

CLINICAL INVESTIGATION

Cervix

COMPUTED TOMOGRAPHY VERSUS MAGNETIC RESONANCE IMAGING-BASED CONTOURING IN CERVICAL CANCER BRACHYTHERAPY: RESULTS OF A PROSPECTIVE TRIAL AND PRELIMINARY GUIDELINES FOR STANDARDIZED CONTOURS

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Purpose: To compare the contours and dose–volume histograms (DVH) of the tumor and organs at risk (OAR) with computed tomography (CT) vs. magnetic resonance imaging (MRI) in cervical cancer brachytherapy.

Methods and Materials: Ten patients underwent both MRI and CT after applicator insertion. The dose received by at least 90% of the volume (D_{90}), the minimal target dose (D_{100}), the volume treated to the prescription dose or greater for tumor for the high-risk (HR) and intermediate-risk (IR) clinical target volume (CTV) and the dose to 0.1 cm³, 1 cm³, and 2 cm³ for the OARs were evaluated. A standardized approach to contouring on CT (CT_{Std}) was developed, implemented (HR- and IR- CTV_{CTStd}), and compared with the MRI contours.

Results: Tumor height, thickness, and total volume measurements, as determined by either CT or CT_{Std} were not significantly different compared with the MRI volumes. In contrast, the width measurements differed in HR- CTV_{CTStd} ($p = 0.05$) and IR- CTV_{CTStd} ($p = 0.01$). For the HR- CTV_{CTStd} , this resulted in statistically significant differences in the volume treated to the prescription dose or greater (MRI, 96% vs. CT_{Std} , 86%, $p = 0.01$), D_{100} (MRI, 5.4 vs. CT_{Std} , 3.4, $p < 0.01$), and D_{90} (MRI, 8.7 vs. CT_{Std} , 6.7, $p < 0.01$). Correspondingly, the IR-CTV DVH values on MRI vs. CT_{Std} differed in the D_{100} (MRI, 3.0 vs. CT_{Std} , 2.2, $p = 0.01$) and D_{90} (MRI, 5.6 vs. CT_{Std} , 4.6, $p = 0.02$). The MRI and CT DVH values of the dose to 0.1 cm³, 1 cm³, and 2 cm³ for the OARs were similar.

Conclusion: Computed tomography-based or MRI-based scans at brachytherapy are adequate for OAR DVH analysis. However, CT tumor contours can significantly overestimate the tumor width, resulting in significant differences in the D_{90} , D_{100} , and volume treated to the prescription dose or greater for the HR-CTV compared with that using MRI. MRI remains the standard for CTV definition. © 2007 Elsevier Inc.

Cervical cancer, Brachytherapy, Computed tomography, Magnetic resonance imaging.

INTRODUCTION

Patients with locally advanced cervical cancer require brachytherapy after external beam radiotherapy (EBRT) to increase the likelihood of survival and to optimize outcomes (1, 2). Several studies have validated the use of high-dose-rate (HDR) brachytherapy (3, 4). Most reports have relied on traditional methods of plain X-ray imaging for treatment planning. The use of three-dimensional (3D) imaging from either computed tomography (CT) or magnetic resonance imaging (MRI) as a diagnostic tool has increased significantly worldwide. Evaluations of both CT and MRI in the

planning of brachytherapy applicator treatment have been previously published (5, 6).

Since 1998, the Medical University of Vienna has used MRI immediately after applicator placement to guide treatment planning for tandem and ring brachytherapy. In 2005, the Group Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) provided recommendations for target delineation using MRI-contoured tumor volumes (7), and definitions were proposed for the gross tumor volume (GTV), high-risk (HR) clinical target volume (CTV), and intermediate-risk (IR)-CTV. Subsequent publications of treatment planning pa-

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parameters for MRI-based tandem and ring brachytherapy have used these guidelines (8). However, the use of CT as related to the GEC-ESTRO recommendations (7) in gynecologic brachytherapy has not previously been evaluated.

Although MRI is superior to CT for imaging the normal anatomy of the female pelvis and for identifying cervical cancer extension (9–11), some institutions do not have access to an MRI unit or their unit is located a significant distance from the radiation oncology clinic. MRI requires special nonmagnetic brachytherapy applicators that are considerably more expensive than metallic applicators. CT scanners are often more widely available than MRI, either for use as dedicated simulators in radiotherapy departments or in close proximity to radiology departments, and may be used for planning 3D treatment. Although nonmetallic brachytherapy applicators produce clearer images on CT, metallic applicators will not harm the patient, and the resultant scatter may be minimized using special scanning algorithms (12).

To assess the validity of CT-based contours using the GEC-ESTRO MRI definitions, we compared the CT and MRI contours of cervical cancer with a tandem and ring applicator in place. A standardized series of CT-based contours was generated after evaluation of the initial CT and MRI contours. The primary endpoint of this trial was to assess the feasibility of using these CT-standardized (CT_{Std}) contours to approximate MRI-based treatment parameters. A secondary endpoint was to determine whether CT and MRI provide dosimetrically similar results for the organs at risk (OARs), including the bladder, rectum, and sigmoid.

METHODS AND MATERIALS

Patient enrollment and EBRT

Between January and December 2005, we obtained informed consent from and enrolled 10 patients with biopsy-proven cervical cancer (Stage IIA–IIIB) in a protocol at the Medical University of Vienna. The pretreatment clinical examination consisted of laboratory studies, including a complete blood count and assessment of renal function; a chest X-ray or chest CT scan to confirm the absence of lung metastases; abdominopelvic CT; and diagnostic MRI of the pelvis. A radiation oncologist and gynecologist performed the initial clinical assessment of the tumor stage.

Diagnostic MRI scans, evaluated by the radiologist and radiation oncologist, depicted the 3D tumor volume and relationship to the adjacent structures before the initiation of radiotherapy. Because 2 patients were transferred from outside institutions solely for brachytherapy, the diagnostic MRI studies from outside the hospital were also evaluated.

All patients underwent pelvic EBRT using a four-field box technique with CT-based treatment planning. Patients with common iliac node involvement also underwent four-field para-aortic nodal radiotherapy. Concurrent weekly cisplatin chemotherapy at 40 mg/m² was administered when feasible. After completing EBRT, patients underwent tandem and ring HDR brachytherapy with a CT/MRI-compatible applicator (Nucletron Systems, Veenendaal, The Netherlands) with a tandem length of 40 or 60 mm, curvature of 45° or 60°, and a ring diameter of 24, 30, or 36 mm. One patient received a tandem and cylinder applicator with

pulse-dose-rate (PDR) brachytherapy because the tumor extended to the lower vagina.

Brachytherapy insertion and treatment

Patient preparation, examination, and the standard insertion procedures have been previously published (8). Patients receiving HDR ¹⁹²Ir brachytherapy were treated with a Nucletron HDR microSelectron in the brachytherapy suite. One patient was treated with a Nucletron microSelectron PDR unit.

CT and MRI technique

All patients underwent both CT and MRI at brachytherapy with the tandem and ring applicator in place. The MRI unit at the Medical University of Vienna is a 0.2-Tesla Magnetom Open (Siemens, Open-Viva, Erlangen, Germany). MRI was performed with a pelvic surface coil. The image acquisition protocol used at the Medical University of Vienna has recently been described (6, 13). The applicator, vaginal packing, bladder balloon, and rectal probe were displayed with low-signal intensity on T₂-weighted images.

The CT scanner at the Medical University of Vienna is a conventional scanner, the Somatom Plus S (Siemens, Erlangen, Germany). The abdominopelvic CT scans at diagnosis were performed for EBRT planning. The CT images at brachytherapy were generated in 4-mm slice intervals from the iliac crest to the ischial tuberosities without intravenous contrast.

The specific techniques used for MRI with the brachytherapy applicator in place have been previously described (6). The section thickness was 5 mm with no intersection gap. Axial images were obtained from the level above the uterine fundus to the inferior border of the symphysis pubis below any vaginal tumor extension; sagittal images were obtained between the internal obturator muscles. The coronal, paracoronar, and para-axial images included the tumor, entire cervix, corpus uteri, parametria, and vagina.

Contouring and brachytherapy treatment planning

Axial T₂-weighted MRI studies taken after brachytherapy applicator placement were contoured on a PLATO workstation (Nucletron) in accordance with the GEC-ESTRO recommendations (7, 14). The GTV was determined by a radiation oncologist as the macroscopic extent of the tumor at brachytherapy, as represented by high-signal-intensity masses on MRI. The MRI-defined HR-CTV (HR-CTV_{MRI}) included the entire cervix and the macroscopic extent of the tumor at brachytherapy plus any pathologic residual tissue in the parametria, uterine corpus, rectum, bladder, and/or vagina. The MRI-defined IR-CTV_{MRI} encompassed the tumor extension at diagnosis or a 1-cm margin around the HR-CTV_{MRI}. Delineation of the outer wall of the OARs was according to the GEC-ESTRO protocol.

The target tissue (HR-CTV_{CT}, IR-CTV_{CT}), bladder, sigmoid, and rectum were contoured on MRI and CT separately. CT contours of the HR-CTV_{CT} and IR-CTV_{CT} were adapted based on the GEC-ESTRO recommendations for MRI. The GTV could not be defined on CT, because tumor tissue has the same signal intensity as normal cervical tissue. The CT contours of the tumor and bladder, rectum, and sigmoid were determined retrospectively by a radiation oncologist (A.V.) for this study using Oncentra Masterplan (Nucletron). No contrast was used in this study. Contours of the rectum began 1 cm above the anus, ended at the sigmoid flexure, and covered the outer wall of the organ. The sigmoid was considered to begin at the level of the rectosigmoid flexure and

ended at the anterior crossing of the sigmoid by the pubic symphysis. The bladder contour included the outer wall of the bladder and ended at the beginning of the urethra.

The CT and MRI volumes were fused using the anatomy-modeling tool of Oncentra Masterplan (Nucletron). Two fusion protocols available in this software system were applied: automatic fusion using mutual registration, and manual fusion using landmarks. The landmarks included the tip of the tandem, center of the ring, tip of bladder, and rectal probes and the tip of the interstitial needles, if used. These fusion methods were assessed qualitatively by comparing the location of the applicator. The fusion with the best agreement between data sets was chosen for additional analysis. After initial contouring on CT and evaluation of the fused images, a consistent approach to contouring was developed, and all patients underwent repeat contouring using the standardized approach, which defined the CT_{Std}-defined HR-CTV_{CTStd} and IR-CTV_{CTStd}.

In this trial, treatment planning for all patients used plain X-ray and MRI scans, as previously described (8). For calculation of the dosimetric parameters, the images were transferred to PLATO BPS and registered to the dose distribution with the EVAL module, ensuring that the identical dose distribution coincided with MRI and CT. After reconstruction of the applicator, an optimized treatment plan was created for the MRI and CT data sets. Dose-volume histograms (DVHs) were evaluated for the bladder, rectum, sigmoid, and tumor. The dose received by at least 90% of the volume (D_{90}), the minimal target dose (D_{100}), the volume treated to the prescription dose or greater for tumor, and the dose to 0.1 cm³, 1 cm³, and 2 cm³ for the bladder, sigmoid, and rectum were calculated from the cumulative DVHs. The dose values are reported in the dose/HDR fraction. To use the values of the 1 PDR case, the PDR dose/fraction was re-normalized to the HDR prescription dose of 7 Gy/fraction.

The values for height, width (at point A), thickness (at point A), and volume were generated for the MRI, CT, and CT_{Std} contours. These values and the volume treated to the prescription dose or greater, D_{90} , and D_{100} of the CT targets (HR-CTV_{CT}, IR-CTV_{CT}, HR-CTV_{CTStd}, and IR-CTV_{CTStd}) were compared with those of the MRI scans (HR-CTV_{MRI} and IR-CTV_{MRI}). The dose to 0.1 cm³, 1 cm³, and 2 cm³ of the OARs of the CT and MRI contours were analyzed. For comparison between the different contouring modalities, a two-sided paired *t* test was performed. *P* values ≤ 0.05 were considered significant.

RESULTS

Patient, tumor, and treatment characteristics

The median patient age was 53 years (range, 34–71 years). Of the 10 patients, 1 had Fédération Internationale de Gynécologie et d'Obstétrique (FIGO) clinical Stage IIA, 5 had IIB, 2 had IIIA, and 2 had IIIB. Patients underwent either CT of the chest ($n = 7$) or a chest X-ray ($n = 3$) at diagnosis as staging for lung metastases. Additional staging studies included positron emission tomography in 1 patient and abdominopelvic CT in all patients. The median dose of EBRT was 45 Gy (range, 45–55 Gy). Para-aortic nodal radiotherapy was administered to 3 patients. The pelvic EBRT fraction size was 1.8 Gy and was 1.6 Gy to the para-aortic nodes, if treated. One patient did not receive cisplatin chemotherapy because she had undergone a kidney

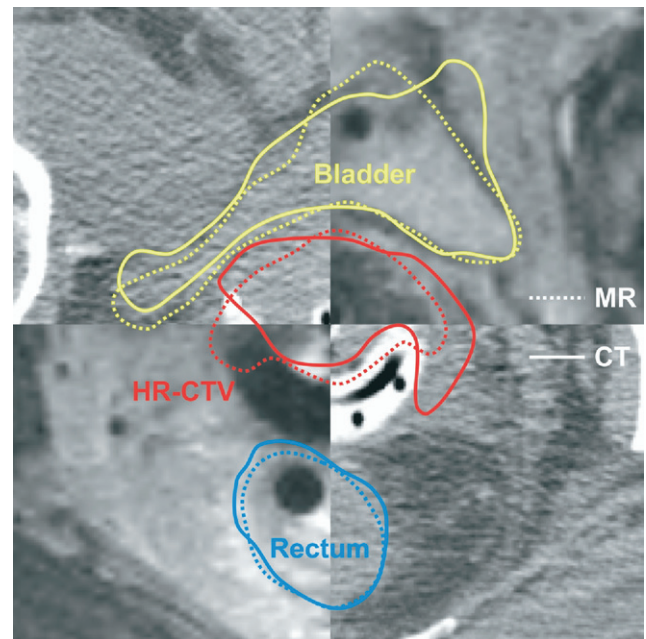


Fig. 1. Example of fusion between axial computed tomography (solid line) and magnetic resonance imaging (dotted line) scans with contours for rectum, bladder, and high-risk clinical target volume in patient with tandem and ring brachytherapy applicator inserted into cervix. Outer rectum contours overlap nicely; bladder contours show only slight deviations. The high-risk clinical target volume contour highlights the difference in lateral extension seen between computed tomography and magnetic resonance imaging and reveals difficulty in accurately assessing the lateral dimension.

transplant. Brachytherapy included HDR ($n = 9$) and PDR ($n = 1$). The HDR fractionation was 7 Gy for four fractions ($n = 8$) or 8 Gy for 3 fractions ($n = 1$). For the 8 patients treated with 7 Gy for four fractions, two insertions were performed approximately 1 week apart. After the insertion, two fractions were administered approximately 16 hours apart. Brachytherapy started during the last week of EBRT in 5 patients and within 1 week after EBRT in 5 patients.

CT_{Std} contouring protocol development

Several limitations were noted in the initial contouring of CT images, including difficulty delineating the superior border of the cervix and the lateral border of the parametria (if involved) and accurate delineation of the OARs. After initial contouring on CT, fused MRI, and CT images were evaluated (Fig. 1). Using the GEC-ESTRO guidelines for MRI, a standardized protocol was created and used to contour the HR-CTV_{CTStd} and IR-CTV_{CTStd} (Appendix). These standardized contours overestimated the cervix size to ensure adequate coverage.

Volumetric and DVH values

Table 1 lists the height, width, thickness, and volume of the tumor contoured for the HR-CTV_{MRI}, HR-CTV_{CT}, and HR-CTV_{CTStd}. A two-sided *t* test comparing the mean values of the height, thickness, and volume showed no significant differences among the three. Table 2 shows

Table 1. Mean values and comparison of volume and dose parameters among high-risk clinical target volume obtained on magnetic resonance imaging, computed tomography, and after formulating standardized computed tomography contours

Parameter	HR-CTV _{MRI}	HR-CTV _{CT}	HR-CTV _{CTStd}
Height (cm)	4.6 ± 1.5	4.4 ± 1.5	4.2 ± 1.0
Width at Point A (cm)	4.5 ± 1.0	5.1 ± 1.8	5.5 ± 1.3 (<i>p</i> = 0.05)*
Thickness at Point A (cm)	3.6 ± 0.6	3.5 ± 1.1	3.8 ± 1.3
Volume (cm ³)	47.3 ± 28.5	43.3 ± 30.5	47.6 ± 23
V ₁₀₀ [†] (%)	96 ± 4	91 ± 11	86 ± 9 (<i>p</i> = 0.01)*
D ₁₀₀ [†] (Gy)	5.4 ± 1.5	4.1 ± 1.7 (<i>p</i> = 0.03)*	3.4 ± 1.0 (<i>p</i> < 0.01)*
D ₉₀ [†] (Gy)	8.7 ± 1.5	7.6 ± 1.9	6.7 ± 1.6 (<i>p</i> < 0.01)*

Abbreviations: HR = high risk; CTV = clinical target volume; MRI = magnetic resonance imaging; CT = computed tomography; HR-CTV_{CTStd} = HR-CTV with standardized CT contours; V₁₀₀ = volume treated to ≥100% of prescription dose; D₁₀₀, minimal target dose; D₉₀ = dose received by ≥90% of volume.

Data presented as mean ± standard deviation.

* Statistically significant values compared with HR-CTV_{MRI}.

[†] Normalized to 7 Gy/fraction.

similar results for IR-CTV_{MRI} and IR-CTV_{CTStd} (all *p* > 0.05). A nonsignificant increase in width was seen from HR-CTV_{CT} to HR-CTV_{CTStd}. However, the tumor width was significantly different for both the HR-CTV_{CTStd} (*p* = 0.05) and the IR-CTV_{CTStd} (*p* = 0.01) compared with the corresponding MRI values.

For the HR-CTV, this difference in width resulted in statistically significant differences in the volume treated to the prescription dose or greater, D₁₀₀, and D₉₀. Similar differences were seen with the IR-CTV between the MRI and CT_{Std} DVH values, including the D₁₀₀ and D₉₀ (Table 2).

No statistically significant differences in the dose to 0.1 cm³, 1 cm³, and 2 cm³ for the OARs were noted (Table 3). A difference in the rectal volume was noted, reflecting that the MRI OAR volumes were not contoured using a standard protocol. This difference was not reflected in the DVH values, because those do not reflect the dose to the entire volume but only to the region most proximal to the greatest dose.

DISCUSSION

The results of this study have shown that, in general, the width of the contoured cervix was greater on CT, particularly after the generation of standardized contours. This increased width resulted in a decrease in the D₁₀₀ and D₉₀. Although the CT contours were typically larger than the MRI contours, this was not seen in the height measurement, because the cervical apex was not always visible on a CT scan. This is the first study to compare the CT and MRI DVH values of the tumor using the GEC-ESTRO guidelines and of the OARs; no difference was noted in any of the OAR values.

Coverage of the tumor volume is imperative, because an insufficient brachytherapy dose to endocervical tumors increases the rate of pelvic relapse (1). Inadequate coverage of the GTV and CTV correlates with persistent disease in patients treated with surgical resection after radiotherapy for cervical

Table 2. Mean values and comparison of volume and dose parameters between intermediate-risk clinical target volume obtained on magnetic resonance imaging and after formulating standardized computed tomography contours

Parameter	IR-CTV _{MRI}	IR-CTV _{CTStd}
Height (cm)	7.1 ± 2.5	6.1 ± 1.3
Width at Point A (cm)	6.7 ± 1.1	8.1 ± 0.9 (<i>p</i> = 0.01)*
Thickness at Point A (cm)	5.3 ± 1.3	4.8 ± 0.9
Volume (cm ³)	115.1 ± 46.9	117.9 ± 45.7
V ₁₀₀ (%)	75 ± 10	71 ± 15
D ₁₀₀ (Gy)	3.0 ± 0.8	2.2 ± 0.5 (<i>p</i> = 0.01)*
D ₉₀ (Gy)	5.6 ± 1.0	4.6 ± 1.2 (<i>p</i> = 0.02)*

Abbreviations: IR = intermediate risk; other abbreviations as in Table 1.

Data presented as mean ± standard deviation.

* Statistically significant values compared with IR-CTV_{MRI}.

Table 3. Volume and dose to organs at risk after importing to Plato, normalized to 7 Gy/fraction

OARs	MRI	CT
Bladder		
Volume (cm ³)	62.5 ± 31.6	84.5 ± 57.5
D _{0.1cm³}	7.5 ± 1.0	6.5 ± 1.5
D _{1cm³}	6.1 ± 0.6	5.5 ± 1.4
D _{2cm³}	5.6 ± 0.6	5.0 ± 1.2
Rectum		
Volume (cc)	45.3 ± 15.3	62.8 ± 16.8*
D _{0.1cm³}	5.0 ± 0.9	5.0 ± 1.1
D _{1cm³}	4.2 ± 0.7	4.2 ± 0.9
D _{0.2cm³}	3.9 ± 0.7	3.9 ± 0.8
Sigmoid		
Volume (cc)	36.5 ± 25.2	29.8 ± 16
D _{0.1cm³}	5.5 ± 1.1	5.5 ± 1.9
D _{1cm³}	4.5 ± 0.9	4.3 ± 1.5
D _{2cm³}	4.0 ± 0.8	3.9 ± 1.4

Abbreviations: D_{0.1cm³} = dose to 0.1 cm³; D_{1cm³} = dose to 1 cm³; D_{2cm³} = dose to 2 cm³; other abbreviations as in Table 1.

* *p* < 0.01.

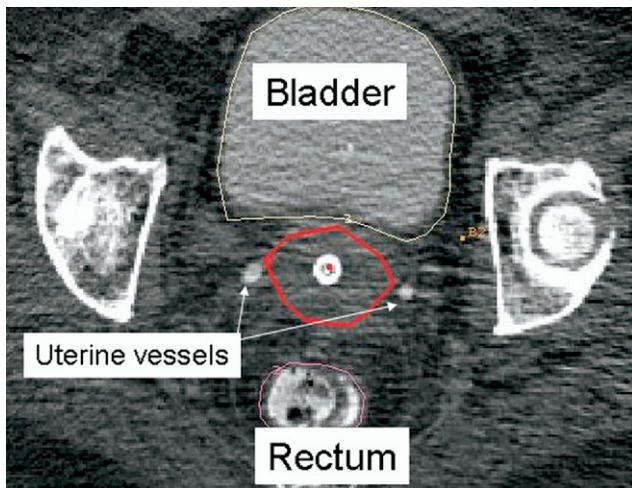


Fig. 2. Axial computed tomography image at level of cervix/uterine interface in Fédération Internationale de Gynécologie et d'Obstétrique Stage IB cervical cancer. Intravenous contrast delineates uterine vessels and may assist with identifying superior border of cervix. Bladder and rectal contrast inserted at computed tomography scanning aid in delineation of these structures.

cancer (15). Proper delineation of the tumor volume using 3D imaging for treatment planning allows optimal radiation delivery to the tumor, while avoiding adjacent OARs.

Although MRI at brachytherapy with the applicator in place is the reference standard (6, 16), MRI may not be available in many institutions. Consensus guidelines for the standardization of the nomenclature for MRI-based cervical cancer brachytherapy have recently been published (7). These recommendations used MRI contours of the tumor with the applicator in place. A validation study showed that contours obtained on MRI were consistent among institutions (17). Treatment planning parameters for cervical cancer brachytherapy have been published for MRI (8), and the results using these parameters with MRI have shown a high rate of local control for patients with locally advanced cervical cancer (18).

To date, no institution has proposed guidelines for CT-based 3D contouring in cervical cancer brachytherapy. Previous studies have shown that CT at brachytherapy is feasible (5) and can be used to verify placement and to ensure that the uterus has not been perforated (19). Several publications have compared radiography and CT-based planning, particularly with regard to the normal tissue dose (20–27). One study found that the dose to Point A overestimated the dose covering the GTV (22). However, a worse-stage tumor had less coverage by the prescribed dose, indicating the importance of 3D assessment of the tumor for all cases. The use of positron emission tomography at brachytherapy has also been described (28).

Computed tomography contouring results can be improved by contrast-enhanced imaging and careful integration of the information obtained from clinical examination, multiplanar imaging, and MRI immediately before brachytherapy. The borders between the OARs and gynecologic

tissues (uterus, cervix, and vagina) cannot be discerned in all cases (29). Contrast may be used to assist with delineation of the OARs (30). Dilute Hypaque contrast placed directly into the bladder can determine the lateral recesses on CT. Barium inserted into a rectal tube placed with the tip in the rectosigmoid before scanning provides adequate sigmoid and rectal contrast and enhances OAR contouring.

Contouring typically occurs on axial planes; however, sagittal images with the applicator in place can ensure that the superior extent of the cervix encompasses the average cervical height of 3 cm. CT, unlike MRI, does not permit a distinction between the corpus and cervix uteri or a clear delineation between tumor and normal cervical tissue. With contrast, the central areas of the cervix are enhanced more than the peripheral regions (31, 32). However, intravenous contrast does not highly enhance the tumor on CT. Therefore, a GTV as recommended by the GEC-ESTRO guidelines for MRI cannot consistently be visualized on CT. Intravenous contrast during CT, after confirmation of a patient's adequate renal function, may identify the uterine vessels, which delineate the cervicouterine junction at the intersection of the uterine vessels and the cervix (Fig. 2). This allows demarcation of the upper border of the cervix and, therefore, could guide contouring of the superior border of the HR-CTV. However, for patients with tumor extension superior to the cervix, only MRI immediately before or at brachytherapy can accurately delineate the superior border of the HR-CTV. If MRI is unavailable, the initial tumor extension into the uterine corpus, or at least the entire uterine

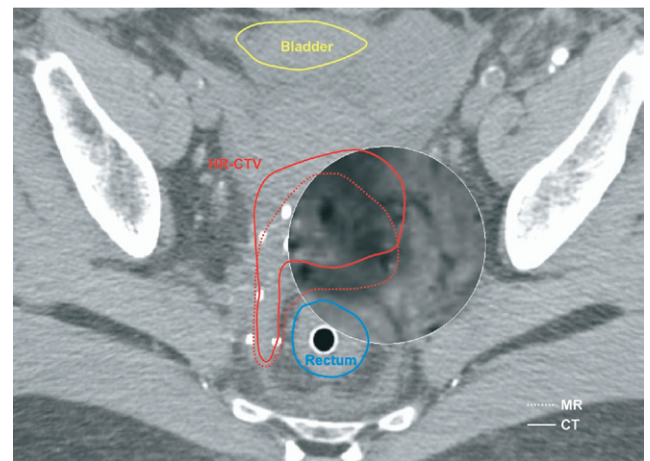


Fig. 3. Axial computed tomography slice at level of uterine cervix of patient with Fédération Internationale de Gynécologie et d'Obstétrique Stage IIIB cervical cancer. High-risk clinical target volume extends into right uterosacral ligament (solid line indicates computed tomography contour; dotted line indicates magnetic resonance imaging contour). For bilateral parametrial coverage of high-risk clinical target volume, combined intracavitary/interstitial approach used. Spyglass viewing revealed underlying magnetic resonance image. On magnetic resonance imaging, low-signal-intensity cervical stroma can be easily differentiated from surrounding tissues, facilitating contouring of cervix. On computed tomography, borders of homogeneous mass, including cervix and parts of surrounding tissues, could not be distinguished, resulting in insignificant differences in delineation of right dorsal parametria.

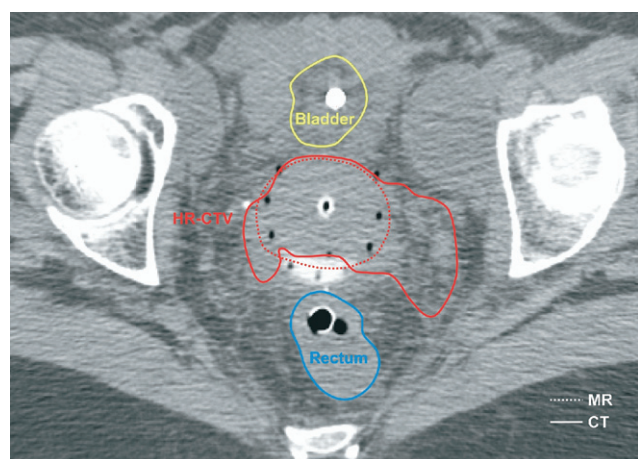


Fig. 4. Axial computed tomography slice of pelvis immediately superior to ring applicator depicting parametrium in patient with Fédération Internationale de Gynécologie et d'Obstétrique Stage IIB cervical cancer. Both magnetic resonance imaging (solid line) and computed tomography (dotted line) contours are superimposed. Bilateral inconsistencies with regard to parametrial extension of high-risk clinical target volume are revealed. Computed tomography contours confirm significantly increased lateral extension of parametrial tissues contoured compared with magnetic resonance imaging contour. Therefore, clinical examination and magnetic resonance imaging before brachytherapy are critical to avoid unnecessarily contouring uninvolved parametrial tissue.

canal, must be contoured superiorly to ensure that the CTV covers the entire extent of potential areas at risk. The parametrial ligaments are depicted with a wide variation in shape and thickness on CT (31, 32). Therefore, wide HR-CTV volumes may be outlined with CT for patients with uterosacral (Fig. 3) or parametrial (Fig. 4) extension.

Accurate delineation of the HR-CTV and IR-CTV requires documentation of the gynecologic examination with drawings at diagnosis and at brachytherapy. For IR-CTV generation, a comparison to the initial extension (as seen on either the clinical diagram or the initial MRI scan) is crucial. Clinical examination may be superior to CT or MRI for the evaluation of vaginal tumor extension. We found that, although each case must be considered individually, certain parameters were similar in all cases (Appendix).

The results of this study showed significantly different D_{90} and D_{100} values when CT_{Std} contours were compared with the MRI-based contours for both HR-CTV and IR-CTV. This resulted from the additional lateral extension of the CT_{Std} contours in the region of the parametrial or lateral cervical tissue, because the standardized contours used in this study overestimated tumor size to ensure adequate tumor coverage. Because this represents the region with a high falloff of dose in a range close to the prescription dose (range, 3–9 Gy), the additional lateral volume on CT accounts for the differences in the dose parameters. However, because this difference is only on the lateral aspects, the differences in the total volumes for the MRI and CT_{Std} contouring protocols were not statistically significant. Therefore, CT-based treatment planning as performed in this study resulted in a slightly greater dose to patients if these guidelines were used for prospective dose optimization. Approximation with careful clinical judgment during treatment planning optimization is imperative to carefully evaluate the larger treatment volumes obtained by CT. However, this dose increase was still limited by the constraints for the OARs.

The limitations of this study included its reliance on a population from a single institution. A small number of patients were enrolled prospectively. The data are preliminary and need to be validated by a larger multi-institutional trial.

This study is the first to directly compare MRI and CT contours of the tumor using the GEC-ESTRO guidelines for definitions and of the OAR. No significant differences between CT and MRI in volume or dose to the OARs were identified. Therefore, contouring normal tissue structures with CT appears to be valid. At present, MRI remains the reference standard for contouring tumor volumes. The proposed standardized contouring protocol provides a framework for generating future guidelines for CT-based cervical cancer brachytherapy. CT may be used for prospective planning, but direct comparison with tumor DVH parameters obtained with MRI may not be valid. Therefore, whenever feasible, an MRI scan should be performed with the brachytherapy applicator in place.

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APPENDIX

CT-standardized Contour Guidelines

- I. Standard contour (disease confined to cervix at brachytherapy), includes all patients with Fédération Internationale de Gynécologie et d'Obstétrique (FIGO) Stage IB cervix-confined disease at diagnosis
 - A. High-risk clinical target volume (HR-CTV)—Contour entire cervix as seen on computed tomography (CT)
 1. Inferiorly, start contour at superior level of ring
 2. Superiorly, contour to level at which uterine vessels first abut cervical tissue (if intravenous contrast administered) to point at which volume expands (indicating presence of uterine tissue), or to point at which uterine cavity appears
 - a. Add two slices of contour (with decreasing diameters) around tandem superiorly to cover conical cervical apex
 - b. Measure height of cervix to ensure adequate coverage (average height approximately 3 cm)
 - B. Intermediate-risk CTV (IR-CTV)—Add 1-cm expansion around HR-CTV, modify for disease extent at diagnosis
 1. Modify volume by deletion of contour extending into the bladder, sigmoid, or rectum

- II. Upper vaginal involvement at the time of brachytherapy (includes FIGO clinical Stage IIA disease confined to the cervix and upper vagina, with residual vaginal disease after external beam radiotherapy [EBRT])
 - A. HR-CTV—Contour entire cervix as seen on CT and any residual vaginal disease as determined from clinical examination at brachytherapy
 1. Follow standard contour (see Section IA)
 2. Modify contour inferiorly to cover most inferior extent of vaginal disease
 - B. IR-CTV—Follow standard contour (see section IB)
- III. Parametrial or uterosacral disease at brachytherapy, with or without upper vaginal disease, not fixed to sidewall (includes FIGO clinical Stage IIB with residual parametrial disease after EBRT)
 - A. HR-CTV
 1. Inferiorly, start contour at superior level of ring or just inferior to vaginal extension if present (see Section IIA)
 2. Superiorly, follow standard contour (see Section IA)
 3. Divide parametria into inner and outer halves
 - a. If inner half is involved on clinical examination at brachytherapy, laterally contour parametrium as butterfly-shaped structure, ≤ 2 cm from edge of cervix
 - b. If outer half is involved at brachytherapy, laterally contour parametrium as butterfly-shaped structure >2 cm from edge of cervix, not to sidewall
 - c. Start parametrial contours at level of ring and extend parametrial contours for entire height of cervix
 - d. If para-uterine extension is visible on MRI immediately before brachytherapy implantation, or visible on CT, contour full extension
 4. Contour uterosacral ligaments, consistent with clinical examination findings or disease seen on CT
 - B. IR-CTV
 1. Follow standard contour (see Section IB)
 2. Ensure coverage of parametrial/uterosacral/vaginal disease present at diagnosis
- IV. Lower vaginal disease at brachytherapy (includes FIGO clinical Stage IIIA disease confined to cervix and lower vagina with or without parametrial involvement, with residual lower vaginal disease at brachytherapy)
 - A. HR-CTV
 1. Inferiorly, start contour below lowest extent of vaginal disease using urethral meatus as landmark to compare CT, MRI, and clinical examination findings. Include entire thickness of tumor into paravaginal tissues if visible on MRI or detected on clinical examination immediately before brachytherapy
 2. Superiorly, follow standard contour (see Section IB)
 3. Laterally, if parametrial or uterosacral disease is present, follow Section IIIA3. If no parametrial extension exists, follow standard contour (see Section IA)
 - B. IR-CTV
 1. Follow standard contour (see Section IB)
 2. Ensure coverage of extent of lower vaginal involvement at diagnosis
- V. Sidewall extension/fixation (includes FIGO clinical Stage IIIB, cervix, and lateral sidewall or posterior uterosacral fixation, or hydronephrosis, with or without vaginal extension), with residual sidewall or uterosacral fixation at brachytherapy
 - A. HR-CTV
 1. Inferiorly, cover vaginal extension of disease, if present (see Section IVA1)
 2. Superiorly, follow standard contour (see Section IB)
 3. Laterally, contour disease to pelvic sidewalls if sidewall fixation is present (with sidewall fixation defined as tumor extension extending to internal obturator muscle or adjacent to pelvic bone)
 4. Posteriorly, if uterosacral ligament fixation is detected, contour to sacral wall
 - B. IR-CTV
 1. Follow standard contour (see Section IB)
 - a. Delete contour that extends into pelvic bone
 2. Ensure coverage of extent of lower vaginal involvement at diagnosis
- VI. Adjacent organ invasion (FIGO clinical Stage IVA cervix plus adjacent organ with or without fistula, parametrial/sidewall extension, or vagina extension) at diagnosis and brachytherapy
 - A. HR-CTV
 1. If feasible, obtain diagnostic MRI scan just before brachytherapy to determine extent of adjacent organ invasion
 2. Inferiorly, add vaginal extension, if present, including paravaginal tissues
 3. Superiorly, contour to superior extent of visible tumor or standard contour (see Section IA)
 4. Laterally, contour disease present on clinical examination at brachytherapy (including parametrial disease, sidewall disease, vaginal disease)
 5. Contour region of tumor invasion into adjacent organ visible either on CT or on pre-brachytherapy MRI—do not contour entire organ
 - B. IR-CTV—Follow standard contour (see Section IB)
 1. Exclude contour extending into OARs, including bladder, sigmoid, rectum, or into normal pelvic bone unless involved with disease