Original Article

Title page

Feasibility of magnetic resonance imaging-ultrasound guided high-dose-rate brachytherapy for localized prostate cancer: Preliminary results from a prospective study

Running Title: Focal therapy for prostate cancer

Nobuhiko Kamitani[a], Yoshiyuki Miyaji[b], Tsutomu Tamada[a], Eisaku Yoden[a], Yujiro Kawata[a], Kenta Watanabe[a], Ryouji Tokiya[a], Atsushi Nagai[b], Kuniaki Katsui[a, *]

[a] Department of Radiology, Kawasaki Medical School, 577 Matsushima, Kurashiki, 701-0192, Japan

[b] Department of Urology, Kawasaki Medical School, 577 Matsushima, Kurashiki, 701-0192, Japan

***Corresponding author**:

Kuniaki Katsui: ORCID ID: 0000-0002-1842-2485

Department of Radiology, Kawasaki Medical School, 577 Matsushima, Kurashiki, 701-0192, Japan

Phone: +81-86-462-1111

E-mail: katsui@med.kawasaki-m.ac.jp

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Abstract

Objective: This study aimed to investigate preliminary outcomes of a prospective trial of magnetic resonance imaging-ultrasound fusion-guided ultrafocal high-dose-rate brachytherapy in localized prostate cancer.

Methods: In our prospective study, data from patients who underwent this treatment between April 1, 2020 and March 31, 2021 were analyzed. In the procedure, the applicator needle was inserted through the perineum to target the lesion on the multi-parametric magnetic resonance imaging, which was fused onto the transrectal ultrasound image. The prescription dose was set at a single fraction of 19 Gy. Data from patients who received whole-gland high-dose-rate brachytherapy were extracted and compared with data from patients who received ultrafocal high-dose-rate brachytherapy to evaluate the frequency of acute adverse events.

Results: Eight patients underwent ultrafocal high-dose-rate brachytherapy with a median observation period of 7.75 months (range: 5.96–15.36 months). No acute genitourinary or gastrointestinal adverse events were observed in this cohort. The planned procedure was completed in all patients, and no unexpected adverse events were observed; however, prostate-specific antigen failure was detected in one patient. In the 25 patients who underwent whole-gland high-dose-rate brachytherapy, acute genitourinary and gastrointestinal adverse events were observed in 88% and 20% of the patients, respectively. Ultrafocal high-dose-rate brachytherapy was a significant factor in avoiding acute adverse genitourinary events in univariate and multivariate analyses ($P<0.001$ and $P=0.032$, respectively).

Conclusions: Magnetic resonance imaging-ultrasound fusion-guided ultrafocal high-dose-rate brachytherapy in localized prostate cancer is a safe and feasible treatment without acute genitourinary and gastrointestinal adverse events. Long-term observation and further investigation are warranted.

Keywords: focal therapy; brachytherapy; prostate cancer; MRI-US fusion; high-dose-rate

Abbreviations & Acronyms: CT, computed tomography; CTV, clinical target volume; GI, gastrointestinal; GTV, gross tumor volume; GS, Gleason Score; GU, genitourinary; HDR-BT, high-dose-rate brachytherapy; HIFU, high-intensity focused ultrasound; LDR-BT, low-dose-rate brachytherapy; mpMRI, multi-parametric magnetic resonance imaging; MRI, magnetic resonance imaging; PSA, prostate-specific antigen; PTV, planning target volume; US, ultrasound; 95% CI, 95% confidence interval.

Introduction

Prostate cancer is a malignancy with increasing incidence worldwide, specifically in Japan, where it is the most common cancer among men.[1,2] Besides widespread prostate-specific antigen (PSA) screening, advances in diagnostic tools such as magnetic resonance imaging (MRI) and biopsy have led to earlier detection and treatment of prostate cancer. Thus, we can often detect prostate cancer at a more localized state and at an earlier stage.[3] Even for early-stage, localized, low-risk prostate cancers, where active surveillance through MRI or biopsy is possible, surgery or radiotherapy are often used to target the whole prostate gland. By targeting the whole prostate gland for treatment, genitourinary (GU) and gastrointestinal (GI) adverse events can occur.[4]

In recent years, focal therapy has been performed to reduce adverse events and has been listed in the guidelines of the Japanese Urological Association as an option for the initial treatment of localized low- and intermediate-risk prostate cancer.[5] Specifically, there are many reports of focal cryotherapy and high-intensity focused ultrasound (HIFU), but only a few reports of focal high-dose-rate brachytherapy (HDR-BT).[6-8] In our institution, HDR-BT has been adopted for the treatment of prostate cancer since 1998, and an MRI-ultrasound (US) fusion-guided system has been introduced to enable targeted prostate cancer biopsies, which allows accurate identification of clinically significant prostate cancer before treatment.[9] To the best of our knowledge, there are no studies on the use of ultrafocal HDR-BT for prostate cancer in Japanese patients. With this background, we launched a prospective clinical study of ultrafocal HDR-BT with an MRI-US fusion-guided system. In this study, we evaluated the safety and acute adverse events of the procedure and compared the results with previous data

from our institution to demonstrate preliminary results.

Methods

Criteria

This study was approved by the Ethics Committee of Kawasaki Medical School (approval numbers: 3813−01 and 5329-00). We performed a prospective clinical trial of patients with prostate cancer who underwent ultrafocal HDR-BT at our institution between April 1, 2020 and March 31, 2021. This study was registered with the Japanese University Hospital Medical Information Network clinical trial center (ID: UMIN000040121). The clinical outcomes of patients who could be followed up for more than 6 months after treatment were analyzed. Multiparametric MRI (mpMRI) was performed in all cases with Ingenia Elition 3.0T (Philips, Amsterdam, the Netherlands) and interpreted by a radiologist specializing in prostate cancer. All patients underwent systematic and targeted biopsy to detect suspected cancer lesions on mpMRI using MRI-fusion US.[9,10] MRI-US fusion-guided prostate biopsy was performed using elastic image fusion and real-time three-dimensional tracking technology, Koelis Trinity® (Koelis, Grenoble, France). The indications for treatment using HDR-BT were based on findings from previous studies.[6,11] In each patient, a targeted biopsy was performed at one lesion where the cancer was suspected by mpMRI, and prostate cancer was detected only at that site. The specific inclusion criteria were as follows: Gleason score (GS) was 3+3 or 3+4, untreated prostate cancer, no evidence of metastasis on computed tomography (CT), initial prostate-specific antigen (PSA) level <20 ng/ml, 20 years or older, performance status 0 to 2, and patients agreed to undergo ultrafocal HDR-BT after being informed about active surveillance and other treatment options. The

exclusion criteria were as follows: cases of prostate cancer bordering the rectum, cancer detected in more than one lesion, history of radiotherapy in the pelvis, inability to follow up with regular MRI, inadequate understanding of this treatment, other serious diseases or conditions, oral corticosteroid or 5-alpha reductase inhibitor use, severe mental disorders, another active cancer, or deemed inappropriate by the principal investigator or researcher. Written informed consent was obtained from all the participants of the ultrafocal HDR-BT study. Final eligibility was determined in a multidisciplinary conference attended by board-certified urologists, diagnostic radiologists, and radiation oncologists. Patients in the control group, those receiving HDR-BT for the whole prostate gland (whole-gland HDR-BT), were given the opportunity to withdraw from this study via a notification on the website. All procedures performed were in accordance with the ethical standards outlined in the Declaration of Helsinki and subsequent amendments.

Treatment

The treatment procedure for ultrafocal HDR-BT was as follows. The patient was anesthetized in the lumbar spine, and mpMRI was used to guide the applicator needle through the perineum to target the lesion, which was fused onto the transrectal US image via the Koelis Trinity® (Figure 1a). One or two applicator needles were placed in the contralateral lobe as anchors to prevent prostate displacement. Additionally, applicator needles were inserted at 5 mm intervals in and around the tumor using a template (Figure 1b, 1c, 1d). The needles were also intended to penetrate 2 cm deeper than the tumor and into the bladder wall to avoid needle displacement. The Foley catheter was removed the next morning. Oncentra version 3.3.3.86 and 4.5.3

(Elekta/Nucletron, Veenendaal, Netherlands) and microSelectron v2 (Elekta/Nucletron, Veenendaal, Netherlands) were used for treatment planning and treatment, respectively. Gross tumor volume (GTV) was determined by identifying the extent of the prostate cancer lesion based on mpMRI at diagnosis and MRI-fusion US images at the insertion of the applicator needles. From the treatment plan for patient No. 5, mpMRI was fused into the treatment planning system, which was utilized as a reference for the contouring of the GTV. This is because the updated version of the treatment planning system made it possible to fuse mpMRI into the plan. A 5 mm margin was added in all directions of the GTV, making up the planning target volume (PTV) to accommodate for instrumental fusion error and micro-invasion extent.[12] In accordance with the previous studies[11,13,14], the prescription dose was set at a single fraction of 19 Gy with the D99 prescription for PTV. In cases where urethral and rectal dose constraints could not be met, dose reduction was accepted with a lower limit of the D95 prescription. Dose constraints for risk organs were set at D1cm^3 ≤12 Gy for the rectum and bladder and D0.1 cm^3 ≤21 Gy for the urethra.[11,13,14] In our study, the time between lumbar anesthesia, replacement of applicator needles, CT scanning, and the end of dose planning was recorded as "in-room-time," and the time between CT scanning and end of dose planning was recorded as "planning time," based on the study by Fischbach et al.[7]

Evaluation and statistics

Medical examinations and PSA measurements were performed at 1, 3, and 6 months after treatment, and MRI was performed at 3 and 6 months after treatment. Acute GU and GI adverse events were evaluated using the Common Terminology Criteria for Adverse Events v5.0. To evaluate the incidence of acute adverse events,

information on patients who underwent the standard treatment of whole-gland HDR-BT between January 2008 and March 2021 at the author's institution, and were observed for at least 3 months, was extracted as the control group to patients receiving ultrafocal HDR-BT. The criteria for selecting whole-gland HDR-BT patients were consistent with those for selecting ultrafocal HDR-BT patients, including T2a or lower disease. In whole-gland HDR-BT, applicator needles were inserted in both lobes, and the whole prostate gland was treated with 18 Gy/2 fractions/day and 39 Gy/13 fractions with conventional external beam radiotherapy using a three-dimensional treatment plan without MRI fusion. The prostate was intended to be surrounded by a 100% line and individually adjusted to meet the dose constraints of the urethra and rectum. The dose constraints for risk organs were 120% or less of the prescribed dose for the urethra and 60% or less for the rectum. The following factors were adopted to evaluate acute adverse events: type of HDR-BT, age, GS, initial PSA, T stage, location of the lesion, and prostate volume. In univariate analysis, the Wilcoxon-Mann Whitney test was used for continuous variables, and the Fisher's exact test was used for categorical variables. Multivariate analysis was performed using Firth's logistic regression analysis of factors with P values <0.1 in univariate analysis. The Wilcoxon rank-sum test was utilized to compare the urethral and rectal doses of ultrafocal HDR-BT and whole-gland HDR-BT. R software (version 4.1.1, The R Foundation for Statistical Computing, Vienna, Austria) was used for all statistical analyses. We adopted Firth's bias-reduced logistic regression to address the separation issue using the package 'logistf' (version 1.24).[15]

Results

Eight patients with adenocarcinoma were treated with ultrafocal HDR-BT with

a median observation period of 7.75 months (range: 5.96–15.36 months). Patient characteristics are shown in Table 1. A hydrogel spacer was inserted in patient No. 5 alone to reduce the rectal dose. The planned procedure was completed in all patients, and no unexpected adverse events were observed.

Figures 1e, 1f, and 2 show the dose distribution and MRI images of tumor lesion changes during a typical course. Prostate MRI 3 months after treatment showed the disappearance of the lesion on diffusion-weighted imaging and diminished enhancement effect on dynamic contrast-enhanced MRI. Moreover, the changes in PSA levels during the observation period for all patients are shown in Figure 3. PSA failure was observed in one patient. In patient No. 1, MRI and planned biopsy results at 12 months showed recurrence inside and outside the PTV, and biochemical failure occurred at 15 months after ultrafocal HDR-BT. In patient No. 2, a planned biopsy 12 months after ultrafocal HDR-BT revealed a new lesion outside the PTV. Median and mean pretreatment PSA levels were 7.31 ng/ml and 7.11 ng/ml (range: 2.37–14.17 ng/ml), respectively. Median and mean post-treatment PSA levels at 6 months were 2.05 ng/ml and 3.06 ng/ml (range: 1.06–7.75 ng/ml), respectively. There was a 51.3% reduction in mean PSA levels.

No acute GU adverse events were observed in the ultrafocal HDR-BT cohort (Figure 4a and Table 2), and no acute GI adverse events were observed in any of the patients (Figure 4b and Table 2). The details of the 25 cases of whole-gland HDR-BT are shown in Table 3. In the 33 total cases, type of HDR-BT (ultrafocal or whole-gland) was a significant predictive factor for the incidence of GU adverse events in univariate and multivariate analyses ($P<0.001$, and $P=0.032$, respectively) (Table 4a). However, the type of HDR-BT was not a predictive factor for GI adverse events in the univariate

analysis (P=0.300) (Table 4b). Doses of D0.1 cm^3, D2 cm^3, and D5 cm^3 for the rectum and D0.1 cm^3, D10%, and D30% for the urethra were significantly lower in ultrafocal HDR-BT than in whole-gland HDR-BT (P<0.001, <0.001, <0.001, =0.031, <0.001, and <0.001, respectively) (Table 5).

Discussion

To the best of our knowledge, this is the first prospective study of MRI-US fusion-guided HDR-BT in patients with localized prostate cancer and the first clinical study of ultrafocal HDR-BT in Japanese patients. In this study, we confirmed the safety and feasibility of the MRI-US fusion-guided ultrafocal HDR-BT procedure. We showed that ultrafocal HDR-BT had no acute adverse events, while whole-gland HDR-BT demonstrated significantly higher acute GU adverse events.

In our procedure, the median in-room time was 275 min (range: 155–464 min), and the most time-consuming process of in-room time was treatment planning, which took a median of 167 min (range: 70–347 min). In a study of the transperineal approach, Peters et al. reported a treatment time of 3 to 4 h.[6] Since our procedure did not remarkably exceed this time frame, it appeared appropriate. Maenhout et al. reported that intraoperative urethral hemorrhage due to premature retraction of the unfolded umbrella catheter occurred in one of thirty patients who underwent focal-HDR BT, while the remaining patients had no intra- or perioperative complications.[11] In our study, there were no unexpected adverse events during the procedure, and using the same transperineal approach used in the study by Maenhout et al. was considered safe.

During the observational period of our study, one patient experienced recurrence inside and outside the PTV, followed by PSA failure. Cash et al. reported that

in a sample of 408 patients with suspected cancer on mpMRI, no cancer was detected in 61 patients by MRI-fusion US-guided targeted biopsy, despite detecting cancer by random biopsy. It was concluded that the primary reason for this was targeted biopsy error.[16] Thus, the recurrence within the PTV in patient No. 1 may be due to a targeting error in the procedure. In a study of the postoperative whole-mount pathology of 101 prostate cancer patients with unilateral disease diagnosed by preoperative mpMRI and MRI-US fusion-guided prostate biopsy who underwent total prostatectomy, 73.27% had bilateral tumors, and only 47.52% would be eligible for focal therapy.[17] More research is needed to determine the appropriate adaptation of ultrafocal HDR-BT. However, this fact does not diminish the advantage of ultrafocal HDR-BT. Maenhout M et al. and Yamada Y et al. reported that ultrafocal therapy with brachytherapy could be safely performed even in patients who had undergone radiotherapy to the whole prostate gland, suggesting that ultrafocal therapy could be repeated with fewer adverse events.[11,18] Marconi L et al. showed that prostatectomy after focal therapy was safe with no increase in toxicity compared with primary prostatectomy.[19] Even if new lesions requiring treatment appear after our ultrafocal therapy, the option for therapeutic intervention remains. We believe that at the time of initial diagnosis, the attending physician can offer another option of ultrafocal therapy to patients who are torn between active surveillance and therapeutic intervention for the whole prostate gland.

The reduction rate of PSA after ultrafocal HDR-BT in this study was 56.9%, whereas, in the study by Fischbach et al., it was 80.6%.[7] Dankulchai et al. reported that in HDR-BT for prostate cancer, the group with fewer needles had lower conformity[20]. Therefore, in the D99 prescription, the irradiated volume is expected to be larger when fewer needles are used. In our study, nine needles (median) were used, while only two

were used in the study by Fischbach et al. Therefore, our irradiated volume may be smaller than theirs, which, coupled with the PSA failure in one case, may be the reason for our low PSA reduction rate. After focal HDR-BT, normal prostate tissue remains, making it difficult to determine recurrence based on PSA alone, and patients should be closely monitored with MRI and planned biopsies.

In our study, no acute GU or GI adverse events were observed after ultrafocal HDR-BT. Additionally, the incidence of acute GU adverse events was significantly lower in the ultrafocal HDR-BT group than in the whole-gland HDR-BT group under other equivalent conditions. Although the biological effects should be taken into account because of the different number of fractions in the two groups, we showed that the doses for the urethra and rectum were significantly lower in the ultrafocal HDR-BT group. Furthermore, no additional external beam radiotherapy was added to the ultrafocal HDR-BT group. Therefore, the significantly lower incidence of GU adverse events in the ultrafocal HDR-BT group is a reasonable result. Thus, for early-stage prostate cancer, ultrafocal HDR-BT appears to be more beneficial than whole-gland HDR-BT in terms of acute GU adverse events. In a study on acute adverse events due to MRI-guided ultrafocal HDR-BT, GU issues were observed in 12 patients with grade 1 and one with grade 2, and GI issues were observed in 18 patients with grade 1 and 21 with grade 2, 1 month after treatment among 30 patients.[6] In contrast, some studies have shown no acute GU or GI adverse events with MRI-guided focal HDR-BT.[7] The median clinical target volume (CTV) reported by Peters et al. was 20.8 cm^3, which was larger than that reported in our study, and the CTV reported by Fischbach et al. was 4.66 cm^3, which was close to our report. The dose was prescribed according to the CTV rather than the PTV in both studies. Lower target volumes may reduce the incidence of acute

GU and GI adverse events. A study of 122 cases of cryotherapy, another modality of focal therapy, showed that complaints of acute GU (urinary bother) were present in 17% of the patients and acute GI (bowel bother) in 10.5%.[21] In a study of 137 patients treated with HIFU, voiding dysfunction was observed in 22.2%, incontinence in 10.8%, urethral stricture in 6.8%, and urinary tract infection in 4.1% as acute adverse events.[22] Compared with focal cryotherapy and HIFU, ultrafocal HDR-BT appears to have an advantage in terms of acute adverse events. Low-dose-rate brachytherapy (LDR-BT) is a well-established treatment for low-risk prostate cancer. Yamada et al. introduced focal therapy as salvage therapy using LDR-BT, and three of these cases were treated only cancer lesions as ultrafocal therapy.[18] Despite high-risk patients being treated with three-dimensional radiotherapy at a dose of 72 Gy, the incidence of acute adverse events ranged from 0% to 67% for grade 1 and 0% for grade 2 or higher, showing the promising result of ultrafocal therapy with LDR-BT. As ultrafocal therapy, brachytherapy, including LDR-BT and HDR-BT, appears to be a promising treatment, although the evidence is insufficient, and further research is needed.

The limitations of our study are the small number of patients and short observation period. The whole-gland HDR-BT group differs from the ultrafocal HDR-BT group in the inclusion of multiple lesions and upper volume limit of 30 cm^3. Propensity matching was not performed because no reasonable factors were identified, and the time periods in which the two types of HDR-BT were performed did not overlap. Further follow-up is needed to evaluate the long-term therapeutic effects and adverse events of ultrafocal HDR-BT.

In conclusion, MRI-US fusion-guided ultrafocal HDR-BT is a safe and feasible treatment with no acute GU or GI adverse events, while PSA failure was observed in

one patient. Long-term observation and further investigation are warranted.

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Disclosure of Ethical Statement: All the participants of this study were given the opportunity to withdraw from this study through a notification on the website. All procedures were performed in accordance with the ethical standards outlined in the Declaration of Helsinki and subsequent amendments.

Conflict of Interest: Nobuhiko Kamitani, Yoshiyuki Miyaji, Tsutomu Tamada, Eisaku Yoden, Yujiro Kawata, Kenta Watanabe, Ryouji Tokiya, and Kuniaki Katsui borrowed the transrectal probe free of charge from AMCO for ultrafocal HDR-BT. The other author declares no conflict of interest.

Approval of the Research Protocol by an Institutional Review Board: This study was approved by the Ethics Committee of Kawasaki Medical School (approval numbers: 3813−01 and 5329-00).

Informed Consent: Written informed consent was obtained from all the participants of ultrafocal HDR-BT study.

Registry and the Registration No. of the Study/Trial: This study was registered with the Japanese University Hospital Medical Information Network clinical trial center (ID: UMIN000040121).

Animal Studies: N/A.

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Figure Legends

Fig. 1 Images of Koelis Trinity® and the radiotherapy treatment planning system. (a)-(c) Images of Koelis Trinity®, (a) MRI-US fusion image, (b) US image, (c) T2WI. The green dots indicate applicator needles, and the red-filled area indicates prostate cancer lesions detected by mpMRI. (d)-(f) Images of radiotherapy treatment planning system. (d) Image without dose distribution. Red and pink indicate GTV and PTV, respectively. (e) Image of axial dose distribution, (f) Image of coronal dose distribution. Abbreviations: MRI, magnetic resonance imaging; US, ultrasound; T2WI, T2-weighted image; GTV, gross tumor volume; PTV, planning target volume.

Fig. 2 The cancer lesion is shown as a focal hyperintense lesion on pretreatment diffusion-weighted imaging (arrow) (a) and as focal early enhancement on pretreatment dynamic contrast-enhanced MRI (arrow) (d). On diffusion-weighted images at 3 months (b) and 6 months (c) after ultrafocal HDR-BT, the hyperintense lesion disappeared completely at 3 months (arrows). On dynamic contrast-enhanced MRI images at 3 months (e) and 6 months (f) after ultrafocal HDR-BT, the enhanced lesion gradually improved (arrows).
Abbreviations: MRI, magnetic resonance imaging; HDR-BT, high-dose-rate brachytherapy.

Fig. 3 Changes in PSA for all patients
Abbreviations: PSA, prostate-specific antigen; pt., patient.

Fig. 4a Comparison of acute GU adverse events between ultrafocal and whole-gland HDR-BT

Abbreviations: GU, genitourinary; HDR-BT, high-dose-rate brachytherapy.

Fig. 4b Comparison of acute GI adverse events between ultrafocal and whole-gland HDR-BT.

Abbreviations: GI, gastrointestinal; HDR-BT, high-dose-rate brachytherapy.

Tables

Table 1

Patient characteristics of ultrafocal HDR-BT

Patient No	1	2	3	4	5	6	7
Age (years)	72	72	77	85	83	79	69
Initial PSA (ng/ml)	6.02	6.04	4.93	9.88	5.39	10.36	2.36
Gleason Score	3+4	3+4	3+3	3+4	3+4	3+3	3+3
T stage	2a	1c	2a	2a	1c	2a	2a
Location of lesion	TZ	TZ	TZ	TZ	PZ	TZ	TZ
PIRADs	4	4	3	3	4	5	4
Number of needles	6	9	10	8	7	11	10
Prostate volume (cm^3)	43.08	42.45	37.8	25.21	52.4	31.57	39.98
GTV (cm^3)	0.32	1.1	0.84	0.22	0.6	0.14	0.14
PTV (cm^3)	2.02	6.78	4.04	4.64	4.7	2.35	3.17
Planning time (min)	105	80	110	70	285	225	347
In-room time (min)	195	155	205	185	385	385	464
Prescribed dose (Gy)	19	19	19	19	19	19	19
Prescription	D95	D98	D95	D96	D99	D99	D95
D100 (%)	60.79	80.22	69.9	75.91	93.65	88.59	72.04
D99 (%)	71.56	98	84.79	88.44	101.01	100	82.07
D95 (%)	100	117.42	100	106.09	111.77	118.78	101.47
D0.1cm^3 urethra (Gy)	8.96	11.66	13.6	20.89	16.14	20.81	19.86
D1cm^3 rectum (Gy)	2.13	2.75	2.51	8.17	5.34	2.58	4.81
D1cm^3 bladder (Gy)	1.26	5.23	2.17	7.88	2.07	2.23	2.06

2.74	2.19	1.26	7.88	
2.3	2.66	2.13	8.17	
15.67	15.9	8.96	20.96	
116.78	116.32	136.24	100	
100	99	115.35	71.56	
89.16	84.4	102.47	60.79	
D99				
19	19	19	19	
345	275	155	464	
245	167	70	347	
4.1	4.07	2.02	6.78	
0.52	0.42	0.14	1.1	
34.01	38.89	25.21	52.4	
10	9.5	6	11	
4				
PZ				
2a				
3+4				
5.36	5.7	2.36	10.36	
65	74.5	65	85	
8	median	max	min	

Abbreviations: HDR-BT, high-dose-rate brachytherapy; PSA, prostate-specific antigen; PIRADs, prostate imaging reporting and data system; GTV, gross tumor volume; PTV, planning target volume.

Table 2.

Adverse events

		Whole-gland HDR-BT (n)		Ultrafocal HDR-BT (n)	
		Grade 1	Grade 2	Grade 1	Grade 2
GU	Urinary frequency	11	9	0	0
	Urinary tract pain	5	2	0	0
	Hematuria	0	2	0	0
	Urinary urgency	0	1	0	0
	Urinary retention	1	0	0	0
	Urinary incontinence	0	1	0	0
GI	Diarrhea	3	0	0	0
	Hemorrhoids	2	0	0	0

Abbreviations: HDR-BT, high-dose-rate brachytherapy; GU, genitourinary; GI, gastrointestinal.

Table 3.

Patient characteristics of whole-gland HDR-BT

Age (years)	median 69	range 54–80
initial PSA (ng/ml)	median 6.3	range 3.7–19.6
Gleason Score		
3+3=6	7 pts	
3+4=7	18 pts	
T stage		
T1c	16 pts	
T2a	9 pts	
Location of lesion		
TZ	10 pts	
PZ	15 pts	
Prostate volume (cm^3)	median 28.6	range 15.4–40.1

Abbreviations: HDR-BT, high-dose-rate brachytherapy; PSA, prostate-specific antigen; TZ, transitional zone; PZ, peripheral zone; pts, patients.

Table 4a.

Univariate and multivariate analyses of factors associated with GU

	Univariate analysis	Multivariate analysis		
	P value	*P* value	Odds ratio	95% CI
Type of HDR-BT	<0.001	0.03	29.13	1.28–760.20
Age	0.02	0.67	0.95	0.71–1.18
Gleason score	>0.99			
Initial PSA	0.37			
T stage	0.06	0.3	0.34	0.03–2.69
Location of lesion	0.72			
Prostate volume	0.02	0.88	0.99	0.80–1.19

Abbreviations: GU, genitourinary; HDR-BT, high-dose-rate brachytherapy; PSA, prostate-specific antigen

Table 4b.

Univariate analyses of factors associated with GI

	Univariate analysis
	P value
Type of HDR-BT	0.3
Age	0.89
Gleason score	0.63
Initial PSA	0.01
T stage	>0.99
Location of lesion	0.66
Prostate volume	0.48

Abbreviations: GI, gastrointestinal; HDR-BT, high-dose-rate brachytherapy; PSA, prostate-specific antigen

Table 5.

Dosimetry of the rectum and urethra according to the type of HDR-BT

	Whole-gland HDR-BT		Ultrafocal HDR-BT		*P* value
	median	range	median	range	
Rectum D0.1cm^3	10.69	8.68–12.90	3.50	3.01–13.47	<0.001
Rectum D0.1cm^3	7.78	6.02–9.98	2.38	1.77–6.65	<0.001
Rectum D0.1cm^3	6.29	4.38–8.22	1.94	1.25–4.70	<0.001
Urethra D0.1cm^3	20.52	18.04–21.97	15.90	8.96–20.89	0.031
Urethra D10%	21.83	20.88–26.04	16.65	9.73–21.86	<0.001
Urethra D30%	21.17	20.02–25.46	12.32	8.08–19.34	<0.001

Abbreviations: HDR-BT, high-dose-rate brachytherapy

Figures

Fig. 1

Images of Koelis Trinity® and the radiotherapy treatment planning system.

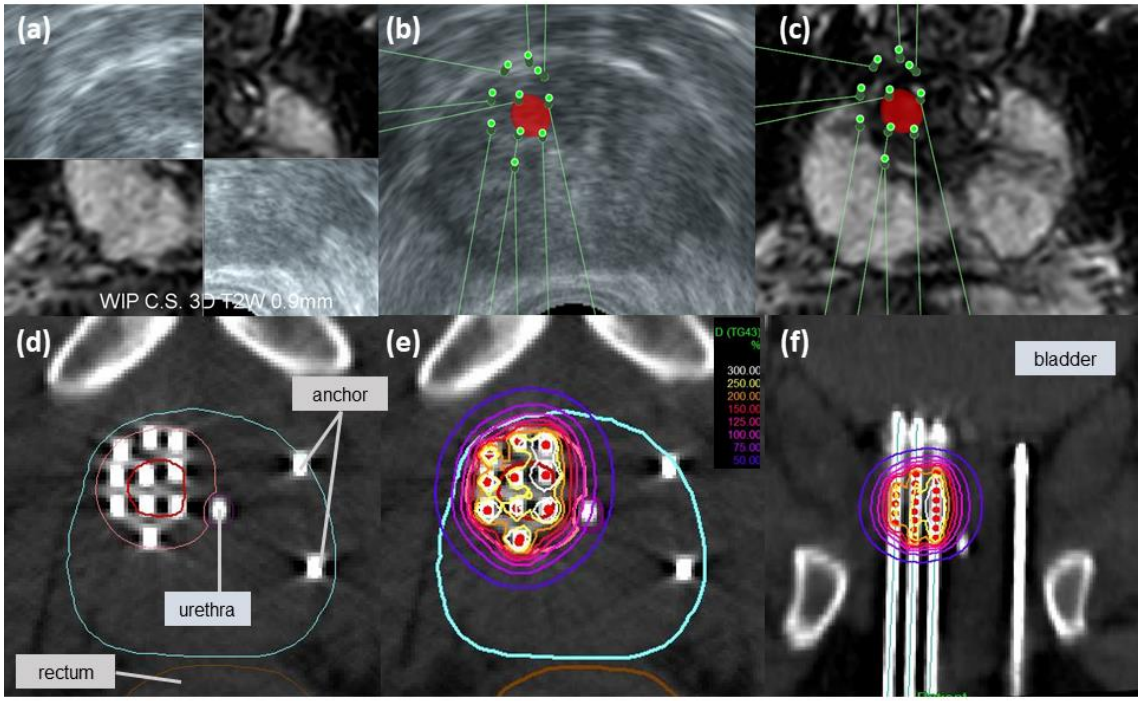

Fig. 2

MRI of tumor lesion changes after ultrafocal HDR-BT during a typical course.

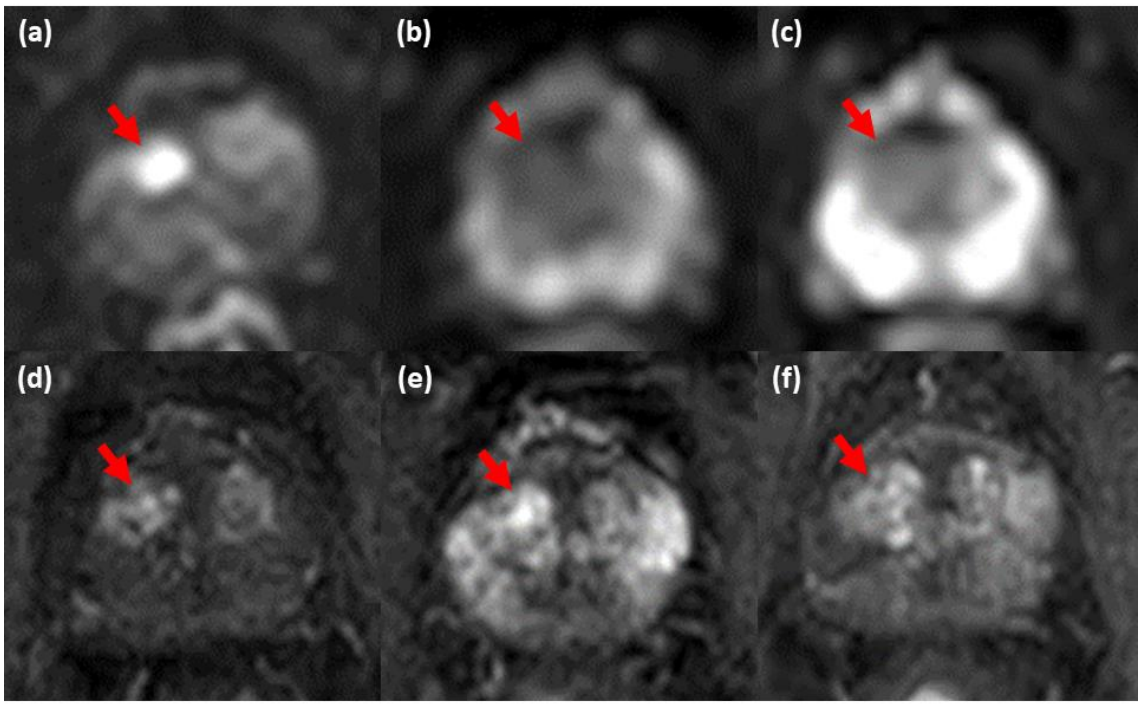

Fig. 3

Changes in PSA for all patients.

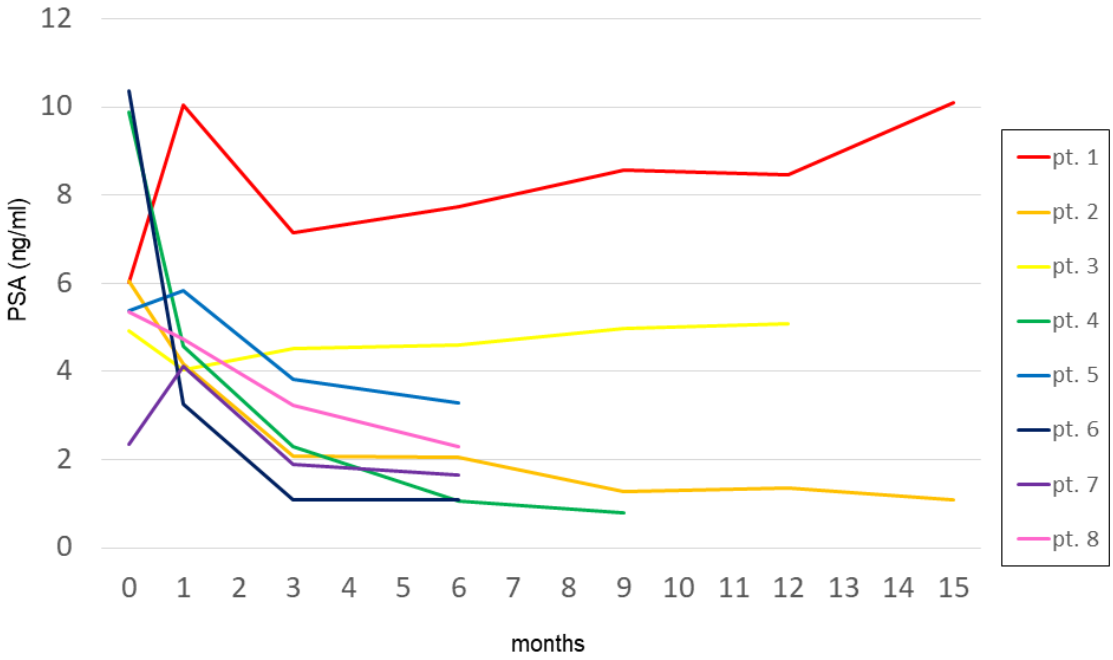

Fig. 4a

Comparison of acute GU adverse events between ultrafocal and whole-gland HDR-BT.

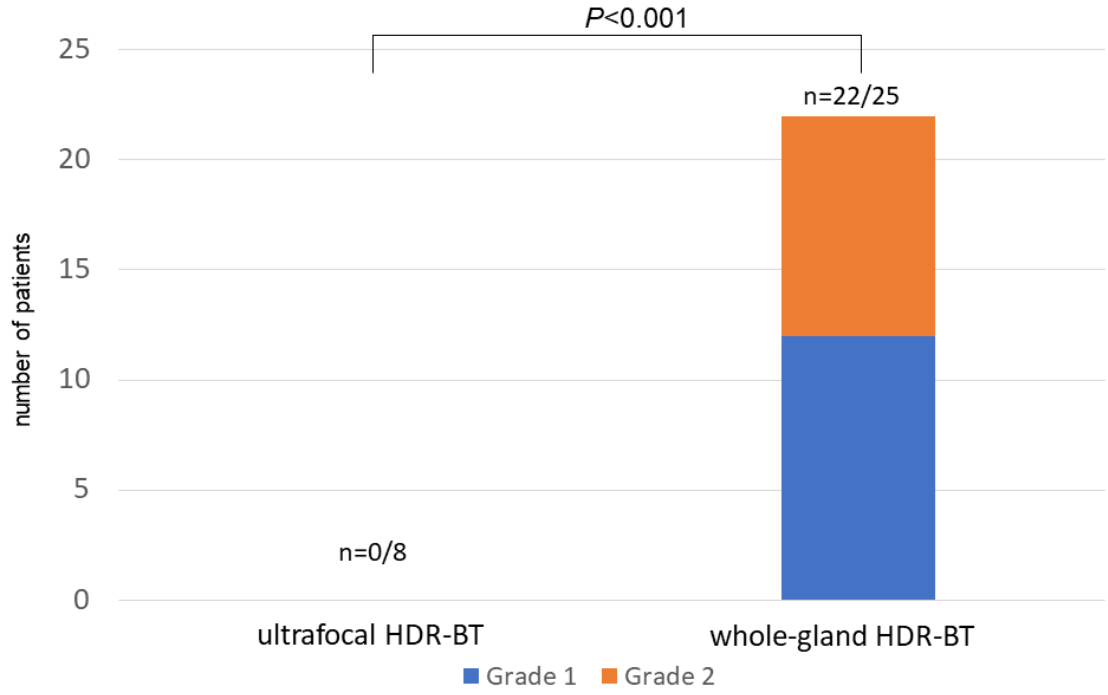

Fig. 4b

Comparison of acute GI adverse events between ultrafocal and whole-gland HDR-BT.