research article

Effects of gold fiducial marker implantation on tumor control and toxicity in external beam radiotherapy of prostate cancer

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Background. Evidence regarding the effects of fiducials in image-guided radiotherapy (IGRT) for tumor control and acute and late toxicity is sparse.

Patients and methods. Patients with primary low- and intermediate-risk prostate cancer, 40 with and 21 without gold fiducial markers (GFM), and treated between 2010 and 2015 were retrospectively included. The decision for or against GFM implantation took anaesthetic evaluation and patient choice into account. IGRT was performed using electronic portal imaging devices. The prescribed dose was 78 Gy, with 2 Gy per fraction. Biochemical no evidence of disease (bNED) failure was defined using the Phoenix criteria. Acute and late gastrointestinal (GI) and genitourinary toxicity (GU) were assessed using the Radiation Therapy Oncology Group criteria.

Results. Most patients did not receive GFM due to contraindications for anaesthesia or personal choice (60% and 25%). Regarding tumor control, no significant differences were found regarding bNED and overall and disease-specific survival ($p = 0.61$, $p = 0.56$, and $p > 0.9999$, respectively). No significant differences in acute and late GI ($p = 0.16$ and 0.64) and GU toxicity ($p = 0.58$ and 0.80) were observed.

Conclusions. We were unable to detect significant benefits in bNED or in early or late GI and GU side effects after GFM implantation.

Key words: prostate cancer; IGRT; fiducials; tumor control; toxicity

Introduction

Prostate cancer can be treated by external beam radiotherapy (EBRT) brachyradiotherapy or radical prostatectomy; for low-risk disease and highly selected intermediate disease, active surveillance can be offered.[1-5] Important factors in patient decision making are, therefore, the duration of treatment, circumstances of treatment, and treatment-induced side effects. Regarding side effects in EBRT, the use of intensity-modulated radiotherapy (IMRT) has been shown to reduce treatment-associated side effects compared with 3D-conformal radiotherapy.[6,7] Further reduction of side effects is expected using image-guided radiotherapy (IGRT)[8], in which fiducials, ultrasound, MRI, CT scans, or electromagnetic responders are used to locate the prostate before and during radiotherapy.[9] However, to our knowledge, there are as yet no data regarding IGRT in the form of randomized controlled trials, although IGRT is recommended by the NCCN[1], EAU[5], British NICE[10], and German S3[4] guidelines.

With this paper, we explore the role of gold fiducial markers (GFM) used for IGRT in primary prostate cancer treatment. There are only a few studies comparing patients with and without GFM. For example, a retrospective study by Zelefsky *et al.*[11] described an advantage after implanting GFM

in regard to genitourinary (GU) side effects in all patients and biochemical no evidence of disease (bNED) rates in high-risk prostate cancer patients. However, this study compared a group of patients treated with IGRT, but without IMRT with an IMRT-only group, making its results difficult to apply to modern day radiotherapy, in which IMRT is always recommended.[1] The same applies to Sveistrup *et al*.[12], Zapatero *et al*.[13] and Wortel *et al*.[7], which compared patients treated with fiducial-marker IGRT and IMRT with patients treated with 3D conformal radiotherapy.[12] Singh *et al*. compared the use of GFM IGRT with no IGRT *et al*.[14] However, to our knowledge, only one study has compared the use of IGRT with and without GFM[15], and it showed no significant benefits regarding tumor control and toxicity.

In our department, we use cone-beam CT scans and ExacTrac (Brainlab, Munich, Germany), as well as routinely implanted GFM for image guidance. As GFM are implanted with the use of anesthesia, the benefit of the GFM has to be larger than the risks from anesthesia, including, but not limited to, nausea, allergic reactions, intraoperative awareness, or death[16,17], and the risk of the intervention itself, such as infections or injuries to adjacent organs. Local anaesthesia reduces the risks of anaesthesia. Some patients have contraindications against anesthesia or refuse the intervention. A more precise patient positioning due to GFM can be expected to lead to greater treatment precision and hence, possibly, to reduced toxicity and increased tumor control. These assumed benefits can justify its routine application in patients with prostate cancer. Without these advantages, the routine use of GFM would not be justified. Therefore, we wanted to compare a group of patients receiving IGRT with GFM with a group receiving only IGRT to evaluate the potential benefits of GFM regarding tumor control and GI and GU toxicity.

Patients and methods

Design, setting, and participants

Our study protocol was approved by the ethical review board of our university according to local regulations (EK Nr: 1533/2020). We included all patients between 2010 and 2015 with localized primary prostate cancer treated with EBRT by the use of volumetric modulated arc therapy (VMAT) with or without GFM implantation. Patients treated before 2010 were excluded, as routinely prescribed doses were below the currently recommended 75.6 Gy with 1.8 Gy per fraction.[1] Due to the implementation of moderate hypofractionation in our department, patients treated after 2015 were excluded to keep the fractionation uniform among patients. The stage had to be cN0/x and cM0/x, with a risk of lymph node involvement < 15% according to the Roach formula[18], and a clinical T category of 1 or 2.

Interventions

Target volumes were defined using CT and MRI for planning. The prescribed doses were 78 Gy with 2 Gy per fraction. Doses were prescribed to 95% of the planning target volume (PTV) according to International Commission on Radiation Units and Measurements report 83.[19] Safety margins were 7 mm after GFM implantation and 10 mm without. Irradiation was performed with the patient in supine position. All patients received a rectal balloon[20] for prostate immobilization. Cone-beam CT control scans were performed daily for the first week, followed by daily ExacTrac (Brainlab, Munich, Germany) controls for the rest of treatment. The clinical target volume (CTV) included the prostate for low-risk tumors and additionally the base of the seminal vesicles for intermediate-risk tumors.

GFM implantation was recommended to all patients. Reasons for not receiving GFM were contraindications against anesthesia, such as pre-existing pulmonary illness, coronary heart disease, or myocardial infarction, or refusal by the patient. Implantation itself was performed transperineally with ultrasound guidance by the radiation oncologist, under mask narcosis performed by an anaesthesiologist. In each patient, 3 GFM were implanted, one on each side of the prostate and one in the apex. Ciprofloxacin 250 mg 1-0-1 was prescribed as postinterventional prophylaxis for 5 days. If patients received androgen deprivation therapy, it was prescribed by the caretaking urologist.

Outcome measurements

Patient follow-ups were immediately after treatment, 3 months after treatment, 12 months after treatment, and every 12 months from then on. At each follow-up, PSA levels and GI and GU side effects were assessed by the physician. bNED failure was defined using the Phoenix criteria (PSA nadir + 2 ng/mL).[21] Acute and late GI and GU side effects were assessed using the RTOG criteria.[22] Survival data were collected using the local death registry.

Dose-volume histogram (DVH) data were collected using our database. They included the vol-

umes, Dmax/D1, and Dmean of the CTV, PTV, rectum, and bladder, as well as the Dmin of the CTV and the V70 and V60 for the rectum and V70, V50, and V30 for the bladder, as these data were used for plan evaluation.

Statistical analysis

The statistical analysis was performed using GraphPad Prism 9.3.1 (GraphPad Software, San Diego, CA, USA) and SPSS 28.0.1.0 (IBM, Armonk, NY, USA). A p-value of < 0.05 was considered statistically significant. bNED, overall survival, and disease-free survival were compared using the Kaplan-Meier method. Side effects were analyzed by use of the Mann-Whitney U test, the Kruskal-Wallis test, and a Cox regression analysis for the onset of late toxicity grade 2 or higher, as well as bNED and overall survival.

Results

Patient characteristics are displayed in Table 1. We also analyzed the reasons for patients not receiving GFM implantation. Among them, most patients (12, 60%) had medical contraindications for anesthesia, 5 patients (25%) refused GFM implantation, and for 3 patients (15%) who did not receive GFM, the reason was unknown.

bNED rates are displayed in Figure 1. bNED ratios after 5 years for patients with and without GFM implantation were 92% and 100%, respective-

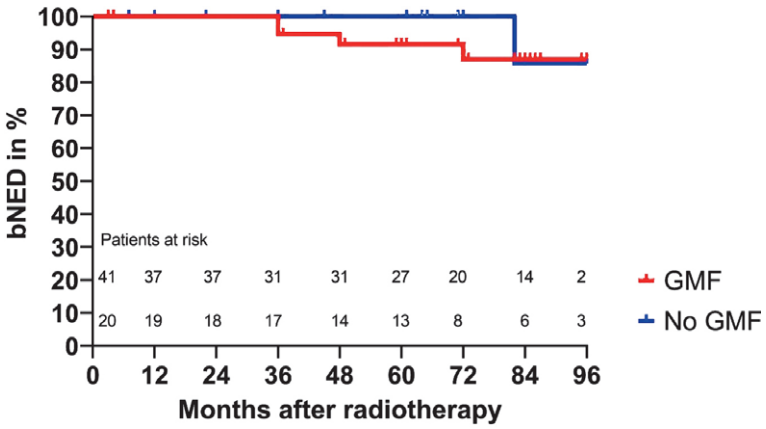

FIGURE 1. Biochemical no evidence of disease (bNED) rates of patients with and without gold fiducial marker (GMF) implantation (p = 0.61).

TABLE 1. Patient characteristics

	GFM	%	No GFM	%
n	41	100%	20	100%
cT category				
1	23	56%	16	80%
2	18	44%	4	20%
iPSA in µg/l, median (IQR)	7 (5.3/8.7)		5.9 (4.4/10.6)	
Gleason score				
6	26	63%	18	90%
7a	12	29%	1	5%
7b	3	7%	1	5%
Risk group				
Low risk	16	39%	10	50%
Intermediate risk	25	61%	10	50%
ADT prescribed	14	34%	3	15%
Median duration of ADT in months (IQR)	9 (3/18)		6 (6/8)	
Median age at RT (IQR)	74 (70/77)		72 (67/72)	
Median follow-up in months (IQR)	72 (49/84)		68 (36/86.5)	

ADT = androgen deprivation therapy; cT = clinical tumor extension; GFM = gold fiducial markers; iPSA = initial prostate-specific antigen; IQR = interquartile range; RT = radiotherapy low risk = PSA < 10 µg/L and Gleason Score 6; intermediate risk = PSA ≥ 10 µg/L or Gleason Score 7a/b

TABLE 2. Maximum acute side effects in patients with and without gold fiducial marker implantation

Grade	Gastrointestinal toxicity		Genitourinary toxicity	
	Gold fiducial markers	No gold fiducial markers	Gold fiducial markers	No gold fiducial markers
0	27%	15%	17%	5%
1	66%	65%	44%	55%
2	7%	20%	39%	40%

No significant differences for acute gastrointestinal and genitourinary side effects were detected (p = 0.15 and p = 0.58, respectively).

TABLE 3. Maximum late side effects in patients with and without gold fiducial marker implantation

Grade	Gastrointestinal toxicity		Genitourinary toxicity	
	Gold fiducial markers	No gold fiducial markers	Gold fiducial markers	No gold fiducial markers
0	59%	50%	37%	35%
1	12%	15%	27%	25%
2	24%	35%	34%	35%
3	5%	0%	2%	5%

No significant differences for late gastrointestinal and genitourinary side effects were detected (p = 0.64 and p = 0.80, respectively).

ly. After 8 years, bNED rates were 87% and 86%, respectively (p = 0.61). We also analyzed disease-specific survival (DSS) and overall survival (OS). Regarding DSS, we did not find a single death due to prostate cancer (p > 0.9999). For OS, survival proportions for patients with and without GFM after 5 years were 93% and 95%, and after 8 years 90% and 95% (p = 0.56).

Maximum acute and late gastrointestinal side effects are displayed in Tables 2 and 3. No significant differences between the two groups were detected. It is noteworthy that at no point was a grade 4 toxicity detected. We also compared late GI and GU toxicity in the two groups after 3, 12, 24, 36, 48, 60, 72, 84, and 96 months, and did not find a significant difference at any point.

For DVH data, we started by comparing the two groups regarding volumes, Dmax/D1, and Dmean of the CTV, PTV, rectum, and bladder, as well as the Dmin of the CTV and the V70 and V60 for the rectum and V70, V50, and V30 for the bladder. Significant differences were found in the PTV (median 124.7 cm^3 with GFM and 157.1 cm^3 without, p = 0.004), the Dmin of the CTV (median 76.0 Gy with GFM and 76.5 Gy without, p = 0.04), the rectal Dmean (median 36.0 Gy with GFM and 39.3 Gy without, p = 0.01), V70 (median 11.4 Gy with GFM and 16.1 Gy without, p < 0.001), and V60 (median 20.0 Gy with GFM and 25.3 Gy without, p < 0.001). An overview of the DVH data is presented in Table 4.

We also performed a univariable, and if more than one variable was significant, a multivariable Cox regression analysis regarding bNED and OS, as displayed in Table 5, as well as the onset of late GI or GU toxicity grade 2 or higher. The results of our Cox regression analysis regarding bNED and OS are displayed in Table 5.

As no patient died of prostate cancer, we did not model a Cox regression for DSS. Analyses including rectal or bladder DVH variables regarding bNED and OS were performed, and none of the variables was significant. Therefore, to improve clarity, we did not add them to Table 5. The results regarding toxicity are displayed in Table 6.

Discussion

As GFM implantation is an invasive procedure, the benefits of implantation have to outweigh the potential risks. There are two categories of risks. The first is the risk due to the implantation itself. Citing our information sheet, these risks are bleeding, injuries of the bladder and urethra, infection including abscess formation, and allergic reactions to the prescribed antibiotic. The second category is risks due to the anaesthesia. Even when only a breathing mask is used to administer anaesthesia, these risks include tissue damage due to patient positioning, allergic reactions, malignant hyperthermia, subsequent confusion, aspiration, and regaining consciousness during anesthesia.[16,17] While these side effects occur rarely in our clinical experience, as well as in the literature[23], they have to be considered in evaluating GFM implantation, aside from its influence on tumor control and side effects.

Several retrospective studies comparing fiducial IGRT with a control group exist. However, most of them compare a 3D conformal group with either an IGRT 3D conformal group[14,24] or an IGRT IMRT group[12], making them hard to apply to today's treatment due to their being outdated or their comparison of two different treatment modalities with inherent differences regarding outcomes. While many international guidelines[1,4,10] suggest the use of IGRT, no study covering this topic is mentioned in the NCCN[1] or NICE[10] guidelines. Napieralska *et al.*[15], to our knowledge the

only other study comparing patients with and without fiducial marker implantation and IMRT, found no significant differences regarding either bNED, with the exception of improved OS in intermediate patients, or late toxicity when comparing fiducial marker guidance and bone structure guidance. A significant difference was found regarding acute GU toxicity. Our results are similar, with no significant differences in acute toxicity. However, the aforementioned study did not include DVH data. Looking at our DVH data, we were unable to translate the differences regarding PTV and rectal variables into differences related to tumor control or toxicity, most likely due to DVH constraints in both groups.

It is quite likely that the most crucial effect regarding potential outcomes in our department is the safety margin reduction by 3 mm in GFM patients, which is absent from the aforementioned studies. The effect of reducing the safety margin by 3 mm can be displayed using math. Assume a spherical form for the prostate, with a radius between 2 and 2.5 cm and safety margins of 7 mm and 10 mm. The radii, including the PTV safety margins, are 2.7 cm and 3 cm, with an initial radius of 2 cm and 3.2 cm, respectively, and 3.5 cm with an initial radius of 2.5 cm. With $4/3*\pi*r^3$ being the formula for the volume of a sphere, reducing the safety margins by 3 mm leads to a decrease in the PTV of 27% for the 2-cm initial radius and 24% for the 2.5-cm initial radius ($2.7^3/3^3$ and $3.2^3/3.5^3$). In our data, the difference in the median volume is 21%, similar to the expected difference. Although this calculation is far from perfect, as the prostate is not a perfect sphere, it allows one to imagine the effect of safety margin variation through the third power of the radius. Zelefsky's conclusion in his IGRT study[11] was that safety margins should be reduced. However, to our knowledge, he has yet to publish any data comparing bNED rates before and after margin reduction.

When comparing our bNED rates with those of groundbreaking studies like those of Peeters *et al.*[25] and Pasalic *et al.*[26], using 78 Gy, and Dearnaley *et al.*[27], using 74 Gy, with bNED rates after 5 years ranging from 64% for Peeters to above 90% for Pasalic, we are leaning toward the top end, with bNED rates after 5 years of 92% and more, while only including patients with low- and intermediate-risk tumors. Regarding late side effects, while there were no significant differences between the two groups, our data, with 29%–35% of maximum GI toxicity at RTOG grade 2 or higher toxicity and approximately 36%–40% of GU toxicity of RTOG grade ≥ 2, are worse than the results presented by Napieralska[15], showing 12% grade ≥ 2 GU side effects and 15%–19% grade ≥ 2 GI side effects, possibly due to differences in side-effect assessment between institutions. Zelefsky reports lower toxicity rates, using CTCAE criteria, complicating a direct comparison.

One weakness of our study is its retrospective nature. On top of that, there is no group of patients with GFM implantation and a safety margin of 10

TABLE 4. Dose-volume histograms for patients with and without gold fiducial markers (GFM)

	GFM	No GFM
PTV prostate cm³ median (IQR)	124.72 (98.68–152.83)	157.12 (128.34–173.66)
PTV Dmax/D1 median (IQR)	81.55 (80.55–82.75)	81.15 (80.46–82.06)
PTV Dmean median (IQR)	78.10 (77.41–78.70)	78.10 (77.00–78.43)
CTV prostate cm³ median (IQR)	44.14 (34.75–64.70)	43.91 (34.40–55.42)
CTV Dmax/D1 median (IQR)	81.24 (80.64–82.57)	81.22 (80.35–81.85)
CTV Dmean median (IQR)	78.58 (77.97–79.47)	78.63 (77.94–79.04)
CTV Dmin median (IQR)	76.00 (75.36–76.32)	76.49 (75.88–77.05)
Rectal volume median (IQR)	113.02 (100.22–134.55)	114.53 (105.57–136.38)
Rectal Dmax median (IQR)	80.06 (78.88–81.98)	80.24 (79.23–81.25)
Rectal Dmean median (IQR)	35.99 (32.94–39.61)	39.30 (37.81–42.99)
Rectal V70 Gy % median (IQR)	11.41 (9.41–13.04)	16.12 (14.55–18.66)
Rectal V70 Gy cm³ median (IQR)	13.21 (11.33–15.93)	18.66 (16.55–21.39)
Rectal V60 Gy % median (IQR)	19.95 (16.39–22.37)	25.25 (23.77–29.26)
Rectal V60 Gy cm³ median (IQR)	23.36 (19.93–25.98)	29.23 (26.74–33.13)
Bladder volume median (IQR)	196.93 (113.66–282.94)	155.76 (127.30–296.44)
Bladder Dmax/D1 median (IQR)	78.78 (77.01–80.53)	79.53 (77.04–80.44)
Bladder Dmean median (IQR)	21.11 (16.92–30.06)	28.10 (18.99–35.20)
Bladder V70 Gy % median (IQR)	7.50 (5.44–11.78)	9.43 (6.06–14.02)
Bladder V70 Gy cm³ median (IQR)	14.14 (10.53–21.16)	19.01 (12.00–22.20)
Bladder V50 Gy % median (IQR)	17.14 (12.00–26,40)	20.81 (13.60–30.86)
Bladder V50 Gy cm³ median (IQR)	34.00 (23.17–42.23)	37.58 (27.16–44.42)
Bladder V30 Gy % median (IQR)	28.24 (21.74–41.73)	41.31 (25.78–51.83)
Bladder V30 Gy cm³ median (IQR)	58.71 (43.43–78.57)	65.38 (48.97–83.61)

CTV = clinical target volume; GFM = gold fiducial marker; IQR = interquartile range; PTV = planning target volume; RT = radiotherapy

TABLE 5. Uni- and multivariable Cox regression of biochemical no evidence of disease (bNED) and overall survival (OS)

bNED	Univariable analysis			Multivariable analysis		
	p-value	exp(HR)	exp(HR) (95% conf.)	p-value	exp(HR)	exp(HR) (95% conf.)
Use of GFM	0.603	1.788	0.200–16.018	-	-	-
Age at RT	0.960	0.996	0.857–1.157	-	-	-
PTV prostate	0.789	1.003	0.980–1.027	-	-	-
PTV Dmax/D1	0.556	1.133	0.747–1.719	-	-	-
PTV Dmean	0.960	0.978	0.410–2.332	-	-	-
CTV prostate	0.006	1.020	1.006–1.035	0.862	0.996	0.947–1.046
CTV Dmax/D1	0.014	0.814	0.690–0.960	0.224	2.583	0.560–11.925
CTV Dmean	0.005	0.858	0.770–0.956	0.298	0.188	0.008–4.393
CTV Dmin	0.005	0.875	0.797–0.960	0.453	2.067	0.310–13.770

OS	Univariable analysis					
	p-value	exp(HR)	exp(HR) (95% conf.)			
Use of GFM	0.564	1.907	0.213–17.063	-	-	-
Age at RT	0.235	1.149	0.913–1.446	-	-	-
PTV Prostate	0.723	1.004	0.984–1.024	-	-	-
PTV Dmax/D1	0.300	0.705	0.364–1.366	-	-	-
PTV Dmean	0.153	0.426	0.132–1.373	-	-	-
CTV Prostate	0.833	1.002	0.980–1.025	-	-	-
CTV Dmax/D1	0.775	0.964	0.747–1.242	-	-	-
CTV Dmean	0.946	0.992	0.791–1.245	-	-	-
CTV Dmin	0.879	1.024	0.758–1.383	-	-	-

bNED = biochemical no evidence of disease; CTV = clinical target volume; GFM = gold fiducial marker; HR = hazard ratio; OS = overall survival; PTV = planning target volume; RT = radiotherapy

mm, complicating the direct comparison of our two groups, as GFM were implanted and the safety margin was reduced to 7 mm together. However, retrospective studies should be used to generate hypotheses, not prove them, and with this study we have generated the hypothesis that the use of GFM for IGRT provides no benefits, but only risks, and should not be performed regularly if other, non-invasive tools for IGRT are in use. Another weakness is the limited sample size.

Regarding strengths, we analyzed a homogeneous patient collective to address this question, with in-depth data including bNED, OS, DSS, and acute and late toxicity, as well as DVH data. Besides, our patient collectives were recruited in parallel, and this reduced any potential bias due to changing treatment modalities over time.

Conclusions

With this study, we have developed the hypothesis that the use of GFM in IGRT does not provide a substantial benefit regarding tumor control or toxicity when other modalities for IGRT are used. To clarify the role of GFM in IGRT, prospective studies based on this hypothesis are needed to possibly reduce the number of unnecessary medical interventions in the treatment of men's most common cancer.

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TABLE 6. Uni- and multivariable Cox regression of the onset of late gastrointestinal or genitourinary toxicity grade 2 or higher

GI	Univariable analysis			Multivariable analysis		
Variable	**p-value**	**exp(HR)**	**exp(HR) (95% conf.)**	**p-value**	**exp(HR)**	**exp(HR) (95% conf.)**
Use of GFM	0.89	0.936	0.368–2.378	-	-	-
Acute GI grade 2	0.09	2.642	0.875–7.981	-	-	-
Age at RT	0.03	1.124	1.010–1.252	0.101	1.092	0.983-1.213
PTV prostate	0.06	0.987	0.974–1.000	-	-	-
PTV Dmax/D1	0.76	1.037	0.824–1.305	-	-	-
PTV Dmean	0.49	1.158	0.767–1.747	-	-	-
CTV prostate	0.03	0.966	0.936–0.996	0.073	0.972	0.942–1.003
CTV Dmax/D1	0.55	1.056	0.884–1.263	-	-	-
CTV Dmean	0.51	1.090	0.843–1.410	-	-	-
CTV Dmin	0.64	1.042	0.877–1.236	-	-	-
Rectal Volume	0.29	1.007	0.994–1.020	-	-	-
Rectal Dmax	0.29	1.125	0.906–1.397	-	-	-
Rectal Dmean	0.25	0.951	0.973–1.036	-	-	-
Rectal V70 Gy %	0.59	0.971	0.875–1.078	-	-	-
Rectal V70 Gy cm^3	0.42	1.040	0.945–1.144	-	-	-
Rectal V60 Gy %	0.42	0.969	0.899–1.046	-	-	-
Rectal V60 Gy cm^3	0.50	1.024	0.955–1.099	-	-	-

GU	Univariable analysis					
Variable	**p-value**	**exp(HR)**	**exp(HR) (95% conf.)**			
Use of GFM	0.93	1.041	0.441–2.459	-	-	-
Acute GU grade 2	0.09	2.042	0.892–4.673	-	-	-
Age at RT	0.50	1.026	0.952–1.106	-	-	-
PTV prostate	0.29	1.006	0.995–1.017	-	-	-
PTV Dmax/D1	0.14	0.808	0.611–1.068	-	-	-
PTV Dmean	0.04	0.573	0.342–0.961	-	-	-
CTV prostate	0.93	0.999	0.989–1.010	-	-	-
CTV Dmax/D1	0.93	1.006	0.895–1.130	-	-	-
CTV Dmean	0.67	1.025	0.916–1.147	-	-	-
CTV Dmin CTV	0.58	1.035	0.918–1.165	-	-	-
Bladder volume	0.72	0.999	0.997–1.002	-	-	-
Bladder Dmax/D1	0.24	0.973	0.696–1.094	-	-	-
Bladder Dmean	0.89	0.997	0.960–1.036	-	-	–
Bladder V70 Gy %	0.49	0.977	0.913–1.045	-	-	-
Bladder V70 Gy cm^3	0.23	0.969	0.921–1.020	-	-	-
Bladder V50 Gy %	0.54	0.988	0.951–1.027	-	-	-
Bladder V50 Gy cm^3	0.29	0.985	0.957–1.013	-	-	-
Bladder V30 Gy %	0.79	0.997	0.974–1.020	-	-	-
Bladder V30 Gy cm^3	0.70	0.997	0.980–1.014	-	-	-

CTV = clinical target volume; GFM = gold fiducial marker; GI = gastrointestinal; GU = genitourinary; PTV = planning target volume; RT = radiotherapy

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