LONG TERM OUTCOMES OF PROSTATE BRACHYTHERAPY

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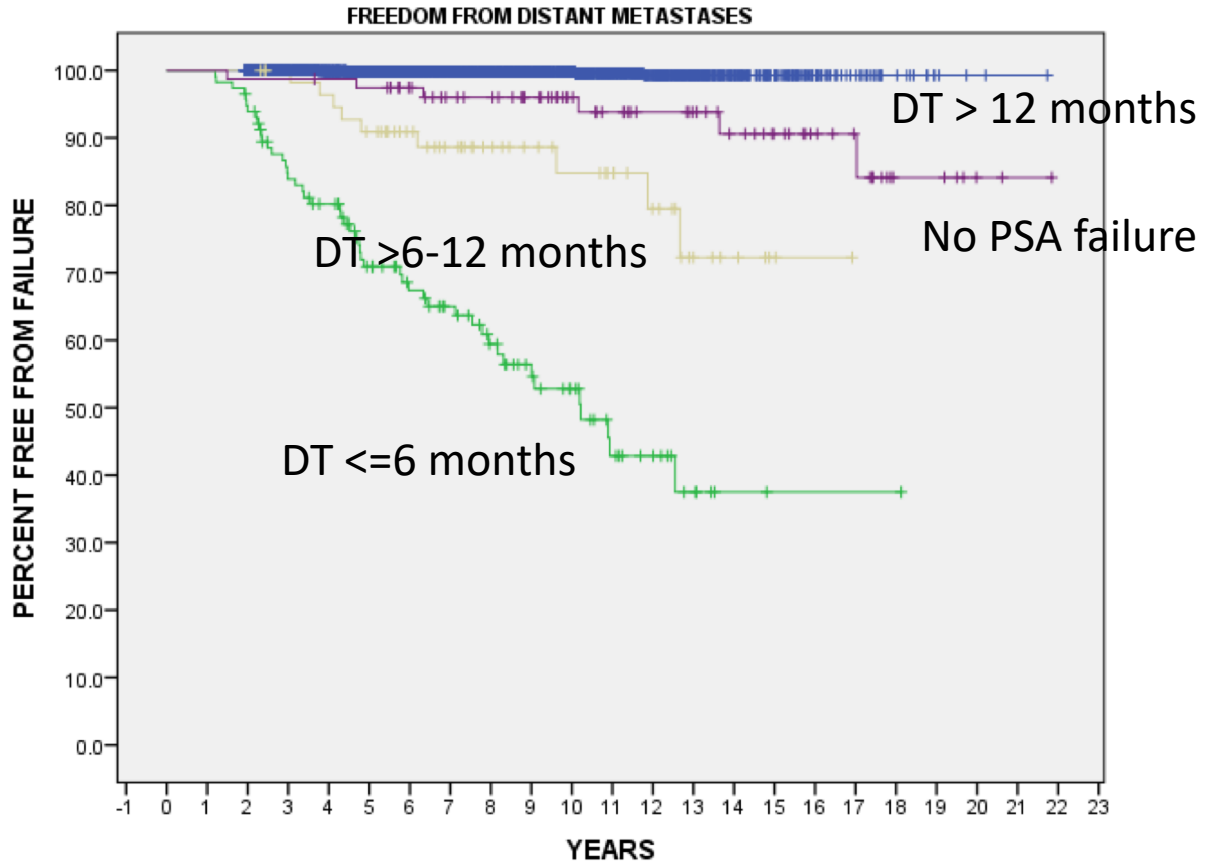
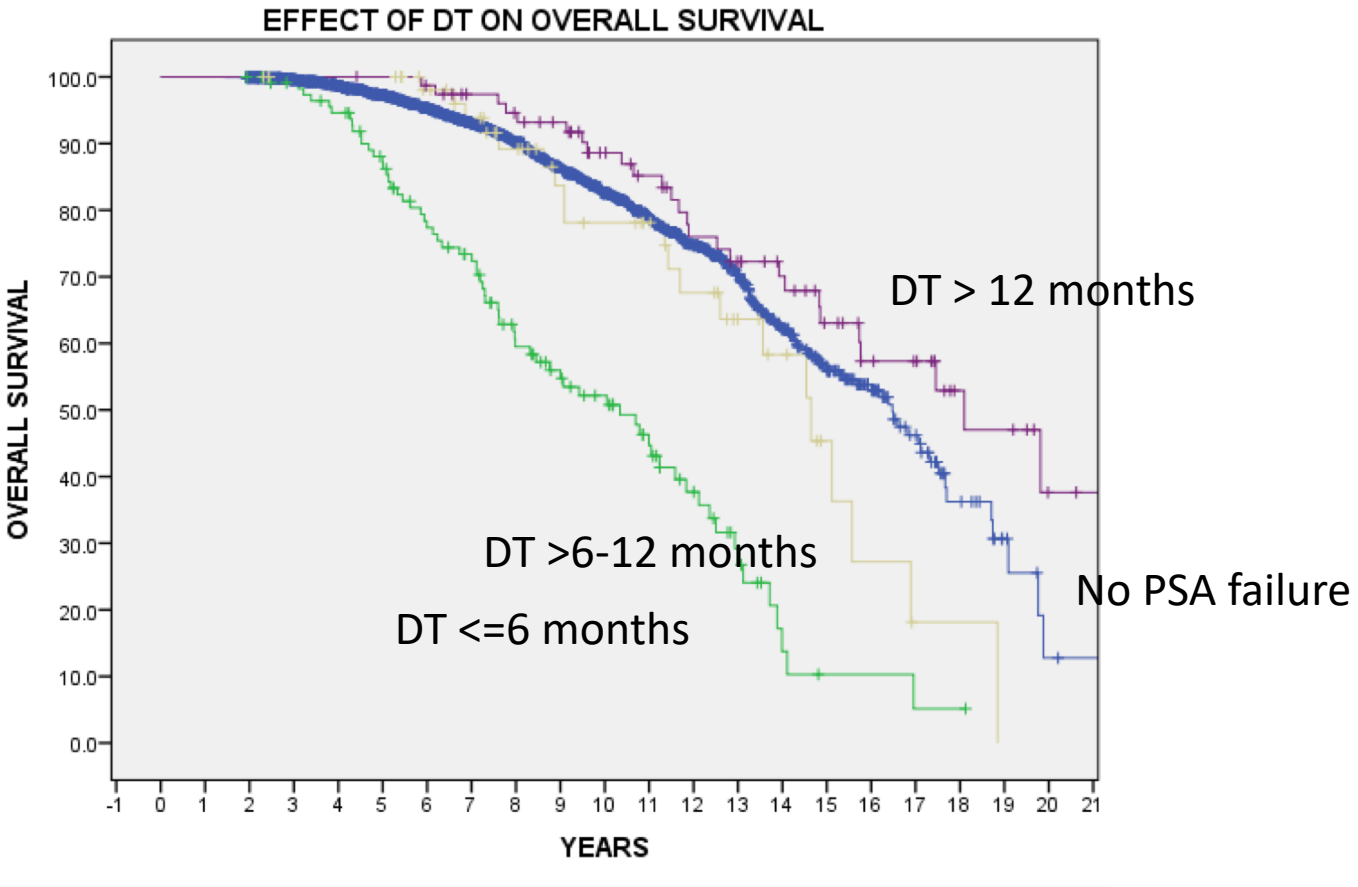
OBJECTIVES

- Review long term outcomes of prostate Brachytherapy
  - PSA control
  - Distant Mets
  - Overall Survival
  - Intermediate Risk Patients
  - High Risk Patients
- Randomized Trials

THE IMPORTANCE OF PSA DOUBLING TIME AS A PREDICTOR OF OUTCOME

- Between 1990 and 2015 2771 patients with localized prostate cancer underwent treatment at the Ichan School of Medicine at Mount Sinai by a single radiation oncologist with low dose rate brachytherapy as a component of definitive radiation therapy.


FREEDOM FROM DISTANT METASTASES
PERCENT FREE FROM FAILURE
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-1 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23
YEARS
DT > 12 months
No PSA failure
DT >6-12 months
DT <=6 months


EFFECT OF DT ON OVERALL SURVIVAL
OVERALL SURVIVAL
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
-1 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
YEARS
DT > 12 months
DT >6-12 months
DT <=6 months
No PSA failure

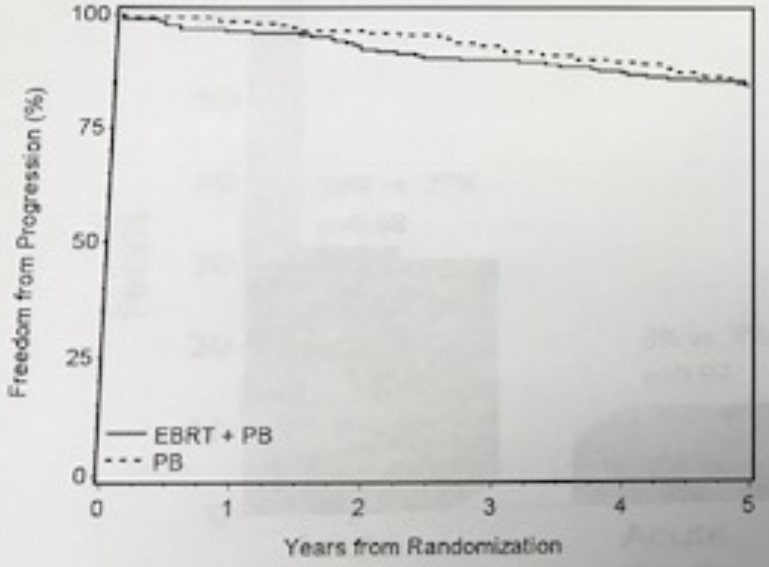
NRG Oncology/RTOG 0232: A Phase lll trial comparing combined external beam and brachytherapy with brachytherapy alone for intermediate risk patients

- Eligibility Criteria:
- Gleason 2-6, PSA >10 , <20
- Gleason 7, PSA <10
- PV <60cc

- No ADT
- IPSS <16
- Node -

- Treatment arms:
- 45 Gy plus 100Gy of Pd103 or I-125 , 110 Gy
- Pd103(125 Gy) or I-125 (145 Gy)

Results: Freedom from Progression



ents at Risk

T + PB	220	212	203	198	192	183
	223	219	213	207	198	186

First Failure	EBRT + PB (n=34)	PB (n=32)	Total (n=66)
BF-ASTRO	23 (68%)	17 (53%)	40 (61%)
LP	1 (3%)	1 (3%)	2 (3%)
LP, DM	1 (3%)	0 (0%)	1 (2%)
Death*	9 (26%)	14 (44%)	23 (35%)

*Not due to prostate cancer

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Outcomes and toxicities in patients with intermediate-risk prostate cancer treated with brachytherapy alone or brachytherapy and supplemental external beam radiation therapy

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Table 1 Patient c

Characteristic	All patients (N = 902)	Brachytherapy alone (n = 390)	Brachytherapy and EBRT (n = 512)	P
Median age, years	68	69	67	<0.001
Median follow-up, months	91	110	81	<0.001
Median pre-implant prostate volume, cm^3	33	32	33	0.131
Median BED, Gy_2	199	176	207	<0.001
ADT, n (%)	622 (69.0)	245 (65.0)	377 (71.8)	0.029
Self-reported race, n (%)				
White	671 (74.4)	307 (81.4)	364 (69.3)	0.001
Black	120 (13.3)	41 (10.9)	79 (15.0)	
Hispanic	69 (7.6)	20 (5.3)	49 (9.3)	
Asian	10 (1.1)	4 (1.1)	6 (1.1)	
Other race	18 (2)	3 (0.8)	15 (2.9)	
Unknown race	14 (1.6)	2 (0.5)	12 (2.3)	
Number of risk factors, n (%)				
1 intermediate risk factor	521 (57.8)	282 (74.8)	239 (45.5)	<0.001
2–3 intermediate risk factors	381 (42.2)	95 (25.2)	286 (54.5)	
Clinical stage, n (%)				
≤T2a	419 (46.5)	165 (43.8)	254 (48.4)	0.171
≥T2b	483 (53.5)	212 (56.2)	271 (51.6)	
Gleason score, n (%)				
≤6	383 (42.5)	277 (73.5)	106 (20.2)	<0.001
7	519 (57.5)	100 (26.5)	419 (79.8)	
Initial PSA level, n (%)				
0–4 ng/mL	69 (8.9)	36 (10.6)	33 (7.7)	0.004
5–9 ng/mL	354 (45.9)	134 (39.3)	220 (51.2)	
10–20 ng/mL	348 (45.1)	171 (50.1)	177 (41.2)	

ADT, androgen deprivation therapy; BED, biologically effective dose; EBRT, external beam radiation therapy.

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Fig. 1 Biochemical Failure in patients with 1 intermediate-risk factor.
$P = 0.433$.

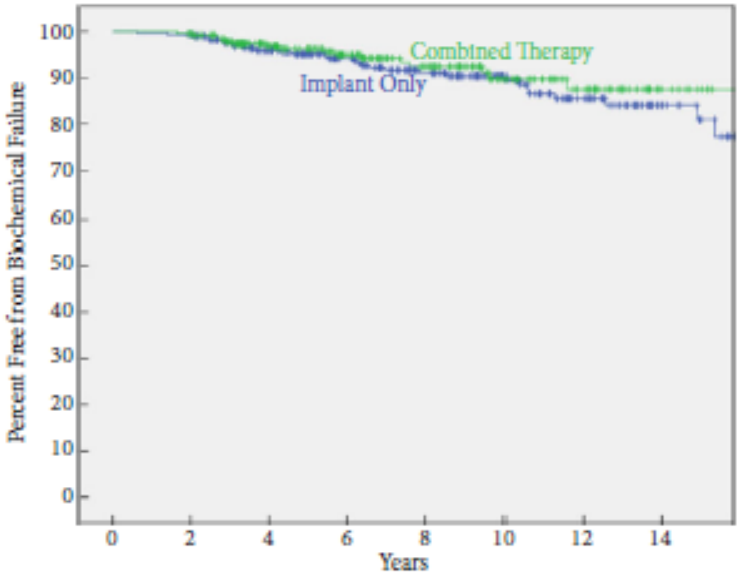


Fig. 2 Biochemical Failure in patients with >1 intermediate-risk factor.
$P = 0.092$.

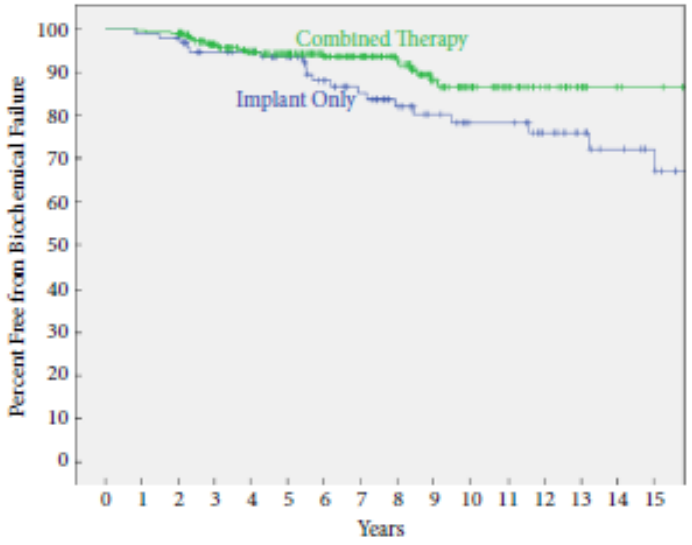
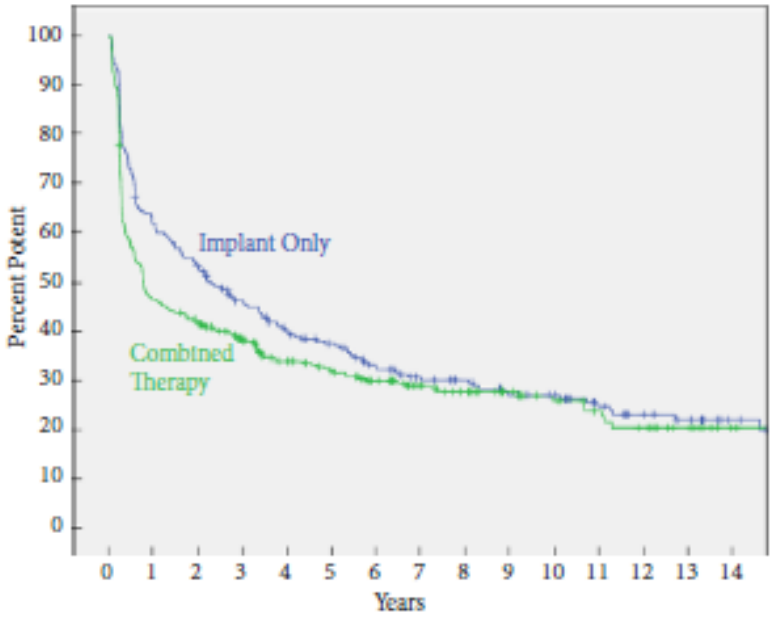


Table 5 Differences in toxicities between treatment groups among all patients.

Factor	Brachytherapy alone	Brachytherapy and EBRT	P
Median (range) change* in IPSS	1 (−21 to 29)	2 (−28 to 27)	0.118
Median (range) change* in IPSS QoL	0 (−6 to 6)	0 (−5 to 5)	0.002
Median (range) change* in SHIM score	−3 (−24 to 24)	−4 (−24 to 20)	0.145
Change* in potency†	−1 (−3 to 3)	−1 (−3 to 3)	0.243
Urge incontinence‡, *n* (%)	34 (9)	114 (22)	<0.001
Dysuria‡, *n* (%)	59 (16)	204 (39)	<0.001
Haematuria‡, *n* (%)	18 (5)	74 (14)	<0.001
Stress incontinence‡, *n* (%)	31 (8)	56 (11)	0.220
Rectal bleeding‡, *n* (%)	22 (6)	41 (8)	0.251
Urinary retention‡, *n* (%)	27 (7)	37 (7)	0.947

*EBRT, external beam radiation therapy; QoL, quality of life; SHIM, Sexual Health Inventory for Men. *Change is calculated as score reported at last follow-up visit minus score reported before treatment. †Change in potency as measured by Mount Sinai erectile function scale score. ‡Toxicity was reported at any follow up visit and in many cases did not persist.*

Fig. 3 Time to impotency in those potent at start of treatment. P = 0.040.



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Low-dose-rate brachytherapy for prostate cancer: outcomes at >10 years of follow-up

BJU Int 2018
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Objective

To examine biochemical control, survival, and late morbidity with definitive low-dose-rate brachytherapy (LDR-BT) for patients with prostate cancer surviving for >10 years after treatment.

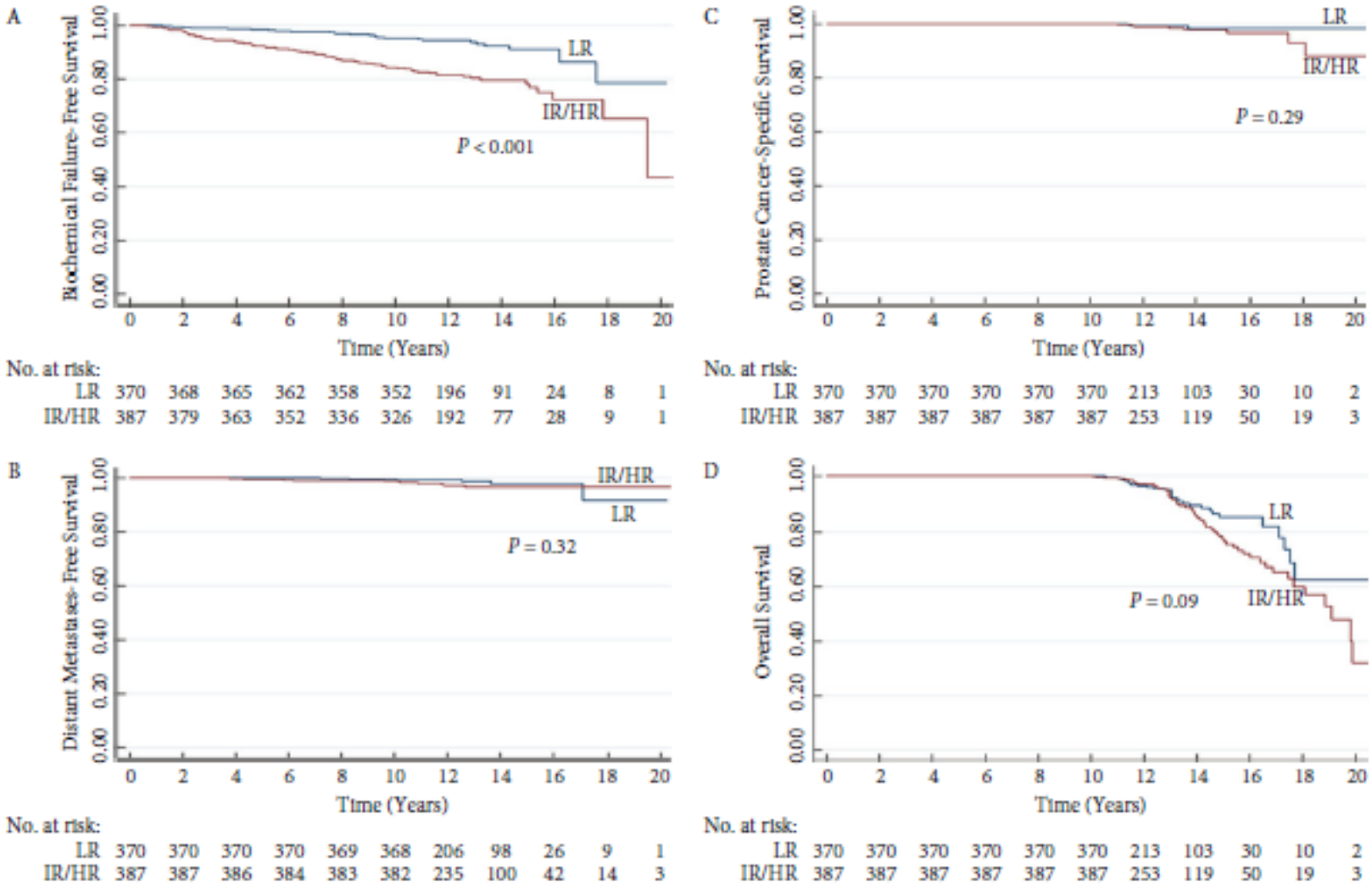
Patients and Methods

We identified 757 men with localised prostate cancer who underwent definitive LDR-BT in the period 1990–2006 and were followed for >10 years at our institution. Biochemical failure-free survival (BFFS), distant metastases-free survival (DMFS), prostate cancer-specific survival (PCSS), and overall survival (OS) were selected as study endpoints. Survival was examined using the log-rank test, Kaplan–Meier method, and Cox regression modelling. Urinary, quality of life (QoL), and potency scores at baseline and last follow-up were recorded.

Table 3 Survival rates by NCCN risk group classification [median (range) follow-up of 12.5 (10.1–21.8) years].

Survival variable, %, (95% CI)	Total *n* = 757 (100%)	Low risk *n* = 370 (48.9%)	Intermediate risk *n* = 170 (22.5%)	High risk *n* = 217 (28.6%)	Log-rank *P*
BFFS					
13-year	87 (0.84–0.89)	94 (0.90–0.96)	87 (0.81–0.92)	75 (0.68–0.80)	<0.001
15-year	84 (0.81–0.87)	91 (0.86–0.94)	84 (0.74–0.90)	73 (0.66–0.79)	
17-year	79 (0.72–0.85)	86 (0.73–0.93)	80 (0.67–0.89)	65 (0.51–0.76)	
DMFS					
13-year	98 (0.96–0.99)	99 (0.96–0.99)	97 (0.92–0.99)	96 (0.92–0.98)	0.27
15-year	97 (0.95–0.98)	98 (0.94–0.99)	97 (0.92–0.99)	96 (0.92–0.98)	
17-year	97 (0.95–0.98)	98 (0.94–0.99)	97 (0.92–0.99)	96 (0.92–0.98)	
OS					
13-year	94 (0.91–0.95)	95 (0.91–0.97)	95 (0.89–0.98)	91 (0.84–0.94)	0.09
15-year	81 (0.76–0.85)	86 (0.78–0.90)	80 (0.68–0.88)	75 (0.65–0.83)	
17-year	72 (0.64–0.78)	82 (0.71–0.89)	73 (0.56–0.84)	60 (0.46–0.71)	
PCSS					
13-year	99 (0.97–0.99)	99 (0.97–0.99)	100	97 (0.92–0.99)	0.02
15-year	98 (0.96–0.99)	98 (0.94–0.99)	100	96 (0.90–0.98)	
17-year	97 (0.94–0.99)	98 (0.94–0.99)	100	94 (0.85–0.97)	

Fig. 1 Kaplan–Meier survival curves for the entire cohort [*n* = 757, median (range) follow-up of 12.5 (10.1–21.8) years]. (**A**) BFFS, (**B**) DMFS, (**C**) PCSS, and (**D**) OS. LR, low-risk; IR/HR, intermediate- and high-risk.



15-Year Cause Specific and All-Cause Survival Following Brachytherapy for Prostate Cancer: Negative Impact of Long-Term Hormonal Therapy

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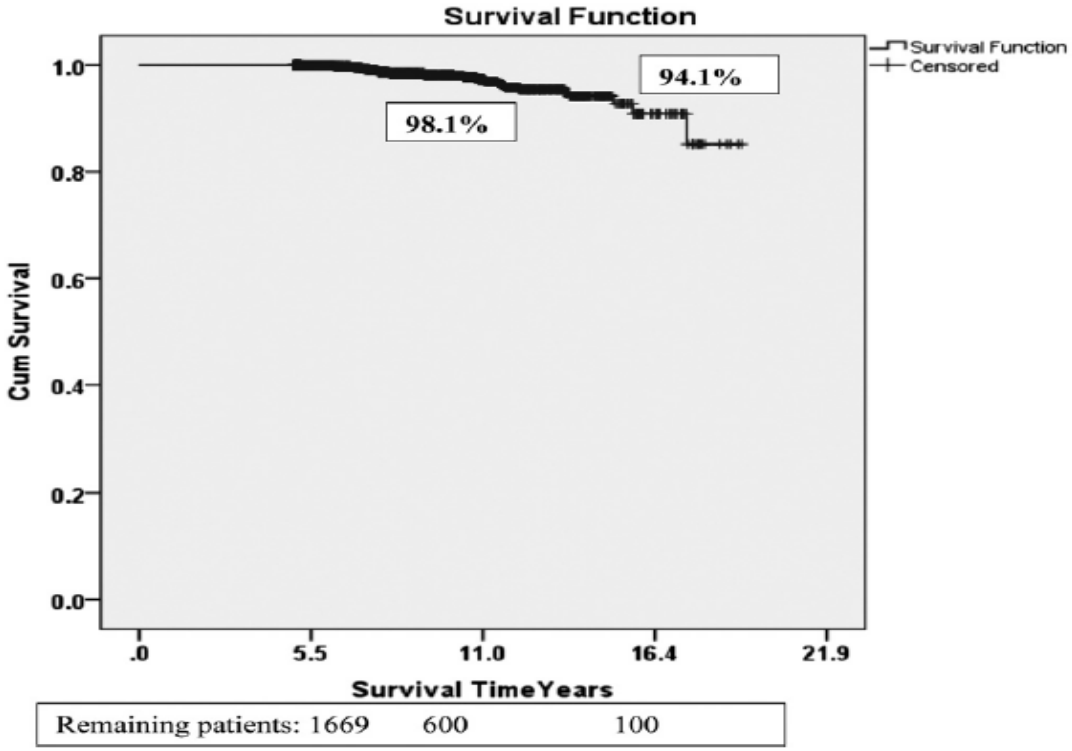

Figure 1. Ten and 15-year CSS

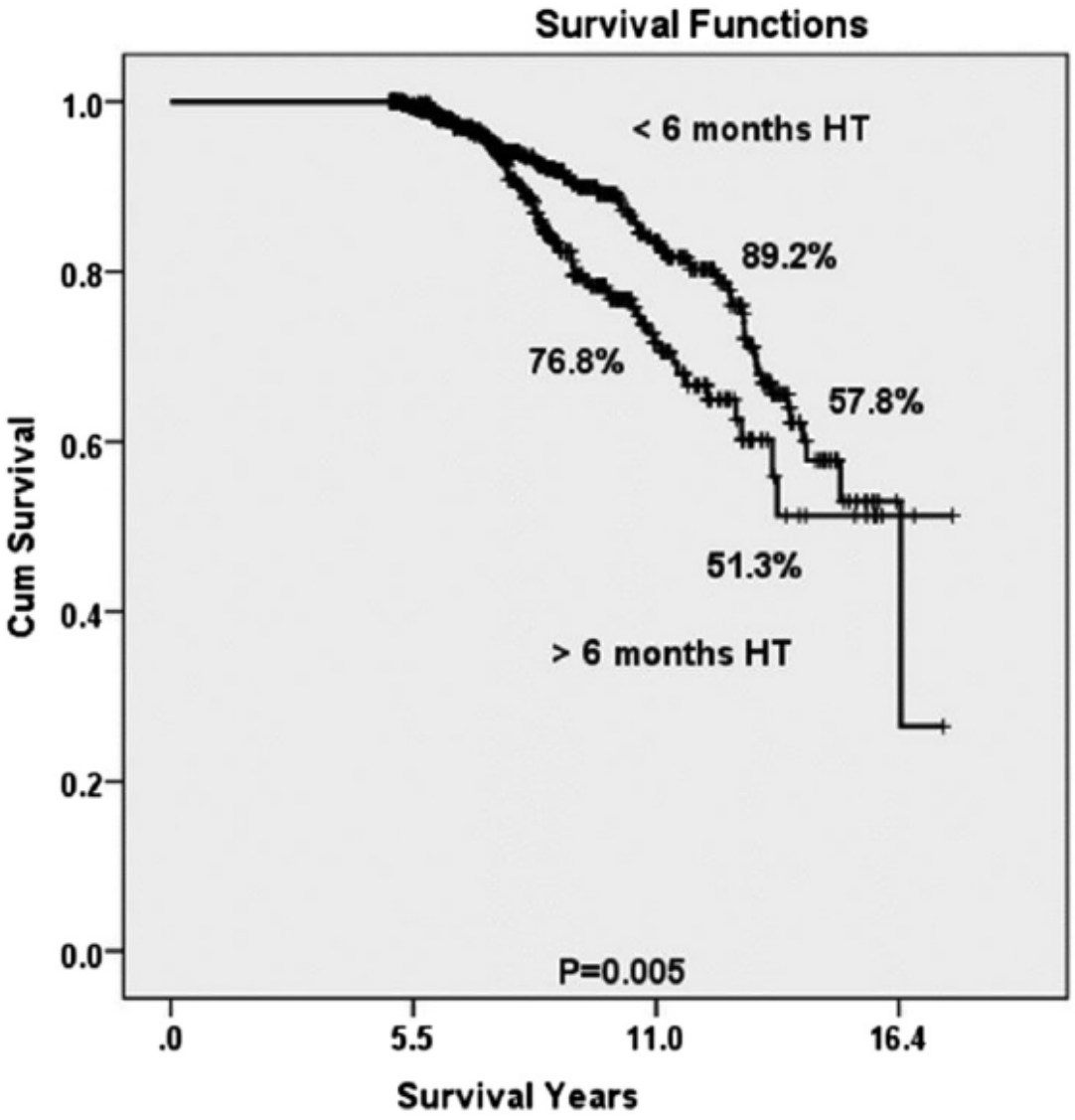

Figure 2. Ten and 15-year ACS in men with 6 months or less vs greater than 6 months of HT (median 6).

Cox Regression: Overall Survival

Factor	p value
Age	<.001
Hormone Therapy	.032
Smoking	.03
DM	.013
Atrial Fib	.04
Emphysema	.04

JAMA | Original Investigation

Radical Prostatectomy, External Beam Radiotherapy, or External Beam Radiotherapy With Brachytherapy Boost and Disease Progression and Mortality in Patients With Gleason Score 9-10 Prostate Cancer

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IMPORTANCE The optimal treatment for Gleason score 9-10 prostate cancer is unknown.

OBJECTIVE To compare clinical outcomes of patients with Gleason score 9-10 prostate cancer after definitive treatment.

DESIGN, SETTING, AND PARTICIPANTS Retrospective cohort study in 12 tertiary centers (11 in the United States, 1 in Norway), with 1809 patients treated between 2000 and 2013.

EXPOSURES Radical prostatectomy (RP), external beam radiotherapy (EBRT) with androgen deprivation therapy, or EBRT plus brachytherapy boost (EBRT+BT) with androgen deprivation therapy.

MAIN OUTCOMES AND MEASURES The primary outcome was prostate cancer–specific mortality; distant metastasis-free survival and overall survival were secondary outcomes.

RESULTS Of 1809 men, 639 underwent RP, 734 EBRT, and 436 EBRT+BT. Median ages were 61, 67.7, and 67.5 years; median follow-up was 4.2, 5.1, and 6.3 years, respectively. By 10 years, 91 RP, 186 EBRT, and 90 EBRT+BT patients had died. Adjusted 5-year prostate cancer–specific mortality rates were RP, 12% (95% CI, 8%-17%); EBRT, 13% (95% CI, 8%-19%); and EBRT+BT, 3% (95% CI, 1%-5%). EBRT+BT was associated with significantly lower prostate cancer–specific mortality than either RP or EBRT (cause-specific HRs of 0.38 [95% CI, 0.21-0.68] and 0.41 [95% CI, 0.24-0.71]). Adjusted 5-year incidence rates of distant metastasis were RP, 24% (95% CI, 19%-30%); EBRT, 24% (95% CI, 20%-28%); and EBRT+BT, 8% (95% CI, 5%-11%). EBRT+BT was associated with a significantly lower rate of distant metastasis (propensity-score-adjusted cause-specific HRs of 0.27 [95% CI, 0.17-0.43] for RP and 0.30 [95% CI, 0.19-0.47] for EBRT). Adjusted 7.5-year all-cause mortality rates were RP, 17% (95% CI, 11%-23%); EBRT, 18% (95% CI, 14%-24%); and EBRT+BT, 10% (95% CI, 7%-13%). Within the first 7.5 years of follow-up, EBRT+BT was associated with significantly lower all-cause mortality (cause-specific HRs of 0.66 [95% CI, 0.46-0.96] for RP and 0.61 [95% CI, 0.45-0.84] for EBRT). After the first 7.5 years, the corresponding HRs were 1.16 (95% CI, 0.70-1.92) and 0.87 (95% CI, 0.57-1.32). No significant differences in prostate cancer–specific mortality, distant metastasis, or all-cause mortality (≤7.5 and >7.5 years) were found between men treated with EBRT or RP (cause-specific HRs of 0.92 [95% CI, 0.67-1.26], 0.90 [95% CI, 0.70-1.14], 1.07 [95% CI, 0.80-1.44], and 1.34 [95% CI, 0.85-2.11]).

CONCLUSIONS AND RELEVANCE Among patients with Gleason score 9-10 prostate cancer, treatment with EBRT+BT with androgen deprivation therapy was associated with significantly better prostate cancer–specific mortality and longer time to distant metastasis compared with EBRT with androgen deprivation therapy or with RP.

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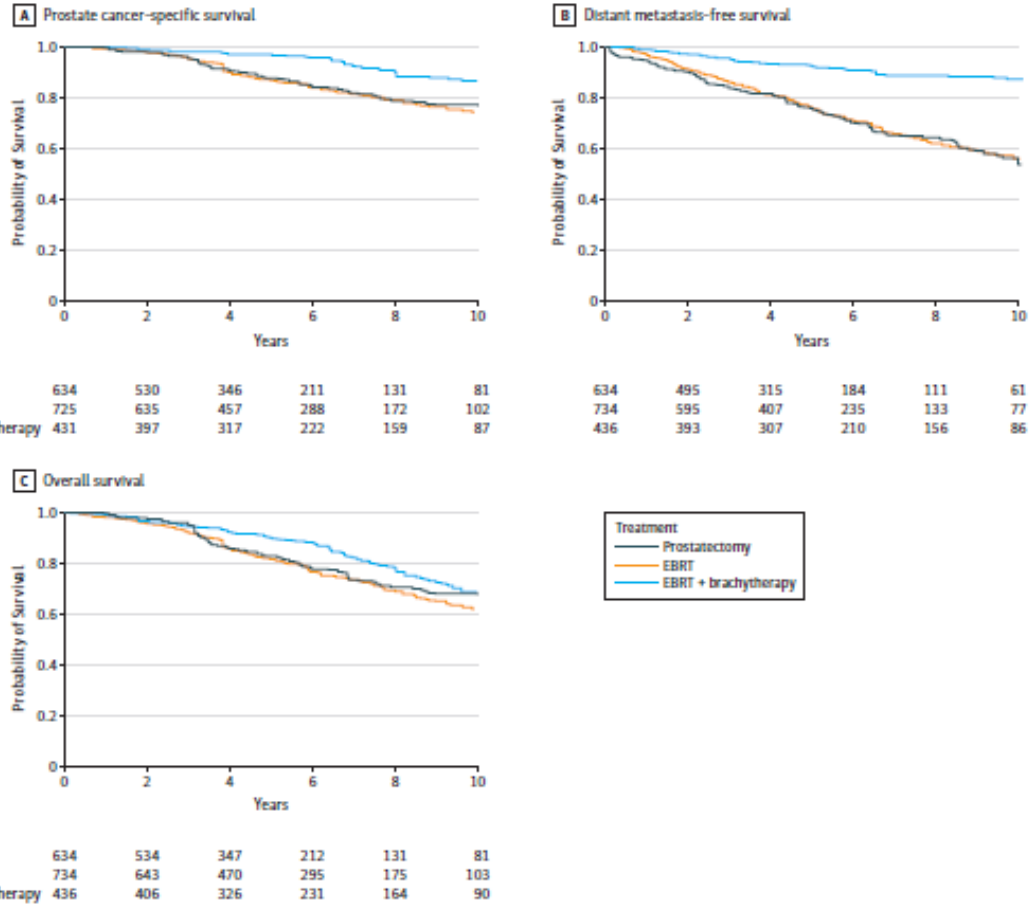
Figure. Adjusted Survival Curves for Prostate Cancer-Specific Survival, Distant Metastasis-Free Survival, and Overall Survival by Treatment Group, Weighted by the Inverse Probability of Treatment



No. at risk

Prostatectomy	634	530	346	211	131	81
EBRT	725	635	457	288	172	102
EBRT + brachytherapy	431	397	317	222	159	87

634	495	315	184	111	61
734	595	407	235	133	77
436	393	307	210	156	86

No. at risk

Prostatectomy	634	534	347	212	131	81
EBRT	734	643	470	295	175	103
EBRT + brachytherapy	436	406	326	231	164	90

EBRT indicates external beam radiotherapy; and EBRT+BT, external beam radiotherapy with a brachytherapy boost. Median follow-up for each treatment cohort was as follows: EBRT, 5.1 years (interquartile range, 2.9-7.7 years); EBRT+BT, 6.3 years (interquartile range, 3.9-9.4 years); and surgery, 4.2 years (interquartile range, 2.5-7.0 years). Adjusted curves were generated with Kaplan-Meier methods with inverse probability of treatment weights, calculated with propensity scores that were determined by using multinomial logistic regression with treatment cohort as the outcome and age, ln(initial prostate-specific antigen level), clinical T stage, and Gleason score as pretreatment, prognostic covariates. Numbers at baseline differ for A from both B and C because not all patients had known cause-of-death information to compute prostate cancer-specific survival.

Clinical Investigation

Androgen Suppression Combined with Elective Nodal and Dose Escalated Radiation Therapy (the ASCENDE-RT Trial): An Analysis of Survival Endpoints for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost to a Dose-Escalated External Beam Boost for High- and Intermediate-risk Prostate Cancer

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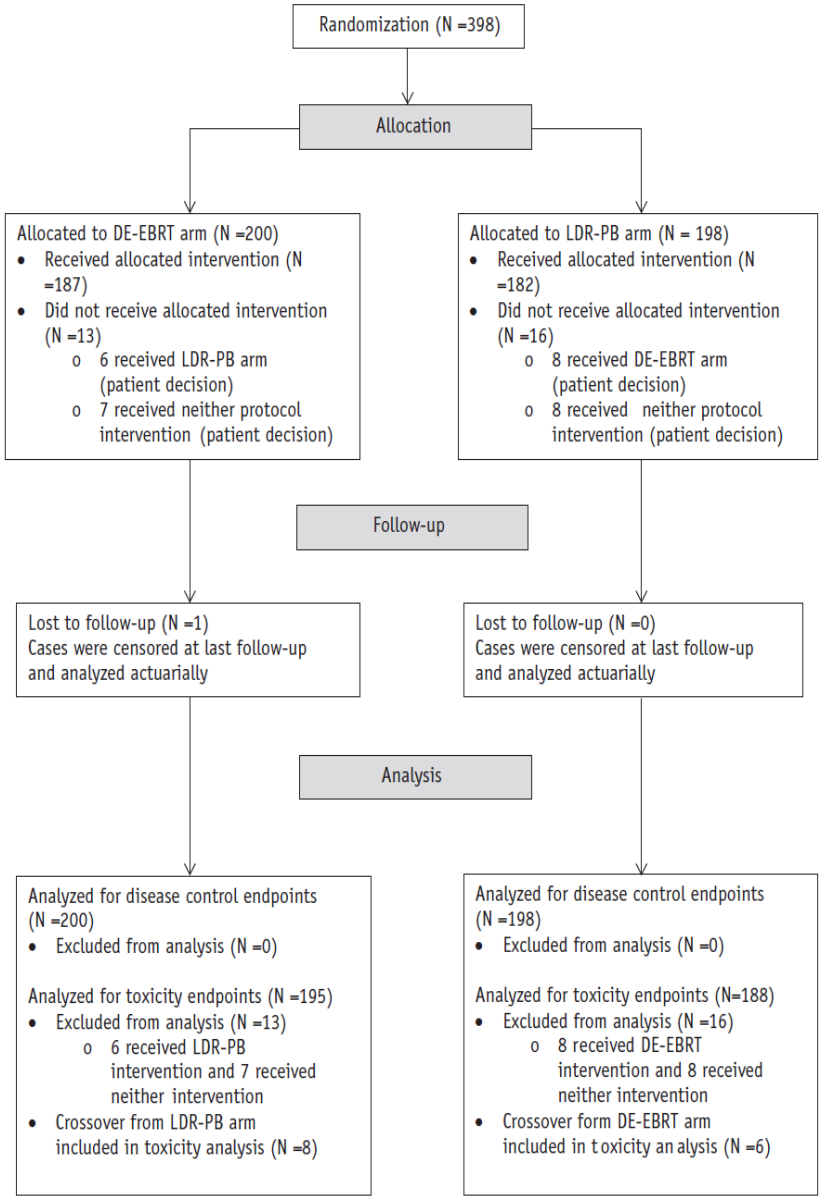

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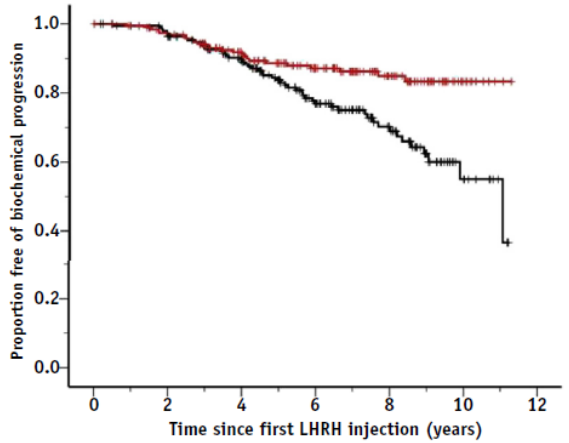
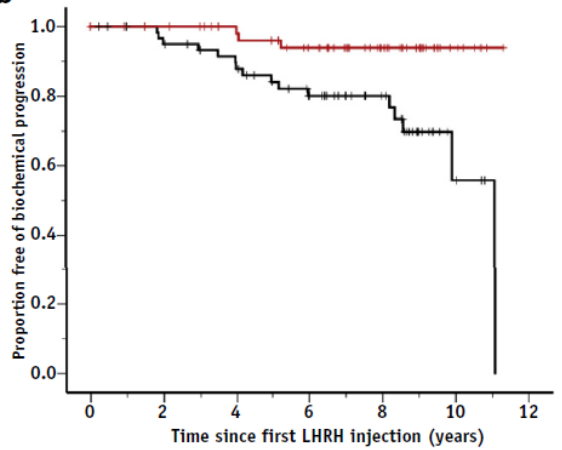


Numbers at risk:

Time (yrs)	0	2	3	4	5	6	7	8	9	10
DE-EBRT	200	186	168	145	119	93	74	52	27	11
LDR-PB	198	184	168	147	127	106	86	59	38	14

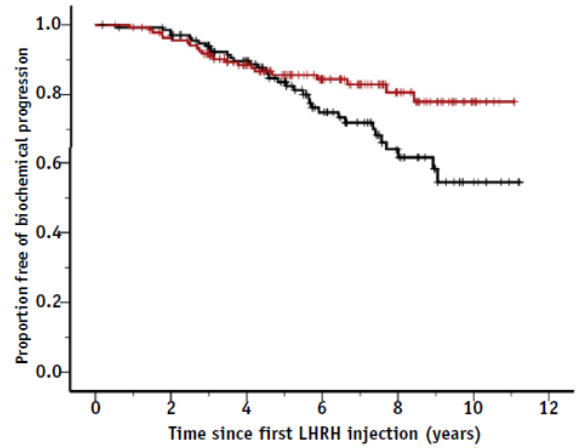
b



Numbers at risk:

Time (yrs)	0	2	3	4	5	6	7	8	9	10
DE-EBRT	63	57	54	49	43	38	30	25	12	4
LDR-PB	59	55	54	50	47	42	35	26	7	6

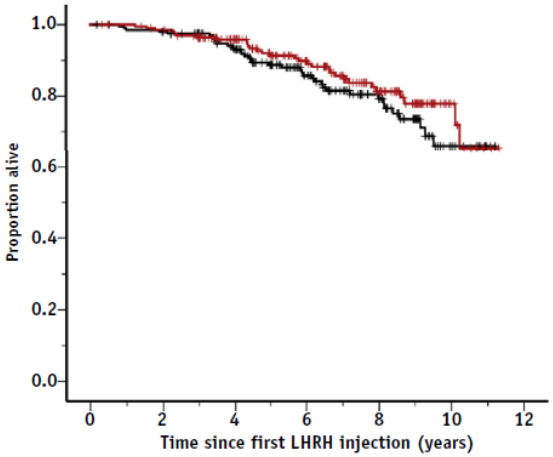
c



Numbers at risk:

Time (yrs)	0	2	3	4	5	6	7	8	9	10
DE-EBRT	137	129	114	96	76	55	44	27	15	7
LDR-PB	139	128	114	97	80	64	51	33	21	8

d



Numbers at risk:

Time (yrs)	0	2	3	4	5	6	7	8	9	10
DE-EBRT	200	192	184	161	134	109	85	66	40	16
LDR-PB	198	191	182	160	137	116	94	65	41	15

Clinical Investigation

ASCENDE-RT: An Analysis of Treatment-Related Morbidity for a Randomized Trial Comparing a Low-Dose-Rate Brachytherapy Boost with a Dose-Escalated External Beam Boost for High- and Intermediate-Risk Prostate Cancer

Sree Rodda, MBBS, MRCP, FRCR,* Scott Tyldesley, MD, FRCPC,*,† W. James Morris, MD, FRCPC,*,† Mira Keyes, MD, FRCPC,*,† Ross Halperin, MD, FRCPC,†,‡ Howard Pai, MD, FRCPC,†,§ Michael McKenzie, MD, FRCPC,*,† Graeme Duncan, MB, ChB, FRCPC,*,† Gerard Morton, MB, MRCPI, FRCPC, FFRRCSI,‖,¶ Jeremy Hamm, MSC,# and Nevin Murray, MD, FRCPC*,**

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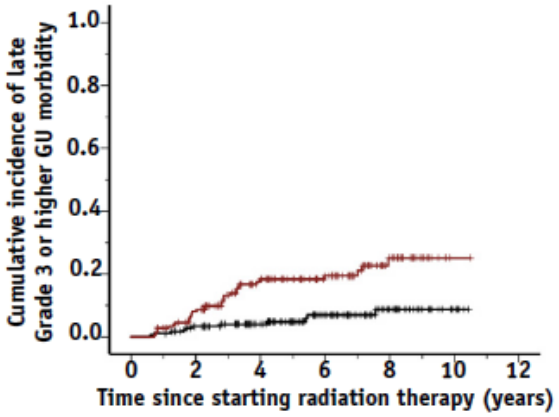
Table 3 Worst grade of late GU and GI toxicity experienced (5-year actuarial cumulative incidence and hazard ratios)

Maximum grade	DE-EBRT (%) (n=195)	LDR-PB (%) (n=188)	Hazard ratio: LDR-PB vs DE-EBRT	*P*
Cumulative incidence of late GU side effects at 5 y				
0	29.6 (23-36)	20.6 (9-32)	0.51 (0.32-0.80)	.003*
1	43.8 (36-51)	33.7 (27-41)	0.75 (0.54-1.04)	.088
2	20.6 (14-27)	32.8 (26-40)	1.97 (1.3-3.00)	.002*
3	5.2 (1-8)	18.4 (12-25)	3.46 (1.7-7.07)	<.001*
4/5	0.6 (0-2)	2.1 (0-6)	2.05 (0.19-22.6)	.559
Cumulative incidence of late GI side effects at 5 y				
0	35.8 (28-42)	31.3 (23-38)	0.83 (0.56-1.23)	.343
1	48.2 (41-56)	42.0 (35-49)	0.86 (0.63-1.16)	.322
2	20.2 (14-26)	31.3 (17-45)	1.33 (0.86-2.08)	.205
3	3.2 (0-6)	8.1 (3-13)	2.16 (0.81-5.75)	.124
4/5	0	1.0	N/A	N/A

Abbreviations as in Tables 1 and 2.
Values in parentheses are 95% confidence intervals.
* Statistically significant.

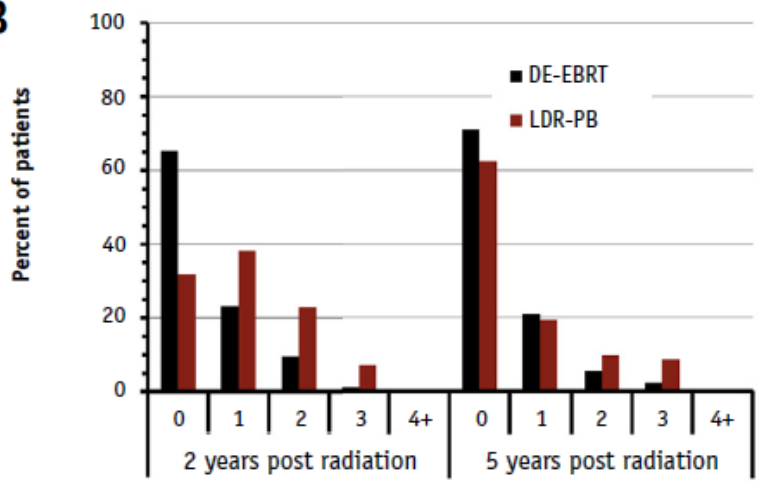
A



Numbers at risk:

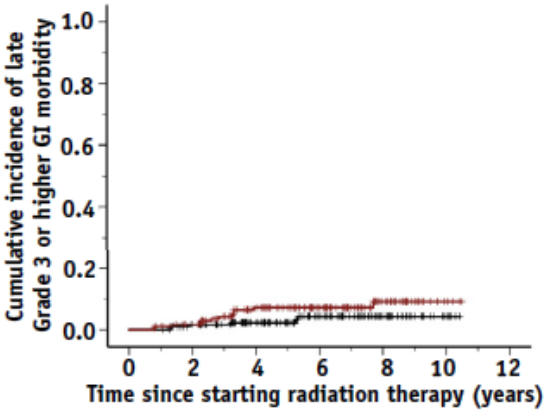
Years	0	2	4	6	8	10
DE-EBRT	195	167	125	79	41	8
LDR-PB	188	158	109	69	28	1

B



The prevalence of late GU morbidity by grade

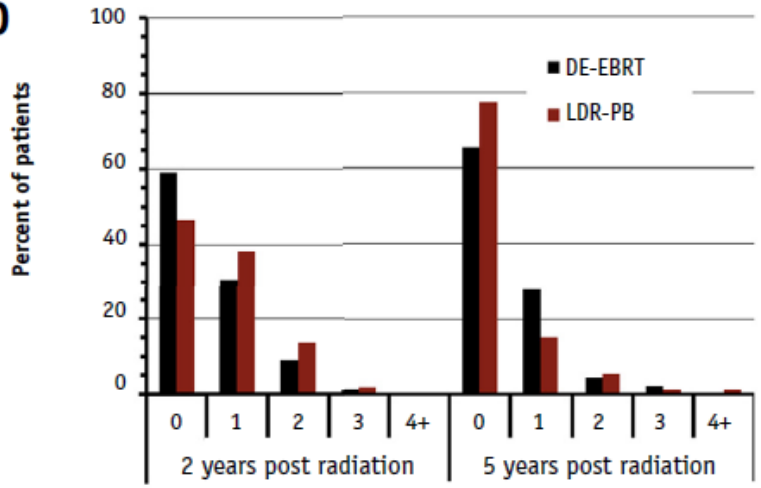
C



Numbers at risk:

Years	0	2	4	6	8	10
DE-EBRT	195	172	129	80	41	9
LDR-PB	188	168	119	80	36	4

D



The prevalence of late GI morbidity by grade