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Treatment results of image-guided high-dose-rate interstitial brachytherapy for pelvic recurrence of uterine cancer

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ABSTRACT

PURPOSE: We analyzed clinical data to evaluate the effectiveness of image-guided high-dose-rate interstitial brachytherapy (HDR-ISBT) for pelvic recurrence of uterine cancer.

METHODS AND MATERIALS: Between 2003 and 2011, 56 patients were treated with HDR-ISBT with or without external beam radiotherapy (EBRT). The median followup time was 33 months (range, 1−109 months). Pre-ISBT treatments included radical hysterectomy for 35 patients (Group A), radical hysterectomy with postoperative radiotherapy for 8 patients (Group B), and radical radiotherapy for 13 patients (Group C). We initiated MRI-assisted CT-based planning for the last 49 patients. The median ISBT single fraction dose was 6 Gy. The median total doses were 30 and 54 Gy with and without EBRT (range, 30−50 Gy) for Group A, respectively and 48 Gy without EBRT for Groups B and C.

RESULTS: The 3-year local control (LC) rates were 85%, 75%, and 46% for Groups A, B, and C, respectively ($p = 0.017$). The 3-year LC rates were 84%, 73%, and 33% for clinical target volume at the time of HDR-ISBT of <10, 10−29, and ≥30 cc, respectively ($p = 0.005$). The 3-year LC results tended to be higher for patients whose D_{100} (clinical target volume) was equal or higher than 67.1 Gy ($p = 0.098$). A total of 13 late complications of Grades 3−5 occurred in 11 patients (20%).

CONCLUSIONS: Our image-guided HDR-ISBT for pelvic recurrence of uterine cancer provided good treatment outcomes. The treatment results for patients who underwent radical surgery with or without postoperative radiotherapy are better than those for patients who underwent radical radiotherapy.

Keywords: Pelvic recurrence; Uterine cancer; Image guided; High-dose-rate interstitial brachytherapy; Magnetic resonance imaging

Introduction

Radical treatment for pelvic recurrence of uterine cancer is difficult because many organs at risk (OARs), such as the rectum, sigmoid colon, small intestine, bladder, and urethra, are near the tumor site. The indications for curative organ-sparing salvage surgery or pelvic exenteration are limited (1). External beam radiotherapy (EBRT) with or without chemotherapy is well tolerated; however, its treatment outcomes are not satisfactory (2).

Interstitial brachytherapy (ISBT) features the potential to salvage such tumors while preserving the function of OARs. The American Brachytherapy Society consensus guidelines show that patients with recurrent cervical, endometrial, or vulvar carcinoma with residual vaginal lesions greater than 0.5-cm thickness are potential candidates for ISBT (3). Several clinical studies have reported good local

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control (LC) with low-dose-rate (LDR) or high-dose-rate (HDR) ISBT (4–19).

Recurrent tumors are often large and with complex shapes that makes it difficult to achieve satisfactory implantation without image guidance. Therefore, image guidance and three-dimensional (3D) dose calculation have the potential to improve ISBT treatment results. The applicability of ultrasonography (4,5), CT (5–14), and MRI (7,13–15) has been investigated for applicator implantation or treatment planning.

In the past, we have installed implants via transrectal ultrasonography (TRUS) guidance and CT treatment planning with MRI assistance (19) using flexible plastic applicators to allow the contours of the gross tumor volume (GTV), clinical target volume (CTV), and OARs to be easily drawn from the CT images without metal artifacts. As a result, no metallic treatment items were used in our patients, thus allowing them to undergo MRI examinations. We have already reported our preliminary experience with this method for previously untreated uterine cervical carcinoma (20).

We report here the 3-year treatment results obtained with our imaging-assisted HDR-ISBT technique for pelvic recurrence of uterine cancer.

Material and Methods

Between May 2003 and January 2011, 63 patients with pelvic recurrences of uterine cancer underwent HDR-ISBT at the Department of Radiation Oncology, National Hospital Organization, Osaka National Hospital, Osaka, Japan. About 7 patients were excluded from this study because of distant metastases or because they were lost to followup in less than 12 months after HDR-ISBT. The median followup times were 33 months (range, 1–109 months) for the remaining 56 patients (median age, 59 years; range, 27–82 years) and 58 months for the survivors (Table 1).

The primary tumor site was the uterine cervix for 45 patients and the uterine corpus for 11. Histological findings revealed 30 squamous cell carcinomas, 2 adenosquamous carcinomas, 23 adenocarcinomas, and 1 endocrine tumor. The GTV was assessed on CT and MRI at the time of ISBT planning. The median maximum tumor diameter before treatment was 25 mm (range, 5–79 mm). The tumor morphological types were superficial and indurative for 9 and 47 patients, respectively. Among the latter, the maximum tumor diameter was less than 50 mm for 39 patients and 50–79 mm for 8 patients. In total, there were 55 N0 and 1 N1 patients.

We divided the patients into three groups according to their previous treatment modalities: patients who underwent radical surgery without postoperative radiotherapy (Group A; $n = 35$), those who underwent radical surgery with postoperative radiotherapy (Group B; $n = 8$), and those who underwent radical radiotherapy (Group C; $n = 13$). The median time interval between the previous radical treatment and our treatment was 15 months; the intervals were 6 months or less for 7 patients, 7–24 months for 30 patients, and more than 24 months for 19 patients.

Table 1
Patient characteristics

Characteristics	Values
Patient number	56 (2003.5–2011.1)
Followup	1–109 mo (median, 33 mo)
Age	27–82 y (median, 59 y)
Histology	Sq:Ad:AdSq:Endocrine = 30:23:2:1
Primary site	Uterine cervix:Corpus = 45:11
N-stage	N0:N1 = 55:1
Maximum tumor diameter	Superficial: <50 mm:50–79 mm = 9:39:8
CTV at the time of ISBT	<10 cc:10–29 cc:≥30 cc = 31:19:6
Previous treatment	Op:Op + PostOp RT:Radical RT = 35:8:13
Recurrence interval	≤6 mo:7–24 mo:>24 mo = 7:30:19
Chemotherapy	(+):(−) = 8:48

Sq = squamous cell carcinoma; Ad = adenocarcinoma; AdSq = adenosquamous cell carcinoma; CTV = clinical target volume; Op = operation; RT = radiotherapy.

About 20 patients in Group A underwent EBRT to the whole pelvis with a median prescribed dose of 30 Gy (range, 30–50 Gy). In addition, 17 patients underwent center-shielded EBRT (median, 20 Gy; range, 10–20 Gy). One patient underwent an additional boost of irradiation for pelvic lymph node metastases (10 Gy). The median overall treatment time (duration of whole EBRT and ISBT) was 46 days (range, 35–56 days). We performed ISBT after whole pelvic EBRT was essentially completed.

About 8 patients (14%) received concurrent chemotherapy before or during EBRT. About 7 of them received intravenous cisplatin, and 1 patient received intravenous carboplatin.

Applicator implantation

Implantation was performed under lumbar anesthesia. We also initiated epidural anesthesia and continued this until the applicator was extracted. We performed a single-applicator implantation with multifractionated HDR-ISBT for all patients. Implantation was monitored with the aid of TRUS (SSD-1000 and Prosound α7; Hitachi Aloka Medical, Ltd., Tokyo, Japan), and flexible needles (ProGuide Sharp Needle; Nucletron an Elekta Company, Veenendaal, The Netherlands) were used for all patients. Before implantation, we implanted three to four titanium markers at the distal, lateral edge of the GTV. We used a template-guided and nonambulatory implant technique for the first 5 patients and a freehand and ambulatory implant technique for the remaining 51 patients. The ambulatory applicator implantation technique has been described elsewhere (21). First, a single flexible needle applicator was inserted through the center of the vaginal stump or uterine cervix. A button stopper was then affixed to the needle and placed