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Point A vs. HR-CTV D_{90} in MRI-based cervical brachytherapy of small and large lesions

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ABSTRACT

PURPOSE: To evaluate the dosimetric benefits of MRI-based brachytherapy in small and large high-risk clinical target volume (HR-CTV) in cervical cancer.

METHODS AND MATERIALS: Twenty-eight fractions obtained from sixteen cervical cancer patients treated with MRI-based high-dose-rate brachytherapy with standard tandem and ovoid applicators were used; original fractions were optimized to HR-CTV D_{90}. Fractions were separated based on the median volume into small and large (HR-CTV <25 cm^3 or >25 cm^3) lesion groups. Retrospective plans prescribed to Point A were created for each fraction. $D_{0.1\ cc}$, $D_{2\ cc}$, and International Commission of Radiation Unit and Measurements (ICRU) points were used to compare Point A vs. HR-CTV D_{90} plans for bladder, rectum, and sigmoid.

RESULTS: In the small lesion group, Point A plans vs. HR-CTV D_{90} plans had significantly higher $D_{0.1\ cc}$, $D_{2\ cc}$, and ICRU points for bladder, rectum, and sigmoid ($p < 0.05$). In the large lesion group, there was no significant difference between Point A and HR-CTV D_{90} plans for $D_{0.1\ cc}$, $D_{2\ cc}$, and ICRU points to the organs at risk (OARs).

CONCLUSIONS: The dosimetric advantages to OARs offered by MRI-based brachytherapy with prescription to HR-CTV D_{90} compared to Point A is most distinct for patients with smaller HR-CTV (<25 cm^3). This study demonstrates sufficient tumor coverage with lower doses to OARs in HR-CTV D_{90} vs. Point A plans in the small lesion group. These improvements were not seen in the large lesion group, indicating a lesser dosimetric advantage of HR-CTV D_{90} compared to Point A planning when the cervical lesion is >25 cm^3. Incorporation of interstitial needles for patients with larger HR-CTV is likely the best method to decrease dose to OARs and improve tumor coverage.

Keywords: MRI-based brachytherapy; Cervical cancer; Point A; HR-CTV D_{90}; Tumor size

Introduction

A combination of concurrent chemotherapy and external beam radiation therapy (EBRT) with brachytherapy is standard of care in the treatment of advanced stages of cervical cancer (1–4). Brachytherapy represents an essential component of definitive radiation therapy for cervical cancer that has been shown to improve overall survival (5). In the past several years, cervical brachytherapy has evolved to integrate three dimensional–based treatment planning with improved local control and decreased toxicity compared to two-dimensional planning (6).

CT scans have frequently been used for treatment planning due to their cost-effectiveness, ease of access, and ability to differentiate organs at risk (OARs). However, CT images are limited by poor soft tissue contrast and reduced ability to differentiate neoplastic tissue from normal soft tissue. This limits the ability to individualize dose distribution to patient tumor volume.

Incorporating MRI into the radiotherapy planning process provides improved soft tissue contrast relative to CT imaging data, allowing for higher confidence in delineation of target volumes and OARs (7). Multiple studies have shown the imaging and dosimetric advantages of using MRI guidance in brachytherapy planning (8–12). MRI-based brachytherapy for gynecologic cancers has

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shifted the paradigm of radiation prescription planning from a more traditional point-based approach to one based on optimization of dose delivered to a target volume (7).

Recommendations from the Groupe Européen de Curiethérapie and the European Society for Radiotherapy & Oncology (GEC-ESTRO) working group introduced new target volumes to receive prescribed doses, such as high-risk clinical target volume (HR-CTV), intermediate-risk clinical target volume, and gross tumor volume (13). Studies have shown that shifting from a point-based to a volume-based radiation prescription in MRI-based brachytherapy allows for dose reduction to OARs while maintaining therapeutic dose delivered to target volume (14). These efforts are being applied as an American Brachytherapy Society survey showed that MRI-based cervical brachytherapy and volume-based prescriptions are increasing in the United States (15).

In this study, we investigate differences in MRI-based brachytherapy treatment planning for small and large HR-CTV when optimized to D_{90} (the minimum dose covering 90% of the volume) vs. Point A. Small HR-CTV may be overcovered and large HR-CTV may be undercovered if prescribing to Point A compared to HR-CTV D_{90}. We aim to quantify these differences to OARs for small and large HR-CTV. We compare tumor coverage and OAR dosage parameters in plans prescribed to Point A vs. plans optimized to HR-CTV D_{90} for patients with either small or large tumors at time of MRI-based brachytherapy.

Methods and materials

In July 2014, we began an MRI-based brachytherapy program for cervical cancer at Loyola University Medical Center and enrolled patients on a prospective IRB approved study. This study reports on the first 16 histologically confirmed cervical cancer patients treated with MRI-based brachytherapy and volume-based prescriptions. Patients had varying stages of cervical cancer, ranging from Stage IB2 to IVB. All patients received EBRT to the whole pelvis ± paraaortic lymph node chain with a prescription dose of 45−50.4 Gy in 25−28 fractions. Our usual brachytherapy regimen is to perform two implants with two fractions delivered per implant (total four fractions) and MRI with the applicator in place at each implant. Brachytherapy planning process starts at 7 Gy per fraction to point A, and then, dose is optimized to maximize coverage of the HR-CTV and minimize dose to OARs according to the GEC-ESTRO guidelines (13). Our treatment goal was to deliver an HR-CTV D_{90} EQD2 (equivalent dose at 2 Gy per fraction) of $\geq$ 87 Gy (16). Brachytherapy doses for larger lesions tended to be lower than for smaller lesions to limit dose to OARs. Most patients received concurrent weekly cisplatin chemotherapy in combination with radiation.

Treatment plans consisted of two implants with two fractions administered per implant per patient for 12 patients. Four patients had one implantation with all fractions delivered. In total, there were 28 implants for use in this project. Treatments for all patients employed an MRI-conditional tandem and ovoid applicator without interstitial needles. With the applicator in place, T2-weighted sequences were obtained in the para-transverse, parasagittal, and paracoronal planes with a 1.5 T MRI.

We retrospectively created alternate plans to deliver the same prescribed dose to Point A by rescaling the plan and adjusting ovoid weighting (max vaginal surface dose) to match the initial plan.

Contours of OARs were delineated according to Radiation Therapy Oncology Group atlas recommendations (17). The outer wall of the bladder, rectum, and sigmoid was contoured to include each organ lumen. In addition to organ delineation, both bladder and rectal International Commission of Radiation Unit and Measurements (ICRU) points were inserted (18). A medical physicist (AD) created each alternate plan, and an attending radiation oncologist (MMH) reviewed each plan to evaluate dose distribution, target volume and OAR delineation, and ICRU point identification.

To determine how size of the HR-CTV affects dose distribution, patients were split into two equally sized groups dividing at the median volume: small volume (<25 cm^3, $N = 14$) and large volume (>25 cm^3, $N = 14$) of the HR-CTV. Dosimetric parameters were obtained using dose-volume histograms generated by the treatment planning software. The dosimetric parameters used to compare groups were HR-CTV D_{90}, D_{100}, and doses to OARs. OAR $D_{0.1\ cc}$ and $D_{2\ cc}$ (minimum dose to maximally irradiated 0.1 cc and 2 cc, respectively) were compared between Point A and HR-CTV plans for both small and large HR-CTV groups. To determine degree of tumor coverage in the Point A plans, the ratio of the HR-CTV D_{90} to the dose delivered to Point A in small vs. large HR-CTV plans was obtained.

For statistical analysis, a Wilcoxon signed rank test was chosen to directly compare differences between HR-CTV D_{90} and Point A dosage parameters in both the small and large HR-CTV groups. For the target coverage ratio between small and large groups, an unpaired t test was used. A value of $p < 0.05$ was set for statistical significance.

Results

The characteristics of the patient population can be found in Table 1. A diagram of the distribution of treatment groups can be found in Fig. 1. The median HR-CTV volume for the entire cohort was 24.6 cm^3. The median HR-CTV volumes were 14.8 cm^3 for the small lesion group and 37.4 cm^3 for the large lesion group.