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High-dose-rate interstitial brachytherapy for the treatment of high-volume locally recurrent endometrial carcinoma

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ABSTRACT

PURPOSE: Limited therapeutic options are available for the treatment of locally recurrent endometrial carcinoma. Our objective was to report an institutional experience using interstitial brachytherapy (IBT) to treat significant recurrent endometrial carcinoma, including previously irradiated disease.

METHODS AND MATERIALS: Between December 2004 and September 2012, 40 patients with high-volume locally recurrent endometrial cancer were treated by high-dose-rate IBT (±external beam radiation therapy (EBRT). Sixteen patients had prior radiotherapy: EBRT alone (n = 5), intracavitary brachytherapy alone (n = 3), or EBRT with intracavitary brachytherapy boost (n = 8). Actuarial outcome rates were calculated using the Kaplan−Meier method and compared using the log-rank test.

RESULTS: Median followup interval was 18 months. Median disease-free interval was 61 months. Actuarial local control, progression-free survival (PFS), and overall survival were 74% and 60%, 70% and 51%, and 83% and 72% at 12 and 24 months, respectively. p-Values for local control, progression-free survival, and overall survival between patient who had prior RT (n = 16) to no prior RT (n = 24) were p = 0.38, 0.32, and 0.90, respectively. Acute toxicities include Grade 1−2 pain (5%), genitourinary (7%), gastrointestinal (12%), soft tissue (5%), and dermatologic (12%). Four patients observed late Grade 3−4 toxicities, including rectal bleeding/fistula and soft tissue necrosis.

CONCLUSIONS: High-dose-rate IBT is an effective treatment for locally recurrent endometrial carcinoma with an acceptable toxicity profile. Outcomes are similar between previously irradiated and nonirradiated patients. In women who have received prior radiotherapy and are often considered for palliative treatment, interstitial brachytherapy is a potentially curative option.

Keywords: Endometrial carcinoma; Salvage; High volume; High dose rate; Interstitial brachytherapy

Introduction

Endometrial carcinoma is the most common gynecologic malignancy in North America (1, 2). The standard curative treatment for endometrial carcinoma involves a hysterectomy at the minimum, and depending on the stage and recurrence risk, can include adjuvant radiotherapy (RT) for improved local control (LC) or chemotherapy. Although patients with limited stage disease have a favorable prognosis, local recurrences of 13% for all patients and <5% for early stage have been reported (3). According to the PORTEC-2 study of early Stage I or IIA endometrial carcinoma patients with high-intermediate risk features, reported 5-year vaginal recurrence rates were 1.8% after vaginal brachytherapy(VBT) and 1.6% after external beam radiation therapy (EBRT); and 5-year locoregional relapse rates (vaginal and/or pelvic) were 5.1% after VBT and 2.1% after EBRT. Most local recurrences occur at the vaginal vault, which is commonly within an area of prior radiation (4, 5).

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Salvage treatment options depend on site and size of recurrence and prior treatment(s). Previously, nonirradiated patients can be treated with curative intent brachytherapy and external beam radiotherapy. However, treatment of patients with locally recurrent disease following initial treatment with pelvic irradiation presents a clinical challenge. Normal tissue dose tolerances may restrict the ability to safely deliver radical doses of radiation necessary to eradicate the disease using standard techniques. As a result, such patients often receive a palliative course of radiation.

Surgical salvage typically involves a pelvic exenteration, which confers a significant risk of operative mortality and morbidity in a disease that affects a predominantly older population. Intracavitary or VBT is a common salvage option for treating recurrent endometrial cancer; however, concerns about dose coverage tend to limit its use to only small nonbulky vaginal recurrences. For bulky or extensive recurrences that cannot be adequately treated by VBT alone, interstitial brachytherapy (IBT) offers a potential and flexible solution.

IBT is not only able to offer better dose coverage as compared to intracavitary brachytherapy (ICB), its optimal dose fall-off to spare normal surrounding tissue is advantageous over external beam radiotherapy. Successful treatment of local vaginal recurrence of endometrial cancer and other gynecologic malignancies has previously been reported; however, the vast majority are in patients initially treated by primary surgery alone without RT or in patients salvaged mainly by vaginal vault brachytherapy. Studies on high-dose-rate (HDR) IBT for recurrent uterine cancer rather than a heterogeneous group of gynecologic cancers are few. Especially in the setting of prior pelvic irradiation with IBT used as salvage treatment, outcomes are lacking and not well reported.

Our objective is to report an institutional experience using HDR IBT, either alone or in combination with EBRT to treat significant locally recurrent endometrial carcinoma (which we defined in our study as large volume, paravaginal extension, lower vaginal disease) including women requiring reirradiation.

Methods

Patient population

Between December 2004 and September 2012, 40 patients with locally recurrent endometrial cancer underwent HDR IBT. These patients were identified from a REB-approved institutional database. This database was compiled from both retrospective and prospective data collection of any patient treated with IBT for gynecologic malignancies, as described previously (6). Additional followup data of patients lost to oncologic followup were further abstracted by outside physician correspondence.

Patients had a clinical diagnosis of locally recurrent endometrial carcinoma and were deemed unsuitable for ICB either alone or with EBRT on the basis of size/thickness of disease (>10 mm thick before treatment or size >2 cm) or location (most commonly the periurethral or paravaginal/parametrial region). Locally recurrent disease was diagnosed via pelvic examination and CT or MRI followed by histologic confirmation by biopsy. When suspected, regional or distant metastatic disease was evaluated by CT/MR imaging. Patients with evidence of regional or distant metastatic disease were excluded.

RT consisted of IBT either alone or in combination with EBRT. Patients previously treated by ICB or EBRT or both were categorized in the prior RT group. Prior RT dosages consisted of 4500 cGy in 25 fractions to the pelvis and prior ICB boost consisted of 2100 cGy in 3 fractions alone or 1500 cGy in 3 fractions in combination with EBRT. Salvage RT pelvic dose was 4500 cGy in 25 fractions and was only given in the setting of a previously untreated pelvis.

Brachytherapy technique

Details of IBT procedure, image acquisition, and treatment planning are available in published literature (6). Briefly, catheter implantation was performed using a perineal implant template with a four-channel vaginal cylinder, and placement was based on prior imaging (CT, MR) and clinical examination at time of recurrence and then subsequently. Postimplant image acquisition by CT scan was obtained, and treatment planning and optimization was performed using BrachyVision (Varian Medical Systems Inc., Palo Alto, CA) treatment planning system. Clinical target volume (ascertained from initial clinical examination, diagnostic imaging, and examination under anesthesia), organ at risks (bladder, rectum, sigmoid, and small bowel), and dwell positions were delineated, and the plan was optimized based on dose volume histogram and isodose distribution curves.

IBT dosages were determined based on biologically effective dose calculation and compared to equivalent 2 Gy fractions (EQD2). In the setting of prior irradiation, dose was determined using the following considerations: (1) dose needed to achieve a reasonable chance of controlling disease, (2) time elapsed from prior radiation to the area, (3) previous radiation dose given, that is EBRT alone vs. EBRT and VBT, (4) location, that is vaginal vault and within previously radiated volume vs. lower vagina and out of the previously radiated field.

Median IBT prescription doses was 700 cGy × 3 fractions and ranged from 500 to 750 cGy × 3 fractions with the exception of 2 patients, one treated with 850 cGy in 2 fractions and the other with 550 cGy in 5 fractions. Assuming no repair from prior treatments, median cumulative EQD2 was 71.1 Gy (63−105.8 Gy EQD2); patients treated with prior RT received a median cumulative EQD2 of 74 Gy (63−105.8 Gy), and those without prior RT received an EQD2 of 71.1 Gy (68.3−77.1 Gy).