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Clinical feasibility of interstitial brachytherapy using a ''hybrid'' applicator combining uterine tandem and interstitial metal needles based on CT for locally advanced cervical cancer

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ABSTRACT

PURPOSE: To explore the dosimetric advantage of target volume and surrounding normal tissue by using interstitial (IS) brachytherapy (BT) based on three-dimensional CT in locally advanced cervical cancer, as a simple and effective clinical treatment approach.

METHODS AND MATERIALS: Fifty-two patients with poor tumor response to external beam radiotherapy and a residual tumor >5 cm at the time of the first BT were included. IS BT was performed using a ''hybrid'' applicator combining uterine tandem and free metal needles based on three-dimensional CT. The high-risk clinical target volume (HR-CTV), intermediate-risk clinical target volume, and organs at risk were contoured. The total dose, including external beam radiotherapy (45 Gy in 25 fractions) and high-dose-rate BT (30 Gy in 5 fractions), was biologically normalized to conventional 2-Gy fractions. D_{90} and D_{100} for HR-CTV and intermediate-risk clinical target volume and D_{2cc} for the bladder, rectum, and sigmoid were analyzed.

RESULTS: The mean D_{90} value for HR-CTV was 88.4 ± 3.5 Gy. Totally, 88.5% of the patients received D_{90} for HR-CTV ≥87 Gy. The D_{2cc} for the bladder, rectum, and sigmoid were 81.1 ± 5.6, 65.7 ± 5.1, and 63.1 ± 5.4 Gy, respectively. The mean number of needles was 6.9 ± 1.3 for each application. IS BT was associated with minor complications.

CONCLUSION: IS BT using the ''hybrid'' applicator provides a dosimetric advantage for target volume and organs at risk in large-volume (>5 cm) tumors and is, thereby, clinically feasible. However, the long-term curative effect and possible toxicity need further clinical observation.

Keywords: Interstitial brachytherapy; Computed tomography; Cervical cancer

Introduction

Patients with locally advanced cervical cancer undergo standard treatment with external beam radiation (EBRT) and concomitant cisplatin combined with brachytherapy (BT), which is an essential integral component of this treatment for curative purposes (1–4). The prescription doses to Point A on traditional two-dimensional treatment planning cannot be based on target volume; therefore, extensive tumors are likely to be undertreated with small BT volumes and doses (5). Image-based BT (IBBT), which provides individual treatment planning for patients by prescribing doses to the target volume as well as potentially limiting the doses to the organs at risk (OAR), is considered more advantageous compared to conventional two-dimensional approaches (6, 7). With IBBT, CT or MRI is used for imaging in most treatment centers worldwide. Studies on three-dimensional (3D) imaging in BT treatment planning have indicated that IBBT may improve local control and decrease treatment-related toxicity (8–10). In 2005, the Group Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology provided recommendations for adaptive target concepts for BT based on MRI: Delineations of a gross tumor volume, the high-risk clinical target volume (HR-CTV), and the intermediate-risk clinical target volume (IR-CTV) were introduced (11, 12).

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Subsequent studies on MRI-based BT have used these guidelines (13, 14).

MRI is the gold standard for target volume delineation owing to its superior soft tissue visualization compared to CT (15, 16). However, it is difficult to preform MRI-based BT in most clinics owing to its high cost, inconvenience because of the absence of MRI facilities in most radiation oncology departments and high time requirement. CT simulators are more widely available, and comparison and consensus guidelines on the delineation of target volume for CT- and MRI-based BT have recently been published (17). Although the width of the contoured parametrial extension was greater on CT than on MRI, the distinction seemed to be minor for patients with severe lateral extension and demonstrating poor EBRT response (17). However, there seemed to be no significant differences between CT and MRI for contouring the OAR (18).

In patients with laterally extended or unfavorable topography with an unfavorable response to EBRT, interstitial (IS) BT is advisable. Combined intracavitary (IC)/IS BT such as the Vienna applicator (tandem ring) and the Utrecht applicator (tandem ovoid) allows additional needles to be inserted via holes in the ring or ovoids, providing an improvement in dose-volume histogram (DVH) parameters (19, 20). However, both these standard IC/IS applicators, especially involving the use of plastic needles that cannot be reused, are very expensive for patients in developing countries, where cervical cancer in the advanced stage is highly prevalent. In contrast, reusable metal needles are much cheaper and available in most centers.

Free needles are always conventionally used for large tumors in most centers, but their accurate freehand implantation is difficult without real-time image guidance. The latter approach was introduced in a case report on IC CT-guided IS brachytherapy (21). However, to the best of our knowledge, dosimetric results for a cohort of patients treated with this method have not been published. Our study aimed to investigate the dosimetric advantage of using IS BT with freehand placement of metal needles under real-time 3D CT guidance for large-volume tumors and/or lateral parametrial extension and to determine the feasibility of its clinical application. This method may provide a simple and effective treatment approach, especially useful for clinical facilities with limited resources.

Methods and materials

Patients and treatment

Consecutive patients with biopsy-proven locally advanced cervical cancer evaluated at our department between October 2013 and November 2015 were analyzed. Pelvic MRI (1.5 T; 5-mm sections) was performed for all the patients before EBRT and 1 day before each BT. Clinical gynecologic examination with drawings was conducted before EBRT and at the time of BT.

All the patients were treated with 45 Gy of 1.8-Gy EBRT in 25 fractions, administered via intensity-modulated radiation therapy or a four-field box radiation (Varian)–based 3D CT; the pathologic lymph nodes were treated with 60 Gy, and 5–6 cycles of weekly cisplatin chemotherapy (40 mg/m^2) were administered. After completing EBRT or during the last week of EBRT, high-dose-rate ^{192}Ir BT was performed for 4–5 days/fraction. For all patients, the overall treatment time was limited to 56 days. All the participants provided written informed consents.

BT implantation and CT guidance

BT was administered to the patient in the lithotomy position under subarachnoid anesthesia. Briefly, a metal intrauterine tandem was placed into the uterine cavity under transabdominal ultrasonography guidance. IS metal needles (length: 16 cm, diameter: 1.3 mm, Elekta) were then inserted into the remaining tumor parallel to the vagina as well as into parametrial or lateral pelvic sidewall extensions at different angles to the vagina, at a depth of approximately 10 mm as a preliminary implantation according to T2-weighted MRI and clinical gynecologic examination. The vagina was packed with gauze to push away the rectum and bladder and fix the uterine tandem and needles. The bladder was filled with 50 mL diluted urografin (dilution 1:20) through a urinary catheter, and CT scans were obtained at 4-mm slice intervals. Then, we adjusted the direction and depth of the metal needles repeatedly until satisfactory distribution was achieved, including accurate needle insertion in the remnant tumor and parametrial extension, to ensure symmetrical distribution in the tumor at a 1-cm distance from the central axis and to provide eligible DVH for the target volume and OAR in the subsequent treatment planning, as observed on multiple CT scans (Fig. 1).

Contouring and treatment planning

HR-CTV, IR-CTV, and OAR, including the bladder, rectum, and sigmoid, were contoured based on CT; HR-CTV and IR-CTV contours were delineated according to the target definition guidelines recommended by the Group Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology for MRI (11). The scope of HR-CTV included the whole cervix and any notable remaining tumor at BT. Specific borders for HR-CTV were set according to the recommendation of Viswanathan *et al.* (18). In particular, in the inferior direction, the contour of the lowest extent of the vaginal tumor was based on the information obtained from clinical examinations if the vagina was involved; in the superior direction, HR-CTV was decided if intrauterine involvement was detected