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FRACTIONATED STEREOTACTIC RADIOTHERAPY BOOST FOR GYNECOLOGIC TUMORS: AN ALTERNATIVE TO BRACHYTHERAPY?

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Purpose: A brachytherapy (BT) boost to the vaginal vault is considered standard treatment for many endometrial or cervical cancers. We aimed to challenge this treatment standard by using stereotactic radiotherapy (SRT) with a linac-based micromultileaf collimator technique.

Methods and Materials: Since January 2002, 16 patients with either endometrial (9) or cervical (7) cancer have been treated with a final boost to the areas at higher risk for relapse. In 14 patients, the target volume included the vaginal vault, the upper vagina, the parametria, or (if not operated) the uterus (clinical target volume [CTV]). In 2 patients with local relapse, the CTV was the tumor in the vaginal stump. Margins of 6–10 mm were added to the CTV to define the planning target volume (PTV). Hypofractionated dynamic-arc or intensity-modulated radiotherapy techniques were used. Postoperative treatment was delivered in 12 patients (2 × 7 Gy to the PTV with a 4–7-day interval between fractions). In the 4 nonoperated patients, a dose of 4 Gy/fraction in 5 fractions with 2 to 3 days' interval was delivered. Patients were immobilized in a customized vacuum body cast and optimally repositioned with an infrared-guided system developed for extracranial SRT. To further optimize daily repositioning and target immobilization, an inflated rectal balloon was used during each treatment fraction. In 10 patients, CT resimulation was performed before the last boost fraction to assess for repositioning reproducibility via CT-to-CT registration and to estimate PTV safety margins around the CTV. Finally, a comparative treatment planning study between BT and SRT was performed in 2 patients with an operated endometrial Stage I cancer.

Results: No patient developed severe acute urinary or low-intestinal toxicity. No patient developed urinary late effects (>6 months). One patient with a vaginal relapse previously irradiated to the pelvic region presented with Grade 3 rectal bleeding 18 months after retreatment. A second patient known to suffer from irritable bowel syndrome presented with Grade 1 abdominal pain after treatment. The estimated PTV margins around the CTV were 9–10 mm with infrared marker registration. External SRT succeeded in improving dose homogeneity to the PTV and in reducing the maximum dose to the rectum, when compared to BT.

Conclusion: These results suggest that the use of external SRT to deliver a final boost to the areas at higher risk for relapse in endometrial or cervical cancer is feasible, well tolerated, and may well be considered an acceptable alternative to BT. © 2005 Elsevier Inc.

Cervix cancer, Endometrial adenocarcinoma, Brachytherapy, Stereotactic radiotherapy, Micromultileaf collimator, Novalis-shaped beam surgery, Intensity-modulated radiotherapy, Comparative treatment planning.

INTRODUCTION

Radiation therapy (RT) is commonly used in the treatment of endometrial and cervical cancer. Patients are frequently treated with external photon irradiation to the whole pelvis (WPRT), followed by intracavitary brachytherapy (BT), either low-dose rate or high-dose rate (HDR), to a boost volume usually including the vaginal vault and, in nonoperated patients, the uterus and parametria. Stereotactic radiotherapy (SRT) may be used to treat the final boost volume in endometrial/cervical cancer patients with time–dose fractionation schedules similar to those with HDR-BT. However, SRT offers several advantages over HDR-BT, including simplified radiation protection, no need for hospitalization, no anesthesia, no narcotics, and a potential improvement in target dose distribution.

Stereotactic RT to relatively small pelvic targets has been made possible thanks to new treatment delivery techniques

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(i.e., dynamic-arc treatment and intensity-modulated radiotherapy [IMRT]) and to the availability of highly accurate immobilization and repositioning systems. Optimal repositioning with infrared (IR) metallic body markers and an inflatable rectal probe has been recently reported for prostate cancer patients (1).

The purpose of this study was to challenge the BT standard for gynecologic tumors by using high-precision linear accelerator–based SRT with micromultileaf collimation. We aimed to assess tolerance and repositioning reproducibility of this new treatment approach, and to evaluate the dose distributions achieved by SRT in the target and surrounding organs at risk (OARs) compared with those attainable using HDR-BT.

METHODS AND MATERIALS

Patients

Since January 2002, 16 consecutive women with either cervical cancer (7 patients) or endometrial cancer (9 patients) have been treated with a final boost to the areas at higher risk for relapse. Patient ages ranged from 33 to 71 years (median, 53 years). Patient, tumor, and treatment characteristics are summarized in Table 1. Four cervix cancer patients (2 Stage IB2, 1 Stage IIB, and 1 Stage IIIB) received adjuvant chemotherapy (cisplatin and 5-fluorouracil). WPRT was delivered to 12 patients before the boost treatment. Three patients were treated to the pelvic and to the para-aortic nodes. In 12 patients, the boost volume included the upper vagina (vaginal vault). In one nonoperated patient, the boost included the entire uterus and both parametria, whereas in a second not radically operated patient, only the parametria and the vaginal vault were included in the boost volume. Finally, the target volume included the tumor in the vaginal stump in 2 patients treated for local relapse after surgery and after radiotherapy, respectively. Patients were staged at diagnosis according to the FIGO classification (2): 9 were Stage I, 6 Stage II, and 1 Stage III.

Table 1. Patient and tumor characteristics

Characteristics	*n*
No. of patients	16
Age (years)	
Median	53
Range	33–71
Tumor site	
Cervix	7
Endometrium	9
Relapse	2 (1 endometrium, 1 cervix)
Histology	
Squamous cell	6
Adenocarcinoma	9
Others	1
Stage	
I/II/III	9/6/1
Hysterectomy	
None	1
Yes	15
Tumor residual before treatment	
Gross disease	3
Subclinical disease	13
Concomitant chemotherapy	4
Para-aortic irradiation	3

Treatment

Most patients were treated first to clinical target volume 1 (CTV1: pelvic lymph nodes ± para-aortic nodes, tumor bed, or tumor residual) with a 4-field "box" technique in the supine position. All fields were treated daily, 5 days a week, with 15-MV X-rays. The prescribed dose to the pelvis was 45–50.4 Gy in 1.8 Gy/fraction.

The treatment boost to clinical target volume 2 (CTV2: vaginal vault, or uterus-parametria, or tumor residual, or tumor relapse) was delivered under stereotactic conditions with a commercially available micromultileaf collimator–based linear accelerator. Such treatment delivers 6-MV X-rays and is able to perform dynamic-arc treatments, as well as IMRT (Novalis, BrainLAB A.G., Heimstetten, Germany). Before the boost dose to CTV2 was delivered, patients were immobilized with a customized vacuum body cast and optimally repositioned with the help of an IR-guided system developed for extracranial SRT (ExacTrac, BrainLAB A.G., Heimstetten, Germany). This system has previously been described in detail by Soete *et al.* (3). Briefly, 5 to 7 IR-reflecting metallic markers are asymmetrically fixed to the skin of the abdomen just before the planning CT is performed. The position of the isocenter with regard to the IR markers is calculated by the planning system. Before each treatment session, the markers are placed back on the patient. Their spatial arrangement is detected by a pair of IR cameras mounted to the treatment room's ceiling to reproduce the same coordinates when the patients are repositioned for daily treatment.

To further limit target motion and to help improve the target defining process in the simulation CT, a magnetic resonance endorectal probe was used for the CTV2 simulation and treatment. Sodium phosphate enemas were used to evacuate the rectum the night before and again 1 to 2 h before each procedure. To reduce anxiety and prevent or alleviate potential painful rectal spasms during the simulation or treatment intervals, alprazolam 0.5 mg *per os* was prescribed. After the probe was introduced into the rectum, 60 mL of air was introduced with a syringe. The inflated probe was then gently pulled toward the anus. No special care was taken to reproduce bladder filling during treatment. Patients were then fitted in their immobilization casts, skin metallic markers were fixed on their respective spots, and the IR-guided setup was undertaken.

Simulation CT images were taken in 3-mm increments over the region of interest. The CTV2 and OARs (i.e., rectum, bladder, small bowel, and femoral heads) were contoured on sequential axial CT slices. The CTV2 was expanded uniformly by 6 to 10 mm in all directions to produce the planning target volume (PTV) (Fig. 1).

Fifteen patients were treated with IMRT to CTV2, 12 using a single isocenter and 5–15 fields and 3 using 2 isocenters and 8–12 fields. One patient was treated with a dynamic-arc technique. In all 12 postoperative cases, a dose of 2 × 7 Gy to the PTV with 4 to 7 days' interval between fractions was prescribed and delivered. In 3 radically treated patients (1 with the primary tumor intact, 1 with nonradical surgery, and 1 with postsurgical local relapse), a dose of 5 × 4 Gy, 2 days a week during 2.5 weeks was prescribed and delivered. The patient with a reirradiation for a relapse in the vaginal stump received a total dose of 8 × 2 Gy daily, 5 days/week followed by 10 × 4 Gy twice-a-week during 5 weeks to the same PTV.

The above-described fractionation schedule for postoperative treatment was selected based on BT-HDR recommendations published by the American Brachytherapy Society (4) and by Orton