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ORIGINAL ARTICLE

Single-isocenter volumetric-modulated Dynamic WaveArc therapy for two brain metastases

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Abstract

Purpose A new irradiation technique, volumetric-modulated Dynamic WaveArc therapy (VMDWAT), based on sequential non-coplanar trajectories, can be performed using the Vero4DRT. This planning study compared the dose distribution and treatment time between single-isocenter volumetric-modulated arc therapy (VMAT) with multiple straight non-coplanar arcs and single-isocenter VMDWAT in patients with two brain metastases.

Materials and methods Twenty patients with two planning target volumes exceeding 2.0 cm^3 were included. Both VMAT and VMDWAT plans were created with single isocenter and a prescribed dose of 28 Gy delivered in five fractions. Target conformity was evaluated using indices modified from the RTOG-CI (mRTOG-CI) and IP-CI (mIP-CI).

Results VMDWAT significantly improved both mRTOG-CI and mIP-CI and reduced the volume of normal brain tissue receiving 25 and 28 Gy compared to VMAT. The two modalities did not significantly differ in terms of the volume of normal brain tissue receiving 5, 10, 12, 15, and 20 Gy. The mean treatment time was significantly shorter in the VMDWAT group.

Conclusion VMDWAT significantly improved dose distribution in a shorter treatment time compared to VMAT in patients treated for two brain metastases. Single-isocenter VMDWAT may thus be a promising treatment for two brain metastases.

Keywords Dynamic WaveArc · Single-isocenter VMAT · Brain metastases · Dosimetric study · Treatment time

Introduction

In the unique design of the Vero4DRT (Mitsubishi Heavy Industries, Ltd., Tokyo, Japan, and Brainlab, Feldkirchen, Germany), the gantry is mounted in the O-ring structure [1]. Non-coplanar beams can be delivered by rotating the O-ring without moving the couch, and the Vero4DRT can rotate both the gantry and the O-ring simultaneously. Because the sequential non-coplanar trajectory created by the simultaneous rotation of both the gantry and the O-ring acts like a wave, it is referred to as Dynamic WaveArc (DWA), a concept further developed as unicursal irradiation [2] (Fig. 1). A new irradiation technique combining DWA and volumetric-modulated arc therapy (VMAT) was developed as volumetric-modulated DWA therapy (VMDWAT). The mechanical accuracy of VMDWAT had been already confirmed to be quite high, which resulted in very small dosimetric errors [3].

Stereotactic irradiation (STI) is a well-established treatment for multiple brain metastases [4]. Although Dynamic conformal arc therapy (DCAT) in linear-accelerator

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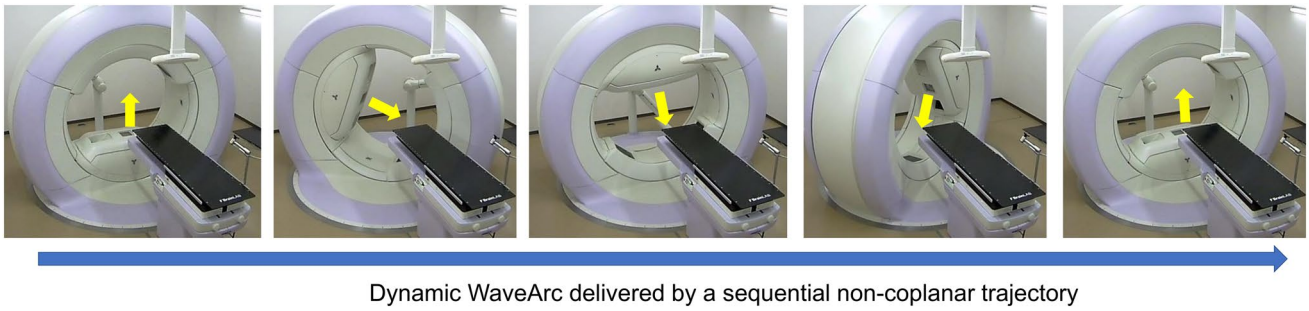

Fig. 1 Representative trajectory of Dynamic WaveArc therapy delivered by a sequential non-coplanar trajectory

(LINAC)-based STI is the standard treatment for 1–4 brain metastases, multiple isocenters must be placed on each target and the treatment time becomes longer, as the number of lesions increases. Single-isocenter VMAT for multiple brain metastases is a new treatment option for LINAC-based STI. Its advantage is a shortened treatment time based on the use of only one isocenter to treat multiple targets with intensity modulation and image-guided radiotherapy. Single-isocenter VMAT has been shown to achieve good local control safely and over a short treatment time [5–7].

Single-isocenter VMAT is delivered with multiple straight non-coplanar arcs to improve target conformity and reduce the doses to normal tissue. When the non-coplanar beams are delivered by conventional LINAC, radiotherapists must enter the treatment room to rotate the couch, thus prolonging the total treatment time compared to treatment with only coplanar arcs. Vero4DRT, however, can deliver non-coplanar beams safely and without couch rotation, resulting in a shorter treatment time than with conventional LINAC [8]. For these reasons, the Vero4DRT should be suitable for STI.

Multiple straight non-coplanar arcs are usually applied for single-isocenter VMAT, but it takes times to rotate the gantry and O-ring between each separate straight arc, even if the Vero4DRT is used. Since, in VMDWAT, sequential non-coplanar DWAs can be delivered and there is no need to use separate straight coplanar and non-coplanar arcs, VMDWAT seems to be able to allow for a shorter treatment time than conventional VMAT with multiple straight non-coplanar arcs. Planning studies using VMDWAT for pituitary adenoma, craniopharyngioma, and some extracranial tumors have been reported [9–11]. By contrast, analyses of the radiotherapy delivered by the Vero4DRT based on a single isocenter for multiple lesions have yet to be published. There are also no reports on the use of VMDWAT for brain metastases.

Therefore, we conducted a planning study to compare the treatment time and dose distributions between conventional VMAT with multiple straight non-coplanar arcs and VMDWAT for use in the treatment of brain metastases.

Materials and methods

This study was conducted in accordance with the 1964 Declaration of Helsinki. Our Institutional Ethical Review Board approved the research (E2276 and R1048). Informed consent was obtained from all participating patients.

We limited our study to patients with two large brain metastases of which planning target volumes (PTVs) > 2.0 cm^3. Because PTVs that exceed 2.0 cm^3 are treated at our institution using hypofractionated stereotactic radiotherapy (HFSRT), to minimize the risk of radiation necrosis. HFSRT, rather than stereotactic radiosurgery (SRS) with single fraction, may minimize the positional deviation that can arise with single-isocenter irradiation for multiple targets. In addition, the mechanical property of the Vero4DRT, with its 5 mm wide multileaf collimeters, was considered to be unsuitable to treat small lesions < 2.0 cm^3 [12]. In fact, it is rare to see patients with three or more large metastases in the brain in daily clinical practice.

Therefore, the study population consisted of 20 patients with two brain metastases, both exceeding 2.0 cm^3. The metastases were treated with STI at our institution from December 2007 to May 2017.

Contouring

Contouring were performed with previously acquired computed tomography (CT) images and RayStation version 4.7 (RaySearch Laboratories, Stockholm, Sweden). CT images were acquired using a Light Speed RT scanner (GE Healthcare, Milwaukee, WI, USA) and SOMATOM Definition AS (Siemens Healthineers, Erlangen, Germany). The thickness of the CT slices ranged from 1 to 1.25 mm. Patients were immobilized using a thermoplastic frameless mask, and contrast-enhanced magnetic resonance images were fused with the CT images. Gross tumor volume (GTV) was defined using the contrast-enhanced lesions. The PTV was created by expanding the GTV with a 1 mm

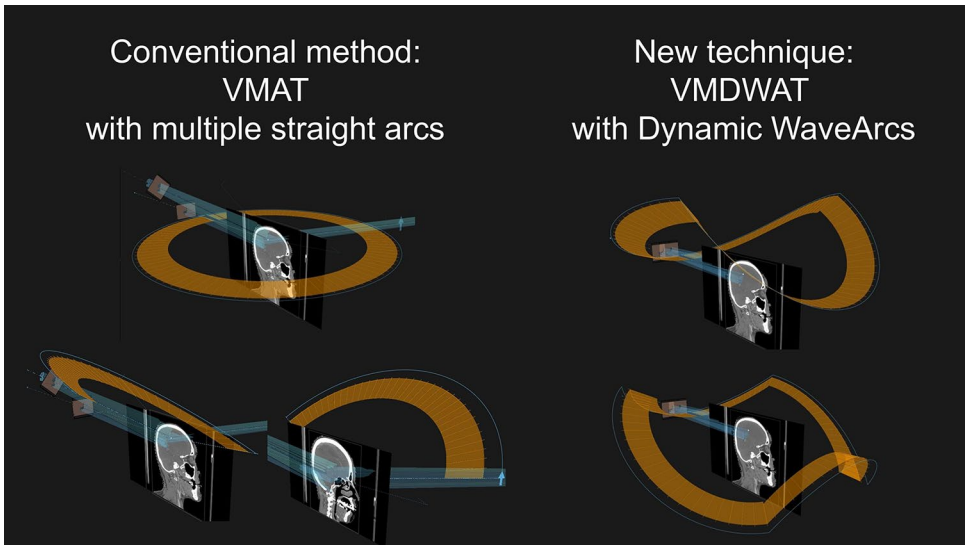

Fig. 2 Arc arrangements in conventional volumetric-modulated arc therapy (VMAT) with multiple straight arcs vs. those of volumetric-modulated Dynamic WaveArc therapy (VMDWAT)

Table 1 The control points of one coplanar and two straight non-coplanar arc trajectories in the volumetric-modulated arc therapy (VMAT) plans

	O-ring angle (°)	Gantry angle (°)
Arc1		
Start	0	182
Stop	0	178
Arc 2		
Start	320	160
Stop	320	20
Arc 3		
Start	40	340
Stop	40	200

Table 2 The control points of two Dynamic WaveArc trajectories in the volumetric-modulated Dynamic WaveArc therapy (VMDWAT) plans

	O-ring angle (°)	Gantry angle (°)
Arc1		
Start	0	182
	40	290
	320	70
Stop	0	178
Arc 2		
Start	0	178
	335	122
	35	38
	325	322
	25	238
Stop	0	182

margin. Normal brain, optic nerves, chiasm, lenses, eyes, and brainstem were contoured as organs at risk (OARs). Normal brain was delineated by whole-brain tissue, except for the PTVs.

Treatment planning

VMAT and VMDWAT plans were retrospectively created for all 20 patients using RayStation version 4.7. The calculation grid size was 1 mm, and the calculation algorithm was collapsed cone convolution. The prescribed dose was 28 Gy delivered in five fractions, with 99.5% of the two PTVs set to be covered by at least 28 Gy ($D_{99.5\%} \geq 100\%$).

VMAT planning

The single isocenter was set at the mid-point between the two PTVs. The VMAT plans consisted of one coplanar and two straight non-coplanar arcs (Fig. 2). The control points of the VMAT with multiple straight arcs are shown in Table 1. Optimization was performed to satisfy the following criteria: 28 Gy isodose lines were fitted to the PTVs to the extent possible, and the dose to normal brain tissue was reduced. The doses covering 2% of the structure ($D_{2\%}$) for the two PTVs, brainstem, optic nerves, chasm, lenses, and eyes were set to below 56, 20, 20, 20, 10, and 20 Gy, respectively.

VMDWAT planning

Similar to VMAT planning, the single isocenter was set at the mid-point between the two PTVs. VMDWAT plans were created using two sequential non-coplanar DWA trajectories (Fig. 2), selected from templates mounted in the RaySta-tion and deliverable without risk of collision. The control points of the two DWA trajectories are shown in Table 2.

The criteria for optimization and the dose constraints for the OARs were as the same as those described for the VMAT plans.

Evaluation of the treatment plans

$D_{2\%}$, $D_{98\%}$, and $D_{50\%}$ for each PTV were evaluated, with $D_{98\%}$ and $D_{50\%}$ defined as the doses covering 98% and 50% of the PTV, respectively.

Although the conformity indices defined by the Radiation Therapy Oncology Group (RTOG-CI) and Paddick et al. (IP-CI) are useful to evaluate target conformity, they cannot be calculated in cases of two close lesions [13, 14]. This is because the isodose lines of the prescribed doses can become merged and thus not separated for each target. Accordingly, we used the modified conformity indices derived from the RTOG-CI (mRTOG-CI) and IP-CI (mIP-CI) and the summed dosimetric parameters of the two PTVs [15]. mRTOG-CI was defined as $V(28)/V\text{PTVs}$, where $V(28)$ is the volume enclosed by an isodose line of 28 Gy and $V\text{PTVs}$ were the sum of the two PTVs. mIP-CI was defined as $([\text{VPTVs}(28)]^2/[V(28) \times V\text{PTVs}])$, where VPTVs(28) is the sum of the two PTVs receiving > 28 Gy. Homogeneity index (HI) was evaluated in the two modalities. The HI was defined as $(D_{2\%} - D_{98\%})/D_{50\%}$.

The volume of irradiated normal brain tissue was evaluated as $V_{5\,\text{Gy}}$, $V_{10\,\text{Gy}}$, $V_{12\,\text{Gy}}$, $V_{15\,\text{Gy}}$, $V_{20\,\text{Gy}}$, $V_{25\,\text{Gy}}$, and $V_{28\,\text{Gy}}$, defined as the volume of normal tissue receiving at least an absorbed dose of 5, 10, 12, 15, 20, 25, and 28 Gy, respectively. Doses to the OARs were evaluated as well, excluding normal brain tissue, using $D_{2\%}$.

Treatment time

The monitor unit (MU), beam-on time, and treatment time were compared between the two modalities. The beam-on time was estimated using RayStation. The treatment time included the beam-on time and the time needed to rotate both the O-ring and the gantry between arcs. The gantry and O-ring rotate at a maximum rate of 6° and 3° per second, respectively.

Statistical analyses

All statistical analyses were performed using EZR version 1.32, a graphical user interface for R (R Foundation for Statistical Computing, Vienna, Austria) [16]. Specifically, EZR is a modified version of R commander version 2.2–3 that facilitates biostatistical evaluations. Data from the two plans were compared using the Wilcoxon signed-rank test and paired *t* test. A p value < 0.05 was considered to indicate statistical significance.

Results

The median PTV was 5.5 (range 2.1–28.3) cm^3. The sum of the two PTVs per patient was 11.4 (range 4.6–45.9) cm^3. The median distance between two brain metastases was 6.44 cm (range 3.53–12.39). The MU in VMDWAT was larger than that in VMAT. While the beam-on time in VMDWAT was longer, the treatment time was significantly shorter than in VMAT (Table 3).

Target conformity and homogeneity

The irradiation field and the sagittal plane of the dose distribution of VMDWAT in a representative case are shown in Fig. 3. Table 4 summarizes the PTV indices. Although there were no significant differences between the two modalities with respect to $D_{2\%}$, $D_{98\%}$, and $D_{50\%}$, VMDWAT significantly improved the mRTOG-CI and mIP-CI compared to VMAT. There was no significant difference in the mean HI between VMAT and VMDWAT (0.231 ± 0.056 and 0.243 ± 0.066, $p = 0.366$).

Normal brain and other OARs

The irradiated volume and doses to the OARs are listed in Table 5. Compared to VMAT, VMDWAT significantly reduced $V_{25\,\text{Gy}}$ and $V_{28\,\text{Gy}}$ of normal brain tissue. The two modalities did not significantly differ in terms of either $V_{5\,\text{Gy}}$, $V_{10\,\text{Gy}}$, $V_{12\,\text{Gy}}$, $V_{15\,\text{Gy}}$, and $V_{20\,\text{Gy}}$ of normal brain tissue or $D_{2\%}$ of brainstem, chiasm, and both optic nerves. While $D_{2\%}$ of both eyes and the left lens were significantly higher in VMDWAT than in VMAT, the absolute doses to those organs were far below the dose constraints.

Discussion

This planning study is the first to evaluate dose distribution of single-isocenter VMDWAT for the treatment of more than one lesion. While both irradiation techniques delivered low to moderate doses to similar volumes of normal brain

Table 3 The monitor unit (MU), beam-on time, and treatment time in VMAT and VMDWAT plans

	VMAT (mean ± SD)	VMDWAT (mean ± SD)	*p* value
MU	1282 ± 375	1446 ± 332	0.011
Bean-on time (s)	229 ± 66	247 ± 39	0.014
Treatment time (s)	278 ± 66	247 ± 39	0.004

SD standard deviation

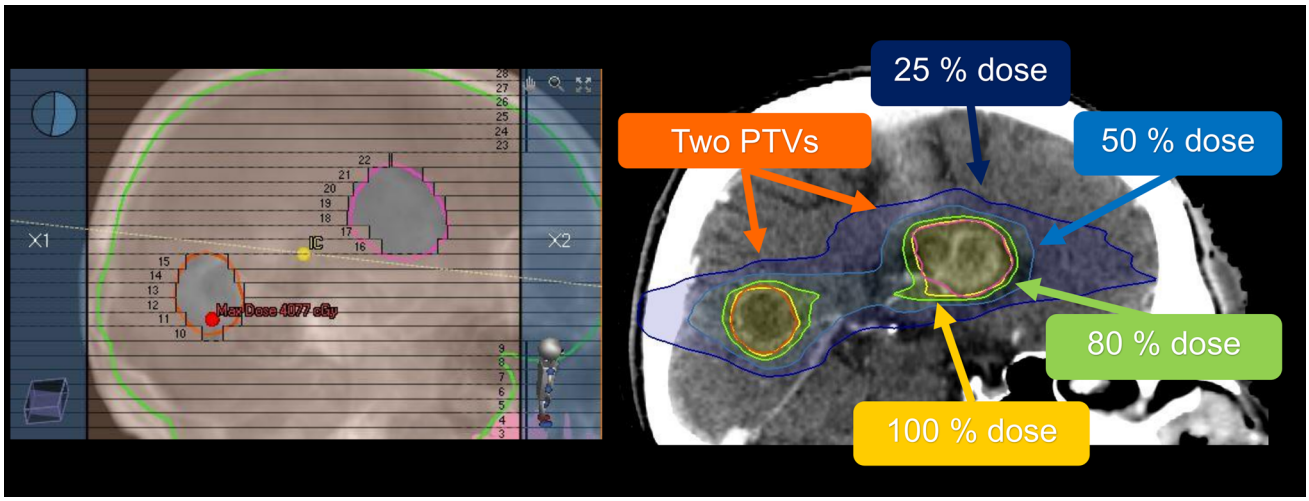

Fig. 3 Irradiation field and sagittal plane of the dose distribution of VMDWAT in a representative case

Table 4 Indices of dose-volumetric parameters for planning target volume

	VMAT (mean ± SD)	VMDWAT (mean ± SD)	*p* value
$D_{2\%}$ (Gy)	37.1 ± 2.2	37.4 ± 2.4	0.563
$D_{98\%}$ (Gy)	29.3 ± 0.5	29.2 ± 0.3	0.307
$D_{50\%}$ (Gy)	33.8 ± 1.3	33.9 ± 1.0	0.822
mRTOG-CI	1.28 ± 0.08	1.24 ± 0.08	0.005
mIP-CI	0.78 ± 0.05	0.80 ± 0.05	0.002

mRTOG-CI modified conformity index (CI) derived from the CI defined by the Radiation Therapy Oncology Group (RTOG) [13], *mIP-CI* modified CI derived from the CI defined by Paddick et al. [14]

tissue, the treatment time was shorter and the conformity significantly improved using VMDWAT for patients with two brain metastases. These observations indicate the use of VMDWAT as a promising treatment option for multiple brain metastases.

Treatment time was significantly shorter in VMDWAT compared to that of VMAT in our study. In conventional single-isocenter VMAT for brain metastases, separate straight non-coplanar arcs are usually needed to achieve high target conformity and reduce the risk of radiation necrosis. However, the delivery of separate straight non-coplanar arcs implies a longer treatment time because of the time needed to rotate the O-ring and the gantry between each arc. DWA

Table 5 The irradiated volume and doses to organs at risks

Organ	Index	VMAT (mean ± SD)	VMDWAT (mean ± SD)	*p* value
Normal brain	$V_{5\,Gy}$ (cm^3)	202.7 ± 98.9	210.2 ± 108.3	0.089
	$V_{10\,Gy}$ (cm^3)	69.3 ± 32.8	71.2 ± 34.6	0.064
	$V_{12\,Gy}$ (cm^3)	50.8 ± 23.9	51.3 ± 24.0	0.455
	$V_{15\,Gy}$ (cm^3)	33.1 ± 15.0	33.1 ± 15.4	0.940
	$V_{20\,Gy}$ (cm^3)	17.1 ± 7.8	16.7 ± 8.2	0.112
	$V_{25\,Gy}$ (cm^3)	7.9 ± 3.9	7.3 ± 3.9	0.002
	$V_{28\,Gy}$ (cm^3)	3.4 ± 1.9	2.9 ± 1.7	0.004
Brainstem	$D_{2\%}$ (Gy)	4.7 ± 3.2	4.5 ± 3.3	0.926
Chiasm	$D_{2\%}$ (Gy)	2.0 ± 1.7	2.1 ± 1.7	0.520
Left optic nerve	$D_{2\%}$ (Gy)	1.2 ± 1.1	1.4 ± 1.5	0.312
Right optic nerve	$D_{2\%}$ (Gy)	1.4 ± 1.0	1.6 ± 1.2	0.100
Left eye	$D_{2\%}$ (Gy)	0.9 ± 0.7	1.4 ± 1.3	0.001
Right eye	$D_{2\%}$ (Gy)	1.3 ± 1.7	1.9 ± 2.2	0.017
Left lens	$D_{2\%}$ (Gy)	0.6 ± 0.5	0.8 ± 0.8	0.031
Right lens	$D_{2\%}$ (Gy)	0.7 ± 0.6	1.0 ± 1.1	0.050

VX volume of normal brain irradiated by X Gy , *DX* doses covering 2% of the organs at risk

trajectories are the only way to safely deliver sequential non-coplanar beams without rotating the couch, thereby shortening the treatment time.

VMDWAT can deliver sequential non-coplanar beams from not only the cranial, but also the caudal direction. A much greater improvement of target conformity seems to be achieved when the trajectories include a wider range of angles. In our study, the VMAT plans applied three arcs, which is one of the standard practices at our institution and did not include beams from the caudal direction. The VMDWAT trajectories, however, consisted of various control points, including a beam from the caudal direction, which presumably improved the target conformity of VMDWAT compared to VMAT. For patients with skull-based tumors, irradiation from the caudal direction results in better conformity and homogeneity when conventional DCAT is used [17]. While at the time of this study, only the templates of the DWA trajectories could be used, with the latest version of RayStation (version 6.2), it is now possible to modify the DWA trajectories manually. Optimization of the DWA trajectories for each patient might improve the dose distribution to a greater extent than using the templates mounted in the RayStation.

VMDWAT reduced the volume of normal brain tissue receiving high doses of radiation. While the prognosis of patients with brain metastases has improved due to advances in systemic therapy, the incidence of brain radiation necrosis increases with an increasing number of years after radiosurgery [18, 19]. In addition, as higher doses are a risk factor for brain necrosis [20], it is important to reduce the volume of normal brain tissue receiving high doses as much as possible. VMDWAT may be a good treatment option for multiple brain metastases to reduce the risk of radiation necrosis. In our study, the $D_{2\%}$ to most of the OARs were similar in the VMDWAT and VMAT groups, excluding both eyes and the left lens. However, the absolute doses in these latter structures were still far below the dose constraints, suggesting that the differences between the two modalities have little impact on clinical outcomes.

This study also had several limitations. First, it was only a planning study; whether an improvement of target conformity and a reduction of high-dose-irradiated normal brain tissue reduce the risk of brain necrosis remains to be determined. Additional studies of VMDWAT will be required to validate the clinical significances in the future. Second, we did not examine whether the arc arrangements of VMAT and VMDWAT used in our study were optimal for each case. The location and spatial relationship of the two metastases differed in each patient. However, because our goal was to compare the dose distributions between VMAT and VMDWAT for two brain metastases, the same arc arrangements were used for each group in this planning study. While these arc arrangements used in this study seemed adequate for multiple brain metastases treated by Vero4DRT, these should be optimized according to tumor location and its relationship to the OARs in the clinical setting. Modification and optimization of the arc arrangement with the latest version of RayStation may lead to an even better dose distribution. Finally, we only analyzed the dose distribution created by Vero4DRT and RayStation; whether comparable results would be obtained with radiotherapy devices other than Vero4DRT remains uncertain. The width of the multileaf collimator, the range of the O-ring or the couch motion, the dose calculation algorithm, and the optimization process differ among treatment devices and treatment planning systems (TPSs). We analyzed only the Vero4DRT and RayStation, to ensure consistency in the evaluation of the VMAT and VMDWAT using the same treatment device and TPS as the first step. Comparisons between other TPSs and radiotherapy devices should be conducted in future studies. For example, the use of 4pi radiotherapy delivered with conventional LINAC by rotating the gantry and couch has been reported for central nervous system tumors [21–24]. In Wilson et al. [24], 4pi trajectory-based SRS by conventional LINAC was used in 10 patients with acoustic neurinomas and 1–3 brain metastases. The authors reported promising results of trajectory-based SRS compared to conventional DCAT and VMAT techniques. Thus, 4pi and VMDWAT should be compared with respect to dose distribution, treatment time, and the level of patient distress during radiotherapy, because the need to continuously rotate the couch during 4pi radiotherapy may be a source of distress for patients. As VMDWAT is delivered by rotating the O-ring and there is no need to rotate the couch, this therapeutic approach may reduce patient distress compared to 4pi radiotherapy.

In conclusion, single-isocenter VMDWAT can improve target conformity compared to conventional VMAT with multiple straight non-coplanar arcs. VMDWAT also reduced V_{25Gy} and V_{28Gy} of normal brain tissue, in addition to significantly shortening the treatment time. Although the mean $D_{2\%}$ of both eyes and the left lens were significantly higher in VMDWAT, the absolute doses of those structures were far below the dose constraints. Together, these results suggest that VMDWAT is useful as a treatment modality for patients with two brain metastases.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Our Institutional Ethical Review Board approved this research (E2276 and R1048).

Informed consent Informed consent was obtained from all participated patients.

References

1. Kamino Y, Takayama K, Kokubo M, Narita Y, Hirai E, Kawawda N, et al. Development of a four-dimensional image-guided radiotherapy system with a gimbaled X-ray head. Int J Radiat Oncol Biol Phys. 2006;66:271–8.
2. Mizowaki T, Takayama K, Nagano K, Miyabe Y, Matsuo Y, Kaneko S, et al. Feasibility evaluation of a new irradiation technique: three-dimensional unicursal irradiation with the Vero4DRT (MHI-TM2000). J Radiat Res. 2013;54:330–6.
3. Hirashima H, Nakamura M, Miyabe Y, Uto M, Nakamura K, Mizowaki T. Monitoring of mechanical errors and their dosimetric impact throughout the course of non-coplanar continuous volumetric-modulated arc therapy. Radiat Oncol. 2018;13:27.
4. Tsao MN, Rades D, Wirth A, Lo SS, Danielson BL, Gaspar LE, et al. Radiotherapeutic and surgical management for newly diagnosed brain metastasis(es): an American Society for Radiation Oncology evidence-based guideline. Pract Radiat Oncol. 2012;2:210–25.
5. Nath SK, Lawson JD, Simpson DR, Vanderspek L, Wang JZ, Alksne JF, et al. Single-isocenter frameless intensity-modulated stereotactic radiosurgery for simultaneous treatment of multiple brain metastases: clinical experience. Int J Radiat Oncol Biol Phys. 2010;78:91–7.
6. Lau SK, Zakeri K, Zhao X, Carmona R, Knipprath E, Simpson DR, et al. Single-isocenter frameless volumetric modulated arc radiosurgery for multiple intracranial metastases. Neurosurgery. 2015;77:233–40.
7. Serna A, Escolar PP, Puchades V, Mata F, Ramos D, Gomez MA, et al. Single fraction volumetric modulated arc radiosurgery of brain metastases. Clin Transl Oncol. 2015;17:596–603.
8. Monzen H, Mizowaki T, Yano S, Fujimoto T, Kamomae T, Utsunomiya S, et al. Impact of the Vero4DRT (MHI-TM2000) on the total treatment time in stereotactic irradiation. J Nucl Med Radiat Ther. 2015;6:238. https://doi.org/10.4172/2155-9619.100023
9. Burghelea M, Verellen D, Poels K, Hung C, Nakamura M, Dhont J, et al. Initial characterization, dosimetric benchmark and performance validation of Dynamic WaveArc. Radiat Oncol. 2016;11:63.
10. Uto M, Mizowaki T, Ogura K, Miyabe Y, Nakamura M, Mukumoto N, et al. Volumetric modulated Dynamic WaveArc therapy reduces the dose to the hippocampus in patients with pituitary adenomas and craniopharyngiomas. Pract Radiat Oncol. 2017;7:382–7.
11. Ono Y, Yoshimura M, Hirata K, Ono T, Hirashima H, Mukumoto N, et al. Dosimetric advantages afforded by a new irradiation technique, Dynamic WaveArc, used for accelerated partial breast irradiation. Phys Med. 2018;48:103–10.
12. Burghelea M, Verellen D, Gevaert T, Depuydt T, Poels K, Simon V, et al. Feasibility of using the Vero SBRT system for intracranial SRS. J Appl Clin Med Phys. 2014;15:4437.
13. Shaw E, Kline R, Gillin M, Souhami L, Hirschfeld A, Dinapoli R, et al. Radiation therapy oncology group: radiosurgery quality assurance guidelines. Int J Radiat Oncol Biol Phys. 1993;27:1231–9.
14. Paddick I. A simple scoring ratio to index the conformity of radiosurgical treatment plans. Technical note. J Neurosurg. 2000;93(Suppl 3):219–22.
15. Uto M, Mizowaki T, Ogura K, Mukumoto N, Katagiri T, Takehana K, et al. Dosimetric comparison between dual-isocentric Dynamic conformal arc therapy and mono-isocentric volumetric-modulated arc therapy for two large brain metastases. J Radiat Res. 2018;59:774–81.
16. Kanda Y. Investigation of the freely available easy-to-use software 'EZR' for medical statistics. Bone Marrow Transpl. 2013;48:452–8.
17. Ogura K, Mizowaki T, Ishida Y, Hiraoka M. Dosimetric advantages of O-ring design radiotherapy system for skull-base tumors. J Appl Clin Med Phys. 2014;15:4608.
18. Kohutek ZA, Yamada Y, Chan TA, Brennan CW, Tabar V, Gutin PH, et al. Long-term risk of radionecrosis and imaging changes after stereotactic radiosurgery for brain metastases. J Neurooncol. 2015;125:149–56.
19. Iuchi T, Shingyoji M, Sakaida T, Hatano K, Nagano O, Itakura M, et al. Phase II trial of gefitinib alone without radiation therapy for Japanese patients with brain metastases from EGFR-mutant lung adenocarcinoma. Lung Cancer. 2013;82:282–7.
20. Shaw E, Scott C, Souhami L, Dinapoli R, Kline R, Loeffler J, et al. Single dose radiosurgical treatment of recurrent previously irradiated primary brain tumors and brain metastases: final report of RTOG protocol 90–05. Int J Radiat Oncol Biol Phys. 2000;47:291–8.
21. Woods K, Lee P, Kaprealian T, Yang I, Sheng K. Cochlea-sparing acoustic neuroma treatment with 4pi radiation therapy. Adv Radiat Oncol. 2018;3:100–7.
22. Yang Y, Zhang P, Happersett L, Xiong J, Yang J, Chan M, et al. Choreographing couch and collimator in volumetric modulated arc therapy. Int J Radiat Oncol Biol Phys. 2011;80:1238–47.
23. Nguyen D, Rwigema JC, Yu VY, Kaprealian T, Kupelian P, Selch M, et al. Feasibility of extreme dose escalation for glioblastoma multiforme using 4pi radiotherapy. Radiat Oncol. 2014;9:239.
24. Wilson B, Otto K, Gete E. A simple and robust trajectory-based stereotactic radiosurgery treatment. Med Phys. 2017;44:240–8.

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