Highly hypofractionated intensity-modulated radiation therapy for nonmetastatic prostate cancer with a simultaneous integrated boost to intraprostatic lesions: A planning study

Authors:

Ryo Ashida, M.D., Ph.D.[1], Kiyonao Nakamura, M. D., Ph.D.[1], Rihito Aizawa, M.D.[1], Hiraku Iramina, Ph.D.[1], Kenji Takayama, M.D.[1], Mitsuhiro Nakamura, Ph.D.[1,2], Takashi Mizowaki, M.D., Ph.D.[1]

[1] *Department of Radiation Oncology and Image-applied Therapy, Graduate School of Medicine, Kyoto University, 53 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto, 606-8507, Japan*

[2] *Division of Medical Physics, Department of Information Technology and Medical Engineering, Human Health Sciences, Graduate School of Medicine, Kyoto University, 53 Kawahara-cho, Shogoin, Sakyo-ku, Kyoto, 606-8507, Japan*

Corresponding author: Takashi Mizowaki

Department of Radiation Oncology and Image-applied Therapy, Graduate School of Medicine, Kyoto University, 54 Shogoin Kawahara-cho, Sakyo-ku, Kyoto, 606-8507, Japan

Phone.: +81-75-751-3417; Fax: +81-75-771-9749; E-mail: mizo@kuhp.kyoto-u.ac.jp

Author contributions

Ryo Ashida and Takashi Mizowaki contributed to the study conception and design. Ryo Ashida, Kiyonao Nakamura, Rihito Aizawa, Kenji Takayama and Takashi Mizowaki collected the data. Hiraku Iramina and Mitsuhiro Nakamura performed patient-specific quality assurance. All authors read and approved the final manuscript.

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Conflict of Interest

The authors declare that they have no conflict of interest.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Ethical Statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Abstract

Purpose

The purpose of this planning study was to develop an acceptable technique for highly hypofractionated intensity-modulated radiation therapy using simultaneous integrated boost technique (SIB-hHF-RT) for nonmetastatic National Comprehensive Cancer Network high-risk prostate cancer.

Materials and methods

We created SIB-hHF-RT plans for 14 nonmetastatic prostate cancer patients with MRI-detectable intraprostatic lesions (IPLs) and without intestines locating close to the seminal vesicle and prostate. We prescribed 57 Gy for IPLs and 54 Gy for the remainder of planning target volume (PTV) in 15 fractions. The IPLs were contoured based on magnetic resonance imaging, and PTV was generated by adding 6–8-mm margins to the clinical target volume. For the dose-volume constraints of organs at risk (OARs), the same constraints as 54 Gy plans were used so as not to increase the toxicity.

Results

All created plans fulfilled the dose-volume constraints of all targets and OARs. The median estimated beam-on time was 108.5 s. For patient-specific quality assurance, the global gamma passing rates (3%/2 mm) with 10% dose threshold criteria were greater than 93% in all cases and greater than 95% in 11 cases.

Conclusion

SIB-hHF-RT plans were developed that fulfill the acceptable dose-volume constraints and pass patient-specific quality assurance. We believe these plans can be applied to selected patients with

nonmetastatic prostate cancer.

Secondary abstract

Highly hypofractionated intensity-modulated radiation therapy plans prescribed 57 Gy for intraprostatic lesions and 54 Gy for the remainder of the planning target volume in 15 fractions using simultaneous integrated boost technique could be developed that fulfill the acceptable dose-volume constraints for 54 Gy plans and pass patient-specific quality assurance.

Keywords

Prostate cancer, hypofractionation, IPLs, SIB-IMRT, dose escalation

Introduction

Prostate cancer is one of the most common cancer types among men [1], and external beam radiation therapy (EBRT) is a major treatment modality for nonmetastatic prostate cancer. Conventionally, EBRT of up to 78 Gy is administered in 2-Gy fractions for 8 weeks [2–5], but recently, hypofractionated radiation therapy (HF-RT) has been administered because of the low α/β value of prostate cancer [6]. HF-RT has been intensively studied in non-metastatic prostate cancer, and guidelines for HF-RT have been issued by the American Society of Clinical Oncology, the American Urological Association, and the American Society for Radiation Oncology [7]. Previously, we performed a pilot study of highly hypofractionated radiation therapy (hHF-RT) using 54 Gy in 15 fractions (3.6 Gy per fraction) over 3 weeks, of which fractionation is in the gap between that of moderately HF-RT and of ultrahypofractionated RT or stereotactic body radiation therapy (SBRT) for the National Comprehensive Cancer Network (NCCN) for very low- to unfavorable intermediate-risk prostate cancer [8]. The tumor equivalent dose for this prescription was approximately equal to 78 Gy in 39 fractions based on an assumption that the α/β ratio for prostate cancer is 1.5 Gy. This study showed good tumor control without severe toxicity at 2 years, which is comparable to the outcomes of conventional fractionated intensity-modulated radiation therapy (IMRT).

However, additional doses may be necessary to control NCCN high-risk prostate cancer [9]. Zaorsky et al. suggested that a biologically effective dose (BED) based on an estimated α/β ratio for prostate cancer of 1.5 Gy ($BED_{1.5}$) to 200 Gy was associated with increased prostate cancer control, while a dose of more than 200 Gy would not have additional clinical benefit. The $BED_{1.5}$ of 54 Gy in 15 fractions was 183.6 Gy; if the irradiation plans finished in 15 fractions, 57 Gy would be necessary to achieve a

$BED_{1.5}$ of 200 Gy ($BED_{1.5}$ 201.4 Gy). Meanwhile, ultrahigh dose irradiation increases gastrointestinal (GI) and genitourinary (GU) toxicity if delivered as EBRT to the whole prostate [10–12]. Therefore, a boost to a small part of the prostate was considered an option to increase the radiation dose [10]. Local recurrence of prostate cancer after radiation therapy usually occurs at the same site where intraprostatic lesions (IPLs) exist at baseline [13]. This supports the usefulness of boosting the biological target volume (BTV), which was derived from biological images made using magnetic resonance imaging (MRI) and positron emission tomography (PET) [14]. In 2018, a systematic review of treatment with focal dose escalation for IPLs was published, which found favorable biochemical control and acceptable toxicity [15]. Several reports have discussed boosting IPLs in SBRT or conventionally fractionated radiation therapy with or without brachytherapy. However, to the best of our knowledge, there is no report of boosting IPLs in hHF-RT using the simultaneous integrated boost (SIB) technique.

We conducted a planning study for prostate cancer patients to develop an acceptable SIB-hHF-RT plan in which 57 Gy in 15 fractions (3.8 Gy per fraction) was prescribed for IPLs. Moreover, we used non-coplanar IMRT to decrease the dose to organs at risk (OARs) [16, 17].

Materials and methods

This study was conducted in accordance with the Declaration of Helsinki, and our institutional ethical review board approved the research (approval numbers C1236 and R1048). Informed consent was obtained from all individual participants included in the study.

Study population

At our institution, a total of 23 patients underwent computed tomography (CT) simulation for nonmetastatic prostate cancer between March and August 2017. The period was determined because we estimated that immediate 6 months will be enough to pick up sufficient cases with various IPL characteristics. Of these patients, six had no identifiable IPLs based on MRI before the therapeutic intervention, and three had intestines close to the seminal vesicle and prostate that were considered difficult to spare from high-dose irradiation. These patients were excluded; therefore, the data from the remaining 14 patients were included in this study, and plans were created using their simulation CT. Patient characteristics are listed in Table 1 and IPL characteristics in Table 2. Because this is a planning study, we included all patients with identifiable IPLs in this study.

CT simulation

Patients were instructed to void the urinary bladder and rectum 1–1.5 hour before CT simulation and were then prohibited from voiding until the end of the simulation [18]. CT simulation was performed in the supine position using a BodyFIX vacuum cushion (Elekta, Stockholm, Sweden). CT images were acquired using a LightSpeed RT scanner (GE Healthcare, Little Chalfont, UK) with a 2.5-mm slice thickness or a Siemens Somatom Definition (Siemens, Erlangen, Germany) with a 2.0-mm slice thickness.

Target and OAR delineation

The targets and OARs are shown in Fig. 1. The total volume of IPLs was contoured as the

BTV in the simulation CT images according to the diffusion-weighted images (DWI) at b values of ≥ 500 s/mm^2 and the T2-weighted images (T2WI) of the pretreatment MRI with ≤5 mm thickness. Because the prostate volume changed between the pretreatment MRI and simulation CT for patients receiving neoadjuvant androgen deprivation therapy, the BTV was contoured using an empirical algorithm, which is mapping algorithm based on the assumption that the prostate deformation is directly proportional in each direction [19]. The clinical target volume (CTV) was defined as the total volume of the prostate and proximal portion of the seminal vesicles. In patients with low- or intermediate-risk prostate cancer as determined by the D'Amico risk group [20], the CTV included the base of the seminal vesicles. In patients with prostate cancer with seminal vesicle invasion, the CTV included all seminal vesicles; in the other patients, the CTV included two-thirds of the proximal seminal vesicles. The planning target volume (PTV) was generated by adding an 8 mm margin elsewhere except for the posterior, where a 6 mm margin was applied, to the CTV. If a planner in charge judged it necessary, manual modifications of reducing the posterior margin to 5 mm were allowed to preserve the rectum from receiving an excessively high dose. The boost volume (PTV-boost) was created by adding isotropic 3-mm margins around the BTV [21], and the PTV-boost was subtracted from the PTV to define the volume in which 54 Gy was prescribed (PTV_54Gy). For OARs, the bladder, rectum, small intestine, and sigmoid colon were contoured. We used an inner bladder wall thickness of 4 mm for the bladder dose evaluation. For the rectal dose, we used an inner rectal wall thickness of 4 mm, ranging from 10 mm below the apex of the prostate to 10 mm above the tips of the seminal vesicles. The CTV, PTV, and OARs had been created using Eclipse version 13.6 (Varian Medical Systems, Palo Alto, CA) for prior radiation therapy, and the BTV, PTV-boost, and

PTV_54Gy were newly generated using RayStation version 4.7 (RaySearch Laboratories, Stockholm, Sweden).

Radiation treatment

We used a Vero4DRT System (Mitsubishi Heavy Industries, Ltd., Tokyo, Japan, and Brainlab, Munich, Germany) with 30 pairs of 5-mm-thick multileaf collimator (MLC) to administer non-coplanar IMRT. The Vero4DRT System has a gantry mounted within the O-ring structure and can rotate the gantry and O-ring simultaneously, delivering radiation therapy with a non-coplanar arc without rotating the couch, which is known as dynamic wave arc (DWA) [22]. This technique can be combined with intensity modulation and volumetric-modulated dynamic wave arc therapy (VMDWAT). VMDWAT plans were created using a single non-coplanar arc trajectory (Fig. 2). The arc trajectory was divided into four segments. The O-ring rotated from 20 to 0°, 0 to 335°, 335 to 25°, and 25 to 340° during the first, second, third, and fourth segments, and the gantry rotated clockwise from 182 to 234°, 234 to 314°, 314 to 42°, and 42 to 178° in each segment, respectively. Treatment planning was performed using RayStation version 4.7. In the plan, 6-MV photon beams and the collapsed cone dose calculation algorithm (version 3.1) was used with a calculation grid size of 2.0 mm. In the current study, 54 Gy in 15 fractions (3.6 Gy per fraction) was delivered to the PTV_54Gy and 57 Gy (3.8 Gy per fraction) to the PTV-boost simultaneously. Referring to the dose-volume indices of prior pilot study [8], new dose-volume constraints were defined as shown in Table 3. The dose-volume constraints of OARs were the same as those used in the prior study to avoid increases in GI and GU toxicity. $D_{X\%}$ was defined as the dose to X% of the target or OAR volume, and V_{XGy} was

defined as the volume receiving at least X Gy. For patient-specific quality assurance (QA), the global gamma passing rates (3%/2 mm) with 10% dose threshold criteria between the measured or reconstructed dose distributions and planned dose distributions were evaluated using ArcCHECK (Sun Nuclear Corp., Melbourne, FL, USA) [23].

Results

The mean volumes ± standard deviation (SD) of the BTV, CTV, PTV, and PTV-boost were 2.40 ± 2.31, 25.64 ± 9.20, 78.37 ± 23.66, and 6.66 ± 5.15 mL, respectively. The axial plane of the dose distribution in a representative case is shown in Fig. 1.

Table 4 summarizes the dose-volume indices of the targets. One patient had a smaller $D_{95\%}$ value of the PTV-boost than the ideal index; another patient had a greater $D_{2\%}$ value of the PTV_54Gy, and four patients (28.6%) had smaller $D_{95\%}$ values of the PTV. However, all plans had allowable indices for the targets.

In all 14 plans, the dose indices of the OARs fulfilled the ideal dose constraints, although in some cases the BTV was located next to the rectum. The dose-volume histograms of the bladder wall and rectum wall are shown in Fig. 3. All dose-volume constraints for the bladder wall and rectum wall were achieved in all cases. The constraints for the small intestine and sigmoid colon were also achieved in all cases (V_{45Gy} of the small intestine: at most 0.03 mL, V_{48Gy} of the sigmoid colon: 0 mL in all cases).

The median estimated delivery time was 108.5 s (range: 104–126 s). For patient-specific QA, the mean gamma passing rates (3%/2 mm) ± SD were 95.9 ± 1.6%, greater than 93% in all cases, and

greater than 95% in 11 cases.

Discussion

The purpose of this study was to develop an acceptable SIB-hHF-RT plan for nonmetastatic prostate cancer in which 57 Gy in 15 fractions was prescribed to the BTV and 54 Gy in 15 fractions was prescribed to other regions of the PTV using the SIB technique. To our knowledge, this is the first study of SIB-hHF-RT that boosts BTV.

The concept of the BTV was first suggested in 2000 [14], but it was considered difficult to achieve a BTV boost at that time because it was difficult to reproduce the BTV position with skin markings or bone matching using on-board kV imaging. The BTV position at the time of treatment often deviates from the position in the simulation CT due to interfractional error derived from the amount of urine and rectal gas present (e.g., [24]). Recently, cone-beam computed tomography (CBCT) on a linear accelerator has become more common, and organ-matching using CBCT can be widely implemented. This technique has made it easier to reproduce the BTV position despite interfractional errors and has made BTV boosting possible.

The delivery of the BTV boost is also difficult due to intrafractional errors. Non-coplanar IMRT decreases the dose delivered to OARs [16, 17] but a lot of time is required to rotate the couch; thus, intrafractional prostate motion and baseline drift increase with time [25], making non-coplanar IMRT difficult to use in radiation therapy for prostate cancer with a BTV boost. However, VMDWAT using the Vero4DRT System, allows sequential non-coplanar trajectories without rotating the couch, by rotating the gantry and O-ring simultaneously. VMDWAT also can shorten the delivery time to

~110 s, which is much shorter than that of non-coplanar radiation therapy delivered by rotating the couch. Therefore, we consider that VMDWAT can reduce baseline drift and improve the accuracy of the BTV position. Meanwhile, the Vero4DRT System has only 5-mm MLCs, although treatment machines with thinner MLCs of 3 or 2.5 mm around the center of the field are increasingly being used. However, 5-mm MLCs are acceptable for creating dose painting plans for prostate cancer [26]. The isotropic 3-mm margins around the BTV to determine the PTV-boost were smaller than the margins around the CTV to determine PTV. This is because the dose distribution outside the PTV should be steeply reduced, but the PTV-boost in the PTV and dose distribution outside the PTV-boost was equivalent to the therapeutic dose for prostate cancer.

In the current study, we prescribed 57 Gy in 15 fractions to PTV-boost and 54 Gy in 15 fractions to the other regions of the PTV with hHF-RT. We used hHF-RT because we think hHF-RT has some advantages over moderately HF-RT or SBRT. The advantage of hHF-RT over moderately HF-RT is the shorter overall treatment time. Although moderately HF-RT takes 4–6 weeks to complete the treatment, hHF-RT is completed over 3 weeks. One of the advantages of hHF-RT over SBRT is its robustness against random errors owing to the higher fraction number of hHF-RT. Another advantage is that hHF-RT does not necessarily require fiducial markers as previously reported [8] owing to its fractionation and short delivery time, the implantation of which is invasive and can delay the start of radiation therapy. SBRT itself takes only 1–2 weeks; however, including the period between implantation of the fiducial marker and the simulation, it takes 3–5 weeks from the implantation to complete the SBRT. This period is almost the same as that for hHF-RT itself. The dose prescription of 57 Gy to PTV-boost and 54 Gy to the other regions of the PTV was based on the following three

assumptions. First, prior hHF-RT study that prescribed 54 Gy in 15 fractions using the Vero4DRT System showed good tumor control without severe toxicity at 2 years, which is comparable to outcomes following conventionally fractionated IMRT [8]. Second, as mentioned above, an increase in $BED_{1.5}$ >200 Gy was associated with increased prostate cancer control [9]. The $BED_{1.5}$ of 57 Gy in 15 fractions was 201.4 Gy, achieving $BED_{1.5}$ >200 Gy. Third, many patients would not have tolerated an ultrahigh dose if it had been delivered as external beam radiation therapy to the whole of the prostate due to GI and GU toxicity [10–12], but a boost to a small part of the prostate was an option to increase the radiation dose [10]. In the current plans, despite a 57-Gy prescription, the dose-volume indices of the OARs were the same as in previous study, which showed no acute rectal or GU toxicity of grade ≥3 and late toxicity of grade ≥2 [8]. Therefore, the toxicity to the bladder and rectum was presumed to be acceptable. Because of the low α/β value of prostate cancer, the effect of the dose difference between PTV-boost and PTV was comparatively larger than its absolute value in a hypofractionated setting. This is an advantage of HF-RT in prostate cancer.

In these plans, a PTV $D_{95\%}$ was difficult to achieve, and 28.6% of the patients (4 of 14 patients) had smaller indices than ideal. However, this was almost equal to that in a prior pilot study (33.3% minor deviation in PTV $D_{95\%}$), and it appears to be unrelated to an increased radiation dose. For patient-specific QA, the American Association of Physicists in Medicine Task Group No. 218 reported that a gamma passing rate of 3%/2 mm and 10% dose threshold should be 95% for the universal tolerance limit and 90% for the universal action limit [27]. In the present study, eleven plans passed the tolerance limit, and the remaining three plans passed the action limit. Therefore, all plans in this study were considered acceptable by these standards.

This study has some limitations. First, we used T2WI and DWI to determine IPLs but did not use PET images. To determine IPLs, some studies have used ^{11}C choline PET [28–31] or prostate-specific membrane antigen-targeted PET [32] images. However, a combination of T2WI and DWI was used in PI-RADS version 2 to improve the detectability of prostate cancer [33, 34]. We considered the combination of T2WI and DWI as an adequate approach to detect IPLs. Second, it is unclear whether GI or GU toxicity will increase even when using allowable dose-volume constraints. In particular, the urethra is not defined as an OAR and would possibly be irradiated with the boost dose. Although the dose-volume effect on the urethra is unclear, toxicity to the urethra might increase. In addition, clinical impacts of boosting IPLs in very high-risk cases such as T3b are currently unclear. We plan to conduct a prospective clinical trial for NCCN high-risk patients to assess this toxicity and evaluate the clinical outcomes.

In conclusion, SIB-hHF-RT plans for 57 Gy in 15 fractions prescribed to IPLs and 54 Gy in 15 fractions to the remainder of the PTV can be developed without exceeding the dose-volume constraints for OARs stated in a prior pilot study using a 54 Gy prescription. These plans comply with patient-specific QA. We believe that these plans can be applied to patients with nonmetastatic prostate cancer. We have conducted a prospective clinical trial using this SIB-hHF-RT protocol and believe this trial will reveal the clinical significance of SIB-hHF-RT.

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Tables

Table 1. Patient characteristics

Age (years)	
Range	62 - 82
Median	75
Clinical T-stage	
T2a	6
T2b	1
T2c	2
T3a	3
T3b	2
iPSA (mg/ml)	
Range	4.1 - 65.8
Median	9.5
Mean	15.8
Gleason Score	
3+3	2
3+4	4
4+3	2
≥4+4	6
NCCN risk classification	
Very low	1
Low	1
Favorable intermediate	3
Unfavorable intermediate	2
High	5
Very high	2

Abbreviation: iPSA = initial prostate-specific antigen, NCCN = National Comprehensive Cancer Network.

Table 2. Characteristics of intraprostatic lesions

Patient No.	IPL No.	Total volume (mL)	Position			
			Base - apex	Anterior - posterior	Left - right	Zone
1	1	0.45	Center	Posterior	Left	PZ
2	2	0.43	Center	Posterior	Right	PZ
3	3	6.73	Base - apex	Anterior	Bilateral	PZ and TZ
4	4	0.50	Center	Anterior	Center	TZ
5	5	2.15	Center	Anterior - center	Left	TZ
6	6	0.15	Center	Posterior	Left	PZ
7	7	2.92	Center	Anterior	Left	TZ
8	8	1.30	Base - center	Anterior	Left	TZ
	9		Center	Anterior	Right	TZ
9	10	1.10	Center	Anterior	Center	TZ
	11		Apex	Anterior	Center	PZ
10	12	1.63	Center	Anterior	Bilateral	TZ
	13		Apex	Center	Left	TZ
11	14	6.06	Base - apex	Anterior	Bilateral	TZ
12	15	0.60	Center	Posterior	Left	PZ
13	16	3.34	Center - apex	Anterior - posterior	Right	PZ
14	17	5.73	Base - apex	Anterior - posterior	Bilateral (mainly left)	PZ, TZ and CZ

Abbreviation: No. = number, IPL = intraprostatic lesion, PZ = peripheral zone, TZ = transitional zone, CZ = central zone

Table 3. Dose-volume constraints

	ideal	allowable
PTV		
$D_{95\%}$	≥ 51.3 Gy (95% of 54 Gy)	≥ 50.22 Gy (93% of 54 Gy)
PTV-boost		
$D_{2\%}$	≤ 59.85 Gy (105% of 57 Gy)	≤ 60.99 Gy (107% of 57 Gy)
$D_{50\%}$	56.43 - 57.57 Gy (99% - 101% of 57 Gy)	-
$D_{95\%}$	≥ 54.15 Gy (95% of 57 Gy)	≥ 53.01 Gy (93% of 57 Gy)
PTV_54Gy		
$D_{2\%}$	≤ 56.7 Gy (105% of 54 Gy)	≤ 57.78 Gy (107% of 54 Gy)
BTV		
$D_{2\%}$	≤ 59.85 Gy (105% of 57 Gy)	≤ 60.99 Gy (107% of 57 Gy)
$D_{98\%}$	≥ 54.15 Gy (95% of 57 Gy)	≥ 53.01 Gy (93% of 57 Gy)
CTV		
$D_{98\%}$	≥ 51.3 Gy (95% of 54 Gy)	≥ 50.22 Gy (93% of 54 Gy)
Bladder wall		
V_{30Gy}	≤ 60%	
V_{50Gy}	≤ 30%	
Rectum wall		
V_{30Gy}	≤ 60%	
V_{45Gy}	≤ 30%	
V_{50Gy}	≤ 20%	
V_{54Gy}	≤ 1%	
Small intestine		
V_{45Gy}	< 0.5 mL	
Sigmoid colon		
V_{48Gy}	< 0.5 mL	

Abbreviations: PTV = planning target volume, BTV = biological target volume, CTV = clinical target volume, $D_{X\%}$ = dose to X% of the volume, V_{XGy} = volume of organs receiving X Gy.

Table 4. Doses-volume indices of the targets and organs at risk

	mean ± SD
PTV	
$D_{2\%}$	57.62 ± 0.55 Gy
$D_{50\%}$	54.95 ± 0.17 Gy
$D_{95\%}$	51.37 ± 0.28 Gy
PTV-boost	
$D_{2\%}$	58.82 ± 0.49 Gy
$D_{50\%}$	57.07 ± 0.13 Gy
$D_{95\%}$	55.04 ± 0.76 Gy
PTV_54Gy	
$D_{2\%}$	56.51 ± 0.21 Gy
$D_{50\%}$	54.81 ± 0.24 Gy
$D_{95\%}$	51.25 ± 0.28 Gy
BTV	
$D_{2\%}$	58.98 ± 0.53 Gy
$D_{50\%}$	57.78 ± 0.28 Gy
$D_{98\%}$	55.94 ± 0.57 Gy
CTV	
$D_{2\%}$	58.27 ± 0.57 Gy
$D_{50\%}$	55.69 ± 0.26 Gy
$D_{98\%}$	53.02 ± 0.41 Gy
Bladder wall	
V_{30Gy}	26.45 ± 7.26%
V_{50Gy}	14.99 ± 4.49%
Rectum wall	
V_{30Gy}	39.36 ± 5.38%
V_{45Gy}	21.04 ± 2.88%
V_{50Gy}	10.44 ± 2.55%
V_{54Gy}	0.09 ± 0.26%

Abbreviations: SD = standard deviation, PTV = planning target volume, BTV = biological target volume, CTV = clinical target volume, $D_{X\%}$ = dose to X% of the volume, V_{XGy} = volume of organs receiving X Gy.

Captions for illustrations

Fig. 1 The structure delineation and dose distribution in a representative case

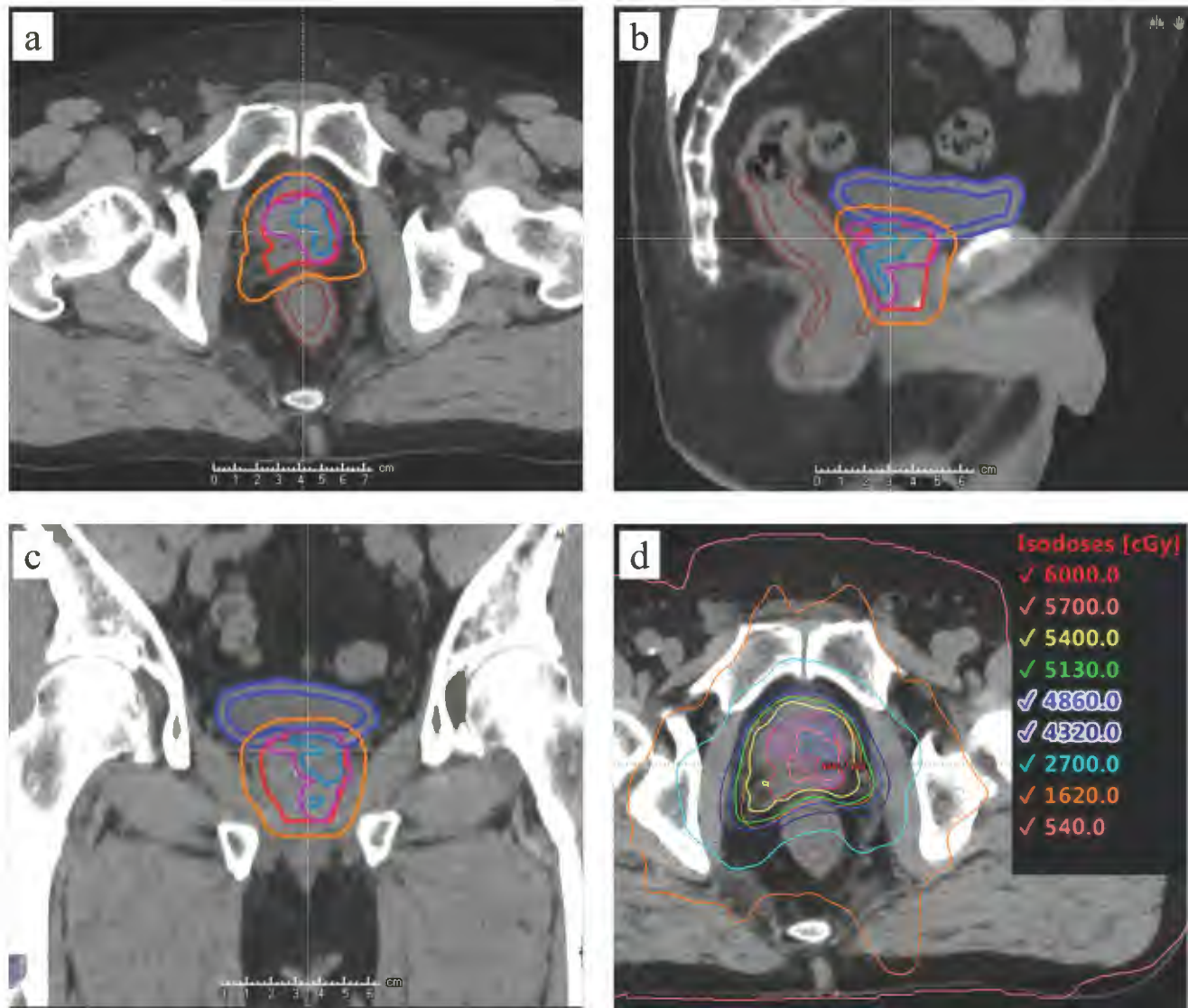
(a–c) The targets and organs at risk (OARs) in the axial, sagittal, and coronal planes, respectively. Each colored line defines the targets and OARs. Cyan: biological target volume (BTV), red: clinical target volume (CTV), orange: planning target volume (PTV), purple: PTV-boost, blue: bladder wall (4 mm thickness), brown: rectum wall (4 mm thickness). (d) Axial plane of dose distribution.

Fig. 2 Arc arrangement of the volumetric-modulated Dynamic WaveArc therapy (VMDWAT) plan

The orange band shows the non-coplanar trajectories of VMDWAT.

Fig. 3 Dose-volume histograms of the bladder wall (a) and rectum wall (b) in each patient

Triangles indicate the dose-volume constraints.


a
b
c
d
Isodoses [cGy]
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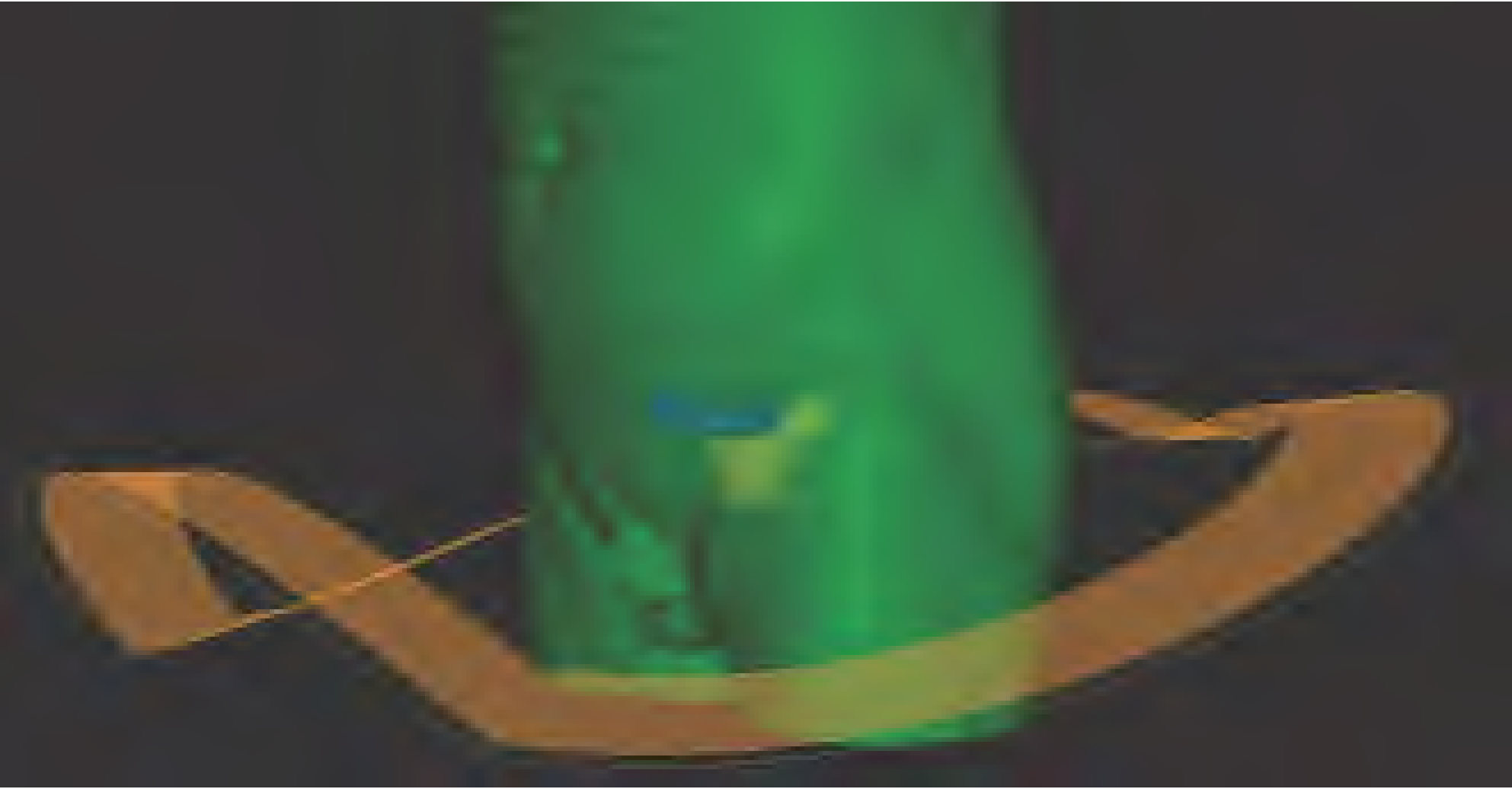
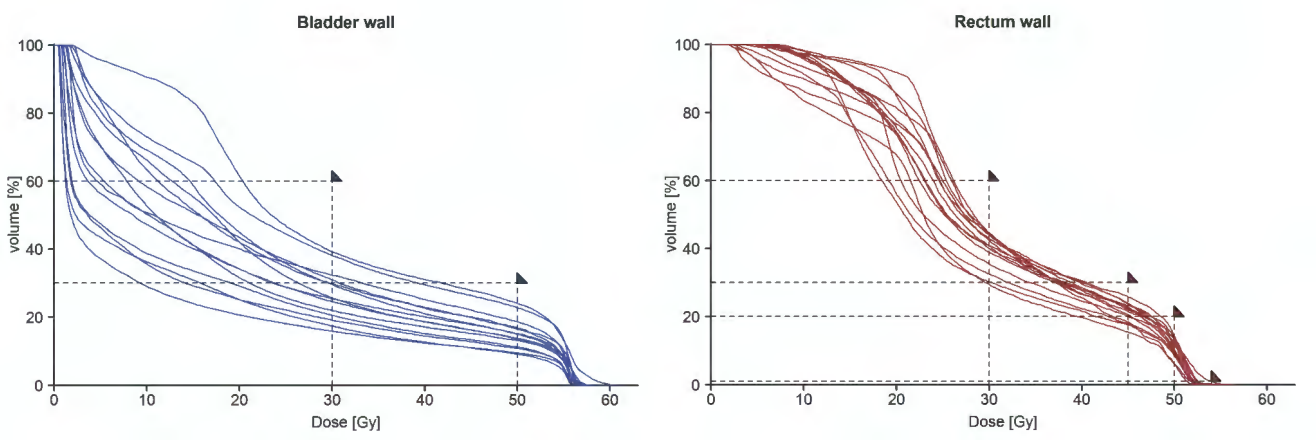
5700.0
5400.0
5130.0
4860.0
4320.0
2700.0
1620.0
540.0




Bladder wall
volume [%]
Dose [Gy]
0
10
20
30
40
50
60
100
80
60
40
20
0
Rectum wall
volume [%]
Dose [Gy]
0
10
20
30
40
50
60
100
80
60
40
20
0