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Computed tomography planned interstitial brachytherapy for recurrent gynecologic cancer

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ABSTRACT

PURPOSE: To report outcomes and identify predictors of toxicity in patients undergoing reirradiation with interstitial brachytherapy (ISBT) for recurrent cancers of the female reproductive tract.
METHODS AND MATERIALS: Twenty-one patients received ISBT performed using ^{192}Ir sources (10 low dose rate and 11 high dose rate) at our institution between 2009 and 2013. Demographic, disease specific, treatment, toxicity, and outcome data were collected. Kaplan−Meier and proportional hazard models were used to estimate survival and logistic regression to model toxicity. A least absolute shrinkage and selection operator penalty was used to identify relevant predictors of outcome and toxicity.
RESULTS: Eleven patients had uterine cancer, 7 patients had cervical cancer, and 3 patients had vulvar cancer. One-year actuarial freedom from local−regional failure, progression-free survival (PFS), and overall survival were 71.5%, 66.0%, and 82.2%, respectively. Tumor size was a significant predictor of worse PFS and overall survival (1 cm increase in tumor size = hazard ratio [HR], 1.61; 95% confidence interval [CI]: 1.16, 2.62 for PFS; HR, 2.02; 95% CI: 1.21, 3.38). Grade 3 or higher vaginal, urinary, and rectal toxicity occurred in 28.5%, 9.5%, and 19% of patients, respectively. Urethra $D_{0.1cc}$ predicted for grade 2 or higher urinary toxicity (one equivalent dose in 2 Gy fraction increase = HR, 1.156; 95% CI: 1.001, 1.335).
CONCLUSIONS: Reirradiation with ISBT is both safe and effective. In patients with recurrent cancer, urethra $D_{0.1cc}$ predicts for increased urinary toxicity. Increased tumor size is a negative prognostic factor in patients receiving ISBT for cancer recurrence.

Keywords: Interstitial brachytherapy; Reirradiation; Gynecologic malignancy

Introduction

Isolated pelvic recurrence of gynecologic cancer, although rare, often presents a management challenge. Many patients previously treated with aggressive surgery, radiotherapy, chemotherapy, or combination therapy have limited treatment options at the time of recurrence. Surgical options are often limited to pelvic exenteration or other morbid procedures. Reirradiation with external beam radiotherapy (EBRT) alone rarely offers long-term control of pelvic recurrences, likely secondary to the high risk of complications with curative doses (1−7). Some investigators have examined other techniques including stereotactic body radiotherapy (8, 9) and seed brachytherapy (10). When reirradiation is necessary to offer local control without the morbidity typically associated with more aggressive surgical procedures, interstitial brachytherapy (ISBT) offers a distinct advantage, either as an adjunct to EBRT or as a stand-alone treatment option.

CT planned ISBT has been well described in patients with newly diagnosed gynecologic malignancies (11−16).

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The advantages of CT planned ISBT are perhaps more important in the reirradiation setting. ISBT allows removable radioactive sources to be implanted in close physical proximity to tumor, minimizing normal (and previously irradiated) tissue's exposure to additional radiation. Furthermore, ISBT allows for greater dose conformality and the ability to safely deliver a higher dose to the target volume. CT planning can aid in postimplant assessment when using low dose rate (LDR) techniques; however, when combined with high dose rate (HDR) techniques, a CT-based plan allows for dose shaping by optimizing source dwell times. This can increase the therapeutic advantage, an especially important consideration when treating a patient who has previously received radiotherapy.

Reirradiation experience with ISBT is limited and not well described in the literature. Many series of ISBT include some patients with recurrent disease who have previously received EBRT or brachytherapy intermixed with patients at the first presentation (12, 13,16−22). In addition to the classic series by Nag *et al.* (23) published in 1998, there has been an increasing number of studies examining reirradiation alone with ISBT for patients with recurrent gynecologic cancer (24, 25). For the first time, prospective evidence is available from Spanish investigators examining the role of ISBT in recurrent gynecologic cancer (26). Despite the growing body of literature, investigators have not yet been able to define the optimal dose prescription in the recurrent setting or establish a clear correlation between dose and toxicity.

At our institution, ISBT is a crucial treatment option for patients with isolated central pelvic recurrences of gynecologic cancer. Many of the previously reported series did not include dosimetric data based on postimplantation CT for patients with recurrent disease. In our series, we expand on the available knowledge by presenting a series of patients planned using modern techniques with a focus on toxicity-related endpoints and predictors of outcome.

Methods and materials

Patients

Records were retrospectively reviewed as part of this IRB approved study. Between 2009 and 2013, 21 patients who had recurrent cancer at time of treatment were identified. Clinical characteristics are shown in Table 1. Eighteen patients received prior pelvic radiation. Median age of patients was 60 years (range, 42−81 years). Median Karnofsky Performance Status was 90%. Eleven patients had uterine cancer, 7 patients had cervical cancer, and 3 patients had vulvar cancer. The indication for ISBT was vaginal involvement in 15 patients, vulva involvement in 3 patients, and pelvic sidewall involvement in 3 patients. Tumors were a median of 3.0 cm (range, 1.5−10 cm). Ten patients received pelvic irradiation at the time of recurrence before ISBT (median dose, 45.0 Gy). Eighteen patients had received previous pelvic radiotherapy including 2 patients who had received brachytherapy alone at the initial presentation.

Table 1
Patient characteristics

Characteristics	Number (%)
Age	
<60 years	9 (42.9)
60−70 years	7 (33.3)
>70 years	5 (23.8)
Karnofsky Performance Status	
90−100	14 (66.7)
80−89	6 (28.6)
<80	1 (4.8)
Diagnosis	
Uterus	11 (52.4)
Cervix	7 (33.3)
Vulva	3 (14.3)
Previous treatment	
Pelvic radiotherapy[a]	18 (85.7)
No previous radiotherapy	3 (14.3)
Current treatment	
ISBT alone	11 (52.4)
ISBT and EBRT	10 (47.6)

ISBT = interstitial brachytherapy; EBRT = external beam radiotherapy.
[a] Including brachytherapy alone.

Brachytherapy technique

All ISBT devices were placed with the patient anesthetized in the operating room. Epidural catheters were used for pain control and kept in place for the duration of the ISBT treatment course (27). Patients were placed in the dorsal lithotomy position, and an examination under anesthesia was performed. Gold seeds were placed in the superior, inferior, and lateral aspects of the palpable tumor if not previously performed. Vaginal obturator was inserted to stabilize the template and needle geometry. Brachytherapists used either the Syed-Neblett GYN III template (Best Medical International, Inc., Springfield, VA) or an institutional template to space needles. The number of needles used was based on clinical and radiographic extent of disease (median, 7 needles; range, 3−14). Needles were placed under fluoroscopic guidance without the use of ultrasound or laparoscopy.

From 2009 until 2011, LDR ISBT was performed using an ^{192}Ir source. Starting in 2011, all patients were treated with HDR technique using an ^{192}Ir source. Eleven patients were treated with HDR techniques, and 10 patients were treated with LDR techniques. Treatment planning was performed with the Varian Eclipse (Palo Alto, CA) treatment planning system. For HDR cases, dose was prescribed to a high-risk clinical target volume delineated in accordance with the GEC-ESTRO guidelines (28). After a CT-based plan was constructed, the patient was brought to the brachytherapy vault and treatments were administered in a B.I.D. fashion