Dosimetric Analysis of HDR Brachytherapy Plus Ultra-Hypofractionated Pelvic RT for High-Risk Prostate Cancer

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ABSTRACT

Purpose: To evaluate dosimetric characteristics and biological dose delivered via abbreviated regimen combining single-fraction HDR brachytherapy (15 Gy) with ultra-hypofractionated elective pelvic radiation therapy (ePUHRT, 25 Gy in 5 fractions) for unfavorable intermediate and high-risk prostate cancer patients.

Materials/Methods: Patients with unfavorable intermediate to very high-risk prostate cancer enrolled in an IRB-approved phase II trial underwent real-time transperineal ultrasound-guided HDR brachytherapy with hyaluronic acid rectal spacer placement, followed by fiducial marker implantation and highly conformal VMAT-based ePUHRT delivered within 2–6 weeks. Biological dose (EQD2) was calculated using α/β ratios of 1.5 Gy for prostate and 3 Gy for organs at risk (OAR). Dosimetric parameters were evaluated for protocol constraint compliance.

Results: Ten high-risk prostate cancer patients (mean prostate volume 41.5 ± 9.8 cc) completed treatment between March and November 2025. HDR brachytherapy achieved excellent target coverage and organ sparing, with mean prostate V100 of 95.9 ± 0.8%, rectum V75 of 0.44 ± 0.32 cc, and urethra D10 of 112.1 ± 1.9%. All patients met key prostate and rectal constraints, and 90% achieved all protocol criteria. ePUHRT plans demonstrated robust coverage (mean PTV 858.0 ± 120.2 cc; V100 98.2 ± 1.2%; D99 99.5 ± 0.7%) with substantial OAR sparing. Mean rectum, bladder, and bowel V25 values were 3.1%, 5.8%, and 2.6%, respectively, corresponding to 61–83% below protocol limits. Composite biological dose analysis confirmed a total prostate EQD2 of 117.1 Gy_2 (HDR 70.7 Gy_2 + ePUHRT 46.4 Gy_2), comparable to ASCENDE-RT, delivered over a median of 44 days with 100% treatment completion.

Conclusion: This abbreviated regimen with an HA rectal spacer and fiducial-based motion management achieves biological dose escalation comparable to conventional 6-week therapy, with excellent dosimetric feasibility and organ-at-risk sparing. The consistent achievement of stringent protocol constraints with substantial safety margins supports continued clinical investigation, with outcome and toxicity analyses ongoing.

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INTRODUCTION

Dose escalation improves biochemical control in unfavorable intermediate- and high-risk prostate cancer but is traditionally delivered with prolonged external beam courses and combined-modality regimens that impose substantial treatment burden. Building on evidence supporting single-fraction 15 Gy HDR brachytherapy boosts and emerging data for 5-fraction pelvic SBRT regimens, an abbreviated protocol that combines single-fraction HDR brachytherapy (15 Gy) with elective pelvic ultra-hypofractionated radiation therapy (ePUHRT, 25 Gy in 5 fractions) was designed. This study reports the dosimetric characteristics and composite biological dose of this regimen, with the goal of achieving ASCENDE-RT–level dose escalation within a substantially shortened overall treatment course while maintaining stringent organ-at-risk (OAR) sparing and clinical feasibility.

METHODS AND MATERIALS

Patients with unfavorable intermediate to high-risk prostate cancer were enrolled on an IRB-approved phase II trial and treated with a combined HDR–ePUHRT protocol. All patients first underwent real-time, transperineal ultrasound-guided HDR brachytherapy delivering 15 Gy in a single fraction to the prostate, with hyaluronic acid (HA) rectal spacer placement to reduce rectal dose. This was followed by fiducial marker implantation and highly conformal VMAT-based ePUHRT to the prostate, seminal vesicles, and elective pelvic nodal volumes (25 Gy in 5 fractions), initiated 2–6 weeks after HDR.

HDR and ePUHRT plans were generated to meet strict protocol constraints for target coverage and OAR sparing. Prostate and OAR dosimetry were recorded using standard parameters including prostate V100, rectum V75, urethra D10 (HDR), and pelvic PTV V100/D99 and rectum/bladder/bowel V25 (ePUHRT). Biological dose was calculated as EQD2 using an α/β of 1.5 Gy for prostate and 3 Gy for OARs, and composite prostate EQD2 from both HDR and ePUHRT components was compared to established dose-escalation regimens such as ASCENDE-RT.

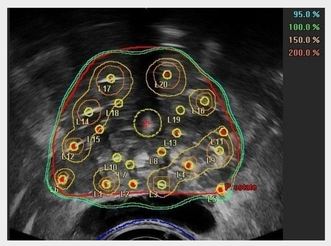

Figure 1. An US image shows the HA rectal spacer displacing the rectum (blue) posteriorly away from the high-dose region. For a 15 Gy prostate HDR treatment, 95%–200% isodose lines are displayed.

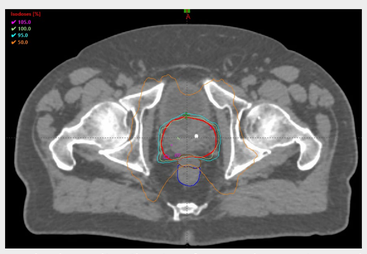

Figure 2. Example dose distribution from volumetric arc therapy plans delivering 25 Gy in five fractions. 50%–105% isodose lines are displayed.

RESULTS

Ten high-risk prostate cancer patients completed the combined regimen between March and November 2025, with a mean prostate volume of 41.5 ± 9.8 cc. HDR brachytherapy produced excellent target coverage and organ sparing, with mean prostate V100 of 95.9 ± 0.8%, rectum V75 of 0.44 ± 0.32 cc, and urethra D10 of 112.1 ± 1.9%; all patients met key prostate and rectal constraints, and 90% met all protocol criteria. The subsequent ePUHRT plans demonstrated robust coverage of a mean pelvic PTV of 858.0 ± 120.2 cc, with V100 of 98.2 ± 1.2% and D99 of 99.5 ± 0.7%

OAR exposure during ePUHRT remained well below protocol limits, with mean rectum, bladder, and bowel V25 values of 3.1%, 5.8%, and 2.6%, respectively, corresponding to reductions of 61–83% relative to allowable thresholds. Composite radiobiological analysis yielded a total prostate EQD2 of 117.1 Gy_2 (HDR 70.7 Gy_2 + ePUHRT 46.4 Gy_2), comparable to ASCENDE-RT–level dose escalation, while the entire regimen was delivered in 6 fractions over a median of 44 days with a 100% treatment completion rate.

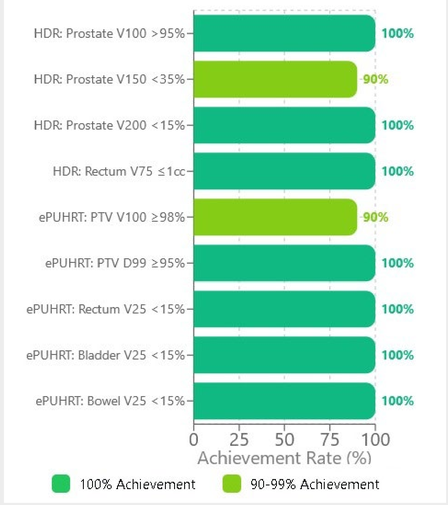

Figure 3 summarizes the primary dosimetric and clinical feasibility findings. (A) Shows 90-100% achievement of all protocol dosimetric constraints across HDR brachytherapy and ePUHRT components (N=10 patients).

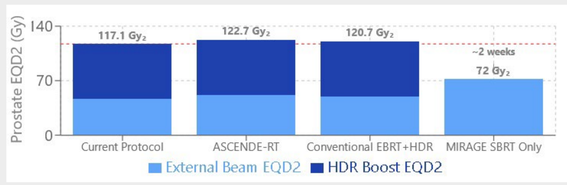

Figure 4 demonstrates biological dose equivalence of current ultra-hypofractionated protocol (117.1 Gy_2) to established dose-escalation regimens while maintaining abbreviated treatment course. EQD2 calculated using α/β = 1.5 Gy for prostate cancer patients.

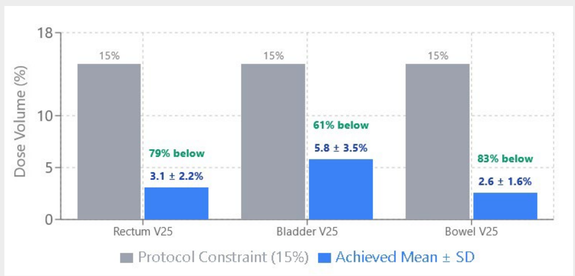

Figure 5 highlights exceptional OAR sparing including rectum V25 with mean doses substantially below protocol thresholds, suggesting superior therapeutic ratio compared to conventional fractionation.

DISCUSSION

This study provides a comprehensive dosimetric and radiobiological evaluation of combining single-fraction 15 Gy HDR brachytherapy with 5-fraction pelvic ePUHRT for unfavorable intermediate- and high-risk prostate cancer. The protocol achieved high rates (90–100%) of dosimetric constraint compliance across HDR and ePUHRT components, with reproducible planning performance across a broad range of prostate volumes (28–59 cc) and consistently low composite OAR doses, supporting a favorable therapeutic ratio. The total prostate EQD2 of 117.1 Gy_2 approximates that of dose-escalation regimens such as ASCENDE-RT, yet is delivered in only six fractions over a median of 44 days, suggesting meaningful reductions in treatment burden, travel demands, and time away from work, particularly relevant for rural or underserved patients.

The incorporation of an HA rectal spacer, real-time ultrasound-guided HDR planning, and fiducial-based VMAT ePUHRT enabled stringent rectal and bladder sparing, with rectal, bladder, and bowel V25 values substantially below protocol thresholds by 61–83%. This high level of OAR protection, combined with consistent protocol adherence and 100% treatment completion, establishes practical benchmarks for clinical implementation of this abbreviated regimen. Ongoing follow-up will determine whether the favorable dosimetric and radiobiological profile translates into comparable disease control and acceptable toxicity relative to conventional 6-week courses, and future work should explore patient-reported outcomes and health system impacts such as resource utilization and access.

CONCLUSIONS

An abbreviated regimen combining single-fraction 15 Gy HDR brachytherapy with 25 Gy in 5-fraction pelvic ePUHRT, delivered with HA rectal spacer and fiducial-based motion management, achieved biological dose escalation (EQD2 117.1 Gy_2) comparable to established 6-week protocols while maintaining excellent target coverage and robust OAR sparing. The high rate of dosimetric constraint compliance, broad applicability across prostate volumes, and 100% treatment completion support the dosimetric feasibility and practicality of this approach. These findings justify continued clinical investigation, with ongoing outcome and toxicity analyses needed to confirm long-term safety and efficacy and to define the role of this ultra-hypofractionated combined-modality strategy in routine practice.

REFERENCES

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