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Dosimetric comparison between simultaneous integrated boost dynamic conformal arc therapy and whole brain radiation therapy techniques in the treatment of patients with multiple brain metastases

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ABSTRACT

Background: Brain metastases are the most common intracranial neoplasm in adults. It is estimated that 8-10% of adults with cancer will develop symptomatic brain metastases during their lifespan. **Aim:** This study aims to compare the dosimetric results of whole brain radiation therapy (WBRT) and simultaneous integrated boost dynamic conformal arc therapy (DCAT) to ascertain the optimal approach for treating brain metastases. **Patients and Methods:** WBRT and DCAT plans were created for 20 patients treated for brain metastases using the Eclipse™ treatment planning system (Varian Medical Systems). WBRT plan was designed to deliver 20.0Gy in 5 fractions while the DCAT plan was designed to deliver 25.0Gy in 5 fractions to the brain metastases planning target volumes (PTVs). Target coverage and sparing of organs at risk (OARs) were compared between both techniques. The total number of monitor units (MUs) and the treatment time were used to assess treatment delivery efficiency. **Results:** In this study, The DCAT technique significantly outperformed the WBRT technique in terms of coverage of Mean PTV25Gy when comparing the means of the two groups (25.64 ± 0.27 Gy Vs 20.84 ± 0.09 Gy) ($P = 0.02$) and also for Maximum PTV25Gy (26.59 ± 0.52 Gy Vs 21.25 ± 0.08 Gy) ($P = 0.001$). Moreover, there are very substantial variations between the WBRT approach and the DCAT technique in terms of number of monitor units (474.95 ± 15.16 Gy Vs 1250.70 ± 20.16 Gy) ($P = 0.01$) & time of treatment (0.76 ± 0.02 min. Vs 0.88 ± 0.02 min.) ($P = 0.01$). For OARs, Hippocampus was also significantly lower using DCAT Vs WBRT (10.91 ± 5.16 Gy vs. 20.64 ± 0.26 Gy) ($p = 0.03$). Optic chiasm Maximum was also significantly lower using DCAT Vs WBRT (7.52 ± 3.33 Gy vs. 20.56 ± 0.34 Gy) ($p = 0.007$), also for left and right optic nerve was significantly lower using DCAT Vs WBRT (left 4.72 ± 0.74 Gy vs. 20.07 ± 0.25 Gy) ($p = 0.006$) & (right 4.64 ± 0.82 Gy vs. 20.80 ± 0.12 Gy) ($p = 0.006$). **Conclusion:** DACT strategies facilitate enhanced radiation delivery to brain metastases while simultaneously safeguarding organs at risk, allowing for escalation of doses in small and large lesions

Keywords: Brain metastases DCAT, Dosimetric evaluation, OARs, Radiotherapy, WBRT

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BACKGROUND

Brain metastases are the leading intracranial neoplasms among adult individuals and are observed in 10-30% of patients diagnosed with cancer (Khauntia et al., 2006). The outlook for individuals afflicted with brain metastases is typically unfavorable, as untreated patients typically have a median survival period of one month, while treated patients typically have a median survival period of 4-6 months (Li et al., 2008).

Many individuals diagnosed with cancer will ultimately experience the occurrence of brain metastases. The established treatment methods for patients with brain metastasis are surgical intervention and radiotherapy. For

many years, the utilization of whole-brain radiotherapy (WBRT) has been implemented in clinical settings. Typically, patients with oligo-brain metastasis undergo surgical removal, chemotherapy, and the utilization of stereotactic radiosurgery (SRS) either as a standalone treatment or in combination with WBRT (Chiesa et al., 2013). SRS is a non-invasive treatment with few side effects compared to WBRT. For patients with multiple brain metastases, WBRT is a commonly used treatment modality. However, SRS seems to be a new standard option (Kraft et al., 2019).

Brain metastases (BMs) are widely recognized as the most prevalent intracranial neoplasms, with a median survival period ranging from 3 to

47 months, as per various histological groups (Lamba et al., 2021; Sperduto et al., 2020). Brain metastases manifest in approximately 20%-40% of cancer patients and are present at the initial diagnosis in 10%-15% of cases (Ostrom et al., 2018). Irrespective of Histology, around 70% of patients exhibit solitary brain metastases (Stark et al., 2011). Nevertheless, the number of brain metastases varies depending on the primary tumor. Notably, melanoma and lung cancer are more prone to develop multiple brain metastases, while breast, renal, and gastrointestinal cancers tend to exhibit a predilection for solitary brain metastases formation (Delattre et al., 1988; Nussbaum et al., 1996).

In the case of individuals afflicted with brain tumors, WBRT aids in the mitigation of intracranial pressure, thereby achieving expeditious palliation of neurological symptoms. This therapeutic option contributes to the enhancement of local tumor control as an adjuvant to surgical intervention or radiosurgery (Norden et al., 2005). Simultaneously it bolsters survival rates in instances where tumor regression manifests (Aebi et al., 2007). Regrettably, it has been demonstrated that WBRT may be associated with enduring, progressive, and irreversible neurological sequelae (Crossen et al., 1994). This includes but is not limited to dementia (Welzel et al., 2008), cerebellar dysfunction (Roman et al., 1995), and a decline in neurocognitive functioning. Monje et al. (2002) posited that symptoms of neurocognitive function decline, such as short-term memory loss and diminished concentration, may manifest months after the administration of WBRT.

Recent advancements in systemic therapy have resulted in a significant improvement in the prognosis of individuals diagnosed with brain metastasis. As a result, stereotactic radiosurgery (SRS) is now being increasingly embraced as a viable substitute for WBRT to attain favorable long-term local control, while simultaneously mitigating the potential for neurocognitive impairment (Brown et al., 2016).

Stereotactic radiosurgery (SRS) is employed in the management of neoplasms with a

maximum diameter that is less than three centimeters. This threshold is chosen due to its ability to yield effective control at the local level while simultaneously reducing the risk of radiation necrosis. The size of the tumor plays a noteworthy role in predicting the likelihood of local recurrence following SRS. Vogelbaum et al. (2006) observed that brain metastases with the longest diameter greater than two centimeters exhibited a heightened rate of local recurrence and radio necrosis as compared to those with a diameter equal to or smaller than two centimeters.

Dynamic conformal arc therapy is a technique for delivering conformal dose distributions which consists of intensity-modulated radiotherapy (IMRT) delivered continuously as the gantry rotates around the patient in a DCAT (Otto et al., 2008). During DCAT delivery the gantry rotation speed, Multileaf Collimator (MLC) field aperture and the dose rate are all simultaneously adjusted (Bedford et al., 2009).

This research aims to compare the radiotherapy dose received by OAR including the brain stem, optic chiasm, pituitary gland, right and left optic nerves, and right and left eyes in patients with multiple large brain metastases treated with simultaneous integrated boost dynamic conformal arc therapy (SIB DCAT) and whole brain radiotherapy (WBRT).

PATIENTS AND METHODS

This prospective study includes twenty patients diagnosed with brain malignancy. In this study, we have compared whole brain radiation therapy (WBRT) and dynamic conformal arc therapy (DCAT) treatment planning techniques for each patient to achieve an optimum plan for a specific target and organ at risk. These two plans were designed using the Varian Eclipse treatment planning system, at Ayadi Al-Mostakbal Oncology Hospital.

We identified all patients with brain metastases treated with WBRT in Ayadi Al-Mostakbal Oncology Hospital, where we have a registry for all patients. We manually reviewed imaging and identified those adult patients who had a pre-treatment T1-contrast MRI sequence, had ten or fewer brain metastases, and at least one ≥ 3 cm in longest diameter.

Informed consent forms were signed by all patients. The study protocol was approved by our local independent ethical committee and conducted in accordance with the Declaration of Helsinki. Before simulation or delivering EBRT for brain cancer, patients were immobilized to maximize accuracy and minimize the movement of the target organ by using a custom Qfix thermoplastic head mask. All the methods described here were performed following the relevant guidelines and regulations.

Patients were scanned in a supine position on headboard with arms at the sides as well as heads extended; the head was put on custom neck cushion support. Before the CT scan, on the head mask are put three orientated points in the crosses of the laser room. Patients were scanned from the top of the head including the brain to the neck, with a scan thickness and index of 3 mm.

The computed tomography images of selected patients were transferred to the treatment planning system, where contouring of the target volumes and organs at risk was done according to Radiation Therapy Oncology Group (RTOG) guidelines. The planning target volumes and OARs were delineated by a radiation oncologist on the CT slices using the contouring tool of Varian eclipse treatment planning system.

For each patient, we fused MRI and planning CT scans and outlined all visible lesions on the volumetric T1-contrast MRI scans as gross tumor volume (GTV). Planning target volume (PTV) was then developed by an isotropic 1 mm margin from GTV. OARs included the normal brain, eyes, lenses, chiasm, optic nerves, brainstem, cochlea, and hippocampi, and they were outlined for dose constraints and evaluation. Hippocampi were outlined according to RTOG contouring atlas.

After simulation and contouring, the radiotherapy plans were performed via Varian eclipse software using AAA algorithm. For WBRT plans, we used the original plan that patients received, using conventional opposed lateral fields. The dose was prescribed to 20 Gy in 5 fractions for all WBRT plans. DCAT plan used a mono-isocenter technique with two coplanar 360°-ARCs. We increased the prescribed dose

to 25 Gy for small lesions (<3 cm in longest diameter); a sum of all small lesions was called PTV_{25Gy}. Whereas maintaining the dose at 20 Gy for large lesions (≥ 3 cm in longest diameter); a sum of all large lesions is called PTV_{20Gy}.

The plans were evaluated qualitatively by comparing, the dose distribution through the patient volume (cut-by-cut) and quantitatively with the use of Dose Volume Histograms (DVHs). The maximum dose, mean dose, and a set of values (Dx%) the percentage dose received by the x% volume of the target volume, and (Vx%) the percentage volume irradiated by x% of the PD, were obtained for OARs.

Statistical analysis

In the current study, statistical analysis of data was carried out using SPSS version 22 software to compare the differences between the two plans regarding dosimetric characteristics for planning target volume and organs at risk. Continuous variables are presented as a mean and standard deviation. The comparisons between the groups were performed using an independent t-test. The p-value (<0.05) was considered a statistically significant difference.

RESULTS

Demographic criteria of patients

With analysis of the data of 20 patients included in this study, the mean age of the patients was 62.05 years. Ten patients (50%) were male and the other ten (50%) were female. Five of the brain metastases cancer patients (25%) had breast cancer as the primary tumor. Four patients (20%) had non-small cell lung cancer (NSCLC) as the primary tumor. Three patients (15%) had esophagus cancer as the primary tumor, besides six patients (30%) have colon, myeloma, and small cell lung cancer (SCLC) cancers as primary tumor divided to equal percent (10%), two patients for each primary tumor. Finally, two patients (10%) had ovary and rectum cancers as primary tumors divided to equal percent (5%) one patient for each primary tumor. All twenty brain metastases cancer patients didn't do neurosurgery before radiotherapy. Nine patients of them (45%) had zero Eastern Cooperative Oncology Group (ECOG) performance, while seven patients (35%) had one (ECOG) performance. Other four

patients of brain metastases cancer patients (20%) had two (ECOG) performances. All twenty brain metastases cancer patients didn't have the status of extracranial metastases. The number of small brain metastases ranged 3-9 as well as the number of large brain metastases ranged 1-2 (Table 1).

We compared the dose received by each PTV in WBRT and DCAT radiotherapy techniques. We used axial, sagittal, and coronal cuts as well as a beam eye view (BEV) as well as DVHs of

Table 1. Demographic criteria of patients and metastases characteristics.

P.NO	Gender	Age	Primary tumor	Neurosurgery before radiotherapy,	Performance (ECOG)	Status of extracranial metastases	Number of small brains metastases <3cm	Number of large brains metastases > 3 cm
1	Male	54	Colon	NO	0	NO	7	2
2	Male	67	NSCLC	NO	2	NO	4	1
3	Female	58	Breast	NO	0	NO	6	2
4	Male	59	Esophagus	NO	1	NO	3	1
5	Female	61	Myeloma	NO	1	NO	6	1
6	Female	53	Breast	NO	2	NO	5	1
7	Male	65	Colon	NO	0	NO	8	2
8	Female	72	Myeloma	NO	0	NO	4	1
9	Female	51	Ovary	NO	0	NO	5	2
10	Male	73	SCLC	NO	1	NO	6	2
11	Male	69	NSCLC	NO	1	NO	9	1
12	Female	50	Breast	NO	0	NO	6	1
13	Female	60	Rectum	NO	2	NO	4	1
14	Male	70	SCLC	NO	1	NO	7	2
15	Female	56	Esophagus	NO	1	NO	3	1
16	Female	62	Breast	NO	0	NO	6	2
17	Male	74	NSCLC	NO	2	NO	8	2
18	Female	61	Breast	NO	0	NO	5	1
19	Male	58	Esophagus	NO	0	NO	6	2
20	Male	68	NSCLC	NO	1	NO	3	1

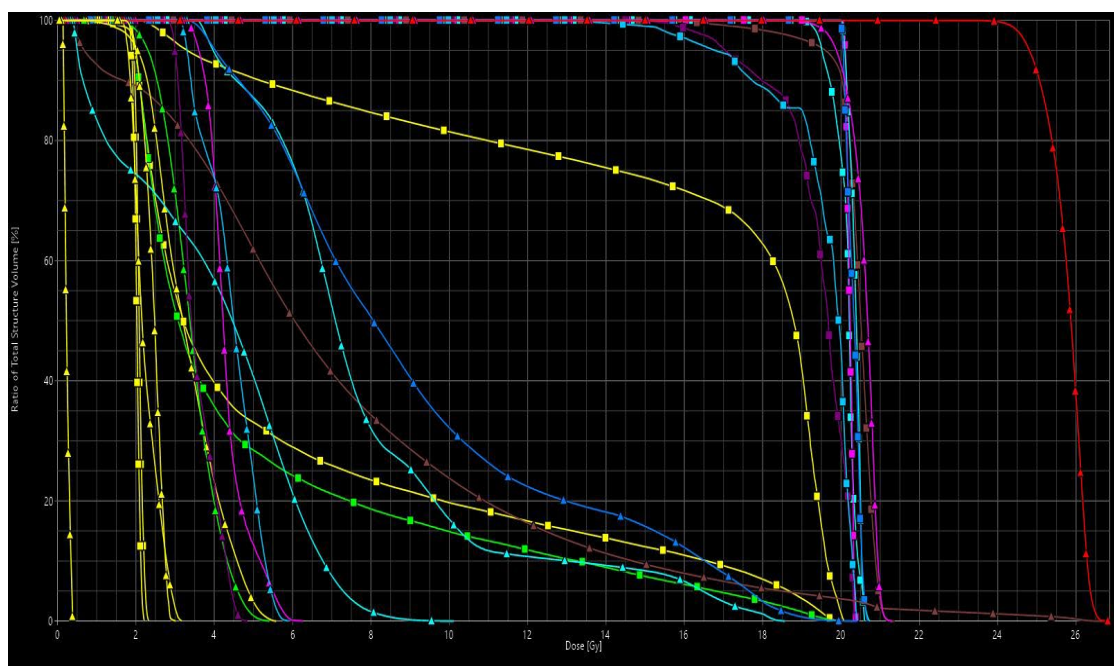


Figure 1. Planning target volumes (PTVs) and organ at risk (OAR) dose comparison between WBRT (square shape) and DCAT (triangle shape) plans of the same patient.

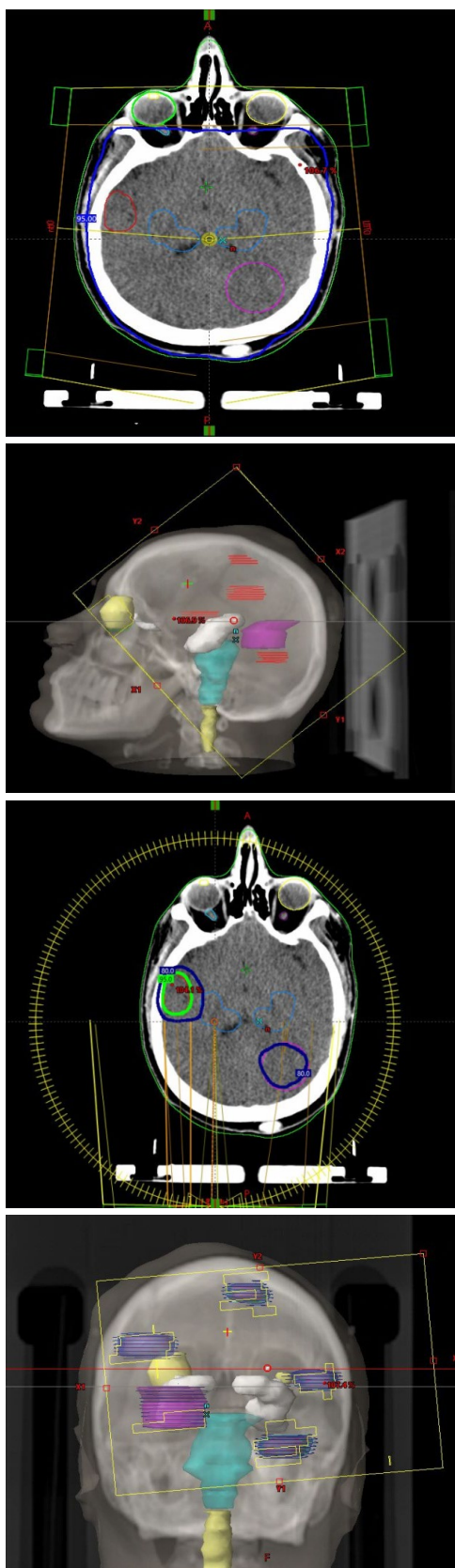


Figure 2. Planning target volumes (PTVs) and organ at risk (OAR's) dose comparison between WBRT (square shape) and DCAT (triangle shape) for a radiation therapy plan of the same patient. (a) axial cut for WBRT, (b) BEV image for WBRT, (c) axial cut for DCAT & (d) BEV image for WBRT.

the two planning techniques for every brain metastasis patient included in this study as represented in Figures 1 & 2. The comparison between the means of the two groups showed significant increase in the coverage of PTV_{20Gy} Mean, PTV_{20Gy} Maximum, PTV_{25Gy} Minimum, PTV_{25Gy} Mean, and PTV_{25Gy} Maximum for DCAT technique than WBRT technique. However, the comparison between the means of the two groups showed highly significant differences in the coverage of PTV_{20Gy} Minimum, as well as the number of monitor unit (MU) and treatment time for WBRT technique than DCAT technique. All the data is presented in Table (2). However, the comparison between the means of the two groups showed significant differences in the coverage of PTV_{20Gy} Minimum, as well as number of mointer unit (MU) and treatment time for WBRT technique than DCAT technique. All the data is presented in Table 2. Regarding the dosimetric parameters of organs at risk (OARs), the comparison between means of two groups for all organs at risk (OAR) shows that the best technique is DCAT with a highly significant difference from WBRT. All the data is presented in Table (3).

DISCUSSION

WBRT has the potential to swiftly alleviate neurologic symptoms and enhance the quality of life, which is particularly advantageous for patients with brain metastases that cannot be surgically accessed or for patients who are unable to undergo neurosurgery (Gaspar et al., 2010). Patients with limited intracranial disease are advised to consider focal therapeutic options, such as neurosurgical resection or stereotactic radiosurgery, to mitigate the risks of cognitive decline and deterioration in learning and memory function that may occur following WBRT. To preserve neurocognitive function in cases of brain metastasis without hippocampal involvement, the hippocampus avoidance whole brain radiation therapy (HA-WBRT) technique may be a viable option (Brown et al., 2020; Yang et al., 2021).

In the context of patients afflicted with brain metastases, it is imperative to exercise caution in administering high levels of radiation to healthy brain tissue to avert the occurrence of

Table 2. Dosimetric parameters (Mean \pm SD) of target volume coverage in WBRT and DCAT plans in patients with brain metastases cancer

Dosimetric parameter	Brain cancer patients (n=20)		P-value
	WBRT	DCAT	
PTV _{20Gy} Minimum	20.03 \pm 0.39 Gy	19.36 \pm 0.58 Gy	0.03
PTV _{20Gy} Mean	20.33 \pm 0.16 Gy	21.71 \pm 0.19 Gy	0.04
PTV _{20Gy} Maximum	20.82 \pm 0.10 Gy	21.03 \pm 0.13 Gy	0.04
PTV _{25Gy} Minimum	20.33 \pm 0.12 Gy	23.19 \pm 0.29 Gy	0.03
PTV _{25Gy} Mean	20.84 \pm 0.09 Gy	25.64 \pm 0.27 Gy	0.02
PTV _{25Gy} Maximum	21.25 \pm 0.08 Gy	26.59 \pm 0.52 Gy	0.01
Monitor Unit (MU)	474.95 \pm 15.16	1250.70 \pm 20.16	0.01
Treatment Time (minute)	0.76 \pm 0.02	0.88 \pm 0.02	0.02

PTV: planning treatment volume, WBRT: whole brain radiotherapy and DCAT: dynamic conformal arc therapy. The means were compared using an independent T-test, where P value <0.05 indicates a significant difference.

Table 3. Dosimetric parameters (Mean \pm SD) of organs at risk in WBRT and DCAT plans in patients with brain metastases cancer

Dosimetric parameter	Brain Cancer Patients (n=20)		P-value
	WBRT (n=20)	DCAT (n=20)	
LT EYE MAX	19.80 \pm 0.17 Gy	4.69 \pm 0.85 Gy	0.002
RT EYE MAX	19.86 \pm 0.10 Gy	4.58 \pm 0.70 Gy	0.003
BRAIN STEM MAX	19.52 \pm 0.48 Gy	11.48 \pm 6.59 Gy	0.04
SPINAL CORD MAX	19.66 \pm 0.45 Gy	0.60 \pm 0.27 Gy	0.008
OPTIC CHAISM MAX	20.56 \pm 0.34 Gy	7.52 \pm 3.33 Gy	0.007
LT OPTIC NERVE MAX	20.07 \pm 0.25 Gy	4.72 \pm 0.74 Gy	0.006
RT OPTIC NERVE	20.80 \pm 0.12 Gy	4.64 \pm 0.82 Gy	0.006
HIPPOCAMPAS MAX	20.64 \pm 0.26 Gy	10.91 \pm 5.16	0.03
HIPPOCAMPAS AVOID MAX	21.06 \pm 0.23 Gy	10.73 \pm 6.26 Gy	0.02
LT LENS MAX	3.01 \pm 0.49 Gy	2.08 \pm 0.84 Gy	0.04
RT LENS MAX	2.88 \pm 0.54 Gy	1.88 \pm 0.57 Gy	0.045
BRAIN 20GY	91.98 \pm 1.08 %	3.90. \pm 0.68%	0.008
BRAIN 15GY	99.85 \pm 0.09 %	8.70. \pm 0.82%	0.007
BRAIN 10GY	100 \pm 0.00 %	22.93 \pm 0.67%	0.008
BRAIN 5GY	100 \pm 0.00 %	59.89. \pm 1.71%	0.009

WBRT: whole brain radiotherapy, DCAT: dynamic conformal arc therapy, LT: left and RT: right. The means were compared using an independent T-test, where P value <0.05 indicates a significant difference.

radio necrosis. This principle holds true not only for low and intermediate doses but also for high doses. The progression of treatment options, which now encompass chemotherapy, molecular target drugs, and immune checkpoint inhibitors, has led to a more favorable prognosis for patients grappling with brain metastasis. Consequently, the utilization of stereotactic radiosurgery (SRS) for brain metastases has witnessed a rise in prevalence. Nonetheless, there exists a subset of patients necessitating additional SRS treatment, particularly when new intracranial brain metastases are detected through follow-up magnetic resonance (MR) imaging. Given the potential for this scenario, it is incumbent upon healthcare providers to

minimize the impact of radiation not only at high doses but also at low and intermediate doses on the normal brain tissue to the greatest extent possible (Blonigen et al., 2010).

There is a wealth of consistent evidence suggesting a direct correlation between the increasing volume of brain metastases and inferior overall survival (OS) and local control (LC). However, the lack of adequate data from randomized clinical trials and concerns regarding the safety of SRS in patients with large lesions have led to WBRT remaining the established treatment regimen for multiple large brain metastases. Regrettably, the outcomes of WBRT have been unsatisfactory.

The patients in our study were selected from a neurooncology center with comprehensive neurosurgical and neurooncology services, including access to SRS. Despite having access to these services, the patients included in this study were those who were ultimately treated with WBRT by their primary consultants (Navarria et al., 2016).

The efficacy of LC is enhanced when the dose administered to the lesions increases. Our study illustrated an augmentation in the dose delivered to the lesions. Regardless of the size of the lesions, both the integral dose and the dose delivered to the target volume experienced a notable increase with the implementation of the DCAT plan. Consequently, these findings indicate that the DCAT model outperforms the administration of a higher dose to the brain metastases, thereby likely achieving a superior LC outcome. It is worth noting that OARs received a significantly reduced dose in the DCAT plan. The integration of the inner-escalated dosing model further signifies the improved preservation of normal tissue with DCAT in comparison to WBRT, thus reducing the probability of radiation-induced toxicity (Abraham et al., 2018; Vogelbaum et al., 2006).

For the treatment target volumes coverage, the mean doses received by PTV_{20Gy} Mean, PTV_{20Gy} Maximum, PTV_{25Gy} Minimum, PTV_{25Gy} Mean, and PTV_{25Gy} Maximum of brain metastases cancer patients show highly significant differences between DCAT in a comparison with WBRT. Except for the PTV_{20Gy} Minimum in favor of the WBRT technique. The analysis of MU and treatment time indicated that WBRT delivered the lowest number of MU (474.95 ± 15.16) in the shortest time (0.76 ± 0.02 min) than DCAT technique but the difference in time is very small due to 1400 dose rate in DCAT technique. The best technique should achieve homogeneous dose distribution to the PTV. The minimum and maximum acceptable radiation doses to the PTV should be (95%-110%) which is achieved by two treatment techniques. However, the comparison between the two planning techniques (PTV_{20Gy} Minimum, PTV_{20Gy} Mean, PTV_{20Gy} Maximum) and (PTV_{25Gy} Minimum, PTV_{25Gy} Mean, and PTV_{25Gy} Maximum) proved that the radiation

dose received in 2DCAT is the best. So, 2DCAT achieved better PTV coverage and dose homogeneity.

Our results agree with the results obtained by Yamamoto et al. (2014) who studied SRS without WBRT for patients with multiple brain metastases. Their study suggests that SRS alone for patients with five to ten brain metastases is non-inferior to that in patients with two to four brain metastases. Stereotaxic radiosurgery is a suitable alternative for patients with up to ten brain metastases.

Regarding dosimetric parameters for organs at risk, the comparison of WBRT and DCAT treatment techniques showed that, the maximum doses delivered to the left eye, right eye, brain stem, spinal cord, optic chiasm, left optic nerve, right optic nerve, hippocampus, hippocampus avoid, left lens, and right lens as well as the present volume of the brain receive 20Gy, 15Gy, 10Gy and 5Gy irradiated with DCAT technique were highly lower than that for WBRT. So, the use of the DCAT technique would be preferable to WBRT during the treatment of brain metastases cancer patients to minimize the OARs long-term complications. All dosimetric parameters for organs at risk were still within the dose tolerance of the brain metastases cancer in WBRT vs. DCAT techniques. The hippocampus is the most important organ at risk in brain metastases cancer. The brain stem is also another important organ that should be protected in brain metastases cancer treatment. So, OARs are better protected in the DCAT technique plan. Blonigen et al. (2010) studied radio necrosis after SRS using a linear accelerator. Their study suggested that V_{10Gy} to normal brain larger than 10.5 cm³ or V_{12Gy} larger than 8 cm³ are associated with the highest risk of symptomatic radio necrosis. This patient should better be considered for hypo-fractionated stereotaxic radiotherapy.

The occurrence of radiation-induced toxicity in individuals receiving WBRT has also been documented in relation to other OARs, such as the parotid glands, scalp, and ear canals, among others. Our investigation has put forth the proposition that an accelerated radiotherapy course in the DCAT plan has the potential to

protect these vital structures while maintaining adequate coverage of WB-PTV. This reduction in clinically significant radiation dose to critical structures may yield enhancements in patient quality of life. Within this study, we have successfully showcased the feasibility of employing the simultaneous integrated boost-accelerated radiotherapy technique (SIB-DCAT) to preserve the hippocampi. Concurrently, a uniform dose distribution to the WB-PTVs and a high-quality dose distribution conforming to multiple brain metastases planning target volumes (m-BM PTVs) within the same treatment setup were facilitated. In forthcoming times, we will furnish an intricate elucidation of the OAR dose analysis (for instance, dose diminution to the scalp, ear canals, parotid glands, cochlea, etc.), exhibiting the clinical potential of the SIB-DCAT planning in mitigating radiation-induced toxicity in normal tissues. We hold the conviction that diminishing hippocampal doses, as well as doses to other OAR, could bestow a superior quality of life, particularly for WBRT patients who display elongated survival, such as those undergoing prophylactic cranial irradiation and pediatric or young adult patients subjected to craniospinal irradiation (Cho et al., 2013; Trignami et al., 2014; Kao et al., 2014).

The primary concern associated with the prescription of a higher dosage is the heightened probability of radio necrosis. Evidence obtained from fractionated SRS employing a 5-fraction regimen indicates anticipated rates of toxicity of 4.8% for V24.4 of 10 cm³ and 8.6% for V24.4 of 20 cm³ of the normal brain. Even though escalated dosing models result in higher V24.4 in the normal brain compared to WBRT, we managed to maintain V24.4 \leq 10 cm³. The average V24.4 range was 1.11–4.30 cm³ across the DCAT plan.

Finally, because of the study's retrospective nature and the limited size of the sample, we have solely demonstrated that the introspective nature of the dosimetry analysis has deviated from the criteria in clinical settings. Therefore, the dilemma does indeed exist in finding a balance between clinical workload and the time-consuming planning that is necessary to meet all the criteria. Consequently, daily treatment may be obtained at the expense of

noncompliance and non-conformity regarding planning targets, even when deviations from the protocol occur. In the process of determining the final plan, the physician's individual choice, in accordance with the patient's clinical situation, may have undoubtedly played a role. In other words, in an actual clinical situation, other clinical factors may have been given higher priority than strict adherence to the criteria. The determination of the patient's projected lifespan or the assessment of the precise tumor dimensions and its placement within the body would have been deliberated upon prior to the ultimate selection of the treatment regimen. Nonetheless, the subsequent occurrence of intracranial malfunction, whether due to insufficient dosage coverage or solely attributable to the malignant nature of the cancer itself, remains an area necessitating further investigation.

CONCLUSIONS

In this article, we have investigated utilizing DCAT for the administration of WBRT with SIB to multiple brain metastases, which encompasses up to 10 brain tumors. It was indeed feasible to spare all organs at risk (OARs) while simultaneously ensuring the delivery of conformal and homogenous dose distributions to WB-PTVs. Furthermore, DCAT possessed the capability to administer radio-surgical equivalent dose distributions to each brain tumor, acting as SIB, within the same timeframe, and on the same treatment machine. The utilization of DCAT with SIB plan significantly shortened total beam-on time (averaging 0.88 minutes), thereby facilitating a rapid and efficacious treatment delivery process that also benefits the convenience of the patients.

AUTHOR CONTRIBUTIONS

Conceptualization, A.M.D.; methodology, A.A.A.; software, N.M., A.M.E.; validation, A.M.D. and A.M.E.; formal analysis, A.M.E.; writing—original draft preparation, A.M.D., A.M.E., N.M., A.A.A.; writing—review and editing, A.M.D, A.M.E., N.M., A.A.A. All authors have read and agreed to the published version of the manuscript.

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INFORMED CONSENT STATEMENT

All patients signed an informed consent form.

DATA AVAILABILITY STATEMENT

Data will be available upon reasonable request.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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