

High Risk Non-Metastatic Prostate Cancer /Point – Counter Point

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Financial Disclosure

- American Cancer Society – Board Member
- CareCore – Advisory Board
- Ferring Pharmaceuticals – Advisory Board: Prostate Cancer
- Molecular Insight – Research on Prostate Cancer Imaging
- Astra-Zeneca – Speakers Bureau



“State-of the Art”

1. Neoadjuvant ADT +/- long term ADT
2. Whole Pelvic Image Guided Intensity Modulated Radiotherapy
3. Brachytherapy or High Dose IMRT Boost



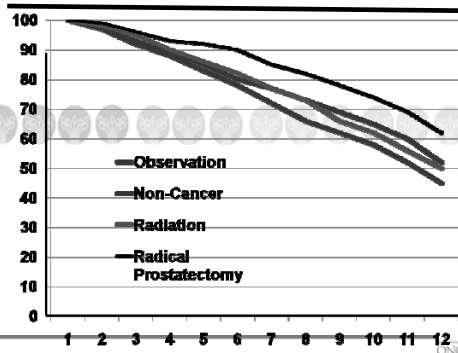
Comparative Risk-Adjusted Mortality Outcomes After Primary Surgery Prostatectomy, Radiotherapy, or Androgen-Deprivation Therapy for Localized Prostate Cancer

Copperberg et al. *Cancer* 116: (2011)

Characteristics	Surgery	Radiation
PSA > 20 ng/ml	4.9%	16.5%
T-Stage T2-3	19.9%	27.4%
Bx GS <7	70.5%	54.2%
4+3 & 8-10	12.7%	26.8%
PPB % >50%	18.2%	31.4%



Limits of Observational Data in Determining Outcomes From Cancer Therapy. Diordano et al. *Cancer* 112: 2456-66(2008)



Metastasis After Radical Prostatectomy or External Beam Radiotherapy for Patients with Clinically Localized Prostate Cancer: A Comparison of Clinical Cohorts Adjusted for Case Mix. Zelefsky et al. *JCO* 28: (2010)

PURPOSE:

... assess the effect RP & EBRT on distant metastases (DM) in pts with localized prostate ca.

PTS & METHODS: stage T1c-T3b prostate ca. were treated with IMRT (>= 81 Gy) or RP. Both cohorts included pts treated with salvage RT or ADT.



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Zelevsky et al. JCO 28: (2010)

The 8-yr prob of freedom from met progression was 97% for RP pts & 93% for EBRT pts.

After adjustment for case mix, RP associated with a reduced risk of mets (HR, 0.35; P < .001).

Results similar for prostate cancer-specific mortality (hazard ratio, 0.32; 95% CI, 0.13 to 0.80; P = .015).

Rates of mets similar for favorable dz (1.9% diff. at 8-yr)

reduced for intermed- & high-risk (9.2% & 7.9%

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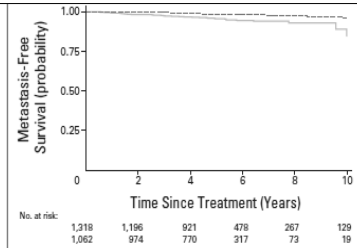


Fig 1. Kaplan-Meier probability of freedom from metastasis by treatment. Dashed blue line: surgery. Solid gold line: radiotherapy.

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Zelevsky et al. JCO 28: (2010)

CONCLUSION:

Metastatic progression is infrequent in men with low-risk Prostate Ca. treated with either RP or EBRT.

RP pts with higher-risk disease treated had a lower risk of met prog & prostate cancer-specific death than EBRT pts.

... may be confounded by differences in the use & timing of salvage Tx. [13 vs 69 mo. for RP & RT pts]

Metastasis After Radical Prostatectomy or External Beam Radiotherapy for Patients with Clinically Localized Prostate Cancer: A Comparison of Clinical Cohorts Adjusted for Case Mix.
Zelevsky et al. JCO 28: (2010)

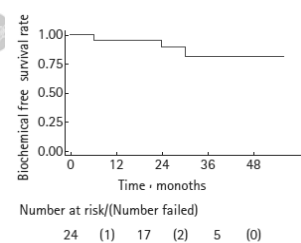
Problems with this Comparison?:

1. IGRT vs IMRT
2. Short term (56%)* only vs long term ADT (0%)
3. Value of Salvage therapy?
4. Risk Stratification for PSA failure vs Mets
5. Brachy high doses than possible with IMRT
6. No treatment of pelvic Lymph Nodes

* Volume reduction or high risk disease

Salvage Permanent Perineal Radioactive-seed implantation For Treating Recurrence of Localized Prostate Adenocarcinoma After external Beam Radiotherapy.
Aaronson et al. BJUI 2009

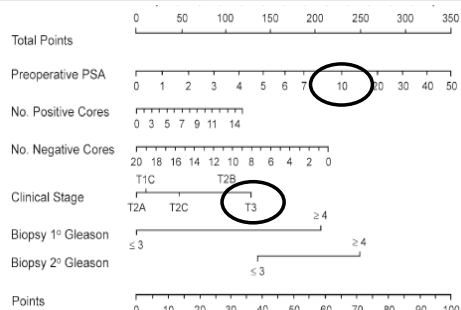
Kaplan-Meier biochemical free survival estimate



Mets After RP or EBRT for Pts with Clinically Localized Prostate Ca: A Comparison ... Adjusted for Case Mix.
Zelevsky et al. JCO 28:

13 vs 69 mo. for RP vs RT pts

Preoperative Nomogram Predicting the 10-Year Probability of Prostate Cancer Recurrence After Radical Prostatectomy
Stephenson ... Kattan. JNCI 98:715-7, 2006



PSA Failure vs Mets (death), Kattan et al.

Modified from Kattan's Model JCO 18:3352-3359, 2000

Modified from Kattan's Bone Mets Model JCO 21:4568-4571, 2003

Predicting 15-Year Prostate Cancer Specific Mortality After Radical Prostatectomy.

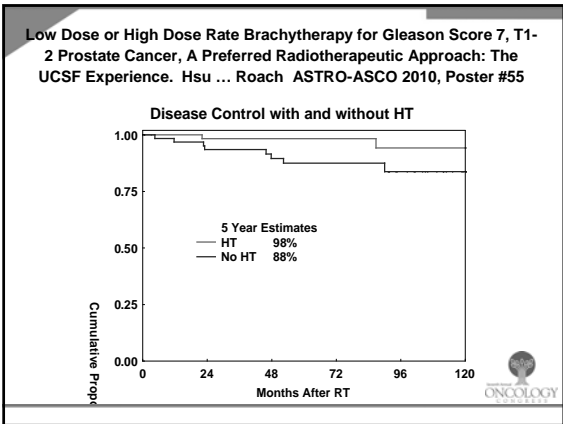
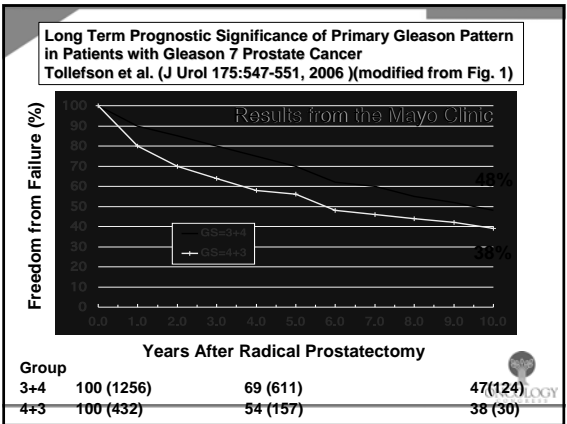
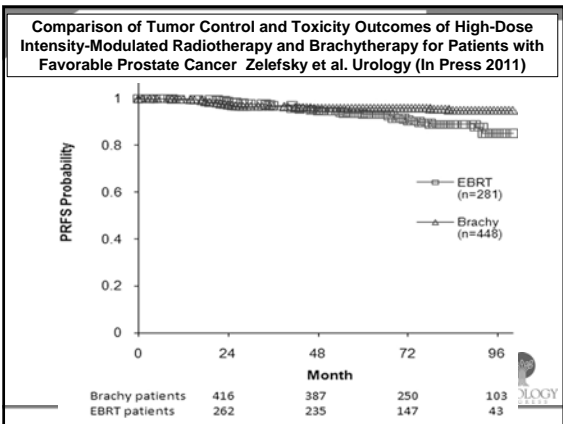
Egner, Scardino, Walsh et al. J Urol 185: 960-75.

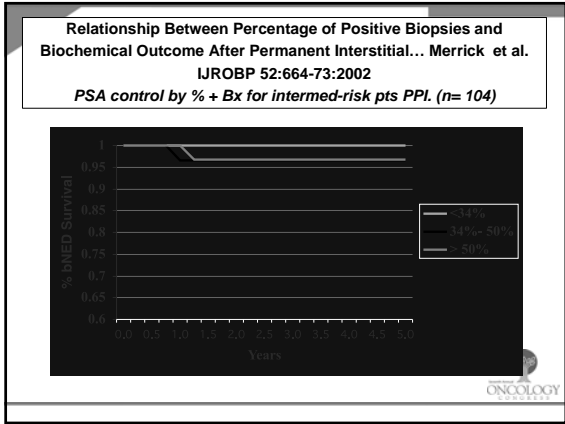
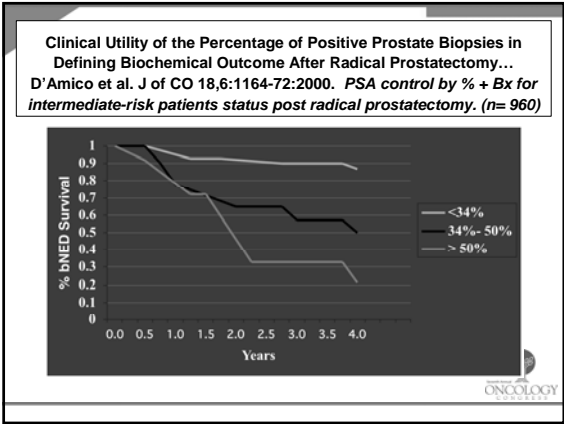
Points	0	10	20	30	40	50	60	70	80	90	100
PSA (Range-Max)											
SV+	No							Yes			
Primary GS1-3										4-5	
Secondary GS	1-3								4-5		
Total Points	0	100				250				450	
Predicted 15-yr PCSM	0.01					0.15				.99	

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Zelevsky et al. JCO 28: (2010)

Characteristics	Surgery	Radiation
PSA (median)	6.2 (4.5-8.7)	7.6 (5.1-12)
Kattan 5-yr PFS	84%	80%
T-Stage		
T1c-2c	95.9%	91%
T3	4.1%	9%
Bx GS <7	96%	87%
7-10	4%	13%





CLINICAL INVESTIGATION Prostate

RETROSPECTIVE COMPARISON OF EXTERNAL BEAM RADIOTHERAPY AND RADICAL PROSTATECTOMY IN HIGH-RISK, CLINICALLY LOCALIZED PROSTATE CANCER

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¹Department of Radiotherapy, ²Laboratory of Medical Physics and Expert System, and ³Department of Urology, Regina Elena National Cancer Institute, Rome, Italy

... to retrospectively compare the results of radical surgery vs ... external beam radiotherapy (EBRT) plus androgen deprivation therapy using an intent-to-treat analysis on two ... concurrently treated, high-risk patient populations.

ONCOLOGY

Retrospective comparison of external beam radiotherapy and radical prostatectomy in high-risk, clinically localized prostate cancer. Arcangeli, G. et al. IJROBP 2010

RESULT:

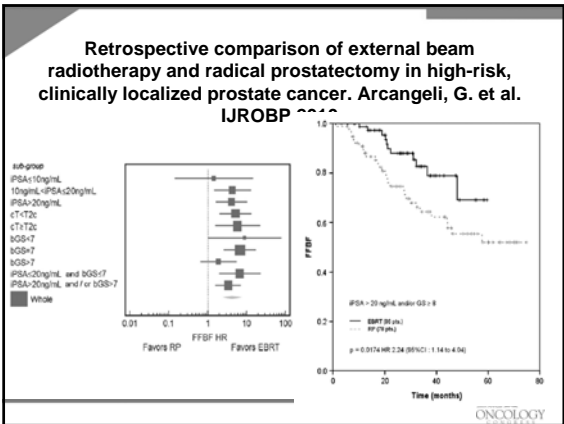
The two groups ... were homogeneous on the basis of the T stage, Bx GS, & initial PSA.

For EBRT and RP the 3yr freedom from PSA failure ... was 86.8% & 69.8% (p = 0.001).

On MVA PSA level & Tx type (EBRT vs. RP) as sign.

CONCLUSION: ... retrospective intention-to-treat analysis showed a better outcome after EBRT than RP

ONCOLOGY



- Conclusions Concerning Radiotherapy & High Risk Prostate Cancer**
1. "Conventional Dose" radiotherapy alone is inadequate treatment for High Risk prostate ca.
 2. Dose escalated IGRT and ADT should be the standard to which all other therapies should be compared
 3. This therapy is less limited by KPS or anatomic constraints (+SVs ...), may not be as dependent on the technical skills of the providers
 4. Post Prostatectomy patients with adverse features or a rising PSA also benefit from Radiotherapy
- ONCOLOGY