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Image-guided adaptive brachytherapy in primary vaginal cancers: A monocentric experience

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ABSTRACT

PURPOSE: Primary vaginal cancer is a rare disease for which treatment has been modeled based on cervical cancer. We report our experience in the use of image-guided adaptive brachytherapy (IGABT) in this indication.

METHODS AND MATERIALS: Patients treated for vaginal cancer with a combination of external beam radiation therapy and IGABT were identified through electronic search. The Groupe Européen de Curiethérapie—European Society for Radiotherapy and Oncology recommendations for cervical cancer have been extrapolated with the definition of two clinical target volumes (CTVs) corresponding to the residual disease after external beam radiation therapy (CTV_{BT}), assessed from clinical and imaging findings, and the so-called CTV_i, comprising the CTV_{BT} with directional margins and at least the initial disease at diagnosis.

RESULTS: Twenty-seven patients were identified. MRI was used for brachytherapy guidance in 82% of the cases. An interstitial component was used in 59% of the cases. The D_{90} CTV_{BT} and D_{90} CTV_i were 73.1 ± 12.8 Gy and 66.6 ± 6.7 Gy, respectively. After a median followup of 40.1 months, nine recurrences in 8 patients were observed of which four were local. Local relapses occurred within the CTV_{BT}. Three-year local control and disease-free rates were 82% and 65%, respectively. At 2 years, the Grade 2—4 gastrointestinal or urinary morbidity accrual rate was 9%. Twelve patients experienced late sexual morbidity, including three patients with Grade 3 stenosis.

CONCLUSION: IGABT is feasible in vaginal cancer with promising outcomes. Harmonizing the definition of CTVs is required to allow comparisons between experiences and to perform multicenter studies.

Keywords: Vaginal cancer; Concurrent chemoradiotherapy; Image-guided adaptive brachytherapy; Dose-volume histograms

Introduction

Primary vaginal cancer is rare, accounting for 2—3% of all gynecological cancers (1). Similarly to cervical cancer, it is usually human papillomavirus related. Because of its rarity, the management of primary vaginal cancer does not rely on randomized or even prospective studies. Surgery is challenging because of the proximity of the bladder,

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rectum, urethra, and anal canal. Therefore, it is usually restricted to local excision in limited T1 lesions or in case of recurrence. The principles of treatment have been extrapolated from cervical cancer and rely on a combination of external beam radiation therapy (EBRT) ± concurrent chemotherapy and brachytherapy (2). The role of brachytherapy has been recently highlighted in a Surveillance, Epidemiology, and End Results (SEER) database analysis, showing a prolongation of median overall survival (OS) for patients who received brachytherapy in addition to EBRT, from 3.6 to 6.1 years ($p \leq 0.001$) (3). Concomitant chemotherapy has been proposed by analogy to cervical cancer, although no randomized study has shown its benefit. However, a recent National Cancer Data Base study reviewing the data from 13,689 patients suggested that median OS was longer with chemoradiation compared to radiation alone (56.2 vs. 41.2 months, $p < 0.0005$) (4).

During the last 2 decades, the treatment of locally advanced cervical cancer has dramatically evolved with the advent of image-guided adaptive brachytherapy (IGABT) (5). This technique allows the definition of the clinical target volume (CTV) on three-dimensional (3D) images, and dose escalation has become possible, without exceeding dose constraints to organs at risk. In 2005, the Groupe Européen de Curiethérapie–European Society for Radiotherapy and Oncology (GEC-ESTRO) published recommendations on CTVs definitions (6). Since then, multiple publications have reported favorable local control and morbidity rates with regard to classical data and IGABT progressively became a standard (7–14). Again, by analogy to cervical cancer, some teams have started to use IGABT in the treatment of vaginal cancer (15–19). However, so far, this experience remains limited to a low number of patients.

The study's aim was to report our experience in the adaptation for vaginal cancer of the GEC-ESTRO recommendations for cervical cancers.

Methods and materials

Patient selection

Patients treated for vaginal cancer with curative intent and receiving a combination of EBRT and IGABT were eligible for this retrospective study. They were identified from the institutional database through electronic search, submitting keywords such as "vaginal primary," "vaginal cancer," "cancer of the vagina," "brachytherapy," and "pulsed-dose rate" to a search machine. Only patients treated after 2004, date of IGABT implementation, were considered. Inclusions were limited to patients with histologically proven primary vaginal adenocarcinoma or squamous cell carcinoma. Patients with vaginal recurrences from cervical or endometrial cancers were excluded. Tumors were staged according to the 2009 *Fédération Internationale de Gynécologie-Obstétrique* classification. They all had a pelvic MRI and a positron emission tomography-computed tomography in the initial workup. Whenever possible (nonobstructing vaginal tumor), a vaginal impression at diagnosis was performed, and a picture of the impression was taken to guide an accurate placement of the catheters within the vaginal mold applicator. Therefore, the initial extent of the disease was taken into account. No marker seeds were used in that intention.

Treatments

External beam radiation therapy

All patients were treated with pelvic EBRT planned on a 3-mm slice thickness planning CT scan. Conventional fractionation was used in all patients (1.8 Gy per fraction, five times a week) for a total dose of 45 Gy with high-energy photons (18–20 MV), except in case of intensity-modulated radiotherapy (IMRT: 6 MV). The centropelvic CTV included the whole vagina, cervix, uterus (if present), the adnexa, and the parametrial and paravaginal tissues. A systematic margin of at least 10 mm in all directions was added to generate the planning target volume. In patients treated with IMRT, the anteroposterior margin was extended to 12–15 mm according to the repletion of the bladder and rectum on the simulation CT. The nodal CTV comprised the bilateral external and internal iliac, ilio-obturator, presacral, and common iliac lymph nodes areas in all cases and bilateral inguinal areas when the lower third of the vagina was involved. The decision of extending the fields to the paraaortic region was based on the positron emission tomography-computed tomography findings and the results of paraaortic laparoscopic staging when performed (upper-third vaginal lesions). In patients with nodal involvement, boosts were delivered to reach a total dose of 60 Gy. In case of IMRT, a simultaneous integrated boost was used with doses ranging from 2.2 to 2.4 Gy per fraction, according to the distance of the involved nodes from the tumor and the expected contribution of brachytherapy. In case of 3D conformal EBRT, boosts were delivered sequentially after evaluation of the brachytherapy contribution. An isotropic margin of 7 mm was added to the nodal CTV to generate a planning target volume. Concomitant chemoradiation was delivered, except in case of contraindication, mainly severe comorbidity, or refusal. The standard regimen was cisplatin 40 mg/m^2 weekly, five cycles concomitantly with EBRT, then a sixth cycle delivered during IGABT.

Image-guided brachytherapy

Pulsed-dose-rate IGABT systematically followed EBRT. Implants were performed under general anesthesia. A personalized vaginal mold applicator was used in all cases, based on a vaginal impression (Fig. 1). This technique allows adaptation of the number and positions of the sources according to the tumor extents (20, 21). Two to four catheters