RESEARCH ARTICLE

**Editorial Process:** Submission:03/18/2017 Acceptance:01/11/2018

# Comparative Evaluation of a 6MV Flattened Beam and a Flattening Filter Free Beam for Carcinoma of Cervix – IMRT Planning Study

**Suresh Tamilarasu[1], Madeswaran Saminathan[2]*, S K Sharma[1], Anjali Pahuja[1], Abhinav Dewan[1]**

## Abstract

**Purpose:** Intensity modulated radiotherapy (IMRT) plan quality, beam on time and integral dose were compared using 6MV FB (Flattened Beam) and FFFB (Flattening filter free beam) for carcinoma of cervix. **Materials and Methods:** Ten patients with stage II–IIIB cervix cancer (Ca.Cx) were retrospectively identified from the department database. Target volume (TV) and organ at risk (OAR) were delineated as per Radiation Therapy Oncology Group (RTOG) cancer guidelines. Dose prescribed to planning target volume (PTV) was 50.4Gy in 28 fractions. Two plans (6MV FB IMRT and 6MV FFFB IMRT) were generated to achieve 95% of prescription dose to PTV and sparing OAR as per normal tissue guidelines. Numbers of beams and their orientations were the same for all plans. The homogeneity index (HI), conformity index (CI), treatment monitor unit (MU), beam on time (BOT) and non-tumor integral dose (NTID) were chosen for comparison. **Results:** FFFB generated plans were clinically acceptable. There was a statistically significant difference among the FB IMRT and FFFB IMRT plans with respect to CI, HI, D50%, D2% in PTV coverage, bladder V50Gy, MU, mean NTID and non-tumor low dose volume. **Conclusions:** 6MV flattened and flattening filter free photon beams produce comparable plans by IMRT . FFF beams allow time efficient treatment delivery and may help reduce the risk of secondary malignances in carcinoma cervix cases.

**Keywords:** Intensity modulated radiotherapy- flatten beam- flattening filter free photon beam- secondary cancer risk

*Asian Pac J Cancer Prev,* **19 (3)**, 639-643

## Introduction

IMRT technique is the treatment choice for gynecologic cancer due to adequate TV coverage and increased OAR's sparing as compared to three dimensional conformal radiotherapy (3DCRT) (Georg, 2006). Historically, flatten beam was used to generate the clinically acceptable doses in TV and for reducing doses to OAR's by 3DCRT or advanced technique such as IMRT or volumetric modulated arc therapy (VMAT). In recent years, utilization of advanced technique increased due to creation of conformal plans. In this technique, flatten beam is modified by fluence modification algorithm to generate required dose distribution, thereby invalidating need for flatten beam. Therefore, flattening filter becomes unnecessary in advanced technique (Georg, 2011).

Kry (2005) and Hall (1995; 2003; 2006) noted that IMRT technique needs higher MU's to achieve the treatment goal and resulted in increased non-tumor integral dose to the patient. Presence of flattening filter increases the leakage and scatter radiation in the treatment head, multiple beam angles contribute to higher volume of non-tumor tissue being exposed to lower doses which may lead to a higher chance of radiation-induced second cancer risk (SCR) after IMRT.

Various authors Cashmore et al., (2008); Kry et al., (2007) and Kragl et al., (2009) showed that that the, flattening filter removed from linear accelerator treatment head resulted in increased dose rate by a factor 2 to 4, reduced collimator scatter factor, head leakage, peripheral dose and neutron leakage in higher energies (>10MV). Present study to analyze, whether FFFB generate clinically acceptable treatment plans and compared them with FB in Carcinoma cervix cases using IMRT modality.

## Materials and Methods

*Patients Characteristics*

Ten cervix cancer (stage II–IIIB) patients were retrospectively selected for this study. Mean PTV volume was 1493.9±264.8cm$^3$ (Ranges 1154.8cm$^3$ to 1859.22cm$^3$). The mean rectum and bladder volumes were 113.462±68.2 cm$^3$ (Ranges 39.83 cm$^3$ to 218.14 cm$^3$) and 346.03±91.8 cm$^3$ (Ranges 168.02 cm$^3$ to 456.36

[1]*Department of Radiotherapy, Rajiv Gandhi Cancer Institute and Research Centre, Rohini, New Delhi,* [2]*Department of Physics, VIT University, Vellore, Tamil Nadu, India. *For Correspondence: madeswaran.s@vit.ac.in*

$cm^3$) respectively. The mean volume was 3137.40±890.83 $cm^3$ (Ranges 742.62 $cm^3$ to 3274.06 $cm^3$). The mean right femur and left femur volumes were 99.03±14.68 $cm^3$ (Ranges 87.2 $cm^3$ to 132.19 $cm^3$) and 100.77±16.26 $cm^3$ (Ranges 88.3 $cm^3$ to 130.41 $cm^3$) respectively. The average anterior-posterior and right–left separation of the patient body was 23.5±2.9cm (Ranges 21.0cm to 29.8 cm) and 35.3±4.2 cm (Ranges 29.8 cm to 44.0 cm), respectively. Average PTV length was 18.9±1.9cm (Ranges 15.5 cm to 22.0 cm).

*Imaging and contouring*

All patients were immobilized with thermoplastic cast (Orfit Industry NV, Belgium), in supine position with the help of All-in One board (AIO, Orfit Industry NV, Belgium), and knee rest support with full bladder protocol. Radio opaque fiducials were placed over the thermoplastic cast to guide the isocenter shift during first day of treatment delivery. CT scans were acquired on a CT-simulator at 3-mm slice intervals using Siemens SOMATOM Sensation Open CT Scanner (Siemens Medical Systems, Germany) CT axial images were obtained from the L2 vertebral body to 5cm below the ischial tuberosithwith intravenous contrast. After CT simulation, DICOM (Digital Imaging and Communications in Medicine) images were transferred to Eclipse Treatment Planning System (version 11.0 Varian Medical Systems, Palo Alto, California, USA).

*Target volume and organs at risk definition*

TV and OAR's were delineated in axial CT slices by radiation oncologists as per the recommendations of International Commission on Radiation Units and Measurements Reports (ICRU) 50 and 62, (ICRU Report 50, 1993; ICRU Report 62, 1999). The gross tumor volume (GTV) includes the cervix with visible tumor extension and the corpus uteri. Clinical target volume (CTV) was created by adding 5 mm margin to the GTV, and, included the external, internal and common iliac and presacral lymph nodes. The CTV was expanded uniformly by 5mm in all directions to produce a planning target volume (PTV). OAR's like bladder, rectum, femoral heads and bowel were also delineated.

*Dose Prescription and Optimization objective used for Inverse Treatment planning*

IMRT technique was used to irradiate the PTV to a dose of 50.4Gy in 28 fractions. Planning objective was to deliver 100% prescription dose (PD) to 95% of PTV with no more than 2% of PTV volume receiving 107% of PD as recommended by ICRU Report 83 (ICRU Report 83, 2010) Normal dose constraint were bladder and rectum $V_{50Gy} \leq 50\%$, Femoral heads and bowel mean dose will be ≤30Gy as per institutional protocol.

*Planning Technique*

Treatment Planning was performed using two photon beams (6MV flatten beam and 6MV flattening filter free photon beam) of Varian True Beam Linear Accelerator equipped with HD 120 MLC (MLC of 60 pair, inner 32 leaf pair of 0.25 cm, and outer 28 leaf pair of 0.50 cm projection width at isocenter and maximum leaf speed of 2.5 cm/s). All the Photon beams were calibrated at 1 $_c$Gy/MU at dmax on the central axis for a 10 cm x10 cm field with SSD of 100 cm, for both flattened and FFF beams as per Technical Reports Series No. 398 (TRS-398) (TRS 398, 2,000) of International Atomic Energy Agency. Plans were optimized selecting a maximum dose rate of 600MU/min in 6MV FB and 1,400MU/min for 6MV FFFB. For all patients, two plans 6MV FB IMRT and 6MV FFFB IMRT were designed using Eclipse Treatment planning system (TPS) version 11.0 (Varian Medical Systems, Palo Alto, CA, USA) using IMRT technique. Anisotropic analytical algorithm with 0.25 cm grid size was used for photon dose calculation for all plans.

*Sliding window IMRT Planning*

A fixed multiple beam arrangement was chosen. Isocentre was placed approximately at the Centre of mass of PTV. Fields were equally spaced at 50° intervals coplanar beams consisting of the following gantry angles: 0°, 50°, 100°, 150°, 200°, 250°, and 300°. IMRT plans were created with inverse planning optimization with dose volume optimizer and AAA for final dose calculation. Collimator rotation of 3° were used in each beam angle to cover the entire PTV and reduce tongue and groove effect which subsequently minimizes inter-leaf leakage (Deng, 2001).

*Plan Evaluation and statistical Methods*

As per ICRU Report 83 (ICRU Report 83, 2010) doses to the TV and OARs were recorded from their respective cumulative dose volume histogram (cDVHs).

*Homogeneity index (HI)*

A ratio evaluating the dose homogeneity ($D_2$%-$D_{98}$%)/$D_{50}$%, in TV, where $D_2$%, $D_{98}$%, and $D_{50}$% are the minimum dose delivered to 2%, 98%, and 50% volume of the TV, respectively. HI of zero indicated homogeneous dose distribution.

*Conformity index (CI)*

A ratio evaluating the coverage of the prescription dose in treatment plans. CI = Volume within 98% isodose line/TV. CI of one indicated the good dose conformity.

Rectum and bladder were evaluated for mean dose and V50Gy, where V50Gy is the volume of rectum and bladder receiving a dose of 50 Gy. Bowel, right and left femoral heads were evaluated for mean doses.

Normal tissue integral dose (D'Souza, 2003) (NTID), defined as the integral of the absorbed dose extending to overall voxels excluding those within the TV. It was calculated to assess the plan quality based on the following formula.

Normal tissue integral dose (NTID) = Mean dose × Volume of normal tissue outside TV.

In addition, treatment parameters including the monitor units (MU) and beam ON time (BOT) for each treatment plan were recorded for evaluation. BOT was defined as the radiation delivery time and did not include gantry movement, the patient positioning and imaging procedures, which was noted while performing QA.

A test of significance was required in order to quantify the differences between parameters in FF and FFF plans. All statistical tests were done using paired sample t-test for comparisons of data performed using the IBM Statistical Package for Social Sciences (SPSS) software (release 20.0, SPSS Inc., Chicago, IL, USA). Statistical significance was defined as $p < 0.05$.

## Results

All the plans satisfied our dosimetric criterion and were evaluated using cumulative dose volume histogram. Dose to PTV and OAR's are tabulated in Table 1.Isodose distribution of axial, coronal and sagittal views of one patient resulted from IMRT planning using 6MV FB and FFF beams were represented in Figure 1.Comparison of the dose volume histograms of TV and OAR's for 6MV FB IMRT and 6MV FFFB IMRT beam represented in Figure 2.

*Target Volume Coverage*

CI and HI of target PTV were improved in 6MV FB IMRT when compared to 6MV FFFB IMRT. There was no big difference in dose distribution between FB and FFFB, except D50% and D2%. The present study indicated that the HI, CI and D2% of target PTV for 6MV FB IMRT in comparison to FFFB IMRT plans, the p value were significant ($p<0.05$). The p values were not significant for D98% and D95% of the PTV coverage. HI and CI of FB are $0.046 \pm 0.005$ and $1.12 \pm 0.03$ respectively and $0.059 \pm 0.007$ and $1.17 \pm 0.046$ for FFFB. 6MV FB IMRT produces more homogenous and highly conformal plans in comparison to FFFB IMRT.

Table 1. Target Parameters, NTID and Low Dose Volume Comparison between 6MV FB and UFB for HI (Homogeneity index), CI ( Conformity index), MU (Monitoring units) and BOT (Beam on time in minutes). Vx is the volume receiving x% of the prescribed dose. Dx% is dose received by x% of volume. SD, Standard deviation; NS, No significant.

| Parameters | 6MV FB IMRT | | 6MV FFFB IMRT | | p value |
|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | |
| $D_{98\%}$ (Gy) | 50.09 | 0.11 | 50.04 | 0.1 | NS |
| $D_{95\%}$ (Gy) | 50.42 | 0.05 | 50.41 | 0.05 | NS |
| $D_{50\%}$ (Gy) | 51.32 | 0.19 | 51.62 | 0.2 | <0.05 |
| $D_{2\%}$(Gy) | 52.48 | 0.2 | 53.11 | 0.37 | <0.05 |
| $V_{107\%}$ | 0 | 0 | 0 | 0 | NS |
| HI | 0.05 | 0.01 | 0.06 | 0.01 | <0.05 |
| CI | 1.12 | 0.03 | 1.17 | 0.05 | <0.05 |
| MU | 1451.6 | 104.83 | 1768.2 | 241.71 | <0.05 |
| BOT (in min) | 2.42 | 0.17 | 1.26 | 0.17 | <0.05 |
| NTID ($10^5$ cGy.cc) | 310.37 | 74.76 | 308.85 | 74.59 | <0.05 |
| $V_{1Gy}$ (cc) | 19668.27 | 5413.3 | 19517.07 | 5423.04 | <0.05 |
| $V_{2Gy}$ (cc) | 15824.42 | 4377.75 | 15767.03 | 4366.6 | <0.05 |
| $V_{3Gy}$ (cc) | 14634.08 | 4907.85 | 14318.68 | 4542.97 | <0.05 |
| $V_{4Gy}$ (cc) | 13366.11 | 4033.35 | 13146.82 | 3936.47 | <0.05 |
| $V_{5Gy}$ (cc) | 12387.08 | 3486.76 | 12188.11 | 3479.27 | <0.05 |

Table 2. OAR'S Comparison between 6MV FB and UFB. Abbreviations: Dmean is mean dose and Dmax is the maximum dose

| Organ | Dose Volume | 6MV FB IMRT | | 6MV FFFB IMRT | | p value |
|---|---|---|---|---|---|---|
| | | Mean | SD | Mean | SD | |
| Bladder | $D_{mean}$ (Gy) | 45.43 | 1.34 | 45.48 | 1.33 | NS |
| | $V_{50}$ Gy (%) | 46.09 | 3.81 | 47.48 | 4.5 | <0.05 |
| Rectum | $D_{mean}$ (Gy) | 42.83 | 3.52 | 43.22 | 3.61 | NS |
| | $V_{50}$ Gy (%) | 33.94 | 10.89 | 33.93 | 10.7 | NS |
| Rt.Femur | $D_{mean}$ (Gy) | 22.28 | 3.06 | 22.21 | 3.03 | NS |
| Lt.Femur | $D_{mean}$ (Gy) | 22.79 | 2.58 | 22.72 | 2.46 | NS |
| Bowel | $D_{mean}$ (Gy) | 18.2 | 4.88 | 18.31 | 4.92 | NS |

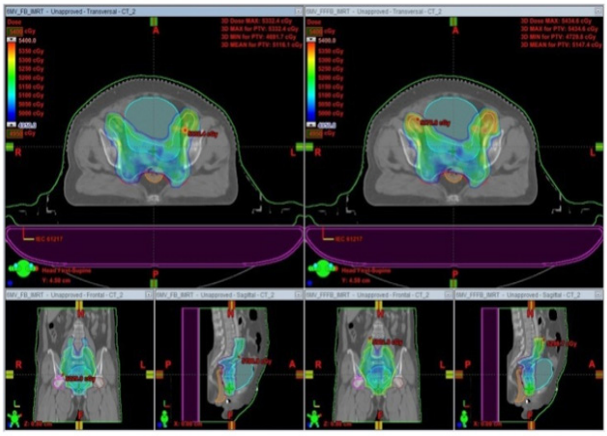

Figure 1. The Isodose Distribution Generated from IMRT Planning in Case of Ca.Cervix for Same Patient in Axial, Coronal and Sagittal Planes with (a) 6 MV FB IMRT and (b) 6 MV FFFB IMRT

*OAR's*

Mean dose to bladder, rectum, femur and bowel were not statistically significant difference between two plans. But V50Gyof bladder was statistically significant ($p<0.05$) and V50Gyofrectum also not significant.

*Non-tumor integral dose and low dose volume on normal tissue*

Difference among two plans in terms of mean non-tumor tissue integral dose and low dose volume was

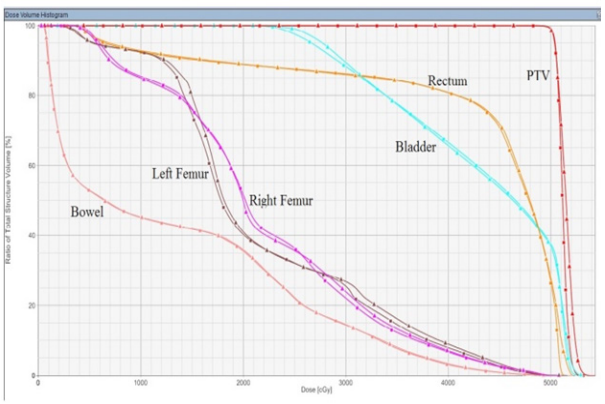


Figure 2. Comparison of the DVH of TV and OAR's for 6MV FB IMRT (Triangle) and 6MV FB FFF Beam (Square).

statistically significant. Non-tumor volume enclosed by 1Gy, 2Gy, 3Gy, 4Gy and 5Gy found to be less in FFFB IMRT plan as shown in Table 1.OAR'S comparison between 6MV FB and FFFB is represented in Table 2.

*MU and Beam on time*

Planned MUs per fraction were significantly lower for the FB plans as compared to the FFFB plan by a factor of 1.21. MU's delivered (mean ± SD) was 1451.6 ± 104 for 6MV FB IMRT planned 1768.2 ± 241 for 6MV FFFB IMRT plan. Dose rate in FFFB plan was 2.3 times higher than FB plan, thereby leading to 48% decrease in beam on time. The difference was statistically significant ($p<0.05$).

## Discussion

There is limited literature reporting impact of FFF beams in Ca. Cervix cases at present. Our study is one of the first few studies reporting on the above aspect. ICRU Report 63, recommends a dose variation to the PTV to within−5% to 7% of the prescription dose. Mundt et al. (2002) reported that the high dose volume V110 (%) and V115 (% ) in the PTV was 9.8% and 0.2% respectively. In our study, V110 (%) and V115 (%) of PTV is zero.

Our results are in contrast to those observed in other studies involving FFF beams for large and complex targets. Nicolini et al., (2012) and Subramaniam et al., (2012) reported that VMAT with FFF beam plans resulted in minor improvement in plan quality, thereby suggesting their applicability for large and complex targets.

Hall et al., (1995; 2003; 2006) Cashmore et al., (2008) reported that absence of flattening filter may be help reduce the amount of radiation reaching OAR's through scatter and leakage. Diallo et al., (2009) studied 115 pediatric patients diagnosed with secondary cancer after radiotherapy and noted that, 22% of the second cancers were 5 cm to 1m from the PTV. The highest incident of secondary malignancy was seen in normal tissues receiving a dose of 2.5 Gy or less. Cashmore et al., (2011) investigated whole-body dose exposure for intracranial tumors of pediatric patients and reported decreased peripheral dose when using FFFB IMRT instead of FB IMRT.

In our study, FFFB needs 22% higher MUs compared to FB in order to achieve dose uniformity within PTV, so more modulation is required to reduce the higher beam intensity near the central axis due to forward heterogeneous peak profile of FFF beam. This higher MU off-set is compensated by higher FFFB dose rate, by a factor 2.3. As a result, delivery time is reduced by about 48% as compared to FB. Statistically significant reduction of normal tissue volume receiving low dose of 1Gy, 2Gy,3Gy 4Gy and 5Gy were observed. Increase in MU did not affect the low dose volume in FFFB as compared to FB.

In contrast, Vassiliev et al. (2006 ; 2007) found a significant 50% decrease in the number of MU for their FFF treatment plans. The reason was that after removal of the flattening filter, recalibration of MU was not performed and found that 6MV FFF x - ray beam, the dose per MU increased by a factor of 2.06 as compared to 6MV FB. In our study, both FB and FFF x - ray beams were calibrated, and the dose per MU was kept as 1 for at 10x10 cm2 field size at a depth of dose maximum.(1cGy=1MU).

Fu et al., (2004) found reduced treatment time by 46% for FFF beam IMRT treatment, depending upon the dose per fraction. This time advantage increased further, when using higher dose per fraction. However, difference was insignificant for standard fractionation of 2Gy per fraction. This study is purely a dosimetric study. Further studies are required to note the clinical impact of FFF beam in cervical cancer cases.

In conclusion, 6MV flattening filter free x-ray beam produces dosimetrically and clinically acceptable plans by IMRT technique. The FFFB has the benefit of faster treatment delivery with lesser dose to normal tissues. Choosing advanced innovative technology plays an important role in modern radiotherapy and will help increase patient safety, reduce patient waiting time and chance of developing secondary cancers after radiotherapy. In this study, we recommended that 6MV FFF x-ray beam was a good choice for Cervical Cancer IMRT. Further clinical and radiobiological studies are needed for other sites.

*Conflict of interest*

Any disclosure or conflict of interest: None

## References


Cashmore J (2008). The characterization of unflattened photon beams from a 6 MV linear accelerator. *Phys Med Biol*, **53**, 1933-46.

Cashmore J, Ramtohul M, Ford D (2011). Lowering whole-body radiation doses in pediatric intensity-modulated radiotherapy through the use of unflattened photon beams. *Int J Radiat Oncol Biol Phys*, **80**, 1220–27.

D'Souza WD, Rosen II (2003). Non-tumor integral dose variation in conventional radiotherapy treatment planning. *Med Phys*, **30**, 2065-71.

Deng J, Pawlicki T, Chen Y, et al (2001). The MLC tongue-and-groove effect on IMRT dose distributions. *Phys Med Biol*, **46**, 1039-60.

Diallo ID, Haddy N, Adiadi E (2009). Frequency distribution of second solid cancer locations in relation to the irradiated volume among 115 patients treated for childhood cancer. *Int J Radiat Oncol Biol Phys*, **74**, 876–83.

Fu W, Dai J, Hu Y (2004). Delivery time comparison for intensity-modulated radiation therapy with/without flattening filter, A planning study. *Phys Med Biol*, **49**, 1535–47.

Georg D, Knoos T, McClean B (2011). Current status and future perspective of flattening filter free photon beams. *Med Phys*, **38**, 1280-93.

Georg P, Georg D, Hillbrand M, Kirisits C, Potter R (2006). Factors influencing bowel sparing in intensity modulated whole pelvic radiotherapy for gynaecological malignancies. *Radiother Oncol*, **80**, 19-26.

Hall EJ (2006). Intensity-modulated radiation therapy, protons, and the risk of second cancers. *Int J Radiat Oncol Biol Phys*, **65**, 1–7.

Hall EJ, Martin SG, Amols H, Hei TK (1995). Photo-neutrons from medical linear accelerators- Radiobiological measurements and risk estimates. *Int J Radiat Oncol Rio Phys*, **33**, 225-30.

Hall EJ, Wu C (2003). Radiation-induced second cancers. The impact of 3D-CRT and IMRT. *Int J Radiat Oncol Biol Phys*, **56**, 83–8.

IAEA (2000). An international code of practice for dosimetry based on absorbed dose to Water, IAEA Technical Series No. 398, absorbed dose determination in external beam radiotherapy. Vienna: IAEA.

ICRU Report 83 (2010). Prescribing, recording, and reporting photon-beam intensity-modulated radiation therapy (IMRT). International commission on radiation units and measurements, Bethesda.

International commission on radiation units and measurements (1999). Supplement to ICRU Report 50, ICRU Report 62, Bethesda.

International commission on radiation units and measurements (1993). Prescribing, recording and reporting photon beam therapy, ICRU Report 50, Bethesda.

Kragl G, AF Wetterstedt S, Knausl B (2009). Dosimetric characteristics of 6 and 10MV unflattened photon beams. *Radiotherapy Oncol*, **93**, 141-6.

Kry SF, Salehpour M; Followill DS (2005). The calculated risk of fatal secondary malignancies from intensity-modulated radiation therapy. *Int J Radiat Oncol Biol Phys*, **62**, 1195–1203.

Kry SF, Titt U, Ponisch F (2007). Reduced neutron production through use of a flattening-filter-free accelerator. *Int J Radiat Oncol Biol Phys*, **68**, 1260-4.

Mundt AJ, Lujan AE; Rotmensch J (2002). Intensity-modulated whole pelvic radiotherapy in women with gynecologic malignancies. *Int J Radiat Oncol Biol Phys*, **52**, 1330–7.

Nicolini G, Ghosh-Laskar S, Shrivastava S, et al (2012). Volumetric modulation arc radiotherapy with flattening filter-free beams compared with static gantry IMRT and 3D conformal radiotherapy for advanced esophageal cancer: a feasibility study. *Int J Radiat Oncol Biol Phys*, **84**, 553–60.

Subramaniam S, Thirumalaiswamy S, Srinivas C, et al (2012) Chest wall radiotherapy with volumetric modulated arcs and the potential role of flattening filter free photon beams. *Strahlenther Oncol*, **188**, 484–91.

Vassiliev ON, Kry SF, Kuban DA (2007). Treatment-planning study of prostate cancer intensity-modulated radiotherapy with a Varian clinic operated without a flattening filter. *Int J Radiat Oncol Biol Phys*, **68**, 1567-71.

Vassiliev ON, Titt U, Ponisch F (2006). Dosimetric properties of photon beams from a flattening filter free clinical accelerator. *Phys Med Biol*, **5**, 1907-17.