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Triple-tandem high-dose-rate brachytherapy for early-stage medically inoperable endometrial cancer: Initial report on acute toxicity and dosimetric comparison to stereotactic body radiation therapy

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ABSTRACT

PURPOSE: Stereotactic body radiotherapy (SBRT) may be appealing in medically inoperable endometrial cancer to avoid procedural risks. We performed a dosimetric comparison to triple-tandem, high-dose-rate (HDR) brachytherapy.

METHODS AND MATERIALS: Six consecutive clinical stage I, grade 1−2, medically inoperable endometrial cancer patients were treated with triple-tandem HDR brachytherapy. We report patient factors and acute toxicity. Also, we performed dosimetric comparison to SBRT using both 3D conformal arc (3DArc) and volumetric-modulated arc therapy. D2cc values for normal tissues were calculated and compared to the HDR plans.

RESULTS: Median age was 57 years. Patient comorbidities included morbid obesity, congestive heart failure, diabetes, and pulmonary emboli. In three patients who received prior external beam radiation (EBRT), median EBRT and HDR doses were 46 Gy and 20 Gy, respectively. The median dose with HDR brachytherapy monotherapy was 35 Gy. Acute toxicities during EBRT included gastrointestinal (3/3 with grade 1−2) and genitourinary (3/3 with grade 1−2). Acute toxicities during HDR brachytherapy were gastrointestinal (2/6 total with grade 1−2) and genitourinary (2/6 total with grade 1). The mean D2cc/Gy of prescription dose for rectum, sigmoid, and bladder were 0.58, 0.40, and 0.47 respectively. Overall, doses to normal tissues were higher for SBRT plans as compared to HDR. Also, the R50 (ratio of the 50% prescription isodose volume to the PTV) was lowest with HDR brachytherapy.

CONCLUSIONS: In medically inoperable, clinical stage I endometrial cancer patients with multiple comorbidities, definitive triple-tandem, HDR brachytherapy results in mild acute toxicity. In addition, HDR brachytherapy achieves relatively lower doses to surrounding normal tissues as compared to SBRT. © 2016 Published by Elsevier Inc. on behalf of American Brachytherapy Society.

Keywords: Endometrial cancer; Brachytherapy; SBRT

Introduction

Endometrial cancer is the most common gynecologic malignancy in the United States, with over 52,000 estimated new cases in 2014 (1). Initial surgical management remains the standard treatment for women diagnosed with early-stage endometrial cancer who are suitable for surgery. However, a small percentage of patients are considered medically inoperable due to significant comorbidities. Definitive radiation therapy, typically incorporating brachytherapy, is an alternative to surgery for these patients. For example, intracavitary brachytherapy has been established as a safe and effective treatment modality for medically inoperable patients with reported 5-year disease-specific survival rates of 85%−87% in large, single-institution series (2, 3). However, placement of brachytherapy applicators is not without risk. Although local anesthesia may be feasible in some patients, the procedure often involves general or regional anesthesia as well as a period of immobilization. These factors may expose these high-risk patients to potential procedural related complications (4).

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Conflict of Interest: none.

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A variety of brachytherapy applicators have been used in this setting, including Heyman capsules as well as single-, dual-, and triple-tandem applicators. The optimal applicator choice is not well defined. Early reports using single-tandem applicators highlight concerns regarding adequate clinical target volume coverage (5). Furthermore, recent dosimetric studies suggest triple-tandem applicators provide superior target coverage while sparing organs at risk compared to double- or single-tandem applicators (6).

In this study, we sought to review our institutional experience with triple-tandem HDR brachytherapy for definitive management of medically inoperable endometrial cancer. We report on patient-related and treatment-related factors, as well as acute toxicity. Furthermore, given the desire to avoid invasive procedures in this patient population, we developed example stereotactic body radiation therapy (SBRT) plans using both static-arc and volumetric-modulated arc therapy (VMAT) techniques as a dosimetric comparison.

Methods and materials

Study patients

With institutional review board approval, we identified six patients with clinical stage I, grade 1−2, endometrial cancer treated with definitive high-dose-rate (HDR) brachytherapy at our institution from 2013 to 2014, with or without preceding external beam radiation therapy (EBRT). All patients were deemed medically inoperable due to severe medical comorbidities. Patients were evaluated in conjunction with a gynecology oncology physician and clinically staged according to the 2010 International Federation of Gynecology and Obstetrics classification system. Staging work-up included physical examination, transvaginal ultrasound, computed tomography (CT) scan of the abdomen and pelvis, and/or MRI when available.

In all cases, a triple-tandem applicator was used for brachytherapy delivery (Universal Endometrial Applicator Set, Varian Medical Systems, Inc. Palo Alto, CA). A single applicator insertion was performed in the operating room under general or spinal anesthesia. Applicator placement was performed jointly with gynecology oncology team, including examination under anesthesia, sounding of the uterus, and successive dilation of the cervical OS, followed by insertion of the triple-tandem applicator. Vaginal packing was used to displace vaginal mucosa, bladder, and rectum and to help secure applicator in place. Subsequently, patients were hospitalized on bed rest for approximately 3 days while receiving twice-daily HDR brachytherapy sessions. Subcutaneous heparin and/or sequential compression devices were ordered for deep venous thrombosis prophylaxis. In addition, patient-controlled anesthesia pumps were prescribed for pain control throughout hospitalization.

After applicator placement, a CT scan was obtained in the treatment position and used for treatment planning. Individualized HDR brachytherapy treatment plans were developed for each patient, using Eclipse v11.0 (Varian Medical Systems, Inc) and delivered with an Iridium-192 source using the VariSource iX afterloader (Varian Medical Systems, Inc). The target volume was defined as the entire uterus, cervix and upper 3 cm of the vagina. When available, MRI images (obtained before applicator placement) were fused to planning CT scan to help define gross tumor volume. Isodose lines were manually adjusted to ensure adequate coverage of gross tumor. Dose was prescribed to a uterine point, defined as a point located 2 cm below the center of a line drawn between the tips of the ends of the triple-tandem applicator extending laterally from the tandem by half the maximum uterine width and 0.5 cm depth along the upper 3 cm of vagina. Bladder, rectum, sigmoid colon, and small bowel were defined as organs at risk. The ensuing plan was then used for each treatment fraction. HDR brachytherapy treatments were delivered in 5−6, twice-daily fractions separated by a minimum interval of 6 hours between treatments. For patients who received prior EBRT, the prescription dose was 20 Gy delivered in five fractions. For patients who received brachytherapy alone, the prescription dose was 35 Gy delivered in five fractions (except for one patient with recurrent endometrial cancer previously treated with definitive radiation therapy for whom the prescribed HDR brachytherapy dose was 21 Gy delivered in six fractions).

For patients who also received EBRT, multiple field technique using a high-energy linear accelerator beam (6 MV) was used to deliver a dose of 45−50.4 Gy in 25−28 fractions. Radiation fields included the entire uterus, pelvic lymph nodes to the level of L5/S1, and upper 4 cm of the vagina. Brachytherapy was initiated within 8 weeks after completion of EBRT.

After completion of treatment, patients received regular clinic follow-up including history and physical examinations including pelvic examination every 3 months. Tumor control was defined as cessation of vaginal bleeding. Recurrence of vaginal bleeding or any suspicious findings on physical examination were further evaluated with cervical cytology and/or biopsy. With institutional review board approval, patient charts were reviewed to report patient and treatment factors. Acute toxicity was evaluated per the National Cancer Institute Common Toxicity Criteria version 4.

We used the Pinnacle Treatment Planning System (version 9.2) to develop stereotactic body radiation therapy (SBRT) treatment plans using both 3D conformal arc (3D-Arc) and VMAT techniques as dosimetric comparisons to the HDR brachytherapy plans (Fig. 1). The clinically approved HDR 100% prescription isodose cloud was used as the gross target volume (GTV) then expanded 5 mm isotropically to form the planning target volume (PTV). The planning goal was to cover at least 99% of the GTV and 90% of the PTV with the prescription dose. Plans would be further optimized to reduce doses to critical organs (sigmoid, rectum and bladder) while maintaining target