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ORIGINAL ARTICLE

Differences Between MRI- and CT-Based Delineation of Target Volume and Organs at Risk in High-Dose-Rate Brachytherapy of Cervix

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Abstract

Aim With superior soft tissue imaging characteristics, MRI is better than CT in determining the local disease extent during intracavitary brachytherapy of carcinoma cervix. The aim of the study is to evaluate the differences in dimensions and volumes of the target and organs at risk and the subsequent changes in dosimetry between MRI- and CT-based plans.

Methods and Materials MRI and CT datasets of 34 locally advanced cervical cancer patients taken up for intracavitary brachytherapy between January and September 2017 were analyzed. The target volumes and organs at risk, namely bladder, rectum and sigmoid, were contoured by the same radiation oncologist on both the MRI and CT images as per the GEC ESTRO guidelines. The dimensions of HRCTV, the dose volume parameters of the target and OAR were recorded for the CT and MRI plans.

Results CT image significantly overestimated the width ($p = 0.000$) and thickness ($p = 0.009$) of HRCTV. The volumes of HRCTV ($p = 0.000$) and IRCTV ($p = 0.041$) were larger with CT image compared to MRI. There was no statistically significant difference between rectal ($p = 0.107$) and sigmoid ($p = 0.365$) volumes on CT and MRI. There was statistically significant difference (all $p < 0.05$) between the dose received by 100%, 98%, 90% and 50% (D100, D98, D90 and D50, respectively) of HRCTV and IRCTV on CT and MRI. There was statistically significant difference (all $p < 0.05$) in the dose delivered to the bladder. However, there was no statistically significant difference (all $p > 0.05$) in the dose received by rectum and sigmoid on CT and MR plans.

Conclusion MRI-based brachytherapy planning has shown considerable improvements in tumor control and reductions in normal tissue toxicity. However, the high cost of MRI and non-availability of MRI preclude its use in many centers. CT, on the other hand, is widely available, but it can lead to overestimation of the target, at the time of brachytherapy. Hence, it is important to identify the subset of patients who will benefit from MRI-based planning at the time of brachytherapy.

Keywords HDR brachytherapy · Cervical cancer · CT planning · MRI planning

Introduction

Concurrent chemoradiation is the standard of care for locally advanced cervical cancers [1–5]. High radiation doses are delivered to the tumor through a combination of external beam radiotherapy and brachytherapy. Conventionally, 2D X-ray-based planning with dose prescribed to point A using tandem-based applicators was used to deliver brachytherapy [6]. With point-based 2D planning, there is poor correlation between point doses and the doses to the target volume and organs at risk.

With the recent advancements in imaging, there is increase in use of 3D image-based brachytherapy. Volume-based dose calculations are feasible with CT and MR imaging. In 2005, the Group European de Curietherapie–European Society for Therapeutic Radiology and Oncology (GEC–ESTRO) developed guidelines for target volume delineation using MRI for image-guided brachytherapy [7, 8]. With superior soft tissue imaging characteristics, MRI is better than CT in determining the local disease extent [9, 10]. Several studies have shown significant

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improvement in tumor control rates with the addition of MRI to brachytherapy planning [11–13].

However, lack of availability of MRI, direct access to MRI and the high cost of MRI-compatible applicators preclude its use in several institutions. CT imaging after brachytherapy application is easier to implement with the widespread availability of CT simulators in the radiation oncology departments. Viswanathan et al [14] developed CT-based contouring guidelines to delineate target volumes and organs at risk on CT.

Very few studies have compared MRI- versus CT-based planning for intracavitary brachytherapy. In the present study, we evaluated the differences in dimensions and volumes of the target and organs at risk and the subsequent changes in dosimetry between MRI- and CT-based plans.

Materials and Methods

MRI and CT datasets of 34 locally advanced cervical cancer patients taken up for intracavitary brachytherapy between January and September 2017 were analyzed. All patients were treated with external beam radiotherapy dose of 50 Gy in 2 Gy per fraction along with weekly cisplatin 40 mg/m^2. Patients were taken up for brachytherapy after completion of external beam radiotherapy. A dose of 7 Gy to point A was delivered per fraction for a total of three fractions. MRI was taken either for the first or second fraction. CT images were taken for all the three fractions. MRI and the corresponding CT datasets were analyzed in the present study.

Brachytherapy Procedure

All the brachytherapy insertions were done under general anesthesia in the operating room. Bladder was catheterized in all patients, and the bladder balloon was filled with 7 ml of nonionic contrast and saline and left to drain continuously. A CT- and MR-compatible tandem ovoid applicator with a curvature of 30° was inserted after serial dilatations into the uterine canal. The most common tandem length used was 5 cm. The most appropriate size of the ovoid was inserted into the vaginal fornices, and the applicator was secured in position. Anterior and posterior vaginal gauze packing was done.

Imaging

All patients underwent MRI scan at the radiology department followed by CT in the radiotherapy department. MRI was done with a 1.5 Tesla MRI with a pelvic surface coil [Siemens, Erlangen, Germany]; 3 mm slice thickness with no intersection gap was taken. Sagittal, coronal and paraaxial images were obtained. CT images with slice thickness of 3 mm were obtained using a CT simulator [Somatom, Siemens, Erlangen, Germany]. All the acquired images were then transferred to Oncentra treatment planning system [Oncentra, an Elekta company, Stockholm, Sweden].

Contouring and Planning

The target volumes and organs at risk, namely bladder, rectum and sigmoid, were contoured by the same radiation oncologist on both the MRI and CT images as per the GEC ESTRO guidelines. Gross tumor volume (GTV) was contoured only on MRI images. High-risk clinical target volume (HRCTV—MR) and intermediate-risk clinical target volume (IRCTV—MR) and the organs at risk were contoured on T2-weighted MRI sequences as per the GEC ESTRO recommendations.

The entire cervix along with any parametrial and vaginal extensions as per the clinical examination at the time of brachytherapy was included in the high-risk clinical target volume (HRCTV—CT) on CT. The bladder wall was contoured from the dome to the urethra. The rectal wall was contoured from the level of ischial tuberosity to the rectosigmoid junction. The sigmoid was contoured from the rectosigmoid junction to the level where it crosses anteriorly.

Applicator reconstruction was done on MRI. Dummy MRI markers were used as surrogate for source position. A standard loading pattern was followed to calculate the dosimetry. The dwell positions for the tandem were 1, 3, 5, 7, 10, 13, 16 and 20 and 3, 4, 5 and 6 for the ovoids. A step size of 2.5 mm was used for all applications. A dose of 7 Gy to point A was prescribed. Dwell time optimization was done in selected cases to meet the GEC ESTRO constraints for the organs at risk. Applicator reconstruction and a similar planning were done for the CT images, and a dose of 7 Gy was prescribed to point A. Dose volume histograms were generated for both MRI and CT plans.

The volumes of HRCTV, IRCTV and OARs were recorded for both the CT and MRI contours. The values of height, maximum width and thickness of HRCTV were recorded for both the MRI and CT contours. The dose received by 100%, 98%, 90% and 50% (D100, D98, D90 and D50, respectively) of HRCTV and IRCTV of the CT and MRI plans was calculated. The volumes of organs at risk and the dose received by 0.1 cc, 1 cc and 2 cc (D0.1 cc, D1 cc and D2 cc, respectively) of the organs at risk were recorded for the CT and MRI plans.

Figures 1, 2 and 3 show the axial and sagittal CT (top) and MR (bottom) images showing the dimensions of width, height and thickness of HRCTV, respectively.

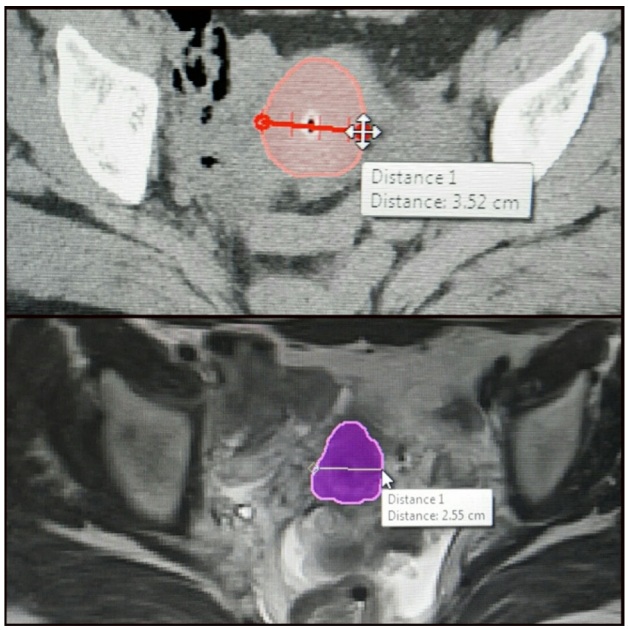

Fig. 1 Axial images showing width of HRCTV on CT (top) and MRI (bottom)

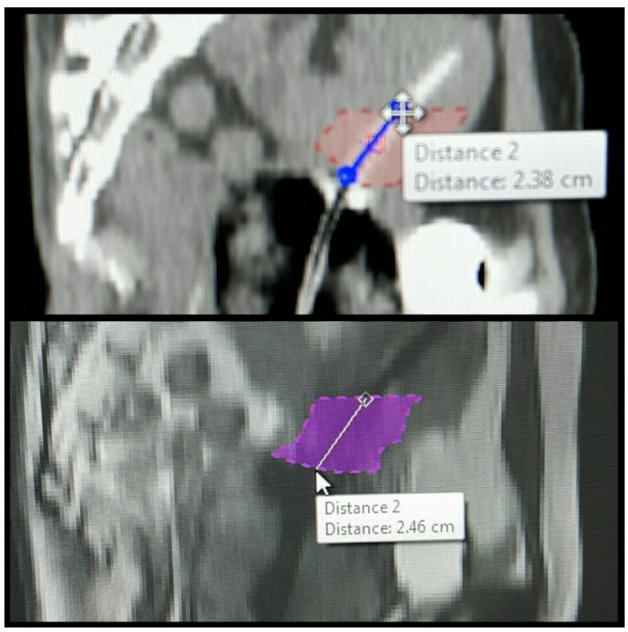

Fig. 2 Sagittal images showing height of HRCTV on CT (top) and MRI (bottom)

Statistical Analysis

Data collected were analyzed using SPSS statistical package version 20 (IBM corporation, New York, USA). Paired two-tailed t test was used to analyze data that were normally distributed. Wilcoxon signed-rank test was used to analyze data that were not normally distributed. A p value of less than 0.05 was considered significant.

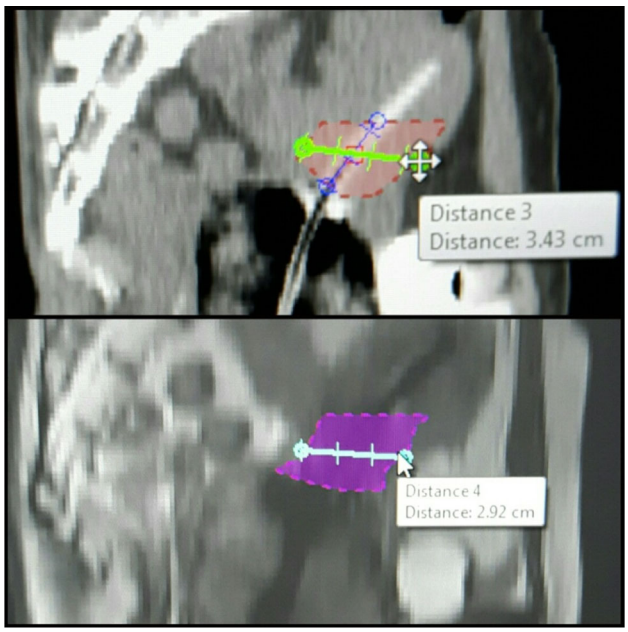

Fig. 3 Sagittal images showing thickness of HRCTV on CT (top) and MRI (bottom)

Results

Thirty-four patients were recruited between January and September 2017. The median age of patients was 50 years (range 37–70). Fifty percentage of patients had stage IIIB disease, 41% had stage IIB disease and 3% had stage IB2, IIA2 and IVA diseases, respectively. All patients received external beam radiotherapy of 50 Gy along with weekly cisplatin. Examination under anesthesia at the time of brachytherapy revealed no residual growth in 53% of patients. 35.2% of patients had central disease with residual growth involving anterior or posterior lips or both, and 11.8% of patients had residual central disease with unilateral parametrial involvement at the time of brachytherapy.

Table 1 Target and organs at risk volumes on CT and MRI

Volumes	CT (cc)	MRI (cc)	p value
HRCTV	22.95 ± 6.7	18 ± 7.2	0.000
IRCTV	53.23 ± 16.6	48 ± 21.9	0.041
Bladder	61.7 ± 32.8	52 ± 38.4	0.002
Rectum	33.8 ± 11.8	30 ± 9.9	0.107
Sigmoid	13.6 ± 8.8	14.3 ± 7.8	0.365

Difference in Volumes of Target and OAR

The difference in volumes of the target and the organs at risk between CT and MRI images is shown in Table 1. The volumes of HRCTV ($p = 0.000$) and IRCTV ($p = 0.041$) were larger with CT image compared to MRI, and the difference was found to be statistically significant. There was no statistically significant difference between rectal ($p = 0.107$) and sigmoid ($p = 0.365$) volumes on CT and MRI images. The difference in bladder volume ($p = 0.002$) can be explained by the time taken between MRI and CT acquisition. In 33% of our patients, there was an average delay of 80 min between MRI and CT acquisition due to logistic reasons.

Difference in Dimensions of HRCTV

The differences in dimensions of HRCTV are tabulated in Table 2. CT images significantly overestimated the width ($p = 0.000$) and thickness ($p = 0.009$) of HRCTV which is similar to that reported by other studies in the literature. There was no significant difference in the height ($p = 0.063$) of HRCTV between CT and MRI images.

Difference in Dose to Target and OAR

The differences in dose to the target and OAR are tabulated in Tables 3 and 4. There was statistically significant difference (all $p < 0.05$) between the dose received by 100%, 98%, 90% and 50% (D100, D98, D90 and D50, respectively) of HRCTV and IRCTV on CT and MRI. There was no statistically significant difference between the dose received by 100% of HRCTV ($p = 0.110$) and IRCTV ($p = 0.218$) (V100) between CT and MR plans. There was statistically significant difference (all $p < 0.05$) in the dose delivered to the bladder due to the delay in CT acquisition as mentioned earlier. The distension of bladder due to the delay in CT acquisition resulted in increased D0.1 cc, D1 cc and D2 cc to the bladder on CT images, and it was found to be statistically significant. However, there was no statistically significant difference (all $p > 0.05$) in the dose received by rectum and sigmoid on CT and MR plans.

Table 2 Dimensions of HRCTV on CT and MRI

Dimensions	CT (cm)	MRI (cm)	*p* value
Width of HRCTV	3.5 ± 0.62	3 ± 0.75	0.000
Height of HRCTV	2.9 ± 0.67	3.1 ± 0.89	0.063
Thickness of HRCTV	2.8 ± 0.57	2.6 ± 0.67	0.009

Table 3 DVH parameters of HRCTV and IRCTV on CT and MRI

DVH parameters	CT (Gy)	MRI (Gy)	*p* value
D100 HRCTV	4.9 ± 1.8	5.4 ± 1.7	0.002
D98 HRCTV	6.1 ± 1.95	6.7 ± 1.9	0.002
D90 HRCTV	7.8 ± 1.79	8.3 ± 2	0.011
D50 HRCTV	13.6 ± 2.2	14.3 ± 3	0.047
V100 HRCTV	92.6 ± 8.1	93.4 ± 9.2	0.110
D100 IRCTV	3.6 ± 1.23	4 ± 1.2	0.011
D98 IRCTV	4.5 ± 1.4	4.9 ± 1.35	0.005
D90 IRCTV	5.7 ± 1.46	6.1 ± 1.34	0.010
D50 IRCTV	10.4 ± 2.7	11.1 ± 3.3	0.000
V100 IRCTV	76.9 ± 17.4	78 ± 19.9	0.218

HRCTV high-risk clinical target volume, *IRCTV* intermediate-risk clinical target volume

Table 4 DVH parameters of organs at risk on CT and MRI

DVH parameters	CT (Gy)	MRI (Gy)	*p* value
D0.1 cc Bladder	9.8 ± 3.1	8.8 ± 2.5	0.012
D 1 cc Bladder	7.7 ± 1.9	7.1 ± 1.7	0.017
D2 cc Bladder	6.8 ± 1.7	6.3 ± 1.5	0.003
D0.1 cc Rectum	5 ± 1.36	4.7 ± 1.38	0.180
D1 cc Rectum	4.1 ± 1	3.9 ± 1	0.40
D2 cc Rectum	3.6 ± 0.98	3.5 ± 0.8	0.107
D0.1 cc Sigmoid	5.5 ± 2.1	5.3 ± 1.9	0.338
D1 cc Sigmoid	4.4 ± 1.6	4.1 ± 1.3	0.105
D2 cc Sigmoid	3.8 ± 1.35	3.5 ± 1.17	0.053

Analysis of dose volume parameters of HRCTV on CT and MRI based on the residual disease at the time of brachytherapy:

Fifty-three percentage of patients had no residual disease at the time of brachytherapy, and 47% of patients had residual disease at the time of brachytherapy. For patients with no residual disease at the time of brachytherapy, HRCTV volume was statistically larger ($p = 0.002$) on CT compared to MRI. The width of HRCTV was more on CT ($p = 0.000$), but there was no statistically significant difference in the height and thickness of HRCTV on CT and MRI (Table 5). Dose parameters like D100 ($p = 0.014$) and D98 ($p = 0.043$) were statistically higher on MRI compared to CT.

For patients with residual disease at the time of brachytherapy, HRCTV volume was more on CT (Table 6) and was statistically significant ($p = 0.000$). There was no statistically significant difference in the height of HRCTV between CT and MRI, but the thickness ($p = 0.031$) and width ($p = 0.000$) of HRCTV were more on CT and it was

Table 5 Dose volume parameters of HRCTV for CT and MRI for patients with no residual disease at the time of brachytherapy

DVH parameters	CT	MRI	*p* value
HRCTV volume	21.6 ± 5.7 cc	17.2 ± 8.1 cc	0.002
Width of HRCTV	3.5 ± 0.7 cm	2.9 ± 0.7 cm	0.000
Height of HRCTV	3 ± 0.69 cm	3.3 ± 1 cm	0.053
Thickness of HRCTV	2.77 ± 0.69 cm	2.5 ± 0.8 cm	0.108
D100 HRCTV	4.95 ± 1.9 Gy	5.5 ± 1.8 Gy	0.014
D98 HRCTV	6.2 ± 2 Gy	6.7 ± 1.9 Gy	0.043
D90 HRCTV	7.9 ± 2 Gy	8.4 ± 2 Gy	0.077
D50 HRCTV	14.4 ± 2.2 Gy	15.1 ± 3.2 Gy	0.111
V100 HRCTV	93.8 ± 7.7 cc	94.4 ± 7.9 cc	0.735

Table 6 Dose volume parameters of HRCTV for CT and MRI for patients with residual disease at the time of brachytherapy

DVH parameters	CT	MRI	*p* value
HRCTV volume	24.8 ± 7.6 cc	19 ± 6.2 cc	0.000
Width of HRCTV	3.5 ± 0.59 cm	3 ± 0.74 cm	0.000
Height of HRCTV	2.9 ± 0.65 cm	3 ± 0.74 cm	0.351
Thickness of HRCTV	3 ± 0.38 cm	2.7 ± 0.4 cm	0.031
D100 HRCTV	4.8 ± 1.6 Gy	5.4 ± 1.6 Gy	0.060
D98 HRCTV	6 ± 1.8 Gy	6.7 ± 1.8 Gy	0.020
D90 HRCTV	7.6 ± 1.5 Gy	8.2 ± 2.1 Gy	0.079
D50 HRCTV	12.7 ± 1.8 Gy	13.4 ± 2.6 Gy	0.243
V100 HRCTV	91.4 ± 8.5 cc	92.3 ± 10.8 cc	0.557

statistically significant. There was no significant difference in the dose volume parameters except D98 ($p = 0.020$).

Discussion

MRI is the gold standard imaging modality for target delineation in 3D image-based brachytherapy of cervix due to better depiction of soft tissue. Detailed information regarding tumor regression after external beam radiotherapy is also well depicted on MRI. CT, on the other hand, provides limited information on post-radiation changes and parametrial disease. The distinction between the corpus and the cervix is also challenging on CT. It is difficult to define the gross tumor volume at the time of brachytherapy on CT images. However, the depiction of the applicator is better with CT compared to MRI.

Comparison between MRI- and CT-based contours of the target and the organs at risk has been reported earlier. In a study conducted at University of Texas Southwestern Medical Center [15], the target and the organs at risk were contoured on MRI and CT image sets. The HRCTV volume was found to be significantly smaller on MRI compared to CT. However, there was no significant difference in the dose delivered to the HRCTV and OAR.

In a study conducted by Eskander et al [16], there was statistically significant overestimation of thickness ($p = 0.004$) and underestimation of height ($p = 0.006$) of HRCTV on CT. However, there was no statistically significant difference in the width and volume of HRCTV and D100, D90 of HRCTV between CT and MRI plans. There was a statistically significant difference in the D2 cc of bladder with MRI and CT values of 87.5 Gy and 91 Gy, respectively ($p = 0.041$). This difference was attributed to the ability to better identify the bladder wall on MRI compared to CT.

Ling Yip et al [17] found an overestimation of volume ($p = 0.001$), width ($p = 0.004$) and thickness ($p = 0.001$) of HRCTV on CT-based plans compared to MRI plans. There was no statistically significant difference between the height ($p = 0.372$) of HRCTV on CT and MRI images. In a similar study conducted on 17 patients [18], there was an underestimated height ($p = 0.001$) and overestimated width ($p = 0.009$) at the level of parametrium on CT images. However, there was no difference in the dose delivered to the target and organs at risk. The present study showed a statistically significant overestimation of width and thickness on CT (Table 7).

Spatial agreement between CT along with pre-brachytherapy MRI and MRI-based HRCTV delineation was analyzed by Federico et al [19]. They found geographical miss of CT-based contouring to be more pronounced for stage IVA cancers in the areas of gross tumor involvement. In a systematic review of 13 clinical studies involving 465 patients [20], width was overestimated and height underestimated on CT. Thickness was comparable between the two imaging modalities. The dose parameters for HRCTV were found to be lower on CT compared to MRI. The dose parameters for HRCTV in the present study were also found to be statistically lower on CT compared to MRI.

Swanick et al [21] recommend MRI-based brachytherapy for patients with higher body mass index and for patients with tumors more than 5 cm with parametrial invasion on MRI at diagnosis. Viswanathan et al [22] found that the CTV contours were identical on CT and MRI for patients with no parametrial extension. They recommend MRI for patients with parametrial invasion at diagnosis with a complete response to teletherapy. The present study shows a statistically significant overestimation of volume, width and thickness of HRCTV on CT compared to MRI for patients with residual disease at the time of brachytherapy. The dose parameters like D100, D98, D90

Table 7 Studies reporting dimensions and volumes of HRCTV

S. no.	Study	Number of patients	Width of HRCTV (cm)	Thickness of HRCTV (cm)	Height of HRCTV (cm)	Volume of HRCTV (cc)
1	Eskander et al. [16]	11	CT 3.3 ± 0.8	CT 4.5 ± 0.9	CT 2.2 ± 0.8	–
			MRI 3 ± 0.6	MRI 3.7 ± 0.7	MRI 2.7 ± 0.5	–
			p value 0.157	*p* value 0.004	*p* value 0.008	–
2	Krishantry et al. [18]	17	CT 5.2 ± 1.1	CT 3.9 ± 0.5	CT 3.7 ± 1	CT 29.1 ± 19.7
			MRI 4.4 ± 1.2	MRI 3.7 ± 0.6	MRI 4.5 ± 1	MRI 35.2 ± 18.2
			p value 0.009	*p* value 0.46	*p* value 0.001	*p* value 0.106
3	Yip et al. [17]	11	CT 5.2 ± 0.9	CT 3.8 ± 0.6	CT 3.4 ± 1	CT 50.7 ± 23.8
			MRI 4.4 ± 1	MRI 3.1 ± 0.7	MRI 3.5 ± 1	MRI 33.2 ± 20.6
			p value 0.004	*p* value 0.001	*p* value 0.372	*p* value 0.001
4	Present study	34	CT 3.5 ± 0.6	CT 2.8 ± 0.5	CT 2.9 ± 0.6	CT 22.9 ± 6.7
			MRI 3 ± 0.7	MRI 2.6 ± 0.6	MRI 3.1 ± 0.8	MRI 18 ± 7.2
			p value 0.000	*p* value 0.009	*p* value 0.063	*p* value 0.000

and D50 were higher with MRI plans, but none were statistically significant except D98.

Though there is statistically significant difference in the volume and dimensions of HRCTV between the CT and MRI images in the present study, there was no statistically significant difference in the dose parameters of the HRCTV(except D98) in both the subset of patients with residual disease and no residual disease at the time of brachytherapy. Hence, CT-based planning is adequate for patients in resource-poor setting. However, it is important to identify the subset of patients who would specifically benefit from a MRI at the time of brachytherapy in a larger study with more number of patients.

Conclusion

MRI-based brachytherapy planning has shown considerable improvements in tumor control and reductions in normal tissue toxicity. However, the high cost of MRI and non-availability of MRI preclude its use in many centers. CT, on the other hand, is widely available, but it can lead to overestimation of the target, at the time of brachytherapy. The present study did not show any statistically significant difference between CT and MRI plans in the dose parameters of the target.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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