

Polish Brachytherapy Society recommendations and expert consensus on radical high-dose-rate brachytherapy for prostate cancer

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Purpose

Purpose: High-dose-rate brachytherapy (HDR-BT) is an established and highly effective modality for the radical treatment of localized prostate cancer. Despite its widespread use in Poland, relevant aspects of patient selection, treatment qualification, dose and fractionation, integration with external beam radiotherapy (EBRT), and target and organ-at-risk definition vary between centers. The aim of this document was to develop national recommendations and expert consensus statements to standardize the use of radical HDR-BT for prostate cancer.

Material and methods: The Polish Brachytherapy Society convened a multidisciplinary panel of radiation oncologists with extensive experience in prostate brachytherapy. Recommendations were developed through a structured literature review focusing on prospective trials, meta-analyses, and large retrospective studies. Evidence quality and strength of recommendations were assessed using the GRADE framework. A modified two-round Delphi process was applied, involving a core expert panel and an extended national panel. Consensus was predefined as $\geq 75\%$ agreement.

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Results: Consensus recommendations were formulated across the entire HDR-BT treatment pathway, including patient assessment, diagnostic work-up, risk stratification, indications for HDR-BT monotherapy and HDR-BT boost combined with EBRT, dose and fractionation schedules, use and duration of androgen deprivation therapy, timing of HDR-BT relative to EBRT, and target volume delineation with organ-at-risk dose constraints. The consensus supports fractionated HDR-BT monotherapy in selected low- and intermediate-risk clinical scenarios, and confirms the role of HDR-BT boost combined with EBRT as a key component of dose-escalation strategies in high- and very high-risk prostate cancer. An EQD₂-based approach to dosimetric constraints was endorsed to enhance treatment safety and consistency.

Conclusions: These recommendations represent the first national expert consensus of the Polish Brachytherapy Society on radical HDR-BT for prostate cancer. They provide a comprehensive, evidence-informed framework to harmonize clinical practice, support decision-making, and improve comparability of outcomes across Polish centers. Regular updates will be required as new clinical evidence emerges.

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Purpose

Prostate cancer (PCa) is the most common malignant neoplasm among men in Poland. In 2019, more than 17,000 new cases were diagnosed. Unfortunately, mortality remains approximately 30% and is higher than in many other European Union countries. The projected incidence for 2026 approaches 29,000 cases, with an estimated number of deaths slightly exceeding 6,600. Moreover, an increasing proportion of patients are younger individuals; one quarter of all diagnoses occur in men aged 45-64 years [1].

Modern brachytherapy (BT) is an effective treatment modality for patients with PCa, and it can be applied as monotherapy or combined with external beam radiotherapy (EBRT) in more advanced disease [2-4]. It remains one of the few proven options for local recurrence after prior radiotherapy [5], reflected in international guidelines that recognize BT as a valuable modality across all risk groups and as a salvage treatment strategy [6, 7].

In Poland, prostate BT was introduced in the 1990s, and is currently available in most centers equipped with dedicated BT units. Its widespread availability has resulted in numerous Polish publications addressing this treatment approach [5, 8-13].

The Polish Brachytherapy Society (PBS) conducted a nationwide survey, outcomes of which were presented during the 4th PBS Congress in 2016. The results demonstrated that most centers follow broadly similar fractionation schedules, but noticeable differences exist in plan evaluation criteria, both for target volumes and organs at risk (OARs). International guidelines, including those developed by the Groupe Européen de Curiothérapie – European Society for Radiotherapy and Oncology (GEC-ESTRO) [3] and the American Brachytherapy Society (ABS) [14], provide an essential framework for prostate brachytherapy. However, these recommendations are not specifically adapted to organizational structure, clinical practice patterns, and treatment availability within specific national healthcare systems. Therefore, variability in clinical implementation may persist, highlighting the need for nationally adapted consensus recommendations.

The present PBS recommendations were developed to standardize the use of iridium-192-based high-dose-rate brachytherapy (HDR-BT) in radical treatment of PCa in Po-

land, and to provide a nationally adapted consensus-based framework for clinical practice. These guidelines focus primarily on clinical aspects of patient qualification, treatment strategy, dose prescription, and integration with EBRT.

Technical and physics-related aspects, including equipment specifications, treatment planning systems, dosimetric algorithms, and quality assurance procedures, were considered beyond the scope of the current clinical consensus, thus not addressed in detail. These important technical domains will be the subject of a separate dedicated consensus initiative, with medical physicists and multidisciplinary experts involved.

Methodology for developing recommendations and reaching consensus

The PBS Executive Board appointed a group of clinicians experienced in the management of PCa to formulate a unified position on the use of HDR-BT. The aim of the project was to develop consensus-based recommendations on patient assessment and diagnostic work-up, treatment indications, dose and fractionation schedules, use of androgen deprivation therapy (ADT), integration of HDR-BT with external beam radiotherapy (EBRT), and target and OARs definition, considering associated dosimetric constraints in HDR-BT for PCa.

A detailed literature review was conducted, focusing on prospective studies, randomized controlled trials (RCTs), meta-analyses, multicenter investigations, and single-center reports. The analysis covered evidence on clinical outcomes and treatment-related toxicity associated with HDR-BT. Available data were assessed using the grading of recommendations assessment, development, and evaluation (GRADE) framework (Table 1) [15], which enables a structured evaluation of the quality of evidence and strength of recommendations based on pre-defined criteria.

Strength of recommendations

- **Strong recommendation:** Issued when the recommendation is supported by high- or moderate-quality evidence, and when the benefits clearly outweigh the risks. Most patients should receive the recommended intervention.

Table 1. GRADE system for rating quality of evidence and strength of recommendations

Quality of evidence	Description
High	High-quality studies, such as well-designed RCTs or meta-analyses, providing a high-level of confidence in the estimated effect
Moderate	Studies with some limitations, which may affect the accuracy and reliability of data, but overall indicate a probable effect
Low	Observational studies or studies with important methodological limitations, suggesting an effect, but with considerable uncertainty regarding the reliability of results
Very low	Very limited evidence, where the estimated effect is highly uncertain

- Weak (conditional) recommendation: Issued when the recommendation is supported by low-quality evidence, or when the balance between benefits and risks is close. Decision-making should be individualized and guided by patient preferences.

Notes on determining recommendation strength

Recommendation strength was determined by a core expert panel using the GRADE framework, considering the quality of evidence, balance of benefits and risks, and expert clinical judgment. Final classification was confirmed through a modified Delphi consensus process and agreement of an extended expert panel.

Consensus development process

The process of establishing recommendations was based on a modified Delphi methodology [16], conducted according to the following steps:

1. Formation of core expert panel: The PBS appointed a seven-member core panel consisting of radiation oncologists and brachytherapy specialists. The panel included representatives from academic and clinical centers, ensuring a broad spectrum of experiences and perspectives.
2. Identification of key clinical questions: Based on literature review and clinical practice, key issues requiring recommendations were identified.
3. Literature review: For each clinical question, a detailed review of literature was performed, including searches of major medical databases (e.g., PubMed, EMBASE) to identify relevant clinical studies, meta-analyses, and guidelines.
4. Assessment of evidence quality and development of preliminary recommendations: The core panel assessed the quality of evidence for each question using the GRADE system. Preliminary recommendations were drafted, with quality of evidence, balance of benefits and risks, and patient values and preferences taken into account.
5. First round – voting by the extended expert panel: Preliminary recommendations were presented to 23 radiation oncologists and brachytherapy specialists, constituting the extended expert panel. Panelists rated their agreement using a Likert scale (from “strongly disagree” to “strongly agree”).
6. Analysis and refinement of recommendations: Recommendations were modified based on voting results

- and expert comments, with particular attention given to areas of disagreement or low concordance.
7. Second round – final consensus: Revised recommendations were circulated for the second round of voting. Consensus was achieved when at least 75% of experts agreed with a given recommendation.
 8. Final approval and publication: Following consensus, the recommendations were approved by the PBS Executive Board and prepared for publication.

Definition of consensus levels

Consensus thresholds were defined a priori according to widely accepted standards for Delphi-based oncology studies:

- Consensus: ≥ 75% agreement among experts;
- Strong consensus: ≥ 90% agreement.

Agreement percentage was calculated as the proportion of “agree” and “strongly agree” responses out of all votes cast. The detailed voting results for individual items are presented in Supplementary Material.

Patient assessment before treatment

General patient evaluation

Effective and safe treatment of PCa requires a comprehensive patient assessment. This evaluation should consider not only chronological age, but also biological fitness, comorbidities, perioperative risk, and geriatric factors (particularly in patients aged ≥ 75 years). A multidisciplinary team may support the decision-making process by jointly weighing the expected benefits and potential risks. The following recommendations outline the key elements of this assessment.

Recommendation 1

The overall health status and comorbidities of the patient should be carefully evaluated, as they may influence:

- Eligibility for anesthesia: Cardiovascular and respiratory diseases, and spinal disorders.
- Tolerance of lithotomy position: Spinal conditions, hip joint disorders, previous fractures of the pelvis or lower limbs, and presence of orthopedic implants.
- Urinary catheterization: Congenital penile anomalies, history of sexually transmitted infections, and prior transurethral urological procedures.

- Insertion of transrectal ultrasound probe and imaging quality: Post-operative conditions involving the anal canal or rectum, anal fissures, and perianal fistulas.
- Periprocedural complications and treatment-associated toxicity: Allergies, hematologic disorders, use of anticoagulants, inflammatory bowel disease, prior pelvic irradiation, connective tissue disorders, and neurological conditions.

Quality of evidence: Low.

Strength of recommendation: Strong.

Rationale: Careful consideration of these factors is essential to minimize perioperative risk and optimize treatment outcomes. Although the evidence is largely based on clinical experience and observational data, this practice is universally applied in routine BT workflows. Within the GRADE framework, it justifies a strong recommendation despite low-quality evidence, given the clear clinical benefit and broad expert consensus.

A strong consensus was reached.

Recommendation 2

In patients aged ≥ 75 years, the geriatric eight (G8) screening tool [17] should be employed, with a full comprehensive geriatric assessment performed when indicated. Patients identified as frail should not be considered candidates for radical treatment.

Quality of evidence: Moderate.

Strength of recommendation: Strong.

Rationale: International guidelines recommend geriatric assessment in older patients to identify individuals unlikely to tolerate radical therapy [17]. Frailty is associated with increased risk of complications, limited therapeutic benefit and, in severe cases, reduced overall survival (OS).

A consensus was reached.

Assessment of genitourinary function

Recommendation 3

Particular attention should be paid to baseline urinary symptoms using the international prostate symptom score (IPSS) [18]. This tool is useful both for initial assessment and monitoring treatment-related toxicity.

Quality of evidence: High.

Strength of recommendation: Strong.

Rationale: IPSS is a proven and widely used instrument for evaluating lower urinary tract symptoms. It should be used during baseline patient assessment to support treatment qualification and risk assessment. It also helps predict potential urological complications, and may be utilized during follow-up to monitor treatment-related toxicity.

A strong consensus was reached.

Recommendation 4

The international index of erectile function (IIEF-5) should be applied to evaluate sexual function [19].

Quality of evidence: High.

Strength of recommendation: Strong.

Rationale: IIEF-5 is a validated tool for assessing erectile function. Baseline evaluation of sexual function is crucial for treatment qualification and counselling patients on potential sexual side effects of treatment.

A consensus was reached.

Assessment of anatomical conditions

Recommendation 5

Large prostate volume should not be considered a contraindication for HDR-BT. Evidence shows that patients with glands > 60 ml can be treated effectively without a significant increase in toxicity [20, 21].

Quality of evidence: Moderate.

Strength of recommendation: Strong.

Rationale: Studies indicate that HDR-BT can be safely delivered in patients with larger prostate volumes without increased treatment-related toxicity and without compromising biochemical disease control.

A consensus was reached.

Recommendation 6

Assessment of the relationship between the prostate and bony pelvis is essential. Pubic arch interference (PAI) may prevent proper needle placement, especially in anterior-lateral regions of the gland, resulting in a sub-optimal implantation [22, 23].

Quality of evidence: Moderate.

Strength of recommendation: Strong.

Rationale: Evaluation of PAI is critical for treatment planning, ensuring adequate implant geometry and dose distribution.

A strong consensus was reached.

Recommendation 7

Transrectal ultrasound (TRUS) examination in the lithotomy position, multiparametric magnetic resonance imaging (mpMRI), or computed tomography (CT), may be used to assess PAI and other relevant anatomical conditions [22, 23].

Quality of evidence: Moderate.

Strength of recommendation: Strong.

Rationale: Imaging modalities, such as TRUS, CT, and mpMRI, provide complementary anatomical information, which support the assessment of prostate anatomy, spatial relationships with surrounding structures, and overall technical feasibility of HDR-BT implantation. Cross-sectional imaging can be particularly useful in selected cases to better evaluate potential anatomical constraints.

A strong consensus was reached.

Recommendation 8

In cases of PAI, after weighing potential benefits and risks, short-course (3 months) neoadjuvant ADT may be considered to reduce prostate volume [24], even in patients without standard indications for ADT.

Quality of evidence: Low.

Strength of recommendation: Weak.

Rationale: Evidence supporting the use of neoadjuvant ADT specifically to overcome PAI is limited. Therefore, decision-making should be individualized.

A consensus was reached.

Recommendation 9

In patients with a history of transurethral resection of the prostate (TURP), HDR-BT can be safely performed at least 3 months after the procedure [25]. Accurate assessment of the location and size of the post-TURP cavity is essential to ensure appropriate dosimetric control in the region of urethra.

Quality of evidence: Moderate.

Strength of recommendation: Strong.

Rationale: Studies indicate that HDR-BT is both safe and effective after TURP, provided that adequate time has passed, and careful treatment planning is undertaken.

A strong consensus was reached.

Diagnostics

Prostate cancer encompasses a heterogeneous spectrum of disease: from clinically insignificant tumors that may remain asymptomatic and not require radical treatment, to cancers with a high-risk of progression. Accurate diagnostic work-up is essential for determining disease stage and assigning patients to the appropriate National Comprehensive Cancer Network (NCCN) risk group [6], thereby guiding optimal oncologic management, including qualification for radical treatment with HDR-BT.

The PBS consensus panel recommends that all patients with suspected PCa undergo a comprehensive diagnostic process that includes:

1. Digital rectal examination (DRE).
2. Serum prostate-specific antigen (PSA) measurement.
3. mpMRI of the prostate.
4. Biopsy (systematic and/or targeted).
5. Imaging studies for assessment of nodal (N) and distant (M) metastases.

The key components of this diagnostic pathway are summarized below, along with specific recommendations.

Digital rectal examination (DRE)

Digital rectal examination remains the fundamental method for initial clinical assessment of T stage (cT), according to the American Joint Committee on Cancer (AJCC) 8th edition [26]. Furthermore, data indicate that a suspicious DRE should prompt mpMRI, even when PSA deviations are small [27, 28].

Recommendation 10

DRE should be routinely performed for cT assessment in all patients with suspected PCa, regardless of PSA level.

Quality of evidence: Moderate.

Strength of recommendation: Strong.

Rationale: DRE is a simple and widely available examination, enabling detection of suspicious findings even

at low PSA values. An abnormal DRE is an indication for further imaging.

A strong consensus was reached.

PSA measurement

Serum PSA is an enzymatic glycoprotein produced by prostatic epithelial cells. Although physiologically present in the bloodstream at low concentrations, its level increases in several conditions, such as PCa, benign prostatic hyperplasia (BPH), and prostatitis.

Both the NCCN [6] and European Association of Urology (EAU) [7] guidelines emphasize the importance of PSA testing in the initial evaluation of patients with suspected PCa, particularly when DRE is abnormal or additional risk factors (e.g., family history, BRCA mutations) are present. PSA must also be measured immediately before qualification for radical treatment, e.g., HDR-BT, to exclude interval disease progression requiring modification of treatment. PSA density improves diagnostic specificity, especially in equivocal mpMRI findings, such as prostate imaging reporting and data system (PI-RADS) category 3 lesions, and may help reduce unnecessary biopsies [29]. Moreover, evidence indicates that both diagnostic PSA density and PSA level obtained on the day of the first HDR-BT fraction are prognostic factors for local recurrence risk post-treatment [30].

Recommendation 11

In men with normal DRE but reproducible PSA > 3 ng/ml, additional diagnostic evaluation for PCa is recommended. PSA density should be considered in equivocal cases to reduce unnecessary biopsies. PSA measurement must be repeated directly before HDR-BT to identify possible interval progression and reassess treatment eligibility.

Quality of evidence: Moderate.

Strength of recommendation: Strong.

Rationale: PSA is a key biochemical marker for detecting clinically significant PCa and assessing disease progression. Elevated or rising PSA levels justify further diagnostic evaluations, even with a normal DRE. PSA density provides additional risk stratification in borderline or ambiguous situations, and improves decision-making in terms of biopsy. Repeating PSA immediately before HDR-BT allows early identification of clinically relevant progression during the diagnostic process, ensuring that only appropriate candidates proceed to radical treatment.

A consensus was reached.

Multiparametric MRI (mpMRI)

The mpMRI protocol (T2W, T1W, DWI, DCE) is essential for lesion localization and assessment of disease extent. Evidence, including a large Cochrane meta-analysis, demonstrate that pre-biopsy mpMRI increases detection of clinically significant PCa and reduces unnecessary biopsies [31].

Recommendation 12

The mpMRI should be performed prior to the first prostate biopsy to improve diagnostic sensitivity and specificity, while reports should follow PI-RADS version 2.1 rules to enhance reproducibility.

Quality of evidence: High.

Strength of recommendation: Strong.

Rationale: The mpMRI before biopsy enhances identification of clinically significant tumors and improves diagnostic precision, enabling better targeting and reducing overdiagnosis.

A strong consensus was reached.

Biopsy

Diagnosis of PCa relies exclusively on histopathological evaluation of biopsy specimens. Contemporary grading and reporting standards are defined by recent consensus statements from the International Society of Urological Pathology (ISUP) and the Genitourinary Pathology Society [32, 33] as well as the World Health Organization classification of tumors, 5th edition [34].

Recommendation 13

A systematic biopsy (minimum 12 cores) should be performed. In patients with suspicious mpMRI lesions (PI-RADS ≥ 4 , or lesions located in the anterior zone), targeted (fusion) biopsy needs to be considered additionally.

A histopathology report should include at least:

- Histologic type;
- Gleason grading for each core, including dominant pattern, and the overall ISUP grade group;
- Presence or absence of intraductal carcinoma or cribriform morphology;
- Presence or absence of atypical intraductal proliferation;
- Number of cancer-positive cores (minimum recommended systematic sampling: 12 cores);
- Tumor extent per core (percentage or millimeters);
- For MRI-targeted sampling, ISUP grade or a detailed benign histologic description when no carcinoma is identified;
- Presence of lymphovascular invasion, extracapsular extension (ECE), or seminal vesicle invasion (SVI), if identified.

Biopsy specimens may be obtained *via* transrectal (TRUS-guided) or transperineal route (TRUS and/or MRI guidance). The transperineal approach and targeted bi-

opsy improve detection of clinically significant anterior tumors and reduce infectious complications [35, 36].

Quality of evidence: High.

Strength of recommendation: Strong.

Rationale: Combining systematic and targeted sampling increases detection of clinically significant PCa, ensuring accurate histopathological grading and risk classification.

A strong consensus was reached.

Imaging for assessment of nodal (N) and distant (M) metastases

Following clinically significant PCa confirmation, additional imaging is typically required to evaluate nodal involvement and distant metastatic spread.

Recommendation 14

Conventional staging studies, i.e., MRI or CT of the abdomen and pelvis and bone scintigraphy, should be performed according to NCCN risk categories [6]. Even in patients who do not formally meet criteria for the above imaging, routine chest X-ray and abdominal ultrasound are advisable. All staging studies should be performed no more than 12 weeks prior to treatment qualification.

Quality of evidence: Moderate.

Strength of recommendation: Strong.

Rationale: Conventional imaging is supported by widely available robust evidence, forming a reliable foundation for staging and treatment planning.

A strong consensus was reached.

Recommendation 15

In patients with high-risk (HR) and very high-risk (vHR) PCa, advanced imaging, including prostate-specific membrane antigen positron emission tomography – computed tomography (PSMA PET-CT) as well as whole-body MRI (WB-MRI), can be considered during initial staging.

Quality of evidence: Moderate.

Strength of recommendation: Weak.

Rationale: Advanced imaging techniques provide superior diagnostic accuracy compared with conventional staging. PSMA PET-CT offers high sensitivity and specificity in detecting nodal and distant metastases [37, 38], while WB-MRI has emerged as a highly sensitive whole-body staging modality, enabling simultaneous assessment of bone and soft-tissue disease with excellent repro-

Table 2. Recommended imaging for staging prostate cancer (PCa) according to PBS (by NCCN risk groups)

NCCN risk group	Prostate mpMRI	Pelvis and abdomen imaging (CT/MRI)	Bone scintigraphy	Advanced imaging (PSMA PET-CT, WB-MRI)
Low	+	–	–	–
Favorable intermediate	+	–	–	–
Unfavorable intermediate	+	+	–	–
High	+	+	+	+*
Very high	+	+	+	+*

*May be considered as an alternative to conventional imaging

ducibility and without ionizing radiation [39]. However, evidence of survival benefit is lacking, while cost and availability remain important limiting factors.

A strong consensus was reached.

The detailed summary of the recommended staging modalities across the NCCN risk groups is presented in Table 2.

Additional opinions of the extended expert panel

Opinion 1: The cT category should always be determined based on correlation between DRE findings and imaging studies (mpMRI preferred).

A strong consensus was reached.

Opinion 2: A suspicious DRE always requires prostate biopsy, irrespective of PSA level.

A consensus was reached.

HDR-BT as monotherapy for low-risk, favorable intermediate-risk, and selected unfavorable intermediate-risk PCa

Clinical studies have demonstrated that dose escalation in hypofractionated radiotherapy improves biochemical control in PCa [40, 41]. HDR-BT is an effective method for delivering ultra-hypofractionated radiotherapy to the prostate. As monotherapy, HDR-BT provides precise dose delivery and a shorter overall treatment time, making it an attractive option for appropriately selected patients.

Two main prostate BT modalities are currently used: ultra-low-dose-rate BT (uLDR-BT) and HDR-BT. Although HDR-BT is a newest technique with limited long-term data available (beyond five years), it has been included in major NCCN [6] and EAU [7] guidelines. In the low-risk (LR) group, active surveillance (AS) or observation are preferred, whereas radical treatment, including HDR-BT monotherapy, should be considered only in cases of progression during AS/ observation, or if the patient does not accept such an approach.

The latest NCCN (2025) recommendations advise the use of HDR-BT in the favorable intermediate-risk (FIR) group, and allow BT monotherapy also in patients with unfavorable intermediate-risk (UIR) disease, together with short-term ADT, unless additional risk assessment suggests a less aggressive disease course or medical contraindications exist. However, for the UIR group, there are no prospective randomized trials evaluating HDR-BT monotherapy exclusively, and the recommendation relies on estimations from retrospective studies, mixed (HDR/uLDR) analyses, and expert consensus.

No prospective randomized trials directly comparing HDR-BT monotherapy with EBRT were identified. However, systematic reviews and meta-analyses indicated that fractionated HDR-BT used as monotherapy provides high rates of disease control with low toxicity [42, 43].

Summary of evidence

Anderson *et al.* [42]: This systematic review and meta-analysis included seven retrospective studies com-

prising 2,123 patients treated with fractionated HDR-BT monotherapy. Risk distribution was 40% for low-, 40% for intermediate-, and 20% for high-risk disease. ADT was used in 31.6% of patients, and 19.8% were classified as high-risk. The median follow-up was 74 months, and the pooled 5-year biochemical relapse-free survival (bRFS) was 95%, increasing to 96% after adjustment for publication bias. Estimated late grade ≥ 3 toxicity was low: 2% genitourinary (GU) and 0.3% gastrointestinal (GI). Fractionated HDR-BT monotherapy was therefore associated with excellent disease control and very low rates of severe toxicity.

Viani *et al.* [43]: This meta-analysis included 14 studies with 3,534 patients treated with HDR-BT monotherapy. The median follow-up was 65 months, and the pooled 5-year bRFS was 92%, with stratified bRFS of 97.5% for low-risk, 93.5% for intermediate-risk, and 91% for high-risk patients. The use of ADT (administered in ~25% of patients) was significantly associated with improved biochemical control. Approximately 10% of the cohort consisted of high-risk patients. Late grade ≥ 3 toxicity was low: 1.4% GU and 0.2% GI, while overall late grade 2-3 GU and GI toxicity occurred in 22.4% and 2.7%, respectively. Higher biologically effective dose (BED), BED per fraction, and number of HDR fractions, were significantly correlated with better biochemical outcomes.

Recommendation 16

HDR-BT monotherapy is recommended as a safe and effective treatment option for PCa, depending on risk group:

- LR: Only in cases of progression during AS/observation, or if AS/observation is not acceptable to the patient;
- FIR: As one of the preferred definitive treatment modalities;
- UIR: In selected cases.

Quality of evidence:

LR, FIR: Moderate;

UIR: Low.

Strength of recommendation:

FIR: Strong;

LR: Conditional;

UIR: Conditional.

Rationale: In LR and FIR diseases, HDR-BT monotherapy provides high disease-control rates with low toxicity, although AS remains the preferred first-line strategy in LR patients. In UIR disease, the recommendation is based on the 2025 NCCN consensus and limited clinical data.

A strong consensus was reached.

Additional opinions of the extended expert panel regarding qualification of UIR patients for HDR-BT monotherapy

Opinion 3: Patients with exactly two intermediate-risk factors (IRF: cT2b-cT2c, grade group 2-3, PSA 10-20 ng/ml) may be considered eligible for HDR-BT monotherapy.

A consensus was reached.

Opinion 4: Patients with three IRFs should preferably be treated with EBRT combined with an HDR-BT boost.

A consensus was reached.

Dose and fractionation

Emerging evidence suggests that radiotherapy for localized PCa can be delivered safely and effectively in fewer than five fractions using HDR-BT or stereotactic body radiotherapy (SBRT) [44]. Long-term data support the effectiveness of HDR-BT monotherapy delivered in 2-4 fractions, whereas single-fraction monotherapy has shown sub-optimal disease control [44-47]. For patients with UIR disease who, according to the latest NCCN recommendations [6], may be treated with HDR-BT monotherapy, there are no prospective randomized trials evaluating optimal fractionation specifically within this group. Fractionation recommendations are therefore based on extrapolation from LR/FIR cohorts and analyses involving mixed-risk populations.

Summary of evidence

Anderson *et al.* [42]: The authors demonstrated that fractionated HDR-BT monotherapy is associated with high disease control and low rates of significant toxicity. The median number of fractions was 5 (range, 2-9), and the median dose per fraction was 8.8 Gy (range, 6-13.5 Gy).

Hudson *et al.* [45]: Their phase II randomized trial compared 27 Gy in 2 fractions with 19 Gy in 1 fraction (median follow-up: 9 years) in low- and intermediate-risk groups patients. The two-fraction regimen yielded superior outcomes, 8-year biochemical disease-free survival (bDFS) of 83.2%, and a local failure (LF) rate of 11.1%. In the single-fraction group, bDFS was 61.5% and LF was 36%. Both regimens were well-tolerated, with minimal high-grade toxicity.

Tsang *et al.* [46]: This study compared HDR-BT (19 Gy in 1 fraction and 26 Gy in 2 fractions) and SBRT (36.25 Gy in 5 fractions). The two-fraction HDR-BT schedule achieved a biochemical control rate (BCR) of 95%, outperforming single-fraction HDR-BT (69%) and demonstrating results comparable with SBRT (92%) with lower toxicity.

Salari *et al.* [47]: The authors found that HDR-BT monotherapy delivered as a single 21 Gy fraction resulted in sub-optimal biochemical control (bRFS of 76.9%) and grade ≥ 2 GU toxicity in 38.5% of patients after a median follow-up of 5.1 years.

Nagore *et al.* [48, 49]: These two prospective reports described outcomes of the same cohort of 120 patients treated with 27 Gy in 2 fractions delivered on the same day. The initial 2018 publication confirmed feasibility and acceptable toxicity, while the 2023 long-term analysis reported a 10-year no biochemical evidence of disease rate of 93.3%. Late grade 2 and 3 GU toxicity occurred in 18% and 1% of patients, respectively. Together, these findings support the durable efficacy and favorable tolerability of the 2 \times 13.5 Gy same-day HDR-BT regimen.

Hoskin *et al.* [50]: The study reported that single-fraction HDR-BT (19-20 Gy) achieved similar biochemical

control and late toxicity compared with 2 (2 \times 13 Gy) and 3 fractions (3 \times 10.5 Gy) in intermediate- and high-risk patients, with low GU and GI toxicity.

Recommendation 17

Fractionated HDR-BT regimens (2-4 fractions) are recommended over single-fraction HDR-BT in monotherapy due to superior biochemical control and acceptable toxicity profile. In UIR patients, fractionated regimens with established effectiveness in LR/FIR populations should be preferred.

Quality of evidence:

LR/FIR: High;

UIR: Low.

Strength of recommendation:

LR/FIR: Strong;

UIR: Conditional.

Rationale: Randomized studies demonstrate superior effectiveness of fractionated schedules compared with single-fraction HDR-BT. In UIR patients, dedicated trials are lacking, but given the higher disease risk, the proven fractionation regimens from LR/FIR cohorts should be used preferentially.

A strong consensus was reached.

Additional opinions of the extended expert panel

Opinion 5: The preferred and recommended fractionation schedule for HDR-BT monotherapy, balancing effectiveness and toxicity, is 2 \times 13.5 Gy. A treatment interval of 7-14 days between applications is recommended.

A strong consensus was reached.

Opinion 6: HDR-BT delivered as a single 19 Gy fraction should be discontinued as a treatment option due to sub-optimal outcomes.

A strong consensus was reached.

Use of androgen deprivation therapy

Androgen deprivation therapy was used in a proportion of patients across the analyzed studies, ranging from 25% to 31.6% of participants [42, 43]. The proportion of high-risk patients varied, reaching up to 19.8%. According to the ABS, the use of ADT in HDR-BT monotherapy for PCa should be considered on an individual basis, depending on the patient risk profile [51].

The most recent NCCN guidelines [6] specify that when HDR-BT is used as monotherapy in patients with UIR disease, ADT should be routinely added unless contraindications exist or additional clinical factors indicate a less aggressive disease course.

Recommendation 18

In HDR-BT monotherapy for UIR patients, ADT (4-6 months) is recommended as a standard practice, provided that no contraindications exist.

For the FIR group, ADT may be considered in selected patients (e.g., those with features indicating higher risk of progression or elevated genomic classifier scores).

Quality of evidence:

FIR: Low;

UIR: Low.

Strength of recommendation:

Strong for ADT use in UIR.

Weak for FIR.

Rationale: Retrospective studies and mixed-modality analyses (HDR/uLDR) indicate a potential improvement in biochemical control, with short-term ADT in higher risk patients. The recommendation for UIR aligns with the current NCCN standards.

A consensus was reached.

Additional opinion of the extended expert panel

Opinion 7: A 6-month duration of ADT combined with HDR-BT is recommended for both intermediate-risk groups.

A consensus was reached.

HDR-BT as a boost combined with EBRT

The integration of external beam radiotherapy (EBRT) with a BT boost represents a well-established dose escalation strategy for localized PCa. By delivering a highly conformal and intensified dose directly to the prostate while limiting radiation exposure to surrounding organs at risk, a BT boost enhances intraprostatic tumor control, and has demonstrated long-term biochemical benefits across multiple risk categories [52]. Early randomized evidence supporting the concept of a BT boost, irrespective of technique, can be found in a trial by Dayes *et al.* [53], which compared EBRT alone with EBRT plus an interstitial iridium-based LDR-BT implant in node-negative, locally advanced PCa patients. The BT-boost arm showed a sustained reduction in biochemical failure in long-term follow-up, while overall survival (OS), metastasis-free survival (MFS), and toxicity profiles remained comparable. Although the implant technique predates modern HDR-BT practice, it provided foundational proof that intraprostatic dose escalation improves oncological outcomes. A second key source of high-level evidence is the ASCENDE-RT trial [54] that evaluated a permanent seed iodine-125 BT boost. The uLDR-BT boost arm demonstrated a marked and durable improvement in biochemical control compared with dose-escalated EBRT, showing similar OS and MFS between treatment groups. These findings further reinforce the clinical value of BT boost as an effective method of dose intensification.

Together, these studies establish the oncological rationale for BT boost. On this foundation, modern HDR-BT offers superior dosimetric precision, procedural reproducibility, and workflow advantages. The following sections summarize the evidence specifically supporting HDR-BT boost in combination with EBRT.

Comparison of EBRT + HDR-BT boost vs. EBRT alone in UIR, HR, and vHR PCa patients

For patients with UIR, HR, and vHR PCa, choosing the most effective radiotherapy strategy is essential, given the higher likelihood of disease progression and met-

astatic spread. This section evaluated clinical evidence comparing EBRT combined with HDR-BT boost versus EBRT alone in these risk groups. The objective was to determine whether integrating HDR-BT boost provides meaningful improvements in survival and biochemical control, while maintaining acceptable toxicity. It should be noted that many studies included patients classified broadly as “intermediate risk” without distinguishing FIR from UIR. This limited the granularity of conclusions, which can be drawn in terms of HDR-BT boost efficacy within intermediate-risk sub-categories.

Summary of evidence

Miszczyk *et al.* [8]: In a large retrospective Polish cohort of 1,457 IR and HR patients treated with either EBRT alone or EBRT + HDR-BT boost, the addition of HDR-BT significantly improved OS, biochemical failure-free survival (bFFS), and MFS. Five-year OS was 88.5% in the combination arm versus 78.5% in the EBRT only arm. Benefits were observed in both intermediate- and high-risk groups. This provides strong population-level evidence supporting HDR-BT boost.

Hoskin *et al.* (2012 & 2021) [55, 56]: These publications presented early and extended follow-up results of a prospective comparative study evaluating EBRT vs. EBRT + HDR-BT boost in intermediate- and high-risk patients. The combination therapy significantly improved bRFS. No significant differences were found in OS or MFS, and toxicity profiles were comparable. Overall, these findings reinforce the conclusion that HDR-BT boost enhances biochemical control.

Kee *et al.* [57]: Although their meta-analysis included different BT techniques, the HDR-BT data within the pooled evidence consistently confirmed a significant improvement in biochemical control compared with EBRT boost, without a corresponding OS benefit. These findings align with HDR-specific prospective data, and strengthen the evidence base supporting HDR-BT boost.

Slevin *et al.* [58]: This systematic review similarly demonstrated improved biochemical outcomes with BT boost, including HDR-BT, while noting that some series reported a higher incidence of late GU toxicity. However, toxicity findings varied substantially across studies, and were influenced by technique, dose, and follow-up. Overall, the review supports HDR-BT boost as an effective dose-escalation strategy, with the caveat of careful GU toxicity vigilance.

Recommendation 19

For patients with HR and vHR PCa, EBRT combined with HDR-BT boost is recommended to improve OS and biochemical control, considering a potentially increased risk of late GU toxicity. The large retrospective analysis by Miszczyk *et al.* provides strong evidence supporting this approach in the Polish population. For UIR patients, since most studies do not distinguish FIR from UIR, the decision regarding monotherapy versus combined treatment should be individualized.

Quality of evidence: High.

Strength of recommendation: Strong.

Rationale: Consistent evidence demonstrate superior oncological outcomes with acceptable toxicity, especially in HR and vHR groups; individualized decision-making is needed for UIR patients.

A strong consensus was reached.

Additional opinion of the extended expert panel

Opinion 8: EBRT + HDR-BT boost should be considered the standard of care for all HR and vHR patients, given the improved outcomes observed in large patient cohorts.

A strong consensus was reached.

HDR-BT boost in patients with node-positive disease (cN1)

In cN1 patients, the standard of care includes pelvic EBRT combined with long-term ADT, while in contemporary practice, systemic treatment intensification (e.g., androgen receptor pathway inhibitors) is also used. The potential added value of prostate dose escalation by using an HDR-BT boost in this group is unclear.

Summary of evidence

MUREBRANO by Bilski *et al.* [59]: This multicenter retrospective analysis evaluated patients with cN1 disease treated with EBRT + ADT with or without an HDR-BT boost, using propensity score matching (PSM). In the overall population, adding HDR-BT did not prolong time to distant metastasis compared with EBRT alone. However, among patients with higher grade tumors (ISUP 4-5), a clear improvement was observed in both MFS and OS. Safety was assessed: late GI toxicity \geq grade 2 was lower in the HDR-BT boost group (2.5% vs. 10.9%; $p = 0.02$), while GU \geq grade 2 toxicity did not differ. The most common regimen was EBRT 50 Gy in 25 fractions combined with a single-fraction HDR-BT boost of 15 Gy. Qualification was partially based on PSMA PET, though not equally for all patients. In conclusion, no benefit of HDR-BT boost was demonstrated in unselected cN1 population, whereas a strong signal of benefit was seen in ISUP 4-5, with favorable late GI toxicity and no increase in GU toxicity. Prospective validation is needed, particularly in the era of widespread PSMA PET and modern systemic intensification. In ISUP 1-3, no improvement in MFS or OS was observed when HDR-BT was employed. Nevertheless, across the entire propensity-matched cohort, late GI \geq grade 2 toxicity was lower and GU \geq grade 2 toxicity was not increased. This may support the selective use of HDR-BT boost in patients where rectal sparing is a priority (e.g., challenging rectal constraints or unfavorable anatomy), provided that the treating team has substantial expertise in BT.

Recommendation 20

For patients with cN1 and ISUP 4-5, EBRT to the pelvis combined with an HDR-BT boost to the prostate (alongside long-term ADT and, according to current standards, systemic intensification) should be considered, as it may

improve MFS and OS with an acceptable toxicity profile. In ISUP 1-3, routine use of HDR-BT boost is not supported by available evidence, and should be individualized.

Quality of evidence: Moderate.

Strength of recommendation: Conditional.

Rationale: Consistent signal of clinical benefit in ISUP 4-5 with improved GI profile and no increase in GU toxicity, but absence of benefit in the overall cN1 population and in ISUP 1-3.

A consensus was reached.

Timing of HDR-BT boost and EBRT

The optimal sequence, in which EBRT and HDR-BT boost should be delivered, has not yet been clearly established.

Summary of evidence

Choudhury *et al.* (2024) [60]: This randomized trial comparing HDR-BT administered before vs. after EBRT demonstrated no significant differences in toxicity or disease-free survival. Both schedules were tolerated well, suggesting that the choice of sequence may depend on institutional protocols and patient preference.

Hetnał *et al.* (2023) [61]: This study suggested that delivering HDR-BT before EBRT allows marker placement, which may improve treatment accuracy and patient comfort.

Recommendation 21

Both sequences, HDR-BT before EBRT and HDR-BT after EBRT, are acceptable. The choice should be guided by institutional practice, patient preference, and logistical considerations.

Quality of evidence: Moderate.

Strength of recommendation: Weak.

Rationale: Available evidence suggest no clinically meaningful difference between the two schedules, therefore, flexibility is appropriate until more definitive data become available.

A strong consensus was reached.

HDR-BT boost dose

Optimal dose and fractionation for HDR-BT boost have been evaluated across multiple prospective and retrospective studies. The available evidence consistently supports a single 15 Gy fraction as an effective and efficient method of dose escalation, while two-fraction regimens ($2 \times \sim 9$ Gy) remains appropriate in selected clinical scenarios.

Summary of evidence

Miszczyk *et al.* [8]: This large retrospective Polish cohort of intermediate- and high-risk patients demonstrated that single-dose of 15 Gy HDR-BT boost after EBRT significantly improved OS and bFFS, with acceptable toxicity.

Hoskin *et al.* [56]: This randomized phase III trial comparing EBRT alone vs. EBRT + HDR-BT boost using $2 \times$

8.5 Gy (single-implant), showed a significant improvement in long-term relapse-free survival using HDR-BT, without an increase in severe GU/GI toxicity, establishing the oncologic benefits of two-fraction regimen.

Morton *et al.* [62]: A comparison of two sequential prospective phase II trials evaluating a 15 Gy \times 1 vs. a 2 \times 10 Gy HDR-BT boost, demonstrated similarly high 5-year bRFS (95-98%) and comparable toxicity and quality of life. These results support the effectiveness and practicality of the single-fraction schedule.

Crook *et al.* [63]: Long-term comparative outcomes of HDR vs. uLDR boost indicated excellent biochemical control and favorable functional recovery with HDR. Importantly, the HDR boost dose was 15 Gy, highlighting the evidence of supporting this schedule in contemporary clinical practice.

Schweizer *et al.* [64]: A protocol-based real-world cohort treated with EBRT 50.4 Gy followed by 2 \times 9-9.5 Gy HDR-BT boost, reported a 7-year bRFS of ~85% and low \geq G3 late toxicity (~4%), supporting the safety and efficacy of two-fraction regimen within the 9 Gy range.

Helou *et al.* [65]: A comparative analysis of 1 \times 15 Gy vs. 2 \times 10 Gy showed excellent long-term biochemical control in both arms (5-year bRFS ~97% vs. ~93%; $p = 0.995$), with no clinically meaningful differences in toxicity, confirming the durability of single-fraction approach. Also, contemporary guidelines, including NCCN [6] and the Patel *et al.* consensus [66], recognized both 1 \times 15 Gy and two-fraction (8.5-10 Gy) HDR-BT boost schedules as standard options.

Recommendation 22

Preferred regimen: 1 \times 15 Gy.

Is recommended as the standard schedule for most patients due to logistical simplicity and strong evidence supporting its effectiveness for bRFS and OS.

Alternative option: 2 \times ~9 Gy (8.5-10 Gy).

Is considered when a single 15 Gy fraction may increase the risk of toxicity to organs at risk, or when specific clinical indications favor a two-fraction approach.

Quality of evidence:

1 \times 15 Gy: High;

2 \times ~9 Gy: Moderate/High.

Strength of recommendation:

1 \times 15 Gy: Strong (preferred regimen);

2 \times 9 Gy: Conditional (appropriate alternative in selected clinical cases).

Rationale: Evidence from prospective and retrospective studies show that 1 \times 15 Gy approach provides oncologic outcomes comparable with multi-fraction regimens indicating added logistical advantages, while 2 \times ~9 Gy remains a safe alternative when a single-fraction dosing is less suitable.

A strong consensus was reached.

Use of ADT in combination with HDR-BT boost

The use of androgen deprivation therapy (ADT) in combination with HDR-BT boost has been extensively investigated in the context of improving oncological outcomes. ADT may enhance the efficacy of radiotherapy by

reducing tumor volume, increasing radiosensitivity of cancer cells, and reducing the risk of microscopic metastatic disease.

Summary of evidence

Hoskin *et al.* [56]: In this study, most patients had intermediate- or high-risk disease. ADT was recommended for 6 months in intermediate-risk and up to 3 years in high-risk patients, with approximately 75-77% of patients in both arms receiving ADT. In multivariable analysis, both the treatment arm and the use of ADT were independent predictors of relapse, indicating that HDR-BT boost provides an additional independent improvement in biochemical control when used together with ADT.

Jackson *et al.* [67]: This network meta-analysis included nine randomized trials: six comparing EBRT \pm ADT ($n = 4,663$) and three comparing EBRT \pm BT boost ($n = 718$). Overall, 84% of patients had intermediate- or high-risk disease. The addition of ADT to EBRT significantly improved OS compared with EBRT alone, whereas the addition of a BT boost did not significantly improve OS. In a network comparison, EBRT + ADT was superior to EBRT + BT boost without ADT, with a 88% probability that EBRT + ADT yields better OS. The authors concluded that omitting ADT in men with intermediate- and high-risk PCa treated with EBRT + BT boost may lead to inferior survival, and that ADT should remain a critical component of treatment regardless of the radiotherapy technique.

Keyes *et al.* [51]: This systematic review of the available literature concluded that the addition of ADT to BT-based regimens can improve biochemical control in patients with UIR and HR disease. Although the evidence was largely retrospective and heterogeneous in terms of ADT duration and BT technique, several included series reported approximately a 10-15% absolute improvement in biochemical control when ADT was combined with BT-based dose escalation. The study emphasized that the benefit appears most relevant in patients with high-risk features, while the role of ADT in lower-risk profiles remains uncertain.

TROG/RADAR trial [68]: In high-risk patients treated with EBRT (with or without BT boost), extending ADT from 6 to 18 months reduced the risk of metastatic progression, irrespective of radiation dose. Patients who received a BT boost, including HDR-BT, also benefited from longer ADT duration, supporting the use of prolonged ADT in dose-escalated settings.

NCCN guidelines [6]: NCCN recommended 4-6 months of ADT for intermediate-risk patients treated with EBRT + BT, and 12-36 months of ADT for patients with high- and very-high-risk (vHR) disease receiving definitive radiotherapy, including combined EBRT + BT.

Comments on NCCN recommendations

It should be emphasized that the NCCN recommendation for 4-6 months of ADT administration in intermediate-risk patients receiving EBRT + BT boost was largely based on extrapolation from trials assessing ADT with

EBRT alone. Pivotal trials underpinning these guidelines, such as RTOG 9408 [69], EORTC 22991 [70], and D'Amico *et al.* studies [71, 72], evaluated the addition of short-term ADT to EBRT without inclusion of BT. There is a lack of direct randomized evidence specifically assessing the combination of HDR-BT boost + ADT in intermediate-risk (especially UIR) patients. Consequently, clinicians should be aware of the extrapolative nature of these recommendations and individualize decision-making, particularly in UIR patients, balancing potential oncological benefits against ADT-related toxicity and associated comorbidities.

Recommendation 23

Patients with HR and vHR disease:

In patients receiving EBRT + HDR-BT boost, the addition of ADT is strongly recommended. A total ADT duration of 12-24 months is advised to improve survival outcomes and reduce the risk of disease progression.

Patients with UIR disease:

The decision to add ADT and define its duration should be individualized. Potential benefits of ADT must be carefully weighed against its side effects and impact on quality of life.

Quality of evidence:

HR and vHR groups: High;

UIR group: Low to moderate.

Strength of recommendation:

HR and vHR groups: Strong;

UIR group: Conditional.

Rationale: Randomized and meta-analytic data support the survival benefit of combining ADT with EBRT + HDR-BT boost in HR/vHR disease, while limited and extrapolated evidence in UIR patients necessitates individualized decision-making.

A strong consensus was reached.

Target volume definition and organs at risk with recommended dose constraints

Accurate delineation of clinical target volume (CTV) and OARs is essential for optimal HDR-BT treatment planning. Precise contouring enables high-dose coverage of the tumor while minimizing toxicity to adjacent structures.

Clinical target volume (CTV)

Although final CTV and OARs delineation is performed after HDR-BT needle implantation to account for the true implant geometry and resulting dose distribution [4, 14, 73], pre-implant contouring of all relevant structures using high-quality TRUS is strongly recommended. This is particularly important because ultrasound image quality often degrades after needle insertion, making it more difficult to precisely visualize the prostate boundaries and neighboring OARs.

Baseline CTV definition

CTV should include the entire prostate gland plus a 2-mm pericapsular margin [73]. When ECE or SVI is

suspected on imaging (mpMRI or PSMA-PET), these regions must be incorporated into CTV [4, 14].

Additional sub-volumes (CTV2, CTV3, etc.)

These may include intraprostatic or periprostatic regions corresponding to areas of higher tumor burden, identified using advanced imaging (e.g., mpMRI, MR spectroscopy, PSMA-PET). In selected cases, targeted dose escalation to these sub-volumes may be considered [4, 73].

Planning target volume (PTV)

Some centers treat a CTV as a PTV; however, contemporary clinical practice recognizes additional uncertainties related to:

- Needle reconstruction accuracy;
- Bladder and rectal filling variation;
- Prostate oedema.

If the initial 2-mm margin accounts only for microscopic spread, an additional 1-2 mm may be applied to create a PTV [73, 74].

Recommendation 24

The CTV should include the entire prostate gland plus a 2-mm pericapsular margin (excluding OARs). This margin may be expanded when ECE or SVI is present. Contouring should be performed both before and after implantation. Pre-implant: To accurately define anatomy on ultrasound; Post-implant: To reflect the true anatomy after implantation, needle geometry, and to optimize dose distribution. Final treatment planning and dose optimization should be based on post-implant contouring.

Key dosimetric parameters for CTV

$V_{100} \geq 95\%$ and $D_{90} \geq 100\%$ of the prescription dose ensure adequate tumor coverage [14, 17]. V_{150} and V_{200} (volumes receiving $\geq 150\%$ or $\geq 200\%$ of the prescription dose) should remain controlled ($V_{150} < 40\%$, $V_{200} < 15\%$) to maintain dose homogeneity and reduce toxicity [49, 75].

Quality of evidence: Moderate.

Strength of recommendation: Strong.

Rationale: Precise CTV definition and adherence to dosimetric parameters ensure reliable tumor coverage and acceptable toxicity, supported by consistent clinical experience and international standards.

A strong consensus was reached.

Organs at risk and dose constraints

Toxicity involving the urinary tract and rectum is a major determinant of quality of life after prostate radiotherapy [76]. In HDR-BT, the rectal wall and urethral dose tolerances frequently limit dose delivery [4]. Therefore, precise delineation and dose monitoring of these structures are essential.

The anterior rectal wall and urethra represent the primary OARs in HDR-BT, which must always be contoured. Additional structures, such as the bladder neck, penile bulb, and neurovascular bundles (NVBs), may also influence treatment-related toxicity, although formal dose constraints have not yet been established [77].

In the absence of robust prostate-specific data, dose constraints for certain OARs may be guided by radiobiological experience from gynecological BT [3, 4, 78], particularly for pelvic structures, with shared anatomical and tolerance characteristics.

For HDR-BT boost delivered in combination with EBRT, the safest strategy is to use the equivalent dose in 2-Gy fractions (EQD₂), and to assess the cumulative OAR dose from both treatment modalities [4].

Additional OARs

Bladder neck: In uLDR-BT, bladder-neck D_{2cm³} has been shown to predict GU toxicity [79], while in HDR-BT, this association has not been consistently observed [80]. Nevertheless, the bladder neck remains a structure of interest, particularly in prospective studies, while ongoing monitoring of the dose to this region is advisable.

Penile bulb: Higher dose to the penile bulb correlates with erectile dysfunction in EBRT series [81]. Although there are no validated HDR-BT dose constraints for this structure; the suggested thresholds include D_{60-70%} < 70 Gy EQD₂ associated with a < 55% risk of severe erectile dysfunction [82]. Further validation is required before these limits can be adopted as formal constraints.

NVBs: No formal dose constraints have been defined. Contouring remains optional, and is most relevant for research protocols or selected clinical scenarios, in which erectile function preservation is prioritized.

Recommendation 25

General contouring principles:

The rectal wall and urethra should be meticulously contoured. Each structure should include a 5-mm cranio-caudal extent of organ tissue immediately adjacent to the CTV/PTV. Urethral contouring on axial images should encompass the Foley catheter with a 1-mm margin.

Contouring of additional structures, particularly the bladder neck, is recommended.

Quality of evidence:

Rectal wall and urethra: Moderate;
Bladder neck, penile bulb, and NVB: Very low.

Strength of recommendation:

Rectal wall and urethra: Strong;
Bladder neck, penile bulb, and NVB: Weak.

Rationale: The rectal wall and urethra require strict contouring due to their dose-limiting role, while additional OARs are considered selective, given very low evidence and potential functional relevance.

A strong consensus was reached.

Recommendation 26

Recommended OARs dose constraints for HDR-BT

For both HDR-BT monotherapy and HDR-BT boost combined with EBRT, the safest approach is to use the

equivalent dose in 2-Gy fractions (EQD₂). The recommended EQD₂ limits are:

Rectum: D_{2cm³} ≤ 75 Gy (EQD₂).

Urethra: D_{0.1cm³} ≤ 120 Gy (EQD₂), D₁₀ < 120 Gy (EQD₂), and D₃₀ < 105 Gy (EQD₂).

Assuming an α/β ratio of 3 Gy for the rectum [83] and 5 Gy for the urethra [84], Table 3 presents regimen-specific percentage equivalents of the EQD₂ constraints defined above, expressed relative to the prescribed HDR-BT dose for the specified fractionation schedules.

Quality of evidence: Moderate.

Strength of recommendation: Strong.

Rationale: EQD₂-based limits provide the safest and most widely accepted approach to minimize GU/GI toxicity in HDR-BT alone or combined with EBRT, despite the absence of prospective validation.

A consensus was reached.

Areas without consensus and future directions

Despite achieving a high-level of agreement across most topics, a small number of issues did not reach the pre-defined threshold for consensus. These areas primarily concern domains, in which the available evidence is limited, heterogeneous, or based predominantly on expert opinion, and where the current body of literature does not allow the formulation of definitive recommendations. Divergence of views was most apparent in selected aspects of risk stratification, potential histopathological modifiers, and detailed considerations surrounding the use and timing of ADT in patients with intermediate-risk disease. A common feature of these topics is that their proposed clinical application currently exceeds the strength of existing evidence, and warrants further validation before they can be incorporated into standard practice.

In accordance with the methodological principles of the GRADE framework and Delphi process, items that did not achieve consensus were not included in the main recommendations. They should instead be regarded as areas requiring further investigation, particularly prospective multicenter research, refinement of pathological definitions, and a clearer understanding of the role of systemic therapies within specific risk sub-groups. Their identification highlights evidence gaps and underscores

Table 3. Regimen-specific percentage equivalents of EQD₂ organ at risk constraints from Recommendation 26, expressed relative to the prescribed HDR-BT dose

Structure/parameter	Monotherapy 2 × 13.5 Gy	Boost 15 Gy
Rectum D _{2cm³}	≤ 80%	≤ 65%
Rectum D _{0.1cm³}	< 100%	< 100%
Rectum D ₁₀	ALARA	< 75%
Urethra D _{0.1cm³}	≤ 130%	≤ 130%
Urethra D ₁₀	≤ 130%	≤ 130%
Urethra D ₃₀	≤ 120%	≤ 115%

ALARA – as low as reasonably achievable

key directions, where the evolution of both Polish and international prostate BT will be especially relevant.

This document represents the first national guidelines and expert consensus of the Polish Brachytherapy Society on radical HDR-BT for PCa. It was developed based on a harmonized review of the literature and a two-round Delphi process involving experts from multiple clinical centers across Poland. These recommendations mark an important step towards standardizing clinical practice, unifying qualification, treatment-planning pathways, and improving comparability of clinical outcomes between centers. We hope that these guidelines will contribute to enhancing the quality of patient care and that, as new scientific data emerge, they will be systematically updated and expanded, supporting the continued consolidation of national standards in prostate HDR-BT.

Future research should focus on prospective evaluation of HDR-BT monotherapy in unfavorable intermediate-risk patients, optimization of androgen deprivation therapy duration in combination with HDR-BT boost, and further refinement of dose constraints and target volume definition based on modern imaging and treatment planning techniques. Additionally, studies evaluating the role of HDR-BT in node-positive disease and integration with emerging systemic therapies, are warranted. These efforts will be essential to further strengthen the evidence base and support continued evolution of clinical practice.

Further prospective studies are warranted to strengthen the evidence base in selected clinical scenarios, where current recommendations rely on limited or extrapolated data, particularly HDR-BT monotherapy in UIR patients, optimal integration and duration of ADT, and the role of HDR-BT boost in node-positive disease patients.

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