



Comparison of dosimetric and clinical outcomes between short- and long-channel cylinder applicators for vaginal brachytherapy in intermediate- and high-risk endometrial cancer

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ABSTRACT

PURPOSE: Vaginal brachytherapy (VBT) using a cylinder applicator is a standard treatment of intermediate- and high-risk endometrial cancer. We conducted a retrospective study of the dosimetric and clinical outcomes at our institution with 2 single-channel applicators in patients receiving VBT. **METHODS AND MATERIALS:** One hundred thirty-six patients with endometrial cancer treated from 2006 to 2016 receiving VBT after definitive surgery were evaluated. Two cylinders were used with the distal dwell position 7.1–12.8 mm from the apex varying by diameter (short channel), and 3.2 mm from the apex (long channel). We prescribed 18–26 Gy in 3–4 fractions at 0.5 cm depth. Measurements of the distance from the apex to the prescription isodose line were taken from CT imaging. Student's *t* test and the Wilcoxon rank-sum test were used with corrections for multiple comparisons.

RESULTS: Patients had International Federation of Gynecology and Obstetrics 2009 Stage I-II disease (70 Stage IA, 58 Stage IB, 9 Stage II). Mean cylinder apex dose was 95.2% and 154.7% of prescription ($p < 0.001$), and mean distance from apex to the prescription isodose line was 0.54 mm and 3.5 mm ($p < 0.001$) for the short- and long-channel cylinders, respectively. There were no significant differences in any toxicity between cylinders. Four patients (2.9%) had vaginal recurrence, all of whom were treated with the short-channel cylinder. Cylinder type was not associated with vaginal recurrence ($p = 0.27$).

CONCLUSIONS: A cylinder applicator with a distal dwell position closer to the apex results in higher doses to the vaginal cuff and increased D_{2cc} to the bladder. All four recurrences were in the short-channel cylinder. Additional investigation into applicator design and impact on patient outcomes in larger cohorts with sufficient followup is warranted. © 2018 Published by Elsevier Inc. on behalf of American Brachytherapy Society.

Keywords:

Vaginal; Brachytherapy; Cylinder; Endometrial; Cancer

Introduction

In 2018, approximately 63,000 patients will be diagnosed with endometrial cancer in the United States (1). The majority of these cases will be early-stage disease. Early-stage patients with high-risk features such as high grade, increased depth of myometrial invasion, lymphovascular space invasion, advanced age, and increased tumor size may be recommended to undergo adjuvant radiation therapy to decrease the risk of locoregional recurrence (2–4). The first Post-Operative Radiation Therapy in Endometrial Cancer study and the Gynecologic Oncology Group 99 study demonstrated decreased locoregional recurrence in early-stage

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patients with adjuvant external beam radiation therapy (EBRT) compared with observation. These studies also identified a high-intermediate-risk group of patients most likely to benefit from adjuvant therapy (2, 3).

In high-intermediate-risk patients, second Post-Operative Radiation Therapy in Endometrial Cancer demonstrated that vaginal brachytherapy (VBT) had a non-inferior rate of vaginal recurrence compared with EBRT but with a more favorable toxicity profile (5). VBT is now a routine option for adjuvant treatment of early-stage, intermediate-risk, and high-intermediate-risk endometrial cancer (2, 3, 5). Five-year recurrence-free survival rates for early stage patients receiving adjuvant radiation therapy are estimated at 95% or greater (2, 3, 5). Despite the high cure rate in this patient population, patients who do recur require more aggressive salvage therapy, have significant rates of salvage therapy failure, and increased risk of treatment-related toxicity (6–12).

3-D image-guided VBT using a single-channel cylinder applicator has become a standard option for early-stage endometrial cancer. A number of vaginal cylinders are now available to administer VBT with variations in their design, leading to different dosimetric profiles to the vaginal cuff and surrounding organs at risk (OAR). These design variations often include different distances between the distal source position and cylinder apex. For single-channel cylinders, small variations in the apical source position will affect the dose to tissue nearest to the apex due to the inherent anisotropy of the high dose rate source. Despite this, reports of comparisons different cylinder applicators are scarce.

We aimed to investigate if different cylinder designs may result in clinically or dosimetrically significant differences in outcomes, even if these differences are small. We report a retrospective study of the dosimetric and clinical outcomes at our institution with two such applicators in patients with early-stage endometrial cancer receiving adjuvant VBT without EBRT.

Materials and methods

After approval from our institutional review board, we reviewed the records of 199 patients treated with VBT as adjuvant therapy after definitive surgery at Loyola University Medical Center from 2006 to 2016. Patients receiving EBRT before their VBT were excluded. We identified 136 patients that met these criteria. We collected information including patient demographics, disease characteristics, and treatment information. All patients diagnosed before 2009 were converted to the International Federation of Gynecology and Obstetrics 2009 staging system (13).

Briefly, our treatment process involves performing a speculum exam to ensure that the vaginal cuff is adequately healed after surgery. The largest diameter vaginal cylinder that the patient's anatomy can comfortably accommodate is placed. An anterior radiograph with a dummy wire in the source tube of the cylinder is taken, and applicator

positioning is verified by CT at the first fraction to ensure that the cylinder was advanced to abut the vaginal cuff. CT is also used to evaluate doses to OAR. The cylinder position is verified on subsequent fractions based on anterior radiograph comparison with the first fraction. Two types of single-channel cylinders were used in our series: a cylinder with the most cephalad dwell position 7.1–12.8 mm from the apex varying by cylinder diameter (short-channel cylinder, Varian Medical Systems GM11004140), and a cylinder with the most distal dwell position fixed within 3.2 mm of the apex (long-channel cylinder, Varian Medical Systems GM11004160). The rectum and bladder were delineated on CT, and the D_{2cc} to these OAR was calculated. Plans were generated by manual optimization of dwell times, which were optimized for delivery of a uniform dose around the cylinder throughout the entire treatment length. We prescribed 18–26 Gy in 3–4 fractions at 0.5 cm depth using a high-dose-rate remote afterloader. Vaginal treatment length ranged from 2 to 6.5 cm.

For the dosimetric analysis, plans for all patients were retrospectively reviewed. Measurements of the apex dose, distance from the apex to the prescription isodose line (IDL), and length of vaginal mucosa treated were performed on the sagittal or coronal center slice of the vaginal cylinder on CT on the plane that best showed a complete cross-section of the cylinder. The apex dose was measured as a point dose at the most superior point of the vaginal cylinder on the center slice (see Fig. 1). If the prescription IDL was located within the vaginal cylinder as a result of anisotropy, the distance from the apex to the prescription IDL was denoted as a negative value.

Minimum dose to the maximally irradiated 0.1, 1, and 2 cc ($D_{0.1cc}$, D_{1cc} , and D_{2cc} , respectively) were collected for both the bladder and rectum from the dose-volume histogram of each plan.

Univariate comparisons between patients treated with the short- and long-channel cylinders were performed using Student's *t* test and the Wilcoxon rank-sum test (Wilcoxon, "Individual comparisons by ranking methods" *Biometrics Bulletin*, 1945), with application of the Bonferroni correction to control the familywise error rate. Toxicities were graded according to Common Terminology Criteria for Adverse Events v4.03 (14). Clinically significant toxicities were considered grade 2 or higher. Toxicities were compared using Pearson's χ^2 test, with Barnard's unconditional test (Barnard, "A new test for 2×2 tables" *Nature*, 1945) used for infrequent toxicities. All statistical calculations were performed in the R open source statistical computing suite (R Foundation for Statistical Computing, Vienna, Austria, Version 3.3.2 2016).

Results

From 2006 to 2016, 136 patients with early-stage endometrial cancer were treated with definitive surgery and adjuvant VBT with a median followup time of 35 months

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