Volumetric-modulated arc therapy versus conventional fixed-field intensity-modulated radiotherapy in a whole ventricular irradiation: a planning comparison study

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ABSTRACT

This study evaluated the dosimetric difference between volumetric-modulated arc therapy (VMAT) and conventional fixed-field intensity-modulated radiotherapy (cIMRT) in whole-ventricular irradiation. Computed tomography simulation data for 13 patients were acquired to create plans for VMAT and cIMRT. In both plans, the same median dose (100% = 24 Gy) was prescribed to the planning target volume (PTV), which comprised a tumor bed and whole ventricles. During optimization, doses to the normal brain and body were reduced, provided that the dose constraints of the target coverage were satisfied. The dose-volume indices of the PTV, normal brain, and body as well as monitor units were compared between the two techniques by using paired *t*-tests. The results showed no significant difference in the homogeneity index (0.064 *vs*. 0.065; $p = 0.824$) of the PTV and conformation number (0.78 *vs*. 0.77; $p = 0.065$) between the two techniques. In the normal brain and body, the dose-volume indices showed no significant difference between the two techniques, except for an increase in the volume receiving a low dose in VMAT; the absolute volume of the normal brain and body receiving 1 Gy significantly increased in VMAT by 1.6% and 8.3%, respectively, compared with that in cIMRT (1044 *vs*. 1028 mL for the normal brain and 3079.2 *vs*. 2823.3 mL for the body; $p < 0.001$). The number of monitor units to deliver a 2.0-Gy

fraction was significantly reduced in VMAT compared with that in cIMRT (354 *vs*. 873, respectively; p <0.001). In conclusion, VMAT delivers IMRT to complex target volumes such as whole ventricles with fewer monitor units, while maintaining target coverage and conformal isodose distribution comparable to cIMRT; however, in addition to those characteristics, the fact that the volume of the normal brain and body receiving a low dose would increase in VMAT should be considered.

Keywords:

Germinoma

Whole-ventricular irradiation

VMAT

Planning study

Introduction

Whole-ventricular irradiation (WVI) has been indispensable to high local/regional control and survival rates in patients with localized intracranial germinoma.[1] Intensity-modulated radiotherapy (IMRT) is an advanced radiation technique that delivers a conformal dose to the target and spares organs at risk (OARs). In WVI, conventional fixed-field IMRT (cIMRT) has shown dosimetric advantages in normal tissue sparing.[2-5] Sparing normal tissue is considered helpful in sustaining cognitive function and social status in long-term survivors with brain tumors that originate during childhood.[6] In addition to the advantage regarding OARs, WVI using cIMRT has been reported to improve target coverage,[5] which can be important in controlling a tumor. WVI using cIMRT may reduce late side effects related to radiotherapy without compromising local/regional control for patients with localized intracranial germinoma.

Volumetric-modulated arc therapy (VMAT), developed by Otto,[7] is now commercially available as the RapidArc system (Varian Medical Systems, Palo Alto, CA). RapidArc can deliver IMRT with dynamic arcs by changing three mechanical parameters: the

gantry rotation speed, multi-leaf collimator motion, and dose rate. The mechanical characteristics of RapidArc result in IMRT with fewer monitor units while maintaining target coverage and OAR sparing that are comparable to cIMRT in planning studies of primary intracranial tumors.[8-10] In WVI, VMAT is expected to reduce monitor units without compromising plan quality, compared with cIMRT; however, to our knowledge, no information is available regarding the planning comparison between VMAT and cIMRT in WVI. One published report of VMAT in WVI was a comparison between VMAT and three-dimensional conformal radiotherapy. [11] The aim of the present study was to reveal the dosimetric differences in WVI between plans using VMAT with the RapidArc system and those using cIMRT.

Methods and materials

Patient characteristics

The present study included 13 patients, who underwent radiotherapy following induction chemotherapy for localized intracranial germinoma at Kyoto University Hospital between

June, 2003 and March, 2010. Induction chemotherapy yielded a complete response in all patients enrolled in the current study. Computed tomography (CT) simulation and magnetic resonance imaging data for 12 of 13 patients were acquired previously for a dosimetric comparison between three-dimensional conformal radiotherapy and cIMRT.[5] Data for one female patient with bifocal localized intracranial germinoma were added to the present study. Details of the CT simulation and the delineation of the planning target volume (PTV) were described previously.[5] In the present study, the normal brain, body, and lens were delineated as the OARs. The normal brain was defined as the brain volume outside the PTV. The region scanned in the CT simulation was from the top of the head to the neck, which was sufficient to include the irradiated volume. The mean age was 17.5 years (range, 5–34 years). The primary sites were the pineal region (n = 4), suprasellar region (n = 5), and bifocal region (pineal and suprasellar; n = 4). The mean volumes of the tumor bed, whole ventricles, PTV, normal brain, and body were 3.6 mL (range, 0.1–15.6 mL), 52.9 mL (range, 33.3–84 mL), 363.4 mL (range, 295.7–425.0 mL), 1048.4 mL (range, 759.3–1210.3 mL), and 4923.5 mL (range, 3724–9549.2 mL), respectively.

Treatment planning

Treatment planning for VMAT and cIMRT was performed using Eclipse (ver. 8.6.15; Varian Medical Systems, Palo Alto, CA). All treatment plans were created with 6-MV photon beams, commissioned for a Varian CL21iX linear accelerator and Millennium 120-leaf multi-leaf collimator (Varian Medical Systems). Dose calculation was performed using the anisotropic analytical algorithm[12] with a calculation grid of 2.5 mm. The isocenter was placed in the center of the PTV.

The cIMRT plans consisted of seven coplanar fields with angles of 0, 55, 105, 155, 205, 255, and 305°. The Varian's Eclipse fluence-based algorithm was used in the optimization. Multi-leaf collimator leaf sequences were generated using the dynamic sliding-window technique.[13] The accuracy of cIMRT dose delivery is affected by the dose rate, although a higher dose rate can theoretically reduce the beam-on time in cIMRT.[14] We set the dose rate for cIMRT as 300 monitor units/min, which is the dose rate adopted for cIMRT plans using the dynamic sliding-window technique at our hospital.

VMAT plans were created for the RapidArc system (Varian Medical Systems) with coplanar double arcs, because RapidArc with a single arc has difficulty in achieving conformal dose distribution for complex target volumes.[15] One arc rotation was clockwise, from -179 to 179°, and the other was counter-clockwise, from 179 to -179°. The couch position was set at 0°. The collimator angles were 45° and 315° in each arc. The maximal dose rate and maximal gantry speed were set as 600 monitor units/min and 4.8°/s, respectively. The coplanar double arcs were optimized simultaneously.

For optimization, dose constraints were prioritized to satisfy the target coverage requirement: D98% (DX% represents the dose covering X% of the structure volume) to the PTV was larger than 98% of the prescribed dose (100% = 24 Gy in 12 fractions), and D2% to the PTV was lower than 107% of the prescribed dose. The planning objectives were set for identical structures; PTV and normal brain, however the parameters for optimization were individually set for each patients to make conformal isodose distribution to the PTV. Provided that the target objectives were satisfied, D2% and the median dose (D50%) to the normal brain were reduced. After optimization, the value of D50% to the PTV in the VMAT plan was

normalized to the same value as that in cIMRT. When the dose indices violated the constraints after the normalization process, optimization of the VMAT plan was restarted until the dose constraints of the PTV were satisfied.

Assessment of endpoints

The mean dose-volume histograms (DVHs) of the PTV, normal brain, and body were created from the dose-volume data of 26 cIMRT and VMAT plans. To compare the target coverage, D2%, D98%, and the homogeneity index (HI) were calculated. HI was defined as (D2%–D98%)/D50% [16]. For the normal brain and body, D50%, and the volume receiving 18, 12, 6, 3, and 1 Gy (V_{18Gy}, V_{12Gy}, V_{6Gy}, V_{3Gy}, and V_{1Gy}) were compared between the two techniques. Additionally, D2% in the normal brain was evaluated. D50% was used to compare the dose to the lens between the two techniques. Conformity was evaluated by the conformation number (CN).[17] The CN was defined as $(TV_{RI}/TV) \times (TV_{RI}/V_{RI})$, where TV_{RI} = the target volume covered by the reference isodose, TV = target volume, and V_{RI} = the volume of the reference isodose. The 95% isodose was used as the reference isodose in the present study. To compare the quality of our plan with that of a previous study,[5] we also

evaluated the maximal dose (Dmax), D95%, D99%, and the percentage volume receiving 100% of the prescribed dose (V100%) of the PTV, as calculated in the previous study. The numbers of monitor units to deliver a 2-Gy fraction were calculated for both techniques.

Statistical analysis

The HIs of the PTV, CN, V_{18Gy}, V_{12Gy}, V_{6Gy}, V_{3Gy}, and V_{1Gy}, and the numbers of monitor units were compared between cIMRT and VMAT using paired *t*-tests. All statistical tests were two-sided. A *p*-value less than 0.05 was deemed to indicate statistical significance. Statistical analyses were conducted using Graphpad software (ver. 5.03; Graphpad Software, San Diego, CA).

Results

Target coverage

The mean D50% to the PTV was 102.4% (range, 101.9–103.1%) of the prescribed dose in both techniques. No significant differences in HI or CN were observed between cIMRT and VMAT (0.064 *vs*. 0.065, respectively, for the HI [$p = 0.824$] and 0.78 *vs*. 0.77 respectively,

for the CN [p = 0.065]). Both techniques resulted in a conformal isodose distribution to the PTV (Fig. 1). The shapes of the mean DVH of the PTV were similar in cIMRT and VMAT (Fig. 2). The mean D2%, D98%, D95% values to the PTV, and V100% of the PTV (standard deviation) were: 104.8% (0.3) *vs*. 105.3% (0.5), 98.2% (0.2) *vs*. 98.7% (0.4), 99.6% (0.2) *vs*. 99.9% (0.3) and 93.3% (1.1) *vs*. 93.9% (1.5), respectively, in cIMRT and VMAT. The absolute differences in these dose indices between the two techniques were 0.3–1.9% of the prescribed dose.

Dose to organs at risk

No significant difference was observed between cIMRT and VMAT regarding D50% to the normal brain (63.2% *vs*. 62.5%, respectively; p = 0.137) and body (14.6% *vs*. 14.3%, respectively; p = 0.549). The shapes of the mean DVH of the normal brain and body were generally similar in cIMRT and VMAT, except for the volume that received a low dose, which was larger in VMAT than in cIMRT (Fig. 2 and Table 1). The V_{1Gy} values for the normal brain and body were significantly higher in VMAT; however, the V_{3Gy} and V_{6Gy}

values for the normal brain and body were significantly lower in VMAT than in cIMRT. The absolute increases in V_{1Gy} in the normal brain and body were 16 and 256.0 mL, respectively. The absolute decreases in V_{3Gy} and V_{6Gy} were 5.0 and 10.1 mL, respectively, in the normal brain, and 21.0 and 41.0 mL, respectively, in the body. The D50% to the lens (standard deviation) was significantly higher in VMAT than in cIMRT (1.6 Gy (0.90) *vs*. 1.2 Gy (0.72), respectively; p <0.001). The mean number of monitor units to deliver a 2.0-Gy fraction was significantly higher in cIMRT than in VMAT (873 *vs*. 354, respectively; p <0.001).

Discussion

VMAT remains a developing technique compared with cIMRT. The shape of whole ventricles includes concave and convex contours. It has been reported that large or complex target volumes cause difficulties in creating VMAT plans that are comparable to those for cIMRT.[8,9] Moreover, the quality of the required plan influences the feasibility of VMAT.[18] In WVI for localized intracranial germinoma, high-quality planning is essential because sufficient target coverage of complex target volumes is indispensable for high local/regional

control and overall survival.[19] We previously reported dose indices of the PTV achieved in WVI using conventional three-dimensional conformal radiotherapy.[5] Compared with that report, the dose indices in the present study show comparable target coverage; the absolute differences in Dmax, D95%, D99%, and V100% of the PTV between the present and previous reports are less than 1–3% of the prescribed dose. As shown in Fig. 1, together with adequate target coverage, the conformal isodose distribution to the PTV spares the normal brain. In WVI, VMAT using double arcs can deliver conformal dose distribution to the PTV while maintaining adequate target coverage, which was comparable to that of cIMRT.

The present study focused on low-dose exposure of the normal brain and body within the irradiation field in VMAT. The whole ventricles were centrally located and surrounded by normal brain and body. In VMAT, the beam reaches the target from multiple angles, presenting the risk of spreading the dose to surrounding normal tissue within the irradiation field. In fact, the current study revealed an increase in low-dose exposure within the irradiation field in VMAT, compared with cIMRT. Intracranial germ cell tumors are most often found in patients in the early pubertal years.[20] The effects of increased low-dose

exposure on normal surrounding tissue raise concerns regarding carcinogenesis. Hence, for clinical use of VMAT, we should consider the dosimetric character: the volume of the normal brain and body within the irradiation field that receives a low dose is higher in VMAT.

In the present study, the increased volume receiving a low dose in the normal brain and body was limited to V_{1Gy}. Although a biological discussion is not the major focus of the current paper, the biological impact in terms of carcinogenesis has been reported to be lower for low-dose exposure than for high-dose exposure.[21] Tubiana suggested that potent defenses against the carcinogenic effects of ionizing radiation were more effective at low doses, based on animal and human data.[21] Some authors have reported that a dose per fraction of less than 120 to 160 mGy cumulating to about 3 Gy caused less carcinogenesis than higher doses per fraction.[22, 23] The effects of the observed increase of V_{1Gy} are small, which would be counterbalanced by the decrease in V_{6Gy} and V_{3Gy} in the normal brain and body. We believe that use of VMAT can be justified provided that the increased irradiated volume of the normal surrounding tissue is limited to the low-dose volume, as observed in the current study.

In this study, the different dose rates were used in each technique. In VMAT, the higher dose rates achieved the smaller number of monitor units by the compensation of gantry speed and multi leaf collimator motion.[24, 25] Thus in VMAT, we selected the maximal dose rate as 600 monitor units/min which was the maximally available dose rate from the previous reports. Differently from VMAT, the dose rate is basically unchanged through beam-on time in cIMRT. It was reported that the higher the dose rates were, the larger the number of monitor units was in cIMRT.[26] The number of monitor units is associated with the amount of transmitted radiation dose through the multi leaf collimator and the treatment time. Considering our clinical practice and published paper's recommendation, we set the dose rates as 300 monitor units/min for cIMRT, although it was smaller dose rate than in VMAT. It is important to select the optimal dose rate in VMAT and cIMRT planning, reflecting that the dosimetric effects from the dose rates differed between two techniques.

The longer beam-on time in cIMRT increases the exposure of normal tissue to low doses outside the irradiation field,[27] as confirmed by dosimetric studies.[4,28] For instance, Mansur *et al*. reported that the dose outside the irradiation field was 1–10 cGy higher in

cIMRT than in conventional radiotherapy when 54 Gy were delivered in 30 fractions to a phantom of a young patient with an intracranial tumor.[28] Matuszak *et al*. emphasized that VMAT reduces low-dose exposure outside the irradiation field because it requires fewer monitor units.[29] They hypothesized that the reduced low-dose exposure may alleviate concerns regarding secondary malignancies in young patients. Most importantly, dose reduction outside the irradiation field is desirable; however, the reported absolute dose reduction outside the irradiation field is relatively small compared with that inside the irradiation field. Biologically, low-dose exposure has been reported to have a minimal impact on carcinogenesis.[21] In fact, 78% of secondary malignancies occur in the area within or surrounding the PTV,[30] where the higher dose is prescribed. Thus, we believe that in considering VMAT planning the focus should be on dose exposure within, rather than outside, the irradiation field.

The lens is particularly sensitive to radiation. The threshold dose for cataract formation has been reported to be 2–10 Gy.[31] The lens is located in the peripheral region of the irradiation field, where VMAT may increase low-dose exposure. In previous reports on

the use of RapidArc for intracranial tumors, the lens received more than 10% of the prescribed dose.[10,32] In the present study, the total dose received by the lens was maintained below 2 Gy, which was 6.6% of the dose prescribed in the VMAT plans. It is thought that the reduced dose to the lens was the result of tilting the patient's head during the radiotherapy treatment. In the CT data used in the present study, the patients were supine with the head tilted, which facilitated sparing of the lens, as was found in a previous study in which a head-tilted technique was used.[9] Our results support the feasibility of sparing the lens in VMAT using the RapidArc system.

In conclusion, VMAT delivers IMRT to a complex target volume, such as whole ventricles, with fewer monitor units while maintaining target coverage and OAR sparing comparable to cIMRT. However, the fact that a greater volume of the normal brain and body within the irradiation field receives a low dose in VMAT should be considered when planning.

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Fig. 1. Multi-plane slices showing isodose distribution for cIMRT and VMAT.

Shaded cyan area = tumor bed before induction chemotherapy; shaded red area = planning target volume. Yellow line indicates 100%; green, 95%; light blue, 90%; dark blue, 80%; orange, 70%; and pink, 50% of the isodose line.

Abbreviations: cIMRT = conventional fixed-field intensity-modulated radiotherapy; VMAT = volumetric-modulated arc therapy using the RapidArc system.

Fig. 2. Mean cumulative dose-volume histograms of the PTV, normal brain*, and body.

Abbreviations: PTV = planning target volume; cIMRT = conventional fixed-field intensity-modulated radiotherapy; VMAT = volumetric-modulated arc therapy using the RapidArc system.

Foot notes: * normal brain = the volume of the brain outside the PTV.

Table

Table 1. Summary of dose-volume histogram analysis of the PTV, normal brain*, and body (mean value [standard deviation]).

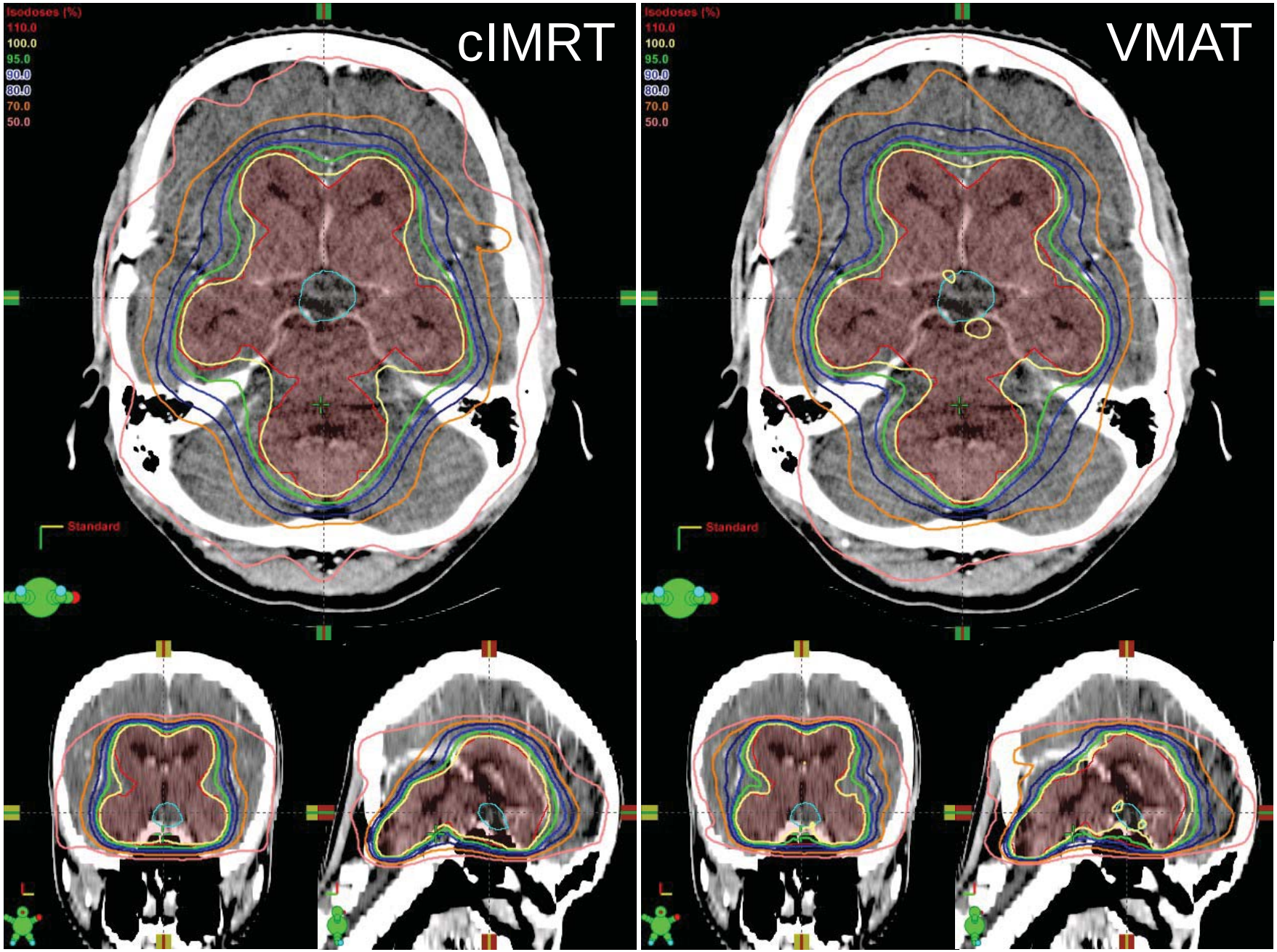
	cIMRT	VMAT	Difference	*p*†
PTV				
Homogeneity index‡	0.064 (0.004)	0.065 (0.006)	+0.001	0.824
Normal brain				
D2% (%)	100.1 (0.7)	100.8 (0.8)	+0.7	0.024
D50% (%)	63.2 (3.1)	62.5 (2.9)	−0.7	0.137
V_{18Gy} (mL)	316.9 (35.8)	313.3 (32.5)	−3.6	0.540
V_{12Gy} (mL)	737.1 (67.8)	741.6 (75.1)	+4.5	0.586
V_{6Gy} (mL)	880.2 (92.9)	870.1 (88.7)	−10.1	0.004
V_{3Gy} (mL)	919.2 (97.9)	914.2 (94.5)	−5.0	0.049
V_{1Gy} (mL)	1028.0 (119.1)	1044.0 (130.2)	+16.0	0.027
Body				

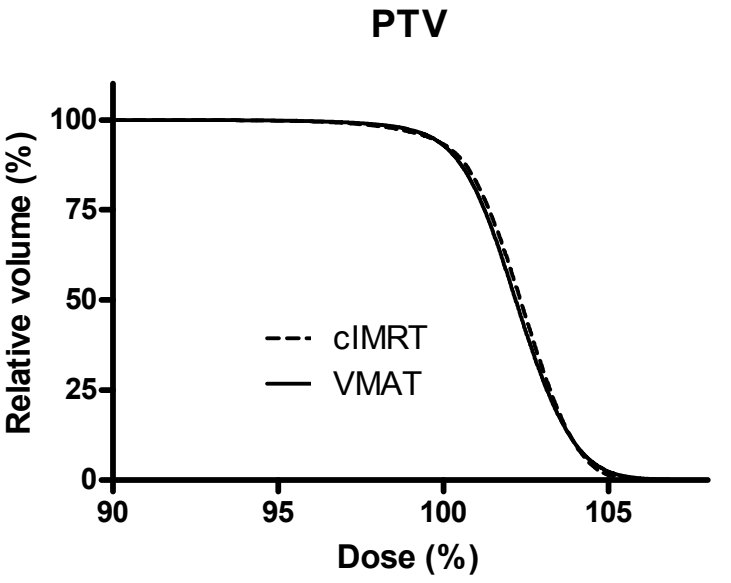
D50% (%)	14.6 (10.3)	14.3 (9.1)	−0.3	0.549
V_{18Gy} (mL)	725.2 (57.7)	719.7 (60.1)	−5.5	0.395
V_{12Gy} (mL)	1352.0 (114.3)	1351.9 (125.6)	−0.1	0.996
V_{6Gy} (mL)	2053.2 (233.2)	2012.0 (227.0)	−41.0	<0.001
V_{3Gy} (mL)	2323.9 (312.5)	2303.5 (312.4)	−21.0	<0.001
V_{1Gy} (mL)	2823.3 (396.5)	3079.2 (427.6)	+256.0	<0.001
Conformation number#	0.78 (0.034)	0.77 (0.034)	−0.01	0.065
Monitor units	873.1 (95.1)	354.1 (28.3)	−519.0	<0.001

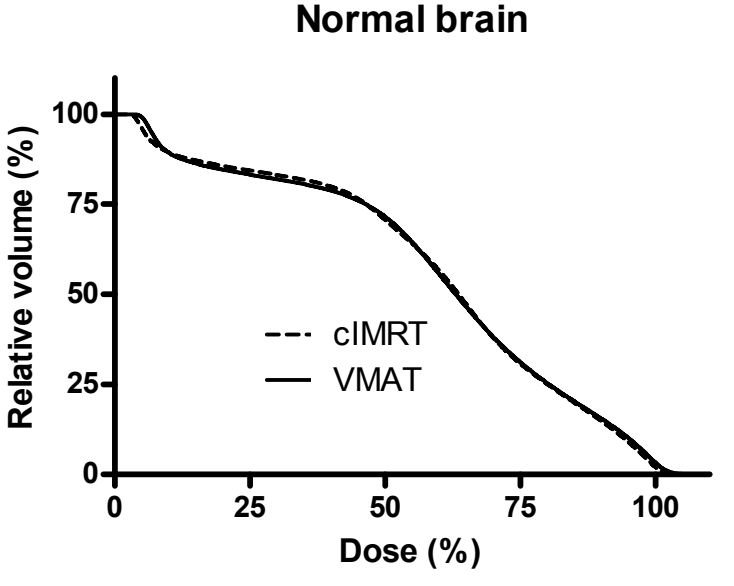
Abbreviations: PTV = planning target volume; cIMRT = conventional fixed-field intensity-modulated radiotherapy; VMAT = volumetric-modulated arc therapy using the RapidArc system; DX% = the dose that covers X% of the structure volume; V_{XGy} = the absolute volume receiving X Gy.

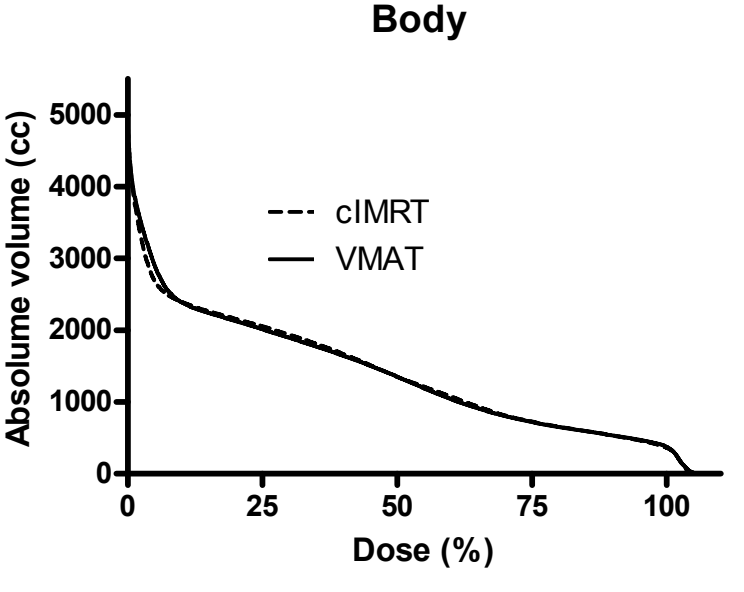
Footnotes: * normal brain = the volume of the brain outside the PTV; † *p*-value with paired *t*-test; ‡ homogeneity index = (D2%−D98%)/D50% [15]; # conformation number = (TV_{RI}/TV) ×

(TV_{RI}/V_{RI}), where TV_{RI} = the target volume covered by the reference isodose, TV = target volume, and V_{RI} = the volume of the reference isodose[16] The 95% isodose was used for the reference isodose


cIMRT
VMAT
Isodoses (%)
110.0
100.0
95.0
90.0
80.0
70.0
50.0
Standard


PTV
Relative volume (%)
100
75
50
25
0
90
95
100
105
Dose (%)
cIMRT
VMAT


Normal brain
Relative volume (%)
100
75
50
25
0
0
25
50
75
100
Dose (%)
cIMRT
VMAT


Body
Absolume volume (cc)
5000
4000
3000
2000
1000
0
0
25
50
75
100
Dose (%)
cIMRT
VMAT