CaP localizado: Comparação da eficácia da Prostatectomia Radical versus RDT

a favor da Cirurgia!!!

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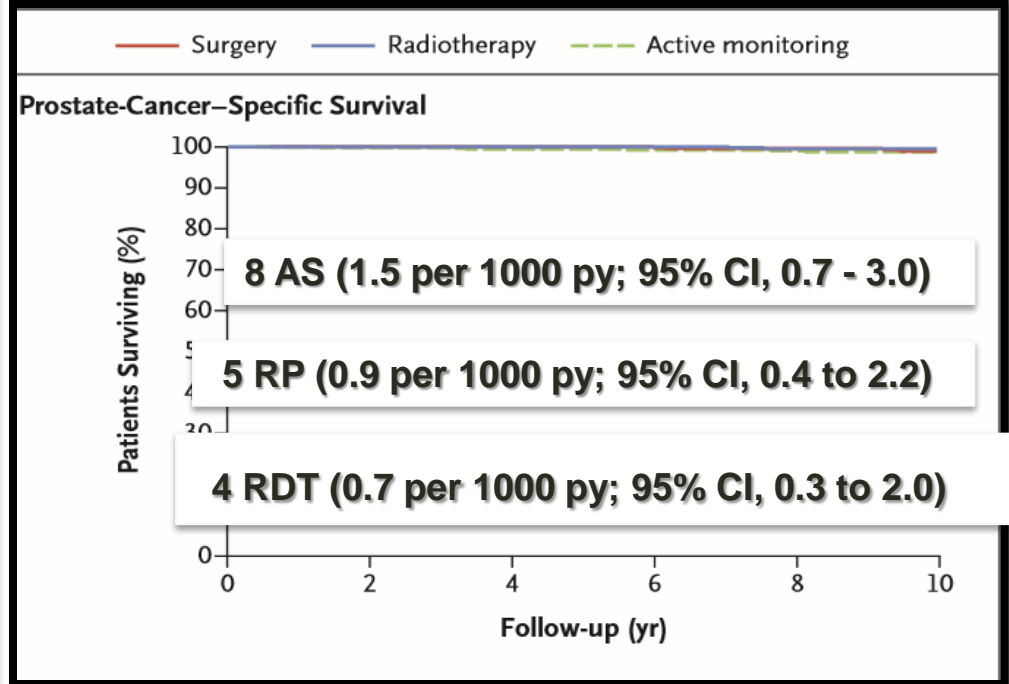
Disclosures

- Nothing to disclosure

- **But…. I'm am high volume prostate surgeon**

10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer

F.C. Hamdy, J.L. Donovan, J.A. Lane, M. Mason, C. Metcalfe, P. Holding, M. Davis, T.J. Peters, E.L. Turner, R.M. Martin, J. Oxley, M. Robinson, J. Staffurth, E. Walsh, P. Bollina, J. Catto, A. Doble, A. Doherty, D. Gillatt, R. Kockelbergh, H. Kynaston, A. Paul, P. Powell, S. Prescott, D.J. Rosario, E. Rowe, and D.E. Neal, for the ProtecT Study Group*

	Active monitoring protocol (n=545)	Surgery (n=553)	Radiotherapy protocol (n=545)
Mean age in years at randomisation (SD[1])	62 (5)	62 (5)	62 (5)
White ethnic origin (%)	535 (99)	542 (99)	529 (98)
Married or living with partner (%)	457 (84)	458 (84)	460 (85)
Managerial / professional occupation (%)	229 (43)	229 (42)	226 (42)
Known family history prostate cancer (%)	43 (8)	32 (6)	44 (8)
Median PSA[2] in ng/ml (IQR[3])	4.7 (3.7, 6.7)	4.9 (3.7, 6.7)	4.8 (3.7, 6.7)
PSA[2] 10+ ng/ml (%)	57 (10)	57 (10)	58 (11)
Gleason score			
6	421 (77)	422 (76)	423 (78)
7	111 (20)	120 (22)	108 (20)
8-10	13 (2)	10 (2)	14 (3)
Missing	0	1	0
Clinical stage			
T1c	410 (75)	410 (74)	429 (79)
T2	135 (25)	143 (26)	116 (21)

Prostate-Cancer–Specific Survival

Surgery — Radiotherapy --- Active monitoring

8 AS (1.5 per 1000 py; 95% CI, 0.7 - 3.0)

5 RP (0.9 per 1000 py; 95% CI, 0.4 to 2.2)

4 RDT (0.7 per 1000 py; 95% CI, 0.3 to 2.0)

Patients Surviving (%) vs *Follow-up (yr)*

At a median of 10 years, PCSM was low irrespective of the treatment assigned, with no significant difference among treatments.

Hamdy FC et al. NEJM. 2016

Rational for RP as primary treatment

- ✓ **Excellent 5-, 10- and 15-year OS and CSS rates have been published. These rates *surpass radiotherapy-alone series and are no different from RT + HT***

- ✓ **Avoid early and late RT toxicity, and second cancers.**

- ✓ **Optimal local control, avoiding LUTS and late local complication.**

- ✓ **Clear-cut situation after RP, and possible adjuvant-salvage RT-**

- ✓ **Obviate the need for HT, or postpone HT.**

Patients with localized Pca with aggressive features benefit the most from Radical Prostatectomy!!!!

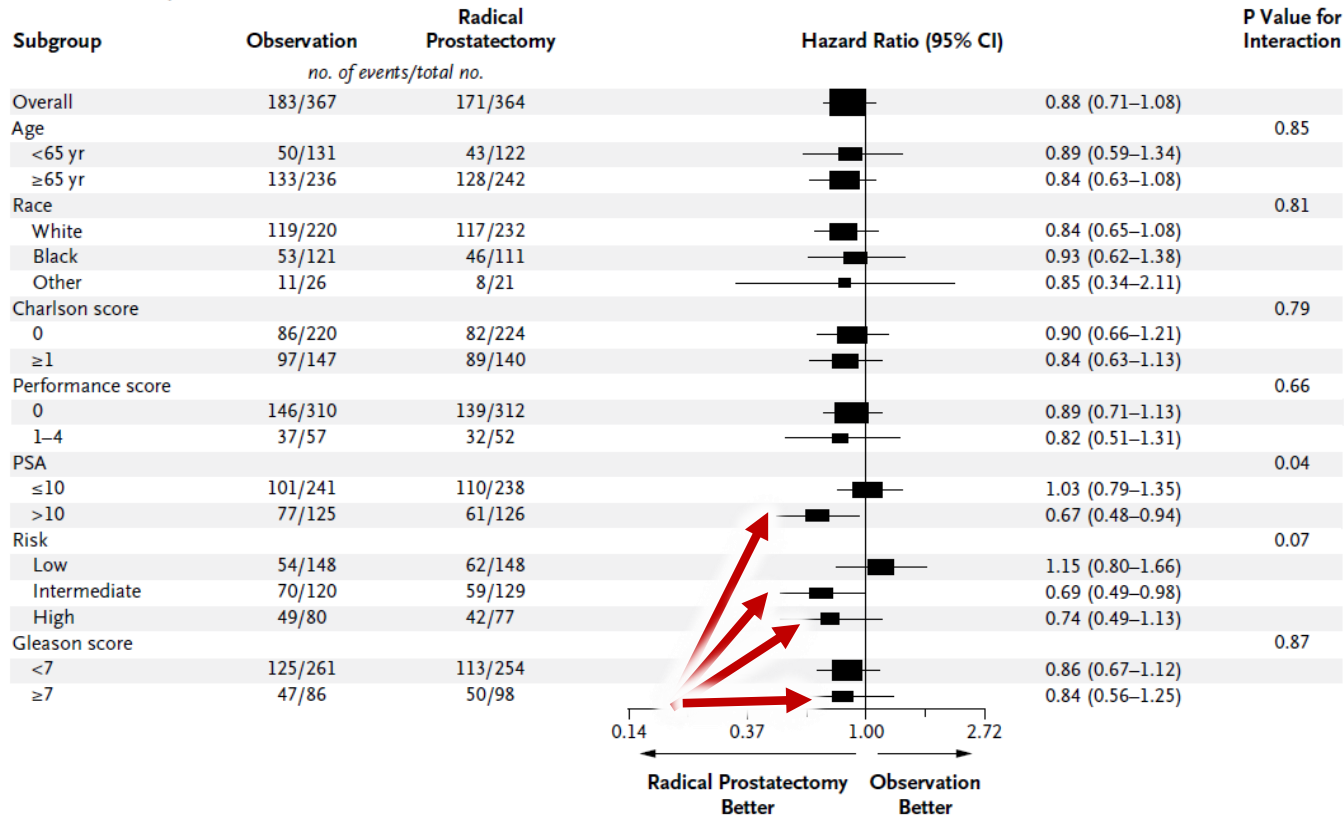"in men with *intermediate and high-risk disease* radical prostatectomy was associated with an *absolute reduction in all-cause mortality of 10.5 percentage points (hazard ratio, 0.71; 95% CI, 0.54 to 0.92; P = 0.01)*"

Individualized Estimation of the Benefit of Radical Prostatectomy from the Scandinavian Prostate Cancer Group Randomized Trial

Andrew Vickers [a,*], Caroline Bennette [b], Gunnar Steineck [c], Hans-Olov Adami [d], Jan-Erik Johansson [e], Anna Bill-Axelson [f], Juni Palmgren [c], Hans Garmo [g], Lars Holmberg [h]

EUROPEAN UROLOGY
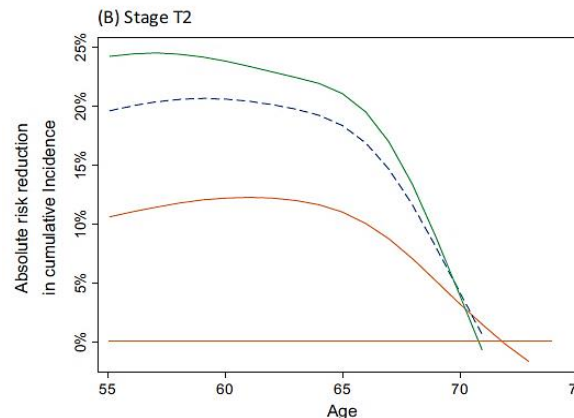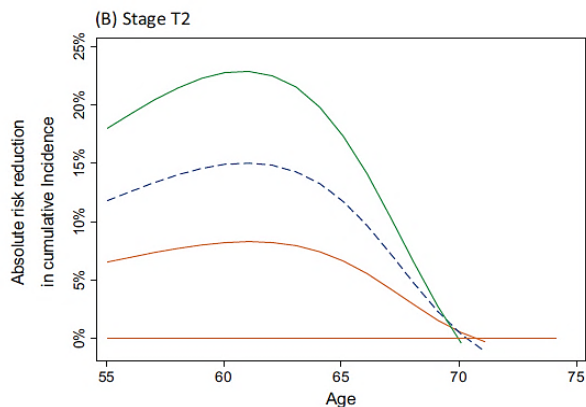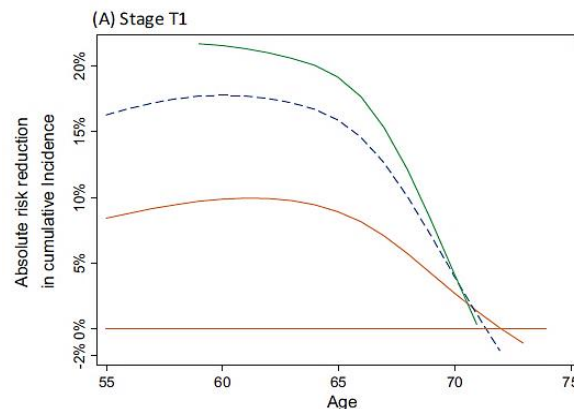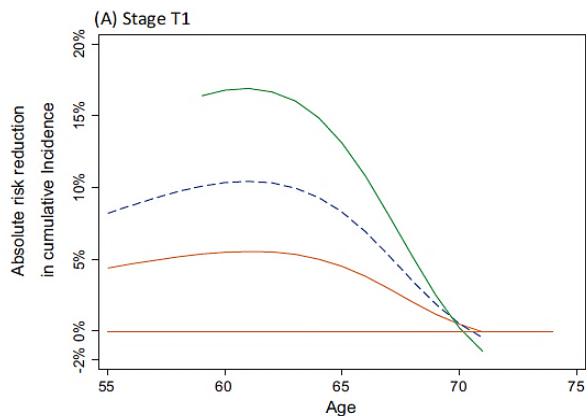
10-yr predicted risk reduction for death from prostate cancer among men treated by RP versus WW

10-yr predicted risk reduction for metastasis among men treated by RP versus WW

younger men with more aggressive disease experienced a larger reduction in risk of prostate cancer death and metastasis with RP than older men with lower risk cancer

Survival Benefit of Radical Prostatectomy in Patients with Localized Prostate Cancer: Estimations of the Number Needed to Treat According to Tumor and Patient Characteristics

Firas Abdollah,* Maxine Sun,*,† Jan Schmitges, Rodolphe Thuret, Marco Bianchi, Shahrokh F. Shariat, Alberto Briganti, Claudio Jeldres, Paul Perrotte, Francesco Montorsi and Pierre I. Karakiewicz

THE JOURNAL of UROLOGY®

Intermediate Risk Disease
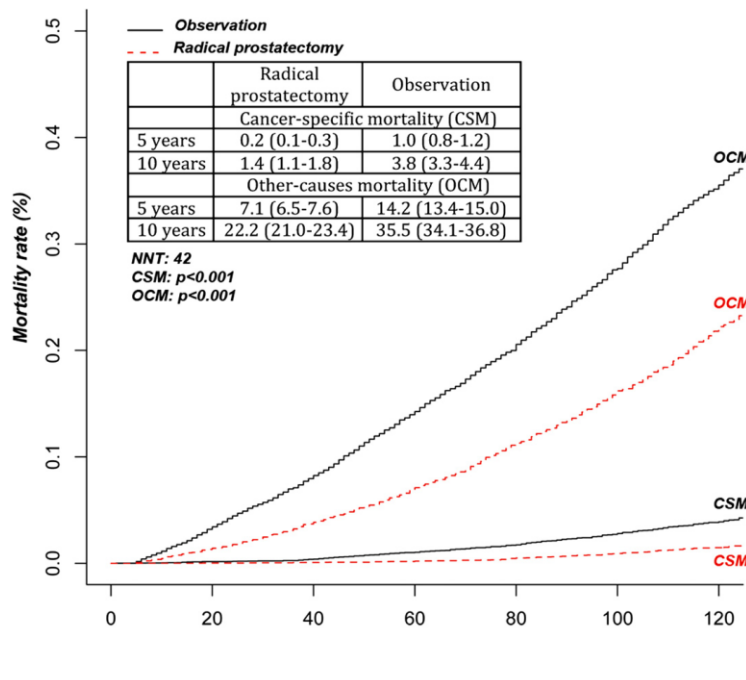
High Risk Disease
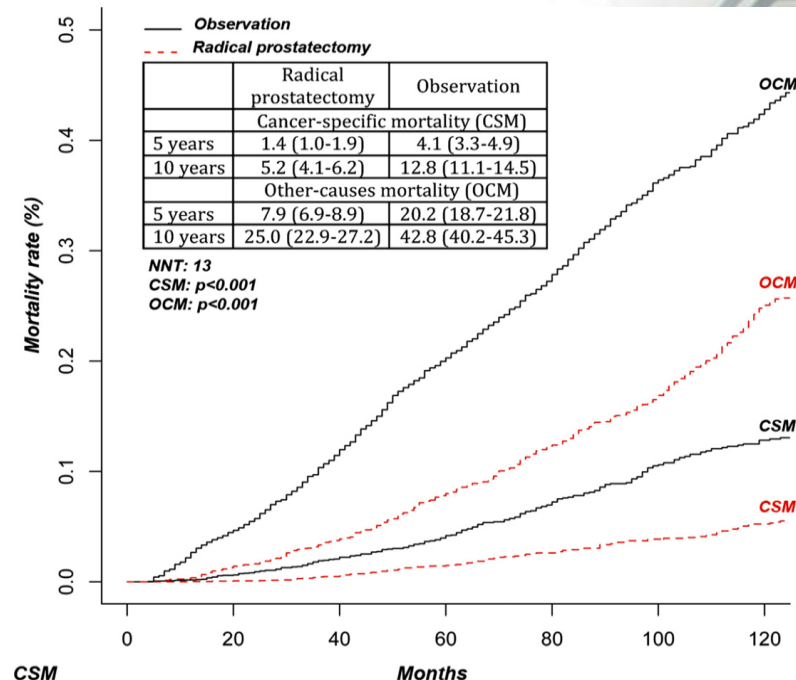
Patients with *high risk prostate cancer benefit the most* from radical prostatectomy.

However in the recent past…..
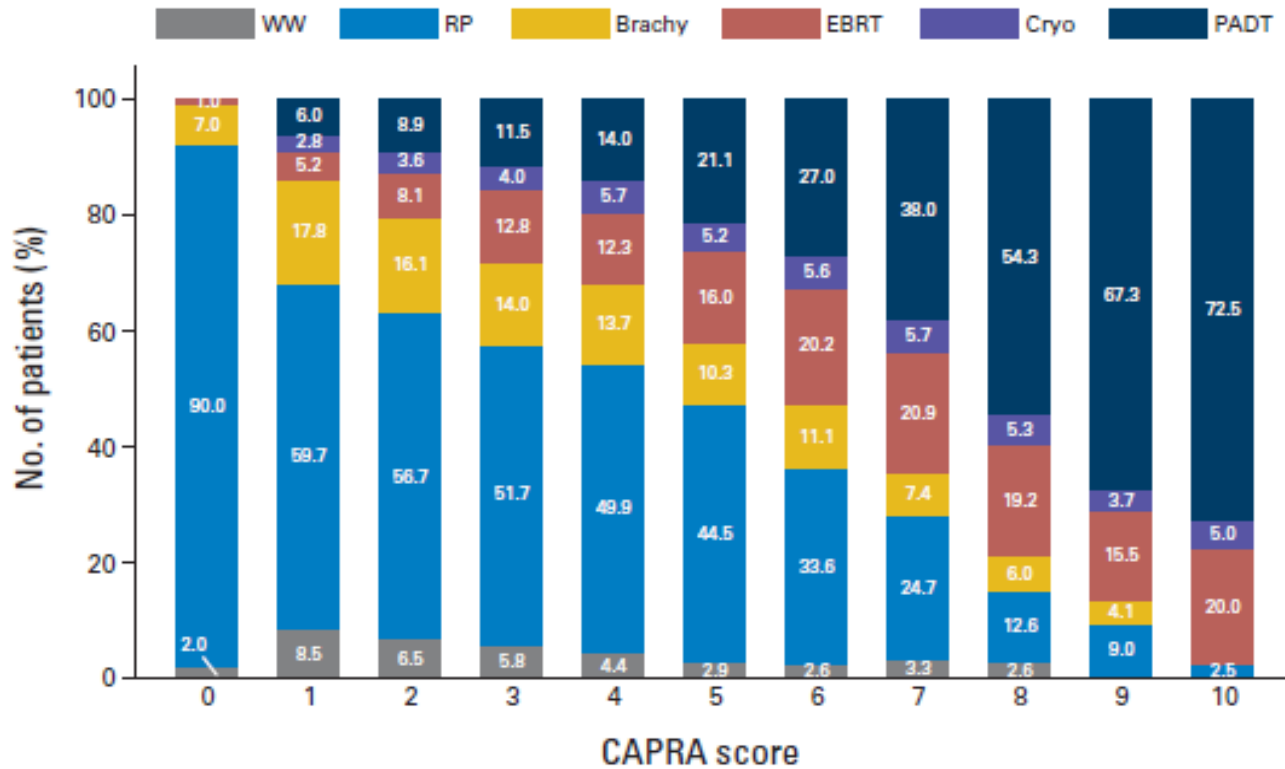
Overtreatment of low-risk disease!!!
Undertreatment of high-risk disease!!!!

Copperberg et al. JCO 2010

ORIGINAL ARTICLE

Contemporary management of men with high-risk localized prostate cancer in the United States

AB Weiner[1], RS Matulewicz[1], EM Schaeffer[1], SL Liauw[2], JM Feinglass[3] and SE Eggener[4]

42%

26%
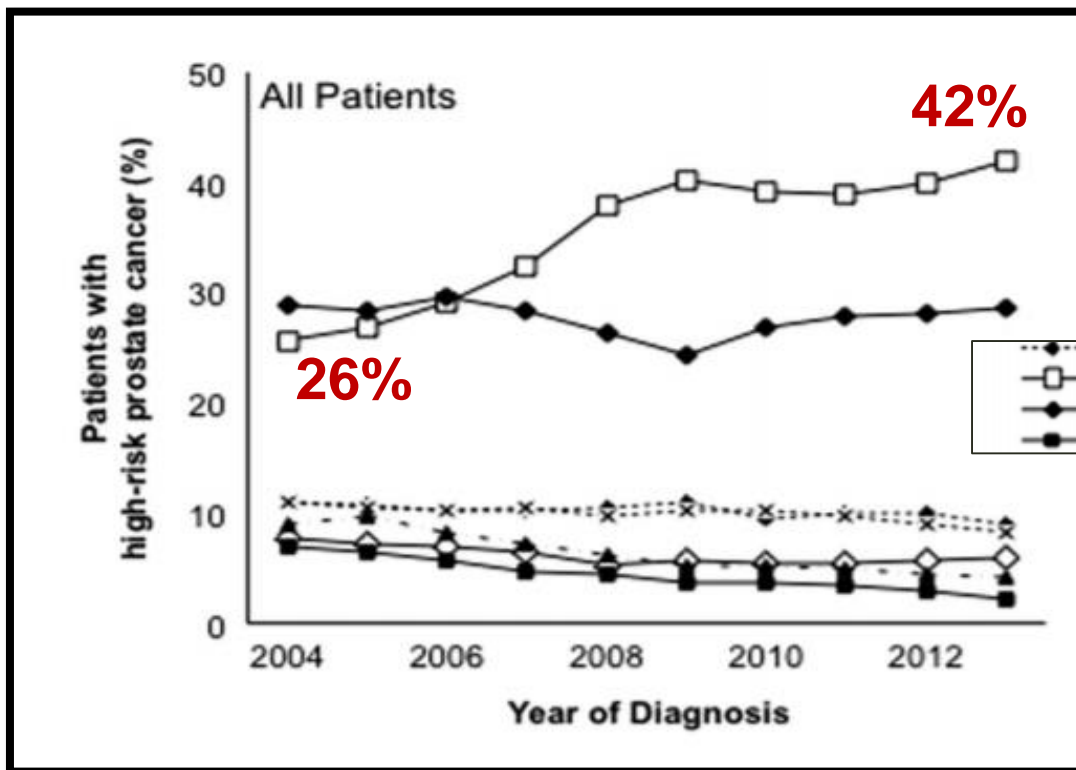
In the United States between 2004 and 2013, the likelihood of receiving RP increased dramatically for high-risk PCa

Trends in Radical Prostatectomy Risk Group Distribution in a European Multicenter Analysis of 28 572 Patients: Towards Tailored Treatment
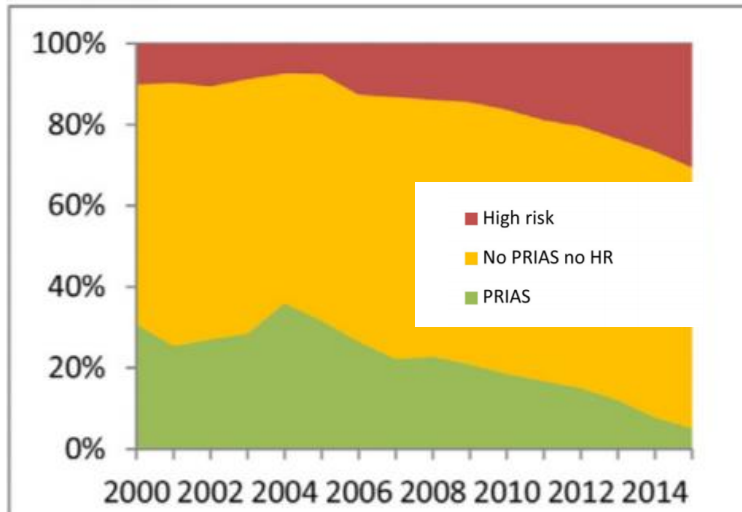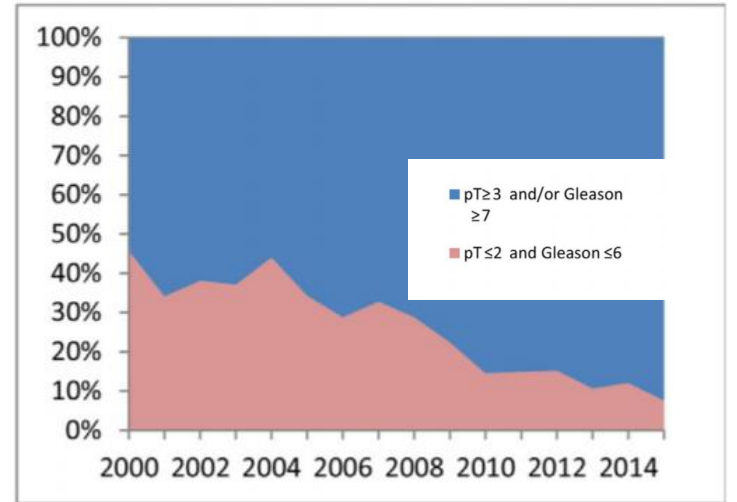
This European analysis confirmed the **risk profile of patients undergoing RP shifting away of the most favorable disease**. High-risk disease comprised an increasing share of all RPs

RP vs. RP+/-HT for Intermediate/High Risk Disease

Oncologic Outcomes

- ## No level I Evidence

Statistics Notes

Absence of evidence is not evidence of absence

BMJ

Douglas G Altman, J Martin Bland

When we are told "there is no evidence" we should first ask whether absence of evidence simply means that there is no information at all or studies were underpowered. When necessary we should seek evidence from case control studies, matched-pair analysis (…)

Altman DG et al . BMJ. 1995

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ORIGINAL REPORT

Metastasis After Radical Prostatectomy or External Beam Radiotherapy for Patients With Clinically Localized Prostate Cancer: A Comparison of Clinical Cohorts Adjusted for Case Mix

Michael J. Zelefsky, James A. Eastham, Angel M. Cronin, Zvi Fuks, Zhigang Zhang, Yoshiya Yamada, Andrew Vickers, and Peter T. Scardino

Table 2. Multivariable Cox Regression Model for the Outcome of Distant Metastases From Prostate Cancer

Predictor	Hazard Ratio	95% CI	P
Age at treatment*	0.98	0.95 to 1.02	.3
Year of treatment*	0.97	0.87 to 1.07	.5
NCCN risk (high v intermediate/low)	6.37	3.89 to 10.5	< .0005
Treatment (surgery v radiotherapy)	0.35	0.19 to 0.63	.001

Abbreviation: NCCN, National Comprehensive Cancer Network.
*Hazard ratio estimates are given for a 1-year increase.

Zelefsky et al, JCO, 2010

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			Kaplan-Meier Probability of Prostate Cancer Death							
			5 Year				8 Year			
			Radiotherapy		Surgery		Radiotherapy		Surgery	
NCCN Risk	No. of Patients	No. of Events	%	95% CI	%	95% CI	%	95% CI	%	95% CI
Low	952	1	0.0		0.0		0.0		0.0	
Intermediate	1,019	10	0.0		0.2	0.0 to 1.7	4.5	1.8 to 10.8	1.9	0.5 to 6.3
High	409	19	3.7	1.8 to 7.4	1.0	0.1 to 7.0	9.5	4.9 to 17.9	3.8	1.2 to 11.5

HR Sx vs. RDT. 0.32 (95% CI, 0.13 to 0.80; *P*.015)

RP patients with higher-risk disease had a lower risk of metastatic progression and prostate cancer–specific death than EBRT patients.

Zelefsky et al, JCO, 2010

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Zelefsky et al, JCO, 2010
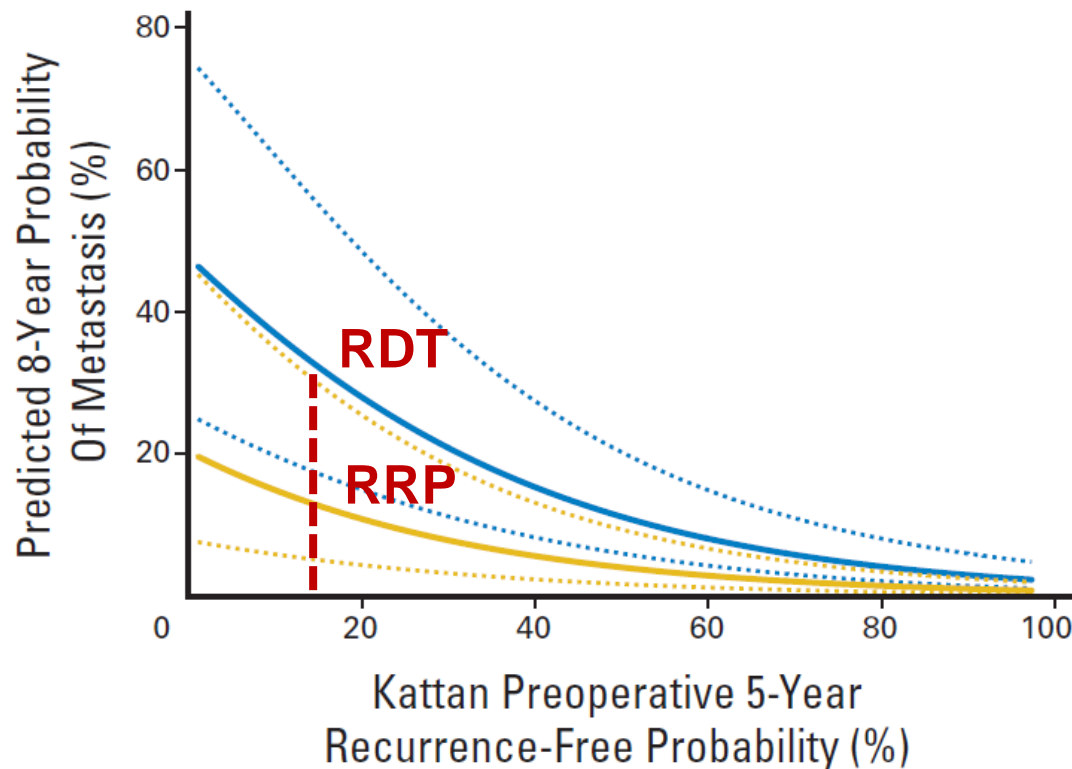
Comparative Risk-Adjusted Mortality Outcomes After Primary Surgery, Radiotherapy, or Androgen-Deprivation Therapy for Localized Prostate Cancer
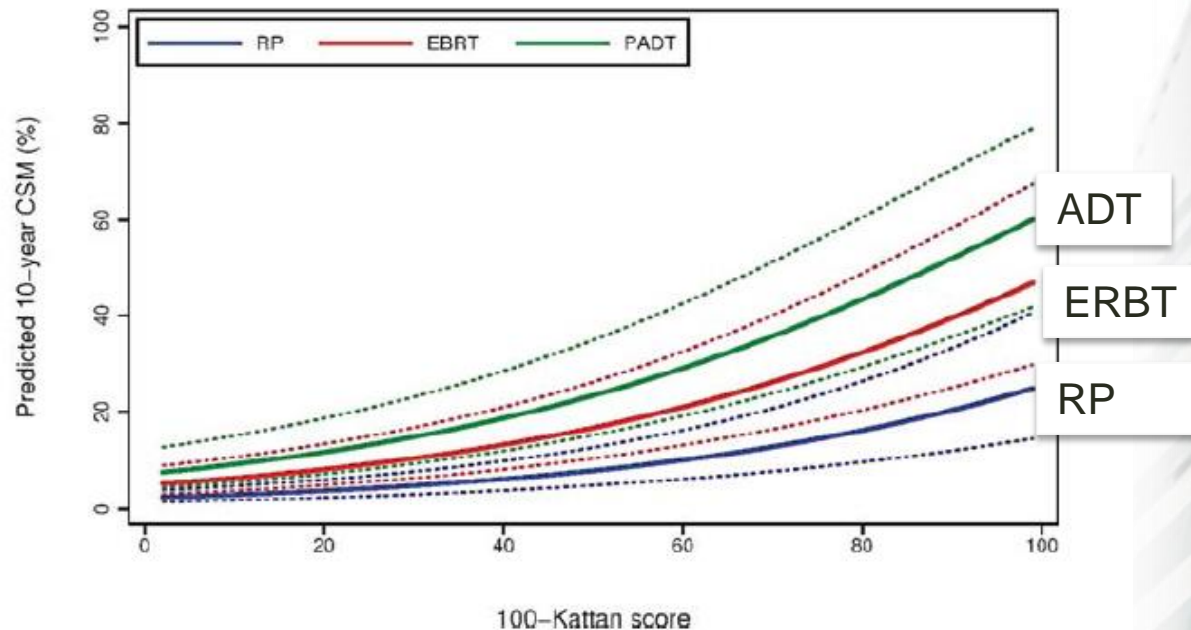
After rigorous case-mix adjustment and multiple sensitivity analyses, we identified roughly 2-fold and 3-fold increases in the risk of PCSM among those who received ERBT or primary ADT, compared with RP, and the greatest differences were observed for higher risk patients

Coopeerberg et al, JCO, 2010

Long-Term Survival After Radical Prostatectomy Versus External-Beam Radiotherapy for Patients With High-Risk Prostate Cancer

Stephen A. Boorjian, MD[1]; R. Jeffrey Karnes, MD[1]; Rosalia Viterbo, MD[2]; Laureano J. Rangel, MS[3]; Eric J. Bergstralh, PhD[3]; Eric M. Horwitz, MD[4]; Michael L. Blute, MD[1]; and Mark K. Buyyounouski, MD, MS[4]

Cancer Specific Survival
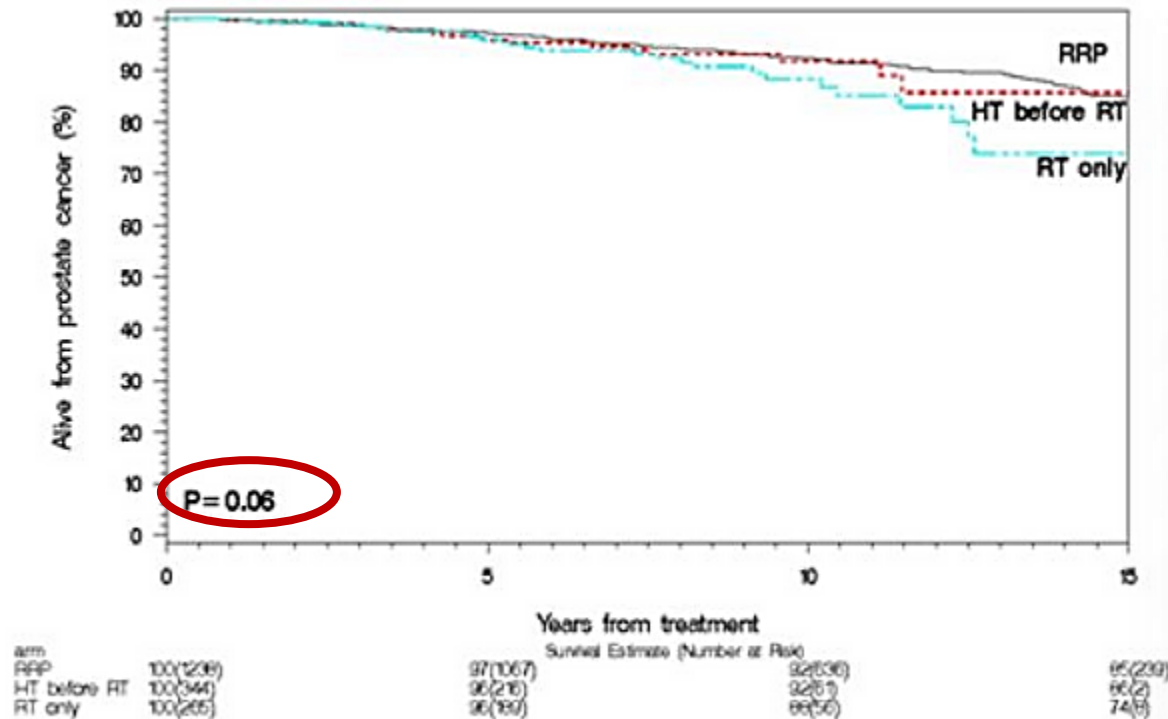
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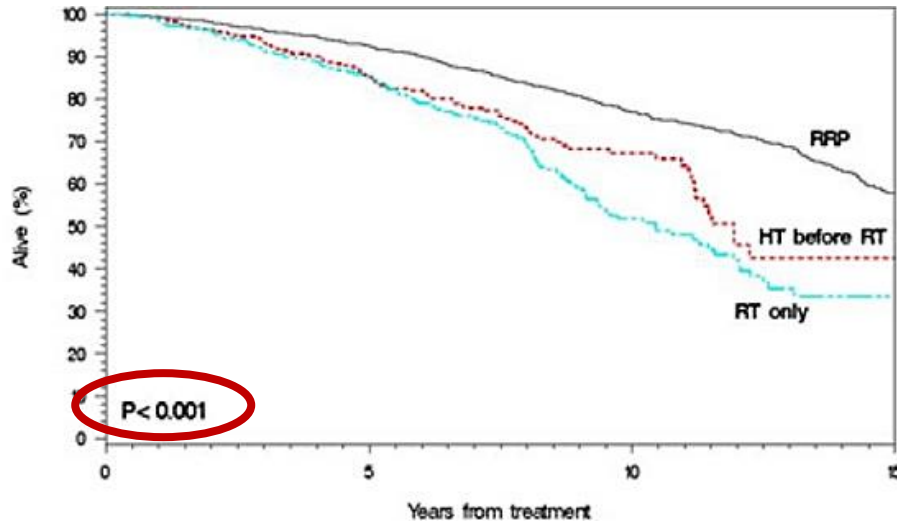
Overall Survival   **Overall Survival – RDT CCI 0/1**
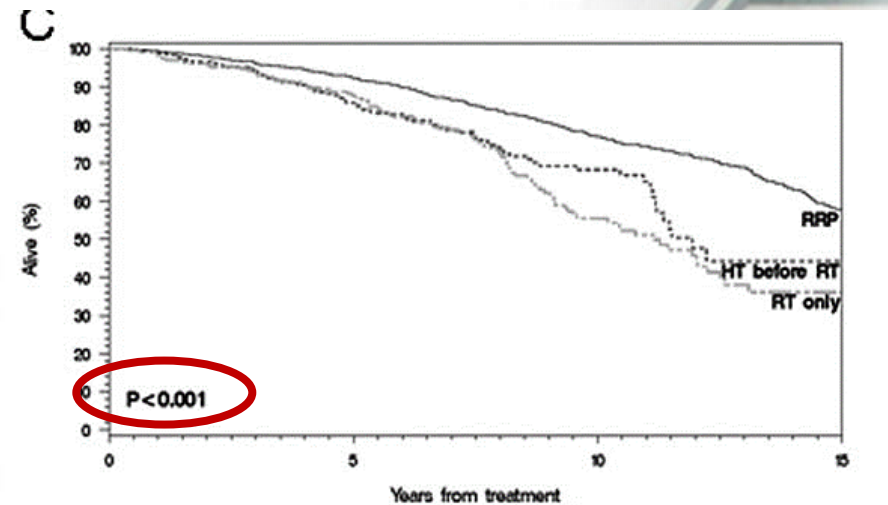
"(…) *no significant differences* in the risks of *prostate cancer death* were seen between patients treated with EBRT + ADT and RRP. The *risk of all-cause mortality was, however, greater after EBRT + ADT* than RRP."

Boorjian et al, Cancer, 2007.

Surgery Versus Radiotherapy for Clinically-localized Prostate Cancer: A Systematic Review and Meta-analysis

a

Study or subgroup	log[hazard ratio]	SE	Weight	Hazard ratio IV, random, 95% CI
Boorjian 2011	0.5988	0.0852	12.1%	1.82 [1.54, 2.15]
Cooperberg 2010	0.4637	0.0911	10.6%	1.59 [1.33, 1.90]
Hoffman 2013	0.5128	0.0792	14.0%	1.67 [1.43, 1.95]
Jeldres 2008	0.7419	0.2255	1.7%	2.10 [1.35, 3.27]
Kibel 2012	0.4886	0.0562	27.8%	1.63 [1.46, 1.82]
Ladjevardi 2010	0.4121	0.0685	18.7%	1.51 [1.32, 1.73]
Merglen 2007	0.8755	0.3537	0.7%	2.40 [1.20, 4.80]
Rice 2013	0.3038	0.2255	1.7%	1.35 [0.87, 2.11]
Sun 2013	0.4187	0.0917	10.5%	1.52 [1.27, 1.82]
Tewari 2007	0.7839	0.2058	2.1%	2.19 [1.46, 3.28]
Total (95% CI)			**100.0%**	**1.63 [1.54, 1.73]**

Heterogeneity: Tau² = 0.00; χ² = 8.85, df = 9 (p = 0.45); I² = 0%
Test for overall effect: Z = 16.56 (p < 0.00001)

Favors radiotherapy — Favors surgery

Overall Survivall

b

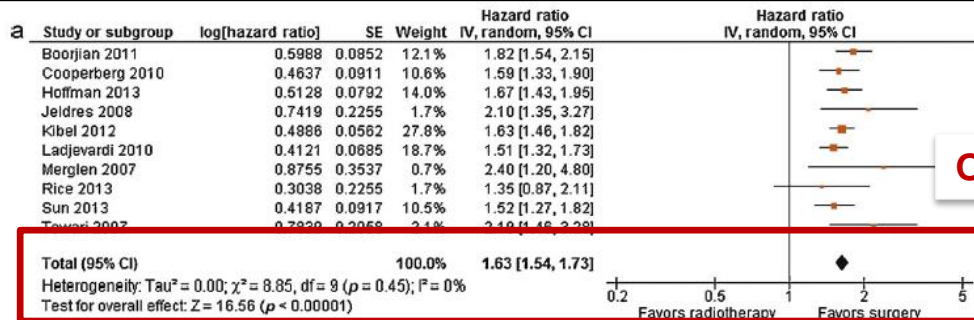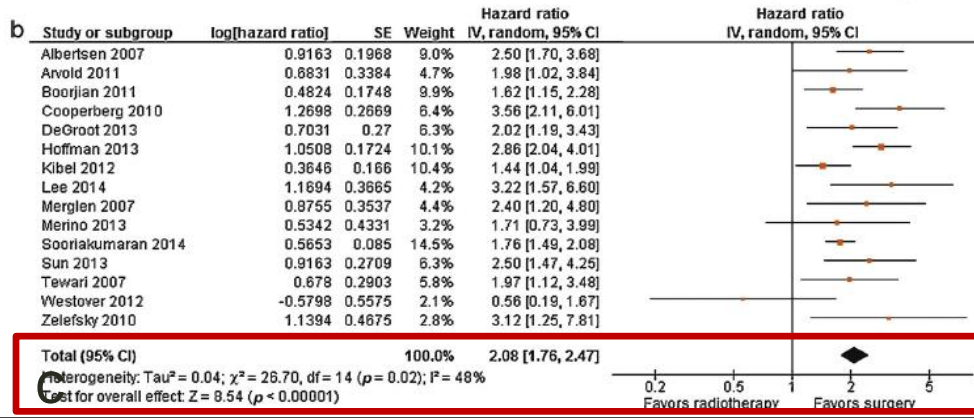| Study or subgroup	log[hazard ratio]	SE	Weight	Hazard ratio IV, random, 95% CI
Albertsen 2007	0.9163	0.1968	9.0%	2.50 [1.70, 3.68]
Arvold 2011	0.6831	0.3384	4.7%	1.98 [1.02, 3.84]
Boorjian 2011	0.4824	0.1748	9.9%	1.62 [1.15, 2.28]
Cooperberg 2010	1.2698	0.2669	6.4%	3.56 [2.11, 6.01]
DeGroot 2013	0.7031	0.27	6.3%	2.02 [1.19, 3.43]
Hoffman 2013	1.0508	0.1724	10.1%	2.86 [2.04, 4.01]
Kibel 2012	0.3646	0.166	10.4%	1.44 [1.04, 1.99]
Lee 2014	1.1694	0.3665	4.2%	3.22 [1.57, 6.60]
Merglen 2007	0.8755	0.3537	4.4%	2.40 [1.20, 4.80]
Merino 2013	0.5342	0.4331	3.2%	1.71 [0.73, 3.99]
Sooriakumaran 2014	0.5653	0.085	14.5%	1.76 [1.49, 2.08]
Sun 2013	0.9163	0.2709	6.3%	2.50 [1.47, 4.25]
Tewari 2007	0.678	0.2903	5.8%	1.97 [1.12, 3.48]
Westover 2012	-0.5798	0.5575	2.1%	0.56 [0.19, 1.67]
Zelefsky 2010	1.1394	0.4675	2.8%	3.12 [1.25, 7.81]
Total (95% CI)			**100.0%**	**2.08 [1.76, 2.47]**

Heterogeneity: Tau² = 0.04; χ² = 26.70, df = 14 (p = 0.02); I² = 48%
Test for overall effect: Z = 8.54 (p < 0.00001)

Favors radiotherapy — Favors surgery

PCSM

c

	Overall mortality		Prostate cancer-specific mortality	
	Adjusted HR (95% CI, p value)	I²	Adjusted HR (95% CI, p value)	I²
Risk category				
Low risk	1.47 (1.19–1.83, p = 0.0004)	59%	1.70 (1.36–2.13, p < 0.00001)	0%
Intermediate risk	1.50 (1.24–1.82, p < 0.0001)	NA	1.80 (1.45–2.25, p < 0.0001)	0%
High risk	1.88 (1.64–2.16, p < 0.00001)	0%	1.83 (1.51–2.22, p = 0.0001)	42%

We identified an increased risk of overall and PCSM for patients treated with radiotherapy compared with surgery after adjustment for common patient and tumor prognostic factors
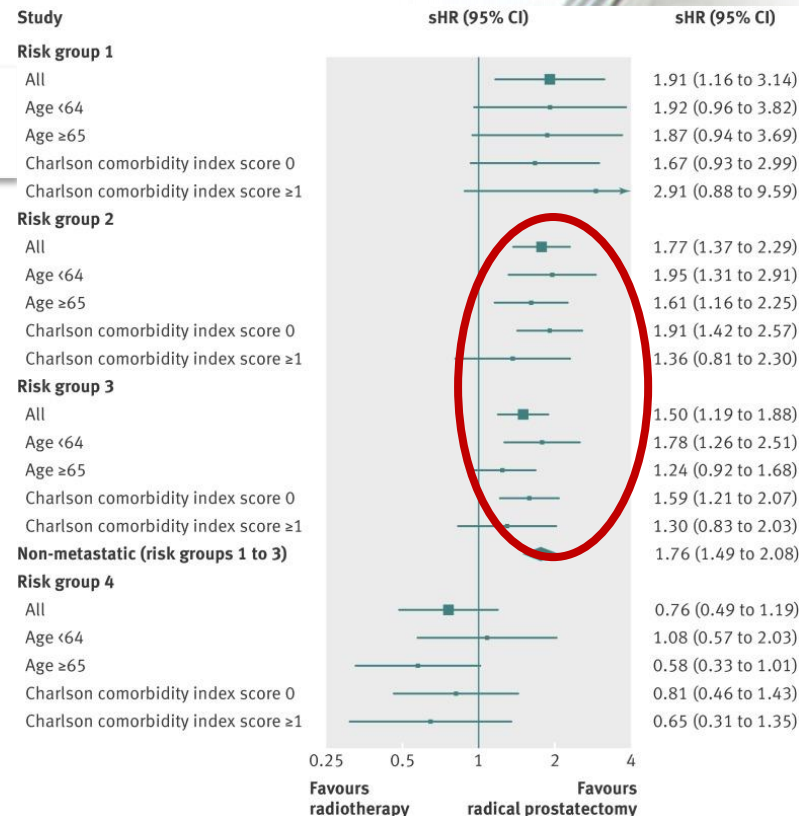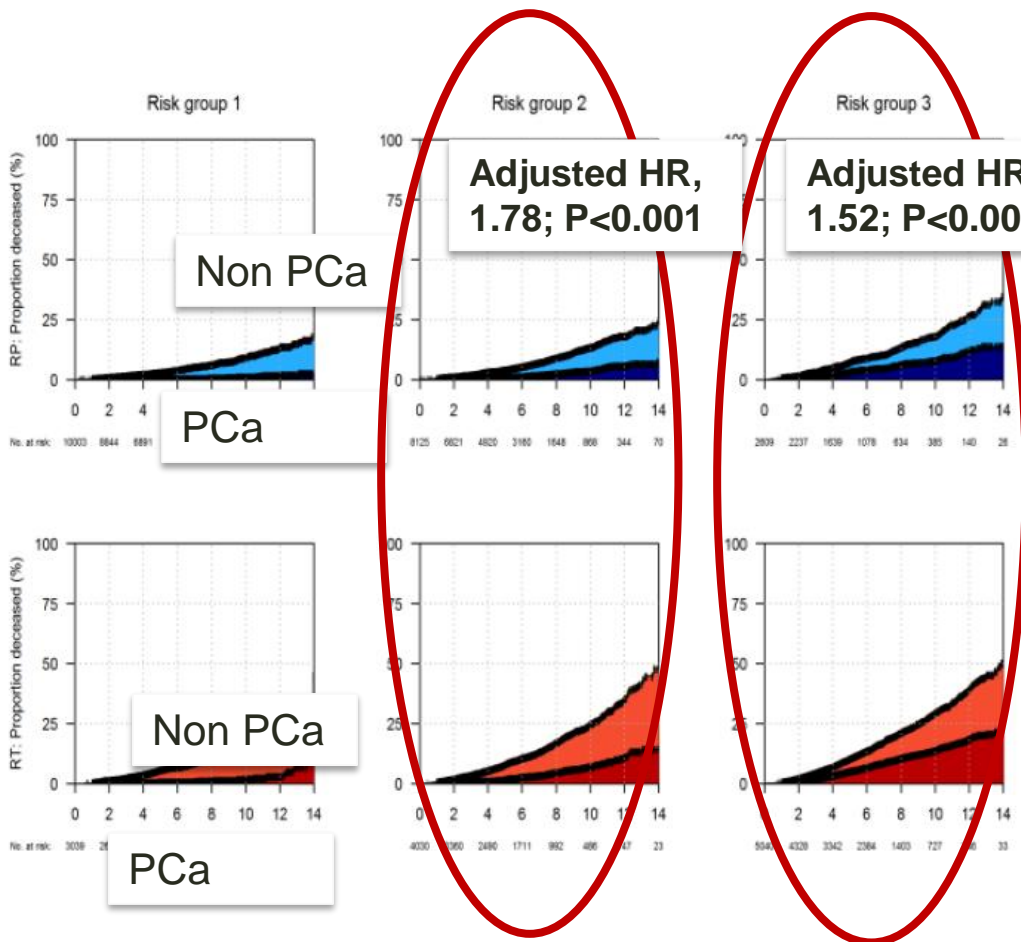
Wallis CJ et al, Eur Urol, 2015

Surgery Versus Radiotherapy for Clinically-localized Prostate Cancer: A Systematic Review and Meta-analysis

Table 3 – Newcastle-Ottawa Scale for risk of bias assessment of studies included in the meta-analysis

Study	Selection				Comparability	Outcome			Overall
	Representativeness of exposed cohort	Selection of nonexposed	Ascertainment of exposure	Outcome not present at start		Assessment of outcome	Adequate follow-up length	Adequacy of follow-up	
Abdollah (2012)	☆	☆	☆	☆	☆☆	☆			7
Albertsen (2007)	☆	☆	☆	☆	☆☆	☆	☆		8
Arvold (2011)	☆		☆	☆	☆☆				5
Boorjian (2011)	☆		☆	☆	☆☆	☆	☆		7
Cooperberg (2010)	☆	☆	☆	☆	☆☆	☆			7
DeGroot (2013)	☆	☆	☆	☆	☆☆	☆	☆		8
Hoffman (2013)	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Jeldres (2008)	☆	☆	☆	☆	☆☆	☆	☆		8
Kibel (2012)	☆	☆	☆	☆	☆☆	☆	☆		8
Ladjevardi (2010)	☆	☆	☆	☆	☆☆	☆		☆	8
Lee (2014)	☆	☆	☆	☆	☆☆	☆	☆		8
Merglen (2007)	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Merino (2013)	☆	☆	☆	☆	☆☆		☆		7
Rice (2013)	☆	☆	☆	☆	☆☆	☆	☆		8
Sooriakumaran (2014)	☆	☆	☆	☆	☆☆	☆	☆	☆	9
Sun (2013)	☆	☆	☆	☆	☆☆	☆		☆	7
Tewari (2007)	☆	☆	☆	☆	☆☆	☆			7
Westover (2012)	☆		☆	☆	☆☆	☆			6
Zelefsky (2010)	☆		☆	☆	☆☆	☆		☆	7

Comparative effectiveness of radical prostatectomy and radiotherapy in prostate cancer: observational study of mortality outcomes

BMJ

Adjusted HR, 1.78; P<0.001

Adjusted HR, 1.52; P<0.001

Study	sHR (95% CI)
Risk group 1	
All	1.91 (1.16 to 3.14)
Age <64	1.92 (0.96 to 3.82)
Age ≥65	1.87 (0.94 to 3.69)
Charlson comorbidity index score 0	1.67 (0.93 to 2.99)
Charlson comorbidity index score ≥1	2.91 (0.88 to 9.59)
Risk group 2	
All	1.77 (1.37 to 2.29)
Age <64	1.95 (1.31 to 2.91)
Age ≥65	1.61 (1.16 to 2.25)
Charlson comorbidity index score 0	1.91 (1.42 to 2.57)
Charlson comorbidity index score ≥1	1.36 (0.81 to 2.30)
Risk group 3	
All	1.50 (1.19 to 1.88)
Age <64	1.78 (1.26 to 2.51)
Age ≥65	1.24 (0.92 to 1.68)
Charlson comorbidity index score 0	1.59 (1.21 to 2.07)
Charlson comorbidity index score ≥1	1.30 (0.83 to 2.03)
Non-metastatic (risk groups 1 to 3)	1.76 (1.49 to 2.08)
Risk group 4	
All	0.76 (0.49 to 1.19)
Age <64	1.08 (0.57 to 2.03)
Age ≥65	0.58 (0.33 to 1.01)
Charlson comorbidity index score 0	0.81 (0.46 to 1.43)
Charlson comorbidity index score ≥1	0.65 (0.31 to 1.35)

Favours radiotherapy — Favours radical prostatectomy

"*Surgery lead to better survival outcomes for the majority of men with localized prostate cancer, especially in younger men and those with lower comorbidity*"

Sooriakumaran P, BMJ, 2014

Survival Outcomes of Radical Prostatectomy Versus Radiotherapy in Intermediate-Risk Prostate Cancer: A NCDB Study

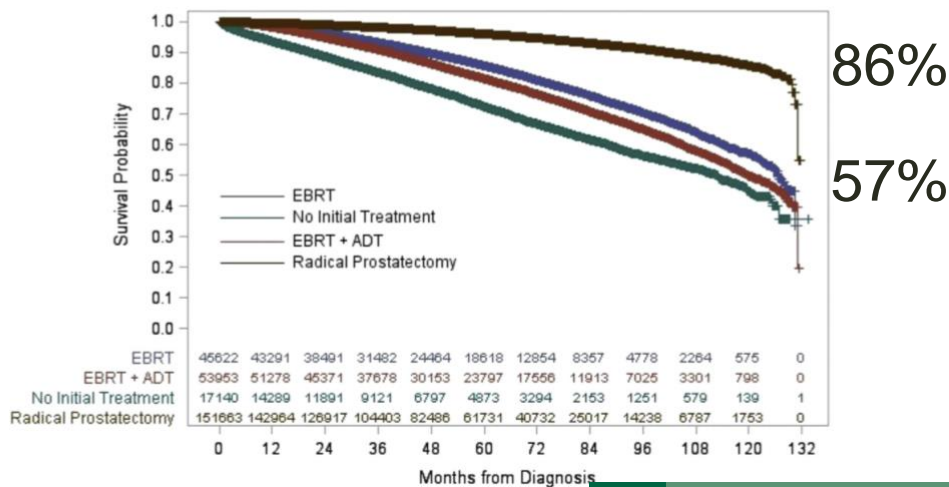**Figure 2** | **Kaplan-Meier Survival Curve by Treatment Cohort**

86%

57%

Table 3 | **Results of Multivariable Cox Regression**

Characteristic	HR	95% CI for HR		P
		Lower	Upper	
Patient Clinical Characteristics				
Treatment				
EBRT vs. no treatment	0.59	0.55	0.62	<.001
EBRT + ADT vs. no treatment	0.58	0.55	0.61	<.001
RP vs. no treatment	0.24	0.23	0.25	<.001
RP vs. EBRT	0.41	0.39	0.43	<.001
RP vs. EBRT + ADT	0.41	0.39	0.43	<.001
EBRT vs. EBRT + ADT	1.01	0.97	1.05	.624
PSA	1.01	1.01	1.01	<.001
Gleason score	1.26	1.23	1.28	<.001

We noted a greater overall survival benefit to patients who underwent RP compared to EBRT, EBRT + ADT, and no initial treatment. The findings support surgical intervention as treatment of choice for intermediate risk Pca
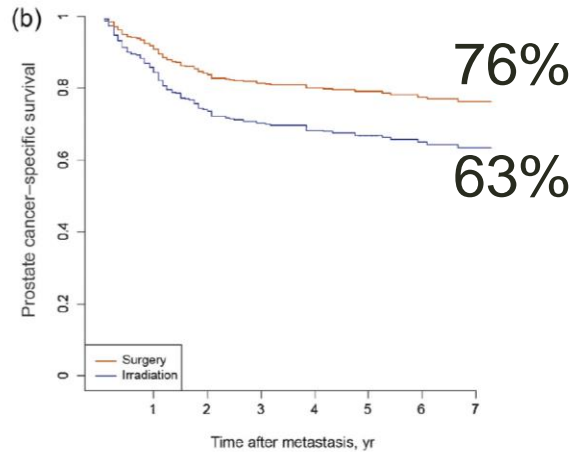
Cancer-specific Survival After Metastasis Following Primary Radical Prostatectomy Compared with Radiation Therapy in Prostate Cancer Patients: Results of a Population-based, Propensity Score–Matched Analysis

EUROPEAN UROLOGY

Low Risk Disease

86%

79%

Intermediate Risk Disease

76%

63%
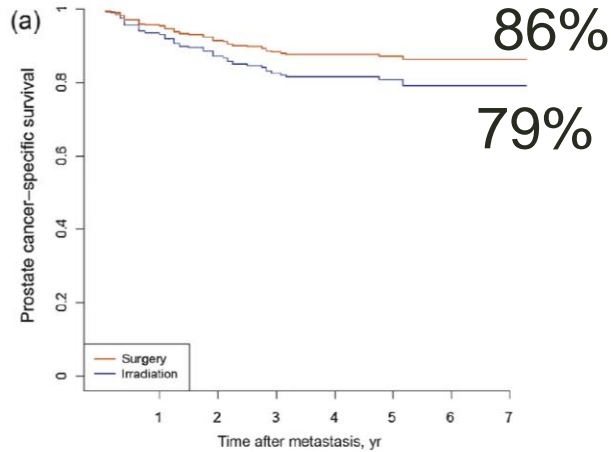
Characteristic	Low Radical prostatectomy vs radiation therapy, HR (95% CI)		Intermediate–high Radical prostatectomy vs radiation therapy, HR (95% CI)	
Overall cohort				
Unadjusted model	0.58	(0.37–0.92)	0.68	(0.52–0.90)
Model adjusted for cancer stage and cancer grade[*]	0.58	(0.37–0.92)	0.67	(0.51–0.89)
Multivariate Cox	0.57	(0.35–0.91)	0.59	(0.44–0.79)

This population-based study suggests that primary treatment modality may affect PCSS after metastasis. Following the development of metastases, men who had received primary RP had a longer PCSS than men who had received primary RT.

Shao YHJ et al, Eur Urol, 2015

Primary Radical Prostatectomy Versus Primary Radiotherapy for Locally Advanced Prostate Cancer: an Open Randomized Clinical Trial (SPCG-15)

Planned follow-up is 10 years

PATIENTS

TREATMENT

RANDOMIZED

- Age ≤75
- Newly diagnosed prostatic adenocarcinoma
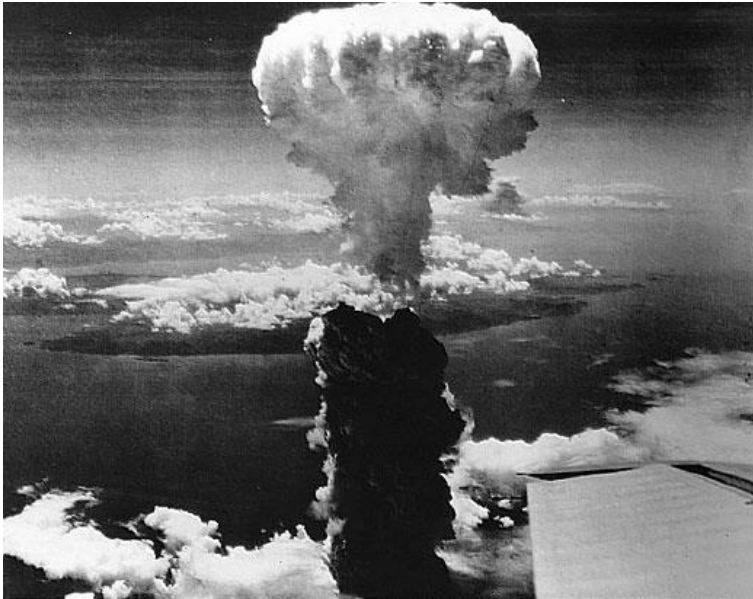- T3 stage Significant extra-capsular tumor extension
- Presence Gleason grade pattern 4

Radical prostatectomy with or without adjuvant or salvage radiotherapy

Radiotherapy with adjuvant androgen deprivation therapy

1:1

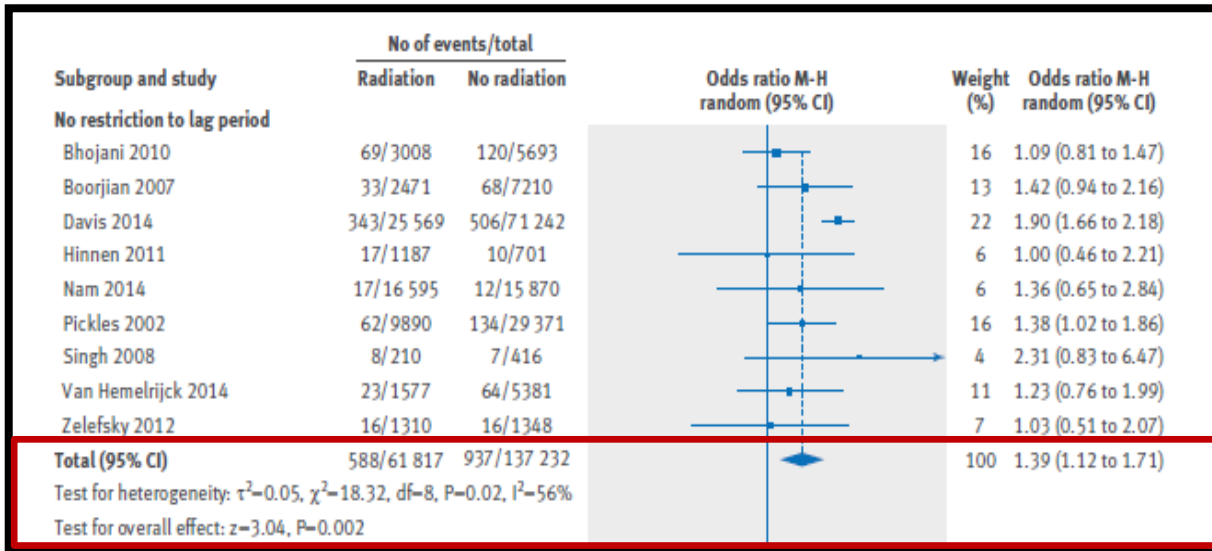N = 1200

Primary efficacy endpoint: Cause-specific survival (CSS)

NCT02102477

RDT+ HT - side effects!!!

Second malignancies after radiotherapy for prostate cancer: systematic review and meta-analysis

BMJ

Bladder cancer

Subgroup and study	Radiation (No of events/total)	No radiation (No of events/total)	Odds ratio M-H random (95% CI)	Weight (%)	Odds ratio M-H random (95% CI)
No restriction to lag period					
Bhojani 2010	69/3008	120/5693		16	1.09 (0.81 to 1.47)
Boorjian 2007	33/2471	68/7210		13	1.42 (0.94 to 2.16)
Davis 2014	343/25 569	506/71 242		22	1.90 (1.66 to 2.18)
Hinnen 2011	17/1187	10/701		6	1.00 (0.46 to 2.21)
Nam 2014	17/16 595	12/15 870		6	1.36 (0.65 to 2.84)
Pickles 2002	62/9890	134/29 371		16	1.38 (1.02 to 1.86)
Singh 2008	8/210	7/416		4	2.31 (0.83 to 6.47)
Van Hemelrijck 2014	23/1577	64/5381		11	1.23 (0.76 to 1.99)
Zelefsky 2012	16/1310	16/1348		7	1.03 (0.51 to 2.07)
Total (95% CI)	588/61 817	937/137 232		100	1.39 (1.12 to 1.71)
Test for heterogeneity: $\tau^2=0.05$, $\chi^2=18.32$, df=8, P=0.02, $I^2=56\%$					
Test for overall effect: z=3.04, P=0.002					

Colorectal cancer

Subgroup and study	Radiation (No of events/total)	No radiation (No of events/total)	Odds ratio M-H random (95% CI)	Weight (%)	Odds ratio M-H random (95% CI)
No restriction to lag period					
Bhojani 2010	33/3079	43/6037		11	1.51 (0.96 to 2.38)
Boorjian 2007	11/2471	20/7210		7	1.61 (0.77 to 3.36)
Davis 2014	310/25 569	557/71 242		17	1.56 (1.35 to 1.79)
Hinnen 2011	25/1187	16/701		8	0.92 (0.49 to 1.74)
Margel 2011	26/2163	168/26 830		12	1.93 (1.27 to 2.93)
Nam 2014	45/16 595	15/15 870		9	2.87 (1.60 to 5.16)
Pickles 2002	234/9890	319/29 371		17	2.21 (1.86 to 2.62)
Rapiti 2008	11/264	8/870		5	4.68 (1.86 to 11.77)
Van Hemelrijck 2014	24/1577	97/5381		11	0.84 (0.54 to 1.32)
Zelefsky 2012	13/1310	9/1348		5	1.49 (0.64 to 3.50)
Total (95% CI)	732/64 105	1252/164 860		100	1.68 (1.33 to 2.12)
Test for heterogeneity: $\tau^2=0.08$, $\chi^2=31.82$, df=9, P<0.001, $I^2=72\%$					
Test for overall effect: z=4.34, P<0.001					

*We identified consistent evidence of an **increased risk of bladder, colorectal, and rectal cancers** in men treated with radiotherapy.*

Secondary Cancer After Radiotherapy for Prostate Cancer: Should We Be More Aware of the Risk?

Peter J. Bostrom [a,b,*], Mark S. Soloway [b]

No. patients
141,761
122,123
85,815
144,162

SEER Epidemiological Studies

Study	Bladder cancer			Rectal cancer		
	Radiation	No radiation/surgery	p-value	Radiation	No radiation/surgery	p-value
Neugut et al. [22]	1.5[a] (95% CI, 1.1–2.0)	1.0[a] (95% CI, 1.0–1.7)	–	0.8[a] (95% CI, 0.4–1.3)	0.8[a] (95% CI, 0.6–1.1)	–
Brenner et al. [30]	1.32[b]	0.75[b]	0.01	1.18[b]	0.55[b]	0.03
Baxter et al. [31]	NA	NA	NA	1.7 (95% CI, 1.4–2.2)[c]	1.0[c]	<0.0001
Moon et al. [28]	1.6[c] (95% CI, 1.44–1.84)	0.78[c,*]	<0.05	1.60[c] (95% CI, 1.29–1.99)	0.92[c,*]	<0.05

- *Radiotherapy for pCa seems to be associated with a increase in secondary cancers. One of 70 patients undergoing radiation for pCa will develop a secondary cancer if they survive more than 10 yr.*
- *Other treatment modalities should be considered for young patients and patients with additional risk factors, such as cigarette smoking.*

THE CALCULATED RISK OF FATAL SECONDARY MALIGNANCIES FROM INTENSITY-MODULATED RADIATION THERAPY

STEPHEN F. KRY, M.S.,* MOHAMMAD SALEHPOUR, PH.D.,* DAVID S. FOLLOWILL, PH.D.,*
MARILYN STOVALL, PH.D.,* DEBORAH A. KUBAN, M.D.,† R. ALLEN WHITE, PH.D.,‡ AND
ISAAC I. ROSEN, PH.D.*

Departments of *Radiation Physics, †Radiation Oncology, and ‡Biomathematics, The University of Texas M. D. Anderson Cancer Center, Houston, TX

| | Conventional | Intensity-modulated radiotherapy | | | | | |
| | 18 MV | 6 MV | | 10 MV | 15 MV | | 18 MV |
Organ site		Varian	Siemens	Varian	Varian	Siemens	Varian
Colon	527	965	1148	655	877	1103	1271
Liver edge	462	930	1148	661	974	1135	1391
Stomach edge	431	699	893	458	810	920	1154
Liver center	265	417	552	344	541	643	869
Stomach center	253	419	533	334	549	610	860
Esophagus edge	252	437	552	333	509	587	770
Lung edge	228	311	484	287	492	610	910
Lung center	138	189	366	189	314	466	560
Esophagus center	105	161	347	166	232	350	439
Thyroid	139	130	372	134	313	448	684
Bone marrow	359	466	639	363	765	812	1213
Percent risk of fatal second malignancy	1.7	2.9	3.7	2.1	3.4	4.0	5.1

"Clinicians should be aware that IMRT treatments have higher out-of-field dose equivalents than conventional treatments and this dose corresponds to a risk of secondary malignancies"

Most patients are treated with RDT + ADT!!!

RISK GROUP	EXPECTED PATIENT SURVIVAL[a]	INITIAL THERAPY	ADJUVANT THERAPY

Intermediate:[e,n]
• T2b-T2c or
• Gleason score 7 or
• PSA 10–20 ng/mL

≥10 y[o]

RP[i] + PLND if predicted probability of lymph node metastasis ≥2%

Adverse features:[j]
EBRT[h]
or
Observation[k]

Lymph node metastasis:
ADT[l] (category 1) ± EBRT[h] (category 2B)
or
Observation (category 2B)[k]

EBRT[h] ± ADT[l] (4–6 mo) ± brachytherapy
or brachytherapy alone[h]

<10 y

Observation[k]

RISK GROUP	INITIAL THERAPY

High:[e]
• T3a or
• Gleason score 8–10 or
• PSA >20 ng/mL

EBRT[h] + ADT[l] (2–3 y) (category 1)
or
EBRT[h] + brachytherapy ± ADT[l] (2–3 y)
or
EBRT[h] + ADT[l] (2–3 y) + docetaxel[p]
or
RP[i] + PLND

National Comprehensive Cancer Network®

Metabolic Complications of Androgen Deprivation Therapy for Prostate Cancer

Philip J. Saylor* and Matthew R. Smith†

From the Department of Oncology, Massachusetts General Hospital Cancer Center, Boston, Massachusetts

of THE JOURNAL UROLOGY®

SEER- 73.196 patients

Adjusted Hazard Ratios	Excess Risk	p value
Diabetes	44%	<0.001
Coronary heart disease	16%	<0.001
Myocardial infarction	11%	0.03
Sudden death	16%	

0.   1.   1.

◄ Better   Worse ►
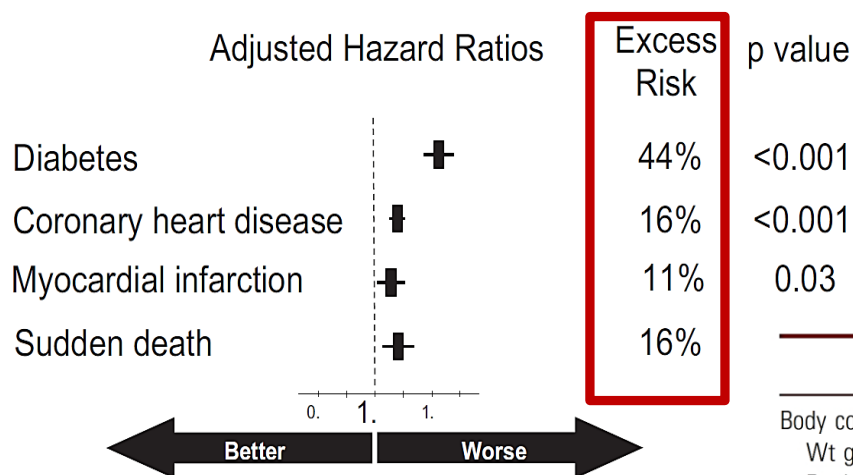
THE METABOLIC SYNDROME

End Points	Observations
Body composition:	
Wt gain	Gain ~2% in 12 mos[15,17,56]
Fat body mass	Gain 4%–8% in 3 mos,[19,20] gain ~10% in 12 mos[15,17,18]
Lean body mass	Lose ~3% in first 3–12 mos[15,17,18,20]
Serum lipids:	
Total cholesterol	Increases 7%–10% in first 3–12 mos of therapy[15,24,25]
Triglycerides	Increases 26% in first 3–6 mos of therapy[15,25]
HDL	Increases 8%–20% in 3–12 mos of therapy[15,24,25]
LDL	No change in 3–6 mos[24,25]
Insulin sensitivity:	
Fasting insulin	Increases 26%–65% in first 12 wks[20,21,24]
Insulin sensitivity index	Decreases ~13% in 12 wks[19,21]

Saylor P & Smith MR, J Urol, 2013

DON'T THINK ONCE, THINK TWICE! THE CARDIOVASCULAR EFFECTS OF ANDROGEN DEPRIVATION THERAPY

FRAMINGHAM HEART STUDY
A Project of the National Heart, Lung and Blood Institute and Boston University

BJUI
BJU INTERNATIONAL

59-year-old patient with high risk PCa.
8 points for age,
2 points for a treated SBP of 136 mmHg
4 points for an cholesterol level of 240 mmol/L,
2 points for diabetes

after ADT

Hard coronary heart disease (HCHD)
(myocardial infarction or coronary death)

Point Total	10-year risk
< 0	< 1
0	1
1	1
2	1
3	1
4	1
5	2
6	2
7	3
8	4
9	5

Point Total	10-year risk
10	6
11	8
12	10
13	12
14	16
15	20
16	25
≥ 17	≥ 30

Risk Score after ADT	25%

The Adult Treatment Panel III, JAMA. 2001

Jefferies ES et al, BJU int, 2011

Androgen Deprivation Therapy for Localized Prostate Cancer and the Risk of Cardiovascular Mortality

Henry K. Tsai, Anthony V. D'Amico, Natalia Sadetsky, Ming-Hui Chen, Peter R. Carroll

*Among the 1015 patients who received ADT, **the median duration of ADT use was 4.1 months** (range = 1.0 – 32.9 months).*
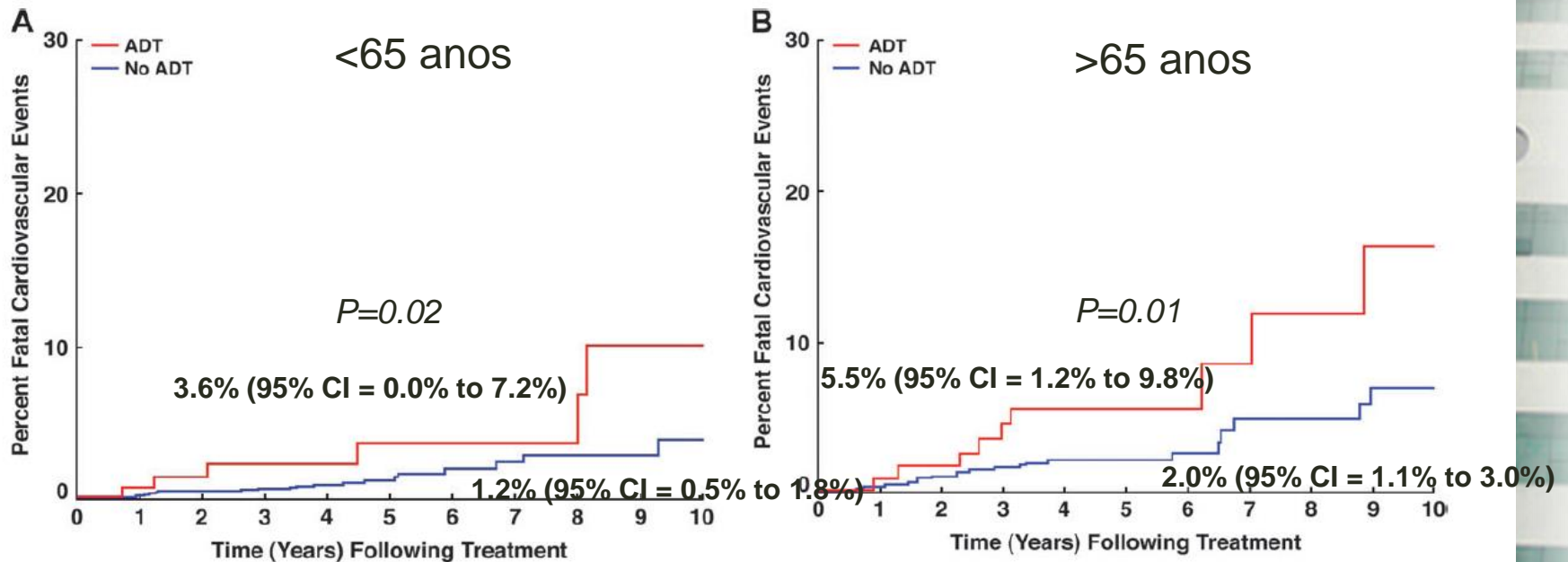
The use of ADT appears to be associated with an increased risk of death from cardiovascular causes

Tsai et al, JNCI, 2007.

Androgen Deprivation Therapy and Future Alzheimer's Disease Risk

Kevin T. Nead, Greg Gaskin, Cariad Chester, Samuel Swisher-McClure, Joel T. Dudley, Nicholas J. Leeper, and Nigam H. Shah
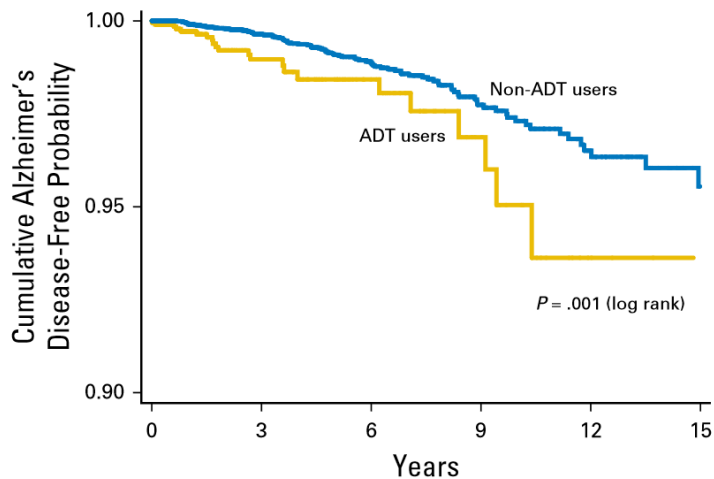
Table 4. Propensity Score–Matched Cox Regression Analysis for the Association of ADT Use With Alzheimer's Disease by Therapy Duration

Duration of ADT Use (Months)	HR (95% CI)	P	P for Trend*
No ADT use	Ref	Ref	.016
ADT users			
< 12 months ADT use	1.62 (0.82 to 3.21)	.165	
≥ 12 months ADT use	2.12 (1.11 to 4.03)	.011	

*In conclusion, we provide support for an **association between the use of ADT in the treatment of prostate cancer and an increased risk of Alzheimer's disease** in a general population cohort*

Surgical Technique
Tailoring RP according risk of EPE

Anatomic Grading of Nerve Sparing During Robot-Assisted Radical Prostatectomy

Schlatoff O , Coelho RF et al, Eur Urol, 2012
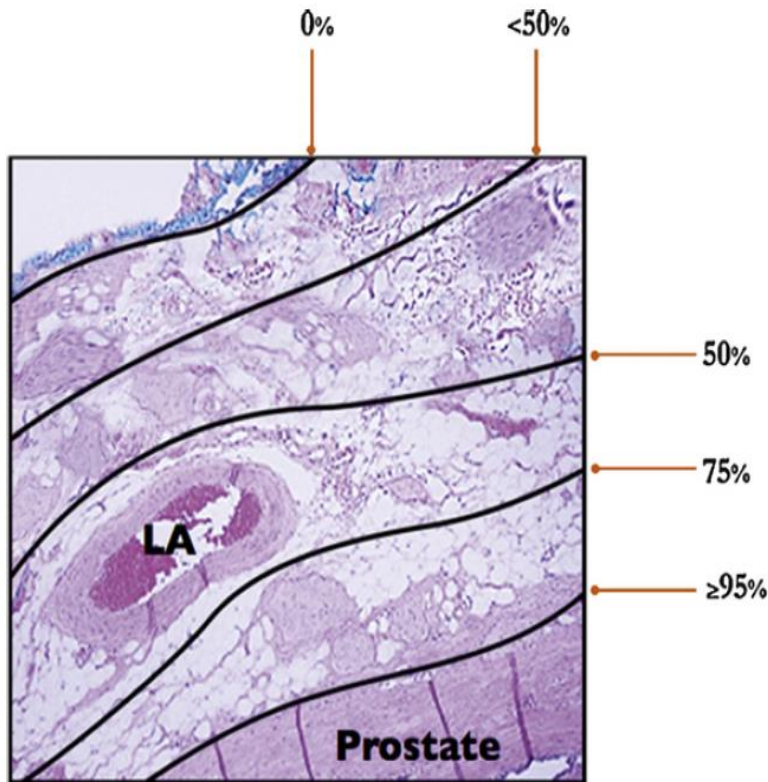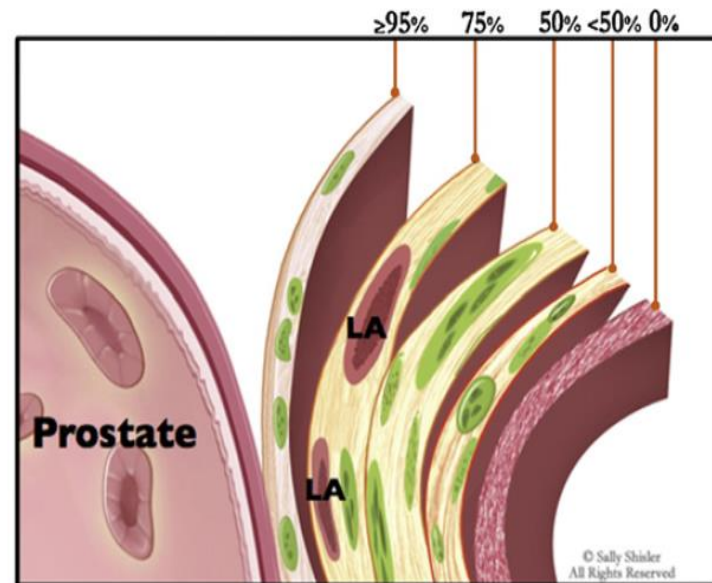
Rationale for partial nerve-sparing

Patients	410 patients with ECE (5217 total)
ECE width min (mm)	0,2
ECE width max (mm)	9
ECE width mean (mm)	1,78 ± 1,39
ECE width median (mm)	1
ECE width <8 mm	99,5%
ECE width <3 mm	89%
ECE width <1 mm	64%

3mm
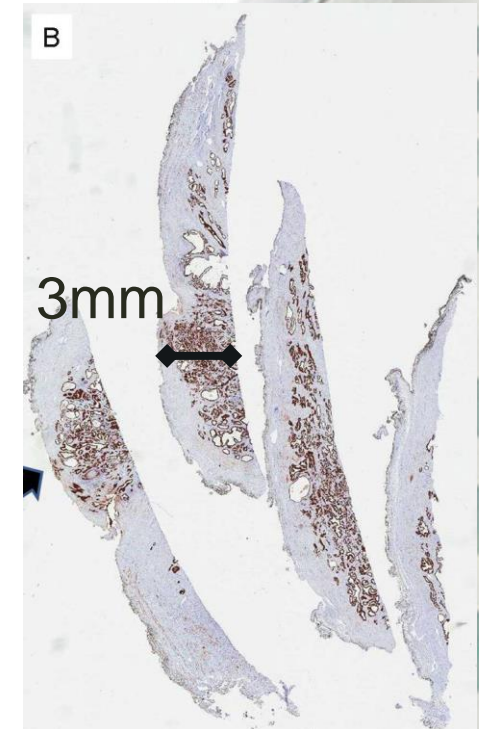
Coelho RF, Patel et al, unpublished data

The Role of the Prostatic Vasculature as a Landmark for Nerve Sparing During Robot-Assisted Radical Prostatectomy

Vipul R. Patel[a,b,], Oscar Schatloff[a], Sanket Chauhan[a,b], Ananthakrishnan Sivaraman[a], Rair Valero[c], Rafael F. Coelho[d], Bernardo Rocco[e,1], Kenneth J. Palmer[a,b], Darian Kameh[a]*
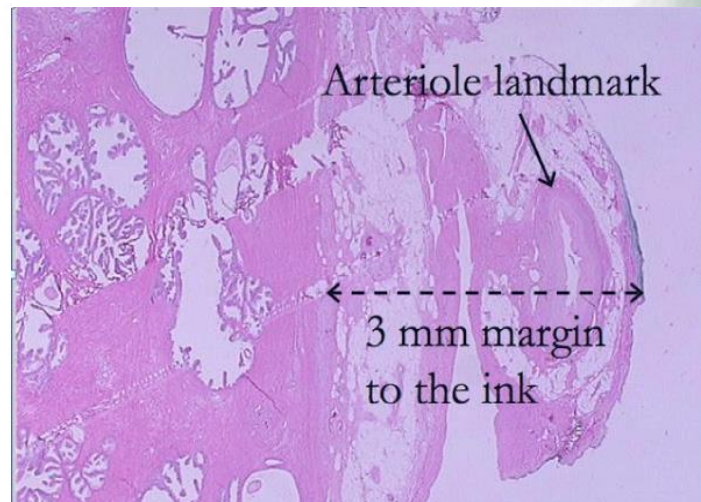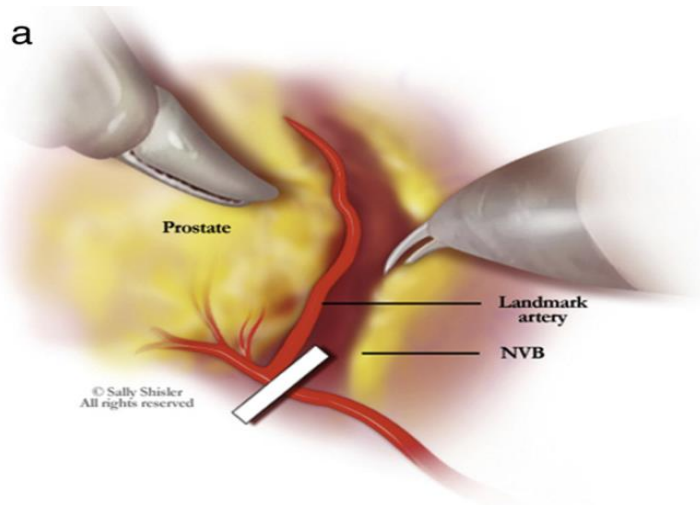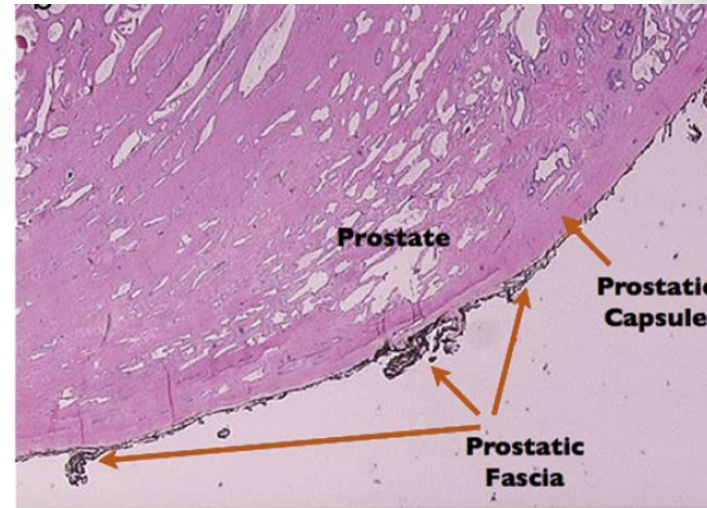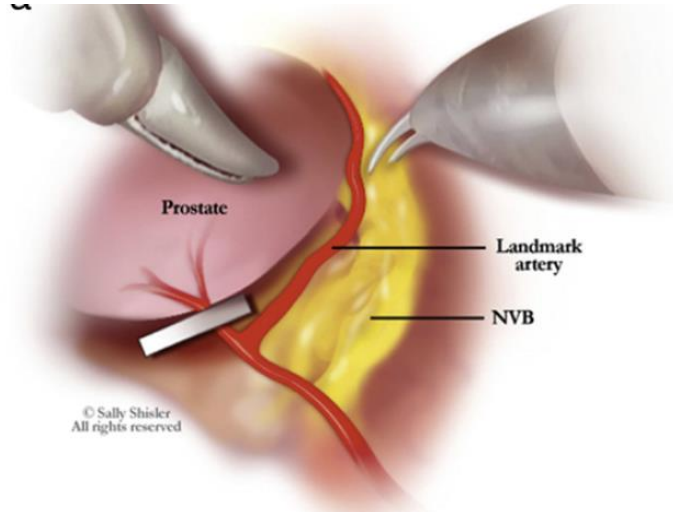
Early Retrograde Release of the NVB
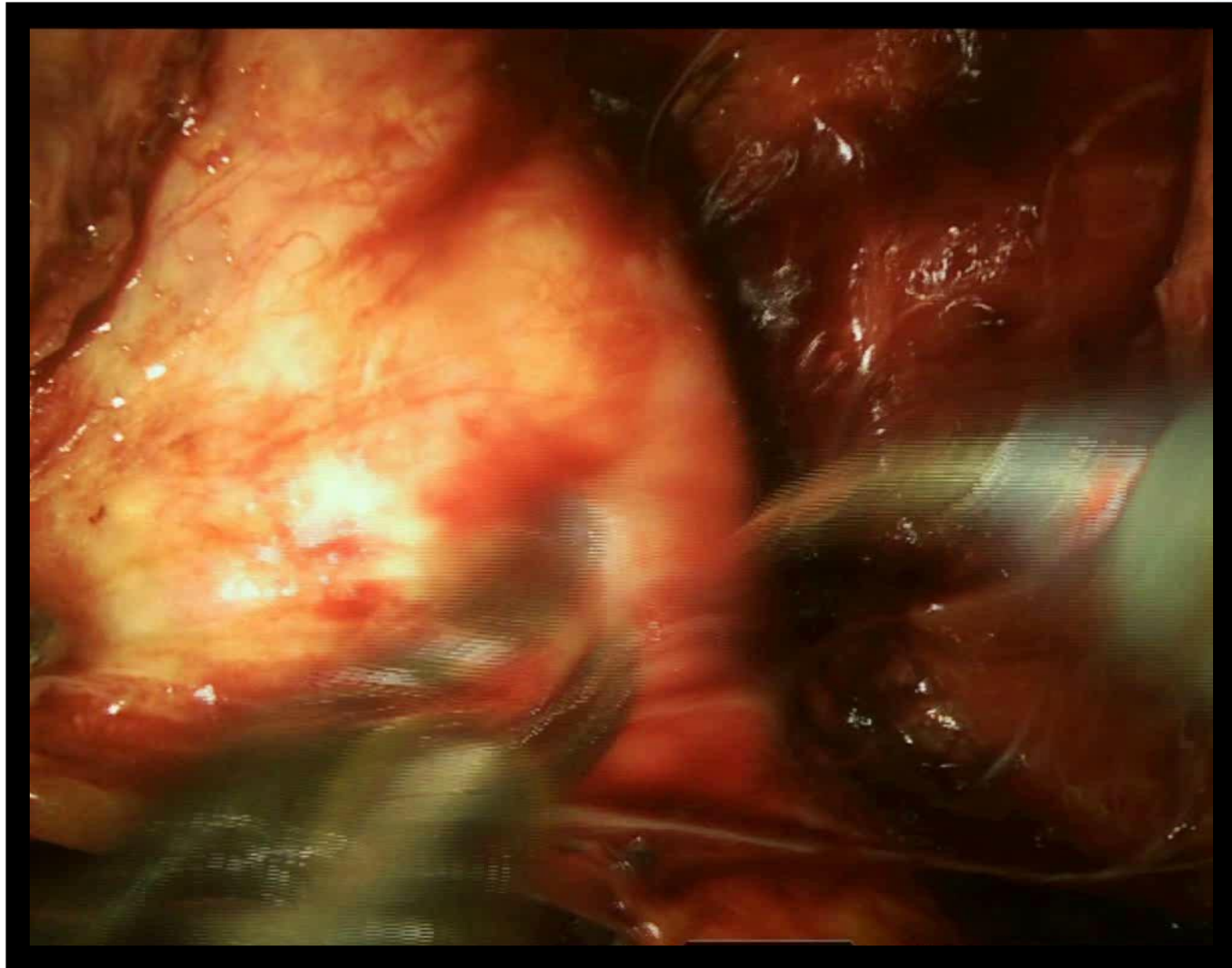
Partial NS - Landmark artery
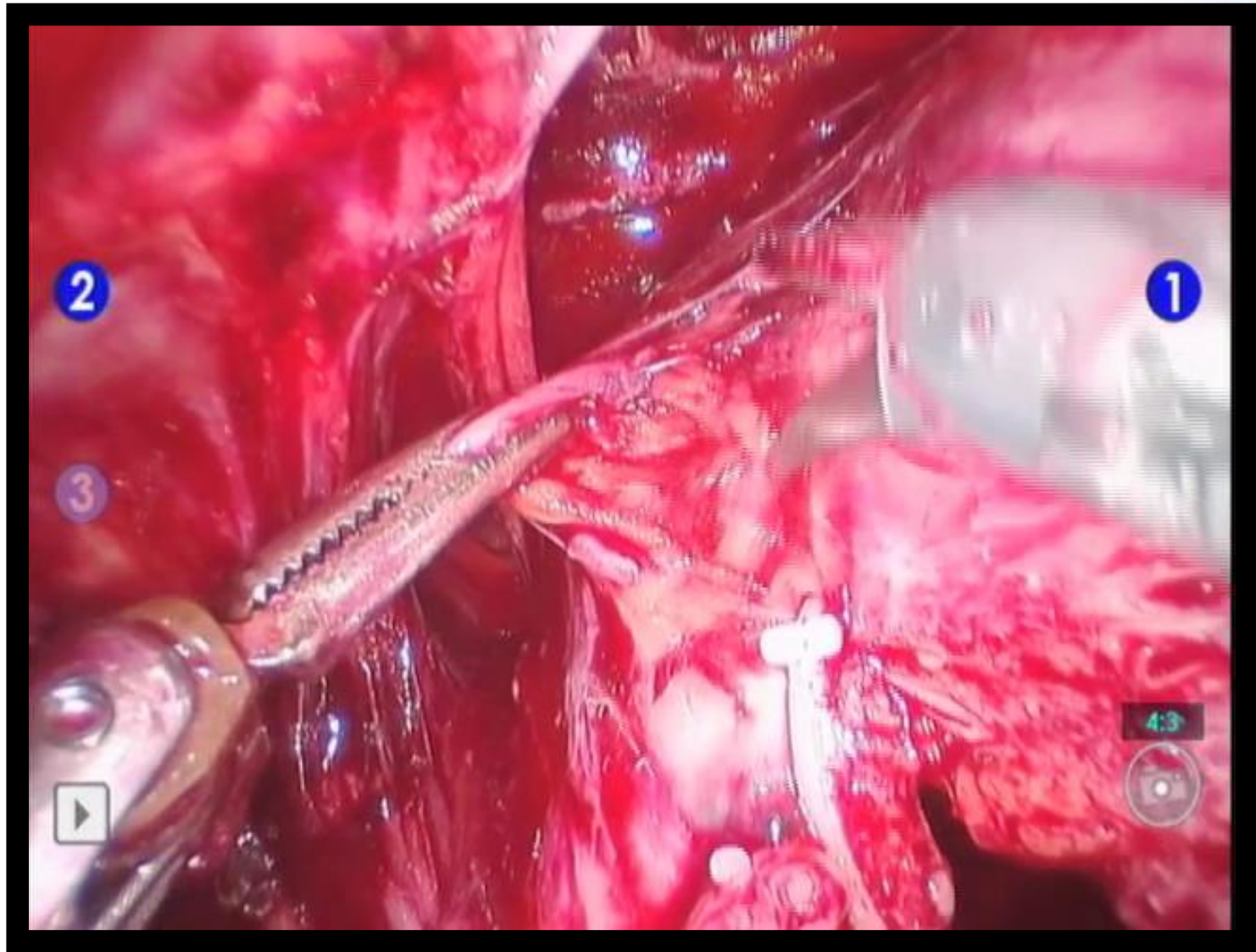
How to plan NS?

The Role of Magnetic Resonance Image-Guided Prostate Biopsy in Stratifying Men for Risk of Extracapsular Extension at RP

MP - MRI	
N	169
ECE	23,1%
Sensitivity	48,7%
Specificity	73,9%
VPP	82,8%
VPN	35,9%
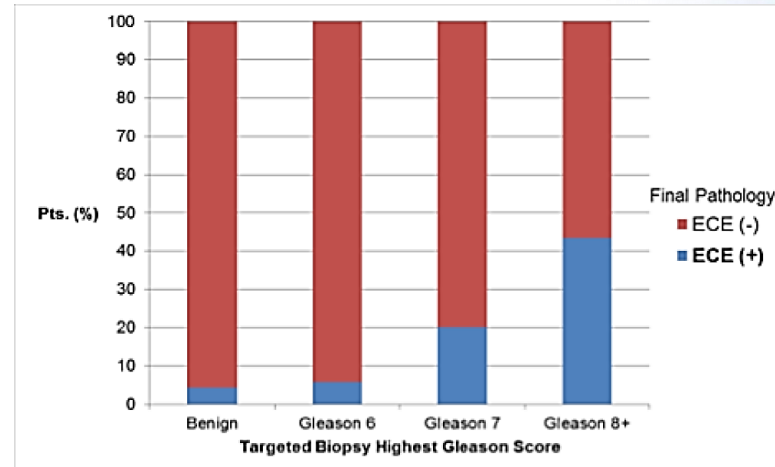
	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age, per year	1.2	1.1 – 1.3	**<0.001***	1.2	1.1 – 1.3	**0.002***
PSA, per ng/mL	1.1	1.0 – 1.2	**0.008***	1.0	1.0 – 1.1	0.259
MP-MRI						
No. lesions, per lesion	0.9	0.5 – 1.3	0.484	-	-	-
Suspicion Level	0.9	0.3 – 2.4	0.562	-	-	-
Biopsy Gleason Score						
Random 12-core	2.5	1.4 – 5.0	**<0.001***	1.5	0.8 – 3.0	0.219
MRI/TRUS fusion-guided	3.0	1.7 – 5.9	**<0.001***	2.0	1.1 – 4.2	**0.032***

Because of the low sensitivity of MP-MRI for ECE, further tools are necessary to stratify men at risk for occult ECE. MRI/TRUS fusion-guided biopsy Gleason score can help identify which men with PCa have ECE that may not be detectable by imaging.

Raskolnikov D et al, J Urol, 2015

A novel tool for predicting extracapsular extension during graded partial nerve sparing in radical prostatectomy

Vipul R. Patel*, Marco Sandri[†], Angelica A.C. Grasso[‡], Elisa De Lorenzis[‡], Franco Palmisano[‡], Giancarlo Albo[‡], Rafael F. Coelho[§], Alexander Mottrie[¶]**, Tadzia Harvey*, Darian Kameh*, Hariharan Palayapalayam*, Peter Wiklund[††], Silvano Bosari[‡‡], Stefano Puliatti[§§], Paola Zuccolotto[¶¶], Giampaolo Bianchi[§§] and Bernardo Rocco[§§]
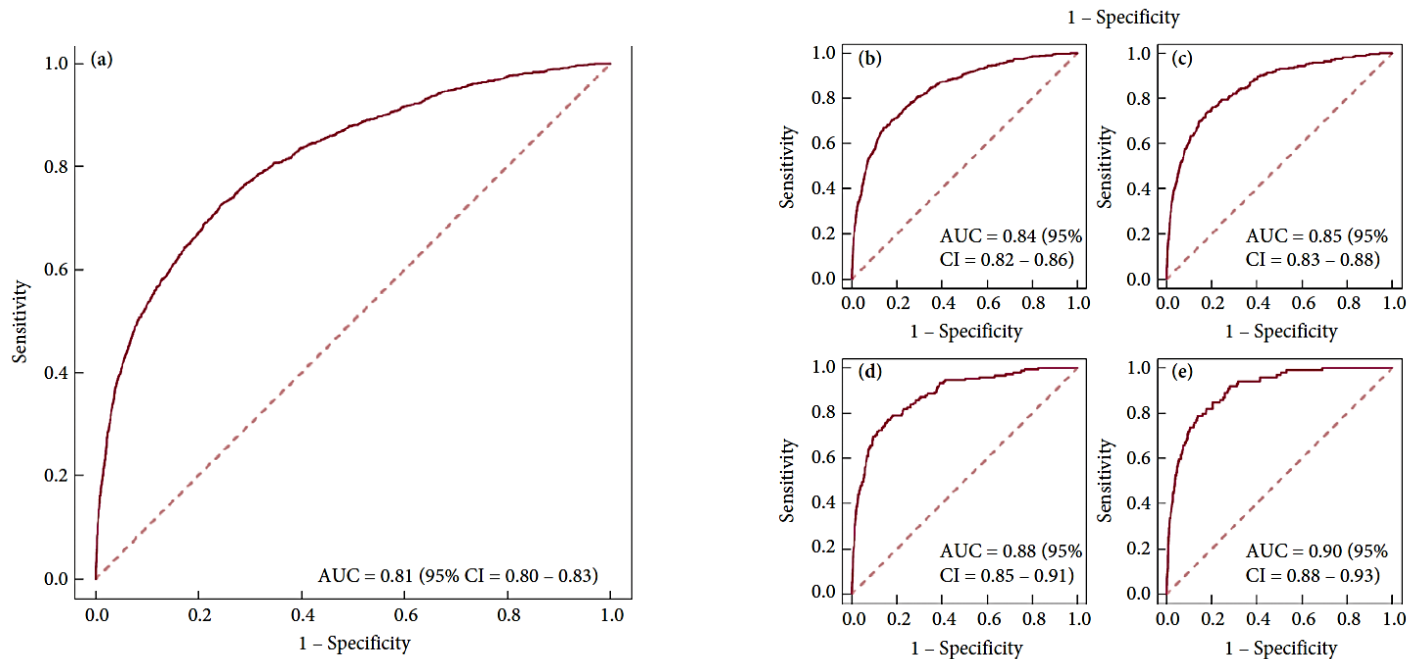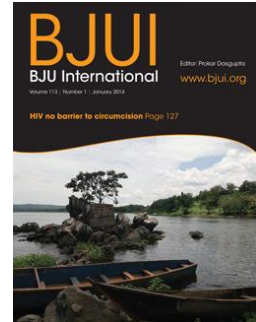
The five logistic models showed good predictive performance, the area under the receiver operating characteristic curve was: 0.81 for ECE, and 0.84, 0.85, 0.88, and 0.90 for ECE width of >1, >2, >3, and >4 mm, respectively.

Patel VR. Coelho RF. BJU Int. 2018

CAPRA score	**Logistic regression**	**0.779 (0.766-0.793)**
Chung JS, Choi HY, Song HR, et al. Preoperative nomograms for predicting extracapsular extension in Korean men with localized prostate cancer: a multi-institutional clinicopathologic study. J Korean Med Sci. 2010 Oct; 25(10):1443-8	Logistic regression	**0.795 (0.781-0.808)**
Crippa A, Srougi M, Dall'Oglio MF, et al. A new nomogram to predict pathologic outcome following radical prostatectomy. Int Braz J Urol. 2006 Mar-Apr;32(2):155-64.	Logistic regression	**0.787 (0.774 – 0.799)**
Graefen M1, Haese A, Pichlmeier U, et al. A validated strategy for side specific prediction of organ confined prostate cancer: a tool to select for nerve sparing radical prostatectomy. J Urol. 2001 Mar;165(3):857-63.	Classification Tree (CART)	**0.698 (0.685 – 0.710)**
Ohori M1, Kattan MW, Koh H, et al. Predicting the presence and side of extracapsular extension: a nomogram for staging prostate cancer. J Urol. 2004 May;171(5):1844-9	Logistic regression	**0.801 (0.788 – 0.814)**
Eifler JB, Feng Z, Lin BM, et al. An updated prostate cancer staging nomogram **(Partin tables)** based on cases from 2006 to 2011. BJU Int. 2013 Jan;111(1):22-9	Multinomial logistic regression	**0.764 (0.750 – 0.778)**
Partin AW, Mangold LA, Lamm DM,et al. Contemporary update of prostate cancer staging nomograms (Partin Tables) for the new millennium. Urology. 2001 Dec;58(6):843-8.	Multinomial logistic regression	**0.774 (0.761 – 0.788)**
Satake N, Ohori M, Yu C, Kattan MW, et al. Development and internal validation of a nomogram predicting extracapsular extension in radical prostatectomy specimens. Int J Urol. 2010 Mar;17(3):267-72.	Logistic regression	**0.776 (0.762 – 0.790)**
Memorial Sloan Kettering Cancer Center https://www.mskcc.org/nomograms/prostate/pre-op/coefficients **Model: Extracapsular Extension**	Logistic regression	**0.777 (0.764 – 0.791)**
Steuber T, Graefen M, Haese A, et al. Validation of a nomogram for prediction of side specific extracapsular extension at radical prostatectomy. J Urol. 2006 Mar;175(3 Pt 1):939-44;	Logistic regression	**0.728 (0.713 – 0.742)**

www.prece.it
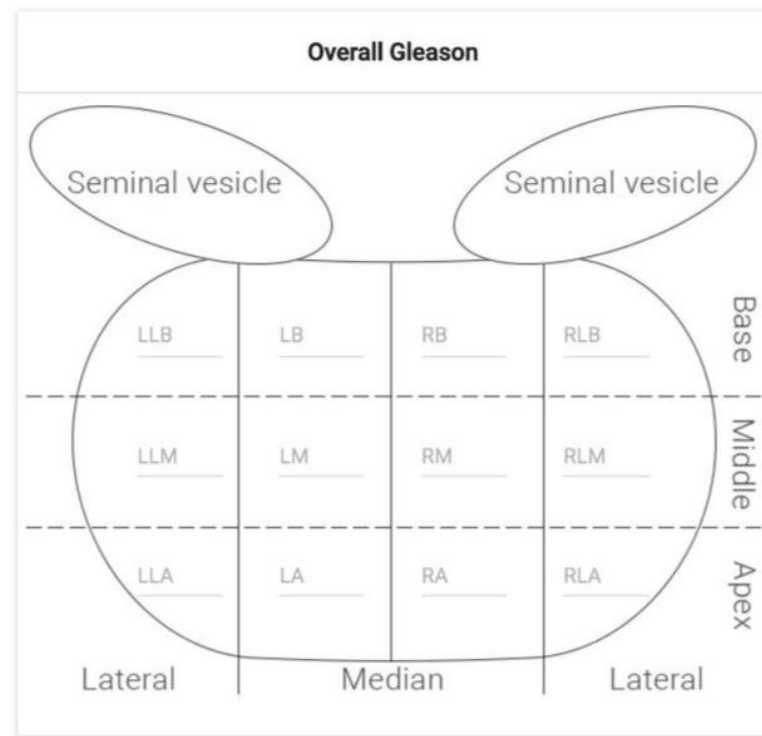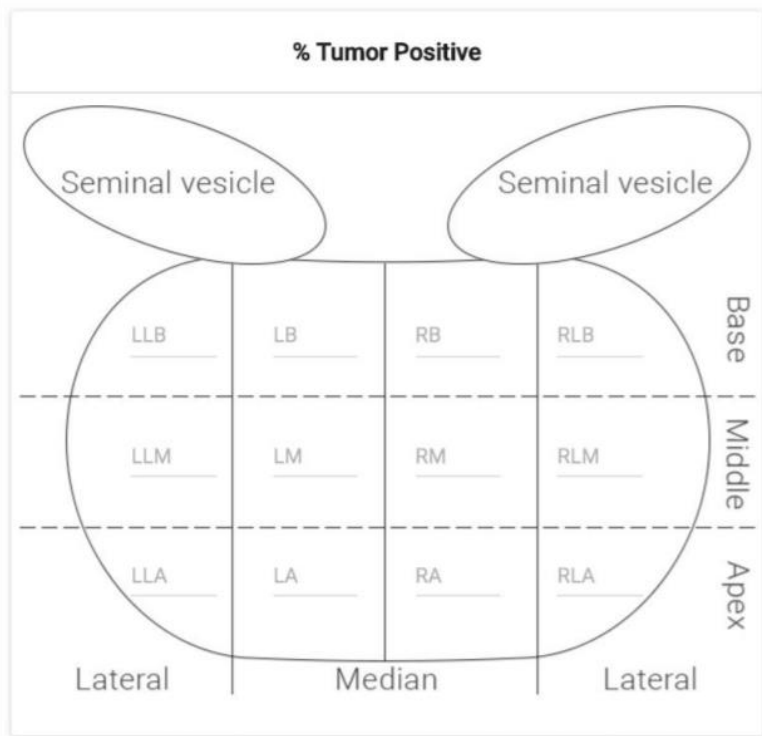
RP - Functional Outcomes

Critical review of 'pentafecta' outcomes after robot-assisted laparoscopic prostatectomy in high-volume centres

Vipul R. Patel*[+], Haidar M. Abdul-Muhsin*, Oscar Schatloff*[+],
Rafael F. Coelho*[+], Rair Valero*[§], Young H. Ko*[¶],

Reference	N patients	Ages, years	Follow-up, months	Continence % at n months				
				Immediate	1	3	6	12
Joseph et al. [11]	325	60	6	24	56	93	96	–
Borin et al. [15]	400	61.2	6	–	70.5	89	97	–
Zorn et al. [54]	300	59.4	24	–	23	47	68	90
Krambeck et al. [20]	294	61	12	–	–	–	–	91.8
Murphy et al. [21]	400	60.2	>18	–	–	–	–	91.4
Rocco et al. [22]	120	63	12	–	–	70	93	97
Novara et al. [52]	304	61.6	12	–	–	–	–	90
Mottrie et al. [13]	184	60	6	–	43	–	95	–
Patel et al. [50]	1100	58	18	–	6 weeks 67.7	85.4	95.7	97.4
Tewri et al. [39]	N* 214	64.3	13	13.1	35.2	50.2	61.9	82.1
	P* 304	62.8	13	27	59	76.6	85.6	91.2
	T* 182	61.2	6	38.4	82.5	91.3	97.1	–
Menon et al. [51]	1142	60.2	12	–	–	–	–	92
van der Poel et al. [53]	151	60	12	–	–	–	54	70
Weighted mean		60.35		25.17	58.54	79.08	87.89	91.85

Patel VR. Coelho RF. BJU Int. 2012

| Reference	N	years	Type of NS, %			Follow-up, months	Potency, %		Overall potency at n months			
			Uni.	Bi.	None		Uni.	Bi.	3	6	12	18
Joseph et al. [11]	325	60	23.6	70	6.4	12	58	80.6	–	77.1	–	–
Zorn et al. [54]	300	59.4	26.4	59.6	14	24	62	83	47	58	74	76.5
Krambeck et al. [20]	294	61	91	9	12	–	–	–	–	70	–	–
Murphy et al. [21]	394	60.2	28.2	65.3	–	12	–	–	–	–	62	–
Rocco et al. [22]	120	63	–	–	–	12	–	–	31	43	61	–
Novara et al. [52]	304	61.6	7	66	27	12	–	–	–	–	49	–
Mottrie et al. [13]	184	62	13	64.5	18.1	6	47	70	–	66.6	–	–
Patel et al. [50]	1100	58	–	–	–	18	–	–	–	68.8	91.5	96.6
Tewari et al. [67]	215	60	11	85	4	12	–	87	–	–	–	–
Menon et al. [51]	1142	60.2	25	33	>18	–	100	–	–	–	70	100
van der Poel and de Block [68]	107	59.6	45.8	54.2	–	6	40.8	63.8	–	53	–	–
Finley et al. [69] with cautery	42	56.5	26	74	–	>18	50	67.8	8.3	14.7	43.2	63.1
Finley et al. [69] without cautery	62	57	26	74	–	>18	80	93	32.1	57.1	76.6	89.6
Weighted mean		59.75	28.64	43.89	15.47		79.42	79.45	38.85	65.49	73.90	95.09

RETROGRADE RELEASE OF THE NVB WITH PRESERVATION OF DORSAL VENOUS COMPLEX

**Demographic and preoperative features
(128 pts – 3.5 months period)**

Variable		
Age, yr, mean ± SD		62,6 ± 0,707
BMI, mean ± SD		27,93 ± 2,984
Charlson comorbidity index, median (IQR)		2 (1-3)
PSA median (IQR)		5,25 (4,1-7,2)
		N° (%)
Clinical stage	T1c	41 (32)
	≥ T2	87 (68)
Biopsy Gleason score	≤6	29 (22,7)
	7	80 (62,5)
	≥8	19 (14,8)
D'Amico risk classification	Low risk	26 (20,3)
	Intermediate risk	70 (54,7)
	High Risk	32 (25)
Prostate weight range, g	20-40	90 (70,3)
	41-60	23 (18,0)
	>60	15 (11,7)
SHIM score, median (IQR)		21,5 (23-20)

RETROGRADE RELEASE OF THE NVB WITH PRESERVATION OF DORSAL VENOUS COMPLEX

% CONTINENCY

% POTENCY

Under review – Eur Urol – Surgery in Motion
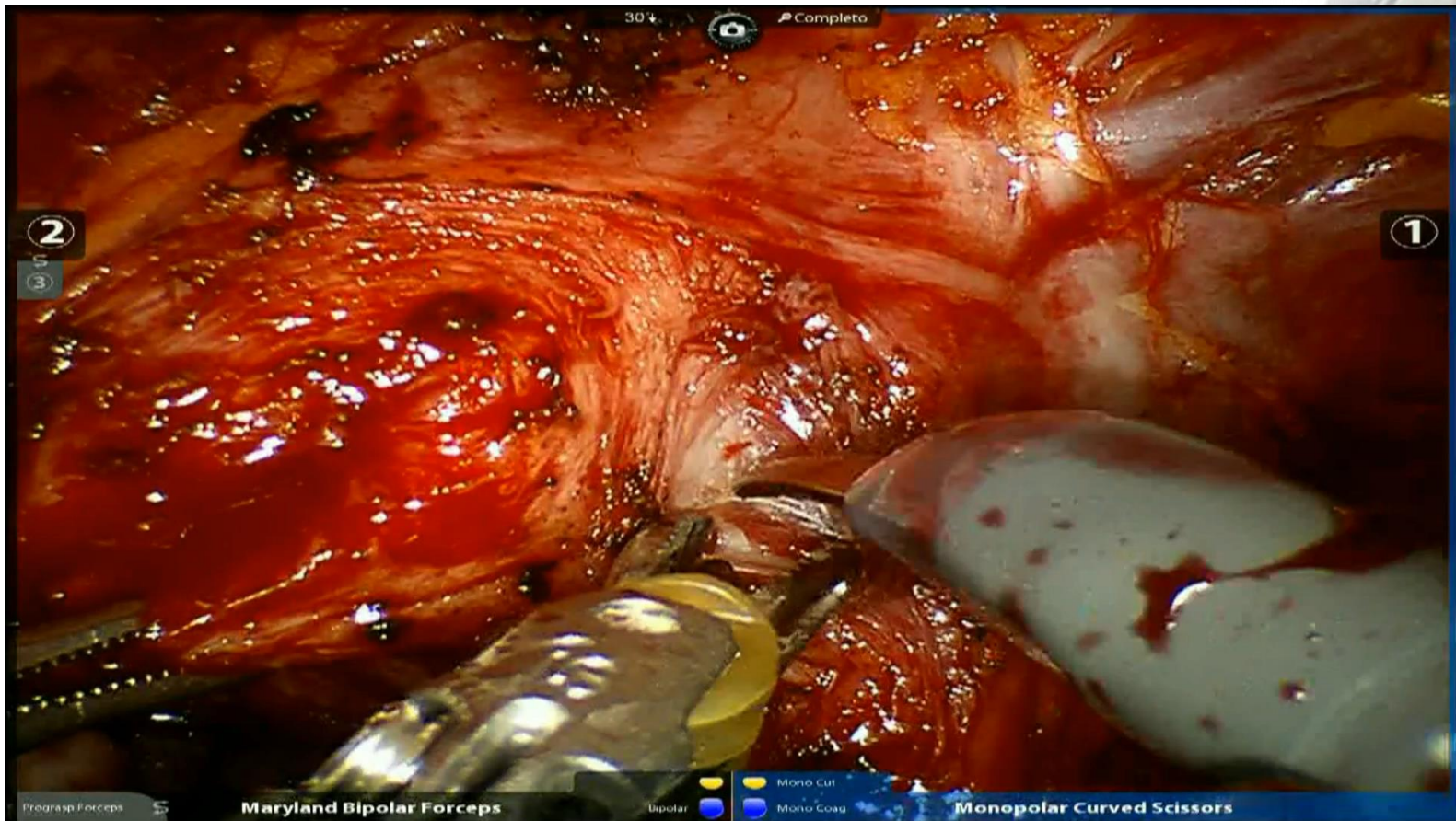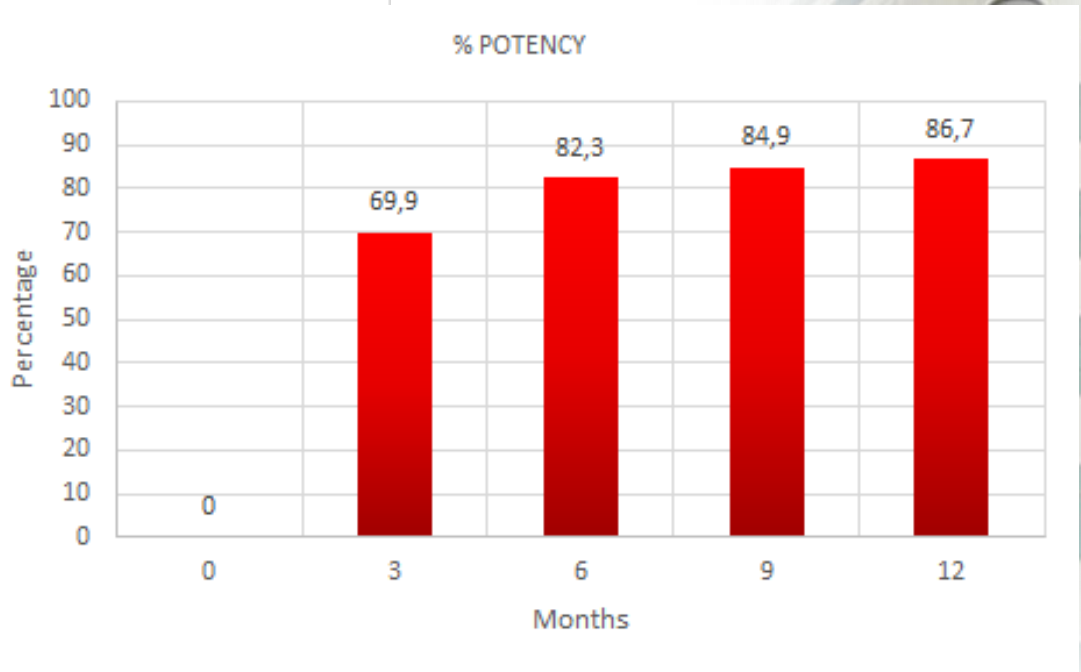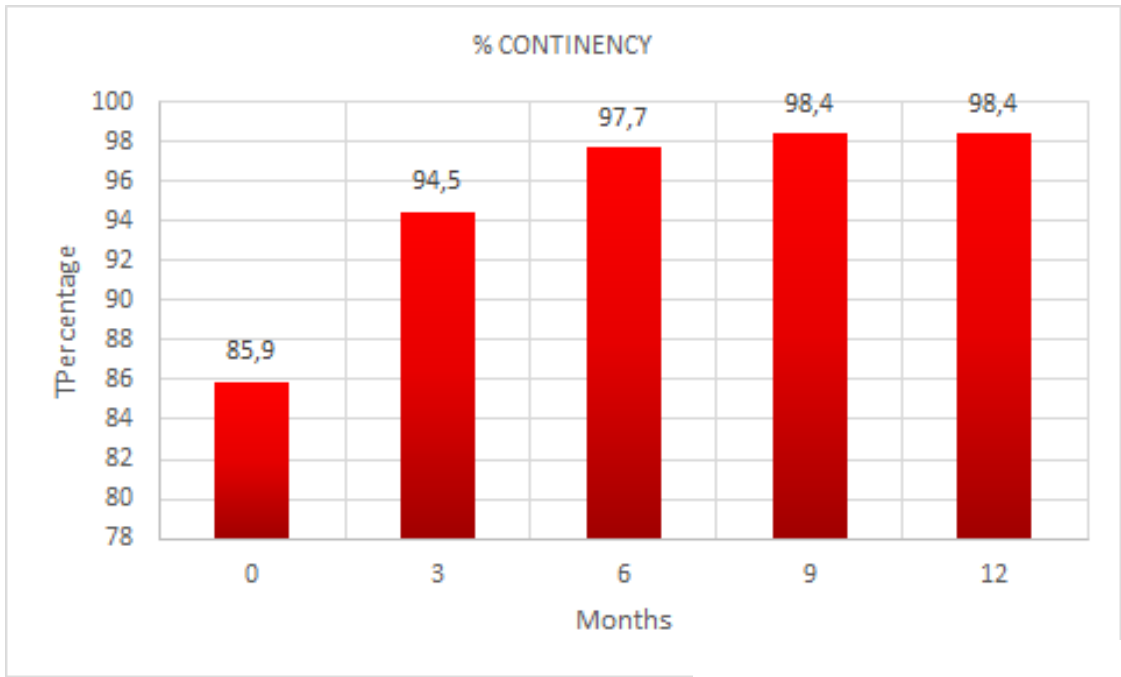
Mr Smith would you consider RDT for your clinically localized Pca?

- You may experience **long term RDT side effects** (bowel dysfunction, second malignancies, worsening LUTS)

- There is no low morbidity **salvage treatment** for BCR

- You will need **ADT** which increases risk of DM, MI, Stroke, Alzheimer, DE, depression, OP

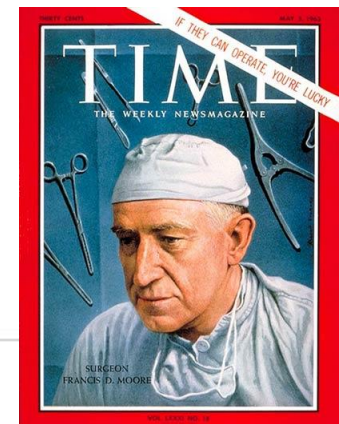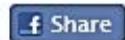- And cancer control, in the available literature, is **worse than RP**

Please take my prostate out, Doc!!

Survey: Surgeons Are The Most Attractive Doctors

And only 6% of women would date a shrink

By Jacob Davidson | Aug. 30, 2013 | 3 Comments

TIME
THE WEEKLY NEWSMAGAZINE
IF THEY CAN OPERATE YOU'RE LUCKY
SURGEON
FRANCIS D. MOORE

Medical school students everywhere take note: if you want a date to go with your degree, it pays to be a surgeon.

According to a survey conducted by UniformDating.com, a dating website "for singles in uniform & for those who like them," surgeons are the most attractive type of doctor. Out of 1,000 men and women polled, 36% of women and 26% of men picked surgeons as the most datable genera of medical professional. Second place went to pediatricians, who received votes from 28% of women and 23% of men.

Jochen Sands / Getty Images

So why did surgeons take the top spot? Respondents believed most are practically minded, possess a high IQ, and can remain calm in difficult situations. The fact that surgeons are likely to be "good with their hands" was cited as an additional plus.