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Pulsed-dose-rate brachytherapy for uterine cervix carcinoma: 10 years of experience with 226 patients at a single institution

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ABSTRACT

PURPOSE: To analyze the long-term results of pulsed-dose-rate (PDR) brachytherapy (BT) in cervical carcinoma patients treated at a single institution.

METHODS AND MATERIALS: All patients with histopathologically proven Stages IB–IVA cervical carcinoma, treated at our institution with PDR intracavitary BT between April 1996 and November 2007, were included in this retrospective analysis. All patients underwent primary pelvic radiotherapy (45 Gy) with concomitant chemotherapy from 1999 and PDR intracavitary BT (16 Gy to the clinical target volume), followed by hysterectomy in 124 patients.

RESULTS: Two hundred twenty-six patients received radiochemotherapy and BT. With a median followup of 81.7 months, the 5-year overall survival, disease-free survival, and local control (LC) were 67%, 65%, and 80%, respectively; seventy-seven relapses were observed including 38 local recurrences. Multivariate analysis showed earlier FIGO (International Federation of Gynecology and Obstetrics) stage and absence of nodal involvement to be associated with better overall and disease-free survivals. Use of three-dimensional image-guided BT planning and absence of nodal involvement were associated with better LC in the multivariate analysis. Late Grade ≥3 toxicity was experienced by 22 patients (9.7%), consisting of gastrointestinal toxicity for 6 patients, urinary tract for 10 patients, lymphatics for 3 patients, and vaginal toxicity for 3 patients.

CONCLUSIONS: This study demonstrates excellent LC rates with few late side effects with PDR BT for cervix carcinoma, similar to those reported in the literature with historical standard low-dose-rate BT. © 2013 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords: Pulsed-dose-rate brachytherapy; Cervical cancer; Image guided; Toxicity (side effects)

Introduction

Brachytherapy (BT) is an integral part of the treatment of cervical carcinomas, offering rapid dose falloff and very high conformational dose distribution in comparison with high-tech external beam irradiation. It offers a good therapeutic index with a high degree of local control (LC) and low toxicity (1–3). Continuous low-dose-rate (LDR) BT has been routinely used for the treatment of cervix carcinoma (1, 4), but high-dose-rate (HDR) BT was proposed as an alternative because of advantages of using a single-stepping source. Published oncologic results available for HDR are similar to LDR. At the beginning of the 1990s, pulsed-dose-rate (PDR) BT was developed combining isodose distribution optimization of HDR BT and radiobiologic advantages of LDR BT. Brenner and Hall (5) and Fowler and Van Limbergen (6) defined the conditions for equivalence of continuous to pulsed LDR BT. Since these publications, despite a lack of reported clinical results, PDR BT has been increasingly used in practice in France, replacing LDR.

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Our experience using PDR intracavitary BT spans across 10 years involving more than 200 patients with over 5 years of followup for most patients. The aim of this clinical retrospective study was to present the results of this decade of experience at our institution for patients with cervical cancer.

Methods and materials

Patient and tumor characteristics

From April 1996 to November 2007, 226 patients with invasive carcinoma of the cervix were treated at our institution with PDR intracavitary BT with curative intent. All patients treated at our institution and for whom medical records were available were selected for inclusion in this retrospective study. Initial locoregional staging included a clinical evaluation performed by a gynecologic surgeon and radiation oncologist (according to the 1995 FIGO (International Federation of Gynecology and Obstetrics) classification (7)). Abdominopelvic MRI was obtained for 168 patients (74.3%) and CT imaging for 160 patients (70.8%). FDG-PET (fluorine-18-fluorodeoxyglucose positron emission tomography) scan was not systematically performed, and no decision has been taken based only on its results; 148 patients (65.4%), mostly Stages I and II, with a good health status and without suspicious lomboaortic nodes at CT or MRI were selected to receive pelvic lymphadenectomy by coelioscopy first. Only 1 patient had a para-aortic lymphadenectomy. Nodal involvement was determined if histologically proven (65 patients) or suspected on CT (24 patients). All patients with positive lymph nodes, including IB1 stage, received first external beam radiation therapy and are included in the study. Stage IB1 patients treated with preoperative intracavitary PDR BT followed with colpohysterectomy were excluded from the analysis (19 patients). Institutional review board approval was obtained for this study, and it was conducted in compliance with the Helsinki Declaration.

Treatment characteristics

All patients received 45 Gy pelvic external beam radiotherapy (EBRT) before PDR BT with a standard four-field technique (190 patients) or a two anterior/posterior opposing fields technique (36 patients) using high megavoltage photons from a linear accelerator (photons × 18 and 25 MeV). EBRT included the para-aortic area when the CT showed enlarged common iliac or para-aortic nodes. When the nodal involvement was histologically proved or suspected on CT, a complementary boost irradiation was delivered after BT to reach a minimum of 60 Gy to the parametria and/or involved pelvic nodes and 55 Gy to the para-aortic nodes, taking into account the dose contribution of BT. From 1999, based on the results of randomized trials (8–12), chemotherapy was given during EBRT for all stages ≥IB2, with intravenous cisplatin 40 mg/m^2 once a week for 5 weeks in 150 of 226 patients (66.4%). Chemotherapy courses were not delivered during the hospitalization for the BT procedure.

PDR-BT procedure and treatment planning

After EBRT, the PDR BT boost was delivered during a single hospitalization, using the PDR Selectron (Elekta, Stockholm, Sweden). At the beginning of the BT procedure, a careful clinical examination was carried out under general anesthesia to assess clinical response to EBRT. A Fletcher applicator was used, and no patient underwent interstitial BT. Pulses were delivered hourly during night and day. Before 1999, the BT treatment planning dosimetry was based on orthogonal radiographs, in accordance with International Commission on Radiation Units (ICRU) 38 (13). The prescribed dose was 16 Gy after radiochemotherapy. The dose was reported according to the ICRU38 guidelines with the 60 Gy isodose, total reference air kerma (TRAK), and dose to critical organs (bladder and rectal reference points). The dose distribution was calculated on orthogonal films for 68 patients. Three-dimensional (3D) computerized-assisted treatment based on CT (CT-based 3D PDR BT) was adopted for treatment of cervical cancer since 1999 and was carried out for 158 patients. CT at BT was performed with CT–MRI compatible Fletcher applicator in place and with intravenous contrast except in cases of renal insufficiency or allergy. Clinical target volume (CTV) and organs at risk (OARs) (rectum, sigmoid, bladder, and small bowel) were delineated. CTV corresponded to the high-risk (HR) CTV of the Brachytherapy Group of the European Society for Therapeutic Radiology and Oncology (GEC ESTRO) guidelines (14) and included the whole cervix and any palpable or macroscopic residual disease. The BT dose was prescribed on the target (HR CTV of GEC ESTRO). The dose was calculated on minimal peripheral dose of the target, and the dose rate prescribed was around 65 cGy/h that we have used previously. Care was taken to obtain a similar TRAK to that used previously with LDR BT. Concerning the OAR, no consensus and guidelines were established in 1999; at the date, we began CT-based 3D PDR BT. Dose in a low volume had been suggested to be well correlated with dose at OAR, and a value of 3 cm^3 was chosen. The dose–volume constraints were dose–volume histograms (DVHs) 3 cm^3 bladder ≤65 Gy (dose cumulated external irradiation EBRT + BT not calculated in EQD_2 [equivalent dose in 2-Gray fractions]) and DVH 3 cm^3 rectum ≤70 Gy. These doses were extrapolated out of our experience with LDR with doses calculated to the ICRU points (bladder and rectum reference points). The dose–volume constraints evolved with current practices and after 2005; the doses were calculated according to GEC ESTRO recommendations on dose reporting (24 patients). Until 2005, dose optimization was performed using only dwell positions, modifications only in the number of dwell positions in the uterine probe and number and position of the dwell positions in the ovoids. After 2005, graphical optimization was used (24 patients).

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