

Original Article

Volumetric modulation arc radiotherapy with flattening filter-free beams compared with conventional beams for nasopharyngeal carcinoma: a feasibility study

Mingzan Zhuang¹, Tuodan Zhang¹, Zhijian Chen¹, Zhixiong Lin¹, Derui Li¹,
Xun Peng¹, Qingchun Qiu² and Renhua Wu³

Abstract

There is increasing interest in the clinical use of flattening filter-free (FFF) beams. In this study, we aimed to investigate the dosimetric characteristics of volumetric modulated arc radiotherapy (VMAT) with FFF beams for nasopharyngeal carcinoma (NPC). Ten NPC patients were randomly selected to undergo a RapidArc plan with either FFF beams (RA-FFF) or conventional beams (RA-C). The doses to the planning target volumes (PTVs), organs at risk (OARs), and normal tissues were compared. The technical delivery parameters for RapidArc plans were also assessed to compare the characteristics of FFF and conventional beams. Both techniques delivered adequate doses to PTVs. For PTVs, RA-C delivered lower maximum and mean doses and improved conformity and homogeneity compared with RA-FFF. Both techniques provided similar maximum doses to the optic nerves and lenses. For the brain stem, spinal cord, larynx, parotid glands, oral cavity, and skin, RA-FFF showed significant dose increases compared to RA-C. The dose to normal tissue was lower in RA-FFF. The monitor units (MUs) were (536 ± 46) MU for RA-FFF and (501 ± 25) MU for RA-C. The treatment duration did not significantly differ between plans. Although both treatment plans could meet clinical needs, RA-C is dosimetrically superior to RA-FFF for NPC radiotherapy.

Key words Flattening filter-free beams, RapidArc, nasopharyngeal carcinoma, volumetric modulated arc therapy, TrueBeam

Radiotherapy is the main component of curative treatment for nasopharyngeal carcinoma (NPC), and it presents a particular challenge in treatment planning. Large and complex target volumes are surrounded by many organs at risk (OARs), such as the brain stem, spinal cord, and parotid glands. Furthermore, more than 70% of NPC patients are diagnosed with stages III-IV tumors with skull base or intracranial invasion, or with cranial nerve symptoms, which increase the

difficulty of treatment planning^[1]. The application of sophisticated techniques is required to minimize the risk of toxicity while delivering adequately curative doses. Several investigators have studied the role of volumetric modulated arc therapy (VMAT) and static gantry intensity-modulated radiotherapy (IMRT). These studies demonstrated the feasibility of VMAT for NPC radiotherapy with the possibility of optimizing the tradeoff between target coverage and OAR protection^[2,3].

Recently, there has been an increasing interest in the clinical usage of flattening filter-free (FFF) beams. Removal of the flattening filter results in a significantly increased dose rate with decreased head scatter and leakage. This may allow faster treatment with reduced out-of-field dose exposure^[4,5]. The present study aimed to determine the role of FFF beams in reducing the involvement of OARs and preserving adequate target coverage in VMAT. It has been demonstrated that for medium and small targets, FFF beams were suitable for IMRT planning and that the out-of-field dose could be

Authors' Affiliations: ¹Department of Radiation Oncology, Tumor Hospital of Shantou University Medical College, Shantou, Guangdong 515000, P. R. China; ²Department of Medical Physics and Computer Application, Shantou University Medical College, Shantou, Guangdong 515000, P. R. China; ³Department of Radiation, The Second Affiliated Hospital of Shantou University Medical College, Shantou, Guangdong 515000, P. R. China.

Corresponding Author: Xun Peng, Department of Radiation Oncology, Tumor Hospital of Shantou University Medical College, No. 7 Raoping Road, Shantou, Guangdong 515000, P. R. China. Tel: +86-13692002110; Email: ppx206@yahoo.com.cn.

doi: 10.5732/cjc.012.10182

significantly reduced, resulting in better OAR protection^[6]. It would be important to demonstrate whether these advantages could be extended to larger targets in a complex anatomic situation.

Materials and Methods

Patient selection

NPC patients who had undergone radiotherapy continuously in the Radiation Oncology Department, Tumor Hospital of Shantou University Medical College between March 2011 and February 2012 were selected.

Delineation of target volumes and OARs

All target volumes were outlined on the treatment planning computed tomography (CT) images according to the International Commission on Radiation Units and Measurements Report 62 guidelines^[7]. Gross tumor volume (GTV) was defined as the gross extent of the tumor shown by CT or magnetic resonance imaging (MRI), covering the primary tumor (GTVnx) as well as all involved regional lymph nodes (GTVnd). Clinical target volume (CTV) was defined as the GTV plus a margin for potential microscopic spread, including the regional lymph node draining areas. Planning target volumes (PTVs), which included PTVnx, PTVnd, and PTV60, were generated by the 3 mm outer margin of GTVnx, GTVnd, and CTV to account for patient set-up and motion uncertainties. The OARs, including the spinal cord, brain stem, lens, optic nerves, parotid glands, oral cavity, and larynx, were contoured following anatomic definitions. Normal tissue was defined as the body volume subtracted by all PTVs and OARs, and the skin was defined as the ring generated by the 3 mm inter margin of the body.

Treatment plan management

A RapidArc plan with FFF beams (RA-FFF) and a RapidArc plan with conventional beams (RA-C) were optimized to assess the usability of these new beams in practice. Considering the large target volumes of the NPC and surrounding complex OARs, two coplanar arcs of 360° were adopted for both RapidArc plans and delivered with opposite rotation (i.e., clockwise and anticlockwise). The maximal dose rate was set to 600 monitor units (MU)/min for RA-C and 1,400 MU/min for RA-FFF. The couch was set to 0°, whereas the collimator rotation was set at 30°.

The Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA) was used for 6 MV

beams with or without flattening filter from a TrueBeam linear accelerator (Varian Medical Systems, Palo Alto, CA). The accelerator was calibrated to deliver 1 cGy/MU to water at a depth of 1.5 cm for a 10 cm × 10 cm field at a source-to-surface distance of 100 cm following the American Association of Physicists in Medicine Task Group 51 report^[8]. The dose constraints for the target volumes and OARs used in this study are listed in Table 1. The optimization methods and parameters used were the same for all patients across both techniques. A calculation grid spacing of 2 mm was used in our study, and the analytical anisotropic algorithm (version 10.0.28) was applied for calculation.

Based on the information from dose-volume histograms (DVHs), dosimetric analysis was performed to compare the two techniques. For the PTVs, the maximum dose, minimum dose, mean dose, target coverage (TC), conformity index (CI), and homogeneity index (HI) were compared. TC was the percentage volume of the PTV at the prescribed dose. CI was calculated using this equation: $CI = (PTV_{ref} / V_{PTV}) \times (PTV_{ref} / V_{ref})$. PTV_{ref} represents the volume receiving the prescribed dose within the target volume. V_{PTV} stands for the volume of the PTV. V_{ref} is the volume that has received the prescribed dose. HI was evaluated as the difference between D1% and D99% (i.e., the dose received by 1% and 99% of the volume) divided by the prescribed dose^[9-11]. The maximum dose was applied to evaluate the doses to the brain stem, spinal cord, optic nerves, and lenses, and the mean dose was applied to evaluate the doses to the parotid glands, larynx, oral cavity, normal tissue, and skin. The treatment delivery time and the MUs of the two techniques were also compared.

Statistical analysis

The SPSS 11.0 software (IBM, Chicago, IL) was used for statistical data management and analysis. To determine statistical significance, the paired-sample *T* test was performed with *P* values <0.05 considered significant. Data are presented as the mean over all patients with standard deviations (SD).

Results

Patient characteristics

Ten NPC patients (6 men and 4 women) were selected. The median age was 53 years (range, 33–76 years). According to the 2002 American Joint Committee on Cancer (AJCC) staging system, 6 patients had stage III tumors and 4 had stage IV tumors.

Table 1. Dose constraints in both RapidArc plans for nasopharyngeal carcinoma (NPC)

Structures	Dose constraint
PTVnx	TC \geq 95%, V110 \leq 1%
PTVnd	TC \geq 95%, V110 \leq 1%
PTV60	TC \geq 95%
Brain stem	Dmax < 60 Gy
Spinal cord	Dmax < 45 Gy
Optic nerves	Dmax < 50 Gy
Lens	Dmax < 10 Gy
Larynx	Dmean < 40 Gy
Oral cavity	Dmean < 40 Gy
Parotid	Dmean < 40 Gy
Normal tissue	As low as possible

PTVnx, planning target volume of the primary nasopharyngeal tumor; PTVnd, planning target volume of involved regional lymph nodes; PTV60, planning target volume receiving 60 Gy; TC, target coverage, the percentage volume of the PTV receiving the prescribed dose; V110, the percentage volume of the PTV receiving 110% of the prescribed dose; Dmax, the maximum dose; Dmean, the mean dose.

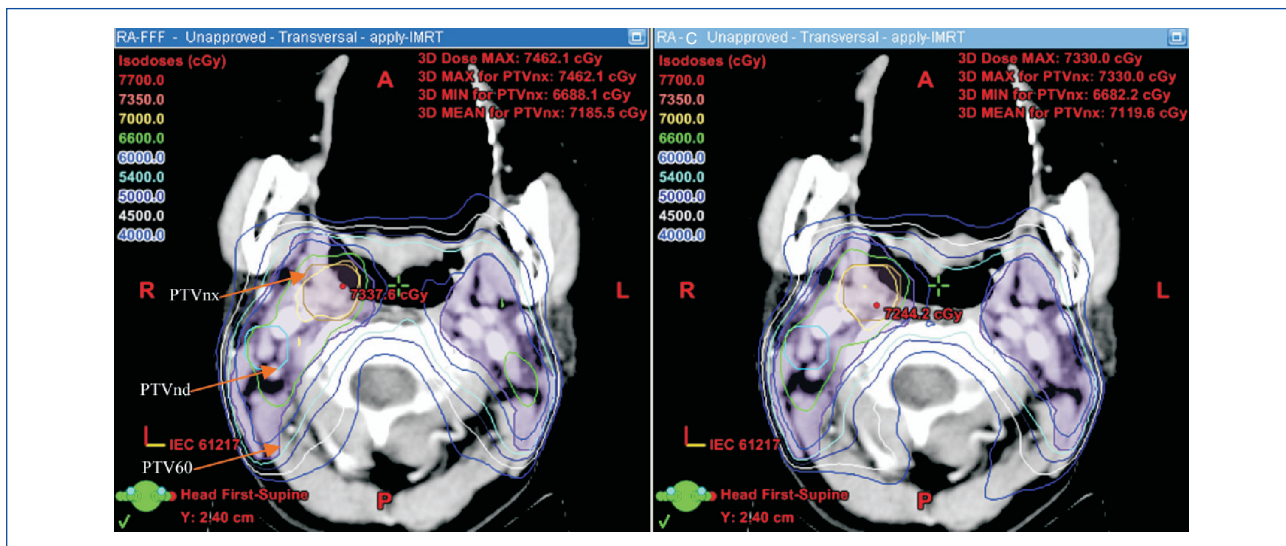


Figure 1. The dose distributions for RapidArc with flattening filter-free (FFF) beams (RA-FFF) and RapidArc with conventional beams (RA-C) in a patient with nasopharyngeal carcinoma. Both techniques delivered adequate dose coverage for the planning target volumes (PTVs). The dose distributions for RA-FFF and RA-C were similar; however, higher dose splashing to normal tissue was noticed in RA-C.

PTV doses

The simultaneous boost plan was used with prescribed doses of 7,000 cGy to PTVnx, 6,600 cGy to PTVnd, and 6,000 cGy to PTV60 in 31 fractions. The median volumes were (51 ± 27) cm³ for PTVnx, (66 ± 33) cm³ for PTVnd, and (537 ± 137) cm³ for PTV60. All plans were normalized so that 95% of the PTVnx received the prescribed dose, resulting in a mean PTVnx dose of $(7,280 \pm 72)$ cGy in RA-FFF and $(7,215 \pm 68)$ cGy in RA-C. The dose distributions for the two plans are shown for

1 patient in Figure 1 with corresponding DVHs shown in Figure 2.

As shown in Table 2, both techniques met the planning requirement for delivering the prescribed dose to at least 95% of the PTVs, and RA-C improved homogeneity and conformity compared with RA-FFF. For PTVs, RA-FFF delivered higher maximum and mean doses than did RA-C. No significant difference in other PTV parameters between the two techniques could be established.

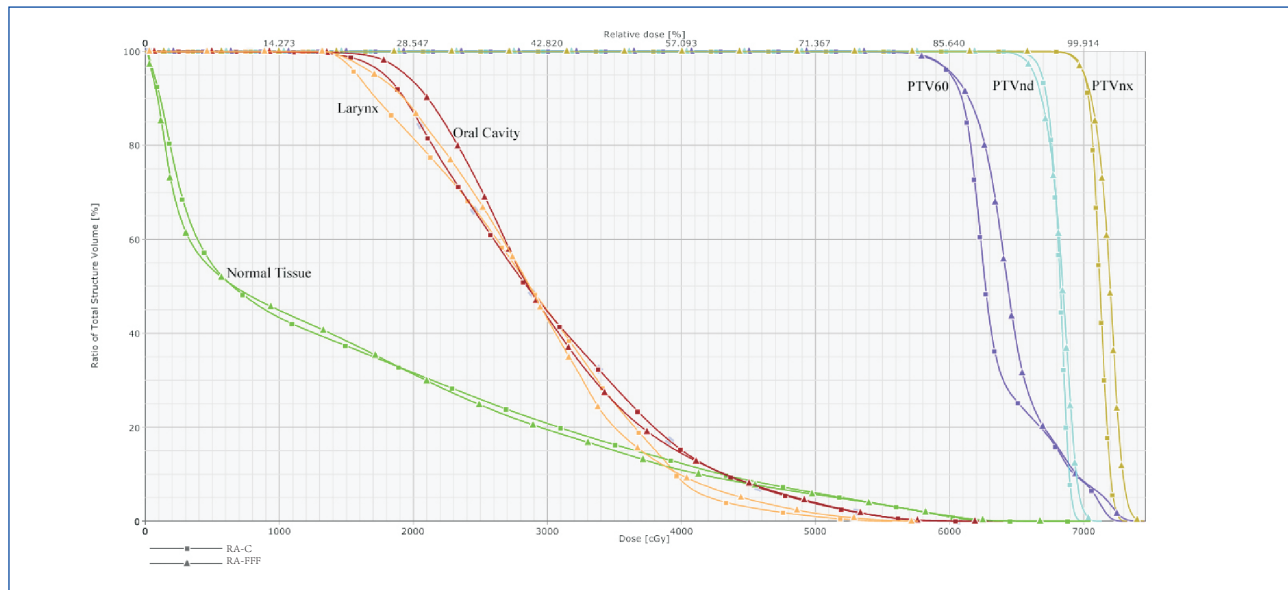


Figure 2. Dose-volume histograms (DVHs) for RA-FFF and RA-C in the same patient. Although both techniques provided good target coverage, RA-FFF delivered higher maximum and mean doses than RA-C to PTVs. To the larynx and oral cavity, RA-FFF showed significantly greater dose exposure compared to RA-C. However, the dose to normal tissue was slightly lower in RA-FFF.

Table 2. Comparison of PTV doses between RA-FFF and RA-C

Target	RA-FFF	RA-C	<i>P</i>	<i>T</i>
PTVnx				
Dmin (cGy)	6,422 ± 246	6,462 ± 198	0.412	-0.860
Dmax (cGy)	7,655 ± 156	7,516 ± 134	0.000	5.986
Dmean (cGy)	7,280 ± 72	7,215 ± 68	0.000	5.753
TC	0.950 ± 0.000	0.950 ± 0.000		
CI	0.486 ± 0.213	0.609 ± 0.199	0.010	-3.225
HI	0.087 ± 0.023	0.067 ± 0.021	0.031	0.953
PTVnd				
Dmin (cGy)	5,933 ± 301	5,881 ± 286	0.320	1.061
Dmax (cGy)	7,412 ± 169	7,267 ± 161	0.000	6.452
Dmean (cGy)	6,967 ± 99	6,890 ± 85	0.004	3.913
TC	0.978 ± 0.010	0.975 ± 0.017	0.588	0.564
CI	0.209 ± 0.074	0.244 ± 0.074	0.027	-2.707
HI	0.108 ± 0.054	0.088 ± 0.052	0.002	4.353
PTV60				
Dmin (cGy)	4,470 ± 362	4,423 ± 406	0.437	0.814
Dmax (cGy)	7,634 ± 141	7,537 ± 167	0.043	2.359
Dmean (cGy)	6,623 ± 93	6,555 ± 108	0.000	5.616
TC	0.964 ± 0.009	0.963 ± 0.010	0.940	0.077
CI	0.793 ± 0.025	0.811 ± 0.023	0.000	-5.397
HI	0.230 ± 0.040	0.217 ± 0.044	0.029	2.585

RA-FFF, RapidArc with flattening filter-free (FFF) beams; RA-C, RapidArc with conventional beams; Dmin, the minimum dose; CI, conformity index; HI, homogeneity index. Other abbreviations as in Table 1.

OAR doses

Both techniques provided similar maximum doses

to the optic nerves and lenses. None of their differences reached statistical significance (Table 3). For the brain stem, spinal cord, larynx, parotid glands, oral cavity, and

Table 3. Comparison of doses to organs at risk (OARs) between RA-FFF and RA-C

Parameter	RA-FFF (cGy)	RA-C (cGy)	P	T
Dmax				
Brain stem	5,891 ± 245	5,715 ± 275	0.002	4.490
Spinal cord	4,272 ± 267	4,082 ± 213	0.004	3.776
Optic nerves	1,971 ± 2,319	2,023 ± 2,209	0.624	-0.507
Lenses	574 ± 256	608 ± 216	0.130	-1.666
Dmean				
Larynx	3,255 ± 297	3,183 ± 269	0.028	2.618
Oral cavity	3,412 ± 223	3,331 ± 190	0.008	3.407
Parotid (right)	3,595 ± 432	3,400 ± 387	0.002	4.307
Parotid (left)	3,467 ± 362	3,347 ± 316	0.001	5.073
Normal tissue	1,624 ± 210	1,641 ± 209	0.012	-3.132
Skin	1,561 ± 214	1,485 ± 203	0.000	5.686

Abbreviations as in Table 2.

skin, RA-FFF delivered a significantly increased dose exposure compared to RA-C. However, the dose to normal tissue was lower in RA-FFF.

MUs and delivery time

The MUs were significantly higher in RA-FFF than in RA-C [(536 ± 46) MU vs. (501 ± 25) MU, $P = 0.024$]. The delivery duration was (152 ± 7) s for RA-FFF and (153 ± 7) s for RA-C.

Discussion

FFF beams have several potential advantages, including increased dose rate, reduced collimator scatter, reduced head leakage, and reduced out-of-field doses to the patient. This study aimed to assess whether FFF beams might be of clinical value, specifically in VMAT for NPC. We found that both treatment plans met clinical needs; however, RA-C outperformed RA-FFF by effectively reducing the dose to most OARs and achieving better conformity and homogeneity for the PTVs.

The increase in dose rate is an obvious effect of removing the flattening filter, and the maximal dose rate was 1,400 MU/min for RA-FFF in our study. However, the average delivery duration was similar for RA-FFF and RA-C because the delivery duration is largely limited by the gantry rotation speed and leaf speed, not the dose rate.

The spectrum of a 6 MV FFF beam is typically softer because the flattening filter acts as a beam hardener. The different spectrum of unflattened beams

is reflected in the depth-dose distribution. Vassiliev *et al.*^[12] found that the depth-dose distribution of unflattened 6 MV beams was similar to that of conventional 4–5 MV beams. Due to the softer spectrum of FFF beams, a slightly higher dose to the skin can be expected. A mitigating factor to the higher dose is that the scattered radiation and electron contamination from the flattening filter are eliminated. RA-FFF delivered a higher mean dose to the skin than RA-C. This could be avoided by using higher energies, e.g., 8 MV instead of 6 MV^[5].

Some degree of collimator rotation is usually performed in VMAT to minimize the cumulative effects of the tongue-and-groove effect and interleaf transmission^[13]. In our study, a 30° collimator angle in RapidArc was chosen. Mans *et al.*^[14] indicated that a better plan quality could be achieved using a collimator rotation between 20° and 30°. Clivio *et al.*^[15], Vanetti *et al.*^[16], and Cozzi *et al.*^[17] reported that a 30°–45° collimator rotation could improve the results.

In this study, RA-FFF showed a lower mean dose than RA-C for normal tissue because removing the flattening filter results in decreased scatter, leakage, and out-of-field doses. However, the MUs in the RA-FFF plans were always greater than in the RA-C plans. The reason for this effect is that the FFF beam intensity abruptly decreases with the off-axis distance, which can be clearly observed in larger field (≥10 cm × 10 cm) open-beam dose profiles. As a result, off-axis distance-dependent modulation is needed for delivering uniform doses to larger target volumes, and this may lead to greater MUs. This drawback will at least partially cancel the potential advantages of FFF beams.

Conclusions

In conclusion, when comparing the RA-FFF and RA-C techniques by the Eclipse planning system for patients with NPC, we found that RA-C was superior to RA-FFF due to its lower dose to most OARs and its better conformity and homogeneity for all PTVs. Although RA-FFF shows potential for the treatment of NPC patients with adequate target coverage and sparing of OARs, RA-C delivers dosimetric superiority compared to RA-FFF, and further studies are required to evaluate their clinical outcomes.

References

- [1] Lin S, Pan J, Han L, et al. Nasopharyngeal carcinoma treated with reduced-volume intensity-modulated radiation therapy: report on the 3-year outcome of a prospective series. *Int J Radiat Oncol Biol Phys*, 2009, 75:1071–1078.
- [2] Lee TF, Ting HM, Chao PJ, et al. Dual arc volumetric-modulated arc radiotherapy (VMAT) of nasopharyngeal carcinomas: a simultaneous integrated boost treatment plan comparison with intensity-modulated radiotherapies and single arc VMAT. *Clin Oncol*, 2012, 24:196–207.
- [3] Lu SH, Cheng JC, Kuo SH, et al. Volumetric modulated arc therapy for nasopharyngeal carcinoma: a dosimetric comparison with TomoTherapy and step-and-shoot IMRT. *Radiother Oncol*, 2012, 104:324–330.
- [4] Scorsetti M, Alongi F, Castiglioni S. Feasibility and early clinical assessment of flattening filter free (FFF) based stereotactic body radiotherapy (SBRT) treatments. *Radiat Oncol*, 2011, 6:113.
- [5] Georg D, Knoos T, McClean B. Current status and future perspective of flattening filter free photon beams. *Med Phys*, 2011, 38:1280–1293.
- [6] Cashmore J, Ramtohl M, Ford D. Lowering whole-body radiation doses in pediatric intensity-modulated radiotherapy through the use of unflattened photon beams. *Int J Radiat Oncol Biol Phys*, 2011, 80:1220–1227.
- [7] International Commission on Radiation Units and Measurements. ICRU report 62: prescribing, recording, and reporting photon beam therapy (supplement to ICRU report 50). Bethesda, ICRU, 1999.
- [8] Tailor R, Hanson W, Ibbott G. TG-51: experience from 150 institutions, common errors, and helpful hints. *J Appl Clin Med Phys*, 2003, 4:102–111.
- [9] Baltas D, Kolotas C, Geramani K, et al. A conformal index (COIN) to evaluate implant quality and dose specification in brachytherapy.

Acknowledgments

We wish to thank Prof. Lei Xing of Stanford University, Prof. Guojun Zhang and Dr. Minjie Luo of Shantou University Medical College for their valuable support. We also like to thank the support from the Li Ka Shing Foundation.

Received: 2012-07-10; revised: 2012-10-21;
accepted: 2012-10-22.

- Int J Radiat Oncol Biol Phys*, 1998, 40:515–524.
- [10] Clivio A, Fogliata A, Franzetti-Pellanda A, et al. Volumetric-modulated arc radiotherapy for carcinomas of the anal canal: a treatment planning comparison with fixed field IMRT. *Radiother Oncol*, 2009, 92:118–124.
- [11] Lin XT, Shun T, Wang CD, et al. Dosimetric comparison of fixed field intensity modulated radiation therapy and RapidArc volumetric modulated arc therapy in treatment of multiple intracranial metastases. *Chin J Radio Med Protect*, 2010, 30:585–589.
- [12] Vassiliev ON, Titt U, Ponisch F, et al. Dosimetric properties of photon beams from a flattening filter free clinical accelerator. *Phys Med Biol*, 2006, 51:1907–1917.
- [13] Rao M, Yang W, Chen F, et al. Comparison of Elekta VMAT with helical tomotherapy and fixed field IMRT: plan quality, delivery efficiency and accuracy. *Med Phys*, 2010, 37:1350–1359.
- [14] Mans A, Remeijer P, Olaciregui-Ruiz I, et al. 3D dosimetric verification of volumetric-modulated arc therapy by portal dosimetry. *Radiother Oncol*, 2010, 94:181–187.
- [15] Clivio A, Fogliata A, Franzetti-Pellanda A, et al. Volumetric-modulated arc radiotherapy for carcinomas of the anal canal: a treatment planning comparison with fixed field IMRT. *Radiother Oncol*, 2009, 92:118–124.
- [16] Vanetti E, Clivio A, Nicolini G, et al. Volumetric modulated arc radiotherapy for carcinomas of the oro-pharynx, hypo-pharynx and larynx: a treatment planning comparison with fixed field IMRT. *Radiother Oncol*, 2009, 92:111–117.
- [17] Cozzi L, Dinshaw KA, Shrivastava SK, et al. A treatment planning study comparing volumetric arc modulation with RapidArc and fixed field IMRT for cervix uteri radiotherapy. *Radiother Oncol*, 2008, 89:180–191.