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Radiotherapy doses at special reference points correlate with the outcome of cervical cancer therapy

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ABSTRACT

PURPOSE: The authors analyzed the correlation between radiotherapy doses at reference points on the uterine edge and the rectal wall and both pelvic control and late rectal complications of cervical cancer therapy.

METHODS AND MATERIALS: Between 1997 and 2005, 57 patients with Stages IB–IVA cancer of uterine cervix were treated with a combination of external beam radiotherapy and high-dose-rate intracavitary brachytherapy. Their high-dose-rate intracavitary brachytherapy was planned by dose-point optimization at six dose points located on the edge of uterus by computed tomography. A rectal reference point located on the anterior wall of the rectum by computed tomography was also used. The pelvic control rate and the rate of late rectal complications were calculated according to the biologically effective dose (BED) at each point and several clinical parameters.

RESULTS: The overall 3-year pelvic control rate was 69.4%. The patients with a BED >80 Gy10 at the point on the edge of the uterine cervix had better pelvic control (78.4% at 3 years) than the patients with a BED $\leqslant 80$ Gy10 (54.4% at 3 years), and the difference was significant. The difference in the BED (Gy3) at the rectal reference point between the patients with Grade 0–1 late rectal complications (median, 114 Gy) and the patients who developed Grade $\geqslant 2$ late rectal complications (median, 178 Gy) was significant. Chemotherapy was a borderline significant parameter in regard to correlation with pelvic control and late rectal complications, but there were no correlations with other dosimetric or clinical parameters.

CONCLUSIONS: The radiotherapy dose at the reference point on the edge of the cervix affected pelvic control more than the clinical parameters, and the dose at the rectal reference point was more strongly correlated with the occurrence of late rectal complications.

Keywords: Uterine cervical cancer; Dose–response relationship; Intracavitary brachytherapy; Pelvic control; Late rectal complication

Introduction

Intracavitary brachytherapy (ICBT) is an integral component of standard radiotherapy for cervical cancer and enables delivery of high dose radiation to the central tumor volume with relative sparing of surrounding normal organs, such as the bladder and rectum. Cervical cancer has traditionally been treated with low-dose rate (LDR) ICBT; however, high-dose-rate (HDR) ICBT has been developed to overcome LDR's potential disadvantages, which are radiation exposure of the medical staff, prolonged treatment time, mandatory hospitalization, and applicator movement. Moreover, one of the main advantages of HDR is the possibility of individualizing treatment by an optimization procedure (1, 2).

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LDR-ICBT for cervical cancer has traditionally been performed by the Manchester system. Use of that system is also the current clinical practice for HDR-ICBT of cervical cancer at most hospitals (3), and HDR-ICBT has yielded results comparable to those obtained by LDR therapy (4–7). However, it may be impossible to expect a better outcome by the Manchester system, because either no correlations between the point A dose and pelvic control or complications have been found (8), or higher doses at point A have been found to correlate with lower pelvic failure rates but with higher complication rates (9).

The dose evaluation at point A in the Manchester system does not reflect the dose to the cervical tumor, because the tumor itself is not imaged (3, 10, 11). In the present study, computed tomography (CT) images were used to identify six dose points on the edge of uterus covering the cervix and tumor extension and one reference point on the rectal wall, and the HDR-ICBT dose was prescribed to the isodose line that was planned by dose-point optimization at the six dose points on the edge of the uterus, but not to exceed the dose to point A. We evaluated pelvic control and late rectal complications that resulted from treatment with a combination of external beam radiotherapy (EBRT) and HDR-ICBT, and analyzed the correlations between outcome and radiotherapy doses at the seven points.

Methods and materials

Patient characteristics

Between September 1997 and November 2005, 96 patients with FIGO Stages IB–IVA cancer of the uterine cervix were treated by HDR-ICBT in the Department of Radiology at Tokyo Medical and Dental University Hospital, and 57 of them received HDR-ICBT according to the dose-point-optimized planning and were analyzed in this study. The other 39 patients did not consent to this study, and they received HDR-ICBT according to the Manchester system. The ages of 57 patients ranged from 32 to 91 years, and their median age was 63 years. Patients were staged on the basis of the results of a physical examination, biopsy, transvaginal sonography, abdomino-pelvic CT, and chest radiography. Cystoscopy and proctoscopy were performed when clinically indicated (Table 1).

Table 1
Patient characteristics

Characteristic	Number of patients (%)
Stage	
IB	5
IIA	2
IIB	15
IIIA	1
IIIB	28
IVA	6
Lymph-node metastasis	
Negative	39
Positive	18
Histological type	
Squamous cell carcinoma	54
Adenocarcinoma	3

Treatment

All patients were treated with a combination of EBRT and HDR-ICBT. EBRT was usually delivered to the whole pelvis (WP) through anterior and posterior parallel-opposed portals in the form of 10-megavolt (MV) X-rays. When central shields (CS) were inserted during EBRT, they were 4-cm wide in the lower half of the field and 2-cm wide in the upper half of the field. The EBRT dose was usually administered at 1.8–2 Gy per fraction, five fractions a week. WP total dose ranged from 39.6 to 54 Gy (median, 50.4 Gy), and CS was inserted after the delivery of 0–50.6 Gy (median, 30.8 Gy) of EBRT.

HDR-ICBT was administered by means of an HDR Microselectron unit (54 patients with a tandem and ovoids inserted; 3 patients with a uterine tube and cylinders inserted) with an ^{192}Ir source and a PLATO treatment planning system (BPS version 13), and it was administered in three to five fractions at a rate of one fraction per week concurrently with EBRT. ICBT planning was achieved by dose-point optimization. Instead of using point A of the Manchester system, to achieve an isodose surface covering the entire uterine cervix and tumor extension into the uterine corpus, six points were identified on CT images scanned before the first ICBT planning procedure with the tandem or uterine tube in place, that is, a point on the right uterine edge and a point on the left uterine edge along the plane of the tandem on the external cervical os (point E_R and E_L), two points on the body of the cervix (point C_R and C_L), and two points on the top of the uterus (point T_R and T_L), and the dose distributions were determined according to the dose-point optimization at these six points (Fig. 1). The prescribed dose for each fraction was individually determined so that point A would receive a dose between 5 and 7.5 Gy, and the total prescribed dose ranged from 9 to 35 Gy (median, 22.5 Gy).

Cisplatinum-based chemotherapy was administered via the internal iliac artery to 8 patients (1 in Stage IB, 3 in Stage IIB, and 4 in Stage IIIB) before radiotherapy (total dose range, 100–400 mg; median dose, 200 mg) between 1997 and 2000, and was systemically administered to 22 patients (6 in Stage IIB and 16 in Stage IIIB) during radiotherapy (total dose range, 70–450 mg; median dose, 175 mg) between 2001 and 2005.

Analysis

A followup examination was usually performed every month. The median followup period of all 57 patients