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Image-guided high-dose-rate intracavitary brachytherapy in the treatment of medically inoperable early-stage endometrioid type endometrial adenocarcinoma

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ABSTRACT

PURPOSE: The purpose of this case series is to describe the treatment and outcomes of a cohort of patients with inoperable early-stage endometrioid endometrial cancer with 3D image-guided high-dose-rate (HDR) intracavitary brachytherapy.

MATERIALS AND METHODS: A review was performed of patients with early-stage endometrial cancer who underwent primary radiation treatment between 2010 and 2016. Staging and treatment planning were performed CT, pelvic ultrasound, and pelvic MRI. Gross tumor volume (GTV) was defined as the MRI or ultrasound demonstrated endometrial stripe width, with the entire uterine corpus, cervix, and proximal vagina representing the clinical target volume (CTV). Dosimetry calculations were performed in each fraction of HDR brachytherapy.

RESULTS: Eight patients received external beam radiation therapy followed by intracavitary HDR brachytherapy. Seven patients underwent intracavitary HDR brachytherapy alone. In all patients, mean cumulative dose to 90% (D_{90}) of GTV was 95.99 Gy in equivalent dose in 2 Gy fractions (EQD_2, $\alpha/\beta = 10$). Mean cumulative D_{90} EQD_2 to CTV was 51.64 Gy. Average follow-up was 29 months. Four patients died from concurrent disease(s) at an average of 2.83 years after completion of treatment. Except for 1 (6.6%) patient who recurred at 9 months following completion of treatment, all patients remained disease-free for the remainder of follow-up.

CONCLUSIONS: In patients who are poor surgical candidates and have early-stage endometrioid type endometrial carcinoma, image-guided HDR intracavitary brachytherapy carries minimal side effects and a high response rate.

Keywords: Endometrioid adenocarcinoma; Intracavitary brachytherapy; Endometrial cancer; Computer assisted dosimetry calculations

Introduction

Endometrial cancer is the most common gynecological cancer and the fourth most common cancer in women in the United States. Approximately 61,000 women with cancer of the uterus will be diagnosed in 2017, and the number of women who die of this cancer is increasing annually (1, 2). The risk of developing endometrial cancer is greatly increased by morbid obesity, and the relative risk of uterine cancer related death in morbidly obese women is 6.25 (3). Obese women are also predisposed to other diseases, such as hypertension or diabetes. A Gynecologic Oncology Group study found a hazard ratio of

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2.77 for mortality from causes other than endometrial cancer in morbidly obese women with the disease (4). Obesity and other comorbidities affect not only risk of developing the disease but in many cases may dictate available treatments.

The standard treatment for endometrial adenocarcinoma includes total hysterectomy, bilateral salpingo-oophorectomy, and complete surgical staging. By nature of the risk factors for endometrial cancer, medical comorbidities may preclude treatment by major surgery, even in the setting of early-stage disease where surgery alone would be curative. In these patients, hormonal or radiotherapy may be offered (5). Hormonal therapy may be successful in populations where not medically contraindicated. The response rate to oral progestins has been reported as 55−78%, whereas recent studies have shown initial response to levonorgestrel intrauterine device to be 85.7% following hysteroscopic resection of visible tumor (6).

In patients with multiple medical comorbidities which preclude surgical therapy, radiotherapy is considered to be the only curative option (7). Historically, whole pelvic radiation, alone or in combination with low-dose-rate intracavitary brachytherapy, was used for treatment. With the advent of iridium-192 high-dose-rate (HDR) brachytherapy, as well as more sophisticated three dimensional CT and MRI, HDR intracavitary brachytherapy dosimetry has become much more precise. This precision allows higher doses to be used for target tissues, with lower doses reaching surrounding structures, such as bladder and bowel (8).

Although intracavitary HDR brachytherapy for endometrial adenocarcinoma has been investigated in large case series in the past (8), fewer studies have investigated the efficacy of image-guided intracavitary brachytherapy (9−12). This retrospective case series reports the experience with the technique at our institution.

Methods and materials

Following institutional Institutional Review Board approval of the study design, cases were selected by review of all image-guided HDR intracavitary brachytherapy given since 2010, when the technique was first used at our institution for endometrial cancer. Inclusion criteria were American Joint Committee on Cancer (AJCC) stage T1a or T1b endometrioid type endometrial cancer, with medical comorbidities precluding surgical management. International Federation of Gynecologic Oncology (FIGO) clinical staging was not used as it does not allow differentiation between depths of myometrial invasion. Exclusion criteria were any evidence of nodal or cervical disease, or histologic types other than endometrioid.

Electronic medical record review of all patients yielded demographic and medical history data, as well as follow-up and outcomes. Imaging and treatment planning were reviewed using Oncentra Brachy (Elekta, Stockholm, Sweden). All treatment planning used CT imaging following placement of HDR applicators (tandem with ring or tandem with ovoids). Prior to 2016, a high-risk clinical target volume was defined by the radiation oncologist as approximately 2 cm myometrial depth from the deepest point of the lesion. All patients received MRI before treatment planning to demonstrate lesion size and depth, ensuring that the high-risk clinical target volume encompassed the entire lesion. However, no specific treatment protocol existed within our institution, and target definition was at the discretion of the radiation oncologist. In 2016, a protocol was initiated where gross tumor volume (GTV) was defined as the width of the visible abnormality as defined by T2-weighted MRI. Clinical target volume was defined as the entire uterine corpus, cervix, and proximal vaginal wall, excluding fibroids. Goal cumulative dose to 90 percent of the tissue volume (D_{90}) in equivalent 2 Gy fractions (EQD_2, $\alpha/\beta = 10$) was 80−90 Gy for GTV and 60 Gy for CTV; however, these goal doses were attenuated as needed based on normal tissue exposure.

The decision to give external beam radiation therapy (EBRT) before brachytherapy was made by the radiation oncologist on the basis of MRI-demonstrated myometrial invasion, indicating increased risk of occult pelvic nodal disease. EBRT was also utilized when it was thought that intracavitary brachytherapy alone would not deliver a sufficient dose to the entire CTV. This occurred most often in the case of a distorted endometrial cavity which would result in a significant dose to normal tissues to attain a therapeutic level in the CTV. EBRT consisted of intensity modulated radiotherapy with daily cone beam CT image guidance in 1.8 Gy fractions.

Before the intracavitary applicator insertion, ultrasound-guided cervical sleeve placement was performed under general anesthesia or monitored anesthesia care by the gynecologic oncology team, and correct placement was confirmed by the radiation oncologist. A CT/MRI compatible single channel intrauterine tandem and two ovoids or a ring were used for all patients except one in whom two uterine tandems were used. Treatment was given twice per week for a total of five fractions in all but 2 patients. Each fraction was given using local analgesia and mild sedation. Before tandem placement, the patients were given lorazepam 1 mg and ibuprofen 600 mg orally, then meperidine intramuscularly in increments of 25 mg (maximum 50 mg). Topical lidocaine (4%) was applied directly to the cervix around the sleeve.

Twelve ounces of oral contrast were given at the time of initiation of tandem placement, allowing visualization of the small bowel by CT following placement. Foley catheter placement allowed instillation of 50 mL contrast into the bladder, and approximately 100 mL contrast was instilled into rectum before CT scan. Following the CT scan for treatment planning, the bladder was drained. At the time of treatment delivery, 50 mL normal saline was instilled into the bladder through the Foley catheter to maintain equal distention. Waiting time from CT scan to HDR delivery was less than 2 hours. CT imaging and treatment planning were performed with each fraction.