Initial Report of NRG Oncology/RTOG 0232: A Phase III Study Comparing Combined External Beam Radiation and Transperineal Interstitial Permanent Brachytherapy with Brachytherapy Alone for Selected Patients with Intermediate Risk Prostatic Carcinoma

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Background

- Low risk prostate cancer may be treated with either surgery, external beam radiation or brachytherapy ("seed implant") equally successfully
- Patients with intermediate risk prostate cancer have conventionally received either external beam radiation alone or in combination with brachytherapy, but not brachytherapy alone
- **Hypothesis:** Patients with intermediate risk prostate cancer who receive External Beam Radiation Therapy (EBRT) + prostate brachytherapy (PB) will have a 10% improvement in FFP at 5 years compared to those receiving PB alone.

Eligibility Criteria

- Histologically confirmed prostate adenocarcinoma, stages T1c-T2b (AJCC 6th Edition)
- Zubrod Performance Scale 0-1
- One of the following combinations of factors:
  - Gleason score 2-6, and prostate-specific antigen ≥10 but < 20
  - Gleason score 7, and prostate-specific antigen < 10
  - Prostate volume < 60 cc
- No prior ADT (beginning < 2 months or > 6 months prior to registration)
- International Prostate Symptom Score (IPSS) < 16
- No distant metastases (*M0*) or clinically or radiographically suspicious nodes

RTOG 0232: Study Schema

STRATIFY	Stage 1. T1c 2. T2a – T2b Gleason Score 1. ≤ 6 2. 7 PSA 1. < 10 2. 10-20 Neoadjuvant Hormonal Therapy 1. No 2. Yes	RECORD	Isotope 1. I-125 2. Pd-103	RANDOMIZE	Arm 1: 45 Gy EBRT Partial pelvis (1.8 Gy/fraction M-F for five weeks) followed 2-4 weeks later by Pd-103 (100 Gy) or I-125 (110 Gy) or Arm 2: Pd-103 (125 Gy) or I-125 (145 Gy)

Methods and Materials: Techniques

External Beam Radiation

Volume: CTV- Prostate + SV, nodes optional. PTV: CTV + 0.5-1 cm margin
Dose: PTV > 98%, 1.8 Gy x 25 = 45 Gy. 43% received IMRT

Brachytherapy – Low Dose Rate

Timing: 2-4 weeks post EBRT
Volume: CTV defined by pre-implant TRUS. PTV: CTV + 2-5 mm margin

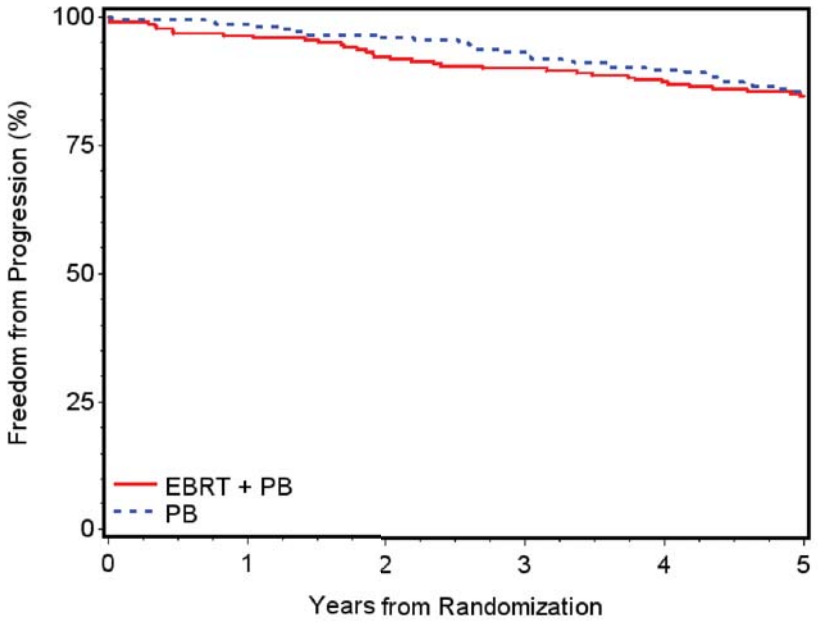
Dose	I-125 (482)	Pd-103 (81)
Monotherapy	145 Gy	125 Gy
Boost	110 Gy	100 Gy
Source Activity	.277 - .548 U	1.29 - 2.61 U

RTOG 0232 Accrual Summary

Date activated	6/11/2003
Date closed	2/8/2012
Target sample size	586

	EBRT + PB	PB	Total
Randomized	292	296	588
Ineligible	5	4	9
Eligible	**287**	**292**	**579**

Results: Freedom from Progression



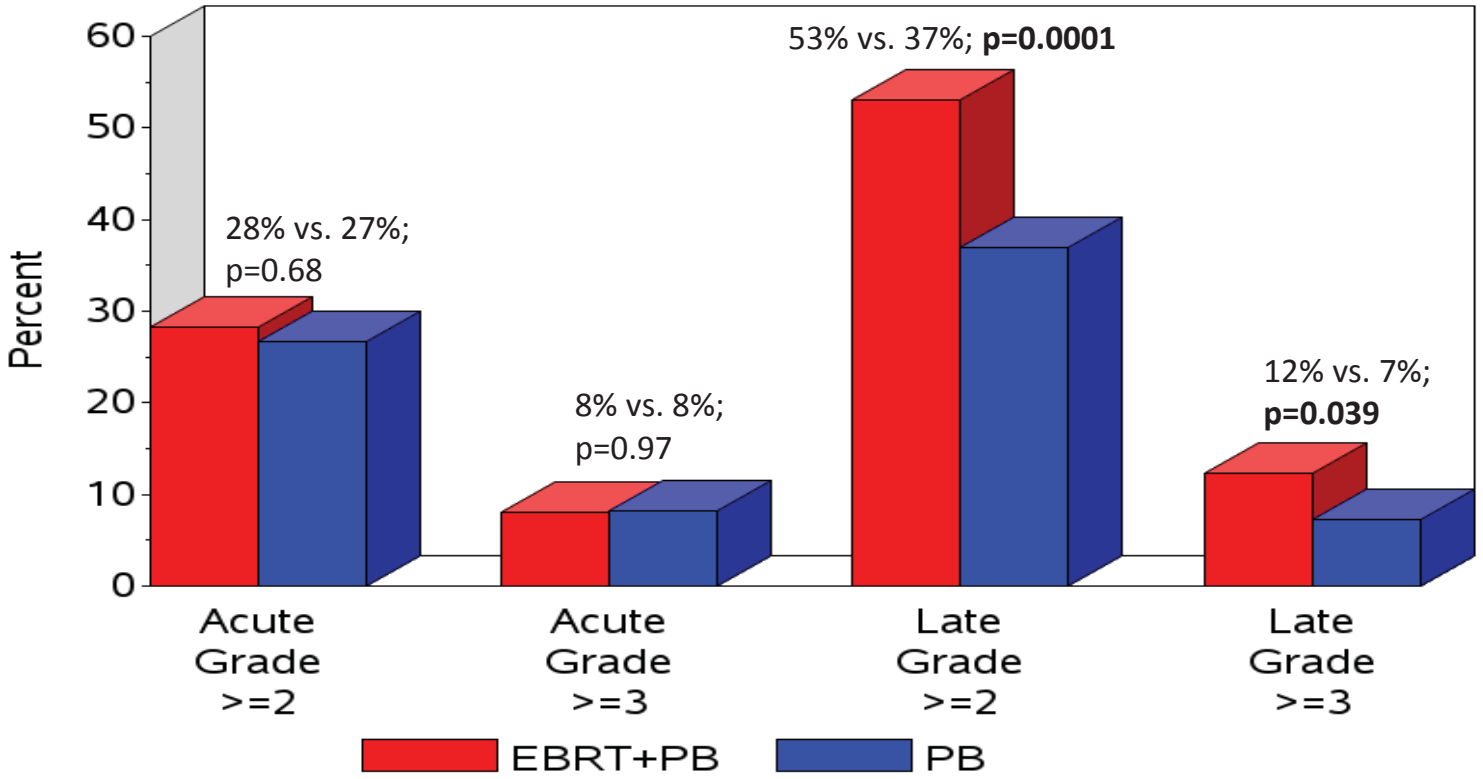
Patients at Risk

EBRT + PB	220	212	203	198	192	183
PB	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

Results: Adverse Events



Conclusions

- Among men with intermediate risk (IR) prostate cancer, the addition of external beam therapy to brachytherapy did not result in superior freedom from progression compared to brachytherapy alone at 5 years in this initial report.
- Toxicity in both groups was limited, but there were fewer late effects, mostly GU, noted in the brachytherapy alone arm.
- Implications for clinical practice: Men with intermediate risk prostate cancer may be well managed with brachytherapy alone.
- Further subset analysis will be required to determine if the unfavorable IR patients do as well as those with favorable IR disease.
- Longer follow up is needed to confirm the durability of the findings.