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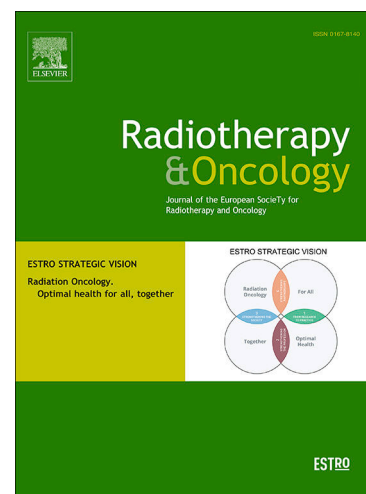
PII: S0167-8140(26)00549-9
DOI: <https://doi.org/10.1016/j.radonc.2026.111710>
Reference: RADION 111710

To appear in: *Radiotherapy and Oncology*

Received Date: 7 July 2026
Accepted Date: 17 July 2026

Please cite this article as: Draulans, C., Tree, A., Zilli, T., Alongi, F., Zamboglou, C., Ost, P., Jereczek-Fossa, B.A., Blanchard, P., Gomez-Iturriaga, A., Faccenda, V., Wolf, F., Roover, R.D., Scherman, J., Alexander, S., Schmidt-Hegemann, N-S., How to optimise prostate SBRT: ESTRO clinical practice consensus recommendations, *Radiotherapy and Oncology* (2026), doi: <https://doi.org/10.1016/j.radonc.2026.111710>

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Highlights

- Comprehensive evidence-based consensus regarding the delivery of prostate SBRT
- Patient selection criteria and follow-up recommendations for prostate SBRT
- Optimal contouring, dose, and fractionation for prostate SBRT
- Minimal advised and optimal treatment techniques for the delivery of prostate SBRT

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Abstract

A steady rise in the number of patients receiving stereotactic body radiation therapy (SBRT) for primary prostate cancer is expected. Consequently, the current European Society for Radiotherapy and Oncology (ESTRO) 'how to' consensus has been developed to offer practical recommendations for the initiation and implementation of prostate SBRT in radiotherapy (RT) departments. A panel of fifteen experts in the field of prostate SBRT reviewed and analysed the literature and, through a Delphi process, answered a ten-item questionnaire addressing areas of controversy in prostate SBRT. Consensus was a priori defined as $\geq 75\%$ agreement in each answer, while $\geq 90\%$ agreement was defined as strong consensus. The aim of this 'how to' consensus recommendations is to define minimum requirements, common practices and additional options for prostate SBRT based on scientific evidence, expert opinion and consensus. This 'how to' clinical practice recommendations cover patient selection and follow-up process, treatment planning and delivery techniques in prostate SBRT.

Keywords

Prostate cancer; Primary external-beam radiotherapy; Stereotactic Body Radiation Therapy (SBRT); Hypofractionation; ESTRO; Consensus recommendations

Background

Prostate cancer is a significant global health concern, impacting millions of men each year. With nearly 1.4 million new diagnoses annually, it remains one of the most diagnosed cancers worldwide and is expected to rise to 2.9 million new cases each year by 2040 [1]. Patients with low- and intermediate-risk prostate cancer can choose from a wide range of treatments with a curative intent or, in selected cases, active surveillance. Advances in radiation therapy (RT) have enabled the safe application of higher doses per treatment fraction while shortening the overall treatment time. Moderate hypofractionated RT, which typically involves 20 to 28 fractions, is currently the standard of care, with several phase III trials demonstrating its oncologic equivalency and a similar side effect profile compared to longer treatment schedules with lower doses per fraction [2–7]. Encouraged by these findings, ultra-hypofractionated RT, administering doses greater than 5 Gy per fraction, has been tested in several phase III trials [8]. The HYPO-RT-PC trial was the first randomised trial comparing ultra-hypofractionated with conventionally fractionated RT in patients with intermediate- to high-risk prostate cancer, showing non-inferiority for ultra-hypofractionated RT [9,10]. Following this, the publications of the PACE trials have further sparked interest in stereotactic body RT (SBRT), confirming with the PACE-B trial that five-fraction SBRT was non-inferior in patients with low- to intermediate-risk prostate cancer to conventional RT delivered in 20 or 39 treatment fractions, respectively [11–13]. The term ultra-hypofractionated RT is commonly used interchangeably with SBRT. However, it must be clarified that ultra-hypofractionated RT strictly refers to the fraction size and dose, whereas the latter refers additionally to steep dose gradients, high geometric precision and precise image guidance and motion management [8]. Given the patients' preference for shorter treatment courses and the reduced cost for healthcare systems [14,15], a steady increase in the number of patients treated with SBRT is anticipated. Thus, the current ESTRO consensus has been developed to provide practical recommendations for the implementation and initiation of SBRT in prostate cancer.

Methods

A task force of ESTRO members reviewed the existing literature, evaluated the current evidence, and developed an initial set of 'how-to' recommendations aimed at facilitating the integration of ultra-hypofractionated prostate SBRT into routine clinical practice. The aim of the clinical practice consensus is to establish minimum requirements for prostate SBRT supplemented by optional practices which could be implemented if desired.

The proposed recommendations were shared with a selected expert panel, partially overlapping with the task force, consisting of eleven radiation oncologists, three medical physicists and one radiotherapy technologist (RTT) for feedback. The experts were purposively selected from nine European countries, namely Germany, Belgium, Italy, the UK, Switzerland, Sweden, Austria, France, Spain and Cyprus. After incorporating feedback from the first round, the recommendations were refined and presented at the ESTRO 2025 meeting in Vienna, Austria, where final adjustments were made to produce the current ESTRO clinical practice consensus. Additionally, the consensus was supplemented with ten multiple-choice consensus questions addressing various areas of controversy. Following the procedure of a Delphi consensus, two rounds of questionnaires were administered via a web-based survey to the radiation oncologists and medical physicists of the expert panel [16]. Levels of consensus were predefined, based on those established by the Advanced Prostate Cancer Consensus Conference (APCCC) [17]. Consensus was defined as $\geq 75\%$ agreement in each answer, while $\geq 90\%$ agreement was defined as strong consensus.

Results & discussion

Patient selection

Careful patient selection is crucial to optimise outcomes and minimise potential side effects of prostate SBRT. The most widely accepted selection criteria typically include the following factors.

1. Disease Risk Stratification

Prostate SBRT is recommended as standard treatment for patients with ISUP grade 2–3, cT1c–cT2c disease, and prostate-specific antigen (PSA) < 20 ng/mL.

Q1: In patients with prostate cancer undergoing RT to the prostate, for patients with the following risk categories, I would recommend SBRT as standard treatment outside a clinical trial:

ISUP

- ISUP 2: 100% (13 votes)
- ISUP 3: 100% (13 votes)
- ISUP 4: 38% (5 votes)
- ISUP 5: 0% (0 votes)
- Abstain/unqualified to answer: 1 vote

cT-stage

- cT1c–cT2a: 100% (13 votes)
- cT2b–cT2c: 100% (13 votes)
- cT3a: 38% (5 votes)
- cT3b: 0% (0 votes)
- cT4: 0% (0 votes)
- Abstain/unqualified to answer: 1 vote

PSA-value

- PSA < 20 ng/mL: 100% (13 votes)
- PSA = 20 – 40 ng/mL: 8% (1 vote)
- PSA > 40 ng/mL: 0% (0 votes)
- Abstain/unqualified to answer: 1 vote

Strong consensus in favour of recommending prostate SBRT as standard treatment for patients with ISUP 2 to 3, cT1c to cT2c prostate cancer with a PSA-value < 20 ng/mL.

Experts treating patients with high-risk disease report that prostate SBRT is generally reserved for cases without a combination of multiple high-risk factors.

Localised disease, typically clinical T1-T2 stage, with a low likelihood of extra-capsular extension, a ISUP Grade Group 2-3, PSA levels <20 ng/mL represents the clinical scenario with the strongest evidence supporting SBRT. Although a large amount of literature is based on data coming from patients with low- and intermediate-risk prostate cancer, the increasing role of active surveillance in low-risk cases means that SBRT will mainly be used for NCCN intermediate-risk prostate cancer [11,12,18]. HYPO-RT-PC is the only phase III trial to date that included high-risk patients and reported oncological outcomes, though they comprised just 11% of participants, while PACE-C has published toxicity data but not yet oncological outcomes [9,13]. Furthermore, data from the SHARP consortium based on multiple phase II trials indicate that the safety and efficacy profile of SBRT for patients with high-risk localised

prostate cancer remains favourable at long term follow-up [19]. Some ongoing randomised trials have begun incorporating prostate SBRT in the de-novo oligometastatic settings, often in combination with systemic therapy [20]. However, these applications are still under investigation.

2. Prostate Gland Size and Anatomy

No strict prostate volume cut-off is recommended for prostate SBRT, although many trials exclude volumes exceeding 80–100 cc.

Q2: In patients with prostate cancer undergoing RT to the prostate, do you use/recommend a maximum prostate volume as cut-off for SBRT? (if yes, please indicate the recommended cut-off)

- Yes: 62% (8 votes)
- No: 38% (5 votes)
- Abstain/unqualified to answer: 1 vote

No consensus.

If experts recommend using a cut-off for the maximum prostate volume, the median value is 90 cc, ranging from 70 cc to 150 cc.

Prostate size could be a critical issue as patients with prostate volumes greater than 80 cc may not be ideal candidates due to the potential difficulty in achieving proper dosimetry endpoints [21–24]. Favourable factors include clear visualisation of the gland, preferably with minimal rectal overlap with the planning target volume (PTV) due to patient's anatomy.

3. Baseline Urinary function

A maximum International Prostate Symptom Score (IPSS) threshold is recommended for prostate SBRT, with caution advised in patients treated after benign prostatic hyperplasia (BPH) surgery.

Q3: In patients with prostate cancer undergoing RT to the prostate, do you recommend using a maximum IPSS as cut-off for SBRT? (if yes, please indicate the recommended cut-off)

- Yes: 85% (11 votes)
- No: 15% (2 votes)
- Abstain/unqualified to answer: 1 vote

Consensus in favour of using a maximum IPSS as cut-off for SBRT.

If experts recommended using a cut-off for the maximum IPSS, the median value is 17, ranging from 10 to 20.

Q4: In the majority of patients with prostate cancer undergoing SBRT to the prostate, do you recommend prophylactic medications such as α 1-blockers corticosteroids, non-steroidal anti-inflammatory drugs or phosphodiesterase-5 inhibitors?

- Yes, in the majority of patients: 15% (2 votes)
- Yes, but only in selected patients: 38% (5 votes)

- No: 46% (6 votes)
- Abstain/unqualified to answer: 1 vote

No consensus.

Q5: In patients with prior surgery for BPH (transurethral resection of the prostate (TURP)/ Holmium Laser Enucleation of the Prostate (HoLEP)/ prostate adenectomy) undergoing RT to the prostate, do you recommend prostate SBRT?

- Yes, without any waiting period, regardless of the BPH surgery cavity: 0% (0 votes)
- Yes, but only in selected patients respecting a certain waiting period and taking into account the BPH surgery cavity (*please indicate the recommended waiting period*): 100% (13 votes)
- No: 0% (0 votes)
- Abstain/unqualified to answer: 1 vote

Strong consensus on recommending prostate SBRT only in selected patients with prior BPH surgery, respecting a certain waiting period and considering the BPH surgery cavity.

The median waiting time recommended by the expert panel is 6 months, ranging from 2 to 12 months.

Patients with significant baseline obstructive urinary symptoms, quantified by an IPSS greater than 11, or especially greater than 19, or those with large post-void residuals, may experience increased genitourinary side effects [25]. Residual volumes >100-200 mL are generally considered as abnormal [26]. In borderline or clearly symptomatic cases, consider correcting urinary flow prior to treatment (e.g., using α 1-blockers or performing surgery for BPH) [27].

4. Life Expectancy and patient factors

Life expectancy and performance status for prostate SBRT should match those required for conventionally fractionated or moderately hypofractionated radiotherapy.

Patients should generally have a life expectancy of at least five to ten years to justify the use of radical treatment and balance the risk-benefit of treatment. Moreover, a good performance status (ECOG 0-2) and the ability to tolerate the treatment, maintaining the correct positioning during therapy, are important issues for the reproducibility of accuracy in SBRT settings.

A relative contraindication for primary prostate SBRT of the prostate gland includes the presence of an active or recent inflammatory bowel disease. Furthermore, bilateral hip replacements are sometimes considered a contraindication, because of the potential for artifacts or image degradation that may compromise accurate anatomical definition and position verification during treatment. In such cases, appropriateness for prostate SBRT should be determined on an individual basis, with particular attention to the feasibility of target delineation and the reliability of image guidance.

Patients undergoing prostate SBRT should be informed about the potential for a late urinary symptom flare. This transient set of symptoms including frequency, urgency, weak stream, and dysuria, occur 6 to 18 months post-treatment in about 10% to 20% of the patients [28]. Although self-limiting, these symptoms can impact quality of life. Anticipatory counselling may help to manage patient expectations and reduce discomfort.

5. Technical considerations

Prostate SBRT requires high-quality imaging for treatment planning, with MRI co-registration strongly recommended for contouring purposes. The capability to undergo dedicated MRI for treatment planning, and the ability to implant fiducial markers for image guidance, if required, are important requirements to consider.

Recommended dose and fractionation schedule

Administering 36.25 Gy in five fractions of 7.25 Gy, with 40 Gy to 95% of the prostate CTV, or delivering 42.7 Gy in seven fractions, is the standard dose regimen for prostate SBRT.

According to the phase III data of the PACE-B trial, administering five fractions of 7.25 Gy, resulting in a total prescribed dose of 36.25 Gy to 95% of the PTV with a dose of 40 Gy to 95% of the prostate clinical target volume (CTV), is the standard dose prescription when performing prostate SBRT in daily clinical practice (Table 1, Figure 1).

As an alternative, the fractionation schedule used in the HYPO-RT-PC study, delivering 42.7 Gy in seven fractions of 6.1 Gy, may be utilised. The HYPO-RT-PC regimen uses a lower biologically effective dose compared with the PACE-B schedule, yet demonstrates non-inferiority, indicating that a 40 Gy dose in five fractions may not be necessary for all patients; however, uncertainties remain regarding dose heterogeneity and the applicability of the linear quadratic model at such high fraction doses. So far, the optimal dose regimen has not yet been fully established, as the recent NRG-GU005 trial demonstrated in a preliminary publication at ASTRO 2025 lower side effects with a reduced dose, 36.25 Gy delivered in five fractions, but potentially at the cost of a slightly higher rate of biochemical relapse after three years follow-up [29]. Further investigation is needed to determine the cause of the slightly higher rate of biochemical relapse.

Whether focal dose-escalation to the imaging-defined intraprostatic gross tumour volume (GTV) with >40-50 Gy in five fractions for high-risk patients (NCT05705921; NCT06330909), or a dose de-escalation approach with 30 Gy in five fractions to the non-tumour suspicious areas within the prostate for lower risk patients (NCT05709496) can be applied widely, and result in improved outcome, is currently being further explored within multiple clinical trials [30,31].

Within the various phase II and III trials conducted on prostate SBRT, the treatment frequency ranged from daily (QD) to weekly (QW) treatment sessions. The PACE-B trial showed comparable acute toxicity patterns independent of treatment frequency with an overall treatment time of one or two weeks [23]. Furthermore, the PACE-C trial did not find a measurable effect of treatment length (1 vs. 2 weeks) when accounting for confounding centre variation [13]. When implementing prostate SBRT using an every-other-day (QOD) or more protracted schedule seems appropriate given a potential increased risk of low-grade side effects was found using a QD schedule [32,33]. So far, no oncological detriment has been demonstrated from protracting the overall treatment time of prostate SBRT [34–36].

Target volumes delineation

1. Prostate

Accurate delineation is essential for SBRT quality assurance, since contouring errors constitute systemic inaccuracies that can affect both treatment outcomes and side effects. The prostate should be delineated on a planning MRI using T2-weighted sequences, properly registered to a planning CT, where used. Be careful to generously cover the prostate apex, which lies posterior to the urethra at its most caudal part. The prostatic apex is typically visualised as a bilaterally symmetric, triangular region of high T2-weighted signal intensity within the peripheral zone, demonstrating clear contrast with the caudally adjacent urogenital diaphragm and the laterally situated levator ani muscle [37]. Cranially ensure not to contour up to urine, but instead purposefully exclude the bladder wall, which curves over the top of the prostate [37]. The seminal vesicles can be omitted from the target volume in low-risk patients, while for intermediate and high-risk patients the seminal vesicles should be included [36]. In the PACE trials, the proximal 1 cm of the seminal vesicles was included in the prostate target volume for all patients. In addition, for intermediate risk patients with Gleason 4+3 or NCCN high risk disease the proximal 2 cm were included to a dose of 30 Gy in 5 fractions.

If the patient has MRI-defined T3b disease the macroscopic disease as seen on MRI should receive the highest prescription dose. If a focal boost is being delivered, contour the GTV based on a reconstruction of the pre-ADT tumour volume [38]. The MRI protocol should be consistent with the PI-RADS guidelines [39]. Regarding focal boost delineation, it is very important to consider all sequences including diffusion-weighted images and contrast-enhanced MRI and where available PSMA PET may also play a role in helping to identify GTVs within the prostate [30,40–42].

2. Pelvic lymph node radiotherapy

Q6: When treating patients with high-risk prostate cancer with SBRT to the prostate, do you recommend elective pelvic lymph node radiotherapy outside a clinical trial?

- Yes: 0% (0 votes)
- No: 100% (12 votes)
- Abstain/unqualified to answer: 2 votes

Strong consensus on not performing elective irradiation of the pelvic lymph nodes along with prostate SBRT outside a clinical trial.

SBRT is not routinely recommended for patients with the need of a pelvic nodal irradiation. Therefore, the contouring of the pelvic nodes is not specifically covered. The role of pelvic SBRT for patients with prostate cancer is currently being investigated, most commonly using 25 Gy in 5 fractions [43].

Organs of interest

Prostate SBRT requires accurate delineation of organs of interest and strict compliance with dose constraints.

Optimising SBRT treatments while minimising treatment-related side effects requires precise delineation of organs of interest (OOIs) and adherence to strict dose constraints (Table 2). Since dose constraints are highly dependent on the dose per fraction, they must be defined for each specific fractionation schedule. Given that most evidence in prostate SBRT stems from five-fraction schedules, which also appear to be the most used, we have focussed our

recommendations on dose guidance for this specific schedule. For other fractionation schedules, we recommend consulting the relevant publications.

The rectum is typically defined from the recto-sigmoid junction to approximately 2 cm below the lowest contour of the prostate apex, while the bladder includes the entire organ, as previously described [37].

Recent advances in understanding radiation-induced urinary toxicity have expanded the range of anatomical structures that can be delineated and spared to help reduce this toxicity [44]. Similar to findings in brachytherapy, optimising doses to the intraprostatic urethra by minimising maximal hotspots has been linked to decreased rates of acute and late urinary toxicity following prostate SBRT [45]. This structure can be identified using T2-weighted MRI sequences, a Foley catheter, urethrogram, or surrogate CT-based contouring techniques [46]. A minimum PRV margin of 2 mm is typically used [45]. Two approaches can be used: urethra steering, which aims to avoid hotspots within the urethra, and urethra sparing, which involves reducing the urethra dose below levels of the surrounding CTV dose prescription [47]. For the latter, a dose reduction of 10% has been successfully implemented and represents an alternative approach [35]. Furthermore, sparing the bladder trigone and enucleation/TURP cavity may further reduce the risks of genitourinary toxicity, including urinary incontinence, dysuria, and haematuria [48–50]. However, evidence regarding the relationship between urinary substructure dose and late toxicity remains heterogeneous. Notably, a recent post hoc analysis of PACE-B did not find significant associations between a higher dose to urinary substructures and late urinary toxicity [25].

The relationship between radiation doses to sexual structures and the development of erectile dysfunction remains poorly understood for SBRT treatments. In patients treated with a seven-fraction schedule, the maximal dose to the penile bulb has been linked to the development of erectile dysfunction [51]. While vessel-sparing techniques, which minimise radiation to the internal pudendal arteries, have shown promising results in reducing erectile dysfunction after conventionally fractionated RT, findings from SBRT trials suggest that limiting doses to the crura may also reduce this risk [52,53]. Although the impact of nerve damage on erectile dysfunction following prostate cancer RT is not well established, the potential benefits of neurovascular bundle sparing are being explored in ongoing trials [54].

Concomitant androgen deprivation therapy

The use of ADT with prostate SBRT should be in line with the international guidelines, independent of fractionation used.

Q7: In patients with prostate cancer undergoing SBRT to the prostate, do you recommend concomitant ADT?

- Yes, according to the existing recommendations for evidence-based use of ADT in combination with radiotherapy, independent of the radiation schedule: 100% (13 votes)
- No: 0% (0 votes)
- Abstain/unqualified to answer: 1 vote

Strong consensus that ADT should be used in line with international guidelines, irrespective of fractionation.

In intermediate-risk prostate cancer, short-term ADT added to conventionally fractionated radiotherapy improves overall and prostate cancer-specific survival by 7%, with no additional benefit beyond approximately four months of therapy [55,56]. This benefit persists in the dose-

escalation era [57]. Moderate hypofractionation trials have reported variable ADT use [3,4,6], but the available evidence supports continued short-term ADT in this group.

In high-risk prostate cancer, combined radiotherapy and long-term ADT consistently improves overall and disease-specific survival, irrespective of dose escalation [58–62]. Moderate hypofractionation trials predominantly included ADT, with median durations ranging from 9 to 32 months and 67–100% of patients receiving therapy [3,5,63].

With ultra-hypofractionated RT or SBRT, prospective trials are limited: HYPO-RT-PC and PACE-B did not permit concomitant ADT, whereas PACE-C included short-term ADT for higher-risk patients. Retrospective analyses have reported conflicting results: Jackson et al. found no significant association between ADT use and biochemical outcomes in a meta-regression model [64], whereas the SHARP consortium demonstrated inferior biochemical relapse-free survival in high-risk patients when ADT was withheld [65].

Overall, there is no evidence that SBRT modifies the established benefit of ADT. Thus, ADT should be prescribed according to established risk-adapted guidelines.

Treatment techniques

Achieving high precision in prostate SBRT requires patient preparation, optimised planning, and accurate delivery supported by strict QA programs with tight tolerances.

1. Patient Preparation

Bladder and bowel preparation protocols are advised to ensure reproducible anatomy and minimise organ motion during treatment.

Q8: When treating patients with SBRT to the prostate, do you recommend a specific bladder or bowel preparation?

- Yes: 100% (14 votes)
- No: 0% (0 votes)
- Abstain/unqualified to answer: 0 votes

Strong consensus in favour of using a bladder and bowel preparation protocol for prostate SBRT.

Since prostate position is highly sensitive to anatomical variations and organ motion, controlled bladder filling and rectal emptying are helpful to ensure target localisation reproducibility and dosimetric consistency between fractions. All major clinical trials in prostate radiotherapy have adopted standardised preparation protocols to minimise such uncertainties. For example, the PACE trial instructed patients to use daily enemas for 2 days prior to, and on the day of CT planning and to restart enemas 2 days prior to starting radiotherapy and each day of treatment. Both the PACE and HYPO-PC-RT trials also advise that for patients with extremely full rectums, due to faeces or gas, on the planning scan, a new planning scan is performed prior to treatment planning.

A comfortably full bladder before simulation CT, MR and each session is also recommended. For shorter treatment durations, this can be accomplished by drinking 300 to 500 mL of water 30 to 60 minutes beforehand. If longer treatment durations are expected, an alternative approach could be to start with a half full bladder, allowing it to fill during treatment.

2. Planning scan

A comfortable patient position with dedicated immobilisation systems that limit hip and leg rotation are essential to improve anatomical reproducibility. The use of knee and foot support is recommended, indexed to the treatment couch. CT scans should extend from the L3/L4 intervertebral space to the external genitalia including the testis and use a slice thickness ≤ 2 mm to improve contouring precision and dose calculation accuracy.

3. Treatment Plan

Treatment plans should balance optimal PTV coverage with OOI protection, while favouring reduced treatment delivery time.

Treatment plans should aim to maximise PTV coverage while ensuring compliance with OOI dose guidance (Table 1-2). Minimum target coverage objectives, as well as maximum allowable doses within the PTV, vary significantly across different planning methods and countries. Typically, at least 95% to 98% of the PTV should be covered by 95% of the prescription dose. When focal boosting and/or urethra sparing are not implemented, maintaining dose homogeneity within the PTV helps minimise hotspots, ranging from 105% to 107% of the prescription dose, as these may increase the risk of urinary toxicity [66]. However, the PACE trials allow for considerable heterogeneity within the PTV, with different prescriptions for the CTV and PTV, and maximum doses reaching 120% to 133% of the prescription, while maintaining acceptable genitourinary adverse events rates [12]. At present, there is no high-level evidence clearly favouring a homogeneous over an inhomogeneous dose distribution in this setting. Therefore, the choice of planning strategy should be primarily guided by urethral dose constraints and OOI protection rather than by the degree of PTV dose homogeneity per se. Since prostate motion probability increases with treatment duration, reducing beam-on time is always beneficial [67]. At the planning level, this can be achieved by minimising the number of beams, avoiding posterior beam entry through the rectum, utilising high dose-rate beams, and optimising the modulation and segmentation parameters within each treatment planning system (TPS) [68].

In the setting of proton therapy (PT) for prostate cancer, the PARTIQoL phase III trial found no significant differences in outcomes or quality of life between conventionally fractionated or moderately hypofractionated PT and IMRT for low- and intermediate-risk prostate cancer, with pencil beam scanning used in only 48% of the cases [69]. Interest in hypofractionated PT has grown, though later than photon-based RT. A meta-analysis on hypofractionated PT, based on observational prospective and retrospective cohort studies has shown favourable grade ≥ 2 acute gastrointestinal adverse events (2% vs. 7%) and favourable five-year biochemical relapse-free survival (95% vs. 91%) compared to photon therapy [70]. However, these findings are derived largely from non-randomised evidence, and further studies are needed to better define the long-term role of PT in both primary treatment and re-irradiation settings. In this context, proton-based SBRT for prostate cancer remains limited by high costs and relevant dosimetric uncertainties, particularly related to range uncertainties and interplay effects. At present, it is not considered a standard of care for localised prostate cancer and remains mainly investigational or restricted to selected indications in specialised centres.

Q9: In patients with prostate cancer undergoing SBRT to the prostate, do you recommend using a rectal spacer?

- Yes, for the majority of patients: 0% (0 votes)
- Yes, but only in selected patients in whom higher gastrointestinal side effects are expected (e.g. inactive ulcerative colitis): 15% (2 votes)
- No: 85% (11 votes)

- Abstain/unqualified to answer: 1 vote

Consensus on not using a rectal spacer for prostate SBRT.

The use of rectal spacers is an option when aiming for further reducing the rectal dose. The risk-benefit profile of using rectal spacer is currently under investigation. So far, two randomised clinical trials have demonstrated their potential efficacy in lowering gastrointestinal toxicity in both conventionally fractionated and hypofractionated schedules, while additional studies are also suggesting their effectiveness in SBRT regimens [71–75]. However, several factors, including the risk of adverse events and suboptimal placement, as well as the need for adequately trained personnel and appropriate procedural volume, may impair the potential benefit of rectal dose reduction. Given the lack of large-scale risk-benefit analyses to date, the use of rectal spacers is not formally recommended.

4. Quality Assurance (QA) program

Rigorous and comprehensive QA procedures are essential to guarantee the accuracy, safety, and reproducibility of SBRT delivery across all treatment platforms.

SBRT presents unique challenges compared to conventional radiotherapy, including the delivery of very high doses per fraction with steep dose gradients, the use of advanced imaging for precise patient alignment, and the critical importance of accurately reproducing the planned dose in a limited number of fractions. Consequently, SBRT requires tighter equipment tolerances and more stringent QA procedures to minimise the risk of clinically significant deviations in target coverage or OOI sparing, in accordance with international recommendations [76].

In particular, essential components of SBRT QA include systematic verification of patient positioning and repositioning, imaging isocenter, geometric distortion and spatial resolution, constancy of treatment unit output, accurate alignment of the radiation and mechanical isocentres, precise multileaf collimator (MLC) performance in shaping complex dose distributions, the use of detectors appropriate for small field dosimetry, and correct modelling of small field sizes in the TPS. These checks should be performed on a planned and regular basis, with tolerances typically $\leq 1\text{--}2$ mm for geometric parameters and $\pm 2\text{--}3\%$ for dosimetric parameters [76].

Before treatment delivery, some form of patient-specific QA (PSQA) should be performed in accordance with institutional protocols and equipment capabilities, ensuring that each individual plan can be safely delivered on the verified treatment machine. Common PSQA approaches include EPID-based dosimetry, phantom measurements, and, more recently, independent MU calculations. Dose comparison is typically performed using gamma analysis to assess agreement between planned and delivered dose distributions [77]. For SBRT plans, tighter gamma criteria, such as 2%/2 mm, 2%/1 mm or even 1%/1 mm, are generally recommended, with a universal passing rate of $\geq 90\%$ considered acceptable [78].

Image-guided radiotherapy & motion management

1. Non-adaptive image-guide radiotherapy

The appropriate use of image guidance and motion management strategies, tailored to PTV margins and treatment duration, is essential to ensure precise and safe prostate SBRT delivery.

Q10a: When treating patients with SBRT to the prostate, which minimum required motion management strategy do you recommend (using a PTV margin ≥ 5 mm)?

- Pre-treatment cone beam computed tomography (CBCT) soft-tissue matching or kV/MV fiducial marker matching: 79% (11 votes)
- Pre-treatment matching in combination with intra-fraction tracking: 21% (3 votes)
- Other: 0% (0 votes)
- Abstain/unqualified to answer: 0 votes

Q10b: When treating patients with SBRT to the prostate, which minimum required motion management strategy do you recommend (using a PTV margin < 5 mm)?

- Pre-treatment cone beam computed tomography (CBCT) soft-tissue matching or fiducial marker matching: 21% (3 votes)
- Pre-treatment matching in combination with intra-fraction tracking: 71% (10 votes)
- Other: 7% (1 vote)
- Abstain/unqualified to answer: 0 votes

Consensus on recommending the use of pre-treatment cone beam computed tomography (CBCT) soft-tissue matching and/or pre-treatment kV/MV fiducial marker-based systems as minimum required motion management strategy for prostate SBRT when using a PTV margin ≥ 5 mm; No consensus on the need for augmentation with intra-fraction tracking when PTV margin is below 5 mm.

Image-guided RT (IGRT) uses imaging to locate the target prior to treatment, compensating for inter-fraction prostate misalignments and ensuring precise dose delivery. Daily IGRT is particularly crucial for advanced techniques like SBRT, where the low number of fractions reduces statistical averaging of setup errors, making precision in each session essential. Online corrections, indeed, help minimise both systematic errors (e.g., setup or positioning issues) and random errors (e.g., day-to-day variations), reducing the required safety margins to account for only residual uncertainties [79]. Even in conventionally fractionated treatments, daily imaging compared to weekly controls has been associated with improved biochemical progression-free survival and reduced rectal toxicity [80].

The minimum standard for IGRT in prostate cancer treatment is the use of daily pre-treatment CBCT soft-tissue matching and/or kV/MV fiducial marker-based systems and all corrections applied online (Table 3). CBCT offers the added benefit of visualizing prostate rotations and deformations, as well as rectum and bladder filling. By combining the use of fiducial markers with CBCT soft-tissue matching, the accuracy will be improved, and inter-observer variability will be reduced, enabling more effective image-guidance strategies [81]. Commonly, only translational corrections are applied, but rotational adjustments can improve accuracy with small PTV margins, especially when the seminal vesicles are included in the CTV [79]. These can be achieved using six-degree-of-freedom (6DoF) couches, robotic systems, or, more recently, adaptive strategies. Daily pre-treatment imaging is generally sufficient when using the commonly adopted margins of 5 mm, which are considered adequate to account for machine performance, setup inaccuracies, and organ motion, provided that treatment times are short [79,82–84]. For linac-based treatments, with typical beam-on times of 1.5 to 3 minutes, smaller margins of 4 mm are increasingly being used, e.g. in some clinical trials such as hypo-FLAME and MIRAGE trial [85]. For treatment plans involving multiple arcs, acquiring additional CBCTs or where fiducials are implanted kV/MV planar imaging between arcs may be considered to further improve localisation accuracy.

To account for intra-fraction prostate motion, especially when smaller PTV margins and/or longer treatment times are employed, incorporation of additional technologies can be

considered [86]. These include online tracking of fiducial markers, electromagnetic (EM) transponders placed into the prostatic urethra using a catheter, transperineal ultrasound systems, single/stereoscopic X-ray imaging of fiducial markers or MRI-guided systems (Table 3). These systems allow monitoring of the prostate during treatment, but their limitations in detecting rapid intra-fraction motion and the uncertainty in the tracking-to-delivery process must be considered [85,86]. For example, intermittent X-ray-based imaging systems require a high imaging frequency (every 15 to 40 seconds) to accurately capture the unpredictable nature of intra-fraction prostate motion, though there is no established consensus on the optimal image acquisition interval [87]. In continuous tracking systems (2 to 30 frames per second), a small latency is inherent, and accurate gating thresholds and maximum allowable time interval beyond the threshold must be set before manual or automatic beam hold. Intra-fraction motion tracking may be beneficial in prostate SBRT, though its impact on side effects and clinical outcomes has yet to be proved [79,88]. Notably, both landmark trials, PACE-B and HYPO-RT-PC, did not incorporate an intra-fraction motion management strategy for most patients. For systems such as MRI-linacs or CyberKnife, which involve longer treatment times of 25–45 minutes, organ motion management techniques are fully integrated. For conventional linacs, these techniques can be additionally implemented. With their use, tighter PTV margins of 2–3 mm may be safely employed [79,82,83].

2. Online adaptive radiotherapy

MRI-Linacs can offer potential advantages over conventional IGRT, integrating high-quality imaging with comprehensive motion management, allowing for accurate, real-time adaptive radiation delivery. MRI-guided RT platforms provide continuous, real-time, and non-ionizing high soft tissue resolution imaging during the entire radiation delivery, enabling precise motion tracking and continuously targeting prostate volume. Moreover, MRI-Linacs account for non-cyclical or erratic motion, such as irregular processes due to passage of gas in the rectum, permitting an improved management of irregular prostate motion [89,90].

Furthermore, recent technological advancements in image guidance, deformable image registration, automated contouring tools, workflow integration, and fast GPU-based dose calculation engines, have facilitated the implementation of online adaptive RT (ART) into both MRI-guided and CBCT-based platforms. These workflows enable real-time adjustments of the treatment plan before delivery to account for daily anatomical variations, aiming at minimising treatment-related toxicity. Online ART involves image acquisition, contour propagation, plan adaptation, review, and an appropriate form of PSQA, all of which must be completed in the shortest timeframe possible, as the patient remains on the treatment couch during the process [91]. Reported timeframes for daily prostate replanning range from 10 up to 45 minutes. While early findings suggest promising toxicity outcomes with this approach [94], the clinical benefit compared with non-adaptive approaches remains to be definitively established.

Moreover, although online ART has proven feasible in several clinical settings [95,96] and is increasingly adopted, practical considerations such as the management of intra-fraction anatomical changes during the adaptive process, resource requirements, staff workload, and the potential for major uncertainties due to the need for rapid execution must be carefully evaluated when implementing this technique. A recent systematic risk analysis across multiple commercial platforms and institutional settings highlighted that online ART introduces additional safety and workflow risks, primarily due to real-time clinical decision-making at the treatment console by staff whose conventional scope of practice did not previously include such responsibilities [97]. The highest-risk failure modes were related to the daily contouring step, largely associated with insufficient manual review, followed by imaging, dose calculation and plan evaluation. Such risk-based analyses are essential to identify priority areas for the

development of appropriate QA programmes for online ART workflows, thereby helping to mitigate risks while maximizing the benefits of adaptation [97].

Post-SBRT PSA kinetics

Early PSA rises after prostate SBRT should be interpreted with caution. Transient PSA bounces are common within the first 12 – 18 months and often resolve spontaneously; therefore, early salvage therapy should generally be avoided in the absence of confirmed biochemical failure.

PSA bounce is a transient increase in PSA levels observed after RT, including SBRT, for prostate cancer [98]. Although generally benign, PSA bounce can be a source of concern for both patients and clinicians. This phenomenon has been documented in patients treated with conventionally fractionated RT or brachytherapy and is now increasingly reported in those receiving SBRT. Various thresholds for defining a bounce exist, the most often used definition is a PSA level increase of ≥ 0.2 ng/mL above the pre-bounce nadir spontaneously dropping to or below the pre-bounce nadir as it was chosen in the HYPO-RT-PC trial [99,100]. In the PACE trials PSA failure was defined after 24 months with the Phoenix definition (i.e. nadir+2 ng/mL) to rule out incorrectly classifying a PSA rise as a PSA failure. The incidence of PSA bounce ranges from 10% to 40%, with most bounces occurring within the first 12 to 18 months post-treatment [101]. The exact mechanism remains unclear, but it is believed to be related to local inflammation, microvascular changes, and tumour cell apoptosis induced by high-dose radiation [102]. A PSA bounce typically resolves over time without affecting overall survival or disease-free survival, but it can be a challenging issue in distinguishing benign fluctuations from true disease recurrence. Thus, clinicians should be cautious in making early decisions about salvage therapies, as a PSA bounce may resolve without intervention. Regular monitoring, with attention to clinical symptoms and imaging, is recommended to differentiate between PSA bounce and actual recurrence.

Conclusion

Prostate SBRT is a standard of care treatment for patients with low- and intermediate-risk localised prostate cancer and is increasingly being used in high-risk disease as well, although its role in this setting is still evolving. These 'how to' clinical practice consensus recommendations, based on the latest available evidence, are developed in cooperation with ESTRO and intended for radiation oncologists, medical physicists and RTTs to jointly implement or optimise prostate SBRT in their radiation oncology department.

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Acknowledgements

The panel would like to thank Eralda Azizaj and Jonas Johansen for providing logistical and administrative support from ESTRO. Furthermore, the authors would like to thank the reviewers Uulke van der Heide, Alan Dal Pra and Simon Spohn for their valuable time, insightful comments and constructive feedback during the review of this manuscript.

Funding

No external funding has been received for the preparation of these consensus recommendations.

Conflict of interest disclosure

AT declares receipt of grants and research support from Elekta, Varian, Accuray and Artera AI; receipt of honoraria or consultation fees from Elekta, Accuray, Janssen, Astellas and Bayer; and a paid role as chair of the MR linac consortium steering committee and as Oncology lead for the UK National Prostate Cancer Audit. **TZ** declares receipt of grants and research support from Varian and Astellas; receipt of honoraria or consultation fees from Janssen, Amgen, Ferring, Debiopharm, Bayer, Astellas, Telix, Mvision, Recordati and Ipsen; and a paid role as chair of the ESTRO guidelines committee. **FA** declares receipt of grants and research support from Elekta and Varian; and receipt of honoraria or consultation fees from Ipsen, Ferring, Recordati, Johnson and Johnson, Bayer and Novartis. **CZ** declares receipt of grants and research support from Elekta and Artera AI. **PO** declares receipt of grants and research support from Bayer, Veracyte and Artera AI; and receipt of honoraria or consultation fees from Astellas Pharma, Telix Pharmaceuticals, AstraZeneca, Janssen, Bayer, Recordati and Micropos. **BJ** declares receipt of grants and research support from Accuray, IBA, AIRC (Italian Association for Cancer Research) and Fondazione IEO-CCM (Istituto Europeo di Oncologia-Centro Cardiologico Monzino); and receipt of honoraria or consultation fees from Bayer, Ipsen, Accuray, Astellas Pharma, AstraZeneca, Pfizer, Accord, Novartis, Seagen, Technologie Avanzate, IBA and Recordati. **PB** declares receipt of grants and research support from Neolys and Boston Scientific; receipt of honoraria or consultation fees from Astellas, Ipsen, Janssen, AstraZeneca, MSD, Bayer, Merck Serono; and a paid role as Editor in Chief of Radiotherapy and Oncology (the Green Journal). **AGI** declares receipt of honoraria or consultation fees from

AAA, Astellas, Bayer, Janssen, Accord, Recordati and Elekta. **NSSH** declares receipt of honoraria or consultation fees from Astellas, Orion Pharma, Bayer, Janssen, MSD and Pfizer. All other authors (**CD**, **VF**, **FW**, **RDR**, **JS** and **SA**) have declared no conflicts of interest.

Legends

Figure 1. Example of standard planning and dose distribution when performing prostate SBRT according to the PACE-B protocol

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Figure 1. Example of standard planning and dose distribution when performing prostate SBRT according to the PACE-B protocol

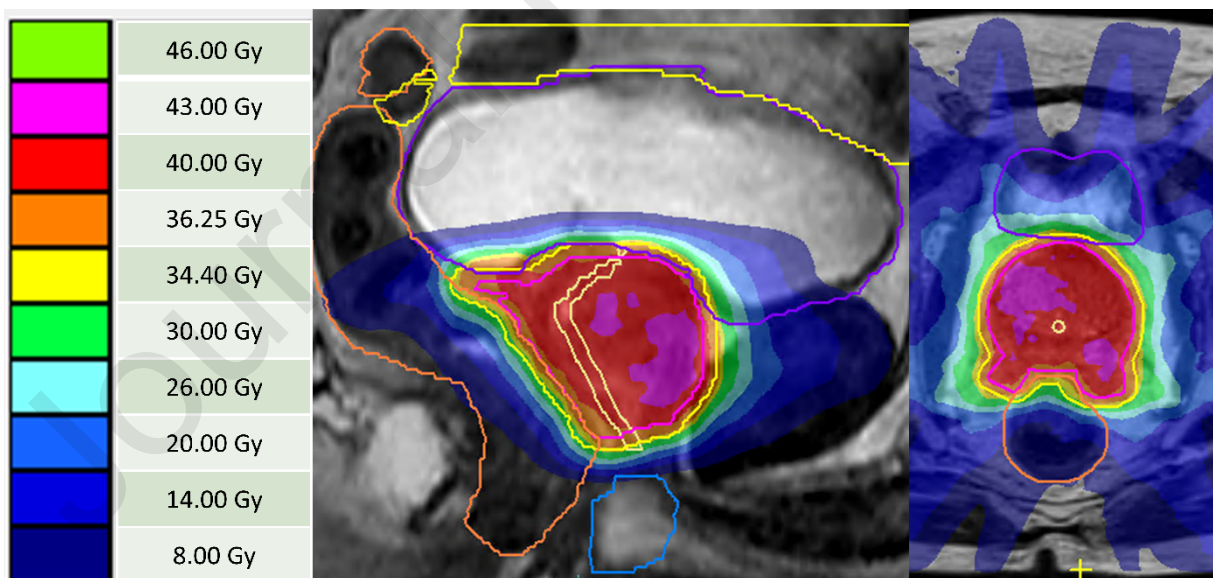


Table 1. Suggested target volume parameters*

Target Volume	Dose guidance (Gy)	Volume	Notes	Source
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CTV	V40	≥95%	Optimal	PACE-B [12]
PTV	V36.25	≥95%	Optimal	PACE-B [12]
	V34.4	≥98%	Mandatory	PACE-B [12]
	<48	Dmax	Mandatory	PACE-B [12]
	<42.8	D2%	Optimal	PACE-B [12]

* Dose parameters for gantry-based SBRT

Table 2. Suggested dose guidance

OOI	Dose (Gy)	guidance	Volume	Notes	Source
Mandatory OOs					
Rectum	V18.1		<50%	Mandatory	PACE-B [12]
	V29		<20%	Mandatory	PACE-B [12]
	V36		<2 cc	Mandatory	PACE-B [12]
	V36		<1 cc	Optimal	PACE-B [12]
Bladder	V18.1		<40%	Mandatory	PACE-B [12]
	V37		<10 cc	Mandatory	PACE-B [12]
	V37		<5cc	Optimal	PACE-B [12]
Femoral heads	V14.5		<5%	Optimal	PACE-B [12]
Bowel*	V18.1		<5cc	Mandatory	PACE-B [12]
	V30		≤1cc	Mandatory	PACE-B [12]
	<35		D0.035 cc	Mandatory	hypo-FLAME [103]

Optional OOs				
Prostatic urethra PRV (urethra steering)	V42**	<50%	Mandatory	PACE-B [12]
	<42	D0.035 cc	Optimal***	hypo-FLAME [103]
Penile bulb	V29.5	<50%	Optimal	PACE-B [12]
Crura	<4.7	Dmean	Optimal	Achard et al. [53]
	<12	D2%	Optimal	Achard et al. [53]

* Based on individual bowel loops

** Based on additional analyses, this PACE-B based dose constraint may be too permissive; hotspots in the urethra should be avoided.

*** The D0.035 cc < 42 Gy constraint is mandatory in the hypo-FLAME trial. In the context of the PACE constraints, this additional constraint could be regarded as an optimal planning objective.

Urethra PRV = mostly defined as urethra + 2mm

Table 3. Minimum image guidance and motion management requirements based on PTV margins and total treatment time

Total treatment time (per fraction)	PTV margin	CBCT soft-tissue matching or fiducial marker-based kV/MV systems	Integration of/use of additional intra-fraction monitoring systems
Fast: ≤5-10 minutes	2-3mm	✓	✓
	4-5mm	✓	
	2-3mm	✓	✓

Prolonged: >10 minutes	4-5mm	✓	✓
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