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Original Research Article

Treatment planning comparison of high-dose-rate brachytherapy vs. robotic and conventional stereotactic body radiotherapy for ultrahypofractionated treatment of prostate cancer

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ABSTRACT

Background and purpose: Ultrahypofractionated radiation therapy is increasingly used in the treatment of prostate cancer. High-dose-rate brachytherapy (HDR-BT) and stereotactic body radiotherapy (SBRT) are representative methods of ultrahypofractionation. This study was performed to compare clinically applied treatment plans for patients who had been treated using HDR-BT vs. conventional or robotic SBRT.

Materials and methods: Calculated dose-volume indices between HDR-BT without a perirectal spacer (n = 20), robotic SBRT without a spacer (n = 40), and conventional (non-robotic) SBRT with a spacer (n = 40) were compared. Percentages against the prescription dose regarding the planning target volume (PTV), bladder, rectum, and urethra were statistically compared.

Results: The D50% of the PTV with HDR-BT (140.5% ± 4.9%) was significantly higher than that with robotic or conventional SBRT (116.2% ± 1.6%, 101.0% ± 0.4%, $p < 0.01$). The D2cm^3 of the bladder with HDR-BT (65.6% ± 6.4%) was significantly lower than those with SBRT (105.3% ± 2.9%, 98.0% ± 1.3%, $p < 0.01$). The D2cm^3 of the rectum with HDR-BT (60.6% ± 6.2%) was also significantly lower than those with SBRT (85.1% ± 8.8%, 70.4% ± 9.6%, $p < 0.01$). By contrast, the D0.1cm^3 of the urethra with HDR-BT (117.1% ± 3.6%) was significantly higher than those with SBRT (100.2% ± 0.7%, 104.5% ± 0.6%, $p < 0.01$).

Conclusions: HDR-BT could administer a higher dose to the PTV and a lower dose to the bladder and rectum, at the cost of a slightly higher dose to the urethra compared with SBRT.

1. Introduction

Radiation therapy (RT) is a standard treatment option for localized or locally advanced prostate cancer with curative intent [1]. RT consists of external beam radiation therapy (EBRT) and brachytherapy (BT). In the history of BT, low-dose-rate BT initially prevailed widely, whereas high-dose-rate (HDR) BT has gained momentum recently. HDR-BT was first used as a boost in combination with EBRT; however, HDR-BT is now also used as monotherapy. HDR-BT monotherapy is an ultimate form of hypofractionation [2]. The first reported HDR-BT monotherapy regimen comprised eight to nine fractions of 6 Gy per fraction [3] followed by other regimens with a smaller number of fractions and a larger dose per fraction [4–6]. Currently, the most widely accepted regimen is two fractions of 13 to 13.5 Gy per fraction [7,8].

In the field of EBRT, a dose of 1.8 to 2 Gy per fraction was used for several decades. The trend recently changed toward hypofractionation. Moderate hypofractionation using 2.4 to 3.4 Gy per fraction [9] has become a standard treatment option [10,11]. The next step was

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ultrahypofractionation, defined as ≥ 5 Gy per fraction [9]. This regimen is now used worldwide, although establishing evidence of its non-inferiority is ongoing [12,13]. The typical dose fractionation regimen is five fractions of 7.25 to 8 Gy per fraction [1,9]. Hence, one may reasonably presume that the most advanced form of hypofractionated RT for prostate cancer as of today is two-fraction HDR-BT monotherapy or five-fraction SBRT.

Several reports have compared treatment planning between HDR-BT monotherapy and SBRT [14–16]. Fuller et al. [14] compared their robotic SBRT treatment planning to "virtual HDR" planning, where HDR-BT had not actually been performed. Later, Chatzikonstantinou et al. [15] performed a similar study, and Spratt et al. [16] compared their HDR-BT treatment planning with virtual SBRT planning. Those reports included one real dose plan and another virtual plan that was not used for the real treatment. Additionally, SBRT could be delivered by a robotic linear accelerator or by a conventional (non-robotic) one, and the dose distribution of each might differ from each other. The aim of this study was to determine whether there are significant differences in dose-volume indices in the real dose plans between these treatment options that would explain intrinsic differences between the treatments and make it easier to interpret future clinical results.

2. Materials and methods

2.1. Patients

This retrospective study was approved by the institutional review boards of the two participating institutions, and the study was conducted in 2022. All 100 patients had biopsy-proven adenocarcinoma; received staging workups comprising bone scintigraphy, computed tomography (CT), and magnetic resonance imaging (MRI); and were diagnosed with T1c-T3aN0M0 prostate cancer. Intermediate- and high-risk patients received 6 months of androgen deprivation therapy (ADT) before RT, and high-risk patients also received 18 months of adjuvant ADT (total ADT duration: 2 years). Patients in one institution received either HDR-BT monotherapy (n = 20) or conventional SBRT (n = 40).

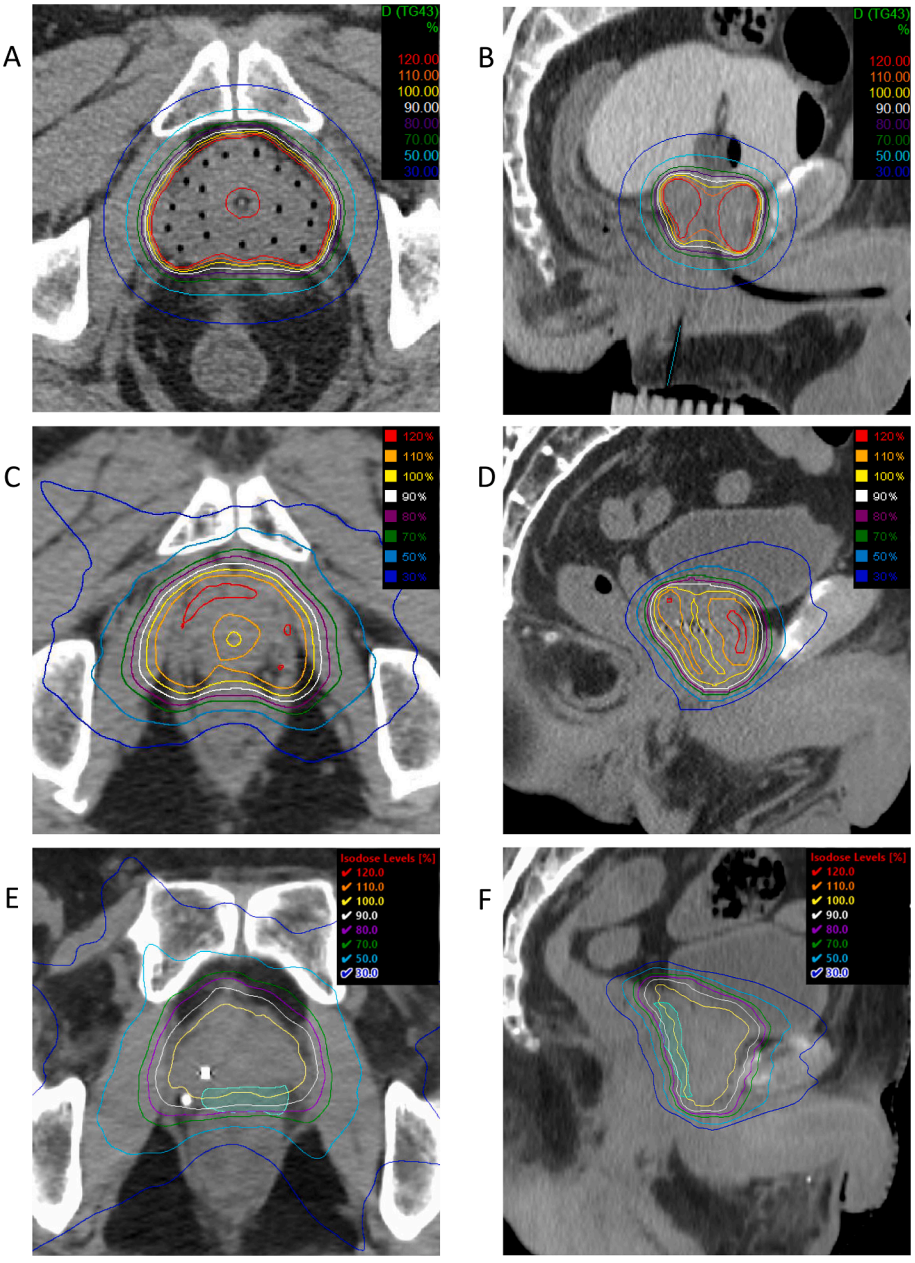

Fig. 1. Representative dose distributions of: (A) high-dose-rate brachytherapy as monotherapy, transverse section, and (B) sagittal section; (C) robotic stereotactic body radiation therapy (SBRT), transverse section, and (D) sagittal section; (E) conventional linear accelerator SBRT, transverse section, and (F) sagittal section. The red isodose line indicates 120% of the prescription dose, orange: 110%, yellow: 100%, white: 90%, purple: 80%, green: 70%, cyan: 50%, and blue: 30%. Light cyan in (E) and (F) represents a perirectal spacer. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Patients in the other institution received robotic SBRT (n = 40). Patients who did not choose either HDR-BT or SBRT (who were not enrolled in this study) received moderately hypofractionated intensity-modulated RT (IMRT) with 70 Gy in 28 fractions (or iodine-125 low-dose-rate BT, if indicated). Data for consecutive patients treated with HDR-BT or conventional SBRT were collected from February 2018 to June 2022, excluding data for six SBRT patients who did not undergo perirectal hydrogel spacer injection for various reasons. Forty patients were treated with robotic SBRT, excluding one patient who underwent spacer injection. The 2-year preliminary clinical results of robotic SBRT, including for these 40 patients, have been published elsewhere [17]. The methods for the three ultrahypofractionated RTs are described below.

2.2. HDR-BT monotherapy

HDR-BT was performed as monotherapy using an HDR iridium-192 source equipped in an HDR unit (microSelectron HDR; Elekta, Stockholm, Sweden). A total of 27 Gy in two fractions was administered in two separate implants under general anesthesia with a 2- to 4-week interval. Typically, 13 outer plastic needles and 4 inner plastic needles were inserted under transrectal ultrasound guidance [3,18]. Next, an in-room CT scanner was used to ensure that the needles were inserted to just beneath the bladder lumen, and the treatment planning was based on the CT images. We did not perform MRI for treatment planning. The clinical target volume (CTV) was defined as the prostate gland plus a 3-mm margin except on the rectal side, and 10% to 75% of the volume of the seminal vesicles was included in the CTV according to the risk classification. The planning target volume (PTV) was equivalent to the CTV. The dose-volume constraints for each organ are shown in Supplemental Table S1, and a representative dose distribution is shown in Fig. 1A and B. The treatment planning was performed using Oncentra Brachy (Elekta). No patients underwent perirectal hydrogel spacer injection.

2.3. Robotic SBRT

The CyberKnife robotic SBRT method has been described elsewhere [17]. Briefly, three fiducial gold markers were implanted in the prostate. CT and MRI were performed on the same day for treatment planning. The CTV was defined as the prostate gland plus a 3-mm margin excluding the bladder and rectum, and the proximal 1 cm of the seminal vesicles was included in intermediate- and high-risk patients. The PTV was defined as the CTV plus a 2-mm margin in all directions. Notably, the urethra was identified in the treatment planning MRI and CT, and the planning goal for the urethra was set at 95% to 102% of the prescription dose. We used the Multiplan treatment planning system (Accuray, Inc., Sunnyvale, CA). The prescription dose was 36.25 Gy in five fractions. It was defined as D95 to the PTV, with an adjustment of 75% to 85% of the peak dose to meet the dose constraints and a PTV minimum dose of greater than 70% of the peak dose. The real peak dose (D2%) in the PTV ranged from 116% to 126% of the prescription dose. The dose-volume constraints for each organ are shown in Supplemental Table S1, and a representative dose distribution is shown in Fig. 1C and D. Irradiation was performed using the CyberKnife M6 (Accuray) on five consecutive weekdays. Before every irradiation, CT was performed to confirm the presence of a full bladder and empty rectum. During irradiation, the prostate position was checked and corrected every 20 to 60 s using fiducial marker tracking. No patients underwent perirectal hydrogel spacer injection.

2.4. Conventional SBRT

The TrueBeam conventional SBRT method was performed in accordance with our experience with more than 500 patients who received IMRT using 2 Gy per fraction [19]. Patients also received daily enemas before irradiation as well as portable ultrasonography to check for a full bladder. Cone-beam CT was performed daily, and the position of the fiducial marker was checked before, during, and after every irradiation using ExacTrac (Brainlab AG, Munich, Germany). Approximately 1 month before irradiation, one fiducial gold marker was implanted in the prostate, and a perirectal hydrogel spacer (SpaceOAR Hydrogel; Boston Scientific Corporation, Marlborough, MA) was injected. Two weeks later, CT and MRI were performed on the same day for treatment planning. The CTV was defined as the prostate gland plus a 3-mm margin excluding the bladder and rectum, with the proximal 2 cm of the seminal vesicles included in intermediate- and high-risk patients. The PTV was defined as the CTV plus a 4-mm margin in all directions. We used the Eclipse treatment planning system (Varian Medical Systems, Inc., Palo Alto, CA). We administered a total dose of 36.25 Gy in five fractions to D98 of the CTV, while keeping D95 of the PTV at 90% of the prescription dose and D50 of the PTV at 100% of the prescription dose. Dose-volume constraints for each organ are shown in Supplemental Table S1, and a representative dose distribution is shown in Fig. 1E and F. The treatment was delivered using a TrueBeam linear accelerator (Varian Medical Systems). Irradiation was performed on five consecutive weekdays.

2.5. Analysis

As mentioned above, one HDT-BT patient had received two implants, each with a different treatment plan. However, those two plans in a single patient might not be considered statistically independent. Therefore, the dose-volume indices of the two implants in the same patient were simply totaled. We averaged the two curves in the cumulative dose-volume histogram of each implant; that is, we added the numbers of the Y-axis at any point of the X-axis and divided by two. Values in the HDR-BT column in Table 1 may be overestimations because hot spots would not have appeared in the same locations for the two implants.

Comparisons of each dose-volume parameter were performed using the two-sided *t*-test. When we compared three groups at once, we used one-way analysis of variance. Regarding repeated comparisons between the three groups (HDR-BT vs. robotic SBRT vs. conventional SBRT), p-values of < 0.01 were considered statistically significant.

3. Results

The results of the comparisons are shown as Fig. 2 in the form of dose-volume histograms, and as Table 1 with the numerical dose-volume indices, between HDR-BT without a spacer, robotic SBRT without a spacer, and conventional SBRT with a spacer. In Fig. 2A, it was visually confirmed that the higher dose than the prescription dose was administered into the CTV in the order of HDR-BT, robotic SBRT, and conventional SBRT. In Fig. 2B and C, the moderate to high dose to the blader and rectum was shown to be lower in HDR-BT than SBRT. Fig. 2D shows that the urethral dose in HDR-BT was higher than robotic SBRT.

As shown in Table 1, the PTV with conventional SBRT (89.3 ± 29.9 cm^3 (average ± standard deviation)) was significantly larger than that with robotic SBRT (51.6 ± 14.8 cm^3, $p < 0.01$), and that with robotic SBRT was significantly larger than that with HDR-BT (34.7 ± 7.7 cm^3, $p < 0.01$). These were in the same order as the width of the CTV-to-PTV margins of 4, 2, and 0 mm. In the reverse order, the D50% of the PTV with HDR-BT (140.5% ± 4.9%) was significantly higher than that with robotic SBRT (116.2% ± 1.6%, $p < 0.01$), and that with robotic SBRT was significantly higher than that with conventional SBRT (101.0% ± 0.4%, $p < 0.01$). The same trend was confirmed for the V100% and D90% of the PTV.

The dose-volume parameters for the bladder and rectum were consistently favorable for HDR-BT with statistical significance. The $D2cm^3$ of the bladder and rectum with HDR-BT (65.6% ± 6.4%, 60.6% ± 6.2%) were smaller than those with robotic SBRT (105.3% ± 2.9%, 85.1% ± 8.8%, both $p < 0.01$) and conventional SBRT (98.0% ± 1.3%,

Table 1
Comparison of the dose-volume indices between HDR-BT, robotic SBRT, and conventional SBRT with or without a perirectal spacer

	HDR-BT without spacer	Robotic SBRT without spacer	Conventional SBRT with spacer	p (HDR-BT vs. Robotic)	p (HDR-BT vs. Conv.)	p (Robotic vs. Conv.)	p (all)
N	20*	40	40				
Prostate volume (cm^3)	N.A.	27.9±11.1	31.2±15.3	N.A.	N.A.	0.21	N.A.
CTV (cm^3)	34.7±7.7	38.9±12.7	50.5±21.1	0.13	<0.01	<0.01	<0.01
PTV (cm^3)	34.7±7.7	51.6±14.8	89.3±29.9	<0.01	<0.01	<0.01	<0.01
PTV_V100% (%)	96.7±1.4	95.6±0.5	58.6±3.5	<0.01	<0.01	<0.01	<0.01
PTV_D90% (%)	111.4±3.4	103.8±0.6	92.6±0.6	<0.01	<0.01	<0.01	<0.01
PTV_D2% (%)	N.A.**	121.9±1.9	103.8±0.5	N.A.	N.A.	<0.01	N.A.
PTV_D50% (%)	140.5±4.9	116.2±1.6	101.0±0.4	<0.01	<0.01	<0.01	<0.01
PTV_Dmean (%)	N.A.***	114.1±1.4	99.3±0.4	N.A.	N.A.	<0.01	N.A.
PTV_D98% (%)	96.6±4.1	97.1±0.8	88.9±0.8	0.57	<0.01	<0.01	<0.01
BladderD1cm^3 (%)	71.8±6.7	109.8±2.7	99.6±0.8	<0.01	<0.01	<0.01	<0.01
BladderD2cm^3 (%)	65.6±6.4	105.3±2.9	98.0±1.3	<0.01	<0.01	<0.01	<0.01
BladderD5cm^3 (%)	54.5±6.2	93.1±5.0	92.1±3.2	<0.01	<0.01	0.31	<0.01
BladderV50% (cm^3)	7.4±2.9	12.8±3.9	28.6±10.1	<0.01	<0.01	<0.01	<0.01
BladderV100% (cm^3)	0.0±0.1	1.8±0.6	0.8±0.5	<0.01	<0.01	<0.01	<0.01
RectumD1cm^3 (%)	68.5±6.1	93.6±6.5	78.4±10.2	<0.01	<0.01	<0.01	<0.01
RectumD2cm^3 (%)	60.6±6.2	85.1±8.8	70.4±9.6	<0.01	<0.01	<0.01	<0.01
RectumD5cm^3 (%)	46.6±5.3	63.0±10.2	55.3±7.5	<0.01	<0.01	<0.01	<0.01
RectumV50% (cm^3)	4.2±1.5	16.4±3.7	6.5±2.1	<0.01	<0.01	<0.01	<0.01
RectumV100% (cm^3)	0.0±0.0	0.9±0.5	0.0±0.0	<0.01	0.13	<0.01	<0.01
UrethraD0.035cm^3 (%)****	119.6±4.1	101.0±0.7	104.7±0.6	<0.01	<0.01	<0.01	<0.01
UrethraD0.1cm^3 (%)****	117.1±3.6	100.2±0.7	104.5±0.6	<0.01	<0.01	<0.01	<0.01
UrethraV110% (cm^3)****	0.4±0.1	0.0±0.0	0.0±0.0	<0.01	<0.01	N.A.	<0.01
UrethraV125% (cm^3)****	0.0±0.0	0.0±0.0	0.0±0.0	0.01	0.01	N.A.	<0.01

Abbreviations: HDR-BT = high-dose-rate brachytherapy, SBRT = stereotactic body radiation therapy, CTV = clinical target volume, PTV = planning target volume. Note: Data are averages ± standard deviations. *Each value for the two implants in a single patient were totaled, and percentages against the total dose are shown. **Values were too high to calculate. ***The treatment planning system could not calculate Dmean. ****Because there was no urethral contour in the coventional SBRT plan, values for PTV were substituted.

70.4% ± 9.6%, both $p < 0.01$). The D1cm^3, D5cm^3, and V50% of the bladder and rectum showed the same trend.

The parameters for the urethra, by contrast, were unfavorable for HDR-BT. The D0.1cm^3 of the urethra with HDR-BT (117.1% ± 3.6%) was significantly higher than that with robotic SBRT (100.2% ± 0.7%, $p < 0.01$) and conventional SBRT (104.5% ± 0.6%, $p < 0.01$). This trend was confirmed also for the D0.035cm^3 of the urethra.

4. Discussion

We performed a comparative study of the real dose plans between HDR-BT monotherapy, robotic SBRT, and conventional SBRT for prostate cancer. To the best of our knowledge, this is the first report to directly compare these three methods of ultrahypofractionated RT, and we found a clear difference in dose-volume indices for bladder, rectum, urethra, and PTV between them.

Some reports have compared two methods, namely HDR-BT monotherapy and any type of SBRT, as already mentioned in the Introduction [14–16]. Two of these three studies showed a significantly lower dose to the rectum with HDR-BT than with SBRT [15,16], whereas the third study showed a similar dose [14]. Regarding the bladder dose, one study showed that HDR-BT was better [15], another showed that SBRT was better [14], and the third showed no significant difference between the methods [16]. Regarding the urethral dose, two of the studies suggested an advantage of SBRT compared with HDR-BT [14,15], whereas the third study did not indicate a significant difference between the methods [16]. Generally, intraprostatic doses were higher with HDR-BT than with SBRT in all three studies [14–16].

The results of the current study are similar to those of the three abovementioned studies. Regarding the bladder and rectum doses, HDR-BT was associated with statistically significantly lower doses than those with robotic SBRT and conventional SBRT. Only rectum V100% showed the same results with HDR-BT and conventional SBRT because both were 0.0 cm^3. This finding could be attributed to the use of a perirectal spacer in conventional SBRT. In contrast, the maximum dose to the urethra was statistically significantly higher with HDR-BT than with both SBRT methods. Intraprostatic doses (i.e., V100%, D90%, and D50% of the PTV) decreased obviously in the following order: HDR-BT, robotic SBRT, and conventional SBRT. Whether a higher dose than the prescription dose for PTV is beneficial or harmful is unknown, as Correa et al. [20] discussed as a matter of the greater heterogeneity in the dose distribution of HDR-BT. One may consider HDR-BT as a "universal boost," presuming a benefit with a higher dose in the PTV, on condition that the organs at risk (bladder, rectum, and urethra) are avoided, based on the positive results of the FLAME study [21]. A benefit could also be presumed on the basis of a uterine cervical cancer study in which an IMRT or SBRT boost was not a substitute for BT [22], or on the basis of the success of BT itself. However, such a presumption, if true, should be endorsed by clinical results; e.g., by showing that HDR-BT or HDR-like robotic SBRT with a heterogeneous dose distribution yields a better local control rate than conventional SBRT with a homogeneous dose distribution.

Comparing robotic SBRT with conventional SBRT was not the main subject of this study; however, this is an interesting issue. Robotic SBRT was intended to provide an HDR-like dose distribution, which meant significantly more volume receiving a higher dose than the prescription dose in the PTV, with statistically significant differences in all PTV-related indices (Table 1). For example, the PTV Dmean of robotic SBRT was 114%, while that of conventional SBRT was 99% of the prescription dose ($p < 0.01$). By contrast, all rectum-related conventional

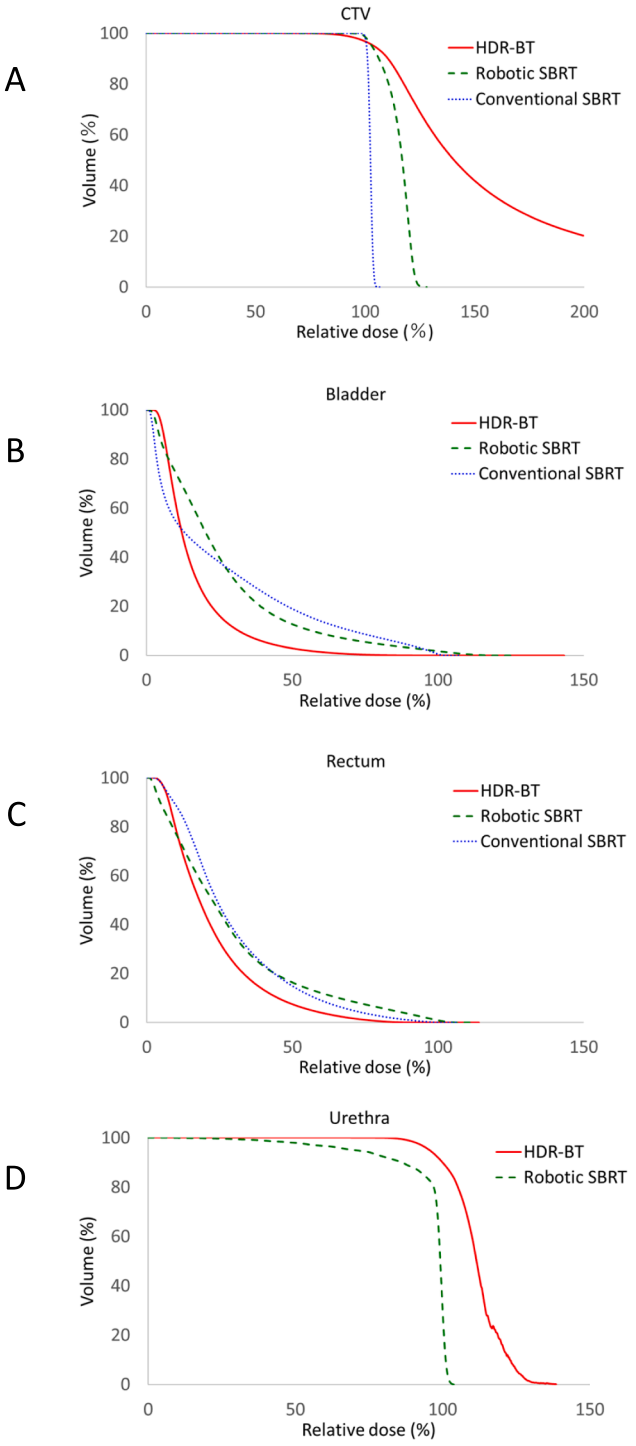

Fig. 2. Dose-volume histograms for the (A) clinical target volume (CTV), (B) bladder, (C) rectum, and (D) urethra. Each curve represents the average of the 40 implants of high-dose-rate brachytherapy (HDR-BT), of the 40 patients treated with robotic stereotactic body radiation therapy (SBRT), or of the 40 patients treated with conventional SBRT. Note that a perirectal spacer was used for the conventional SBRT cases only.

SBRT indices were significantly better than those of robotic SBRT, although the CTV-to-PTV margin of conventional SBRT (4 mm) was larger than that of robotic SBRT (2 mm). This could be attributed to the effect of the perirectal spacer used with conventional SBRT, consistent with a previous study [23]. The maximum urethral dose in robotic SBRT was constrained below 100% to 102% of the prescription dose, which resulted in a significantly lower urethral dose than the dose with HDR-BT. One may speculate that HDR-like robotic SBRT had superiority over the other two modalities because it was incorporating the benefits while ignoring the drawbacks of HDR-BT and conventional SBRT. This meant a moderate dose escalation in the PTV with robotic SBRT while keeping the urethral dose equal to the prescription dose.

Technological innovation, such as MRI-linear accelerator (MRI-linac), may cause a change in the treatment planning especially for SBRT. It was reported by den Hartogh et al. [24] that SBRT with focal ablative boosting using MRI-linac was feasible without deterioration of plan quality. Tetar et al. [25] and Yang et al. [26] reported that MRI-guided prostate SBRT with daily online plan adaptation was feasible by showing their practice strategy and successful experience. Willigenburg et al. [27] conducted a comparative planning study to evaluate the feasibility of delivering a single 19 Gy dose to a local recurrent prostate cancer lesion using a 1.5 Tesla MR-linac system. The simulated MR-linac plans were compared to clinically delivered focal salvage HDR-BT plans. They concluded that they could create an acceptable and comparable MR-linac plan for the majority of the patients who were actually treated with HDR-BT.

The major strength of this study is that it includes real dose plans from patients that were treated according to the plan. The authors emphasize that real dose plans were compared and that this was not a planning study. This may at the same time be a weakness of the study in that the three groups were not completely comparable. Notably, the patients treated with HDR-BT were suitable candidates for invasive procedures including general anesthesia, suggesting that they were healthier and younger than those treated with the other modalities. Only conventional SBRT patients had received perirectal hydrogel spacer injection, which made it difficult to interpret the differences in rectal dose-volume parameters. In addition, this study was solely a comparison of treatment planning and was not accompanied by clinical results. Differences in dose-volume indices by themselves are not fully meaningful unless clinical results verify differences in oncologic outcomes or toxicities. Other groups have begun studies involving such clinical comparisons, although there are few published reports to date [20,28,29], and the superiority or inferiority of HDR-BT or SBRT is unknown. It will take some years until our own clinical results are mature.

In conclusion, the current study clearly showed a difference in dose-volume parameters between HDR-BT and SBRT regardless of whether SBRT was used with a robotic chasing system or a perirectal spacer. HDR-BT without a spacer could yield a more favorable dose distribution, including a higher dose to the PTV and a lower dose to the bladder and rectum, at the cost of a slightly higher dose to the urethra. Future comparisons of mature clinical results are warranted.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.phro.2023.100445.

References

[1] National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN guidelines®). Prostate Cancer. Version 4.2022. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed on July 1, 2022.

[2] Zaorsky NG, Davis BJ, Nguyen PL, Showalter TN, Hoskin PJ, Yoshioka Y, et al. The evolution of brachytherapy for prostate cancer. Nat Rev Urol 2017;14:415–39. https://doi.org/10.1038/nrurol.2017.76.

[3] Yoshioka Y, Nose T, Yoshida K, Inoue T, Yamazaki H, Tanaka E, et al. High-dose-rate interstitial brachytherapy as a monotherapy for localized prostate cancer: treatment description and preliminary results of a phase I/II clinical trial. Int J Radiat Oncol Biol Phys 2000;48:675–81. https://doi.org/10.1016/s0360-3016(00)00687-8.

[4] Hauswald H, Kamrava MR, Fallon JM, Wang PC, Park SJ, Van T, et al. High-dose-rate monotherapy for localized prostate cancer: 10-year results. Int J Radiat Oncol Biol Phys 2016;94:667–74. https://doi.org/10.1016/j.ijrobp.2015.07.2290.

[5] Martinez A, Pataki I, Edmundson G, Sebastian E, Brabbins D, Gustafson G. Phase II prospective study of the use of conformal high-dose-rate brachytherapy as monotherapy for the treatment of favorable stage prostate cancer: a feasibility report. Int J Radiat Oncol Biol Phys 2001;49:61–9. https://doi.org/10.1016/s0360-3016(00)01463-2.

[6] Zamboglou N, Tselis N, Baltas D, Buhleier T, Martin T, Milickovic N, et al. High-dose-rate interstitial brachytherapy as monotherapy for clinically localized prostate cancer: treatment evolution and mature results. Int J Radiat Oncol Biol Phys 2013;85:672–8. https://doi.org/10.1016/j.ijrobp.2012.07.004.

[7] Hoskin P, Rojas A, Lowe G, Bryant L, Ostler P, Hughes R, et al. High-dose-rate brachytherapy alone for localized prostate cancer in patients at moderate or high risk of biochemical recurrence. Int J Radiat Oncol Biol Phys 2012;82:1376–84. https://doi.org/10.1016/j.ijrobp.2011.04.031.

[8] Morton G, McGuffin M, Chung HT, Tseng CL, Helou J, Ravi A, et al. Prostate high dose-rate brachytherapy as monotherapy for low and intermediate risk prostate cancer: efficacy results from a randomized phase II clinical trial of one fraction of 19 Gy or two fractions of 13.5 Gy. Radiother Oncol 2020;146:90–6. https://doi.org/10.1016/j.radonc.2020.02.009.

[9] Morgan SC, Hoffman K, Loblaw DA, Buyyounouski MK, Patton C, Barocas D, et al. Hypofractionated radiation therapy for localized prostate cancer: executive summary of an ASTRO, ASCO, and AUA evidence-based guideline. Pract Radiat Oncol 2018;8:354–60. https://doi.org/10.1016/j.prro.2018.08.002.

[10] Dearnaley D, Syndikus I, Mossop H, Khoo V, Birtle A, Bloomfield D, et al. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial. Lancet Oncol 2016;17:1047–60. https://doi.org/10.1016/S1470-2045(16)30102-4.

[11] Lee WR, Dignam JJ, Amin MB, Bruner DW, Low D, Swanson GP, et al. Randomized phase III noninferiority study comparing two radiotherapy fractionation schedules in patients with low-risk prostate cancer. J Clin Oncol 2016;34:2325–32. https://doi.org/10.1200/JCO.2016.67.0448.

[12] Widmark A, Gunnlaugsson A, Beckman L, Thellenberg-Karlsson C, Hoyer M, Lagerlund M, et al. Ultra-hypofractionated versus conventionally fractionated radiotherapy for prostate cancer: 5-year outcomes of the HYPO-RT-PC randomised, non-inferiority, phase 3 trial. Lancet 2019;394:385–95. https://doi.org/10.1016/S0140-6736(19)31131-6.

[13] Brand DH, Tree AC, Ostler P, van der Voet H, Loblaw A, Chu W, et al. Intensity-modulated fractionated radiotherapy versus stereotactic body radiotherapy for prostate cancer (PACE-B): acute toxicity findings from an international, randomised, open-label, phase 3, non-inferiority trial. Lancet Oncol 2019;20:1531–43. https://doi.org/10.1016/S1470-2045(19)30569-8.

[14] Fuller DB, Naitoh J, Lee C, Hardy S, Jin H. Virtual HDR CyberKnife treatment for localized prostatic carcinoma: dosimetry comparison with HDR brachytherapy and preliminary clinical observations. Int J Radiat Oncol Biol Phys 2008;70:1588–97. https://doi.org/10.1016/j.ijrobp.2007.11.067.

[15] Chatzikonstantinou G, Keller C, Scherf C, Bathen B, Köhn J, Tselis N. Real-world dosimetric comparison between CyberKnife SBRT and HDR brachytherapy for the treatment of prostate cancer. Brachytherapy 2021;20:44–9. https://doi.org/10.1016/j.brachy.2020.07.011.

[16] Spratt DE, Scala LM, Folkert M, Voros L, Cohen GN, Happersett L, et al. A comparative dosimetric analysis of virtual stereotactic body radiotherapy to high-dose-rate monotherapy for intermediate-risk prostate cancer. Brachytherapy 2013;12:428–33. https://doi.org/10.1016/j.brachy.2013.03.003.

[17] Ito M, Yoshioka Y, Takase Y, Suzuki J, Matsunaga T, Takahashi H, et al. Stereotactic body radiation therapy for Japanese patients with localized prostate cancer: 2-year results and predictive factors for acute genitourinary toxicities. Jpn J Clin Oncol 2021;51:1253–60. https://doi.org/10.1093/jjco/hyab094.

[18] Yoshioka Y, Suzuki O, Isohashi F, Seo Y, Okubo H, Yamaguchi H, et al. High-dose-rate brachytherapy as monotherapy for intermediate- and high-risk prostate cancer: clinical results for a median 8-year follow-up. Int J Radiat Oncol Biol Phys 2016;94:675–82. https://doi.org/10.1016/j.ijrobp.2015.05.044.

[19] Sasamura K, Soyano T, Kozuka T, Yuasa T, Yamamoto S, Yonese J, et al. Outcomes of intensity-modulated radiation therapy for intermediate- or high-risk prostate cancer: a single-institutional study. Jpn J Clin Oncol 2022;52:170–8. https://doi.org/10.1093/jjco/hyab167.

[20] Correa RJM, Morton G, Chung HT, Tseng CL, Cheung P, Chu W, et al. Two-fraction stereotactic ablative radiotherapy (SABR) versus two-fraction high dose rate (HDR) brachytherapy for localized prostate cancer: does dose heterogeneity matter? Radiother Oncol 2022;169:51–6. https://doi.org/10.1016/j.radonc.2022.02.007.

[21] Kerkmeijer LGW, Groen VH, Pos FJ, Haustermans K, Monninkhof EM, Smeenk RJ, et al. Focal boost to the intraprostatic tumor in external beam radiotherapy for patients with localized prostate cancer: results from the FLAME randomized phase III trial. J Clin Oncol 2021;39:787–96. https://doi.org/10.1200/JCO.20.02873.

[22] Gill BS, Lin JF, Krivak TC, Sukumvanich P, Laskey RA, Ross MS, et al. National Cancer Data Base analysis of radiation therapy consolidation modality for cervical cancer: the impact of new technological advancements. Int J Radiat Oncol Biol Phys 2014;90:1083–90. https://doi.org/10.1016/j.ijrobp.2014.07.017.

[23] Hamstra DA, Mariados N, Sylvester J, Shah D, Karsh L, Hudes R, et al. Continued benefit to rectal separation for prostate radiation therapy: final results of a phase III trial. Int J Radiat Oncol Biol Phys 2017;97:976–85. https://doi.org/10.1016/j.ijrobp.2016.12.024.

[24] den Hartogh MD, de Boer HCJ, de Groot-van Breugel EN, van der Voort van Zyp JRN, Hes J, van der Heide UA, et al. Planning feasibility of extremely hypofractionated prostate radiotherapy on a 1.5 T magnetic resonance imaging guided linear accelerator. Phys Imaging. Radiat Oncol 2019;11:16–20. https://doi.org/10.1016/j.phro.2019.07.002.

[25] Tetar SU, Bruynzeel AME, Lagerwaard FJ, Slotman BJ, Bohoudi O, Palacios MA. Clinical implementation of magnetic resonance imaging guided adaptive radiotherapy for localized prostate cancer. Phys Imaging Radiat Oncol 2019;9:69–76. https://doi.org/10.1016/j.phro.2019.02.002.

[26] Yang J, Vedam S, Lee B, Castillo P, Sobremonte A, Hughes N, et al. Online adaptive planning for prostate stereotactic body radiotherapy using a 1.5 Tesla magnetic resonance imaging-guided linear accelerator. Phys Imaging. Radiat Oncol 2021;17:20–4. https://doi.org/10.1016/j.phro.2020.12.001.

[27] Willigenburg T, Beld E, Hes J, Lagendijk JJW, de Boer HCJ, Moerland MA, et al. Focal salvage treatment for radiorecurrent prostate cancer: A magnetic resonance-guided stereotactic body radiotherapy versus high-dose-rate brachytherapy planning study. Phys Imaging Radiat Oncol 2020;15:60–5. https://doi.org/10.1016/j.phro.2020.07.006.

[28] Hegde JV, Collins SP, Fuller DB, King CR, Demanes DJ, Wang PC, et al. A pooled analysis of biochemical failure in intermediate-risk prostate cancer following definitive stereotactic body radiotherapy (SBRT) or high-dose-rate brachytherapy (HDR-B) monotherapy. Am J Clin Oncol 2018;41:502–7. https://doi.org/10.1097/COC.0000000000000311.

[29] Tsang YM, Tharmalingam H, Belessiotis-Richards K, Armstrong S, Ostler P, Hughes R, et al. Ultra-hypofractionated radiotherapy for low- and intermediate risk prostate cancer: high-dose-rate brachytherapy vs stereotactic ablative radiotherapy. Radiother Oncol 2021;158:184–90. https://doi.org/10.1016/j.radonc.2021.02.028.