

# Comparison between flattening filter-free (FFF) and flattened photon beam VMAT plans for the whole brain radiotherapy (WBRT) with hippocampus sparing

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## Abstract

**Purpose:** To evaluate and investigate the feasibility of flattening filter-free (FFF) beam for the whole-brain radiotherapy (WBRT) with hippocampus sparing.

**Methods:** Eighteen patients with volumetric-modulated arc therapy (VMAT) plans in FFF and conventional beam modes were included in this study. The prescribed dose was 30 Gy in 10 fractions. The conformity index (CI), heterogeneity index reported by TPS (HI-M), and homogeneity index (HI) for planning target volume (PTV) were evaluated. Subsequently, the following parameters for PTV were calculated and compared:  $D_{2\%}$ ,  $D_{98\%}$ ; the mean dose, maximum dose, and minimal dose for OARs. Plan modulation index, total MUs, and the gamma index were used to evaluate the plan quality.

**Results:** HI-M results were similar for the two techniques (1.239 vs. 1.247, respectively,  $p = 0.048$ ); FFF beam plans yielded lower  $D_{2\%}$  compared to FF beam plans (3,416.3 cGy vs. 3,437.2 cGy,  $p = 0.22$ ), mean dose (3,177.5 cGy vs. 3,195.2 cGy,  $p = 0.009$ ), and CI (0.884 vs. 0.876,  $p = 0.001$ ) for PTV. Significant differences were observed between the two beam modes (FF model vs. FFF model) for the maximum dose (1,612.9 cGy vs. 1,470.2 cGy, respectively,  $p < 0.001$ ), minimum dose (987.6 cGy vs. 898.8 cGy, respectively,  $p < 0.001$ ), and the mean dose (1144.4 cGy vs. 1047.3 cGy, respectively,  $p < 0.001$ ) to the hippocampus, and the maximum dose to the eyes (2,792.6 cGy vs. 2,751.3 cGy, respectively,  $p < 0.001$ ). The average total MUs for FFF-VMAT plans was significantly greater than FF-VMAT plans. However, differences for the plan modulation index and the gamma index were negligible.

**Conclusion:** In comparison with FF beam, the FFF beam mode offers a clear benefit with respect to WBRT with hippocampal sparing.

## KEYWORDS

flattening filter-free, hippocampal sparing, volumetric-modulated arc therapy, whole-brain radiotherapy

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## 1 | INTRODUCTION

Whole-brain radiotherapy (WBRT) is a fundamental treatment for patients with metastases in brain,<sup>1</sup> which is one of the most common brain tumors in adults.<sup>2</sup> However, WBRT imparts side effects including neurocognitive dysfunction.<sup>3,4</sup> To prevent such side-effects from irradiation, modern intensity modulated radiotherapy techniques have been developed and to reduce the hippocampus dose during WBRT.<sup>5–10</sup>

The flattening filters equipped in the treatment head of linac were used to generate a relatively uniform dose at a certain depth. However, the flattening filters have become unnecessary in modern treatment techniques, because of the varying fluence patterns needed in these techniques.<sup>11</sup> FFF beams have relatively distinctive dosimetric features, including sharper penumbra, less head scatter, and less peripheral dose, which have shown a lower probability of normal tissue complications. The purpose of this study was to investigate the benefit of FFF beams in the VMAT of hippocampal sparing considering plan quality, modulation index, and plan verification. This is a retrospective paper where all cases have been treated with FF beam mode.

## 2 | MATERIALS AND METHODS

### 2.1 | Contouring and planning

Eighteen patients treated with FF beam model were included. Brain computed tomography (CT; SOMATOM, Siemens Healthcare GmbH) was used to obtain 1.5 mm sliced images of the patients. The Philips scanner (Philips, Cleveland, OH, USA) was used to obtain MR images and the slice thickness was 1.5 mm. The CT and MRI datasets were registered in the Monaco (Elekta AB, Stockholm, Sweden) for target volume contouring.

All of the cases were treated under VersaHD unit (Elekta AB) with Agility head of this study. The 80-pair interdigitating MLCs in the head have a projected lead width of 5 mm at the isocenter. For each case, the coplanar VMAT with four arcs were optimized in the Monaco TPS. The four full arcs optimized simultaneously and to be delivered in one beam (clock-counterclockwise-clock-counterclockwise). The flattening filter free (FFF) with 6-MV photon beams energy were selected. In order to ensure confidence in accuracy of dose calculation and delivery, these studies were referred.<sup>12,13</sup>

The hippocampus was delineated on the MR images according to the RTOG 0933 protocol. The margin of 5 mm was used to treatment plan for the tolerance of setup. The same radiation oncologist delineated the other OARs, including the eyes and lenses.

### 2.2 | Prescription and OAR constraints

The prescription dose was 30 Gy/10F to the PTV. All plans needed at least 90% of PTV covered by 100% of the prescribed dose. The hippocampus dose was constrained according to the protocol of RTOG 0933. The maximal doses limited for the lens and the eyes were 8 and

30 Gy respectively. Both FF-VMAT and FFF-VMAT plans were normalized to achieve prescription dose to PTV and limited dose to the OARs.

### 2.3 | Plan evaluation

The conformity index reported by Monaco (CI), heterogeneity index reported by Monaco (HI-M), and the homogeneity index (HI) for PTV were evaluated. The following dose volume parameters for PTV and OARs were recorded, using PTV  $D_{2\%}$  as the “maximum dose,” PTV  $D_{98\%}$  as the “minimum dose,” by TPS to evaluate the dose “tail.”

The CI formula used by Monaco is defined as:

$$CI = \frac{V_{RX}^2}{TV \times V_{RI}}$$

where TV is the volume of PTV,  $V_{RX}$  is the volume of target covered by prescription dose, and  $V_{RI}$  is the total volume of the prescription dose. The CI describes how the volume of prescribed dose conforms to the shape and size of the target volume.

The formula of HI-M by Monaco is:

$$HI - M = D_{5\%} / D_{95\%}$$

The HI-M describes the uniformity of dose within a target volume. Although the  $D_{5\%}$  is defined as the dose delivered to the hottest 5% of the tissue. The  $D_{95\%}$  is the minimum dose received by 95% of the tissue. The values close to 1 are considered to be optimal.

The HI is defined as:

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{median}}$$

where  $D_{2\%}$  and  $D_{98\%}$  is the same as previously defined.  $D_{median}$  is the median dose to the PTV. HI is used to describe the uniformity of dose distribution as well; in contrast to HI-M values, the values close to 0 are considered optimal.

### 2.4 | Plan quality

The complexity of plan, the Gamma index of plan verification, and the total MU were used to evaluate the plan quality. Several studies have given the suggestions of using modulation indices to predict VMAT delivery accuracy.<sup>14</sup> This study used the modulation complexity score for VMAT (MCSv)<sup>15</sup> evaluation, which is a previously suggested modulation index for IMRT.<sup>16</sup>

For each plan, the verification plans were generated and evaluated with the ArcCHECK™ (Sun Nuclear Corporation, Melbourne, FL, USA). For the local gamma evaluation, the 3% per 3 mm gamma criteria was used, which is the most commonly used in other sites.<sup>17</sup>

### 2.5 | Statistical analysis

Statistical comparisons of the results were performed using Origin, version 2018 (OriginLab Corporation, Northampton, MA, USA) by

paired-sample *t* tests. A two-sided *p*-value < 0.05 indicated a statistically significant difference.

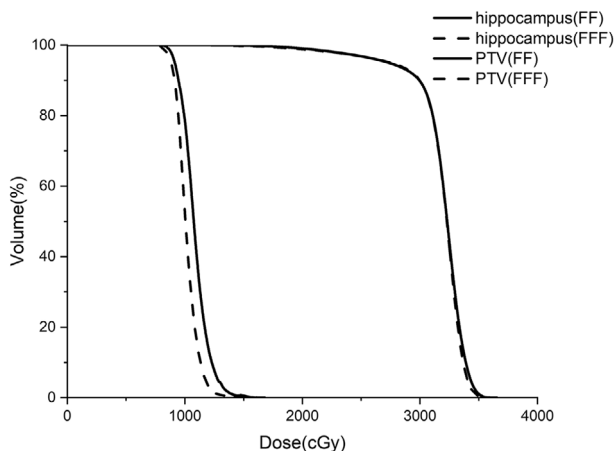
### 3 | RESULTS

#### 3.1 | Dose for PTV

PTV dose parameters (mean ± SD) for the different beam modes are presented in Table 1. The  $D_{98\%}$ ,  $D_{2\%}$ ,  $D_{\text{mean}}$ ,  $D_{\text{max}}$ , CI, HI-M, and HI for PTV were also compared. After values were normalized to 90% of PTV covered 100% prescription dose, the two beam modes provided similar  $D_{98\%}$ . FFF-VMAT provided the lower average  $D_{2\%}$  ( $3,416.3 \pm 36.17$  cGy) and mean dose ( $3,177.5 \pm 23.8$  cGy) for PTV, and no significant differences in the  $D_{\text{max}}$  were found between the modes. Although there are some statistically significant significances for PTV, these are not clinically significant. According to the HI-M formula by TPS, the better target dose heterogeneity would be achieved by FFF beam plans ( $1.239$ ,  $p = 0.048$ ). The two modes provided similar CIs ( $0.876$  vs.  $0.884$ ). No statistically significant difference in HI was found between the two beam modes. Figure 1 shows average DVHs for the dose to PTV for each of the two beam modes.

**TABLE 1** Dose parameters for PTV

	FF	FFF	<i>p</i>
PTV, $D_{98}$ (cGy)	$2282.4 \pm 123.5$	$2283.8 \pm 139.8$	0.028
PTV, $D_2$ (cGy)	$3437.2 \pm 43.6$	$3416.3 \pm 36.17$	0.022
$D_{\text{Mean}}$ (cGy)	$3195.2 \pm 29.6$	$3177.5 \pm 23.8$	0.009
$D_{\text{Max}}$ (cGy)	$3635.7 \pm 41.1$	$3623.7 \pm 56.1$	0.138
CI	$0.876 \pm 0.015$	$0.884 \pm 0.015$	0.001
HI-M	$1.247 \pm 0.036$	$1.239 \pm 0.038$	0.048
HI	$0.388 \pm 0.052$	$0.385 \pm 0.047$	0.661



**FIGURE 1** PTV average dose–volume histograms for treatment planning with the two beam modes

**TABLE 2** Dose to Hippocampus and other OARs

	FF	FFF	<i>p</i>
Hippocampus, $D_{\text{max}}$ (cGy)	$1612.9 \pm 175.3$	$1470.2 \pm 136.3$	<0.001
Hippocampus, $D_{\text{min}}$ (cGy)	$987.6 \pm 189.8$	$898.8 \pm 140.5$	<0.001
Hippocampus, $D_{\text{mean}}$ (cGy)	$1144.4 \pm 81.1$	$1047.3 \pm 51.8$	<0.001
Lens, $D_{\text{max}}$ (cGy)	$671.2 \pm 42.0$	$668.2 \pm 43.5$	0.373
Eyes, $D_{\text{max}}$ (cGy)	$2792.6 \pm 321.8$	$2751.3 \pm 326.3$	0.031

**TABLE 3** Plan quality

	FF	FFF	<i>p</i>
MSCv	$0.144 \pm 0.014$	$0.141 \pm 0.014$	0.234
Gamma index	$98.7 \pm 0.6$	$98.3 \pm 0.7$	0.072
MU	$1641.9 \pm 177.2$	$1955.8 \pm 198.6$	<0.001

#### 3.2 | Dose for Hippocampus and other OARs

The dose parameters comparisons for hippocampus are shown in Table 2. Significant differences in  $D_{\text{max}}$  ( $1,470.2 \pm 136.3$  cGy,  $p < 0.001$ ),  $D_{\text{min}}$  ( $898.8 \pm 140.5$  cGy,  $p < 0.001$ ), and  $D_{\text{mean}}$  ( $1047.3 \pm 51.8$  cGy,  $p < 0.001$ ) were observed between the two beam modes. Compared to FF-VMAT, FFF beam plans yielded lower average maximum doses, minimum doses, and mean doses to the hippocampus. For eyes and lenses, both beam modes met the dose constraints we set. Plans in FFF mode yielded the slightly lower average maximum doses to eyes ( $p < 0.05$ ). There were no statistically significant differences observed for the dose to lens. Figure 1 shows average DVHs for the dose to hippocampus in the two beam modes.

#### 3.3 | Plan quality

The plan quality for each plan is compared in Table 3. The FFF-VMAT plans generated significantly more MUs than the FF plan ( $1,955.8$  vs.  $1,641.9$ , respectively,  $p < 0.001$ ). No significant differences were observed in the MSCv and Gamma index between the two beam modes.

### 4 | DISCUSSION

The two beam modes achieved PTV target coverage, they provided similar  $D_{98\%}$  and CI values. The  $D_{\text{mean}}$ ,  $D_{2\%}$ , and HI-M values for FFF VMAT was lower than those with the FF beam plan, but this difference could be negligible. There were no statistically significant differences in the  $D_{\text{max}}$  and HI between the modes. Thus, the FFF beams yielded a little bit better results in target volume coverage and conformity than the FF beams. The dosimetry advantage for target can be neglected by the FFF mode; these results are similar to those of other studies.<sup>18,19</sup> The FFF mode can increase the peripheral dose of the target area with nonuniform tissues, such as SBRT for lung cancer.<sup>20</sup>

The development of advanced techniques is increasing the feasibility of hippocampal avoidance during WBRT, resulting in greater memory preservation and quality of life of patients.<sup>21</sup> Lower average maximum, minimum, and mean doses to the hippocampus were achieved by the FFF beams VMAT. Meanwhile, FFF also significantly reduced the eye dose. Other studies have also confirmed the ability to protect OARs in FFF mode.<sup>22,23</sup> These can be attributed to the unique dosimetry characteristics of the FFF such as smaller leakage. At the same time, the high-speed moving blade, a collimator speed of 9 cm/scan,<sup>24</sup> also better utilize the high dose rate characteristics of the FFF mode.

Because the FFF mode requires more MUs for a point in a segment far away from the central axis to achieve the same depth dose as the point in the central, the average total MUs for FFF-VMAT plans was greater than that of the FF-VMAT plans. This finding is in line with the results from previous studies.<sup>19,25,26</sup> However, there was no significant difference observed in the plan quality among the two beam modes. Although our results show that the FFF-VMAT plan can produce very good protection of the hippocampus, it is important to note that the FFF beams increased the total MUs about 20%.

One limitation of this study is that the experience of the dosimetrist has a greater impact on the quality of the modern intensity-modulated radiotherapy plan.

## 5 | CONCLUSIONS

From a dosimetric perspective, the FFF beam mode can offer a clear benefit for WBRT with hippocampal sparing when compared to the FF beam plans. The plan verification showed that both of the FF and FFF plans had acceptable results. Therefore, by the results of this study, it is suggested that the use of the FFF beam is feasible and also provides efficacious treatment for WBRT with hippocampal sparing if carefully applied.

## CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

## AUTHORS' CONTRIBUTIONS

T. Ji designed the study; F. Cai and S. Lu collected the patients' clinical data and delineated target volume; T. Ji and G. Li optimized and expert reviewed the patients' treatment plans; T. Ji analyzed the data and wrote the paper. All authors read and approved the final manuscript.

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