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Tumor size before image-guided brachytherapy is an important factor of local control after radiotherapy for cervical squamous cell carcinoma: analysis in cases using central shielding

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ABSTRACT

We analyzed the local control (LC) of cervical squamous cell carcinoma treated by computed tomography (CT)-based image-guided brachytherapy (IGBT) using central shielding (CS). We also examined the value of tumor diameter before brachytherapy (BT) as a factor of LC. In total, 97 patients were analyzed between April 2016 and March 2020. Whole-pelvic (WP) radiotherapy (RT) with CS was performed, and the total pelvic sidewall dose was 50 or 50.4 Gy; IGBT was delivered in 3–4 fractions. The total dose was calculated as the biologically equivalent dose in 2 Gy fractions, and distribution was modified manually by graphical optimization. The median follow-up period was 31.8 months (6.3–63.2 months). The 1- and 2-year LC rates were 89% and 87%, respectively. The hazard ratio was 10.11 (95% confidence interval: 1.48–68.99) for local recurrence in those with a horizontal tumor diameter $\geq$ 4 cm compared to those with $<$ 4 cm before BT. In CT-based IGBT for squamous cell carcinoma, favorable LC can be obtained in patients with a tumor diameter $<$ 4 cm before BT. However, if the tumor diameter is $\geq$ 4 cm, different treatment strategies such as employing interstitial-BT for dose escalation may be necessary.

Keywords: cervical cancer; tumor size; squamous cell carcinoma; image-guided brachytherapy (IGBT); central shielding (CS)

INTRODUCTION

In cervical cancer, improving local control (LC) of the primary lesion is considered to have a direct effect on disease control and survival [1]. The standard radiation therapy regimen for patients with cervical cancer consists of external beam radiotherapy (EBRT) and brachytherapy (BT) [2]. Accordingly, 3-dimensional image-guided brachytherapy (3D-IGBT) using computed tomography (CT) or magnetic resonance imaging (MRI) is widely employed [3, 4]. The 2017 Japan Society of Gynecologic Oncology guidelines for the treatment of uterine cervical cancer differs from those of Europe and the United States. These guidelines indicate the use of central shielding (CS) [5–7]. In previous studies of LC after 3D-IGBT based on the Japanese treatment schedule, histological type, tumor diameter, and dose have been reported to be important factors associated with LC [8–11]. However, these

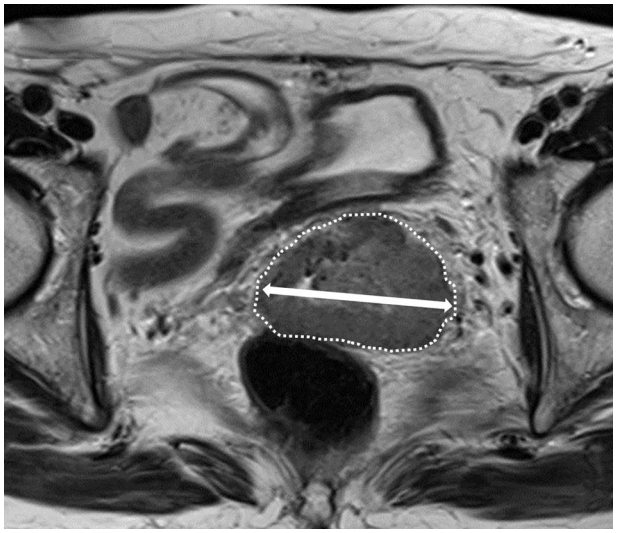

Fig. 1. The horizontal tumor diameters were measured based on the axial T2-weighted MRI.

reports analyzed LC among various histological types which impact LC. Moreover, no report has evaluated whether the tumor diameter before the start of treatment or BT is a significant factor of LC in the Japanese treatment schedule. Here, we retrospectively analyzed the LC of cervical squamous cell carcinoma from a treatment schedule employing CS and examined the value of pre-BT tumor diameter as a factor of LC.

MATERIALS AND METHODS

Patients

This study was approved by the Institutional Ethics Committee (No. 2112–024) of the Okayama University Hospital, Okayama, Japan. In total, 97 patients with pathologically proven, previously untreated cervical squamous cell carcinoma treated at our hospital with high-dose-rate (HDR) CT-based 3D-IGBT between April 2016 and March 2020 were included in this study. All patients underwent a pelvic examination, CT scan, MRI, and blood test, including patients with the 2008 International Federation of Gynecology and Obstetrics (FIGO) stage IB1–IVB disease and those with para-aortic node metastasis. All radiotherapy (RT) and concurrent chemoradiotherapy (CCRT) were performed as definitive treatments. The horizontal tumor diameters were measured based on the axial T2-weighted MRI images for analysis in this study (Fig. 1).

Chemotherapy

Concurrent chemotherapy of cisplatin (40 mg/m^2) and nedaplatin (35 mg/m^2) was administered weekly in 73 (75%) patients with FIGO Stage IB2, IIA2, and IIB-IV, or pelvic and para-aortic lymph node metastases. However, chemotherapy was not performed on patients with impaired organ function or those aged $\geq$80 years. Nedaplatin was selected when patients with impaired renal function were observed with para-aortic lymph node metastasis. Supportive treatments, such as blood transfusions, were performed during RT/CCRT. Postponement of chemotherapy was considered when grade 3 or higher adverse events in Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 appeared.

External beam radiotherapy

Radiation therapy was delivered using 10-MV photons from a linear accelerator (Primus; Canon Medical Systems, Tochigi, Japan). A superposition dose calculation algorithm with heterogeneity correction was used (Xio version 4.8.0; Elekta, Stockholm, Sweden) with a radiation therapy planning system. The clinical target volume (CTV) for EBRT included sites such as the primary tumor, whole uterus, bilateral parametrium, the upper half of the vagina, and pelvic lymph nodes (common, internal, external iliac, obturator, and presacral). The planning target volume (PTV) was defined as the CTV plus a margin of 2 cm for the primary tumor and uterus body. Three-dimensional conformal RT with an anterior–posterior parallel-opposed field or a 4-field box was used for whole pelvic (WP) irradiation. After WP irradiation, the anterior–posterior parallel-opposed field with CS of 4 cm in width was delivered according to the Japanese guideline treatment schedule [5]. CS position was set to the S2/3 level to cover the presacral area. The total pelvic dose (WP-dose plus CS-dose) administered was 50 Gy in 25 fractions or 50.4 Gy in 28 fractions.

Brachytherapy

BT was initiated after WP-EBRT and performed weekly for three or four sessions. An HDR ^{192}Ir source was used for BT, and all patients were treated by intracavitary (IC) BT. MicroSelectron digital (HDR-V3) BT afterloader (Elekta Inc., Stockholm, Sweden) with a combination of either tandem and ovoid or tandem and vaginal cylinder applicators was used to administer and perform ICBT. CT-based 3D-IGBT was performed in each BT session. The high-risk CTV (HR-CTV) and organs at risk (OARs) were contoured on the planning CT with Oncentra® (Elekta Inc.) according to several guidelines [12–14] using MRI images acquired at diagnosis and within one week of the first BT session. The HR-CTV included the entire cervix and the macroscopic residual tumor at the time of the BT. All radiation doses were biologically converted to equivalent doses in 2 Gy (EQD2) by a linear-quadratic model using an alpha/beta ratio of 10 Gy for the HR-CTV and 3 Gy for OARs. The dwell times and dose distributions were modified manually using graphical optimization to meet our dose constraints as follows: (i) for each BT session, the HR-CTV D90 (minimum dose administered to 90% of the volume with the highest irradiation) was $\geq$ 6 Gy, and bladder and rectum D2 cc (minimum dose to the most irradiated 2 cm^3) was $<$ 7 Gy; and (ii) the total HR-CTV D90 was $\geq$ 60 Gy, bladder D2 cc was $<$ 90 Gy, and rectum D2 cc was $<$ 75 Gy.

In calculating the total HR-CTV and OAR doses, all EQD2 values of whole pelvic external beam radiotherapy (WP-EBRT) (not including central shielding external beam radiotherapy (CS-EBRT)) and HDR-BT were summed according to previous reports [8, 11].

Follow-up

Gynecologists followed up with each patient every one to three months for the first two years and every three to six months from the third year after completion of treatment. Tumor status and adverse events were

assessed using patient interviews, physical and gynecological examinations, and blood tests. Patients generally underwent MRI and ^{18}F-fluorodeoxyglucose positron emission tomography one to two months after treatment to evaluate the therapeutic effects and every six to 12 months after that. The recurrence was determined when a lesion was observed on CT or MRI findings and was confirmed through biopsy. LC duration was defined as the period between the initiation of RT and a diagnosis of local recurrence or the date of the last follow-up. Late adverse events were defined as adverse events emerging ≥ 90 days after completion of RT and were graded according to the CTCAE version 4.0.

Statistical analysis

Descriptive analysis was performed for patient and tumor characteristics, as well as treatment details according to tumor size before BT (≥ 4 cm vs < 4 cm). The Shapiro–Wilk normality test was used to examine the normality. To compare the characteristics of the groups, we used Fisher's exact test (categorical variables), Student's t-test (normally distributed continuous variables), and Mann–Whitney U test (non-normally distributed continuous variables). The 1- and 2-year LC rates were analyzed using the Kaplan–Meier method. We also examined LC by pre-treatment and pre-BT tumor diameter using the Kaplan–Meier method. Hazard ratios and their 95% confidence intervals for local recurrence were estimated through Cox proportional hazard regression analysis. Although the cut-off value was determined using median values (age, D90–100, body mass index, SCC-antigen, overall treatment time), the cut-off value of tumor size before treatment and BT was intentionally determined from the results of the receiver operating characteristic (ROC) analysis, the value of previous reports [6, 7, 11], and the ease of use in daily clinical practice. The Multivariable Cox regression analyses examined the association between the tumor sizes and local recurrence, adjusting for total HR-CTV D90 and age at diagnosis. These variables were selected based on the previous reports [6, 11, 15]. A two-sided *P*-value < 0.05 was identified to be statistically significant. All statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) [16].

RESULTS

Patient and tumor characteristics and treatment details are summarized in Tables 1 and 2, respectively. The median follow-up period was 31.8 months (range 6.3–63.2 months). Additionally, 12 patients (12%) developed local recurrence. The 1- and 2-year LC rates were 89% and 87%, respectively (Fig. 2). Table 3 shows the baseline data comparison between tumor size groups. As shown in Table 4, tumor size before treatment (≥ 5 cm) ($P = 0.002$) and before BT (≥ 4 cm) ($P < 0.001$) were significant factors in simple Cox hazard regression analysis. When LC by pre-treatment and pre-BT tumor diameter was evaluated, no recurrence was observed in those whose tumor diameter was ≥ 5 cm before treatment and shrank to < 4 cm before BT ($n = 13$) (Fig. 3).

Only tumor size before BT was a significant factor of LC in multiple regression analysis (Table 5). The hazard ratio was 10.11 (95% confidence interval: 1.48–68.99) for local recurrence in those with a tumor diameter ≥ 4 cm compared to those with a tumor diameter < 4 cm before BT. Figure 4 shows a scatter plot of tumor diameter before BT and D90. When the tumor diameter before BT was ≥ 4 cm, recurrence was observed regardless of D90. Here, two cases of recurrence were described despite the tumor diameter being < 4 cm before BT. One

Table 1. Patient and tumor characteristics ($n = 97$)

Characteristics			
Median age at diagnosis (years) (IQR)		57	(47–68)
Median body mass index (IQR)		22.1	(20–25.1)
FIGO 2008 (%)	IB1	13	(14%)
	IB2	12	(12%)
	IIA1	6	(6%)
	IIA2	2	(2%)
	IIB	44	(45%)
	IIIA	1	(1%)
	IIIB	17	(18%)
	IVA	1	(1%)
	IVB	1	(1%)
Histologic type (%)	SCC	97	(100%)
Median value of tumor marker: SCC-antigen (ng/ml) (IQR)		6.4	(3–15.9)
Median tumor size before treatment (mm) (IQR)		41	(32–54)
Median tumor size before BT (mm) (IQR)		29	(21–37)
Median HR-CTV at initial BT (ml) (IQR)		51	(38.5–66.5)

Abbreviations: IQR = interquartile range, SCC = squamous cell carcinoma, FIGO = International Federation of Gynecology and Obstetrics, BT = brachytherapy, HR-CTV = high-risk clinical target volume

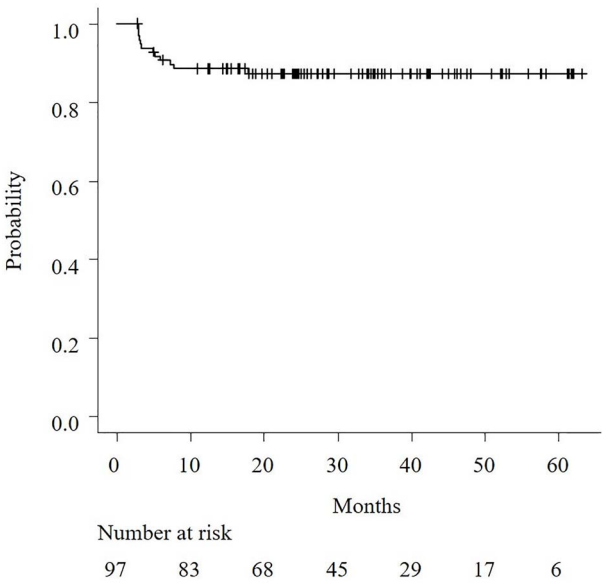

Fig. 2. Kaplan–Meier curves for LC. The LC rate was 89% for 1 year and 87% for 2 years.

Table 2. Treatment details and histogram parameters ($n = 97$)

Characteristics			
Median overall treatment time (days) (IQR)		49	(45–52)
Chemotherapy (%)			
Without		24	(25%)
With	wCDDP	58	(60%)
	wCDGP	15	(15%)
EBRT (%)			
WP dose (Gy)	19.8/20	19	(20%)
	30/30.6	69	(71%)
	39.6/40	9	(9%)
CS dose (Gy)	10/10.8	9	(9%)
	19.8/20	69	(71%)
	30/30.6	19	(20%)
Brachytherapy			
Median number of fractions	3	10	(10%)
	4	87	(90%)
Applicator (%)	Tandem + Ovoids	85	(88%)
	Tandem + Cylinder	12	(12%)
Histogram parameters calculated by EQD2			
Median total HR-CTV D90 (Gy) (IQR)		66.3	(62–70.4)
Median total HR-CTV D95 (Gy) (IQR)		61	(57.7–65.8)
Median total HR-CTV D100 (Gy) (IQR)		50.5	(47.2–53.7)
Median rectum D2 cc (Gy) (IQR)		66.9	(60.9–72)
Median bladder D2 cc (Gy) (IQR)		80.4	(73.5–87.2)

Abbreviations: IQR = interquartile range, WP = whole pelvis, CS = central shielding, EBRT = external beam radiotherapy, CDDP = cisplatin, CDGP = nedaplatin, HR-CTV = high-risk clinical target volume, EQD2 = equivalent dose in 2 Gy, D90–100 and D2 cc = minimum dose received by the 90–100% and 2 cc volume with highest irradiation

case relapsed because BT did not adequately cover the vaginal submucosal infiltration. The other was a case of adenosquamous carcinoma diagnosed following salvage surgery when the lesion remained after three months from chemoradiotherapy completion.

Late adverse events in the rectum, bladder and sigmoid are shown in Table 6. A grade 3 adverse event of the rectum, sigmoid colon and bladder was defined as hemorrhage requiring transfusion.

DISCUSSION

Clinical outcomes regarding the LC of CT-based 3D-IGBT for squamous cell carcinoma were analyzed in this study. The LC rate was 89% at 1 year and 87% at 2 years. Furthermore, multivariate analysis showed that pre-BT tumor diameter was a significant factor of LC and had a higher hazard ratio than pre-treatment tumor diameter. Several studies have reported factors of LC from treatment schedules with CS. For example, Murakami *et al.* [8] reported a 3-year LC of 91.7% in an analysis of 51 cases (48 cases of squamous cell carcinoma and three cases of adenocarcinoma). In contrast to the current study, their analysis included cases with and without CS and non-squamous cell carcinoma. As a result of univariate analysis, they reported that an HR-CTV D90 $\geq$ 60 Gy was a significant factor of LC. However, in their report, the effect of tumor diameter before BT on LC was not fully investigated. Moreover, Kawashima *et al.* [11] reported a 3-year LC of 89% in an analysis of 84 cases (71 cases of squamous cell carcinoma and 13 cases of adenocarcinoma). Their report, like ours, analyzed only cases of IC irradiation and those with CS. Multivariate analysis in their study identified histological type (adenocarcinoma) and pre-treatment tumor diameter ($\geq$4.5 cm) to be risk factors for local recurrence. However, they analyzed the HR-CTV as a variable, not the tumor diameter at the time of the first BT.

In the current study, we considered the tumor diameter before BT and the HR-CTV at the first BT as potential factors of LC. However, pre-BT tumor diameter was evaluated as it can be measured by MRI, making it a more reproducible variable since these factors as correlated. Moreover, the effect of histological type on LC has already been reported [11, 17]. The analysis that included adenocarcinoma was considered problematic as adenocarcinoma is a risk factor for local recurrence. This study examined only squamous cell carcinoma and performed MRI analysis before BT in all cases to increase reliability.

Dimopoulos *et al.* [6] reported that cases with tumor diameters > 5 cm at the time of diagnosis had different control rates depending on whether they were 2–5 or > 5 cm at BT. They performed MRI-based treatment without CS for a group of subjects with various histological types. They reported that an HR-CTV D90 $\geq$ 87 Gy is required to achieve 95% LC. Our results showed an LC rate of 97% in the group with a pre-BT tumor diameter < 4 cm. Even if the tumor diameter is 5 cm or more before the start of treatment, excellent results can be obtained if the tumor responds well to EBRT. The reason is that the tumor diameter before BT reflects the radiosensitivity and

Table 3. Summary of baseline data comparison between tumor size group ≥ 4 cm and < 4 cm

Variable		Tumor size before BT		
		≥ 4 cm ($n = 23$)	< 4 cm ($n = 74$)	P
Age at diagnosis (years)				0.2*
	median	51	59.5	
	IQR	44.5–66	47.3–67.8	
Body mass index (kg/m^2)				0.38*
	median	21.8	22.5	
	IQR	13.2–37.2	15.9–42.4	
Tumor size before EBRT (%)				< 0.001¶
	< 5 cm	3 (13%)	61 (82%)	
	≥ 5 cm	20 (87%)	13 (18%)	
Chemotherapy (%)				0.42¶
	With	19 (83%)	54 (73%)	
	Without	4 (17%)	20 (27%)	
Total HR-CTV D90 (Gy)				0.011†
	median	63.5	67.7	
	IQR	60.7–66.8	63–71.4	
Total HR-CTV D95 (Gy)				0.031†
	median	59	62.6	
	IQR	57.2–63.3	58.3–66.4	
Total HR-CTV D100 (Gy)				0.23†
	median	49.6	51.1	
	IQR	47.4–52.6	46.7–54.6	
Overall treatment time (days)				0.77†
	median	49	47.5	
	IQR	47–51	45–52	

Abbreviations: BT = brachytherapy, EBRT = external beam radiotherapy, HR-CTV = high-risk clinical target volume, IQR = interquartile range, D90–100 = minimum dose received by the 90–100% volume with highest irradiation
*= Mann–Whitney U test ¶= Fisher's exact test †= Student's t-test

tumor volume. Furthermore, baseline D90 was significantly lower in the pre-BT tumor diameter ≥ 4 cm group (Table 3). In larger tumor diameter groups, tumor dose may have decreased to meet dose constraints of OARs. Ohno *et al.* [18] reported that the 5-year LC rate of tumors > 6 cm before treatment was also 94% using Trocar Point Needles (Nucletron; Elekta, Stockholm, Sweden) in combination with IC-BT. Their study divided tumor diameter before treatment into three groups: ≤ 4 cm, 4–6 cm, and ≥ 6 cm. When the HR-CTV D90 values were compared, no significant difference was observed in the D90 values among the groups. Thus, interstitial-BT (IS-BT) makes it possible to irradiate large tumors with a sufficient dose and may improve LC. HR-CTV D90 values previously reported as an LC factor [6, 7] were not significant in this study. Ohno *et al.* [18] reported excellent treatment outcomes with a median HR-CTV D90 of 66.5 Gy and a 5-year LC rate of 94% using CS-EBRT with a 3 cm width for pretreatment tumor diameter > 6 cm group. This study's CS width was 4 cm; thus, IC-BT for tumors over 5 cm before treatment showed 30% recurrence (Table 4). Kawashima *et al.* [11] also performed a 4 cm wide CS-EBRT as treatment with a median of 73.4 Gy of HR-CTV D90. They reported 23% local failure in the pretreatment tumor diameter of 45 mm or larger group, which is consistent with our result. The LC rate differs greatly between Ohno *et al.* and this study because the contribution of CS-EBRT dose to the tumor could not be accurately evaluated for each width of CS. Using a phantom, Tamaki *et al.* [19, 20] reported the contribution of dose to tumors of 3 cm and 4 cm wide CS-EBRT. In clinical practice, tumor locations and extents vary, making it more difficult to analyze CS-EBRT's dose contribution to tumors than phantom analysis. One of the reasons HR-CTV D90 was not an LC factor in this study may be that the effect of CS-EBRT on tumors has not been fully evaluated.

This study had several limitations. The retrospective and single institutional nature of this study is a limitation. In addition, while our outcomes are based on a higher number of cases than those previously reported, our report is limited to cases of CT-based treatment schedules using CS of 4 cm width, squamous cell carcinoma, and IC-BT. Furthermore, CS hinders the accurate evaluation of the dose to the tumor and normal organs. Although Tamaki *et al.* [19, 20] reported measuring the effects of CS on tumors and normal organs using a phantom, the dose contribution of EBRT with the CS technique to the HR-CTV is unclear.

In this study, the pre-BT tumor diameter (≥ 4 cm) was the most important factor of LC. Favorable results are obtained from the current treatment using IC-BT for patients with a pre-BT tumor diameter < 4 cm. However, if the tumor diameter is ≥ 4 cm before BT, it may

Table 4. Simple regression analysis for LC (*n* = 97)

					Simple regression analysis		
Factors		Total	Local failure, n (%)		Hazard ratio	95% CI	P
Tumor size before BT	≥ 4 cm	23	10	(43%)	19.44	4.25–88.87	< 0.001
	< 4 cm	74	2	(3%)			
Tumor size before EBRT	≥ 5 cm	33	10	(30%)	11.33	2.48–51.76	0.002
	< 5 cm	64	2	(3%)			
Age at diagnosis (years)	≥ 58 years	48	3	(6%)	0.31	0.08–1.13	0.075
	< 58 years	49	9	(18%)			
Total HR-CTV D90 (EQD2)	≥ 66.3 Gy	49	5	(10%)	0.73	0.23–2.31	0.6
	< 66.3 Gy	48	7	(15%)			
Total HR-CTV D95 (EQD2)	≥ 61.0 Gy	49	5	(10%)	0.73	0.23–2.31	0.6
	< 61.0 Gy	48	7	(15%)			
Total HR-CTV D100 (EQD2)	≥ 50.5 Gy	50	7	(10%)	0.71	0.22–2.22	0.55
	< 50.5 Gy	47	7	(15%)			
Body mass index	≥ 22.1	49	6	(12%)	0.92	0.3–2.87	0.89
	< 22.1	48	6	(13%)			
FIGO stage	IIB-IV	64	11	(17%)	5.96	0.77–46.19	0.087
	I-IIA	33	1	(3%)			
Tumor marker: SCC-antigen	≥ 6.4 ng/ml	49	7	(14%)	1.35	0.43–4.26	0.61
	< 6.4 ng/ml	48	5	(10%)			
Applicator	T + O	85	11	(13%)	1.63	0.21–12.65	0.64
	T + C	12	1	(8%)			
Chemotherapy	With	73	10	(14%)	1.7	0.37–7.77	0.49
	Without	24	2	(8%)			
Number of BT	3 fractions	10	7	(20%)	1.78	0.39–8.11	0.46
	4 fractions	87	7	(11%)			
Overall treatment time	≥ 49 days	49	7	(14%)	1.38	0.44–4.33	0.59
	< 49 days	48	7	(10%)			

BT = brachytherapy, HR-CTV = high-risk clinical target volume, EBRT = external beam radiotherapy, FIGO = International Federation of Gynecology and Obstetrics, SCC = squamous cell carcinoma, D90–100 = minimum dose received by the 90–100% volume with highest irradiation, CI = confidence interval

Table 5. Hazard ratios for local recurrence (*n* = 97)

	Multiple regression analysis		
Variables	Hazard ratio	95% CI	P
Tumor size before BT, ≥ 4 cm vs < 4 cm	10.11	1.48–68.99	0.018
Tumor size before EBRT, ≥ 5 cm vs < 5 cm	2.56	0.4–16.32	0.32
Total HR-CTV D90 (Gy)	1	0.89–1.12	0.98
Age at diagnosis (years)	0.98	0.94–1.03	0.48

Abbreviations: BT = brachytherapy, EBRT = external beam radiotherapy, HR-CTV = high-risk clinical target volume, CI = confidence interval, D90 = minimum dose received by the 90% volume with highest irradiation

Table 6. Number of patients with late complications (Graded according to CTCAE version 4.0)

Grade	0	1	2	3	4	5
Rectum (%)	70 (72%)	18 (19%)	3 (3%)	5 (5%)	0	1 (1%)
Sigmoid (%)	92 (95%)	1 (1%)	1 (1%)	3 (3%)	0	0
Bladder (%)	89 (92%)	6 (6%)	1 (1%)	1 (1%)	0	0

Abbreviations: CTCAE = Common Terminology Criteria for Adverse Events

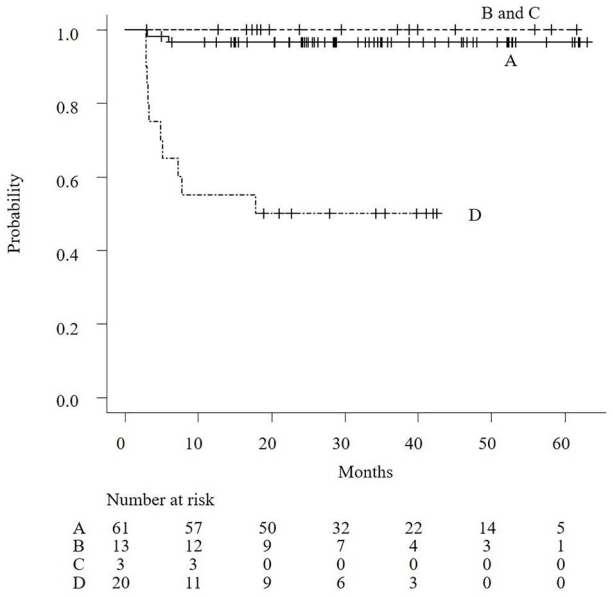

Fig. 3. Kaplan–Meier curves for LC. (A) Tumor size before treatment < 5 cm and before BT < 4 cm (n = 61, 2-year LC rate was 97%). (B) Tumor size before treatment ≥ 5 cm and before BT < 4 cm (n = 13, 2-year LC rate was 100%). (C) Tumor size before treatment < 5 cm and before BT ≥ 4 cm (n = 3, 2-year LC rate was 100%). (D) Tumor size before treatment ≥ 5 cm and before BT ≥ 4 cm (n = 20, 2-year LC rate was 50%). Line B and C overlap.

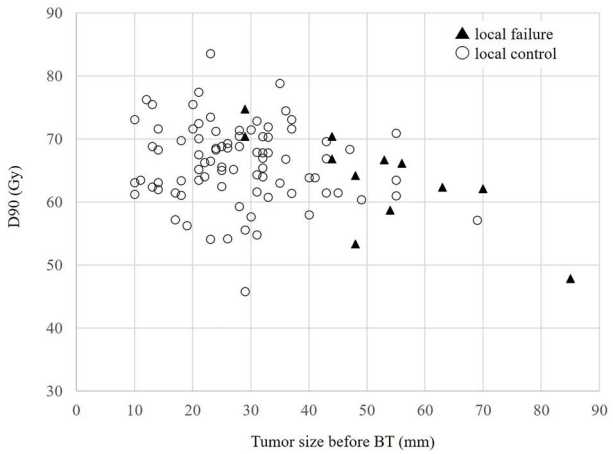

Fig. 4. Scatter diagrams of tumor size before BT and D90 of 97 patients. Open circles indicate patients without LC, and a filled triangle indicates local failure.

be necessary to consider trying interstitial (IS)-brachytherapy (BT) or the influence of CS-EBRT on the tumor as a possible optimal treatment method.

CONFLICT OF INTEREST

The authors declare they have no conflicts of interest.

PRESENTATION AT A CONFERENCE

The content of this study is to be presented at the 81st annual meeting of the Japanese Radiological Society.

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