ELSEVIER

Brachytherapy ■ (2016) ■

BRACHYTHERAPY

Contribution of image-guided adaptive brachytherapy to pelvic nodes treatment in locally advanced cervical cancer

Warren Bacorro[1,2], Isabelle Dumas[3], Antonin Levy[1], Eleonor Rivin Del Campo[1], Charles-Henri Canova[1], Tony Felefly[1], Andres Huertas[1], Fanny Marsolat[3], Christine Haie-Meder[1], Cyrus Chargari[1,4,5], Renaud Mazeron[1,*]

[1]*Department of Radiation Oncology, Brachytherapy Unit, Gustave Roussy, University of Paris Saclay, Villejuif, France*
[2]*Department of Radiation Oncology, Benavides Cancer Institute, University of Santo Tomas Hospital, Manila, Philippines*
[3]*Department of Medical Physics, Gustave Roussy, University of Paris Saclay, Villejuif, France*
[4]*Institut de Recherche Biomédicale des Armées, Bretigny-sur-Orge, France*
[5]*French Military Health Academy, Ecole du Val-de-Grâce, Paris, France*

ABSTRACT

PURPOSE: With the increasing use of simultaneous integrated boost in the treatment of cervical cancer, there is a need to anticipate the brachytherapy (BT) contribution at the level of the pathologic pelvic lymph nodes. This study aimed to report the dose delivered at their level during BT.
METHODS AND MATERIALS: Patients with pelvic nodal involvement and treated with a combination of chemoradiation followed by image-guided adaptive pulsed-dose-rate BT were selected. On per BT three-dimensional images, pelvic lymphadenopathies were delineated, without planning aim. For the purposes of the study, D_{100}, D_{98}, D_{90}, and D_{50} were reviewed and converted in 2-Gy equivalent doses, using the linear quadratic model with an α/β of 10 Gy.
RESULTS: Ninety-one patients were identified, allowing evaluation at the level of 226 lymphadenopathies. The majority of them were external iliac (48%), followed by common iliac (25%), and internal iliac (16%) regions. The 2-Gy equivalent doses D_{98} were 4.4 ± 1.9 Gy, 5.4 ± 3.1 Gy, and 4.3 ± 2.1 Gy for the obturator, internal iliac, and external iliac, respectively, and 2.8 ± 2.5 Gy for the common iliac. The contribution to the common iliac nodes was significantly lower than the one of external and internal iliac ($p < 0.001$).
CONCLUSIONS: BT significantly contributes to the treatment of pelvic nodes at the level of approximately 5 Gy in the internal, external, and obturator areas and 2.5 Gy in the common iliac, allowing the anticipation of nodal boost with the simultaneous integrated boost technique. However, important individual variations have been observed, and evaluation of the genuine BT contribution should be recommended.

Keywords: Image-guided adaptive brachytherapy; Cervix cancer; Simultaneous integrated boost; Node; Dose

Introduction

The management of locally advanced cervical cancer relies on a combination of external beam radiotherapy (EBRT) and brachytherapy (BT) (1). The first component aims to cover the low-risk clinical target volume (CTV), including the lymph nodes areas. The second aims to escalade the dose to the cervical tumor itself. The recommended dose to cover the low-risk CTV varies from 44 to 50 Gy, even if a lower EBRT dose favors the ability to achieve the BT planning aims (2). This dose range is considered as effective to treat microscopic disease but is too weak to treat macroscopic lymph nodes. It is therefore recommended to boost pathologic nodes, although the optimal dose to reach remains debated (3). The total dose delivered to pelvic nodes results in the summation of the pelvic radiotherapy, nodal boost, and BT doses. This last component contributes inhomogeneity to their treatment, according to the distance between the implant and the target nodes. Before the era of three-dimensional (3D) image guidance, dose-point calculations have been used to evaluate

Received 19 September 2016; received in revised form 1 November 2016; accepted 22 November 2016.

Conflict of interest: The authors declare no conflict of interest with the topic of this work or the content of the manuscript.

* Corresponding author. Radiation Oncology, Gustave Roussy, 114, Rue Edouard Vaillant, 94805 Villejuif Cedex, France. Tel.: 00-33-1-42-11-45 66; fax: 00-33-1-42-11-52-08.

E-mail address: renaud.mazeron@gustaveroussy.fr (R. Mazeron).

1538-4721/$ - see front matter
http://dx.doi.org/10.1016/j.brachy.2016.11.016

the BT contribution. The Point B as well as the Fletcher lymphoid trapezoid, or the Chassagne pelvic wall points, have been proposed as surrogates of the dose delivered to the pelvic lymph nodes areas (Additional Figs. 1 and 2) (4). These methods, based on construction of points from the applicator or bony landmarks, have indeed limitations (5, 6). The advent of 3D imaging, such as CT or MRI, allows accurate delineation of each node, generation of dose-volume histogram, and reporting of BT contribution (7).

Nodal boosting has been performed for years using sequential boosts allowing to account for prior BT contribution. However, this management delays the boost until after BT and thus increases the overall treatment time of lymph nodes and probably decreases its efficiency. Intensity-modulated radiotherapy allows more conformal plans with a better sparing of organs at risk (OAR) and is increasingly used in routine in the treatment of locally advanced cervical disease (8, 9). This technique also allows the use of simultaneous integrated boost (SIB) in the pathologic nodes, requiring the integration in the initial treatment plan of the dose contribution to pelvic nodes during BT. Presently, limited data on dose contribution from image-guided adaptive brachytherapy (IGABT) to the pelvic nodes have been reported (10, 11). The aims of this study were to refine these findings by investigating the contribution of BT in a large number of pathologic nodes and to propose SIB dose/fractionation.

Methods and materials

Patient' selection

Patients were identified retrospectively from the department database. They were all treated for a locally advanced cervical carcinoma including pelvic nodal involvement. In all cases, the treatment relied on a combination of EBRT and image-guided adaptive BT, given with curative intent. Those treated for squamous cell, adenosquamous or adenocarcinoma subtypes, with no prior history of hysterectomy (total or subtotal) were retained. The institutional review board of Gustave Roussy approved the study.

Pretreatment evaluation and nodal staging

During the study period, the initial workup has evolved, notably regarding the use of positron emission tomography−computed tomography and pretreatment laparoscopic para-aortic staging. All patients had at least a pelvic MRI and an abdomino-pelvic CT in their workup. For the purposes of the study, pathologic nodes were considered as such according to the conclusions of the examinations performed at the time of the treatment. Criteria used to define pathologic nodes were as follows: enlargement (short axis ≥ 1 cm), shape (rounded), heterogeneous enhancement, and significant TEP uptake when performed (in regard to the noise and primary tumor uptake). Another criterion used for doubtful adenopathies was the response to chemoradiation. In case of any doubt, the node was usually considered as pathologic and thus boosted. All cases were discussed at that time at tumor board before treatment, in the presence of a radiologist who confirmed the nodal involvement, based on the available information. From 2007, laparoscopic para-aortic node dissection was offered in patients without para-aortic node uptake on the positron emission tomography−computed tomography to eliminate false negatives (12).

Treatment

In most patients, EBRT consisted in 3D conformal radiotherapy techniques with high-energy photons (18−20 MV). A conventional fractionation (1.8−2.0 Gy per fraction, five fractions a week) was used in all patients. The decision of extending the fields was based on the imaging or on para-aortic staging results, when performed. Concurrent chemotherapy, usually weekly cisplatinum, was systematically administered, except in case of refusal or contraindication. The pelvic CTV encompassed all pelvic lymph node areas up to the iliac bifurcation. In case of para-aortic irradiation, the upper limit was raised to T12−L1 or T11−T12 according to the height of the highest pathologic node. PTVs were generated using an automatic expansion of 7 mm in all directions. Further details on EBRT techniques and volumes are available in a previous publication (13).

Pulsed-dose-rate (PDR) IGABT was performed within 2 weeks after completion of pelvic EBRT. A detailed description of the procedure can be consulted elsewhere (14, 15). A personalized vaginal mold applicator, previously manufactured from a vaginal impression, was used in most applications (16). After the implant, 3-mm-thick, T2-sequence MRI scans in axial, sagittal, and coronal planes were acquired, with dummy sources inserted in the catheters to facilitate applicator reconstruction. Alternatively, 3-mm-thick, iodine contrast-injected CT simulation scans were performed. The images were then transferred to Oncentra (Nucletron, an Elekta company, Stockholm, Sweden) or Brachyvision (Varian medical systems, Palo Alto, CA). High-risk and intermediate-risk clinical target volumes (CTV_{HR} and CTV_{IR}), as defined by the Groupe Européen de Curiethérapie−European Society for Radiation Oncology, and OAR (bladder, rectum, and sigmoid) were delineated, as well as the pathologic node remnants (17, 18). Planning objectives, summing EBRT, and BT in 2-Gy equivalent doses obtained by applying the linear quadratic model with $\alpha/\beta = 10$ Gy and a half-time repair of 1.5 h, consisted in $D_{90} \geq 85$ Gy and ≥60 Gy for the CTV_{HR} and CTV_{IR}, respectively. The OAR dose constraints were 75 Gy, 75 Gy, and 85 Gy to the maximally exposed 2-cm^3 volumes (D_{2cm3}) of the rectum, sigmoid, and bladder, respectively ($\alpha/\beta = 3$ Gy). Dosimetry was initiated using a standard loading pattern then manually optimized to meet the above objectives. No planning objective was applied to the lymphadenopathies, but the BT contribution at their level was