Prostate cancer: the case for radiotherapy when survival outcomes are similar

Evidence to support radiotherapy discussions for referral, MDT, and care decision-making

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When long-term survival is similar, treatments should be assessed not only on disease control, but on their long-term impact on urinary, bowel, and sexual function, and on patients' day-to-day quality of life. This document brings together evidence to support treatment discussions when choosing between radiotherapy, surgery, and systemic therapy, in settings where survival outcomes are comparable.

About this document

This resource summarizes selected clinical evidence and patient-reported outcomes to inform referral and multidisciplinary (MDT) discussions.

It is not a clinical guideline and does not replace specialist assessment, multidisciplinary discussion, or local protocols.

Sections

When survival is similar, treatment choice matters

Prostate cancer is the second-most diagnosed cancer in men globally, and the most commonly diagnosed cancer in men in 118 of 185 countries.[1] Long-term (15-year) survival in men diagnosed with localized or locally advanced disease is above 95%.[2,3] The combination of high incidence and excellent survival rates means millions of men live for many years after treatment, making long-term side effects and quality of life central considerations in treatment selection.[3]

What are the treatment options for newly diagnosed localized prostate cancer?

For men with localized or locally advanced prostate cancer, management options typically include active monitoring, surgery (radical prostatectomy), radiotherapy, and, in higher-risk settings, systemic therapy such as androgen deprivation therapy (ADT). These approaches differ not in their ability to control disease in appropriately selected patients, but in how they affect the body and what patients live with over time.

Treatment selection is influenced by disease stage, patient factors, and local practice. The table below summarizes how these approaches are typically considered across the pathway.

Table 1: Prostate Cancer Treatment Options by Disease Stage

	Watch and Wait	Radical Prostatectomy	Radiotherapy	Androgen Deprivation Therapy (ADT)	Systemic Therapy
Localized	Option*	Primary option	Primary option		
Locally advanced		Option*	Primary or in combination	In combination	
Recurrent/ Oligometastatic			Primary or in combination	Option (may be delayed)	Option*

* Option = may be considered depending on disease characteristics, patient preference, and MDT judgement.

How prostate cancer treatments differ in practice

In practice, treatment decisions typically involve surgery, radiotherapy, or drug-based systemic therapies. These approaches differ not in their ability to control disease, but in how they affect the body and what patients live with over time.

Each option has potential advantages and limitations, and there is rarely a single “best” choice for everyone. Many men with early prostate cancer do well regardless of the approach taken. Where possible, involving both urology and radiation oncology in treatment discussions can help patients make decisions that reflect their values and lifestyle.

Active surveillance or monitoring

Active surveillance is often used for men with slow-growing prostate cancer. Rather than immediate treatment, doctors monitor the cancer with blood tests, MRI scans, and biopsies, starting therapy only if the cancer advances. This approach can help avoid or delay side effects while ensuring prompt intervention if needed.

Surgery

Surgery (radical prostatectomy) removes the prostate and nearby tissue. It can provide effective disease control in appropriate patients, but carries perioperative risks (for example bleeding, infection, and anesthetic risk) and can be associated with urinary incontinence and erectile dysfunction. The likelihood and severity of these effects depend on a patient’s pre-treatment urinary, sexual, and bowel function, as well as treatment technique and recovery.

Systemic therapies/ADT

Systemic drug treatments such as Androgen Deprivation Therapy (ADT) affect the whole body, not just the prostate. ADT can be associated with hot flushes, sexual dysfunction, fatigue, metabolic changes, bone health effects, and cardiovascular risk, among others. The balance of treatment depends on disease risk, treatment intent, and duration of therapy.

Radiotherapy

Radiotherapy treats the prostate locally without removing the gland. It can be used as a primary treatment, after surgery (for example as salvage or adjuvant radiotherapy in selected cases), or alongside systemic therapy in higher-risk settings. Techniques and schedules vary (including conventional fractionation, moderate hypofractionation, and stereotactic body radiotherapy in selected patients). Adaptive radiotherapy is a newer approach described later in this document.

When prostate cancer shows signs of being more aggressive, clinicians may recommend adding hormone therapy to radiation. By lowering testosterone levels, hormone therapy can make radiation more effective by slowing or shrinking the cancer.

What long-term data show about function and quality of life after treatment for prostate cancer

Long-term efficacy data from the Prostate Testing for Cancer and Treatment (ProtecT) trial are frequently referenced in treatment discussions and guidelines for men with localized or locally advanced prostate cancer. This trial evaluated outcomes in 1,643 men who underwent monitoring, surgery, or radiotherapy.[2]

At 15-year follow-up, prostate cancer-specific and overall survival were similar across all groups.[2] When survival outcomes are similar, differences in long-term functional outcomes become critical.[2,4]

At 12 years:
- Urinary incontinence was more common after surgery
- Sexual function declined in across all treatments, but is most affected by surgery
- Bowel side effects were more commonly reported after radiotherapy

These functional differences persist many years after treatment and directly affect quality of life.[4]

No single treatment is best across all functional outcomes. Differences in urinary, bowel, and sexual function should be considered alongside disease control when supporting treatment decisions.[2,4]

Table 2: Summarizes the differences of the ProtecT 12-Year Functional Outcomes[4]

	Watch and Wait	Radical Prostatectomy	Radiotherapy
Urinary function			
>1 pad per day	11%	24%	8%
Urinary leakage	11%	15%	7%
Urinary voiding difficulties	48%	37%	48%
Urinary symptoms with "somewhat" or "a lot" of impact on quality of life	11%	11%	7%
Sexual function			
Moderate to severe impact on quality of life	37%	42%	30%
Bowel function			
Fecal leakage	6%	6%	12%

Modern radiotherapy and treatment precision

Radiotherapy techniques have advanced significantly since the patients in the ProtecT trial were treated.

Modern approaches allow treatment to be delivered more precisely and, in many cases, in fewer sessions, reducing treatment burden while maintaining disease control.

A key development is the ability to adapt treatment to daily anatomical variation. During a course of radiotherapy, the prostate and surrounding organs can shift from day to day. Online adaptive radiotherapy uses in-room imaging at the point of treatment to account for these changes, allowing treatment to be adjusted to the patient's anatomy at each session.

This improved precision can:

- maintain accurate targeting of the prostate
- reduce treatment margins
- limit dose to surrounding organs such as the bladder and rectum

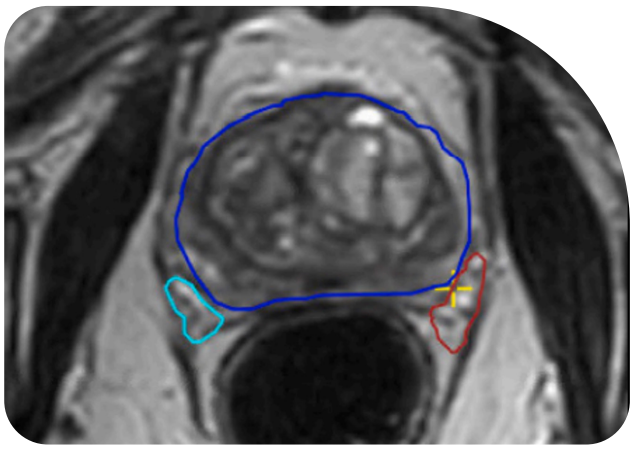
MRI-guided radiotherapy improves visualization of the prostate compared with conventional CT-based approaches, allowing smaller treatment margins. In the MIRAGE trial (NCT04384770), MRI-guided Stereotactic Body Radiotherapy (SBRT) significantly reduced urinary and bowel side effects compared with conventional SBRT treatment, with benefits sustained at two years.[7]

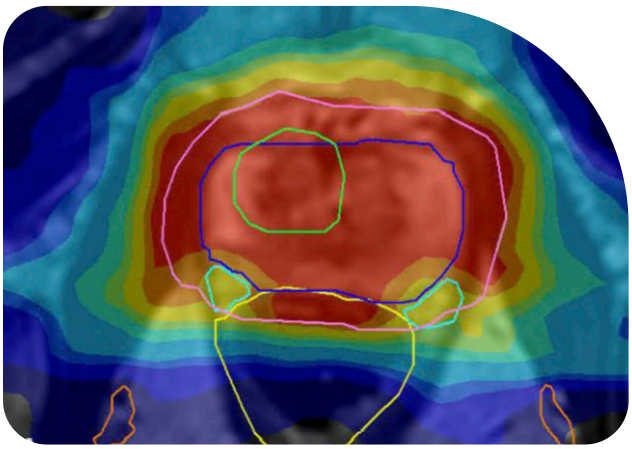
Online adaptive approaches build on this by using in-room MR or CT imaging during treatment. Evidence shows this can lower rates of urinary and bowel toxicity and improve patient-reported outcomes.

Supporting evidence includes:

- **MOMENTUM study:** low rates of moderate-to-severe urinary and bowel toxicity with five-fraction MR-guided adaptive radiotherapy[11]
- **HERMES trial** (NCT04595019): acceptable toxicity with two-fraction adaptive regimens[9]
- **ERECT trial:** improved preservation of erectile function compared with conventional radiotherapy[10]

Taken together, these studies (summarized in Table 3) show that improving treatment precision and adapting to daily variation can reduce side effects and better protect long-term function.





Figures 1 & 2. Images from an MR-Linac illustrating how radiotherapy can be shaped to the prostate while limiting dose to surrounding organs such as the bladder and rectum.

Optimizing disease control (FLAME)

The Phase 3 FLAME trial showed that external beam radiotherapy (EBRT), (77 Gy in 35 fractions to the whole prostate gland) can be optimized by delivering a focal boost of up to 95 Gy to lesions that were visible on magnetic resonance imaging (MRI) in men with intermediate- and high-risk prostate cancer (NCT01168479).

This approach improved disease control outcomes without increasing long-term toxicity, demonstrating that EBRT can be tailored to tumor biology and anatomy.[11]

MR-guided radiotherapy can be used to deliver evidence-based hypofractionated prostate schedules while visualizing daily anatomical variations.

Shorter treatment courses without compromising outcomes

Several trials show that radiotherapy can be delivered in fewer sessions without compromising outcomes:

- **CHHiP Phase 3 trial** (ISRCTN97182923): 20 fractions non-inferior to 37 fractions for safety and efficacy.[5]
- **PACE-B trial** (NCT01584258): 5-fraction SBRT non-inferior for biochemical or clinical failure.[6]
- **SHORTER Phase 2 trial** (NCT04422132): 5-fraction salvage radiotherapy without increased toxicity.[12]
- **POPSTAR:** single-fraction SBRT with excellent local control and delayed need for ADT.[13]

Together, these studies show that shorter treatment schedules

- reduce treatment burden
- maintain disease control
- may delay the need for systemic therapy in some patients

The following studies, in table 3, illustrate how advances in precision, treatment delivery, and fractionation have translated into improved clinical and patient-reported outcomes.

Table 3: Summary of Recent Advances in Prostate Cancer Radiotherapy

Trial	Key Findings	Clinical Impact
Localized/locally advanced prostate cancer		
CHHiP[5]	60 Gy in 20 fractions was non-inferior to 74 Gy in 37 fractions with respect to 5-year safety and efficacy outcomes.	Hypofractionated regimens reduce patients' treatment burden without compromising efficacy or safety
PACE-B[6]	5-fraction SBRT was non-inferior to control radiotherapy with respect to biochemical or clinical failure at median follow-up of 74 months.	
MIRAGE[7]	MRI-guided reductions in margins can better protect organs and tissues around the prostate compared with CT-guided reductions, leading to significant reductions in grade > 2 GU and GI side effects and improved patient-reported quality of life. 2-year follow-up data showed sustained benefit of MRI guidance with respect to grade >2 GU and GI side effects, bowel function and sexual health.	Advanced MRI-guided/ adapted radiotherapy technologies enhance dosing to tumor and enable reduced margins that better protect healthy tissue and reduce GU and GI side effects.
MOMEN-TUM[8]	Reductions in grade > 2 GU and GI side effects with 5-fraction online MR-guided adaptive radiotherapy compared with previously reported rates without MR-guided adaptation.	
HERMES[9]	Patients can receive treatment in two sessions without increasing grade >2 GU side effects compared with 5 fractions.	
ERECT[10]	Advanced RT imaging and delivery technologies can help preserve erectile function in men treated for prostate cancer.	
FLAME[11]	A focal boost of 95 Gy to lesions visible on MRI added to a conventional dose 77 Gy in 35 fractions to the entire prostate improved multiple DFS outcomes.	
Salvage therapy		
SHORTER[12]	A 5-fraction regimen was not associated with an increase in GI or GU toxicity as salvage therapy in men who had undergone prostatectomy and had biochemical recurrence or persistently detectable PSA levels.	5-fraction radiotherapy can reduce treatment burden without increasing GI or GU toxicity compared with a 20-fraction regimen in men who have failed prostatectomy.
Oligometastatic disease		
POPSTAR[13]	Single-fraction SABR demonstrated one- and two-year rates of local progression-free survival of 97% and 93%, and distant progression-free survival rates of 58% and 39%. For men who entered the study not on ADT, the 2-year freedom from ADT was 48%.	Single-fraction SABR provides excellent progression-free survival outcomes while delaying the need for ADT, which can improve patient quality of life.

Radiotherapy across the prostate cancer pathway

Radiotherapy can be used at different stages of prostate cancer care, depending on disease characteristics and treatment goals.

It may be used:
- as a primary treatment
- after surgery (salvage)
- in oligometastatic disease

In oligometastatic disease, radiotherapy may delay the need for ADT in some patients, potentially postponing cumulative systemic side effects.[8]

In oligometastatic disease, targeted radiotherapy has been shown to delay the initiation of ADT in a proportion of patients, potentially postponing the cumulative side effects associated with long-term systemic therapy.[8]

What this means for MDT decision-making

When survival outcomes are similar, treatment choice should be guided by long-term side effects and patient experience.[2,4]

- Surgery is invasive and irreversible.
- Systemic therapies affect the whole body and are associated with cumulative long-term side effects.[4,8]
- Radiotherapy offers local disease control without removing the prostate and, with modern techniques, can reduce treatment burden and long-term toxicity.[5–7, 10–13]

Advanced such as hypofractionation and online adaptive radiotherapy have further improved the side-effect profile of radiotherapy, strengthening the case for its early consideration in appropriate patients.[5–7, 10–13]

When survival is similar, long-term side effects matter.

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