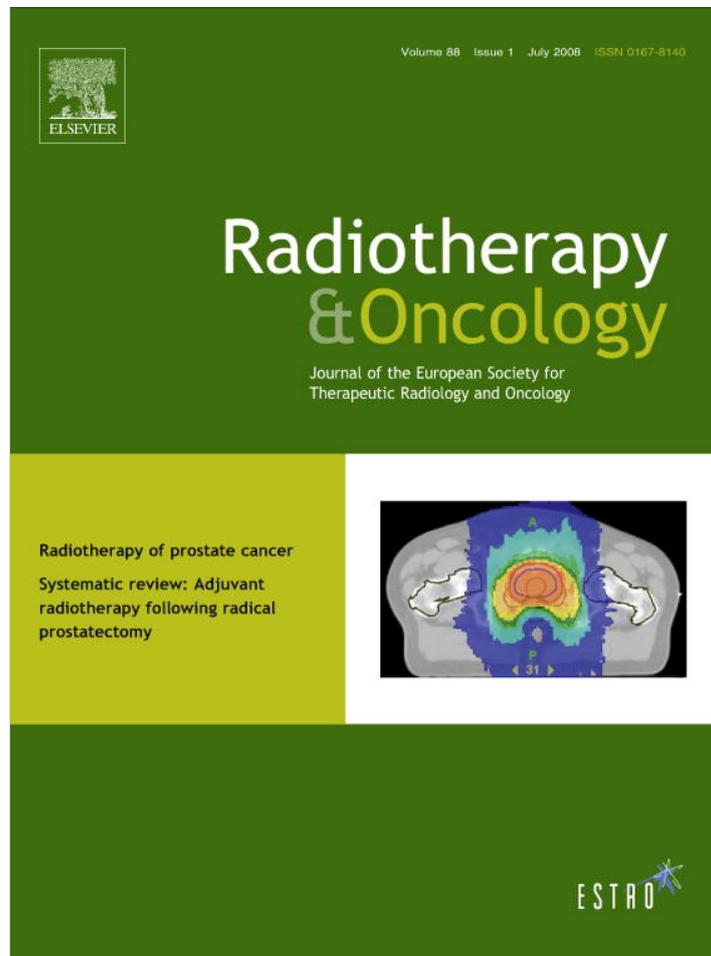


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## Prostate brachytherapy

## MRI-based preplanning in low-dose-rate prostate brachytherapy

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## Abstract

**Purpose:** To compare the dosimetric results between MRI-based and TRUS-based preplanning in permanent prostate brachytherapy, and to estimate the accuracy of MRI-based preplanning by comparing with CT/MRI fusion-based postimplant dosimetry.

**Methods and materials:** Twenty-one patients were entered in this prospective study with written informed consent. MRI-based and TRUS-based preplanning were performed. The seed and needle locations were identical according to MRI-based and TRUS-based preplanning. MRI-based and TRUS-based preplanning were compared using DVH-related parameters. Following brachytherapy, the accuracy of the MRI-based preplanning was evaluated by comparing it with CT/MRI fusion-based postimplant dosimetry.

**Results:** Mean MRI-based prostate volume was slightly underestimated (0.73 cc in mean volume) in comparison to TRUS-based volume. There were no significant differences in the mean DVH-related parameters except with rectal V<sub>100</sub>(cc) between TRUS-based and MRI-based preplanning. Mean rectal V<sub>100</sub>(cc) was 0.74 cc in TRUS-based and 0.29 cc in MRI-based preplanning, respectively, and the values demonstrated a statistical difference.

There was no statistical difference in mean rectal V<sub>150</sub>(cc), and rectal V<sub>100</sub>(cc) between MRI-based preplanning and CT/MRI fusion-based postimplant dosimetry.

**Conclusion:** Prostate volume estimation and DVH-related parameters in MRI-based preplanning were almost identical to TRUS-based preplanning. From the results of CT/MRI fusion-based postimplant dosimetry, MRI-based preplanning was therefore found to be a reliable and useful modality, as well as being helpful for TRUS-based preplanning. MRI-based preplanning can more accurately predict postimplant rectal dose than TRUS-based preplanning.

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**Keywords:** Prostate brachytherapy; MRI; CT; TRUS; Preplanning

Transperineal prostate brachytherapy has become an increasingly popular treatment over the past 15 years [11,12]. Image-based preplanning is an important part of the modern practice of permanent prostate brachytherapy. Transrectal ultrasound (TRUS) images enable multiplanar visualization of the prostate capsule, bladder, rectum, and, with the introduction of a catheter or contrast agent, the urethra [1,2,7,13,15,22–24]. Based on TRUS-based preplanning, the exact number of seeds required for the implant (plus a few extra) is ordered for each individual patient [3]. However, TRUS-based preplanning is inconvenient and uncomfortable due to the insertion of a probe into the rectum.

The discrepancies between Computed tomography (CT)-based, Magnetic resonance imaging (MRI)-based and TRUS-based prostate volume have been well discussed [1,2,5–7,9,14–16,20]. Narayana et al., using two different approaches for preplanning (CT-based vs. TRUS-based), found

a significant difference in the CT volumes, which were markedly greater (47%) than the TRUS volumes [13]. On the other hand, several authors have reported the TRUS-based prostate volume to be similar to the MRI-based prostate volume [1,7,15,24]. The cost for performing MRI is still high, but recently, it has been used to detect the location of prostate cancer and extracapsular extension to establish a pretreatment diagnosis [4]. We hypothesized that MRI could be replaced as an imaging modality for preplanning of permanent prostate implants. If similar results as accurate as those obtained through TRUS-based preplanning could be obtained by MRI-based preplanning, then it would be comfortable and convenient for patients. Therefore, the accuracy of MRI-based preplanning was estimated through comparisons with TRUS-based preplanning. In addition, we also estimated the accuracy of MRI-based preplanning by comparing it with CT/MRI fusion-based postimplant dosimetry.

## Methods and materials

Between April 2006 and December 2006, 21 patients with local prostate cancer were entered in this prospective study. All patients gave their written informed consent before entry into the study. The patient's ages ranged from 62 to 74 years and nine patients underwent neoadjuvant hormone therapy. All patients were treated with loose  $^{125}\text{I}$  radioactive seeds with an activity of 0.432U (0.34 mCi) per source (Oncoseed; Nihon Medipysics Co., Tokyo, Japan) using a Mick applicator (Mick Radio-Nuclear Instruments, Inc., Bronx, New York, USA). Thirteen patients with low-risk prostate cancer (prostate-specific antigen [PSA] <10 ng/mL, Gleason score <7, Union Internationale Contre le Cancer 1997 clinical stage T1–T2b) were treated with an implant of 145 Gy alone. Eight patients with intermediate-risk prostate cancer (PSA 10–20 ng/mL and Gleason score 6, or Gleason score 7 and PSA <10 ng/mL) were treated with an implant boost of 104 and 40 Gy of external beam radiotherapy 4 weeks after implantation. All patients underwent CT-based, MRI-based and TRUS-based prostate volume studies 4 weeks before implantation. Simultaneously, MRI-based and TRUS-based preplanning was performed. The mean number of seeds and needles was 53.6 and 15.3, respectively.

### CT, MRI, and TRUS preplanning image acquisition and organ contouring

Preplanning CT, MRI, and TRUS were obtained within 2 h (Fig. 1). Initially, CT was obtained using a CT scanner with 16 detector arrays (LightSpeed Ultra 16; GE Healthcare, WI) in supine position. Axial CT images of 5-mm thickness with a 5-mm interval were obtained. A field of view of 15 cm, a 512-square matrix, and a standard reconstruction algorithm were used. No i.v. contrast material was used. The patients were not catheterized for a CT scan and MRI. The CT images were transported to the Variseed system (Variseed 7.1; Varian Medical Systems, Inc., Palo Alto, CA) to calculate the CT-based prostate volume by a radiation oncologist (Fig. 1a). CT-based preplanning was not performed because prostate volume contoured by CT was very different from that done by TRUS, as previously reported [2,6].

Next, MRI was also performed using an MR imager (Intera Achieva 1.5T. Pulsar, Philips Medical Systems, Eindhoven, the Netherlands). MRI was performed within 1 h after CT in supine position. MRI was performed using a five-channel sense cardiac coil (5-mm section thickness with no intersection gap, and a 16-cm field of view). The MR imaging sequence was a T2-weighted fast spin-echo (repetition time [TR]/echo time [TE] in millisecond: 3000/80). The MR images were transported to the Variseed system to calculate the MRI-based prostate volume and to perform the MRI-based preplanning. The radiation oncologist contoured the urethra under the guidance of the MRI, but in some cases, the urethra was contoured as a surrogate when visualization was difficult based on the MRI findings. The surrogate urethra was drawn as a 5-mm diameter circle. It was contoured through the geometric center at the apex to the base which was slightly posterior to the center at the base of the prostate on each MR image based on subjective judgments. This method was derived because Lee et al. demonstrated the location of the actual urethra at the base

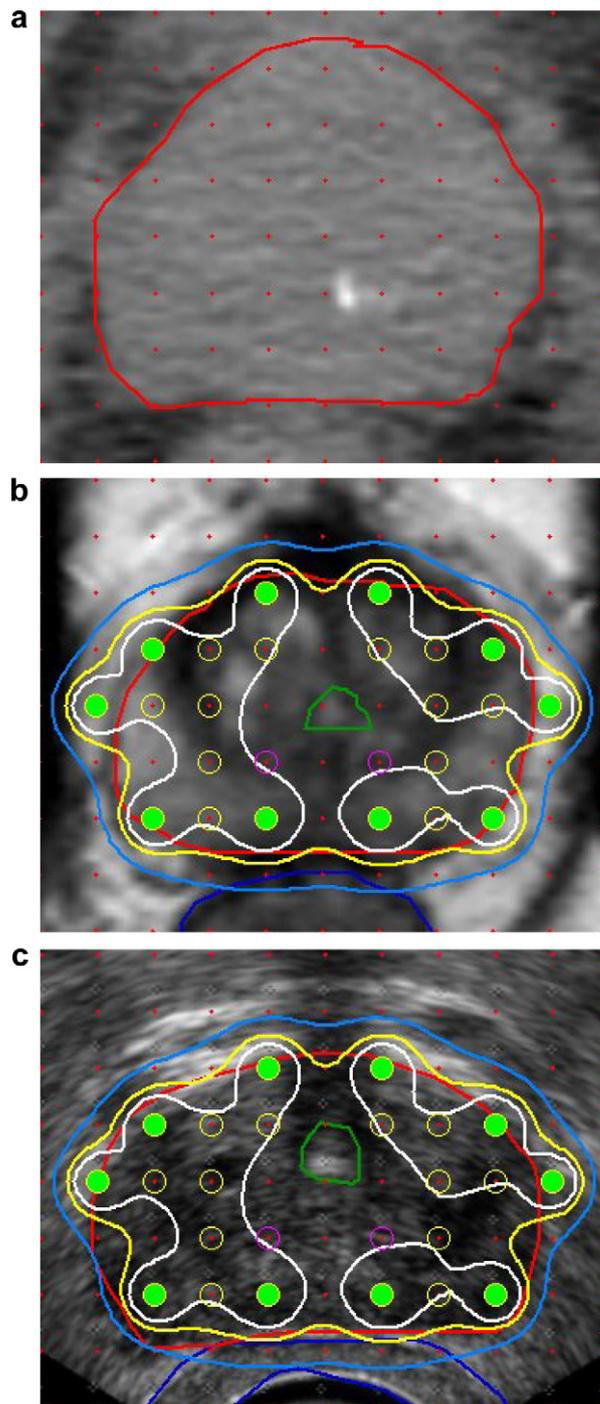


Fig. 1. Comparison between the three modalities at the same slice level in preplanning imaging. (a) Computed tomography (CT)-based prostate volume study. (b) Magnetic resonance imaging (MRI)-based preplanning. (c) Transrectal ultrasound (TRUS)-based preplanning. Red lines represent the prostate. Green circles represent the urethra. Blue lines posterior to the prostate represent rectum. Green dots represent the seeds and yellow circles represent needles. Blue, yellow and white lines represent 100%, 150% and 200% of the prescription dose, 145 Gy.

of the prostate to be more anterior than the geometric center of the prostate [10]. The rectum was contoured as a whole outer wall.

### Preplanning (seed and needle location)

Preplanning was performed by the radiation oncologist using a Variseed system, following a modified peripheral seed placement approach (Fig. 1b). The planning target volume (PTV) was formed by adding margins to the prostate contours in accordance with RTOG protocol P-0019 guidelines, namely 3 mm anteriorly and laterally, and 5 mm cranially and caudally. No margin was added posteriorly at the rectal interface. The seed locations were chosen manually within a volume extending not more than 3 mm outside the PTV, to meet the following dose-volume constraints: prostate  $V_{100} > 96\%$ , prostate  $D_{90} > 120\%$ , urethra  $D_{90} < 150\%$ , and rectum  $V_{100} < 1$  cc ( $V_n$  denotes the percentage (or cc) of a structure volume receiving  $n\%$  of the prescribed dose and  $D_n$  denotes the percentage of the prescribed dose covering  $n\%$  of the structure).

TRUS-based preplanning in the lithotomy position was performed by a urologist using ALOKA transrectal ultrasound machine with a rectal biplanar transducer (UST-672/7.5). CIVCO Assist Stabilizer and EXII Stepper were used in all patients. A urethral catheter was used for TRUS-based preplanning. The urethra was contoured on the catheter and only the anterior one-third of the rectal wall was contoured, because the TRUS field is restricted to this area. After organ contouring on TRUS, the MRI-based preplanning (seed and needle locations) was manually fused to the TRUS-based contouring image on the Variseed system (Fig. 1c).

We compared the accuracy of MRI-based preplanning with TRUS-based preplanning. This analysis included a comparison of the prostate volume, prostate  $V_{100}(\%)$ , prostate  $D_{90}(\%)$ , urethral  $D_{30}(\%)$ , urethral  $D_5(\%)$ , urethral  $V_{150}(\text{cc})$ , rectal  $V_{150}(\text{cc})$ , and rectal  $V_{100}(\text{cc})$ .

### Brachytherapy procedure

The required number of seeds (plus a few extra) was ordered based on MRI-base preplanning except in one patient. The required number of seeds was identical to the MRI-based preplanning except in this patient. The prostate volume of this patient was 11.5 cc on preplanning MR imaging and 14.9 cc on preplanning TRUS imaging, therefore we ordered the seeds based on TRUS-based preplanning. Following organ contouring on TRUS in the operating room, MRI-based preplanning (seed and needle locations) was manually fused to the TRUS-based intraoperative image on the Variseed system. In 2 of 21 cases, MRI-based preplannings were partly modified using TRUS-based intraoperative image before implantation (however, the number of seeds was identical to the number determined using MRI-based preplanning, and therefore the location of the seeds was moved.), because a prostate volume or shape varied from MRI-based preplanning.

### CT/MRI fusion-based postimplant dosimetry

Postimplant CT and MRI were obtained on the day after the procedure. The CT and MRI axial images (3-mm section thickness with no intersection gap, 15-cm displayed field of view for CT, 16-cm field of view for MR imaging) were obtained within 30 min of each other. The MR imaging sequence was T2-weighted fast spin-echo (TR/TE: 3000/80). The details of the CT/MRI fusion-based postimplant dosimetry have been previously reported [21]. The accuracy of the

MRI-based preplanning was evaluated by comparing it with CT/MRI fusion-based postimplant dosimetry.

### Statistical methods

The comparison of TRUS and MRI prostate volume was estimated by measuring the agreement methods. The group comparisons for the volumes and dosimetric parameters were performed using a paired  $t$  test and a  $p$  value of  $<0.05$  was considered statistically significant.

## Results

### Comparison of the prostate volume between TRUS-based, MRI-based, and CT-based preplanning

The mean prostate volume was  $20.00 \pm 8.71$  cc,  $19.26 \pm 8.15$  cc and  $23.42 \pm 8.43$  cc in TRUS-based, MRI-based and CT-based preplanning, respectively. The prostate volume contoured by MRI was slightly underestimated in comparison to that done by TRUS (however, the difference in the mean prostate volume was less than 1 cc), the prostate volume as contoured by MRI thus closely agreed with that done by TRUS (Fig. 2). The prostate volume contoured by CT was overestimated by about 1.17 times (3.4 cc) in comparison to that done by TRUS.

### Comparison of the DVHs between TRUS-based and MRI-based preplanning

The mean DVH-related parameters estimated by TRUS-based and MRI-based preplanning are shown in Table 1. Although we found some discrepancies in the DVH related parameters between TRUS-based and MRI-based preplanning due to the prostate deformations caused by examinations with or without the rectal probe, there were no significant differences in the mean DVH related parameters except between rectal  $V_{100}$ .

Prostate  $V_{100}$  were over 96% both on MRI-based and TRUS-based preplanning in most cases, but there was one case with 99.0% on MRI-based preplanning and 84.6% on TRUS-based preplanning (Fig. 3a). Regarding prostate  $D_{90}$ , this case shows 130.6% on MRI-based preplanning and 86.62% on TRUS-based preplanning (Fig. 3b) The prostate volume of this case was 11.5 cc on MR imaging and 14.9 cc on TRUS imaging, about 1.3 times.

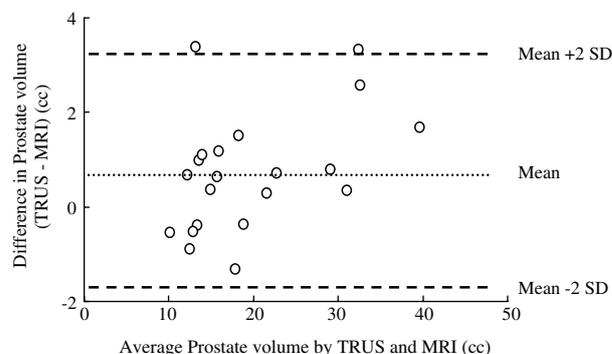


Fig. 2. Prostate volume measured with TRUS and MRI. Differences against mean for prostate volume.

**Table 1**  
Comparisons between TRUS-based preplanning, MRI-based preplanning and CT/MRI fusion-based postimplant dosimetry in the prostate volume and dose volume histograms

	TRUS-based preplanning	MRI-based preplanning	CT/MRI-based postimplant dosimetry
Prostate volume (cc)	20.00 ± 8.71	19.26 ± 8.15	27.01 ± 8.80
	0.73 (p=0.015)		7.75 (p<0.001)
Prostate V100 (%)	97.50 ± 3.47	98.45 ± 0.97	91.19 ± 4.58
	0.95 (p=0.221)		7.26 (p<0.001)
Prostate D90 (%)	131.75 ± 15.68	133.30 ± 6.54	103.86 ± 11.31
	1.55 (p=0.601)		29.44 (p<0.001)
Urethral D30 (%)	165.40 ± 19.82	162.37 ± 15.64	143.30 ± 11.00
	3.03 (p=0.120)		19.06 (p<0.001)
Urethral D5 (%)	180.81 ± 27.55	175.35 ± 19.36	161.61 ± 16.30
	5.46 (p=0.145)		13.74 (p=0.005)
Urethral V150 (cc)	0.25 ± 0.16	0.25 ± 0.14	0.21 ± 0.17
	0.01 (p=0.760)		0.04 (p=0.290)
Rectal V150 (cc)	0.08 ± 0.21	0.01 ± 0.02	0.02 ± 0.05
	0.07 (p=0.127)		0.01 (p=0.652)
Rectal V100 (cc)	0.74 ± 0.61	0.29 ± 0.23	0.21 ± 0.31
	0.46 (p=0.001)		0.07 (p=0.243)

Urethral  $D_{30}$ ,  $D_5$  and  $V_{150}$  showed agreement between MRI-based and TRUS-based preplanning. Rectal  $V_{100}$  and  $V_{150}$  contoured by TRUS were overestimated in comparison to that done by MRI.

**Comparison of MRI-based preplanning and CT/MRI fusion-based postimplant dosimetry**

A mean prostate volume and DVH-related parameters are shown in Table 1. The postimplant prostate volumes increased by prostatic edema in comparison to preplanning. Postimplant prostate  $V_{100}$  and  $D_{90}$  were decreased in comparison to the MRI-based preplanning. However, there was no statistical difference in the rectal  $V_{150}$ (cc), and rectal  $V_{100}$ (cc) values between MRI-based preplanning and CT/MRI fusion-based postimplant dosimetry. The rectal  $V_{100}$ (cc) value between MRI-based preplanning and CT/MRI fusion-based postimplant dosimetry showed a close correlation (Fig. 4). The time course of postimplant dosimetry in comparison to the preplanning findings was similar to that reported in previous studies.

**Discussion**

**Prostate volume and dose**

TRUS is commonly used before implantation to determine the prostate volume and boundaries. These determinations have been shown to correlate closely with the

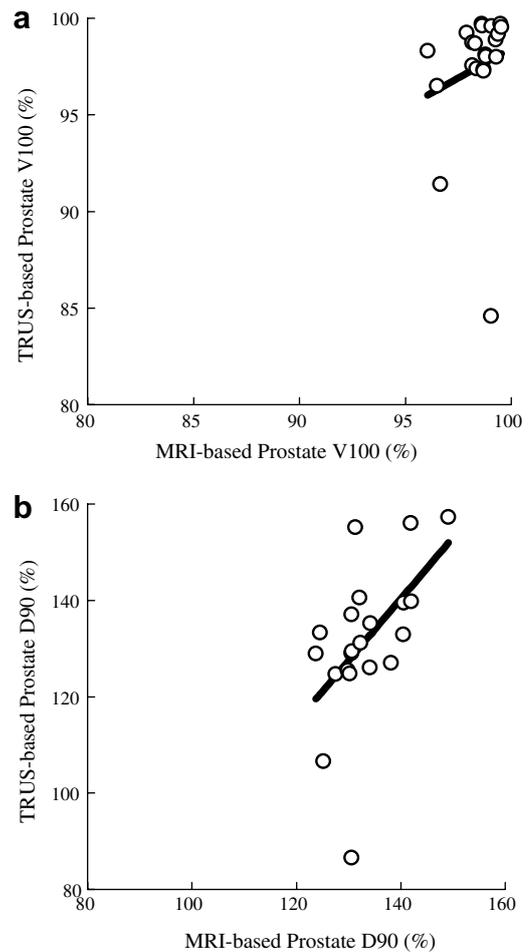


Fig. 3. (a) Comparison of the prostate  $V_{100}$  value between TRUS-based preplanning and MRI-based preplanning.  $R^2 = 0.1704$ . (b) Comparison of the prostate  $D_{90}$  value between TRUS-based preplanning and MRI-based preplanning.  $R^2 = 0.5322$ .

volume of the prostate during pathologic evaluations [3,12]. Sosna et al. in a series of 20 patients found a

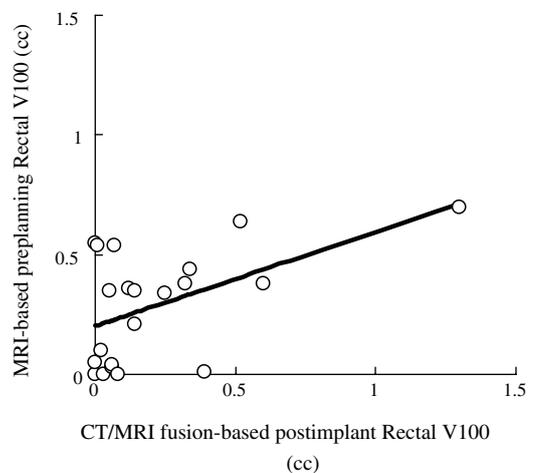


Fig. 4. Comparison of the rectal  $V_{100}$  between MRI-based preplanning and CT/MRI fusion-based postimplant dosimetry.  $R^2 = 0.5115$ .

strong correlation between volumes calculated from MRI with pathologic specimens [19]. Hricak et al. measured prostate volume using US and MRI in 15 patients prior to undergoing a radical prostatectomy [7]. The accuracy of US and MRI was evaluated by recording the difference between prostate size using imaging and that of the actual surgical specimen. Both US and MRI predicted the prostate size with a high degree of accuracy. Hoffelt et al. reported a comparison of CT and TRUS-based prostate volume in 36 patients with untreated prostate cancer [6]. A strong correlation was found between the CT and TRUS measurements of the prostate volume, however, CT overestimated the prostate volume by approximately 50%. Roach et al. compared CT with MRI-measured prostate volume. The mean prostate volume in the 10 patients studied was 32% larger using CT than with MRI [18]. Kagawa et al. also reported a 26% mean overestimation when delineating prostate volume with CT images in comparison to MRI images [9]. Based on the above studies, the prostate can be identified with a high degree of accuracy with MRI or US imaging but, at least in the hands of some investigators, CT overestimates the size of the prostate considerably and is associated with a high interobserver variation.

Our current results correlated with previous findings in the literature. The mean MRI-based prostate volume was similar to the mean TRUS-based prostate volume (the difference in the mean prostate volume was less than 1 cc), and the mean CT-based prostate volume was 17% larger than mean TRUS-based prostate volume. A strong correlation was found between the MRI and TRUS measurements of the prostate volume. Although MRI was performed in supine position and TRUS was performed in lithotomy position, there was no statistical difference in the prostate volume or the prostate DVH-related parameters regarding preplanning.

The prostate  $V_{100}$  and  $D_{90}$  values in MRI-based preplanning were correlated to those of TRUS-based preplanning except in one patient. The prostate volume of this patient was 11.5 cc on MRI and 14.9 cc on TRUS imaging. The number of seeds was identical between the TRUS-based and MRI-based preplanning, therefore the seeds required according to TRUS-based preplanning were insufficient in comparison to those required based on MRI-based preplanning. The fact that an underestimation of the prostate volume strongly influences the DVH-related parameters in the postimplant setting has been thoroughly described by Polo et al. [14]. In our series, the discrepancy between the TRUS and MRI prostate volume for this patient was caused by the miscontouring of either the apex or the base of the prostate because the prostate size was too small. The MRI-based prostate volume was similar to TRUS-based one in most patients, we believe that the MRI-based volume estimation is useful, and comfortable in comparison to TRUS-based.

The CT/MRI fusion-based postimplant prostate volumes increased due to prostatic edema in comparison to preplanning by approximately 40% (7.7 cc). DVH-related parameters decreased in postimplant dosimetry in comparison to the preplanning parameters.

### Urethral location and dose

Lee et al. reported that using a surrogate urethra at the geometric center of the prostate may significantly overestimate the urethral dose in a postimplant setting [10]. We used the T2-weighted spin echo MRI which helps to determine the urethra in the prostate. A surrogate urethra was used when the urethra was unable to be visualized on MRI, a 5-mm diameter circle was drawn at the geometric center at apex to posterior slightly than center at the base of the prostate (not at the geometric center through the prostate) on each MR image. Fig. 1 shows that urethral discrepancy was found in A–P direction between MRI-based and TRUS-based preplanning, but we found no significant difference in urethral dose between them. This was due to better urethral visualization on MRI in some cases and contouring the modified surrogate urethra as shown above. Using a urethral catheter is the best way to visualize the urethra, but using T2-weighted imaging and a new surrogate model is therefore sometimes reliable in MRI-based preplanning. There was no statistical difference in urethral  $V_{150}(\text{cc})$  between the preplanning and postimplant dosimetry findings. As a result, we believe that MRI-based preplanning is thus a reliable modality for predicting the appropriate urethral dose in postimplant dosimetry.

### Rectal location and dose

We found a significant difference in the MRI-based and TRUS-based preplanning findings regarding the rectal dose. On TRUS-based preplanning, the shape of the rectum changes with the insertion of the probe, namely it tends to take on an unnaturally straight course [8]. On MRI-based preplanning and CT/MRI fusion-based postimplant dosimetry, the shape of the rectum maintains its natural form. Therefore, the rectal dose tended to be overestimated in TRUS-based preplanning in comparison to MRI-based preplanning, due to the increased surface of the rectal wall adjacent to the prostate in the TRUS-based preplanning findings (Fig. 1). Although using an endorectal coil MRI is similar to using the TRUS image, it is uncomfortable and the shape of the rectum is unnatural such as in TRUS position. In fact, we found no significant difference in the rectal dose between the MRI-based preplanning and CT/MRI fusion-based postimplant dosimetry. Based on these findings, MRI-based preplanning are thus considered to be superior to TRUS-based preplanning in predicting rectal dose.

During the implant procedure, we did not experience any pubic arch interference in the examined patients. One reason for this is considered to be due to the fact that our patients mostly have relatively small prostate volumes. In addition, MRI-based preplanning helps to predict pubic arch interference such as TRUS-based preplanning. Recently, intraoperative planning has been used at many centers to eliminate the need for a preplan volume study [25]. However, the use of an operating room has now become a very expensive cost factor, and the cost of performing intraoperative planning in an operating room is far greater than that done in an outpatient examination room. Reynier et al. reported that using MRI linked with TRUS improves TRUS image segmentation, and this may significantly modify the prostate volume definition and therefore strongly influence

the treatment planning [17]. At a center which uses intraoperative planning, MRI-based preplanning may thus shorten the intraoperative planning time by combining MRI-based preplanning with TRUS-based intraoperative planning.

Although prostate volume estimation in very small prostates may show a significant difference between the findings determined by TRUS-based and MRI-based imaging, usual or larger prostate volumes tend to be the same for both TRUS-based and MRI-based imaging. We believe that MRI-based preplanning is therefore equally useful to that of TRUS-based preplanning, while it can more accurately predict the rectal dose than TRUS-based preplanning.

## Conclusions

To our knowledge, our series is the first to report the findings of dosimetric comparisons between TRUS-based and MRI-based preplanning. Prostate volume estimation and DVH-related parameters, with the exception of the rectal dose, on MRI-based preplanning is almost identical to TRUS-based preplanning. From the results of the CT/MRI fusion-based postimplant dosimetry, MRI-based preplanning is therefore considered to be a reliable and useful modality, in addition to TRUS-based preplanning. Besides, we found no significant difference in the rectal dose between the MRI-based preplanning and CT/MRI fusion-based postimplant dosimetry. MRI-based preplanning can therefore more accurately predict the postimplant rectal dose than TRUS-based preplanning.

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