

The Case for Radiotherapy

High-Risk Prostate Cancer: RT vs RP

Piet Ost

**For men with high-risk prostate cancer —
should we operate or irradiate?**

This is not a debate about preferences.

This is a debate about evidence.

Who Are We Talking About?

≥T3

CLINICAL STAGE

Extracapsular extension
or seminal vesicle invasion

GS 8–10

GLEASON / ISUP 4–5

High-grade disease
at biopsy

PSA>20

OR NODE-POSITIVE (N1)

Elevated biochemical
burden at diagnosis

Remember: High-risk is a spectrum — from T3a GS7 to GS 9-10 with PSA >40 and N1. They are not the same patient. This distinction will matter.

"High-Risk" Is Not One Disease

Low end of high-risk

- T3a, Gleason 7 (ISUP 3)
- PSA 12–15 ng/mL
- Young, fit, low comorbidity

True high-risk — the debate

- GS 9-10 (ISUP 5)
- PSA >40 ng/mL
- Node-positive (cN1)

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1. Surgery
2. Radiotherapy
3. Both are good

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The Numbers Don't Lie

5+

Phase III RCTs
for RT + ADT

EORTC · RTOG · DART · GETUG-AFU · STAMPEDE

0

Phase III RCTs
for Primary RP

SPCG-15 ongoing — no OS data yet

This is not bias. This is decades of scientific investment that surgery never matched.

EVIDENCE HIERARCHY

Five+ Phase III RCTs. All Showing Benefit.

RT+ADT > ADT

SPCG-7 / SFUO-3 NCIC CTG PR.3 /
MRC PR07 STAMPEDE H

OS benefit

RT+ LT ADT > RT+ STADT

RTOG 92-02 EORTC 22863 STAMPEDE M0
RTOG 85-31 DART 01/05

OS benefit

These trials define the standard of care for high-risk PCa.

BREAKING DOWN THE DOGMAS

Radiotherapy First or Surgery First: A One-Way Door?

RT

1%

patients ultimately receive
salvage local therapy

RP

50%

patients ultimately receive
salvage local therapy

TRIMODALITY TRAP

Surgery First: is NOT a One-Way Door

40–60%

of RP patients ultimately receive
postoperative RT + ADT

- Positive surgical margins → salvage RT
- pN1 at pathology → RT + long ADT
- PSA persistence post-RP → adjuvant RT
- Each step adds toxicity without proven OS gain

You are not offering patients a choice between surgery OR radiotherapy.
You are often offering surgery THEN radiotherapy THEN ADT.

TWO LOCAL THERAPIES

DOUBLE TROUBLE

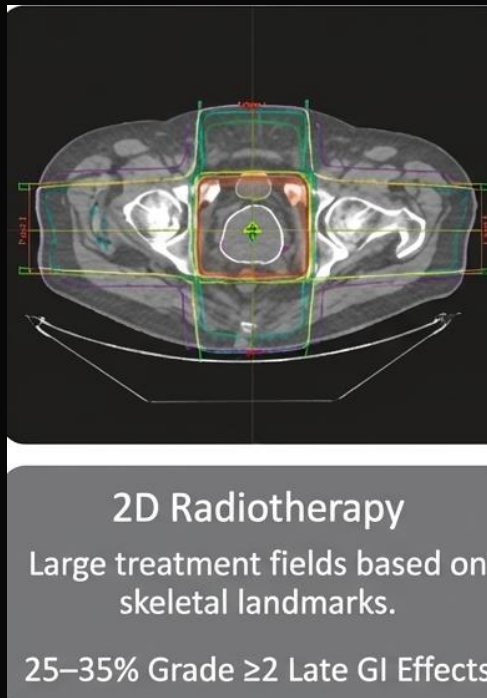
Bruner et al. ASTRO 2023: Trimodality therapy is associated with a significantly higher cumulative toxicity burden — without a demonstrated survival advantage over primary RT + ADT.

MORE TOXICITY · NO PROVEN OS GAIN

The key reframe

Today RT is not the RT of 1900s.

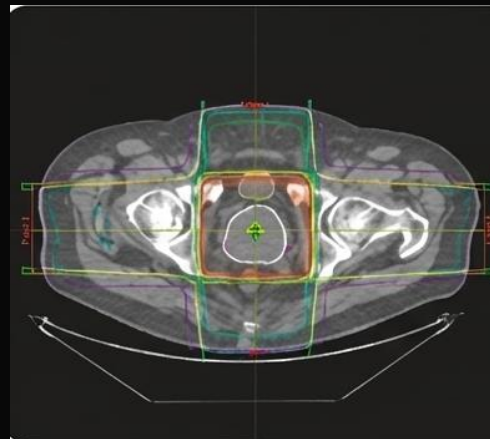
MODERN $\neq$ VINTAGE



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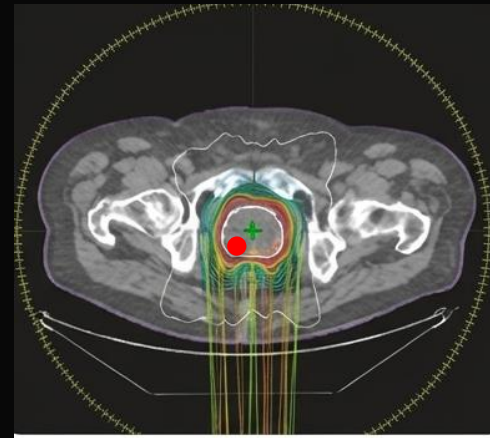
MODERN $\neq$ VINTAGE



2D Radiotherapy

Large treatment fields based on skeletal landmarks.

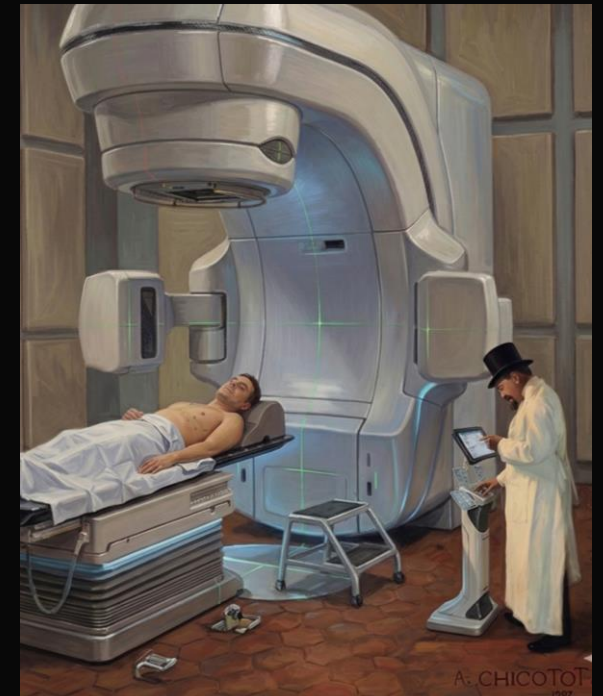
25–35% Grade ≥ 2 Late GI Effects



VMAT / SABR

Intensity-modulated arcs bend dose into concavities.

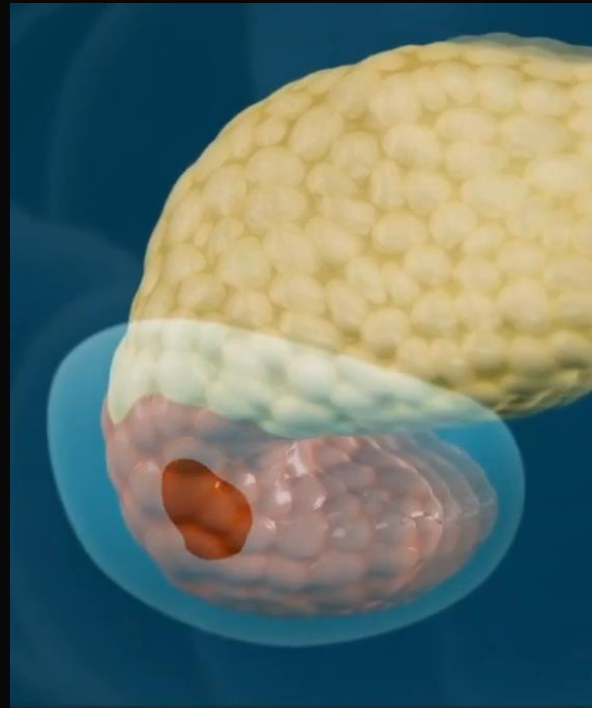
4–7% Grade ≥ 2 Late GI Effects



The key reframe

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MODERN ≠ VINTAGE



RT is Getting Smarter: AI Can Now Personalise ADT Duration

BIOMARKER POSITIVE (66%)

✓ **LONG-TERM ADT**

STANDARD 24-28 MONTHS

15-Year Distant Metastasis Rate

19%

With LT-ADT



33%

With ST-ADT

14% ABSOLUTE BENEFIT

Significant Reduction in Metastasis (P<0.001)

Biomarker negative (34%)

✗ **SHORT-TERM ADT**

DE-ESCALATE TO 4-6 MONTHS

15-Year Distant Metastasis Rate

11%

With LT-ADT



11%

With ST-ADT

0% ABSOLUTE BENEFIT

Spare 2 Years of ADT Toxicity

~1 in 3 high-risk men can safely avoid long-term ADT

Adding It All Up

RT + long-term ADT

- Urinary: mild LUTS — mostly transient
- Bowel: low-grade proctitis — manageable
- Sexual: erectile dysfunction (modifiable)
- ADT: fatigue, metabolic effects
- Single treatment. Known, manageable profile.

RP → postop RT → ADT

- RP: urinary incontinence, erectile dysfunction
- Post-op RT: on top of surgical changes
- Bowel & urinary: compounded effects
- ADT: added to already compromised QoL
- Three treatments. Every side effect stacks.

Both RT and RP have toxicity. Only trimodality has all of it at once.

RT + ADT remains the only treatment with Level I evidence for high-risk prostate cancer.

-
- Multiple phase III RCTs — with decades of follow-up
 - Consistent overall survival benefit shown across studies
 - Guideline-endorsed by EAU, ESMO, NCCN, ASTRO

Ask for the same quality of evidence from surgery. It does not exist — yet.



A new scientific truth is usually not propagated in such a way that opponents become convinced and discard their previous views. No, the adversaries eventually die off, and the upcoming generation is familiarised anew with the truth.

— *Max Planck* —

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Radiotherapy has most evidence
Surgery: a reasonable discussion

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Radiotherapy is the only valid option



Science advances one funeral at a
time.

— *Max Planck* —