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Effect of bladder distension on doses to organs at risk in Pulsed-Dose-Rate 3D image-guided adaptive brachytherapy for locally advanced cervical cancer

Jean Philippe Nesseler[1,*], Claire Charra-Brunaud[1], Julia Salleron[2], Jean François Py[1], Andres Huertas[1], Emilie Meknaci[3], Florent Courrech[3], Didier Peiffert[1], Sophie Renard-Oldrini[1]

[1]*Department of Radiotherapy and Brachytherapy, Institut de Cancérologie de Lorraine, Vandoeuvre-Lès-Nancy, France*
[2]*Department of Biostatistics and Data Management, Institut de Cancérologie de Lorraine, Vandoeuvre-Lès-Nancy, France*
[3]*Department of Radiation Physics, Institut de Cancérologie de Lorraine, Vandoeuvre-Lès-Nancy, France*

ABSTRACT

PURPOSE: To evaluate the impact of bladder distension on doses to organs at risk in patients treated with 3D image-guided adaptive pulsed-dose-rate (PDR) brachytherapy (BT) for locally advanced cervical cancer.

METHODS AND MATERIALS: Twenty-two patients who had previously been treated by external beam radiation therapy (EBRT), underwent BT treatment planning to a pelvic MRI (or a CT scan in case of contraindication) after their bladder was filled with 100 cc of physiological saline (full bladder). This was immediately followed by a CT scan after emptying of the bladder. A fusion of these two examinations was conducted, and the dosimetry was duplicated for the study with an empty bladder. Equieffective doses of 2 Gy per fraction from EBRT and BT of bladder/rectum/sigmoid colon/small bowel were compared.

RESULTS: A full bladder condition was found to be non-inferior in terms of the bladder D2cc (a difference of −0.9 Gy; 97.5% CI [−∞; 2.6]), and it resulted in a reduction in the bladder D0.1cc ($p = 0.038$). Bladder expansion resulted in a significant reduction of maximum doses received by the small bowel, both in terms of the D0.1cc (51.2 Gy vs. 63.4 Gy, $p < 0.001$) and the D2cc (48.5 Gy vs. 53.6 Gy, $p < 0.001$). A negative correlation was seen between the difference in the small bowel D2cc and the body mass index; ($r = -0.55$; $p = 0.008$). No differences were noted in regard to doses to the rectum and sigmoid colon.

CONCLUSIONS: Bladder distension with 100 cc of physiological saline can reduce maximum doses received by the small bowel without the alteration of the doses received by the other organs at risk during a 3D image−guided adaptive PDR BT for locally advanced cervical cancer. However, the maintenance of a predefined bladder volume is difficult to achieve with PDR BT, whereas it could be easily managed before each session in case of high-dose-rate BT.

Keywords: Brachytherapy; Cervical cancer; Organs at risk; Small bowel; Bladder volume

Introduction

The standard treatment for locally advanced cervical cancer (stages IB2 to IVA according to the 2009 FIGO classification) consists of concurrent chemoradiation with weekly cisplatin (1−3), followed by intracavitary brachytherapy (BT) (4). The overall treatment time must be less than 56 days in order not to compromise local control (5, 6).

The additional dose delivered by BT compared with external beam radiation therapy (EBRT) provides a higher rate of local control, thus improving disease-free and overall survival (7, 8).

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Conflict of interest: The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

* Corresponding author. Département de radiothérapie, Institut de Cancérologie de Lorraine, 6 avenue de Bourgogne, 54 519 Vandoeuvre-lès-Nancy, France.

E-mail address: jpnesseler@gmail.com (J.P. Nesseler).

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Pulsed-dose-rate (PDR) BT mimics and has comparable radiobiological benefits as low-dose-rate BT. In addition, it allows for optimization of the dose distribution by modulation of positions and dwell times of the radioactive source. Locally advanced cervical cancers are treated by PDR BT or high-dose-rate (HDR) BT.

Three-dimensional imaging by MRI or CT scan for BT treatment planning has improved local control, and it has reduced grade 3–4 toxicities compared with two-dimensional imaging techniques (9), due to an improvement of the dose-volume distribution and histogram parameters (10, 11).

Uterovaginal BT can cause urinary, digestive, or vaginal late toxicity. In PDR BT, the risk of late complications is related to the total dose and the dose rate to organs that are at risk.

At our institution, PDR uterovaginal BT is performed with a full bladder, thereby moving parts of its anterior wall away from the most irradiated areas, with the potential risk of bringing parts of its posterior wall closer to the maximum dose areas. Maintaining a fixed bladder volume throughout the PDR BT treatment can, however, not be achieved with certainty.

The primary aim of our study was to demonstrate the non-inferiority of BT in a full bladder condition compared with an empty bladder condition in terms of the minimum dose to the maximally irradiated 2 cc (D2cc) of the bladder. The secondary aim was to determine if bladder filling modified the dose distribution to the other organs at risk, that is, the rectum, sigmoid colon, and small bowel. In case there was a difference, we also wanted to assess whether the effect of bladder filling was influenced by the body mass index (BMI), FIGO stage, type of applicator, or clinical target volume (CTV) absolute volumes.

Patients and methods

Patients were prospectively included between September 2015 and August 2016.

All patients with histologically proven stage IB2 to IVa cervical cancer for whom an indication of uterovaginal BT had been recommended by a multidisciplinary tumor board received an information brochure regarding the protocol as well as a consent form.

A prior treatment by pelvic ± para-aortic irradiation was performed, delivering 45 Gy in 25 fractions, with a nodal dose boost to an average of 60 Gy in case of lymphadenopathy. This was in association with concomitant weekly cisplatin chemotherapy.

Patients who were minors, pregnant or lactating, or who had previously undergone pelvic surgery or radiotherapy, as well as patients with a recent joint prosthesis (<3 months) or who otherwise had restricted movement were excluded from the study.

Implantation of the BT applicator was performed in the operating room under general or spinal anesthesia with bladder catheterization. The applicator was either a customized vaginal mold or a Utrecht applicator for combined intracavitary/interstitial BT treatment if there was residual parametrial tumor at the end of the EBRT.

Dosimetric imaging was either by 3D T2-weighted MRI or by a noninjected pelvic CT scan in the case of contraindication to MRI. This first imaging procedure was performed after filling of the bladder with 100 cc of isotonic physiological serum.

A second pelvic imaging by noninjected CT scan was then performed after emptying of the bladder by unclamping of the urinary catheter.

These two studies, with filled and emptied bladders, were then exported to the ONCENTRA (Elekta Brachytherapy Solutions) BT planning system.

Treatment planning was conducted using the imaging results obtained with a full bladder. Indeed, at our institution, PDR BT is performed with a full bladder. Patients are informed before starting the treatment that they can unclamp the urinary catheter, but only after a pulse and without complete emptying of the bladder.

Target volumes (i.e., GTV, high-risk CTV, intermediate-risk CTV) and organs at risk (e.g., the bladder, rectum, and sigmoid colon) were delineated according to the recommendations of GYN GEC-ESTRO (12) and ICRU 89 (13). The small bowel was defined as the peritoneal cavity containing the small bowel and the colon.

The dose prescription was based on the recommendations of GYN GEC-ESTRO (14). The equieffective dose of 2 Gy per fraction (EQD2) from EBRT and BT was calculated by applying the linear quadratic model, using an α/β of 10 Gy for the CTVs ($EQD2_{10}$) and 3 Gy for organs at risk ($EQD2_3$), and a half-time for sublethal damage repair of 1.5 h, assuming that the small volumes studied in BT (0.1 and 2 cc) received 100% of the prescribed EBRT dose.

A dosimetric optimization was performed manually and graphically, for good coverage of the CTVs and/or up to maximum dose to an organ at risk. If parametrial needle positions were activated, they had to deliver a dose that remained below 15% of the total BT dose.

Organs at risk were also delineated on the CT scan study with an empty bladder.

Both studies were then exported to AQUILAB software and automatically fused with a manual correction if necessary. The dosimetry was then duplicated for the study with an empty bladder.

We compared the two modalities of bladder filling according to the D0.1cc and D2cc, that is, the minimum doses to the maximally irradiated 0.1 cc and 2 cc respectively, for each organ at risk.

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