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Early outcomes and impact of a hybrid IC/IS applicator for a new MRI-based cervical brachytherapy program

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ABSTRACT

PURPOSE: The purpose of this study was to report early outcomes and assess the learning curve in a new MRI-based cervical brachytherapy program.

METHODS: We accrued 33 patients prospectively, and only patients with ≥3 months' followup ($n = 27$) were assessed for disease control and toxicity. Eras were defined as first half and second half for the intracavitary (IC)-only era ($n = 13$ each), and the intracavitary/interstitial (IC/IS) era was separated by difference in applicator availability ($n = 7$). Dose to 90% of the high-risk clinical target volume (D_{90} HR-CTV) and minimum dose to the maximally irradiated 2 cubic centimeters (D_{2cc}) to organs at risk were used to assess dosimetry. Statistics were performed with *t* tests and Kaplan−Meier method.

RESULTS: Median followup was 14.7 months. Median treatment duration was 50.5 vs. 57 days for patients treated with external beam radiation therapy at our institution vs. an outside institution ($p = 0.03$). One-year local control, noncervical pelvic control, distant metastasis−free rate, and overall survival were 84.0%, 96.0%, 78.5%, and 91.3%, respectively. When comparing the first half and second half eras of IC only, there were no differences in median D_{90} HR-CTV or D_{2cc} of the bladder, rectum, or sigmoid. Comparing the entire IC era to the IC/IS era, median D_{90} HR-CTV trended higher from 88.0 Gy to 92.9 Gy ($p = 0.11$). D_{2cc} rectum decreased from 69.3 Gy to 62.6 Gy ($p = 0.01$), and D_{2cc} bladder trended lower from 87.5 Gy to 83.6 Gy ($p = 0.09$).

CONCLUSIONS: There was no significant difference between the first half and second half eras with IC-only MRI-based brachytherapy. Incorporation of an IC/IS applicator generated the greatest dosimetric improvement. Early results of the MRI-based brachytherapy program are favorable. Published by Elsevier Inc. on behalf of American Brachytherapy Society.

Keywords: MRI-based brachytherapy; Cervical cancer; Learning curve; Intracavitary; Intracavitary/interstitial

Introduction

Locally advanced cervical cancer is standardly treated with external beam radiotherapy (EBRT) with concurrent cisplatin chemotherapy followed by brachytherapy [1−5]. Classic 2D-brachytherapy was prescribed using milligram-Radium hours or point-based systems [6−8]. More recently, 3D-based brachytherapy with CT or MRI has become more commonly used and demonstrates superior local control and decreased toxicity to the classic 2D prescription systems [9−15]. MRI has superior soft-tissue delineation compared to CT allowing for superior delineation of the gross tumor volume and high-risk clinical target volume (HR-CTV) [16, 17]. This improved visualization has resulted in improved local control and decreased toxicity with MRI-based brachytherapy compared to CT-based brachytherapy [11−13,15]. Compared to point A, volume-based prescriptions can prevent overdosing patients with small HR-CTV and underdosing those with large HR-CTV [18].

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Hybrid intracavitary/interstitial (IC/IS) applicators have been developed to incorporate interstitial needles through the intracavitary (IC) vaginal applicator (most commonly rings or ovoids). These applicators afford additional versatility to deliver dose to targets with challenging topography [19, 20].

Our institution initiated an MRI-based cervical brachytherapy program, and our challenges and solutions to start our program have been previously described [21]. As our program evolved, we minimized the imaging protocols, moving to MRI-only planning rather than MRI/CT-based planning [22], and we subsequently added a hybrid IC/IS applicator.

The purpose of this study was to report the early outcomes of our MRI-based cervical brachytherapy program and analyze if a learning curve exists to improve coverage of the HR-CTV and decrease dose to organs at risk (OARs).

Methods and materials

Loyola University Medical Center began an MRI-based cervical brachytherapy program in July 2014 and accrued patients on an institutional review board−approved prospective study (LU206907). All patients were implanted by one of two gynecologic brachytherapists (MH and WS). Methods of our procedures have been previously reported [21]. Briefly, patients were treated with EBRT with concurrent platinum-based chemotherapy, most commonly weekly cisplatin 40 mg/m^2, followed by brachytherapy. Our standard brachytherapy regimen comprised two implants with MRI performed with the applicator in place for each implant, beginning within 1 week after completion of EBRT. Implants were separated by 1−2 weeks with two doses delivered during each implant for a total of four doses. The workflow comprised placement of the applicator in the operating room under general anesthesia with X-ray for intraoperative confirmation of appropriate placement. After recovery, MRI was performed with the applicator *in situ*. We then performed treatment planning and treatment delivery of the first fraction on Day 1. The patient stayed overnight in the hospital. On Day 2, an X-ray was taken to verify whether the applicator position is consistent with the intraoperative X-ray. If there was any concern for applicator motion, then CT was performed on Day 2. After verification of proper applicator position, the second fraction was delivered in the morning of Day 2. The applicator was then removed and the patient was discharged. The process was repeated for the second implant.

Our initial workflow included CT for all patients for applicator reconstruction, but we have since then discontinued CT for IC-only applicators after we found no significant difference in target volume coverage or doses to OARs with applicator reconstruction on the MRI [22]. Our current workflow is to perform CT only when interstitial needles are present to facilitate needle reconstruction. When CT images are acquired, a rigid registration is performed to align the applicator with the MR images.

We initially used an IC Fletcher-Suit-Delclos MRI conditional tandem and ovoid applicator (Varian Medical Systems, Palo Alto, CA). A hybrid IC/IS applicator was obtained in May 2016. The plan was initially created to deliver 7 Gy per fraction to point A using a standard loading pattern. The dose was then optimized to improve coverage of the HR-CTV. The goal dose at the beginning of the program was a 2 Gy equivalent dose to a minimum dose to 90% (D_{90}) HR-CTV of ≥85−87 Gy based on our prior experience with the point A−based system and data from the University of Vienna [23−25]. Availability of interstitial needles with the IC/IS applicator allowed us to increase the goal dose range of D_{90} HR-CTV to 90−95 Gy based on data from retroEMBRACE and the goals of EMBRACE II [26, 27].

We accrued 33 patients who completed definitive EBRT at either our institution or an outside institution. All patients underwent MRI-based cervical brachytherapy at our institution. Twenty-seven patients with ≥3 months followup (including IC/IS patients with ≥3 months followup) were included in the assessment of disease control and toxicity. Common Terminology Criteria for Adverse Events version 4.03 was used to assess toxicity with late toxicity defined as ≥3 months from completion of radiotherapy [28]. All 33 patients were included in the dosimetric analysis. We assessed D_{90} HR-CTV and minimum dose to the maximally irradiated 2 cubic centimeters (D_{2cc}) of the OARs such as bladder, rectum, and sigmoid colon. Eras were defined arbitrarily into first half and second half for the IC-only era (n = 13 each) as has been done in a similar prostate brachytherapy learning curve analysis [29]. The IC/IS era included 7 patients and was separated by the difference in applicator availability, 6 of whom were treated with the hybrid IC/IS applicator (n = 6). Patients were considered for the IC/IS applicator if they had lateral parametrial extension at diagnosis, residual parametrial disease after EBRT, large HR-CTV, and/or irregular tumor topography. The eras with applicable dates of first fraction of brachytherapy are shown in Fig. 1.

Median doses and interquartile ranges are reported where appropriate. Doses between eras, HR-CTV volumes, and overall treatment time analysis were compared with *t* tests. Kaplan−Meier method was used to estimate disease control and survival.

Results

Among 27 patients with ≥3 months followup, the median followup was 14.7 months (range 3.8−26.9 months). Patient characteristics are described in Table 1. Median treatment duration was 50.5 days for patients treated with EBRT at our institution vs. 57.0 days for patients treated with EBRT at an outside institution (p = 0.03). There