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Stereotactic Body Radiation Therapy as an Alternative to Brachytherapy in Vaginal Cancer: A Case Report

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Abstract

Treatment for vaginal cancer not amenable to surgical excision often consists of primary chemoradiation followed by a brachytherapy (BT) boost. Cumulative dose to the high-risk clinical target volume should ideally be at least 80 Gy equivalent dose in 2 Gy fractions. BT is a critical component in the treatment of vaginal cancer, allowing high doses to be delivered to the tumor and low doses to critical structures. However, select patients may have medical comorbidities or anatomical variants that preclude the administration of BT. Here, we present a case in which a patient with vaginal cancer had an anatomical variant of her vaginal introitus at birth that was surgically corrected, which prohibited the introduction of a vaginal cylinder. Therefore, a stereotactic body radiation therapy (SBRT) boost was used as a replacement. The patient was successfully treated with an SBRT boost with no significant radiation-induced toxicity and remains tumor-free at 12 months. This case demonstrates the feasibility of an SBRT boost when BT is not possible and adds to comparable literature in other gynecologic malignancies.

Categories: Obstetrics/Gynecology, Radiation Oncology, Oncology
Keywords: brachytherapy, ebrt, external beam radiation therapy, sbrt, stereotactic body radiation therapy, vaginal carcinoma

Introduction

Vaginal cancer, of which approximately three-quarters are caused by human papillomavirus (HPV), is a relatively rare malignancy with an incidence of 0.2-0.7 per 100,000 women [1], with a median age at diagnosis of 68-75 years. Radiation therapy (RT) is the primary treatment for vaginal cancer, and its application is determined by the International Federation of Gynecology and Obstetrics (FIGO, 2021) stage. Stage I options include brachytherapy (BT) alone for favorable cases (lesion <2 cm or thickness ⩽5 mm) or external beam radiation therapy (EBRT) with BT, with an option for platinum-containing chemotherapy [2]. Stages II-IVA require chemoradiation (CRT) and BT. BT is a critical step and has been shown to increase five-year progression-free survival (PFS) and disease-specific survival (DSS) when compared to EBRT alone [3,4]. This is because BT is able to achieve much sharper dose falloff than EBRT, and therefore is more easily able to deliver curative doses to the tumor while limiting dose to organs at risk (OARs) and thereby toxicity. BT applicators also result in fixed anatomy, which eliminates the need for a planning target margin (PTV) to account for motion.

BT application options for vaginal cancer include interstitial (ISBT) and intracavitary (ICBT) approaches. ICBT is generally appropriate for tumors with ⩽5 mm gross disease thickness and can be performed using single-channel, multichannel, or partially shielded vaginal cylinder applicators. For tumors >5 mm gross disease thickness, ISBT is often preferred to prevent excessive doses to OARs.

While BT remains a preferred step in the treatment of vaginal cancer, some patients may require alternative approaches. Examples include patients with anatomic variants of their vaginal introitus or medical comorbidities that preclude placement of a BT implant [3]. These patients may require treatment with EBRT alone, with one option being delivery of the boost using stereotactic body radiation therapy (SBRT). An advantage of SBRT is the ability to deliver high doses in a conformal manner by achieving sharper dose falloff through increasing hotspots in the tumor, thereby trying to mimic the general dosimetric distribution achieved by BT. There is limited data on the use of SBRT for primary treatment of gynecologic malignancies given how strongly preferred BT is. Data are primarily available for cervical and endometrial cancer, which are far more prevalent than vaginal cancer [5,6]. To our knowledge, prospective data for vaginal cancer SBRT are limited to a single, unpublished trial [7].

In this case presentation, we detail a patient with vaginal cancer who was unable to undergo a BT boost and therefore was treated with SBRT boost.

Case Presentation

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A 75-year-old female presented for care following discovery of a left vaginal sidewall mass near the introitus. Her past medical history included stroke, resulting in hemiparesis of the left side. She also had a history of endometriosis treated with hysterectomy and bilateral salpingo-oophorectomy at age 19. At baseline, she was bedbound with incontinence, requiring care at a skilled nursing facility. The mass was identified by her caretaker due to discharge being noted when changing her diaper. Biopsy was performed and was consistent with HPV-associated verruciform squamous cell carcinoma with focal lymphovascular space invasion. Positron emission tomography/computed tomography (PET/CT) was performed for staging, which revealed mass-like vaginal soft-tissue thickening extending to the vaginal skin surface with a standardized uptake value (SUV) of 22. An MRI with gel was obtained, which showed the tumor was confined to the vagina and measured approximately 3 cm. There was no evidence of lymphadenopathy or distant metastasis, and she was clinically staged as FIGO Stage Ib. She was subsequently referred to radiation oncology for definitive radiation with concurrent weekly cisplatin.

During consultation, the patient was noted to have a very narrow vaginal introitus, and the patient reported being born without a vaginal opening and therefore required one to be created surgically shortly after birth. With the size of the mass before EBRT, it was uncertain if a vaginal cylinder could be passed into the vagina to facilitate ICBT. ISBT was ruled out due to medical comorbidities and performance status. Therefore, the plan was to determine if BT would be feasible upon completion of EBRT.

The patient was simulated for treatment in the frog-leg position without contrast. She was immobilized using a vacuum bag. Due to her hemiparesis and incontinence, neither a full bladder nor an empty rectum could be achieved. EBRT treatment volumes consisted of a clinical target volume (CTV) that included the entire vagina, parametria, and nodal volumes. Nodal volumes included inguinal, obturator, internal iliac, external iliac, and presacral nodes. An isotropic 7 mm PTV was used. Representative contours are shown in Figure *1*. EBRT was prescribed to 4,500 cGy in 25 fx with weekly cisplatin 40 mg/m^2. EBRT was well tolerated with only grade 1 nausea and fatigue.

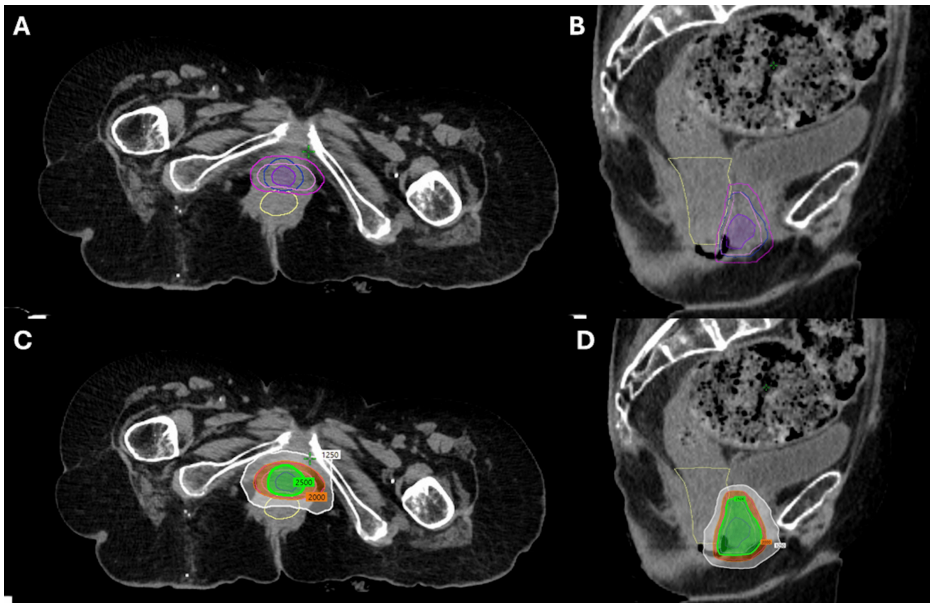


FIGURE 1: Representative contours and dose distribution.

(A) Representative axial slice of contours (purple: GTV, pink: CTV, blue: PTV_2500, magenta: PTV_2000, yellow: rectum). (B) Representative sagittal slice of contours. (C) Representative axial slice of dose distribution. (D) Representative sagittal slice of dose distribution.

GTV = gross tumor volume; CTV = clinical target volume; PTV = planning target volume

Upon completion of EBRT, an attempt was made to perform an ICBT boost. Although there was significant shrinkage of the vaginal tumor, the 1 cm vaginal cylinder was unable to be passed into the vagina, and therefore attempts at BT were aborted. The plan pivoted to an SBRT boost. The patient was simulated similarly to her prior EBRT course; due to the relationship of the high-dose volume to the bladder, it was not thought to be necessary to insert a Foley catheter and balloon to ensure consistent filling. A dose of 2,500 cGy/5 fractions was prescribed to the gross tumor volume (GTV), while 2,000 cGy/5 fractions was prescribed to a CTV consisting of the length of the vagina. An isotropic 5 mm PTV margin was used, with the exception of 4 mm posteriorly to limit rectal dose. Representative contours are shown in Figure *1*. The prescription dose was selected to ensure the cumulative target D90 was comparable to goals that would be used in the setting of BT. Target dose objectives were based on minimum dose received by the most irradiated 2 cc

volume of OAR (D2cc) from the institutional protocols. Cumulative dosimetry is reported in Table *1*, using an α/β of 10 for tumor and 3 for OARs. Representative dose distribution is shown in Figure *1*.

Metric	EBRT	SBRT	EBRT + SBRT
CTV D90	45.22	34.34	79.56
Bladder D2cc	46.67	6.89	53.56
Rectum D2cc	45.43	26.24	71.67
Bowel D2cc	46.26	6.26	52.52

TABLE 1: Radiation course dosimetry in EQD2 (Gy).

EQD2 = equivalent dose in 2 Gy fractions; CTV = clinical target volume; D90 = minimum dose received by 90% of the volume; D2cc = minimum dose received by the most irradiated 2 cc volume of organs at risk; EBRT = external beam radiation therapy; SBRT = stereotactic body radiation therapy

SBRT was successfully delivered with daily cone-beam CT without significant radiation-induced toxicity. PET/CT at the three-month follow-up showed resolution of the vaginal thickening and uptake. No new sites of disease were noted. On clinical examination, the mass had resolved with thickened skin but no nodularity. At the one-year follow-up, there remained no evidence of disease, and the patient reported no adverse effects from treatment.

Discussion

The treatment of malignancy requires an individualized approach that accounts for patient comorbidities and anatomic variants, which may limit the feasibility of conventional radiotherapy techniques. In the present case, such factors precluded the use of BT, thereby necessitating consideration of SBRT as an alternative treatment modality. In cases when BT is preferred but not feasible, SBRT offers the potential to achieve favorable dosimetric coverage in gynecologic malignancies. Prior studies in cervical cancer have demonstrated comparable outcomes between matched BT and SBRT cohorts [8], supporting the potential applicability of SBRT in the management of vaginal cancer as well.

One of the principal concerns regarding the use of SBRT in gynecologic malignancies is setup uncertainty and increased inter- and intrafraction motion resulting from physiologic changes in patient anatomy, including variations in bladder and rectal filling, which requires the use of a PTV and, in some cases, an internal target volume (ITV). In contrast, BT mitigates this limitation by placing the radiation source in direct proximity to the target lesion [9]. Consequently, SBRT may confer a greater risk of radiation exposure to surrounding OARs compared with BT due to requiring a PTV and, in some cases, an ITV. Nevertheless, available evidence suggests that SBRT is generally well tolerated in gynecologic malignancies, with grade 3 toxicities reported infrequently [9-12]. A notable exception is the phase II trial that sought to use SBRT as a boost for cervical cancer, with two-year cumulative grade ⩾3 toxicity of 26.7%, though this trial used a conformality factor of 1.3, causing plans to be more homogeneous than classical SBRT plans, which limits rapid dose falloff [13].

Notably, there remains a paucity of data specifically evaluating SBRT in vaginal cancer, as most published literature has focused on cervical, endometrial, and ovarian malignancies, with only limited representation of vaginal cancer cases (which in part may be due to the relative rarity of primary vaginal cancer). Relevant studies and case reports are summarized in Table *2*. Pooled findings from these reports suggest that patients with vaginal cancer treated with SBRT experienced low rates of grade III toxicity and achieved meaningful disease-free survival, with some patients demonstrating complete clinical response.

Study	Disease site and histology	Number of patients (n)	Total dose of SBRT boost/fractions	DFS	Oncologic outcomes	Reported toxicities
Higginson et al., 2011 [9]	Primary vaginal SCC	2	25 Gy in 5 fractions	5 months (n = 1); 17 months (n = 1)	One patient developed pulmonary metastases at 17 months; both patients DOD	One patient experienced acute grade II radiation cystitis; no grade III or higher toxicities reported
Hadi et al., 2022 [10]	Recurrent vaginal SCC	3 of a cohort of 10	8.0–28.0 Gy in 2–4 fractions (treatment protocol not separately specified for vaginal cancer subgroup)	Not specified for vaginal cancer subgroup	Outcomes not separately specified for vaginal cancer subgroup	No grade III or higher toxicities reported
Kubicek et al., 2013 [12]	Primary vaginal	2	25 Gy in 5 fractions; 22.5 Gy in 5 fractions	DFS not specifically reported	Both patients were alive without evidence of recurrence at the last follow-up, with a median follow-up of 14 months	No grade III or higher toxicities reported
Schonewolf et al., 2022 [14]	Primary vaginal mucosal melanoma	2	30 Gy in 5 fractions	16 months (n = 1); 29 months (n = 1)	Complete response without recurrence; one patient demonstrated an abscopal effect following treatment of the index lesion	Grade I: thigh dermatitis, diarrhea; grade II: perianal dermatitis; no grade III toxicities

TABLE 2: Published reports of SBRT utilized as an alternative to brachytherapy in vaginal malignancies.

SBRT = stereotactic body radiation therapy; DFS = disease-free survival; DOD = dead of disease; SCC = squamous cell carcinoma

For patients in whom SBRT is selected as an alternative to BT, adherence to OAR dose constraints remains a critical consideration. Published guidance regarding SBRT-specific dose constraints for vaginal cancer is limited. As such, treatment planning principles derived from other gynecologic malignancies, including the EMBRACE I and II protocols for cervical cancer, may provide a useful framework [15,16]. The EMBRACE studies standardized OAR delineation and dose constraints for gynecologic BT, identifying the bladder, rectum, rectovaginal point, sigmoid colon, and bowel as critical structures. The dose constraints outlined in these protocols are readily accessible and were adhered to in all studies summarized in Table *2*, as well as in the present case. Importantly, adherence to these constraints was associated with the absence of grade III toxicities, supporting the feasibility and safety of SBRT in carefully selected patients. These findings further underscore the need for prospective studies aimed at defining optimal dosimetric parameters and treatment protocols for vaginal cancer treated with SBRT. Existing data from SBRT for cervical or endometrial cancer demonstrate that this technique should be performed with care, and patients should be appropriately counseled about the potential risk of high-grade toxicity and possible inferior local control relative to BT.

The present case contributes to the limited body of literature describing patients in whom BT was not technically feasible, necessitating the consideration of alternative approaches to achieve therapeutic radiation dosing. Review of the literature reveals relatively few reported cases in this clinical context. The favorable outcome observed in the current patient, together with those summarized in Table *2*, supports continued investigation into the role of SBRT as an alternative to BT in select patients with vaginal cancer. Further research is warranted to better characterize appropriate patient selection, establish standardized dosimetric constraints, and optimize treatment protocols for this population.

Conclusions

While BT remains an integral aspect of the treatment of vaginal cancer, its application may be limited by anatomical variants or medical comorbidities. In such cases, it may be appropriate to consider the use of SBRT as an alternative. Future studies should seek to characterize overall treatment response, efficacy, and toxicity of such an approach.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Kazim Apaydin, Colton Ladbury

Drafting of the manuscript: Kazim Apaydin, Colton Ladbury

Acquisition, analysis, or interpretation of data: Colton Ladbury

Critical review of the manuscript for important intellectual content: Colton Ladbury

Supervision: Colton Ladbury

Disclosures

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