

Clinical Investigation

# Comparison and Consensus Guidelines for Delineation of Clinical Target Volume for CT- and MR-Based Brachytherapy in Locally Advanced Cervical Cancer



Akila N. Viswanathan, MD, MPH,\* Beth Erickson, MD,<sup>†</sup>  
David K. Gaffney, MD, PhD,<sup>‡</sup> Sushil Beriwal, MD,<sup>||</sup>  
Sudershan K. Bhatia, MD, PhD,<sup>¶</sup> Omer Lee Burnett III, MD,<sup>#</sup>  
David P. D'Souza, MD,\*\* Nikhilesh Patil, MD,\*\*  
Michael G. Haddock, MD,<sup>††</sup> Anuja Jhingran, MD,<sup>‡‡</sup>  
Ellen L. Jones, MD, PhD,<sup>§§</sup> Charles A. Kunos, MD, PhD,<sup>||||</sup>  
Larissa J. Lee, MD,\* Lilie L. Lin, MD,<sup>¶¶</sup> Nina A. Mayr, MD, PhD,<sup>##</sup>  
Ivy Petersen, MD,<sup>††</sup> Primoz Petric, MD,<sup>\*\*\*,†††</sup> Lorraine Portelance, MD,<sup>‡‡‡</sup>  
William Small Jr, MD,<sup>§§§</sup> Jonathan B. Strauss, MD,<sup>|||||</sup>  
Kanokpis Townamchai, MD,\* Aaron H. Wolfson, MD,<sup>†††</sup>  
Catheryn M. Yashar, MD,<sup>¶¶¶</sup> and Walter Bosch, DSc<sup>§</sup>

\*Brigham & Women's Hospital/Dana-Farber Cancer Institute, Boston, Massachusetts, <sup>†</sup>Medical College of Wisconsin, Milwaukee, Wisconsin, <sup>‡</sup>University of Utah Huntsman Cancer Hospital, Salt Lake City, Utah, <sup>§</sup>Washington University, St. Louis, Missouri, <sup>||</sup>University of Pittsburgh Cancer Institute, Pittsburgh, Pennsylvania, <sup>¶</sup>University of Iowa, Iowa City, Iowa, <sup>#</sup>University of Alabama, Birmingham, Alabama, \*\*London Health Sciences Centre and Western University, London, Ontario, Canada, <sup>††</sup>Mayo Medical Center, Rochester, Minnesota, <sup>‡‡</sup>University of Texas MD Anderson Cancer Center, Houston, Texas, <sup>§§</sup>University of North Carolina, Chapel Hill, North Carolina, <sup>||||</sup>Case Western Reserve University, Cleveland, Ohio, <sup>¶¶</sup>University of Pennsylvania, Philadelphia, Pennsylvania, <sup>##</sup>University of Washington, Seattle, Washington, <sup>\*\*\*</sup>Division of Radiotherapy, Institute of Oncology Ljubljana, Ljubljana, Slovenia, <sup>†††</sup>Department of Radiation Oncology, National Center for Cancer Care and Research, Doha, Qatar, <sup>‡‡‡</sup>University of Miami Miller School of Medicine, Miami, Florida, <sup>§§§</sup>Loyola University Strick School of Medicine, Chicago, Illinois, <sup>|||||</sup>The Robert H. Lurie Comprehensive Cancer Center of Northwestern University, Chicago, Illinois, and <sup>¶¶¶</sup>University of California, San Diego, California, Washington University, St. Louis, Missouri

Received Mar 3, 2014, and in revised form May 28, 2014. Accepted for publication Jun 2, 2014.

Reprint requests to: Akila N. Viswanathan, MD, MPH, Department of Radiation Oncology, Brigham and Women's Hospital/Dana-Farber Cancer Institute, Harvard Medical School, 75 Francis St, ASB 1, L2, Boston, MA 02115. Tel: (617) 732-6331; E-mail: [aviswanathan@lroc.harvard.edu](mailto:aviswanathan@lroc.harvard.edu)

Presented at the 55th Annual Meeting of the American Society for Radiation Oncology, Atlanta, GA, September 22-25, 2013. Endorsed by the American Brachytherapy Society.

Support through National Institutes of Health R21 167800 to A. N. Viswanathan. The Advanced Technology Consortium (ATC) has received support through National Institutes of Health Grant CA81647.

## Summary

Consensus contours generated by a large group of expert gynecologic radiation oncologists using computed tomography (CT) and 3 Tesla magnetic resonance imaging (MRI) were compared. MRI-contoured volumes were smaller than CT volumes, particularly in locally advanced cervical cancer cases with parametrial extension and this difference was dependent on the amount of tumor regression. CT has a higher level of agreement, which may be due to the more distinct contrast between tissues on the images at the time of brachytherapy. A 95% consensus volume was generated for CT and for MR online contouring atlases available for instruction at <http://www.nrgoncology.org/Resources/Contouring-Atlases/GYNCervical-Brachytherapy.aspx> on the basis of these results.

**Objective:** To create and compare consensus clinical target volume (CTV) contours for computed tomography (CT) and 3-Tesla (3-T) magnetic resonance (MR) image-based cervical-cancer brachytherapy.

**Methods and Materials:** Twenty-three experts in gynecologic radiation oncology contoured the same 3 cervical cancer brachytherapy cases: 1 stage IIB near-complete response (CR) case with a tandem and ovoid, 1 stage IIB partial response (PR) case with tandem and ovoid with needles, and 1 stage IB2 CR case with a tandem and ring applicator. The CT contours were completed before the MRI contours. These were analyzed for consistency and clarity of target delineation using an expectation maximization algorithm for simultaneous truth and performance level estimation (STAPLE), with  $\kappa$  statistics as a measure of agreement between participants. The conformity index was calculated for each of the 6 data sets. Dice coefficients were generated to compare the CT and MR contours of the same case.

**Results:** For all 3 cases, the mean tumor volume was smaller on MR than on CT ( $P < .001$ ). The  $\kappa$  and conformity index estimates were slightly higher for CT, indicating a higher level of agreement on CT. The Dice coefficients were 89% for the stage IB2 case with a CR, 74% for the stage IIB case with a PR, and 57% for the stage IIB case with a CR.

**Conclusion:** In a comparison of MR-contoured with CT-contoured CTV volumes, the higher level of agreement on CT may be due to the more distinct contrast medium visible on the images at the time of brachytherapy. MR at the time of brachytherapy may be of greatest benefit in patients with large tumors with parametrial extension that have a partial or complete response to external beam. On the basis of these results, a 95% consensus volume was generated for CT and for MR. Online contouring atlases are available for instruction at <http://www.nrgoncology.org/Resources/ContouringAtlases/GYNCervicalBrachytherapy.aspx>. © 2014 Elsevier Inc.

## Introduction

Women with locally advanced cervical cancer require treatment with external beam radiation (EBRT) combined with brachytherapy (BT) to maximize both local and regional tumor control. Survival rates decrease significantly for patients who cannot receive BT to the primary tumor for various reasons (1, 2). BT requires that a tandem be inserted into the uterus (3) to bring the primary cervical tumor to doses in the range of 80 to 90 Gy, depending on tumor size, with the dose historically recorded at point A (4). Proper applicator placement significantly improves local control and disease-free survival (5). The advantages of 3-dimensional (3D) imaging at the time of BT include assurance of proper applicator placement, more accurate definition and treatment of the tumor volume, and delineation of outlines of the organs at risk (OAR) for volume-based dose calculations.

Surveys in the United States and Europe demonstrate the increasing use of 3D image-based BT, with dose given to the at-risk volume rather than to a prespecified point (6, 7).

Three-dimensional image-based BT results in outstanding local control and a significant reduction in toxicity for patients with cervical cancer (8-10). Over the past decade, research has evaluated real-time 0.5-T MR guidance (11) or postinsertion MR imaging to assist with tumor delineation and tumor dosimetry. MR-based planning (12) has shown favorable results compared with traditional point A plans (13-15). Contouring guidelines have been published by the GEC-ESTRO to aid the physician in contouring on 0.2- to 1.5-T MR in a standardized fashion (16, 17). A report using 3-T MR for both intracavitary and interstitial gynecologic BT shows the feasibility of using high-strength 3-T MR for gynecologic BT (18).

Contouring accurately on the 3D imaging obtained after applicator placement is critical to ensure an optimal treatment plan that adequately doses the tumor and minimizes the dose to the normal tissue structures. However, no consensus atlas has been available in the United States to teach those transitioning from 2-dimensional film-based to 3D image-based BT. Prospective clinical trials in cervical

cancer with MR (12) or CT (9) have shown an advantage in reducing toxicity and increasing local control with image-based BT. An atlas will be useful for future clinical trial and routine practice.

With the increasing availability of CT simulators in radiation oncology departments, CT imaging after BT applicator insertion is easy to implement. MR imaging is feasible but more difficult for most clinics, given the typical location of MR scanners outside of the radiation oncology department. CT/MR-compatible tandem-and-ring and tandem-and-ovoid applicators are widely available, with or without the addition of interstitial needles. CT contouring guidelines were generated in a previous study that compared with MRI; the contours on CT were consistently wider in the lateral direction (19). A CT scan can define a clinical target volume (CTV) around the lateral borders of the cervix and include any obvious parametrial extension seen on the scan (19). Uterosacral ligaments may be clearly visualized on CT when involved with tumor and included in the CTV contours. However, the gross tumor volume (GTV) may not be adequately delineated on CT because of difficulty in identifying the tumor consistently even with intravenous (IV) contrast medium. Furthermore, the superior border of the cervix is not well visualized on CT, but rather the entire tandem length is activated, and the top dwell is optimized to reduce dose to the sigmoid and small bowel. To create a safety margin around the visualized volume, both CT-CTV (19) and MR (17) high risk clinical target volume (HR-CTV) contouring recommendations state that the parametrial tissues should be included when involved at diagnosis.

The aim of this study was to compare the contours achieved by a large group of expert physicians on CT-based and MR-based BT cases representing 3 commonly seen scenarios and to generate consensus contours for CT and MR BT atlases to be available on the Internet for online training of physicians.

## Methods and Materials

Representative physicians from the Radiation Therapy Oncology Group Gynecologic Cancer Working Group and other gynecologic cancer experts received the same 3 cervical cancer cases as Digital Imaging and Communications in Medicine (DICOM) files, which could be uploaded into their institutions' contouring software. Physicians responded to a questionnaire asking whether they used MR, CT, plain radiographs, or a combination of these imaging modalities for the majority of their cases. In each case, a 3-T MRI was performed at diagnosis, an MRI and a CT were performed at the time of BT (within an hour of applicator insertion), and clinical drawings based on the examination at diagnosis and at the time of BT were available for physician review. The T2-weighted images were used for contouring. A CTscan (120 kVP, 200 mA, 30-cm field of view, 1.25-mm slice thickness) at the time of BT was performed without IV contrast medium for all 3 cases. A

previous contouring study generated a normal-tissue atlas, and therefore contouring of the OAR was not required (20).

## Case descriptions

Case 1 was that of a patient with a stage IIB bulky adenocarcinoma of the cervix. The tumor involved both the full length of the uterus and the cervix, with bilateral parametrial involvement. At the time of BT, she had a near-complete response to EBRT. A tandem and ovoid applicator was inserted. To treat the full length of the tumor, a tandem was inserted to the top of the fundus. Because of the presence of tumor, the tandem extended slightly through the tip of the fundus, as was noted on CT, indicating a perforation. Perforations require reinsertion. In general, perforations of the uterus most commonly occur in the posterior myometrium and require immediate repositioning into the uterine canal and antibiotics, followed by treatment. In this case, the tandem was in the uterine canal and required only slight inferior retraction before planning and treatment. The doses were optimized to minimize dose to the adjacent rectum and sigmoid.

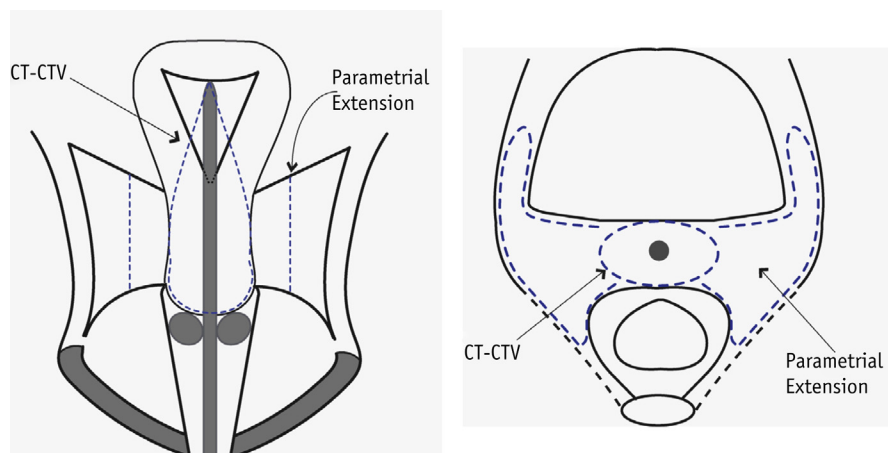
Case 2 was that of a patient with a large stage IIB cervical cancer, with a poor response and difficult anatomy after EBRT. A cavity formed in the region where the cervical tumor had originally filled the vault, and this area was stiff and noncompliant. Given the large amount of residual tumor remaining after EBRT, a decision was made to insert a tandem and ovoids with the addition of needles through the ovoids. An air gap was inevitable between the cervix and the ovoids, even though small ovoids were inserted, given the stiffness of the tissue and the cavitary formation of the upper vault. Therefore, it was thought that needles could provide dose around the cavity and parametria where a gap existed adjacent to the ovoids.

Case 3 was that of a patient with a stage IB2 cervical cancer that was bulky at diagnosis, with a complete response to chemoradiation, treated with a tandem and ring.

## CT-based contouring

The instructions mandated that CT contouring be done first without viewing the MRI scan done at the time of BT. Clinical drawings of the disease at diagnosis, disease extension at the time of BT, and the MRI scan done at diagnosis could be viewed for CT-based contouring. For CT contouring, physicians drew a CTV cervix that included the cervix and any notable parametrial extension at the time of BT (Figure 1), but not the entire parametrial region if not involved, similar to the HR-CTV for MRI. The cervix contours started at the level of the applicator. Modification of the previously published CT-based guidelines did not mandate setting a parametrial edge other than what was perceived on the scan. On the axial CT, borders were set as follows:

1. Inferiorly at the level of the ring, contour tissue inside the central ring. For ovoids, contour tissue to the level of



**Fig. 1.** A generated CT atlas and an MR atlas based on the consensus contours for case 1.

the ovoids. Add vaginal tissue adjacent to the ring if involved at the time of BT. Do not include the ring or voids in the CTV contours.

2. Superiorly, contour superiorly to the level where the uterus indents (internal os); draw the next 1 cm as a pointed shape (cone). The approximate height of cervix should be approximately 3 cm.
3. Laterally, parametrial extension should be included in the CT-CTV (not a separate structure) if it appears “grey/white” on the CT (ie, a density similar to that of the cervix). There is no need to draw the parametrial region if it does not have stranding visible on the CT or if it is not noted in the clinical drawing. IV contrast medium was not mandated. Bowel may have a similar density and be immediately adjacent to the cervix and parametria. Careful evaluation to minimize dose to such bowel while not compromising tumor coverage is recommended.

## MR-based contouring

The MR-defined CTV (MR-CTV), which was identical to the GEC-ESTRO defined HR-CTV (17), included the entire cervix as seen on MRI plus any parametrial or vaginal extension (called “grey zones” by the GEC-ESTRO nomenclature on a low-Tesla MR scan) seen on MRI and on clinical examination at the time of BT (16). The Steering Committee determined that physicians would not be asked to contour the GTV or other structures because the primary focus was on comparison of CT-CTV with MR-CTV. A comparison of historical versus current CT and MR contouring guidelines is summarized in Table 1.

## Analysis

The DICOM files were sent to the Advanced Technology Consortium (ATC) for analysis. The Computerized

Environment for Radiation Research (CERR), an open-source MATLAB (The MathWorks, Natick, MA)-based radiation therapy planning analysis tool (21), was used to analyze the contours and generated the expectation maximization algorithm for simultaneous truth and performance level estimation (STAPLE) contours (22, 23). MIM software (MIM Software, Inc., Cleveland, OH), was used to smooth the edges of any irregularities. For example, a small portion of the contours extended into the applicator and were removed from the CTV volume.

The clinical cases were then analyzed for consistency and clarity of target delineation using STAPLE, with  $\kappa$  statistics as a measure of agreement between participants. The conformity index, defined as the ratio between the common (mean) and encompassing (union) volume of a given pair of contours was calculated for each of the data sets independently for MR and for CT. STAPLE sensitivity and specificity values were generated (24, 25).

Consensus atlases were packaged for review using the FullAccess software package (Radiologica, St. Louis, MO) and approved by the NRG Oncology Radiotherapy Committee before posting on the website ([www.nrgoncology.org](http://www.nrgoncology.org)). The software allows viewing of the CT contour alone or in conjunction with the MR contour.

## Dosimetric comparison

Dosimetric calculations of the D90 and D2cc to the bladder, rectum, and sigmoid were performed using a standard point A plan and CT-optimized and MR-optimized plans. Optimization ensured that the CT or MR-CTV D90 was maximized while reducing doses to the OAR, sigmoid, rectum, and bladder as far as was feasible.

## Results

A total of 23 physicians contoured as part of this protocol. Approximately 50% of physicians reported using MR for



**Table 1** Comparison of historical and current CT and MR contouring guidelines for the CTV in locally advanced cervical cancer

Imaging Modality	Clinical target volume contouring guidelines
MR (2005)	<p>Contour the whole cervix and the presumed extracervical tumor extension at time of brachytherapy (BT). Tumor extension is defined by clinical examination (visualization and palpation) and by MRI findings at time of BT, taking into account tumor spread at diagnosis as indicated on clinical examination and initial MRI for staging.</p> <p>Pathologic residual tissue(s) as defined by palpable indurations and/or residual grey zones in parametria, uterine corpus, vagina or rectum, and/or bladder on MR are included in HR-CTV. No safety margins are added.</p>
CT (2007) (19)	<p>Contour entire cervix as seen on CT</p> <ol style="list-style-type: none"> <li>1. Inferiorly, start contour at superior level of applicator.</li> <li>2. Superiorly, contour to level at which uterine vessels first abut cervical tissue (if intravenous (IV) vessels first abut cervical tissue (if intravenous (IV) contrast medium administered) to point at which volume expands (indicating presence of uterine tissue), or to point at which uterine cavity appears.               <ol style="list-style-type: none"> <li>a. Add 2 slices of contour (with decreasing diameters) around tandem superiorly to cover conical cervical apex.</li> <li>b. Measure height of cervix to ensure adequate coverage (average height approximately 3 cm). Divide parametria into inner half and outer half. Contour parametria throughout the entire height of the cervix.</li> </ol> </li> </ol>
CT (2014, Figure 1)	<ol style="list-style-type: none"> <li>1. Inferiorly at the level of the ring, contour tissue inside the central ring. For ovoids, contour tissue to the level of the ovoids. Add vaginal tissue adjacent to the ring if involved at the time of BT.</li> <li>2. Superiorly, contour to the level where the uterus indents (internal os); draw the next 1 cm as a pointed shape (cone). The approximate dimension (height) of cervix should be 3 cm.</li> <li>4. Laterally, parametrial extension should be included in the CT-CTV (and not a separate structure) if it appears “grey/white” on the CT (ie, a similar density to the cervix). There is no need to draw the parametrial region if it does not have stranding visible on the CT or it is not noted in the clinical drawing. IV contrast medium is not mandated. Do not include bowel directly adjacent to the cervix that may be difficult to distinguish.</li> <li>5. Take into account tumor present on clinical examination and MRI findings at time of BT if available. Disease extension on clinical exam and MRI at the time of diagnosis should be contoured in a low-dose region (intermediate risk [IR]-CTV).</li> <li>6. Pathologic residual tissue(s) identified in the uterus, vagina, rectum, and/or bladder are included in the CT-CTV.</li> </ol>

Abbreviations: CT = computed tomography; CTV = clinical target volume; MR = magnetic resonance; MRI = magnetic resonance imaging; HR-CTV = high risk clinical target volume.

BT contouring routinely; 90% used CT for BT planning either in addition to or instead of MR routinely. The mean, minimum, and maximum tumor volumes for each of the 3 cases on CT and MR are listed in Table 2. The mean tumor volume was smaller on MR than on CT for all 3 cases ( $P < .001$ ). Sensitivity and specificity were similar between

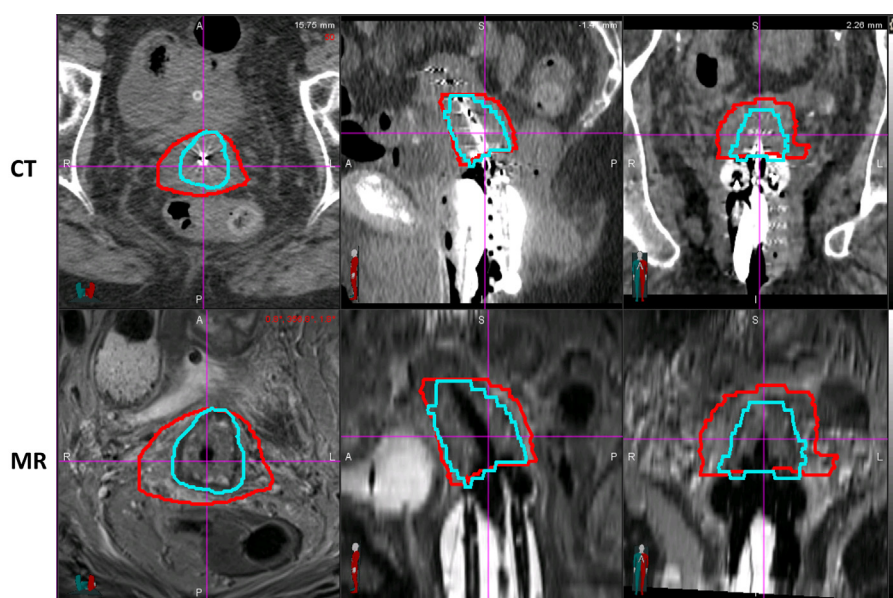
CT and MR, indicating very little apparent difference in contours. The  $\kappa$  estimates showed substantial agreement among physicians' contours and were significantly higher for CT compared to MR ( $P = .048$ ), with a mean value on CT of 0.69 versus 0.66 on MR. The conformity index was significantly higher for CT than for MR ( $P = .048$ ),

**Table 2** Results from contouring 3 cases on CT- and MR-based brachytherapy by physician experts

Structure measure	Case 1 CT	Case 1 MR	Case 2 CT	Case 2 MR	Case 3 CT	Case 3 MR
Sensitivity	72%	73%	68%	72%	75%	66%
Specificity	98%	98%	99.8%	98.5%	98%	99.6%
Vol mean/min/max* (SD)	32.9/13.5/49.5 (10.3)	16.2/5.7/28.4 (6.3)	55.16/19.9/96.3 (16.1)	39.77/16.14/63.12 (11.9)	59.36/32.0/95.6 (15.45)	44.54/9.9/81.98 (15.5)
STAPLE/intersection/union vol*	38.2/9.06/75.2	17.50/4.4/42.3	77.63/10.8/116.1	45.21/7.4/107.7	69.20/13.74/123.85	59.68/0.84/106.7
$\kappa$	0.65	0.64	0.71	0.67	0.70	0.66
Conformity index	0.44	0.38	0.48	0.37	0.48	0.42

Abbreviations: CT = computed tomography; max = maximum; min = minimum; MR = magnetic resonance; SD = standard deviation; STAPLE = simultaneous truth and performance level estimation; vol = volume.

\* in cubic centimeters.



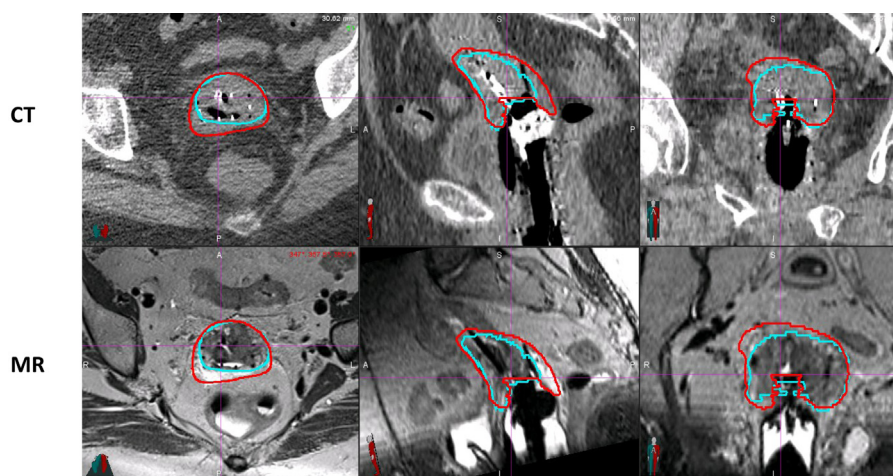
**Fig. 2.** Axial, sagittal, and coronal computed tomographic (CT) and magnetic resonance (MR) images for case 1 showing a tandem and ovoid applicator with consensus contours for MR (light blue) and for CT (red).

indicating a higher level of agreement on CT. Dice coefficients of the 95% consensus volumes comparing CT with MR were 57% for case 1, 74% for case 2, and 89% for case 3. A CT atlas and an MR atlas were generated based on the consensus contours for case 1 (Fig. 2), case 2 (Fig. 3), and case 3 (Fig. 4). The individual physician contours on CT and MR are shown for case 2 (Fig. 5) and case 3 (Fig. 6). The highest Dice coefficient was found for case 3, which had a smaller initial tumor with no parametrial involvement, and a small amount of residual disease to contour, with clear edges of the cervix visible on CT and MR (Fig. 4). Case 1, the case of a patient with a large tumor at diagnosis with parametrial extension that had a good response to EBRT, had the lowest Dice

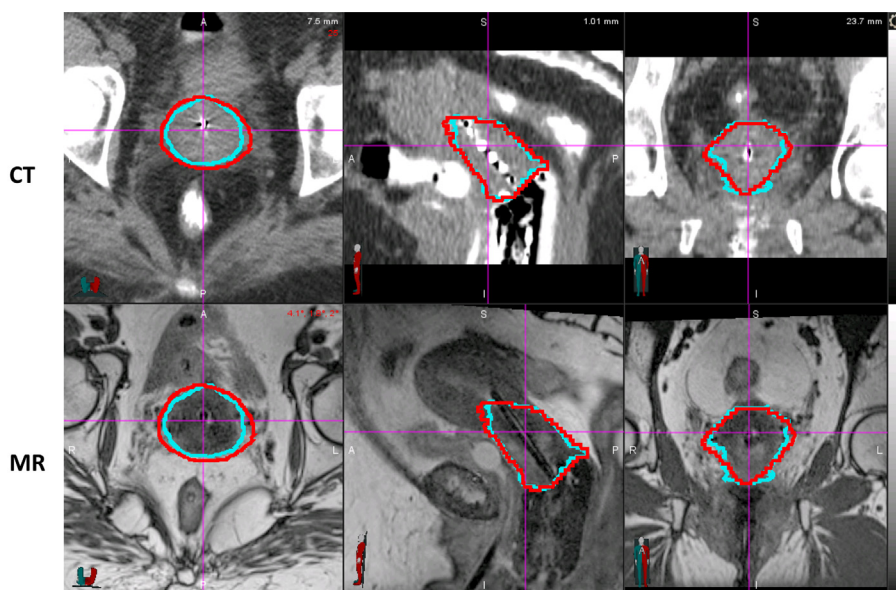
coefficient because of the appearance of parametrial extension on the CT but not on the MR (Fig. 2). The patient in case 2 had a large tumor at diagnosis and large residual disease at the time of BT; the contours for this case on both CT and MR (Fig. 3) were large, indicating a good level of concordance between consensus contours in this clinical scenario.

## Discussion

This study analyzed detailed contouring from a large group of expert gynecologic cancer radiation oncologists using 3 different types of BT applicators to generate CT-based and



**Fig. 3.** Axial, sagittal, and coronal computed tomographic (CT) and magnetic resonance (MR) images for case 2 showing a tandem and ovoid applicator with needles with consensus contours for MR (light blue) and for CT (red).

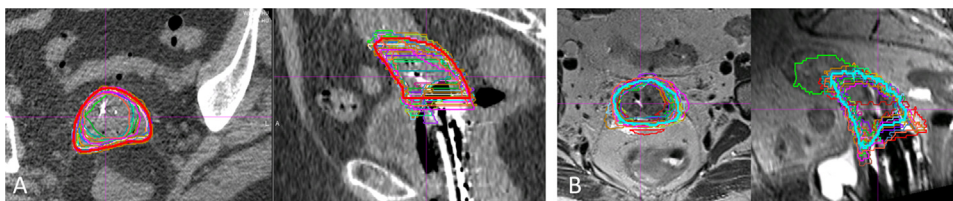


**Fig. 4.** Axial, sagittal, and coronal computed tomographic (CT) and magnetic resonance (MR) images for case 3 showing a tandem and ring applicator with consensus contours for MR (light blue) and for CT (red).

3-T MR-based cervical cancer BT atlases. These atlases can be used in future cervical cancer trials and in clinical practice. In the 3 different clinical scenarios analyzed, the CT-generated CTV contours were more similar among physicians than were the MR-based contours, indicating a higher degree of reliability. Both CT and MR had high sensitivity and specificity. There was greater discordance between CT and MR in cases with parametrial extension and a good response to EBRT than in either cases with no parametrial extension and a small tumor with a good response to EBRT or cases with parametrial extension and a poor response to EBRT. This indicates that the greatest advantage from the addition of MR is in patients with large tumors and a complete response. The comparison between MR and CT validates earlier findings showing that the MR-contoured volume was consistently smaller than the CT-contoured CTV (19) and clarifies that this discrepancy is greatest in patients who have parametrial extension at diagnosis and a good response to treatment. Case 1, the case of a patient with a large tumor at diagnosis with parametrial extension that had a good response to EBRT, had the lowest Dice coefficient because of the appearance of parametrial extension on the CT but not on the MR. CT

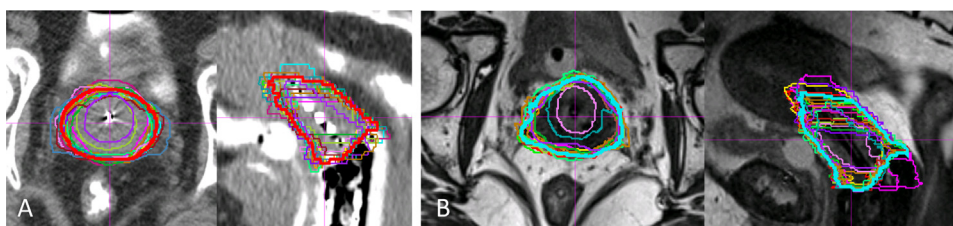
may overestimate volume in patients with parametrial extension at diagnosis whose tumors have a good response to EBRT. Conversely, it is possible that with 3-T MR, parametrial regions that were initially involved may no longer enhance due to scar tissue, particularly in patients who have had a complete clinical response. Whether this lack of enhancement means that micrometastatic residual disease may still be present is not known. The incidence of parametrial recurrence in patients who have had a good response on 3-T MR but have residual parametrial extension on CT must be analyzed by large prospective series. In order to clarify whether the large volume is covered by CT otherwise the smaller volume covered by MR is safer.

Accurate delineation of the tumor and OAR is critical for optimal treatment planning. Owing to the rapid fall-off of dose, imprecise contouring can change dosing to the tumor and to the adjacent normal tissue. In this study, the conformity indices (ratio between common and encompassing volumes) of over 20 gynecologic radiation oncology experts were between 0.37 and 0.48. For each clinical scenario, the conformity index was slightly higher for CT than for MR, likely because of the distinction on CT between involved “grey” region and noninvolvement of the



**Fig. 5.** Individual physician contours shown on axial and sagittal images for case 2 with consensus contour depicted on A) CT (red) and B) MRI (light blue).





**Fig. 6.** Individual physician contours shown on axial and sagittal images for case 3 with consensus contours depicted on A) CT (red) and B) MR (light blue).

parametria. All 3 cases underwent 3-T MRI, which provides excellent soft-tissue resolution.

In a study analyzing the agreement between target volumes, as delineated by 2 observers on 2 different MR image planes, the interobserver and interplanar conformity indices ranged from 0.7 to 0.8 (24), with small volumetric and dosimetric variations (25). The conformity indices in our analysis were lower because of the complexity of the cases and the large number of expert physicians contouring, although all the physicians had had significant experience contouring on both MR-based and CT-based gynecologic brachytherapy implants.

In a report of 6 cervical cancer cases contoured on MR by 10 physicians, results showed that, owing to lower delineation uncertainties in comparison with GTV and intermediate risk (IR)-CTV, the HR-CTV may be considered the most robust volume for dose prescription and optimization (26). In that study, no comparison to CT was made. The dosimetric consequence on MR-CTV was a single fraction mean relative standard deviation of 8% to 10% and a cumulative whole-treatment uncertainty of  $\pm 5$  Gy (27). Similarly, in this study, we chose to only focus on the MR-CTV on MR and the CT-CTV on CT. Institutional series using CT-based cervical cancer brachytherapy confirm high rates of local control (>90%) are achievable with low rates of grade 3 or higher morbidity (28, 29, 30).

The Dice coefficient of the 95% consensus volumes comparing CT with MR was highest (89%) for the case with no parametrial extension and a good response to EBRT, the scenario most often taught in contouring workshops. These cases are therefore the least likely to benefit from the use of MR, and CT may be adequate thought both are better than plain x-ray.

By contrast, the scenario with a large tumor volume at diagnosis that had a near complete response had the lowest Dice coefficient (57%), with significant differences between CT and MR contours in the region of the parametria (Fig. 2). In this scenario, caution must be exerted in that even among expert physicians, when MR is used to contour the CTV, the parametria may appear to have a complete response, whereas on CT, this region appears as scar and is treated to full dose as part of the CTV. Whether MR may have a higher rate of parametrial failure as a consequence of this potential undercontouring, or whether CT may overdose the parametria, OAR, or both in this scenario, is

unknown. To safely treat all patients presenting with this scenario, caution in covering the parametria is recommended at this time. The limitations of intracavitary techniques in the setting of bulky parametrial involvement, however, must be realized, and when appropriate, interstitial techniques may need to be considered.

In the scenario with a large tumor that had an incomplete response, an applicator that incorporates interstitial needles into the ovoids was used. This scenario resulted in a Dice coefficient of 74% comparing CT with MR consensus volumes. The highest discrepancy was again in the parametrial region, but more parametrial tissue was contoured on the MR than in case 1, resulting in the higher Dice coefficient. This reiterates the importance of careful evaluation of the parametria on MR. For centers where only a CT is available, the CT suffices to cover adequate parametrial extension in all scenarios if the contours extend to the most lateral aspect of the parametrial tissue.

Based on these 3 scenarios, parametrial extension may help clarify when patients may benefit from MRI at the time of BT. In cases with no parametrial extension, MR and CT have nearly identical CTV contours. For cases with parametrial extension and a poor response to treatment, MR and CT have similar CTV contours and either imaging modality may be acceptable. Cases with parametrial extension with a complete response benefit the most from the use of MRI in locally advanced cervical cancer brachytherapy. We compared consensus contours generated by a large group of expert gynecologic radiation oncologists using CT and 3-T MR in locally advanced cervical cancer brachytherapy.

MRI-contoured volumes are smaller than CT volumes, particularly in cases with parametrial extension, and depend on the amount of tumor regression. CT has a higher level of agreement that may be due to the more distinct contrast between tissues on the images at the time of BT. A 95% consensus volume was generated for CT and for MR online contouring atlases that are available for instruction at <http://www.nrgoncology.org/Resources/ContouringAtlases.aspx>, based on these results.

## References

1. Montana GS, Hanlon AL, Brickner TJ, et al. Carcinoma of the cervix: Patterns of care studies: Review of 1978, 1983, and 1988-1989 surveys. *Int J Radiat Oncol Biol Phys* 1995;32:1481-1486.



2. Lanciano RM, Martz K, Coia LR, et al. Tumor and treatment factors improving outcome in stage III-B cervix cancer. *Int J Radiat Oncol Biol Phys* 1991;20:95-100.
3. Viswanathan AN, Cormack R, Rawal B, et al. Increasing brachytherapy dose predicts survival for interstitial and tandem-based radiation for stage IIIB cervical cancer. *Int J Gynecol Cancer* 2009;19:1402-1406.
4. Viswanathan AN, Thomadsen B. American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part I: General principles. *Brachytherapy* 2012;11:33-46.
5. Viswanathan AN, Moughan J, Small W Jr., et al. The quality of cervical cancer brachytherapy implantation and the impact on local recurrence and disease-free survival in Radiation Therapy Oncology Group prospective trials 0116 and 0128. *Int J Gynecol Cancer* 2012;22:123-131.
6. Viswanathan AN, Erickson BA. Three-dimensional imaging in gynecologic brachytherapy: A survey of the American Brachytherapy Society. *Int J Radiat Oncol Biol Phys* 2010;76:104-109.
7. Viswanathan AN, Creutzberg CL, Craighead P, et al. International brachytherapy practice patterns: A survey of the Gynecologic Cancer Intergroup (GCIg). *Int J Radiat Oncol Biol Phys* 2012;82:250-255.
8. Charra-Brunaud C, Harter V, Delannes M, et al. Impact of 3D image-based PDR brachytherapy on outcome of patients treated for cervix carcinoma in France: Results of the national STIC prospective study. *Radiother Oncol* 2012;103:305-313.
9. Potter R, Georg P, Dimopoulos JC, et al. Clinical outcome of protocol based image (MRI) guided adaptive brachytherapy combined with 3D conformal radiotherapy with or without chemotherapy in patients with locally advanced cervical cancer. *Radiother Oncol* 2011;100:116-123.
10. Haie-Meder C, Chargari C, Rey A, et al. MRI-based low dose-rate brachytherapy experience in locally advanced cervical cancer patients initially treated by concomitant chemoradiotherapy. *Radiother Oncol* 2010;96:161-165.
11. Viswanathan AN, Szymonifka J, Tempny-Afdhal CM, et al. A prospective trial of real-time magnetic resonance-guided catheter placement in interstitial gynecologic brachytherapy. *Brachytherapy* 2013;12:240-247.
12. Kirisits C, Potter R, Lang S, et al. Dose and volume parameters for MRI-based treatment planning in intracavitary brachytherapy for cervical cancer. *Int J Radiat Oncol Biol Phys* 2005;62:901-911.
13. Lindegaard JC, Tanderup K, Nielsen SK, et al. MRI-guided 3D optimization significantly improves DVH parameters of pulsed-dose-rate brachytherapy in locally advanced cervical cancer. *Int J Radiat Oncol Biol Phys* 2008;71:756-764.
14. Jurgenliemk-Schulz IM, Tersteeg RJ, Roesink JM, et al. MRI-guided treatment-planning optimisation in intracavitary or combined intracavitary/interstitial PDR brachytherapy using tandem ovoid applicators in locally advanced cervical cancer. *Radiother Oncol* 2009;93:322-330.
15. De Brabandere M, Mousa AG, Nulens A, et al. Potential of dose optimisation in MRI-based PDR brachytherapy of cervix carcinoma. *Radiother Oncol* 2008;88:217-226.
16. Potter R, Haie-Meder C, Van Limbergen E, et al. Recommendations from Gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy-3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology. *Radiother Oncol* 2006;78:67-77.
17. Haie-Meder C, Potter R, Van Limbergen E, et al. Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): Concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. *Radiother Oncol* 2005;74:235-245.
18. Kapur T, Egger J, Damato A, et al. 3-T MR-guided brachytherapy for gynecologic malignancies. *Magn Reson Imaging* 2012;30:1279-1290.
19. Viswanathan AN, Dimopoulos J, Kirisits C, et al. Computed tomography versus magnetic resonance imaging-based contouring in cervical cancer brachytherapy: Results of a prospective trial and preliminary guidelines for standardized contours. *Int J Radiat Oncol Biol Phys* 2007;68:491-498.
20. Gay HA, Barthold HJ, O'Meara E, et al. Pelvic normal tissue contouring guidelines for radiation therapy: A Radiation Therapy Oncology Group consensus panel atlas. *Int J Radiat Oncol Biol Phys* 2012;83:e353-e362.
21. Deasy JO, Blanco AI, Clark VH. CERR: A computational environment for radiotherapy research. *Med Phys* 2003;30:979-985.
22. Warfield SK, Zou KH, Wells WM. Simultaneous truth and performance level estimation (STAPLE): An algorithm for the validation of image segmentation. *IEEE Trans Med Imaging* 2004;23:903-921.
23. Allozi R, Li XA, White J, et al. Tools for consensus analysis of experts' contours for radiotherapy structure definitions. *Radiother Oncol* 2010;97:572-578.
24. Petric P, Dimopoulos J, Kirisits C, et al. Inter- and intraobserver variation in HR-CTV contouring: Intercomparison of transverse and paratransverse image orientation in 3D-MRI assisted cervix cancer brachytherapy. *Radiother Oncol* 2008;89:164-171.
25. Dimopoulos JC, De Vos V, Berger D, et al. Inter-observer comparison of target delineation for MRI-assisted cervical cancer brachytherapy: Application of the GYN GEC-ESTRO recommendations. *Radiother Oncol* 2009;91:166-172.
26. Petric P, Hudej R, Rogelj P, et al. Uncertainties of target volume delineation in MRI guided adaptive brachytherapy of cervix cancer: A multi-institutional study. *Radiother Oncol* 2013;107:6-12.
27. Hellebust TP, Tanderup K, Lervag C, et al. Dosimetric impact of interobserver variability in MRI-based delineation for cervical cancer brachytherapy. *Radiother Oncol* 2013;107:13-19.
28. Tan LT, Coles CE, Hart C, et al. Clinical impact of computed tomography-based image-guided brachytherapy for cervix cancer using the tandem-ring applicator: The Addenbrooke's experience. *Clin Oncol (R Coll Radiol)* 2009;21:175-182.
29. Kang HC, Shin KH, Park SY, et al. 3D CT-based high-dose-rate brachytherapy for cervical cancer: Clinical impact on late rectal bleeding and local control. *Radiother Oncol* 2010;97:507-513.
30. Kaplan S, Townamchai K, Newhouse C, Viswanathan AN. Determining dosimetric factors related to local control in CT-based brachytherapy. *Brachytherapy* 2012;11. S111.