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ORIGINAL ARTICLE

Evaluation of the dosimetric impact of applying flattening filter-free beams in intensity-modulated radiotherapy for early-stage upper thoracic carcinoma of oesophagus

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Abstract

Introduction: Flattening filter-free (FFF) radiation beams have recently become clinically available on modern linear accelerators in radiation therapy. This study aimed to evaluate the dosimetric impact of using FFF beams in intensity-modulated radiotherapy (IMRT) for early-stage upper thoracic oesophageal cancer. **Methods:** Eleven patients with primary stage upper thoracic oesophageal cancer were recruited. For each patient, two IMRT plans were computed using conventional beams (Con-P) and FFF beams (FFF-P), respectively. Both plans employed a five-beam arrangement and were prescribed with 64 Gy to (planning target volume) PTV1 and 54 Gy to PTV2 in 32 fractions using 6 MV photons. The dose parameters of the target volumes and organs at risks (OARs), and treatment parameters including the monitor units (MU) and treatment time (TT) for Con-P and FFF-P were recorded and compared. **Results:** The mean D_5 of PTV1 and PTV2 were higher in FFF-P than Con-P by 0.4 Gy and 0.3 Gy, respectively. For the OARs, all the dose parameters did not show significant difference between the two plans except the mean V_5 and V_{10} of the lung in which the FFF-P was lower (46.7% vs. 47.3% and 39.1% vs. 39.6%, respectively). FFF-P required 54% more MU but 18.4% less irradiation time when compared to Con-P. **Conclusion:** The target volume and OARs dose distributions between the two plans were comparable. However, FFF-P was more effective in sparing the lung from low dose and reduced the mean TT compared with Con-P. Long-term clinical studies are suggested to evaluate the radiobiological effects of FFF beams.

Introduction

Oesophagus carcinoma is a common malignancy in China and its incidence in 2009 was 22.1 per 100,000 population.[1] Higher incidence has been reported in southern China including Shantou. About 15% of oesophageal cancers arise in the upper thoracic region of the oesophagus. Because of its more posteriorly located anatomy and proximity to major nerves and blood vessels which make surgery less accessible, radiotherapy is one of the main treatment modality for upper thoracic carcinoma of oesophagus.[2] However, radiotherapy is not without challenges because these tumours are anatomically close to the spinal cord and the treatment region always experiences great changes in body contour.[3] Recently, static beam conventional beam intensity-modulated radiotherapy (IMRT) has been proven to have dosimetric advantages over the conventional three-dimensional radiotherapy by some studies, in which better dose coverage to the target and sparing of organs at risk (OARs) have been reported.[4–6] However, conventional IMRT requires a relatively longer treatment time (TT), which may increase the risk of patient movement during treatment,[7] resulting in a less accurate treatment. Since the target dose demonstrate great dose gradients at the boundary, a slight shift by the patient can result in dramatic dosimetric changes leading to detrimental results to the patient.

To overcome the problem, a recently developed technology utilising flattening filter-free (FFF) radiation beams has been introduced to the linear accelerator. The main purpose of FFF is to accelerate the speed of dose delivery because the attenuation of radiation by the flattening filter at the gantry head has been removed.[8,9] Because of this, a dose rate of as high as 2400 MU/min can be delivered, which is about four times faster than the commonly used dose rate. Another accompanied advantage of FFF is that the dose just outside the treatment field can be reduced due to the reduction of side scatter radiation and multileaf collimator (MLC) leakage.[10] For the FFF beams, with the use of the modulation effect of dynamic MLC in IMRT, the problem of a nonuniform, conical fluence distribution can be largely solved. Recent trials of FFF have demonstrated its applications in IMRT and stereotactic body radiotherapy (SBRT) for various malignant diseases.[11–13] Apart from the potential reduction of treatment delivery time, our study aimed to evaluate the dosimetric impact of using FFF beams in IMRT for early-stage upper thoracic oesophageal cancer. If the dosimetric outcome of the FFF plans were comparable or superior to the conventional IMRT plans, they would have the potential to become a more favourable treatment due to its expected shortened TT.

Methods

Eleven patients (eight males and three females) with primary stage I and II upper thoracic oesophageal cancer treated by radiotherapy between March and September 2010 were retrospectively recruited. The study was approved by the institutional review board of the cancer hospital and all patient information was anonymised throughout the study. The length of the lesions ranged between 4.5 and 10.5 cm, with the gross tumour volume (GTV) ranging from 19.5 to 51.0 cm^3 (mean 35.1 ± 8.5 cm^3).

During CT, patients lied in supine position with both arms placed at the side of the body. A thermoplastic shell was used to immobilise the head and neck region. The CT was conducted using Brillance Big Bore (Philips, Eindhoven, the Netherlands) with patients under normal breathing condition. The scan covered the whole volume of the lung with a slice thickness of 3 mm. The DICOM CT data of each patient were transferred to the Eclipse treatment planning system (TPS) (Version 10.0; Varian Medical Systems, Palo Alto, CA). The target volumes and OARs were delineated in the respective CT slices. The GTV contained the oesophageal tumour and the adjacent major nodes. The clinical target volume that was prescribed a dose of 64 Gy (CTV_{64}) included the GTV plus the high-risk region, which was to add margins of 15–20 mm and 15 mm in the longitudinal and transverse direction, respectively. The CTV_{54} (clinical target volume was prescribed 54 Gy) was delineated by adding the mediastinal and supraclavicular lymphatics to the CTV_{64}. The planning target volume (PTV) was formed by expanding the CTV by 5 mm in all directions. The OARs included the lungs and spinal cord. A margin of 5 mm was added to form the planning organ at risk of the spinal cord (PRV). Because the lesion at upper thoracic of the thoracic oesophagus was at considerable distance from the heart and the dose to this organ was expected to be very low, it was not included as OAR in the study.

For each patient, two IMRT plans were computed using conventional beams (Con-P) and FFF beams (FFF-P), respectively. Both plans employed a 5-beam arrangement with gantry angles at 0°, 72°, 144°, 216°, and 288°, which was a standard practice in the local department. The intensity-modulated beams were generated by dynamic MLC from the TrueBeam linear accelerator (Varian Medical Systems) using 6 MV photons. The dose rates were set at 600 MU/min and 1400 MU/min for the Con-P and FFF-P, respectively. The maximum dose rate 2400 MU/min was not used because the dosimetric reliability was not yet verified. Both plans were prescribed with 64 Gy to PTV1 and 54 Gy to PTV2 in 32 fractions. The optimisation parameters including the dose constraints of the targets and OARs were set for the optimisation of both Con-P and FFF-P plans according to the local protocol as shown in Table 1. All plans were computed by the same planner and the dose calculation was done using the analytical anisotropic algorithm (AAA) with grid size of 0.25×0.25 cm^2.

Table 1. Dose constraints for target volume and organs at risk in the computation of conventional IMRT plan (Con-P) and flattening filter-free IMRT plan (FFF-P).

Structures	Dose constraints
PTV1	95% $\geq$ 64 Gy $V_{105} \leq 5\%$ $D_{\min} \geq 60$ Gy $D_{\max} \leq 70$ Gy
PTV2	95% $\geq$ 54 Gy
Spinal cord	$D_{\max} \leq 40$ Gy
Spinal cord PRV	$D_{\max} \leq 45$ Gy
Lung	$V_{20} \leq 25\%$ $V_{30} \leq 20\%$

PTV, Planning target volume; PRV, planning organ at risk volume; $D_{\min}$, minimum dose; $D_{\max}$, maximum dose; V_{105}, volume of structure receiving 105% dose level; V_{20} and V_{30}, volume of structure receiving 20 Gy and 30 Gy respectively.

After the production of the treatment plans, the doses to the targets and OARs were recorded from their respective dose volume histograms (DVHs). For the dose analysis of PTV1 and PTV2, their D_{mean} (mean dose), D_5 (dose received by 5% of volume), D_{min} (minimum dose), V_{95} (volume received 95% prescribed dose), and V_{105} (volume received 105% prescribed dose) were used. In addition, the conformity index (CI) and homogeneity index (HI) were also used for PTV1. The calculation of CI was using the $(V_{\mathrm{T,ref}}/V_{\mathrm{T}}) \times (V_{\mathrm{T,ref}}/V_{\mathrm{ref}})$ formula,[14] while the HI was calculated by D_5/D_{95},[15] where $V_{\mathrm{T,ref}}$ was the volume of PTV1 received the prescribed dose 64 Gy, V_{T} was the volume of PTV1, V_{ref} was the volume of the 64 Gy isodose volume, D_5 and D_{95} were the doses received by 5% and 95% of PTV1, respectively. For CI and HI, the closer the value to 1.0, the better would be the target conformity and homogeneity, respectively. D_{max} was used for the recording the dose to spinal cord and its PRV, while for the lung, V_5, V_{10}, V_{20}, and V_{30} (volume of lung received 5, 10, 20, and 30 Gy, respectively) were used. In addition, the treatment parameters including the monitor units (MU) and TT for each treatment plan were also recorded for evaluation. The TT was defined as the radiation delivery time and did not include the setup time. The TT and MU were generated from the TPS. The mean values (and standard deviations) of all the parameters for Con-P and FFF-P in all the patients were calculated and compared. Paired *t*-test or Wilcoxon signed-rank test was used to evaluate the significance of their differences depending on the normality of the data, and P value of <0.05 was defined as significant difference.

Results

All IMRT treatment plans produced met the dose requirements set for optimisation. Based on the DVHs of the target volumes (Fig. 1), the dose patterns were fairly similar between Con-P and FFF-P. Both the PTV1 and PTV2 of FFF-P showed higher D_5 than that of Con-P ($P = 0.046$ and 0.043, respectively) (Table 2) and there was no significant different in the CI and HI between the two plans. For the OARs, all the dose parameters did not show any significant difference between the two sets of plans except for the V_5 and V_{10} of the lung, in which the FFF-P presented with a significantly lower dose (Table 3 and Fig. 1). For the treatment delivery parameters, an increase of 54% in the mean MU was found in the FFF-P relative to the Con-P ($P < 0.001$), while the mean TT, which was the average of the TT for the 11 patients, was reduced by 18.4% when compared with the Con-P ($P = 0.021$) (Table 4).

Discussion

Five beam IMRT has been a routine technique used to treat upper thoracic oesophageal cancer in the local department. The introduction of FFF beams in the more advanced linear accelerators greatly accelerates the

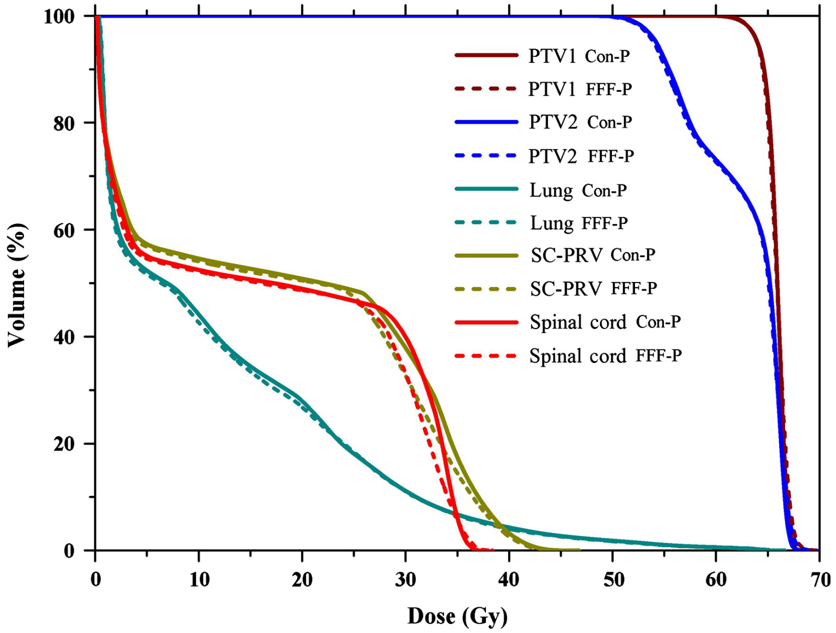

Figure 1. Comparison of dose volume histograms (DVHs) for the targets and organs at risk between Con-P and FFF-P. Con-P, conventional IMRT plan; FFF-P, flattening filter-free IMRT plan; PRV, planning organ at risk volume; PTV, planning target volume; SC, spinal cord.

Table 2. Comparison of target volume dose parameters between Con-P and FFF-P.

Structure	Parameter	Con-P Mean ± SD	FFF-P Mean ± SD	*P* value
PTV1	D_{mean} (Gy)	66.5 ± 0.4	66.5 ± 0.3	0.990
	D_5 (Gy)	68.3 ± 0.7	68.7 ± 0.6	0.046*
	D_{min} (Gy)	58.1 ± 1.5	58.4 ± 1.8	0.676
	V_{95} (%)	99.9 ± 0.1	99.9 ± 0.1	1.000
	V_{105} (%)	32.4 ± 15.5	32.8 ± 12.3	0.165
	CI	0.86 ± 0.03	0.85 ± 0.03	0.444
	HI	1.07 ± 0.01	1.07 ± 0.01	1.000
PTV2	D_{mean} (Gy)	63.0 ± 1.1	63.0 ± 1.1	1.000
	D_5 (Gy)	68.1 ± 0.6	68.4 ± 0.6	0.043*
	D_{min} (Gy)	45.9 ± 1.0	45.7 ± 1.3	0.690
	V_{95} (%)	99.7 ± 0.2	99.6 ± 0.2	0.255
	V_{105} (%)	97.9 ± 0.7	94.9 ± 5.6	0.093

HI, homogeneity index; CI, conformity index; PTV, planning target volume; D_{mean}, mean dose; D_5, dose received by 5% of volume; D_{min}, minimum dose; V_{95}, volume received 95% prescribed dose; V_{105}, volume received 105% prescribed dose; SD, standard deviation. *Significant difference.

Table 3. Comparison of organs at risk dose parameters between Con-P and FFF-P.

Structure	Parameter	Con-P Mean ± SD	FFF-P Mean ± SD	*P* value
Spinal cord	D_{max} (Gy)	38.6 ± 0.8	38.4 ± 0.8	0.564
Spinal cord-PRV	D_{max} (Gy)	45.3 ± 1.6	45.2 ± 1.7	0.888
Lung	D_{mean} (Gy)	32.4 ± 15.5	32.8 ± 12.3	0.947
	V_5(%)	47.3 ± 13.6	46.7 ± 13.5	0.045*
	V_{10}(%)	39.6 ± 11.5	39.1 ± 11.1	0.043*
	V_{20}(%)	24.7 ± 6.8	24.1 ± 6.6	0.836
	V_{30}(%)	8.6 ± 2.5	8.7 ± 2.5	0.726

D_{max}, maximum dose; D_{mean}, mean dose; V_5, V_{10}, V_{20} and V_{30}, volume of lung received 5, 10, 20 and 30 Gy respectively; PRV, planning organ at risk volume; SD, standard deviation. *Significant difference.

Table 4. Comparison of monitor unit (MU) and treatment time (TT) between Con-P and FFF-P.

Parameter	Con-P Mean ± SD	FFF-P Mean ± SD	*P* value
MU	663 ± 71	1020 ± 106	<0.001*
TT (sec)	174 ± 20	142 ± 12	0.002*

SD, standard deviation. *Significant difference.

treatment speed and shortens the beam on time in such treatments. In the radiotherapy of oesophageal cancer patients who are often physically weak, reducing the TT will certainly be a benefit to the patients. Since hypofractionation treatment for oesophageal cancer has been a current trend, which involves higher dose per fraction so as to improve the biological effect of radiation, the application of FFF in such scheme would be useful to keep TT short. Recent studies reported that the advantages of FFF increased the beam output near the central axis and reduced the out-of-field and whole body dose during irradiation.[16] This would lower the risk of complication and development of secondary cancer due to low-dose irradiation.

Our study showed that the IMRT plans using both conventional beams (Con-P) and FFF beams (FFF-P) met the dosimetric requirements for the treatment of upper thoracic oesophageal cancer patients. Many of the dose parameters from the plans of the two different treatment delivery methods were similar (Fig. 2). Although the FFF-P produced a relatively higher D_5 (indicator of the maximum dose) in the PTVs, it was not expected to produce any clinical difference compared with the Con-P in these patients because the absolute difference was minimal. There was also not much difference in the OAR doses between the two different plans. This implied that there was no obvious advantage of the FFF-P over the Con-P in the sparing of OARs. However, the significant difference in the low-dose volume of the lung (V_5 and V_{10}) implied that FFF-P may be able to reduce the stochastic effect to the

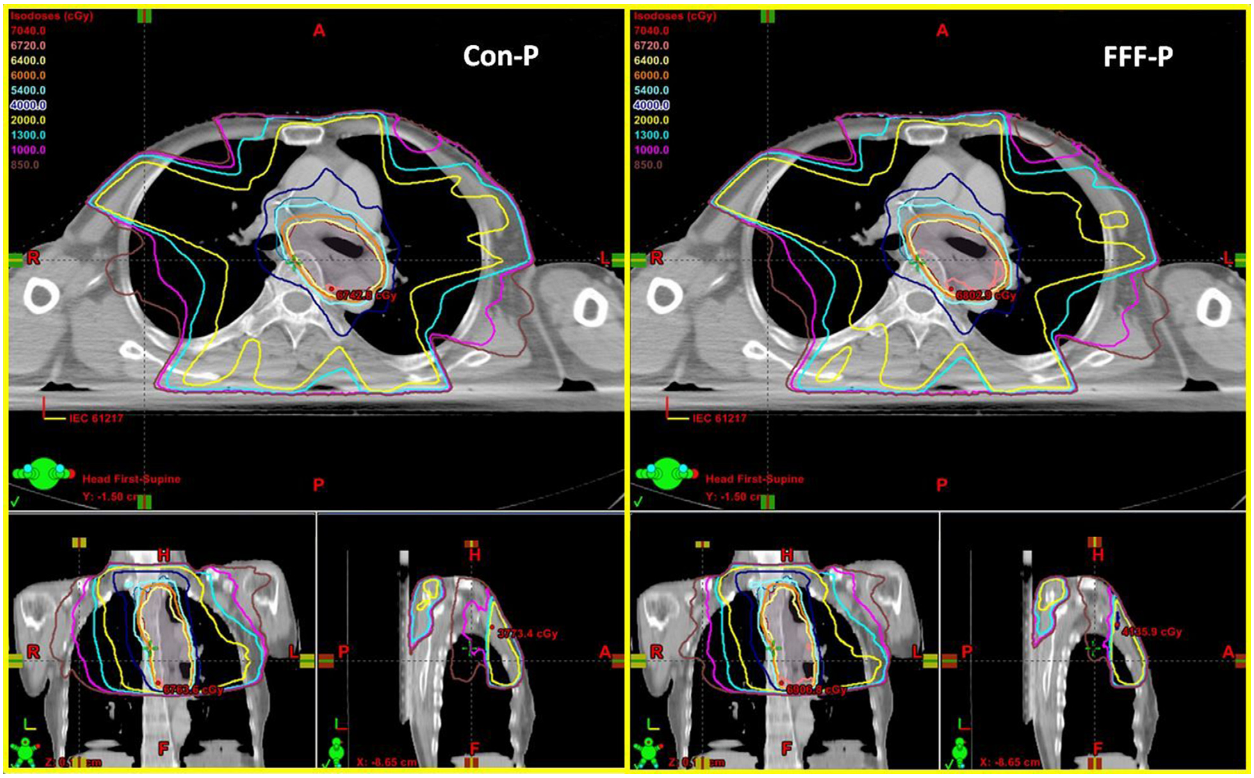

Figure 2. Comparison of dose distribution of a representative case in transverse, coronal and sagittal planes between Con-P (Left) and FFF-P (Right). Con-P, conventional IMRT plan; FFF-P, flattening filter-free IMRT plan.

lung, such as carcinogenesis. Such advantage could be accounted by the less scatter radiation from the FFF beam relative to the conventional beam.

Our results were slightly different from a similar study on advanced oesophageal cancers, which reported that FFF beams had the potential of reducing the dose to OARs and the healthy tissues.[17] The main reason for this difference was because our study was focused on early-stage patients with relatively small tumour volume (GTV < 51.0 cm^3). Smaller tumours were usually more distant from the OARs and therefore both techniques could perform well in sparing these organs resulting in relatively small dosimetric differences. One should note that the calculation algorithm of the TPS would have an impact on the dosimetric outcome as the treatment region was at the thorax, where there was interface between low-density lung tissue and high-density bone. The AAA algorithm used in this study was proved to be better than the pencil beam convolution algorithm.[18] However, it was expected that the calculation accuracy would further be improved if the Acuros XB algorithm[19] was used.

With regard to the treatment delivery parameters, FFF-P required higher MU but a shorter TT. This phenomenon could be explained by the fact that the un-flattened beam with a much higher intensity around the central axis, this required more MLC modulations to produce a more uniform dose profile and therefore created higher MU for the radiation beams. However, removal of the flattening filter has greatly increased the dose output by two to threefold and the time required to deliver the total MU was reduced, which had outweighed the time needed by the increased MU. This was in line with the several previous studies in which reduction of TT of 20–50% have been reported.[17,20,21] Because of this advantage, the use of FFF beams has been extended to VMAT treatment of nasopharynx[22] and prostate[23] cancers. Nevertheless, despite the FFF beam technology demonstrated attractive practical advantages over the conventional beam IMRT, the understanding of the biological effect of such a high dose rate treatment on body tissues which may have consequence on late toxicities is still not certain and needs to be proven by longer term clinical studies.

Conclusion

IMRT with conventional beams (Con-P) and FFF beams (FFF-P) were able to achieved satisfactory dosimetric outcome for early stage upper thoracic oesophageal cancer patients. FFF-P was more effective in sparing the lung tissue from low dose and reduced the mean TT by ~20% compared with Con-P. Long term clinical studies are recommended to evaluate the radiobiological effects of FFF beams.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Chen W, He Y, Zheng R, Zhang S, Zeng H, Zou X, He J. Oesophageal cancer incidence and mortality in China 2009. *J Thorac Dis* 2013; **5**: 19–26.
2. Gu S, Yin W, Yu Z. Pp. 546–74 *in* Radiation Oncology, 4th edn. Chinese Xie He Medical University Publisher, Beijing, 2008.
3. Chang W, Chen Z, Li D. Dosimetric comparison between intensity modulated radiotherapy and conformal radiotherapy for upper oesophageal cancers. *Ai Zheng* 2009; **28**: 1127–31.
4. Wu Q, Manning M, Schmidt-Ullrich R, Mohan R. The potential for sparing of parotids and escalation of biologically effective dose with intensity-modulated radiation treatments of head and neck cancers: a treatment design study. *Int J Radiat Oncol Biol Phys* 2000; **46**: 195–205.
5. Wu VW, Kwong DL, Sham JS. Target dose conformity in 3-dimensional conformal radiotherapy and intensity modulated radiotherapy. *Radiother Oncol* 2004; **71**: 201–6.
6. Chandra A, Guerrero TM, Liu HH, et al. Feasibility of using intensity-modulated radiotherapy to improve lung sparing in treatment planning for distal oesophageal cancer. *Radiother Oncol* 2005; **77**: 247–53.
7. Verhey LJ. Comparison of three-dimensional conformal radiation therapy and intensity-modulated radiation therapy systems. *Semin Radiat Oncol* 1999; **9**: 78–98.
8. Zwahlen DR, Lang S, Hrbacek J, Glanzmann C, Kloeck S, Najafi Y, Streller T, Studer G, Zaugg K, Luetolf UM. The use of photon beams of a flattening-filter-free linear accelerator for hypofractionated volumetric modulated arc therapy in localized prostate cancer. *Int J Radiat Oncol Biol Phys* 2012; **83**: 1655–60.
9. Stieler F, Fleckenstein J, Simeonova A, Wenz F, Lohr F. Intensity modulated radiosurgery of brain metastases with flattening filter-free beams. *Radiother Oncol* 2013; **109**: 448–51.
10. Georg D, Knoss T, McClean B. Current status and future perspective of flattening filter free photon beams. *Med Phys* 2011; **38**: 1280–93.
11. Spruijt KH, Dahele M, Cuijpers JP, Jeulink M, Rietveld D, Slotman BJ, Verbakel WF. Flattening filter free vs flattened beams for breast irradiation. *Int J Radiat Oncol Biol Phys* 2011; **85**: 506–13.
12. Salter BJ, Sarkar V, Wang B, Shukla H, Szegedi M, Rassiah-Szegedi P. Rotational IMRT delivery using digital linear accelerator in very high dose rate “burst mode”. *Phys Med Biol* 2011; **56**: 1931–46.
13. Manscosu P, Castiglioni S, Reggiori G, Shukla H, Szegedi M, Rassiah-Szegedi P. Stereotactic body radiation therapy for live tumors using flattening filter free beam: dosimetric and technical considerations. *Radiat Oncol* 2012; **7**: 16.
14. van’t Riet A, Mak AC, Moerland MA, Elders LH, van der Zee W. A conformation number to quantify the degree of conformality in brachytherapy and external beam irradiation: application to the prostate. *Int J Radiat Oncol Biol Phys* 1997;**37**:731–6.
15. Gong Y, Wang J, Bai S, Jiang X, Xu F. Conventionally-fractionated image-guided intensity modulated radiotherapy (IG-IMRT): a safe and effective treatment for cancer spinal metastasis. *Radiat Oncol* 2008; **3**: 11.
16. Cashmore J. The characterization of unflattened photon beams from a 6 MV linear accelerator. *Phys Med Biol* 2008; **53**: 1933–46.
17. Nicolini G, Ghosh-Laskar S, Shrivastava SK, et al. Volumetric modulation arc radiotherapy with flattening filter-free beams compared with static gantry IMRT and 3D conformal radiotherapy for advanced oesophageal cancer: a feasibility study. *Int J Radiat Oncol Biol Phys* 2012; **84**: 553–60.
18. Amankwaa-Frempong E, Vernimmen F, Blay S, Ezhilalan R. Irradiation of lung and esophagus tumors: a comparison of dose distributions calculated by anisotropic analytical algorithm and pencil beam convolution algorithm, a retrospective dosimetric study. *Int J Cancer Ther Oncol* 2014; **2**: 020210.
19. Rana S. Clinical dosimetric impact of Acuros XB and analytical anisotropic algorithm (AAA) on real lung cancer treatment plans: review. *Int J Cancer Ther Oncol* 2014; **2**: 02019.
20. Prendergast BM, Fiveash JB, Popple RA, et al. Flattening filter-free linac improves treatment delivery efficiency in stereotactic body radiation therapy. *J App Clin Med Phys* 2013; **14**: 64–71.
21. Kretschmer M, Sabatino M, Blechschmidt A, Heyden S, Grunbery B, Wurschmidt F. The impact of flattening-filter-free beam technology on 3D conformal RT. *Radiat Oncol* 2013; **8**: 133.
22. Fu G, Li M, Song Y, Dai J. A dosimetric evaluation of flattening filter-free volumetric modulated arc therapy in nasopharyngeal carcinoma. *J Med Phys* 2014; **39**: 150–5.
23. Rout BK, Muralidhar KR, Ali M, Shekar MC, Kumar A. Dosimetric study of RapidArc plans with flattened beam (FB) and flattening filter-free (FFF) beam for localized prostate cancer based on physical indices. *Int J Cancer Ther Oncol* 2014; **2**: 02046.