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Investigation of fusion dose distribution for locally advanced cervical cancer under different bladder statuses for intensity-modulated radiotherapy combined with intracavitary brachytherapy

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Abstract

Objective: Intensity-modulated radiotherapy (IMRT) combined with intracavitary brachytherapy (ICBT) is a standard radiotherapy technology for locally advanced cervical cancer (LACC), and bladder status is a common factor that affects dose distribution of the target and organs at risk (OARs). Under different bladder statuses, fusion dose distribution of IMRT combined with ICBT is unclear. The aim of the present study was to analyze the fusion dose distribution of targets and OARs for IMRT combined with ICBT in LACC under different bladder statuses.

Methods: A total of 20 patients with LACC who were treated in our department from 1 January 2015 to 31 July 2015 underwent magnetic resonance imaging and simulation computed tomography (Sim-CT) scans under filled and empty bladder status. The magnetic resonance imaging and Sim-CT scans were transmitted by Sim-CT to the Oncentra treatment planning system and fused. The gross tumor volume (GTV) was delineated in the magnetic resonance imaging, and the clinical target volume (CTV), planning target volume (PTV) and OARs (intestine, bladder, rectum, left, and right femoral head) were delineated in Sim-CT. The IMRT plan was designed with seven fields and 3-D ICBT in the treatment planning system, and the radiation sources were X-ray (6 MV) and 192Ir. The doses of the targets (D95%, D90%, D85%, D80%) and OARs (D1 cc and 2cc for intestine, D5%, 10%, and 30% for bladder, D1cc, 2cc, and 5cc for rectum, D1% for femoral head) were planned separately with IMRT and ICBT, and the geometric sum was used as the geometric dose. The treatment planning system plan used the superposition function to superimpose the IMRT and ICBT plans as a fusion plan, and the doses of the targets and OARs were calculated as a fusion dose. The relationship between the geometric and fusion doses of the targets and OARs was analyzed under different bladder statuses, and the dose contribution rates to the targets and OARs were calculated from ICBT.

Results: For the empty bladder: D95% (uGTV = 3.92, tCTV = 11.28, tPTV = 10.79), D90% (uGTV, CTV = 3.92, uPTV = 3.25), and D85% (u = 3.92), D80% (u = 3.92). The geometric doses of the targets were lower than the fusion doses. For the full bladder: D95% (uGTV, PTV = 3.92, tCTV = 15.96), D90% (uGTV = 3.81, uCTV, PTV = 3.92), D85% (u = 3.92), and D80% (uGTV = 4.70, uCTV, PTV = 3.92). The geometric doses of the targets (D95%, D90%, D85%, D80%) were lower than the fusion doses at $P < 0.001$. The dose difference rate of GTV under the filled bladder condition was lower than that of the empty bladder (0.17–0.93% and 0.32–1.07%,

respectively), whereas these values were similar in the empty bladder condition for CTV and PTV (1.10–2.75% and 1.22–3.40%, and 0.98–2.29% and 0.94–3.17%, respectively). For the empty bladder, the geometric doses of OARs (uintestine = 3.92; tintestine = 11.59; ubladder=3.92, 3.92, 3.36; urectum = 3.92; tfemoral head = 4.77 and 6.06) were higher than the fusion doses. For the full bladder, the geometric doses of OARs (tintestine = 10.27 and 8.84; tbladder = 10.69, 11.77, and 4.91; urectum = 3.36, 3.21, and 3.25) were higher than the fusion doses at $P < 0.005$. The average geometric dose differences of D30% for the bladder and D1cc, 2cc, and 5cc for the rectum were higher than those of the fusion dose (1.90 Gy, 1.01 Gy, 0.87 Gy, 0.86 Gy and 1.86 Gy, 0.95 Gy, 0.79 Gy, 0.59 Gy). The D1% values for the right and left femoral head were 0.76 Gy, 0.41 Gy, 0.26 Gy, and 0.73 Gy. For the empty bladder: D95% (uGTV = 3.92, tCTV = 11.40, tPTV = 10.84), D90% (uGTV = 3.92, uCTV = 3.29, tPTV = 6.00), D85% (uGTV = 3.92, tCTV = 17.29, tPTV = 13.87), and D80% (uGTV = 3.92, tCTV = 16.60, tPTV = 15.41). The geometric dose contribution rate of ICBT to the targets was lower than that of the fusion dose; for the full bladder: D95% (uGTV = 9.87, uCTV = 15.78, uPTV = 10.65), D90% (uGTV = 3.81, tCTV = 20.70, tPTV = 17.64), D85% (tGTV = 8.31, tCTV = 23.27, tPTV = 19.78), D80% (tGTV = 4.68, uCTV = 3.92, tPTV = 19.90). The geometric dose contribution rate to the targets was lower than that of the fusion dose at $P < 0.005$. The highest dose contribution rate of ICBT was to GTV. The geometric and fusion contribution rates were 51.12–63.89% and 48.10–60.80%, and 49.52–63.35% and 46.74–60.52% under the empty and filled bladder conditions, respectively. These values were <10.00% for CTV and PTV. For the empty bladder, the geometric dose contribution rate of ICBT to OARs (uintestine = 3.92; ubladder = 3.92, 3.92, and 3.36; urectum = 3.92; tfemoral head = 4.67 and 6.16) was higher than that of fusion. For the filled bladder, the geometric dose contribution rate to OARs (tintestine = 10.14 and 8.77; tbladder = 10.74, 11.82, and 4.93; urectum = 3.25, 3.21, and 3.21) was higher than that of fusion at $P < 0.005$. Comparing the empty bladder with the filled bladder case, the dose contribution rates of ICBT to the rectum were 47.77–59.45% and 40.87–52.40%, and 47.82–58.78% and 41.61–52.00%, respectively, and the dose contribution rates to the bladder were 27.60–45.17% and 26.04–41.80%, and 23.36–43.67% and 21.89–40.22%, respectively. The dose contribution rates to the intestine were 30.90–36.90% and 28.85–34.79%, and 20.68–25.13% and 18.69–22.88%, respectively, with <10% to the femoral head.

KEYWORDS

bladder status, cervical cancer, dose distribution, intensity-modulated radiotherapy, intracavitary brachytherapy

1 | INTRODUCTION

The incidence of cervical cancer was ranked at #10 and #7 for Chinese tumors in 2010 and 2011, respectively.[1,2] A total of 3561 hospitalized patients occurred in the top five.[3] Intensity-modulated radiotherapy (IMRT) is an external irradiation technique commonly used in locally advanced cervical cancer (LACC).[4,5] For LACC, the 5-year overall survival rate was 15.1–24%, and the disease-free survival rate was 11.6% when treated with external irradiation alone.[6] For LACC treatment with external beam radiation therapy in combination with intracavitary brachytherapy (ICBT), the overall survival rate was 68% at 2 years, and reached 47% at 5 years. The overall Local Control (LC) rate was 71% at 2 years and 58% at 5 years.[7] It is suggested that ICBT is an indispensable technique for LACC. Most of the current treatment planning systems (TPSs) separately evaluate the doses of the targets and organs at risk (OARs) in IMRT and ICBT plans, which prompts the following questions: How do the dose distributions of the targets and OARs compare in the IMRT/ICBT fusion plan? Are the results consistent for the dose evaluation alone? How does the relationship change with bladder status? Related research on this topic is lacking. To determine the dose distribution of the IMRT/ICBT fusion plans, the present study used the integration function of Oncentra TPS to fuse the IMRT and 3-D ICBT plans, and to analyze the dose distributions of the targets and OARs for 20 LACC cases with different bladder conditions, and compared them with the single-dose evaluation to supply a reference for clinical dosimetry of LACC radiotherapy.

2 | METHODS

2.1 | Case selection and general information

LACC patients treated from 1 January 2015 to 31 July 2015 were selected from the Department of Oncology, Affiliated Hospital of Southwest Medical University, Luzhou, China. The Inclusion criteria were: (1) patients aged 18–70 years with Karnofsky Performance Status (KPS) score >80; (2) clear pathological diagnosis according to (3) the 2009 International Federation of Gynecology and Obstetrics stage IIb–IVa; (4) digestive tract infections without involvement of the urinary tract; (5) abdominal and pelvic joints without metal implants;

(6) no metastasis; and (7) willingness to accept radiotherapy. According to the selection criteria, 20 patients were randomly selected using the envelope method. The ages of the patients ranged from 35 to 64 years, and the median age was 52.5 years. All patients were diagnosed with squamous cell carcinoma of the cervix with International Federation of Gynecology and Obstetrics staging in 16 cases of stage IIb, two cases in stage IIIa, and two cases in stage IIIb.

2.2 | Image acquisition and fusion

2.2.1 | Simulated positioning for computed tomography scan

For indwelling catheter and bladder emptying, three Fletcher afterloading source applicators were placed in the empty bladder and filled bladder status (rapid injection of 200 mL saline) for computed tomography (CT) simulation scanning (model LIGHTSPEEDPLUS4; American GE Company, Connecticut, Fairfield, USA). At the same time, image contrast enhancement was applied by intravenous injection of 98 mL of 35% iodine fluoride alcohol (Jiangsu Hengrui Pharmaceutical Limited by Share Ltd in China) and an injection speed of 3 mL/s. The CT scan parameters were 150 KV, 200 MA, interval of 2.5 mm, and scan range from the third lumbar superior margin to the lower margin of the obturator lower margin of 5 cm.[8]

2.2.2 | Magnetic resonance imaging scan

The indwelling catheter in the empty bladder and filled bladder status (rapid injection of 200 mL saline) maintained the same position as the simulated positioning CT with a line magnetic resonance imaging (MRI) T2 weighted image (Intera 1.5T Nova; Holland PHILPS, Amsterdam, Holland) scan using T2 weighted image scanning parameters of TR 6000 ms, TE 86.5 ms, 2.5 mm thickness, layer spacing of 0.5 mm, and scanning range from the fifth lumbar superior margin to the obturator lower margin of 5 cm.[9]

2.2.3 | Fusion of CT and MRI images

Simulated CT and MRI scanning images were transferred to the Oncentra TPS (Holland Nucletron, 4.3.0. 410). According to the pelvic bone markers, the empty bladder and filled bladder CT and MRI images were fused by rigid registration and formation of the empty and filled bladder CT/MRI fusion images.

2.3 | Targets, OAR delineation and dosimetric evaluation

2.3.1 | Target delineation and dosimetric evaluation

Target delineation and dosimetric evaluation were carried out by one experienced radiologist, according to the International Commission Radiation Units and Measurements Report No. 62 delineation principle,[10] and based on the principle of naming and delineation of the targets in the literature.[8,9,11] The targets were delineated in the TPS according to gross tumor volume (GTV) delineated by MRI, including cervical cancer, uterine and pelvic lymph node metastasis, and clinical target volume (CTV) delineated by CT, including regional lymph nodes (common iliac, internal iliac, external iliac and obturator, and presacral lymph drainage area), uterus and adjacent tissues, the upper portion of the vagina (vaginal invasion of up to one-third including the entire vagina), and planning target volume (PTV) in CTV on the expansion of 0.3 cm all around. Finally, the delineation was confirmed by three people, including a radiologist and a physical therapist. GTV, CTV, and PTV were assessed by the D95%, D90%, D85%, and D80% volume doses.

2.3.2 | OAR delineation and dosimetric evaluation

The OARs were delineated by adjusting the CT/MRI window width and window position in the TPS. The upper bound of the small intestine exceeded a PTV of 2 cm, the entire bladder, the left and right femoral heads, and the rectal delineation ranged from dentate line to S3 plane. For D1ccm 2cc of the small intestine, D5%, 10%, and 30% of the bladder, D1cc, 2cc, and 5cc of the rectum, and D1% of the femoral head, doses were evaluated.

2.4 | Treatment planning design and validation

The IMRT plan was designed with seven fields (0o/51o/102o/153o/207o/258o/309o) under the empty and filled bladder conditions in the TPS. The radiation sources were 6-MV X-ray, prescription dose of Dt = 50 Gy/25 Fr, the targets of PTV were D95% ≥45Gy, the maximum dose ≤110%, and the minimum dose ≥93%. The conformity index and homogeneity index were determined according to the literature[12,13] computation for conformity index ≥0.70 and homogeneity index ≤1.20. For the OAR requirements, D2% of the unilateral femoral head <50 Gy, D50% of bladder <30 Gy, D50% of small intestine <25 Gy, and D50% of rectum <50 Gy were used. Comprehensive evaluation was carried out based on the combined iso-dose curve and dose volume histogram. The ICBT plan was designed under the empty and filled bladder conditions in the TPS. The radiation sources were 192Ir and the prescription dose of Dt = 24 Gy/4 F[14] (EQD2 = 32 Gy, $\alpha/\beta = 10$). In the ICBT plan, the dose was calculated as 32 Gy. The following doses were calculated according to EQD2: dose requirements for D80% of GTV ≥26 Gy (EQD2).

2.5 | Dose calculation

After confirming compliance with the requirements of the plan, we calculated the geometric dose, fusion dose, and the dose contribution rates of ICBT to the targets and OARs. The geometric dose was defined as the sum of the dose of the IMRT plan and the dose of ICBT plan purely in the same volume; that is, the dose of IMRT + ICBT. The fusion dose is defined with the use of the Oncentra TPS overlay function, and superposition of the IMRT and ICBT plans to form the IMRT/ICBT fusion plan and calculation of the targets and OAR doses in the fusion plans. The dose contribution rate of ICBT to the targets and OARs under the same volume = (IMRT/ICBT fusion dose − IMRT dose) / IMRT plan dose × 100%. At the same volume, the fusion dose and the geometric dose difference = fusion dose − geometric dose. Under the same volume of fusion dose and geometric dose, the difference rate = (fusion dose − geometric dose) / geometric dose × 100%

2.6 | Statistical analysis

SPSS 22.0 statistical analysis software (IBM) was used in analysis. For data in accordance with the normal distribution, the paired *t*-test was used, and otherwise, the signed rank sum test was used. The statistic for the parameter test was set to t, the statistic of the nonparametric test was set to u, and the test level was $\alpha = 0.05$.

3 | RESULTS

3.1 | Comparison of target dosimetry

Under different bladder conditions, the geometric doses of the targets were lower than the fusion doses ($P < 0.05$). The geometric and fusion dose difference rate of GTV was the smallest for the filled bladder, and the dose difference rate in PTV was the largest. The average fusion dose difference of GTV was greater than that of the average geometric dose, but the values were similar for CTV and PTV (Table 1).

3.2 | Comparison of OAR dosimetry

Under different bladder conditions, the geometric doses of OARs were higher than the fusion doses. For the empty bladder, the geometric and fusion doses were higher than those for the filled bladder. The average geometric dose differences of D30% for the bladder and D1cc, 2cc, and 5cc for the rectum were higher than those of fusion (1.90 Gy, 1.01 Gy, 0.87 Gy, 0.86 Gy, and 1.86 Gy, 0.95 Gy, 0.79 Gy, 0.59 Gy; Table 2).

3.3 | Dose contribution rate of ICBT to targets

Under different bladder conditions, the geometric dose contribution rate of ICBT to the targets was lower than the fusion dose contribution rate ($P < 0.05$). The dose contribution rate of ICBT to GTV was the highest, and had the same dose contribution to CTV and PTV (Table 3).

3.4 | Dose contribution rate of ICBT to OARs

Under different bladder conditions, the geometric dose contribution rate of ICBT to OARs was higher than the fusion dose contribution rate. For the empty and full bladder, the contribution rate of the geometric dose from ICBT to the rectum, bladder and intestine was higher than that of the fusion dose, and the geometric and fusion dose contribution rate of ICBT to the right and left femoral head was <10% (Table 4).

4 | DISCUSSION

For LACC, the radiotherapies for IMRT and ICBT were both based on CT to evaluate the dose distribution of the target and OARs.[15,16] The accuracy of CT in evaluating the targets is poor, which leads to a lack of recognition of the targets or too much recognition.[17] The primary concern of IMRT/ICBT in cervical cancer is how to accurately determine the targets of LACC radiotherapy.[17] MRI can effectively evaluate the shape and extent of the tumor, and is the preferred imaging technique for cervical cancer.[18,19] The CT/MRI fusion image has no effect on the dose distribution OARs.[20] LACC radiotherapy of IMRT combined with ICBT is feasible and safe, and it is helpful for accurately delineating the targets.[21] In the present study, CT/MRI fusion images were used to delineate targets of the LACC, which is consistent with the requirements of the literature.[20,21]

Bladder status is the main factor that affects the dose distribution of the target and OARs for LACC radiotherapy.[22] Research indicated that full bladder plans showed a significant reduction in small intestine D2cc from 2.81 Gy to 1.83 Gy, and a reduction in D0.1cc from 4.07 Gy to 2.57 Gy ($P < 0.05$). Similarly, the sigmoidal D2cc was significantly reduced from 4.24 Gy to 3.87 Gy ($P < 0.05$), and D0.1cc was reduced from 6.12 Gy to 5.61 Gy ($P < 0.05$).[23] Another research study showed that with a full bladder, the mean small bowel D(2cc) significantly decreased from 6.77 to 4.08 Gy, and the mean bladder D(2cc) did not increase significantly. Bladder distention decreased the mean D(50%) for both the bladder and the rectum.[24] A bladder volume of >140 cm^3 was beneficial for protection of OARs.[25] The bladder capacity in the present study was 200 mL, similar to that reported in the literature.[25]

The present study showed that under different bladder conditions, the geometric doses of the targets were lower than the fusion doses ($P < 0.05$). For the empty bladder, the geometry and fusion dose of the targets were higher than those of the filled bladder. For the filled bladder geometry, the fusion dose difference rate of GTV is lower than that of the empty bladder (0.17–0.93% and 0.32–1.07%). The average geometry and fusion dose difference value of GTV is >1 Gy, and the average dose difference value of CTV and PTV is <0.20 Gy. Under different bladder conditions, the geometric dose contribution rate of ICBT to the targets was lower than that of the fusion dose ($P < 0.05$). The dose contribution rate to GTV was the highest. For the empty and filled bladder, the fusion dose contribution rate was higher than that of the geometric dose (51.12–63.89% and 48.10–60.80%, and 49.52–63.35% and 46.7–60.52%, respectively). The dose contribution rate to CTV and PTV is <10.00%. This study showed that for LACC radiotherapy of IMRT combined with ICBT, the bladder status primarily affected the dose of GTV, and had little effect on the dose of CTV and PTV, and the geometric dose evaluation might underestimate the dose of GTV. ICBT is the main contribution to the dose of GTV, and it also has a dose contribution to CTV and PTV. The geometric dose contribution rate is less than the contribution rate of fusion. In addition to considering the dose of ICBT to GTV, the dose effect of ICBT on CTV and PTV should be taken into consideration.

Under different bladder conditions, the geometric doses of OARs were higher than the fusion doses ($P < 0.05$). For theempty bladder, the geometric and fusion doses were higher than those for the filled bladder. The average geometric dose differences of D30% for the bladder and D1cc, 2cc, and 5cc for the rectum were higher than that of fusion (1.90 Gy, 1.01 Gy, 0.87 Gy, 0.86 Gy,and1.86 Gy, 0.95 Gy, 0.79 Gy, 0.59 Gy, respectively).Under different bladder conditions, the geometric dosecontribution rate of ICBT to the rectum, bladder and small intestine was higher than that of the fusion dose, and no significant difference was noted between the geometric and fusion dose contribution rates of the femoral head. These observations show that for LACC radiotherapy of IMRT combined with ICBT, bladder condition

TABLE 1 Comparison geometric and fusion doses of targets under empty and filled bladder conditions for intensity-modulated radiotherapy/intracavitary brachytherapy fusion plan

	GTV				CTV				PTV			
	D95%	D90%	D85%	D80%	D95%	D90%	D85%	D80%	D95%	D90%	D85%	D80%
Empty bladder												
Geometric dose	75.49 ± 4.28	78.93 ± 4.41	81.56 ± 4.57	83.90 ± 4.82	49.43 ± 0.94	50.89 ± 1.04	51.92 ± 1.09	52.81 ± 1.13	48.01 ± 0.83	49.98 ± 1.01	50.98 ± 0.94	51.89 ± 0.98
Fusion dose	76.30 ± 4.27	79.46 ± 4.44	81.92 ± 4.65	84.17 ± 4.84	50.56 ± 1.01	51.74 ± 1.02	52.59 ± 1.09	53.33 ± 1.14	49.53 ± 0.93	50.84 ± 0.89	51.68 ± 0.93	52.38 ± 0.98
Difference value	0.81 ± 0.31	0.53 ± 0.19	0.36 ± 0.20	0.27 ± 0.14	1.13 ± 0.45	0.86 ± 0.26	0.68 ± 0.17	0.52 ± 0.14	1.52 ± 0.63	0.86 ± 0.66	0.70 ± 0.23	0.49 ± 0.14
Difference rate (%)	1.07	0.67	0.44	0.32	2.29	1.69	1.31	0.98	3.17	1.72	1.37	0.94
Statistic	3.92*	3.92*	3.92*	3.92*	11.28	3.92*	3.92*	3.92*	10.79	3.25*	3.92*	3.92*
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Filling bladder												
Geometric dose	74.41 ± 4.98	77.66 ± 4.85	80.25 ± 4.73	82.60 ± 4.63	49.50 ± 0.93	50.90 ± 0.95	51.88 ± 1.01	52.76 ± 1.05	47.94 ± 0.92	49.81 ± 0.86	50.92 ± 0.90	51.82 ± 0.94
Fusion dose	75.10 ± 4.91	78.04 ± 4.82	80.56 ± 4.73	82.75 ± 4.65	50.86 ± 0.80	51.94 ± 0.90	52.68 ± 1.00	53.34 ± 1.08	49.58 ± 0.98	51.02 ± 0.76	51.81 ± 0.84	52.45 ± 0.93
Difference value	0.69 ± 0.31	0.38 ± 0.22	0.31 ± 0.17	0.14 ± 0.13	1.36 ± 0.38	1.04 ± 0.22	0.80 ± 0.15	0.58 ± 0.16	1.63 ± 0.68	1.21 ± 0.30	0.89 ± 0.20	0.63 ± 0.14
Difference rate (%)	0.93	0.49	0.39	0.17	2.75	2.04	1.54	1.10	3.40	2.43	1.75	1.22
Statistic	3.92*	3.81*	3.92*	4.70	15.96	3.92*	3.92*	3.92*	3.92*	3.92*	3.92*	3.92*
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Total $n = 20$, Gy, ± S.

*Non-parametric test results. CTV, clinical target volume; GTV, gross tumor volume; PTV, planning target volume.

TABLE 2 Comparison of geometric and fusion doses of organs at risk under empty and filled bladder conditions for intensity-modulated radiotherapy/intracavitary brachytherapy fusion plan

	Small intestine		Bladder			Rectum			Left femoral head	Right femoral head
	D1cc	D2cc	D5%	D10%	D30%	D1cc	D2cc	D5cc	D1%	D1%
Empty bladder										
Geometric dose	68.41 ± 3.64	65.04 ± 3.26	72.73 ± 6.35	68.41 ± 5.26	59.59 ± 3.45	81.31 ± 7.23	78.24 ± 6.63	73.66 ± 5.95	51.30 ± 2.22	50.05 ± 2.78
Fusion dose	67.35 ± 3.51	64.03 ± 3.13	71.04 ± 6.33	66.76 ± 5.23	58.86 ± 3.14	77.69 ± 6.98	74.67 ± 6.50	70.20 ± 5.76	51.17 ± 2.24	49.76 ± 2.74
Difference value	−1.05 ± 0.39	−1.02 ± 0.39	−1.69 ± 0.90	−1.65 ± 0.81	−0.73 ± 0.65	−3.62 ± 2.45	−3.56 ± 2.22	−3.46 ± 1.92	−0.13 ± 0.12	−0.28 ± 0.21
Difference rate (%)	−1.53	−1.57	−2.32	−2.41	−1.23	−4.45	−4.55	−4.70	−0.25	−0.56
Statistic	3.92*	11.59	3.92*	3.92*	3.36*	3.92*	3.92*	3.92*	4.77	6.06
P	<0.001	<0.001	<0.001	<0.001	0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Filling bladder										
Geometric dose	62.40 ± 3.75	59.81 ± 3.24	72.17 ± 4.43	67.29 ± 3.54	57.69 ± 2.21	80.30 ± 8.01	77.37 ± 7.30	72.80 ± 6.48	50.54 ± 3.22	50.31 ± 2.89
Fusion dose	61.28 ± 3.74	58.82 ± 3.20	70.43 ± 4.40	65.43 ± 3.44	57.00 ± 2.01	76.74 ± 8.05	73.88 ± 6.96	69.61 ± 5.95	50.76 ± 2.43	50.49 ± 2.69
Difference value	−1.12 ± 0.49	−0.99 ± 0.50	−1.74 ± 0.73	−1.86 ± 0.71	−0.69 ± 0.63	−3.56 ± 3.36	−3.48 ± 3.26	−3.19 ± 3.04	0.21 ± 2.20	0.18 ± 1.57
Difference rate (%)	−1.79	−1.66	−2.41	−2.76	−1.20	−4.43	−4.50	−4.38	0.42	0.36
Statistic	10.27	8.84	10.69	11.77	4.91	3.36*	3.21*	3.25*	0.43	0.50
P	<0.001	<0.001	<0.001	<0.001	<0.001	0.001	0.001	0.001	0.67	0.62

Total $n = 20$ Gy, ± S.
*Non-parametric test results.

TABLE 3 Comparison of geometric and fusion doses contribution rates of targets from intracavitary brachytherapy for intensity-modulated radiotherapy/intracavitary brachytherapy fusion plan

	GTV				CTV				PTV			
	D95%	D90%	D85%	D80%	D95%	D90%	D85%	D80%	D95%	D90%	D85%	D80%
Empty bladder												
Geometric contribution rate (%)	49.52 ± 9.42	55.00 ± 9.64	59.37 ± 9.87	63.35 ± 10.27	4.68 ± 1.57	6.16 ± 1.78	7.46 ± 1.86	8.73 ± 1.90	4.32 ± 1.43	5.60 ± 1.61	6.73 ± 1.67	7.82 ± 1.70
Fusion contribution rate (%)	51.12 ± 9.44	56.05 ± 9.74	60.08 ± 10.03	63.89 ± 10.35	7.07 ± 1.63	7.94 ± 1.74	8.86 ± 1.90	9.80 ± 1.98	7.62 ± 1.71	7.43 ± 2.02	8.19 ± 1.61	8.83 ± 1.71
Differences rate (%)	1.60 ± 0.61	1.05 ± 0.38	0.71 ± 0.39	0.53 ± 0.28	2.39 ± 0.94	1.79 ± 0.54	1.40 ± 0.36	1.07 ± 0.29	3.30 ± 1.36	1.83 ± 1.36	1.46 ± 0.47	1.01 ± 0.29
Statistic	3.92[a]	3.92[a]	3.92[a]	3.92[a]	11.40	3.29[a]	17.29	16.60	10.84	6.00	13.87	15.41
P	<0.001	<0.001	<0.001	<0.001	<0.001	0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Filling bladder												
Geometric contribution rate (%)	46.74 ± 9.73	51.95 ± 9.43	56.40 ± 9.19	60.52 ± 9.03	4.66 ± 1.56	6.00 ± 1.64	7.22 ± 1.70	8.44 ± 1.77	4.34 ± 1.45	5.51 ± 1.50	6.54 ± 1.56	7.57 ± 1.61
Fusion contribution rate (%)	48.10 ± 9.61	52.69 ± 9.39	57.02 ± 9.21	60.80 ± 9.11	7.55 ± 1.45	8.17 ± 1.55	8.88 ± 1.67	9.63 ± 1.77	7.90 ± 2.05	8.08 ± 1.39	8.40 ± 1.48	8.89 ± 1.58
Differences rate (%)	1.36 ± 0.62	0.74 ± 0.42	0.61 ± 0.33	0.28 ± 0.26	2.89 ± 0.82	2.16 ± 0.47	1.65 ± 0.32	1.19 ± 0.33	3.57 ± 1.50	2.57 ± 0.65	1.86 ± 0.42	1.31 ± 0.30
Statistic	9.87	3.81[a]	8.31	4.68	15.78	20.70	23.27	3.92[a]	10.65	17.64	19.78	19.90
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Total $n = 20$, Gy, ± s.

[a] Non-parametric test results.

TABLE 4 Comparison of geometric and fusion dose contribution rates of organs at risk from intracavitary brachytherapy for intensity-modulated radiotherapy/intracavitary brachytherapy fusion plan

	Small intestine		Bladder			Rectum			Left femoral head	Right femoral head
	D1cc	D2cc	D5%	D10%	D30%	D1cc	D2cc	D5cc	D1%	D1%
Empty bladder										
Geometric contribution rate (%)	36.90 ± 7.23	30.90 ± 6.34	45.17 ± 11.94	38.54 ± 10.12	27.60 ± 6.87	59.45 ± 13.10	54.85 ± 11.80	47.77 ± 9.93	9.15 ± 1.45	8.62 ± 1.82
Fusion contribution rate (%)	34.79 ± 7.02	28.85 ± 6.12	41.80 ± 11.97	35.20 ± 10.11	26.04 ± 6.26	52.40 ± 13.27	47.84± 12.25	40.87 ± 10.36	8.86 ± 1.47	8.02 ± 2.02
Differences rate (%)	−2.11 ± 0.76	−2.05 ± 0.78	−3.37 ± 1.79	−3.34 ± 1.63	−1.56 ± 1.38	−7.06 ± 4.71	−7.01 ± 4.28	−6.90 ± 3.71	−0.29 ± 0.27	−0.60 ± 0.44
Statistic	3.92[a]	3.92[a]	3.92[a]	3.92[a]	3.36[a]	3.92[a]	3.92[a]	3.92[a]	4.67	6.16
P	<0.001	<0.001	<0.001	<0.001	0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Filling bladder										
Geometric contribution rate (%)	25.13 ± 7.73	20.68 ± 6.67	43.67 ± 8.97	35.81 ± 7.46	23.36 ± 5.19	58.78 ± 15.57	54.47 ± 13.99	47.82 ± 11.95	9.17 ± 1.82	8.42 ± 2.15
Fusion contribution rate (%)	22.88 ± 7.66	18.69 ± 6.56	40.22 ± 9.04	32.07 ± 7.43	21.89 ± 5.11	52.00 ± 18.26	47.79 ± 16.40	41.61 ± 14.22	9.91 ± 7.17	8.90 ± 5.04
Differences rate (%)	−2.25 ± 0.99	−1.99 ± 1.02	−3.45 ± 1.44	−3.74 ± 1.41	−1.47 ± 1.34	−6.78 ± 6.73	−6.68 ± 6.75	−6.21 ± 6.42	0.74 ± 5.97	0.49 ± 3.65
Statistic	10.14	8.77	10.74	11.82	4.93	3.25[a]	3.21[a]	3.21[a]	3.14[a]	2.17[a]
P	<0.001	<0.001	<0.001	<0.001	<0.001	0.001	0.001	0.001	0.002	0.03

Total $n = 20$ Gy, ± s.
[a]Non-parametric test results.

affects the dose distribution of OARs, a filled bladder can reduce the dose of OARs, the geometric dose assessment might overestimate the dose of OARs, and the fusion dose evaluation might be more objective in response to the OARs dose.

In conclusion, for LACC radiotherapy of IMRT combined with ICBT, bladder status influences the radiated dose of targets and OARs, and certain limitations exist in the simple geometric calculation of the radiated dose of targets and OARs. Fusion dosimetric analysis is the best choice. Bladder filling is beneficial to protection of the OARs and reduction of the radiated dose of OARs. The bladder can maintain an appropriate volume when radiotherapy of IMRT is combined with ICBT for locally advanced cervical cancer. Many deficiencies and many factors of intervention exist in the present study. Additionally, no actual dose monitoring and follow up were carried out, and this topic requires further study and improvement.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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