A dosimetric evaluation of flattening filter-free volumetric modulated arc therapy in nasopharyngeal carcinoma

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ABSTRACT

Purpose: To explore the dosimetric effects of flattening filter-free (FFF) beams in volumetric modulated arc therapy (VMAT) of nasopharyngeal carcinoma via a retrospective planning study. **Materials and Methods:** A linear accelerator (LINAC) was prepared to operate in FFF mode and the beam data were collected and used to build a model in TPS. For 10 nasopharyngeal carcinoma (NPC) cases, VMAT plans of FFF beams and normal flattened (FF) beams were designed. Differences of plan quality and delivery efficiency between FFF-VMAT plans and filter filtered VMAT (FF-VMAT) plans were analyzed using two-tailed paired t-tests. **Results:** Removal of the flattening filter increased the dose rate. Averaged beam on time (BOT) of FFF-VMAT plans was decreased by 24.2%. Differences of target dose coverage between plans with flattened and unflattened beams were statistically insignificant. For dose to normal organs, up to 4.9% decrease in V35 of parotid grand and 4.5% decrease in averaged normal tissue (NT) dose was observed. **Conclusions:** The TPS used in our study was able to handle FFF beams. The FFF beam prone to improve the normal tissue sparing while achieving similar target dose distribution. Decreasing of BOT in NPC cases was valuable in terms of patient's comfort.

Key words: Flattening filter-free; nasopharyngeal carcinoma; radiotherapy; volumetric modulated arc therapy

Background

LINACs operated in a flattening filter-free (FFF) mode is becoming of increasing interest in recent years. Started in the 1990s, the early research work was focused on the increased dose rate for radiosurgery[1] or the physics characteristics of unflattened beams.[2-4] In 2000s, several groups addressed the issue of using FFF beams in IMRT.[5-7] Rotational IMRT or VMAT has recently become a promising and commercial treatment option.[8] During the past years, feasibility of treating various cancers including prostate, lung, larynx, chest wall, and esophagus using unflattened beams have been reported.[9-16] Also exclusive use of a linear accelerator in FFF mode in 3D CRT planning has also been reported to be feasible.[17] From all these published results, a reduced beam on time (BOT) and comparable plan quality seem to have been confirmed for VMAT plan with unflattened beams. Advantages of removing flattening filter in LINACs thus become more and more convincing. Nevertheless, studies published so far are limited to cases with relatively small planning target volume (PTV) with less peripheral organs at risk (OARs).

Nasopharyngeal carcinoma (NPC) is one of the most frequently occurred cancers in certain regions of East Asia and Africa. Although radiotherapy is the choice of NPC treatment, more treatment fractions and longer treatment time per fraction makes it prominent to further improve the treatment efficiency. At the same time, planning of NPC cases proved to be challenging due to the large PTV volumes and the numerous close proximity normal structures. In the present work, using of FFF beams in NPC-VMAT is studied to evaluate whether and to what extent the higher dose rate of FFF beams could be of a

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solution to the efficiency problem and, to illustrate the performance of FFF-VMAT for NPC cases.

Our work was carried out in three steps: (1) A FFF photon beam was modeled in a commercial TPS using the measured beam data from a LINAC operated in FFF mode. (2) Ten NPC cases previously treated in our department were randomly selected. For each case, a VMAT plan using flattened beams (FF-VMAT) and unflattened beams (FFF-VMAT) were designed, respectively. (3) Plan quality and delivery efficiency between FFF-VMAT plans and FF-VMAT plans were compared.

Materials and Methods

An Elekta Synergy LINAC (Elekta, Crawley, UK) was used for beam data collection and treatment delivery undertaken in this study. Beam data of 6 MV photon with and without FF were collected and used to model the LINAC in the Pinnacle^3 (V9.0) (Philips Radiation Oncology, Fitchburg WI) TPS. The SmartArc module of Pinnacle^3 was used to generate the VMAT plans.

Beam data collection and beam modeling

The usual method of obtaining a FFF beam was to replace the FF with a thin plate composed of various materials.[7,18] As an exploratory study, an easier and safer way was adopted in our study: The 6MV photon FF was replaced with the 6MeV electron scatter foil. In such a way, only the configurations of the LINAC control software needed to be changed and the LINAC could be easily restored to its original clinical mode when the research work done. The FFF beam in our study was not suitable for clinical use, but it should be sufficient for exploratory studies. In order to enable the FFF beam delivery in the LINAC, flatness relevant interlocks were bypassed under the guidance of service engineers. Other beam-steering parameters were kept unchanged.

Beam data with and without the FF were collected according to the Pinnacle Photon Beam Data Collection (Philips Radiation Oncology, Fitchburg WI) using a ScanditronixRFAPlusphantom(ScanditronixAB,Husbyborg, Sweden) with a compact ionization chamber (Scanditronix/ Wellhofr RK Compact Chamber) for depth dose-curve measurements and a diode detector (PFD^{3G} IBA Dosimetry GmbH, Germany) for profile measurements. Data including percent depth dose curves, output factors (S$_{cp}$) and profiles were measured at various depths for a range of field sizes. The FF beam used in our department was calibrated according to the IAEA TRS-277 protocol using Dose1 electrometer and FC65-G 0.6cc farmer ion-chamber (Scanditronix Medical AB). As Xiong *et al.* concluded that when FF was removed, the original stopping-power ratios as function of %dd(10) x can still be used but with a slightly higher uncertainty.[19] The FFF beam in the present work was thus calibrated using the same methods as FF beam.

Modeling a regular LINAC in Pinnacle^3 had been described by Starkschall and Bedford.[20,21] Similar process had been adapted in our study except that the relative incidence fluence was defined by an arbitrary profile in the TPS to account for the conical shape of the unflattened beam.

Case selection and planning

The cases selected were diagnosed with early stage carcinoma (T1) and were clinically treated with nine fields IMRT by means of a simultaneously integrated boost (SIB) technique. Two planning target volumes were defined: PTV1, the target volume of the primary lesion, which was given to 60.06 Gy in 33 fractions, and PTV2, the target volume of electively treated region, which was given to 50.96 Gy in 28 fractions or 60.06 Gy in 33 fractions depends on the clinical observation (only the latter case was examined in our study). The boost target volume, including the planning primary tumor (PGTVnx, GTV extended 2 mm) and the involved periphery lymph nodes (GTVnd), were treated to 69.96 Gy in 33 fractions. Typical targets layout and corresponding dose levels were exemplified in Figure 1. The dose constraints to OARs were listed in Table 1.

The planning process was started by optimizing a 2-arc (360 deg per arc) FFF-VMAT plan according to the clinical requirements. Depending on the optimization results, fine-tuning of optimization parameters and re-optimizing of the plan might also be applied. The plan was finalized when all clinical requirements were met. Finally, the resulting set of

Table 1: OAR constraints for NPC cases

OAR	Constraints
Parotid glands	$V_{35} < 50\%$
Spinal cord	Dmax<45 Gy
Brain stem	Dmax<54Gy
Lens	Dmax<9 Gy
Optic nerves	Dmax<54 Gy

OAR: Organs at risk, NPC: Nasopharyngeal carcinoma

PTV1 60.06 Gy

PGTVnx 69.96Gy

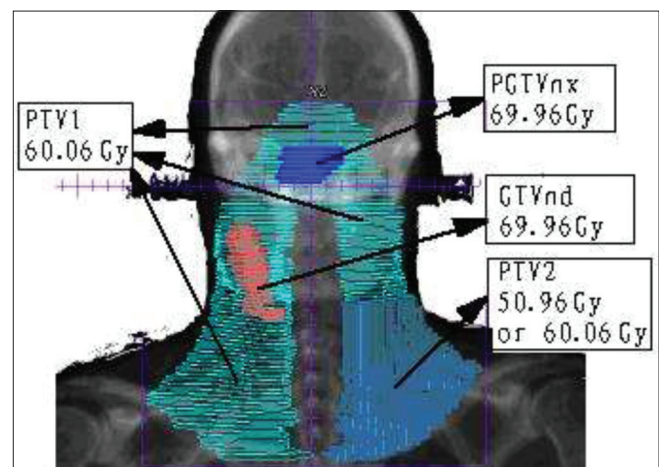GTVnd 69.96Gy

PTV2 50.96 Gy or 60.06 Gy

Figure 1: Typical target layout and corresponding dose levels

optimization parameters were then applied to a FFF-VMAT plan and FF-VMAT plan using the same process: Beams were reset and plan was optimized for 70 iterations followed by a "warm up" optimization (optimization was started from the plan's current photon fluence) of 30 iterations. As can be seen, this study did not optimize treatment delivery parameters specifically for flattened beams. Treatment plans with flattened beams used the same number of arcs, dose constraints, and planning priorities as used for unflattened beams.

When the planning process was done, the collapsed cone convolution superposition algorithm was employed for the final dose calculation. The dose grid was set to 3 × 3 ×3 mm for all cases. Dry runs of all plans were performed on the LINAC to check the real deliverability of the treatment. BOT measured in dry run was used for comparison.

Plan comparison

Target dose, dose to organs at risk (OARs), and normal tissue (NT), plan delivery efficiency were compared using two-tailed, paired t-tests. The NT was defined as the body volume subtracted by all target volumes. For ease of comparison, plans were renormalized such that 95% of PGTVnx received 100% of the prescription dose. Finally, all plans were delivered on the LINAC and the delivery efficiency was evaluated using the actually measured BOT.

Dose homogeneity index (HI) and conformity index (CI) were used as comparison metrics between plans generated with and without a flattening filter. The HI as described by Wu *et al.*[22] was used:

$$HI = \frac{(D_2 - D_{98})}{D_p} \times 100\% \tag{1}$$

where D_P, D_2, and D_{98} represent the prescription dose, dose to 2% and 98% of the target, respectively. By this definition, lower HI value indicates better dose homogeneity. As the dose distribution inside PTV was non-uniform, the HI was

only calculated for PGTVnx. The CI used to evaluate the dose conformity was defined as[23]:

$$CI = PTV\_p \times ISO\_p \tag{2}$$

Where PTV_p is the percentage of PTV volume receiving a dose no less than the prescription dose, and ISO_p is the portion of the prescribed iso-dose volume account for by the target. The CI values range from 0 to 1, where 1 is the ideal value. In this work, PTV1 and PTV2 were merged together to create a new target (PTV1 + PTV2) for conformity evaluation.

In the evaluation of OAR dose, parameters for comparison were selected accordingly: Percent of volume covered by the clinically concerned threshold dose were used for parallel organs and maximum dose were used for serial organs. If no volume of a parallel organ received the threshold dose, mean dose was applied. The maximum dose was defined as the dose to 1cc or 1% of the organ volume, whichever is less. Percent volume covered by 35 Gy iso-dose lines (V_{35}) was used for left and right parotid, and maximum dose was used for spinal cord, brain stem, left and right lens, left and right optic nerves.

Results

Beam data and beam model

With respect to beam modeling in the TPS, errors between the measured profiles and TPS calculated profiles were usually used to evaluate fitness of the resulting model. Figure 2 illustrated the comparison results of a 20 × 20 cm^2 field PDD and profiles (dashed line was the calculated). The maximum differences were 0.7% and 1.2% for PDD beneath the buildup region and profile at 10-cm depth, respectively. Figure 3 was the resulting relative energy spectrum of FF and FFF beam (normalized at 2 MeV). The enhanced lower energy component of the dashed line indicated a softer FFF beam resulting from the absence
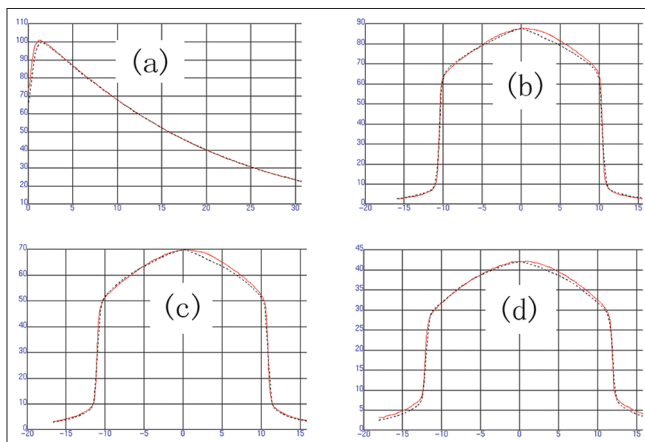

Figure 2: Comparison between the calculated and measured PDD (a) and profiles at depth 5 cm (b), 10 cm (c), 20 cm (d) of 20 cm × 20 cm field for FFF beam
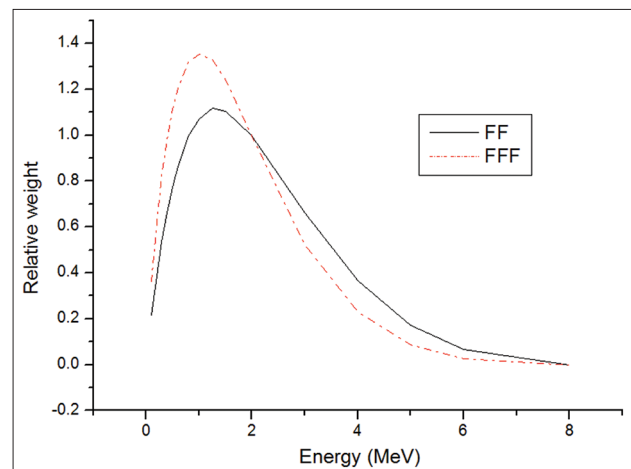

Figure 3: Energy spectrum of FF and FFF beam

of the hardening effects of the FF. The maximum value of the FFF beam spectrum was shifted approximately 1 MV toward the lower energy, making it resembles a 4-5MV FF beam. The absolute dose output ratio of FFF beam to FF beam measured in a 30s beam on duration (SSD 90 cm, 10 × 10 cm field) was 2.225. The result was very close to the data reported by other groups.[5,21]

Plan Comparison

Table 2 listed the average values, standard deviations and *t*-test *P* values of the selected parameters for both groups of plans. Differences were considered as significant at $P < 0.05$. The listed averaged BOT was calculated from the plan dry-run process in which all plans were delivered successfully.

As for target dose coverage, the maximum difference of averaged dose (for PTV2) was less than 1% and the difference was close to statistically significant. For other targets, dose to 95% of the target was almost the same. Comparison of HI value reveals that difference of dose homogeneity was insignificant. Although the difference of CI was statistically significant, the averaged CI values are very close to each other. Visual check of the DVH curves also confirmed that the dose conformity of targets is close. In general, target dose coverage of FFF-VMAT plan was similar to FF-VMAT plans.

For dose to normal organs, though *P* values for some of the metrics (parotid glands, brain stem, right lens, and NT) indicated a statistically significant difference, the average values were relatively close to each other. The most notable difference was observed for the right parotid gland, in which the percent volume covered by 35 Gy iso-dose lines

Table 2: Plan comparison results of NPC cases

	Average		Std. dev.		P value
	FFF	FF	FFF	FF	
PTV1 D_{95}(cGy)	59.86	59.85	0.81	0.94	0.93
PTV2 D_{95}(Gy)	59.67	60.09	0.74	1.03	0.058
GTVnd D_{95}(Gy)	69.88	69.85	0.27	0.40	0.82
HI	0.074	0.085	0.016	0.026	0.091
CI	0.88	0.85	0.028	0.031	<0.001
Parotid L V_{35} (%)	42.27	43.49	4.12	3.83	0.022
Parotid R V_{35} (%)	41.29	43.39	5.46	3.83	0.025
Spinal Cord (Gy)	31.08	30.99	1.54	2.42	0.88
Brain Stem (Gy)	35.81	37.67	2.98	3.26	0.027
lens L (Gy)	4.83	5.26	1.28	0.94	0.083
Lens R (Gy)	4.34	4.87	0.89	0.85	0.034
Optic nerve L (Gy)	42.44	43.91	1.31	15.41	0.42
Optic nerve R (Gy)	39.98	41.96	1.40	16.39	0.30
NT Mean (Gy)	21.27	22.27	0.68	1.143	0.015
MU	533.5	598.6	38.50	43.54	9.6E-06
BOT (s)	273	360	18.70	16.59	<0.001

NPC: Nasopharyngeal carcinoma, PTV: Planning target volume, FFF: Flattening filter-free, FF: Flattened, BOT: Beam on time, NT: Normal tissue, HI: homogeneity index, CI: conformity index, MU: Monitor unit, GTV: Gross target volume

of FFF-VMAT plans was decreased by 4.9%. Max dose to other organs was also decreased to some extent. For NT mean dose, a dose fall-off of 4.5% was observed for plans using unflattened beams. Overall, although the difference was slight, plans were consistently better with the filter removed, and surely they were no worse. Concerning the plan delivery efficiency, averagely ∼24% of the BOT decrease was observed for FFF-VMAT plans and the difference was statically significant.

Discussion

Clinical use of unflattened beams has been investigated from different perspectives; mainly beam modeling, plan verification, and case planning. The most particular work of modeling an unflattened beam in TPS is obviously the way to account for the conical shape of the beam profile. This has been previously accomplished by replacing the conical reduction which simulating the FF with a negative reduction.[11] In the present work, the energy fluence was modeled by an easier way of providing the TPS with an arbitrary profile. The resulting model, as presented in the previous section, was satisfying. Although no modeling details presented, successful modeling of FFF beam in other TPS had also been exemplified.[13] It seems that handling unflattened beams in today's TPS is no longer a problem.

Several groups working on FFF beams have presented IMRT verification using various phantoms and measurement devices in their work.[11,12,15,24] All the results reported could well meet the clinical criteria. From all these investigations, it could be extrapolated that dose calculation accuracy in state-of-the-art TPS will certainly not be impaired when removing the FF. Considering that the FFF-VMAT plans are not intended for clinical use, dosimetric verification was thus not presented in this work.

In a whole, for the NPC cases used in the present work, similar target dose distributions were achievable when unflattened beams were used instead. As the flattening filter (FF) is one of the main scattering elements in the treatment head[25], a better OAR sparing is reasonably expected when applying FFF beam in clinical treatment. Peripheral doses in IMRT and SBRT treatment were reported to be significantly decreased in anthropomorphic phantom measurements.[26,27] As dose to organs close to the target, though the extent of improvement was much less, a better OAR protection for unflattened beams had also been confirmed by a number of authors.[9,10,14,26] According to Table 2, the results in our study generally support these reported data. Whereas, a similar planning study of advanced NPC cases using Eclipse TPS and Varian TrueBeam LINAC performed by Zhuang *et al.* showed that OAR sparing of unflattened beam VMAT plans was somewhat inferior to that of flattened beam.[24]

This may indicate that in a comparison planning study of VMAT technique, patient characteristics, planning processes, TPSs, and LINACs can affect the comparison results. As VMAT and FFF are relatively new techniques in radiotherapy, to further explore their potentials, planning experiences may need to be accumulated and inter-comparison of various TPSs and LINACs may also needed to be carried out.

The increase in dose rate is one of the most obvious and attractive effects when removing the FF. Due to the variety in treatment techniques, the increased dose rate does not necessarily directly translate into shorter treatment times.[5,17] Experimental data from various authors can serve as good references. Up to now, BOT reduction of more than 70% had been reported in SRT treatment[12,13,28,29] and ~33% in breast and prostate treatment.[14,15] The BOT in our study was ~24% less for FFF-VMAT plans, which was remarkably lower than the above mentioned data. Obviously, in terms of treatment time, treatments with small target size and less MLC movement could benefit more from the increased dose rate of the FFF beam. Planning study of various cases using field in field technique illustrated that segments number ratio of FFF beam to FF beam increase with an increased PTV volume.[17] This explains why the relative time decreasing of FFF beam in NPC VMAT cases is less than the reported value. Although the percentage reduction of BOT in complicated NPC case was relatively less, the actual time saved was still beneficial in terms of patient comfort as well as patient outcome.

In our study, the optimization parameters were changed over multiple iterations in order to produce the FFF-VMAT plan that meets all the DVH criteria. One issue of such planning process is termed the "weight paradox" by Deasy, whereby the optimal choices for the relative weights of different PTV and OAR optimization criteria are not known and may take many iterations of trial and error to determine.[30] Choosing criteria that are too constraining for the OAR can compromise the target coverage, or vice versa.[30] In the optimizing of a FF-VMAT plan using parameters derived from a FFF-VMAT plan in our study, there's always a possibility that the resulting FF-VMAT plan was suboptimal. Our way to avoid this problem was tried to make the optimization parameters as general as possible in the optimization process. To be specific, the number of optimization parameters and iterations of trial and error were kept as fewer as possible. To achieve this goal, the optimization process was performed by a highly experienced planner. Our results showed that almost all the doses to targets and OARs of the FF-VMAT plans met the clinical requirements. This means that the "weight paradox" problem was alleviated in our study.

Conclusions

The beam modeling and planning process demonstrated that commercial TPS used in our study was able to handle unflattened beams. The plan comparison results revealed that in the NPC treatment, the FFF beam when compared to the FF beam, prone to improve the normal sparing while achieving similar target dose distribution. Decreasing of beam-on time in NPC cases was less notable but remains beneficial.

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