

Clinical Cases

 **Pierpaolo Dragonetti**

 pierpaolo.dragonetti@guest.policlinicogemelli.it

 **Policlinico Universitario Fondazione Agostino Gemelli**

Gemelli



Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore

GART
Advanced Radiation Therapy



FC, Male, 63 years old

Comorbidities: Hypertension treated with Ramipril 5 mg/day

- (11.2024) iPSA: 7 ng/ml
- (17.03.2025) Multiparametric prostate MRI: PIRADS 4 left apical lesion involving <50% of the lobe. Prostate volume: 30 cc
- (14.04.2025) Biopsy: adenocarcinoma GS 3+4, 2/7 cores in the left lobe (target zone)
- (16.05.2025) Bone scintigraphy: negative for bone metastases
- (13.05.2025) CT TAP with contrast: oncologically negative

TO SUMMARIZE:

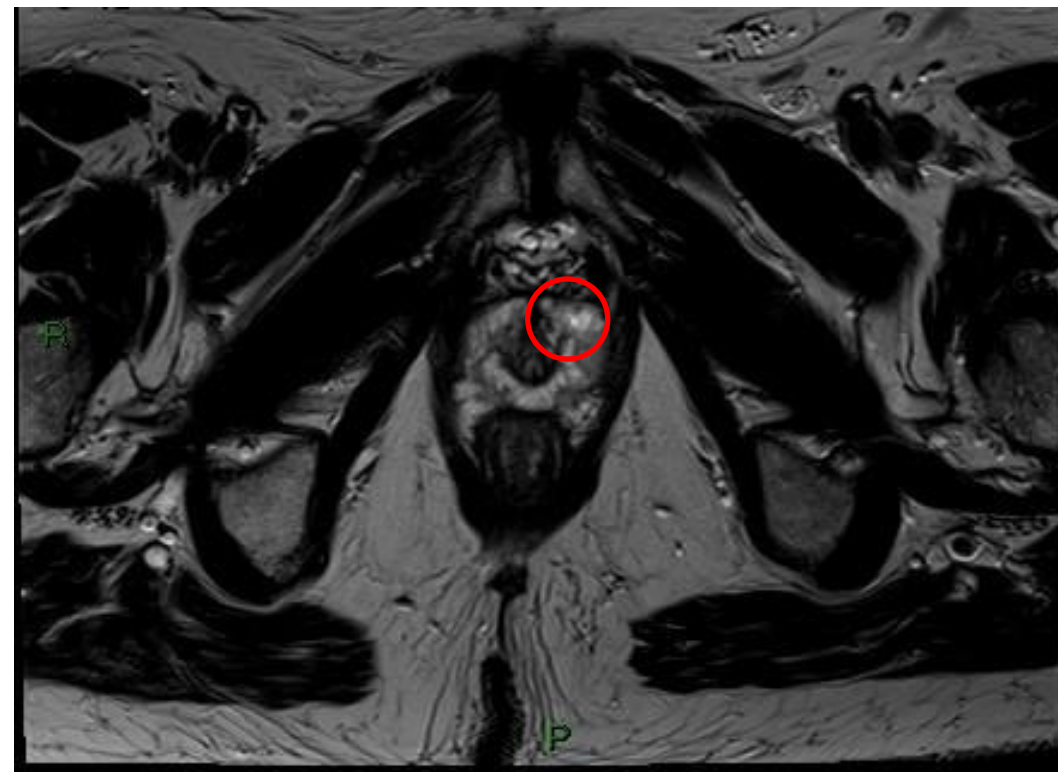
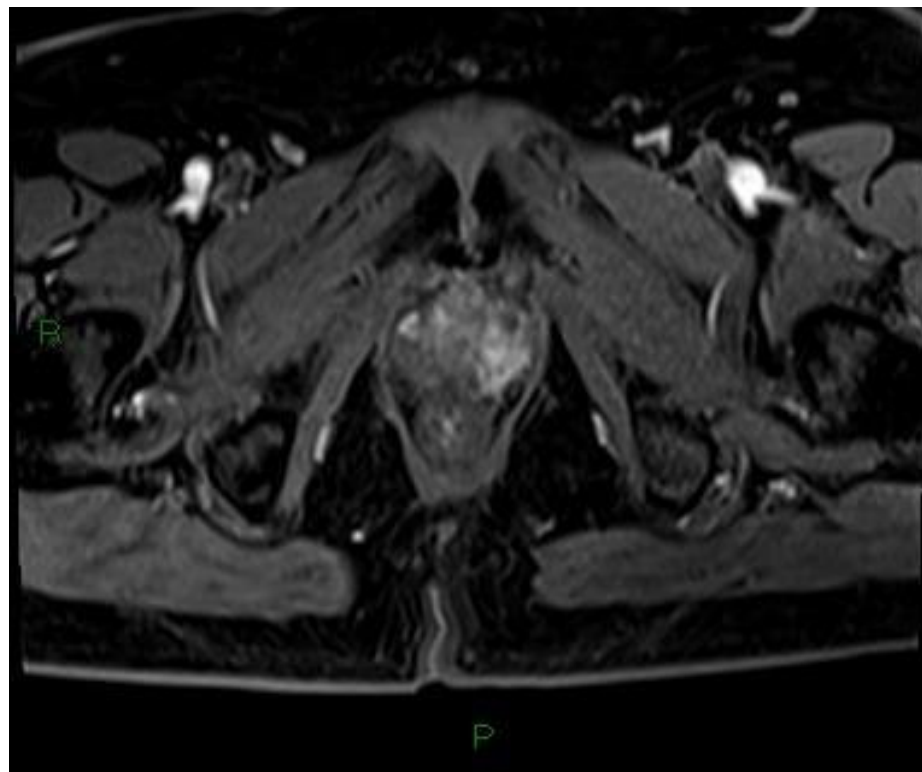
iPSA: 7 ng/ml

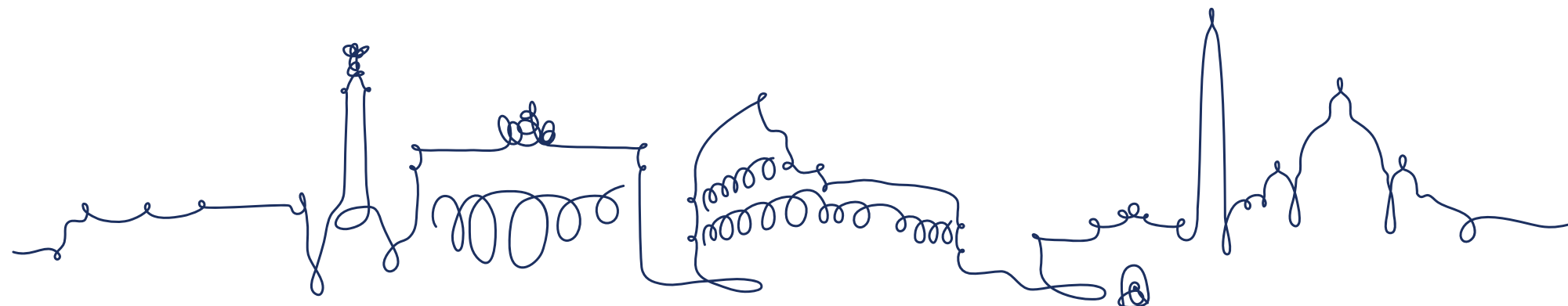
Gleason score: 3+4, 2/7 positive cores in the left lobe

cT2a N0 M0

FC, Male, 63 years old

Multiparametric prostate MRI: PIRADS 4 left apical lesion involving <50% of the lobe. Prostate volume: 30 cc





Which treatment strategy do you believe to be the most appropriate in this scenario?

1. Active surveillance
2. Surgery +/- Hormonal Therapy
3. External Beam RT +/- Hormonal Therapy
4. Interventional RT (Modern Brachytherapy) +/- Hormonal Therapy
5. Hormonal Therapy alone



MRO.35: Equity and research in oncology. The subtle balance between personalized medicine and accessibility to care

26-27-28 OCTOBER 2025 – Fondazione Policlinico Universitario A. Gemelli IRCCS

SCAN ME!



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GSTeP

Gemelli Science and Technology Park

From Guidelines to living practice Panel discussion on local therapy: clinical cases

Prof. Bernardo Rocco

Dir. UOC Urologia – Fondazione Policlinico Gemelli, Roma



Recommendations for intermediate risk Pca (favorable)

Table 4.3: EAU risk groups for biochemical recurrence of localised and locally-advanced prostate cancer (based on systematic biopsy)

Definition				
Low-risk	Intermediate-risk		High-risk	
	Favourable	Unfavourable		
ISUP grade 1 and PSA < 10 ng/mL and cT1-2a*	ISUP grade 2 and PSA < 10 ng/ml and cT1-2b* Or ISUP grade 1 and PSA 10 – 20 ng/ml and cT1-2b* Or ISUP grade 1 and PSA < 10 ng/ml and cT2b*	ISUP grade 2 and PSA 10 – 20 ng/ml and cT1-2b* Or ISUP grade 3 and cT1-2b*	ISUP grade 4/5 Or PSA > 20 ng/ml Or cT2c*	cT3-4* and/or cN+** any ISUP grade* any PSA
Localised				Locally advanced

GS = Gleason score; ISUP = International Society for Urological Pathology; PSA = prostate-specific antigen.

* Based on digital rectal examination.

** Based on CT/bone scan.

Active surveillance for favorable intermediate risk Pca? Maybe yes, BUT ...



6.3.2.6 Recommendations for the management of intermediate-risk disease*

Recommendations	Strength rating
Expectant management	
Offer watchful waiting in asymptomatic patients with life expectancy < 10 years (based on comorbidities and age).	Strong
Offer active surveillance (AS) to selected patients with ISUP grade group 2 disease e.g., < 10% pattern 4, PSA < 10 ng/mL, ≤ cT2a, low disease extent on imaging and low extent of tumour in biopsies (≤ 3 positive cores with Gleason score 3+4 and ≤ 50% cancer involvement/core), or another single element of intermediate-risk disease with low disease extent on imaging and low biopsy extent, accepting the potential increased risk of metastatic progression.	Weak

Overall, the Panel interpreted these data to show that a subset of patients with favorable intermediate-risk prostate cancer and life expectancy greater than 10 years may be considered for active surveillance. However, the precise inclusion criteria and follow-up protocols need continued refinement. Patients must understand that a significant proportion of those clinically staged as having favorable intermediate-risk prostate cancer may have higher risk disease.²⁷⁴⁻²⁷⁷ Particular consideration to active surveillance may be appropriate for those patients with a low percentage of Gleason pattern 4 cancer, low tumor volume, low PSA density, and/or low genomic risk (from tissue-based molecular tumor analysis), but should be approached with caution, include informed decision-making, and use close monitoring for progression.

=> Only to those with low disease extent, low genomic risk and counsel for potential increased risk of metastasis

Favorable intermediate risk Pca with potential aggressiveness

MY choice?

ACTIVE
SURVEILLANCE

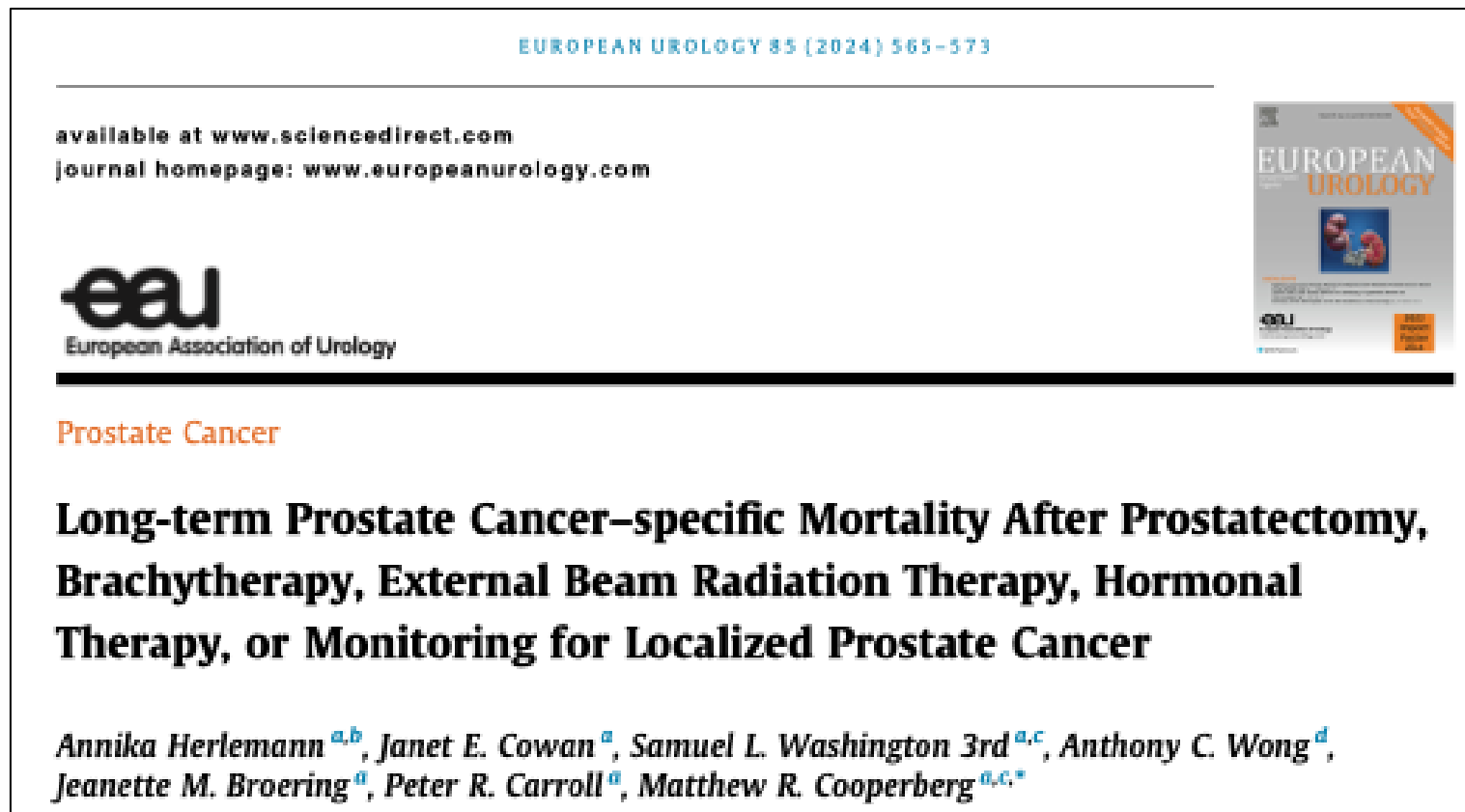


RADIATION TREATMENT
FOCAL TREATMENT

**ROBOTIC RADICAL
PROSTATECTOMY**

Adequate survival outcomes with surgery

Long term PC specific mortality stratified by primary treatment of Pca



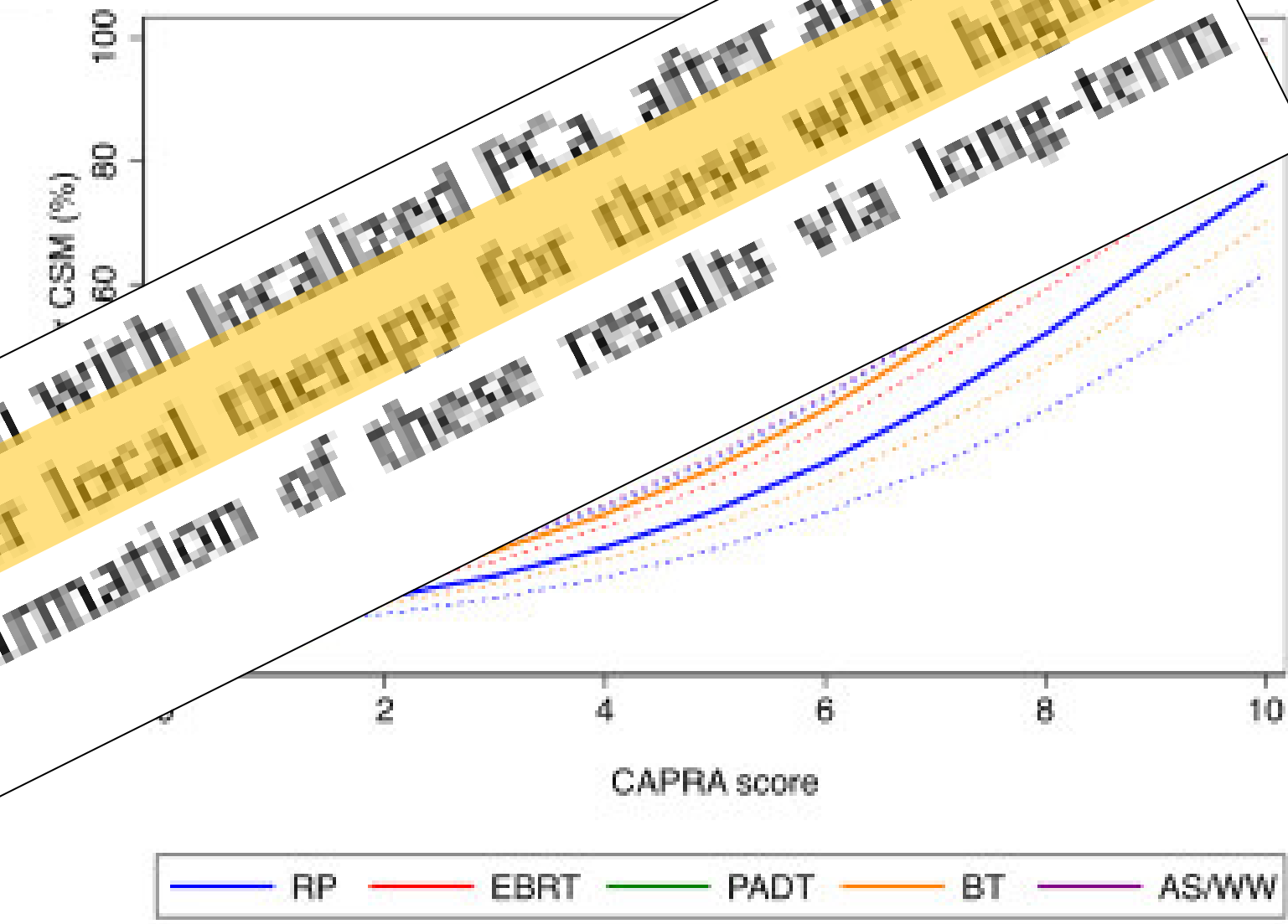
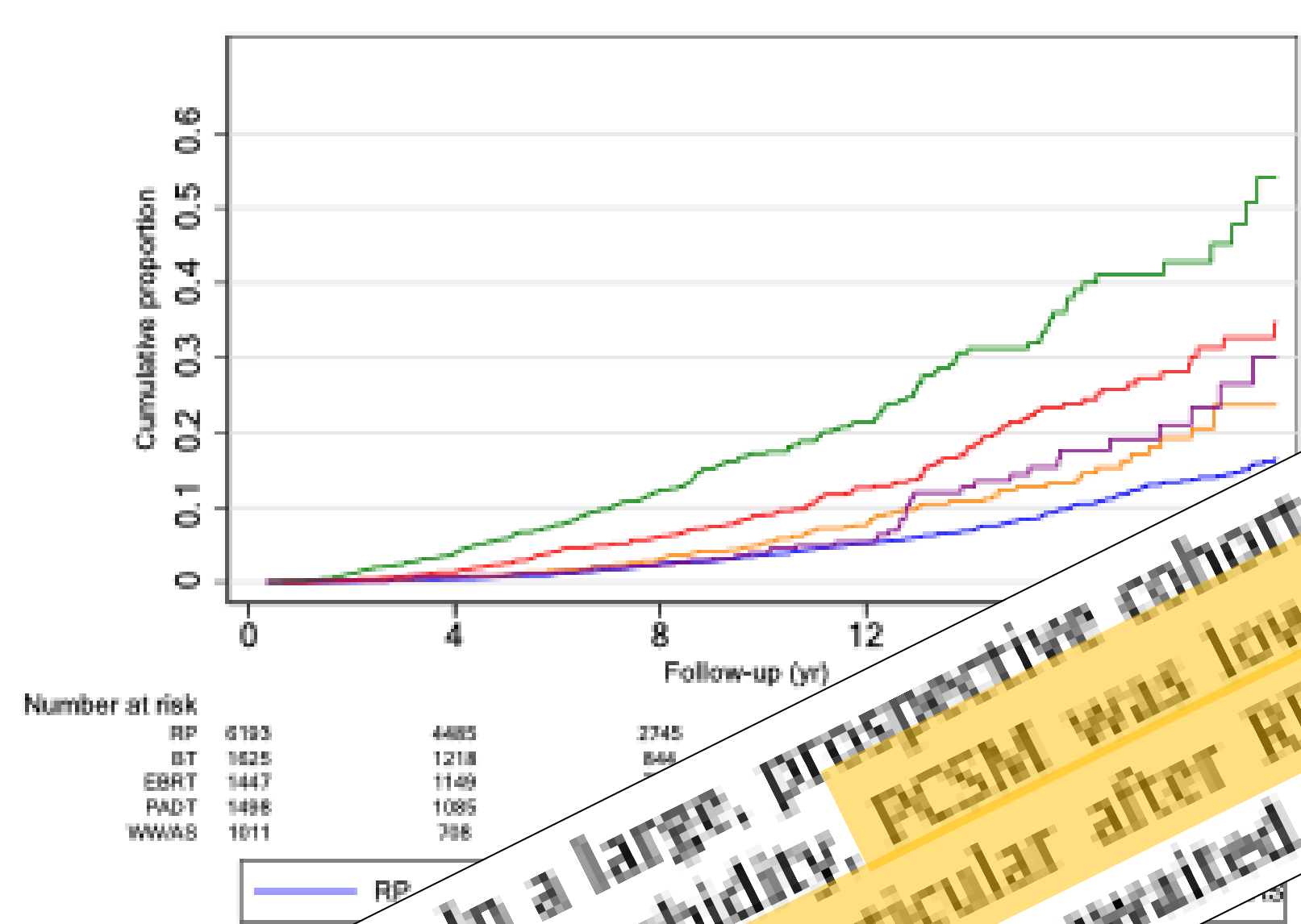
Methods:

- Cohort study with long-term follow-up from the multicenter, prospective, largely community-based Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) registry
- Endpoint: PCSM and all-cause mortality by primary treatment

Results :

- **11 864 men**, 6227 (53%) RP, 1645 (14%) BT, 1462 (12%) EBRT, 1510 (13%) PADT, and 1020 (9%) were managed with AS/WW.
- At a **median of 9.4 yr** (IQR 5.8–13.7) after treatment, **764 Pca deaths**

PCSM by primary treatment



Conclusions: In a large, prospective cohort of men with localized PCA, after adjustment for age and comorbidity, PCSM was lower after local therapy for those with higher-risk disease, and in particular after RP. Confirmation of these results via long-term follow-up of ongoing trials is awaited.

With adjustment for age and comorbidity, the hazard ratio for PCSM was lower for:

- RP (HR 0.45; 95% CI 0.35–0.58; $p < 0.001$) for BT
- RP (HR 0.41; 95% CI 0.31–0.54; $p < 0.001$) for EBRT
- RP (HR 0.41; 95% CI 0.31–0.54; $p < 0.001$) for PADT
- RP (HR 0.45; 95% CI 0.35–0.58; $p < 0.001$) for AS/WW.

Differences in PCSM were negligible for low-risk disease and increased progressively with risk.

Robotic surgery may improve survival outcomes compared with open surgery



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journal homepage: euoncology.europeanurology.com



Robotic Versus Open Radical Prostatectomy, Differences in Prostate Cancer-specific Survival—12 Years of Follow-up in the LAParoscopic Prostatectomy Robot Open Trial

Anna Lantz^{a,b,c,*}, Ying Li^{d,e}, Stefan Carlsson^{a,b}, Johan Stranne^{f,g}, Eva Angenete^{d,h}, Olof Akre^{a,b}, Anders Bjartell^{i,j}, Mehdod Mansoori^{i,j}, Carolina Ehrencrona^d, Peter Wiklund^{a,b,k}, Eva Haglund^{d,h}



Methods

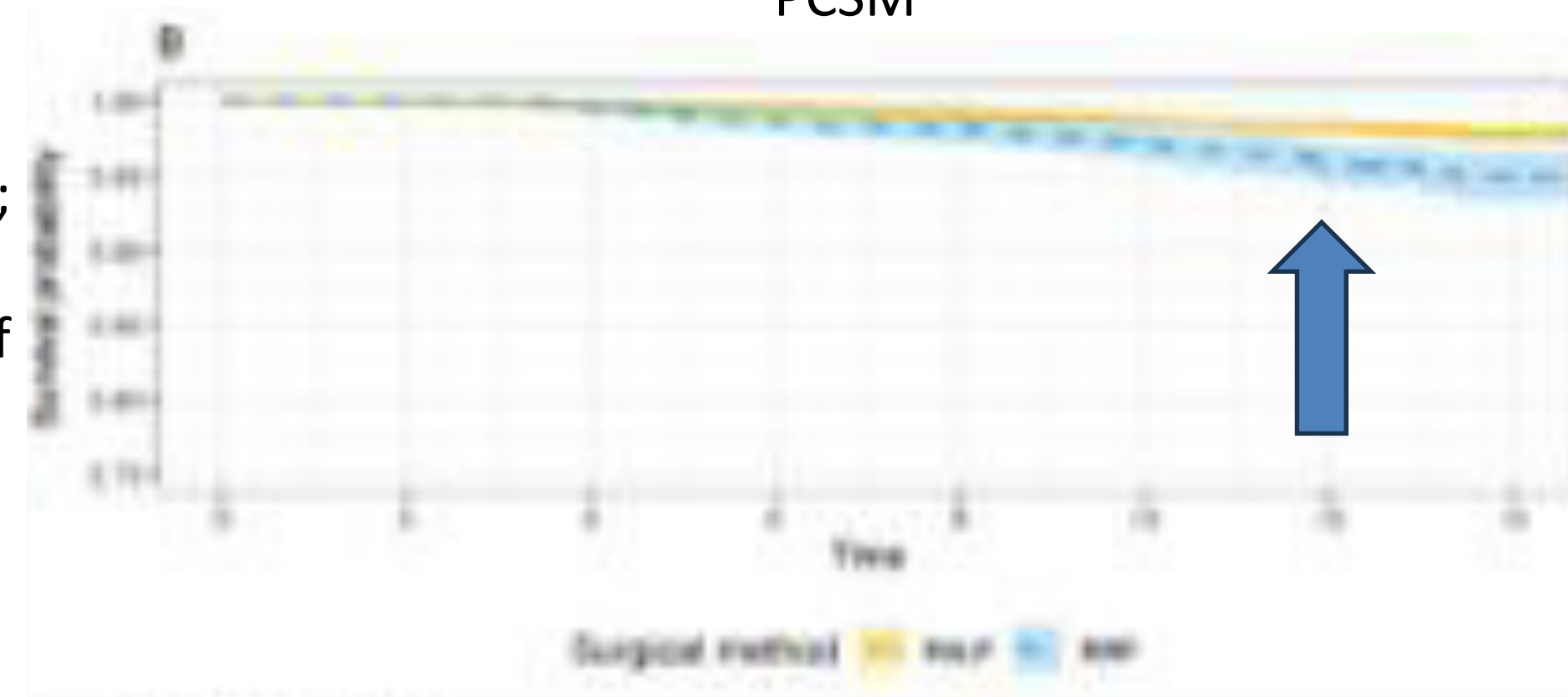
- The non-randomized multicenter observational study LAParoscopic Prostatectomy Robot Open (LAPPRO) trial enrolled patients from 2008 to 2011
- 3583 pts, of whom 2698 (75%) underwent RALP and 885 (25%) RRP.

=> Comparison between robotic and open RP in terms of PCSM

Results:

- At 12 yrs, PCSM significantly lower after RALP (2.0% vs 4.5%; adjusted HR: 0.36, 95% [CI] 0.23–0.55).
- Difference was more pronounced at 12 yr than at 8 yr of follow-up; significant difference in all-cause mortality as well.

PCSM



When stratifying by D’Amico risk group, the mortality difference between RALP and RRP was seen primarily in the high-risk group

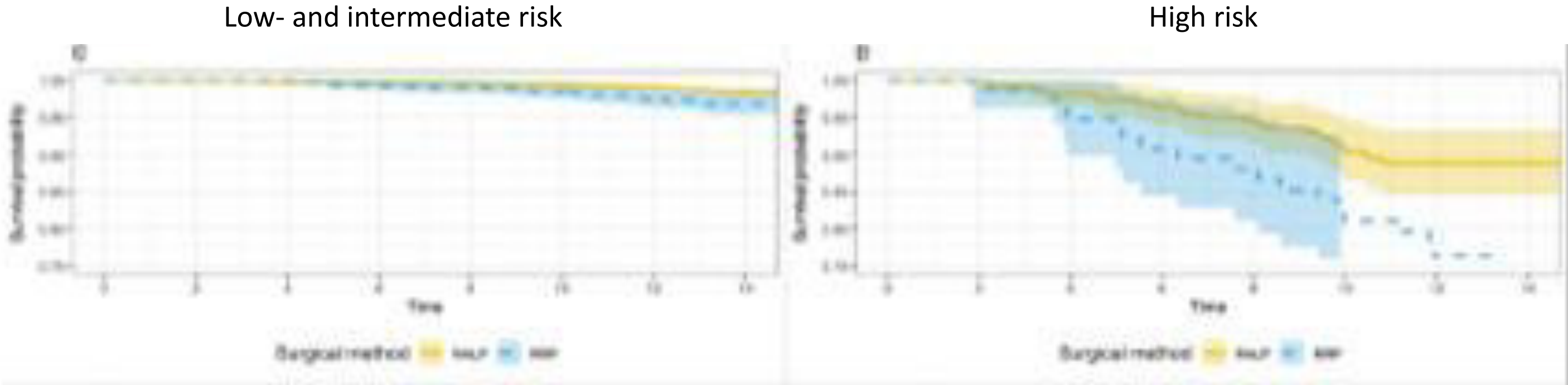


Table 2 – Oncological outcomes in patients undergoing RALP versus RRP 12 yr after surgery

	Main analysis		Sub group analysis 1 ^a			
	Overall		D'Amico low and intermediate risk		D'Amico high risk	
	RALP (n = 2698)	RRP (n = 885)	RALP (n = 2443)	RRP (n = 779)	RALP (n = 220)	RRP (n = 77)
Residual disease, n/total (%)	74/2639 (2.8) ^b	31/841 (3.7) ^b			14/214 (6.5) ^b	14/70 (20) ^b
Relative risk, unadjusted (95% CI)	0.76 (0.50–1.15)				0.33 (0.16–0.65) ^c	
Relative risk, adjusted ^c (95% CI)	Not converged				Not converged	
Elevated PSA, n/total (%)	411/2620 (16)	156/854 (18)	334/2381 (14)	125/762 (16)	76/205 (37)	24/63 (38)
Hazard ratio, unadjusted (95% CI)	0.83 (0.69, 1.00)		0.83 (0.68, 1.02)		0.94 (0.60, 1.49)	
Hazard ratio, adjusted ^d (95% CI)	0.83 (0.67, 1.02)		0.91 (0.72, 1.14)		0.92 (0.55, 1.54)	
Recurrence, n/total (%)	616/2620 (24)	211/854 (25)	509/2381 (21)	172/762 (23)	99/205 (48)	29/63 (46)
Hazard ratio, unadjusted (95% CI)	0.93 (0.80, 1.09)		0.93 (0.79, 1.11)		1.03 (0.68, 1.56)	
Hazard ratio, adjusted ^d (95% CI)	0.91 (0.76, 1.08)		0.99 (0.82, 1.19)		0.97 (0.62, 1.52)	
Overall mortality, n/total (%)	371/2698 (14)	145/885 (16)	314/2443 (13)	114/779 (15)	54/220 (25)	27/77 (35)
Hazard ratio, unadjusted (95% CI)	0.83 (0.68, 1)		0.87 (0.70, 1.08)		0.66 (0.44, 1.04)	
Hazard ratio, adjusted ^e (95% CI)	0.81 (0.66, 0.99)		0.84 (0.66, 1.06)		0.75 (0.44, 1.28)	
Prostate cancer-specific mortality, n/total (%)	55/2698 (2)	40 /885 (5)	32/2433 (1)	22/779 (3)	23/220 (10)	18/77 (23)
Hazard ratio, unadjusted (95% CI)	0.45 (0.26, 0.87)		0.48 (0.25, 0.86)		0.42 (0.23, 0.78)	
Hazard ratio, adjusted ^f (95% CI)	0.36 (0.23, 0.55)		0.43 (0.25, 0.74)		0.40 (0.21, 0.77)	

In the high-risk group, the rates of residual disease was significantly lower for RALP than for RRP (6.5% vs 20%; risk ratio 0.33, 95% CI 0.16–0.65)

Robotic surgery provides adequate functional outcomes



Retrograde release of NVB

EUROPEAN UROLOGY 77 (2020) 628–635

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Surgery in Motion

Retrograde Release of the Neurovascular Bundle with Preservation of Dorsal Venous Complex During Robot-assisted Radical Prostatectomy: Optimizing Functional Outcomes

Paulo Afonso de Carvalho^{a,*}, João A.B.A. Barbosa^a, Giuliano B. Guglielmetti^a,
Maurício Dener Cordeiro^a, Bernardo Rocco^b, William C. Nahas^a, Vipul Patel^c,
Rafael Ferreira Coelho^{a,d,e,*}

12 mo continence rate: 98,4%
12 mo potency rate: 86%

Hood technique

EUROPEAN UROLOGY 80 (2021) 213–221

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Surgery in Motion

Hood Technique for Robotic Radical Prostatectomy—Preserving Periurethral Anatomical Structures in the Space of Retzius and Sparing the Pouch of Douglas, Enabling Early Return of Continence Without Compromising Surgical Margin Rates

Vinayak G. Wagaskar^{a,*}, Ankur Mittal^b, Stanislaw Sobotka^a, Parita Ratnani^a, Anna Lantz^a,
Ugo Giovanni Falagario^a, Alberto Martini^a, Zach Dovey^a, Patrick-Julien Treacy^a,
Prachee Pathak^a, Suit Nair^a, Berryhill Roy^a, Dimple Chakravarty^a, Sara Lewis^c,
Kenneth Haines III^d, Peter Wiklund^a, Ash Tewari^a

48 wk continence rate: 95%

Retzius sparing

EUROPEAN UROLOGY 79 (2021) 839–857

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journal homepage: www.europeanurology.com

eau
European Association of Urology

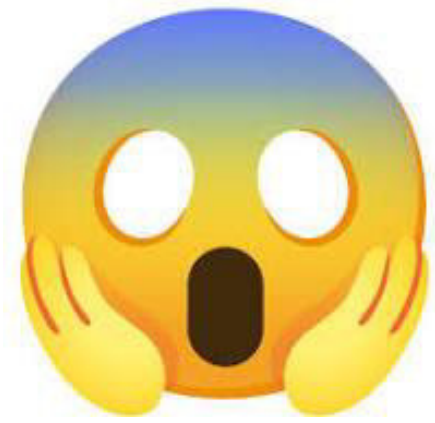
Surgery in Motion

Retzius-sparing Robot-assisted Radical Prostatectomy Leads to Durable Improvement in Urinary Function and Quality of Life Versus Standard Robot-assisted Radical Prostatectomy Without Compromise on Oncologic Efficacy: Single-surgeon Series and Step-by-step Guide

Jillian Egan^a, Shawn Marhamati^a, Filipe L.F. Carvalho^a, Meghan Davis^a, John O'Neill^a,
Harry Lee^a, John H. Lynch^a, Ryan A. Hankins^a, Jim C. Hu^b, Keith J. Kowalczyk^{a,*}

12 mo continence rate: 97,6%

Is continence a real issue of surgery?



The PACE-A RCT compared surgery and radiation for local treatment of PCa:
INcontinence after surgery as high as 50%! BUT ...

EUROPEAN UROLOGY 86 (2024) 566–576

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

 European Association of Urology



Original Article – Editor's choice
Editorial by Markus Graefen, Alberto Bossi on pp. 577–578 of this issue

Radical Prostatectomy Versus Stereotactic Radiotherapy for Clinically Localised Prostate Cancer: Results of the PACE-A Randomised Trial

Nicholas van As^{a,b,*}, Binnaz Yasar^{a,b}, Clare Griffin^b, Jaymini Patel^b, Alison C. Tree^{a,b}, Peter Ostler^c, Hans van der Voet^d, Daniel Ford^e, Shaun Tolan^f, Paula Wells^g, Rana Mahmood^h, Mathias Winklerⁱ, Andrew Chan^j, Alan Thompson^a, Chris Ogden^a, Olivia Naismith^{a,k}, Julia Pugh^b, Georgina Manning^b, Stephanie Brown^b, Stephanie Burnett^b, Emma Hall^b

50 surgeries (small sample size ...)
32 with full data (data completeness?)
42 robot + 8 lap (different techniques ?)

«accrual of 50 RP over a ten-year period
across 8 centers»
(slow recruitment)

«The minimum annual surgical caseload was
specified as at least 25 cases»
Low volume centers

Designing a RCT does not allow drafting conclusions on surgical outcomes

=>>>> Surgery is not a drug and the way it is «administered» matters!



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Minerva Urology and Nephrology 2025 mese;77(0):000-000
DOI: 10.23736/S2724-6051.25.06422-5

EDITORIAL COMMENT

Should every randomized controlled trial be considered Level 1 evidence?

Bernardo ROCCO ¹ *, Maria C. SIGHINOLFI ¹, Alessandro ANTONELLI ²,
Andrea MINERVINI ³, Vipul PATEL ⁴, Rafael COELHO ⁵, Marcio COVAS MOSCHOVAS ⁴,
Michele AMENTA ⁶, Filippo ANNINO ⁷, Riccardo BERTOLO ², Marco BORGHESI ⁸,
Pierluigi BOVE ⁹, Giorgio BOZZINI ¹⁰, Giovanni CACCIAMANI ¹¹, Antonio CELIA ¹²,
Carlo CERUTI ¹³, Orietta DALPIAZ ¹⁴, Roberto FALABELLA ¹⁵, Mario FALSAPERLA ¹⁶,
Antonio Galfano ¹⁷, Fabrizio GALLO ¹⁸, Francesco GRECO ¹⁹, Paolo PARMA ²⁰,
Antonio PASTORE ²¹, Giovanni PINI ²², Angelo PORRECA ¹⁹, Carmine SCIORIO ²³,
Riccardo SCHIAVINA ²⁴, Silvia SECCO ¹⁷, Tommaso SILVESTRI ¹², Virginia VARCA ²⁵,
Domenico VENEZIANO ²⁶, Paolo VERZE ²⁷, Alessandro VOLPE ²⁸, Stefano ZARAMELLA ²⁹,
Marco SANDRI ³⁰, Cristian FIORI ³¹, Luigi SCHIPS ³², Francesco PORPIGLIA ³¹

The continence rates reported in the PACE-A trial significantly diverge from those observed in contemporary studies, underscoring the need for transparency regarding surgical expertise and techniques employed. The individual volume of surgeons participating to the PACE-A is not reported, and “the minimum annual caseload specified as at least 25 cases” is seemingly attributable to the hospital level.

CLINICAL CASE DISCUSSION ON PC:

Radiation Oncology point of view



PROF FILIPPO ALONGI,

–Direttore dip. Radioterapia oncologica avanzata, IRCCS OSPEDALE SACRO CUORE DON CALABRIA , NEGRAR DI
VALPOLICELLA,

–Professore Ordinario, UNIVERSITA'DI BRESCIA

Gemelli

Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore



GART

Advanced Radiation Therapy



CLINICAL INDICATION:
INTERNATIONAL GUIDELINES

**EAU - EANM - ESTRO -
ESUR - ISUP - SIOG
Guidelines on
Prostate Cancer**

P. Cornford (Chair), D. Tilki (Vice-chair), R.C.N. van den Bergh, E. Briers, Patient Advocate (European Prostate Cancer Coalition/Europa UOMO), D. Eberli, G. De Meerleer, M. De Santis, S. Gillissen, A.M. Henry, G.J.L.H. van Leenders, J. Oldenburg, I.M. van Oort, D.E. Oprea-Lager, G. Ploussard, M. Roberts, O. Rouvière, I.G. Schoots, J. Stranne, T. Wiegel
Guidelines Associates: T. Van den Broeck, O. Brundkhorst, A. Farolfi, G. Gandaglia, N. Grivas, M. Lardas, M. Liew, E. Linares Espinós, P.-P.M. Willems
Guidelines Office: J. Darraugh, E. Smith, N. Schouten



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PROSTATE CANCER - LIMITED UPDATE MARCH 2025

6.3.2.6 Recommendations for the management of intermediate-risk disease*

Recommendations	Strength rating
Expectant management	
Offer watchful waiting in asymptomatic patients with life expectancy < 10 years (based on comorbidities and age).	Strong
Offer active surveillance (AS) to selected patients with ISUP grade group 2 disease e.g., < 10% pattern 4, PSA < 10 ng/mL, ≤ cT2a, low disease extent on imaging and low extent of tumour in biopsies (≤ 3 positive cores with Gleason score 3+4 and ≤ 50% cancer involvement/core), or another single element of intermediate-risk disease with low disease extent on imaging and low biopsy extent, accepting the potential increased risk of metastatic progression.	Weak
Patients with ISUP grade group 3 disease should be excluded from AS protocols.	Strong
Re-classify patients with low-volume ISUP grade group 2 disease included in AS protocols, if repeat non-MRI-based systematic biopsies performed during monitoring reveal > 3 positive cores or maximum CI > 50%/core of ISUP grade group 2 disease.	Weak
Radical prostatectomy (RP)	
Offer RP to patients with a life expectancy of > 10 years.	Strong
Radical prostatectomy can be safely delayed for at least three months.	Weak
Offer nerve-sparing surgery to patients with a low risk of extra-capsular disease on that side.	Strong
Radiotherapeutic treatment	
Offer low-dose rate (LDR) brachytherapy to patients with good urinary function and NCCN favourable intermediate-risk disease.	Strong
Offer intensity-modulated radiotherapy (IMRT)/volumetric modulated arc therapy (VMAT) plus image-guided radiotherapy (IGRT), with a total dose of 76–78 Gy or moderate hypofractionation (60 Gy/20 fx in 4 weeks or 70 Gy/28 fx in 6 weeks), in combination with short-term androgen deprivation therapy (ADT) (four to six months).	Strong
Offer focal boosting to MRI-defined dominant intra-prostatic tumour when using conventionally fractionated IMRT/IGRT (1.8-2.0 Gy per fraction) ensuring that Organ at Risk constraints are not exceeded	Weak
Offer ultra-hypofractionated IMRT/IGRT or SBRT, using either 36.25 Gy (40 Gy to prostate) in 5 fx or 42.7 Gy in 7 fx delivered alternate days.	Weak
Offer LDR brachytherapy boost combined with IMRT/VMAT plus IGRT to patients with good urinary function and NCCN unfavourable intermediate-risk disease, in combination with short-term ADT (four to six months).	Weak
Offer high-dose rate (HDR) brachytherapy boost combined with IMRT/VMAT plus IGRT to patients with good urinary function and NCCN unfavourable intermediate-risk disease, in combination with short-term ADT (four to six months).	Weak
Other therapeutic options	
Only offer whole-gland ablative therapy (such as cryotherapy, high-intensity focused ultrasound, etc.) or focal ablative therapy within clinical trials or registries.	Strong
Do not offer ADT monotherapy to asymptomatic men not able to receive any local treatment.	Weak

*All recommendations are based on conventional imaging with isotope bone scan and CT/MR abdomen/pelvis.

INTERMEDIATE (FAVOURABLE)



FC, Male, 63 years old

Comorbidities: Hypertension treated with Triatec 5 mg/day

- (11.2024) iPSA: 7 ng/ml
- (17.03.2025) Multiparametric prostate MRI: PIRADS 4 left apical lesion involving <50% of the lobe. Prostate volume: 40 cc
- (14.04.2025) Biopsy: adenocarcinoma GS 3+4, 2/7 positive cores in the left lobe
- (16.05.2025) Bone scintigraphy: negative for bone metastases
- (13.05.2025) CT TAP with contrast: oncologically negative

TO SUMMARIZE:

iPSA: 7 ng/ml
Gleason score: 3+4, 2/7 positive cores in the left lobe
cT2a N0 M0

INTERMEDIATE (UNFAVOURABLE)



PB, Male, 69 years old

Comorbidities: None

- (10.2024) iPSA: 14 ng/ml
- (28.11.2024) Multiparametric prostate MRI: PIRADS 3/4 Bilateral prostatic lesions without capsular involvement. Prostate volume: 25 cc
- (12.2024) Genitourinary MDT: staging cT2c
- (20.12.2024) Biopsy: adenocarcinoma GS 4+3, 8/12 positive cores bilaterally
- (02.02.2025) F-PSMA PET/CT: pathological uptake in the prostate bilaterally. No seminal vesicle involvement. No pathological pelvic lymph node uptake. Indeterminate uptake at right 7th rib.

TO SUMMARIZE:

iPSA: 14 ng/ml
Gleason score: 4+3, 8/12 positive cores bilaterally
cT2c N0 M0

CLINICAL INDICATION:
INTERNATIONAL GUIDELINES

National
Comprehensive
Cancer
Network®

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NCCN Guidelines Version 2.2026

Prostate Cancer

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[Discussion](#)

INITIAL RISK STRATIFICATION AND STAGING WORKUP FOR CLINICALLY LOCALIZED DISEASEⁱ

Risk Group	Clinical/Pathologic Features (Staging, ST-1)		Additional Evaluation ^{9,i}	Initial Therapy	
Low ^j	Has all of the following: • cT1–cT2a • Grade Group 1 • PSA <10 ng/mL		• Confirmatory testing can be used to assess the appropriateness of active surveillance (PROS-F 2 of 5)	PROS-3	
Intermediate ^l	Has all of the following: • No high-risk group features • No very-high-risk group features • Has one or more intermediate risk factors (IRFs): ▶ cT2b–cT2c ▶ Grade Group 2 or 3 ▶ PSA 10–20 ng/mL	Favorable intermediate	Has all of the following: • 1 IRF • Grade Group 1 or 2 • <50% biopsy cores positive (eg, <6 of 12 cores)^k	• Confirmatory testing can be used to assess the appropriateness of active surveillance (PROS-F 2 of 5)	PROS-4
		Unfavorable intermediate	Has one or more of the following: • 2 or 3 IRFs • Grade Group 3 • ≥50% biopsy cores positive (eg, ≥6 of 12 cores)^k	• Soft tissue imaging and consider bone imaging ⁹ ▶ If regional metastases are found, see PROS-7 ▶ If distant metastases are found, see PROS-14 for Low-Volume M1 (Metachronous or Synchronous) or Synchronous Oligometastatic^h CSPC or PROS-15 for High-Volume M1 CSPC	PROS-5
High	Has one or more high-risk features, but does not meet criteria for very high risk: • cT3–cT4 • Grade Group 4 or Grade Group 5 • PSA >20 ng/mL		Bone and soft tissue imaging ⁹ ▶ If regional metastases are found, see PROS-7 ▶ If distant metastases are found, see PROS-14 for Low-Volume M1 (Metachronous or Synchronous) or Synchronous Oligometastatic^h CSPC or PROS-15 for High-Volume M1 CSPC	PROS-6	
Very high	Has at least two of the following: • cT3–cT4 • Grade Group 4 or 5 • PSA >40 ng/mL		Bone and soft tissue imaging ⁹ ▶ If regional metastases are found, see PROS-7 ▶ If distant metastases are found, see PROS-14 for Low-Volume M1 (Metachronous or Synchronous) or Synchronous Oligometastatic^h CSPC or PROS-15 for High-Volume M1 CSPC	PROS-6	

INTERMEDIATE (FAVOURABLE)



FC, Male, 63 years old
Comorbidities: Hypertension treated with Triatec 5 mg/day

- (11.2024) iPSA: 7 ng/ml
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- (16.05.2025) Bone scintigraphy: negative for bone metastases
- (13.05.2025) CT TAP with contrast: oncologically negative

TO SUMMARIZE: iPSA: 7 ng/ml
Gleason score: 3+4, 2/7 positive cores in the left lobe
cT2a N0 M0

INTERMEDIATE (UNFAVOURABLE)



PB, Male, 69 years old
Comorbidities: None

- (10.2024) iPSA: 14 ng/ml
- (28.11.2024) Multiparametric prostate MRI: PIRADS 3/4 Bilateral prostatic lesions without capsular involvement. Prostate volume: 25 cc
- (12.2024) Genitourinary MDT: staging cT2c
- (20.12.2024) Biopsy: adenocarcinoma GS 4+3, 8/12 positive cores bilaterally
- (02.02.2025) F-PSMA PET/CT: pathological uptake in the prostate bilaterally. No seminal vesicle involvement. No pathological pelvic lymph node uptake. Indeterminate uptake at right 7th rib.

TO SUMMARIZE: iPSA: 14 ng/ml
Gleason score: 4+3, 8/12 positive cores bilaterally
cT2c N0 M0



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NCCN Guidelines Version 2.2026 Prostate Cancer

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[Discussion](#)

PRINCIPLES OF RADIATION THERAPY

All patients diagnosed with intermediate-, high-, very-high-, regional-risk, low-volume mCSPC, biochemically recurrent, low-volume metastatic castration-sensitive prostate cancer (mCSPC) and oligometastatic mCRPC are recommended to be evaluated by a radiation oncologist as part of a multidisciplinary discussion of treatment options.

General

• EBRT

- ▶ **Treatment Planning:** Intensity modulated RT (IMRT) is recommended over 3-dimensional conformal RT to improve dose conformity.
- ▶ **Image Guidance:** Methods to improve accuracy of treatment delivery, thereby enabling reduction in planning target volume (PTV) margins, which generally result in reduced toxicity are encouraged and may include one or more of the following:
 - ◊ Image guidance with daily 3D imaging is recommended with either a cone beam CT (CBCT) or MRI.
 - ◊ Devices that assist with optimal image guidance (fiducial markers) or reduce motion (endorectal balloons).
 - ◊ Real-time intrafraction volumetric tracking.
 - ◊ Online adaptive radiotherapy if target is near mobile organs (ie, performing a simultaneous integrated boost to a positive pelvic lymph node adjacent to bowel).
- ▶ **Beam Type:** Photon and proton RT are acceptable forms of EBRT and appear to have similar outcomes in regard to toxicity, QOL, and tumor control. Potential financial toxicity should be discussed with patients.
- ▶ **Fractionation:** An extensive list of fractionation schedules have been studied. These are grouped into three categories, conventional fractionation (1.8–2 Gy/fraction), moderate hypofractionation (>2.5 to 4 Gy/fraction), and ultra-hypofractionation (>6 Gy/fraction).¹ Common dose/fraction schedules are shown in Table 1. In general, iso-effective moderate hypofractionation dosing has demonstrated noninferior tumor control, toxicity, and QOL over conventional fractionation and is more convenient for patients and thus preferred. Similarly, ultra-hypofractionation has been demonstrated to be noninferior to both moderate hypofractionation and conventional fractionation.² Thus, use of conventionally fractionated radiotherapy is no longer preferred for localized prostate cancer.
 - ◊ Ultra-hypofractionation encompasses stereotactic body radiation therapy (SBRT), which requires precision treatment setup and required additional image guidance techniques.

MODERATE HYPOFRACTIONATION & PROSTATE CANCER

- ✓ Trials investigating the clinical and toxicity outcomes of moderate hypofractionation schedules (**CHHiP, RTOG 0415, PROFIT**) **have sufficient follow-up** data to show that the efficacy and toxicity of these schedules are similar to those of conventionally fractionated regimens (**non-inferiority of all Hypo arms, excluding HYPRO**)
- ✓ More specifically, based on **evidence level 1B**, dose-escalated conventionally fractionated RT with IMRT appears to have similar outcomes and toxicities to hypofractionated RT with IMRT.



CLINICAL INDICATION: LITERATURE PUBLISHED EVIDENCE



HYPO-RT-PC IN 7 FX

This large phase III clinical trial enrolled 1,200 men with intermediate-to high-risk localised prostate cancer. Participants were randomly assigned to receive either:

1. Short-course radiotherapy: 42.7 Gray (Gy) delivered in 7 sessions over 2.5 weeks
2. Standard-course radiotherapy: 78.0 Gy delivered in 39 sessions over 8 weeks

Key outcomes after 10 years:

- Failure-free survival: 72% in the short-course group vs 65% in the standard group.
- Overall survival: 81% for short-course vs 79% for standard
- Prostate cancer-specific mortality: 4% in both groups
- Side effects: Urinary and bowel symptoms were similar in both groups, and most were mild to moderate.

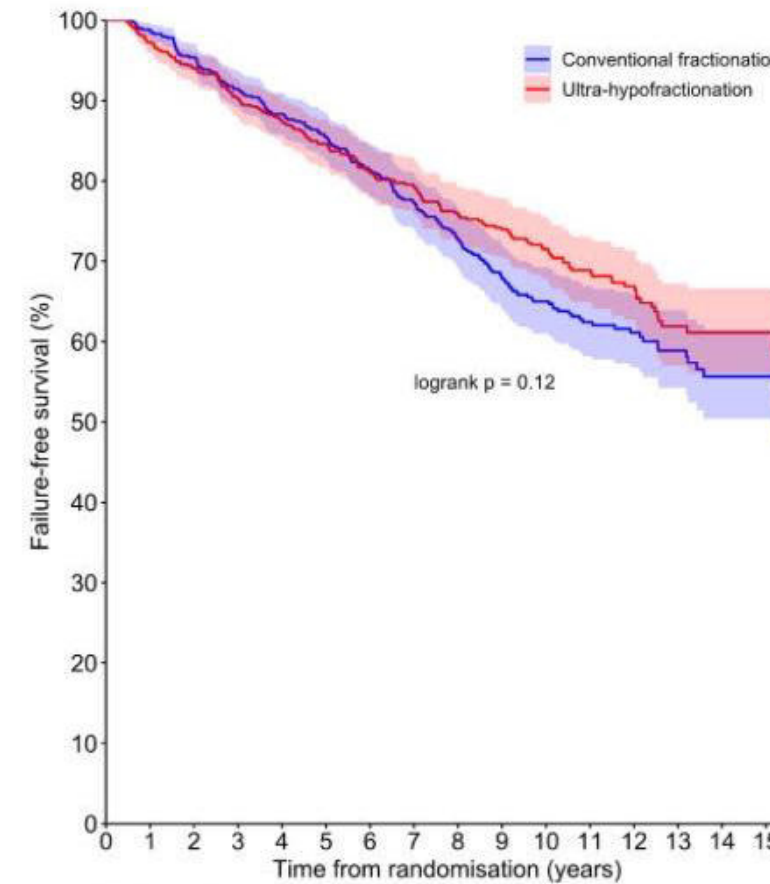


Figure 1. Failure-free survival (freedom from biochemical or clinical failure).

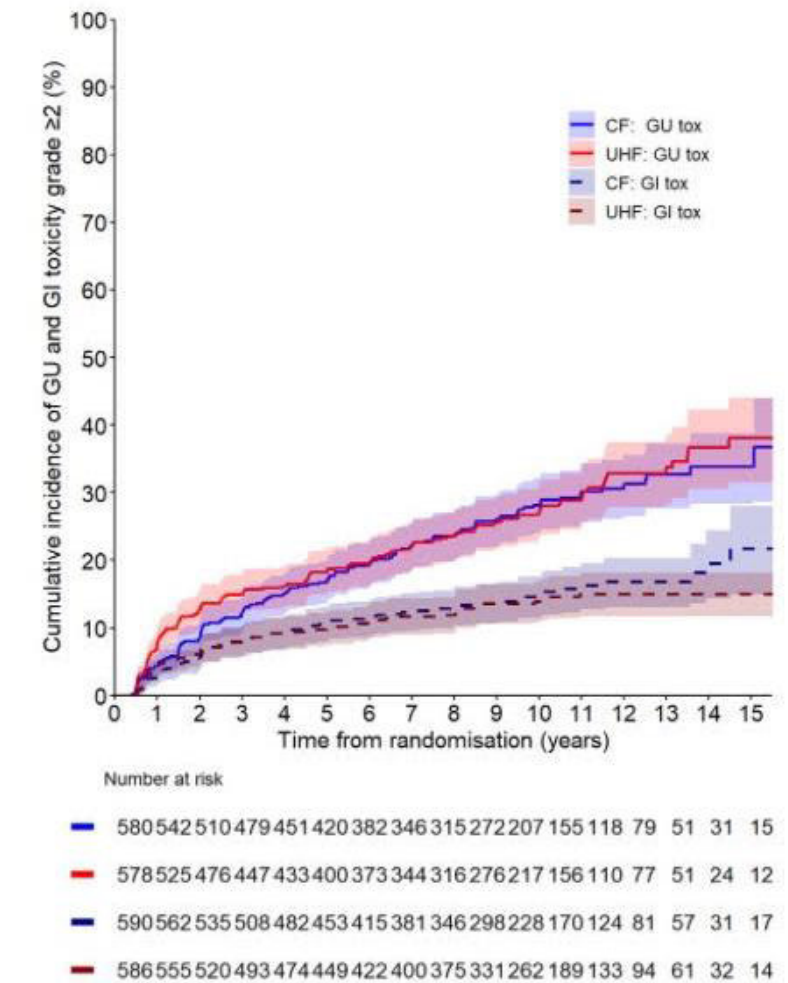
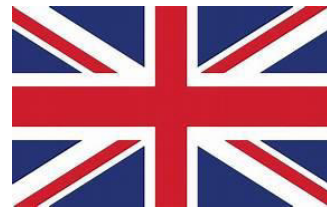


Figure 2. Cumulative incidence of the first occurrence of physician-recorded late grade ≥ 2 GU and GI toxicity, assessed using the RTOG morbidity scale.

CONCLUSIONS:

These findings confirm that the shorter course does not increase long-term side effects and provides equally durable cancer control”, added **Camilla Thellenberg-Karlsson, MD, PhD**, at Umeå University, who presented the results at the ESTRO meeting

CLINICAL INDICATION: LITERATURE PUBLISHED EVIDENCE



RCT: PACE A

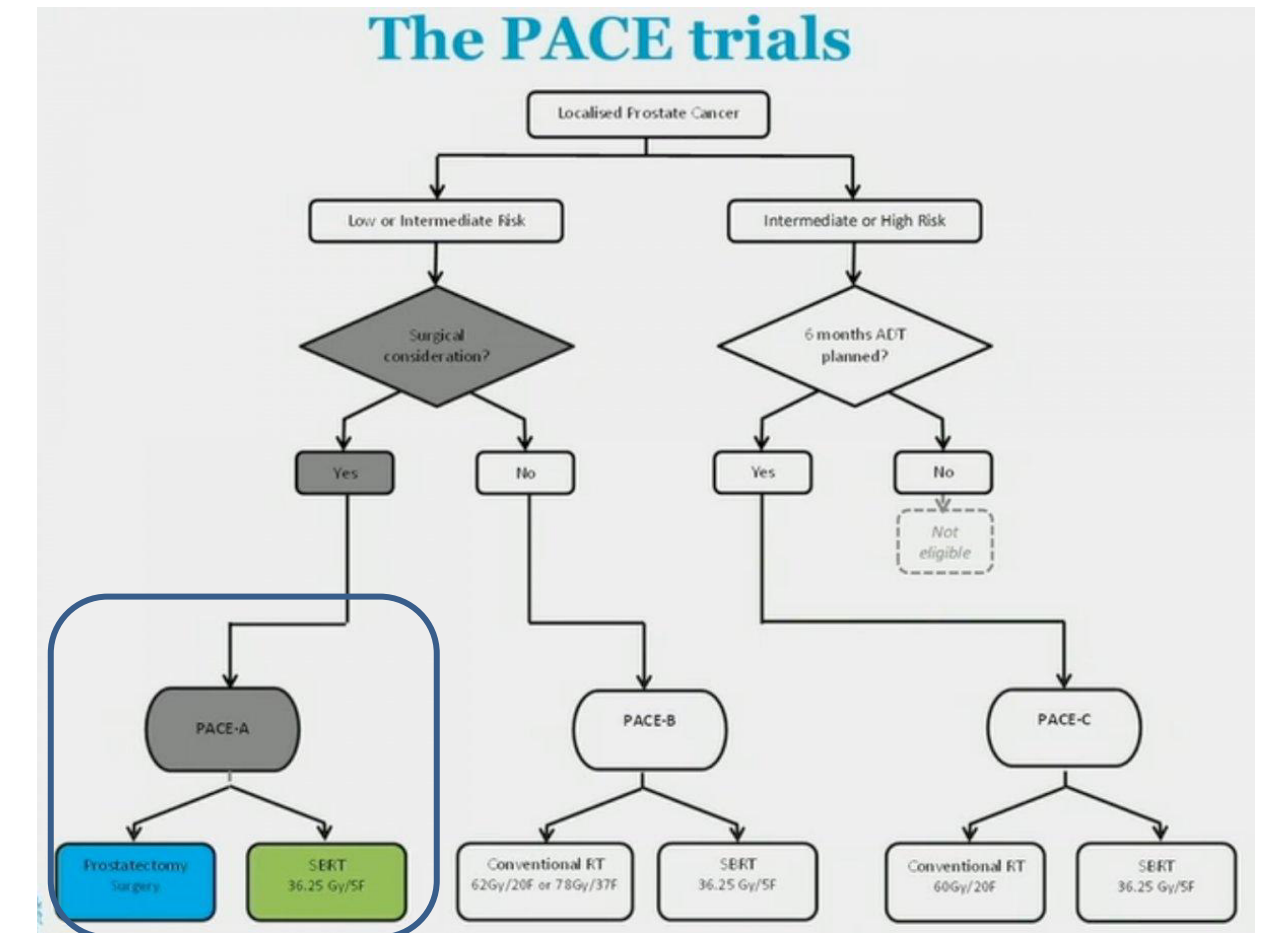
available at www.sciencedirect.com
journal homepage: www.europeanurology.com



Original Article

Radical Prostatectomy Versus Stereotactic Radiotherapy for Clinically Localised Prostate Cancer: Results of the PACE-A Randomised Trial

Nicholas van As^{a,b,*}, Binnaz Yasar^{a,b}, Clare Griffin^b, Jaymini Patel^b, Alison C. Tree^{a,b}, Peter Ostler^c, Hans van der Voet^d, Daniel Ford^e, Shaun Tolan^f, Paula Wells^g, Rana Mahmood^h, Mathias Winklerⁱ, Andrew Chan^j, Alan Thompson^a, Chris Ogden^a, Olivia Naismith^{a,k}, Julia Pugh^b, Georgina Manning^b, Stephanie Brown^b, Stephanie Burnett^b, Emma Hall^b



- **Phase 3** open-label multiple-cohort RCT. In PACE-A, people with LPCa, T1-T2, Gleason≤3+4, PSA≤20ng/mL & suitable for surgery were randomised (1:1) to SBRT or surgery. SBRT dose was 36.25Gy/5 fractions in 1-2 weeks; surgery was laparoscopic or robotically assisted prostatectomy
- From Aug 2012 to Feb 2022, 123 men from 10 UK centres were randomised
- **Compared to surgery, pts receiving SBRT had better urinary continence & sexual bother score;** clinician reported GI toxicity was low but SBRT pts reported more bowel bother at 2 years

The results suggest that stereotactic body radiotherapy may lead to lower rates of urinary incontinence and sexual dysfunction compared to radical prostatectomy, albeit with a potential increase in bowel dysfunction.

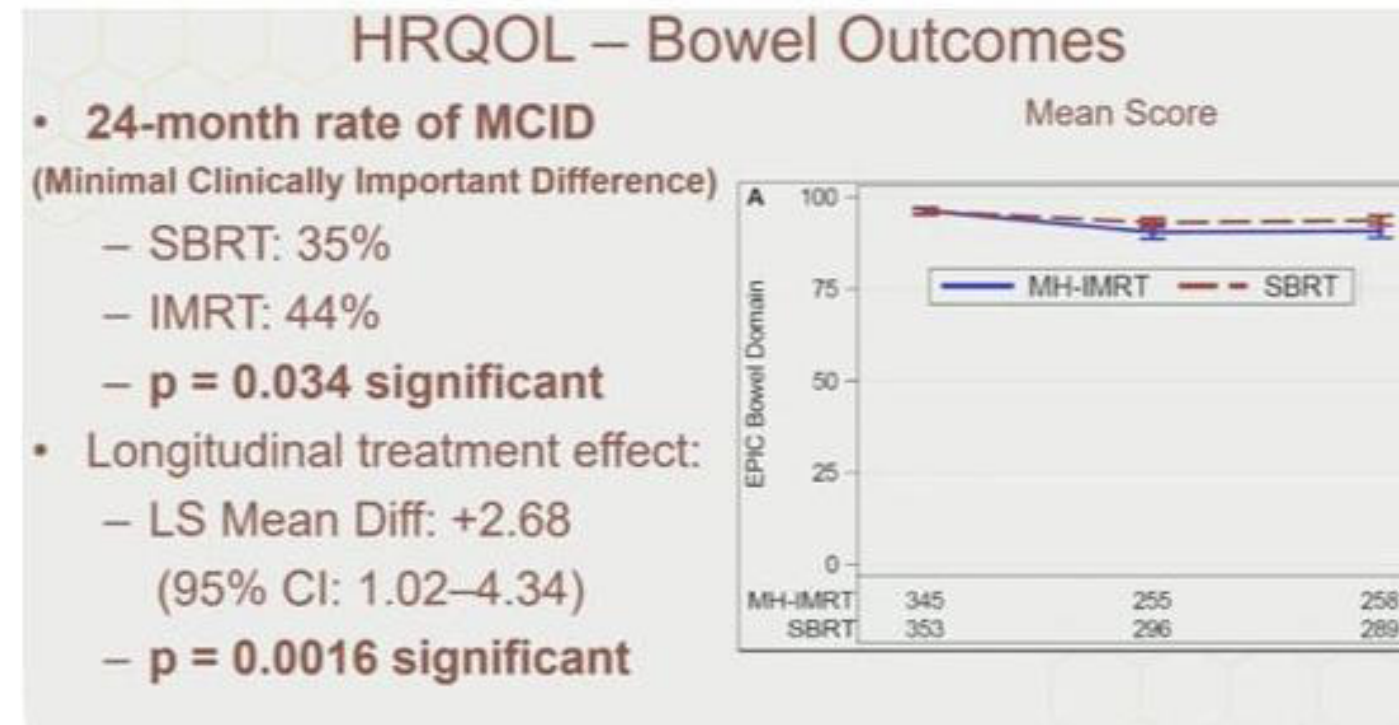


NRG-GU005

Study Design: NRG GU005 Randomized Phase III Trial

N=698 intermediate-risk prostate cancer patients (accrued 11/2017 to 6/2022)

S T R A T I F I C A T I O N	<u>Risk Group</u>	R A N D O M I Z E
	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	
	<u>Use of Rectal Manipulation</u>	
	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		
	<u>Arm 1: IMRT</u>	
	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	
	<u>Arm 2: SBRT</u>	
	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	



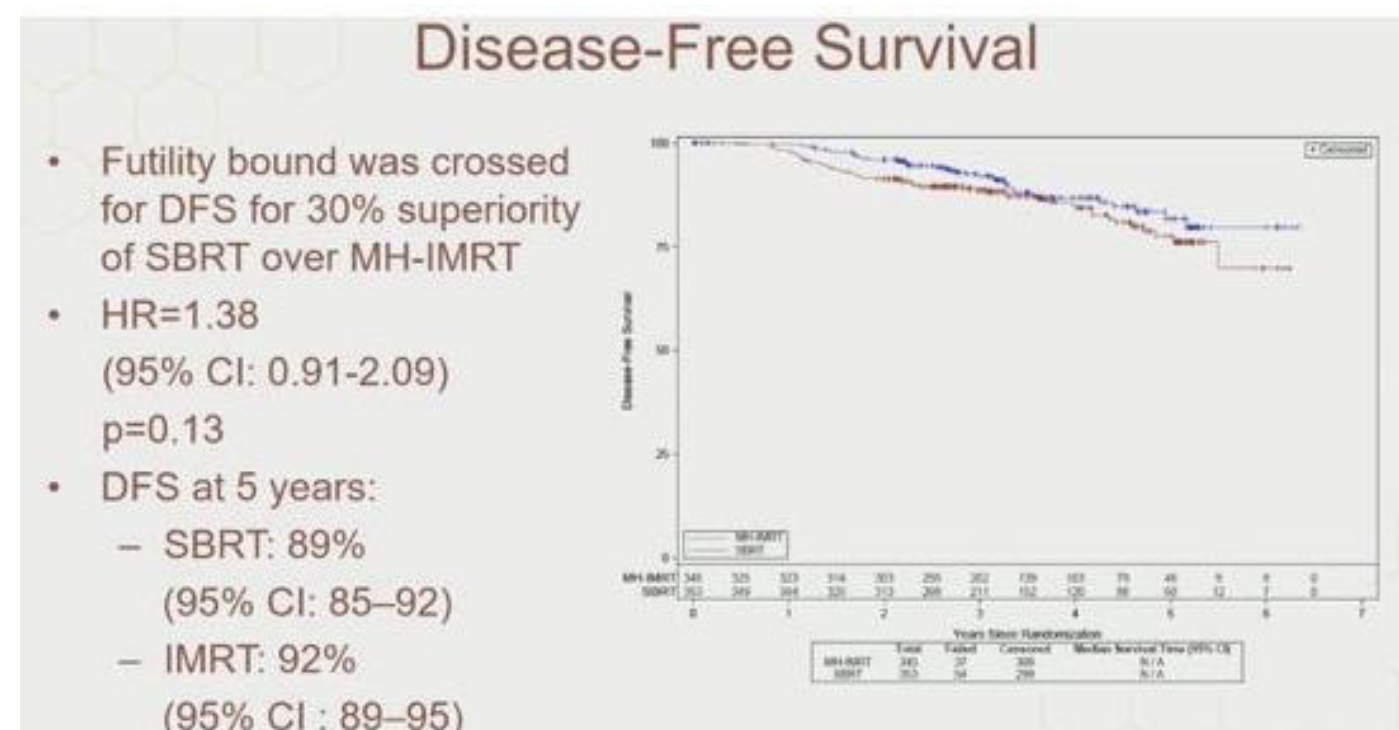
NRGGU005 Phase III: 698 pts with intermediate-risk [Prostate Cancer](#) RCT; SBRT (n=353) vs M-IMRT (n=345)

✓ SBRT → better bowel HRQOL (MCID 35% vs 44%, p=0.03)

⚖ No diff in urinary HRQOL; EPIC continence favours SBRT

✗ futile for DFS; IMRT had ↓ 3-yr biochemical failure (4.2% vs 7.8%)

SBRT safe, better QoL, **!?** but not superior for DFS [ASTRO25](#) [RadOnc](#) [PCSM](#)



The Role of interventional radiotherapy (modern brachytherapy) in favorable intermediate risk prostate cancer

LUCA TAGLIAFERRI - MD, PhD

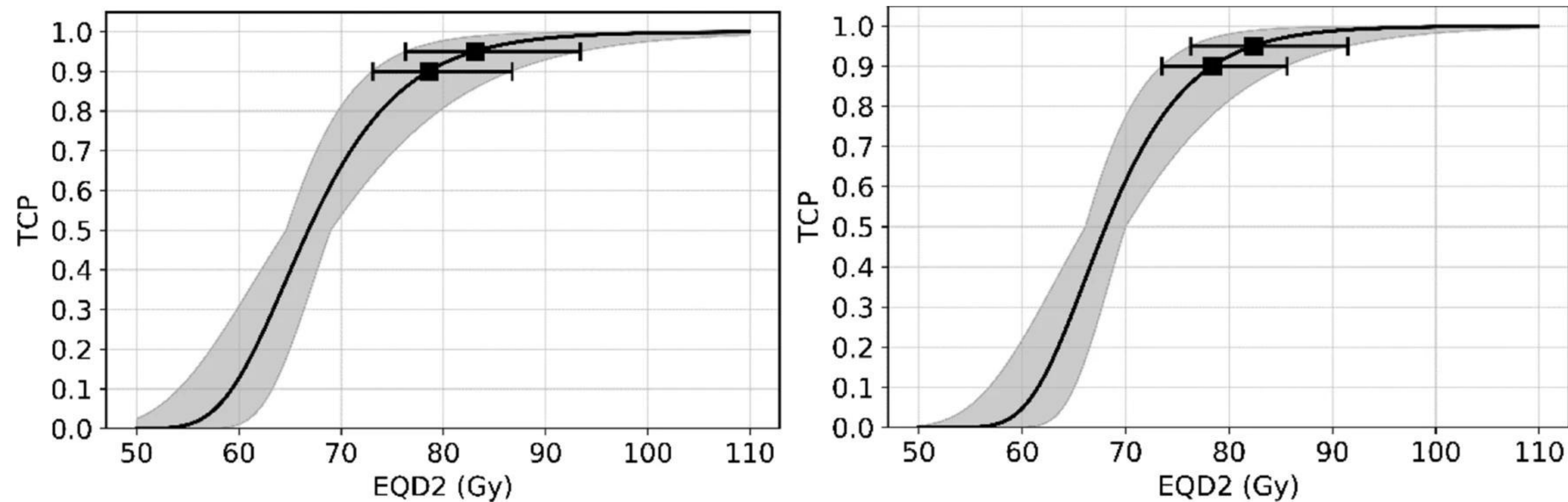
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Gemelli ART (Advanced Radiation Therapy) - Interventional Oncology Center (IOC)



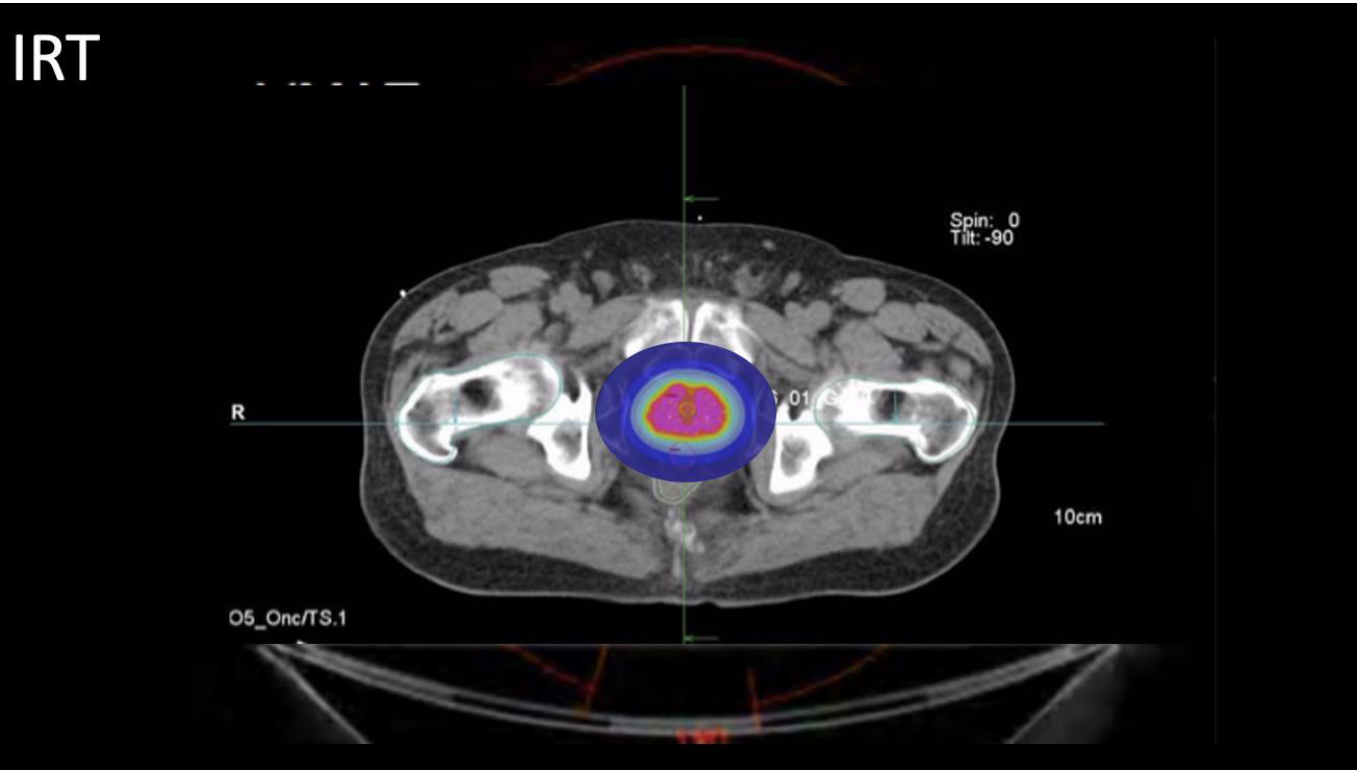
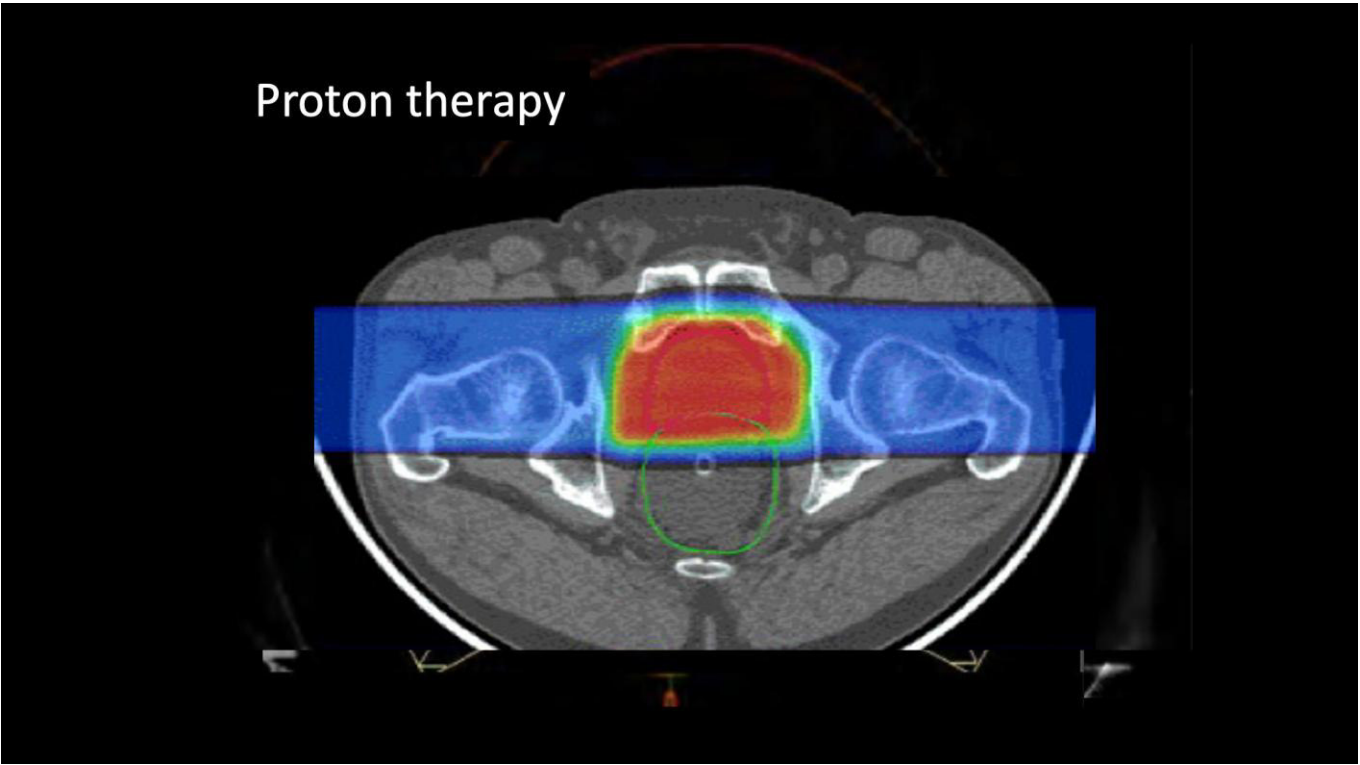
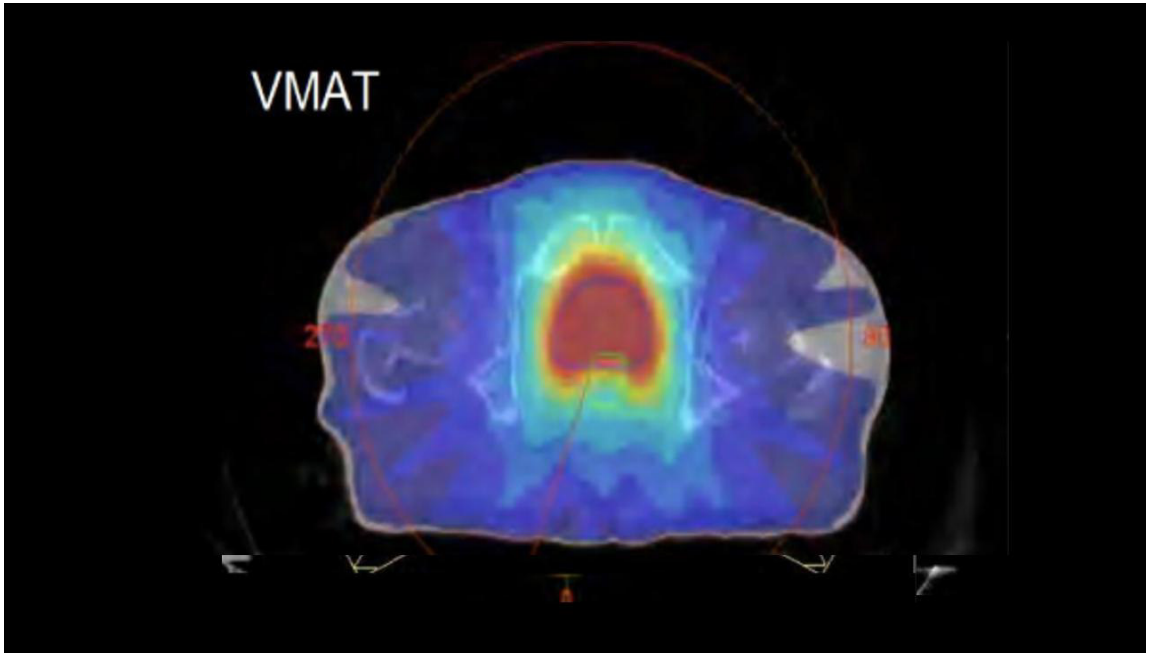
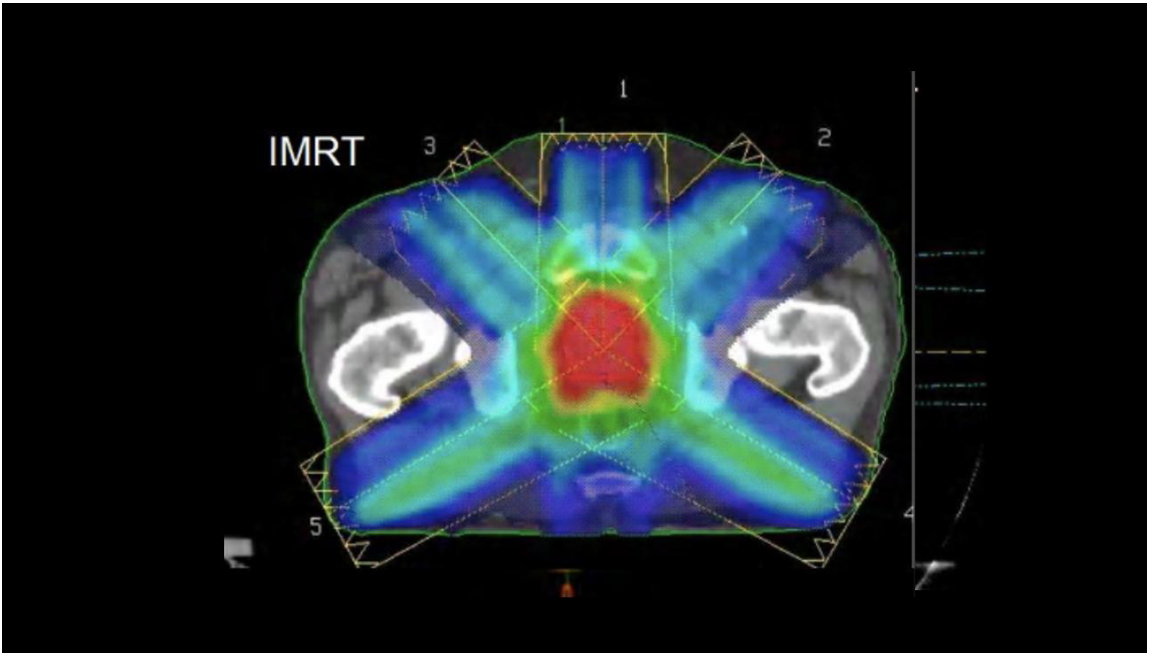
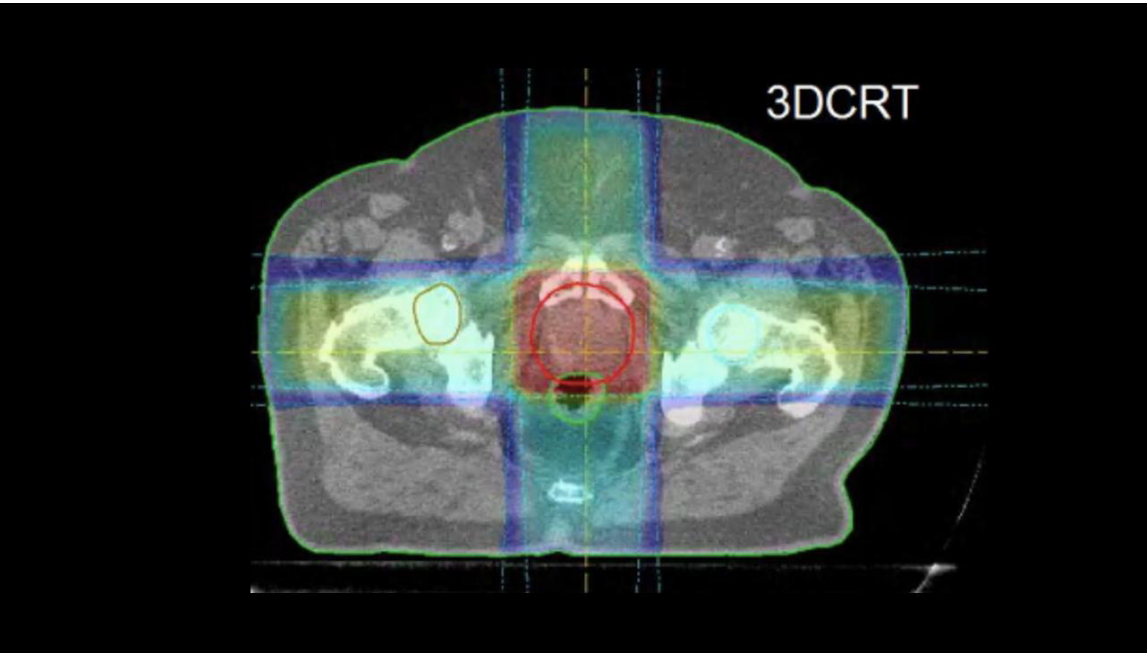
27th October 2025

TUMOR CONTROL PROBABILITY



Response curves of linear-quadratic Poisson model for prostate gland with $\alpha/\beta = 1.3$ Gy (left) and for mpMRI-GTV with $\alpha/\beta = 2.9$ Gy (right). Grey area represents the 95% CI.

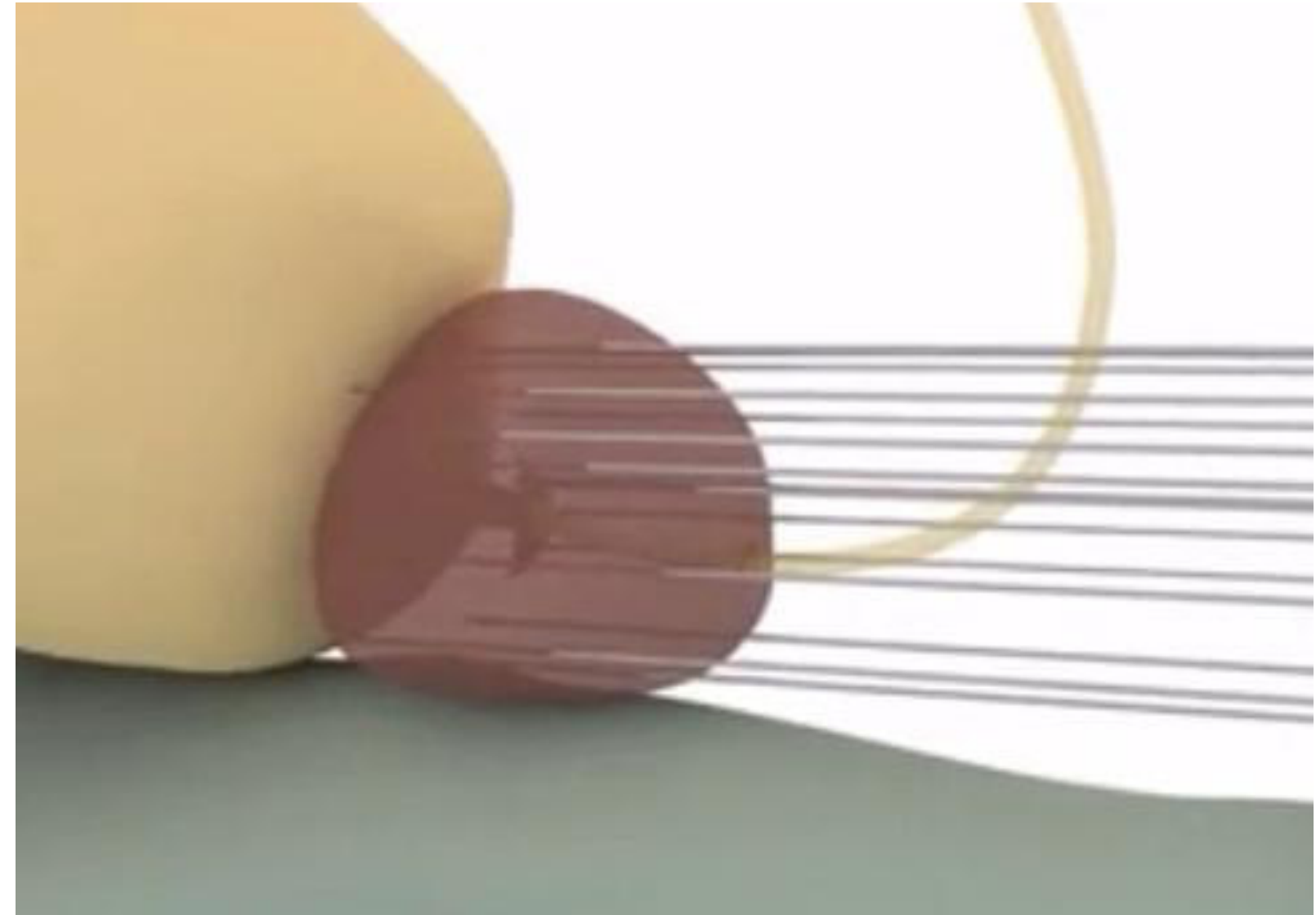
INTERVENTIONAL RADIO THERAPY (BRACHYTHERAPY)



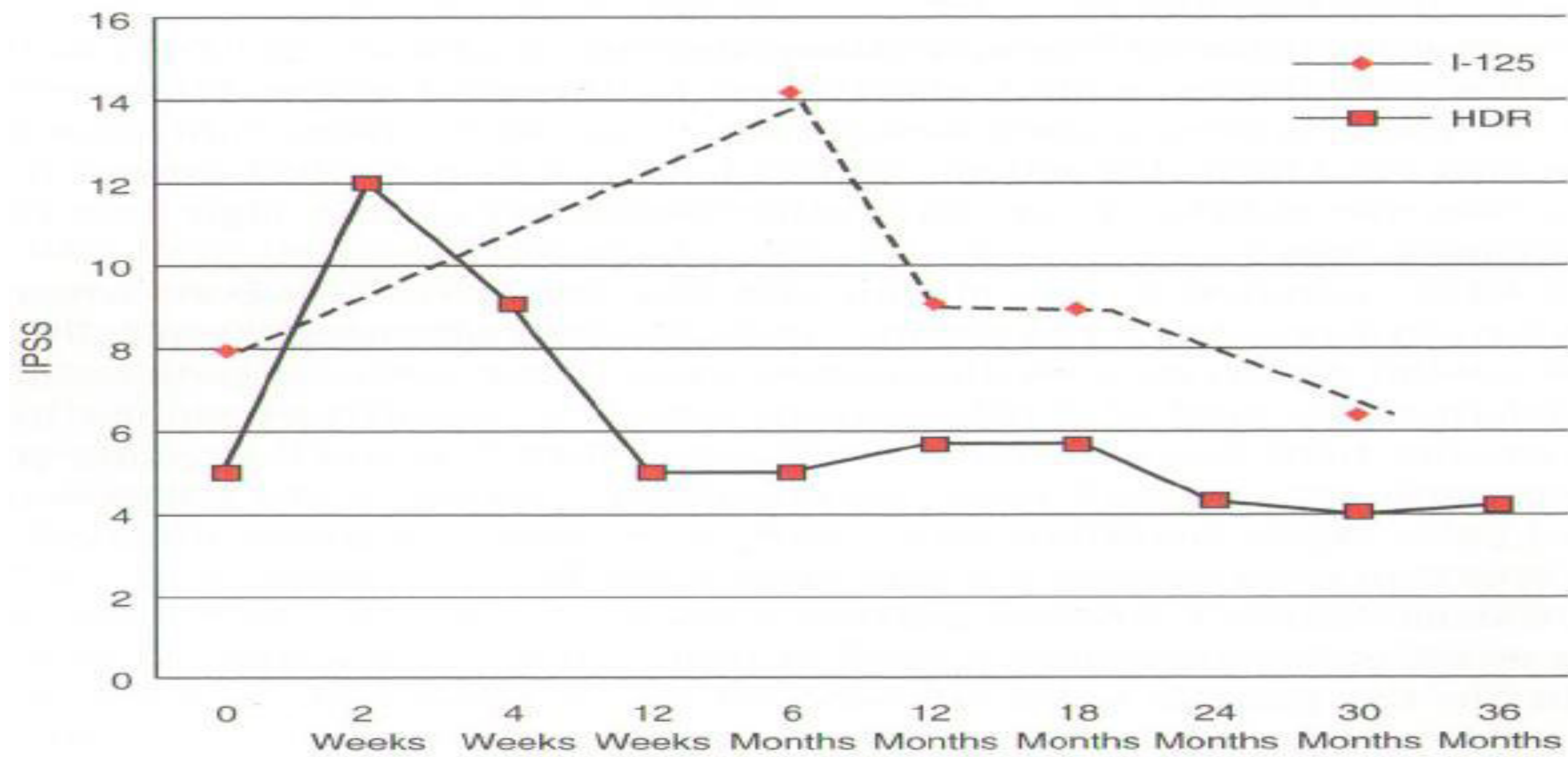
INTERVENTIONAL RADIOOTHERAPY (BRACHYTHERAPY)

MODERN HDR INTERVENTIONAL RT

- Intensity modulated IRT
- Image guided RT

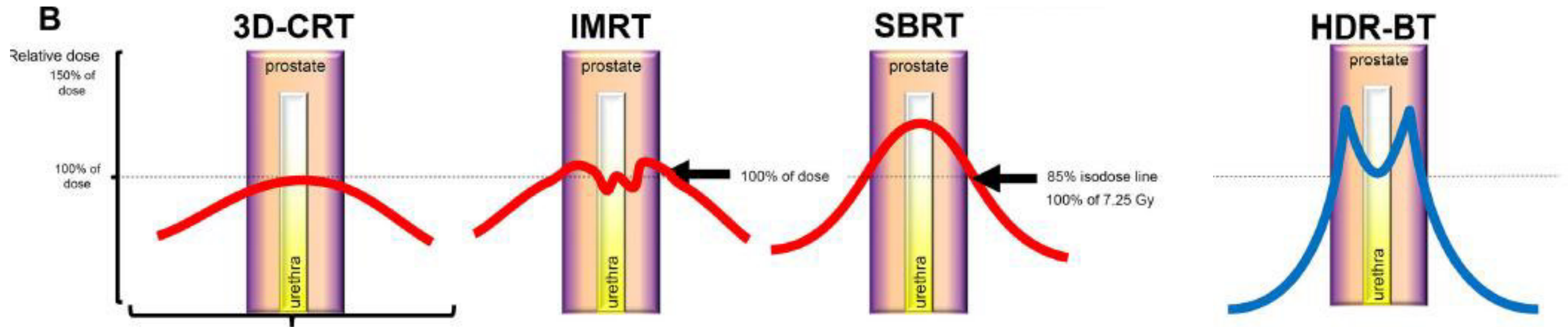


INTERVENTIONAL RADIOOTHERAPY (BRACHYTHERAPY)



• IPSS scores after LDR and HDR prostate brachytherapy. In: Kovács & Hoskin (Eds) *Interstitial prostate brachytherapy*, Chapter 14: HDR versus LDR seeds, Springer, 2013

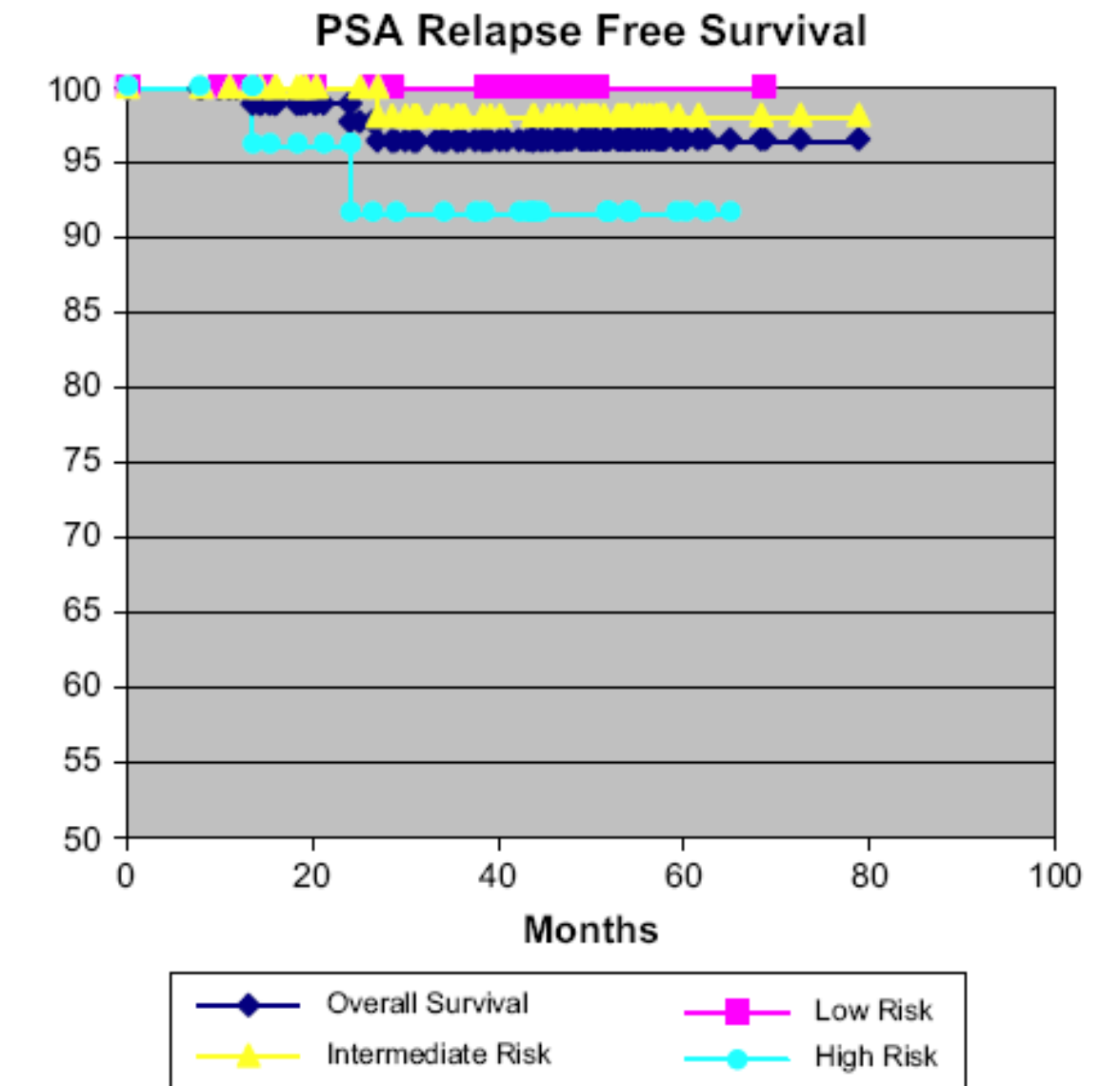
INTERVENTIONAL RADIOOTHERAPY (BRACHYTHERAPY)



HDR Interventional Radiotherapy (monotherapy)

Author	year	# pts	HDR	ADT	Risk	F-up	BNED	GI gr3	GU gr3
Hauswald Demanes	2016	448	6 x 7.25	9%	LR IR	6.5 Max15	98% (10)	0	4.7%
Hoskin	2017	293	1 x 19-20 2 x 13 3 x 10.5	75% 6m	IR HR	4.1 5.2 9	94% (4y) 93% 91%	0 1%	2% 11%
Jawad Martinez Krauss	2016	494	4 x 9.5 2 x 12 2 x 13.5	14%	LR IR	5.5 3.5 2.9	97% 87% 90%	0	2% str 2% inc 7% hem
Patel	2017	190	6 x 7.25	0	IR	6.2	97% (5) 90% (8)	0	3.7% Str/inc
Prada	2016	60	1 x 19	33%	LR IR	6	66% (6)	0	0
Strouthos	2017	450	3 x 11.5	13%	IR HR	4.8	95%	0	0.8%
Yoshioka	2017	524	2 x 13.5 7 x 6.5-7 9 x 6	70%	LR IR HR	5.9	95% 94% 89%	0	1%

N=2459



Y. Yamada et al. / Brachytherapy 5 (2006) 157–164

HDR Interventional Radiotherapy (monotherapy)

Table 4. Comparison of patient satisfaction between treatment groups up to 48 months

The "Other" category comprises "Uncertain", "Dissatisfied" and "Extremely dissatisfied"

Time	Patient satisfaction	Brachytherapy	Robotic Prostatectomy	P-value
12 Months				<0.001
	Extremely Satisfied	113(74.3%)	63(50.4%)	
	Satisfied	29(19.1%)	37(29.6%)	
	Other	10(6.58%)	25(20%)	
24 Months				<0.001
	Extremely Satisfied	112(75.2%)	50(51%)	
	Satisfied	29(19.5%)	31(31.6%)	
	Other	8(5.37%)	17(13.4%)	
36 Months				0.04
	Extremely Satisfied	105(72.4%)	43(55.8%)	
	Satisfied	27(18.6%)	25(32.5%)	
	Other	13(9%)	9(11.7%)	
48 Months				0.06
	Extremely Satisfied	71(71.7%)	44(55%)	
	Satisfied	19(19.2%)	22(27.5%)	
	Other	9(9.1%)	14(17.5%)	

PB, Male, 69 years old

Comorbidities: None

- (10.2024) iPSA: 14 ng/ml
- (28.11.2024) Multiparametric prostate MRI: PIRADS 3/4, Bilateral prostatic lesions without capsular involvement. Prostate volume: 49 cc, PSAd: 0,28
- (12.2024) Genitourinary MDT: staging cT2c
- (20.12.2024) Biopsy: adenocarcinoma GS 4+3, 8/12 positive cores bilaterally
- (02.02.2025) F-PSMA PET/CT: pathological uptake in the prostate bilaterally. No seminal vesicle involvement. No pathological pelvic lymph node uptake. Indeterminate uptake at right 7th rib.

TO SUMMARIZE:

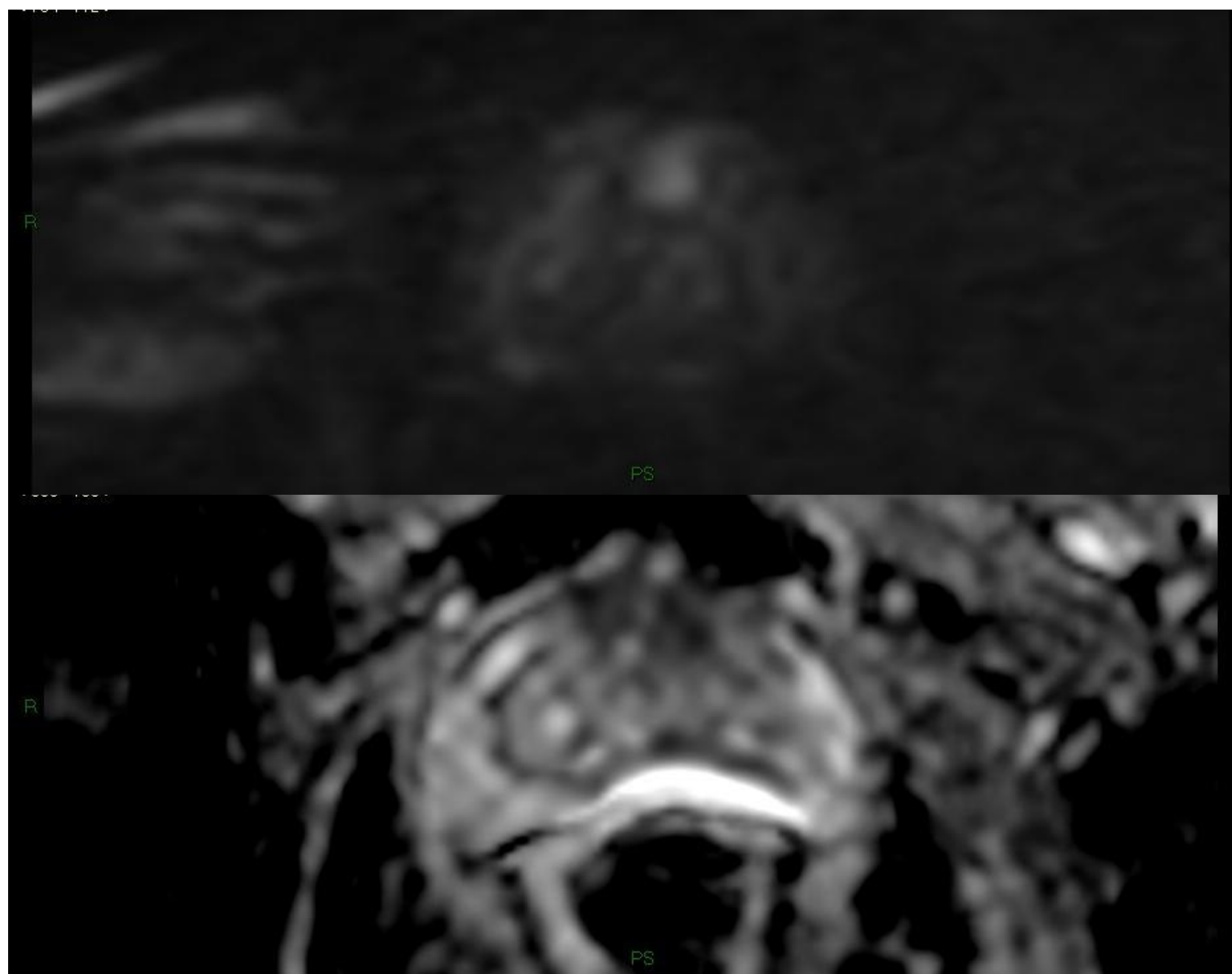
iPSA: 14 ng/ml

Gleason score: 4+3, 8/12 positive cores bilaterally

cT2c N0 M0

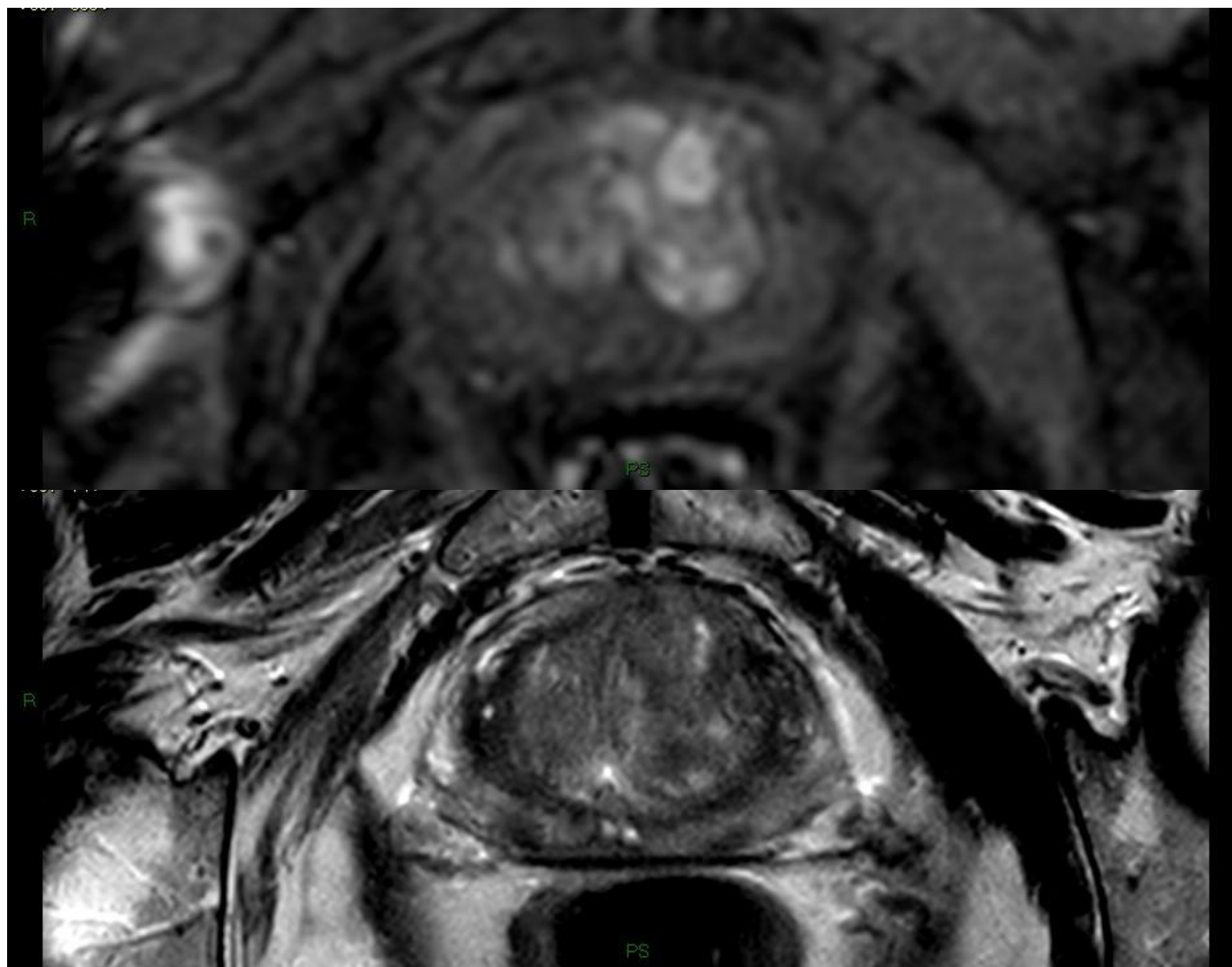
PB, Male, 69 years old

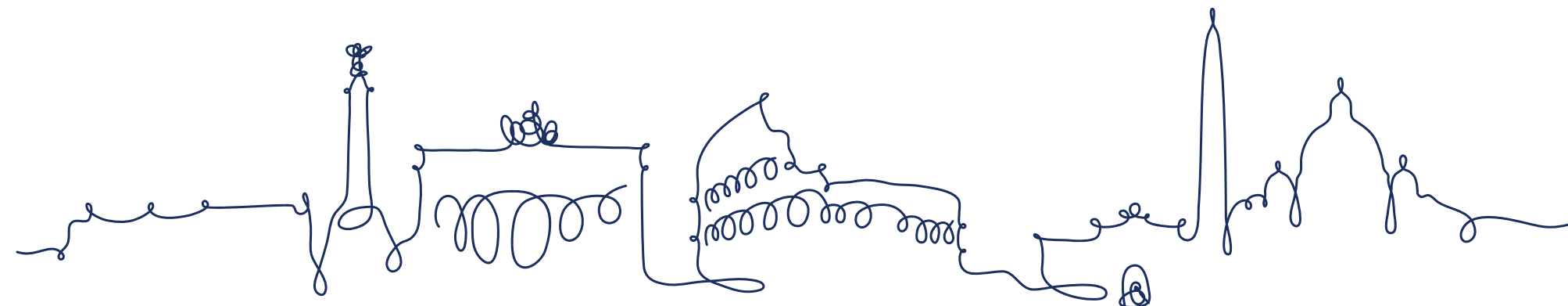
Multiparametric prostate MRI: PIRADS 3/4 Bilateral prostatic lesions without capsular involvement. Prostate volume: 49 cc, PSAd: 0,28



PB, Male, 69 years old

Multiparametric prostate MRI: PIRADS 3/4 Bilateral prostatic lesions without capsular involvement. Prostate volume: 49 cc, PSAd: 0,28





Which treatment strategy do you believe to be the most appropriate in this scenario?

1. Active surveillance
2. Surgery +/- Hormonal Therapy
3. External Beam RT +/- Hormonal Therapy
4. Interventional RT (Modern Brachytherapy) +/- Hormonal Therapy
5. Hormonal Therapy alone



MRO.35: Equity and research in oncology. The subtle balance between personalized medicine and accessibility to care

26-27-28 OCTOBER 2025 – Fondazione Policlinico Universitario A. Gemelli IRCCS

SCAN ME!



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Gemelli

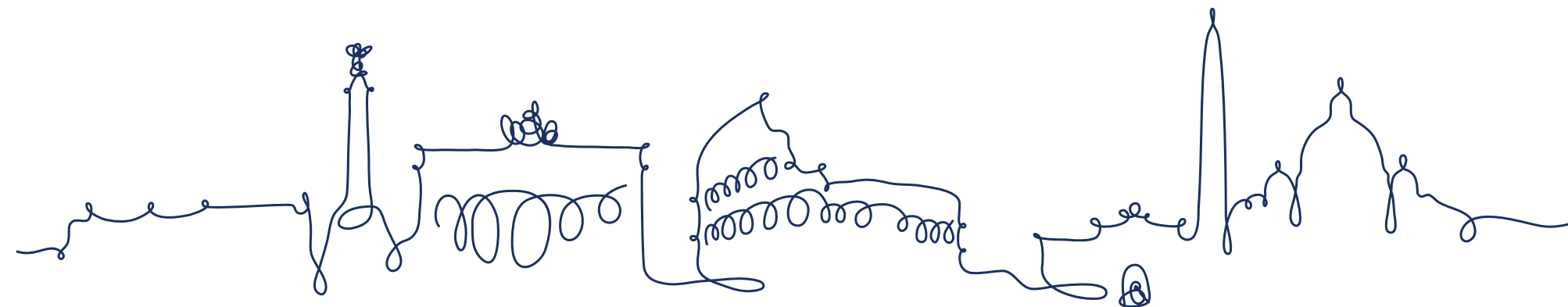


Fondazione Policlinico Universitario Agostino Gemelli IRCCS
Università Cattolica del Sacro Cuore

GART

Advanced Radiation Therapy

Prof. Bernardo Rocco



CLINICAL CASE DISCUSSION ON PC:

Radiation Oncology point of view



PROF FILIPPO ALONGI,

–Direttore dip. Radioterapia oncologica avanzata, IRCCS OSPEDALE SACRO CUORE DON CALABRIA , NEGRAR DI
VALPOLICELLA,

–Professore Ordinario, UNIVERSITA'DI BRESCIA

Gemelli

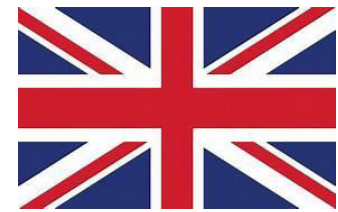
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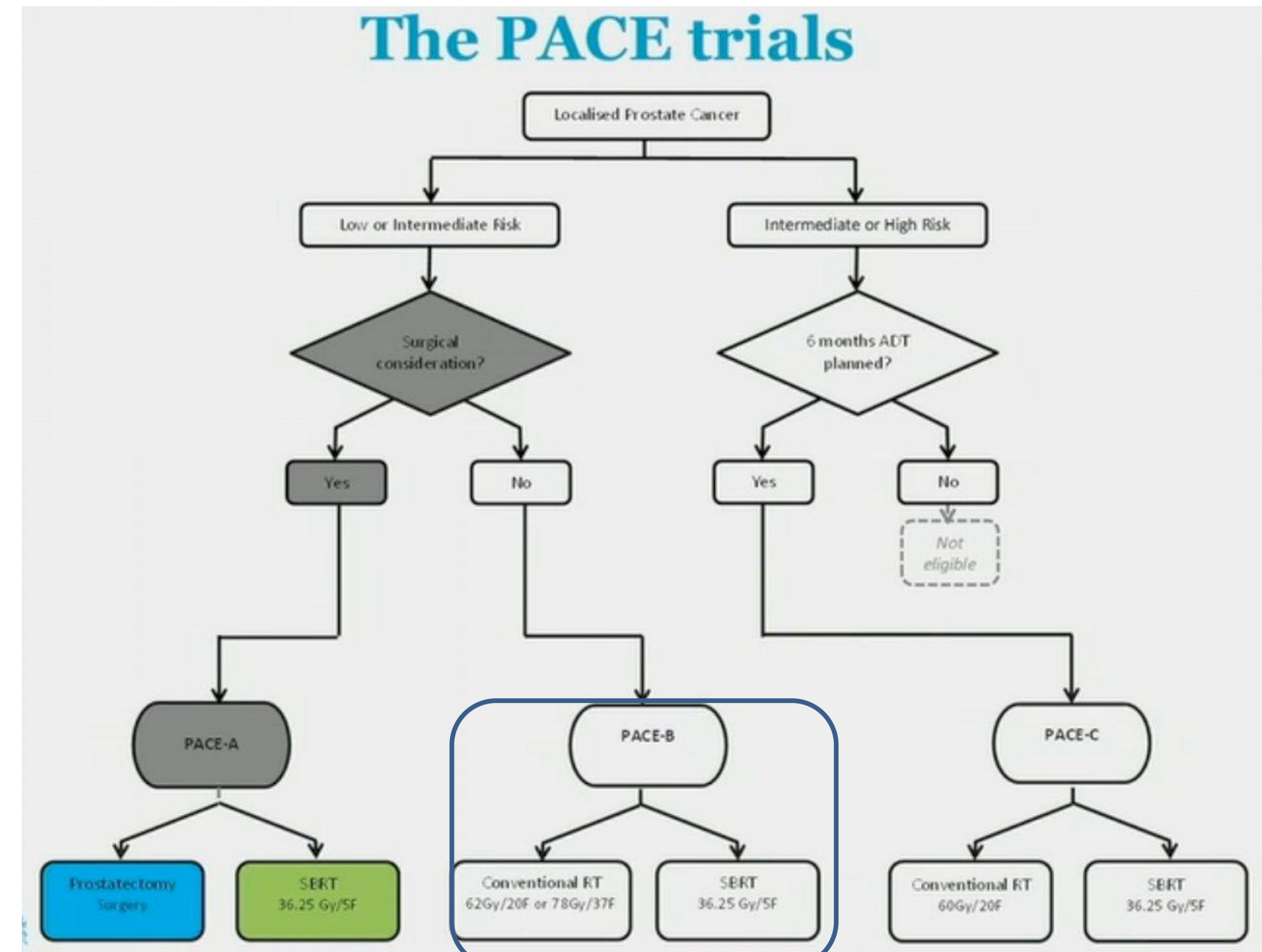
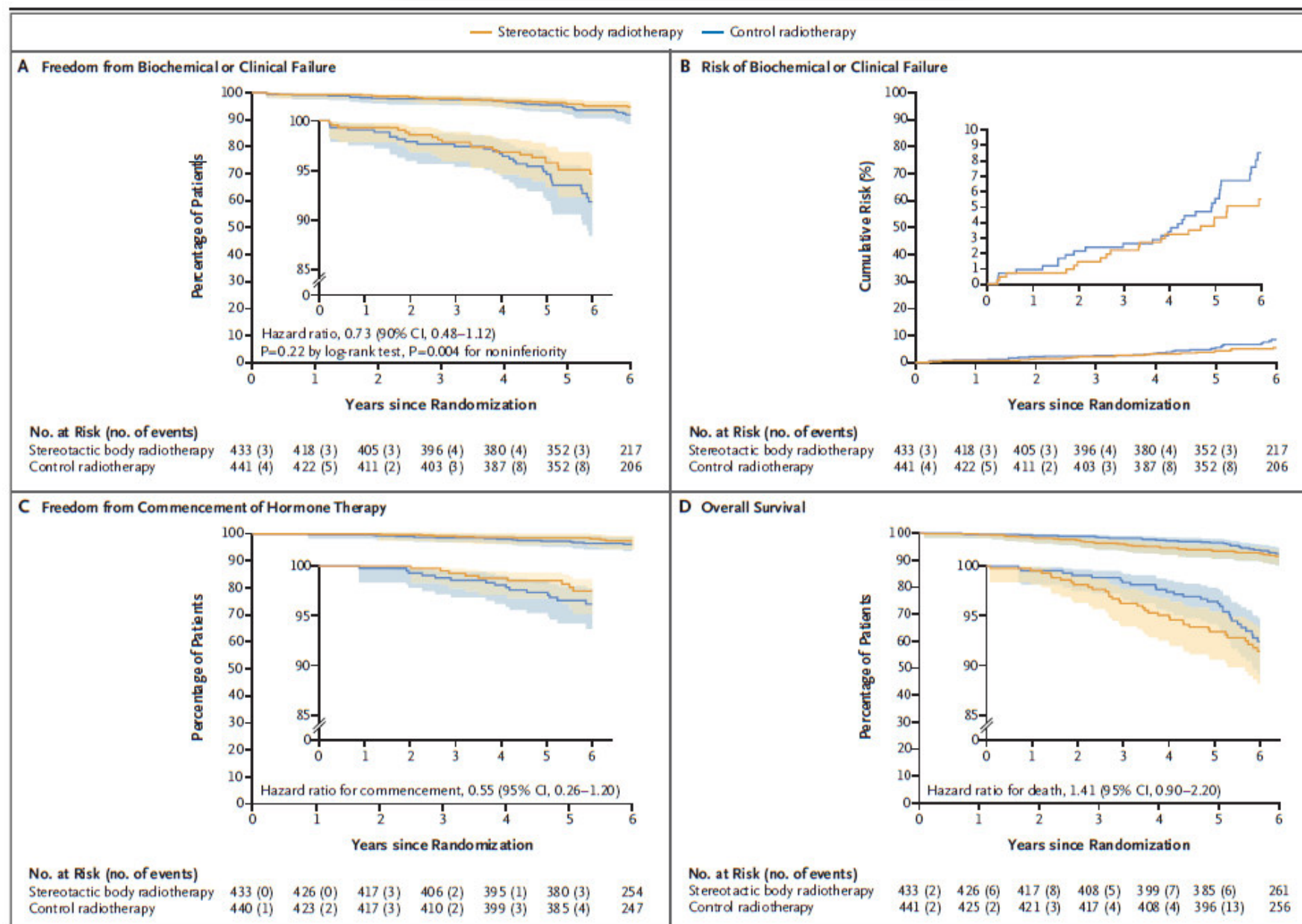
GART

Advanced Radiation Therapy



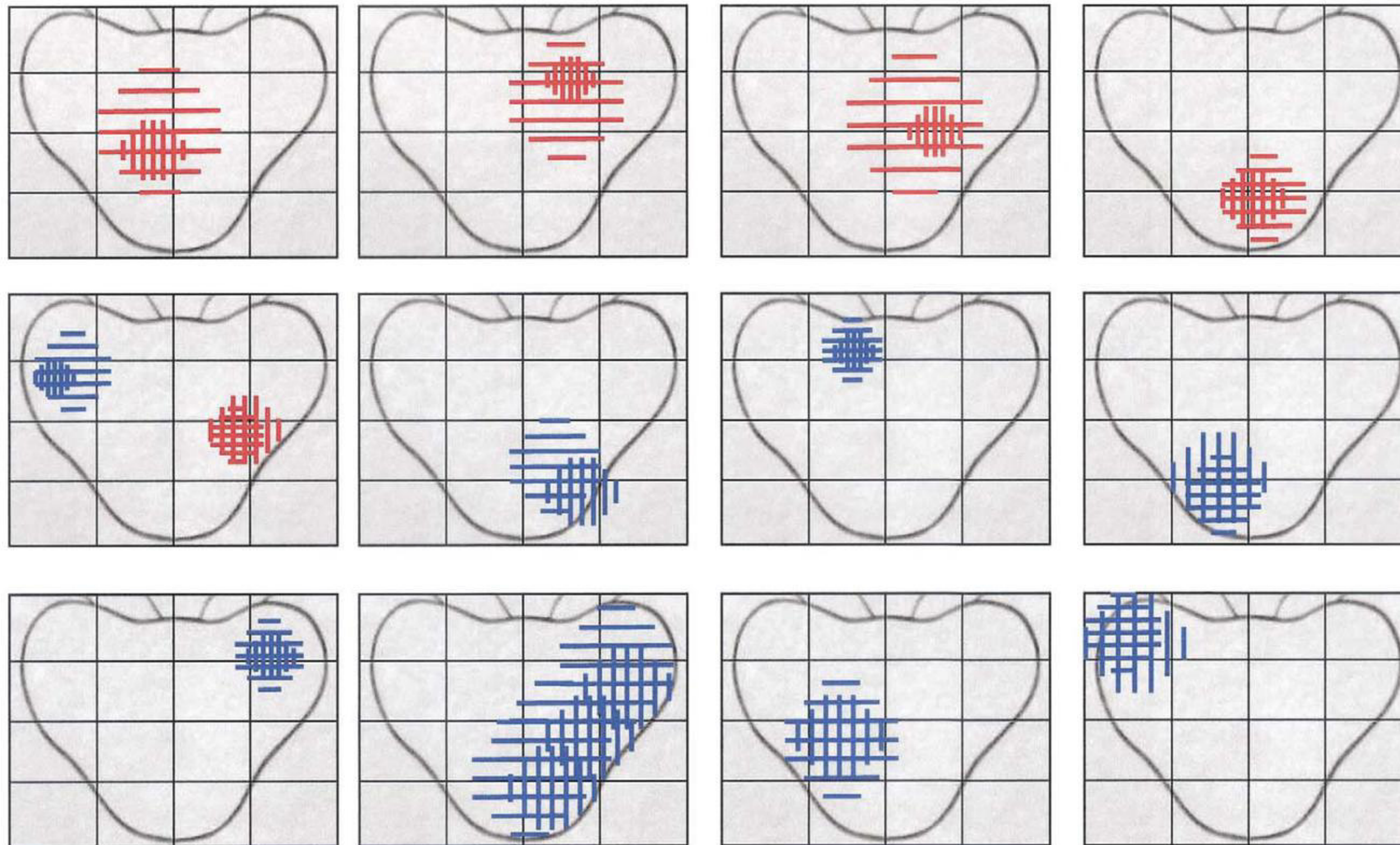


RCT: PACE B



CONCLUSIONS: Five-fraction SBRT was non inferior to control radiotherapy with respect to biochemical or clinical failure and may be an efficacious treatment option for patients with low-to-intermediate-risk localized prostate cancer as defined in this trial.

CLINICAL INDICATION: LITERATURE PUBLISHED EVIDENCE



local recurrence usually originates in the primary tumor

- Cellini N, Morganti AG, Mattiucci GC, Valentini V, Leone M, Luzi S, Manfredi R, Dinapoli N, Digesu' C, Smaniotto D. Analysis of intraprostatic failures in patients treated with hormonal therapy and radiotherapy: implications for conformal therapy planning. Int J Radiat Oncol Biol Phys. 2002

CLINICAL INDICATION: LITERATURE PUBLISHED EVIDENCE

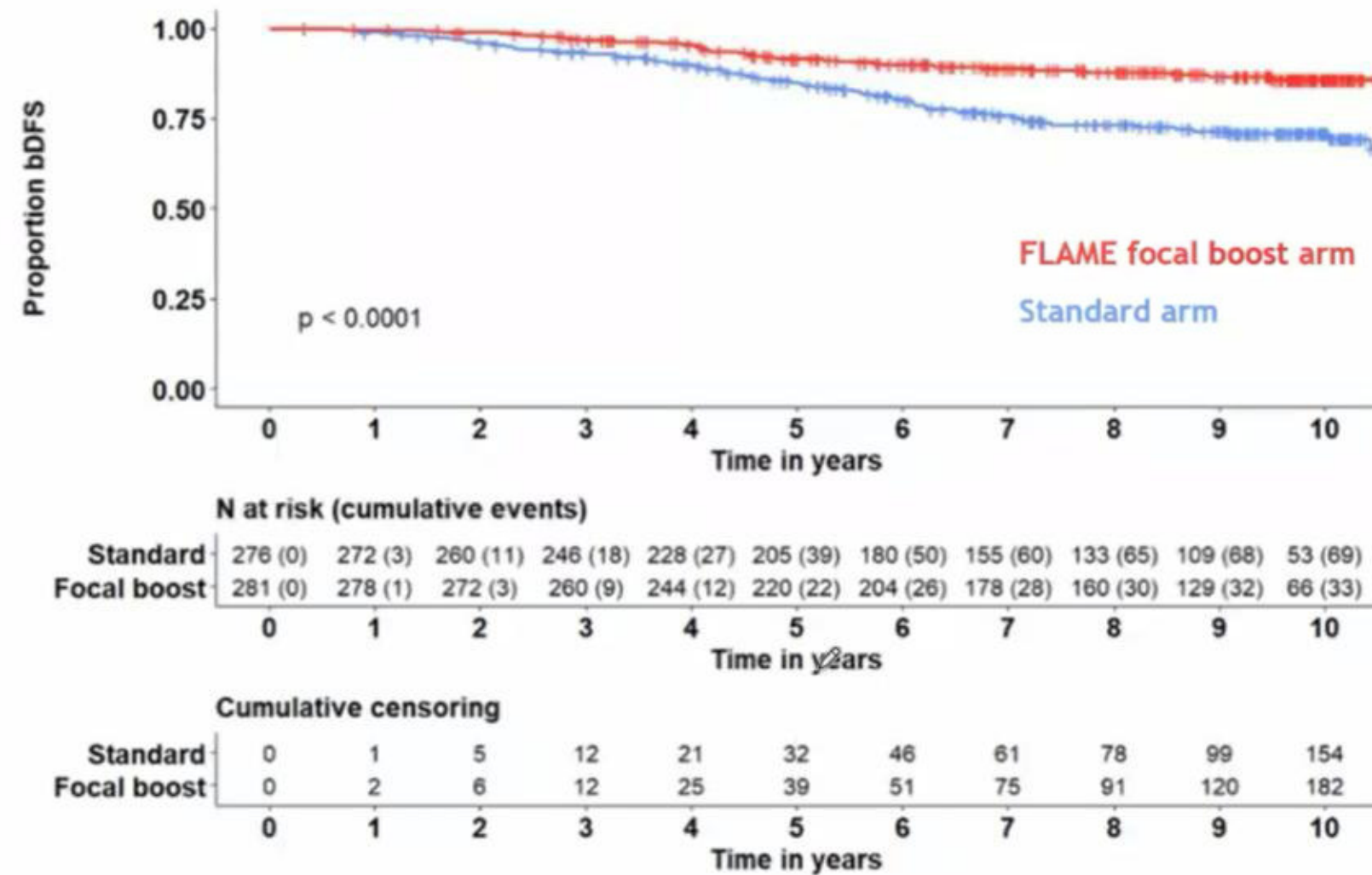
PURPOSE: This study investigates whether **focal boosting of the macroscopic visible tumor** with external beam radiotherapy **increases biochemical disease-free survival (bDFS)** in patients with localized prostate cancer

Standard treatment	FLAME (NCT01168479; phase III)	hypo-FLAME (NCT02853110; phase II)	hypo-FLAME 2.0 (NCT04045717; phase II)
OTT = 7-8 weeks	OTT = 7 weeks	OTT = 29 days	OTT = 15 days
35-40 fractions, 5x/week	35 fractions, 5x/week	5 fractions, 1x/week	5 fractions, 2x/week
Whole gland irradiation	Whole gland irradiation ± focal tumour boost	Whole gland irradiation + focal tumour boost	Whole gland irradiation + focal tumour boost
Prostate Tumour	Prostate Tumour	Prostate Tumour	Prostate Tumour

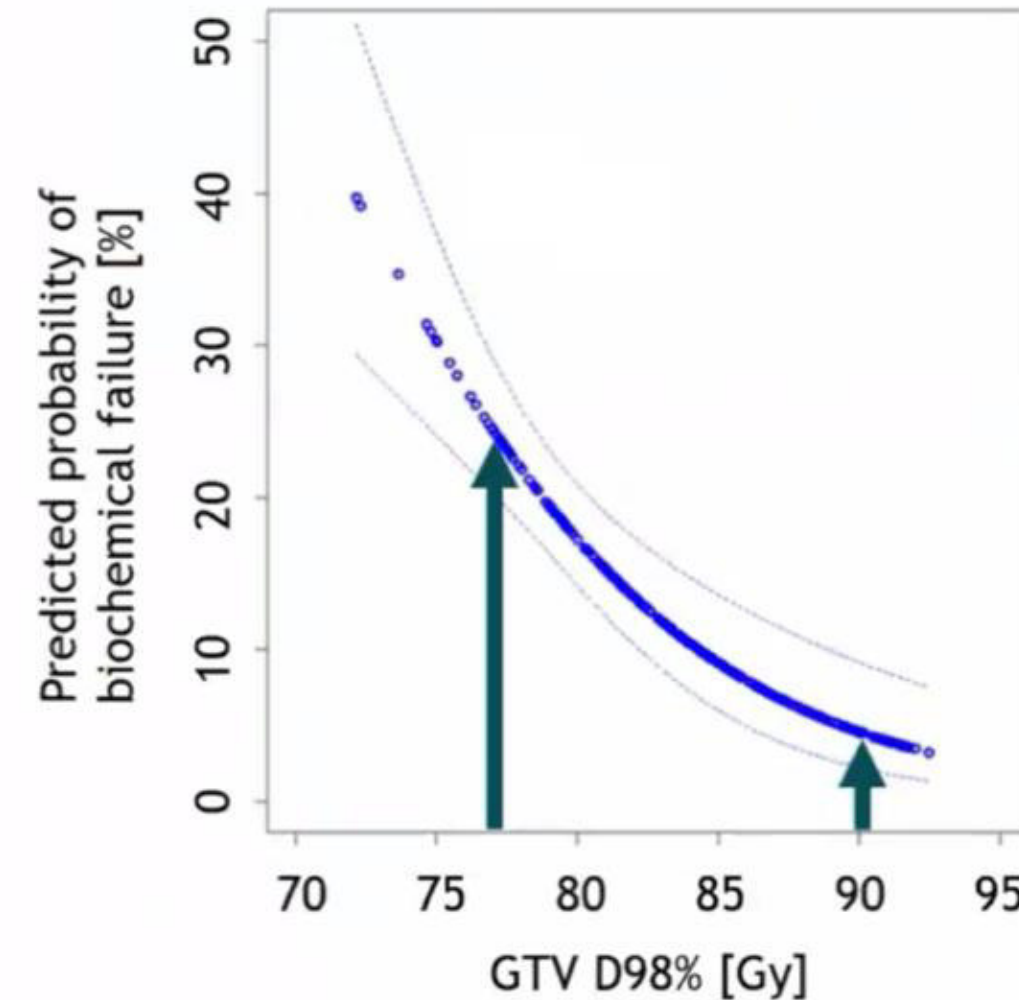
Figure 1. Overview of the FLAME consortium trials investigating focal boosting strategies in prostate cancer

- <https://www.urotoday.com/recent-abstracts/urologic-oncology/prostate-cancer/122180-sbrt-and-the-boost-a-love-story-primary-endpoint-analysis-of-the-phase-ii-hypo-flame-trial-beyond-the-abstract.html>

Biochemical disease-free survival



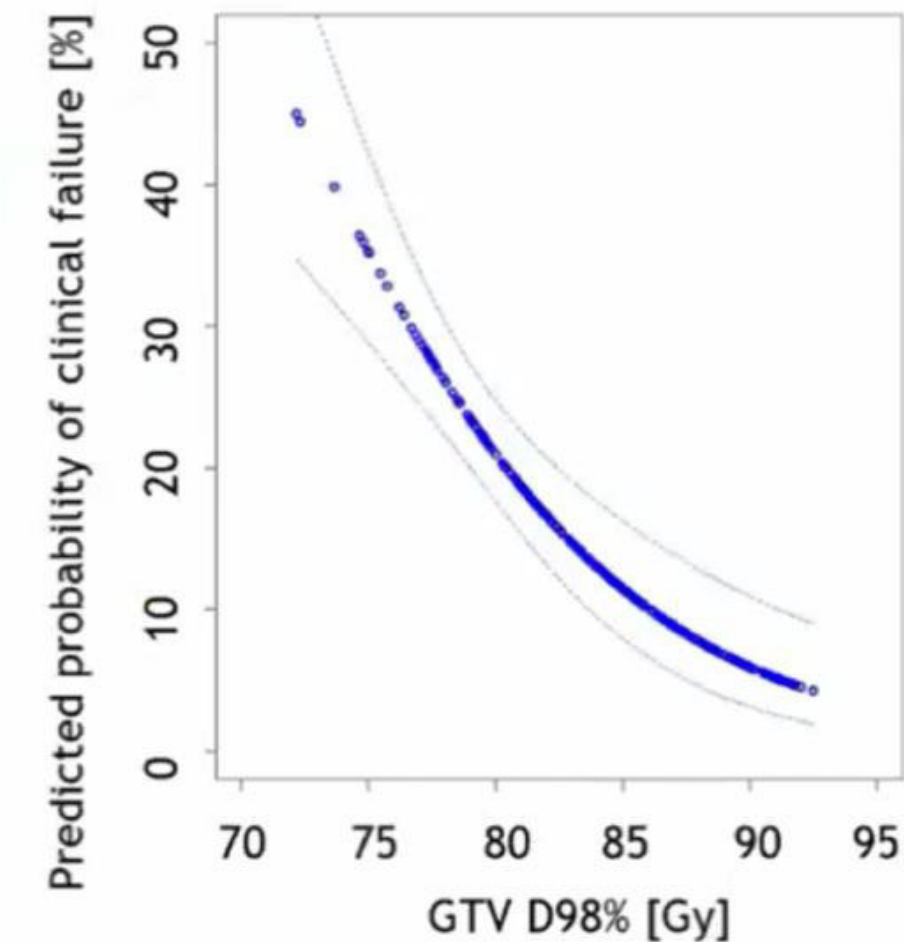
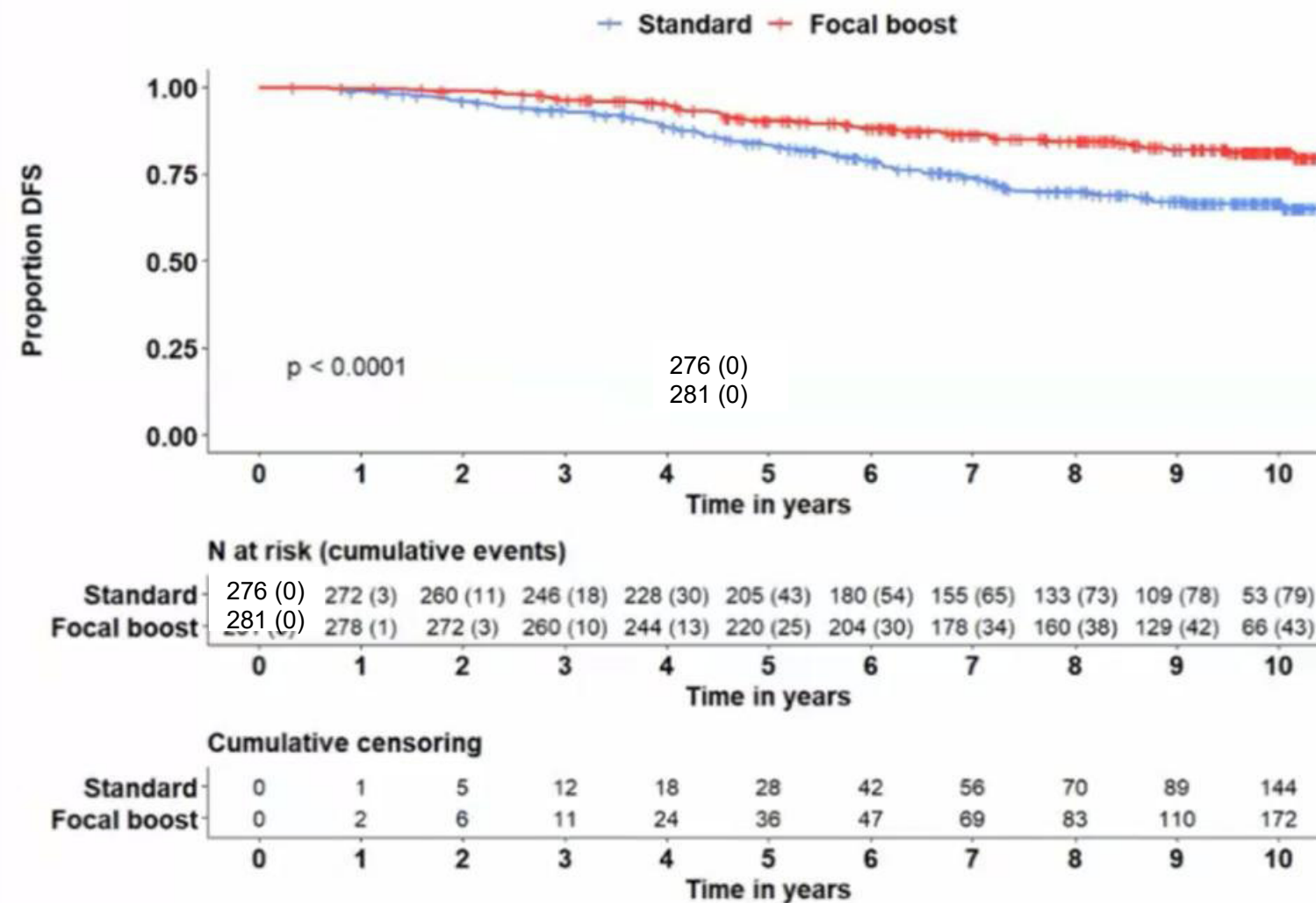
Dose-response curve (bDFS) at 10 years



For biochemical survival at 10 years, the dose-response data revealed that the biochemical failure rate at 77 Gy (the standard dose) was approximately 25%. However, at doses of 90 Gy or higher, the failure rate dropped to 5%, suggesting that **higher doses to the GTV are crucial for improved outcomes**

- ESTRO 2025 – Menne-Guricova Karolina
- Images downloaded from: ESTRO 2025 app and <https://oncoday.com/science/flame-trial-estro-2025> and ESTRO2025

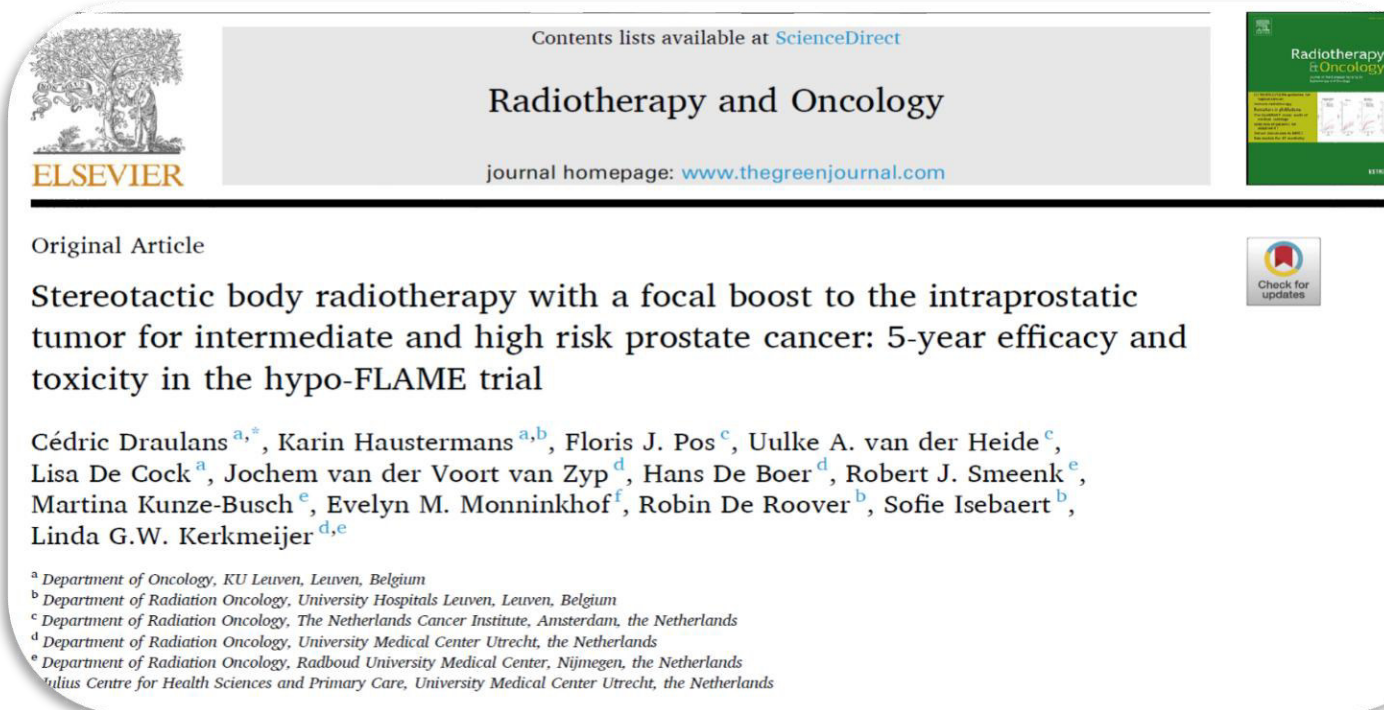
Disease-free survival (DFS)



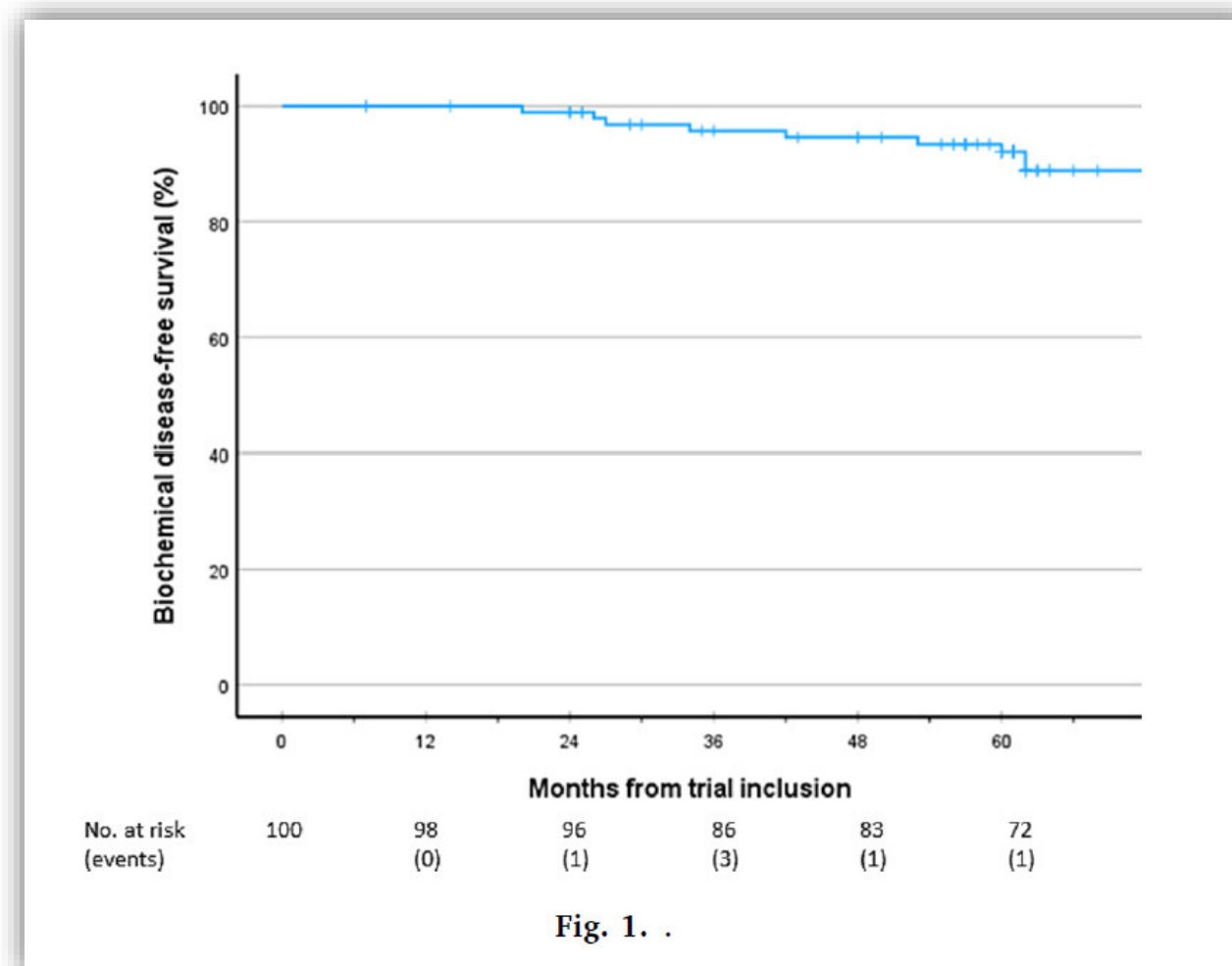
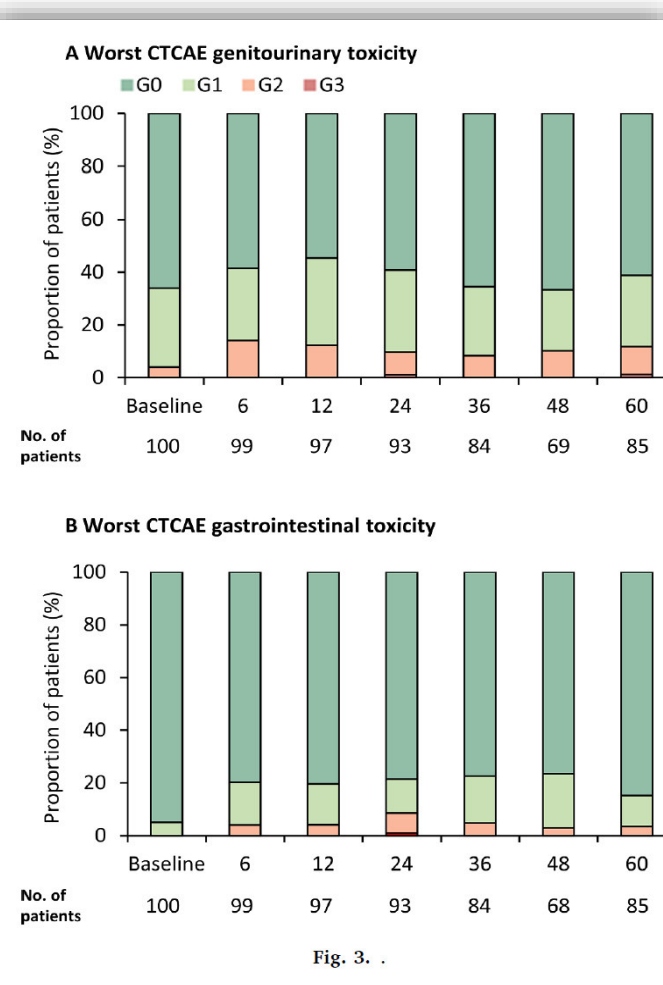
The focal boost arm had a 10-year DFS of 81% compared to 67% in the standard treatment arm. This outcome showed a strong association between **dose escalation and better survival**, supporting the efficacy of focal boosting.

- ESTRO 2025 – Menne-Guricova Karolina
- Images downloaded from: ESTRO 2025 app and <https://oncodayly.com/science/flame-trial-estro-2025> and ESTRO2025

FUTURE DIRECTIONS: DOSE ESCALATION (BOOST)



- 100 Patients with intermediate-high-risk PCa were enrolled in the phase II hypo-FLAME trial.
- All were treated with 35 Gy in 5 weekly fractions to the whole prostate gland with an integrated boost up to 50 Gy to the multiparametric MRI-defined tumor(s).
- If the dose constraints to the normal tissues would be exceeded, these were prioritised over the focal boost dose.
- F-up 61 months



- ✓ At 5 years, the prevalence of grade 2 + GU and GI toxicity was 12 % and 4 %, respectively.
- ✓ The estimated 5-year bDFS was 93 %.

Ultra-hypofractionated focal boost SBRT is associated with encouraging biochemical control up to 5-year follow-up in pts with intermediate and high-risk PCa

The Role of interventional radiotherapy (modern brachytherapy) in unfavorable intermediate risk prostate cancer

LUCA TAGLIAFERRI - MD, PhD

Fondazione Policlinico Univeristario «Agostino Gemelli» IRCCS

Gemelli ART (Advanced Radiation Therapy) - Interventional Oncology Center (IOC)



27th October 2025



INTERVENTIONAL RADIOOTHERAPY AS A BOOST TECHNIQUE



Single fraction
Simultaneous Integrated Boost

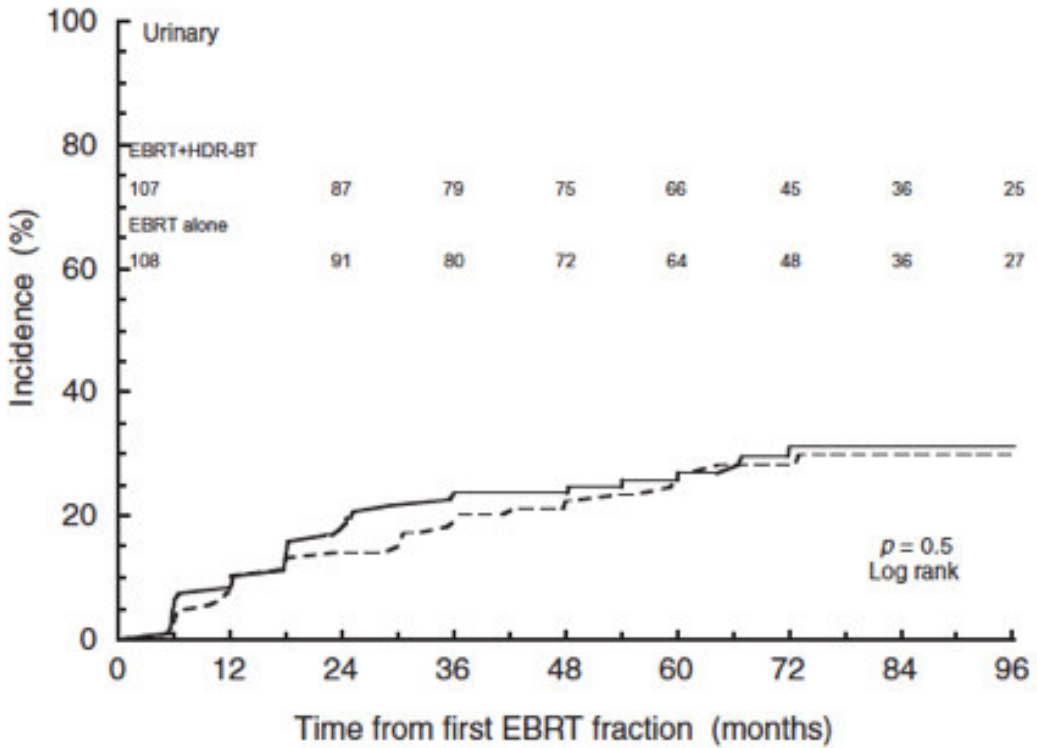
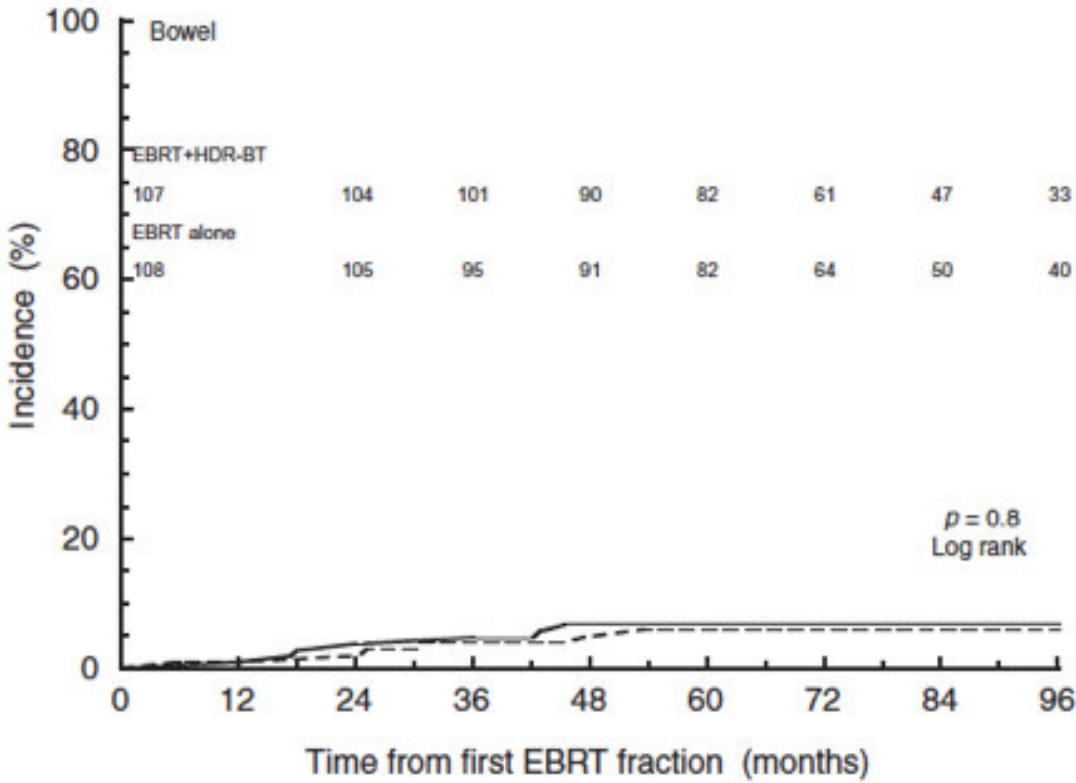
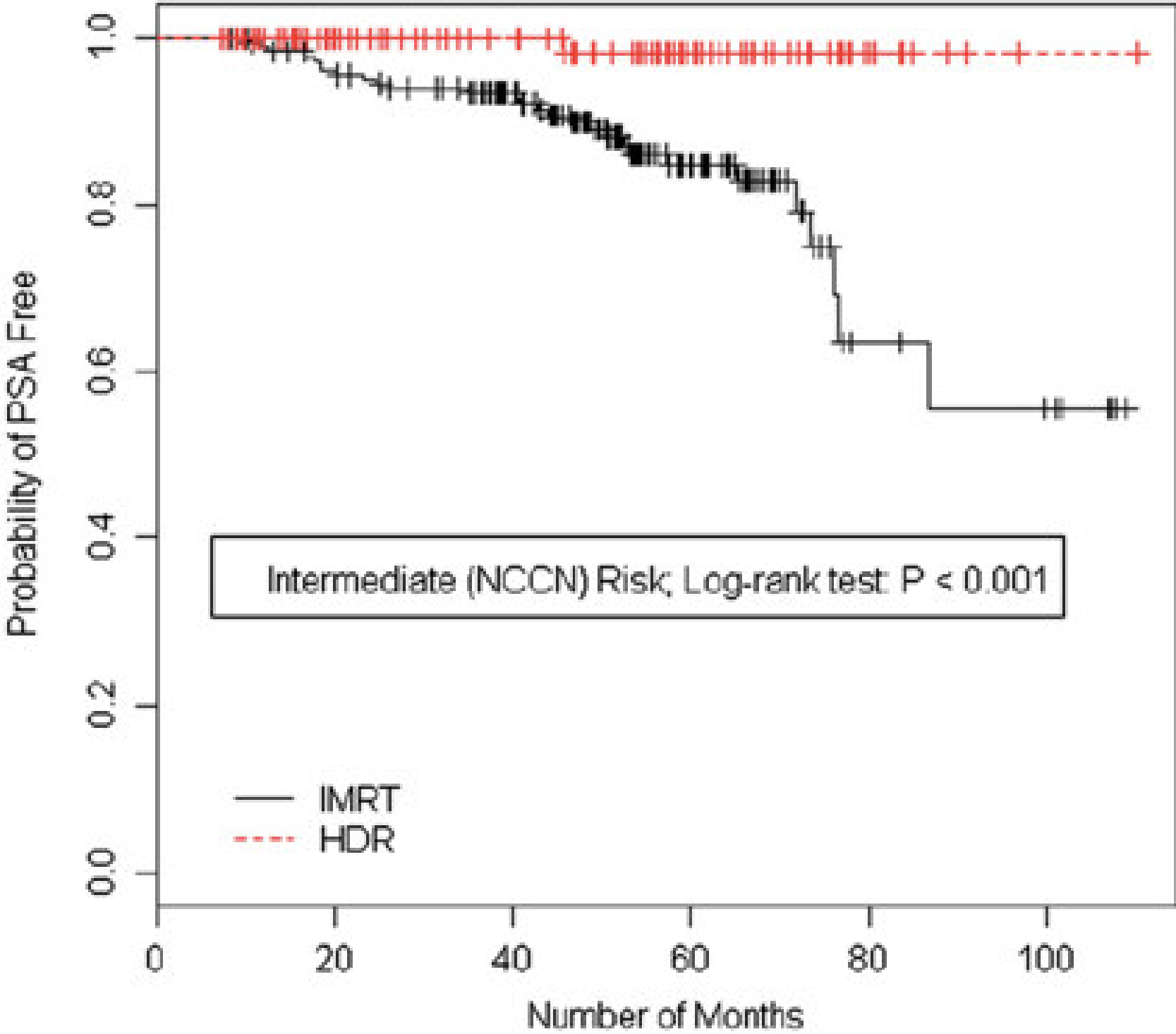
CTV1 10 Gy – Prostate

CTV2 12 Gy – Peripheral prostate area

CTV3 15 Gy – Dominant Intraprostatic Lesion (DIL)

ERT (46Gy – 2Gy/die) + IRT – SIB (10-15Gy)

INTERVENTIONAL RADIOOTHERAPY AS A BOOST TECHNIQUE



• Hoskin PJ, Motohashi K, Bownes P, Bryant L, Ostler P. High dose rate brachytherapy in combination with external beam radiotherapy in the radical treatment of prostate cancer: initial results of a randomised phase three trial. *Radiother Oncol.* 2007

INTERVENTIONAL RADIOOTHERAPY AS A BOOST TECHNIQUE

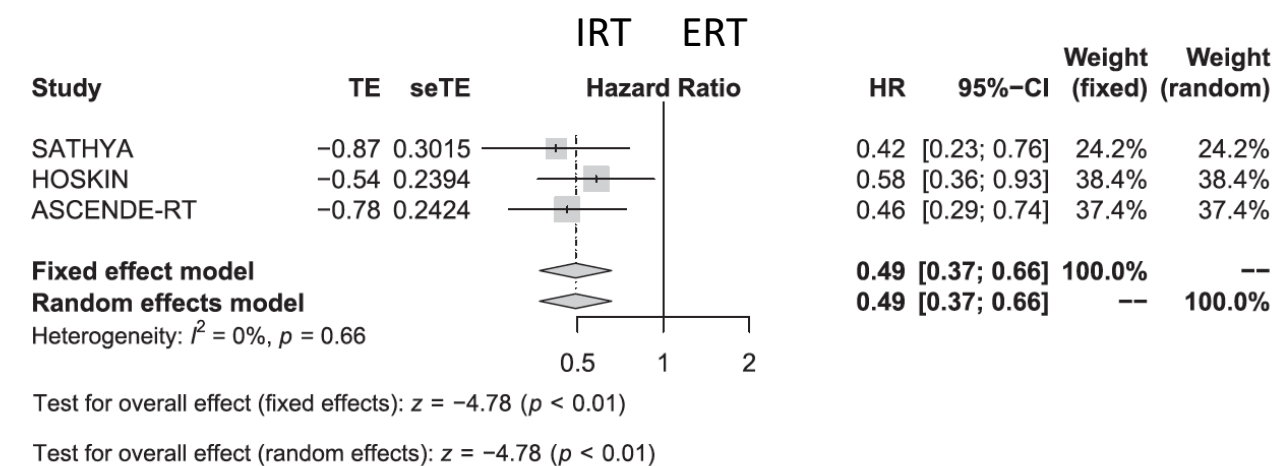


Fig. 2. Forest plots of 5-year biochemical progression free survival for brachytherapy boost versus external beam boost in intermediate and high-risk prostate cancer.

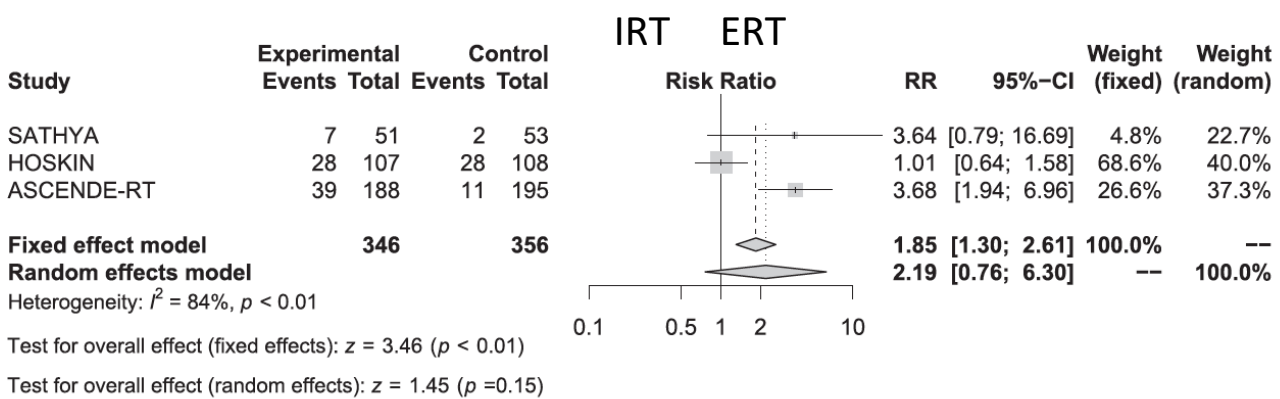


Fig. 4. Forest plots of 5-year rates of late genito-urinary $\geq$ G3 toxicity for brachytherapy boost versus external beam boost in intermediate and high-risk prostate cancer.

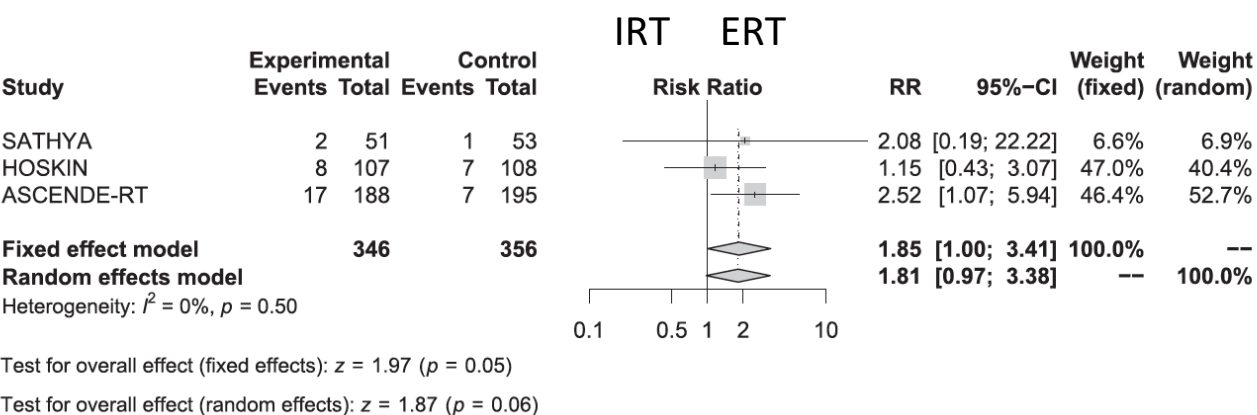


Fig. 5. Forest plots of 5-year rates of late gastro-intestinal $\geq$ G3 toxicity for brachytherapy boost versus external beam boost in intermediate and high-risk prostate cancer.

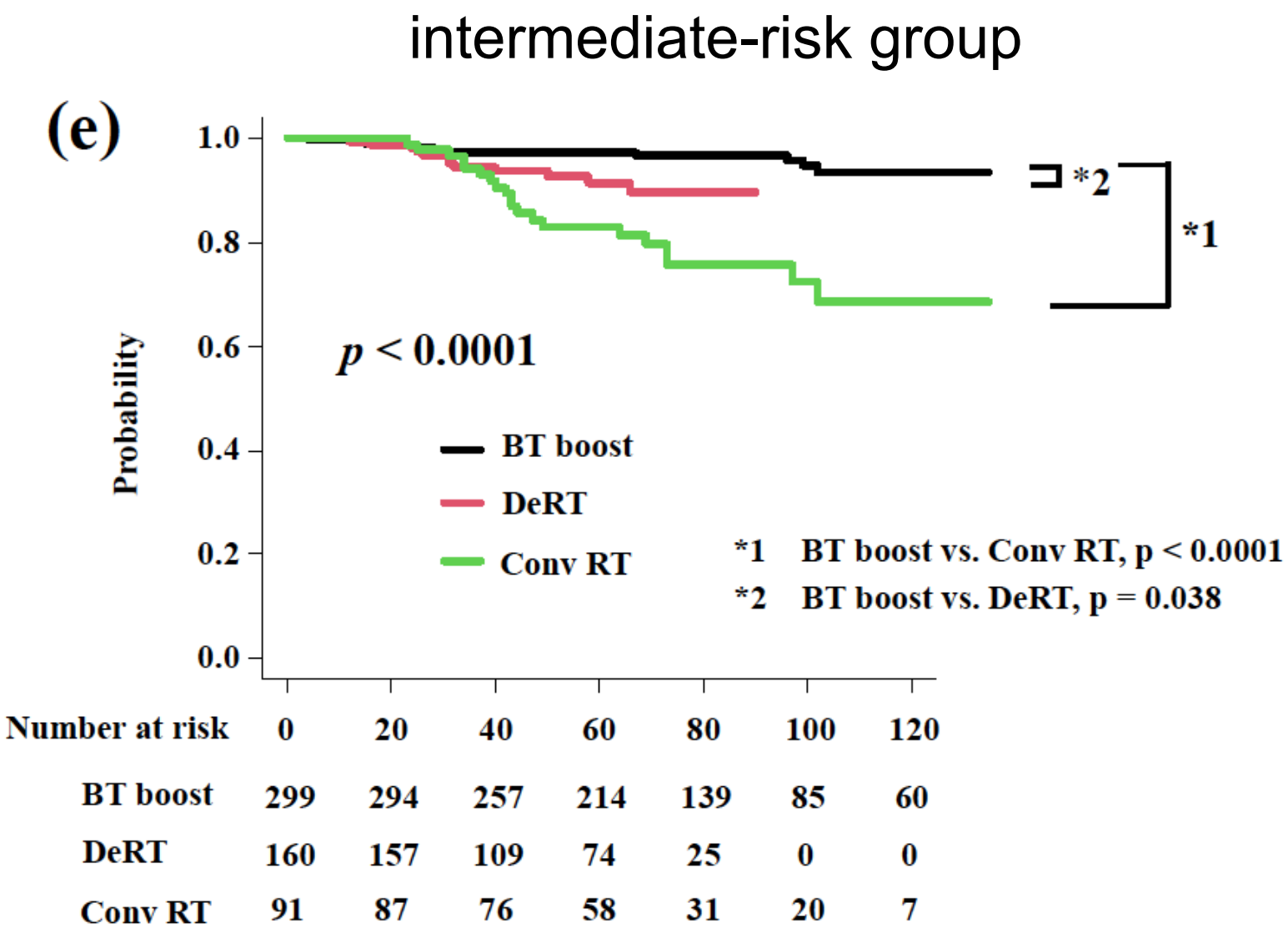
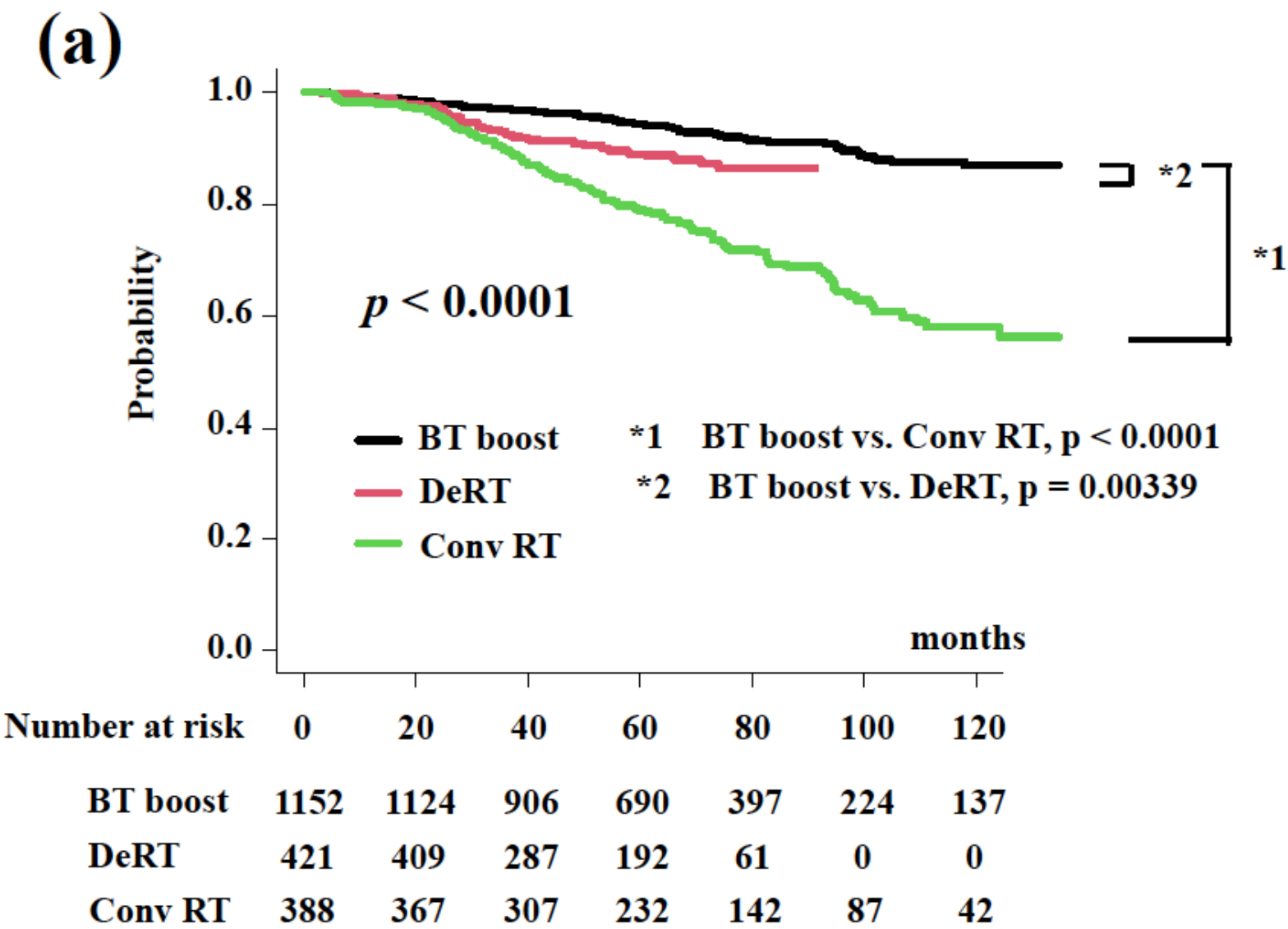


This meta-analysis provides further evidence
in favor of BT boost for intermediate and
high-risk prostate cancer in terms of b-PFS
improvement, leading to suggest
**BT boost as level I and grade A
recommendation.**

However, the risk of grade ≥ 3 late toxicity
must be carefully investigated.

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Biochemical disease-free survival rate (bDFS)



DeRT: Dose Escalation RT

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