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Flattening-filter-free beam-line Multiple-X

Y. Dzierma, F. Nuesken, N. Licht, Ch. Ruebe

Answers for life.

Flattening-filter-free beam-line Multiple-X

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Introduction

Historically, flattening-filters have been added to the beam path of medical linear accelerators in order to create fields with uniform intensity for radiation therapy planning; today, this need has become obsolete for advanced planning techniques such as intensity-modulated radiation therapy (IMRT) and stereotactic radiosurgery (SRS). While con-formal radiation therapy (CRT) treatment planning still relies on a uniform dose distribution throughout the open field, inverse methods as IMRT or modulated arc (mARC) can take into account any kind of beam profile in the planning algorithm; SRS mainly uses small fields for which the absence of a flattening-filter does not significantly affect beam flatness. These techniques are hence well suited for treatment planning with flattening-filter-free (FFF) beams; they also benefit most from FFF treatment because the highly increased dose rate counteracts the increase in treatment time with respect to CRT. In addition to the enhanced dose rate, FFF beams offer the advantage of a decrease in head scatter and out-of-field dose, which may entail a lower risk of radiation-induced secondary malignancies.

The purpose of this work is to introduce the properties of the Multiple-X 7 MV beam line available at the Siemens ARTISTE, both as a reference for the physicist (dosimetric properties, commissioning, verification and treatment planning) and with practical examples of clinical cases. We present the beam characteristics of the Siemens ARTISTE FFF 7 MV beam measured at the Department of Radiation Oncology of the Saarland University Medical Centre in Homburg/Saar (Germany). This accelerator is equipped with a FFF 7 MV and flat 6 MV beam line, which will serve for comparison, and a 160 MLC multileaf collimator. Commissioning and treatment planning is performed in the Philips Pinnacle treatment planning system (TPS). Details on the dosimetric measurements, stability, commissioning and treatment planning can be found in Dzierma et al. (2012) and Dzierma et al. (submitted, 2012).

Physics background

a) Dosimetric properties of the Multiple-X 7 MV beam

The approach chosen for the Siemens ARTISTE was to compensate for the spectral softening caused by the elimination of the flattening-filter from the beam path by a slight increase in beam energy. As a result, the FFF 7 MV and flat 6 MV beams are similar with regards to depth dose curve, energy spectrum and surface dose. Since the strong attenuation of the beam in the flattening-filter is eliminated in the FFF 7 MV beam, the maximum dose rate is drastically increased; dose rates between 500 MU/min and 2000 MU/min (approx. 5-20 Gy/min at maximum depth) are available for the FFF 7 MV beam, vs. 50 MU/min to 500 MU/min (about 0.5-3 Gy/min at maximum) for the flat beams (6 MV or, where available, 18 MV).

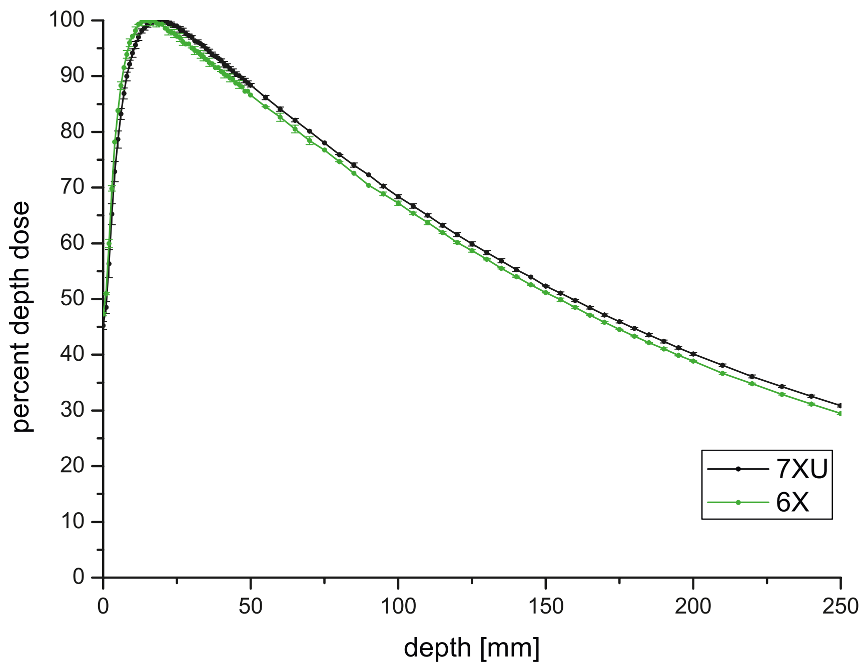

Figure 1: Percent depth dose curve for the FFF 7 MV beam (black line) compared with the flat 6 MV beam (green) for a 10 x 10 cm² field. Error bars shown in this and the following figures correspond to three standard deviations from a suite of three or more measurements repeated on the same day. (Figure from Dzierma et al., 2012)

The depth dose curve measured in a PTW MP3 water phantom with a pinpoint ionisation chamber (PTW type 31016) for the FFF 7 MV and flat 6 MV beams is displayed in Fig. 1. The maximum dose is reached at a depth of 19 mm for the FFF 7 MV beam and 16 mm for the flat 6 MV beam.

The surface dose measured with standard ionisation chambers is an overestimate because of volume averaging by the detector diameter. This can be remedied by using a plane-parallel soft x-ray ionisation chamber (PTW 23342), with an entrance window of 0.03 mm thickness. Measurements of the percent depth dose curve in an acrylic phantom reveal a dose at the surface of 25% for both the 7 MV and 6 MV beams, measured in a 10 x 10 cm² field.

The beam profiles of the FFF 7 MV beam show the characteristic cone-shaped dose fall-off from the central axis, which is compensated by the flattening-filter in the case of the flat 6 MV beam (Figure 2).

For fields smaller than 5 x 5 cm², the profiles are narrow enough to be considered reasonably flat (less than 15% dose deviation over the central 80% of the field opening for the 5 x 5 cm² field).

The 160 MLC leaf transmission and inter-leaf leakage are intrinsic MLC properties and hence display a very similar pattern for the flat 6 MV and FFF 7 MV beams (Fig. 3), with somewhat higher absolute transmission for the 6 MV beam close to the central axis (approximately by 0.6%).

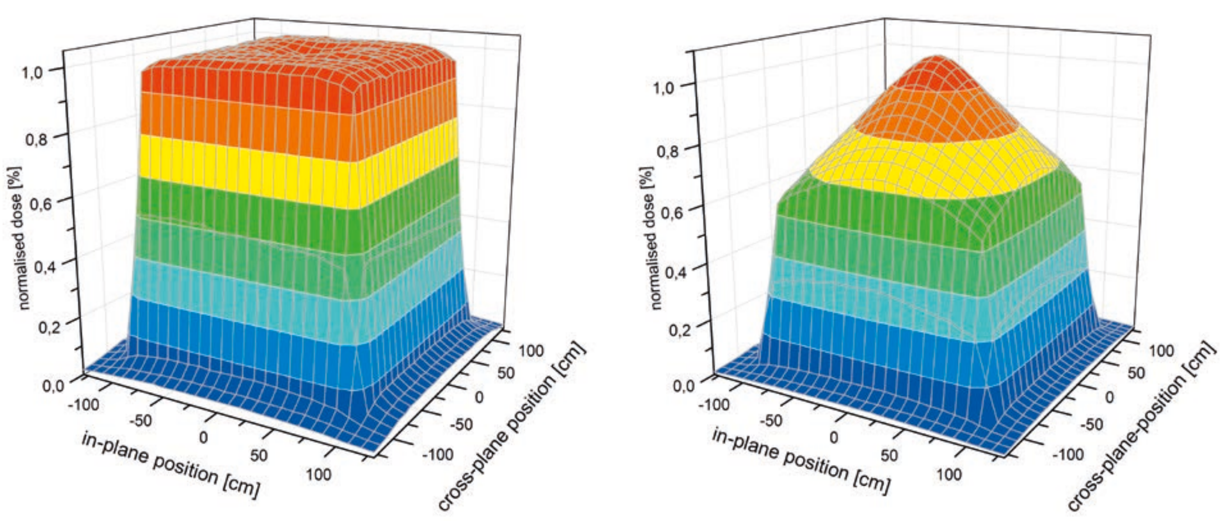

Figure 2: Beam profiles of the flat 6 MV and FFF 7 MV beams for a 20 x 20 cm² field. Note that in fact, the dose is higher for the FFF beam; the flat profile of the 6 MV beam is produced by "cutting off" the high-dose peak.

b) Commissioning in the TPS and dosimetric verification

Many treatment planning systems do not require commissioning by the user, but rely on a set of measurements sent to the company for in-house modelling of the beam properties (e. g. Prowess, Elekta). In the case where commissioning must be performed by the user, the same procedure applies as for flat beams, with just small modifications and caveats which we here present for the practical example of Philips Pinnacle.

The measurements for commissioning are explained in the physics guide of the TPS and should be followed for flat and FFF beams alike. For import into the TPS, measured profiles should be symmetrised, in some cases it may be useful to measure each curve a number of times and average over the different measurements; otherwise smoothing may reduce fluctuations in the profiles. To match the measured FFF beam shape, it is important to use the "arbitrary beam profile" facility. A starting spectrum close to the flat 6 MV model spectrum, or alternatively a Mohan spectrum can be used for the inversion. Our tests have shown that the choice of starting spectrum does not strongly influence the model results, as long as the spectrum covers the complete energy range (e. g., Pinnacle cannot "add" values at higher energies). For modelling the FFF 7 MV beam, a starting spectrum extending to 10 MV was deemed adequate. The automatic modelling routine in Pinnacle copes well with the FFF beam, producing a good model with a fit quality comparable to flat beams. Only the out-of-field dose was slightly overestimated by the model and needed to be manually adjusted to achieve a good fit (Figure 4).

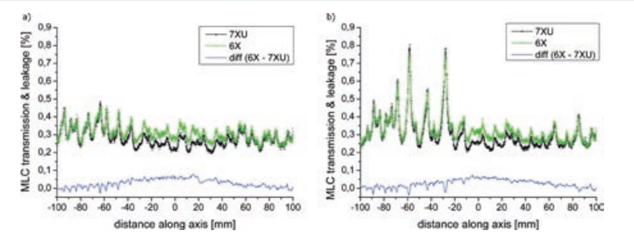

Figure 3: MLC transmission and interleaf leakage for the FFF 7 MV (black) vs. flat 6 MV (green) beam, in percent of the open field dose. The difference (7 MV – 6 MV) is plotted in blue. The MLC is closed at position -10 cm (left) and +10 cm (right). (Figure from Dzierma et al., 2012)

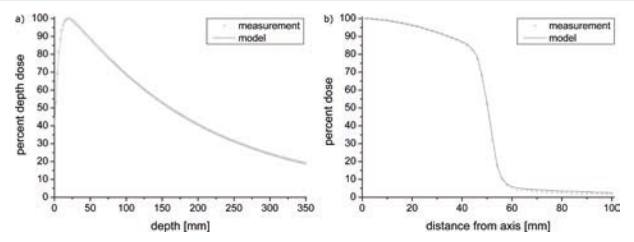

Figure 4: Modelling results from the Pinnacle automatic modelling algorithm: a) percent depth dose curve of the FFF 7 MV beam, 10 x 10 cm² field; b) in-plane profile of the 10 x 10 cm² field at 19 mm depth. (Figure from Dzierma et al., 2012)

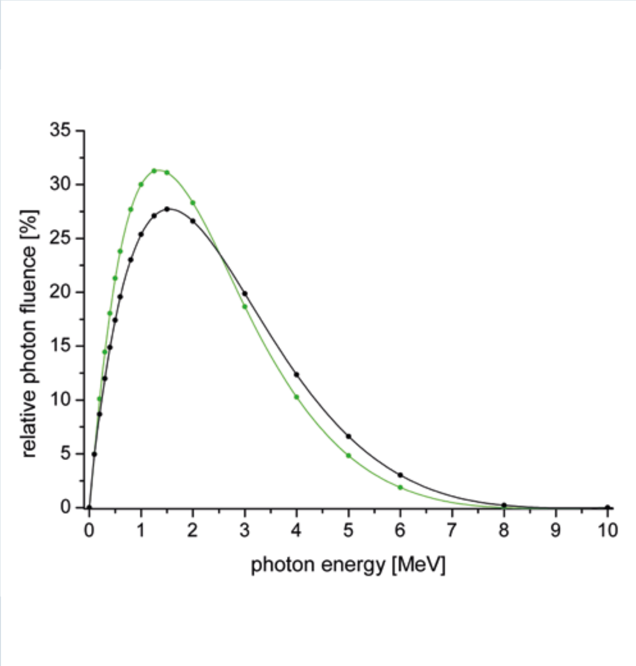

Figure 5: Photon fluence from the Pinnacle modelling algorithm, for the FFF 7 MV beam (black) vs. flat 6 MV beam (green). (Figure from Dzierma et al., 2012)

The relative energy fluence calculated by the TPS inversion is shown in Fig. 5. For photon energies below ca. 2.5 MeV, the spectrum of the FFF 7 MV beam has a lower photon fluence than the 6 MV beam, and correspondingly higher fluence above. As a result, the mean energy is slightly higher (2.5 MeV vs. 2.2 MeV for the FFF 7 MV and flat 6 MV beams, respectively), and the maximum energy fluence is reached at higher energy (2.8 MeV vs. 2.4 MeV).

Several IMRT and SRS plans were created and verified with point dose measurements in an acrylic phantom in the way we perform routine IMRT verification. The dose distribution was furthermore verified using the PTW 2D array and GafChromic film in the same way as is done for flat fields; in all cases, the agreement was within the usual specifications (maximum 3 mm distance to agreement and 3 % dosimetric deviation). For IMRT and mARC plans using flat and FFF beams, verification was furthermore performed using the PTW Octavius with 729 2D-Array, which provides a 3D dose distribution. Again, a criterion of 3 mm distance to agreement and 3% deviation in local dose was applied and satisfied by over 95% of the measured points.

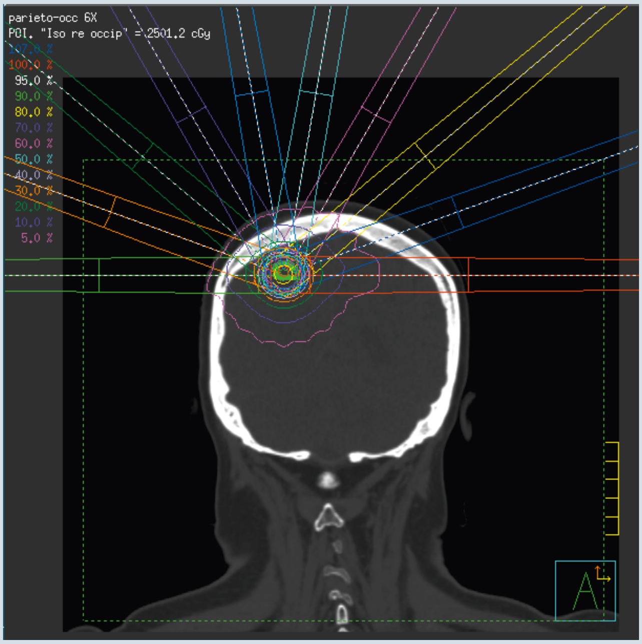

Figure 6: Example of a treatment plan showing the 10 non-coplanar arcs, which each span 140°. The isocentre is placed centrally in the PTV. The dose distribution shown is for the 6 MV plan treated clinically. (Figure from Dzierma et al., under review)

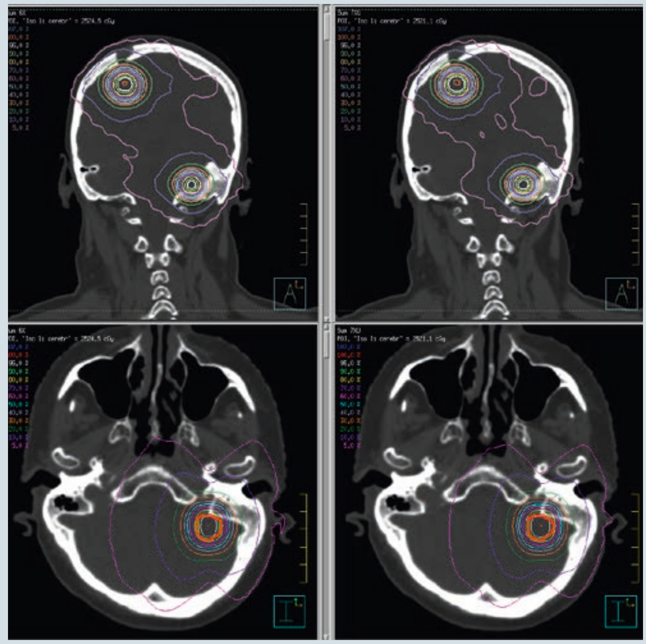

Figure 7: Transverse and coronal example slices for a flat 6 MV plan (left) vs. FFF 7 MV plan (right), for a patient with two metastases.

Treatment planning with the FFF beam

a) Stereotactic radiosurgery of brain metastases

Intrinsically, medical indications requiring high single-fraction doses and relying on small field sizes are optimally suited for FFF beams. In these cases, the axially decaying beam profile does not significantly affect planning, since the beam profiles can be reasonably assumed to be flat and "standard" conformal plans can be applied. At the same time, the high dose rate will be of greatest advantage for extremely hypofractionated treatments, where large single-fraction doses are applied. Both conditions are ideally met for stereotactic radio-surgery (compare Bayouth et al., 2007).

Within the field of radiosurgery, the treatment of brain metastases with multiple non-coplanar beams stands out as a straightforward application of FFF beams. For this case, we performed planning for the Multiple-X FFF 7 MV beam in the same way as usually done for the flat 6 MV beam, based on CT planning data. The plans have 10 non-coplanar arcs of 140° each with table angles between 280° and 20°; an identical plan was made for the 6 MV and FFF 7 MV beam (Fig. 6). In this example, the planning procedure for the FFF 7 MV beam is particularly straightforward, since the plan itself is not changed from the standard flat 6 MV plan. Dose computation in Pinnacle used the collapsed cone algorithm and was performed on a dose grid of spacing 0.2 cm.

For absolute dosimetric verification all treatment plans were mapped onto an acrylic phantom and measured with a PTW 0.235 cm³ ionisation chamber (31010); this is the standard procedure for IMRT verification measure-

Quality index	6 MV – mean	6 MV – std. dev.	FFF 7 MV – mean	FFF 7 MV – std. dev.	p
OR	0.778	0.058	0.738	0.057	5e-4
UR	0.918	0.043	0.953	0.033	5e-4
CI	0.713	0.054	0.703	0.056	0.151
HI	0.359	0.073	0.339	0.081	5e-4
GI	4.26	0.71	3.72	0.51	5e-4
V(80 %) (cm^3)	3.83	1.93	4.15	2.00	5e-4
V(40 %) (cm^3)	15.2	6.4	14.6	6.1	5e-4
V(5 %) (cm^3)	286	102	261	91	5e-4
σPTV/PTVmean (%)	6.85	0.97	6.10	1.03	5e-4
treatment time (min)	14.1	2.5	7.4	0.5	0.002

Table 1: Measures of plan quality. Values which show a statistically significant improvement (based on a level of significance of 0.05 for the Wilcoxon signed-rank test of paired data) are printed in blue. Quality measures are defined as follows: OR = TVPIV/PIV and UR = TVPIV/TV are Paddick's overdose and underdose ratios, where PIV is the volume of the prescribed isodose (80% in our case), TV is the target volume, and TVPIV is the volume of the target receiving the prescribed dose or higher. CI = OR x UR is the conformality index, HI = (PTVmax – PTVmin)/PTVmean the homogeneity index, and GI = V(40%)/V(80%) the gradient index (compare Shaw et al., 1993; Paddick, 2000; Paddick & Lippitz, 2006).

Organ at risk	Minimum	Mean	Maximum	Median	p
Lens (left)	0	10.2	16.9	9.2	0.001
Lens (right)	-4.3	10.1	33.6	8.2	0.001
Eye ball (left)	2.2	5.8	9.5	5.7	0.016
Eye ball (right)	-17.8	4.6	14.8	7.5	0.078
N. Opticus (left)	0.9	6.3	13.3	6.2	5e-4
N. Opticus (right)	3.1	8.9	17.3	7.9	5e-4
Inner ear (left)	1.4	7.7	16.3	6.3	0.004
Inner ear (right)	-1.5	8.7	14.6	9.6	0.012
Chiasma	2.8	6.8	14.3	6.3	5e-4
Brain stem	-0.7	4.4	9.2	4.4	0.061

Table 2: Percentage improvement in OAR sparing by the FFF 7 MV plan, considering the maximum dose to the OAR, as defined by S = 2(D6MV – D7MV)/(D6MV – D7MV). Blue colour marks those values which show a statistically significant improvement (based on a level of significance of 0.05 for the Wilcoxon signed-rank test of paired data).

ments at our clinic. In addition to the point dose measurements, the planar dose distribution was assessed for a plan calculated on an Alderson head and thorax phantom and measured with GafChromic film. The plan quality was assessed for 7 patients with a total of 12 lesions by Dzierma et al. (submitted, 2012). The main effect is that the FFF 7 MV beam has a slightly steeper gradient, which is expressed by two observations: the volume of high-dose isoregions (and hence the PTV coverage) is slightly enhanced, while the volume of low-dose isoregions (and hence dose to most organs at risk) is reduced. Taken together, the FFF 7 MV plans are improved over the flat 6 MV plans, although in some cases the improvement may be so slight to elude clinical relevance. An overview of plan quality measures and dose to organs at risk is given in Tables 1 and 2, example plans are shown in Figure 7.

	7 beams	11 beams	18 beams
Gantry angles (collimator angle)	0° (90°) 50° (0°) 80° (0°) 150° (90°) 210° (90°) 280° (0°) 310° (0°)	0° (90°) 30° (0°) 65° (0°) 100° (0°) 135° (90°) 170° (90°) 190° (90°) 225° (90°) 260° (0°) 330° (0°)	0° (0°) 180° (0°) 20° (0°) 200° (0°) 40° (0°) 220° (0°) 60° (0°) 240° (0°) 80° (0°) 260° (0°) 100° (0°) 280° (0°) 120° (0°) 300° (0°) 140° (0°) 320° (0°) 160° (0°) 340° (0°)
Max. # segments	70	70	50
Min. segment	Area: 7 cm², MU: 5		
Min. lamella	Pairs: 2, distance: 1.5 cm		
Isocentre	Automatically placed inside PTV, then manually shifted to front edge of spine		

Table 3: Plan characteristics and IMRT inversion parameters for three different beam arrangements.

While the plan quality as assessed by these measures differs only marginally between the two plans, the Multiple-X FFF 7 MV plans offer two additional advantages, which are clinically more relevant. Firstly, the treatment time is reduced almost by half from an average of 14 minutes (flat 6 MV plans) to 7 minutes (FFF 7 MV). For the FFF 7 MV plans, the treatment time is no longer determined by the time required to deliver the dose (radiation time), but rather by constraints on the gantry rotation velocity and table angles.

Secondly, the out-of-field dose is decreased (compare Kragl et al., 2011), as is verified by phantom measurements at different locations on the thorax. For five locations (larynx, sternum, clavicles and navel), the measured skin dose at the phantom (for two different PTV locations in the brain) was reduced by between 20% and 50% (Dzierma et al., submitted, 2012).

b) Stereotactic body radiation therapy – IMRT

Stereotactic body radiosurgery, in particular for bronchial carcinoma, is generally treated with IMRT plans at our institution. The small PTV diameter makes this indication a straightforward application of FFF beams, since the effect of the non-flat beam profile on the PTV homogeneity is minor. Planning can hence proceed along very similar lines to usual flat beam IMRT stereotaxy, with no necessity of adjusting the constraints for FFF beams. An issue in treating lung lesions, however, is the effect of respiratory motion on the plan delivery. Here, the higher dose rate available for Multiple-X FFF beams is of great advantage where gated treatment is planned. In the case of non-gated treatment, however, the MLC interplay effect is aggravated by the reduced treatment time per segment. Whether this problem is relevant for each patient must be carefully estimated before treatment; respiratory-correlated CT imaging for planning is hence desirable (Dzierma et al., 2013).

c) IMRT – head & neck cases

IMRT can be calculated for FFF beams in the same way as for flat beams in Pinnacle; however, creating a homogeneous PTV coverage is more challenging for FFF beam profiles, and it is not evident a priori that the same set of constraints will result in a good plan for both flat and FFF fields.

We selected a collective of 8 head & neck patients to compare IMRT plan quality for 6 MV and FFF 7 MV plans, which were inverted using identical beam arrangement, inversion parameters, and constraints. Three scenarios were considered: a "standard" IMRT plan with 7 beams, an improved IMRT plan with 11 beams, and a multi-beam plan intended to simulate rotational treatments (18 beams) – see Table 3 for a summary of plan characteristics. Different sets of constraints were applied to optimise both the flat 6 MV and FFF 7 MV plans.

Comparing a number of different choices of constraints for the IMRT inversion, we find that most objectives/

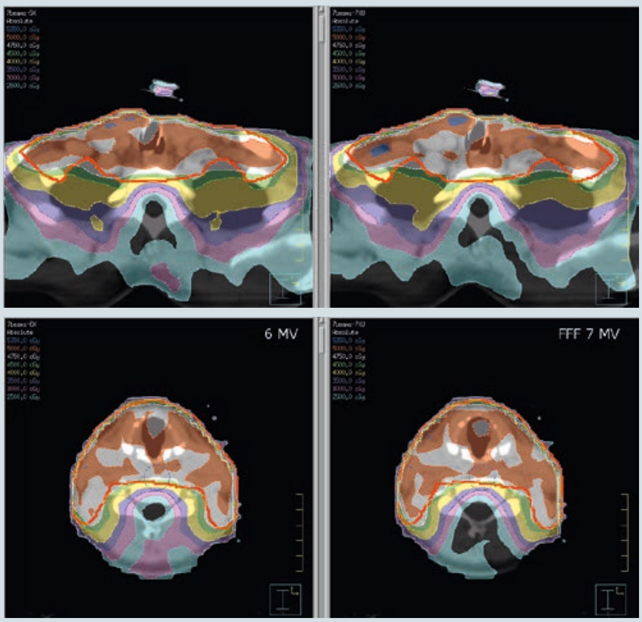

Figure 8: Example head & neck plan using 7 beams, 6 MV (left) vs. FFF 7 MV (right).

constraints generally used for plans consisting of flat 6 MV beams can be easily taken over to the FFF 7 MV. The main difference in planning with the FFF 7 MV is that we find a necessity of including a homogeneity constraint for the PTV, which forces 5% homogeneity. This constraint hardly influences the flat 6 MV plans, which generally comply with this criterion even when it is not explicitly stated (it is included in the PTV_max, PTV_uniform, PTV_ring or sometimes PTV_min constraints), but it improves the FFF 7 MV plans to a point of becoming comparable to the 6 MV plans in homogeneity (the other requirements are usually satisfied). If the homogeneity constraint is set too low (3% or lower), the 6 MV plans are influenced, which is not desired in our case, where the standard constraints produce good quality 6 MV plans. By adding a homogeneity 5% constraint, we can therefore work with the same set of constraints for 6 MV and FFF 7 MV beams. The final set of objectives/constraints that gave best quality plans is given in Table 4, example plans are shown in Figures 8-9.

Different choices of objectives/constraints are certainly able to create equally good plans – we here present one example. All plans were revised by an experienced radio-oncologist, and were considered clinically acceptable. The quality of the plans (6 MV vs. FFF 7 MV) was generally very similar. In most cases, the 11 beam arrangement offered improved plan quality over the 7 beam arrangement, both from the point of view of PTV coverage and sparing of organs at risk. Moving to 18 beams, the quality was sometimes improved (in particular for 6 MV plans), sometimes reduced (mostly for the FFF 7 MV plans). Even in cases where the 18 beam plans were better than the 11 beam plans, the improvement was so slight to be clinically insignificant. In the clinical setting, the shorter treatment time for the 11 beam plans would always have resulted in a decision to treat with these plans.

Depending on the patient, either the 6 MV or FFF 7 MV plans (11 beams) were preferred – in all cases, the differences were minor. For the collective of patient, no

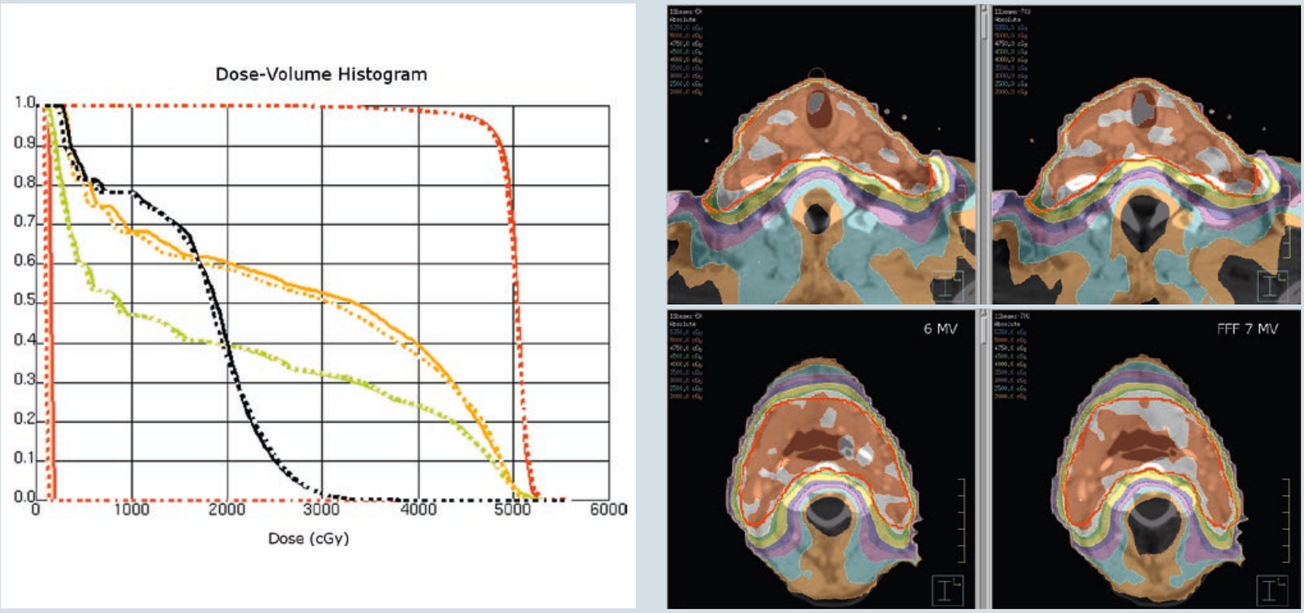

Fig. 9. Example head & neck plan using 11 beams, 6 MV (left) vs. FFF 7 MV (right). Top shows slices through the dose distribution (absolute dose, prescribed dose to PTV is 50 Gy), bottom panel shows dose volume histogram (DVH).

significant difference was found in the quality indices of 6 MV vs. FFF 7 MV plans of equal beam arrangement (overdose and underdose ratio, conformity index, homogeneity index). With a good choice of objectives/ constraints, the FFF beam can hence be applied in IMRT planning with equivalent quality results as the standard flat beams, but with the option to increase the dose rate and hence reduce treatment times. Since the treatment times usually required for IMRT are generally much longer than standard conformal treatment, several studies have pointed out that this might reduce the biological effectiveness of the treatment – a drawback which might be circumvented by Multiple-X irradiation.

d) Backup concept – what if the Multiple-X beam is not available?

In some institutions such as ours, only one linac may be equipped with the Multiple-X beam line. In such cases, a failure at one machine must be compensated by irradiating at another machine with a different energy.

For the presented case of brain metastases, we did not change any parameters between the flat 6 MV plans and FFF 7 MV plans except for the energy. In this case, the 6 MV plan provides an alternative and nearly equivalent plan with the same prescribed dose, very similar dose distribution, slightly higher scattered dose and increased treatment time, which can be calculated easily in a very short time (Figure 7).

For the HNO IMRT cases we considered, the same constraints were set for the flat and FFF beams. Here, creating an alternative plan will involve an additional optimisation. Still, as long as a good set of constraints has been defined from the onset, the optimisation should perform with little problems. Only in complicated cases which cannot be planned with a straightforward IMRT template, the creation of an alternative plan with a flat beam will become more difficult. In these cases, replanning may take as long to create as did the original plan, and hence mean duplicating the work load for these patients in case of linac maintenance.

Structure	Objective	Weight
PTV (excluding parotids where only edge of parotids reaches into PTV)	Uniform dose 50 Gy	20
	Max dose 50.42 Gy	20
	Min dose 48.75 Gy (95 %)	20
	Homogeneity 5 %	Fixed constraint
	Min DVH 95 % 47.5 Gy	Fixed constraint
	Max DVH 5 % 50.25 Gy	Fixed constraint
PTV-Ring (+ 3mm to +7mm)	Max dose 45 Gy (90 %)	20
External – PTV	Max dose 40 Gy (80 %)	20
	Max dose 25 Gy (50 %)	1
Spinal cord	Max dose 33.33 Gy	20
	Max dose 25 Gy	20
Parotids	Max DVH 30 % 14.17 Gy	20

Table 4: Final optimised inversion constraints.

Clinical applications

While the biological effectiveness off the treatment might be improved by the use of FFF beams, the effects of an increase in dose rate have not been investigated in detail so far. In particular, the irradiated segments receive a higher dose rate than in conformal treatment – only the summation over all segments will give an irradiation time comparable to conformal treatment. While there is still a need for detailed studies of the effects of high dose rate percutaneous radiation, this issue is solved to some degree by the option to perform Multiple-X beam treatment in the low dose rate mode (500 MU/min, similar to the high dose rate mode of flat beams). In the clinical setting, we have treated a small number of patients with brain metastases using the Multiple-X beams, with no evidence of different treatment tolerance or side effects.

Up to now, treatment at our institution has mainly applied the Multiple-X beam to stereotactic brain surgery, with dose rates of up to 1000 MU/min. After detailed planning studies for IMRT cases, the FFF beam has been found to be suitable for clinical treatment. A particular advantage lies in the combination with Siemens' novel mARC technique, which allows for even faster treatment. A number of mARC treatments with the Multiple-X 7 MV beams were successfully performed, and will become more routine in the coming months.

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