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Five-fraction SBRT Versus Other RT Modalities in Prostate Cancer

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New York, USA

Disclosures

Speaking Honorarium

Received honorarium and travel support for participation in this meeting

Research Collaborations

Montefiore Medical Center maintains ongoing research collaboration agreements with Accuray and Varian Medical Systems

Outline

- SBRT and IMRT
  - Meta-analysis
  - Hypo-RT-PC
  - Pace-B
  - NRG-GU005
  - Dose escalation
- SBRT and Brachytherapy
  - LDR
  - HDR

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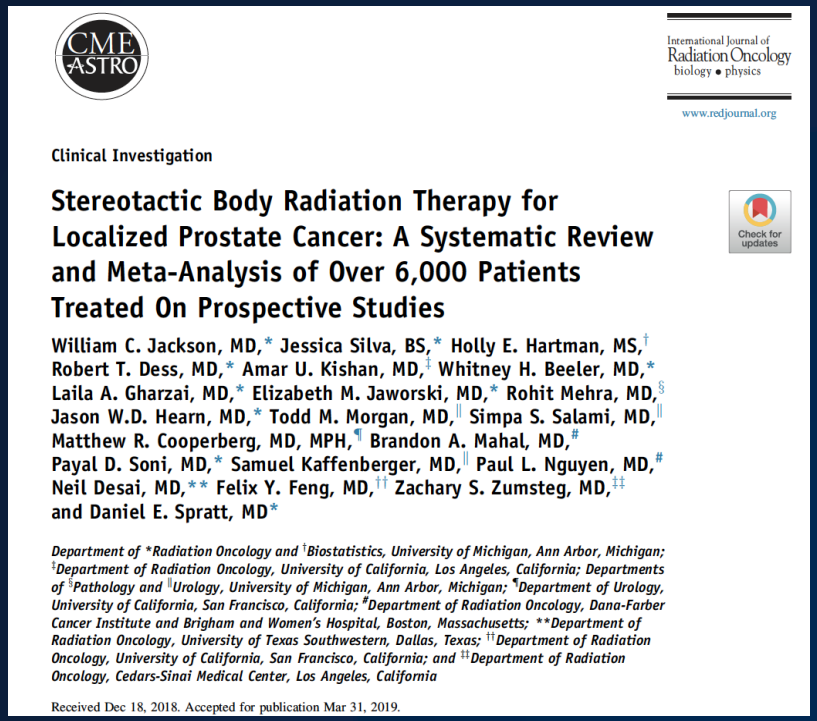

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Clinical Investigation

Stereotactic Body Radiation Therapy for Localized Prostate Cancer: A Systematic Review and Meta-Analysis of Over 6,000 Patients Treated On Prospective Studies

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Prospective series assessing curative intent SBRT for localized prostate cancer

- bRFS
- Physician reported toxicity
- Patient reported outcomes

- Thirty-eight unique prospective series were identified comprising of 6116 patients.

- Articles: 1/1990 to 1/ 2018
- Abstracts: 1/ 2013 to 3/2018

- Median follow-up: 39 months

- Risk group breakdown:
  - 45% low risk
  - 47% intermediate risk
  - 8% high risk

- Mean Dose/ Fraction 7.4 Gy (5-10 Gy)
- Mean Fractions 5 (4-9)

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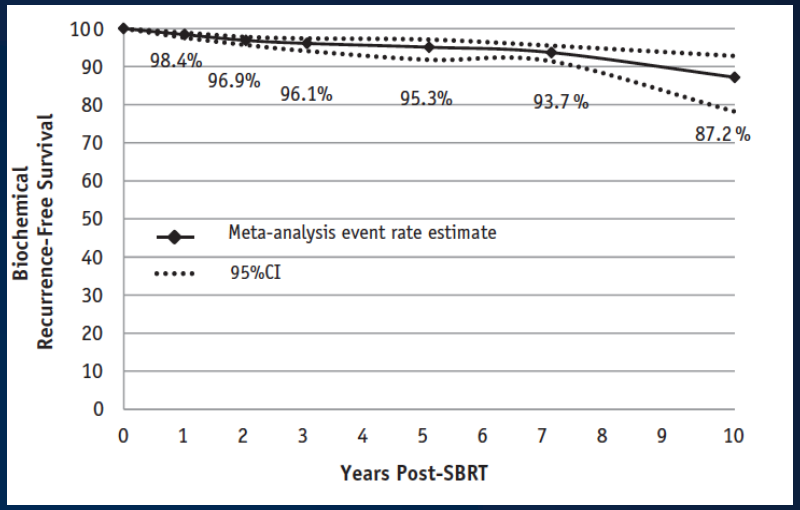
Meta-analysis

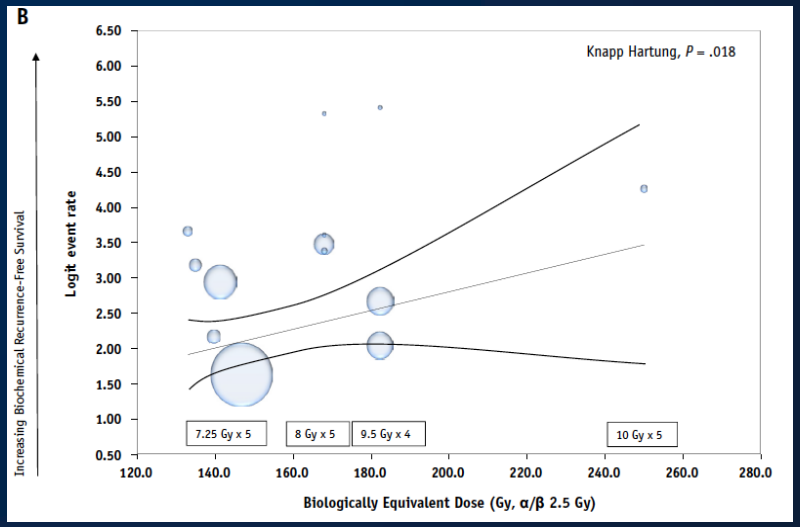
Overall b-RFS rates:

5-year: 95.3% (95% CI, 91.3%-97.5%)
7-year: 93.7% (95% CI, 91.4%-95.5%)



Increasing SBRT dose:

Improved biochemical control (P < .018)
Worse late Gr. 3 GU toxicity (P < 0.014)



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Toxicity

Estimated late toxicity:

Grade 3+ GU: 2.0% (95% CI, 1.4%-2.8%)
Grade 3+ GI: 1.1% (95% CI, 0.6%-2.0%)

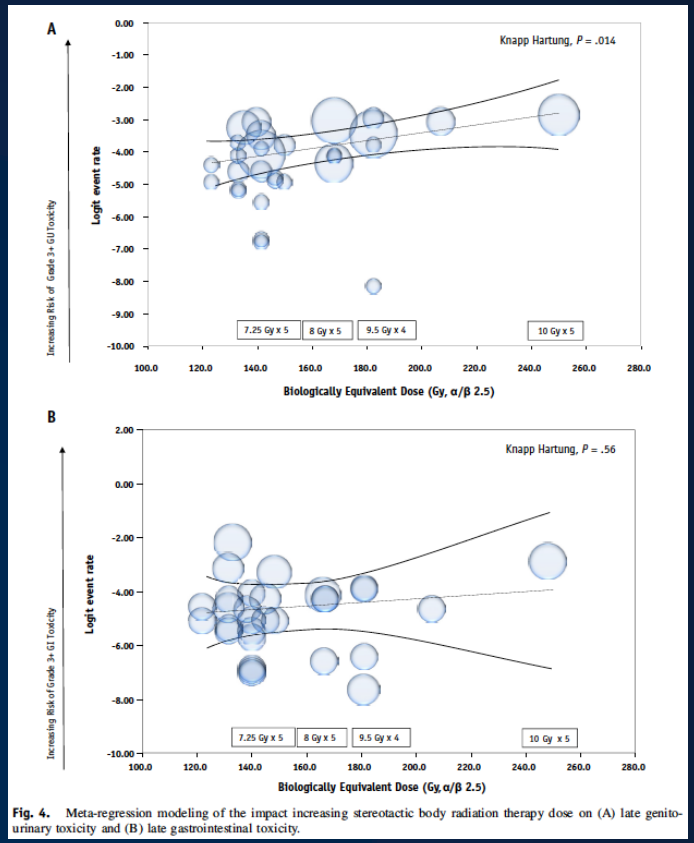
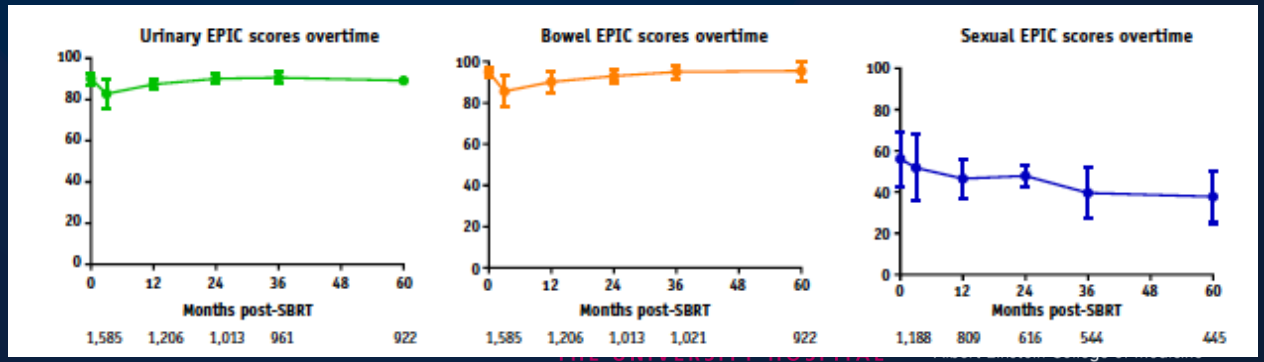


Fig. 4. Meta-regression modeling of the impact increasing stereotactic body radiation therapy dose on (A) late genitourinary toxicity and (B) late gastrointestinal toxicity.

By 2 years post-SBRT, EPIC urinary and bowel domain scores returned to baseline



Scandinavian trial (HYPO-RT-PC)

Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial

Anders Widmark, Adalsteinn Gunnlaugsson, Lars Beckman, Camilla Thellenberg-Karlsson, Morten Hoyer, Magnus Lagerlund, Jon Kindblom, Claes Ginman, Bengt Johansson, Kirsten Björnlinger, Mihajl Seke, Måns Agrup, Per Fransson, Björn Tavelin, David Norman, Björn Zackrisson, Harald Anderson, Elisabeth Kjellén, Lars Franzén, Per Nilsson

- Randomized phase III Non-inferiority trial
- N = 1200 patients from 12 centers
  - Intermediate (89%) or high risk (11%)
  - T1c-T3a + PSA (10-20) or T3a or GS > 7

- Treatment arms:
  - 78 Gy (2Gy / fx) over 8 weeks versus
  - 42.7 Gy (6.1Gy / fx) over 2.5 weeks (every other weekday including 2 weekends)
  - No ADT allowed

- Primary end point: FFS at 5 years
- Secondary end point: QOL

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Hypo-RT-PC: Radiation Details

- RT technique:
  - 80% 3D-CRT
  - 20% IMRT/VMAT
- Image-guidance:
  - 10% BeamCath
  - 90% gold fiducials
- MRI not mandatory
- No rectal spacer

- Targets:
  - CTV: prostate only (no SV)
  - CTV to PTV margins:
    - BeamCath:
      - SBRT: 6mm, 4 mm posteriorly
      - Conventional: 6mm, 4mm posteriorly for first 4 fx --> 10-15mm
    - Gold fiducials: 7mm all around (both groups)

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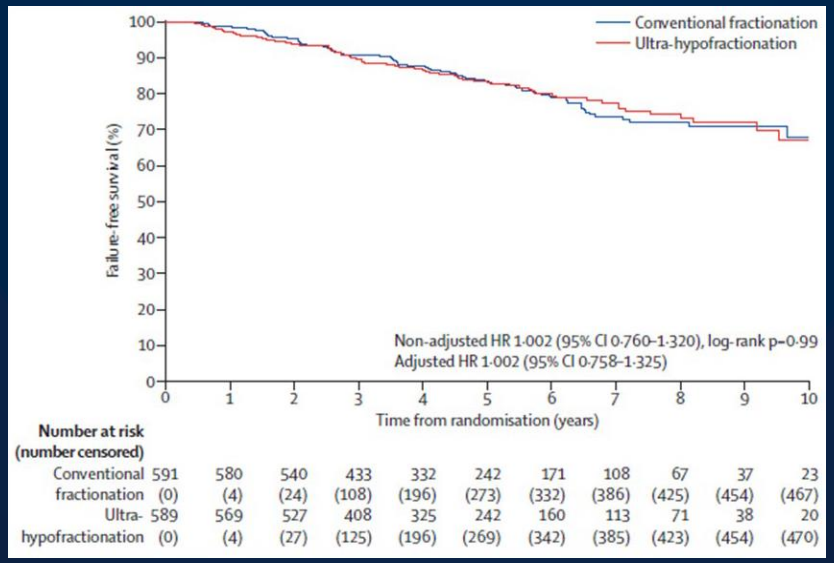
Results

Failure free survival

	5 year (%)
78Gy in 39 fx	83.8
42.7 Gy in 7 fx	83.7

Overall survival

	5 year (%)
78Gy in 39 fx	96
42.7 Gy in 7 fx	94



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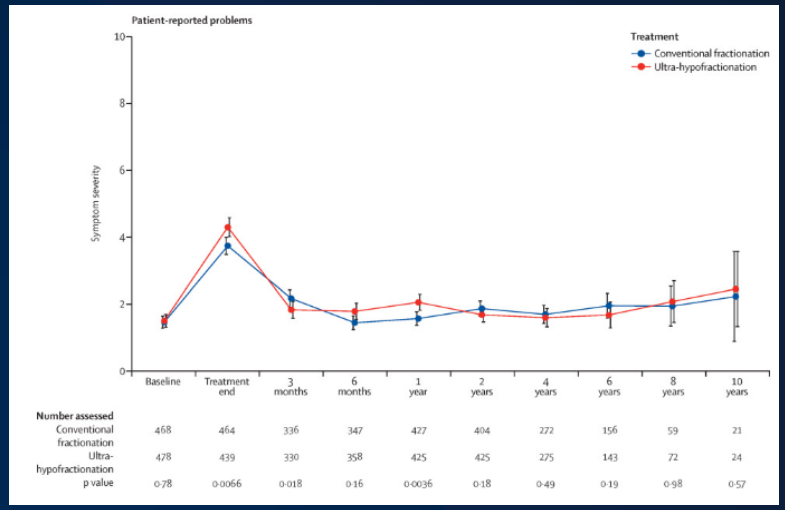
Results: Toxicity (Grade 2+)

GU (conventional vs SBRT)

Acute: 23% vs 28% (p=0.057)

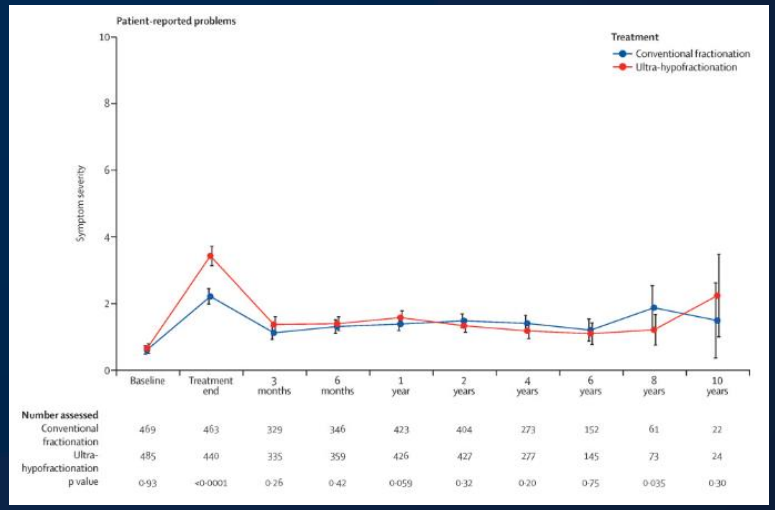
1 year: 2% vs 6% (p<0.01)



GI (conventional vs SBRT)

Acute: 23% vs 28% (p=0.26)

1 year: 4% vs 1% (p=0.059)



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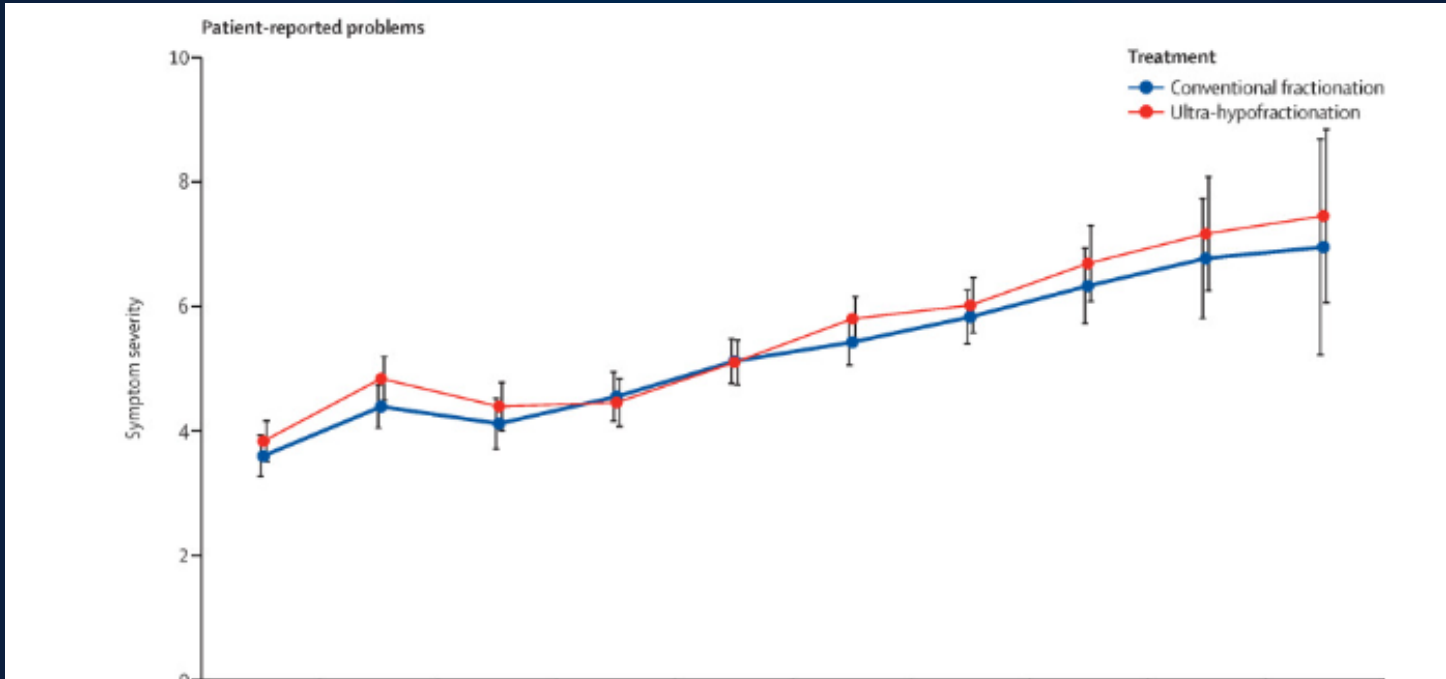
Hypo-RT-PC: Erectile Function



Number assessed	Baseline	Treatment end	3 months	6 months	1 year	2 years	4 years	6 years	8 years	10 years
Conventional fractionation	453	443	318	331	412	396	266	153	61	21
Ultra-hypofractionation	470	414	319	346	410	405	260	135	66	22
p value	0·31	0·066	0·28	0·62	0·74	0·18	0·57	0·41	0·47	0·90

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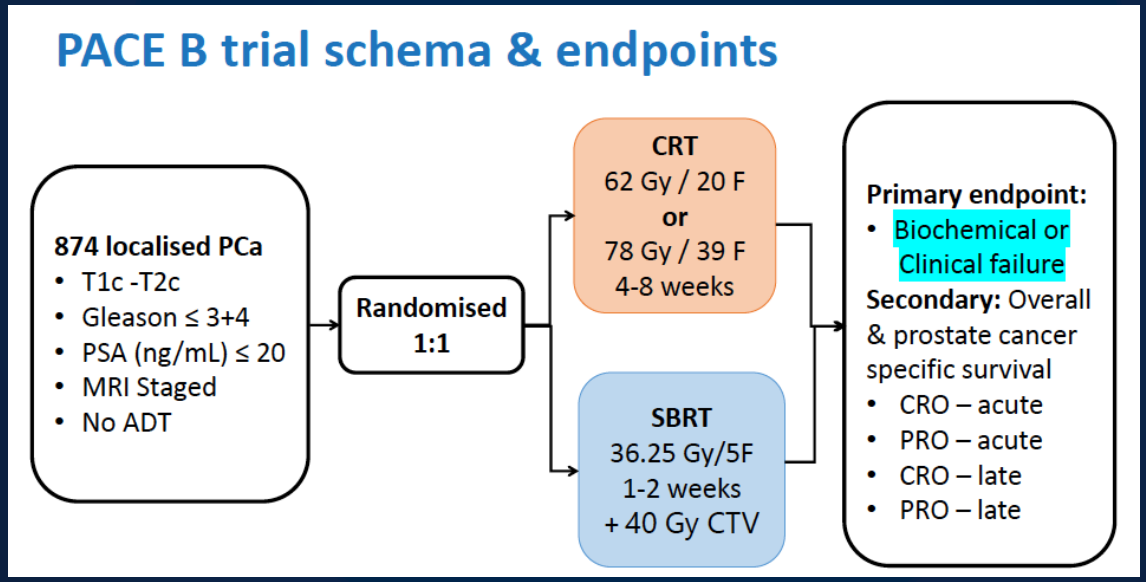
PACE-B: A Phase III randomized controlled trial of Stereotactic Body Radiotherapy in localized prostate cancer

- Randomized Phase-III, non-inferiority trial
- N = 874 patients from 38 sites across UK, Ireland, Canada



N Engl J Med. 2024 October 16; 391(15): 1413–1425. doi:10.1056/nejmoa2403365.

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Patient Characteristics

Baseline Characteristics	CRT (N=441)		SBRT (N=433)		Total (N=874)	
	n	%	n	%	n	%
PSA<10	303	(68.7)	297	(68.6)	600	(68.7)
PSA 10-20	138	(31.3)	136	(31.4)	274	(31.6)
Percentage positive cores						
<50%	304	(68.9)	287	(66.3)	591	(67.6)
≥50%	137	(31.1)	146	(33.7)	283	(32.4)
NCCN risk group						
Low	41	(9.3)	32	(7.4)	73	(8.4)
Intermediate	400	(90.7)	401	(92.6)	801	(91.7)
Favorable	106	(26.5)	86	(21.5)	192	(24.0)
Unfavorable	294	(73.5)	315	(78.6)	609	(76.0)
Prostate volume						
<40 mL	163	(37.0)	192	(44.3)	355	(40.6)
40 - <80 mL	223	(50.6)	198	(45.7)	421	(48.2)
80+ mL	28	(6.3)	22	(5.3)	51	(5.8)
Unknown	27	(6.1)	20	(4.6)	47	(5.4)
Testosterone [μmol/L]						
Median (IQR)	11.3	(8.7, 15.0)	11.5	(9.0, 15.0)	11.3	(8.9, 15.0)
N (Range)	407	(0.4, 30.6)	403	(0.4, 30.5)	810	(0.4, 30.6)
Unknown	34		30		64	
Baseline IPSS grade						
None	21	(4.8)	16	(3.7)	37	(4.3)
Mild	197	(44.7)	202	(46.7)	399	(45.7)
Moderate	141	(32.0)	136	(31.4)	277	(31.7)
Severe	23	(5.2)	20	(4.6)	43	(4.9)
Unknown	59	(13.4)	59	(13.6)	118	(13.5)

SBRT Technique:

- PTV36.25 margin: 4-5 mm, Posterior 3-5 mm;
- CTV40: no expansion.
- Proximal 1cm SV included for Int-risk.

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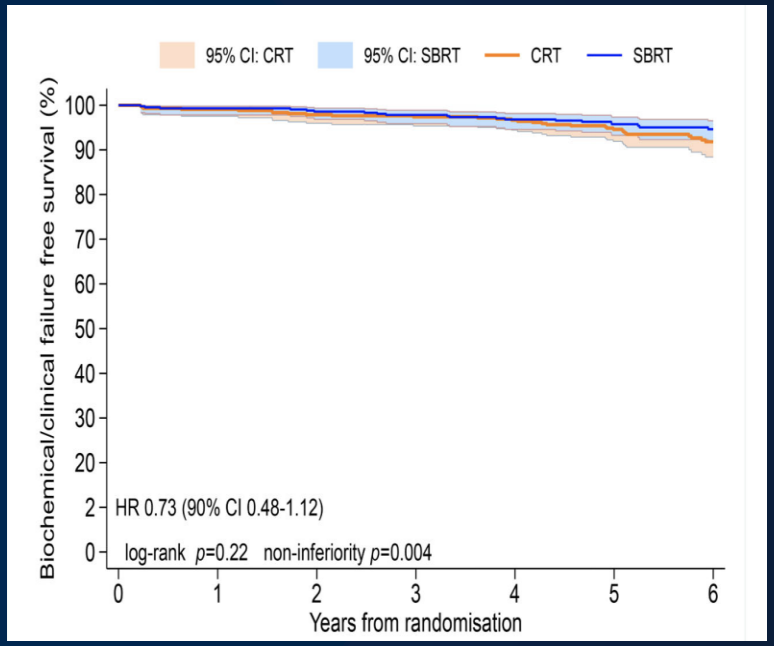
PACE-B: Results

- Median follow-up: 74.0 months
- 5-year biochemical/clinical failure free-rate
  - 94.6% CRT vs 95.8% SBRT
- ***SBRT was non-inferior to CRT***
  - Unadjusted HR 0.73 (90% CI: 0.48, 1.12; p-value for non-inferiority 0.004)



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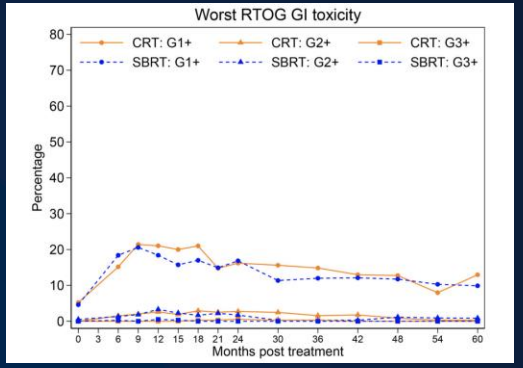
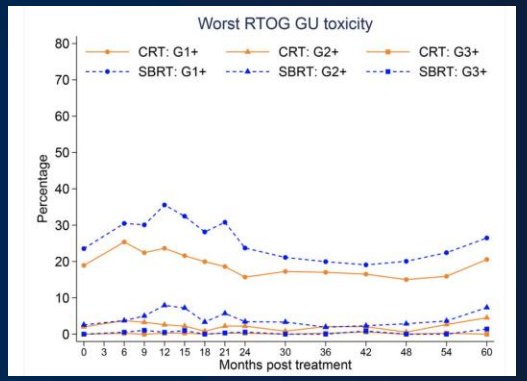
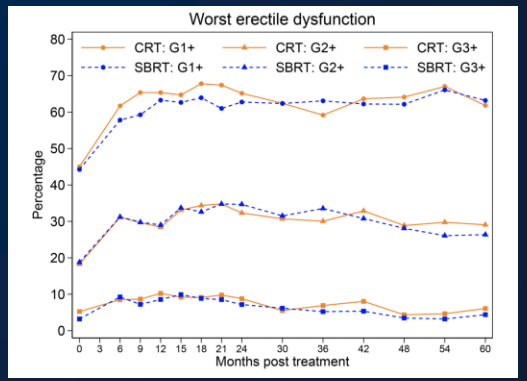
PACE-8
Gr2+ RTOG Toxicity:
5-year cumulative rates

Toxicity	CRT	SBRT	p value
Genitourinary	18.3%	26.9%	P<0.001
Gastrointestinal	10.2%	10.7%	P=0.94
Erectile dysfunction	29.1%	26.4%	P=0.46







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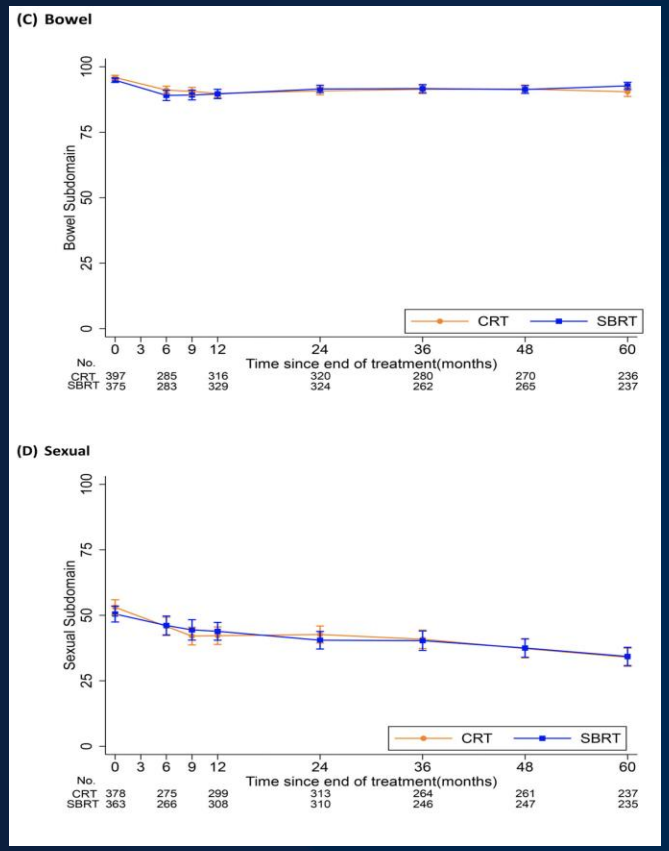
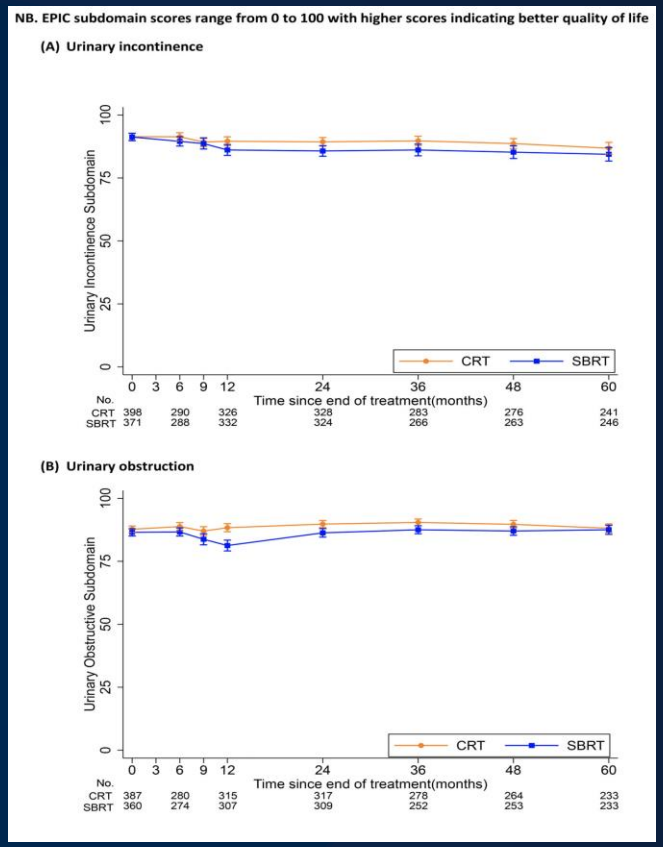
PRO (EPIC-26)





Participants reported stable urinary and bowel symptoms from 2 to 5 years, with little difference between treatment groups

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NRG-GU005:

A phase III trial of SBRT vs. hypo-fractionated IMRT for localized intermediate risk prostate cancer

- ***Hypothesis:*** SBRT is superior to moderately hypofractionated IMRT
- ***Primary endpoints:***
  - **DFS:** Time to biochemical failure, local failure, regional failure, distant metastasis or death from any cause
  - **QOL (PRO):** GI and GU toxicity as measured by EPIC-26 bowel and urinary domains, at 24 months by minimal clinically important difference (MCID)

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NRG-GU005: Trial Schema

STRATIFY	***Risk Group*** 1.Gleason score 7(3+4) with PSA <10 ng/mL 2.Gleason score 7(3+4) with 10 ng/mL <= PSA < 20 ng/mL 3.Gleason score 6(3+3) with 10 ng/mL < PSA < 20 ng/mL ***Use of Rectal Manipulation*** 1. No 2. Rectal balloon 3. SpaceOAR 4. SpaceOAR and rectal balloon IMRT Standard Arm 1) 70 Gy in 28 fractions 2) 60 Gy in 20 fractions	RANDOMIZE	**Arm 1: IMRT** 70 Gy in 28 fractions of 2.5 Gy to the prostate or 60 Gy in 20 fractions of 3 Gy +/- proximal 1cm of seminal vesicles Minimal Margins: 8 mm uniform in expansion, 5 mm posteriorly **Arm 2: SBRT** 36.25 Gy in 5 fractions of 7.25 Gy to the prostate +/- proximal 1 cm of seminal vesicles Minimal Margins: 5 mm superior inferior & laterally, 3 mm anterior & posterior

Mandatory MRI fusion

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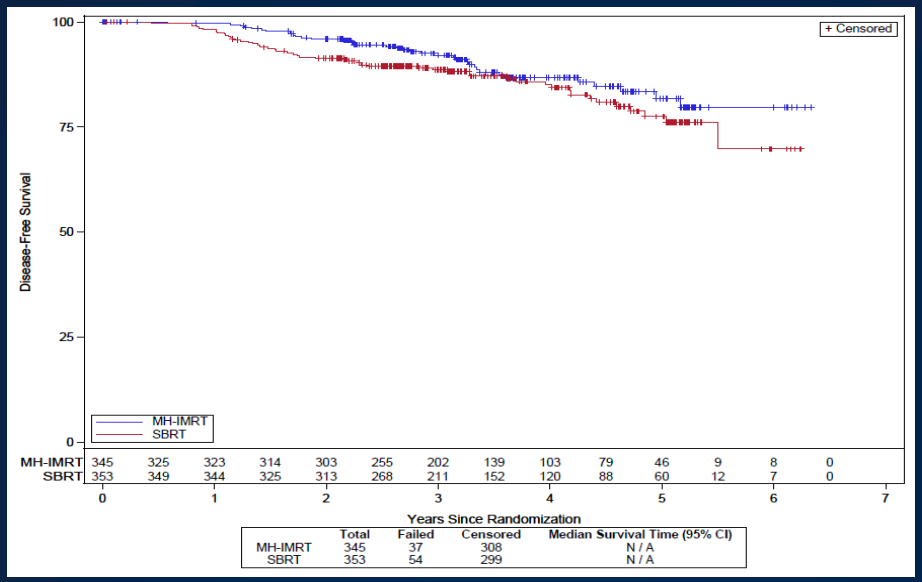
NRG GU-005 Results: IMRT vs SBRT

N = 698 (accrued between 11/2017 to 6/2022)



	IMRT	SBRT	Comments
DFS @3-years	92%	89%	Lack of SBRT superiority
bFailure @3-years	4%	8%	P=0.037
OS @ 5-years	94%	91%	P=0.66

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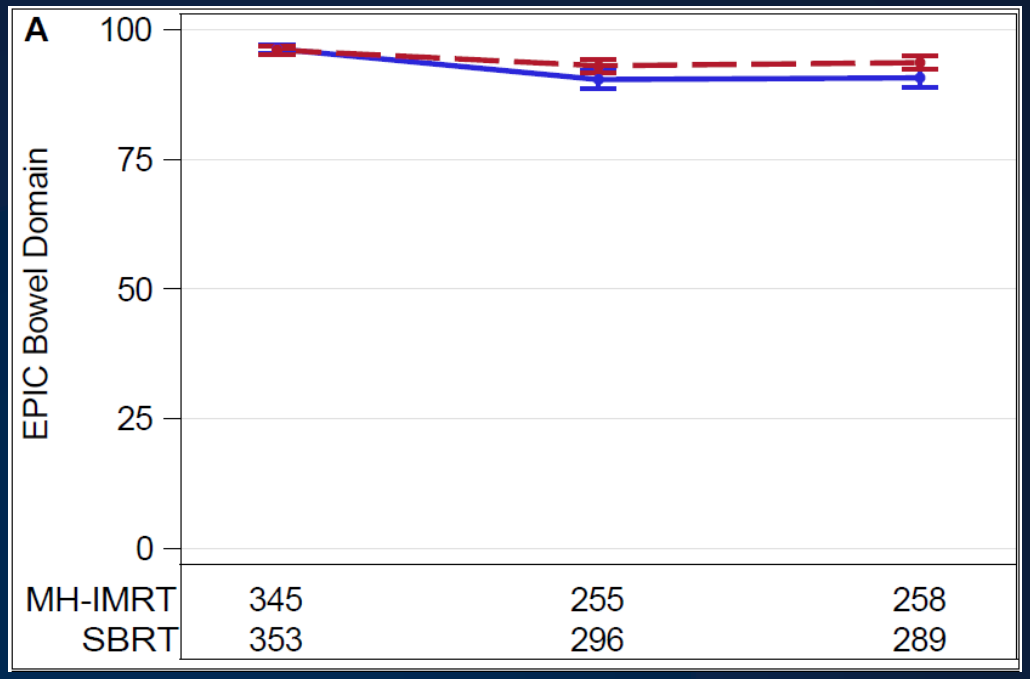
NRG GU-005: Rectal toxicity



24-month rate of MCID:

- SBRT=35% vs. IMRT=44% (**P=0.034 - *significant)***

Longitudinal treatment effect:

- LS Mean Diff= +2.68 (95% CI: 1.02–4.34) (**P=0.0016 -*significant*)**

Endpoint for reduced risk of rectal toxicity with SBRT was met

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•Urinary incontinence: SBRT patients had significantly better scores at two years (25.9% vs. 34.7%, p=0.023).

NRG GU-005: HRQOL Secondary EPIC Outcomes

- ***Sexual function:*** SBRT patients reported less decline in function at one year (34.3 % vs. 43.9%, p=0.026).
- ***Urinary incontinence:*** SBRT patients had significantly better scores at two years (25.9% vs. 34.7%, p=0.023).

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MSKCC - Montefiore - Northwell Phase I SBRT Dose Escalation Trial

Eligibility:

- Low / intermediate risk disease
- Max prostate volume 60 cc
- No ADT

- Accrued 136 patients

Int J Radiat Oncol Biol Phys. 2019 May 01; 104(1): 42–49. doi:10.1016/j.ijrobp.2018.12.045.

Five-Year Outcomes of a Phase 1 Dose-Escalation Study Using Stereotactic Body Radiosurgery for Patients With Low-Risk and Intermediate-Risk Prostate Cancer

Michael J. Zelefsky, MD[*], Marisa Kollmeier, MD[*], Sean McBride, MD[*], Melissa Varghese, BA[*], Borys Mychalczak, MD, Richard Gewanter, MD[*], Madhur K. Garg, MD[§], Laura Happersett, MS[†], Debra A. Goldman, MS[‡], Isaac Pei, PhD[*], Mary Lin, BA[*], Zhigang Zhang, PhD[‡], Brett W. Cox, MD[‖]

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Treatment:

- SBRT with initial dose level 32.5 Gy in 5 fractions
- Dose escalation to 35 Gy, 37.5 Gy, and 40 Gy in 5 fractions

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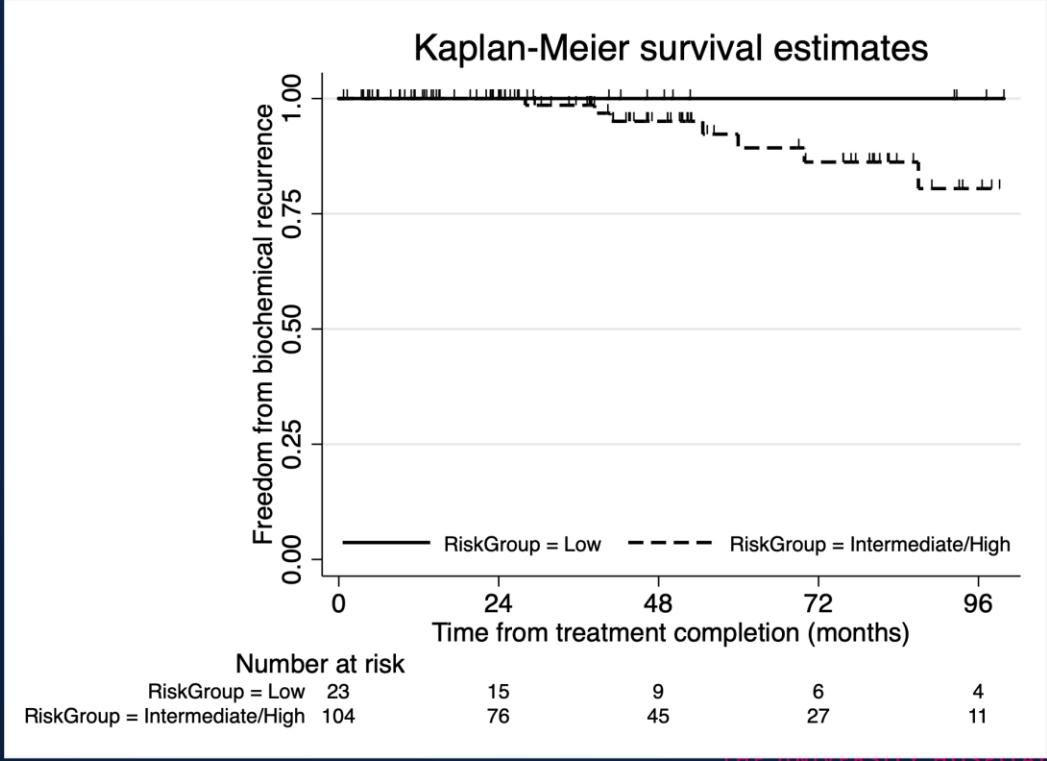
Phase I SBRT Dose Escalation Trial Results

Dose Level	32.5 Gy	35 Gy	37.5 Gy	40 Gy
PSA failure @5-years	15%	6%	0%	0%
Positive biopsy @2-years (p=0.13)	47.6%	19.2%	16.7%	7.7%



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Toxicity Results

- No significant differences in acute or late GI and GU toxicity among the different dose levels
- Significantly different patterns of urinary symptoms and their time to symptom resolution during the follow-up period for the treated cohorts.

Toxicity outcomes for treated patients for each dose cohort

Toxicity		All patients	Dose 32.5 Gy	35 Gy	37.5 Gy	40 Gy	*P* value
Acute GI toxicity grade ≥2	Grade 2	6 (4.4)	0(0)	1 (2.9)	1 (2.8)	4 (11.4)	.16
Acute GU toxicity grade ≥2	Grade 2	22 (16.2)	5 (16.7)	8 (22.9)	3 (8.3)	6 (17.1)	.43
Late GU toxicity grade ≥2	Grade 2	37 (27.2)	7 (23.3)	9 (25.7)	10 (27.8)	11 (31.4)	.88
	Grade 3	1 (0.7)	0(0)	0(0)	0(0)	1 (2.9)	
Late SD toxicity grade ≥2	Grade 2	45 (33.1)	10 (33.3)	14 (40)	8 (22.2)	13 (37.1)	.36
	Grade 3	2 (1.5)	0 (0)	0(0)	2 (5.6)	0(0)	

Model for IPSS scores over time with interaction effect between dose and time

Characteristic			PE	95% CI	*P* value	Overall *P* value
Radiation therapy dose	-	35	1.20	−0.97 to 3.37	.28	0.15
		37.5	−0.72	−2.71 to 1.27	.47	
		40	0.02	−2.01 to 2.04	>.95	
		32.5	Ref			
Time point	12 mo		−0.02	−1.56 to 1.53	>.95	<.001 *
	24 mo		0.22	−1.37 to 1.81	.78	
	36 mo		1.02	−1.02 to 3.06	.32	
	Baseline		Ref			
Interaction between Time and Dose	12 mo	35	0.19	−2.06 to 2.44	.87	0.033 *
		37.5	2.29	0.01 to 4.57	.049 *	
		40	5.19	2.19 to 8.19	<.001	
		32.5	Ref			
	24 mo	35	0.14	−2.21 to 2.48	.91	
		37.5	1.49	−0.75 to 3.74	.19	
		40	2.31	−0.14 to 4.75	.06	
		32.5	Ref			
	36 mo	35	1.10	−2.11 to 4.32	.50	
		37.5	−0.07	−2.65 to 2.52	>.95	
		40	1.23	−1.73 to 4.18	.41	
		32.5	Ref			
	Baseline	35	Ref			
		37.5	Ref			
		40	Ref			
		32.5	Ref			

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Stereotactic body radiation therapy for prostate cancer: review of experience of a multicenter phase I/II dose-escalation study

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Introduction: Stereotactic body radiation therapy (SBRT) is an area of active investigation for treatment of prostate cancer. In our phase I dose-escalation study, maximum-tolerated dose (MTD) was not reached, and subsequently phase II study has been completed. The purpose of this article is to review our experiences of dose-escalated SBRT for localized prostate cancer.

Methods and materials: Patients enrolled to phase I/II study from 2006 to 2011 were reviewed. Prescription dose groups were 45, 47.5, and 50 Gray (Gy) in five fractions over 2.5 weeks. Toxicity and quality of life questionnaire data were collected and analyzed. Descriptive statistics were obtained in the form of means, medians, and ranges for the continuous variables, and frequencies and percentages for the categoric variables.

Results: Ninety-one patients were enrolled from five institutions. Median follow-up for prostate specific antigen (PSA) evaluation was 42 months. PSA control remains at 99%. While the MTD was not reached in the phase I study, excess high grade rectal toxicity

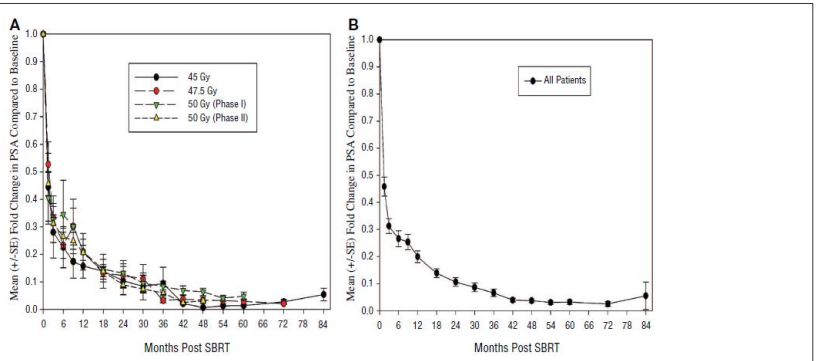

FIGURE 1 | Plot of mean fold change in PSA compared to baseline levels (A) by individual dose groups and (B) for all patients. S.E., standard error; PSA, prostate specific antigen; Gy, gray.

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Table 2 | Worst acute and delayed rectal toxicity in patients treated to 50 Gy dose in phase I and phase II studies.

Rectal toxicity	All patients ($n=91$)		50 Gy phase I ($n=14$)		50 Gy phase II ($n=47$)	
Grade	Acute No. (%)	Late No. (%)	Acute No. (%)	Late No. (%)	Acute No. (%)	Late No. (%)
0	39 (42.9)	38 (41.8)	5 (35.7)	5 (35.7)	18 (38.3)	15 (32)
1	33 (36.3)	27 (29.7)	7 (50)	6 (43)	16 (34)	15 (32)
2	17 (18.7)	21 (23.1)	2 (14.3)	2 (14.3)	11 (23.4)	13 (27.7)
3	1[a] (1.1)	3 (3.3)	0 (0)	0 (0)	1[a] (2.1)	3 (6.4)
4	1 (1.1)	2 (2.2)	0 (0)	1 (7.1)	1 (2.1)	1 (2.1)
Number of patients w/grade 3+ toxicity	6 (6.6%)		1 (7.1%)		5 (10.6%)	

[a] *For this patient, toxicity occurred on day 225 (acute period), but persisted to day 470, well into the delayed toxicity time period. Therefore, this patient was reported as having high grade acute and delayed toxicity. While seven total toxicities are reported, this occurred in a total of six patients.*

Table 2 Worst acute and delayed rectal toxicity in patients by radiation prescription dose level

	All patients (n=91)		45 Gy (n=15)		47.5 Gy (n=15)		50 Gy (n=61)	
Grade	Acute	Late	Acute	Late	Acute	Late	Acute	Late
0	39 (42.9)	38 (41.8)	9 (60.0)	10 (66.7)	7 (46.7)	8 (53.3)	23 (37.7)	20 (32.8)
1	33 (36.3)	27 (29.7)	6 (40.0)	4 (26.7)	4 (26.7)	2 (13.3)	23 (37.7)	21 (34.4)
2	17 (18.7)	21 (23.1)	0	1 (6.7)	4 (26.7)	5 (33.3)	13 (21.3)	15 (24.6)
3	1* (1.1)	3 (3.3)	0	0	0	0	1* (1.6)	3 (4.9)
4	1 (1.1)	2 (2.2)	0	0	0	0	1 (1.6)	2 (3.3)

Values are number (percentage).

* For this patient, toxicity occurred on day 225 (acute period) but persisted to day 470, well into the delayed toxicity time period. Therefore this patient was reported as having high-grade acute and delayed toxicity. Although 7 total toxicities are reported, this occurred in a total of 6 patients.

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SBRT – Elective Nodal RT (Ongoing Trials)

SATURN

SABR Including Regional Lymph Node Irradiation for Patients With High Risk Prostate Cancer (SATURN) (SATURN)

The safety and scientific validity of this study is the responsibility of the study sponsor and investigators. Listing a study does not mean it has been evaluated by the U.S. Federal Government. Read our disclaimer for details.

ClinicalTrials.gov Identifier: NCT01953055

Recruitment Status: Active, not recruiting
First Posted: September 30, 2013
Last Update Posted: July 3, 2018

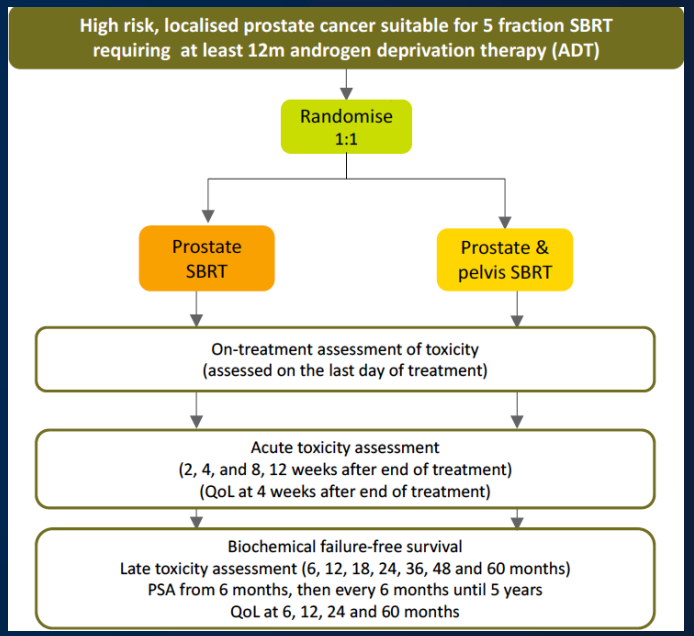
Sponsor:
Sunnybrook Health Sciences Centre

Information provided by (Responsible Party):
Andrew Loblaw, Sunnybrook Health Sciences Centre

Arms and Interventions

Arm
Experimental: Stereotactic ablative radiotherapy 40 Gy in 5 fractions over 4 weeks to prostate; 25 Gy in 5 fractions over 4 weeks to pelvic lymph nodes given simulataneously.

PACE-NODES



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SBRT + pelvic nodal RT is tolerable

Clinical Oncology 30 (2018) 442–447

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Original Article

Early Results of Extreme Hypofractionation Using Stereotactic Body Radiation Therapy for High-risk, Very High-risk and Node-positive Prostate Cancer

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Received 9 December 2017; received in revised form 7 February 2018; accepted 19 February 2018

Table 3
Acute and late toxicity outcomes

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Acute genitourinary toxicity	32 (47%)	27 (41%)	8 (12%)	0	0
Acute gastrointestinal toxicity	53 (85%)	7 (11%)	3 (4%)	0	0
Late genitourinary toxicity	52 (77%)	11 (16%)	3 (4.5%)	2 (2.5%)	0
Late gastrointestinal toxicity	58 (86%)	7 (10%)	3 (4%)	0	0

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SBRT vs Brachytherapy

Radiotherapy &Oncology

Prostate-specific antigen kinetics and biochemical control following stereotactic body radiation therapy, high dose rate brachytherapy, and low dose rate brachytherapy: A multi-institutional analysis of 3502 patients

Rebecca Levin-Epstein [a] · Ryan R. Cook [a] · J. Karen Wong [b] · ... · Eric M. Horwitz [b] · Naomi Y. Jiang [a] · Amar U. Kishan [a] ... Show more

N = 3502 men

- Risk group
  - Low (*n* = 2223; 63.5%),
  - Favorable intermediate (*n* = 869; 24.8%),
  - Unfavorable intermediate (*n* = 410; 11.7%)
- Treatment
  - SBRT (*n* = 1716; 49.0%),
  - HDR-BT (*n* = 512; 14.6%),
  - LDR-BT (*n* = 1274; 36.4%)

- Results:
  - No differences in nadir PSA <0.4 ng/mL at 4 years ($p \geq 0.51$)
  - BCRFS was similar for all three modalities ($p \geq 0.27$)

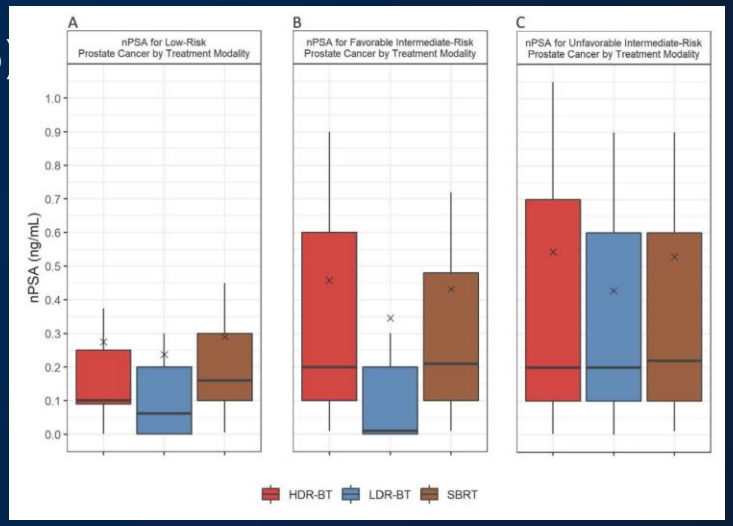

Fig. 1. Median nadir prostate-specific antigen (nPSA) values with interquartile range, minimum, maximum (outliers exceeding 1.5 times the third quartile value not presented), and mean (represented by x) after stereotactic body radiation therapy (SBRT), high dose rate brachytherapy (HDR-BT) and low dose rate brachytherapy (LDR-BT), individually presented for (A) low-risk, (B) favorable intermediate-risk, and (C) unfavorable intermediate-risk prostate cancer.

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Brachytherapy- HDR & LDR

INTERNATIONAL JOURNAL OF
RADIATION ONCOLOGY • BIOLOGY • PHYSICS
ASTRO

Biochemical Control and Toxicity Outcomes of Stereotactic Body Radiation Therapy Versus Low-Dose-Rate Brachytherapy in the Treatment of Low- and Intermediate-Risk Prostate Cancer

Emile Gogineni, DO · Zaker Rana, MD · Danielle Soberman, BS · Baho Sidiqi, MD · Vincent D'Andrea, MD · Lucille Lee, MD · Louis Potters, MD FACR FASTRO · Bhupesh Parashar, MD Show less

- N = 219 treated with LDR (125.0 Gy)
- N = 118 treated with SBRT (42.5Gy in 5 fractions)

- Five-year biochemical control: 91.6% LDR vs 97.6% SBRT (*P* = 0.108)
- LDR patients had a larger increase in mean AUA scores at 1 month (17.2 vs 10.3, *P* < .001) and 3 months posttreatment (14.0 vs 9.7, *P* < .001), and in mean EPIC scores at 1 month (15.7 vs 13.8, *P* < .001)

- No difference in late grade 3 GU toxicity (0.9% LDR vs 2.5% SBRT, *P* = .238)
- LDR had lower rates of late grade 3 GI toxicity (0.0% vs 2.5%, *P* = .018)

AMERICAN JOURNAL OF CLINICAL ONCOLOGY

A Pooled Analysis of Biochemical Failure in Intermediate-risk Prostate Cancer Following Definitive Stereotactic Body Radiotherapy (SBRT) or High-Dose-Rate Brachytherapy (HDR-B) Monotherapy

Hegde, John V. MD*; Collins, Sean P. MD†; Fuller, Donald B. MD‡; King, Christopher R. PhD, MD*; Demanes, D. Jeffrey MD*; Wang, Pin-Chieh PhD*; Kupelian, Patrick A. MD*; Steinberg, Michael L. MD*; Kamrava, Mitchell MD*

Retrospective, multi-institutional analysis of 437 patients with intermediate-risk PC treated with SBRT (N=300) or HDR-B (N=137)

- SBRT - 35 to 40 Gy in 4 to 5 fractions
- HDR-B - 42 Gy in 6 fractions
- BRFS rate (Phoenix definition): 96.3%

- No difference when stratifying by treatment modality or BED1.5

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SBRT vs HDR Boost

INTERNATIONAL JOURNAL OF
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ASTRO

Stereotactic Body Radiation Therapy and High-Dose-Rate Brachytherapy Boost in Combination With Intensity Modulated Radiation Therapy for Localized Prostate Cancer: A Single-Institution Propensity Score Matched Analysis

William C. Chen, MD * · Yun Li, MD, PhD * · Ann Lazar, PhD †,‡ · ... · Alexander Gottschalk, MD, PhD * · I-Chow Hsu, MD * · Mack Roach, III, MD * ... Show more

- Patients: 68.8% high risk, 26.0% unfavorable intermediate risk
  - 94.3% received ADT
- Boost:
  - SBRT boost (21 Gy and 19 Gy in 2 fractions); N = 139
  - HDR brachytherapy boost (19 Gy in 2 fractions); N = 101
  - Propensity-score (PS) matching and multivariable Cox regression were used for analysis
  - Median follow-up: 73.4 and 186.0 months, respectively
- Results:
  - BCRF (5 and 10 year): 88.8% and 85.3% for SBRT and 91.8% and 74.6% for HDR boost (log-rank P = 0.3)
    - After adjusting for covariates or PS matching, there was no statistically significant difference
  - Grade 3+ GU and GI toxicity:
    - SBRT: 4.6% and 1.5%
    - HDR: 3.0% and 0.0%
    - (P = 0.4, Fisher exact test)

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NCCN position on SBRT

EBRT Regimen	Preferred Dose/Fraction	Definitive RT						Post-Treatment RT			Advanced Disease	
								Post-RP		Post-RT	Primary Tumor	Metastases
		Low	FIR	UIR	High	Very-High	Regional	aRT	sRT	sRT	mCSPC M0 CRPC mCRPC	MDT
Conventional	1.8–2 Gy x 37–45 fx			☼	☼	✓	✓				☼	
	1.8–2 Gy x 30–39 fx							✓	✓		☼	
Moderate Hypofractionation	3 Gy x 20 fx (preferred)[a] 2.7 Gy x 26 fx 2.5 Gy x 28 fx	☼	✓	✓	✓	✓	✓			☼	☼	☼
	2.63–2.75 Gy x 20 fx 2.5 Gy x 25 fx							✓	✓	☼	✓	☼
Ultra Hypofractionation (SBRT)	9.5 Gy x 4 fx 7.25–8 Gy x 5 fx 6 Gy x 6 fx 6.1 Gy x 7 fx	☼	✓	✓	✓	☼	☼		☼	✓	✓	✓
	9–10 Gy x 3 fx 12 Gy x 2 fx 16–24 Gy x 1 fx											✓
	6.2–6.4 Gy x 5 fx								☼			
EBRT Boost Techniques												
EBRT with simultaneous integrated boost	See footnote b.		☼	✓	✓	☼	☼		☼	☼	☼	
EBRT with sequential SBRT boost	*Prostate:* 1.8 Gy x 23–28 fx *Boost:* 6 Gy x 3 fx 9.5 Gy x 2 fx			☼	☼	☼						

(✓ Preferred; ☼ Acceptable based on clinical and medical need; Regimens shaded gray are not recommended)

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Conclusions

- SBRT is non-inferior to Conventional RT (Meta-analysis, Pace-B, Hypo-RT-PC)
  - 5-year b-DFS rates >90%
  - Higher G2 + GU toxicity with SBRT however, EPIC scores similar at 2-5 years.

- NRG GU-005 met a primary endpoint of decreased rectal toxicity (but not DFS) with SBRT vs MH-IMRT
  - ~60% had rectal spacer; 5 mm vs 3 mm post margin. MRI mandatory
  - Biochemical failure at 3 years: IMRT: 4% Vs SBRT: 8% (p = 0.037);
  - Final results are awaited however higher dose might be needed.
  - Analysis of dose distribution effects, patters on recurrence and detailed planned parameters should also be revealing.

- Randomized studies underway for high-risk patients (pelvic nodes, hormones)

- Brachytherapy (LDR/HDR) and SBRT: Non-randomized data shows equivalent results

- *Importance of patient selection, planning and delivery parameters and data collection*
- *Importance of perfection in SBRT execution to be emphasized in future studies*

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