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Dosimetric research into target regions and organs at risk in three-dimensional intracavitary brachytherapy techniques for Chinese patients with cervical carcinoma

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ABSTRACT

The present study aimed to compare the dosages of target regions and organs at risk (OARs) in 3D intracavitary brachytherapy (ICBT) and conventional 2D ICBT for Chinese patients with cervical carcinoma. ICBT was performed in a total of 66 patients with Stage IB to IVA cervical carcinoma who had not received surgery but who had received whole-pelvic external-beam radiotherapy (EBRT). Plans for the 3D-ICBT and the conventional 2D-ICBT were individually designed for every patient. The dosages differences between the target regions and the OARs in patients with each of the various stages of cervical carcinoma were compared between the two ICBT plans. There was no significant difference in the dose at Point A between the two ICBT plans. However, the CTVhr-D_{90}, CTVhr-D_{100} and CTVir-D_{90} in 3D-ICBT were much higher than in 2D-ICBT, especially in Stage IIB ($P < 0.05$). As compared with conventional 2D-ICBT, the dosages of D_{ICRU} and $D_{2.0cm^3}$ in the rectum/bladder, and $D_{2.0cm^3}$ in the sigmoid/small bowel were decreased significantly in 3D-ICBT ($P < 0.05$). For patients with Stage IIA, IIB and IIIB, the $D_{2.0cm^3}$ in the rectum/bladder was significantly reduced in 3D-ICBT ($P < 0.05$). It was demonstrated that, in Chinese patients, 3D-ICBT for cervical carcinoma could optimize the target coverage and reduce the dosages to the OARs compared with conventional 2D-ICBT.

Keywords: cervical carcinoma; three-dimensional brachytherapy; target volume; organs at risk; dosimetry

INTRODUCTION

Cervical carcinoma is one of the most common malignancies in China. The incidence of cervical carcinoma in Chinese married women ranks first in female malignant tumors. It is also the cancer that causes the greatest number of deaths in women. Radiotherapy is an excellent modality for the treatment of cervical carcinoma, and intracavitary brachytherapy (ICBT) is an important part of standard clinical treatments. Conventional 2D-ICBT uses the recommended Point A and reference points of organs at risk (OARs) (rectum and bladder) from the International Commission on Radiological Units (ICRU) Report 38 to estimate the dose. However, the estimated dose does not necessary reflect the actual radiation dose in the target and OARs in 3D space [1]. Recently, an image-guided (computed tomography– or magnetic resonance imaging–guided) 3D-ICBT technique has been widely used in cervical carcinoma clinical treatment. The advantages of the 3D-ICBT technique are the possibilities for conforming the dose given by BT to the anatomy of each target volume, at the same time, taking into account both tumor regression and the position of nearby OARs [2]. In China, there are only a few units with the capacity to perform 3D-ICBT for cervical carcinoma with less experience. The dosimetric and clinical feasibility of this technique for use in a larger Chinese patient group with

cervical carcinoma has yet to be demonstrated. In this work, we studied the use of the 3D-ICBT technique to boost the radiation dose for the treatment of patients with cervical carcinoma with the aim of improving target dose coverage without compromising the OARs. The present dosimetric study compared the treatment plans of 3D- and 2D-ICBT to provide data for clinical applications in Chinese patients with cervical carcinoma.

MATERIALS AND METHODS

Patients and tumor characteristics

We recruited a total of 66 patients with cervical carcinoma with a Karnofsky performance status (KPS) of ≥70, of whom 64 had squamous cell cancer and 2 had adenocarcinoma. The mean age of the patients was 52.10 (range 41–62) years. These subjects were all Chinese of Han origin and came from the north-east area of China. The patients were admitted to the China–Japan Union Hospital of Jilin University in the period between September 2008 and June 2010. The initial locoregional staging resulted in a clinical evaluation of IB (4 cases), IIA (14 cases), IIB (21 cases), IIIA (6 cases), IIIB (18 cases) and IVA (3 cases), performed by a well-trained gynecologic surgeon and radiation oncologist, according to the 1995 Federation International of Gynecology and Obstetrics (FIGO) classification.

All patients received 45 Gy to 50.4 Gy pelvic EBRT with either a 3D conformal radiotherapy (3DCRT) technique (58 patients) or an intensity-modulated radiotherapy (IMRT) technique (8 patients) before 3 to 4 fractions of 3D-ICBT (once a week) with a prescribed dose (PD) of 7 Gy were administered to the high-risk clinical target volume (CTVhr). Chemotherapy was given during the EBRT in the form of intravenous cisplatin 30 to 40 mg/m^2 once a week for 5 weeks in 45 of 66 patients (68.18%). The present study was approved by the ethics committee of Jilin University, Changchun, China.

Equipment and applicator

The Micro-Selectron High-Dose-Rate ^{192}Iridium Brachytherapy System (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden), Fletcher System Applicator (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden), Digital X-rays Simulator (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden), PLATO Treatment-Planning System (Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden) and Large-Aperture CT Simulator (Siemens, Germany) were employed.

ICBT procedure and image acquisition

All patients underwent pre-BT gynaecological examination in the lithotomy position. The cancer topography in regard to the location of the cervical os was diagrammatically depicted. A Foley urinary catheter was inserted and fixed against the bladder neck, with a bladder balloon filled with 7 ml of saline-diluted meglumine diatrizoate injection. It was left open to drain out completely and then continuously. After this, all patients underwent high-dose-rate (HDR) ICBT with an applicable applicator. The vagina was then packed with gauze to push away the rectum and bladder and to fix the applicator. The strip of narrow, thin gauze was soaked in diluted barium sulfate in order to determine the location of the posterior wall of the vagina. A tube with an interval of 1 cm per two marks was inserted into the rectum and held in position in order to determine the direction of the rectum, and to provide dose-monitoring observation points.

The patients underwent the X-ray simulation with two perpendicular (0 and 90 degrees) digital radiographs (DRs) in order to determine the tandem and ovoid position. Patients were kept in the same position for the pelvic CT scan, ranging from the sacroiliac joints to 2 cm below the ischial tuberosity, with 2 mm for layer spacing and layer thickness. The images were reconstructed on the CT simulation system workstation. For the 2D-ICBT plan, the source loading pattern was based on the Manchester system, using tandem and ovoid applicators. The loading of the source position into the 3D-ICBT plan was determined by a physicist according to the shape of the target region.

Treatment planning

Based on the recommendations of the Gynecologic Groupe European de Curietherapie, European Society for Therapeutic Radiology and Oncology (GEC-ESTRO), the target regions and OARs in patients were contoured, while referencing MRI images before/after EBRT. The regression of the tumor might vary from patient to patient after EBRT. The target regions included the CTVhr (including the residual tumor at the time of brachytherapy application, the whole cervix, and the adjacent residual pathologic tissue, if present) and the intermediate-risk clinical target volume (CTVir); OARs included the bladder, rectum, sigmoid and small bowel. Planning was performed using pre-treatment CT data transferred to a planning computer.

According to the coordinate system of the applicator set on the CT data, planes similar to those of the DR images were mapped to determine the recommended reference points from the ICRU Report 38 for the 2D-ICBT plan. Point A was defined as a point 2 cm up from the flange of the intrauterine source and 2 cm lateral from the central canal. The ICRU rectal reference point was located on the axis of the intravaginal ovoid applicator 5 mm behind the posterior vaginal wall. The ICRU bladder reference point was taken on an anterio–posterior line drawn through the centre of the Foley balloon at its posterior surface.

For all patients, two different treatment plans were created. The 3D-ICBT plans were optimized and were clinically used for patient treatment. The 2D-ICBT plans were designed to compare the dosimetric differences. On the basis of CT images, the 2D-ICBT plans were given 3 to 4 fractions with a PD of 7 Gy for Point A, so the dose at Point A was optimized without exceeding the dose constraints of D_{ICRU} of the bladder and rectum. The 3D-ICBT plans were optimized for CTVhr-D_{90} (the lowest dose for 90% of the CTVhr) and $D_{2.0cm^3}$ (the minimum dose to the most irradiated 2 cm^3 volume) of OARs. When the dose constraints of the CTVhr/ir and the OARs were not realized simultaneously, the dose constraints of the OARs were used as the conditions for priority satisfaction. Dose calculation and reporting were based on the total (EBRT + BT) biologically equivalent dose in 2-Gy fractions (EQD2). The linear quadratic (LQ) model for radiation damage repair was used with $\alpha/\beta = 10$ Gy for the tumor target, and $\alpha/\beta = 3$ Gy for the OARs. The EQD2 of the EBRT and the BT was then added to evaluate the optimized plan with regard to the dose–volume-histogram (DVH) constraints. The goal of the combined EBRT and BT was to achieve

that (i.e. 3D-ICBT plan: CTVhr-$D_{90} \geq 85$ Gy, CTVir-$D_{90} \geq 60$ Gy, bladder $D_{2.0cm^3} \leq 90$ Gy, rectum/sigmoid/small bowel $D_{2.0cm^3} \leq 75$ Gy; 2D-ICBT plan: 80–90 Gy at point A, bladder $D_{ICRU} \leq 90$ Gy, rectum $D_{ICRU} \leq 75$ Gy) [3, 4]. The DVH and the reference doses were used to design the treatment plans. The dose at Point A (left A1, right A2), CTVhr-D_{90}/D_{100} and CTVir-D_{90}/D_{100} of target were calculated in the 2D and 3D-ICBT plans, respectively. D_{ICRU} of the bladder and rectum, and the $D_{2.0cm^3}$ of the OARs (bladder, rectum, sigmoid and small bowel) were compared in the two treatment regimens.

Data processing and statistical analysis

Data were presented as mean ± standard deviation. Comparison of the data for the two groups was made using a paired *t*-test. Statistical significance was set at $P < 0.05$ at a two-sided level. All statistical analysis were performed using SPSS (version 17.0; SPSS, Chicago, IL, USA).

RESULTS

Dosimetric comparison of target volumes in two plans

The isodose distribution in the 2D/3D-ICBT plans is shown in Fig. 1. There was no significant difference between the dose of Point A in the two treatment plans. The CTVhr-D_{90}, CTVhr-D_{100}, CTVir-D_{90} and CTVir-D_{100} in the 3D-ICBT plans were higher than those in the 2D-ICBT plans, and there was a statistically significant difference in the CTVhr-D_{90}, CTVhr-D_{100} and CTVir-D_{90} between the two treatment plans ($P < 0.05$) (see Table 1). The CTVhr-D_{90} in Stage IIA to IVA, CTVhr-D_{100} in Stage IIA and IIB, and CTVir-D_{90} and CTVir-D_{100} in Stage IIB in 3D-ICBT plans were significantly higher than those in 2D-ICBT plans ($P < 0.05$) (see Table 2). The results suggested that 3D-ICBT has a significant advantage compared with 2D-ICBT in dose coverage of the tumor target, especially in Stage IIB.

Dosimetric comparison of OARs in the two treatment plans

Compared with the 2D-ICBT plans, the D_{ICRU} of the bladder and rectum, and the $D_{2.0cm^3}$ of the bladder/rectum/sigmoid/small bowel in the 3D-ICBT plans were significantly lower ($P < 0.05$) (see Table 3). In the 3D-ICBT plans, the bladder D_{ICRU} for Stage IB, IIA and IIIB, the rectum D_{ICRU} with Stage IB, the bladder $D_{2.0cm^3}$ with Stage IB, IIA, IIB and IIIB, and the rectum $D_{2.0cm^3}$ with Stage IIA to IIIB were reduced significantly compared with the equivalents in the 2D-ICBT plans ($P < 0.05$) (see Table 4). Our results showed that the dose to the OARs in the 3D-ICBT plans could be significantly reduced compared with that in the 2D-ICBT plans, especially the dose to the bladder and rectum for Stage IIA, IIB and IIIB cervical carcinoma. According to the basic assessment standard for planning (fulfilled simultaneously: CTVhr-$D_{90} \geq 80$ Gy, bladder $D_{2.0cm^3} \leq 90$ Gy, and rectum $D_{2.0cm^3} \leq 75$ Gy), the standard-reaching rate (qualified number with planning aim dose of CTVhr-D_{90} and dose constraints of OARs/total number of patients × 100%) was 36.36% in the 2D-ICBT plans (Stage IB with 100.00%, IIA with 42.86%, IIB with 28.57%, IIIA with 33.33%, IIIB with 22.22% and IVA with 66.67%, respectively), but 96.97% in the 3D-ICBT plans, because only two patients with Stage IIIB failed to achieve the assessment standard. However, only 7.58% of 2D-ICBT plans (Stage IB with 75.00%, IIA with 14.29%, IIB with 0.00%, IIIA with 0.00%, IIIB with 0.00% and IVA with 0.00%, respectively) could meet the higher assessment standard (CTVhr-$D_{90} \geq 85$ Gy) compared with 59.09% in the 3D-ICBT plans (Stage IB with 100.00%, IIA with 100.00%, IIB with 71.43%, IIIA with 50.00%, IIIB with 5.56% and IVA with 66.67%, respectively) (see Table 5).

DISCUSSION

The combination of ICBT and EBRT is considered to be the standard treatment for cervical carcinoma. Historically, the dosing parameters for BT have used a system that specified the dose to standardized reference points from the ICRU Report 38. This system, based on 2D images, is still used in the majority of current clinical practice in China. Because of the high probability of insufficient tumor dose and excessive exposure to normal tissue in 2D-ICBT plans, the 3D-ICBT is becoming the new gold standard for cervical carcinoma BT [5–7]. Research into the development of the 3D-ICBT technique has been a major focus for cervical carcinoma radiotherapy in China.

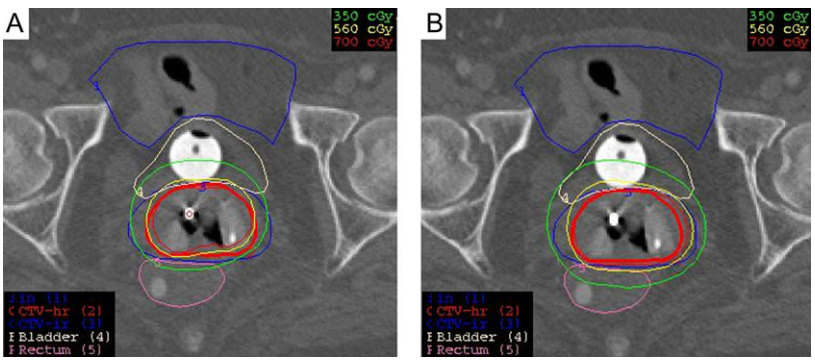

Fig. 1. The isodose distribution in the 2D- and 3D-ICBT plans. 2D-ICBT (A) and 3D-ICBT (B) plan images with crosscut view showing CTVhr (bold red delineation) and CTVir extension (dark blue delineation). The fine red line is the 100% isodose line, yellow was 80%, and green was 50%. White, purple and cyan-blue area showed bladder, rectum, and small bowel, respectively. 3D-ICBT plan (B) with optimized dose distribution resulting in better target volume coverage.

Table 1. Comparison of target dose distribution in two treatment plans

Target	Equivalent dose (Gy)		*t*-value	*P*-value
	2D-ICBT plan	3D-ICBT plan		
ICRU-A1	78.06 ± 5.07	77.94 ± 9.16	0.12	0.91
ICRU-A2	78.15 ± 5.52	77.47 ± 8.59	0.77	0.45
CTVhr-D_{90}	82.25 ± 3.58	86.09 ± 4.15[a]	−7.86	0.00
CTVhr-D_{100}	70.05 ± 4.66	71.32 ± 3.37[a]	−2.79	0.01
CTVir-D_{90}	69.50 ± 3.35	70.74 ± 3.10[a]	−3.40	0.00
CTVir-D_{100}	60.03 ± 3.50	60.71 ± 2.63	−1.96	0.06

[a]$P < 0.05$ vs 2D-ICBT plan.

In recent years, more sophisticated recommendations have been published that put emphasis on using 3D-ICBT to optimize the dose coverage to the tumor while reducing the dose to adjacent critical structures [8–10]. The target concept according to the recommendations is based in principle on three CTVs [the CTVhr, the CTVir and the low-risk clinical target volume (CTVlr)] according to tumor load (and hence risk for recurrence) [11]. The CTVhr has a major risk of local recurrence because of residual macroscopic disease. The intent is to deliver as high a total dose as possible that is appropriate for eradicating all residual macroscopic tumor (usually >80 Gy). The CTVir has a major risk of local recurrence in areas that correspond to the initial macroscopic extent of disease, with, at most, residual microscopic disease at the time of BT. The intent is to deliver a total radiation dose appropriate for curing significant microscopic disease in cervical carcinoma, which corresponds to a dose of ≥60 Gy. The CTVlr should be given a subclinical controlled dose, mainly by external irradiation. The guideline recommends the use of the CTVhr as the primary evaluation index, and the CTVir as an auxiliary evaluation index (CTVhr-$D_{90} \geq 85$ Gy, CTVir-$D_{90} \geq 60$ Gy). OARs in cervical carcinoma BT include the bladder, rectum, sigmoid and small bowel. If the whole volume of the OARs receive over 60 to 70 Gy, inflammation, ulcers, necrosis, fibrosis and other side effects may occur [12, 13].

In this study, Chinese patients with cervical carcinoma in Stage IB to IVA, mainly IIA to IIIB, were studied in order to make a dosimetric comparison between 3D-ICBT and conventional 2D-ICBT planning for target volumes and OARs. The results showed that the CTVhr-D_{90}, CTVhr-D_{100} and CTVir-D_{90} in 3D-ICBT were significantly higher than those in conventional 2D-ICBT in the case of a similar dose for Point A in the two plans. The 3D-ICBT was better than 2D-ICBT in terms of optimizing the target dose in Chinese patients. For most Chinese patients with a small uterus, and tumor-susceptible invasion to the dorsal part of cervix, Point A (2 cm above and 2 cm lateral to the cervical os) is usually outside the target region. In addition, due to the preferential consideration of dose constraints to the OARs in 2D/3D-ICBT plan optimization, our results showed no significant difference in the dose at Point A between 2D- and 3D-ICBT plans. Using the CTVhr instead of Point A as the cervical carcinoma target evaluation index might respond better to the target dose. Several other studies have confirmed that 3D-ICBT could improve the prescription dose to the target volume and that point dose assessment might not be accurate [14–16].

However, the effect of 3D-ICBT on the target volume in Chinese patients with cervical carcinoma of different stages has not been fully clarified. According to the analysis for different stages of cervical carcinoma, it was demonstrated that the CTVhr-D_{90}/D_{100} of Stage IIA, the CTVhr-D_{90}/D_{100} and the CTVir-D_{90}/D_{100} of Stage IIB, CTVhr-D_{90} of Stage IIIA, IIIB and IVA in 3D-ICBT plans were significantly higher than those in 2D-ICBT plans. 3D-ICBT plans could achieve a significantly higher target dose coverage in cervical carcinoma of Stage IIA to IVA, especially Stage IIB. The reason may be that a tumor of Stage IIB is large and has parametrial invasion, but no extension to the pelvic wall. It is possible to achieve relatively good target dose coverage by 3D-ICBT dose optimization while minimising the dose to the OARs. In consideration of the local extension of the tumor in Stage IIB, the target dose coverage might benefit from the ICBT combined with interstitial BT technique. A comparative study based on an expanded number of patients should be integrated in future prospective validation. For patients with Stage IIIB, with simple application of ICBT it might be difficult to achieve the required dose because the tumor extends to the pelvic wall and has a larger and more eccentric target area.

There is an inhomogeneous dose distribution in the tissues adjacent to the sources with ICBT. The hollow OARs walls adjacent to the applicator, such as the inferior–posterior bladder wall, the anterior rectal wall and sigmoid colon wall, are irradiated by the ICBT sources with a high inhomogeneous dose. D_{ICRU} to the the bladder and rectum could be recognized as evaluation parameters in 2D-ICBT, but the dose to the sigmoid and small bowel could not be evaluated because there are no dose evaluation standards for them. However, in some patients, the sigmoid and small bowel which are closer to the tumor, might receive a higher irradiation dose than the rectum. So, the evaluation parameters for the OARs in 2D-ICBT are not comprehensive. Junfang *et al.* reported that CT-guided 3D-ICBT for Chinese patients with cervical carcinoma did not significantly increase the irradiation dose to the OARs [16]. Several investigators have reported the relationship between these 3D dose–volume parameters and dose-limiting toxicities of OARs. These data suggest that the ICRU bladder/rectal point were not the exact location in the bladder/rectum receiving the highest dose, and the $D_{2.0cm^3}$ of the bladder/rectum may possess good predictive value for bladder and rectal injury [17, 18]. Many reports have demonstrated that the increase in the $D_{2.0cm^3}$ of the rectal wall was positively correlated with the incidence of radiation-induced proctitis, and they suggested that the dose constraint had contributed to the low rate of rectal complication [19, 20]. In the present study, we found a significant difference between the dose to the D_{ICRU}/$D_{2.0cm^3}$ of the bladder and rectum, and the $D_{2.0cm^3}$ of the sigmoid and small bowel in 3D-ICBT as compared with the corresponding dose in 2D-ICBT. Our results indicated that the actual dose to the OARs that may be exposed to high doses of irradiation in 3D-ICBT is lower than that in 2D-ICBT. This is in good agreement with some studies that reported that 3D-ICBT could significantly reduce the risk of

Table 2. Comparison of dose distribution between two treatment plans in different stages of cervical carcinoma

Stage	Number	Target	Equivalent dose (Gy)		*t*-value	*P*-value
			2D-ICBT plan	3D-ICBT plan		
IB	4	ICRU-A1	75.98 ± 6.45	71.81 ± 5.63	1.16	0.33
		ICRU-A2	77.87 ± 7.09	73.00 ± 9.17	0.81	0.48
		CTVhr-D_{90}	88.01 ± 4.42	89.98 ± 6.36	−0.67	0.55
		CTVhr-D_{100}	75.49 ± 4.15	73.44 ± 3.70	1.51	0.23
		CTVir-D_{90}	72.20 ± 5.09	71.99 ± 4.13	0.09	0.93
		CTVir-D_{100}	62.40 ± 4.37	61.21 ± 2.60	0.47	0.67
IIA	14	ICRU-A1	79.67 ± 3.54	79.97 ± 10.27	−0.12	0.91
		ICRU-A2	81.41 ± 4.38	80.61 ± 10.09	0.42	0.68
		CTVhr-D_{90}	84.34 ± 2.29	89.39 ± 4.43[a]	−3.55	0.00
		CTVhr-D_{100}	71.06 ± 4.10	72.34 ± 4.24[a]	−2.47	0.03
		CTVir-D_{90}	71.03 ± 2.50	72.25 ± 3.25	−1.90	0.08
		CTVir-D_{100}	60.85 ± 4.02	60.78 ± 2.84	0.13	0.90
IIB	21	ICRU-A1	79.06 ± 3.08	78.26 ± 9.78	0.43	0.67
		ICRU-A2	78.06 ± 3.46	77.14 ± 8.52	0.53	0.60
		CTVhr-D_{90}	82.39 ± 3.45	86.80 ± 2.65[a]	−6.22	0.00
		CTVhr-D_{100}	69.01 ± 5.11	71.38 ± 2.46[a]	−2.55	0.02
		CTVir-D_{90}	68.76 ± 3.78	71.03 ± 2.32[a]	−3.79	0.00
		CTVir-D_{100}	59.43 ± 3.57	61.15 ± 2.43[a]	−2.66	0.02
IIIA	6	ICRU-A1	76.79 ± 4.45	80.03 ± 4.14	−2.51	0.05
		ICRU-A2	77.95 ± 5.54	80.06 ± 4.95	−2.23	0.08
		CTVhr-D_{90}	79.47 ± 3.74	85.21 ± 2.50[a]	−3.50	0.02
		CTVhr-D_{100}	68.57 ± 6.01	70.58 ± 2.32	−0.95	0.39
		CTVir-D_{90}	67.62 ± 4.36	69.40 ± 3.25	−1.41	0.22
		CTVir-D_{100}	57.60 ± 2.36	58.91 ± 1.81	−2.23	0.08
IIIB	18	ICRU-A1	78.16 ± 6.29	76.42 ± 9.30	1.11	0.28
		ICRU-A2	77.48 ± 6.41	75.98 ± 8.57	1.00	0.33
		CTVhr-D_{90}	80.44 ± 1.96	82.38 ± 2.03[a]	−2.95	0.01
		CTVhr-D_{100}	70.16 ± 3.77	70.55 ± 3.76	−0.48	0.64
		CTVir-D_{90}	69.25 ± 2.25	69.45 ± 3.34	0.29	0.77
		CTVir-D_{100}	60.43 ± 3.10	60.71 ± 3.08	−0.40	0.69
IVA	3	ICRU-A1	68.15 ± 4.53	79.25 ± 10.98	−1.92	0.19
		ICRU-A2	68.37 ± 4.67	74.76 ± 6.34	−1.71	0.23

Continued

Table 2. Continued

Stage	Number	Target	Equivalent dose (Gy)		*t*-value	*P*-value
			2D-ICBT plan	3D-ICBT plan		
		CTVhr-D_{90}	80.19 ± 3.02	84.68 ± 3.29[a]	−5.64	0.03
		CTVhr-D_{100}	67.57 ± 2.43	69.51 ± 3.06	−0.70	0.56
		CTVir-D_{90}	69.27 ± 1.71	70.32 ± 1.61	−0.56	0.63
		CTVir-D_{100}	59.61 ± 1.61	60.27 ± 1.16	−0.43	0.71

[a]$P < 0.05$ vs 2D-ICBT plan.

Table 3. Comparison of dose parameters of OARs in two treatment plans

Dose parameters of OARs	Equivalent dose EQD_2 (Gy)		*t*-value	*P*-value
	2D-ICBT plan	3D-ICBT plan		
Bladder				
D_{ICRU}	80.95 ± 8.74	76.70 ± 8.92[a]	4.52	0.00
$D_{2.0cm^3}$	80.24 ± 9.28	75.17 ± 6.64[a]	5.02	0.00
Rectum				
D_{ICRU}	73.25 ± 3.13	71.20 ± 5.10[a]	2.97	0.00
$D_{2.0cm^3}$	72.37 ± 8.07	67.55 ± 5.51[a]	5.72	0.00
Sigmoid				
$D_{2.0cm^3}$	66.24 ± 7.54	63.24 ± 6.62[a]	3.51	0.00
Small bowel				
$D_{2.0cm^3}$	66.98 ± 6.63	64.61 ± 6.45[a]	2.90	0.01

[a]$P < 0.05$ vs 2D-ICBT plan.

excessive exposure from the dose to the OARs [21, 22]. Analysis according to each stage group showed that 3D-ICBT was more effective in protecting the $D_{2.0cm^3}$ of the bladder and rectum in Stage IIA, IIB and IIIB cervical carcinoma. Our study suggested that the use of 3D-ICBT in patients with cervical carcinoma with a larger tumor size, obvious parametrial invasion and extension to the pelvic wall could significantly reduce the dose to the bladder and rectum while increasing the dose to the target. For patients with Stage IIIA cervical carcinoma, 3D-ICBT could reduce the $D_{2.0cm^3}$ to the rectum significantly compared with 2D-ICBT. The radiotherapy target range for Stage IIIA generally needs to extend a lot in the vaginal direction because the tumor involves the lower third of the vagina, and that results in an increase to the rectal and bladder irradiation volume. Among the six patients with Stage IIIA, four patients had involvement of the lower third of the vagina anterior wall in this study. Thus, the rectal protection for Stage IIIA was more obvious in 3D-ICBT.

The American Brachytherapy Society (ABS) has recommended the planning aim dose to the CTVhr and the dose constraints of the OARs [23]. It is recommended that the CTVhr has a basic dose of 80 Gy; isoequivalent dose limits of 90 Gy for the bladder and 75 Gy for the rectum are generally accepted. In the present study, only approximately one-third of patients with 2D-ICBT plans could meet these basic requirements. However, the total standard-reaching rate was >95% in the 3D-ICBT plans. Several papers have been already reported that the D_{90} of the target should receive ≥80 Gy for smaller tumors, and ≥85 Gy for larger ones in order to achieve acceptable local control [24]. If the planning aim dose to the CTVhr-D_{90} reaches 85 Gy, only 7.6% of patients with 2D-ICBT plans could fulfill the assessment standard compared with 59.09% of those with 3D-ICBT plans. According to this data, the 2D-ICBT plans for patients with early Stage IB could completely achieve the basic planning aim dose (CTVhr-D_{90} > 80 Gy), but the 2D-ICBT plans for patients in Stage IIB and IIIB with parametrial invasion would have difficulty meeting the requirement of the assessment standard. In the case of patients in Stage IVA with bladder and/or rectal invasion, the ratio of external irradiation dose (usually 50.4 Gy) to the total therapeutic dose was relatively higher than in other stages, and the invaded parts of the bladder and rectum were included in the CTVhr or CTVir. Although there was no significant difference in the dose parameters between 3D-ICBT and 2D-ICBT with Stage IVA, we considered that the practical value of 3D-ICBT for Stage IVA could not be ignored, because the target area in 3D-ICBT could be observed better and the treatment of the bladder/rectal involvement might be more accurate and have better protection of the OARs.

This study indicated that when using the 2D-ICBT technique, it was difficult to meet most of the clinically prescribed requirements. However, 3D-ICBT was suitable for early-stage cervical carcinoma, and the use of the interstitial brachytherapy (ISBT) technique (instead of parametrial supplemental external irradiation) might have a definite dosimetric advantage in locally advanced cervical carcinoma. It has been pointed out that 3D-ICBT combined with ISBT could significantly increase the target dose and reduce the dose to the OARs, especially for the protection of the bladder and rectum [4, 25, 26]. It is worth noting that in 3D-ICBT, precise definition of the target volume is of the utmost importance. MRI-based contouring became the gold standard for cervical carcinoma targets [10]. Some published data has demonstrated the feasibility and

Table 4. Comparison of dose parameters in OARs with different stages of cervical carcinoma in two treatment plans

Stage	Number	Dose parameters of OARs	Exposure dose (Gy)		*t*-value	*P*-value
			2D-ICBT plan	3D-ICBT plan		
IB	4	Bladder D_{ICRU}	83.63 ± 2.69	75.53 ± 2.09[a]	11.83	0.00
		$D_{2.0cm^3}$	80.70 ± 1.74	74.19 ± 3.88[a]	3.69	0.04
		Rectum D_{ICRU}	74.20 ± 0.67	63.63 ± 2.74[a]	6.63	0.01
		$D_{2.0cm^3}$	69.25 ± 8.28	64.15 ± 4.54	2.08	0.13
		Sigmoid $D_{2.0cm^3}$	62.59 ± 7.31	59.53 ± 6.17	0.73	0.52
		Small bowel $D_{2.0cm^3}$	64.35 ± 8.29	60.73 ± 7.53	1.73	0.18
IIA	14	Bladder D_{ICRU}	77.95 ± 10.40	74.10 ± 8.51[a]	2.31	0.04
		$D_{2.0cm^3}$	81.16 ± 9.65	76.92 ± 7.09[a]	2.26	0.04
		Rectum D_{ICRU}	73.61 ± 2.58	71.79 ± 4.66	1.37	0.19
		$D_{2.0cm^3}$	73.06 ± 8.59	67.85 ± 5.97[a]	3.04	0.01
		Sigmoid $D_{2.0cm^3}$	68.51 ± 6.66	64.97 ± 7.09	1.99	0.07
		Small bowel $D_{2.0cm^3}$	66.13 ± 5.68	64.10 ± 5.51	1.38	0.19
IIB	21	Bladder D_{ICRU}	81.75 ± 7.91	78.21 ± 10.67	1.66	0.11
		$D_{2.0cm^3}$	80.04 ± 10.89	73.25 ± 5.15[a]	2.64	0.02
		Rectum D_{ICRU}	73.10 ± 3.35	71.82 ± 5.09	0.89	0.38
		$D_{2.0cm^3}$	71.43 ± 8.15	67.72 ± 4.40[a]	2.26	0.04
		Sigmoid $D_{2.0cm^3}$	65.33 ± 7.09	62.43 ± 5.88	1.91	0.07
		Small bowel $D_{2.0cm^3}$	67.97 ± 7.71	65.95 ± 6.40	1.33	0.20
IIIA	6	Bladder D_{ICRU}	77.44 ± 11.24	74.15 ± 10.11	1.35	0.24
		$D_{2.0cm^3}$	74.22 ± 10.91	74.68 ± 11.01	−0.42	0.69
		Rectum D_{ICRU}	74.74 ± 0.25	73.43 ± 2.34	1.30	0.25
		$D_{2.0cm^3}$	75.74 ± 13.02	66.56 ± 6.91[a]	3.22	0.02
		Sigmoid $D_{2.0cm^3}$	72.65 ± 4.99	69.32 ± 5.19	1.07	0.33
		Small bowel $D_{2.0cm^3}$	66.44 ± 9.29	63.09 ± 7.36	1.53	0.19
IIIB	18	Bladder D_{ICRU}	82.16 ± 8.58	76.74 ± 6.96[a]	3.26	0.01
		$D_{2.0cm^3}$	81.26 ± 7.56	75.84 ± 6.63[a]	3.85	0.00
		Rectum D_{ICRU}	72.77 ± 3.75	71.57 ± 5.13	1.04	0.31
		$D_{2.0cm^3}$	72.68 ± 6.52	67.67 ± 6.42[a]	3.01	0.01
		Sigmoid $D_{2.0cm^3}$	64.86 ± 6.46	60.70 ± 6.38	1.85	0.08
		Small bowel $D_{2.0cm^3}$	66.93 ± 6.55	64.93 ± 7.13	1.00	0.33

Continued

Table 4. Continued

Stage	Number	Dose parameters of OARs	Exposure dose (Gy)		*t*-value	*P*-value
			2D-ICBT plan	3D-ICBT plan		
IVA	3	Bladder D_{ICRU}	85.55 ± 6.01	84.75 ± 10.66	0.14	0.90
		$D_{2.0cm^3}$	82.69 ± 9.25	78.62 ± 7.56	2.50	0.13
		Rectum D_{ICRU}	71.23 ± 5.03	67.61 ± 6.39	1.19	0.36
		$D_{2.0cm^3}$	71.22 ± 4.09	70.87 ± 4.05	0.62	0.60
		Sigmoid $D_{2.0cm^3}$	67.43 ± 3.37	68.88 ± 2.77	−0.54	0.64
		Small bowel $D_{2.0cm^3}$	68.92 ± 8.23	63.89 ± 5.67	1.58	0.26

[a]$P < 0.05$ vs 2D-ICBT plan.

Table 5. The standard-reaching rate of assessment standard for planning in different stages of cervical carcinoma

Stage	Number	CTVhr-D_{90} > 80 Gy				CTVhr-D_{90} ≥ 85 Gy			
		2D-ICBT plan		3D-ICBT plan		2D-ICBT plan		3D-ICBT plan	
		Qualified number	Standard-reaching rate %	Qualified number	Standard-reaching rate %	Qualified number	Standard-reaching rate %	Qualified number	Standard-reaching rate %
IB	4	4	100.00	4	100.00	3	75.00	4	100.00
IIA	14	6	42.86	14	100.00	2	14.29	14	100.00
IIB	21	6	28.57	21	100.00	0	0.00	15	71.43
IIIA	6	2	33.33	6	100.00	0	0.00	3	50.00
IIIB	18	4	22.22	16	88.89	0	0.00	1	5.56
IVA	3	2	66.67	3	100.00	0	0.00	2	66.67
Total	66	24	36.36	64	96.97	5	7.58	39	59.09

precision of MRI-based planning [27, 28], but at present, most 3D-ICBT plans are based on CT images in China. On the basis of this study, we are gradually carrying out MRI image localization. Our preliminary findings are also consistent with the above conclusions [29].

In conclusion, direct comparison of 2D- and 3D-ICBT appears to favor the 3D approach, which generally increases the tumor dose coverage and reduces dosages to the OARs, compared with the 2D-ICBT plans. This research suggests that 3D-ICBT for cervical carcinoma as an individualized precise treatment model will be beneficial in decision-making regarding the treatment of Chinese patients. However, the appropriate BT technique for Chinese patients with the various stages of cervical carcinoma, anatomical characteristics and economic situations remain to be clarified.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests, and all authors confirm the accuracy of this report.

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