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Vaginal dose assessment in image-guided brachytherapy for cervical cancer: Can we really rely on dose-point evaluation?

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ABSTRACT

PURPOSE: Although dose−volume parameters in image-guided brachytherapy have become a standard, the use of posterior−inferior border of the pubic symphysis (PIBS) points has been recently proposed in the reporting of vaginal doses. The aim was to evaluate their pertinence.

METHODS AND MATERIALS: Nineteen patients who received image-guided brachytherapy after concurrent radiochemotherapy were included. Per treatment, CT scans were performed at Days 2 and 3, with reporting of the initial dwell positions and times. Doses delivered to the PIBS points were evaluated on each plan, considering that they were representative of one-third of the treatment. The movements of the applicator according to the PIBS point were analysed.

RESULTS: Mean prescribed doses at PIBS −2, PIBS, PIBS +2 were, respectively, 2.23 ± 1.4, 6.39 ± 6.6, and 31.85 ± 36.06 Gy. Significant differences were observed between the 5 patients with vaginal involvement and the remaining 14 at the level of PIBS +2 and PIBS: +47.60 Gy and +7.46 Gy, respectively ($p = 0.023$ and 0.03). The variations between delivered and prescribed doses at PIBS points were not significant. However, at International commission on radiation units and measurements rectovaginal point, the delivered dose was decreased by 1.43 ± 2.49 Gy from the planned dose ($p = 0.019$). The delivered doses at the four points were strongly correlated with the prescribed doses with R^2 ranging from 0.93 to 0.95. The movements of the applicator in regard of the PIBS point assessed with the Digital Imaging and Communications in Medicine coordinates were insignificant.

CONCLUSION: The doses evaluated at PIBS points are not impacted by intrafractional movements. PIBS and PIBS +2 dose points allow distinguishing the plans of patients with vaginal infiltration. Further studies are needed to correlate these parameters with vaginal morbidity.

Keywords: Image-guided adaptive brachytherapy; Cervical cancer; Vagina; Doses; Posterior−inferior border of the pubic symphysis (PIBS)

Introduction

Image-guided brachytherapy offers the ability to optimize dosimetries with dose escalation to the targets, while mastering accurately the dose delivered to the organs at risk (OARs) with dose−volume histograms. Volumetric assessment and reporting of doses are standard in image-guided brachytherapy for cervical cancer because the Groupe Européen de Curiethérapie−European Society for Radiation Oncology recommended to report doses delivered to OARs in small volumes (0.1 and 2 cm^3) (1, 2). Reports are encouraging with high local control rates and limited morbidity reported (3−7). For the bladder and rectum, recent studies showed clear dose−volume relationships between these parameters and the probability of occurrence of late morbidity (8, 9). It is therefore possible to balance the

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risk of late radiation-induced morbidity with the benefit of achieving local control based on volumetric dosimetric parameters (10, 11).

However, radiotherapy is responsible for late sexual morbidity, an important issue in many cases, whereas reporting the dose delivered to the vagina remains a challenge (12). First, vagina is both a target volume and an OAR. It is at least partly included in the intermediate risk clinical target volume (IR-CTV) and therefore subject to the planning aim of at least 60 Gy. Residual vaginal disease should be included in the high risk CTV (HR-CTV) and therefore treated at the level of 85−90 Gy (1). Second, the vicinity of the vagina to the radioactive sources leads to the delivery of very high doses, whereas part of the organ is subject to low doses with a rapid fall off of the dose. Third, the maximal doses delivered to the vagina are difficult to assess, as the vaginal mucosa is located in an area of high dose gradients. Therefore, uncertainties in the delineation of the vaginal wall or in the reconstruction the catheters lead to large margins of error while calculating the dose distribution. For instance, Berger *et al.* (13) concluded that geometrical shifts of 1 mm lead to variations of the estimated dose of 25% in the vagina.

In addition, vaginal toxicities are poorly reported in the literature, and therefore, there has been no consistently documented dose−response relationship with regards to toxicity. Actually, there are no reliable dose constraints or even consensual dosimetric parameters for the vagina.

Recently, Westerveld *et al.* (14) proposed an innovative strategy for vaginal dose reporting, defining points according to a bony structure. They defined three points according to the posterior−inferior border of the pubic symphysis (PIBS), located at the level of the inferior border of the symphysis, PIBS +2 and PIBS −2, located 2 cm cranially and caudally, respectively. PIBS represents the transition zone between the middle and lower third of the vagina; PIBS +2, the anatomic midvagina and PIBS −2, represents the vaginal introitus. The system can be used both for two-dimensional and three-dimensional brachytherapy planning, as the PIBS is definable on plain radiographs, CT scans, and MRI. The points can be used in external beam radiation therapy (EBRT) and brachytherapy, and therefore, both contributions can be summed. In their original publication, Westerveld *et al.* concluded that PIBS points offer the possibility to distinguish the dose distribution of the three parts of the vagina.

However, it can be argued that reporting doses in points might be incongruous in the three-dimensional era. One of the main advantages of brachytherapy is that the radioactive sources follow the targets throughout the treatment. However, recent studies suggest that OAR movements may influence the doses delivered. For instance, it has been shown that the estimated delivered rectal minimal dose in the maximally exposed 2 cm3 (D_{2cm^3}) has a trend to be higher than the planned D_{2cm^3} in patients treated with pulsed-dose rate brachytherapy (15−17). The vaginal points described by Westerveld *et al.* are fixed, constructed according to bony structures, whereas the implant and the surrounding OARs are moving.

The aims of this study were:

- To report vaginal doses using the PIBS points and to evaluate their ability to discriminate plans in which the vagina was infiltrated.
- To estimate the impact of organ movement and deformation on the estimated delivered dose they receive in regard to the prescribed dose.

Methods and materials

Patients

Nineteen patients were included in a prospective study aiming to evaluate the impact of organ movement during brachytherapy. Details on this study are available in a previous publication (15). Briefly, patients diagnosed with cervical carcinoma, staged IB2 to IVB (limited to paraaortic lymph node metastases) according to Fédération Internationale de Gynécologie Obstétrique, and treated with curative intent were eligible. All patients received 45 Gy pelvic external beam radiotherapy delivered in 25 fractions of 1.8 Gy, with concomitant (chemotherapy, before brachytherapy).

Brachytherapy and imaging procedure

Brachytherapy consisted in a pulsed-dose rate intracavitary MRI-guided adaptive technique, with a personalized vaginal mold containing one intrauterine and two vaginal catheters. Intracavitary brachytherapy applications were performed under general anesthesia in all patients in lithotomy position. The procedure was always preceded by a careful clinical examination to note the extent of residual disease and performed under ultrasound guidance to facilitate the placement of the intrauterine catheter. Full details of this procedure have been described elsewhere (5, 18).

Following the application, an MRI of the pelvis was performed in all patients, with 3-mm slice thickness without gap. Images were transferred to Brachyvision 8.9 platform (Varian Medical Systems, Palo Alto, CA). Treatment planning was done with the objective of delivering at least 60 Gy to 90% of the IR-CTV (D_{90}) and a minimum of 85 Gy to 90% of the HR-CTV in 2-Gy equivalent (EqD2), as the sum of the brachytherapy (BT) and EBRT doses, and applying the linear-quadratic model with an α/β ratio of 10 Gy, and a repair half-time of 1.5 hours for both radiation techniques. Dose constraints to the OARs were 75 Gy EqD2 to the maximally exposed 2 cm^3 (D_{2cm^3}) of the rectum and sigmoid and 85 Gy for the D_{2cm^3} of the bladder (α/β of 3 Gy). No specific constraint was applied to the vagina or the International commission on radiation units and measurement (ICRU) points of the bladder and