

DOSIMETRIC ANALYSIS OF LIMITING PELVIC BONE
DOSE IN INTENSITY-MODULATED RADIOTHERAPY FOR
CERVICAL CANCER

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Abstract

Numerous studies have indicated the significant importance of pelvic dose in the radiotherapy process for cervical cancer patients. However, research on the actual pelvic bone dose in the treatment of cervical cancer patients using different techniques is currently relatively limited. In this study, we selected 50 postoperative cervical cancer patients. For each patient, three treatment plans with pelvic dose constraints were designed: sIMRT, VMAT, and HT. Statistical analysis was conducted on the target area and organ at risk parameters of the three groups of plans. The results indicate that all three treatment plans meet the clinical requirements. Regarding organs at risk, compared to the sIMRT and VMAT groups, the HT group showed a reduction of 11.85% and 11.07%, respectively, in V40 of bladder. Additionally, compared to the sIMRT and HT groups, the VMAT group exhibited a reduction of 14.94% and 9.53%, respectively, in V10 of pelvic bone. Furthermore, compared to the sIMRT and HT groups, the VMAT group showed a reduction of 10.76% and 6.75%, respectively, in V20 of pelvic bone, and these differences were also statistically significant ($t = 21.630$, $t = -16.621$, $P < 0.05$). In summary, individualized treatment design can be conducted in clinical practice based on the specific conditions of patients.

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Introduction. Cervical cancer is a common gynecological malignancy among women in China [1]. The National Comprehensive Cancer Network (NCCN) in the United States explicitly states in relevant guidelines that pelvic radiation therapy is widely applicable to cervical cancer at all stages [2]. With the advancement of radiation therapy techniques, various technologies and optimization algorithms can reduce complications after radiation therapy by delivering the prescribed dose to the target volume while minimizing the dose to normal tissues. However, the protection of the pelvic region is often overlooked in clinical practice. For patients receiving radiation therapy (RT) alone or concurrent chemoradiation (cCRT), both radiation and chemotherapy drugs can impair bone marrow function, increasing the incidence of acute hematological toxicity [3]. According to the grading criteria of the Radiation Therapy Oncology Group (RTOG), if grade 3 or higher acute hematological toxicity occurs, radiation therapy needs to be interrupted [4]. Previous studies have shown that the occurrence of hematological toxicity in patients is related to the volume of pelvic bone marrow irradiation [5,6].

This study aims to delineate the pelvic region as a separate organ at risk and investigate the dosimetric differences in pelvic dose constraints among three radiation therapy techniques: step and shoot intensity-modulated radiotherapy (sIMRT), volumetric modulated arc therapy (VMAT), and helical tomotherapy (HT) for cervical cancer patients. The findings will provide technical references for reducing the incidence of hematological toxicity in clinical practice.

Dataset and method. Patient choice. Inclusion criteria: Fifty postoperative cervical cancer patients were enrolled from April 2022 to December 2022 at the First Affiliated Hospital of Bengbu Medical College, with ages ranging from 26 to 82 years and a median age of 51 years. Patients were selected based on clinical, pathological, and radiological examinations confirming cervical cancer and according to the International Federation of Gynecology and Obstetrics (FIGO) staging criteria, including patients with stages IB1, IB2, and IIA1.

Simulated localization. Four hours prior to positioning, the patient empties the bladder and orally drinks 400 ml of warm water along with 40 ml of 60% iodinated contrast agent. One hour before positioning, the patient is instructed to hold urine. The patient's position is fixed using a low-temperature thermoplastic membrane. The simulation and positioning are conducted using the Philips Brilliance CT Big Bore 4D scanner for enhanced imaging. The scanning range extends from the level of the second lumbar vertebra to 5 cm below the ischial tuberosity, with a slice thickness of 5 mm.

Delineation of target volume and organs at risk. The target volumes of patients were delineated using the Pinnacle³9.8 treatment planning system, following the guidelines of the International Commission on Radiation Units (ICRU)

Report 83 [7]. The clinical target volume (CTV) was defined as the known tumour and potentially involved tissues, including the primary tumour, surgical bed of the cervix, parametrial tissues, adequate vaginal margins, and pelvic lymphatic drainage areas. Considering the application of image-guided techniques, the planning target volume (PTV) was generated by expanding the CTV by 5 mm in three dimensions. Organs at risk (OARs) included the bladder, rectum, small intestine, femoral heads, and pelvic bones. The pelvic contour started 2 cm above the upper edge of the PTV and encompassed all bone tissues from the sacrum to the level of the ischial tuberosity plane, including the L4 and L5 vertebrae.

Treatment plan design. The plans were designed by a medical physicist using Pinnacle³9.8 and TomoTherapy treatment planning systems and the prescription dose is set to 48.6 Gy. For the sIMRT plan, a fixed 7-field coplanar arrangement was used with gantry angles of 232°, 284°, 336°, 24°, 76°, 128°, and 180°. The optimization was performed using direct machine parameter optimization (DMPO) with a maximum of 100 subfields, a minimum subfield area of 8 cm², and a minimum subfield segment of 8 MU. The VMAT plan utilized coplanar dual-arc irradiation with rotation angles ranging from clockwise 180.1° to 180° and counterclockwise 180° to 180.1°. The HT plan employed a 2.512 cm field width, 0.430 pitch, and 2 modulation factors.

Plan evaluation. The dose-volume histogram (DVH) analysis was performed to evaluate the dose parameters of the target volume and OARs. The dose parameters for the target volume included D98%, D2%, mean dose (Dmean), homogeneity index (HI), and conformal index (CI). The HI is calculated as $(D2\% - D98\%) / D50\% \times 100\%$. The CI is calculated as $V_{t,ref} / V_t \times V_{t,ref} / V_{ref}$, where V_t is the volume of target, V_{ref} is the volume covered by reference isodose line, and $V_{t,ref}$ is the volume of target covered by reference isodose line. The evaluation of OARs mainly includes the assessment of the rectum, bladder, and femoral heads in terms of V40 and mean dose (Dmean). For the pelvic bone, the evaluation is based on V10 to V40 and Dmean. The small bowel is evaluated based on V40 and maximum dose (Dmax). By analyzing these dose parameters, the dosimetric characteristics of the target volume and OARs can be assessed, including dose coverage, dose uniformity, conformity, and the dose received by specific volumes or regions of interest.

Statistical analysis. The dose parameters of the target volume for the three treatment plans were normalized to maintain consistency in dose requirements. Statistical analysis of the target volume and OAR parameters for the three plans was performed using SPSS 26.0 software. A paired *t*-test analysis was conducted to compare the parameters between the two plans. The results were presented as mean \pm standard deviation ($\bar{X} \pm S$), and a *P*-value of less than 0.05 ($P < 0.05$) was considered statistically significant for differences.

Results. Target dose distribution. The dose parameters of the target volume for the sIMRT, VMAT, and HT plans are shown in Table 1. The HT plan

demonstrated the most optimal target dose distribution, while the sIMRT plan showed a slightly inferior distribution. Both the VMAT and HT plans exhibited superior CI (0.878 ± 0.020 , 0.870 ± 0.020) and HI (0.074 ± 0.013 , 0.052 ± 0.009) compared to the sIMRT plan (0.851 ± 0.019 , 0.083 ± 0.011). With the same target prescription dose coverage of 95%, the HT plan showed significant reductions in approximate D2% (50.60 ± 0.034 Gy) and Dmean (50.13 ± 0.32 Gy) compared to the sIMRT (52.30 ± 0.51 Gy, 50.46 ± 0.20 Gy) and VMAT (52.11 ± 0.43 Gy, 50.34 ± 0.24 Gy) plans, with statistically significant differences ($P < 0.001$). When comparing sIMRT and VMAT, D98% and D2% were similar, with no statistically significant differences, but the Dmean of the sIMRT plan was higher than that of the VMAT plan (sIMRT vs. VMAT: 50.46 ± 0.20 Gy vs. 50.34 ± 0.24 Gy, $P < 0.001$).

T a b l e 1

Dosimetric comparison of PTV in the three groups (Mean \pm SD)

Variable	IMRT	VMAT	HT	P^*		
				IMRT vs. VMAT	IMRT vs. HT	VMAT vs. HT
D2% (Gy)	52.30 \pm 0.51	52.11 \pm 0.43	50.60 \pm 0.034	0.016	<0.001	<0.001
D98% (Gy)	48.37 \pm 0.12	48.40 \pm 0.14	48.09 \pm 0.12	0.262	<0.001	<0.001
Dmean (Gy)	50.46 \pm 0.20	50.34 \pm 0.24	50.13 \pm 0.32	<0.001	<0.001	0.001
CI	0.851 \pm 0.019	0.878 \pm 0.020	0.870 \pm 0.020	<0.001	<0.001	0.077
HI	0.083 \pm 0.011	0.074 \pm 0.013	0.052 \pm 0.009	<0.001	<0.001	<0.001

Note: P values are the results of paired-sample t -tests between each plan

Pelvic bone dose distribution. The conventional OARs dose parameters for all patients are listed in Table 2. The pelvic contour map can be seen in Fig. 1a-c. The detailed pelvic dose volume parameters are provided in Table 3 and Fig. 1d. Compared to sIMRT, both VMAT and HT groups showed significant reductions in pelvic dose ($P < 0.001$). In the VMAT group, pelvic V10 and V20 were significantly better than in the HT group, with reductions of 9.53% and 6.75%, respectively, and these differences were statistically significant (VMAT V10 vs. HT V10: $70.69 \pm 2.26\%$ vs. $80.22 \pm 1.20\%$, $P < 0.01$; VMAT V20 vs. HT V20: $60.82 \pm 2.94\%$ vs. $67.58 \pm 0.97\%$, $P < 0.001$). However, V40 was slightly higher in the VMAT group compared to the HT group, and this difference was statistically significant (VMAT V40 vs. HT V40: $32.26 \pm 4.20\%$ vs. $28.99 \pm 2.40\%$, $P < 0.001$).

Distribution of conventional organs-at-risk doses. In terms of other OARs, the HT group showed significant advantages in V40 of bladder preservation compared to sIMRT and VMAT (sIMRT vs. HT: $50.82 \pm 4.17\%$ vs. $38.97 \pm 2.28\%$, $P < 0.001$; VMAT vs. HT: $50.04 \pm 2.36\%$ vs. $38.97 \pm 2.28\%$, $P < 0.001$). The HT group also had a slightly better Dmean than sIMRT and VMAT,

Table 2

Comparison of organs-at-risk dosimetry among the three groups (Mean \pm SD)

OARs	Variable	IMRT	VMAT	HT	P^*		
					IMRT vs. VMAT	IMRT vs. HT	VMAT vs. HT
Bladder	V40 (Gy)	50.82 \pm 4.17	50.04 \pm 2.36	38.97 \pm 2.28	0.089	<0.001	<0.001
	Dmean (Gy)	39.76 \pm 0.67	39.46 \pm 0.54	38.07 \pm 0.43	0.014	<0.001	<0.001
Rectum	V40 (Gy)	68.63 \pm 8.61	63.30 \pm 5.41	61.58 \pm 2.32	<0.001	<0.001	0.014
	Dmean (Gy)	42.24 \pm 1.14	41.31 \pm 1.00	41.21 \pm 0.62	<0.001	<0.001	0.489
Small intestine	V40 (Gy)	12.70 \pm 6.75	12.91 \pm 6.70	11.96 \pm 7.34	0.376	0.039	0.019
	Dmean (Gy)	52.35 \pm 0.76	52.10 \pm 0.68	50.71 \pm 0.37	0.096	<0.001	<0.001
Left femoral head	V40 (Gy)	12.19 \pm 2.42	4.47 \pm 2.82	4.52 \pm 2.34	<0.001	<0.001	0.915
	Dmean (Gy)	27.58 \pm 1.19	18.55 \pm 4.11	26.28 \pm 1.24	<0.001	<0.001	<0.001
Right femoral head	V40 (Gy)	11.11 \pm 3.57	3.40 \pm 4.70	3.39 \pm 2.37	<0.001	<0.001	0.989
	Dmean (Gy)	27.09 \pm 1.88	18.61 \pm 4.21	25.83 \pm 1.59	<0.001	<0.001	<0.001

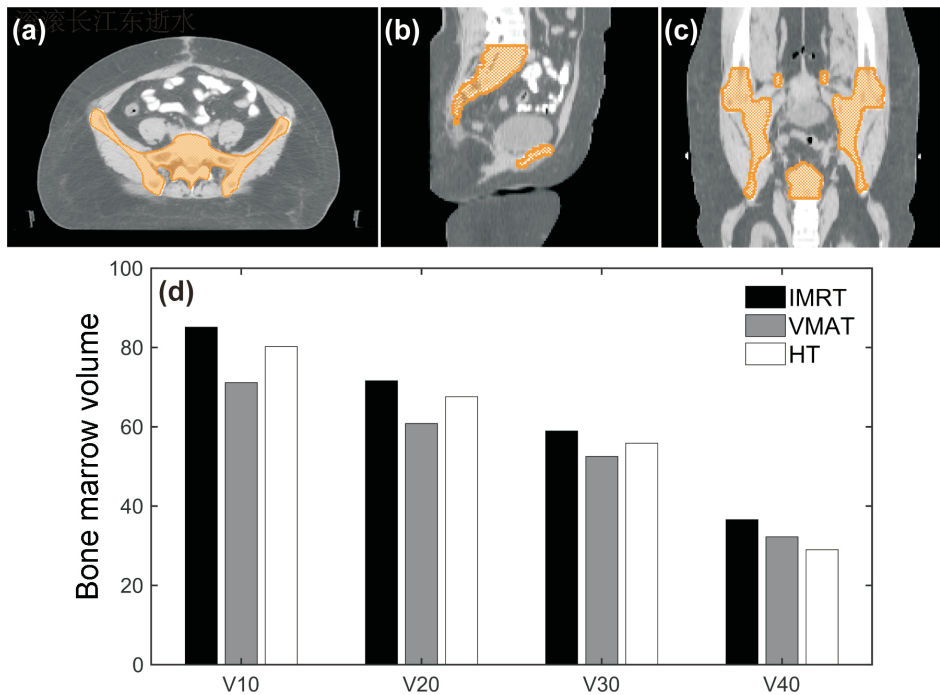


Fig. 1. Typical figures of pelvic bone contour (panel (a) for axial, panel (b) for sagittal, and panel (c) for coronal) and three planned pelvic bone dose volume histograms (d)

with statistically significant results ($P < 0.001$), although the absolute differences were small. The VMAT group and HT group showed similar protection of the rectum, both of which were superior to the sIMRT group. Regarding small bowel

T a b l e 3

Comparison of pelvic bone dosimetry in three groups (Mean \pm SD)

Variable	IMRT	VMAT	HT	P^*		
				IMRT vs. VMAT	IMRT vs. HT	VMAT vs. HT
V10 (Gy)	85.63 \pm 1.91	70.69 \pm 2.26	80.22 \pm 1.20	<0.001	<0.001	<0.001
V20 (Gy)	71.59 \pm 2.95	60.83 \pm 2.94	67.58 \pm 0.97	<0.001	<0.001	<0.001
V30 (Gy)	58.94 \pm 2.86	52.41 \pm 2.32	55.83 \pm 1.78	<0.001	<0.001	<0.001
V40 (Gy)	36.57 \pm 3.57	32.26 \pm 4.20	28.99 \pm 2.40	<0.001	<0.001	<0.001
Dmean (Gy)	31.23 \pm 0.57	27.66 \pm 0.89	29.11 \pm 0.52	<0.001	<0.001	<0.001

protection, the HT group had a significant advantage in small bowel Dmax (sIMRT vs. HT: 52.35 \pm 0.76% vs. 50.71 \pm 0.37%, $P < 0.001$). The VMAT and HT groups were slightly better than sIMRT in V40 of small bowel, with statistical significance ($P = 0.039$ and $P = 0.019$, respectively), but the absolute differences were not significant. For bilateral femoral heads, VMAT and HT showed similar results in V40 femoral head, with no statistically significant differences ($P = 0.915$ and $P = 0.989$, respectively), and both were significantly better than sIMRT. However, VMAT had the optimal mean dose.

Discussions and conclusions. For patients undergoing pelvic radiotherapy for cervical cancer, acute bone marrow suppression is one of the main side effects of radiation therapy, and the hematologic toxicity reactions that occur during patient treatment have become a clinically significant issue that cannot be ignored.

Adult pelvic bones contain more than 50% actively proliferating bone marrow [9]. The primary cause of bone marrow suppression is the damage to hematopoietic stem cells (HSCs) within the red bone marrow [10]. Previous retrospective studies have shown a significant correlation between low-dose radiation to the pelvic bones and the incidence of bone marrow suppression [11-13]. Among them, the RTOG0418 clinical trial demonstrated that pelvic bone marrow V10 \geq 85%, V40 $>$ 37%, and Dmean $>$ 34.2 Gy are all associated with grade 2 or higher hematologic toxicity [14].

Previous studies have shown that bone marrow sparing intensity-modulated radiation therapy (BMS-IMRT) for pelvic irradiation can effectively reduce the radiation dose to the bone marrow while maintaining the original target dose distribution and protecting critical organs [15]. CHEN et al. [16] compared the performance of HT and VMAT in bone marrow sparing plans for pelvic radiotherapy in cervical cancer patients. The average dose to the pelvic bone marrow was similar for both techniques, with values of 28.2 Gy and 29.7 Gy, respectively, which is consistent with the results of this study [16]. However, this study found that VMAT plans demonstrated significant advantages in protecting the pelvic

bone in terms of V10, V20, and the femoral head, while HT plans showed clear advantages in target dose distribution and V40 of bladder dose.

In summary, HT plans demonstrate superior target dose distribution and high-dose region distribution near critical organs. VMAT plans significantly outperform the other two techniques in terms of dose distribution in the low-dose region of the pelvic bones. Therefore, for patients in clinical need of reducing the incidence of hematologic toxicity, personalized treatment using VMAT technology is recommended.

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