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Parametrial boosting in locally advanced cervical cancer: Combined intracavitary/interstitial brachytherapy vs. intracavitary brachytherapy plus external beam radiotherapy

Sandy Mohamed[1,2,*], Jesper Kallehauge[3], Lars Fokdal[1], Jacob Christian Lindegaard[1], Kari Tanderup[4,5]

[1]*Department of Oncology, Aarhus University Hospital, Aarhus, Denmark*
[2]*Department of Radiation Oncology, National Cancer Institute, Cairo University, Cairo, Egypt*
[3]*Department of Experimental Clinical Oncology, Aarhus University Hospital, Aarhus, Denmark*
[4]*Department of Medical Physics, Aarhus University Hospital, Aarhus, Denmark*
[5]*Institute of Clinical Medicine, Aarhus University, Aarhus, Denmark*

ABSTRACT

PURPOSE: Parametrial boost (PB) with external beam radiotherapy (EBRT) aims to increase the dose in the parametrial regions where the contribution from intracavitary brachytherapy (IC BT) is insufficient. An alternative technique for parametrial boosting is combined intracavitary and interstitial (IC−IS) BT. We compared doses delivered by IC BT plus EBRT PB with doses delivered by IC−IS BT.

METHODS AND MATERIALS: We reviewed 51 consecutive patients with locally advanced cervical cancer with parametrial involvement at diagnosis. At BT, 23 patients had persistent parametrial involvement and were treated with IC−IS BT. For the 23 patients, we simulated a treatment of IC BT combined with EBRT PB and compared it with the delivered IC−IS BT. Equivalent total doses in 2-Gy fractions of the target and organs at risk were evaluated, and the normal tissue volume irradiated to at least 60 Gy (V_{60}).

RESULTS: The mean high-risk clinical target volume D_{90} was comparable ($p = 0.8$) for both techniques. However, with the EBRT PB scenario, 3 patients received high-risk clinical target volume D_{90} of <79 Gy, whereas IC−IS BT resulted in D_{90} of >84 Gy for all patients. Organs at risk D_{2cm^3} were significantly higher by a mean of 4−6 Gy ($p < 0.001$) with EBRT PB. The PB scenario resulted in a significantly higher V_{60} of 594 ± 596 cm^3 as compared with 228 ± 82 cm^3 with IC−IS BT ($p = 0.004$).

CONCLUSIONS: Combined IC−IS BT is superior than IC BT + EBRT PB both in terms of organ sparing and target coverage. The IC−IS BT was more conformal with less normal tissue exposure to intermediate doses (V_{60}).

Keywords: Cervical cancer; Parametrial boost; Interstitial brachytherapy; Image-guided brachytherapy; Midline block

Introduction

Brachytherapy (BT) is an integral component in the treatment of locally advanced cervical cancer. During the last decade, the development of three-dimensional (3D) image-guided adaptive BT (IGABT) has allowed the four-dimensional adaptive assessment of the tumor extension in relation to the position of neighboring organs during treatment (1, 2), which has improved not only the dosimetric parameters but also the clinical outcome (3−7).

In cervical cancer, the parametrial lymph nodes are a major path for direct invasion and lymphatic spread (8), and parametrial involvement carries poor prognosis (9−11). The extent of parametrial involvement and infiltration to the pelvic walls correlates with poor disease-specific survival (12).

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Conflict of interest: None to report.

* Corresponding author. Department of Radiation Oncology, National Cancer Institute, Cairo University, Kasr El-Aini st, Fom El-Khalig, Cairo, Egypt. Tel.: +2-0223632665.

E-mail address: sandy_mohamed@cu.edu.eg (S. Mohamed).

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In combating cervical cancer, it is crucial to obtain a high dose to achieve local control with definitive radiotherapy. Dose to the BT target, that is the high-risk clinical target volume (HR-CTV), has been shown to correlate with local control with a D_{90} >86 Gy (13). However, with large tumors, it is a challenge to cover the entire target volume with high dose when using intracavitary BT (IC BT) because of the dose limiting nearby organs at risk (OARs).

Bi- or unilateral external beam radiotherapy (EBRT) fields with midline block have been used to boost parametrial extension in patients in whom the contribution from IC BT is insufficient (14). However, its effectiveness is poorly documented, and there is no strong evidence to validate its routine use. Midline blocks can be either simple standard rectangular blocks or customized blocks that conform to an isodose line (15), or step-wedge filter that conforms to multiple isodose lines (16).

The combined intracavitary and interstitial BT (IC−IS BT) is an alternative technique in which IS needles are implanted to target the parametrial tumor extension. IC−IS BT was reported to be feasible and achieved good target coverage in large tumors (17−19). IGABT with IC−IS application resulted in 85−95% local control rates in large or poorly responding (IIB/III/IV) cervical cancer, with a moderate rate of normal tissue toxicity (6, 7).

One of the challenges related to administration of parametrial EBRT boost is to accurately assess doses to targets and OARs (20). Because of high-dose gradients from both BT and EBRT, it is not possible to directly add dose−volume histogram (DVH) parameters as recommended by the Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology for addition of whole pelvis EBRT and BT. A spatial addition of dose matrices is needed. Furthermore, because the dose per fraction changes throughout the treatment volume, there is a need to convert each dose distribution to equivalent total dose in 2-Gy fractions (EQD2) before spatial dose addition. Because currently available treatment planning systems do not provide this option, we developed a special program for summation of doses of the parametrial boost (PB) field and the IC BT in 3D EQD2 dose maps and not in physical doses.

The aim of this study was to systematically compare parametrial irradiation by EBRT PB plus IC BT vs. IC−IS BT implantation in terms of target coverage and doses to OARs for the treatment of locally advanced cervical cancer.

Methods and materials

Patients with parametrial involvement at diagnosis treated during the period October 2008−August 2011 were reviewed. Patients who had persistent parametrial involvement at BT and who were treated with combined IC−IS BT were included in this study. A PB scenario consisting of IC BT plus midline-blocked EBRT PB field was modeled (Fig. 1) and was compared with the actually delivered IC−IS BT.

All patients received whole pelvis irradiation by intensity-modulated radiation therapy (IMRT) of 45−50 Gy in 25−30 fx. The gross tumor volume (GTV) was determined clinically and/or radiologically for the primary tumor (GTV_T) and any pathological nodes (GTV_N). The CTV included the GTV and surrounding subclinical disease. CTV included the uterus, parametrial tissue, upper vagina, and broad and uterosacral ligaments. All pelvic lymph nodal stations were included in the CTV with a recommended 7 mm margin around the blood vessels. Internal target volume included the CTV plus a margin to account for internal organ movements. Planning target volume included the internal target volume plus margin to account for setup and delivery uncertainties.

In the final 2−3 weeks of an overall treatment time of 7 weeks, two fractions of pulsed-dose-rate BT (BT1 and BT2) were delivered about 1 week apart, each comprising 15−20 hourly pulses. The planning aim was to obtain a dose to 90% of the volume (D_{90}) of at least 85 Gy EQD2 in the HR-CTV from EBRT and BT combined. One week before BT1, a preplanning MRI was routinely performed (BT0), which allowed the assessment of tumor topography and provided information to prospectively decide which application type is to be used for BT1 and BT2 (17). The pulsed-dose-rate BT application and MRI technique have been previously described (4). Briefly, MRI at BT was done with the applicator *in situ*. Imaging, target and OARs contouring, and applicator reconstruction were done according to the Groupe Européen de Curiethérapie-

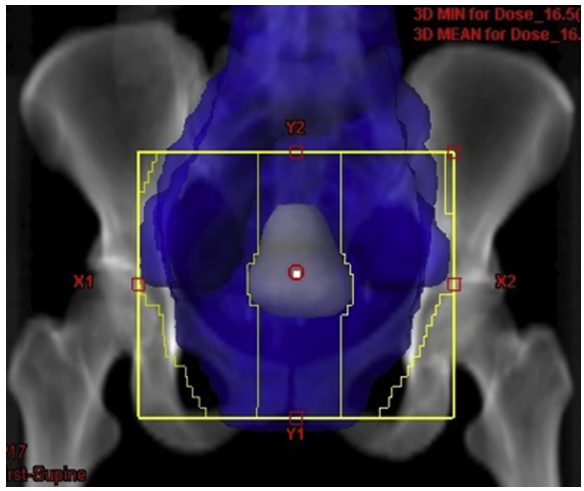

Fig. 1. The parametrial boost field borders, which were planned on the external beam radiotherapy (EBRT) planning CT. The central block is created at least 4 cm in width and furthermore increased in width as needed to conform to the isodose line corresponding to a total of 85 Gy equivalent total dose in 2-Gy fraction dose (pear-shaped gray color structure). The blue color wash showing the EBRT whole pelvic field planning target volume. (For interpretation of references to color in this figure legend, the reader is referred to the web version of this article.)