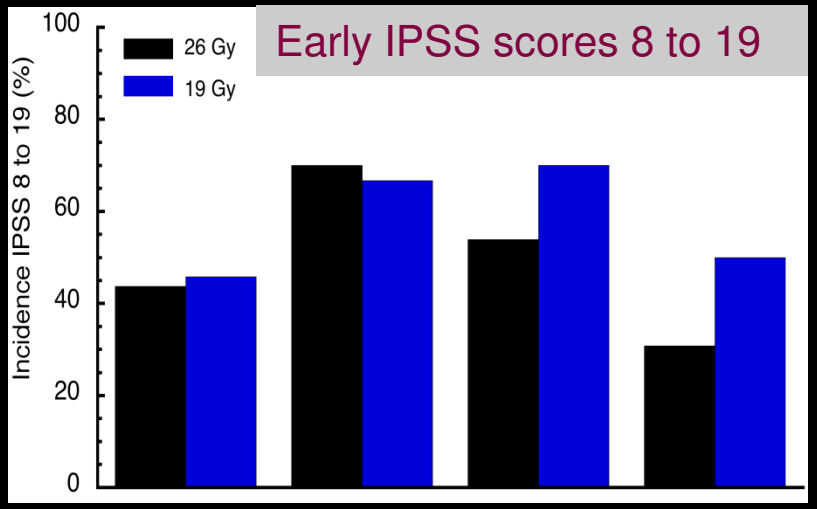
Variable	Risk ratio	Lower CI	Upper CI	*p*
Dose	0.573	0.277	0.934	0.02
Risk group	0.182	0.026	0.848	0.03
TnPSA	0.855	0.722	0.944	0.0002
[nPSA]	4.971	2.123	12.856	< 0.0001

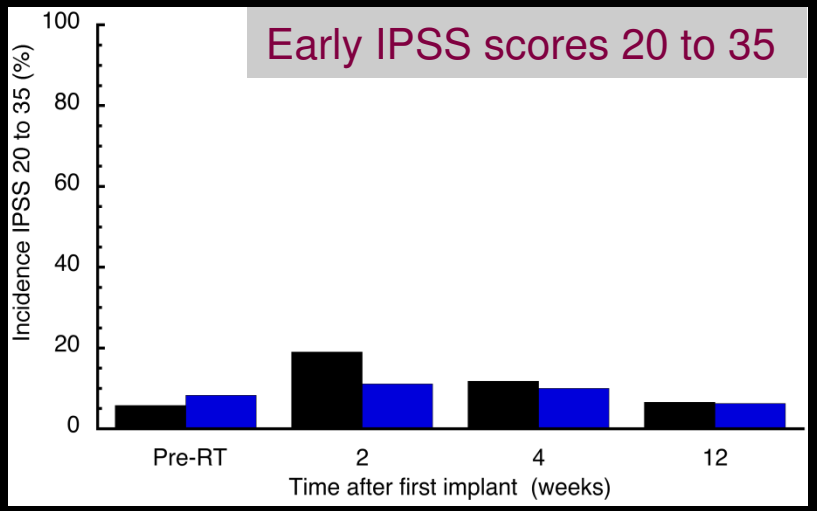
Single dose HDR monotherapy

- Biology
  - Unknown!
    - ? Effect on vasculature as well as tumour cell
    - No reoxygenation, repair, reassortment,repopulation
- Delivery
  - High QA essential .....only one chamce!
  - OAR tolerances more difficult to achieve

MV single dose HDR monotherapy

- 19Gy: 26 patients
- 20Gy: 14 patients





Current issues in HDR prostate brachytherapy

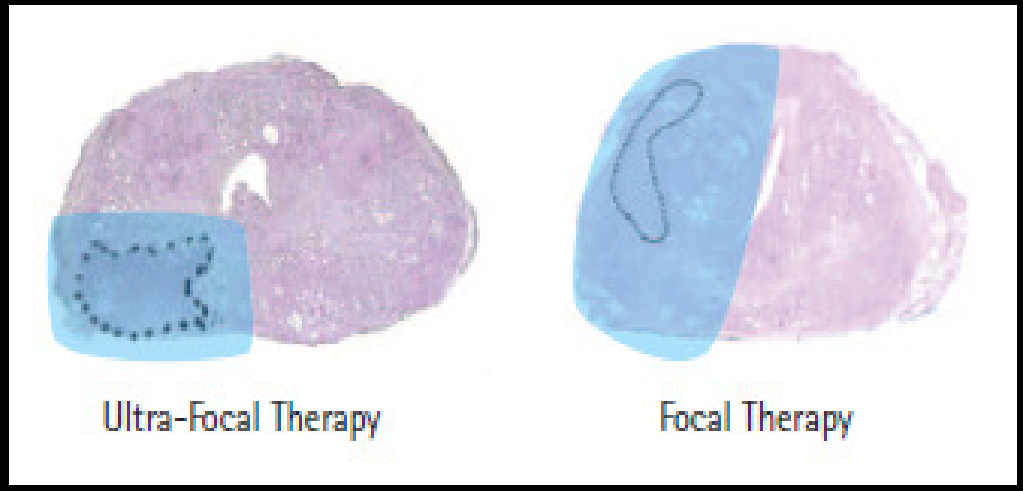
- Optimal dose for boost
- Relative efficacy vs modern high dose IMRT

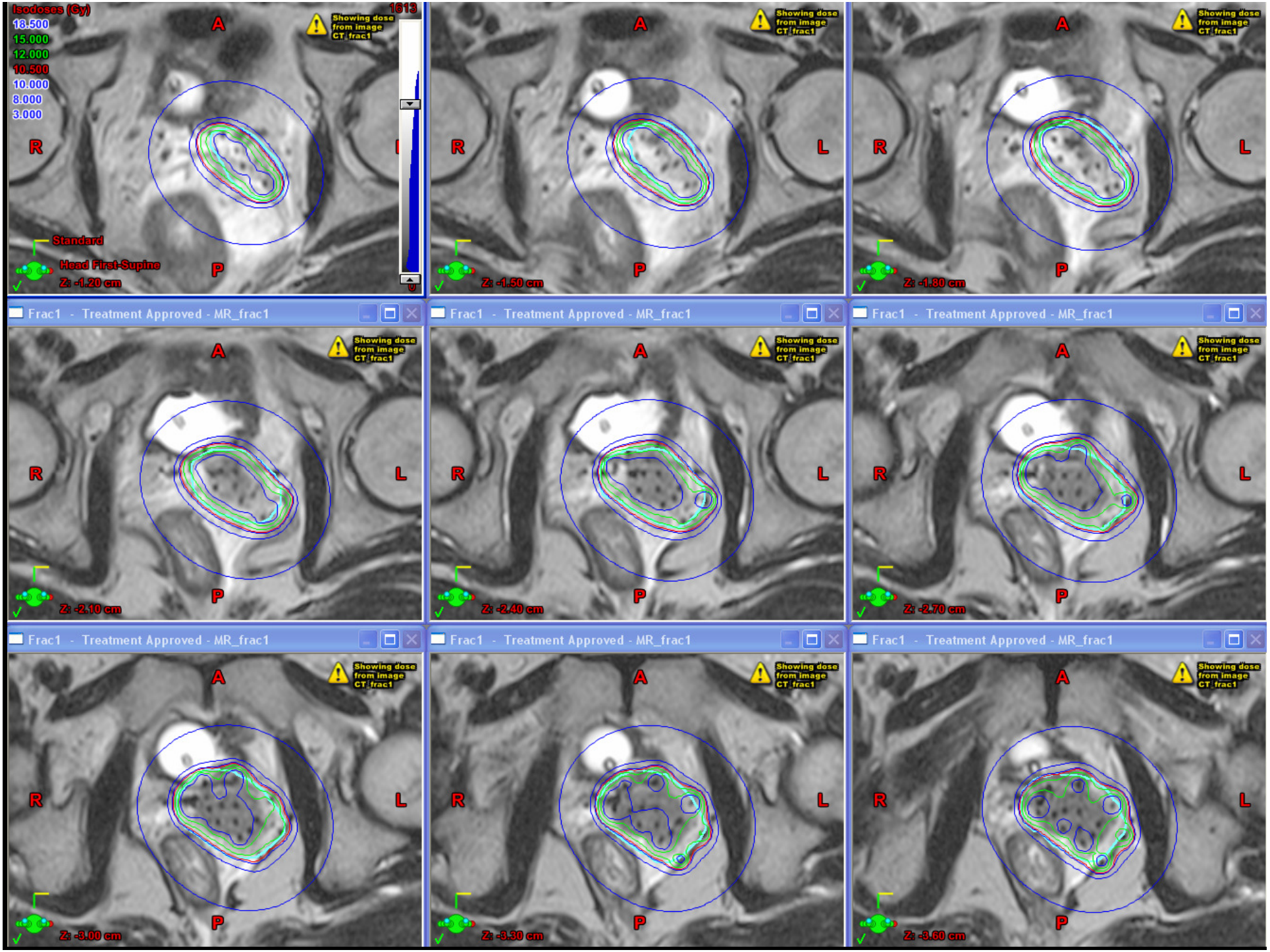
- Role of monotherapy
- Optimal dose for monotherapy
- Monotherapy as focal treatment

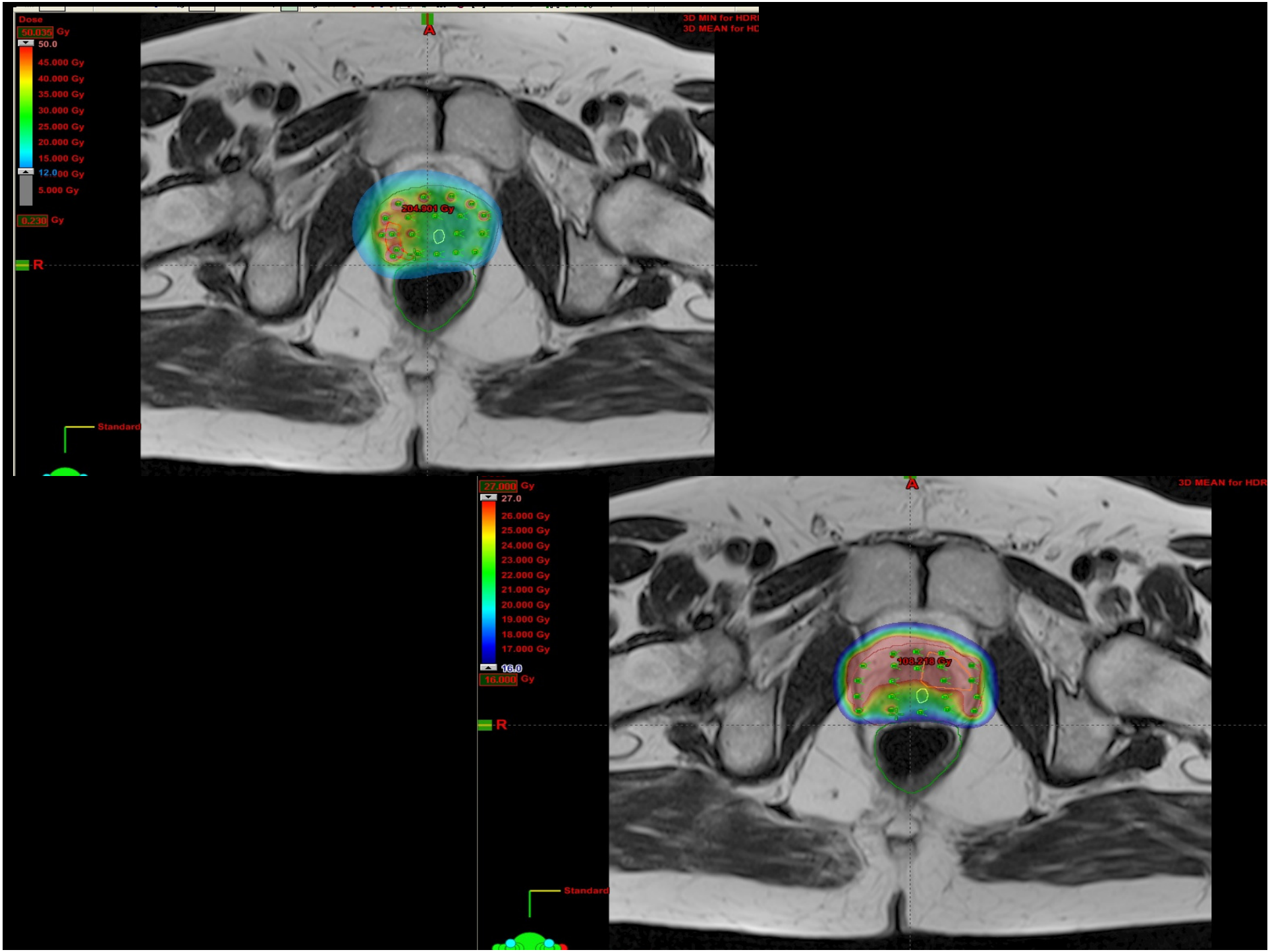
- HDR salvage

Focal therapy with brachytherapy

- HDR:
  - Afterloading HDR source
  - Infinite dose variation by altering dwell times

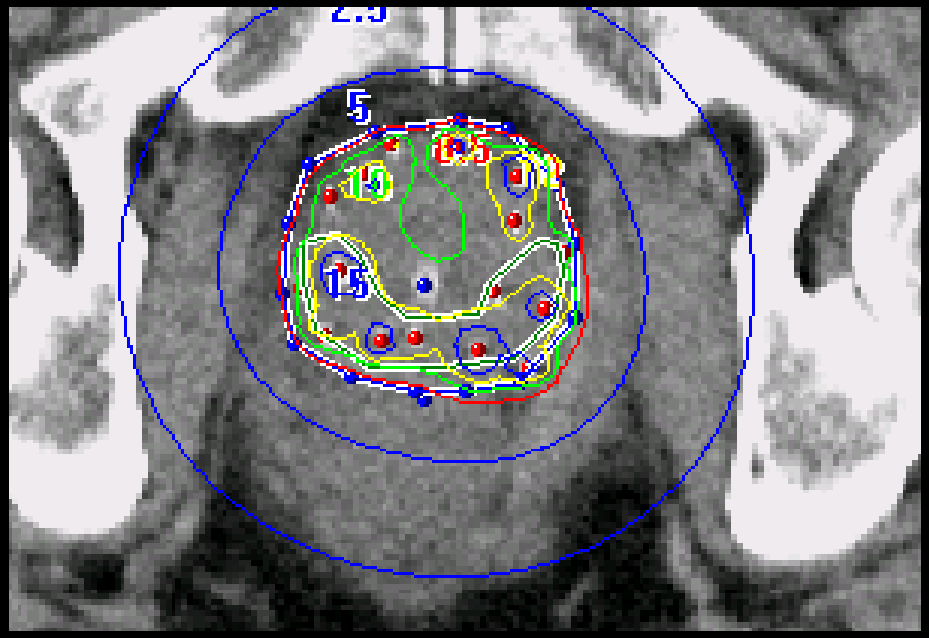



Isodoses (Gy)
18.500
15.000
12.000
10.500
10.000
8.000
3.000
1613
A
P
R
L
Showing dose from image CT_frac1
Standard
Head First-Supine
Z: -1.20 cm
Z: -1.50 cm
Z: -1.80 cm
Frac1 - Treatment Approved - MR_frac1
Z: -2.10 cm
Z: -2.40 cm
Z: -2.70 cm
Z: -3.00 cm
Z: -3.30 cm
Z: -3.60 cm


Dose
50.035 Gy
50.0
45.000 Gy
40.000 Gy
35.000 Gy
30.000 Gy
25.000 Gy
20.000 Gy
15.000 Gy
12.000 Gy
5.000 Gy
0.230 Gy
A
3D MIN for HDRI
3D MEAN for HD
204.901 Gy
R
Standard
27.000 Gy
27.0
26.000 Gy
25.000 Gy
24.000 Gy
23.000 Gy
22.000 Gy
21.000 Gy
20.000 Gy
19.000 Gy
18.000 Gy
17.000 Gy
16.0
16.000 Gy
A
3D MEAN for HDR
108.218 Gy
R
Standard

HDR for subvolume boosts

- CTV1: whole gland defined by capsule
  - Margin around capsule may be added 3 –5 mm
- CTV2: peripheral zone
- CTV3: GTV
- PTV = CTV

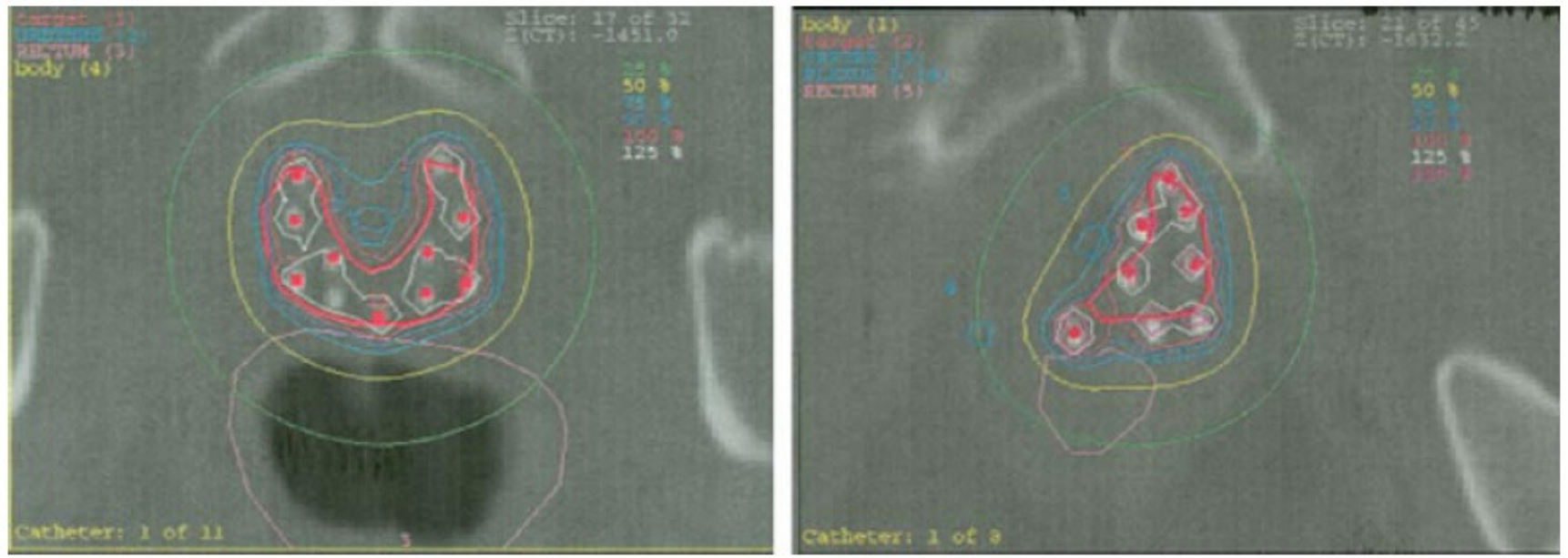


High-Dose-Rate Brachytherapy Boost to the Dominant Intra-Prostatic Tumor Region: Hemi-Irradiation of Prostate Cancer

Ulrike Schick,[1] Youri Popowski,[1] Philippe Nouet,[1] Sabine Bieri,[2] Michel Rouzaud,[1] Haleem Khan,[3] Damien Charles Weber,[1] and Raymond Miralbell[1]*

77 high risk patients: 20 with unliateral tumours on biopsy mapping and MR

64Gy in 32 fractions + 12/14/18Gy in 2 fractions; whole gland or hemigland



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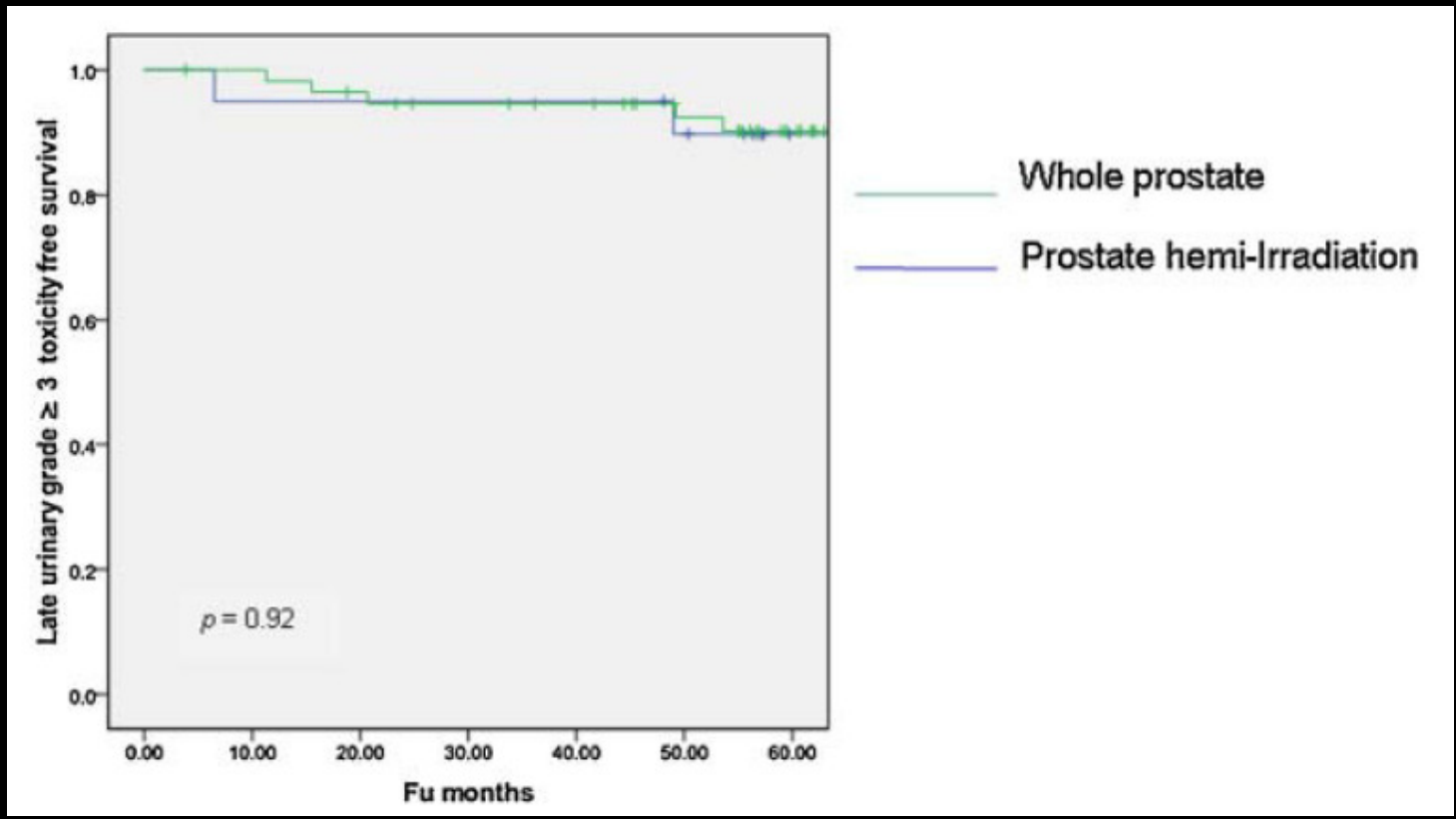

Current issues in HDR prostate brachytherapy

- Optimal dose for boost
- Relative efficacy vs modern high dose IMRT

- Role of monotherapy
- Optimal dose for monotherapy
- Monotherapy as focal treatment

- HDR salvage

BJUI SUPPLEMENTS

Brachytherapy for the treatment of recurrent prostate cancer after radiotherapy or radical prostatectomy

Francisco Gomez-Veiga*, Alfonso Mariño†, Luis Alvarez*, Ignacio Rodriguez*, Carlos Fernandez†, Sonia Pertega§ and Arturo Candal†

*Urology Department, Complejo Hospitalario Universitario A Coruña, †Centro Oncológico de Galicia and §Statistical Unit, University Hospital, A Coruña, Spain

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Study	No. of patients	Median follow-up (months)	% bDFS (timepoint)	Dosage
Wallner *et al.* [17]	13	36	51 (5 years)	170 Gy ^{125}I
Loening and Turner [18]	31	23	67 (5 years)	100–200 Gy ^{198}Au
Grado *et al.* [19]	49	64	34 (5 years)	160 Gy ^{125}I or 170 Gy ^{103}Pd (median)
Beyer [20]	17	62	53 (5 years)	120 Gy ^{125}I or 90 Gy ^{103}Pd
Koutrouvelis *et al.* [21]	31	30	87 (5 years)	144 Gy ^{125}I or 120 Gy ^{103}Pd
Wong *et al.* [22]	17	44	75 (4 years)	120 or 126 Gy ^{125}I or 103.5 or 112.5 Gy ^{103}Pd
Nguyen *et al.* [23]	25	47	70 (4 years)	137 Gy ^{125}I
Lee *et al.* [24]	21	19	89 (2 years)	HDR implants 36 Gy in six fractions
Burri *et al.* [25]	37	86	54 (10 years)	128.8 Gy ^{125}I or ^{103}Pd (median)
Aaronson *et al.* [26]	37	30	88 (3 years)	108–122 Gy ^{125}I or ^{103}Pd
Moman *et al.* [27]	31	108	20 (5 years)	145 Gy ^{125}I

FEASIBILITY OF HIGH-DOSE-RATE BRACHYTHERAPY SALVAGE FOR LOCAL PROSTATE CANCER RECURRENCE AFTER RADIOTHERAPY: THE UNIVERSITY OF CALIFORNIA–SAN FRANCISCO EXPERIENCE

BRIAN LEE, M.D., PH.D.,* KATSUTO SHINOHARA, M.D.,† VIVIAN WEINBERG, PH.D.,‡ ALEXANDER R. GOTTSCHALK, M.D., PH.D.,* JEAN POULIOT, PH.D.,* MACK ROACH III, M.D.,* AND I-CHOW HSU, M.D.*

*Department of Radiation Oncology, University of California–San Francisco, San Francisco, CA and †Department of Urology, University of California–San Francisco, San Francisco, CA, and ‡Comprehensive Cancer Center Biostatistics Core, University of California–San Francisco, San Francisco, CA

Int. J. Radiation Oncology Biol. Phys., Vol. 67, No. 4, pp. 1106–1112, 2007

21 patients
Median follow up 18 months

HDR brachytherapy: 6 x 6Gy

12 peripheral catheters
4 periurethral catheters

CT defined CTV

Age at recurrence (y)	
Mean	68
Range	58–81
Initial treatment (no. patients)	
EBRT	18
PPI	2
Proton	1
Dose for primary radiation	
Median (range)	72 Gy (63–78 Gy)
Time to first recurrence	
Mean	63.6 mo
Range	24–125 mo
≤24 mo	1 patient
>24 mo	20 patients
Presalvage PSA (ng/ml)	
Median	5.9
Range	1.4–9.5
Tumor grade – initial diagnosis	
GS 5	3
GS 6	10
GS 7	8
GS 8	0
Tumor grade – first recurrence	
GS 5	0
GS 6	1
GS 7	10
GS 8	7
GS 9	1
Unknown	2
Tumor stage at recurrence (no. of patients)	
T1c	2
T2a	7
T2b	1
T2c	2
T3a	5
T3b	4
Doubling time	
Median (range)	12.1 mo (4–51 mo)
<6 mo	3 patients
>6 mo	15 patients
Hormonal treatment presalvage (no. of patients)	
+HT	11
−HT	10
Metastases at recurrence	0%
Bx confirmation of local recurrence	100%
% ≥ 2 y initial DFI	100%
PSADT: % >6 mo	83% (15/18)
% GS ≤6 (at recurrence)	11% (2/19)
PSA <10 ng/ml (at recurrence)	100%
% Extracapsular extension	19% (4/21)
% Seminal vesicle invasion	24% (5/21)

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Toxicity

	Grade 1–2	Grade 3	Grade 4
Genitourinary	18	3	0
Gastrointestinal	3	0	0
Sexual dysfunction	18	2	0

PSA response:

13: nadir <0.1ng/ml

1 biochemical failure at 24mo

ELSEVIER

Brachytherapy 4 (2005) 141–145

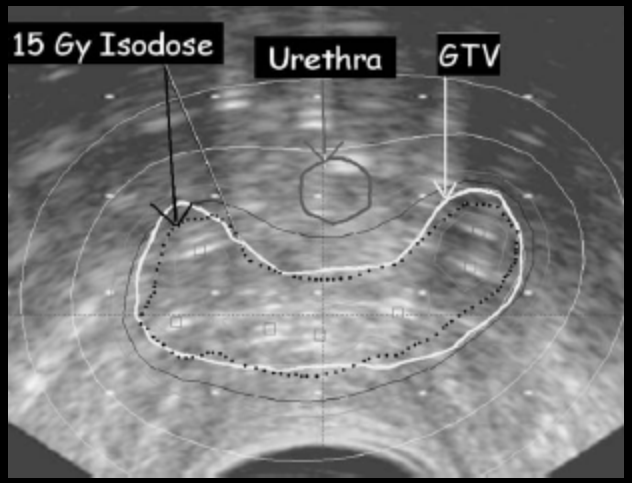
BRACHYTHERAPY

Feasibility and preliminary outcome of salvage combined HDR brachytherapy and external beam radiotherapy (EBRT) for local recurrences after radical prostatectomy

Peter Niehoff[1], Tilmann Loch[2], Niels Nürnberg[1], Razvan Galalae[1], Jan Egberts[1], Peter Kohr[1], György Kovács[1,*]

[1]*Interdisciplinary Brachytherapy Centre, Schleswig-Holstein University Hospital, Kiel, Germany*
[2]*Department of Urology, Diakonie Flensburg, Flensburg, Germany*

	30 Gy EBRT	40 Gy EBRT	Total
No. of patients	21	14	35
Mean iPSA*	33.2 (2–73.2)	11.64 (0.6–17.3)	27.62 (0.6–73.2)
Initial grading	Grade 2: 11 Grade 3: 10	Grade 2: 8 Grade 3: 6	Grade 2: 19 Grade: 16
Time to PSA increase after prostatectomy	42 (7–73) months	42 (6–103) months	42 (6–103) months
T-stage			
No. of patients	pT2a-b: 6 pT3a-b: 14 pT4: 1	pT2a-b: 4 pT3a-b: 10 T4: 0	pT2a-b: 10 pT3a-b: 24 pT4: 1
Mean age at BT (years)	66 (61–77)	65 (52–77)	66 (52–77)
Mean/Median PSA at BT (ng/mL)	5.32/3 (0.8–20.6)	4.68/2.8 (0.14–17.8)	5.02/2.9 (0.14–20.6)



Feasibility and preliminary outcome of salvage combined HDR brachytherapy and external beam radiotherapy (EBRT) for local recurrences after radical prostatectomy

Brachytherapy 4 (2005) 141–145

Mean follow up: 29 months (30Gy) and 26 months (40Gy)

TOXICITY
Acute
6: Grade I/II dysuria
16: Grade I/II GI changes
Late
15: 'some degree of incontinence'
3: strictures
10: impotent

PSA RESPONSE

30Gy: 5/21 progression free

40Gy: 6/14 progression free

ELSEVIER

Brachytherapy 7 (2008) 231–236

BRACHYTHERAPY

Prostate high-dose-rate brachytherapy as salvage treatment of local failure after previous external or permanent seed irradiation for prostate cancer

Morgan Tharp[1,2,*], Michael Hardacre[1,2], Rick Bennett[3], W. Terry Jones[3], David Stuhldreher[3], Jeff Vaught[3]

[1]*Radiation Oncology, Central Indiana Cancer Centers, Indianapolis, IN*
[2]*US Oncology, Houston, TX*
[3]*Urology of Indiana, Indianapolis, IN*

Previous treatment and disease parameters

Pt no	Previous treatment	Initial PSA	Initial Gleason
1	^{125}I Seeds, 24 mCi	NR	NR
2	^{125}I Seeds (dose unknown)	19.3	6
3	XRT, 7200 cGy	8.7	6
4	XRT, 4000 cGy + ^{125}I 108 Gy	4.7	4
5	XRT, 6660 cGy	9.3	6
6	^{125}I Seeds 160 Gy(Prvs TURP)	15.5	6
7	XRT, 6840 cGy (Prvs TURP)	16	6

Salvage treatment used, by previous treatment

Pts nos	XRT	HDR regimen
Patients with prior external beam only		
3, 5, 7	None	Two implants, 700 cGy × 3 each implant
Patients with prior seed-implant only		
6	36 Gy conformal	Two implants, 900 cGy × 1 each implant
1	45 Gy conformal	Two implants, 600 cGy × 2 each implant
2	45 Gy conformal	One implant, 700 cGy × 3 each implant
Patients with prior external beam plus seed implant		
4	None	Two implants, 700 cGy × 3 each implant

Prostate high-dose-rate brachytherapy as salvage treatment of local failure after previous external or permanent seed irradiation for prostate cancer

Brachytherapy 7 (2008) 231–236

Summary of complications, by patient

Pt no	Rectal injury	Urinary injury	Perineal pain
1	None	Gr 2 Stx; Gr 3 necrosis, AS → cont channel	None
2	None	None	None
3	Gr 2 bleeding	Gr 2 Stx dil ×2	None
4	None	Gr 2 Stx; Gr 3 necrosis, AS	Gr 3 pain
5	None	None	None
6	None	Gr 2 Stx dil ×3	Gr 3 pain
7	None	Gr 2 Stx dil ×4; self-caths	None

Gr = grade; AS = artificial urethral sphincter; cont channel = continent catheter channel construction required; Stx = stricture; dil = dilated; self-caths = intermittently self-catheterizes to maintain urethral patency. Only symptoms requiring medical management are reported.

Disease control

No recurrence

Pt no	Length FU	PSA Nadir	Last PSA
1	58 mo	0	0
3	57 mo	0	0.02
5	63 mo	0	0
6	52 mo	0	0.27 (DOC)
7	63 mo	0	0

Recurrence

Pt no	Time to failure	PSA at failure	Survival postsalvage
2	27 mo	7.18	34 mo
4	53 mo	N.R.	54 mo

HDR brachytherapy salvage: recent abstracts

ABS 2010

Use of Prostate HDR as Salvage for Local Failure after Prior Prostate Cancer Therapy

David N. Lowther, M.D.[1], Robert S. Cowles, M.D.[2], Nayha Dixit, M.S.[3]

11 patients
No toxicity
Falling PSA in all

ABS 2011

HDR Salvage Treatment of PSA Only Recurrent Prostate Cancer After Radical Prostatectomy: Update of a Feasibility Study in 5 Patients

Rufus J. Mark, MD, Paul J. Anderson, MD, Robin S. Akins, MD,

5 patients
36Gy/6fractions
Median F/u 36 months
No complications
PSA<0.1 in 3/5

Salvage High-Dose-Rate Brachytherapy for Recurrent Prostate Cancer After Ultra High Intensity Modulated Radiotherapy: Results of a Prospective Study

Lisa K. Morikawa, MD, Michael J. Zelefsky, MD, Gil'ad N. Cohen, MS, DABMP, Marco Zaider, PhD, Sherri M. Donat, MD, Yoshiya Yamada, MD.

29 patients
22 post>81Gy
Median F/u 23 months
79% bRFS
G1/2 rectal: 37%
G1/2 urinary: 24%
No G3/4

ESTRO 2011

SALVAGE HDR BRACHYTERAPHY FOR LOCAL RECCURANCES OF PROSTATE CANCER PRELIMINARY RESULTS

M. Gawkowska-Suwinska[1], M. Fijalkowski[1], B. Bialas[1], S. Kellas-Sleczka[1], et al

23 patients
10Gy x 3
Mean F/u 12 months
Retention in 3
G1 rectal toxicity in 1
4: distant mets
Median PSA in 19: 0.19

Current issues in HDR prostate brachytherapy

- Optimal dose for boost
- Relative efficacy vs modern high dose IMRT

- Role of monotherapy
- Optimal dose for monotherapy
- Monotherapy as focal treatment

- HDR salvage

Acknowledgements to the Mount Vernon Team

- Oncologists
  - Peter Ostler
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  - Linda Bryant
  - Caroline Chapman
- Research Nurses
  - Jess Milner
  - Helen Cladd
  - Jane Gregory
- Data managers
  - Meriele Woodruffe
  - Penny King


NATIONS
RBS
Admiral