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Cone-beam CT-based adaptive planning improves permanent prostate brachytherapy dosimetry: An analysis of 1266 patients

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Purpose: To evaluate adaptive planning for permanent prostate brachytherapy and to identify the prostate regions that needed adaptation.
Methods and materials: After the implantation of stranded seeds, using real-time intraoperative planning, a transrectal ultrasound (TRUS)-scan was obtained and contoured. The positions of seeds were determined on a C-arm cone-beam computed tomography (CBCT)-scan. The CBCT-scan was registered to the TRUS-scan using fiducial gold markers. If dose coverage on the combined image-dataset was inadequate, an intraoperative adaptation was performed by placing remedial seeds. CBCT-based intraoperative dosimetry was analyzed for the prostate (D_{90}, V_{100}, and V_{150}) and the urethra (D_{30}). The effects of the adaptive dosimetry procedure for Day 30 were separately assessed.
Results: We analyzed 1266 patients. In 17.4% of the procedures, an adaptation was performed. Without the dose contribution of the adaptation Day 30 V_{100} would be < 95% for half of this group. On Day 0, the increase due to the adaptation was 11.8 ± 7.2% (1SD) for D_{90} and 9.0 ± 6.4% for V_{100}. On Day 30, we observed an increase in D_{90} of 12.3 ± 6.0% and in V_{100} of 4.2 ± 4.3%. For the total group, a D_{90} of 119.6 ± 9.1% and V_{100} of 97.7 ± 2.5% was achieved. Most remedial seeds were placed anteriorly near the base of the prostate.
Conclusion: CBCT-based adaptive planning enables identification of implants needing adaptation and improves prostate dose coverage. Adaptations were predominantly performed near the anterior base of the prostate. [https://doi.org/10.1002/mp.12156]

Key words: adaptive dosimetry, adaptive radiotherapy, brachytherapy, I-125, prostate

1. INTRODUCTION

Postimplant dosimetry forms an essential feature of permanent prostate brachytherapy, as the results of postimplant dosimetry correlate with clinical outcome.[1–4] For ^{125}I-implants GEC/ESTRO, ABS, and AAPM recommend to perform this postimplant dosimetry approximately 30 days after the implantation procedure.[5–8] However, at Day 30, dose coverage of the prostate may be lower than intended during the implantation procedure.

A lower D_{90} (dose that covers 90% of the prostate)[8–10] and V_{100} (% of the prostate that receives at least 100% of the prescription dose)[8–11] at Day 30 correlate with poorer treatment outcome. Insufficient target coverage cannot be overcome by increasing the overall dose; an excessive dose might harm the organs at risk. A high V_{150} is correlated with urethral,[12–14] bowel,[12,14] and erectile[16] toxicity. Therefore, during implantation a balance needs to be found between a high V_{100} and a low V_{150}. Dose to urethra, bladder, and rectum should be kept below critical levels.

Intraoperative dosimetry procedures have been developed to generate high-quality implants. Intraoperative planning takes the actual size and shape at the day of implantation into account. With interactive planning, the treatment is adapted according to the needle tracks, mostly determined using transrectal ultrasound (TRUS), resulting in improved dosimetry[17] and clinical outcome.[18] Dynamic planning introduces an interactive procedure in which the actual shape of the prostate and positions of the deposited seeds are dynamically updated, allowing a higher overall accuracy.[17]

Since 2007, we routinely apply an intraoperative C-arm cone-beam CT (CBCT)-based adaptive dosimetry technique.[19] With the patient still anesthetized, source positions identified with CBCT are registered to a TRUS scan, resulting in accurate dosimetry. This enables immediate, fast adaptation of the implant. We report the dosimetric results of this procedure for 1266 patients. We identified the regions of the prostate where remedial seeds were placed and show resulting effects on dosimetry. To our best knowledge, this is the first study to present large-scale intraoperative dosimetry results for an adaptive planning procedure and the dosimetrical consequences at Day 30.

2. METHODS AND MATERIALS

2.A. Patients

In the period of October 2007–March 2016, we treated 1314 patients with localized prostate cancer (T1b – T2c) with ^{125}I brachytherapy. Patients were included in the analysis if they received the standard treatment and clinical follow-up. We excluded patients with incomplete datasets. Of the 1266 included cases, 81% (1026 cases) received a monotherapy treatment of 145 Gy and 17% (211 cases) was treated with a boost of 110 Gy, 2% (29 cases) with a boost of 100 Gy. The boost treatment was given approximately 2 weeks after completion of external beam radiotherapy (EBRT).

2.B. Treatment technique

The implantation procedure, including all time points at which images were obtained or dosimetry was performed, is visualized in Fig. 1. Implantations were performed with patients under spinal anesthesia in dorsolithotomy position. Fluoroscopy (Siemens Arcadis Orbic 3D; Siemens Medical Systems, Erlangen, Germany) and ultrasound (Falcon 2101 EX and Flex Focus 400, BK Medical; Herlev, Denmark) were utilized to provide image feedback during implantation.

The implantation procedure started with the placement of four cylindrical fiducial gold markers (⌀1 × 5 mm; Heraeus GmbH, Hanau, Germany). The markers were used to register TRUS and CBCT at the end of the procedure and provided reference points in the prostate that facilitated navigation with fluoroscopy and TRUS. Patients receiving a boost had already four markers implanted prior to the preceding EBRT treatment for position verification.

After marker placement, a TRUS-scan (TRUS 1) was obtained, and the prostate (without margin), urethra, and rectum were contoured. The urethra was contoured as a circle with fixed 5 mm diameter. On this dataset, an intraoperative initial plan was made which served as a starting point for interactive, real-time implantation of seeds. The intraoperative starting point (Plan II) was based on a volume study (Plan I) that was made several weeks before implantation to exclude pubic arch interference and to determine the amount and strength of the ^{125}I seeds to be ordered. In our workflow, we improved intraoperative efficiency by editing Plan I instead of generating a plan anew. Plan II was modified according to the actual shape of the prostate and organs at risk contours on TRUS 1. Subsequently, the implantation was performed (Plan III) using an interactive,[17] real-time planning technique. Plan III is a key element of the adaptive planning procedure, in contrast to Plan I and Plan II that are specific for our implementation to improve the efficiency.

During the implantation, the position of stranded seeds (2007 – June 2008: IBt 1251L, Seneffe, Belgium; June 2008 – March 2010: IBt-Bebig I25.SO6, Berlin, Germany; March 2008 – 2016: Bard STM1251, Murray Hill, NJ USA) was recorded on live TRUS images during release from the needles. First, seeds were implanted in the periphery of the prostate. Seed positions, visible on TRUS, were recorded in the TPS and the dose distribution was recalculated. The treatment plan was updated, and the planned positions of the remaining seeds were reoptimized. Next, seeds were implanted in the dorsal side of the prostate. Also these seed positions were recorded, and after calculating the actual dose distribution, the remaining, central seed positions were reoptimized. Finally, the central seeds were placed and with their updated, optimized positions, final intraoperative TRUS-based dosimetry was obtained (Plan III).[20]

Following implantation the dosimetry of the implant was assessed. First, the legs of the patient were lowered as far as possible, with the feet of the patient remaining in the support. The pressure of the TRUS probe to the rectum was minimized to reduce possible deformation of the prostate. A TRUS-study (TRUS 2) was obtained with 2.5 mm spaced slices, on which the prostate and urethra were immediately contoured.

Directly after removal of the TRUS-probe and leg-support system a CBCT (CBCT 1) was acquired with the C-arm system that was also used for fluoroscopy. A transversal CT reconstruction with 2.5 mm thick slices was generated. Both the TRUS and the CBCT dataset were sent to the treatment planning system (TPS) (Variseed 7.2 – 8.0.2; Varian Medical Systems, Inc., Palo Alto, CA, USA). The seedfinder of the TPS identified the source-positions in the CBCT dataset. Resulting seed positions were visually inspected and, if necessary, corrected. In all cases, the TPS identified the fiducial gold markers as seeds. Furthermore, occasionally, seeds close together were identified as one seed and seeds not displaying a bright spot on CBCT were not automatically found.

The TRUS study was registered to the CBCT dataset using the fiducial markers as reference points. The registration was visually checked by identifying the fiducial markers, seeds and urethral catheter in both datasets and manually adjusted if necessary.

A dose distribution (Plan IV) was calculated and inspected for underdosages. In case the radiation oncologist observed a critical underdosage, that was mostly also represented by a low V_{100}, the implant was adapted. In addition to the dosimetry, the decision to adapt was made by clinical considerations, such as the absolute value of the underdosage, and the location of the underdosage with respect to the index lesion. An updated plan (Plan IV.a) was made, using the CBCT-based postplan as starting point. Remedial seeds were implanted

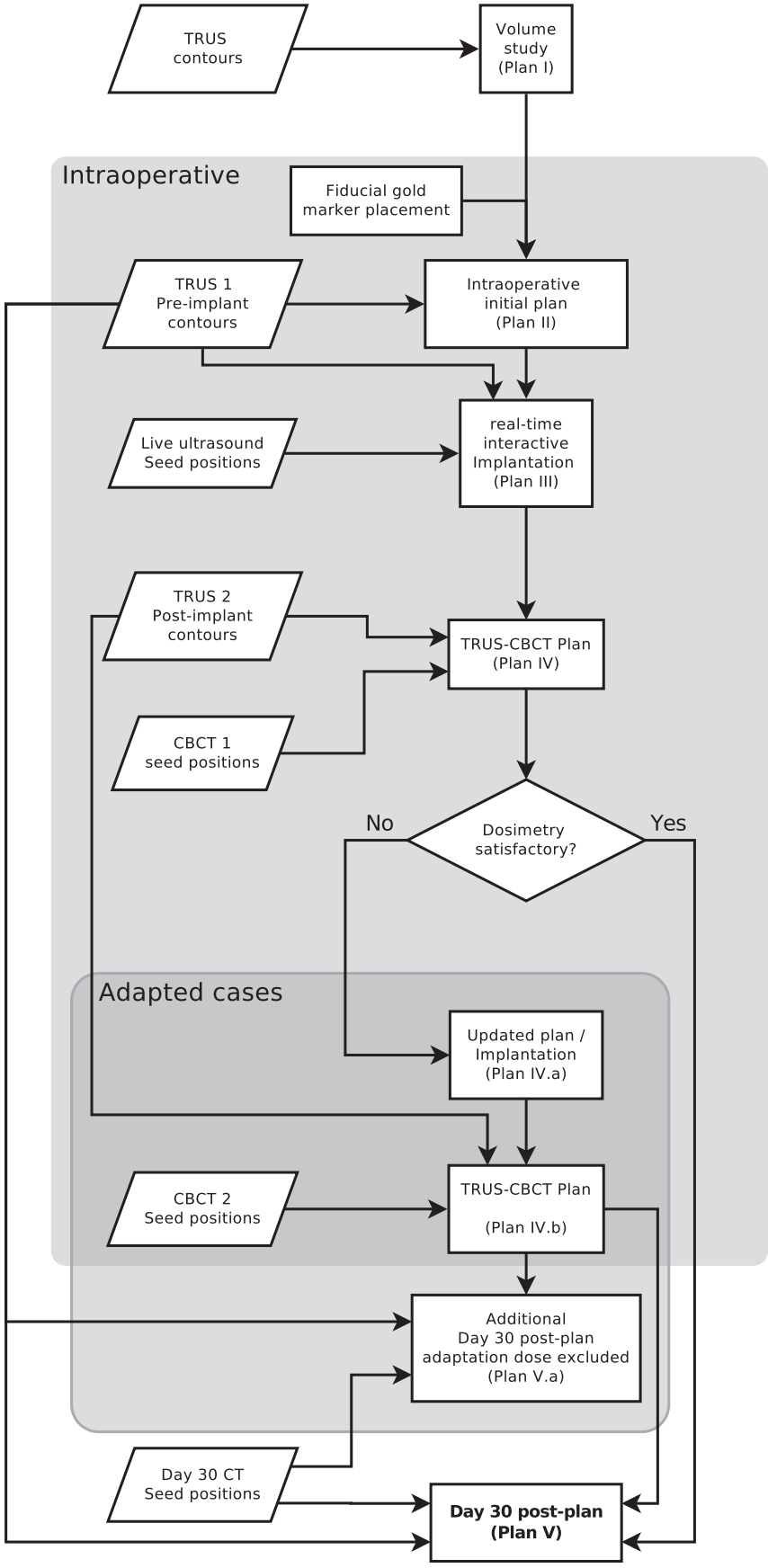

FIG. 1. Imaging and (adaptive) dosimetry. The trapezoidal boxes (left) show input of image data with corresponding contours and/or seed positions. The rectangles (right) show all plans. Plan IV, IV.a, IV.b, V, and V.a include TRUS-(CB)CT registration.

with the patient back in dorsolithotomy position and an additional CBCT-image (CBCT 2) dataset was acquired with the patient in imaging position. An extra postplan (Plan IV.b) based on CBCT 2 and the postimplant TRUS 2 (Fig. 1) was made after the implantation procedure had finished. Plans were made using the TG-43 line source approximation for seeds.[21] Seeds had an average air kerma strength of 0.59 U (range 0.37−0.77 U) during placement. Figure 2 gives an example of de consequences of the adaptation on dosimetry. More details of the clinical procedure have been described before.[19,20] In that study, Day 0 dosimetry was assessed solely to show the feasibility of the procedure for a group of 20 patients.

2.C. Day 30 dosimetry

Day 30 dosimetry (Plan V) was performed. To locate the sources, a CT-dataset (Brilliance Big Bore 16 Slice; Philips,

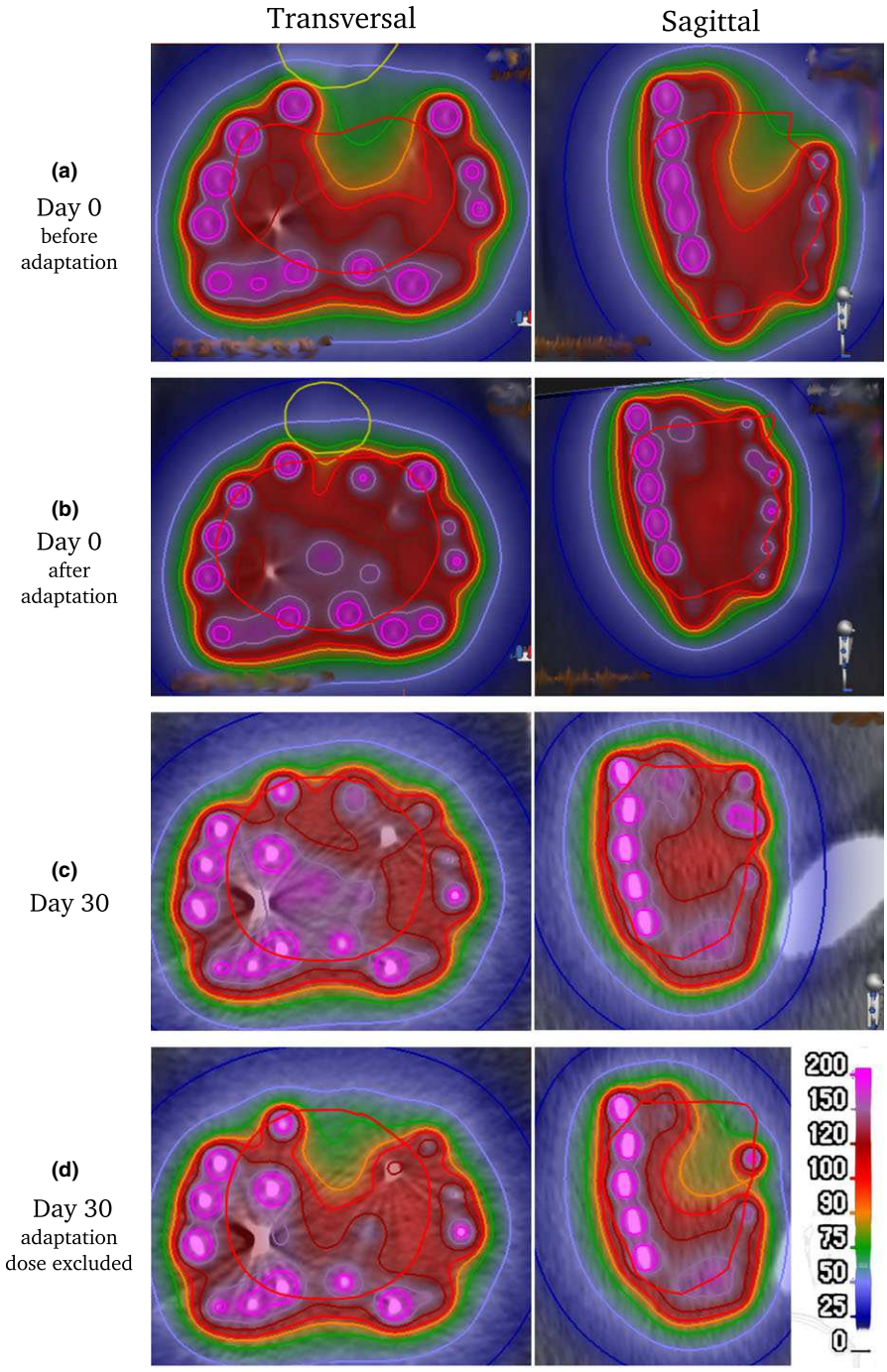

FIG. 2. This example showed poor initial dose coverage (a), Fig. 1:Plan IV. The underdosages were adapted by placing remedial seeds (b), Plan IV.b. At Day 30 dose coverage was adequate (c), Plan V. However, excluding the adaptation of the remedial seeds, dose coverage would have been insufficient at Day 30 (d), Plan V.a. The color bar represents the percentage of the prescribed dose (145 Gy). The prostate is contoured in red, the bladder in yellow.

Best, the Netherlands) was obtained with 2 mm thick slices. TRUS 1, that is not affected by edema,[20] was registered to the CT-dataset using the fiducial markers as reference points. If needed, the registration was manually adjusted. This method is similar to the methodology presented by Bowes *et al.*;[22] we use fiducial markers instead of the urethra for registration of the TRUS and CT data. Bowes *et al.* showed that this method results in similar values as MRI-CT dosimetry at Day 30.

The dosimetry for each patient was recorded. In case an implant had been adapted in the operating theatre, an additional postplan (Plan V.a) was made where we excluded the dose contribution of the remedial seeds, providing a situation as if no adaptation had been performed. An experienced technologist located remedial seeds visually, comparing intraoperative and postimplant seed distributions. This additional plan was used to quantify the dosimetric effects of the adaptation. Figure 2 shows an example of the changes in isodoses as a consequence of the adaptation.

2.D. Analysis

The prostate D_{90}, V_{100}, V_{150} and the urethral D_{30} were determined for the adapted and the nonadapted group, for Day 0 (intraoperative) as well as Day 30. Dosimetry of adapted and nonadapted cases was visualized as density plots at various points in time (Plan III – V). The dose homogeneity index (HI) was calculated for Day 30 as $(V_{100} - V_{150})/V_{100}$.

Seed positions from 128 adapted implants were extracted from DICOM RTPlan objects. Seeds present in Plan V but not in Plan V.a were identified as remedial seeds (Fig. 1). Projections of implants for the three main axes were displayed with the remedial seeds highlighted in a contrasting colour.

Density distributions were constructed for the left–right (LR), anterior–posterior (AP), and cranio–caudal (CC) axes to compare the positions of the remedial seeds with the positions of the initially implanted seeds.

3. RESULTS

For the 1266 patients in our analysis, adaptive CBCT-based planning led to an adaptation in 218 (17.4%) cases. On average 71 seeds (range 36–94) were implanted. A median of 4 (range 1–10) remedial seeds were added during the implantation procedure.

The distributions of D_{90}, V_{100}, and V_{150} at Day 0 are shown in Fig. 3 for several points in time at which dosimetry was obtained (see also Fig. 1). Figure 3 separately shows the distributions for adapted cases without the dose contribution of remedial seeds. The individual intraoperative dosimetry changes, resulting from adaptation, are displayed in Fig. 4.

CBCT acquisition, registration, and dose review took approximately 10 minutes. The adaptation, including a second CBCT was performed in 1/4 h on average. This resulted in a mean procedure time (anesthetized patient to finished implant) of $1^1/_2$ h in case of an adaptation and $1^1/_4$ h if no adaptation was performed. In the adapted group, at Day 30, only 50% would have reached the preferred level of V_{100} if the adaptation would not have been performed. The adaptation increased this number to 90%. At Day 30, 89% of all cases had a $V_{100} > 95\%$, 99% showed a $V_{100} > 90\%$. The percentage of implants meeting the dosimetry criteria at Day 0 and Day 30 is displayed in Table I.

In Table II, the dosimetry at Day 0 and Day 30 is presented for both the adapted and the nonadapted cases. For all adapted cases, two Day 30 plans were made: one with and one without the dose contribution of the remedial seeds. The adaptation led to an immediate (Day 0) average increase in D_{90} of 11.8 ± 7.2% (1 SD), V_{100} showed a mean increase of 9.0 ± 6.4%. Comparing the corresponding Day 30 plans, an increase in D_{90} of 12.3 ± 6.0% and an increase in V_{100} of 4.2 ± 4.3% were observed as a result of the dose contribution of the remedial seeds. The volume of adapted implants, contoured after implantation (Plan IV), was smaller (35.1 ± 9.8 cm^3) than that of nonadapted implants (39.3 ± 10.9 cm^3).

Taking the average of dosimetry of all implants at Day 30, we observed a D_{90} of 119.6 ± 9.1%, a V_{100} of 97.7 ± 2.5%, a V_{150} of 57.0 ± 12.6% for the prostate and a D_{30} of 139.5 ± 16.2% for the urethra. The mean HI at Day 30 equaled 0.42 ± 0.12. At Day 30, the mean HI for the adapted group was 0.40 ± 0.12 and for the nonadapted group was 0.42 ± 0.12.

Figure 5 shows the locations where the remedial seeds were placed. The orthogonal 2D projections and the 3D-view show that remedial seeds were predominantly placed at the base, anterior in the prostate.

4. DISCUSSION

The dosimetric consequences of our adaptive planning technique are visualized in Figs. 3 and 4. For the vast majority of cases, D_{90} and V_{100} move from unacceptable values (below 100% and 90% respectively) to acceptable values. Only 1% of the cases showed a $V_{100} < 90\%$ at Day 30. For most cases (89%), the preferred level of at least 95% for V_{100} was achieved. If no adaptations would have been performed, only 51% of the adapted group would have had a preferred V_{100} (> 95%). The adaptation improved this number considerably to 90%. This shows that our procedure enabled identification of patients needing adaptation and that the selection at Day 0 correctly identified the group that otherwise would have shown coverage problems at Day 30.

Table II shows that V_{150} for the adapted group is lower than for the nonadapted group at Day 0 but higher at Day 30. In the adapted group, dosimetry is based on CBCT 2 (Plan IV.b), which is acquired about 15 min later in the implant procedure compared to CBCT 1 (Plan IV), used for dosimetry in the nonadapted group at Day 0. Therefore, in the adapted group, dosimetry may be more affected by edema, resulting in increase of prostate volume and lower V_{150}. At Day 30, edema has resolved and V_{150} is 2.7% higher for the adapted group.[20]

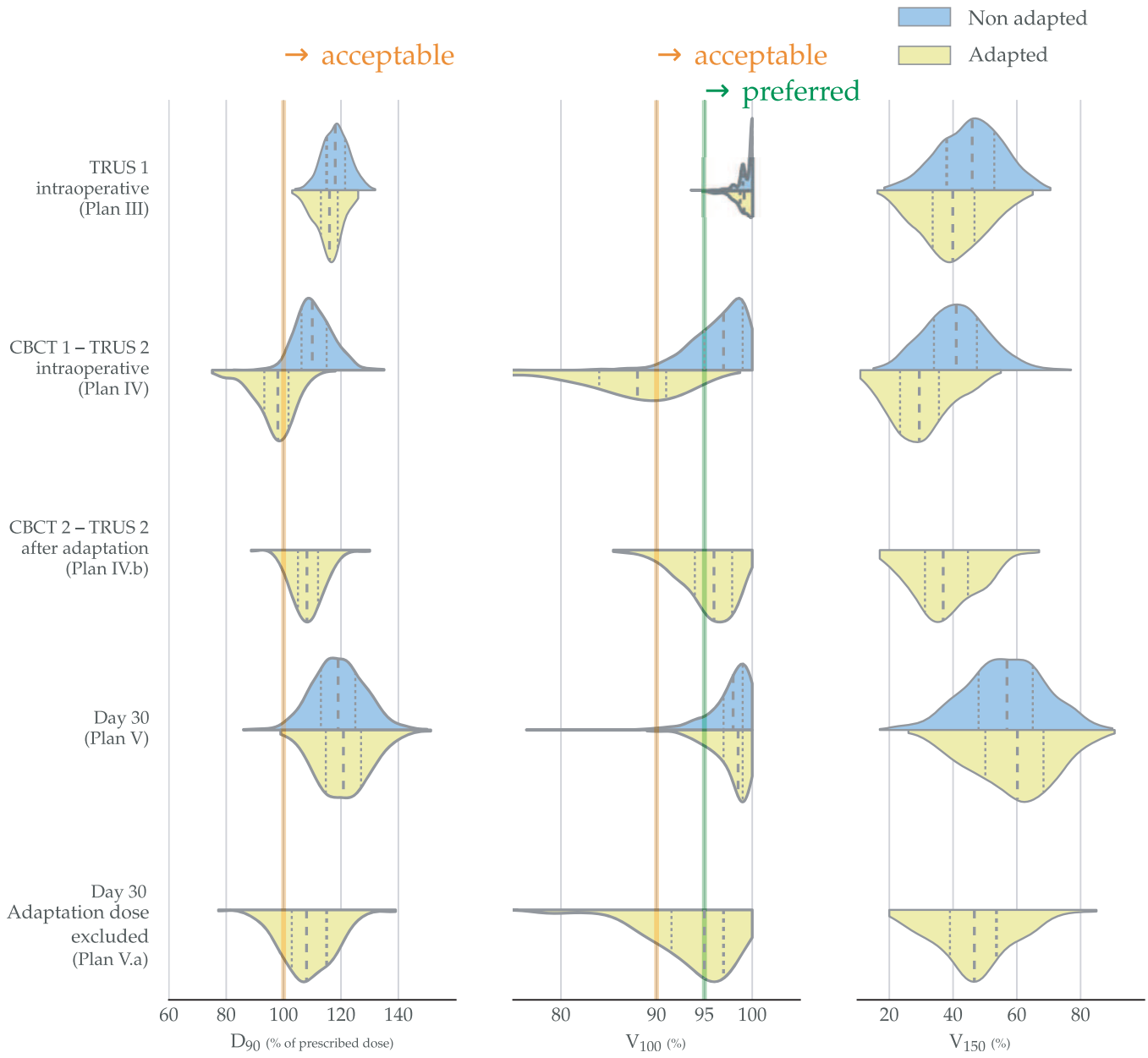

FIG. 3. After adaptation (Plan IV.b, Plan V), dosimetry of the adapted cases is similar to the nonadapted cases, before (Plan IV) and excluding the adaptation dose (Plan V.a) D_{90} and V_{100} are substantially poorer. The top half of each plot shows the nonadapted cases and the bottom half the adapted cases. Dotted lines present the quartiles, dashed lines the median values. Timing of plans is clarified in Fig. 1. Areas under the curves are normalized. [Color figure can be viewed at wileyonlinelibrary.com]

Considering the adapted group, Table II and Figs. 3 and 4 show that, at Day 30, dosimetry would have been considerably poorer without adaptation. After the adaptation however, dosimetry almost equaled the nonadapted group, both immediately after implantation and at Day 30. Not all patients showed Day 30 dosimetry above preferred levels, this is possibly caused by seed displacements.[20]

We compared Day 30 dosimetry after introduction of the CBCT technique to the dosimetry of 100 randomly selected patients (20 per yr) from the period 2002−2006. Target coverage was improved from 110 ± 17 to 120 ± 9% for D_{90} and 94 ± 5 to 98 ± 3% for V_{100}, at the same time V_{150} decreased from 60 ± 11 to 57 ± 13% and the urethral D_{30} decreased from 145 ± 19 to 140 ± 16%. This shows that the CBCT technique allowed more optimal implants, both for improving target coverage and for lowering dose to critical structures. Furthermore, the introduction of the CBCT technique significantly improved treatment outcome. For low-risk prostate cancer, 7-year biochemical disease-free survival (BDFS) improved from 87.2%to 93.5% (log rank: $P = 0.04$), for intermediate risk from 75.9% to 88.5% ($P < 0.001$), and for high risk from 57.1% to 85.0% ($P < 0.001$) with the introduction of CBCT-based adaptive planning.[23]

It is interesting that, using a state of the art, real-time intraoperative planning technique, implants may still show poor dosimetry. In previous work, we compared the dosimetric

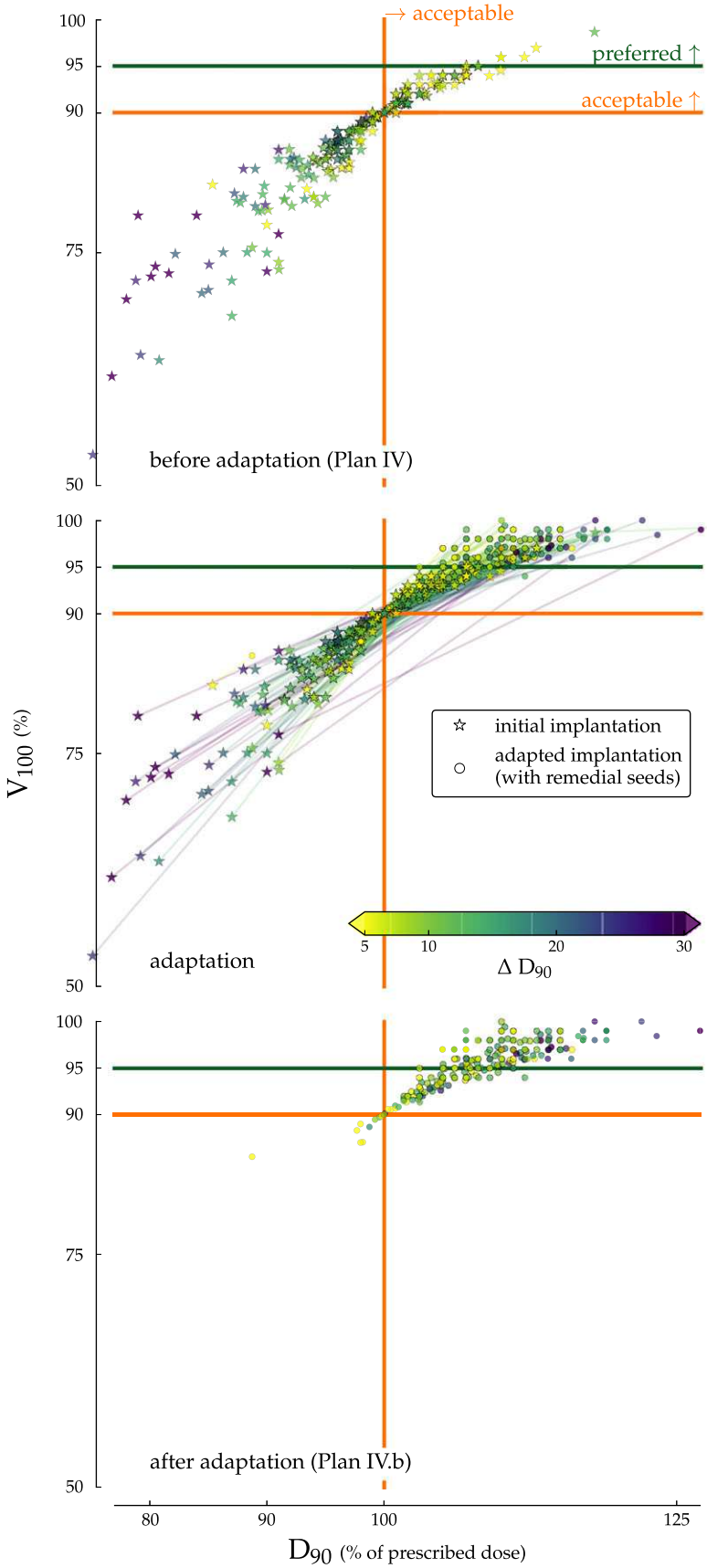

FIG. 4. The adaptation of the adaptive planning procedure improves intraoperative dosimetry considerably for implants that initially show inadequate dose coverage of the prostate. Dosimetry is acceptable with a $V_{100} > 90\%$ and a $D_{90} > 100\%$, preferably V_{100} is above 95%. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE I. Percentage of implants with acceptable ($D_{90} > 100\%$ of prescribed dose, or equivalently, $V_{100} > 90\%$ of total volume) or preferable ($V_{100} > 95\%$ of total volume) dosimetry of the prostate.

		Percent of implants with $D_{90} > 100\%$[a]	
		$V_{100} > 90\%$[b]	$V_{100} > 95\%$[b]
Day 0	Nonadapted	97	76
	Adapted: before adaptation	35	4
	Adapted: after adaptation	94	66
Day 30	Nonadapted	98.8	89
	Adapted: adaptation dose excluded	85	51
	Adapted: adaptation dose included	99.5	90

[a]% of prescribed dose.
[b]% of prostate volume.

results of our real-time intraoperative planning with that obtained with intraoperative CBCT. We found that edema and seed displacements were the major causes of underdosages needing adaptation.[20] In contrast to TRUS imaging, CBCT imaging allows for an accurate localization of all final seed locations and is thus able to display dosimetry including intraoperative edema and seed displacements.

We compared our results to other large-scale studies (>150 patients), reporting postimplant dosimetry. Techniques that relied on (intraoperative) preplanning showed an average postoperative D_{90} of 100−111%, a V_{100} of 89−94%, and a V_{150} of 56–61%.[24–26] Intraoperative real-time techniques showed a mean postoperative D_{90} of 105−126%, a V_{100} of 93−97%, and a V_{150} of 32–70%.[27–31] In the present study, Day 30 dosimetry shows an average D_{90} of 120%, a V_{100} of 98%, and a V_{150} of 57%. Compared to values reported in literature, the present study shows high values for V_{100} and D_{90}. This was realized by starting with a state of the art real-time interactive implantation procedure and adaptations of underdosages in 17% of the cases.

We realized a HI of 0.42 on average, which is relatively high compared to values in recent literature, ranging from 0.29 to 0.41.[24,26,29,32] This indicates that our adaptive technique allows for sparse implantation reducing V_{150} and associated risks of urethral,[12–14] bowel,[12,15] and erectile[16] toxicity as the technique provides the possibility to add remedial seeds if deemed necessary.

The final urethral D_{30} on Day 0 was comparable for the adapted (116%) and nonadapted group (117%, Table II). The absolute urethral D_{30} values on Day 30 have limited value as the urethra contour originated from the intraoperative procedure (Fig. 1, TRUS 1) and, because of the absence of a urinary catheter, the urethra may not have the same shape at Day 30.

In the treated population, an adaptation at Day 0 was deemed necessary in 17% of the cases. This seems a relatively large fraction. There are multiple reasons to adapt an implant. If the dosimetry is below the preferred level, and the dose at a clinically relevant volume is relatively low, the radiation oncologist usually decides for adaptation. The additional time to perform the adaptation is approximately 1/4 hour, allowing remedial seeds to be placed with low effort. On average two needles were sufficient to place the four remedial seeds. To further improve efficiency of the procedure TRUS 2, CBCT 2, Plan I, Plan II, Plan IV.b, and Plan V.a could be omitted, reducing overall workload at the expense of the loss of intermediate dosimetry data.

Immediately after introduction of the CBCT-based technique in our clinic, we performed adaptations more often than in recent years. Still, after almost 10 years of experience, we

TABLE II. Dosimetric effects of adaptation.

			Prostate			Urethra
			D_{90}[a]	V_{100}[b]	V_{150}[b]	D_{30}[a]
Day 0	Nonadapted	Mean[c]	110.7 ± 6.5	96.4 ± 3.0	41.1 ± 10.1	117.0 ± 10.6
		n[d]	1048	1048	1048	1047
	Adapted: before adaptation	Mean	96.9 ± 7.1	86.4 ± 7.0	29.9 ± 9.0	108.8 ± 11.9
		n[e]	218	218	218	216
	Adapted: after adaptation	Mean	108.6 ± 5.5	95.4 ± 2.7	37.8 ± 9.7	115.5 ± 9.9
		n[e]	214	214	214	213
Day 30	Nonadapted	Mean	119.3 ± 9.1	97.6 ± 2.5	56.5 ± 12.5	139.1 ± 16.3
		n[d]	1048	1048	1048	1045
	Adapted: adaptation dose excluded	Mean	108.6 ± 8.9	93.7 ± 5.1	46.9 ± 11.8	131.2 ± 15.7
		n[e]	218	218	218	218
	Adapted: adaptation dose included	Mean	120.9 ± 9.0	97.8 ± 2.0	59.2 ± 12.6	141.1 ± 15.9
		n[e]	218	218	218	218

[a]% of prescribed dose.
[b]% of prostate volume.
[c]Mean ± standard deviation.
[d]Missing data if < 1048.
[e]Missing data if < 218.

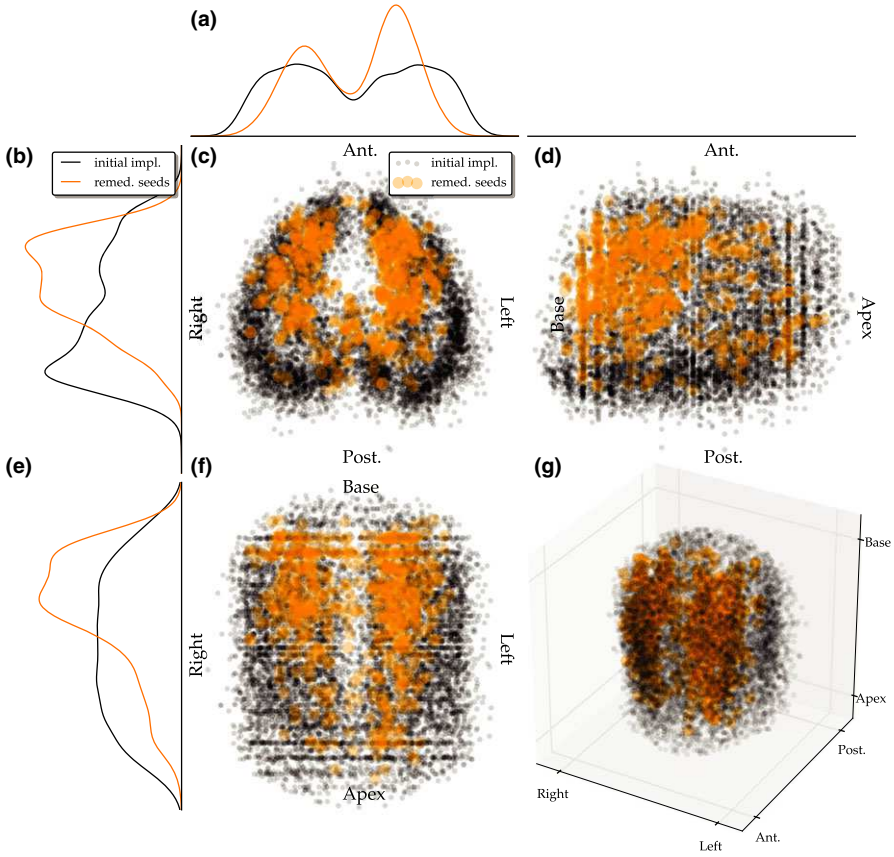

FIG. 5. Remedial seeds were predominantly placed near the anterior base of the prostate. (a), (b), (e) Relative density of the distribution of positions of initially placed seeds compared with the positions of remedial seeds. (a) Right–Left. (b) Posterior–Anterior. (e) Apex–Base.(c), (d), (f) 2D views of the placement of initial and remedial seeds. (g) 3D view. Areas under the curves are normalized.

perform an adaptation in more than one in ten implants. The relative ease to adapt an implant may have affected the initial implantation procedure. We can intentionally start with relatively sparse implants to reduce V_{150} and the OAR dose, knowing that the adaptive planning procedure allows eradication of cold spots by placing remedial seeds. However, we always ensure that dosimetry is adequate after finishing the real-time intraoperative planning (Plan III).

Figure 5 shows that remedial seeds were predominantly implanted in the anterior base of the prostate. Jastaniya *et al.*[33] and Moerland *et al.*[30] also observed most coverage problems in this region. McParland *et al.*[34] report the placement of extra seeds in this region. Some studies indicate that full coverage of this region might not be necessary,[35,36] while other studies show that cancerous tissues may also be found in the anterior base.[37,38]

In a separate analysis of the data we showed that, generally, seeds in the anterior base of the prostate have a tendency to displace caudally. Furthermore, deeper implanted seeds tend to diverge from the central axis of the prostate.[20,39] Both mechanisms can cause the observed underdosages in the anterior base but the extent of the deviations cannot be predicted for an individual patient.

In a previous study,[20] we showed that it is not possible to give an accurate individual prediction of Day 30 dosimetry during the implantation procedure. Using CBCT-based adaptive planning however, we were able to identify a subgroup of implants that needed adaptation, preventing insufficient target coverage at Day 30 for this subgroup (Figs. 3 and 4, Table II).

The use of intraoperative MRI is an attractive yet expensive and scarcely available alternative for performing dynamic dosimetry. It has potential to further increase the accuracy of the implantation procedure by providing visualization of lesions that may be boosted or focally treated.

Our adaptive planning technique would benefit from the inclusion of preoperative MRI. With MRI it is possible to define intraprostatic structures that cannot be visualized with TRUS. The addition of MRI may also improve the definition of the base and apex of the prostate.[40] However, the registered preoperative MRI may show a different prostate shape and size than the actual situation during implantation. Furthermore, the addition of preoperative MRI involves image registration, leading to registration uncertainties.

Registration and contouring uncertainties may have affected the results presented in the current study. In a separate study, we found that the observed registration and contouring variability is smaller than underdosages that are adapted during the adaptive planning procedure.[41] Registration and contouring uncertainties result in uncertainties near the outer contour of the prostate, this region only partly

overlaps with adapted underdosages. These adapted underdosages were located near the anterior base of the prostate but extended centrally. This is displayed in Fig. 5, which shows remedial seeds spread throughout the volume between the center and base of the (anterior) prostate.

The use of multiple modality imaging during the implantation procedure provides an opportunity to independently check the implant while the patient is still anesthetized, thereby reducing the probability on errors.

In other studies, an O-arm CBCT has been used to assess intraoperative dosimetry.[42,43] These studies consider a limited amount of patients without applying the dosimetry feedback to improve the implant. Kuo *et al.* described a dynamic image guidance system using TRUS and fluoroscopy[44] that was tested on 37 patients. To our best knowledge, no large-scale dosimetry study has been published about this interesting approach.

Currently, interest is growing in focal treatments[45] and differential dose prescription strategies.[46] These techniques have the potential to reduce toxicity of the treatment without sacrificing outcome. Seed positioning becomes more critical when treating smaller targets.[47] A rapid adaptive planning feedback loop, as reported in the current study, may be beneficial to warrant high-quality implants for smaller targets. The adaptive nature allows an immediate dose assessment of implants, possibly shortening the learning curve of new strategies.

5. CONCLUSION

We present large-scale (1266 patients) adaptive dosimetry results for permanent prostate brachytherapy. The addition of CBCT-imaging and intraoperative adaptation to the implantation procedure proves valuable, resulting in excellent Day 0 and Day 30 dosimetry. The presented technique is, quick, routinely feasible and allows a sparse implantation strategy, limiting V_{150}. Remedial seeds are predominantly placed near the anterior base of the prostate.

CONFLICTS OF INTEREST

The authors have no relevant conflicts of interest to disclose.

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