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Fixed field technique for hippocampal avoidance whole-brain radiotherapy: A feasibility study using Elekta system

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ABSTRACT

***Background*:** Treatment planning for Hippocampal avoidance whole-brain radiotherapy (ha-WBRT) is demanding and time-consuming due to the position of the Hippocampus and low dose tolerances. This study evaluates the feasibility of fixed field volumetric modulated arc therapy (fVMAT) for ha-WBRT using the Elekta Agility™ collimator system and Monaco treatment planning system. ***Materials and Methods*:** Fifteen patients treated for WBRT were subjected to fVMAT and conventional VMAT (cVMAT) planning with similar optimisation criteria. Jaws were restricted above and below the Hippocampus for the fVMAT plans with isocenter positioned at the brain's center, dividing the brain target into two. In contrast, Jaws were not restricted for cVMAT plans. Plans were compared in terms of dose constraints, dose conformity, and dose homogeneity. Plan complexity was compared in terms of modulation degree (MD), and delivery efficiency was checked by performing patient-specific quality assurance. ***Results*:** Both plans met the RTOG-0933 dose requirements. The fVMAT plans showed statistically significant improved target coverage ($D_{98\%}$, V_{30Gy}), target homogeneity, and conformity. There was no statistically significant change in hippocampus doses between the two plans. The fVMAT plans showed lesser plan complexity with average MD of 3.34±0.5 compared to cVMAT plans (average MD of 4.21±0.4, p=0.00011). The increased plan complexity was reflected in the delivery efficiency as cVMAT showed higher average gamma failure for patient3.84% (p=0.0004) and a target volume 7.13% (p=0.0359) structures. ***Conclusions*:** According to the obtained results, the Elekta Agility™ collimator system and Monaco treatment planning system can generate better ha-WBRT plans using the fVMAT technique.

INTRODUCTION

Prophylactic whole-brain radiotherapy (WBRT) after chemotherapy is the conventional treatment approach for non-small cell lung carcinoma patients to minimize the risk of brain metastasis [1-2]. Poor patient prognosis, such as neurocognitive decline and ear loss after WBRT, has constantly interrogated better treatment approaches. Stereotactic radiosurgery (SRS) techniques are also gaining popularity in improving the quality of life of patients treated for multiple brain metastasis [3]. However, several groups have proven that WBRT still has a notable role in managing patients with brain metastasis [4-5]. Radiation Therapy Oncology Group (RTOG)-0933 [6] trial proved that the neurocognitive deficit followed by WBRT is primarily due to the detriment caused by radiation to the hippocampus neural stem cells, which is located at the brain's centre responsible for cognitive function and memory. This phase-2 multicentered trial used the intensity-modulated radiotherapy (IMRT) technique to reduce hippocampus dose, which proved beneficial in preserving patients' memory and increasing quality of life [6].

IMRT methods are extensively used wherever sharp dose falloff is required between tumor cells and organs at risk (OAR). Various authors have used different IMRT techniques such as static gantry IMRT, helical tomotherapy, and volumetric modulated arc therapy (VMAT) for hippocampal avoidance whole-brain radiotherapy (ha-WBRT) [7-9]. The ha-WBRT planning with VMAT is challenging because of the location of the Hippocampus inside the large target, which is to be spared with almost one-third of the prescription dose. Lee *et al.* [10] compared IMRT and VMAT techniques for ha-WBRT and reported that the VMAT plans were superior to IMRT plans in terms of target dose homogeneity and coverage. Studies [11-13] have evaluated the possibility of fixed field optimisations for radiotherapy treatment planning for different sites. Field fix optimizations depend upon the target geometry, the capability of the linear accelerator (Linac) collimator systems, which mainly include the multi-leaf collimator [MLC] and collimator jaw movements, and the properties of the treatment planning system (TPS). The possibility of fixed field optimisation for ha-WBRT has been

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evaluated for Varian Linacs with a tertiary collimator system and Eclipse treatment planning system (TPS) (Varian, PaloAlto, CA) [14,15]. The Elekta Agility™ MLC system has higher MLC speed and lesser leaf transmission than the Varian tertiary collimator system, which could be advantageous in VMAT planning and execution [16]. Nevertheless, as of our knowledge, no studies have evaluated the possibility of field fix optimisation in Elekta linear accelerators, which have a secondary collimator system (upper X-jaws are replaced with MLCs). A three-dimensional dosimetric validation of such complex treatment planning is necessary before treatment execution; in this study, we have used the most modern transmission type 2D detector array for dosimetric validation of fixed field volumetric modulated arc therapy ha-WBRT. The primary objective of this study is to evaluate the feasibility of fixed field optimisation for ha-WBRT using the Elekta Agility™ MLC system (Elekta, Stockholm, Sweden) and the Monaco TPS (ver. 5.11, Elekta, Stockholm, Sweden).

MATERIALS AND METHODS

After obtaining approval from the institutional ethics committee, the data for fifteen patients are retrospectively analysed in this study. The patient characteristics are given in table-1. Patients were simulated in a head-first supine posture with three clamps thermoplastic face mask on a wide bore 64 slice General Electric computed tomography (CT) (GE Healthcare, Milwaukee, WI, USA) simulator. The CT images were imported into Monaco TPS. These images had to be retrieved from the Monaco database for this study, and target and OAR volumes were contoured retrospectively. The patient's T1 weighted Magnetic Resonance Images (MRI) were imported into the TPS and registered with the planning CT images obtained to delineate the Hippocampus properly. Hippocampus was drawn in the MRI images, and a 5 mm margin was added to create a hippocampal avoidance zone (HAZ), which was subtracted from the planning target volume (PTV) created.

Table 1. Patient demographic information.

Patient characteristics	
Median Age (range)	59 (43-74)
Gender	8 Females: 7 Male
Diagnosis	13 patients for Prophylactic whole-brain radiotherapy (WBRT) for non-small cell lung carcinoma. 2 patients for multiple brain metastasis with primary carcinoma of the stomach.
Mean target volume	1533.88 ± 165.34 cc

The VMAT plans were created according to RTOG-0933 trial criteria [6]. The whole-brain PTV was prescribed with 30 Gy over ten fractions. Along with Hippocampus and HAZ, other OARs such as the brainstem, eye lens, eyes, and cochlea were also considered in treatment plan optimisation. For each patient, a conventional VMAT plan without the jaw fixed (cVMAT), as well as another plan with the jaw fixed (fVMAT), was created. Two gantry arcs of 360^0 were used in both the plans and the collimator was angled into 85^0 and 95^0 for better hippocampal avoidance. The Isocentre was placed in the medial plane of the brain at the centre of both the Hippocampus. In an fVMAT plan, the first arc was set to treat the upper hemisphere of the brain by fixing the jaws one cm above the isocentre, and the second arc was used to treat the lower hemisphere as the Jaws were fixed one cm below the isocentre as shown in figure 1. This particular arrangement results in a region of two cm overlap between arcs. In the c-VMAT plans, jaws were not fixed, and both arcs were utilised to treat the entire target. Both types of plans were optimized with these same optimisation objectives. All plans are delivered on Elekta Versa HD Linac (Elekta, Stockholm, Sweden) with Agility MLC system.

The RTOG 0933 dosimetric constraints were extracted for both the plans and compared. The homogeneity index (HI) [17] and Paddick conformity index (CI) [18] were calculated for the target using equations 1 and 2 and compared.

$$CI = \frac{TV_{iso}}{TV} \times \frac{TV_{iso}}{V_{iso}} \quad (1)$$

TV_{iso} is the PTV volume covered by the reference isodose line, chosen to be 98% isodose line as per RTOG 0933, TV is the PTV volume, V_{iso} is the total volume of the reference isodose line.

$$HI = \frac{D_{2\%} - D_{98\%}}{D_{50\%}} \quad (2)$$

Where $D_{2\%}$, $D_{98\%}$ and $D_{50\%}$ represents 2%, 98% and 50% dose levels.

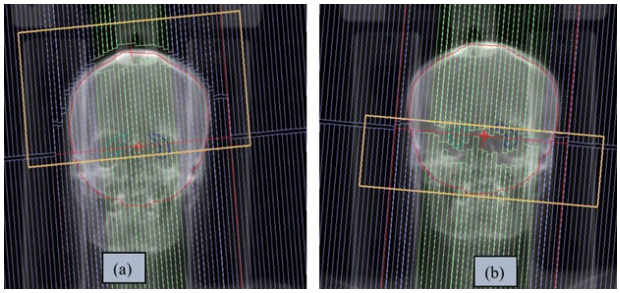

Figure 1. Field placement for fVMAT plans. The Isocentre was placed in the medial plane of the brain at the center of both the hippocampus. The target is divided into two hemispheres, with jaws fixed one cm below and above the isocentre for the upper **(a)** and lower hemisphere **(b)**, respectively. This specific arc geometry results in two cm overlap between the arcs.

The plan complexity was analysed in terms of modulation degree (MD) [19] and total monitor units (MUs). The MD is defined by equation 3 and was calculated using an in-house python script.

$$MD = \frac{Total\ MU}{\frac{\sum(Segment\ area \times Segment\ MU)}{Total\ beam\ area}} \quad (3)$$

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Where Total MU is the total MU of the plan evaluated, Segment area and segment MU are the areas and MU information of each control point of the plan. For a three-dimensional conformal plan, MD is one, while for intensity-modulated fields, this value will be more than one; a plan with high MD indicates a highly modulated plan [19]. The treatment plans' delivery efficiency was checked via pre-treatment patient-specific QA using Dolphin detector™ and Compass dosimetry system™ from IBA Dosimetry (Schwarzenbruck, Germany). Figure 2 depicts the pre-treatment patient-specific QA analysis using the compass dosimetry system. The reference distribution is given in the upper left window, while the upper right window shows the Dolphin measured distribution reconstructed using the compass system. The difference between evaluated and reference distribution is given in the right bottom window. Gamma analysis was conducted between the planned and measured dose distributions with a distance to agreement criteria (DTA) of 2 mm and dose deviation criteria of 3 % with a 10 % dose threshold. The percentage points with gamma greater than one (percentage gamma failing points (%GF)) were noted for PTV and patient structures. The student's t-test was performed for statistical analysis in Minitab® 18.1 version; a p-value of less than 0.05 was considered statistically significant.

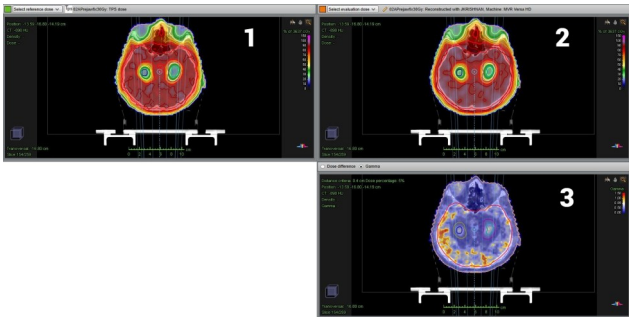

Figure 2. Pre-treatment QA analysis using Compass dosimetry system. **1)** TPS dose distribution; **2)** The Dolphin measured fluence is three-dimensionally reconstructed by the compass system. **3)** The differences between the two distributions in terms of gamma index.

RESULTS

Table 2 compares the obtained dosimetric constraints for PTV and OAR between fVMAT and cVMAT plans. The average value of target HI and CI are also shown in the table. It is evident from the table that there is a statistically significant increase in target coverage (V_{30Gy} (%), p = 0.0022; $D_{98\%}$ (cGy), p=0.0405), dose homogeneity (p = 0.0297), and conformity (p= 0.0014) for fVMAT plans compared to cVMAT. However, there was no significant difference in neither the hippocampus ($D_{100\%}$ (cGy): p = 0.3940 (Right hippocampus), p=0.8294 (Left hippocampus)) nor the HAZ doses p=0.0776 (Right hippocampus): p=0.2206 (Left hippocampus)) between the two plans. The fVMAT plans showed decreased hotspots in the brainstem compared to cVMAT plans (p=0.0264), but the right cochlea doses increased for fVMAT cases (p=0.0259). No other OAR exhibited a statistically significant dose difference.

The MD values are plotted in figure 3 for all fifteen patients. fVMAT showed lesser MD values for all patients with an average MD of 3.34±0.5 compared with cVMAT plans (average MD of 4.21±0.4, p=0.00011). The average MUs for fVMAT plans were 2213.19±262, while for cVMAT, it was 2289±252 (p=0.4038). Though the increased MD values resulted in higher average MUs for cVMAT plans, differences in MUs between the two plans were not statistically significant.

Table 2. Comparison of obtained average dosimetric constraints between fixed field volumetric modulated arc therapy (fVMAT) and conventional VMAT (cVMAT) plans. Parameters represented in bold depict statistically significant results ($p < 0.05$).

Structures	Dosimetric parameters	fVMAT	cVMAT	p - Value
PTV	$D_{2\%}$ (cGy)	3410.5±64	3589.21±69	0.2744
	$D_{98\%}$ (cGy)	**2474.25±297**	**2389±328**	**0.0405**
	$D_{50\%}$ (cGy)	3277.63±50	3257.87±32	0.4231
	V_{30Gy} (%)	**93.45±2**	**91.68±1**	**0.0022**
	HI	**0.32±0.08**	**0.36±0.09**	**0.0297**
	CI	**0.78±0.02**	**0.74±0.02**	**0.0014**
Right Hippocampus	$D_{100\%}$ (cGy)	829.51±63	847.65±47	0.3940
	D_{max} (cGy)	1539.25±118	1457.92±90	0.0645
	D_{min} (cGy)	867.45±63	883.63±43	0.4650
Left Hippocampus	$D_{100\%}$ (cGy)	830.82±54	836±44	0.8294
	D_{max} (cGy)	1478.85±96	1459.68±98	0.3055
	D_{min} (cGy)	870.3±51	868±42	0.9272
Right HAZ	D_{max} (cGy)	2456.63±132	2390±145	0.0776
Left HAZ	D_{max} (cGy)	2405.5±113	2357.87±94	0.2206
Brain stem	**D_{max} (cGy)**	**3250±45**	**3439.4±204**	**0.0264**
Lens Right	D_{max} (cGy)	777.32±53	782.8±98	0.8551
Lens Left	D_{max} (cGy)	773.12±58	775±83	0.9214
Right Eye	D_{max} (cGy)	2576.18±477	2544.56±408	0.6382
	D_{mean} (cGy)	1252.92±83	1419.53±439	0.3073
Left Eye	D_{max} (cGy)	2643.42±442	2580.47±307	0.5714
	D_{mean} (cGy)	1259.46±88	1245.18±74	0.6907
Left Cochlea	D_{mean} (cGy)	2790.56±99	2745.2±234	0.5030
Right Cochlea	**D_{mean}** (cGy)	**2784±184**	**2695.88±245**	**0.0259**

fVMAT: fixed field volumetric modulated arc therapy; cVMAT: conventional VMAT; PTV: Planning target volume; HI: Homogeneity index; CI: Conformity index; HAZ: hippocampal avoidance zone.

Figure 4 shows the pre-treatment patient-specific QA results for cVMAT and fVMAT plans, given in terms of %GF points ($\gamma > 1$) for structures patient and PTV. The QA passed for all plans except for three cVMAT cases, and one fVMAT case as the patient %GF was more than 5%. For all the cases, the cVMAT plans exhibited higher %GF for the patient and PTV structures with an average %GF of 3.84% (p=0.0004) for the patient and 7.13% (p=0.0359) for PTV structure.

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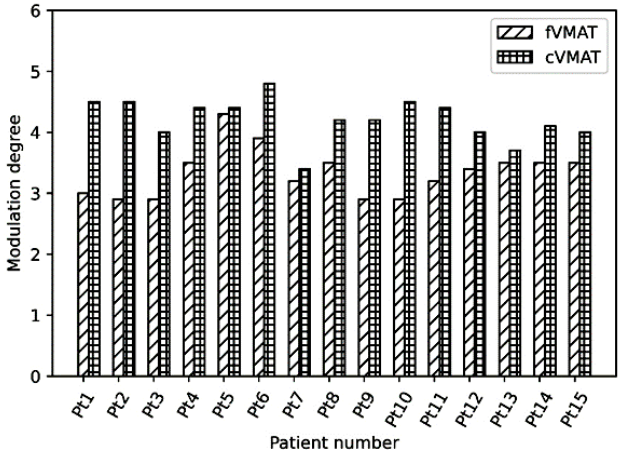

Figure 3. Comparison of Modulation degree between f-VMAT and c-VMAT plans. fVMAT showed lesser MD values for all patients with an average MD of 3.34±0.5 compared with cVMAT plans (average MD of 4.21±0.4, p=0.00011).

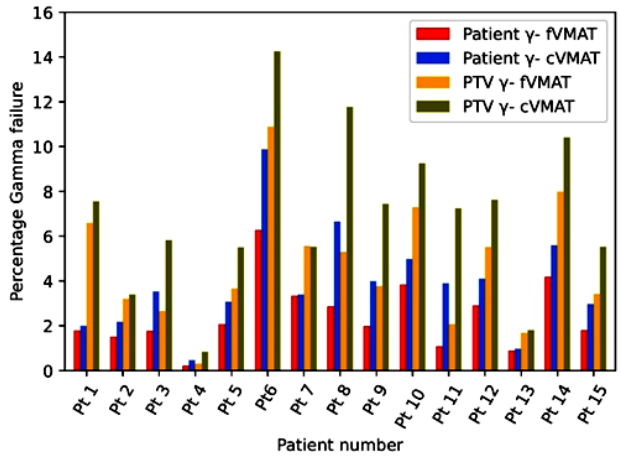

Figure 4. Variation of percentage of gamma failure rates for fVMAT and cVMAT cases. GF failures for patient and PTV structures are shown for both types of plans.

DISCUSSION

This study demonstrates fixed-field optimisation for ha-WBRT for Linacs with secondary collimators systems. Shen *et al.* [14] introduced the usage of partial arcs with fixed field optimisation for ha-WBRT using Varian Linac with tertiary MLC and Eclipse TPS. They contoured the PTV into separate compartments and used it for optimisation. They were able to meet the RTOG 0933 planning objectives with this technique, and their obtained HI and CI values matched our study (0.3±0.01 and 0.72±0.02, respectively). They reported that all plans passed the pre-treatment QA with 4%, 5 mm gamma criteria. They also evaluated the effect of MLC size on ha-WBRT planning by comparing 2.5 mm thickness high-definition MLC with the standard 5mm Millennium 120 MLC and reported that a finer MLC could minimise the hippocampus dose.

Even though the latest collimator systems have jaw tracking options during IMRT delivery, various authors [11-13] have proved that the fixed jaw technique can be advantageous in sparing OARs in different sites. Fixing the fields according to the specific orientation of OARs can keep these structures away from the beam eye view during the whole gantry rotation [13]. Leakage through jaws can significantly affect OARs with very low dose thresholds such as ovary, eye lens, and hippocampus [20]. The measured maximum Jaw leakage for the Elekta Agility system in our center is 0.77%, with an average of 0.39% for 6MV beam, while for MLC's, these values are 0.52% and 0.33%, respectively. The Varian Millenium and high-definition MLC systems have higher average leaf transmission (~ 2% and ~ 2.5%, respectively), which might increase the dose to the Hippocampus. This increase was evident as Shen *et al.* [14] reported a higher average $D_{100\%}$ dose to the Hippocampus (8.5Gy±0.2 Gy) with Varian systems as compared with our study (8.2951±63 Gy). During the treatment of large targets, restrictions due to leaf over travel can create undesired MLC patterns in specific gantry angles, which can adversely affect the quality of the treatment plan [21]. Agility MLC systems have leaf overtravel restriction of 15 cm to the opposite side, compared to Varian tertiary MLC systems, which have more freedom in over travel by 20 cm. Fixing the fields can reduce the restrictions related to leaf overtravel, especially for larger targets. Thus, in terms of leaf overtravel restrictions, Jaw-fixed optimization can be more advantageous for the Agility MLC system to treat larger targets. The increased target homogeneity and conformity associated with fVMAT plans could be due to these reasons. Rossi *et al.* [21] reported that the limitation in MLC speed from one gantry angle to another could deteriorate the IMRT plan quality, especially for larger targets. The Agility MLC system has a higher MLC speed (6.5 cm/s combining the leaf and leaf carrier speed) than the standard Varian millennium 120 MLC (3.7 cm/s combining the leaf and leaf carrier speed). Thus, the Agility systems could deliver the ha-WBRT plans more efficiently than Varian millennium 120 MLCs.

Chen *et al.* [11] suggested that fixed field optimisation cannot be used in all cases as field fixing can increase the MUs, increase the peripheral doses, and impose radiation safety concerns. In our study, the cVMAT plansshowed an average increase of 3.4% in MUscompared to fVMAT cases, which does notsignificantly increase the treatment time. However, other studies [11-13] have reported a significant increase in MUs up to 1.4 times for fixed field VMAT cases for larger targets. The MD is a direct indicator of plan complexity [22]; the decreased MD associated with fVMAT plans has also decreased overall optimisation time by a median of four minutes as the optimiser achieved the objectives in lesser time compared with cVMAT plans. The fVMAT plans were closer to the Monaco TPS calculated dose distribution in terms of dose delivery than cVMAT plans. Increased MD values for cVMAT plans have been

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reflected in the delivery efficiency, as these plans exhibited higher GF rates. Four plans which failed in the pre-treatment QA passed with relaxed gamma criteria of (4mm, 4%), indicating no significant difference between planned and delivered distributions in both the techniques.

CONCLUSIONS

This study demonstrated ha-WBRT with field-fixed optimisation using the Elekta agility MLC system and Monaco TPS. The comparative study between fVMAT and cVMAT plans shows that the fixed field optimization can generate better treatment plans for ha-WBRT using the Elekta agility MLC system and Monaco TPS.

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

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***Ethical statement*:** All applicable institutional and/or national guidelines for the care and use of animals were followed. The work was approved by the institutional Ethical committee (IEC) Ref No: IEC/2021/IV/23; Date: 09/05/2021.

***Author contribution*:** V.R: Constructing hypothesis for the manuscript; Planning methodology to reach a conclusion; Literature review; Data collection and analysis; Manuscript preparation. R.G.R: M.S.O, NP: Organising and supervising the course of the project or the article and taking the responsibility; Reviewing the article before submission not only for spelling and grammar but also for its intellectual content.

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