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Plan Quality Comparison Between Hippocampus-Sparing Whole-Brain Radiotherapy Treated With Halcyon and Tomotherapy Intensity-Modulated Radiotherapy

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Abstract

Objective: Hippocampus-sparing whole-brain radiotherapy using Halcyon, an instrument dedicated to volumetric modulated arc therapy, has not been studied till date; hence, we aimed to examine whether it can meet the RTOG0933 criteria. Based on this, we compared Halcyon to Tomotherapy, which also uses an O-ring-type linear accelerator. **Methods:** This exploratory, experimental, and retrospective study used 5 sets of computed tomography images in the head area to investigate the planning target volume, hippocampal doses, and irradiation time. Calculations were performed from 1 to 4 arcs to determine the optimal number of arcs in the Halcyon plan, which were compared to those of Tomotherapy. **Results:** The Radiation Therapy Oncology Group 0933 criteria could not be satisfied in Halcyon with 1 arc. With 2 arcs, the condition D_{max}<16 Gy was not satisfied for 1 case in the hippocampus. Since there were no significant differences between 3 and 4 arcs, including the irradiation time, 3 arcs were considered the best. We compared Halcyon at 3 arcs with tomotherapy and found that tomotherapy was inferior to Halcyon at $D_{98\%}$; however, it was superior to Halcyon in other dose parameters. In contrast, the irradiation time in Halcyon was overwhelmingly superior, with the irradiation time for Halcyon being 1/ninth the time for Tomotherapy. **Conclusion:** Halcyon was effective in handling hippocampus-sparing whole-brain radiotherapy. We believe that 3-arc radiation is best suited for this procedure. Although Halcyon was inferior to Tomotherapy in terms of dose distribution excluding $D_{98\%}$, it was overwhelmingly superior in terms of irradiation time.

Keywords

Halcyon, tomotherapy, volumetric modulated arc therapy, irradiation time, hippocampus-sparing whole-brain radiotherapy

Abbreviations

CT, computed tomography; DX%, dose reaching X% of the volume; HS-WBRT, hippocampus-sparing whole-brain radiotherapy; IMRT, intensity-modulated radiotherapy; LINAC, linear accelerator; MLC, multileaf collimator; PTV, planning target volume; RTOG, radiation therapy oncology group; VMAT, volumetric modulated arc therapy

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Introduction

Halcyon is a volumetric modulated arc therapy (VMAT) instrument with an O-ring type linear accelerator (LINAC), and only 12 units have been installed in Japan (as of January 2022). There have been reports comparing it to VMATs using C-arm type LINACs in treating cervical cancer,[1] breast cancer,[2] and prostate cancer;[3] however, reports comparing Halcyon to

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tomotherapy, an apparatus dedicated to helical intensity-modulated radiotherapy (IMRT) that also employs the O-ring type LINAC, have been limited. Panda et al[4] have reported that in the treatment of cervical cancer, the Halcyon-based treatment plan is equivalent to the helical Tomotherapy-based treatment plan.

IMRT is essential for hippocampus-sparing whole-brain radiotherapy (HS-WBRT), but the treatment planning takes time. The "how-to" guide/criteria in the Radiation Therapy Oncology Group (RTOG) 0933 study[5,6] showed that cognitive impairment can be effectively reduced using HS-WBRT.[7] In recent years, IMRT methods have evolved, and the main approach to the treatment is changing from multifield IMRT to VMAT. There are reports on HS-WBRT performed using VMAT irradiation,[8–11] which suggest that both multifield IMRT and VMAT irradiations use noncoplanar irradiation, except in tomotherapy. However, noncoplanar irradiation is not possible with Halcyon, and it requires a different protocol from VMAT, which employs a C-arm type accelerator.

To the best of our knowledge, there have been no reports of HS-WBRT using Halcyon. Therefore, in this study, we aimed to verify whether HS-WBRT using Halcyon meets the RTOG0933 protocol and compare Halcyon to Tomotherapy.

Table 1. The Optimization Objectives Volume

	Volume (cm^3)	Range
Planning target volume (PTV)	1745.65	1543.18-2044.69
Hippocampus	4.08	2.33-4.75
Eye	15.98	8.59-21.61
Lens	0.19	0.15-0.24

Material and Methods

This is an exploratory, experimental, and retrospective study using 5 sets of computed tomography (CT) plan data from patients with brain metastases. For CT imaging, Aquarion LB (Toshiba) was used for contouring the brain, hippocampus, eye, lens, optic nerve, and optic chiasm simultaneously, based on images taken using magnetic resonance imaging T2-weighted and gadolinium contrast-enhanced T1-weighted scans. The hippocampal zone to be avoided was delineated with a 5 mm margin. The planning target volume (PTV) was defined as the volume of the brain minus the 5 mm margin hippocampal zone, and contour information was fused to CT data using RayStation (Ray Research Laboratories). Table 1 lists the contours used.

Halcyon planning was performed using Eclipse (version 15.6; Varian Medical Systems), and AcurosXB was used as the calculation algorithm. Calculations were performed from 1 to 4 arcs with a single arc of 360° rotation. The isocenter of

Table 2. Irradiation Fields for Halcyon (2 to 4 arcs)

Field ID	Gantry angle (deg)	Collimetor angle (deg)	Field X1	Field X2
Field 1	179.0 −181.0 CCW	10	− 2.0 cm	14.0 cm
Field 2	181.0 −179.0 CW	280	−14.0 cm	2.0 cm
Field 3	179.0 −181.0 CCW	10	− 2.0 cm	14.0 cm
Field 4	181.0 −179.0 CW	280	−14.0 cm	2.0 cm

Fields 1 and 2 were used for 2 arcs.
Fields 1 to 3 were used for 3 arcs.
Fields 1 to 4 were used for 4 arcs.
Abbreviations: CCW: counter clockwise; CW: clockwise

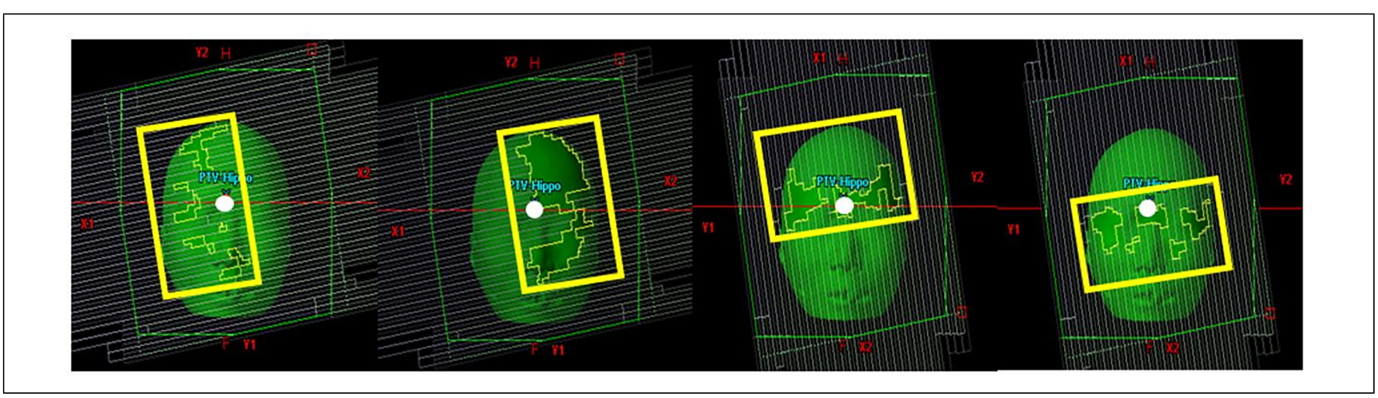

Figure 1. Image showing the 4-arc irradiation field setting with Halcyon. The white dots indicate the isocenter.

each beam was automatically set using Eclipse. The irradiation field was fitted to the PTV with a collimator angle of 45° for 1 arc and multileaf collimator (MLC) in the middle contact. For irradiation with 2 to 4 arcs, the collimator angle was 280° or 10° (Table 2), with an asymmetric irradiation field where 1 of the 2 sides of the MLC direction had an opening of 2 cm from the isocenter. Figure 1 shows an image of the 4-arc irradiation. Optimization was performed by fixing 1 parameter so that the differences between the arcs could be compared, as shown in Table 3. Tomotherapy was optimized using the Tomotherapy Planning Station, as shown in Table 4 (version 5.1.1.6; Accuray Incorporated).

The results were compared with the dose constraints of the PTV and hippocampus, according to RTOG0933 (Table 5). A *t*-test was used to analyze the differences. Statistical significance was set at $P < .05$. All statistical analyses were performed using Microsoft Excel 2019 software package (Microsoft).

Table 3. Optimization Constraints (Halcyon)

	Type	Vol (%)	Dose (Gy)	Priority
Planning target volume (PTV)	Upper	0.0	30.0	400
	Lower	100.0	28.0	300
Hippocampus	Upper	0.0	10.0	300
Lens	Upper	0.0	3.0	100
Eye	Upper	0.0	10.0	100

$D_{95\%} = 30$ Gy in 10 fractions.

Table 4. Optimization Constraints (Tomotherapy)

	Block type	Max dose	Dose-volume histogram (DVH) volume/dose	Importance and penalty
Hippocampus	Unblocked	12 Gy	$D_{50\%} = 6$ Gy	200
Lens	Directional	2.5 Gy	$D_{70\%} = 1.5$ Gy	40
Eye	Directional	3 Gy	$D_{20\%} = 2$ Gy	20
External	Unblocked	30 Gy	$D_{10\%} = 5$ Gy	1

$D_{95\%} = 30$ Gy in 10 fractions. Max dose and min dose: 30 Gy. Importance and penalty: 400. Jaw size: 1 cm, pitch = 0.215, modulation factor = 3.0

Results

Table 5 shows the data according to the number of arcs in Halcyon irradiation. The study shows that for Halcyon at 1 arc, D_{min} of the hippocampus met the dose constraints of RTOG0933 and that HS-WBRT would be intolerable with 1 arc. Moreover, with 2 arcs, 1 case did not meet the criterion of $D_{max} < 16$ Gy in the hippocampus. However, all dose constraints were met at 3 and 4 arcs, and tomotherapy.

Table 6 shows the results of statistical studies on the number of arcs. In the analysis with 2 and 3 arcs, the results for 3 arcs were significantly better in terms of the $D_{2\%}$ and $D_{50\%}$ of PTV, and D_{max} of the hippocampus. There was no significant difference in the irradiation time between 2 and 3 arcs and there were

Table 6. Consideration Based on the Number of Arcs in Halcyon Irradiation

Structure	Parameter	Two arcs versus 3 Arcs	Three arcs versus 4 Arcs	Three-Arc versus Tomotherapy
Planning target volume (PTV)	$D_{2\%}$	0.002	0.51	< 0.001 T
	$D_{98\%}$	0.25	0.17	< 0.001 H
	$D_{50\%}$	0.002	0.78	< 0.001 T
Hippocampus	D_{max}	0.07	0.90	< 0.001 T
	D_{min}	0.90	0.61	0.19
	$D_{50\%}$	0.61	0.40	0.57
Eye	D_{max}	0.30	0.81	< 0.001 T
Lens	D_{max}	0.70	0.62	0.002 T
Monitor unit		0.48	0.40	N/A
Irradiation time		0.48	0.38	< 0.001 H

Note: Two arcs versus 3 arcs: Three-arc irradiation was better for all items with a significant difference.
Three-Arc versus tomotherapy: The column on the right shows the one that was superior (T: tomotherapy, H: Halcyon 3-arc irradiation).

Table 5. Dose Constraints in RTOG0933 and the Results of the Irradiation Doses

Structure	Parameter	RTOG0933 Criteria	Halcyon				Tomotherapy
			1 Arc	2 Arc	3 Arc	4 Arc	
PTV	$D_{2\%}$	< 37.5 Gy	42.36 ± 1.24	35.58 ± 0.23	34.65 ± 0.34	34.47 ± 0.38	33.07 ± 0.34
	$D_{98\%}$	> 25 Gy	22.82 ± 1.86	28.48 ± 0.11	28.35 ± 0.19	28.04 ± 0.36	25.34 ± 0.61
	$D_{50\%}$		38.78 ± 1.04	33.21 ± 0.13	32.62 ± 0.21	32.67 ± 0.27	31.60 ± 0.32
Hippocampus	D_{max}	< 16 Gy	18.76 ± 1.24	15.92 ± 1.34	14.32 ± 0.40	14.28 ± 0.41	12.63 ± 0.60
	D_{min}	< 9 Gy	6.83 ± 0.33	6.36 ± 0.15	6.35 ± 0.17	6.43 ± 0.28	6.15 ± 0.22
	$D_{50\%}$		10.09 ± 0.22	7.80 ± 0.27	7.89 ± 0.17	8.02 ± 0.24	8.02 ± 0.44
Eye	D_{max}		30.14 ± 6.41	20.63 ± 1.71	19.45 ± 1.24	19.72 ± 1.75	12.47 ± 2.18
Lens	D_{max}		14.36 ± 3.00	9.37 ± 2.46	8.78 ± 1.66	9.50 ± 2.25	3.32 ± 0.56
Monitor unit			1464 ± 77	1947 ± 219	2052 ± 172	2160 ± 172	N/A
Irradiation time	second		118.7 ± 6.3	157.9 ± 17.8	166.4 ± 14.0	175.4 ± 13.8	1539.9 ± 95.5

Abbreviations: RTOG: Radiation Therapy Oncology Group; PTV: planning target volume.

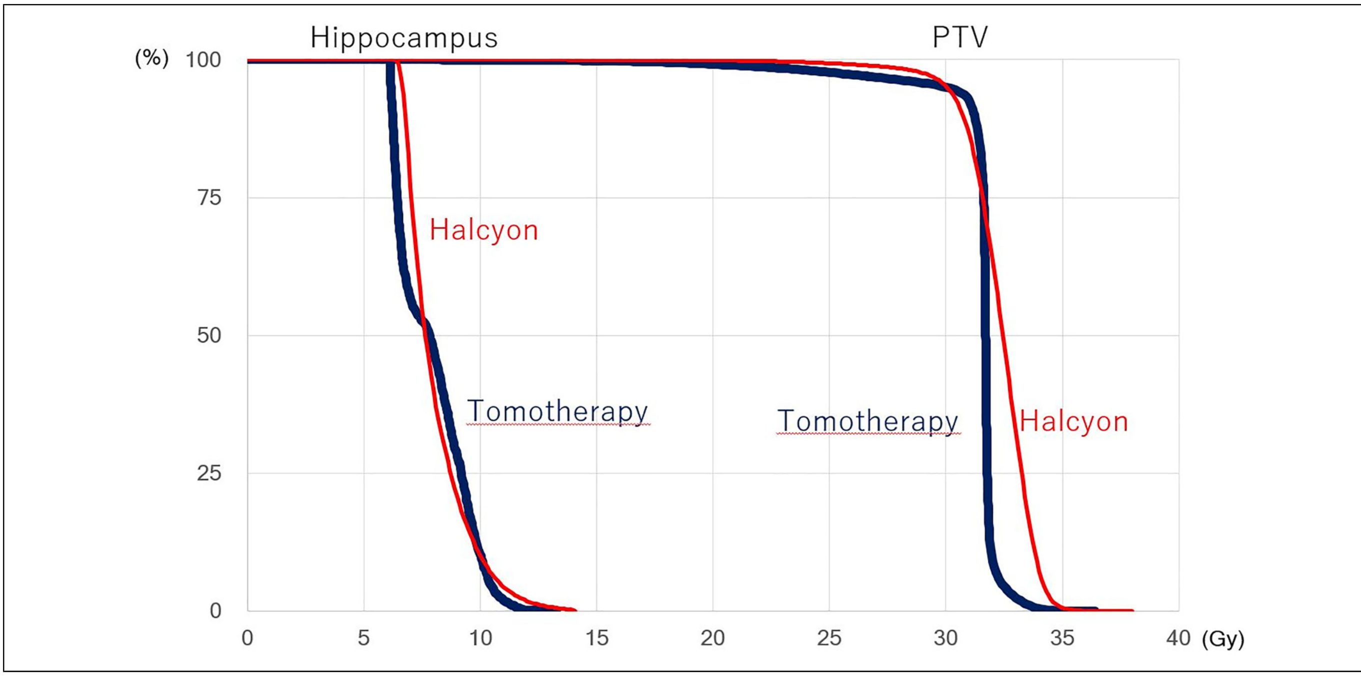

Figure 2. Dose volume histogram of Halcyon 3-arc irradiation and tomotherapy

no other significant differences between 3 and 4 arcs. However, the monitor unit and irradiation times were shorter with 3 arcs; therefore, 3-arc irradiation was considered better for HS-WBRT with Halcyon.

Table 6 shows a comparison between 3-arc irradiation and tomotherapy. Figure 2 shows the dose-volume histogram for 1 case. The $D_{98\%}$ of tomotherapy was inferior compared to that of Halcyon. However, for many other dose parameters, tomotherapy was superior. With respect to irradiation time VMAT showed superiority, with the irradiation time being < 3 min using VMAT as opposed to 25 min using tomotherapy.

Discussion

When the RTOG0933 study was conducted, it was proposed that 9-field IMRT irradiation or helical IMRT using tomotherapy be performed for HS-WBRT.[7] Since then, the IMRT method has evolved, and the main approach is changing from multifield IMRT to VMAT. Even if VMAT is used for HS-WBRT, a treatment plan comparable to IMRT can be performed.[8,9]

Generally, noncoplanar beams are used to consider HS-WBRT, excluding tomotherapy. Gondi et al[7] used 9 noncoplanar IMRT fields with 7 different couch angles for plan optimization. Nevelsky and coauthors used the LINAC-based 9-field IMRT and 2 different couch angles to shorten the treatment time. The maximum dose to the hippocampus in Nevelsky et al's[12] study was lower than the dose reported by Gondi et al. Krayenbuehl et al[10] studied 4-arc radiation with VMAT. They used coplanar radiation for 2 arcs and noncoplanar radiation for the remaining 2 arcs. However, noncoplanar irradiation is not possible in Halcyon. Therefore, a new protocol is required for VMAT.

According to our results, 1-arc irradiation is insufficient for HS-WBRT using Halcyon, and at least 2 arcs are needed. Furthermore, this study demonstrated that 4-arc irradiation was not superior to the 3-arc irradiation. Therefore, we determined that 3-arc irradiation is suitable. We believe that the irradiation field and optimization constraints shown in this study could serve as a guideline for HS-WBRT procedures using Halcyon.

Wang et al[13] reported that 8 out of 10 patients who underwent VMAT using 2 coplanar arcs had minimum and maximum hippocampus doses exceeding the recommended dosage in the RTOG0933 protocol, which may indicate the usefulness of Halcyon compared to the LINAC-based VMAT with the same number of arcs.

Therefore, HS-WBRT using tomotherapy has a better dose distribution compared to LINAC-based IMRT and VMAT.[13,14] The results of this study also showed that tomotherapy is better than the VMAT-dedicated devices, such as Halcyon, in terms of many parameters. Miura et al[15] also suggested that tomotherapy is useful for VMAT in risky organs, such as the hippocampus and lens, and the dose distribution for PTV does not change. In this study, the dose of Tomotherapy was significantly lower in the eyeball and lens. It should be noted that Tomotherapy was found to be inferior in terms of the hippocampal $D_{98\%}$ in the study by Wang et al[13] and our study. In contrast, Halcyon is overwhelmingly superior to tomotherapy in terms of irradiation time. Miura et al[15] reported that the irradiation time was reduced by approximately 10% after applying tilt in tomotherapy. Ishibashi et al[16] reported a reduction in the irradiation time by 30% after reducing the modulation factor. Moreover, Shimizu et al reported that irradiation time can be shortened to 6 min using a 2.5 cm jaw.[17] However, even if these factors are taken into consideration, the superiority of Halcyons' irradiation time remains unchanged. This is because tomotherapy requires a higher number of revolutions due to the helical IMRT, although both systems use the same O-ring system. As in this study, 66–75 rotations, with each rotation lasting for 21–23 s, were used for HS-WBRT; at least 11.8 s per revolution is required for tomotherapy.[16,18]

Determining the superiority of a device superior among all the IMRT-dedicated radiotherapy devices using an O-ring type LINAC is difficult. As evident from the data of the present study, tomotherapy produces a better dose distribution; however, the irradiation time is considerably longer. Panda et al[4] compared treatment plans for cervical cancer between Halcyon and tomotherapy, and reported that there was no difference in the quality of the treatment plans. On the other hand, the irradiation time was 2.4 min for Halcyon (lymph node negative cases) and 3.6 min for tomotherapy, and although a difference was observed, the difference was not as great as that in our study. In this study, we used a complicated irradiation plan, HS-WBRT, which could be a limitation of this study. Due to the higher complexity of HS-WBRT compared to cervical cancer treatment planning, a more complex treatment, tomotherapy may be a better option, but it is desirable to consider it for other diseases in the future. Thus, at this time, the treatment policy of the facility and the number of patients will decide which device will be introduced.

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Authors' Note

Our study was approved by the Ethics Committee of Affiliated JCHO Tokyo Shinjuku Medical Center (approval no. R2-21 and R2-42) and the Ethics Committee of National Cancer Center (approval no. 2020-385).

Authors' Contributions

Conception and design was done by Kazutoshi Yokoyama, Hiromasa Kurosaki. Administrative support was provided by Hajime Oyoshi and Kosei Miura. Provision of study materials or patients was handled by Hiromasa Kurosaki, Kosei Miura, and Nobuko Utsumi. Collection and assembly of data was done by Kazutoshi Yokoyama, Hiromasa Kurosaki, Hajime Oyoshi, and Kosei Miura. Data analysis and interpretation was carried out by Kazutoshi Yokoyama, Hiromasa Kurosaki, Hajime Oyoshi, Nobuko Utsumi. Manuscript writing was performed by all authors.

Declaration of Conflicting Interests

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