Original Article

Comparative Analysis of Radiotherapy Plans for Post-Operative Primary Brain Tumors Using Coplanar Volumetric Modulated Arc Therapy (Co-Rapid Arc) And Non-Coplanar Vmat (Nc-Rapid Arc)

Sulabh Singh , Anirudh Pradhan.

Abstract

Objectives

The aim of this study was to compare the quality of radiotherapy plans for post-operative primary brain tumors using coplanar Rapid arc therapy and non-coplanar Rapid arc.

Methods

A retrospective selection of 20 patients who underwent treatment for primary brain tumors was conducted for this study. Identical CT sets with structures were used for both CO-rapid arc and NC-rapid arc planning in each patient. CO-RAPID ARC utilized one full arc and two coplanar half arcs, while NC-RAPID ARC employed one full coplanar arc and two non-coplanar half arcs with couch rotation of either 315° or 45°. Dose constraints were based on the RTOG 0614, RTOG 0933 protocols. Dose volumetric parameters were collected for statistical analysis.

Results

NC-RAPID ARC demonstrated significant dose reduction in the contralateral hippocampus, both temporal lobes, cochleae, and other organs at risk (OARs), while maintaining similar plan qualities. Specifically, NC-RAPID ARC resulted in an average dose-reduction of 1.67 Gray in the contralateral hippocampus, 6.29 Gy and 2.8 Gy in the temporal lobes for the ipsilateral and contralateral sides, respectively, and 5.34 Gy and 0.97 Gy in the ipsilateral and contralateral cochlea, respectively. Overall, there was a 5.4% reduction in the volume of normal brain tissue receiving low-dose irradiation.

Conclusion

The proposed NC-rapid arc technique exhibited superior plan quality compared to CO-rapid arc for primary brain tumors, particularly in terms of sparing the OARs located contralateral of the tumors.

Advances in knowledge: NC-rapid arc offers the potential to decrease radiation doses to the hippocampi, both neocortex, cochleae, & OARs located contralateral to primary brain tumors during radiotherapy.

JK-Practitioner2024;29(4):40-47.

Introduction

Radiation therapy is frequently used as a crucial or post-operational adjuvant treatment for the majority patients diagnosed with crucial brain tumors.This treatment modality has been exposed to enhance confined tumour control and improve the complete response of patients compared to those who undergo surgery [1].

Author Affiliations

Sulabh Singh , Department of Radiation Oncology, Capitol Hospital, Jalandhar, and Department of Physics, GLA University, Mathura;

Anirudh Pradhan ,Centre for Cosmology, Astrophysics and Space Science, GLA University, Mathura.

Uttar Pradesh, India

Correspondence

Sulabh Singh , Department of Radiation Oncology, Capitol Hospital, Jalandhar
Sulabhm123@gmail.com

Indexed

EMBASE, SCOPUS , IndMED, ESBCO, Google Scholar besides other national and International databases.

Cite this article as

Singh S , Pradhan A. Comparative Analysis of Radiotherapy Plans for Post-Operative Primary Brain Tumors Using Coplanar Volumetric Modulated Arc Therapy (Co-Rapid Arc) And Non-Coplanar Vmat (Nc-Rapid Arc).JK Pract2024;29(4):40-47.

Full length article available at **jkpractitioner.com** one month after publication

Keywords

Brain , radiotherapy tumour .

Using alternative radiotherapy techniques has emerged as a new trend in the treatment of cranial tumors, which includes methods such as IGRT and cyberknife [2,3].
Rapid arc therapy is an innovative radiation practice that enables the precise delivery of radiation dose to the target volume through the use of numerous intensity modulated arcs. This approach achieves confined dose distribution by combining variations in gantry revolving pace, healing field shape, dose-rate. VMAT (Rapid arc) has been widely adopted as a treatment method for various anatomical location, with head and neck regions [4], brain part [5–7], and rest regions of the body. When using Rapid arc for the treatment of crucial brain tumors, it is tricky to minimize the radiation dose to normal brain tissue due to the trajectories involved. This is because primary brain tumor VMAT planning typically entails a large planned target volume, making it difficult to avoid irradiating normal brain tissue.
Non-coplanar radiotherapy involves the utilization of multiple radiation fields which intersect at the same isocenter but do not lie within the similar geometric surface related to the patient [8]. This technique allows for the maximum radiation dose to be delivered on the isocenter, whereas the opening dose may be spread across dissimilar planes. Consequently, the dose to the PTV volume stays unchanged, while the dosage to organs at risk (OARs.) may be low. The temporal lobe plays a vital role within the cerebral cortex of the human brain, accounting for approximately 20% of the entire cerebrum size. It serves various functions, with the superior neocortex being involved in lingo skill , while the low grade and agile regions play a crucial role in challenging nomenclature. Additionally, the middle part of the temporal lobe is responsible for connecting with middle structures, with the hippocampi, which drives a vital role in remembrance & awareness [9]. Furthermore, located adjacent to the temporal lobe is the cochlea, which is responsible for hearing. Several prior researches have indicated that patients could experience neurocognitive and aural impairments following skull irradiation [7,10] The concept of hippocampail-scant has been suggested in total brain radiation therapy [5], as well as in the treatment of brain-metastases [6] and craniopharyngiomas [11], by various radiation therapy treatment such as 7F IMRT, Rapid dual arc, and coplanar Rapid arc. conversely, there is limited research on the appliance of coplanar and non-coplanar Rapid arc for the purpose of sparing multiple organs at risk for the treatment of primary brain-tumors.
The objective of this study is to compare the plan quality of coplanar VMAT (CO-rapid arc) with non-coplanar VMAT (NC-rapid arc) in the radiotherapy treatment of primary brain tumors. The focus is on evaluating the efficacy of both techniques in sparing several organs at risk.

Methods and Materials

Patient range

This retrospective study included 20 patients who underwent treatment for primary brain tumors using the IGRT practice. The patients were chosen from the medical oncology department of capitol hospital Jalandar Punjab. The eligibility criteria for participation in the study were patients who had been identified with a common brain tumor. Patients identified with brain mets, those who underwent craniospinal irradiation, or those with a planning target volume (PTV) overlapping both hippocampus were not included in the study

Radiotherapy simulation

The simulation process involved using a 3-mm slice thickness with a Philips-Brilliance 16 CTscanner at capitol hospital. Patients were positioned in a supine position & immobilized using a base plate, head support, and immobilize cast, which is the typical system for brain tumor management at capitol hospital. CT images were acquired without the use of a contrast agent. MRI scans, obtained from diagnostic centers and given via patients, were also utilized in the study.

Delineation

To enhance the accuracy of description, MRI-images and CT-images be co-registered prior to radiation planning. This process involved aligning and overlaying the two image sets. The oncologists contoured the planning target volumes (PTVs) based on these co-registered images.
Radiation therapists at hospital delineated the organs at risk (OARs) with the brainstem, optic chiasm, cochleae, eyes, lens, optic nerves, spinal cord, TM joint, and temporal lobes. This contouring process involved accurately outlining these structures based on the imaging data and clinical expertise.
In this study, the hippocampus were manually marked by the oncologist with the assistance of radiation therapists at capitol. The contouring process was guided by the online RTOG guidelines. Before radiotherapy planning, the medical dosimetrists at TMH reviewed and approved the delineated structures. To ensure patient privacy, all MRI, CT images, and structure sets were anonym zed during the study.

Treatment planning: coplanar VMAT and noncoplanar VMAT

The Eclipse Radiotherapy Treatment Planning System, version 15.6 (Varian Medical Systems, Palo Alto, CA), was used for the planning process. The prescribed dose was 1.8 Gray/fr, with 5 sessions administered each week for a sum of 30 fractions, resulting in a cumulative dose of 54 Gy. The treatment plans were created using a Varian true beam linear accelerator (Varian Medical Systems, Palo Alto, CA), which was operational having Varian High Definition 120multileaf-collimator. The plans utilized 6MV ionbeam with highest dose-rate of 600 moniter units (MU) / 60second. In all treatment plans, the dose rate was maintained at 600 MU/min, have gantry speed of 4.8° per second. The MLC

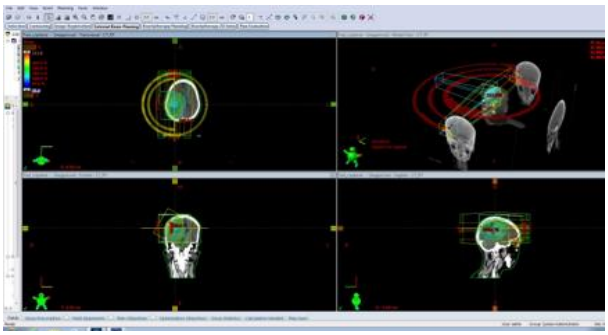

Fig1. ARC coplanar plan.

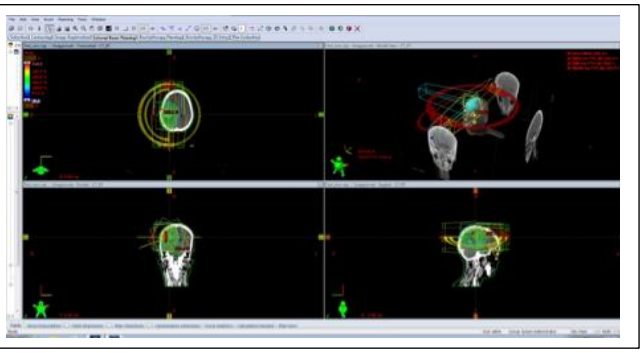

Fig2. ARC Non coplanar plan.

movement used in these plans was sliding window. A solo isocenter has established at the middle of the tumor for every treatment plans. The field sizes were customized using the arc geometry tool within the Eclipse treatment planning system. To minimize inter-leaf transmission between the multi leaf collimator (MLC), the collimator rotation angles were set at 30° for clockwise arcs and 330° for counterclockwise arcs. This configuration aimed to reduce any potential leakage b/w MLC leaves. In the CO-rapid arc plans, a configuration of one full arc spanning from 179° to 181° and two semi arcs were used. The table angle for all fields was maintained at 0° throughout the treatment. In cases where the planning target volume (PTV) was located on the left part of the brain, the gantry angles for the two semi arcs were configured to span starting 0° to 179° and from 179° to 0°, respectively.

This configuration ensured comprehensive coverage of the target volume from different angles. In cases where the planning target volume (PTV) was located at the right part of the brain, gantry angles for the two semi arcs were put to span from 0° to 181° and starting 181° to 0°, respectively. This specific arc pattern for the CO-RAPID ARC method is illustrated in Fig. 1. The NC-rapid arc tactics consisted of one complete arc spanning from 179° to 181° and two semi arcs. The table angle for the complete arc has set to 0° in all plans. In cases where the planning target volume (PTV) was situated on the left part of the brain, the table angle for the two semi arcs was set to 315°. The gantry angles for these semi arcs were configured to cover the range from 0° to 179° and from 179° to 0°, respectively. This setup allowed for optimal treatment delivery to the left-sided PTV. In cases where the planning target volume (PTV) was located on the right part of the brain, the table angle for the two semiarcs was set to 45°. Gantry angle for these arcs were configured to cover the range from 0° to 181° and starting 181° to 0°, respectively. The specific arc and table arrangement for the NC-rapid arc plan can be seen in Fig. 2. The progressive resolution optimizer (PRO3, v. 15.6, Varian Medical Systems, Palo Alto, CA) was used to optimize both the CO-rapid arc and NC-rapid arc plans. During the optimization process, dose constraints were applied based on the Quantec protocol. The specific details of these dose constraints can be found in Tables 1 and 2. Following the optimization process, dose calculations were carried out with the Anisotropic Analytical Algorithm (AAA) within the Eclipse system. The grid-size for dose calculation was set to 1.25 mm.

Interplanner Variability

All treatment plans were developed by a team of two planners, each possessing a comparable level of clinical experience in radiation treatment planning. Each physicist was assigned to create both CO-rapid arc and NC-rapid arc plans for a total of ten patients. In order to standardize the planning procedures and reduce variations between planners, 3 sets of CT-scans were chosen as representative sample. This selection aimed to establish consistency in the planning process. The planners utilized these three sets of CT scans for the planning process, and standard dose-volume matrix commonly employed in medical practice were utilized to evaluate the presentation of the planners. This assessment aimed to gauge the quality and effectiveness of their planning techniques. Prior to commencing the creation of treatment plans for this study, all planners successfully achieved the predetermined planning goals.

Evaluation of treatment plans

The treatment plans were evaluated and accepted by a certified medical physicist using the below criteria: The treatment plans underwent thorough examination and approval by a competent clinical physicist based on the below criteria:

The prescribed dose of 54 Gy should be delivered to at least 98% of the Planning Target Volume (PTV).

The maximum dose received by 2% of the PTV should not exceed 58.32 Gy (108% of the prescribed dose).

The maximum point dose, which includes hotspots outside the PTV, should be kept below 108% of the prescribed dose.

The following parameters were collected and calculated for each treatment plan:

Overall MUs were recorded.
Planning Target Volumes (PTVs) have:
Max.-dose (D_{max})
Min.-dose (D_{min})
Average-dose (D_{mean})
Dose for(2%, 50%, 98% & 1cc) of the PTV size (D2%, D50%, D98%& D1cc)
The volume of regular brain tissue receiving 30% of the given dose ($V_{30\%}$) can considered.
Top of Form

The measurement of the homogeneity indicator& conformity indicator , may have been widely utilized as evaluation metrics for radiotherapy plans, was conducted. The calculation of the homogeneity index was performed using the following formula:
$HI = (D_{2\%} - D_{98\%})/ DP_{(givendose)}$
Here $D_{2\%}$ represents the dose attained by 2% of the PTV, $D_{98\%}$ represents the dosage attained by 98% of the tumor volume, and DP is the given dose, which in this case is 54 Gy.

The calculation of the conformity indicator involved the use of the below formula:
CI = (Vtar^2) / (VT × Vprd)
Here, Vtar represents, volume of the planning target volume (PTV) that receives the prescribed dose of 54 Gy, VT represents the total volume of the PTV, and Vprd represents the volume enclosed by the isodose of the prescribed dose (54 Gy)
The maximum dose (Dmax) and mean dose (Dmean) were calculated for the pituitary, chiasm, and brainstem. Additionally, the dose-volumetric parameters (Dmax and Dmean) were calculated for various structures including the both side temporal lobes, TM joint, optic nerve, cochlea, lens and eyeball. and In the case of the hippocampus, calculations were performed for D_{mean},D_{max}& $D_{40\%}$.

Statistical analysis

The statistical study was conducted using IBM-SPSS software. In this study, statistical significance was defined as p-values below 0.05. All 40 treatment plans underwent thorough clinical evaluation and were approved by competent medical physicists. The presented results are derived from these 32 plans that received the necessary scrutiny and acceptance.

Results

Patient demographics

The study included a total of 20 patients, whose ages ranged from 26 to 71 years old. The gender distribution was 11 males and 9 females. Among the patients, 15 were diagnosed with glioblastoma multiforme, while 5 were diagnosed with meningioma. Prior to undergoing radiotherapy, all patients had undergone surgical procedures. The volume of the gross tumor varied between 1.11 and 7.21 cm, with the measurements taken in the maximum dimension.

Dose–volumetric of PTV and total monitor units

Table 1 presents dose-volumetric parameters for the planning target volume (PTV) for both conformal arc volumetric-modulated arc therapy (CO-rapid arc) and non-conformal arc volumetric-modulated arc therapy (NC-rapid arc). The general dose-volumetric parameters for CO-rapid arc and NC-rapid arc were found to be related, with minimal differences and no significant variation. The mean monitor units (MU) for CO-rapid arc and NC-rapid arc were 472 ± 51.62 and 489 ± 73.09, respectively (p = 0.536).

Dose volume parameters PTV	Co-planar VMAT (avg±SD)	Non Co-planar VMAT (avg ±SD)	P-Value
Maximum dose Gy	57.95±0.37	58.18±0.30	0.197
Mean Dose	55.98±0.17	55.25±0.41	1
Minimum Dose	43.59±7.75	45.04±6.67	0.23
$D_{98\%}$	54.17±0.22	54.12±0.30	0.569
$D_{2\%}$	56.30±0.32	56.32±0.33	.244
$D_{50\%}$	55.27±0.19	55.27±0.13	0.605
D_{1cc}	56.66±0.29	56.72±0.35	0.171
HI	0.0384±0.0067	0.0395±0.0064	0.537
C I	0.938±0.0182	0.943±0.0129	0.303

Table 1

Dose–volumetric parameters of centrally located OARs

Table 2 displays the dose-volumetric parameters of the centrally located organs at risk (OARs) for both conformal arc volumetric-modulated arc therapy (CO-rapid arc) and non-conformal arc volumetric-modulated arc therapy (NC-rapid arc). The complete dose-volumetric parameters for the brainstem pituitary, andchiasm in NC-rapid arc were less compared to CO-rapid arc. However, these differences have not found to be statistically significant, except for the mean dose (Dmean) of the brainstem. The average dose to the brainstem in NC-rapid arc was 1.35 Gray lower than that in CO-rapid arc (p = 0.02).

Dose–volumetric factors of rest OARs –

Tumor side

Table 3 presents the dose-volumetric parameters of the other organs at risk (OARs) located on the same side of tumor for both coplanar arc volumetric-modulated arc

Dose Volume Parameters centrally located OAR's		Coplanar VMAT (avg ± SD)	Non Coplanar VMAT (avg ± SD)	P Value
Pituitary	D_{max}	9.71 ± 0.38	6.778 ± 4.82	0.155
	D_{mean}	15.3 ± 5.77	7.96 ± 8.15	0.091
Chiasm	D_{max}	20.55 ± 11.93	18.37 ± 11.79	0.259
	D_{mean}	11.66 ± 7.65	8.91± 5.06	0.09
Brainstem	D_{max}	23.4 ± 13.96	22.27 ± 11.89	0.878
	D_{mean}	6.06 ± 3.97	4.67 ± 2.55	0.03

Table 2

therapy (CO-rapid arc) and non-coplanar arc volumetric-modulated arc therapy (NC-rapid arc).

The dose-volumetric parameters for the hippocampus, optic nerve, lens, and eyeball were higher in COrapid arc compared to NC-rapid arc, but these differences were not statistically significant. However, the mean dose of the temporal-lobes, cochlea, & temporomandibular joint were significantly high in CO-rapid arc than in NC-rapid arc.

Dose–volume parameters of other OARs – Contralateral part

The dose-volumetric measure of the organs at risk (OARs) placed on the contralateral part of the tumor for both conformal arc with CO-rapid arc and non-conformal NC-rapid arc The dose-volume parameters of thelens,optic nerve, temporomandibular (TM) joint, temporal lobe, eyeball,hippocampus and cochlea in CO-RAPID ARC were found to be significantly advanced compared to NC-rapid arc (entire with $p < 0.05$). Regarding temporal lobe, the maximum dose (Dmax) and mean dose (Dmean) for conformal arc volumetric-modulated arc therapy (CO-rapid arc) were 20.12 Gy and 6.48 Gy, respectively, while for non-conformal arc volumetric-modulated arc therapy (NC-rapid arc), these values were 11.561 Gy ($p = 0.0001$) & 3.68 Gy ($p = 0.0001$), respectively. As such cochlea, the D_{max}& D_{mean} for CO-RAPID ARC were 2.881 Gy & 2.301 Gy, respectively, while for NC-rapid arc, these values were 1.61 Gy ($p = 0.0001$) and 1.33 Gy ($p = 0.0001$), respectively.

Normal brain tissue low dose volume (V30%)

The volume of ordinary brain tissue receiving a lesser dose (30% of the given dose, i.e., 16.2 Gy) in conformal arc volumetric-modulated arc therapy (CO-rapid arc) and non-conformal arc volumetric-modulated arc therapy (NC-rapid arc) was measured to be 1230.93 cm3 and 1167.18 cm3, respectively.

Discussion

Significance of the study

In this research, the non-conformal arc volumetric-modulated arc therapy (NC-rapid arc) demonstrated comparable dose-volumetric parameters in the planning target volume (PTV) and overall plan quality, while exhibiting more favorable dose-volumetric parameters in the organs at risk (OARs) compared to conformal arc volumetric-modulated arc therapy (CO-rapid arc). Bottom of Form

The dose-volumetric parameters for each organ at risk

DV parameters Ipsilateral OAR's		Coplanar VMAT (avg ± SD)	Non Coplanar VMAT (avg ± SD)	P Value
Hippocampus	D_{max}	41.93 ± 17.09	38.94 ± 20.47	0.678
	D_{mean}	26.93 ± 16.82	24.93 ± 18.55	0.484
	$D_{40\%}$	25.03 ± 16.78	16.54 ± 20.28	0.797
Temporal-Lobe	D_{max}	54.74 ± 7.15	52.74 ± 13.46	0.309
	D_{mean}	31.82 ± 12.75	25.53 ± 17.56	0.005
Choclea	D_{max}	16.07 ± 14.46	9.43 ± 14.11	0.003
	D_{mean}	11.97 ± 11.69	6.63 ± 9.77	0.003
TM joints	D_{max}	20.32 ± 9.75	5.45 ± 8.16	0.0002
	D_{mean}	14.15 ± 8.67	3.36 ± 4.14	0.0002
Optic Nerve	D_{max}	14.52 ± 8.45	13.46 ± 11.27	0.719
	D_{mean}	10.37 ± 5.49	9.33 ± 7.09	0.757
Lens	D_{max}	5.73 ± 1.13	5.63 ± 1.77	0.677
	D_{mean}	4.39± 1.07	4.28 ± 1.63	0.279
Eye Ball	D_{max}	16.19 ± 5.62	16.14 ± 5.02	0.957
	D_{mean}	7.15 ± 1.93	6.63 ± 2.96	0.439

Table 3

(OAR) located on the contralateral side of the tumor were consistently lower in non-coplanar arc volumetric-modulated arc therapy (NC-rapid arc) compared to coplanar arc volumetric-modulated arc therapy (CO-rapid arc). This indicates that the delivered doses to the contralateral OARs were always lower in NC-rapid arc. Additionally, for OAR's placed on the sameface of the tumor, the temporal lobe, temporomandibular& cochlea received significantly lower doses in NC-Rapid arc compared to CO-rapid arc.

Hippocampus sparing

Hippocampus sparing radiotherapy has emerged as a promising strategy to develop tardyevokein individuals who have get total brain radiation therapy. Two significant clinical trials, namely Phase III RTOG 0614

and Phase II RTOG 0933, have been conducted to assess its effectiveness. These trials aimed to evaluate the impact of hippocampus sparing radiotherapy on patients' delayed recall compared to conventional whole brain radiotherapy. The findings of these studies have provided valuable evidence regarding the potential benefits of this innovative approach in enhancing cognitive function after radiation therapy. The standard given dose for total brain radiation therapy is typically 30 Gy. Nevertheless, when it comes to local brain tumors, the prescribed dose is higher, ranging from 54 to 60 Gy. Delivering radiotherapy to primary brain tumors presents a greater challenge in minimizing radiation exposure to nearby critical organs at risk (OARs). The proximity of these OARs to the tumor makes it more difficult to spare them from receiving high radiation doses during treatment. Therefore, reducing the radiation dose to OARs while effectively treating primary brain tumors remains a complex task in radiotherapy planning. In a study conducted by Gondi et al. in 2014, it was proposed that a dose greater than 7.3 Gy to 40% (D40%) of bilateral hippocampi could result in lengthy-spanmutilation in tardy evoke following radiation. The research revealed that from 20 patients, 12 of them had the entire ipsilateral hippocampus overlapping with the planning target volume (PTV). As a result, it was unavoidable to deliver a substantial dose to the ipsilateral hippocampus in these cases. These findings highlight the challenge of minimizing radiation exposure to critical structures such as the hippocampus during radiotherapy, mostly where the tumor iscloseness to these regions. The D40% values for the same side hippocampus were 25.08 Gy and 16.57 Gy in CO-rapid arc and NC-Rapid arc, respectively. On the other hand, both CO-rapid arc and NC-Rapid arcgain doses lesser than 7.30 Gy for the D40% of the contralateral hippocampus, with NC-Rapid arc demonstrating a extensively lesser dose compared to CO-rapid arc (5.751 Gy and 3.81 Gy, correspondingly). These findings indicate that the NC-rapid arc technique was more effective in reducing the radiation dose to the contralateral hippocampus compared to CO-rapid arc.

In a study conducted by Tsai et al. in 2015, it was observed that vocalremembrance impairment was correlated with the radiation-dose & volume of irradiation to the hippocampi. The use of NC-rapid arc was found to result in lower radiation doses delivered to both hippocampi, potentially contributing to the preservation of their functionality. This application of NC-rapid arc could be particularly advantageous for pediatric and youngishpeople of brain tumors, as they tend to have wider life expectancies following treatment. By reducing the radiation-related damage to the hippocampus, this technique may help mitigate long-term cognitive effects and improve the quality of life for these individuals.

Temporal lobe sparing

Radiation-induced injury to the temporal lobe has been a widely discussed side effect in patients with nasopharyngeal carcinoma. A study conducted by Kazda et al. in 2014 proposed that when the temporal lobe receives a average radiation dose of more than 45 Gy, it is linked with a rejection in longitudinal-IQ. This finding suggests that higher radiation doses to the temporal lobe can have a detrimental impact on cognitive function over time. It emphasizes the importance of optimizing treatment plans to minimize radiation exposure to critical brain structures such as the temporal lobe, particularly in patients with nasopharyngeal carcinoma, to reduce the risk of long-term cognitive decline.

Furthermore, a study conducted by Hsiao et al. in 2010 found that the mean dose of temporal-lobe (Dmean) may be kept below 36 Gy to minimize the risk of neurocognitive damage. In our study, we observed that CO-rapid arc and NC-rapid arc techniques delivered Dmean doses of 31.8 Gy and 25.5 Gy, correspondingly, to the ipsilateral temporal lobe. It is noteworthy that NC-rapid arc achieved a significantly lower Dmean dose compared to CO-rapid arc, with a reduction of 19.8%. These findings indicate that NC-rapid arc is more effective in limiting the radiation dosage to the ipsilateral temporal- lobe, potentially reducing potential neurocognitive impacts associated with higher radiation doses.

Cochlear sparing

Radiation-induced acousticnoxious can lead to sensor neural hearing loss. It has been observed that a average radiation dosage of 47 Gy for the cochlea can effect in the development of serious high-frequency sensor neural acoustic loss. In our study, all dose-volumetric parameters for both the ipsilateral and contralateral cochlea were below 47 Gy, indicating that the radiation doses delivered were within safe limits. Notably, the NC-rapid arc technique demonstrated a significant reduction in the radiation dose to both the ipsilateral and contralateral cochlea, with a reduction of 41.3% and 44%, respectively, compared to CO-rapid arc. This reduction in radiation dose achieved by NC-rapid arc may help minimize the risk of auditory toxicity and preserve hearing function in patients undergoing radiotherapy.

Low dosage irradiation to ordinary brain tissue

Exposure of ordinary brain tissue to radiation can result in a decrease in microgliacreation and subsequent cognitive mutilation, even in the absence of visibleharm to explicit brain structures. My research found that the volume of normal brain tissue exposed to a low dose was 5.4% less in NC-rapid arc than in CO-rapidarc. This finding aligns with the results of a study conducted by Audet et al. in 2011, which demonstrated that the use of NC rapid arcs can effectively decrease the low dose gained by regular brain tissue. By employing non-coplanar arcs in NC-rapid arc, the radiation dose to normal brain tissue can be minimized, potentially

reducing the risk of cognitive impairment associated with radiation therapy.

Delivery competence

It has been noted that dose delivery time for high-grade glioma radiation therapy treatment is longer for non-coplanar plans compared to coplanar plans. Specifically, delivering a 1.8 Gy session of brain treatment using coplanar VMAT takes approximately 2 minutes. However, in the case of NC-rapid arc (non-coplanar VMAT) in this research, which requisite 1 couch rotation, the delivery time increased by abonus 1 minute if shiftedphysically, and 20 seconds if shiftedmechanicallyvia dynamic table rotation. Despite this increase, the treatment duration remained relatively short byNC-rapid arc in these particular patients

Patient safety

A primary considerations associated with NC-rapid archaving potential risk of collision between the linac& the patient immobilization mask. The likelihood of such a collision occurring depends on several factors, including the location of the tumor, the specific immobilization devices being used, the size of the patient, and the degree of couch rotation [13]

The present research found that a 45-degree couch rotation increased the risk of collision during NC-rapid arc. However, this risk may be lesser by installing a couch-top annex on the advanced component of the table. It is important to note that the entire NC-Rapid arc plans in this research were replicated on a linac, & no collisions were found during the simulation process. In order to incorporate non-coplanar treatment into a clinical setting, it is crucial to thoroughly examine and approve the immobilization devices and predefined trajectories before proceeding with plan optimization. Consequently, it is recommended to conduct plan setup trials and perform manual couch rotations for each new non-coplanar treatment. By utilizing collision prediction techniques and patient modeling, it is possible to minimize the potential risks of collisions.

Limitation of the study

This study had certain limitations, one of which was the diverse nature of brain tumors. Brain tumors can originate in various locations within the brain and exhibit different shapes and sizes. Consequently, the location of the planning target volume (PTV) and its proximity to the hippocampus varied among patients. It was observed that minimizing the dose to the hippocampi was achievable when the PTV was situated at a considerable distance from them. In a study conducted by Korkmaz Kirakli & Oztekin (2017), the distance between several brain metastases & hippocampus was calculated to assess the possibility of reappearance following total-brain radiation therapy [12]. However, in the current study being referred to, the focus was on treating a primary single tumor rather than multiple metastases. The plan optimization process in this study followed a simple approach of prescribing the dose to the planning target volume (PTV) while minimizing the dose to the organs at risk (OARs). Notably, the normal brain tissue, which falls outside the PTV, received a significantly lower dose compared to whole brain radiotherapy. The goal was to ensure that the dose delivered to the normal brain tissue was kept as low as possible. The measurement of the distance among the planning target volume (PTV) and the opposite hippocampus was not taken into account in the current research. In hippocampus-sparing radiotherapy, it's important to recognize that the region surrounding the spared hippocampus may receive a lower dose compared to other parts of the brain or the planning target volume (PTV).While hippocampus sparing radiotherapy is generally considered a safe technique, it has been reported that there is a 2% growth in the absolute chance of reappearance associated with hippocampisaving irradiation [11]. In future investigation, it would be valuable to include the distance between the planning target volume (PTV) and the hippocampus as a factor to find the chance of disease reappearance. By incorporating this parameter, a better understanding of the relationship between PTV-hippocampus distance and recurrence risk can be gained. The configuration of the non-coplanar path used in this research could potentially be a matter of concern. In contrast to a previous research handling by Uto et al. (2016) [10], where they achieved a majorprogress in the homogeneity index with NC-rapid arc plans compared to CO-rapid arc plans [7], our study did not observe a significant difference in the homogeneity index. The lack of significant difference in the homogeneity index observed in our study compared to the study administered by Uto et al. (2016) [7] could be attributed to differences in plan settings. In our study, we utilized a rotation of collimator of 330° or 30° in both directions arcs, whereas we employed a rotation of collimator of 0° in every arc. This disparity in collimator rotation settings between the two studies may have contributed to the varying outcomes in terms of homogeneity index. The small selection size of this research is worth acknowledging. To mitigate the potential impact of the small sample size, we aimed to minimize its effect by including all the patients we collected in the generation of both CO-Rapid arc and NC-Rapid arc plans. By including the entire patient cohort in our analysis, we aimed to enhance the reliability and generalizability of the study findings despite the limitation imposed by the small sample size. In this study, the planning and implementation of the entire treatment plans were performed using a Varian truebeam linac. A study conducted by Snyder et al. (2014) demonstrated that the implementation of jaw tracking in both intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) for spine radiosurgery resulted in a reduction in dose to the spinal cord without compromising calculation accuracy. It is worth exploring the potential for additionaldeclination in radiation dosage to organs at risk (OARs) &ordinary brain part (outside-PTV brain volume) in CO-rapid arc and NC-rapid arc techniques by the integration of jaw

tracking ability. However, such an analysismight be pursued in upcoming studies. In the present research, a table angle of 45° or 315° was selected for NC-rapid arc treatment when dealing with tumors located on the left or right side of the brain, respectively. While our main focus was to demonstrate the benefits of OAR sparing in NC-Rapid arc, it could be valuable to incorporate multiple beam arrangement of NC-rapid arc for comparative analysis in upcomingresearch. This approach would allow for the identification of optimal configurations that can achieve the most effective OAR sparing effects for patients with brain tumors.

Conclusion

In the case of common brain tumor radiation therapy, the NC-rapid arcpractice proposed in this study demonstrated treatment qualities that were equivalent to the CO-rapid arc plans. By implementing NC-rapid arc, there was a notable reduction in dose to critical structures such as the, temporal lobes, temporomandibular,brainstem and cochlea. Furthermore, NC-rapid arc facilitated a decrease in dose to the opposite hippocampus, , eyeball optic nerve, andlens. As a result, NC-rapid arc shows promise as a potential new standard of concern for brain tumor patients, as it helps to conserve neurocognitive function & protects the function of organs at risk (OARs) following radiotherapy.

Conflict of interest – No

References

1. Rampling R. The present and future management of malignant brain tumours:surgery, radiotherapy, chemotherapy. *Journalof Neurology, Neurosurgery & Psychiatry*2004; **75**(suppl_2): ii24–30. doi: https:// doi.org/ 10. 1136/ jnnp. 2004. 040535
2. Beadle BM, Liao K-P,Elting LS, BuchholzTA, Ang KK, Garden AS, et al. Improvedsurvival using intensity-modulated radiationtherapy in head and neck cancers: a SEER-Medicare analysis: survival with IMRT inhead and neck cancer. *Cancer* 2014; **120**:702–10.
3. Zhang S, Yang R, Shi C, Li J, Zhuang H, Tian S, et al. Noncoplanar VMAT for brain metastases: a plan quality and delivery efficiency comparison withcoplanar VMAT, IMRT, and CyberKnife. *Technol Cancer Res Treat* 2019; **18**:153303381987162. doi: https:// doi. org/ 10.1177/ 1533033819871621
4. Han G, Liu D, Gan H, Denniston KA, Li S, Tan W, et al. Evaluation of the dosimetric feasibility of hippocampal sparing intensity-modulated radiotherapy in patients with locally advanced nasopharyngeal carcinoma. *PLoS One* 2014; **9**: e90007. doi: https:// doi. org/ 10. 1371/ journal. pone. 0090007
5. Li J, Tang X-B,Wang B-H,Chen X-M,ChenD, Chai L. Comparison between dual Arc VMATand 7F-IMRT in the protection of hippocampus for patients during whole brain radiotherapy. *J Xray Sci Technol* 2016; **24**: 457–66. doi: https:// doi. org/ 10. 3233/ XST-160561
6. Awad R, Fogarty G, Hong A, Kelly P, Ng D, Santos D, et al. Hippocampal avoidance with volumetric modulated arc therapy in melanoma brain metastases - the firstAustralian experience. *Radiat Oncol* 2013; **8**:62. doi: https:// doi. org/ 10. 1186/ 1748-717X- 8- 62
7. Sood S, Pokhrel D, McClinton C,Lominska C, Badkul R, Jiang H, et al.Volumetric-modulated Arc therapy (VMAT) for whole brain radiotherapy:not only for hippocampal sparing, but also for reduction of dose to organs at risk. *Med Dosim* 2017; **42**: 375–83. doi:https:// doi. org/ 10. 1016/ j. meddos. 2017. 07. 005
8. Webb S. *The physics of three-dimensional radiation therapy: conformal radiotherapy, radiosurgery, and treatment planning*. Bristol,UK ; Philadelphia: Institute of Physics Pub;2001
9. Buchtel HA. *Temporal Lobes, in Encyclopedia of the Human Brain*. Amsterdam: Elsevier; 2002. pp. 569–73.
10. Tsai P-F,Yang C-C,Chuang C-C,HuangT-Y, Wu Y-M, Pai P-C, et al. Hippocampal dosimetry correlates with the change inneurocognitive function after hippocampal sparing during whole brain radiotherapy: a prospective study. *Radiat Oncol* 2015; **10**(no.1)vol.. doi: https:// doi. org/ 10. 1186/ s13014-015- 0562-x
11. Uto M, Mizowaki T, Ogura K, Hiraoka M. Non-coplanar volumetric-modulated Arc therapy (VMAT) for craniopharyngiomas reduces radiation doses to the bilateralhippocampus: a planning study comparing dynamic conformal Arc therapy, coplanar VMAT, and non-coplanarVMAT. *Radiat Oncol* 2016; **11**: 86. doi: https:// doi. org/ 10.1186/ s13014- 016- 0659-x
12. Scoccianti S, Detti B, Gadda D, Greto D,Furfaro I, Meacci F, et al. Organs at risk in the brain and their dose-constraints in adults and in children: a radiation oncologist's guide for delineation in everyday practice.*Radiother Oncol* 2015; **114**: 230–8. doi:https:// doi. org/ 10. 1016/ j. radonc. 2015. 01. 016
13. Nelms BE, Robinson G, Markham J, Velasco K, Boyd S, Narayan S, et al. Variation in external beam treatment plan quality: an Inter-Institutional study of planners andplanning systems. *Pract Radiat Oncol* 2012;**2**: 296–305. doi: https:// doi. org/ 10. 1016/ j.prro. 2011. 11. 012.