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Preserving memory function in whole-brain radiation Therapy: Efficacy of HyperArc and Coplanar VMAT techniques

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► ***Original article***

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ABSTRACT

Background: This study assessed the efficacy of HyperArc planning for whole-brain radiation therapy (WBRT) with hippocampal sparing, comparing it to conventional coplanar volumetric modulated arc therapy (VMAT) techniques using high-definition multileaf-collimators (HDMLC) and millennium MLC (MMLC). ***Materials and Methods:*** In this retrospective study, 25 patients with brain metastases received hippocampus-sparing WBRT by RTOG-0933 trial guidelines. Three treatment plans (HyperArc, VMAT-HDMLC, VMAT-MMLC) were created using Eclipse v16.1 Treatment Planning System (TPS), with a prescribed dose of 30Gy in 10 fractions. The Dosimetric parameters assessed included D98%, D2%, HI, Dmax for PTVeval, and Dmax, Dmean, and D100% for hippocampus and other critical structures. Additionally, Monitor Units (MUs) and delivery checks using portal dosimetry were considered. ***Results:*** All plans met RTOG-0933 criteria for PTV and OARs. HyperArc matched VMAT-HDMLC in D98% (28.41 Gy vs. 28.38 Gy), outperforming VMAT-MMLC (28.04 Gy). HyperArc surpassed both VMAT techniques in D2% (32.83 Gy vs. 33.24 Gy vs. 34.06 Gy), HI (0.14 vs. 0.15 vs. 0.18), and Dmax (34.84 Gy vs. 35.5 Gy vs. 36.36 Gy). In hippocampus sparing, HyperArc achieved lower Dmax (12.99 Gy vs. 13.73 Gy vs. 14.76 Gy), Dmean (9.58 Gy vs. 10.23 Gy vs. 10.64 Gy), and D100% (8.25 Gy vs. 8.70 Gy vs. 8.85 Gy) values. Further, the HyperArc method provided better organ-at-risk sparing and higher gamma results. ***Conclusion:*** All three methods met RTOG-0933 dosimetric goals, with HyperArc outperforming VMAT. Optimized VMAT collimator angles at 0° and 90° improved organ-at-risk doses, exceeding conventional planning in PTV coverage and hippocampal sparing.

INTRODUCTION

The hippocampus, a crucial brain region responsible for learning, memory, and spatial processing, is highly susceptible to radiation-induced damage due to its limited regenerative capacity [1]. Whole-brain radiation therapy (WBRT) is a widely accepted treatment method for various intracranial lesions but often leads to neurocognitive deficits due to acute and chronic changes in the hippocampus [2, 3]. The Radiation Therapy Oncology Group (RTOG) 0933 trial has demonstrated the potential benefits of hippocampal avoidance WBRT (HA-WBRT) in preserving memory function [4]. This trial focused on utilizing Intensity Modulated Radiotherapy (IMRT) techniques to spare the hippocampus during WBRT. Recent studies have assessed the practicality of adhering to RTOG 0933 dose limits via Volumetric Modulated Arc Therapy (VMAT), incorporating both coplanar and non-coplanar beam configurations [5-7].

IMRT and VMAT techniques allow precise targeting of tumours while minimizing radiation dose to critical structures like the hippocampus. These techniques offer improved control over the dose distribution, reducing the risk of radiation-induced damage. Varian Medical Systems has developed HyperArc, a specialized approach for planning and treating intracranial lesions. HyperArc simplifies planning by autonomously choosing the best isocenter and collimator angles while also implementing non-coplanar arc configurations. It aims to achieve precise treatment delivery while minimizing radiation exposure to surrounding healthy tissue [8]. HyperArc utilizes a combination of up to four arcs, including one full coplanar arc and three partial non-coplanar arcs, and employs conventional positioning aids to ensure collision prevention [9]. The primary difference in planning lies between standard VMAT techniques and HyperArc, Additionally, HyperArc enhances delivery efficiency through seamless couch transitions between successive treatment arcs [10,11].

However, this technique led to extended planning and treatment times due to multiple non-coplanar beams. The crucial roles of collimator angles and multileaf-collimator (MLC) thickness in optimizing coplanar VMAT plans became evident, influencing parameters like dose conformity, dose fall-off, and critical organ preservation. Optimal collimator angles allowed precise dose modulation, while MLC thickness optimization achieved a smoother dose fall-off, minimizing healthy tissue exposure [12, 13]. These adjustments enhanced overall plan quality, improving dose distribution in the target area and reducing radiation exposure to normal structures. To address this, the study explores optimizing coplanar VMAT plans, as default collimator angles of 30° and 330° inadequately spared the hippocampus's specific anatomical location while maintaining target coverage. This strategic change not only enhanced plan quality but also reduced both planning and delivery durations.

The newly developed HyperArc Technique automates isocenter placement, beam arrangements, and collimator optimization, reducing manual workloads. This study assesses its effectiveness in WBRT with hippocampal sparing, following RTOG 0933 guidelines. Limited research has validated HyperArc's efficacy in this context. Additionally, the study aims to match HyperArc's plan quality using coplanar VMAT plans with high-definition MLC (HDMLC) and millennium MLC (MMLC), adjusting collimator angles.

MATERIALS AND METHODS

Patient selection, imaging procedures, and organ delineation

Twenty-five patients with brain metastases were involved in this retrospective planning research. All patients had a history of cerebral metastases and a prior primary tumor diagnosis. Each patient underwent imaging, comprising a Computed Tomography (CT) scan using a Philips Brilliance BigBore scanner with slices of 3 mm thickness, and a T1-weighted Magnetic Resonance Image (MRI) acquired with a Philips Ingenia Ambition 1.5T MRI scanner (Philips Healthcare, Amsterdam, The Netherlands). The MRI and CT images were combined to assist in hippocampal delineation. The hippocampal regions were delineated according to the guidelines of the RTOG 0933 contouring protocol. Avoidance areas surrounding each hippocampus were defined by expanding them by 5 mm. Contours were also created for the eyes, optic chiasm, lenses, optic nerves, and brainstem. PTV evaluation (PTVeval) encompassed the WBRT PTV excluding the hippocampal avoidance regions. This parameter was utilized to assess the outcomes of each treatment plan, following the recommendations of the RTOG 0933 trial (table 1).

Dose prescription and planning

All patients received a prescribed dose of 3 Gy per fraction, totalling 30 Gy administered in 10 fractions. Three different treatment plans were generated for each patient.

Table 1. RTOG 0933 dosimetric compliance criteria for hippocampal sparing.

Organ	Dose constraints
Whole brain PTV	$D_{2\%} < 37.5$ Gy, $D_{98\%} > 25$ Gy and $V_{30} > 90\%$
Hippocampus	$D_{100\%} < 9$ Gy and $D_{max} < 16$ Gy

HyperArc planning

The HyperArc plans were developed with Truebeam technology from Varian Medical Systems, Palo Alto, CA, USA, utilizing a 6 MV beam at a maximum rate of 600 monitor units per minute (MU/min). The plans included four arcs arranged by software: one full arc with the couch set at 0°, and three half arcs in non-coplanar configurations with couch rotations at 315°, 45°, and 270°. The isocenter was positioned centrally within the PTV, and collimator angles were optimized based on the target's shape and position. The normal tissue dose objective for stereotactic radiosurgery (SRS NTO) is typically activated as a standard feature in HyperArc plans to uphold strict dose gradient standards. However, it was omitted during the optimization process due to the non-SRS nature of WBRT with hippocampal sparing.

VMAT planning

Two VMAT plans were created, each utilizing two full arcs. Co-planar VMAT plans were generated for each patient using TrueBeam equipped with high-definition Multileaf Collimators (VMAT-HDMLC) and TrueBeam with Millennium Multileaf Collimators (VMAT-MMLC). Both plans utilized a 6 MV beam with a peak dose rate of 600 monitor units per minute (MU/min). Collimator angles are crucial for optimizing coplanar VMAT plans. Our experimentation, guided by prior studies and standard configurations, demonstrated that employing collimator angles of 0° and 90° with two full arcs produced optimal outcomes for enhancing plan quality in coplanar VMAT plans. The planning process employed the Eclipse v16.1 TPS from Varian Medical Systems, Palo Alto, CA, USA, integrating the Photon Optimizer (PO) and Anisotropic Analytical Algorithm (AAA) at a calculation resolution of 0.25 cm.

Evaluation of plans and statistical analysis

The normalization of all treatment plans aimed to achieve 95% coverage of the PTVeval. Dosimetric parameters used for evaluation included V_{30Gy}, $D_{98\%}$, $D_{2\%}$, Homogeneity Index (HI), and D_{max} of PTVeval. For the hippocampus, D_{max}, D_{mean}, and $D_{100\%}$ were evaluated. Hippocampal avoidance, lens, optic nerve, lacrimal gland, and eye were also assessed based on their D_{max} and D_{mean} values. Moreover, the monitor unit (MU) count was taken into consideration. Statistical comparisons among the strategies of the three techniques were performed using a paired t-test. Analyses were conducted using SPSS Version 25 (IBM, USA), with statistical significance set at $p<0.05$.

Quality assurance

Patient treatment delivery accuracy was evaluated with the Varian Medical Systems' aS1200 Digital Megavolt Imager (DMI) system, applying a 2% / 2 mm criteria. The Varian aS1200 Digital Megavolt Imager (DMI) detector features a small pixel size of 0.0336 cm and a large area of 40 × 40 cm^2. It effectively supports FFF beams across varying source-to-detector distances without saturation [14-16].

RESULTS

All the plans met the dosimetric criteria of RTOG 0933 for both PTV and OARs, as shown in table 2. HyperArc plans demonstrated significant improvements across all investigated dosimetric parameters.

Table 2. Dosimetric compliance with RTOG 0933 criteria for PTV and OARs.

Dosimetric Evaluation Parameters		Mean ± Standard Deviation			p-value	
		HyperArc	VMAT-HDMLC	VMAT-MMLC	HyperArc vs VMAT-HDMLC	HyperArc vs VMAT-MMLC
PTV	$D_{98\%}$	28.41±0.55	28.38±0.60	28.04±0.53	0.63	< 0.05
	$D_{2\%}$	32.83±0.63	33.24±0.74	34.06±0.82	< 0.05	< 0.05
	HI	0.14±0.03	0.15±0.0	0.18±0.03	< 0.05	< 0.05
	$D_{max(Gy)}$	34.84±0.75	35.5±0.68	36.36±0.70	< 0.05	< 0.05
Hippocampus	$D_{max(Gy)}$	12.99±0.91	13.73±0.86	14.76±0.93	< 0.05	< 0.05
	$D_{mean(Gy)}$	9.58±0.39	10.23±0.39	10.64±0.59	< 0.05	< 0.05
	$D_{100\%}$	8.25±0.49	8.70±0.43	8.85±0.54	< 0.05	< 0.05
HA	$D_{mean(Gy)}$	27.62±1.0	28.59±1.57	28.80±0.96	< 0.05	< 0.05
Other - OARs	Lens - $D_{max\ (Gy)}$	5.55±0.13	5.89±0.37	6.33±0.38	< 0.05	< 0.05
	ON - $D_{max(Gy)}$	30.47±0.27	30.75±0.34	31.27±0.46	< 0.05	< 0.05
	Eye - $D_{mean(Gy)}$	9.78±0.53	10.88±0.52	11.14±0.39	< 0.05	< 0.05
	LG - $D_{mean(Gy)}$	8.38±0.51	9.00±0.41	9.07±0.54	< 0.05	< 0.05
MUs		914±61	1010±77	910±69	< 0.05	0.76
PSQA (2%/2mm)		99.48±0.16	99.59±0.14	99.20±0.24	0.12	< 0.05

Abbreviations: HA - Hippocampus Avoidance, ON - Optic Nerve, LG - Lacrimal Gland, OARs - Organ At Risk, MUs - Monitor Units, PSQA - Patient-Specific Quality Assurance.

Target coverage

Evaluation of PTV parameters showed no significant differences in $D_{98\%}$ between HyperArc and VMAT-HDMLC ($p=0.63$), with values of 28.41±0.55 and 28.38±0.60, respectively. VMAT-MMLC had significantly less coverage ($p<0.05$) with 28.04±0.53. For $D_{2\%}$, HI, and D_{max} (Gy), HyperArc performed significantly better ($p<0.05$) with values of 32.83±0.63, 0.14±0.03, and 34.84±0.75, compared to VMAT-HDMLC's 33.24±0.74, 0.15±0.03, and 35.5±0.68, and VMAT-MMLC's 34.06±0.82, 0.18±0.03, and 36.36±0.70.

Dose to hippocampus

Regarding hippocampus doses, HyperArc plans provided significantly better sparing ($p<0.05$) with D_{max}, D_{mean} and $D_{100\%}$ values of 12.99±0.91, 9.58±0.39, and 8.25±0.49, respectively, compared to VMAT-HDMLC's 13.73±0.86, 10.23±0.39 and 8.70±0.43 and VMAT-MMLC's 14.76±0.93, 10.64±0.59 and 8.85±0.54.

Dose to other organ at risk

Statistically significant differences ($p < 0.05$) were observed in the maximum doses delivered to the optic nerves and lens, as well as in the mean doses received by the eye and lacrimal gland among the three planning techniques. HyperArc plans achieved doses of 5.55±0.13, 30.47±0.27, 9.78±0.53 and 8.38±0.51, respectively. VMAT-HDMLC plans achieved doses of 5.89±0.37, 30.75±0.34, 10.88±0.52 and 9.00±0.41, respectively. VMAT-MMLC plans achieved doses of 6.33±0.38, 31.27±0.46, 11.14±0.39, and 9.07±0.54, respectively.

Monitor units and QAs

Regarding MUs comparison, the HyperArc plan requires significantly fewer MUs compared to VMAT-HDMLC and is similar to VMAT-MMLC ($p=0.76$). In contrast, VMAT-HDMLC necessitates significantly more MUs than VMAT-MMLC ($p<0.05$). PSQA conducted with aS1200 portal dosimetry demonstrates that HDMLC plans to achieve a higher pass percentage compared to MMLC plans as indicated in table 1.

Figure 1 illustrates the Dose-Volume Histogram (DVH), highlighting that HyperArc plans achieved better dosimetric outcomes compared to VMAT plans. VMAT-HDMLC plans outperformed VMAT-MMLC plans. The VMAT-MMLC plan had higher $D_{2\%}$, D_{max}, and HI values, indicating a more heterogeneous dose distribution. Additionally, it resulted in higher doses to the hippocampus and other OARs.

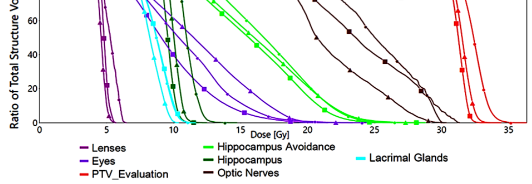

Figure 1. Example case 1: A comparison of DVHs obtained for hippocampal sparing WBRT using HyperArc (square), VMAT-HDMLC (triangle), and VMAT-MMLC (circle).

DISCUSSION

The HA-WBRT presents several challenges in implementation despite its advanced technology and precision. Accurate hippocampi delineation is crucial to balance neuroprotection and disease control. Consistent, high-quality treatment plans must be produced quickly for rapid symptom relief in brain metastasis patients. Efforts are needed to reduce treatment times and minimize operating errors [17]. This planning study assessed various techniques-HyperArc, VMAT-HDMLC and VMAT-MMLC-for treating 25 patients with brain metastases. All treatment plans successfully adhered to the criteria specified by RTOG 0933. The radiation dosage to the hippocampus and other critical structures was minimized, maintaining full coverage of the whole-brain planning target volume (PTV) and staying below the threshold linked to cognitive decline from radiation exposure, as described by Gondi *et al.* [4].

Recognizing the extended planning and treatment times associated with non-coplanar beams in HyperArc [18], we shifted our focus towards enhancing coplanar VMAT plans to achieve comparable quality. Given the crucial roles of collimator angles and MLC thickness in achieving dose conformity, precise modulation, and smooth dose fall-off, especially for the hippocampus, we set out to optimize coplanar VMAT [19-21].

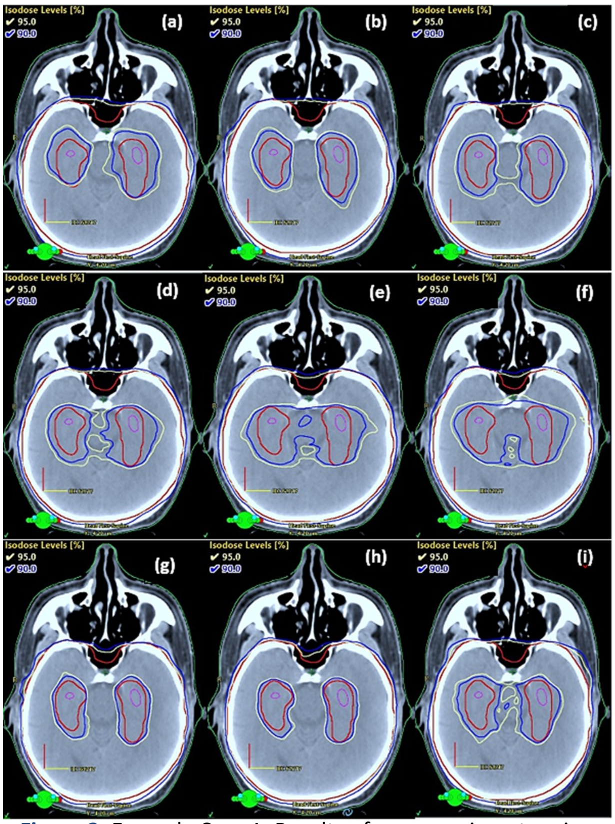

Figure 2. Example Case 1: Results of our experiments using HDMLC collimator rotation with two full arc plans, shown in panels **(a)** to **(g)**: **(a)** 0°-0°, (b) 15°-345°, **(c)** 30°-330°, **(d)** 45°-315°, **(e)** 60°-300°, **(f)** 90°-90°, and (g) 0°-90°. Additional results are shown for **(h)** using HyperArc and **(i)** 0°-90° using MMLC, depicting the coverage of 95% (yellow) and 90% (blue) of the target volume.

The researcher experimented with various collimator rotation combinations using two full arc plans in VMAT-HDMLC, as shown in figure 2. The 0° and 90° collimator angle combination demonstrated superior beam modulation and dosimetric advantages over other combinations, as seen in figure 2(g). By strategically implementing these angles across two full arcs, independent of default settings or previous research, we not only enhanced plan quality but also reduced planning and delivery times. Figure 2(h) indicates that HyperArc plans achieved superior coverage and more effectively spared organs at risk, likely due to the increased number of arcs and directions compared to coplanar VMAT plans. Conversely, figure 2(i) shows that VMAT-MMLC plans did not fully utilize the dosimetric benefits, possibly because of the varying MLC thickness ranging from 2.5 mm to 5.0 mm. To assess the efficacy of our plans, we benchmarked our results against previous studies on WBRT with hippocampal sparing, where the standard practice involves using collimator rotations at 30° and 330°. Sood *et al.* [22] reported PTV D_{max}, $D_{2\%}$, $D_{98\%}$, and HI values of 34.9 Gy, 33.2 Gy, 26.0 Gy, and 0.23, respectively, with hippocampal doses of 8.4 Gy at 100% and a maximum dose of 15.6 Gy. In contrast, our VMAT-HDMLC coplanar plans showed a 2.04% improvement in $D_{98\%}$ and a 0.84 Gy reduction in hippocampus D_{max}, while maintaining consistent D_{max}, HI for PTV, and $D_{100\%}$ for the hippocampus. Compared to the study by Rong *et al.* [23], our VMAT-HDMLC coplanar plans exhibited a 1.58% improvement in PTV $D_{98\%}$ and a 0.07 improvement in HI, with consistent hippocampus dosing. Yuen *et al.* [7] performed two sets of VMAT planning with MMLC, one with default collimator rotation and another with a split arc technique using various collimator angles. Our VMAT-MMLC coplanar plans showed improvements of 1.93% and 2.2% in D_{98}% for coplanar and split arc plans, respectively, and a 1.57 Gy reduction in hippocampus D_{max}. Finally, Sprowls *et al.* [24] compared HyperArc and VMAT plans using Millennium MLC. Our HyperArc HDMLC plans demonstrated a 2.81 Gy reduction in hippocampus D_{max}, and our VMAT-MMLC plans showed a 0.84 Gy reduction in hippocampus D_{max}, both maintaining consistent PTV dosimetric coverage.

Our optimized coplanar VMAT plans met the dosimetric criteria set by the RTOG compared to HyperArc plans. The coplanar VMAT-HDMLC plan achieved comparable PTV coverage to HyperArc. This suggests coplanar VMAT with meticulous collimator angle and MLC thickness selection as a viable alternative to HyperArc. In our comparison, VMAT-HDMLC plans surpassed other PTV coverage studies while maintaining the hippocampus dose. VMAT-MMLC plans achieved enhancements without compromising organ-at-risk dose.

Limitations of this study include the integration of Automatic Lower Dose Objectives (ALDO) and

Stereotactic Normal Tissue Objectives (SRS NTO) in HyperArc planning, which ensure 98% target coverage and a significant decrease in dose beyond target-specific levels [25]. These features were not employed in our research, as our approach did not involve stereotactic radiosurgery (SRS). Furthermore, non-coplanar arcs were not utilized in the VMAT plans with HDMLC and MMLC for comparison with the HyperArc plans. We employed automatic Normal Tissue Objectives (NTO) in this study and did not explore the use of manual NTO.

CONCLUSION

HyperArc and optimized coplanar VMAT plans with 0° and 90° collimator angles met all dosimetric goals set by RTOG-0933. VMAT-HDMLC coplanar plans matched HyperArc's coverage, while both VMAT-HDMLC and VMAT-MMLC plans improved organ-at-risk doses, surpassing conventional planning approaches in PTV and hippocampal sparing.

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