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FACE-TO-FACE AND LIVE STREAMING

16-18 SEPTIEMBRE 2026

Espacio Maldonado, Madrid

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SBRT for High-Risk prostate cancer

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Istituto Euopeo di Oncologia, Milan Italy

University of Milan

High-Risk Prostate Cancer: what definition?

Different guidelines – different criteria – same clinical challenge

Sundi – Very high-risk prostate cancer

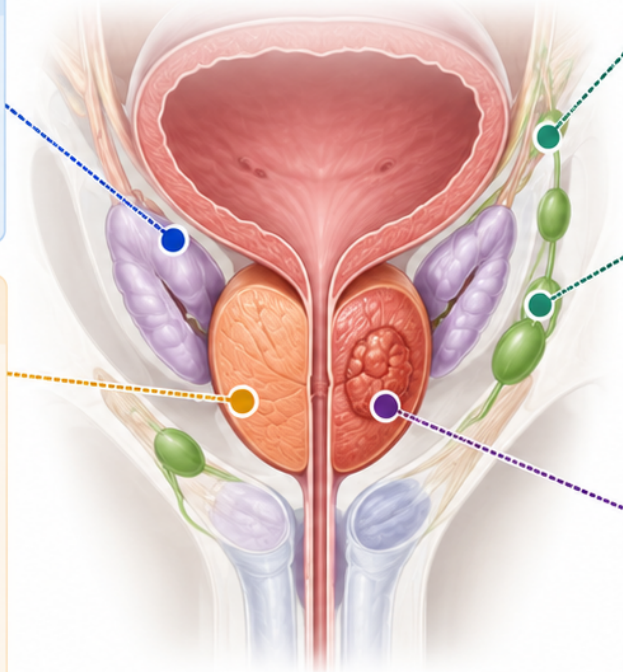
- Primary Gleason pattern 5
- or ≥4 biopsy cores with Gleason sum 8–10
- or multiple NCCN high-risk features (Gleason sum 8–10 or PSA >20 ng/mL or clinical stage ≥T3a)

EAU – High-risk (localised)

- PSA >20 ng/mL
- or Gleason sum ≥8
- or clinical stage ≥T3a

EAU – Locally advanced high-risk

- Any PSA, any Gleason sum
- and either clinical stage T3–T4
- or clinical positive lymph nodes



NCCN – High-risk prostate cancer

- PSA >20 ng/mL
- or Gleason sum ≥8
- or clinical stage ≥T3a

NCCN – Very high-risk prostate cancer

- Primary Gleason pattern 5
- or clinical stage T3b–T4
- or ≥4 biopsy cores with Gleason sum 8–10

D'Amico – High-risk prostate cancer

- PSA >20 ng/mL
- or Gleason sum ≥8
- or clinical stage ≥T2c

High-risk prostate cancer is a heterogeneous group, defined by a higher risk of local progression, regional spread and distant metastases.

Adapted from Lamont J, Wilkins et al. Nat Rev Urol. 2020.

IEO European Institute of Oncology | UNIVERSITÀ DEGLI STUDI DI MILANO

Heterogeneity in Definitions of High-risk Prostate Cancer
and Varying Impact on Mortality Rates after Radical Prostatectomy

Mossanen M et al.
Eur Urol Oncol. 2018;1:143–148

STUDY POPULATION

25,741 men
radical prostatectomy
(1988–2011)

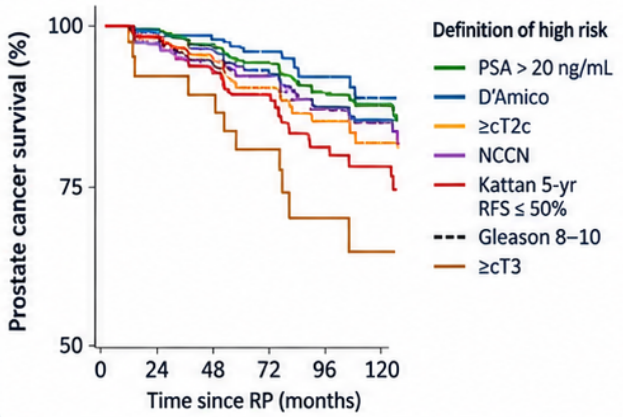
AIM

To evaluate how different definitions of high-risk prostate cancer affect oncological outcomes after radical prostatectomy.

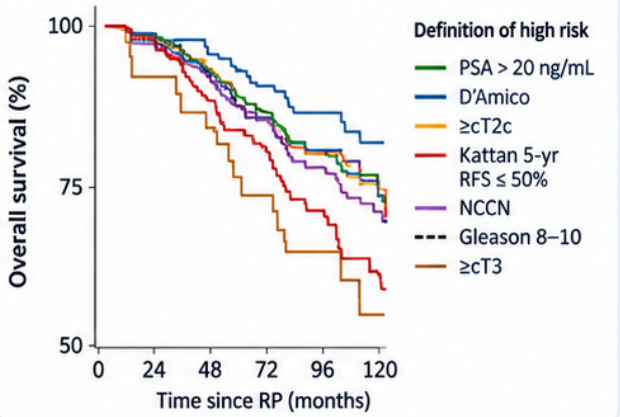
METHODS

- Retrospective analysis
- Multiple high-risk definitions
- Kaplan–Meier estimates
- Prostate cancer–specific and overall survival

Prostate cancer–specific survival



Overall survival



Definition of high risk	Criteria	10-year PCa-specific survival (%)	10-year overall survival (%)
PSA > 20 ng/mL	PSA > 20 ng/mL	~ 90	~ 78
D'Amico	PSA > 20 or GS ≥ 8 or cT ≥ T2c	~ 88	~ 74
≥cT2c	Clinical stage ≥ T2c	~ 86	~ 70
NCCN	PSA > 20 or GS ≥ 8 or cT ≥ T3a	~ 84	~ 67
Kattan 5-yr RFS ≤ 50%	Nomogram-based risk	~ 80	~ 62
Gleason 8–10	Gleason score 8–10	~ 77	~ 59
≥cT3	Clinical stage ≥ T3	~ 69	~ 54

KEY MESSAGES

1. Definitions of high-risk prostate cancer vary substantially across guidelines and studies.
2. Oncological outcomes after radical prostatectomy differ meaningfully depending on which definition is applied.
3. This heterogeneity has important implications for patient counselling, trial design and comparison of treatment outcomes.
4. "High-risk" is not a single disease, and risk stratification remains a moving target.

This variation in outcome according to definition is important for patient counselling, because patients can have different predicted outcomes depending on which definition is applied to identify their PCa risk category.

Radiotherapy in High-Risk Prostate Cancer

From heterogeneous risk to personalized local treatment – where does SBRT fit?

A HETEROGENEOUS DISEASE

Different definitions, different outcomes

High tumour burden
Higher risk of local persistence

Regional risk
Occult nodal disease still possible with modern imaging

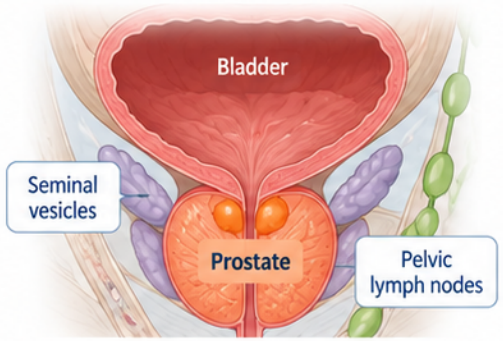
Systemic risk
Higher probability of distant metastases

Heterogeneous definitions
Different criteria across guidelines and studies with variable outcomes

"High-risk" is not a single disease. Risk stratification matters for treatment and for patient counselling.

WHY RADIOTHERAPY?

Local treatment still plays a key role



- Improves local control and biochemical control
- Reduces risk of metastatic progression in selected patients
- Enables dose intensification (whole gland or focal)
- Can include seminal vesicles and pelvic nodes in selected cases

Local treatment is only one component of high-risk management, but it remains essential.

SBRT: A RATIONAL OPTION?

Treatment compression without compromising effectiveness

Radiobiological rationale
- Low α/β ratio
- High tumour BED with large fractions

Shorter treatment course
- 5 fractions (± 1–2 weeks)
- Improved convenience for patients and departments

Opportunities for intensification
- Whole-prostate dose escalation
- MRI-guided focal boost (FLAME, hypo-FLAME)

Potential for pelvic treatment
- Elective nodal irradiation in 5 fractions (early evidence, e.g. SHARP 25 Gy/5)

SBRT can shorten treatment, while maintaining — and potentially increasing — the biological intensity of local therapy.

KEY OPEN QUESTIONS BEFORE ADOPTION

- Which patients are the best candidates for SBRT?
- What is the optimal dose and fractionation?
- How should we treat seminal vesicles and pelvic lymph nodes?
- Can SBRT be safely integrated with long-term ADT and systemic intensification (e.g. ARPI)?
- Will oncological outcomes be non-inferior in high-risk disease? (HIGH FIVE)

AND WHAT DO THE GUIDELINES SAY?

Let's see how current guidelines address the use of radiotherapy and, in particular, SBRT in high-risk prostate cancer...

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PRINCIPLES OF RADIATION THERAPY

Table 1: Below are examples of regimens that have shown acceptable efficacy and toxicity. The optimal regimen for an individual patient warrants evaluation of comorbid conditions, voiding symptoms, and toxicity of therapy. Additional fractionation schemes may be used as long as sound oncologic principles and appropriate estimate of BED are considered.

See treatment pages and Principles of ADT (PROS-G) for other recommendations, including recommendations for neoadjuvant/concomitant/adjuvant ADT.

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

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

Footnotes on PROS-J 8A of 11

Note: All recommendations are category 2A unless otherwise indicated.

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

6.3.3.c. Recommendations for the management of high-risk localised disease*

Radiotherapeutic treatment	
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 four weeks or 70 Gy/28 fx in six weeks), in combination with long-term androgen deprivation therapy (ADT) (two to three years).	Strong
Offer focal boosting to magnetic resonance imaging (MRI)-defined dominant intraprostatic tumour when using normo-fractionated IMRT/IGRT (1.8-2.0 Gy per fraction) ensuring that Organ at Risk constraints are not exceeded.	Strong
Offer patients with good urinary function IMRT/VMAT plus IGRT with brachytherapy boost (either high-dose rate or low-dose rate) in combination with long-term ADT (two to three years).	Weak
Other therapeutic options	
Do not offer either whole gland or focal therapy.	Strong
Only offer ADT monotherapy to those patients unwilling or unable to receive any form of local treatment if they have a prostate-specific antigen (PSA)-doubling time < 12 months, and either a PSA > 50 ng/mL or a poorly differentiated tumour.	Strong

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

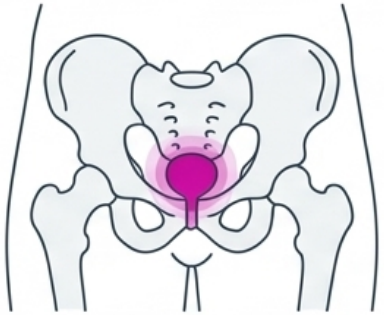
6.3.4.d. Recommendations for management of locally advanced disease*

Radiotherapeutic treatments	
Offer patients with cN0 disease intensity-modulated radiation therapy (IMRT)/volumetric modulated arc therapy (VMAT) plus image-guided radiation therapy in combination with long-term androgen deprivation therapy (ADT).	Strong
Offer patients with cN0 disease and good urinary function, IMRT/VMAT plus IGRT with brachytherapy boost (either high-dose rate or low-dose rate), in combination with long-term ADT.	Weak
Offer long-term ADT for at least two years.	Strong
Offer IMRT/VMAT plus IGRT to the prostate in combination with long-term ADT and two years of abiraterone to cN0M0 patients with ≥ 2 high-risk factors (cT3-4, Gleason ≥ 8 or prostate-specific antigen ≥ 40 ng/mL).	Strong
Offer IMRT/VMAT plus IGRT to the prostate plus pelvis in combination with long-term ADT and two years of abiraterone to cN1M0 patients.	Strong
Other therapeutic options	
Do not offer whole gland treatment or focal treatment.	Strong

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

High-Risk Biology Demands Comprehensive Management, Not Just Fraction Compression

Local Disease



High intraprostatic tumor burden (e.g., T3a disease, bulk). Carries a greater risk of local persistence.

UI

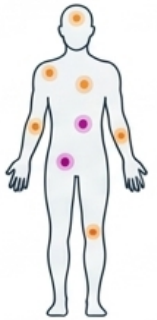
Requires focal dose intensification while respecting urethral ceilings.

Regional Disease



Higher probability of microscopic pelvic nodal involvement and complex seminal vesicle extensions.

Systemic Disease



Greater risk of occult metastatic dissemination.

UI

Demands strict integration with systemic therapy.

High-risk biology does not necessarily require more fractions—it requires more comprehensive treatment.

Gemini Notebook

Establishing the Foundation: SBRT Safety in Lower-Risk Disease

PACE-B

36.25 Gy / 5 fx | Low/Int Risk

- Established non-inferiority with 95.8% 5-year biochemical control.
- No ADT used.
- Excellent long-term safety profile.

HYPO-RT-PC

42.7 Gy / 7 fx | 11% High Risk

- 10-year follow-up validates non-inferior long-term disease control (84% 5y bDFS).
- No ADT used.

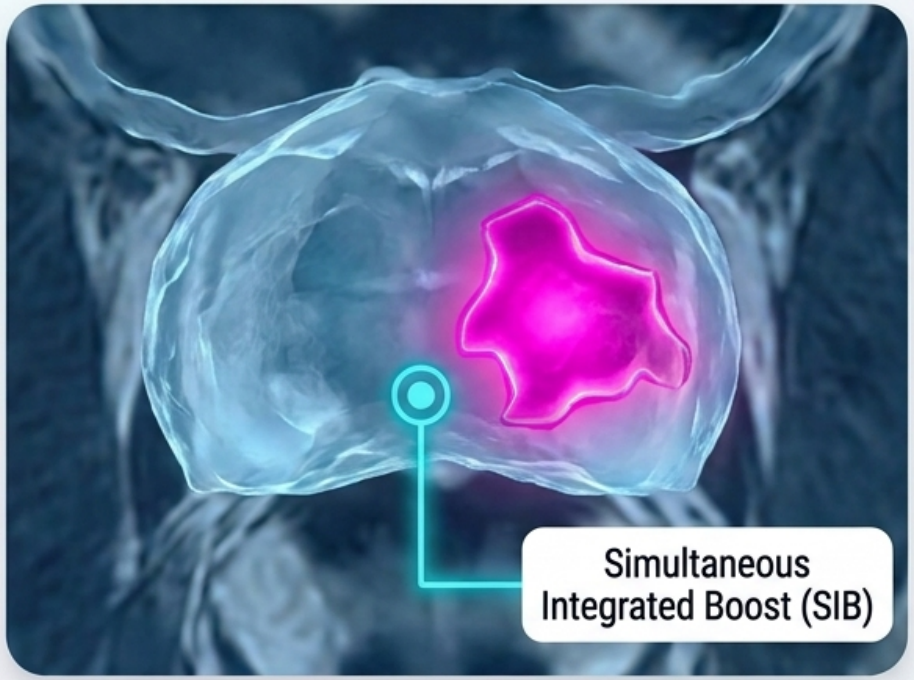
NRG-GU005

36.25 Gy / 5 fx | Ment/Int Risk | Superiority Design

- Shorter treatment requires flawless technical execution to maintain safety.
- SBRT was not superior for DFS.
- Showed acute HRQoL decline at 2 years vs. standard 60 Gy.

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Local Intensification: Eradicating Bulk with Focal Boosting



FLAME (10-Year Follow-up)

Conventional 35-fraction RT + MRI-defined focal boost up to 95 Gy.

Improved 10-year bDFS from 71% to 86%.

hypo-FLAME (Phase II)

SBRT (35 Gy/5 fx) + SIB up to 50 Gy to the DIL.

Achieved a 93% 5-year bDFS

Minimal late toxicity (GU 12%, GI 4%).

Treatment shortening and local dose intensification are not mutually exclusive.

Gemini Notebook

Androgen deprivation therapy use and duration with definitive radiotherapy for localised prostate cancer: an individual patient data meta-analysis

MARCAP consortium (34,823 patients)

MARCAP CONSORTIUM
Individual patient data meta-analysis

STUDY OVERVIEW

34,823 patients
from 4 randomized trials

Individual patient data meta-analysis

Definitive radiotherapy for localised prostate cancer

OBJECTIVE

To evaluate the use and duration of ADT with definitive RT and its impact on oncological outcomes.

RISK STRATIFICATION

Primary analysis according to NCCN risk groups

KEY FINDINGS

1 Adding ADT to radiotherapy improves outcomes

Significant improvement in metastasis-free survival and overall survival

Number needed to treat (NNT) to prevent one distant metastasis at 10 years: 8–18 (NCCN risk group)

2 Longer ADT duration further improves outcomes

Adjuvant ADT ≥ 18 months in conjunction with RT significantly improves metastasis-free survival and overall survival compared with short-term ADT.

NNT to prevent one distant metastasis at 10 years: 10 (high-risk disease)

3 Extending neoadjuvant ADT does not improve outcomes

Extension of neoadjuvant ADT was not associated with improved biochemical recurrence, distant metastasis, metastasis-free survival, or overall survival.

Should not be routinely recommended.

CLINICAL IMPLICATIONS

ADT combined with RT is standard of care in high-risk localised prostate cancer.

An adjuvant ADT duration of at least 18 months should be considered.

Prolonged neoadjuvant ADT does not provide additional benefit and should not be routinely used.

Treatment decisions should be individualised based on NCCN risk group and patient characteristics.

KEY TAKEAWAY

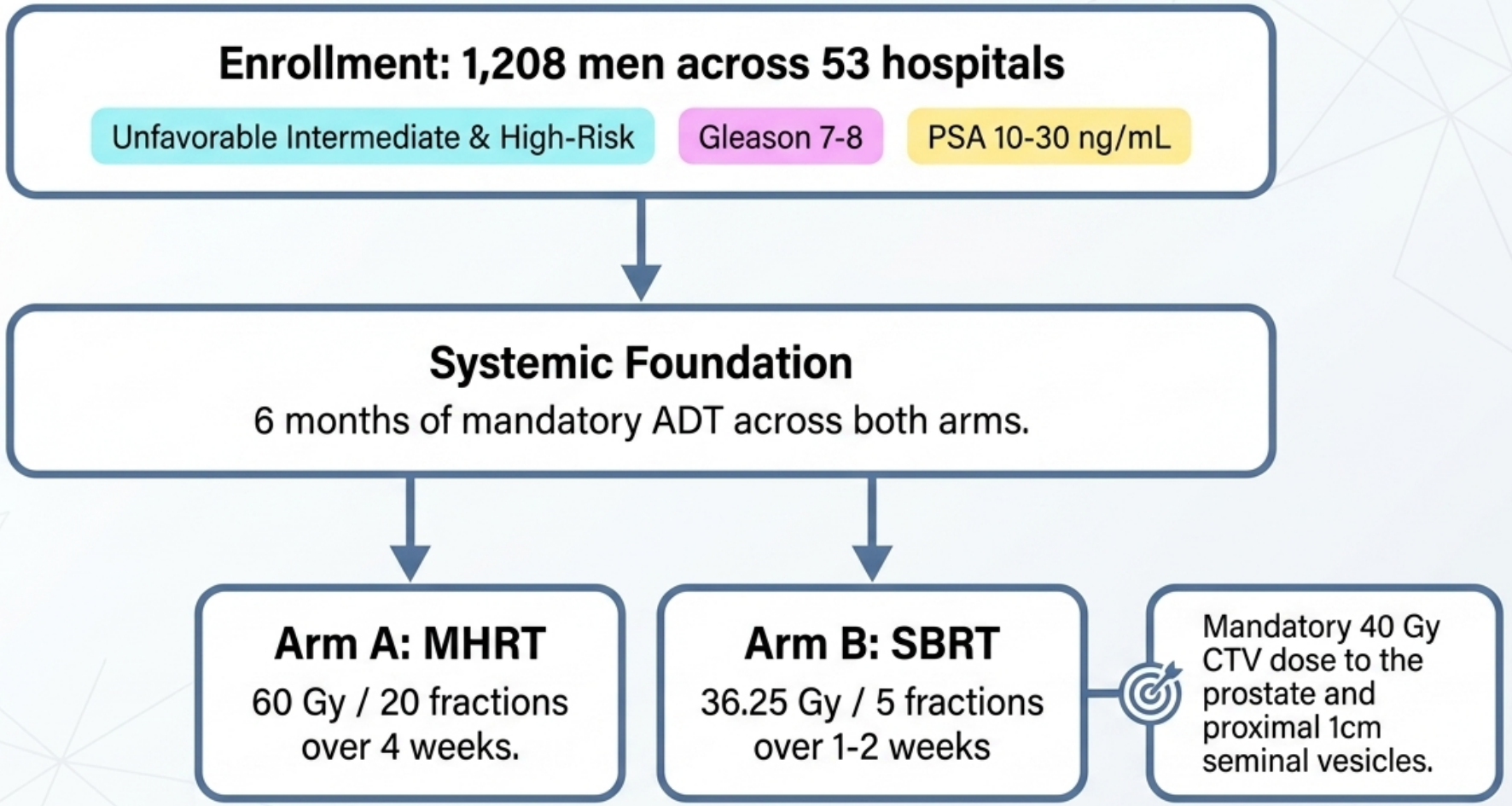
The integration and appropriate duration of ADT with definitive radiotherapy is crucial for optimizing long-term outcomes in high-risk localised prostate cancer.

Urokhan A. et al.
MARCAP Consortium
Lancet 2022; 399: 447–460.

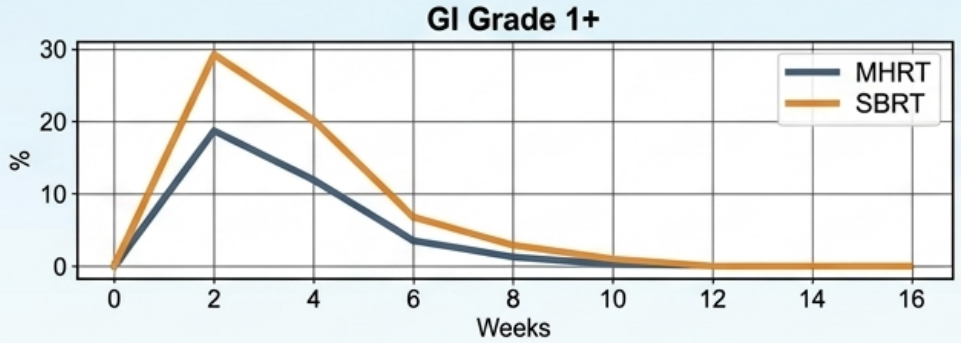
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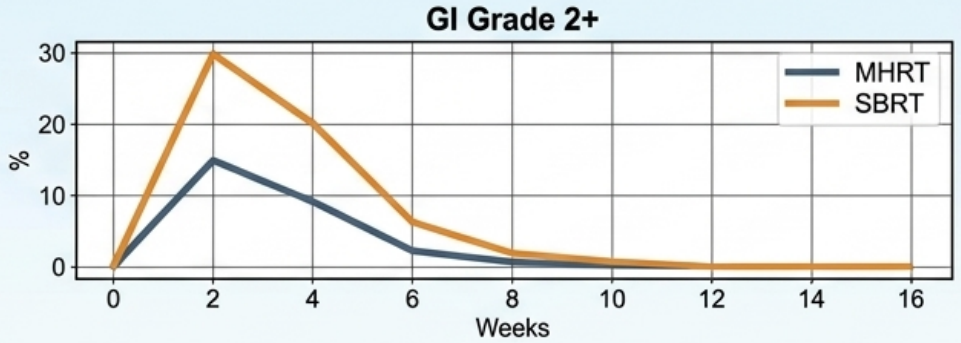
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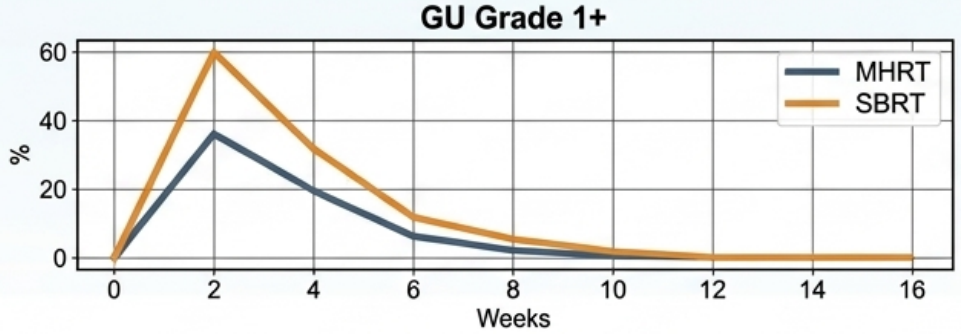
The Latest Evidence: PACE-C Phase III Trial Architecture

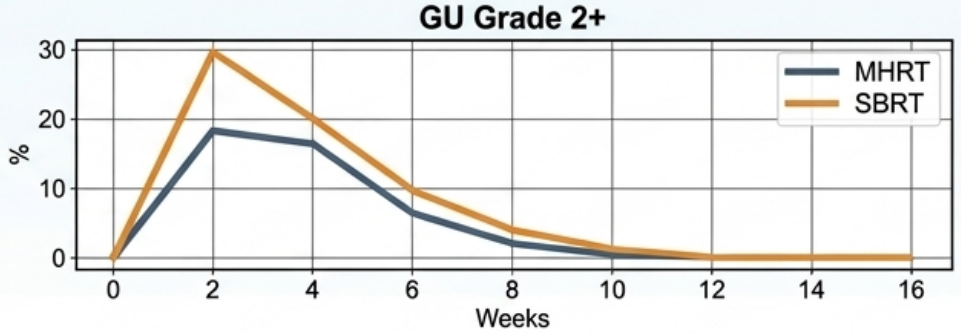


PACE-C Early Toxicity Dynamics: The 12-Week Resolution









Gastrointestinal (GI)

Higher initial symptom flare for SBRT (17% vs 10% CTCAE G2+). Both arms resolved entirely by 12 weeks with no significant long-term difference.

Genitourinary (GU)

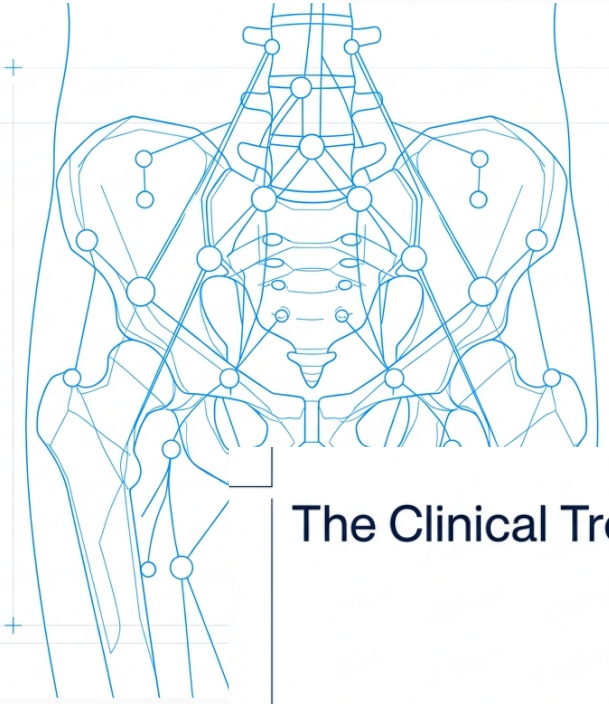
RTOG G2+ nearly identical between arms (28% SBRT vs 27% MHRT). CTCAE showed borderline higher early symptoms heavily influenced by baseline function.

Severe toxicity (Grade 3+) remained extremely rare (<1% to 1%) across both modalities.

Gemini Notebook

The SHARP Update on Pelvic SBRT

Evaluating Efficacy and Safety in High-Risk Localized Prostate Cancer



Data synthesized from the 440-patient SHARP Consortium (Median Follow-up: 60.4 Months).

The Clinical Trepidation

Does the oncologic benefit of elective pelvic nodal SBRT justify the perceived toxicity risks in high-risk localized prostate cancer?

Oncologic Benefit

Despite NCCN inclusion of SBRT for HRLPC, fear of outsized toxicity—particularly when treating pelvic lymph nodes—has driven clinical hesitation and abandonment of SBRT in high-risk populations.

Late Toxicity

We need to definitively map the long-term safety profile and oncologic efficacy of nodal inclusion using 60-month follow-up data.

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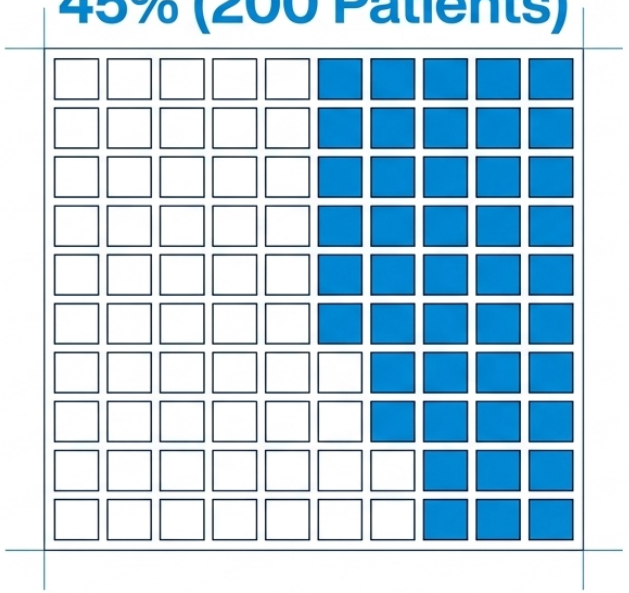
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RD CONSORTIUM

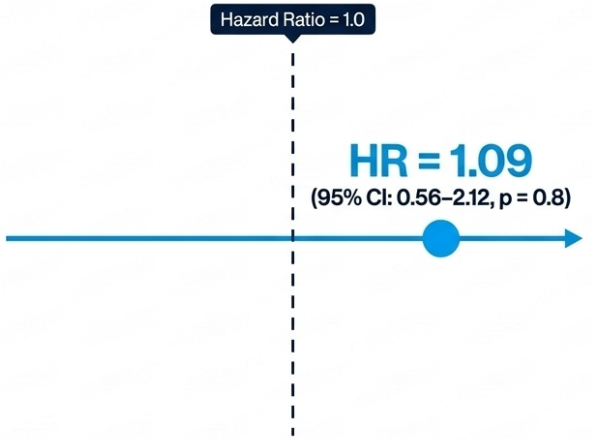
Isolating the Nodal Cohort

45% (200 Patients)



- Out of 440 total HRLPC patients in the SHARP consortium, 200 underwent elective pelvic nodal radiotherapy.
- Treatment Parameter: Target dose of 25 Gy delivered in 5 fractions.
- Cohort Composition: 74% of the intensified treatment group and 38% of the standard treatment group received pelvic RT.
- Exclusion: Node-positive patients were excluded at baseline.

The Efficacy Finding: No Statistical Reduction in Distant Metastasis



- After adjusting for age, PSA, T-category, and Grade Group, treating pelvic lymph nodes as an alternative intensification strategy did not statistically reduce Distant Metastasis (DM).
- This neutral outcome persisted even within the extremely dose-escalated subset (≥8 Gy/fraction to the prostate), yielding an HR of 1.21 (p = 0.7).

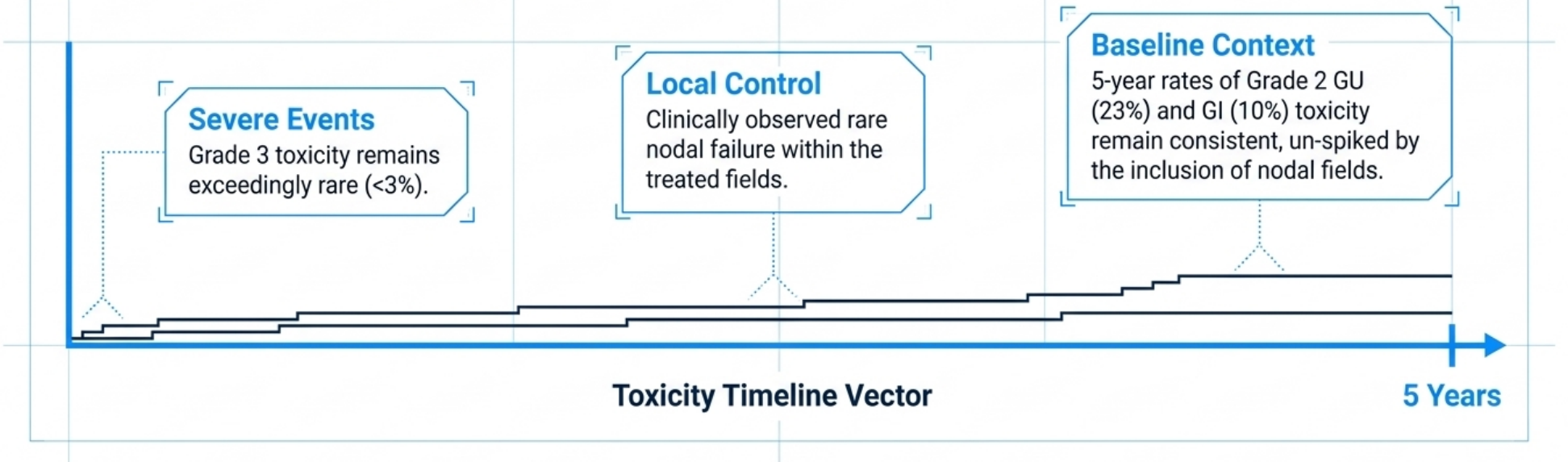
Takeaway: Expanding the RT field to the pelvic nodes does not appear to provide a significant oncologic control advantage for DM based on current data.

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The Safety Finding: A Highly Favorable Toxicity Profile

The data reveals no obvious signals for **increased late toxicity** or decreased efficacy when SBRT is used to treat **pelvic lymph nodes**.



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Clinical Synthesis & The Path Forward

Efficacy vs. Safety Diagnostic Matrix

Oncologic Efficacy

Finding: Flat/Neutral Outcome.

Pelvic SBRT (25 Gy) does not independently drive down Distant Metastasis in HRLPC.

Toxicity & Safety

Finding: Positive/Reassuring Outcome.

The regimen is fundamentally safe, does not compromise the baseline toxicity profile, and results in rare nodal failure.

Pelvic nodal SBRT remains a viable, highly safe option for shared decision-making. Definitive validation of oncologic benefit awaits the results of prospective, randomized level-1 trials: RTOG 0924 and PivotalBoost.

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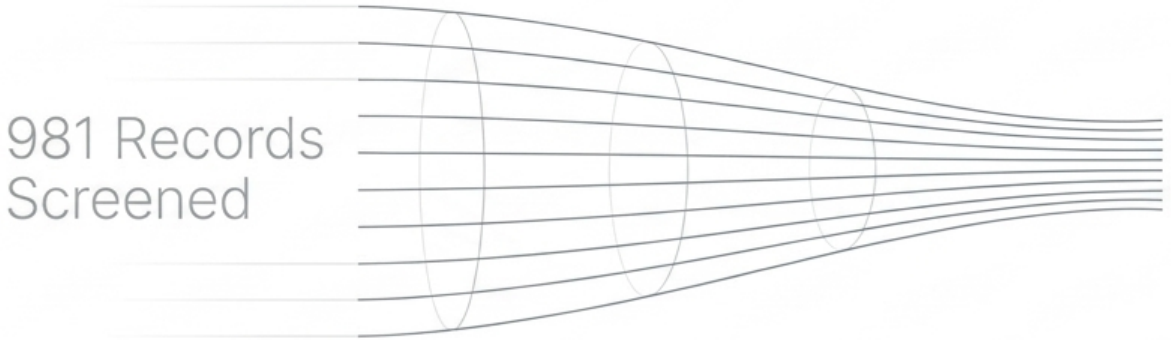
Stereotactic Body Radiation Therapy for High-Risk Prostate Cancer: A Systematic Review of the Literature

Authors: Raffaella Lucchini, Rodrigo Cartes, Ciro Franzese, Lorenzo Lo Faro, Luciana Di Cristina, Giuseppe Roberto D"Agostino, Marco Badalamenti, Andrea Girlando, Rosario Mazzola, Stefano Arcangeli, Marta Scorsetti.

Affiliations: IRCCS Humanitas Research Hospital, Humanitas University, Humanitas Istituto Clinico Catanese, Humanitas Gavazzeni Hospital, University of Milan Bicocca, Fondazione IRCCS San Gerardo dei Tintori.

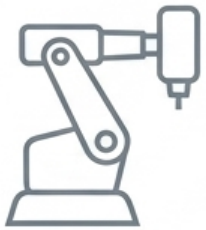
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The Evidence Base for High-Risk Cohorts



30 Studies
1,354 Patients

Highly variable follow-up, but consistently favorable outcomes



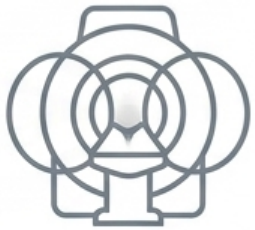
CyberKnife®
14 studies



LINAC
10 studies



TomoTherapy®
2 studies



MR-LINAC
1 study

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Biochemical Control: The Efficacy Spectrum

RETROSPECTIVE SERIES	PROSPECTIVE TRIALS
Demonstrated long-term Biochemical Control (BC) rates ranging from 74.1% to 95.2% (follow-up ≥ 5 years).	Reported BC rates between 65% and 96.7% across 5 to 8 years of follow-up.

The SHARP Consortium

Pooled prospective data solidifies SBRT as a highly viable primary treatment for HRPC.

81.7% BC Rate at 4 Years

(n = 344 prospectively treated patients)

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Long-Term Survival Outcomes

Long-term data (3 to 7 years) confirms that extreme hypofractionation provides durable systemic control and exceptional overall survival in high-risk patients.

The Outcomes Dashboard



Distant Metastasis-Free Survival (DMFS)

Overall Survival (OS) at 5 Years

Cancer-Specific Survival (CSS) at 5 Years

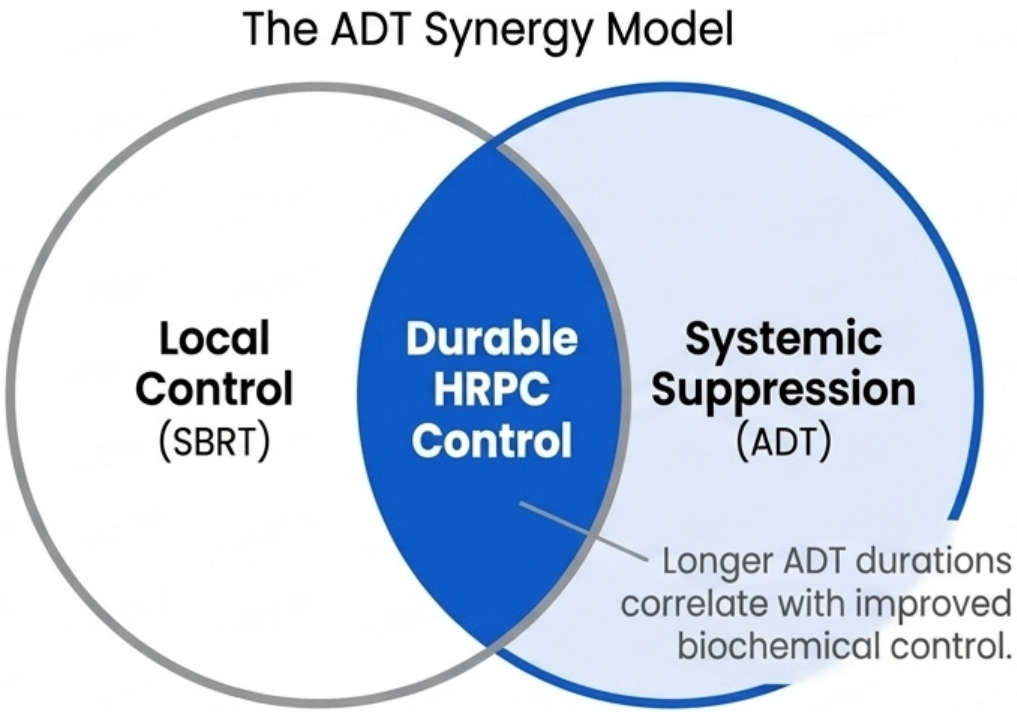
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The Non-Negotiable Catalyst: Androgen Deprivation Therapy

High-risk prostate cancer is a systemic threat requiring a dual-modality approach.

ADT protocols were utilized in 93% (28 of 30) of the reviewed studies, ranging from 4 to 42 months.

Extreme dose escalation (e.g., 135 Gy) alone cannot replace the biochemical benefit of ADT in high-risk populations.



Gemini Notebook

Why Local Control Matters in High-Risk Prostate Cancer
Insights from the FLAME trial



Groen et al.
Eur Urol. 2020

1 Background

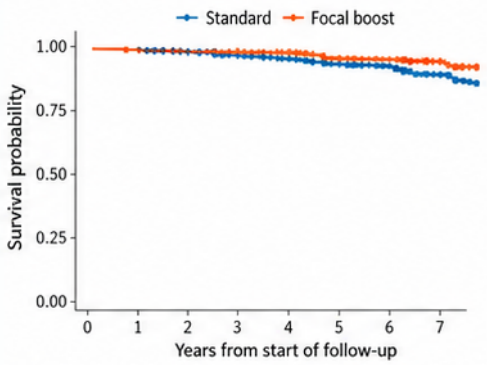
Prostate cancer has a long natural history
Surrogate endpoints are used to measure treatment efficacy.

Distant metastatic failure occurs more frequently in high-risk disease
Is micrometastatic spread present at diagnosis or the result of insufficient local control?

Key endpoints
- Local failure–free survival (LFS)
- Regional + distant metastasis–free survival (rdMFS)

2 Impact of focal boost on outcomes (FLAME)

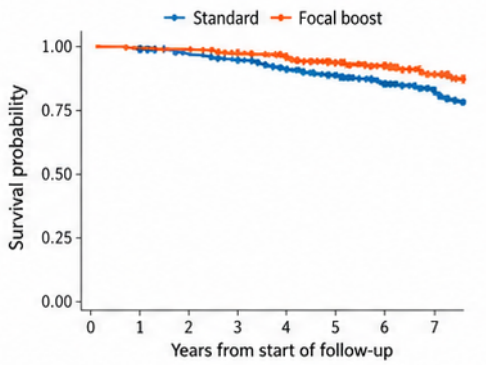
Local failure–free survival (LFS)



N at risk (cumulative events)

Standard	271 (0)	271 (0)	264 (1)	253 (4)	239 (5)	199 (9)	140 (12)	76 (17)
Focal boost	264 (0)	263 (0)	258 (0)	250 (0)	236 (0)	184 (4)	135 (4)	78 (7)

Regional + distant metastasis-free survival (rdMFS)



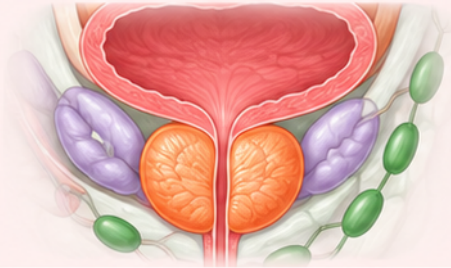
N at risk (cumulative events)

Standard	271 (0)	270 (1)	259 (7)	246 (14)	228 (23)	187 (30)	130 (36)	73 (42)
Focal boost	264 (0)	262 (1)	256 (3)	248 (6)	232 (8)	180 (16)	130 (20)	76 (24)

3 Patterns of failure

Prevalence of total clinical failure per anatomical site

	Petients (n)	
	Standard arm (*N* = 271)	Focal boost arm (*N* = 264)
Local failure	21	7
Regional failure	22	7
Distant failure		
Distant lymph node	13	11
Bone	15	12
Visceral	6	2
Treatment after recurrence		
Systemic therapy	24	15
Local therapy prostate	5	4
Metastasis-directed therapy (oligometastases)	9	5
Palliative radiotherapy	1	1
Other	1	1



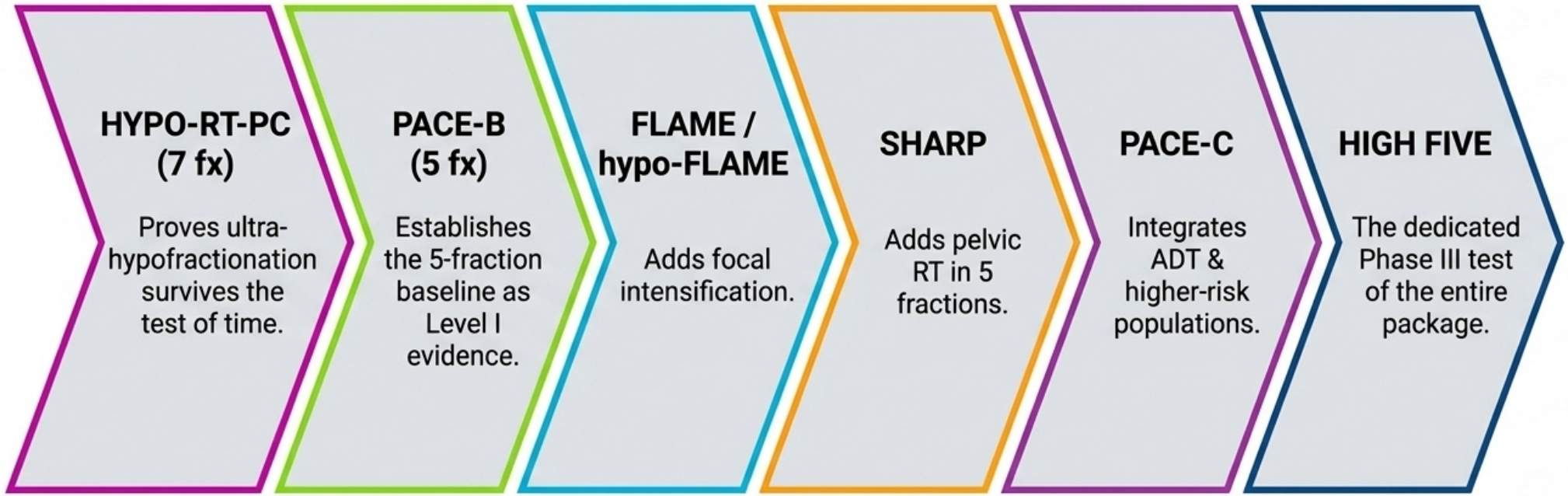
Better local control with focal boosting translates into fewer regional and distant metastases, supporting a causal role of the primary tumour in metastatic progression.

Focal boosting should be considered the standard of care in EBRT for high-risk prostate cancer.

#guardsymposium2026
@GuardConsortium

GUARD CONSORTIUM

PROGRESSIVE HYPOFRACTIONATION & INTENSIFICATION



We have progressively moved from shortening treatment to asking whether we can preserve the entire therapeutic package of high-risk disease within an SBRT strategy.

Gemini Notebook

Where is the biological characterization?

It is really only a matter of dose and focal boosting?

BEYOND ANATOMY.
TOWARDS
PERSONALIZED CARE.

Same clinical diagnosis...



Patients with high-risk prostate cancer

- Similar clinical features
- Similar stage
- Similar Gleason score
- Similar PSA

...but different biology

...different biological profiles

Genomic alterations
DNA repair defects
(ATM, BRCA1/2), TP53, RB1...

Transcriptomic signatures
Aggressive molecular subtypes

Tumour microenvironment
Immune infiltration,
hypoxia, stromal features

Liquid biopsy
Circulating tumour DNA,
molecular dynamics

Clinical–radiological features
PSMA PET, tumour volume,
pattern of spread

Different risks, different outcomes



→ No benefit + higher toxicity



→ Benefit + acceptable toxicity



→ Major benefit + low toxicity



→ No benefit + low toxicity

Towards personalized treatment



Moving from a one-size-fits-all approach to biologically informed, individualized treatment.

"The right patient with the right drug at the right dose at the right time."

So where does SBRT fit in high-risk prostate cancer?

Can we shorten radiotherapy without de-intensifying treatment?

GOALS OF TREATMENT

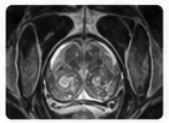
- Eradicate/ablate local disease
- Control regional disease
- Prevent distant progression
- Maintain quality of life

HIGH-RISK PROSTATE CANCER

HETEROGENEOUS BIOLOGY – MULTIMODAL TREATMENT REQUIRED

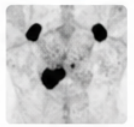
MODERN STAGING AND RISK ASSESSMENT

Multiparametric MRI



- Local extent
- Dominant intraprostatic lesion
- Seminal vesicle involvement

PSMA PET/CT



- Occult nodal disease
- Distant metastases
- Stage migration

Clinical and molecular factors



- PSA, Gleason, stage
- Genomic classifiers
- Biomarkers (emerging)

PATIENT-CENTRED INTEGRATION

PERSONALIZED MULTIMODAL TREATMENT

RIGHT TARGET | RIGHT DOSE | RIGHT SYSTEMIC THERAPY | RIGHT PATIENT

LOCAL INTENSIFICATION

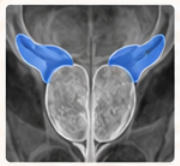
SBRT AS A STRATEGY FOR TREATMENT COMPRESSION



PROSTATE ± FOCAL BOOST

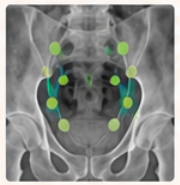
- 35–40 Gy / 5 fractions
- Focal boost to dominant lesion
- Based on MRI/PSMA

FLAME
hypo-FLAME



SEMINAL VESICLES

- Include when indicated
- Careful delineation and motion management
- Feasible in 5 fractions



PELVIC NODAL TREATMENT

- Consider in selected high-risk patients
- 25 Gy / 5 fractions feasible
- High regional control rates

SHARP
(pelvic SBRT)

SYSTEMIC INTENSIFICATION

TREAT THE BIOLOGY



ANDROGEN DEPRIVATION THERAPY

- Standard in high-risk disease
- Duration according to risk
- Do not shorten ADT because of SBRT



ANDROGEN RECEPTOR PATHWAY INHIBITORS

- Proven benefit in high-risk non-metastatic disease
- Consider in selected patients
- Systemic intensification is independent from RT fractionation

STAMPEDE



EARLIER INTENSIFICATION

- ARPI moving into localized high-risk disease
- Perioperative and neoadjuvant strategies
- Reflects the presence of occult systemic disease

PROTEUS

KEY TRIALS INFORMING THIS APPROACH

FLAME Focal boost improves bDFS (10-year results)	**hypo-FLAME** Focal boost with SBRT (5-year results)	**SHARP** Pelvic SBRT feasible (high regional control)	**STAMPEDE** Systemic intensification improves MFS and OS	**PROTEUS** Intensification moving earlier in localized disease	**HIGH FIVE** Phase III high-risk trial Can we do it in 5 fractions?

SBRT in High-Risk Prostate Cancer

Key take-home messages

SHORTER TREATMENT.
SAME AMBITION.

1 High-risk disease requires multimodal treatment



High-risk prostate cancer has a substantial risk of local, regional and distant progression. Radiotherapy should be combined with long-term ADT and, in selected patients, systemic intensification (e.g. ARPI).

2 SBRT is a feasible option



SBRT allows treatment compression (5 fractions) with acceptable toxicity in selected high-risk patients, and enables integration of focal boests and pelvic nodal treatment when indicated (emerging evidence).

3 Efficacy data are maturing but remain limited



- Retrospective and phase II data show promising biochemical and early oncological outcomes.
- Randomized evidence in high-risk disease is still lacking (HIGH FIVE ongoing).
- Longer follow-up is needed to confirm non-inferiority in terms of metastasis-free and overall survival.

4 Patient selection is key



- Consider favourable high-risk patients with adequate urinary function.
- Integrate modern imaging (MRI, PSMA PET).
- Discuss pelvic nodal treatment and focal boost when appropriate.
- Multidisciplinary decision is essential.

5 Current guidelines remain conservative



- EAU 2026 does not recommend SBRT as standard for high-risk disease.
- Recommended approach remains conventional or moderate hypofractionation (76–78 Gy or 60/20 or 70/28) with long-term ADT.
- SBRT can be considered in intermediate-risk disease (weak recommendation).

OVERALL CONCLUSION



SBRT is not yet standard of care for high-risk prostate cancer,
but it is a promising and feasible approach in selected patients within a multimodal strategy.
Ongoing randomized trials (e.g. HIGH FIVE) will clarify its role.

¡Gràcias!

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