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# Comparison between Dual Arc VMAT and 7F-IMRT in the protection of hippocampus for patients during whole brain radiotherapy

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**Abstract**.
**PURPOSE:** The purpose of this study was to compare the dosimetric characteristics for protection of the hippocampus between dual arc VMAT (volumetric modulated arc therapy) and 7 fields intensity-modulated radiation therapy (7F-IMRT) for patients with brain metastases from lung cancer under the whole brain radiotherapy.
**METHODS:** Based on ten cases with brain metastases from lung cancer, two types of radiotherapy plans were designed, namely, dual arc VMAT and 7F-IMRT. Provided that the clinical requirements were satisfied, the comparisons of target dose distribution, conformity index (CI), homogeneity index (HI), dose of organs at risk (OARs), monitor units (MU) and treatment time between dual arc VMAT and 7F-IMRT were investigated for their dosimetric difference.
**RESULTS:** Both treatment plans met the requirements of clinical treatments. However, the PTV-HA conformity and homogeneity of dual arc VMAT were superior to those of 7F-IMRT ($P < 0.05$). As to OARs, the mean maximum doses ($D_{max}$) of hippocampus, eyes and optic nerves in the dual arc VMAT plan were all lower than those in 7F-IMRT plan ($P < 0.05$), but the result had no statistical significance ($P < 0.05$) for the maximum dose of lens. Compared with 7F-IMRT, dual arc VMAT reduced the average number of MU by 67% and the average treatment time by 74%.Therefore, treatment time was shortened by dual arc VMAT.
**CONCLUSION:** With regards to the patients with brain metastases from lung cancer under the whole brain radiotherapy, the PTV-HA conformity and homogeneity of dual arc VMAT were superior to those of 7F-IMRT under the precise of meeting the clinical requirements. In addition, dual arc VMAT remarkably reduced the irradiation dose to OARs (hippocampus, eyes and optic nerves), MU and treatment time, as well, guaranteed patients with better protection.

Keywords: Brain metastases from lung cancer, 7F-IMRT, dual arc VMAT, hippocampus protection, dosimetry parameter comparison

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## 1. Introduction

Radiotherapy is designed to increase locoregional disease control rate by enhancing the radiation dose applied to the target and/or reducing the dose applied to the normal tissues surrounding the target, and to increase survival rate and/or improve the quality of life. For patients with brain metastases from malignant cancer, whole-brain radiation therapy (WBRT) is an effective method to control the development of cerebral disease [1–4]. However, a proportion of patients develop cognitive impairment within 3–6 months after receiving WBRT in clinical application. Patients with mild symptoms suffer from a decline in memory function and those with severe symptoms suffer from dementia, which severely affects their quality of life [5]. The RTOG (Radiation Therapy Oncology Group) –0214 trial [6] and the study of Vinai et al. [7] have demonstrated that brain metastases is a major cause of early cognitive decline. Gondi et al. [8, 9] also have investigated the correlation between irradiation dose to hippocampus and neurocognitive impairment in patients with low-level intracranial tumors received fractionated stereotactic radiotherapy (FSRT). The results have showed that hippocampus bilaterally receiving dose >7.3 Gy can cause neurological impairment. The hippocampus is the part of the brain mainly responsible for learning and memory [10, 11]. Short-term memories are stored in hippocampus, and when certain memory fragments are mentioned repeatedly within a short period of time, they are eventually transmitted to the cerebral cortex and become permanent memory. When the hippocampus gets injured, part or all of the memories are lost, depending on the level of hippocampal damage. For patients who receive WBRT with brain metastases resulting from lung cancer, the protection of hippocampus is attracting increasing attention, in addition to the protection for lens, eyes and other organs at risk (OARs) [12–14].

IMRT (intensity-modulated radiation therapy) increases the probability of local tumor control probability (LTCP) and reduces the radiation-induced normal tissue complication probability (NTCP) [15, 16]. However, the problems of IMRT are its long treatment time, high dosage output, low-dose irradiation of a large normal tissue volume, high dose of leakage and transmission radiation, scattered radiation and the risk of secondary cancer [17–19]. VMAT(volumetric modulated arc therapy) is a latest intensity-modulated arc therapy technique [20]. In this technique, the gantry can rotate 360° around the patient in a single arc for isocentric treatment and certain parameters, such as the leaf position of the multileaf collimator (MLC) and the dose rate of accelerator, and the gantry angle can be automatically adjusted according to the requirements during rotation. Besides, the optimized intensity distribution of inverse planning can be realized by superimposing intensity at each single point of arcs. Mehta et al. [21] have investigated the MLC position accuracy, changes and controls of the dose rate and dynamic MLC movement speed during gantry rotation of VMAT radiation. The experimental results show that MLC movement and changes of the dose rate are controlled precisely. Therefore, the treatment accuracy can be significantly improved.

It has been recently demonstrated that VMAT may be used to treat tumors in different parts of human body, including head and neck, cervical and prostate cancer. A number of studies have reported that VMAT is capable of providing a better dose gradient and reduce the dose to OARs and the number of MU [22, 23]. In this study, patients with metastases to the brain resulting from lung cancer were investigated to study the dosimetric difference between dual arc VMAT and 7F-IMRT, and to understand the advantages and disadvantages of VMAT and IMRT, which may be helpful in clinical application.

## 2. Materials and methods

### *2.1. Case selection*

From February 2014 to May 2015, ten patients with multiple brain metastases were randomly selected for investigation at Subei People's Hospital (Jiangsu, P. R. China). The age of patients ranged from 58

to 79 years and the median age was 68 years. Written informed consent was obtained from all patients or their families. All the procedures of this study were approved by the Ethical Committee of Nanjing University of Aeronautics and Astronautics.

### 2.2. Immobilization and CT scan

The patients were treated with supine position, C/B pillow in comfortable position, and fixed using the carbon fiber position fixing device and thermoplastic marks. An enhancement CT (GE Medical Systems) scan was performed with a large aperture of 80 cm and slice thickness of 2.5 mm. The scanning range included the whole brain plus 5 cm margins isotropically. After simulation, the CT images were transmitted into the Eclipse treatment planning system (TPS, Version 8.6, Varian Medical Systems).

### 2.3. Target lineation

After merging the CT images with magnetic resonance (MR) images obtained in the same position, the radiotherapist delineated clinical target volume (CTV) of the entire brain and OARs (hippocampus, eye, lens, optic nerves), and defined the region with a margin of 4 mm around hippocampus to achieve hippocampal avoidance (HA) of the optimally designed plan; planning target volume (PTV) included CTV plus 5 mm margins isotropically, and PTV-HA was obtained subtracting HA from PTV, as shown in Fig. 1.

### 2.4. Plan designing

7F-IMRT and dual arc VMAT plans were designed with Varian IX medical electron linear accelerator. The delivered dose was 300 cGy $\times$ 10 times. And the designing process was as follows:

i) 7F-IMRT: the dose rate of the irradiation field was 300 MU/min. There were 7 planning fields with isocentric irradiation. The field angles were adjusted according to the factual condition, as shown in Fig. 2.

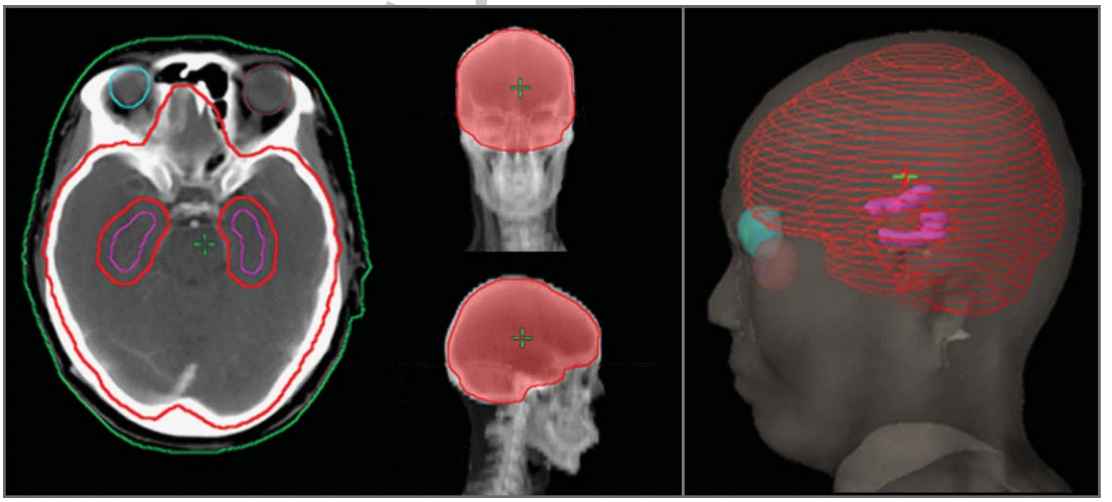

Fig. 1. PTV-HA and OARs (Purple represents hippocampus, and Red represents PTV-HA).

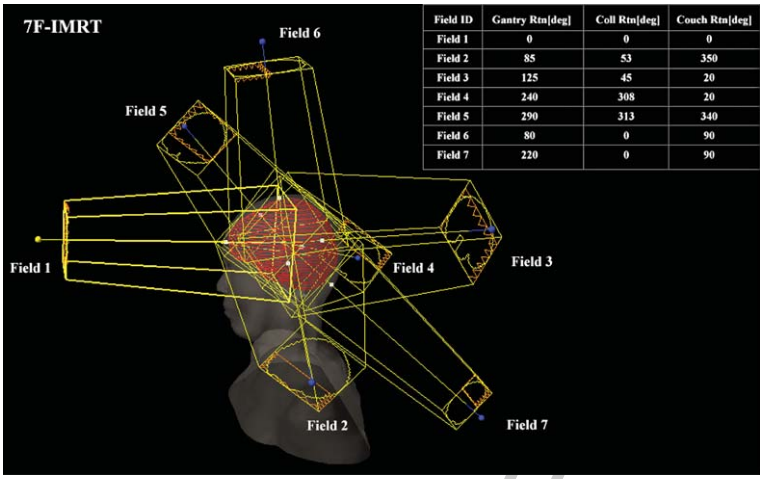


Fig. 2. Beam-on fields of 7F-IMRT for one patient.

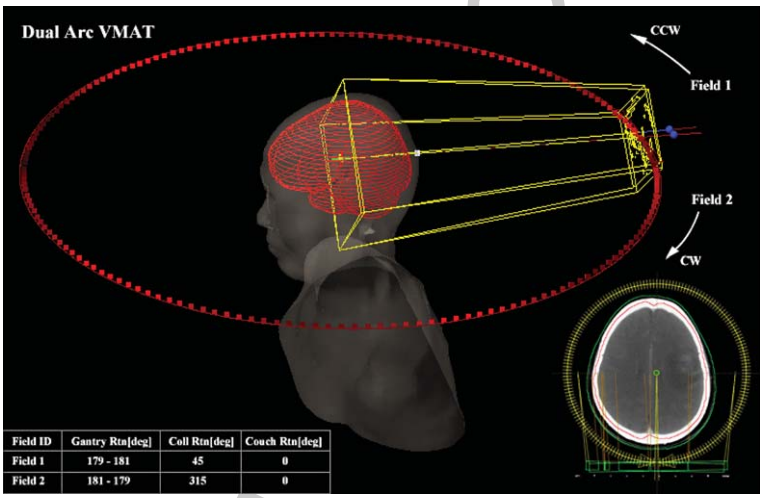


Fig. 3. Beam-on fields of dual arc VMAT for one patient.

ii) Dual Arc VMAT: the peak dose rate of the irradiation field was 600 MU/min. For dual arc irradiation, one rotated from 179° to 181° counterclockwise while the other rotated from 181° to 179° clockwise, the angles of collimator were 45° and 315°, respectively, and the treatment couch angle was 0°, as shown in Fig. 3.

The optimized parameters of the two plans were identical. The maximum dose to OARs was defined as 50 Gy for optic nerves, 45 Gy for eyes and 10 Gy for lens, the maximum dose for hippocampus cannot be more than 20 Gy. MU was not limited in the optimization process for the VMAT plan. The dose was calculated adopting Anisotropic Analytical Algorithm (AAA) algorithm, and the grid for dose calculation was 2.5 mm.

### *2.5. Plan evaluation*

The OARs were hippocampus ($D_{max}$), eyes ($D_{max}$), lens ($D_{max}$) and optic nerves ($D_{max}$). Target conformity and homogeneity for 7F-IMRT and dual arc VMAT plans were compared and evaluated by conformity index (CI) and homogeneity index (HI). CI was obtained by Equation (1):

$$CI = \frac{V_{t,ref}}{V_t} \times \frac{V_{t,ref}}{V_{ref}} \quad (1)$$

where $V_t$ represents the PTH-HA volume, $V_{t,ref}$ stands for the volume of PTH-HA surrounded by reference isodose surface, and $V_{ref}$ is the reference isodose surface volume. CI ranges from 0 to 1, and the higher CI value indicates the better conformity [24]. HI was obtained by Equation (2):

$$HI = \frac{D_2 - D_{98}}{D_p} \times 100\% \quad (2)$$

where $D_2$ represents the dose received by 2% of the PTH-HA volume in dose volume histogram (DVH), and may be considered as the "maximum dosage". $D_{98}$ represents the dose received by 98% of the PTH-HA volume in DVH and may be considered as the "minimum dosage". $D_p$ is the planned prescription dosage. HI ranges from 0 to 1, and the lower HI value indicates the better homogeneity [25].

### 2.6. Statistical method

All the statistical analyses were performed with SPSS 13.0 software for Windows (StaSoft Inc., Tulsa, OK, USA). Paired *t*-test was used to analyze the errors, and $P < 0.05$ was considered statistically significant.

## 3. Results

### 3.1. Comparison of dose distribution and DVH

The dose distributions (range from 80% to 107%) of transverse section, sagittal section and coronal sections of the same CT slice in the 7F-IMRT and dual arc VMAT plans for one patient were analyzed using the Varian Eclipse 8.6 three-dimensional treatment planning system, as shown in Fig. 4, purple stood for hippocampus with less than 2000cGy, the dose of other color regions ranged from 2000 cGy to 3210 cGy. The deeper the color was, the higher the dose was. Moreover, Fig. 4 revealed

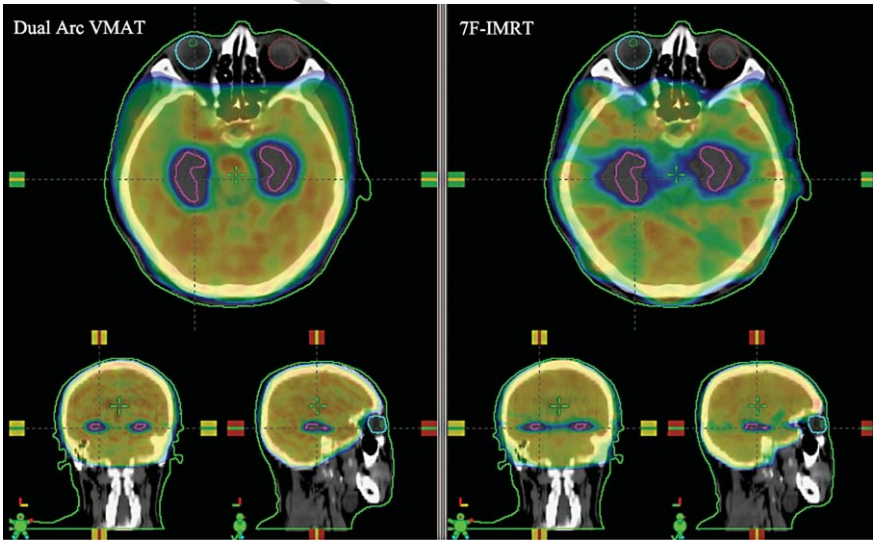


Fig. 4. Comparison of dose distribution between dual arc VMAT and 7F-IMRT plans.

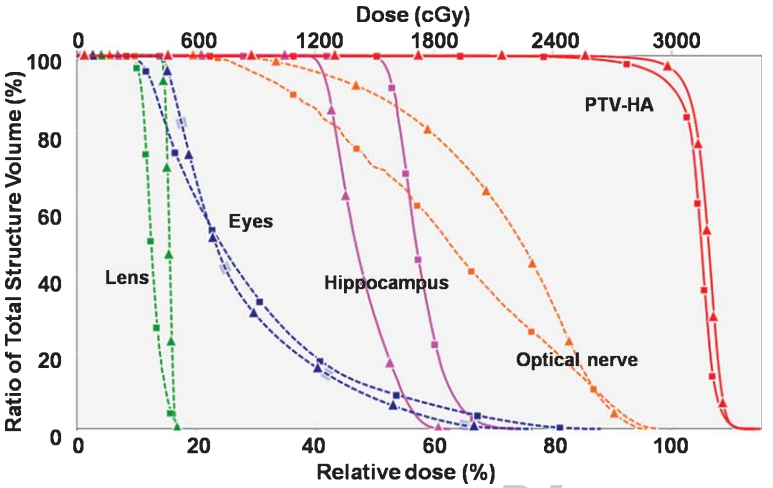


Fig. 5. Comparison of DVH between dual arc VMAT and 7F-IMRT plans (curve with ▲ represents dual arc VMAT plan, and curve with ■ represents 7F-IMRT plan).

that hippocampus was well protected in both 7F-IMRT and dual arc VAMT plans, but the color regions covered more area as to the target surrounding hippocampus in dual arc VMAT compared with 7F-IMRT, which indicated dual arc VMAT plan can obtain better dose distribution of the target to ensure the effects of radiotherapy.

Compared with 7F-IMRT, the dose values in DVH curve of PTV-HA were relatively higher for dual arc VMAT, the curve was rather "steeper", and the dose values of 85%–100% of the PTV-HA volume were remarkably higher, meanwhile, as to 0%–2% of this volume, the dose values were lower as shown in Fig. 5. Meanwhile, the dose for each OAR in dual arc VMAT was generally lower than that in 7F-IMRT. Therefore, DVH of OARs and PTV-HA in dual arc VMAT plan were superior to those in 7F-IMRT plan.

### *3.2. PTV-HA comparison*

Table 1 shows that dose received by the target volume, D2, D95, D98, Dmean and D50 of PTV-HA in dual arc VMAT were higher (better) than that in 7F-IMRT plan, which had statistically significant difference ($P < 0.05$); The PTV-HA receiving 100%, 95% and 105% of the prescription dose in dual arc VMAT were higher (better) than that in 7F-IMRT plan, which had statistically significant with

Table 1
PTV-HA dosimetric parameters comparison between 7F-IMRT and dual arc VMAT

| PTV-HA | 7F-IMRT | Dual Arc VMAT | *T* | *P* |
|---|---|---|---|---|
| $D_{98}$ cGy | 2777 ± 11 | 2970 ± 24 | –7.962 | 0.001 |
| $D_{95}$ cGy | 2936 ± 14 | 3029 ± 12 | –9.384 | 0.000 |
| $D_2$ cGy | 3281 ± 2 | 3286 ± 1 | –2.982 | 0.031 |
| $D_{mean}$ cGy | 3134 ± 8 | 3169 ± 6 | –8.375 | 0.000 |
| $D_{50}$ cGy | 3154 ± 9 | 3182 ± 6 | –4.112 | 0.009 |
| $V_{95}$ % | 97.0 ± 0.2 | 99.2 ± 0.1 | –14.4 | 0.000 |
| $V_{100}$ % | 91.6 ± 0.9 | 96.4 ± 0.6 | –8.178 | 0.000 |
| $V_{105}$ % | 52.4 ± 5.3 | 68.9 ± 3.5 | –4.425 | 0.007 |
| CI | 0.815 ± 0.011 | 0.888 ± 0.004 | –9.135 | 0.000 |
| HI | 0.170 ± 0.004 | 0.105 ± 0.007 | 9.690 | 0.000 |

Table 2
Comparison of dose parameters for OARs between 7F-IMRT and dual arc VMAT

| OARs | Dose parameters | 7F-IMRT | Dual Arc VMAT | $t$ | $P$ |
|---|---|---|---|---|---|
| Hippocampus | $D_{max}$ cGy | $2167 \pm 41$ | $1884 \pm 24$ | 4.941 | 0.004 |
| | $D_1$ cGy | $1990 \pm 37$ | $1739 \pm 8$ | 6.089 | 0.002 |
| Lens | $D_{max}$ cGy | $481 \pm 21$ | $517 \pm 8$ | –2.020 | 0.099 |
| Eyes | $D_{max}$ cGy | $2549 \pm 43$ | $2034 \pm 64$ | 7.313 | 0.001 |
| Optical Nerves | $D_{max}$ cGy | $2940 \pm 82$ | $2930 \pm 69$ | 0.100 | 0.925 |

Table 3
Comparison of MU and treatment time between 7F-IMRT and dual arc VMAT

| Plan | Maximal MU | Minimal MU | Mean MU | Mean treatment time (s) |
|---|---|---|---|---|
| 7F-IMRT | 3319 | 2338 | 2863 | 573 |
| Dual Arc VMAT | 1120 | 840 | 935 | 150 |

$P < 0.05$; the CI for PTV-HA was higher (better) in dual arc VMAT than that in 7F-IMRT; and HI for PTV-HA in dual arc VMAT was lower (better) than that in 7F-IMRT plans,which had statistically significant difference.

### 3.3. Comparison of irradiation dose of OARs

Comparison in Table 2 between dual arc VMAT and 7F-IMRT plans showed that the maximum doses received by hippocampus and eyes in dual arc VMAT plan were all lower than those in 7F-IMRT plan, which was considered statistically significant with $P < 0.05$. By contrast, the maximum dose ($D_{max}$) received by lens and optical nerves had no statistically significant difference in these two plans ($P > 0.05$). These data indicated that the results obtained under irradiation dose could harm organs in dual arc VMAT, which were better than those obtained in 7F-IMRT.

### 3.4. Comparison of MU and treatment time

To evaluate the performance of dual arc VMAT and 7F-IMRT plans, MU and treatment time were compared between the two plans and listed in Table 3. For the ten patients, MU in 7F-IMRT reached a maximum of 3,319, a minimum of 2,338, with a mean of 2,863. While MU in dual arc VMAT reached a maximum of 1120, a minimum of 840 and an average of 935. Compared with 7F-IMRT, dual arc VMAT reduced MU by 67% ($P < 0.05$). The mean treatment time was 573 s in IMRT and 150 s in dual arc VMAT. Compared with 7F-IMRT, dual arc VMAT reduced the mean delivery time by 74% ($P < 0.05$). Therefore, dual arc VMAT plan significantly reduced MU and treatment time, and following with better treatment efficiency.

## 4. Discussion

In this study, the results obtained by evaluating the parameters between dual arc VMAT and 7F-IMRT plans manifested that both of them could meet the clinical requirements. For dose distribution of PTV-HA, dual arc VMAT increased the percentage of dose coverage of the PTV-HA, effectively controlled target dose distribution and significantly improved target dose homogeneity and conformity.

Compared with 7F-IMRT, dual arc VMAT was proved to be superior regarding the protection for OARs, significantly reduced the irradiation dose delivered to OARs. Furthermore, compared with 7F-IMRT, dual arc VMAT reduced the mean MU by 67% and the mean delivery time by 74%, significantly shortening treatment time and improving the efficiency of accelerator.

In order to reduce inertia error as much as possible during gantry rotation, VMAT flexibly adjusts the dose rate according to the target dose and positions of OARs on the premise that the gantry rotates at a uniform velocity. Then, the treatment can be completed in one circle or a few arcs. Due to the shortened treatment time, VMAT increases the patients comfort. In addition, VMAT improves treatment accuracy by relatively reducing the errors caused by organ motion and target shift that exists in traditional radiotherapy. As VMAT plan has more variables (dose rate, MLC velocity, angle of arc, etc.) compared with the conventional IMRT technique, the number of optimization variables increases and the optimization process becomes more complicated [26–28]. For the same case, it requires a longer time to design a plan for VMAT in contract with IMRT to meet the clinical requirements. Therefore, improving the efficiency and radiobiological effect of VMAT requires further investigation.

As regards protection of hippocampus for patients with brain metastases from lung cancer in WBRT, there are several fields in IMRT. As a result, implementing the plan is complicated. Gondi et al. [29] have compared the protection of hippocampus (prescription dose of 3Gy $\times$ 10 times) between helical tomotherapy and 9-field non-coplanar linear accelerator-based IMRT in WBRT and found that $D_{median}$ and $D_{max}$ to the hippocampus in the 9-field non-coplanar linear accelerator-based IMRT plan were 7.8 Gy and 15.3 Gy, respectively. A 7-field coplanar IMRT plan was adopted in the present study, and the experimental results demonstrated that $D_{max}$ and $D_1$ were marginally higher (21.67 Gy and 19.90 Gy, respectively). In addition, the coverage rate of the target volume was relatively low, which is in relation to the number of fields and field angles.

Research reported by both Palma et al. [30] and Cozzi et al. [31] has demonstrated that VMAT plan reduced the dose delivered to normal tissues, provided a better coverage rate of the target volume and resulted in shorter treatment time, ultimately achieving effects equivalent or superior to those of IMRT. In the present study, we attempted to protect hippocampus with VMAT in WBRT. The conventional dual-arcs were used to design a VMAT plan to achieve equal or better the dose distribution of target volume and nearly equivalent OARs dose in IMRT [32]. Significant differences were observed between VMAT and IMRT plans. Under normal circumstances, the field settings in IMRT are usually in close agreement with three requirements, namely, coplanar field, equiangular beams and odd number of fields. Optimizing templates can be used to form a satisfied dose distribution in a short time. The adjustable factors of IMRT encompass gantry angle, collimator angle, MLC, etc. However, several factors in VMAT optimization, such as the number of arcs, collimator angle, MLC speed and dose rate, can be adjusted. Therefore, designing a superior VMAT plan is affected by a number of factors, such as the number of arcs, the start angle of rotation, the angle of collimator, the couch angle, the position and the size of secondary collimator, limit optimization settings, optimization weight settings and control of the optimization process. As a result, more time is required to design a plan that meets clinical requirements compared with IMRT for the same case. However, many radiotherapists consider VMAT as the new IMRT and taking advantage of this new technique requires study and practice. As the application of VMAT in WBRT is still in an early stage, how to improve the efficiency of designing a VMAT plan and minimize the hippocampus dose while ensuring an adequate dose of the target volume require further investigation.

## 5. Conclusion

In summary, both plans meet the requirements of hippocampus protection. 7F-IMRT is relatively simple, practical and ensures a good protection for hippocampus; however, its disadvantages are the

low dose coverage rate of the target volume and the complexity of implementation. By contrast, dual arc VMAT exhibits a better coverage rate of the target volume, a better conformity and homogeneity, and a better protection for hippocampus, with high efficiency and high-speed process.

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