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CT or MRI for Image-based Brachytherapy in Cervical Cancer

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Objective: To compare volumes and doses of tumour and organs at risk with computed tomography vs. magnetic resonance imaging in cervical cancer brachytherapy.
Methods: Seventeen previously untreated patients with cervical cancer suitable for radical treatment were included. All patients underwent brachytherapy using a magnetic resonance imaging-compatible applicator followed by both computed tomography and magnetic resonance imaging. The tumour and organs at risk (bladder, rectum, sigmoid and intestines) were contoured on computed tomography using only clinical findings and on magnetic resonance imaging using GEC-ESTRO guidelines. The volume and doses for tumour and organs at risk were evaluated using two-sided *t*-test.
Results: When magnetic resonance imaging information is not included in contouring on computed tomography images, there is significant underestimation of tumour height and overestimation of the width ($P < 0.05$). However, there was no significant difference in V_{100}, D_{90} and D_{100} for high- and intermediate-risk clinical target volume in computed tomography and magnetic resonance imaging. The volumes and doses to 0.1, 1 and 2 cc for organs at risk were also similar.
Conclusions: Magnetic resonance imaging remains the gold standard for tumour delineation, but computed tomography with clinical information can give comparable results, which need to be studied further. Computed tomography-based contouring can be used comfortably for delineation of organs at risk.

Key words: cervical cancer – brachytherapy – computed tomography – magnetic resonance imaging

INTRODUCTION

Cervical cancer is one of the most common cancers in the women in developing countries (1). The current treatment of choice includes external beam megavoltage radiation (EBRT) with weekly cisplatin followed by intracavitary brachytherapy (2,3). Recently, recommendations were given for target and organs at risk (OAR) delineation and dose prescription on magnetic resonance imaging (MRI) for image-based brachytherapy in cervical cancer by the GEC-ESTRO (4,5).

MRI is a superior imaging modality for cervical cancer brachytherapy planning (6–9) but it is a disease of less developed countries where most institutions do not have MRI or do not have a direct access to MRI or it is at a significant distance from the radiation oncology unit. The computed tomography (CT) scanners are still more widely available as simulators in the department of radiotherapy and can be easily used. Also, MRI requires special non-magnetic brachytherapy applicators that are more expensive than usual metallic applicators, which can be used for CT-based planning.

Previous studies have shown that CT at brachytherapy is feasible (10–14), but very few authors have compared MRI- vs. CT-based planning. In 2007, Viswanathan et al. (15) proposed guidelines for contouring CT images using MRI information. However, the availability and cost is still a

determinant for application of these guidelines in routine, as MRI information is still required for contouring on CT.

This study was conducted to compare the contouring of target volume and the OARs on CT and MRI, using only clinical information with consideration for GEC-ESTRO guidelines of target and OARs definition.

PATIENTS AND METHODS

Between October 2008 and March 2009, 17 patients with biopsy-proven cervical cancer were prospectively enrolled in the study protocol approved by the institute ethical committee.

Pre-treatment Work-up

Routine investigations (blood counts, kidney and liver function test, chest X-ray) and diagnostic MRI of the pelvis were done for all patients. A detailed pelvic examination was made, and findings were depicted with a proper diagram.

EBRT Treatment

All patients underwent pelvic EBRT using a four-field box technique (46 Gy in 23 fractions, 2 Gy per fraction) with CT-based treatment planning (CT simulator Helical CT scanner, VXR 16, GE Medical Systems), with or without concurrent weekly cisplatin (40 mg/m^2) chemotherapy. At the last week of completion of EBRT, all patients were found clinically suitable for intracavitary application.

Brachytherapy Application

All patients underwent pre-brachytherapy gynaecological examination under general anaesthesia, in the lithotomy position. The tumour topography (dimensions) in regard to location of the cervical os was diagrammatically depicted. A urinary catheter was inserted and fixed against the bladder neck, with bladder balloon filled with 7 ml of saline-diluted gadolinium and non-ionic contrast (dilution 1:1:1). It was left open to drain out completely and then continuously. After this, all patients underwent tandem and ring high-dose rate brachytherapy, with a CT/MRI-compatible ring applicator (Nucletron Systems, Veenendaal, The Netherlands) having a tandem length of 4 or 6 cm, a curvature of 45° and a ring diameter of 3 or 3.4 cm (4,5). The applicators were impregnated in a water-soluble gel for external surface enhancement on MRI. After implantation of the tandem–ring applicator, the vagina was additionally filled with a water-soluble gel to remove air pockets around the applicator. This was done to enhance the visibility of applicators on MRI scans. Vagina was then packed with a gauze to push away the rectum and bladder and to fix the applicator. This gauze was also soaked in a water-soluble gel.

CT and MRI Technique

All patients underwent CT scans followed by contouring on CT as described later followed by MRI and then MRI-based planning. The CT was done in the radiotherapy department with dummy markers. For optimal reconstruction of the ring on CT, a slice thickness of 2.5 mm was taken from 3 cm above the tip of tandem up to the superior plane of the ring, a slice thickness of 0.625 mm was taken from the superior surface of the ring up to the inferior surface of the ring and below the slice thickness of 5 mm for a distance of 4 cm. No intravenous contrast was used. MRI was done in the radiodiagnosis department [1.5 Tesla Magenatron Vision Plus MRI in 14 patients and 3 Tesla Magnetron Veiro System (Siemens, Erlangen, Germany) in 3 patients] with pelvic surface coils as per the protocol described by Dimopoulos et al. (7). The 5 mm sections with no intersection gap were taken from the level above the uterine fundus to the inferior border of the symphysis pubis below any vaginal tumour extension on axial slices. Similarly, sagittal, coronal, para coronal and para-axial images were obtained, including the tumour, entire cervix, corpus uteri, parametria and vagina.

Contouring and Brachytherapy Treatment Planning

First, CT images were obtained and contoured for high-risk clinical target volume (HR-CTV$_{CT}$), intermediate-risk clinical target volume (IR-CTV$_{CT}$) and OAR on PLATO Sunrise brachytherapy planning workstation (Nucletron B.V., The Netherlands). The tumour contouring was based on clinical findings and CT information. The HR-CTV$_{CT}$ always included the whole of the cervix as per GEC-ESTRO guidelines, and the parametrial and vaginal extensions were included as per the clinical examination under anaesthesia findings at the time of brachytherapy application. All patients were examined in detail under general anaesthesia before application was performed, which included per speculum, per vaginal, per rectal and abdominopelvic bimanual examination. This information was used for diagrammatic depiction of findings, which were later used for contouring. The upper limit of the cervix was defined as the conical two slices above the starting of uterine budge, while the endocervical extensions were contoured as suspected clinically. The IR-CTV$_{CT}$ was contoured based on the adaptation of GEC-ESTRO recommendations with 1 cm margin to HR-CTV respecting the normal tissue boundaries. The bladder, rectum and sigmoid were contoured as the outer wall of the organ. The intestines were contoured as the entire bowel other than sigmoid and rectum, where the sigmoid extended from the level of the rectosigmoid flexure to the crossing anteriorly by the pubic symphysis. Applicator reconstruction was done directly on CT, with metallic dummy markers being used as the surrogate for source position. Dosimetric calculations were done with the standard loading protocol of our department. The dwell positions for a typical

application of 6 cm uterine tandem were 3, 6, 9, 12, 15, 18, 21 and 24 and for 3.4 cm ring 7, 8, 9, 10, 25, 26, 27 and 28 with a step size of 2.5 mm. Point A was defined as 2 cm above the superior surface of the ring and 2 cm lateral along the uterine axis. Dose of 9 Gy per fraction was prescribed at Point A, with two sessions done 1 week apart.

The MRI axial images were used on PLATO Sunrise to contour Gross Tumour Volume (GTV_{BT}), HR-CTV ($HR\text{-}CTV_{MRI}$), IR-CTV ($IR\text{-}CTV_{MRI}$) and conventional OAR (bladder, rectum and sigmoid) in accordance with the GEC-ESTRO recommendations (4,5). The intestines were also contoured as described earlier on MRI. The standard planning was followed for these MRI images as described by GEC-ESTRO. The dose was prescribed as described for CT plans. The standard plans were then evaluated for bladder and rectum doses, and when ICRU bladder point dose >80% of Point A and rectal point dose >70% of Point A, dose re-planning was done by optimizing dwell times to treat the patients.

The values for the height, maximum width at any level, width at Point A, maximum thickness at any level, thickness at Point A and volume were generated for the MRI and CT contours of HR-CTV and IR-CTV. The dose received by at least 90% of the volume (D_{90}) and the minimal target dose (D_{100}), as well as percentage of volume receiving 100% or more than the prescribed dose (V_{100}) were calculated using cumulative dose–volume histograms (DVHs) of the CT ($HR\text{-}CTV_{CT}$ and $IR\text{-}CTV_{CT}$,) and MRI ($HR\text{-}CTV_{MRI}$ and $IR\text{-}CTV_{MRI}$).

The volumes of the bladder, rectum, sigmoid and intestines (OAR) were compared for both CT and MRI. DVHs were evaluated for the dose to 0.1, 1 and 2 cm^3 for the OAR. The dose values for tumour and OAR are reported in the dose/HDR fraction. For a comparison between CT and MRI contours, a two-sided paired *t*-test was performed on SPSS-14, and *P* values <0.05 were considered significant.

RESULTS

The patients were of the age group 35–60 years (mean 47.12 years). There were 13 patients of Stage IIB (76.5%) and four patients of Stage IIIB (23.5%). All patients received external beam radiation to a dose of 46 Gy in 23 fractions with concurrent cisplatinum-based chemotherapy followed by two sessions of 9 Gy brachytherapy. The total dose to Point A, bladder point and rectum point was 74.5 Gy EQD2, 68.8 Gy EQD2 and 64.8 Gy EQD2, respectively {$EQD2 = D \times [(d + \alpha/\beta)/(2 + \alpha/\beta)]$, where D is the total dose, d the dose/fraction and α/β is 3 for the OAR and 10 is for the tumour}. The mean values of the height, maximum width (at any level), width at point A, maximum thickness (at any level), thickness at Point A and volume of the tumour contoured for the $HR\text{-}CTV_{MRI}$, $HR\text{-}CTV_{CT}$ and $IR\text{-}CTV_{MRI}$, $IR\text{-}CTV_{CT}$ are shown in Table 1. A two-sided paired *t*-test showed that CT underestimated the height, as both clinical examination and CT fail to assess the exact endocervical disease extension, while there was an overestimation of maximum width, which is usually at the level of parametrium. Similar results were seen for $IR\text{-}CTV_{MRI}$ and $IR\text{-}CTV_{CT}$. The dosimetric results of HR-CTV and IR-CTV are shown in Table 2. There was no statistically significant difference between V_{100}, D_{90} and D_{100} for both HR-CTV and IR-CTV.

The volumes and doses to the bladder, rectum, sigmoid and intestines are shown in Table 3. There was no statistically significant difference in volumes or doses to the bladder, rectum, sigmoid and intestines in CT or MRI (dose to ICRU rectal and bladder point, 0.1, 1 and 2 cc).

Table 1. HR-CTV and IR-CTV volume and dimensions comparison

	MRI (mean ± SD)	CT (mean ± SD)	*P* value
HR-CTV			
Height (mm)	45.5 ± 10.81	37.9 ± 10.01	0.001
Maximum width (mm)	44.1 ± 12.21	52.8 ± 11.41	0.009
Width Point A (mm)	32.3 ± 7.61	33.9 ± 12.24	0.571
Maximum thickness (mm)	37.9 ± 7.62	39.0 ± 5.46	0.46
Thickness Point A (mm)	27.4 ± 5.32	25.1 ± 9.52	0.1
Volume (cc)	35.2 ± 18.26	29.1 ± 19.79	0.106
IR-CTV			
Height (mm)	66.0 ± 12.36	51.7 ± 10.21	0.001
Maximum width (mm)	59.8 ± 10.80	69.2 ± 10.48	0.001
Width Point A (mm)	45.1 ± 10.42	52 ± 10.20	0.031
Maximum thickness (mm)	46.8 ± 7.14	48.4 ± 4.90	0.01
Thickness Point A (mm)	33.2 ± 5.69	33.2 ± 7.88	0.966
Volume (cc)	69.1 ± 39.64	64.5 ± 32.69	0.434

MRI, magnetic resonance imaging; SD, standard deviation; CT, computed tomography.

Table 2. HR-CTV and IR-CTV DVH analysis

	MRI	CT	*P* value
HR-CTV			
V_{100} (%)	90.57%	91.16%	0.849
D_{100} (Gy)	6.57 ± 3.86	5.07 ± 1.79	0.148
D_{90} (Gy)	10.6 ± 2.9	10.5 ± 2.9	0.946
IR-CTV			
V_{100} (%)	77.07%	77.07%	1
D_{100} (Gy)	4.9 ± 11.01	4.6 ± 1.67	0.493
D_{90} (Gy)	7.3 ± 1.93	7.4 ± 1.95	0.78

Table 3. OAR volumes and dose analysis

OAR	CT (mean ± SD)	MRI (mean ± SD)	*P* value
Bladder			
Volume (cc)	83.9 ± 34.74	76.6 ± 39	0.089
ICRU Pt (Gy)	6.1 ± 2.4	6.3 ± 2.9	0.435
2 cc	9.0 ± 2.8	9.0 ± 2.1	0.911
1 cc	10.0 ± 3.21	10.0 ± 2.37	0.783
0.1 cc	13.0 ± 4.59	12.4 ± 3.06	0.549
Rectum			
Volume (cc)	48.7 ± 17.01	45.6 ± 10.16	0.377
ICRU Pt (Gy)	4.3 ± 1.4	4.3 ± 1.21	0.964
2 cc	4.5 ± 1.2	4.6 ± 0.9	0.67
1 cc	4.9 ± 1.4	5.1 ± 1.0	0.603
0.1 cc	6.1 ± 1.9	6.4 ± 1.6	0.443
Sigmoid			
Volume (cc)	44.22 ± 15.94	50.42 ± 25.92	0.288
2 cc (Gy)	5.6 ± 1.8	6.1 ± 1.9	0.377
1 cc	6.3 ± 2.1	6.9 ± 2.2	0.392
0.1 cc	8.0 ± 2.5	8.4 ± 3.7	0.699
Intestines			
Volume (cc)	99.81 ± 62.05	92.16 ± 39.81	0.435
2 cc (Gy)	6 ± 2.7	6.4 ± 2.4	0.33
1 cc	5.2 ± 2.7	6.2 ± 2.1	0.31
0.1 cc	7.5 ± 3.5	9.2 ± 3.2	0.21

OAR, organs at risk.

DISCUSSION

It is well known that CT alone is inferior to MRI images, and so MRI is taken to be the standard imaging for image-based contouring at brachytherapy (15,16). This is because the tumour definition especially in the endocervical and in the parametrial extension is more easily depicted on MRI than on CT. This study is unique, in that it compares the CT-based contouring using clinical findings with MRI-based contouring.

It was seen that although the various dimensions of HR-CTV and IR-CTV differ significantly for CT and MRI at different levels, the overall dose coverage of these volumes was not different in two modalities. A typical case of endocervical growth extension at brachytherapy is shown in Fig. 1, with corresponding levels of axial cuts from MRI (Fig. 1a and b) and CT (Fig. 1c and d). The observation that residual endocervical tumour above the level of cervix (Fig. 1b) is easily identified on MRI and not on CT can lead to disparities in volumes and dimension of contours for HR-CTV in two modalities, but dosimetrically coverage is not impacted to that extent.

It has been seen previously that OAR are better delineated on MRI than on CT, as the walls of these organs are better seen on MRI (15,16). However, many studies have shown that CT images are comparable to MRI for contouring OAR. In this study also, it was seen that the volumes and doses to OAR (bladder, rectum and sigmoid) were similar for both CT and MRI. However, it is for the first time that doses and volumes have been reported for intestines and it was seen that 2 cc doses of intestines are comparatively higher than sigmoid and rectum doses on both CT and MRI. Further

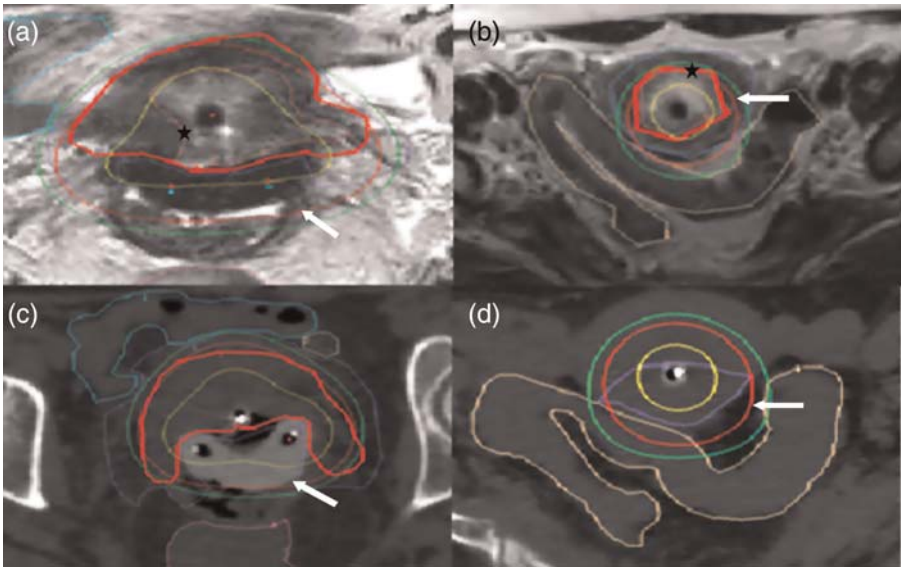

Figure 1. Axial images of magnetic resonance imaging and computed tomographic planning: (a and c) at the level of mid-cervix and (b and d) 1 cm above the point A, respectively. GTV_{BT} (light red; *), HR-CTV (red), IR-CTV (deep blue), rectum (pink), intestine (light blue) and sigmoid (orange) are seen; 100% isodose line (red; arrow pointer). The endocervical extension is clearly seen on MRI (b; marked as *) and not on CT (d) but this region is well covered by the 100% isodose line in both images, shown with an arrow.

implications of this finding are not known as toxicities are not reported in this study. Also the intestines are mobile and it is difficult to estimate the total dose received by a particular part of intestine during the entire treatment (EBRT and brachytherapy) and correlate it with toxicity. However, it is proposed that in future studies, intestines should also be contoured and taken as OAR and that doses received should be consistently recorded and reported for future correlation with acute and chronic toxicity.

It is an important study for countries where MRI is not that readily available or MRI-based planning is not feasible at every session due to logistics. It shows that OARs can be easily contoured on CT, which gives comparable results to MRI for dose volume estimation. Also, the target volume can be contoured precisely if clinical findings are properly documented and implemented in contouring of CT images. These results stand adjuvant to the results of Viswanathan et al. (15) in which MRI information can be easily translated on CT images with comparable results when at brachytherapy MRI information is available. So, it is proposed that if pre or at brachytherapy, MRI scans are available, then with the help of clinical findings and MR information, CT contouring will be much more equitable with MRI-based contouring. This can especially avoid the need of MRI-based planning for all sessions of brachytherapy planning, and CT can be easily used. However, further studies will be required in this context.

The limitations of this study included non-availability of fusion facility, which would have more clearly shown the areas of discrepancies, and helped us to improve clinical interpretation of contouring slice by slice. The number of patients studied is small but it is an important initial experience to guide further studies for CT-based contouring using clinical and MRI information.

Conflict of interest statement

None declared.

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