

LETTERS TO THE EDITOR

Plan quality and delivery accuracy of flattening filter free beam for SBRT lung treatments

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To the Editor,

Stereotactic body radiation therapy (SBRT) or alternatively stereotactic ablative radiotherapy (SABR) is today an important treatment option for a steadily increasing fraction of the cancer patient population. Flattening filter free (FFF) beams have a number of potential dosimetric benefits compared to the conventional filter flattened beams (FF) [1]. Higher dose rate, higher dose per pulse, reduced lateral changes in beam hardening, reduced leakage and out-of-field dose, are all characteristics of FFF beams and could potentially improve treatment plans [2–4]. Significant reduction of lung treatment delivery time has been reported by various radiotherapy centres using FFF beams, created on Eclipse (Varian Medical Systems, Palo Alto, CA, USA) and delivered on Varian accelerators [5–12]. However, it is important to stress that the treatment delivery time and plan quality are highly dependent on many vendor specific factors, e.g. dose rate, MLC leaf speeds, gantry speed, beam quality, MLC segmentation algorithm in the treatment planning system (TPS), as well as patient-related factors such as target size and tumour location. Most of the technical factors are very different between the Varian and Elekta (Elekta AB, Stockholm, Sweden) linacs and MLCs and Eclipse and Philips Pinnacle TPS (Philips Healthcare, DA Best, Netherlands). For the Varian FFF beam the beam quality is lower than the FF beam, due to the unchanged (cf. FF beam) electron

energies used to produce the x-ray beam. For an Elekta accelerator the linac is retuned so that the FFF beam quality is matched to the FF beam quality by increasing the incident electron energy. This difference in beam quality approach has been shown to influence the ratio between central dose and out-of-field dose [2–4]. Also the capabilities of the MLC motions (speeds) are different for the two vendors. Furthermore, the plan optimisation algorithms (e.g. segmentation algorithm) are quite different between Eclipse and Pinnacle. All these differences will influence the plan deliveries and impact the plan quality [13,14]. It is therefore of interest to investigate if the combination of the Pinnacle TPS and the new Versa HD™ accelerator from Elekta [15], can produce and deliver acceptable FFF SBRT treatment plans.

The aim of the current study was to investigate the impact of FFF beams on plan quality, delivery time and delivery accuracy for lung SBRT treatments using a volumetric modulated arc therapy (VMAT) technique delivered on a Versa HD™ accelerator and created using the Pinnacle TPS.

Methods

A cohort of 21 consecutive patients treated with a dual arc VMAT SBRT technique for primary or metastatic tumours of the lung was selected for this study. All patients were treated between January and

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May 2013 at Odense University Hospital, Denmark. The inclusion criteria were single target with a diameter < 7 cm and a prescription dose of 66 Gy to the gross tumour volume (GTV) (95% of 66 Gy to cover GTV – no constraint on the maximum dose to GTV) and 45 Gy to the PTV in 3 fractions according to the Scandinavian SBRT phase II trial SPACE protocol [16]. The GTV was defined as the solid tumour contoured on the mid-ventilation phase and the PTV had a 5 mm expansion left, right, anterior and posterior and 10 mm expansion cranial and caudal [10 phase four dimensional computed tomography (4DCT) planning scan]. New plans were generated in Pinnacle ver. 9.2 using the same objectives as used for the clinically delivered VMAT plans. For each patient three plans were created: 1) dual VMAT arc FF beams (dFF) – similar to the clinical plans; 2) dual VMAT arc FFF beams (dFFF); and 3) single VMAT arc FFF beam (sFFF).

Plan comparison

Plan comparison metrics were based on dose-volume histograms (DVHs) exported from Pinnacle with a resolution of 0.01 Gy (no normalisation of plans was performed since Pinnacle works with absolute and not relative doses). For each patient the following conformity indexes were calculated:

- 1) Conformity index (CI), defined as the ratio of the prescribed isodose and the target volume ($CI_{GTV} = V_{62.7Gy}/V_{GTV}$ and $CI_{PTV} = V_{45Gy}/V_{PTV}$ where the 62.7 Gy is 95% of the prescribed dose of 66 Gy).
- 2) Dose spillage conformity ($CI_{spillage} = V_{22.5Gy}/V_{PTV}$), defined as the ratio of the volume enclosed by the 22.5 Gy iso-dose and PTV volume, where 22.5 Gy is 50% of the prescription dose for the PTV.

Across the patient population

- 3) Organ- and target-specific population mean DVH.
- 4) D_V , the population mean of individual D_V values, given by the cumulative DVH.
- 5) V_D , the population mean of individual V_D values, given by the cumulative DVH.
- 6) CI, the population mean of the individual CI.

where D_V is the dose in Gy for a given volume V in percent ($D_{2\%}$ and $D_{98\%}$ used) and V_D is the volume V in percent for a given dose in Gy (V_{6Gy} , V_{12Gy} , $V_{22.5Gy}$, $V_{45.0Gy}$, $V_{48.2Gy}$, $V_{62.7Gy}$ and $V_{70.6Gy}$ used).

Accelerator setup

The MLC head on the Versa HD™ accelerator is the 'Agility', which is equipped with two MLC banks

each having 80 leaves with a projected width of 5 mm at the iso-centre. The maximum leaf speed is 6.5 cm/s (incl. 3 cm/s dynamic leaf guide motion) and the leakage is reported to be less than 0.5% [17].

Delivery and verification

Beams were delivered on the Versa HD™ linac and actual beam on times were recorded. The dose rate efficiency was defined as average dose rate observed during delivery divided by the maximum dose rate. Treatment dose rate was defined as prescribed dose divided by delivery time.

Delivered dose distributions for each treatment plan were measured using the Sun Nuclear ArcCHECK phantom [18]. The delivered dose was evaluated by a gamma analysis ($\Gamma_{3\%, 3mm}$), using dose criteria of 3% of maximum measured dose and a distance to agreement of 3 mm. Only detector readings above 10% of maximum dose were included in the pass rate evaluation. Pass rates above 95% were considered as clinically acceptable.

In order to compare the calculated integral dose ($ID_{calculated}$) from the planning system with measurements, the measured signals from all 1386 detectors in ArcCHECK were summed and the ratio of dFFF and dFF reported ($ID_{measured}$). Since the $ID_{measured}$ values are only available at the detector positions and the $ID_{calculated}$ is based on the entire volume within the external contour of the patients (patients were scanned from the caudal part of the mandible to the caudal part of the liver), the two values are not directly comparable, but a strong correlation should be expected between the values if $ID_{calculated}$ differences are real and not just an artefact of a suboptimal modelling of the accelerator's out-of-field properties in the planning system.

Statistics

All uncertainties are reported as one standard deviation. A two-sided Wilcoxon-signed rank test was used to test the differences between mean metric for each plan type (dFF, dFFF, sFFF). Differences were considered statistically significant for p-values < 0.05. The population mean DVHs were calculated for each volume of interest to visualise the average dose distribution. To highlight dose regions in which significant differences exist between the mean DVHs of the two techniques, a two-sided Wilcoxon-signed rank test was calculated for each dose level [19]. To test the correlation between $ID_{measured}$ ratio (from ArcCheck) and $ID_{calculated}$ ratio (from DVH's) a Spearman's rank correlation analyses was used.

Results

All the FF and FFF plans were reviewed by a senior physician and found to be clinically acceptable in terms of target doses, with no unnecessary dose outside target and OAR specified doses in accordance with the SBRT constraints as defined in the (Supplementary method section to be found online at <http://informahealthcare.com/doi/abs/10.3109/0284186X.2014.956184>).

In general, the dose within the GTV and the PTV was similar for the two dual arc plans, dFFF and dFF (Table I). The GTV mean dose was significantly higher ($p < 0.05$) for the single arc plan (sFFF) compared to the dual arc plans (dFF and dFFF).

However, even with the higher mean GTV dose, the average minimum dose ($D_{98\%}$) of the sFFF plan was significantly lower than both dual arc plans. Nevertheless, these differences are likely of no clinical relevance (Table I).

The conformity of the GTV was similar for all three types of plans but the PTV conformity was significantly (but not clinically) better for the dFFF and dFF plans compared to sFFF plans. The dose spillage conformity (CI_{spillage}) was significantly inferior for the dFF plans compared to the FFF plans (Table I).

The mean dose to the entire CT scanned part of the patient minus the target (External – Target) was

Table I. Mean target and OAR doses and conformity indexes for the GTV and PTV. Mean dose and D_V are given as percent of the dose prescribed to the specific target. The dose to targets are in Gy and V_D are in % volume. Uncertainties of all values are reported as one standard deviation, except for the target median volume where ranges are reported. All p-values are obtained from a paired two-sided Wilcoxon-signed rank test. Statistically significant differences are shown in bold.

Parameter	dFF	dFFF	sFFF	dFF vs. dFFF	dFF vs. sFFF	dFFF vs. sFFF
GTV (66 Gy)				p	p	p
Median volume	7.6 (1.0–28.2)					
Mean dose (Gy)	66.6 ± 1.0	66.7 ± 1.0	66.9 ± 1.1	0.74	0.01	0.01
Std of dose (Gy)	2.6 ± 0.7	2.7 ± 0.7	2.8 ± 0.7	0.13	0.01	0.07
$D_{2\%}$ (Gy)	71.1 ± 1.9	71.3 ± 2.0	71.6 ± 1.9	0.19	0.04	0.48
$D_{98\%}$ (Gy)	61.1 ± 1.1	61.1 ± 1.1	60.9 ± 1.2	0.69	0.04	0.02
$V_{62.7 \text{ Gy}}$ (%)	91.7 ± 5.1	91.8 ± 5.2	91.1 ± 5.8	0.93	0.23	0.05
$V_{70.6 \text{ Gy}}$ (%)	7.9 ± 11.0	8.2 ± 7.9	11.5 ± 13.4	0.80	0.01	0.06
PTV (45 Gy)						
Median volume	39.4 (10.8–87.5)					
Mean dose (Gy)	56.9 ± 1.5	56.9 ± 1.5	57.0 ± 1.5	0.43	0.43	0.09
Std of dose (Gy)	6.9 ± 0.8	6.9 ± 0.8	6.9 ± 0.9	0.74	0.74	0.07
$D_{2\%}$ (Gy)	69.9 ± 1.9	70.0 ± 1.9	70.4 ± 2.1	0.22	0.22	0.09
$D_{98\%}$ (Gy)	45.7 ± 1.0	45.7 ± 1.0	45.7 ± 0.9	0.99	0.99	0.79
$V_{45.0 \text{ Gy}}$ (%)	98.8 ± 1.2	98.8 ± 1.1	98.8 ± 1.0	0.43	0.43	0.79
$V_{48.2 \text{ Gy}}$ (%)	89.4 ± 4.0	89.6 ± 4.0	89.9 ± 4.1	0.23	0.23	0.61
CI						
$V_{62.7 \text{ Gy}}/V_{\text{GTV}}$	1.03 ± 0.16	1.03 ± 0.16	1.05 ± 0.19	0.82	0.39	0.39
$V_{45.0 \text{ Gy}}/V_{\text{PTV}}$	1.18 ± 0.09	1.18 ± 0.09	1.20 ± 0.10	0.50	0.02	0.02
$V_{22.5 \text{ Gy}}/V_{\text{PTV}}$	7.01 ± 1.7	6.68 ± 1.5	6.9 ± 1.8	0.0002	0.04	0.002
Spinal cord						
Mean (Gy)	2.10 ± 1.0	1.98 ± 1.0	2.00 ± 1.0	0.002	0.12	0.79
D2 (Gy)	9.5 ± 4.2	9.2 ± 4.2	9.3 ± 4.1	0.15	0.61	0.57
Heart						
Mean (Gy)	1.4 ± 1.9	1.3 ± 1.8	1.4 ± 2.0	0.002	0.06	0.01
D2 (Gy)	5.2 ± 5.6	4.9 ± 5.2	5.4 ± 5.8	0.002	0.59	0.02
V12 Gy (%)	1.1 ± 2.3	0.8 ± 1.7	1.4 ± 3.1	0.02	0.74	0.05
Ipsilateral lung						
Mean (Gy)	5.6 ± 1.7	5.4 ± 1.7	5.4 ± 1.7	0.0001	0.001	0.64
V22.5 Gy (%)	7.3 ± 2.6	7.1 ± 2.6	7.2 ± 2.7	0.002	0.50	0.02
V12 Gy (%)	14.8 ± 4.4	14.7 ± 4.5	14.7 ± 4.5	0.09	0.64	0.19
Contralateral lung						
Mean (Gy)	1.24 ± 0.4	1.19 ± 0.5	1.17 ± 0.4	0.0001	0.001	0.34
V12 Gy (%)	0.02 ± 0.1	0.02 ± 0.1	0.02 ± 0.1	0.88	0.13	1.00
V6 Gy (%)	1.6 ± 1.9	1.5 ± 1.9	1.3 ± 1.5	0.09	0.02	0.21
External – Target						
Mean (Gy)	1.84 ± 0.5	1.77 ± 0.5	1.77 ± 0.5	0.0001	0.0001	0.52
V22.5 Gy (%)	1.16 ± 0.5	1.10 ± 0.5	1.14 ± 0.5	0.001	0.05	0.003
V12 Gy (%)	4.04 ± 1.4	3.86 ± 1.4	3.92 ± 1.4	0.0001	0.003	0.04

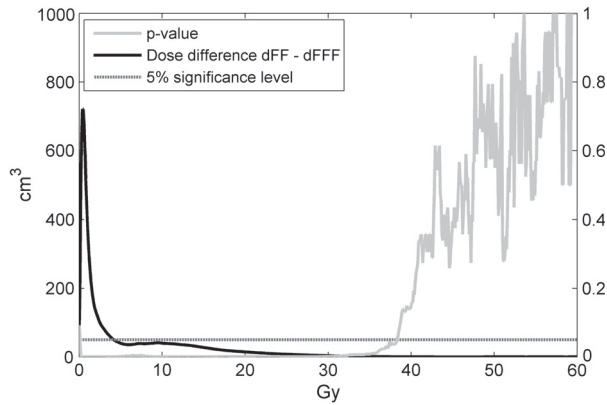


Figure 1. Mean difference in DVH between dFF and dFFF plans in absolute volumes (solid black) for the external – PTV ROI. p-Values are obtained from a paired two-sided Wilcoxon-signed rank test. The grey dotted line indicates the level of 5% statistical significance. Between 0.2 Gy and 38.4 Gy the volume is statistically significant lower for dFFF compared to dFF.

significantly lower for the FFF plans compared to the dFF plan (Table I). This was also shown in the average DVH which was consistently lower across the whole dose range and in the average difference between DVHs for dFFF and dFF (Figure 1). Figure 1 shows that between 0.2 Gy and 38.4 Gy the dose was significantly lower ($p < 0.05$) for dFFF plans compared to dFF plans. This led to an average reduction in $ID_{\text{calculated}}$ between dFFF plans and dFF plans. As an example of the reduced $ID_{\text{calculated}}$, the average volume with a dose reduction larger than 2 Gy was $126 \pm 90 \text{ cm}^3$ (range 10–325 cm^3) (Figure 1). The reduced dose for the FFF plans was also observed for both ipsilateral as well as contralateral lung. For the spinal cord and the heart the reduction was only significant between dFFF and dFF plans. Comparing the dFFF and sFFF plans the heart dose was greater in the sFFF plans. The $V_{22.5 \text{ Gy}}$ (22.5 Gy = 50% PTV dose) was larger for both the ipsilateral lung and the External – PTV volume (Table I).

The treatment times were reduced significantly for the FFF treatments. The average reduction was 234 s for dFFF. The time difference between dFFF

and sFFF was only 2 s. In 18 of the 21 plans the dFFF plans had lower MU than dFF. For all 21 plans the lowest number of MU were obtained in the sFFF plans (Table II). The average dose rate efficiency relative to maximum dose rate was 97.3% for FF and decreased to 89.2% and 87.6% for dFFF and sFFF, respectively (Table II).

The gamma analysis on the measured ArcCHECK phantom showed good agreement between planned and delivered doses for both FF and FFF plans. The average 3%/3 mm pass rates were 99.3%, 98.0% and 98.0% for dFF, dFFF and sFFF, respectively. The higher pass rate of dFF was statistically significant from the two others (Wilcoxon-signed rank, $p < 0.05$ – Table II). All plans passed the 95% pass rate criteria and the detectors failing the 3% and 3 mm criteria were generally few and isolated.

The relative ID_{measured} between dFFF and dFF, over all 1386 ArcCHECK detectors, was statistically significant different from unity (0.987 ± 0.01 , $p = 0.001$), showing that dFFF had the lowest ID_{measured} . The ID_{measured} ratio is strongly correlated to the $ID_{\text{calculated}}$ ratio (Spearman's rank correlation, $\text{Rho} = 0.82$, $p < 10^{-5}$). On average, 70% of the detectors measured less than 10% of the max dose.

Discussion

For all patients, clinically acceptable plans were achievable and deliverable for both FF and FFF treatments.

The beam on time of 2.5 min, which is achieved as a combination of a fast MLC (Elekta Agility) and an efficient segmentation algorithm (Pinnacle), appears to be the fastest commercially available combination when compared to former publications of SBRT VMAT FFF treatments for tumours in the lung (Supplementary Table I to be found online at <http://informahealthcare.com/doi/abs/10.3109/0284186X.2014.956184>). The average treatment dose rate for the Varian 6 MV FFF treatments is approximately 4–5 Gy/min, whilst the Elekta 6 MV FFF treatments are above 8 Gy/min. The 10 MV

Table II. Results for the delivery efficiency and accuracy. The accuracy is given by the mean dosimetric result of the ArcCheck measurements. The numbers are percentages of measuring points passing the gamma deviation criteria of 3 mm and 3%. Uncertainties of all values are reported as one standard deviation. p-Values are obtained from a paired two-sided Wilcoxon-signed rank test. Statistically significant differences are shown in bold.

	dFF	dFFF	sFFF	dFF vs. dFFF	dFF vs. sFFF	dFFF vs. sFFF
Delivery accuracy				p	p	p
Gamma pass rate	99.3 $\pm$ 1.0	98.0 $\pm$ 1.1	98.0 $\pm$ 1.7	0.0004	0.001	0.64
Delivery efficiency						
MU	2877 $\pm$ 231	2841 $\pm$ 237	2743 $\pm$ 223	0.01	0.0001	0.0003
Beam-on time (s)	382 $\pm$ 30	148 $\pm$ 12	146 $\pm$ 12	0.0001	0.0001	0.01
Dose rate (%)	97.3 $\pm$ 0.8	89.2 $\pm$ 1.2	87.6 $\pm$ 0.9	0.0001	0.0001	0.01

FFF treatment dose rates vary from 3 to 8 Gy/min, indicating large variety in plan complexity. To create a treatment plan for a complex anatomy and/or complex treatment protocol, a lack of sufficient MLC speed will often result in reduced dose rate to compensate for the finite MLC speed. Plan differences are typically also seen between planning systems for complex treatments in which some systems use quite small field openings which is associated with an increased number of monitor units. Thus, other things being equal, an efficient delivery time depends not only on the maximum nominal dose rate of the accelerator but just as much on the capability of using high dose rates during a major part of the delivery, i.e. high dose rate efficiency. The observed time differences are thus likely related to the high speed of the Versa HD™ Agility MLC [20] and an efficient segmentation algorithm in Pinnacle [14].

The dose rate efficiencies for the dFF deliveries were close to 100% whereas for the FFF beam they were under 90%, indicating that the full potential of the increased dose rate was not clinically obtainable due to MLC and gantry motion restrictions. For the sFFF plans, the MLC modulation had to be performed over a single 200° arc which required the dose rate to drop for a greater proportion of the delivery to allow for the planned MLC motion, hence, the dose rate efficiency was lowest for the single arc delivery.

The dose spillage (e.g. Figure 1) of the FFF plans was significantly lower than the FF plans. This observation could potentially be a treatment beam model artefact resulting from a different modelling of the out-of-field part of the FFF beam. However, a reduction in ID_{measured} was also observed by ArcCHECK, and furthermore ID_{measured} was strongly correlated to $ID_{\text{calculated}}$, which indicates that the observed reduction of dose spillage is real and not a beam model artefact. The reduction in dose spillage is thus likely related to the reduced scatter of the FFF beam. Similar findings were made by Cashmore et al. 2011, and Kragl et al. 2011 who found that the peripheral doses were reduced using FFF beams [2,4] for the Elekta systems. The OAR mean doses were significantly lower for the dFFF plans compared to the dFF plans, which could be related to the reduced dose spillage. The difference between the Varian and Elekta FFF beams is the beam quality, Q_i . Both systems have reduced head scatter, but the lower Varian energy increases the phantom scatter, resulting in increased out-of-field dose up to 15 cm from the field edge as reported by Kry et al. [3]. In contrast Kragl et al. found that for a fixed value of Q_i removal of the flattening filter decreases the out-of-field dose for FFF right from the field edge [4]. These observations show that dose spillage values probably are vendor-

specific and the small but significant improvement in dose spillage in the current study cannot be expected to be reproduced for accelerators for which Q_i is not matched during removal of the flattening filter.

The dFF and dFFF plans were very similar, even though the gains in reduced dose spillage and OAR mean doses for the dFFF plans were statistically significant. The gains are sufficiently small that any related clinical gains will likely be undetectable, however reduced dose in OARs is always a desired result, if it comes 'free of charge', i.e. without compromising any other clinical requirement. In summary there is no indication from the current study that use of FFF beams could increase the patients' radiation-induced toxicity.

The plan quality for dual arc FF and FFF plans for SBRT lung produced in Pinnacle 9.2 and delivered on a Versa HD™ was equivalent and only very small statistically significant differences were observed. The energy difference between vendors could potentially be important for the dose spillage, which was reduced for the FFF plans.

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Supplementary material available online

Supplementary Methods and Table I to be found online at <http://informahealthcare.com/doi/abs/10.3109/0284186X.2014.956184>