Dosimetric Comparison and Plan Evaluation of Different Stereotactic Radiosurgery Plans for Treatment Multiple Brain Metastasis Using Single and Dual Isocenter

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ABSTRACT

Introduction: stereotactic radiosurgery (SRS)is the most proper treatment for multi brain metastasis for enhanced good coverage and minimizing dose to organs at risk (OARs). This study aims to compare single and dual isocenter SRS plans and discuss which technique we can use with a range distance between two lesions was 4-8cm and maximum of total planning target volumes was 36cc.

Material and Methods: twelve patients with multi brain metastasis underwent two different SRS treatment planning techniques including single isocenter and dual isocenter. We quantitatively assessed plans qualities by dose-volume metrics for two groups according to distance between targets less or more than 6 cm. Conformity index (CI), Confirmation Number (CN), heterogeneity index (HI), gradient distance (GD), Gradient index (GI), and selectivity index. OARs were evaluated and the dose to the normal brain was evaluated using V6, and V12 Gy.

Results: There is an insignificant difference between single and dual isocenter plans in CI, CN, HI, GD, GI, for two plans with separate distance less than 6 cm.in addition to second group have a significant difference in CN, GI, and GD. Dual isocenter plan have lower volume of normal brain received 6Gy than single isocenter plan with separate distance more than 6 cm.

Conclusion: Plan quality of single isocenter was equal to dual isocenter for SRS treatment of multi brain lesions. Dual isocenter took time during setup and matching for CBCT and has little difference in dose spillage for more than 6cm distance between targets.

Keywords: SRS, SI, DI and VMAT.

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Introduction

The most prevalent intracranial malignancy is brain metastases and occurs in approximately 10 percentage to 20 percentage of adult cancer patients and being 10 times more common than initial brain tumors (1). The treatment of brain metastases with radiotherapy has progressed dramatically during the last few decades. Whole brain radiation therapy (WBRT) has a historically been used to improve locoregional control after surgical resection (2).

While surgery is normally reserved for single or symptomatic metastases, whole brain radiation therapy (WBRT)has traditionally been the treatment of choice for numerous intracranial metastases. Stereotactic radiosurgery (SRS), a high dose and precise compliance radiotherapeutic treatment, is rapidly being employed as an alternative to WBRT for controlling intracranial cancer while providing superior normal tissue with less cognitive damage (3,4).

stereotactic radiosurgery was later demonstrated as a viable and safe treatment option for recurring brain malignancies in the setting of prior brain radiotherapy (5). Yamamoto et al.

indicated that treating 5-10 brain metastases with SRS is a safe alternative with comparable survival to those treated for 2-4 brain metastases (6).

Many methods, such as gamma knife (GK) and linear accelerators (LINAC), are available to treat various brain metastases. SRS treatment with multiple brain metastases has used GK and LINAC equipment. Many research has been conducted to compare the plan qualities of Gamma Knife with the single isocenter VMAT approach employing a LINAC equipment for the treatment of numerous brain metastases (7-9).

Volumetric Modulated Arc Therapy (VMAT) is a novel treatment technique that makes use of inverse planning optimization. It can generate extremely conformal dose distributions by regulating the simultaneous modification of multi-leaf collimator angles, dose rate, and gantry motion during treatment delivery gantry rotation around the patient. Efficient treatment delivery provides accurate and precise treatment in a very short period of time (10,11).

Non coplanar arc plan is known as oblique treatment plane with using couch movement, where coplanar arc is known as treatment plane without couch rotation. In comparison to intensity-modulated radiation therapy (IMRT), coplanar VMAT, and noncoplanar VMAT therapy produced better conformity and faster dose reduction. Noncoplanar VMAT provided a similar dose reduction at high dose levels and a lower dose reduction at middle to low dosage levels when compared to CyberKnife. Noncoplanar VMAT plans included a fewer beam on time and smaller monitor units than CyberKnife plans (12). Clark et al. (13) evaluated the plan quality for single isocenter cranial radiosurgery with VMAT. For single targets, one or two arc single isocenter designs are frequently sufficient, however 2-4 arcs may be more favourable for numerous targets.

The main objective of our study to investigate the best plan for improving normal brain tissue and OARs by compare single isocenter and dual isocenter SRS in terms of dosimetric effect for multiple lesions. Taking into account the difference in the distances between the targets, which lead to dividing the cases into two groups according to this factor with constant number of arcs.

Methods and Materials

Contouring and simulation

Twelve cases have multiple brain metastases with different lesions size, number, and distance apart each other were simulated in the supine position. For SRS, patients were immobilized using a standard thermoplastic head and neck mask. Table (1) show basic characteristic of the studied patients.

Table (1): Basic characteristics of the studied patients.

Basic characteristics	The studied brain metastasis patients	
	Number	Percent
Age (years)		
Mean±SD	66 ± 5.59	

Median (Range)	67.50 (57 – 73)	
Number of lesion		
Two lesions	9	75%
Three lesions	2	16%
Four lesions	1	8%
Location		
Right cerebral hemisphere	3	25%
Left cerebral hemisphere	3	25%
Both hemispheres	6	50%
Three-dimensional distance (cm)		
Mean±SD	6.10 ± 1.28	
Median (Range)	6 (4 – 8)	

A magnetic resonance imaging (MRI) scan with contrast medium and a slice thickness of 1mm was performed for planning purposes. This sequence was aligned with the planning computed tomography (CT) scan (1 mm slice thickness). The period between the MRI and the planned CT was kept as short as workable, but no more than one week. To improve co-registration, contrast media was used for the planning CT. Contouring of target volume and organs at risk (OARs) was done by radiotherapist. Planning target volumes (PTV) was introduced by 1mm margin from Gross tumor volumes (GTV). Brainstem, lenses, eyeballs, optical nerves, optic chiasm, cochlea, and hippocampi are among the organs at risk.

Treatment planning

All patients were applied to two different techniques of VMAT SRS plans single isocenter (SI) and dual isocenter (DI). Between the lesions in each case, a single isocenter was inserted. VMAT inverse optimization was carried out to achieve optimal target coverage and maximum sparing of normal tissue by using 4 partial arcs coplanar or non-coplanar (couch angle range 5 to30 degree). To prevent interleaf leakage, the collimator angle was adjusted at 355° for CCW and 5° for CW, respectively. All treatment plans were performed with the Eclipse treatment planning system (TPS) version 13.6. The anisotropic analytical algorithm (AAA) was used for dose calculations.

A dose of four patients is 24Gy in 3 fractions, three patients 30Gy in 5 fractions and five patients 18Gy in 1fractions. All targets in each plan received the same dose. The goal was to achieve dose coverage of at least 99% for each lesion.

Following that, the SRS treatment plans for all cases were replanned using dual isocenter technique. The plans were created utilising four partial arcs, just like a single isocenter plan. Jaw tracking and collimator rotations were used. All of the planning objectives, including the OARs parameters for optimization and avoidance ring constructions, were the same as in the single isocenter plan. Dosimetric parameters for target coverage and neighbouring OARs, including normal brain, were assessed.

Plan evaluation

Numerical indices derived from dose-volume metrics and separated into target coverage and dose spillage parameters are used to evaluate a radiosurgery plan.

We quantitatively assessed plan qualities with the following parameters: The RTOG conformance index (CI)(14) is calculated by dividing the prescribed treatment volume (PIV) by the target volume (TV).

$$CI = \frac{PIV}{TV}$$

In an ideal case, CI = 1.0, indicating a completely conformal plan. The RTOG recommended for the CI is< 1.2, with values between 1.2 and 1.5 acceptable with slight variations. Homogeneity (RTOG)(HI) is d_{max} divided by prescription dose.

$$HI = \frac{D_{max}}{D_{Rx}}$$

Selectivity Index or Overtreatment Ratio or Healthy Tissues Conformity Index

$$Selectivity\ index = \frac{TV_{PIV}}{PIV}$$

where TV_{PIV} is the target volume covered by the full prescribed dose and PIV is the prescription isodose volume.

Paddick CI/Conformation Number (CN) suggested by Ian Paddick (15) is determined as follows:

$$CN = \frac{TV_{PIV}}{TV * PIV}$$

where TV_{PIV} represents the target volume covered by the prescription isodose volume, TV represents the target volume, and PIV represents the prescription isodose volume. The optimal value for CN is one, although it is always one and approaches unity by raising plan quality from below. Furthermore, the Paddick GI (16) is one of the most often used gradient indices.

$$GI = \frac{PIV_{50\%}}{PIV}$$

Where $PIV_{50\%}$ is Volume receiving at least 50 percent of the prescription dose. All parameters of dose volume histogram for the single isocenter and dual isocenter plans were assessed. The dose to the normal brian was determined using V12 and V6Gy in accordance with RTOG recommendations.

Treatment Delivery

All single isocenter plans were treated on the treatment machine was a Varian TrueBeam SN1397 linear accelerator with 120 high definition multileafs collimator (MLC). All plans used 6 X-FFF energy with dose rate 1400MU/min. Each clinical plan evaluates delivery parameter, total number of monitor units (MU) and measured beam-on time (BOT). BOT was determined by dividing total MU by average applied dose rate.

Statical analysis

SPSS 20 for Windows (IBM Corp., Armonk, NY, USA) and Microsoft Office Excel 2010 for Windows were used to gather, tabulate, and statistically analyse all data (Microsoft Cor., Redmond, WA, USA). To compare two dependent groups of non-normally distributed data, the Wilcoxon signed ranks test was utilised. The significant threshold was $P < 0.05$

Results

Twelve patients have multiple brain metastases of variable targets number, size, and distance apart each other were simulated in the supine position. Table 2 outlines details of the total volume of delineated targets. All VMAT SRS plans for single isocenter and dual isocenter met RTOG criteria for high target coverage (CI, HI) and dose spillage parameter (GI and selectivity index).

Table (2): Total volume (cc) of delineated targets among brain metastasis patients.

Total volume (cc) of delineated targets	Mean	±SD	Median	(Range)
Combined GTV volume (cc)	7.70	±6.48	5.50	(1 – 18)
Combined PTV volume (cc)	12.90	±11.06	9.50	(1 – 36)

Target coverage and dose spillage

Table 3 showed that there is an insignificant difference between the two techniques of plans for brain metastasis patients with distance between target less than 6cm for all parameters. where target coverage (CI, CN, and HI) and dose spillage (p value of GI was 0.715 and p value of selectivity index was 0.705) were similar for two techniques.

Table (3): Comparison between single isocenter plan and dual isocenter plan as regards dose-volume histogram (DVH) parameters of target lesions among brain metastasis patients with distance between targets<=6cm. n. s.=not significant values. SD= standard deviation.

parameters	Single isocenter plan	Dual isocenter plan	p-value
Target coverage	Mean±SD(Range)		
GTV: D_{mean} (Gy)	109.62±3.4 (107 - 114)	108±1.93 (106 - 111)	n.s.
GTV: D_{min} (Gy)	100.47±1.06 (99.4 - 101.7)	100.2±0.76 (99.6 - 101.2)	n.s.
GTV: D_{max} (Gy)	120±6.6 (115 - 130)	118±4.93 (113 - 125)	n.s.
CI	1.07±0.11 (0.98 - 1.23)	1.08±0.08 (0.99 - 1.19)	n. s.

Paddick CN	0.93±0.05 (0.87 - 0.98)	0.92±0.03 (0.89 - 0.96)	n. s.
HI	1.2±0.06 (1.15 - 1.3)	1.18±0.05 (1.13 - 1.25)	n. s.
Dose spillage			
GI	5.08±1.89 (3.8 - 7.9)	5.08±1.46 (4.04 - 7.25)	n. s.
GD (cm)	1.26±0.11 (1.15 - 1.4)	1.26±0.29 (0.92 – 1.6)	n. s.
Selectivity index	0.94±0.06 (0.85 – 0.98)	0.93±0.08 (0.82-1.01)	n. s.

Table 4 illustrates CI remains equal for two plans with p value 0.344 for large distance more than 6 cm, so that target coverage (CI and HI) remains insignificant for the two plans with variation distance. In addition to Paddick conformity number have a significant difference with p value 0.027 for large distance between two targets. Our results indicated that there is a significant difference between single and dual isocenter plans with large distance for dose spillage (p value of GI and GD was 0.025).

Table (4): Comparison between single isocenter plan and dual isocenter plan as regards dose-volume histogram (DVH) parameters of target lesions among brain metastasis patients with distance between target >6cm. n. s.=, not significant values.SD= standard deviation.

parameters	Single isocenter plan	Dual isocenter plan	p-value
Target coverage	Mean±SD(Range)		
GTV: D_{mean} (Gy)	108.9±2.45 (106 – 113.3)	108.26±2.53 (104.6 – 111.2)	n.s.
GTV: D_{min} (Gy)	100.68±0.84 (99.6 - 102)	100.26±0.94 (99.2 - 101.3)	n.s.
GTV: D_{max} (Gy)	118.6±4.8 (110 - 125)	117.8±4.4 (112 - 124)	n.s.
CI	1.18±0.12 (1.02 - 1.37)	1.17±0.08 (1.05 - 1.3)	n. s.
Paddick CN	0.88±0.04 (0.84 - 0.95)	0.92±0.04 (0.85 - 0.97)	s.

HI	1.18±0.04 (1.1 - 1.25)	1.17±0.04 (1.12 - 1.24)	n.s.
Dose spillage			
GI	4.92±0.9 (4.02 – 6.5)	4.63±0.85 (3.8 – 6)	s.
GD (cm)	1.6±0.36 (1.1 – 2.1)	1.26±0.29 (0.86 – 1.9)	s.
Selectivity index	0.89±0.02 (0.86 – 0.92)	0.91±0.03 (0.86-0.97)	n. s.

Dosimetric parameter of normal brain

In every case, the OARs limitations satisfied their tolerance criteria for single and dual isocenter treatment plans (accepted by RTOG guidelines). Figures 1 show the statistical results for normal brain where the only statical major variations between the two plans was V6 Gy with p value 0.04 for large distance between two targets more than 6cm.

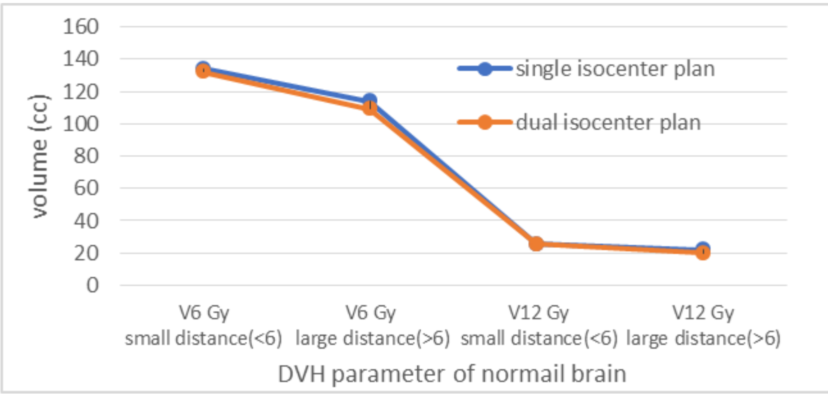

Figure (1): chart shows comparison between single isocenter plan and dual isocenter plan as regard dose volume histogram (DVH) parameters (Volume limits) of OAR (normal brain) among brain metastasis patients; marker represent mean, Y-error bar represent 95%CI (confidence interval of mean).

In addition to, total number of monitor units and measured beam-on time indicate significant differences among the two techniques (p value was 0.028). The mean total number of MUs for single isocenter VMAT plans was 2724(range 2089 -3267MUs). The maximum dosage rate of 1400 MU/min for the 6XFFF beam was employed in all cases reported here. The average total number of MUs for dual isocenter plans was 3060 (range: 2436 -3791MUs).

We took a case as an example who received treatment for two lesions The total planning tumor volume (PTV) was 4.6cc, with lesion 1 (PTV1) = 2.9cc and lesion 2 (PTV2) =1.7cc with a separate distance of 7 cm between the two targets. For each lesion, the patient got asynchronous SRS therapy with a total dose of 18Gy in one fraction. Figures 2 and 3 indicate that a dual isocenter plan reduces dose to all OARs better than a single isocenter plan.

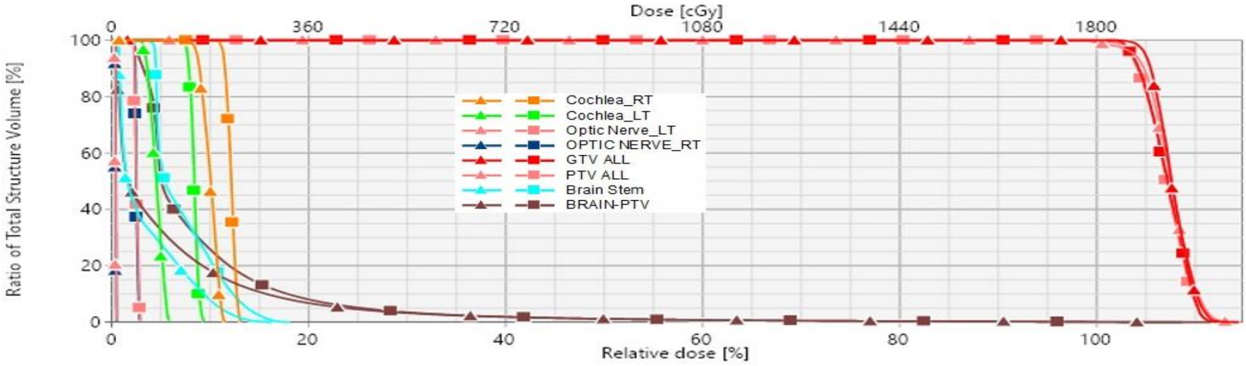

Figure (2): The dose-volume histogram comparison for the target coverage and organ at risk. The square symbols represent the single-isocenter plan, and the triangle symbols represent the dual isocenter plan.

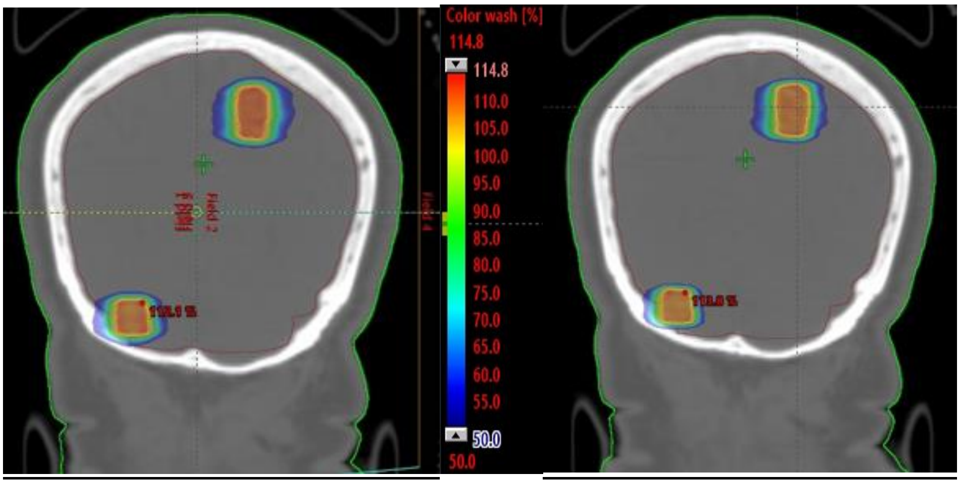

Figure (3): The colour wash of isodose distributions in a coronal view for a patient. In the left plane, a single-isocenter location (automatic between two lesions). The right plane for the dual isocenter plane.

Discussion

A comparative analysis of VMAT stereotactic radiosurgery plan technique using single and dual isocenter for treatment multi brain metastases lesions was investigated in this study and that's to identify the most efficient treatment method in terms of good dose distribution (target coverage) and as low as possible to all OARs and healthy brain tissue to reduce acute and late toxicity effect of treatment. To remove any influence in treatment planning, all planning conditions were kept the same, while creating VMAT plan using single and dual isocenter. Our study is divided to two groups, first group include six patients have distance between any two targets less than 6 cm and second group with separate distance more than 6 cm.

The present work shows that the target coverage (CI, paddick CN, and HI) and dose spillage (GI, GD, and D_{2cm}) are similar between the two techniques of single and dual isocenter SBRT VMAT plans for the first group.

Conformity indexes (CI) remain the same with variation of separate distance of all targets for single and dual isocenter that is compatible with recent studies, but Clark et al (17) improved the CI slightly when compared to single isocenter with single arc and triple isocenter with triple arc. Lwin Lwin Kyaw et al (18) and Clark et al (17) reported that GI is decreased when more arcs were employed since the greater the number of arcs, the greater the capacity to optimise the dose. So, we investigate difference between single and dual isocenter with stable number of arcs by using four partial arc as constant factor for two techniques.

Single-isocenter multitarget stereotactic radiosurgery given in one to five fractions provides excellent local control with minima toxicity by follow-up for 173 patients with 1014 brain metastases (19). Kuntz et al (20) discussed single isocenter arc therapy treatment planning through Brain lab Element system using 3 to 5 non coplanner arcs and multi isocenter VMAT planning with two coplanar arcs.

Hofmaier et al (21) prefer dynamic conformal arc therapy (DCAT) than traditional volumetric modulated arc therapy (VMAT) for enhancing treatment efficiency and sparing of normal brain, especially for roughly spherical lesions. but they favour VMAT with unevenly shaped planning target volumes.

The data presented in this report for the first group (table 3) founded that all target coverage and dose spillage parameters haven’t any significant difference for small separate distance between targets, therefore we favour applied single isocenter than dual isocenter for VMAT SRS multitarget close together with distance not more than 6 cm to reduce treatment time. The second group (table 4) showed that CI and HI the same for two techniques but CN has a significant difference. In addition to the major difference between two groups is dose spillage where GI and GD have p value equal 0.027. that make our results don’t consistent with Clark et al (17) weren’t seen a difference in GI for triple arc triple isocenter vs triple arc single isocenter.

One possible source of concern for multi brain lesions VMAT-SRS plan was dose spillage in the healthy brain tissue, like as V6, V10 and V12 Gy. Kuntz et al (20) make subgroups for number of metastases, multi isocenter plans give higher significant difference for V10Gy and slightly higher but not significant for V12Gy.Lwin et al (18) make subgroups for number of arcs, six Arcs double isocentres showed slightly lower in both V6 and V12 Gy than three arcs single isocenter, which significantly lower than two arcs single isocenter for normal brain. In our investigation, we create two categories according to distance between two lesions where normal brain for dual isocenter improvement in dose there isn’t significant difference in V6 and V12Gy that compatible with Morison (22) but only statical significant differences between the two plans was V6 Gy for large distance between two targets more than 6cm.

conclusion

It was observed that the single isocenter technique is similar to dual isocenter with normal tissue issues and target coverage. Dual isocenter took time during setup and matching for CBCT and has little difference in dose spillage for more than 6cm distance between targets. But in some cases, dual isocenter will provide good distribution and coverage for target volume and reduce doses to organs at risk with a very slight difference from the other treatment plan. Although the difference was decimal, we can recognize that the distance between lesions and their volumes has a more important impact on our choice of plan.

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