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The effect of beam shape on physical parameters of head and neck simultaneous-integrated boost intensity-modulated radiation therapy

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ABSTRACT

Aim: To evaluate the influence of the beam shape created by X-rays with "flat beams" and without "flattening-filter-free [FFF] beams" a flattening filter, and the isocenter locations for FFF beams on the treatment of a large irradiated volume for tumours.

Background: The increase of dose rate and the decrease of out-of-field dose can be expected for FFF beams and lead to effective and safety radiotherapy. On the other hand, the bell-shaped dose profile is thought to be a factor of negating these advantages.

Materials and methods: Treatment plans for 15 patients with head and neck cancer were created using XiO (Elekta, Stockholm AB, Sweden) in fixed-gantry step-and-shoot delivery under the same dose constraints. Seven fields of FFF beams with 7 MV and flat beams with 6 MV were used with the technique of intensity-modulated radiation therapy (IMRT). We compared the dose homogeneity and conformity of targets and dose constraints for organs as the plan quality and evaluated physical parameters: monitor unit (MU) values, number of segments and their locations from the isocenter in beam's-eye-view.

Results: No significant differences were found in the plan quality. The isocenter locations do not affect the physical parameters for FFF beams. It has been confirmed that the number of segments and MU values were 40% higher with FFF beams than with flat beams ($p < 0.05$).

Conclusion: This study demonstrates flat dose distribution is more suitable for IMRT with large and complex targets.

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1. Background

Advances in radiation therapy have brought about the invention of intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT), a technique that creates a high gradient of dose distribution at the border of a treated volume. They have the advantages over conventional radiation therapy of increasing the target dose while sparing normal tissues. However, they often require an increased treatment time because of the increased modulation level to deliver adequate doses to the complex targets.[1] Most of the X-ray radiation therapy machines used in hospitals have a flattening filter inside its beam line to give flat beam fluence inside the treatment field. The flat dose distribution (hereafter, 'flat beams') is of importance, especially for 3D-CRT, to deliver a uniform dose to the irradiated volume effectively because the dose homogeneity is generally recommended inside the target volume.[2] However, this filter decreases the dose rate, and causes scatter and energy variations away from the central axis, leading to a longer treatment time and non-uniform dose distribution with depth.[3]

Removal of the flattening filter, known as the 'flattening-filter-free' mode (hereafter, 'FFF beams'), has been conducted in the clinical use of radiation therapy. FFF beams generally increase the dose rate by more than approximately a factor of two (depending on the electron energy impinging on the target), decrease the variation in off-axis beam hardening and decrease head scatters by approximately 50% because of the lack of attenuation and scatter caused by the flattening filter. These advantages can be expected to result in shortening of the irradiation time, decreasing field-size-dependent energy variations and decreasing leakage outside of the beam collimation.[3–7] Moreover, studies have shown that these dosimetric properties of FFF beams might improve the dose calculation accuracy. For example, less electron contamination might make modelling in treatment planning easier.[4,8]

FFF beams are expected to be useful for IMRT and VMAT comprising many segments because the profile of FFF beams is thought to be equivalent to that of flat beams in a small field of $4 \times 4\,\mathrm{cm}^2$ and below, depending on beam energies.[9] Moreover, in this situation, higher the dose rate the more it is advantageous for clinical use. Comparative planning studies of FFF beams and flat beams have shown that the plans created by the two beams have equivalent qualities, and that FFF beams can reduce the damage to normal tissues outside the treatment field.[10,11] The treatment time has also been compared, with some studies reporting that the irradiation time, monitor unit (MU) values and number of segments were reduced using FFF beams. Moreover, even if the MUs and numbers of segments increased, the application of FFF beams to IMRT resulted in shorter treatment times for smaller irradiated volumes, as with SBRT and IMRT for prostate cancer.[10,12–14]

However, the use of FFF beams may not be suitable for large targets. For large target volumes, FFF beams are reported to be able to deliver a dose to the target as adequate as with flat beams, although the MU values and number of segments increased.[12,15] This increase is mainly caused by the bell-shaped profile of FFF beams and the delivery of a uniform dose to the target. However, it is unclear whether the advantages of FFF beams are suitable for IMRT with large treatment volumes consisting of complex targets (e.g., simultaneous-integrated boost intensity-modulated radiation therapy [SIB-IMRT]) because more segments and higher MU values may be necessary to deliver uniform doses to the target.

2. Aim

Evaluating the influence of the profile of FFF beams on the plan quality (dose homogeneity and conformity of targets, dose constraints to organs) and physical parameters of IMRT (MU values, number of segments and the distribution of segments in the irradiated field) for large and complex target volumes is essential for the clinical use of FFF beams. Our study investigated the effect of the beam profile on the physical parameters by comparing the treatment plans of head and neck SIB-IMRT created for use with flat and FFF beams. In addition, we assessed the relations between the location of isocenter and physical parameters for FFF beams.

3. Materials and methods

3.1. *Treatment plans*

Treatment plans for 15 patients with head and neck cancer were created using the XiO (version 4.8) treatment planning system (Elekta, Stockholm AB, Sweden) with the superposition algorithm and the segment weight optimization using a dose grid resolution of 2.0 mm in each direction, in fixed-gantry step-and-shoot delivery of the Siemens Artiste (Siemens Healthcare, München, Germany).[16] Minimum segment size, MU values, which are deliverable in the IMRT, were set to $2.0 \times 2.0\,\mathrm{cm}^2$ and 5 MU, respectively. Seven gantry angles were used (0°, 51°, 102°, 153°, 207°, 258° and 309°) for head and neck IMRT. Two kind of treatment plans were created for each patient for retrospective analysis. One is with flat beams and another is with unflat beams. Then we compared parameters obtained by two different plans. The energies of primary electrons are 7 MV for FFF beams and 6 MV for flat beams, the physical characteristics of which are similar with regard to depth-dose curve, energy spectrum and surface dose.[17] This similarity makes it possible to evaluate the effect of beam profile alone.[4]

Applied constraints for organs at risk (OAR) followed the protocol of this institute. The total planning target volume (PTV) for each patient included PTV_{70}, PTV_{63} and PTV_{56}, with the subscripted numbers indicating the prescribed dose in Gy. The isocenter of the treatment plans for SIB-IMRT was set to the center of the total PTV (sum of the volumes of PTV_{70}, PTV_{63} and PTV_{56}) for comparing the treatment plans of both beams, because of the large size of the total PTV and delivering the dose to each PTV effectively. The average location of PTV_{70} in all cases was 6.6 ± 1.9 cm from the isocenter. Moreover, the effect of the isocenter location on physical parameters for FFF beams was also investigated because the suitable location of the isocenter may depend on the shape of beam profiles.

Table 1 shows the dose constraints for OAR and for each PTV. The same dose constraints used in the optimization were applied to the use of each beam type. Statistical differences

Table 1 – Prescribed dose to PTVs, dose constraints for OARs and actual average values of each criterion of each plan. Statistical analyses have been performed in accordance with the results of Shapiro–Wilk test, shown in 5th column. Except for PTV_{70}, PTV_{63}, spinal cord and lens, there is no significant difference between plans created by the flat and FFF beams. The ranges are shown in parentheses.

PTV/OAR	Constraints	Flat beam	FFF beam	Shapiro–Wilk test *p* value	*p* value
PTV_{70}	$D_{50} = 70$ Gy	70.0 (70–70.1)	70.1 (70.0–70.3)	**<0.05**	**<0.05**
	$V_{75} < 1\%$	0.4 (0–1.5)	0.1 (0–0.5)	**<0.05**	**<0.05**
PTV_{63}	$D_{50} = 63$ Gy	63.9 (62.7–65.0)	63.6 (62.8–64.7)	0.9075	**<0.05**
	$V_{70} < 1\%$	0.9 (0.0–7.7)	0.5 (0.0–3.9)	**<0.05**	0.206
PTV_{56}	$D_{50} = 56$ Gy	56.9 (55.7–58.4)	56.9 (55.8–58.2)	0.467	0.995
	$V_{63} < 1\%$	1.6 (0.0–9.3)	1.1 (0.0–7.5)	0.222	0.544
Spinal cord	Max < 45 Gy	43.9 (41.3–44.9)	42.9 (40.9–44.8)	0.746	**<0.05**
Brainstem	$D_1 < 54$ Gy	0.0 (0.0–0.0)	0.0 (0.0–0.0)	–	–
Optic nerve	Max < 50 Gy	15.8 (0.3–49.3)	16.0 (0.3–49.9)	**<0.05**	0.247
Contralateral parotid	$V_{26} < 50\%$	38.5 (0.0–50.9)	37.8 (0.0–58.1)	0.902	0.886
Mandible	1 cc < V_{70} (cc)	1.1 (0.0–9.5)	0.9 (0.0–7.2)	**<0.05**	0.492
Ipsilateral parotid	$V_{26} < 50\%$	55.5 (37.5–100)	54.7 (35.0–100)	0.124	0.920
Eye	Max < 5 Gy	16.1 (0.3–75.3)	15.5 (0.3–74.2)	**<0.05**	0.068
Lens	Max < 5 Gy	6.1 (0.3–54.5)	5.7 (0.3–49.8)	**<0.05**	**<0.05**

FFF beam, flattening-filter-free beam; OAR, organs at risk; PTV, planning target volume.

in two plans for each beam were compared using a two-tailed paired *t*-test or Wilcoxon signed-rank test, depending on whether the population was normal, as determined by the Shapiro–Wilk test. Statistical significance was set at $p < 0.05$. R statistical software (Ver. 3.3.1; R foundation, Vienna, Austria) was used for all the statistical analyses.

3.2. *Evaluation of the target homogeneity and plan conformality*

To evaluate the target homogeneity and the degree of conformality of the plans, the homogeneity index (HI) and conformation number (CN)[18] was used. These parameters are defined as follows. The higher homogeneity inside the target and the plan conformality demand that HI and CN are close to 1.0.

$$HI = \frac{D_{2,\mathrm{PTV}}}{D_{98,\mathrm{PTV}}} \quad (1)$$

$$CN = \frac{TV_{ref}}{TV} \times \frac{TV_{ref}}{V_{ref}} \quad (2)$$

wherein $D_{2,\mathrm{PTV}}$ and $D_{98,\mathrm{PTV}}$ in Eq. (1) are the doses received by 2% and 98% volumes of each PTV, which represent near maximum and minimum doses inside a PTV, respectively. In Eq. (2), *TV* is the volume of a PTV, TV_{ref} is the volume covered by 95% of prescribed dose of each PTV and V_{ref} is the volume receiving 95% of prescribed dose for each PTV.[18]

3.3. *Comparison of physical parameters*

3.3.1. *MU values, number of segments and segment locations*

The MU values, number of segments and segment locations, which in this study are defined as physical parameters closely related to beam shape, were investigated.

The number of segments and MU values were extracted from the treatment planning system, and the segment location was determined using an in-house software. The segment location is the distance between the center of mass of a segment and the isocenter in beam's-eye-view for each gantry angle. Estimation of these parameters, in particular, their dependence on the segment location, was performed. The values derived by multiplying the number of segments by the MU value at each location were used as a measure of segment locations.

3.3.2. *Estimated irradiation time*

To estimate the irradiation time for the treatment plan created by each beam type, the empirically-derived equation for step-and-shoot IMRT of ARTISTE machine was used in this study.[10]

Table 2 – Comparison of target homogeneity and the conformality of each plan between beam types. Except HI of PTV_{63} and PTV_{56}, significant differences are observed between those obtained by flat and FFF beams.

PTV	Target homogeneity (HI)/plan conformality (CN)	Flat beam	FFF beam	Shapiro–Wilk test*p* value	*p* value
PTV_{70}	HI	1.13	1.12	0.096	**<0.05**
	CN	0.580	0.641	0.521	**<0.05**
PTV_{63}	HI	1.20	1.19	0.205	0.140
	CN	0.166	0.181	0.080	**<0.05**
PTV_{56}	HI	1.21	1.20	**<0.05**	0.173
	CN	0.258	0.299	**<0.05**	**<0.05**

FFF beam, flattening-filter-free beam; PTV, planning target volume.

Table 3 – Average number of segments and MU values for each treatment plan. There is a difference of about 40% about these parameters between FFF and flat beams.

Physical parameters	Flat beam	FFF beam	Shapiro–Wilk test*p* value	*p* value
Average number of segments	55.3 ± 8.1	77.5 ± 13.7	0.619	**<0.05**
Average MU value	540.5 ± 76.6	770.6 ± 143.8	0.471	**<0.05**

FFF beam, flattening-filter-free beam.

The formula for calculating the irradiation time is as follows:

$$T_{rad} = (n_{beams} - 1) \times t_{gantry} + (n_{segments} - n_{beams} - 1) \times t_{segments} + \frac{MU}{d}, \quad (3)$$

wherein n_{beams} and $n_{segments}$ are the number of fields and segments, respectively, and t_{gantry} and $t_{segment}$ are the average transit time of gantry and the average time necessary for creating segments, respectively. The d is the dose rate for each beam mode, and MU is the total MU value for each plan.

3.4. *Evaluation of isocenter locations for FFF beams*

The effective dose delivery depends on the location of isocenter and the suitable location for bell-shaped profile of FFF beams may be different from the one for flat beams. To investigate the effect of isocenter locations for FFF beams, the center of PTV_{70}, which requires the highest prescription dose, and the center of total PTV were set as an isocenter and then the physical parameters of the treatment plans for both isocenters, which are described in Section 3.3.1, were compared.

4. Results

4.1. *Comparison of plan quality*

Treatment plans were created for 15 patients using the two different beams for the same dose constraints. The plans are compared, and the results are presented in Tables 1 and 2. Table 1 shows the dose constraints for all PTVs and OARs, spinal cord, brainstem, optic nerve, contra- and ipsilateral parotid, mandible, eye and lens and the results for each constraint. The target homogeneity and the plan conformality for each PTV were evaluated using Eqs. (1) and (2), as shown in Table 2.

The results indicate significant differences between the flat and FFF beam plans with respect to the dose in PTV_{70}, PTV_{63}, the spinal cord and lens (Table 1). Clear statistically significant differences were observed, although the absolute differences are quite small. For PTV_{70}, a mean of 70.0 Gy was prescribed in the plans with flat beams and 70.1 Gy in the plans with FFF beams. For PTV_{63}, the average prescribed dose was 63.9 Gy with flat beams and 63.6 Gy with FFF beams. The maximum dose to the spinal cord was 1.0 Gy lower for FFF beams than for flat beams, and the maximum dose to the lens was 0.4 Gy lower for FFF beams than for flat beams, decreasing from 6.1 Gy for flat beams to 5.7 Gy for FFF beams. On the other hand, there were no significant differences despite the fact that the relatively large absolute differences were observed, because the results of statistical analysis depend on the population.

These results in Table 1 show that both types of beams can deliver doses to PTVs while sparing OARs at the same clinical level, although the significant differences were observed in the target homogeneity and plan conformality (Table 2). Thus, evaluating the influence of beam shape under the same plan-quality condition is possible in this study.

4.2. *Evaluation of physical parameters for beam delivery*

4.2.1. *Total number of segments, MU values and the relationship between physical parameters and segment locations*

The number of segments and the MU values for each treatment plan were calculated. Table 3 shows the comparisons of the average number of segments and MU values between the treatment plans. FFF beams increased the number of segments and MU values by 40% over those of flat beams ($p < 0.05$).

The difference in dose profiles affects not only the number of segments and MU values, but also their distribution inside the irradiated volume. Fig. 1 shows the histograms for flat beams and FFF beams, indicating the relationship between these physical parameters and the distance of each segment from the isocenter. The horizontal axis of this figure is the seg-

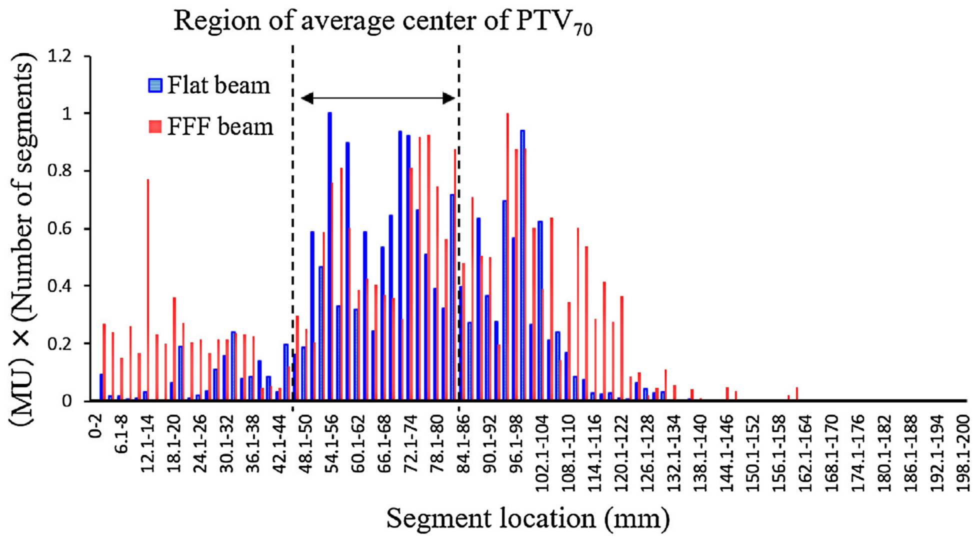

Fig. 1 – The effect of the dose profile on the distribution of physical parameters inside the irradiated volume. The physical parameters for FFF beams gather not only around the PTV_{70}-location but also at locations away from that position. FFF beam, flattening-filter-free beam; MU, monitor unit.

ment locations, and vertical axis is the multiplied values of the number of segments and the MU values at a given distance. The values of the vertical axis are normalised to the maximum value for the product of the number of segments and the MU value.

The multiplied values imply that MU values were weighted to the number of segments, both of which were delivered at a given distance. This parameter represents the number of modulations and MU values at the same distance, which is important for intensity modulations; in addition, it clarifies the intensity level at a distance. The physical parameters for flat and FFF beams gather around PTV_{70} (6.6 ± 1.9 cm from the isocenter) because most modulations and MU values are necessary in that region, and they decrease as away from the location of PTV_{70}. However, the difference between both beams in the distribution shape of physical parameters can be observed. To reveal the dependence of physical parameters on segment locations, the cumulative distributions for this parameter as a function of the distance were shown in Fig. 2. In the region (1) of Fig. 2, which is close to the isocenter, FFF beams deliver more physical parameters than flat beams. As for the region (2), which is away from the PTV_{70}, physical parameters with FFF beams are still in increase, indicating that FFF beams require more MU values and segments in the region away from the PTV_{70}. Conversely, physical parameters created by flat beams increase more rapidly between 50 mm and 100 mm from the isocenter than FFF beams, showing the effective delivery of physical parameters with flat beams.

4.2.2. *Estimation of irradiation time*

The estimated irradiation times for each beam, as calculated using Eq. (3), are shown in Table 4.

The dose rates for flat and FFF beams were set to maximum values of 300 and 2000 MU/min, respectively, under the assumption that these maximum dose rates could be used for each plan during treatment. From these results based on Eq. (3), the use of FFF beams may require a 10% longer irradiation time than does the use of flat beams ($p < 0.05$).

4.3. *Comparison of physical parameters for different isocenter locations*

Treatment plans using FFF beams with different isocenter locations, the center of total PTV and PTV_{70} respectively, were compared to investigate the effect of the isocenter locations for the beam having the bell-shaped beam profile on the physical parameters. The plans were created under the same dose constraints shown in Table 1. The results which show significant difference were presented, and the target homogeneity and the plan conformality were shown in Fig. 3, respectively.

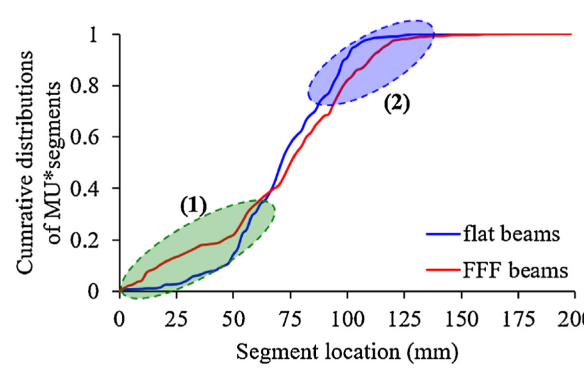

Fig. 2 – The cumulative distribution of the multiplied values of numbers of segments and MU values at a given distance is shown. The green area (1) represents the region close to the isocenter, and blue area (2) shows the region away from the PTV_{70}. The physical parameters with flat beams increase more rapidly around the PTV_{70} than those with FFF beams. Conversely, in the regions 1 and 2, the increases of physical parameters with FFF beams was observed. FFF beam, flattening-filter-free beam; MU, monitor unit.

Table 4 – Comparison of irradiation times estimated by Eq. (3) between beam types. There is a significant difference between them ($p < 0.05$).

	Flat beam	FFF beam	Shapiro–Wilk test*p* value	*p* value
Average irradiation time (s)	517 ± 68.6	587 ± 99.8	0.489	**<0.05**

FFF beam, flattening-filter-free beam.

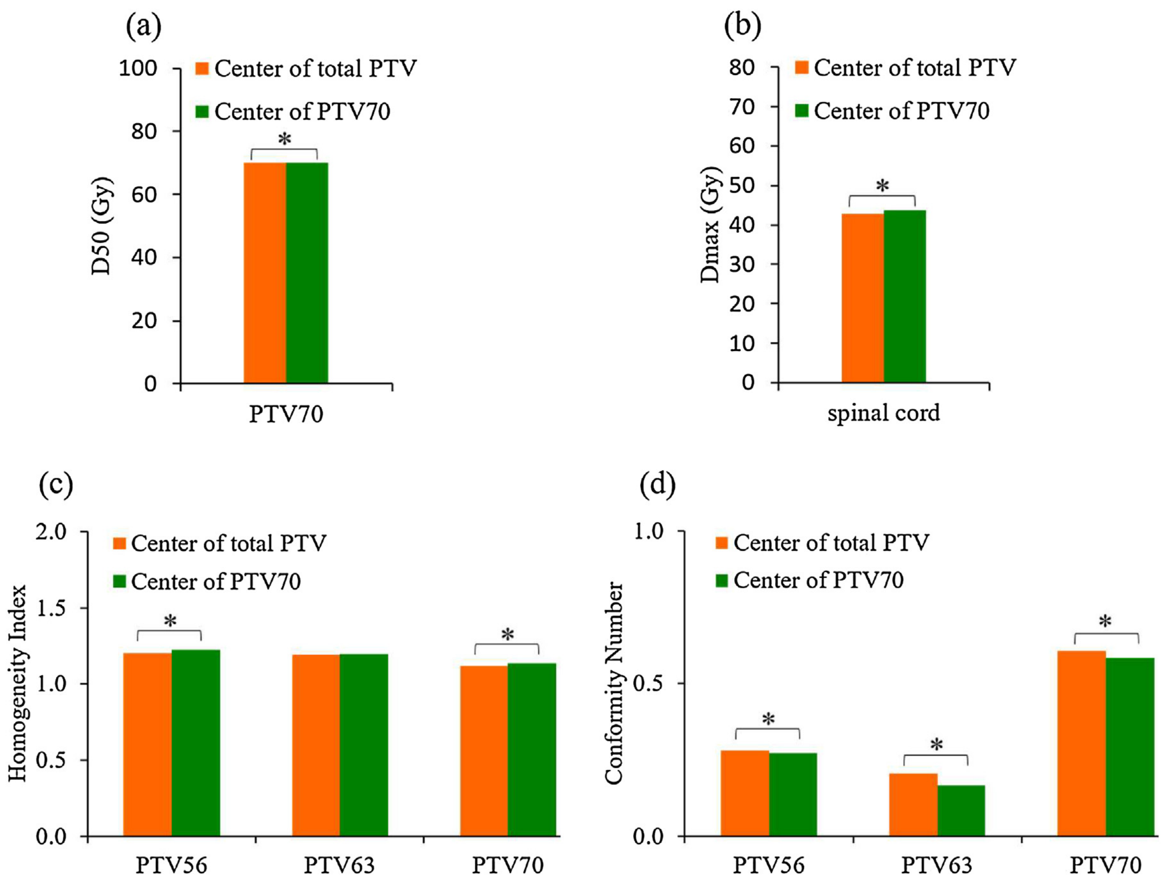

Fig. 3 – Comparisons between plans using FFF beams with different isocenter locations were performed. Except for (a) PTV_{70} and (b) spinal cord, there is no significant difference. Regarding (c) target homogeneity and (d) plan conformality, significant differences are observed except for HI of PTV_{63}.

Significant differences between plans using FFF beams with different isocenter locations were observed in PTV_{70} and the spinal cord (Fig. 3). In addition, except for HI of PTV_{63}, Fig. 3 shows significant differences ($p < 0.05$). However as mentioned in Section 4.1, the absolute differences are quite small, indicating that the comparison of the physical parameters can be performed.

Fig. 4(a) and (b) show the comparisons of the average number of segments and MU values between the treatment plans using FFF beams with different isocenters. There were no significant differences between them.

The cumulative distributions for the multiplied values of physical parameters described in Section 4.2.1, which represent the dependence of physical parameters on segment locations, is shown in Fig. 4(c). In the region (1) of Fig. 4(c), the different tendencies of the distributions were observed. However, in the region (2), physical parameters needed for both plans are still in increase, which means that the conical beam profile of FFF beams needs physical parameters in the region away from the isocenter, regardless of the locations. These results indicate that the location of isocenter does not have an influence on the physical parameters for FFF beams.

5. Discussion

To determine the effect of the beam shape on the treatment plan for head and neck cancer, we evaluated the physical parameters created by flat and FFF beams. The results indicate that these two types of beams provide comparable plan quality but the difference in the beam shape has a great effect on the physical parameters. Moreover, to confirm whether the isocenter locations affect the physical parameters needed for FFF beams, the treatment plans using FFF beams with different isocenters, the center of total PTV and PTV_{70}, were evaluated. We found that the location does not affect the physical parameters for FFF beams.

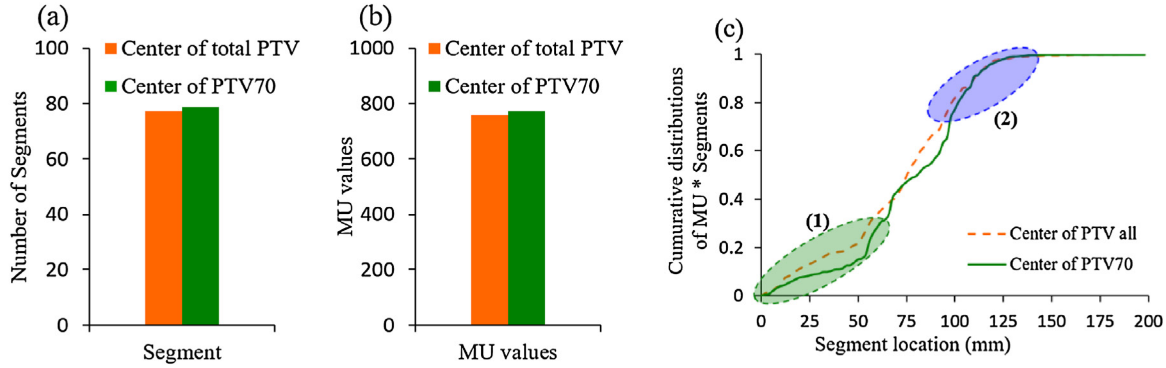

Fig. 4 – Comparisons of (a) average number of segments and (b) MU values between treatment plans with different isocenters. There is no significant difference. (c) The cumulative distributions for the multiplied values of the physical parameters as a function of the distance are shown.

The significant differences of target homogeneity and plan conformality between treatment plans of different beam profiles (Table 2) or different isocenter locations for FFF beams (Fig. 3) were observed, respectively. It is assumed that these differences are caused by the different dose distributions due to the different beam profiles or different isocenter locations. However as mentioned in Sections 4.1 and 4.3, the absolute differences are small, leading to the quantitative evaluations of the physical parameters under the equivalent plan qualities.

The number of segments and the MU values were 40% higher for FFF beams than for flat beams. To assure delivery of the dose to the whole target volume, FFF beams require additional modulations in the region away from the PTV_{70} location as shown in Figs. 1 and 2, where the most modulations are necessary. The results show that the effect of the conical beam profile on these parameters for large treatment volumes is much greater than that of flat beams, and that these effects may cause uncertainty in dose delivery due to the inter/intrafraction motions and the superposition of many smaller segments, although the effect on dose delivery may be small.[19] Moreover, the effects of the conical beam profile seem to be much larger for the higher electron energy, because the conical beam profile becomes steeper as the energy increases, indicating that the effect appears remarkably for body radiation therapies.[5,9] The increase in physical parameters with FFF beams may lead to extension of the required irradiation time by approximately 10% although the estimated irradiation times in this study were based on the empirically-derived equation. The results of this study indicate that the differences in the physical parameters between FFF and flat beams in head and neck SIB-IMRT are remarkable. Given that the potential advantages of FFF beams, accuracy of beam modelling or low dose out of the field are marginal, then the sizable increase of physical parameters negates them even if a treatment planning system reproduces FFF beams well.

Lower head scatter and a softer X-ray spectrum can be obtained using FFF beams. These features are advantageous for requiring a lower out-of-field dose and lower leaf transmission factor, resulting in protection of OAR.[20] However, our study shows that for larger and more complex target structures, such as head and neck SIB-IMRT, many more segments and higher MU values are necessary for IMRT with FFF beams, leading to an increase in transmission dose and out-of-field dose. This result indicates that IMRT with FFF beams for such cases might not have dosimetric advantages and may increase the probability of a secondary cancer induced by low doses of radiation.[21]

VMAT has been developed recently to reduce treatment time while maintaining the dosimetric characteristics obtained by fixed field IMRT.[22–25] The comparison of FFF beams and flat beams in VMAT revealed that MU values and the number of segments have increased, although the plan qualities of these beams were equivalent, as we observed in this study with step-and-shoot IMRT.[26,27]

Some limitations of this study have also been observed. The irradiation times for each treatment plan were estimated from the empirically-derived equation instead of measuring them. This equation dose not take the variable dose rate of FFF beams into account. However, this equation has been shown to be well-estimated formula, which enables it to roughly estimate and compare the irradiation times of both FFF and flat beams. In addition, the treatment machine used in this study is no longer commercially available. However, we focused on the beam shapes, and the effect of their difference on physical parameters in a treatment showed the similar tendency for different irradiation techniques.[26,27]

Our study and other studies have revealed a limitation related to the large and complicated target volume when FFF beams are applied to 3D-CRT, IMRT and VMAT, which is caused by unflat dose distribution.[15,26,27] To break this limitation related to the shape of a beam profile, some research groups tried to improve beam profiles without a flattening filter.[28–30] They focused on electrons before colliding on the target, and proposed methods to create a flat dose distribution by defocusing or converging them. They showed their effectiveness by simulations. If their techniques were realised, the limitation related to the clinical use of FFF beams in complicated and large target volumes could be eliminated.

6. Conclusion

We investigated the influence of flat and FFF beam shape, and the isocenter location for FFF beams on the physical parameters of head and neck SIB-IMRT. It was revealed that the number of segments and MU values were 40% higher with FFF beams than with flat beams, and significant difference in the physical parameters for FFF beams with different isocenter locations was not observed. In addition, the conical beam profile of FFF beams required additional modulations in various regions inside the treatment volume compared with flat beams and the increase in these parameters may cause longer irradiation times with FFF beams, indicating that flat dose profile is more suitable for IMRT with large and complicated target volumes.

Conflict of interest

None declared.

Financial disclosure

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