

# A dosimetric evaluation of flattening filter-free volumetric modulated arc therapy for postoperative treatment of cervical cancer\*

Fuli Zhang, Huayong Jiang, Weidong Xu, Yadi Wang (✉), Junmao Gao, Qingzhi Liu, Ping Wang, Na Lu, Diandian Chen, Bo Yao, Jun Hou, Heliang He, Jianping Chen

Radiation Oncology Department, The PLA Army General Hospital of China, Beijing 100700, China

## Abstract

**Objective** The aim of the study was to compare flattening filter-free (FFF) beams and conventional flattening filter (FF) beams in volumetric modulated arc therapy (VMAT) for cervical cancer after surgery, through a retrospective planning study.

**Methods** VMAT plans of FFF beams and normal FF beams were designed for a cohort of 15 patients. The prescribed dose was 45 Gy to 1.8 Gy per fraction, and at least 95% of the planning target volume received this dose. Doses were computed with a commercially available treatment planning system using a Monte Carlo (MC) algorithm. Plans were compared according to dose-volume histogram analysis in terms of planning target volume homogeneity and conformity indices (HI and CI), as well as organs at risk (OAR) dose and volume parameters.

**Results** FFF-VMAT was similar to FF-VMAT in terms of CI, but inferior to FF-VMAT considering HI. No statistically differences were observed between FFF-VMAT and FF-VMAT in following organ at risks including pelvic bone marrow, small bowel, bladder, rectum, and normal tissue (NT).

**Conclusion** For patients with cervical cancer after hysterectomy, the FFF beam achieved target and OAR dose distribution similar to that of the FF beam. Reduction of beam-on time in cervical cancer is beneficial.

**Key words:** flattening filter-free (FFF); cervical cancer; dosimetry; volumetric modulated arc therapy (VMAT)

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In recent years, volumetric modulated arc therapy (VMAT) has been introduced in clinical practice to overcome some of the limitations associated with fixed field intensity modulated radiation therapy (IMRT) and three-dimensional conformal radiation therapy (3DCRT). VMAT allows the continuous delivery of radiation by simultaneously varying the dose rate, the positions of the multileaf collimator (MLC), and the gantry rotation speed. Some studies demonstrated that VMAT could achieve highly conformal dose distributions, with improved target volume coverage and sparing of normal tissues, compared with conventional IMRT [1–10]. In addition, VMAT has the potential to offer additional advantages over conventional static gantry IMRT in treatment delivery efficiency, because of the reduction in both treatment delivery time and monitor units (MU) usage. More recently, linear ac-

celerators with flattening filter-free (FFF) beams such as Varian's TrueBeam™ (Varian Medical System, Palo Alto, CA) and Elekta's Versa HD™ (Elekta Versa HD, Elekta Oncology systems, Stockholm, Sweden) were introduced into clinical operation [11–17]. FFF beams are characterized by high-dose rates, which combined with VMAT result in greater treatment efficiency compared to traditional fixed field techniques. According to these published results, a further reduced treatment delivery time and comparable plan quality seem to have been verified for VMAT plans with FFF beams.

Many studies on the application of VMAT in various tumor locations including cervical cancer usually choose 6-MV beam energy, although some researchers suggest that there is still a value to higher energies ( $\geq 10$  MV) for deep-seated pelvic/abdominal targets, as the volume

✉ Correspondence to: Yadi Wang. Email: wangyadi@hotmail.com

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of the target increases<sup>[18]</sup>. In addition, some studies published on FFF beams are limited to cases with relatively small planning target volume (PTV), including the prostate, lungs, larynx, chest wall, and esophagus<sup>[11, 14, 19-30]</sup>. Few studies on the dosimetric effects of the FFF beam on VMAT planning for cervical cancer after surgery have been conducted, while faster treatments could have a clinical impact on cervical cancer patients in terms of comfort on the treatment table, immobility, and minimization of internal organ status changes, such as bladder or rectum filling changes over time, as well as the reduction of intra-fractional patient motion. Therefore, we present a planning comparison of VMAT of flattening filter (FF) beams with 6-MV and 10-MV energy (6FF-VMAT and 10FF-VMAT) versus VMAT of FFF beams with 6-MV and 10-MV (6FFF-VMAT and 10FFF-VMAT) for treatment of cervical cancer after hysterectomy. The study was also motivated by the expectation that changes in nominal energy and penumbra of FFF beams may influence the dosimetric outcome for this specific deep-seated treatment location, as changes in secondary build-up may have an impact on target coverage and sparing of organs at risk (OAR).

## Patients and methods

### Patient selection, positioning, and computed tomography

Fifteen cervical cancer patients who had been treated with postoperative radiotherapy after hysterectomy from May 2012 to November 2013 were chosen for retrospective analysis. The mean and median ages were 53.9 and 55.5 years, respectively. Computed tomography (CT) scans of all patients in the treatment position were obtained on our departmental CT scanner (Brilliance Bigbore CT, Philips Medical systems, Cleveland, OH, USA) using 5-mm slice interval and thickness. The CT scans were extended from the T11 vertebral body to mid-thigh and were imported to the Monaco planning system (version 5.0, Elekta AB, Stockholm, Sweden). Before implementing CT, a contrast agent was administered orally or intravenously. In addition, to minimize intra-fractional setup variability and maintain inter-fractional repeatability as much as possible, a custom immobilization device (Thermoplastic mold, MedTec Inc, USA) was fabricated with each patient in the treatment position. The study was approved by the ethics committee of the PLA Army General Hospital of China. All patients provided written consent for storage of their medical information in the hospital database and for research use.

### Target volumes

The clinical target volume (CTV) and OAR for all patients were delineated by a single radiation oncologist with

extensive experience in the treatment of cervical cancer on individual CT slices. Based on the ICRU 62 report<sup>[31]</sup> and some published guidelines<sup>[32, 33]</sup>, the CTV included the upper one-half of the vagina and the stump, parametrial tissue, and pelvic lymph nodes. Because nonenlarged lymph nodes are poorly visualized on CT, contrast-enhanced vessels plus a 2-cm margin were used to define the common, external, and internal iliac nodal regions to the level of the L4-5 interspace. The presacral region was included to the bottom of the S3 vertebral body to ensure coverage of the presacral lymph nodes and attachment of the uterosacral ligament. The PTV was generated using a 1.0-cm uniform expansion of the CTV. The PTV mean volume in this study was  $(1368.90 \pm 644.12)$  cm<sup>3</sup>. All plans were normalized to deliver 45 Gy to 95% of PTV in 25 fractions.

### Critical structures

OAR included the rectum, bladder, bowel, pelvic bone marrow (PBM) and normal tissue (NT). The rectum was defined from the level of the sacral promontory to the ischial tuberosities. The contour of the bladder in full-filling condition was delineated. The peritoneal cavity (excluding the rectum and bladder) from the level of L4-5 was used to define the small bowel region and the individual loops of small bowel were not separately contoured. The PBM comprised the lumbosacral bone marrow, iliac bone marrow, and ischium, pubis, and proximal femoral bone marrow and femoral heads. The NT was defined as the whole body volume covered by the CT scan minus the PTV.

### Treatment planning

For each patient, four VMAT plans were designed using FFF and FF beams of nominal energy 6-MV (6FF-VMAT, 6FFF-VMAT) and 10-MV (10FF-VMAT, 10FFF-VMAT) photons of Elekta Versa HD<sup>TM</sup> accelerator on the Monaco planning system (version 5.1, Elekta AB, Stockholm, Sweden), respectively. VMAT plans were generated using 2 full arcs of clockwise rotation from the initial angle of 180 degrees to the end angle of 180 degrees. All plans were normalized to cover 95% of the PTV with the prescription dose using an identical set of PTV and OAR dose-volume constraints. The dose-volume constraints used for the targets and critical structures are listed in Table 1, which summarized our clinical experience while combining the guidelines of Radiation Therapy Oncology Group (RTOG) 0418, and were kept the same for all plans.

### Dosimetric comparisons

The dose-volume histograms (DVH) of four types of VMAT plans were compared in terms of homogeneity index (HI), conformity index (CI), Dmax, Dmin, and Dmean

of PTV, V10, V20, V30, and V40 of the rectum (fraction of rectum volume receiving > 10 Gy, 20 Gy, 30 Gy, 40 Gy); V20, V30, and V40 of the bladder; V10, V20, V30, and V40 of the bowel; V5, V10, V20, V30, and V40 of PBM; and V10, V20, V30, and V40 of NT. The HI was defined as minimum dose in 5% of the PTV (D5) / minimum dose in 95% of the PTV (D95). Smaller values of HI correspond to more homogenous irradiation of the target volume. A value of 1 corresponds to absolute homogeneity of dose within the target. The CI reflected the degree of conformity and was defined as follows [22]: CI = the percentage of the PTV volume receiving at least prescription dose × the ratio of the volume of the PTV receiving at least prescription dose to the total volume covered by prescription dose. The perfect conformity is 1 and the higher (closer to 1) the CI, the better the dose conformity. Dmax represents the minimum absorbed dose received by 2% of the PTV while Dmin represents the minimum absorbed dose received by 98% of the PTV [34].

### Statistical analysis

Statistical analysis was performed using SPSS software (version 18.0, SPSS Inc., Chicago, IL, USA). Quantitative data were expressed in the form of mean ± standard deviation ( $\bar{x} \pm s$ ). The statistical significance was tested using factorial design analysis of variance (ANOVA). A *P*-value ≤ 0.05 was considered statistically significant, and the 95% confidence intervals (CI) were calculated.

## Results

### PTV coverage

Table 2 summarizes the PTV coverage for four types of VMAT plans. Significant differences for HI were found (*P* = 0.039), with FF-VMAT showing better heterogeneity while CI was similar (*P* = 0.288, *P* = 0.294, and *P* = 0.499, respectively). In addition, Dmax also demonstrated significant differences between FFF-VMAT and FF-VMAT (*P* = 0.039).

### Comparison of dosimetric parameters of OAR for four modalities

Dosimetric parameters of OAR including the PBM, small bowel, bladder, rectum, and NT are listed in Table

**Table 1** Dose-volume constraints for targets and critical structures

Structures	Volume (%)	Dose (Gy)
PTV	95	45
Pelvic bone marrow	≤ 90	10
	≤ 80	20
Small bowel	≤ 30	25
Bladder	≤ 25	30
Rectum	≤ 60	40

3. No significant difference was observed for V5, V10, V20, V30, and V40 of the PBM (*P* > 0.05); V10, V20, and V30 of the small bowel (*P* > 0.05); V20, V30, and V40 of the bladder (*P* > 0.05); V10, V20, V30, and V40 of the rectum (*P* > 0.05); and V10, V30, V40, and Dmean of NT (*P* > 0.05). Only V10 of NT showed significant difference (*P* = 0.039).

### Comparison of monitor units (MU) and beam-on time (BOT) for two modalities

The data of monitor units (MU) and beam-on time (BOT) are listed in Table 4. The BOT of FFF-VMAT reduced delivery time compared with FF-VMAT.

## Discussion

It was demonstrated that for medium- and small-size targets, FFF beams might be suitable for IMRT planning and that the out-of-field dose could be significantly reduced owing to the lower contamination from head scatter, resulting in better OAR risk protection [35]. It would be important to demonstrate whether the two effects could also be confirmed for larger targets in complex anatomic situation.

Spruijt *et al* [15] compared FF and FFF beams for breast cancer using four IMRT techniques and pointed out that all four IMRT techniques allowed FFF beams to generate acceptable plans for breast cancer. Nicolini *et al* [16] carried out a feasibility study by using 6FFF-VMAT on advanced esophageal cancer and concluded that 6FFF-VMAT plans acquired minor improvements in plan quality, but with the potential for additional useful reduction in the treatment time. A study by Kretschmer *et al* [17]

**Table 2** Comparison of HI, CI, Dmax, Dmin, and Dmean for 6FF-VMAT, 10FF-VMAT, 6FFF-VMAT, and 10FFF-VMAT

	6FF-VMAT (%)	10FF-VMAT (%)	6FFF-VMAT (%)	10FFF-VMAT (%)	<i>P</i> value
Dmax	50.45 ± 1.61	50.56 ± 1.86	51.01 ± 1.73	52.16 ± 2.56	0.220*, 0.039**, 0.310***
Dmin	43.59 ± 0.57	43.61 ± 0.50	43.65 ± 0.50	43.52 ± 0.50	0.667*, 0.917**, 0.607***
Dmean	47.95 ± 0.90	48.04 ± 1.07	48.12 ± 0.85	48.66 ± 1.16	0.233*, 0.130**, 0.394***
HI	1.11 ± 0.03	1.11 ± 0.04	1.12 ± 0.03	1.14 ± 0.05	0.194*, 0.039**, 0.294***
CI	0.78 ± 0.06	0.78 ± 0.07	0.78 ± 0.06	0.75 ± 0.06	0.288*, 0.294**, 0.499***

\*, represents the effect of energy; \*\*, represents the effect of flattening filter; and \*\*\*, represents the interactive effect of energy and flattening filter

**Table 3** Comparison of dosimetric parameters of OARs for four modalities

OARs parameters	6FF-VMAT(%)	10FF-VMAT(%)	6FFF-VMAT(%)	10FFF-VMAT(%)	P value
<b>PBM</b>					
V5	98.20 ± 3.22	98.78 ± 2.39	98.73 ± 2.59	98.46 ± 2.99	0.831*, 0.885**, 0.565***
V10	87.32 ± 6.07	89.69 ± 4.87	89.96 ± 4.76	89.70 ± 5.40	0.444*, 0.337**, 0.342***
V20	72.25 ± 7.50	73.59 ± 6.62	73.12 ± 6.50	73.20 ± 6.98	0.692*, 0.894**, 0.725***
V30	54.86 ± 9.67	55.73 ± 9.55	55.07 ± 9.44	56.43 ± 8.03	0.640*, 0.848**, 0.920***
V40	28.85 ± 10.40	30.03 ± 11.67	29.25 ± 10.57	30.68 ± 11.04	0.646*, 0.853**, 0.964***
<b>Small bowel</b>					
V10	74.66 ± 24.42	75.65 ± 24.58	76.25 ± 24.93	75.78 ± 24.67	0.967*, 0.893**, 0.909***
V20	46.51 ± 18.79	46.61 ± 17.94	46.91 ± 17.84	46.46 ± 18.53	0.970*, 0.979**, 0.954***
V30	25.44 ± 12.90	25.43 ± 12.96	25.66 ± 12.29	26.13 ± 13.16	0.945*, 0.888**, 0.943***
<b>Bladder</b>					
V20	86.42 ± 11.51	87.67 ± 12.14	86.67 ± 11.00	89.68 ± 10.54	0.468*, 0.700**, 0.766***
V30	59.09 ± 18.14	60.57 ± 17.90	60.37 ± 17.84	61.96 ± 17.52	0.740*, 0.773**, 0.991***
V40	39.74 ± 22.38	40.90 ± 23.87	40.26 ± 22.06	41.03 ± 23.34	0.872*, 0.957**, 0.974***
<b>Rectum</b>					
V10	97.71 ± 4.53	97.71 ± 4.50	97.68 ± 4.61	97.81 ± 4.42	0.955*, 0.971**, 0.957***
V20	93.61 ± 5.83	93.43 ± 6.26	93.44 ± 5.86	92.79 ± 5.88	0.788*, 0.792**, 0.880***
V30	70.65 ± 18.09	72.38 ± 17.61	71.47 ± 17.16	71.19 ± 18.26	0.875*, 0.967**, 0.827***
V40	46.13 ± 27.32	45.96 ± 27.06	46.74 ± 26.50	46.95 ± 28.69	0.998*, 0.910**, 0.978***
<b>NT</b>					
V10	43.93 ± 9.09	44.21 ± 8.71	44.40 ± 8.62	44.74 ± 8.74	0.220*, 0.039**, 0.310***
V20	24.52 ± 7.17	24.69 ± 6.91	24.43 ± 6.73	24.95 ± 7.01	0.864*, 0.887**, 0.889***
V30	11.71 ± 4.80	11.73 ± 4.79	11.61 ± 4.56	12.64 ± 5.15	0.706*, 0.697**, 0.638***
V40	4.55 ± 2.81	4.74 ± 3.05	4.55 ± 2.79	5.16 ± 3.25	0.642*, 0.751**, 0.755***
Dmean	11.42 ± 2.36	11.46 ± 2.37	11.48 ± 2.28	11.68 ± 2.46	0.842*, 0.813**, 0.898***

\*, represents the influence of energy on parameters; \*\*, represents the influence of flattening filter on parameters; and \*\*\*, represents the influence of interaction between energy and flattening filter on parameters

**Table 4** Comparison of monitor units (MU) and beam-on time (BOT) for two techniques

	MU	BOT (sec)
6FF-VMAT	1275.9 ± 227.4	243 ± 28
10FF-VMAT	1138.1 ± 209.1	246 ± 36
6FFF-VMAT	1724.7 ± 255.1	216 ± 26
10FFF-VMAT	1746.7 ± 272.2	206 ± 31
P value	0.358*, 0.000**, 0.207***	0.642*, 0.000**, 0.376***

\*, represents the effect of energy, \*\*, represents the effect of flattening filter, and \*\*\*, represents the interactive effect of energy and flattening filter

compared FF and FFF beam field-in-field plans in several tumor locations, including breast, neurocranium, lung, and bone metastases, and demonstrated that the exclusive use of a linear accelerator in FFF mode is feasible in 3DCRT. Bell *et al* [35] probed the used of modulated arc (mARC) technique using FFF and FF beams for prostate treatment, respectively. The conclusion was that the combination of the high dose rate with mARC appears to be the preferable option as it benefits from a marked decrease in treatment time and out-of-field dose. Bahrainy *et al* [36] investigated the influence of FFF beam on breast cancer with simultaneous integrated boost in the hybrid

plan technique and concluded that in comparison to the FF-based plan, the FFF mode allowed further reduction of the average left anterior descending artery (LAD) dose for comparable target volume coverage without adverse low-dose exposure of contralateral structures.

The purpose of our study was to compare FFF beams and conventional FF beams in VMAT of cervical cancer after surgery through a retrospective planning study, focusing on the extent of BOT reduction and feasibility of clinical use of FFF beams. Considering that the FFF-VMAT plans are not intended for clinical use, dosimetric verification was thus not presented in this work.

In our study, FFF-VMAT achieved inferior heterogeneity compared to FF-VMAT while the conformity of the modalities was similar. In terms of dosimetric parameters of OAR, no significant difference was observed for dose-volume parameters for the PBM, small bowel, bladder, rectum, and NT, excluding V10 of NT.

The increase in dose rate is one of the most obvious and attractive effects when removing the FF. The increased dose rate can translate into shorter treatment times for the same technique. The BOT in our study was approximately 11% less for 6FFF-VMAT plans and approximately 16% less for 10FFF-VMAT plans. Obviously, in terms

of treatment time, patients could benefit more from the increased dose rate of the FFF beam for cervical cancer to improve comfort on the treatment table, immobility, minimize internal organ movement such as bladder or rectum filling changes over delivery, and reduce intra-fractional patient motion.

## Conclusion

For patients with cervical cancer after hysterectomy, the FFF beam achieved similar target and OAR dose distribution as the FF beam. Reduction of BOT in cervical cancer is beneficial.

## Conflicts of interest

The authors indicated no potential conflicts of interest.

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