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3T multiparametric MRI−guided high-dose-rate combined intracavitary and interstitial adaptive brachytherapy for the treatment of cervical cancer with a novel split-ring applicator

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ABSTRACT

PURPOSE: To evaluate the role of 3T-MRI−guided adaptive high-dose-rate (HDR) combined intracavitary and interstitial brachytherapy for cervical cancer using a novel intracavitary split-ring (ICSR) applicator adapter.

METHODS AND MATERIALS: We retrospectively reviewed all HDR brachytherapy cases from 2013 to 2015 using an ICSR applicator. Initial optimization was performed using 3T multiparametric MRI (mpMRI) series with an applicator in place. The mpMRI series were discretionarily acquired before subsequent fractions for possible target adaptation. When necessary, interstitial needles (ISNs) were inserted through a novel ICSR adapter or freehand. Dosimetric parameters, clinical outcomes, and toxicities were compared between groups.

RESULTS: Seventeen patients were included, with a mean followup of 32 months. An mpMRI series preceded each initial fraction and 52.9% of patients underwent ≥1 additional pretreatment mpMRI. Among these subsequent fractions, the high-risk clinical target volume was reduced in 80% vs. 41% without pretreatment mpMRI. Five patients had ISN placement (seven insertions) to improve extracervical target coverage. Mean D_{90} (Gy) per fraction to the high-risk clinical target volume and intermediate-risk clinical target volume with and without an ISN were 7.51 ± 1.07 vs. 6.14 ± 0.52 (p = 0.028) and 6.35 ± 0.75 vs. 5.21 ± 0.49 (p = 0.007), respectively. Mean fractional D_{2cc} (Gy) for organs at risk was comparable. No Grades 3−4 toxicity was reported. Disease-free survival and local control for the ICSR-ISN and ICSR-alone groups were 29.8 months/80.0% and 31.2 months/83.3%, respectively.

CONCLUSIONS: The mpMRI acquisition with ICSR applicator in place immediately before HDR brachytherapy for cervical cancer guided successful adaptive treatment optimization and delivery. Our initial experience with a novel interstitial adapter for the split-ring applicator demonstrated excellent target coverage without compromising organs at risk, resulting in good local control and disease-free survival.

Keywords: Cervix cancer; MRI-guided; Brachytherapy; Intracavitary; Interstitial; Split-ring

Introduction

Although ultrasound and CT have historically been used in image-guided brachytherapy for locally advanced cervical cancer, MRI has recently been shown to yield more precise visualization of target regions and organs at risk (OARs) (1−4). Both the American and European flagship societies (American Brachytherapy Society, Gynaecological Groupe Européen de Curiethérapie - European SocieTy

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for Radiotherapy & Oncology) have incorporated MRI-based target delineation into their most recent guidelines (5–7). This improved visualization has revealed that often, standard intracavitary applicators are limited in their ability to achieve optimal target coverage (8–10), leading to the development of combined intracavitary/interstitial techniques (11, 12). Reports on the Vienna (tandem and ring) and Utrecht (tandem and ovoid) applicators have been encouraging (13–15).

In addition to the commonly used tandem and ring and tandem and ovoid, another new applicator, the tandem and split ring is used for high-dose-rate (HDR) brachytherapy for treating cervical cancer. The proximal ring configuration has been shown previously to yield point A and OAR doses comparable to ovoids with a slightly smaller total dose volume (16–19), and it appears that the split-ring configuration creates a more natural dose-distribution pattern (20) hypothesized as beneficial for certain tumor configurations and locations. Furthermore, the ability to open the ring components (half rings) symmetrically and asymmetrically provides a high degree of versatility to accommodate anatomical variations in vaginal canal diameter and shape.

To further improve target coverage and avoidance of normal structures, we developed a novel detachable adapter for interstitial needle (ISN) insertion, the "Ellis interstitial cap," compatible with a common split-ring applicator (Eckert & Ziegler BEBIG, Berlin, Germany), producing a custom combined intracavitary/interstitial (IC-IS) device. We have implemented this MRI-compatible set in the delivery of HDR brachytherapy with 3T multiparametric MRI (mpMRI)–guided adaptive treatment planning and present a feasibility report, dosimetric analysis, and initial outcomes using this approach.

Methods and materials

Patients

Between January 2013 and December 2015, 17 patients with International Federation of Gynecology and Obstetrics Stage IB2–IVA (IB2–three, IIB–eight, IIA/IIIA/IIIB–one each, IVA–three) biopsy-proven cervical cancer were treated with curative intent using a split-ring applicator in our radiation oncology department. Independent assessment by both a gynecological oncologist and a radiation oncologist was followed by interdisciplinary institutional tumor board review. Complete staging workup included an examination under anesthesia, CT abdomen/pelvis, pelvic MRI, and occasionally, positron emission tomography (PET)–CT scan.

Treatment

All patients underwent daily CT-based conventional 3D-conformal whole-pelvic external beam radiation therapy (EBRT) via a four-field technique on a linear accelerator to a dose of 45 Gy in 25 fractions (biologically equivalent doses in 2 Gy fractions, EQD2 = 44.2 $Gy_{\alpha/\beta 10}$), followed by a parametrial and/or nodal boost where indicated, along with 5–-6 weekly cycles of concurrent radiosensitizing cisplatin, delivered weekly at 40 mg/m^2. Brachytherapy began either 1–2 weeks after EBRT (nine cases) or overlapped with the latter portion of EBRT (eight cases). Outpatient HDR brachytherapy was delivered 1–2 times per week for five fractions using the MRI-compatible ICSR applicator and an afterload technique. Patients received five fractions of 6 Gy per fraction (three patients were given 5.5 Gy per fraction), to achieve a total EQD2 of ≥84.3 Gy (reference fractional dose 2 Gy, α/β_{tumor} = 10). Our compositional goal was to deliver a dose of ≥80 Gy to 90% (D_{90}) of the high-risk clinical target volume (HR-CTV) (actual range: 81.4–178.7 Gy), meeting OAR constraints of $bladder_{2cc} \leq 90$ Gy, $rectum_{2cc} \leq 75$ Gy, sigmoid $colon_{2cc} \leq 75$ Gy, and small $bowel_{2cc} \leq 75$ Gy (5, 21, 22), as well as a conservative vaginal wall constraint of ≤120 Gy (α/β_{OAR} = 3) based on previously reported recommendations with deference to the inherent challenge of accurate dosimetry associated with this structure (23, 24).

Applicator

The split-ring applicator set is a titanium MRI–compatible dual closed/split-ring system with four possible diameter distances deployed symmetrically or asymmetrically. Ring angles of 30°, 45°, and 60° can be configured with differing intrauterine tube lengths for further customization (Fig. 1a). It is our practice to separate the split rings laterally to the maximal distance from midline that the patient can reasonably tolerate, which limits the risk of either lateral or proximal/distal displacement of the applicator. The custom-modified interstitial caps, individual polyresin adapters, are independently affixed to the anterolateral surface of each of the bilateral rings (Fig. 1b). Each adapter contains 10 equally spaced holes in an inner/outer ring configuration through which ISNs can be reproducibly inserted (Fig. 1c). Easy removal of the Ellis caps from the applicator allows for proper sterilization.

Imaging/treatment planning

All patients underwent a diagnostic pelvic 3T-mpMRI (Philips PET/MRI). Acquired sequences were as follows: axial, sagittal, and coronal haste; axial and sagittal T2 Fast Spin Echo with and without fat saturation; Diffusion Weighted Imaging; pre- and post-gadolinium (14-mL MultiHance) dynamic axial T1 gradient echo (Volumetric Interpolated Breath Hold Examination); and delayed postgadolinium sagittal and coronal haste. Four patients received skull vertex to midthigh PET imaging as well.

The gross tumor volume (GTV) was defined as gross disease on multimodality imaging and physical