

Gynecologic Oncology

# Computed tomography–planned interstitial brachytherapy for locally advanced gynecologic cancer: Outcomes and dosimetric predictors of urinary toxicity

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## ABSTRACT

**PURPOSE:** To identify dosimetric predictors of outcome and toxicity in patients receiving CT-planned interstitial brachytherapy (ISBT) for gynecologic cancers.

**METHODS AND MATERIALS:** Patients who received ISBT between 2009 and 2014 were reviewed. Demographic, disease specific, treatment, and toxicity data were collected. Logistic regression was used to model toxicity. A least absolute shrinkage and selection operator penalty was used to identify relevant predictors. Receiver operating characteristic curves were used to analyze the relation between dosimetric factors and urinary toxicity.

**RESULTS:** Seventy-three patients received ISBT (21 at time of cancer recurrence and 52 at the first presentation). Thirty-six patients had cervical cancer, 16 had vaginal cancer, 13 had uterine cancer, and 8 had vulvar cancer. ISBT was performed using both high-dose-rate and low-dose-rate <sup>192</sup>Ir sources (27 low dose rate and 46 high dose rate). With a median followup of 12 months, Grade 3 vaginal, urinary, and rectal toxicity occurred in 17.8%, 15.1%, and 6.8% of patients, respectively. No patients experienced Grade 4 or 5 toxicity. Dose to 0.1cc of urethra predicted for development of Grade 3 urinary toxicity (area under the curve of 0.81; 95% confidence interval: 0.66, 0.96). A 10% probability of a Grade 3 urinary toxicity associated with a dose of 23.1 equivalent dose in 2 Gy fractions (95% confidence interval: 9.51, 36.27 equivalent dose in 2 Gy fractions).

**CONCLUSIONS:** ISBT is a safe treatment for gynecologic malignancies. The dose to 0.1cc significantly predicts for severe urinary toxicity. Our data suggests that dose to a small urethral volume may be the most significant predictor of urinary toxicity in patients receiving ISBT for gynecologic cancer. © 2016 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

## Keywords:

Gynecologic cancer; Interstitial brachytherapy; Dosimetric predictors of toxicity; Cervical cancer; Vaginal cancer; Endometrial cancer; Vulvar cancer; Brachytherapy

## Introduction

Brachytherapy (BT) is an essential component in the successful treatment of many gynecologic malignancies.

Locally advanced or recurrent gynecologic tumors present several challenges for clinicians. Largely as a result of failure to control the primary tumor, survival remains poor after treatment despite the use of modern surgical techniques, chemotherapy, and radiotherapy. Given the aggressive therapies often used, both acute toxicity and late effects of treatment can be significant. Efforts to replace BT in these patients with external beam radiotherapy have resulted in inferior survival (1). BT delivers a high dose to the primary tumor while providing a sharp dose falloff to nearby normal tissues. Even with the inherent physical advantages of BT,

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traditional intracavitary techniques are sometimes not adequate in patients with locally advanced disease.

Interstitial brachytherapy (ISBT) can improve on some of these limitations by allowing radioactive sources to be implanted in close physical proximity to the tumor, maximizing the therapeutic ratio. The American Brachytherapy Society recommends ISBT for patients with any stage vaginal cancer, gynecologic cancers with significant vaginal involvement, large cervical tumors, or when patient anatomy would result in poor fit of inter-cavitary BT (2, 3).

Although ISBT has traditionally been planned using orthogonal x-rays, CT-planned ISBT, described by Erickson *et al.* (4), offers several distinct advantages. Most importantly, three-dimensional (3D) imaging allows for more precise clinical target definition and delineation of nearby organs at risk (OARs). This prevents loading interstitial needles that were inadvertently placed adjacent to critical organs. Complementing this, high-dose-rate (HDR) techniques can be used in conjunction with 3D planning by varying source dwell times to better optimize the dose distribution (5). Furthermore, clinically available algorithms for heterogeneity calculation are now becoming available which can use CT data to give a more accurate prediction of dose delivery.

Although previous series have demonstrated encouraging clinical outcomes for patients treated using CT-planned ISBT (6–11), few published studies have focused on dosimetric predictors of toxicity (12–14). Establishing predictors of toxicity using dose-volume information is an important step in transitioning from empiric dosing for ISBT to dose selection which optimizes the therapeutic ratio. This has been difficult given the relatively small numbers of patients treated using 3D-planned ISBT.

ISBT is used for cases of locally advanced gynecologic cancer routinely at our institution. Since 2009, we have used 3D planning for all ISBT cases. Both HDR and low-dose-rate (LDR) techniques were used. In this study, we present clinical outcomes for patients treated with modern ISBT techniques using CT planning. Furthermore, we seek to identify the most important predictors of toxicity using dosimetric parameters.

## Methods and materials

### Patients

Records were retrospectively reviewed as part of this institutional review board approved study. Between 2009 and 2014, 73 patients with locally advanced or recurrent gynecologic cancer treated at our institution were identified. Twenty-one patients (29%) were treated at time of disease recurrence, and 52 (71%) were treated at the first presentation. Patients were referred for this specialty procedure from throughout the region, and therefore, all external beam plans were not available in our electronic medical record. The median reported external beam dose from

available documentation was 45.0 Gy. Thirty-six patients had cervical cancer, 16 had vaginal cancer, 13 had uterine cancer, and 8 had vulvar cancer. All 13 uterine cancer cases were treated for salvage after vaginal recurrence. Clinical characteristics of patients are shown in Table 1. Patients were evaluated for standard intracavity BT; however, patients were selected for ISBT for varying reasons. The indication for ISBT was vaginal or vulvar involvement in 40 patients, pelvic sidewall involvement in 19 patients, anatomy not suitable for inter-cavitary BT in 10 patients, and dose-escalation and dose shaping in 4 patients. Median tumor size was 4 cm (range, 1.5–12.5 cm).

### BT technique

At the time of the procedure, patients were anesthetized in the operating room. Epidural analgesia was used for pain control and kept for the duration of the treatment course (15). Examination under anesthesia was performed by the brachytherapist to evaluate disease extent, necessary needle length, and the number of needles needed for implantation. Gold markers were placed at the margins of palpable tumor (or in the cervix if present) for reference on fluoroscopy and CT imaging. Patients were placed in the dorsal lithotomy position, and a vaginal cylinder was inserted into the vagina for template stabilization. The treating physician used either a Syed-Neblett GYN III template (Best Medical International, Inc., Springfield, VA) or a custom institutional template to space needles at least 1 cm apart and 1 cm beyond the boundaries of the gross tumor. Plastic flexible needles or stainless steel needles (Best Medical International, Inc., Springfield, VA) with stylets fully inserted were placed under fluoroscopic guidance (Fig. 1). The number and location of needles was based on the clinical and radiographic location and extent of disease (median 10 needles; range, 3–18). A rectal examination was

Table 1  
Patient characteristics

Characteristics	Number (%)
Age	
<45 years	12 (16.4)
45–59 years	30 (41.0)
60–70 years	14 (19.1)
>70 years	17 (23.2)
Karnofsky Performance Status	
90–100	52 (71.2)
80–89	14 (19.1)
<80	7 (5.4)
Primary site	
Cervix	36 (49.3)
Vaginal	16 (21.9)
Uterine	13 (17.8)
Vulva	8 (10.9)
EBRT	
Pelvic radiotherapy	62 (84.9)
No pelvic radiotherapy	11 (15.0)

EBRT = external beam radiotherapy.

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