Dosimetric comparison between single and double isocenters VMAT for SRT with multiple targets

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Abstract. The focal irradiation approach for brain metastasis (BMs) Stereotactic Radiosurgery (SRS) or Stereotactic Radiotherapy (SRT) has emerged as an important modality for multiple BMs. This study aimed to evaluate the dosimetric effects between single isocentre (SI) and double isocentres (DI) VMAT SRT of multiple brain metastases. Eighteen VMAT SRT plans with varying lesions size, number and distance were simulated on patient CT image using Eclipse treatment planning system version 15. The plan consists of 3 techniques in: 2 coplanar arcs SI, 1 coplanar combine with 2 non-coplanar arcs SI and 2 non-coplanar and 1 coplanar arc DI. The VMAT plans were generated with 21Gy prescription dose to all lesions in 3 fractions. The plans were evaluated in terms of Gradient index (Paddick GI), Conformity index (Paddick CI), and Homogeneity index (ICRU HI) for PTV and V_{12Gy} and V_{6Gy} for normal brain. The same dose constraints were used to optimize for all cases. On the average result from 3 techniques, 3 arcs SI plans and DI were better in GI (14.79±5.83, 13.70±4.72) and CI (0.63±0.08, 0.62±0.09) than 2 arcs SI (17.56±6.15, 0.62±0.11), while HI values was comparable for all techniques. For normal brain, V_{12Gy} for 2 arcs and 3 arcs SI plans were comparable with DI and the volumes of normal brain receiving 6 Gy in 3 arcs SI and DI (77.40 ± 34.30 cm³, 68.94 ± 30.50 cm³) were better than 2 arcs SI (108.10 ± 57.20 cm³). Moreover, the number of arcs, monitoring units and treatment time were also increased and inconvenience in practice in DI. In conclusion, 3 arcs non-coplanar SI VMAT technique presents the suitable in dosimetric evaluation in 2-5 lesions metastases SRT.

Keywords: SRT, SI, DI and VMAT.

1. Introduction
Nowadays, brain metastases are the most common diagnosis in patients who are complications of systemic malignant disease as morbidity and mortality rates are high in patients who develop brain metastasis. The incidence rate of 54% has been reported for brain metastases in patients with adenocarcinoma of the lung. [1, 4] Due to the significant of these diseases, the use of better treatment techniques also may have contributed to a higher survival rate for brain metastases. The different types of radiation treatment to brain that are led from whole brain treatment to advanced SRS VMAT.
Historically, whole brain radiation therapy (WBRT) was the major role treatment for patients with brain metastases but it leads to acute and late toxicities effects to patients. Today, advances in radiation therapy have played as a role to treat brain metastases such as Stereotactic Radiation therapy (SRT), an important modality for multiple BMs and small targets. \[2\] SRT called knifeless surgery that can treat small tumor in head region with few fractions, high dose per fraction, very high dose to tumor especially gross tumor volume (GTV) and rapidly dose fall off for normal tissue sparing. SRT needs to use specific immobilization device for patient fixation because it performs to treat very small and highly precise dose to tumor.

Volumetric Modulated Arc Therapy (VMAT) is a novel treatment technique using inverse planning optimization. \[2\] It can achieve highly conformal dose distributions by modulating the simultaneous variation of multi-leaves collimator positions, dose rate, and gantry speed during gantry rotate around the patient for treatment delivery. \[2, 3\] Efficient treatment delivery gives in very short time and gets accurate and precise treatment. VMAT has been used for linear accelerator based SRT for multiple targets to be treated simultaneously using single plan with single isocenter. The treatment on axial plane without the use of couch rotation is called coplanar, while the treatment on oblique plane using couch rotation is called non-co-planar arc technique. VMAT SRT can plan by using co-planar arc on axial plane and non-coplanar arc on oblique plane with single or multiple isocenter for brain metastases.

There are different types of machine to treat multiple brain metastases such as gamma knife (GK) and linear accelerators (LINAC). GK and LINAC machines have been used for SRT treatment with multiple brain metastases. However, GKRT has some limitations for other parts because it can use only for brain and head and neck treatment. Additionally, it uses rigid fixation that is inconvenience for patient. Moreover, many researchers compared single isocenter VMAT SRS by LINAC and GK for multi-targets and the result showed VMAT based on LINAC was higher conformity index (CI) than GKRT. \[9,10\]

Nakamura et al. \[5\] and Korytko et al. \[6\] showed that clinical application for GKRT SRS was higher radiation toxicity and risk of symptomatic radiation necrosis. Therefore, LINAC SRT has been involved as an advance technique to treat brain metastases disease in recently. Traditionally, LINAC based SRT technique for multiple metastases treatment has been used a multi-isocenter technique, for each isocenter around the individual metastatic lesions. Clark GM et al. compared single and multiple isocenters for multi-targets and approached by using single isocenter for multi target than multi-isocenter. The duration of treatment time for a multi-isocenter technique is longer than single isocenter technique. \[2\] However, this paper was limitation number of targets and spatially distant of each lesion and they preferred to need further studies for large number of targets because they used three lesions to compare plan. \[2\] Thus, we would like to compare single isocenter and double isocenter SRT in terms of dosimetric effect for multiple lesions by varying target number, size and distance between targets.

2. Methods and Materials

2.1. Simulated brain metastases
Simulated lesions were created on treatment planning of CT image by varying lesions size (1, 1.5 and 2 cm), distance between lesions (3 and 6 cm) and different number of lesions (2, 3 and 5). Each variation applies to three techniques, while the rest were fixed as standard case design.

2.2. Treatment planning system
Eighteen VMAT SRT plans were generated with varying lesions size, number and distance apart each other by using 3 beam arrangement techniques which are single isocentre for 2 coplanar arc, single isocenter for 1 coplanar combine with 2 non-coplanar arcs, and double isocentres for 2 non-coplanar and 1 coplanar arc per isocenter. VMAT SRT plans were optimized on original treatment plan image by Eclipse Treatment Planning System version 15 and the same optimization parameters were used for
all plans. Re-planning from single isocentre plan to double isocentres plan were performed with same optimization criteria. The machine of Varian True Beam LINAC with 120 multileaves collimator (MLC) was selected. All plans were used 6 MV FFF beam energy with a high dose rate of 2400 MU per minute. The prescription dose was 21 Gy in three fractions. Anisotropic Analytical Algorithm (AAA) was used for dose calculation and plans was normalized to deliver 100% prescribe does to 95% volume of PTV.

In our study, the approach of Clark et al. [2] was modified to compare single isocentre (SI) and double isocentres (DI) for multiple lesions. Three planning techniques were compared for each variation, which are 2 arcs single isocentre (2 Arcs SI), 3 arcs single isocentre (3 Arcs SI) and 6 arcs double isocentres (6 Arcs DI). Simulated lesions were created as difference sizes, distance and lesion number on planning image. Then, all lesions were combined as a PTV for each variation. For the placement of isocentre, automated isocentre from Eclipse TPS was set on the centre of whole PTV for single isocentre, while the double isocentre technique was placed the isocenters on the average of the number of lesions by manual. After selecting the technique, it was applied to patient’s planning image in clinical part.

2.3. Planning techniques

The parameters shown in table 1 are the summarized of three planning techniques (2 Arcs SI, 3 Arc SI, and 6 Arcs DI) for arc geometry setting up in both coplanar and non-coplanar techniques.

2.3.1. 2 Arcs single isocentre (2 Arcs SI): The 2 Arcs SI was performed by 0° couch angle, 2 full arc co-planar, which the gantry angle was full rotation from 179° to 181° with both counter clockwise (CCW) and clockwise (CW) directions. The collimator angle was set at 355° and 5° for CCW and CW, respectively to prevent interleaf leakage.

2.3.2. 3 Arcs single isocentre (3 Arcs SI): The 3 Arcs SI was set the angle of couch rotation at 0°, 45° and 315° for each respective arc to perform two non-coplanar arcs. The gantry angle was set one full coplanar arc with 179° to 181° CCW and combined 2 half non-coplanar arc with gantry angle from 150° to 30°(CCW) and 210° to 330°(CW) with collimator angle of 5°and 355°, respectively.

2.3.3. 6 Arcs double isocentres (6 Arcs DI): The 6 Arcs DI was planned with couch angle, gantry angle and collimator rotation the same setting as 3 Arcs SI plan, but 3 arcs per each isocentre were set.

| Table 1. Arc geometry by couch rotation, gantry angle and collimator rotation. |
|---------------------------------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Plan               | Gantry start angle | Gantry stop angle | Gantry direction | Couch angle | Collimator angle |
| 2Arcs SI           | 179               | 181              | CCW              | 0             | 355             |
|                    | 181               | 179              | CW               | 0             | 5               |
| 3Arcs SI           | 179               | 181              | CCW              | 0             | 355             |
|                    | 150               | 30               | CCW              | 45            | 5               |
|                    | 210               | 330              | CW               | 315           | 355             |

performed by cumulative dose volume histogram (DVH) that referred to qualitative evaluation tools with Paddick GI, Paddick CI and ICRU HI for PTV. Mean does of V$_{6Gy}$ and V$_{12Gy}$ were recorded for normal brain and total monitoring units (MU) was also collected.

Paddick GI that represented the rapid fall-off doses outside PTV, was defined as the ratio of half of the dose prescription volume to prescription volume (PV) as shown in following equation;
\[ GI_{\text{PADDICK}} = \frac{PV_{50\%}}{PV} \]

Where, \( PV_{50\%} \) is the prescription volume at 50% isodose line coverage and \( PV \) is prescription volume.

Paddick CI was defined as the ratio of tumor volume within the prescription isodose volume squared to the tumor volume multiplied by the prescription isodose volume as following equation:

\[ CI_{\text{PADDICK}} = \frac{(TV_{PV})^2}{TV \times PV} \]

\( TV_{PV} \) is the target volume within the prescribed isodose surface, and \( TV \) is the target volume. Paddick CI value should be in the range between 0.6 and 1. The ideal plan would have a CI value close to unity and the lower the ratio means poor conformity.

ICRU homogeneity index HI was defined as the difference between the maximum dose delivered to 2% of target volume (\( D_{2\%} \)) and the minimum dose to 98% of target volume (\( D_{98\%} \)) divided by median dose (\( D_{50\%} \)) of target volume as shown in following equations;

\[ HI_{\text{ICRU}} = \frac{D_{2\%} - D_{98\%}}{D_{\text{Median}}} \]

Smaller value of HI value corresponds to more homogenous irradiation of target of volume.

Normal tissue is defined as the organs surrounding and outside the PTV. 12Gy isodose volume (\( V_{12\text{Gy}} \)) and 6Gy isodose volume (\( V_{6\text{Gy}} \)) of brain were record as a normal tissue volume dose.

2.5. Application in Clinical patient plan

After selecting technique and then apply for 10 patients plan in clinical situation. The dosimetric plan evaluated by using GI\text{PADDICK}, CI\text{PADDICK}, HI\text{ICRU} for PTV and \( V_{12\text{Gy}}, V_{6\text{Gy}} \) for normal brain.

3. Results

3.1. The plan quality indices comparison of three variations

The GI\text{PADDICK}, CI\text{PADDICK}, and HI\text{ICRU} for variation of size, distance and number of PTV are shown in Table 2. The effect of PTV size variation was lesser than distance variation in GI\text{PADDICK}. The size variation described that 3 Arcs SI showed comparable results with 6 Arcs DI in GI (10.25 ± 6.61, 9.55 ± 5.75) and significantly better than 2 Arcs SI (12.24 ± 7.29), while CI remains the same for all technique. HI is slightly greater in DI than SI techniques (0.19 ± 0.01, 0.19 ± 0.00, 0.17 ± 0.01). In addition, 3 Arcs SI and 6 Arcs DI were greater result than 2 Arcs SI for GI in distance and number of lesions variation, while CI is not significantly difference in distance variation (0.56 ± 0.03, 0.60 ± 0.01, 0.60 ± 0.01) among 3 gantries setting up techniques. Moreover, 3 Arcs SI is the best for CI in lesion number variation (0.58 ± 0.16).

Table 4 shows that GI\text{PADDICK} and CI\text{PADDICK} of these two techniques were not significantly showed in results with p value (GI\text{PADDICK}; p value = 0.705, CI\text{PADDICK}; p value = 0.830, V12Gy; p value = 0.764, V6Gy; p value = 0.608) while HI is slightly significant (HI\text{ICRU} p value= 0.014). As our result, 3 Arcs SI was comparable with 6 Arcs DI.

3.2. Normal brain tissue

Table 3 illustrates the normal brain volume at 6 and 12 Gy isodose for each technique. The 6 Arcs DI showed slightly lower normal brain volume in both 6 and 12 Gy than 3 Arcs SI, while 2 Arcs SI showed significantly higher normal brain volume in both than 3 Arcs SI for all PTV size, distance and number variation. For V12Gy of normal brain, the greatest dose volume differences were found at 2 Arcs SI and 6 Arcs DI (31.97 ± 19.12, 24.50 ± 15.22), while 3 Arcs SI is slightly increased volume.
than DI \((25.57 \pm 15.64, 24.50 \pm 15.22)\) in size variation. The 2 Arcs SI plan generated a total 6 Gy volume of \((139.27 \pm 70.98 \text{ cm}^3)\), the 3 Arcs SI plan yielded \((96.33 \pm 36.56 \text{ cm}^3)\) and 6 Arcs DI plan generated \((88.70 \pm 40.08 \text{ cm}^3)\) in size variation. The 2 Arcs SI plan produced for total 6 Gy is larger in distance and number of lesions variation. Total monitor units in 3 Arcs SI plan was slightly lower than the other techniques.

Table 2. Plan evaluation for each technique according to variation of lesions size, location and number

| Variable forms | Lesions Variable | Plan Technique | Average \( \text{GI}_{\text{PADDICK}} \) | Average \( \text{CI}_{\text{PADDICK}} \) | Average \( \text{HI}_{\text{ICRU}} \) |
|----------------|------------------|----------------|-------------------------------|--------------------------------|----------------|
| Size           | 1, 1.5 & 2 cm    | 2 Arcs SI      | 12.24 ± 7.29                  | 0.76 ± 0.06                    | 0.19 ± 0.01 |
|                |                  | 3 Arcs SI      | 10.25 ± 6.61                  | 0.71 ± 0.04                    | 0.19 ± 0.00 |
|                |                  | 6 Arcs DI      | 9.55 ± 5.75                   | 0.72 ± 0.03                    | 0.17 ± 0.01 |
| Distance       | 3 & 6 cm         | 2 Arcs SI      | 21.20 ± 0.85                  | 0.56 ± 0.03                    | 0.18 ± 0.01 |
|                |                  | 3 Arcs SI      | 16.35 ± 7.43                  | 0.60 ± 0.01                    | 0.20 ± 0.03 |
|                |                  | 6 Arcs DI      | 14.58 ± 4.55                  | 0.60 ± 0.01                    | 0.18 ± 0.01 |
| Number         | 2, 3 & 5         | 2 Arcs SI      | 20.44 ± 5.46                  | 0.53 ± 0.14                    | 0.18 ± 0.01 |
|                |                  | 3 Arcs SI      | 18.29 ± 3.58                  | 0.58 ± 0.16                    | 0.21 ± 0.21 |
|                |                  | 6 Arcs DI      | 17.26 ± 0.49                  | 0.54 ± 0.02                    | 0.18 ± 0.01 |

Table 3. Plan evaluation of parameters for normal brain.

| Variable forms | Lesions Variable | Plan Technique | Average \( V_{12Gy} \) (cm\(^3\)) | Average \( V_{6Gy} \) (cm\(^3\)) | Total MU |
|----------------|------------------|----------------|----------------------------------|---------------------------------|----------|
| Size           | 1, 1.5 & 2 cm    | 2 Arcs SI      | 31.97 ± 19.12                   | 139.27 ± 70.98                 | 3159 ± 585 |
|                |                  | 3 Arcs SI      | 25.57 ± 15.64                   | 96.33 ± 36.56                  | 2326 ± 127 |
|                |                  | 6 Arcs DI      | 24.50 ± 15.22                   | 88.70 ± 40.08                  | 2354 ± 162 |
| Distance       | 3 & 6 cm         | 2 Arcs SI      | 13.55 ± 2.33                    | 92.75 ± 26.80                  | 2940 ± 508 |
|                |                  | 3 Arcs SI      | 11.15 ± 3.75                    | 60.50 ± 7.50                   | 2321 ± 309 |
|                |                  | 6 Arcs DI      | 9.85 ± 1.77                     | 54.85 ± 0.21                   | 2814 ± 166 |
| Number         | 2, 3 & 5         | 2 Arcs SI      | 20.07 ± 15.87                   | 87.23 ± 60.87                  | 2532 ± 54  |
|                |                  | 3 Arcs SI      | 16.70 ± 12.41                   | 69.83 ± 42.79                  | 2526 ± 655 |
|                |                  | 6 Arcs DI      | 13.80 ± 7.43                    | 58.57 ± 26.53                  | 2713 ± 130 |

Table 4. The average dosimetric evaluation in all variations of three planning techniques.

| Plan Technique | \( \text{GI}_{\text{PADDICK}} \) | \( \text{CI}_{\text{PADDICK}} \) | \( \text{HI}_{\text{ICRU}} \) | \( V_{12Gy} \) (cm\(^3\)) | \( V_{6Gy} \) (cm\(^3\)) | Total MU |
|----------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|----------|
| 2 Arcs SI      | 17.56±6.15                   | 0.62±0.11                     | 0.18±0.01                     | 22.90±14.52                  | 108.10±57.20                  | 2869±470 |
| 3 Arcs SI      | 14.79±5.83                   | 0.63±0.08                     | 0.20±0.02                     | 18.64±11.62                  | 77.40±34.30                   | 2400±390 |
| 6 Arcs DI      | 13.70±4.72                   | 0.62±0.09                     | 0.18±0.01                     | 16.83±10.48                  | 68.94±30.50                   | 2603±246 |

3.3. Application in Clinical patient plan
As our result, 3 Arcs SI (NC) plan was equivalent in dose fall off and conformity to 6 Arcs double isocentres (NC) VMAT. However, DI is inconvenience in practice and treatment time was also longer than SI. Therefore, 3 Arcs SI (NC) technique was selected to apply for 10 patients plan in clinical situation with multiple target in range 2-5 targets. The results of dosimetric evaluation are shown in table 5. The multiple target volumes were in range 1.3 to 25.8 cm³. The GI was the highest of 9.46 in patient 8, while the other patients for GI value is around 5. CI and HI value for all patients were quite constant with difference in real clinical situations. When total target volume increased, the result showed that the volume 6 Gy receiving to normal brain was high as presented in case number 6 and 9.

Table 5. Clinical application result by applying 3 Arcs SI (NC) technique.

| Patient | TV (cm³) | No. of targets | GI<sub>PADDICK</sub> | CI<sub>PADDICK</sub> | HI<sub>ICRU</sub> | V<sub>12Gy</sub>(cm³) | V<sub>6Gy</sub>(cm³) |
|---------|---------|----------------|---------------------|---------------------|------------------|-----------------|-----------------|
| 1       | 5.4     | 2              | 5.10                | 0.79                | 0.18             | 20.00           | 88.00           |
| 2       | 9.3     | 2              | 4.06                | 0.60                | 0.17             | 28.30           | 96.60           |
| 3       | 19.8    | 3              | 3.65                | 0.74                | 0.17             | 53.80           | 173.80          |
| 4       | 10.5    | 3              | 4.31                | 0.60                | 0.18             | 32.50           | 132.40          |
| 5       | 15.1    | 4              | 4.64                | 0.79                | 0.19             | 50.70           | 261.70          |
| 6       | 23.6    | 2              | 5.00                | 0.75                | 0.21             | 89.40           | 315.70          |
| 7       | 8.6     | 5              | 5.51                | 0.61                | 0.19             | 34.30           | 197.10          |
| 8       | 1.3     | 3              | 9.46                | 0.59                | 0.19             | 8.70            | 43.30           |
| 9       | 25.8    | 4              | 4.00                | 0.69                | 0.19             | 75.00           | 322.30          |
| 10      | 15.6    | 5              | 4.23                | 0.67                | 0.19             | 48.90           | 246.80          |

4. Discussion
In this study, 3 arcs single isocenter (NC) plan presented the high plan quality in terms of gradient index and conformity for varying number of lesions, size and location. Table 4 shows that GI is minimized when more arcs are used because the larger arc number increase the chance to optimize the dose. Clerk et al. reported that multiple arcs produce better plan quality. They also revealed that when lesions are spaced closely together or close to critical structures, it might be effectiveness to use multiple noncoplanar arcs to generate a better GI. Both GI value and the area of low dose in brain such as V<sub>6Gy</sub> and V<sub>12Gy</sub> are reduced by using more non-coplanar arcs. However, the larger number of arcs should be trade off with the treatment time. As comparison of SI and DI, the gradient index is reduced in DI and it is more suitable in large number of lesion as well as it may give the dose precisely to each tumour for far distance lesions. On the other hand, DI does more complicated treatment planning with more monitoring unit. As our result, 3 arcs single isocentre with non-co-planar technique was generated not only equivalence plan quality with double isocentre but also reduced treatment set up error and convenience in practice. Clark et al. also stated that single isocentre non-co-planar can be used to deliver instead of double isocentres in multiple brain metastases, but his study varied by 3 different size and 3 lesions and 2 distance apart. In our study, we modified to 5 lesions and applied technique by various situations in clinical part. According to Clark et al., the dosimetry of NC Arc with SI using VMAT with multi lesions are highly conformal and similar dose gradient by using DI with multiple brain metastases. As Morrison J’s investigation, multiple isocentres does not provide substantial improved about 0.9% ± 12.7% in GI, 2.6% ±4.6%, 2.6% ± 5.2% in CI and HI in distal location from each lesion for multiple targets. As their studies, DI is not significantly improved compare with SI. So, our results agreed with the studies by Clark et al. and Morrison J. Thus, 3 Arc SI (NC) was selected and applied in 2-5 metastases patients in clinical part.
4.1. Clinical application study

In clinical situation, 3 Arcs SI plan applied to 10 patients plan by different situations. Results for plan quality indices are not statistically significant for all variation. But small lesions or total target volume produced higher GI value in result. The highest of GI value as shown in patient 8, while the other patients for GI value is less differences. It might be because of very small volume in this case (TV = 1.3 cm³). Clark et al. reported a mean GI of 3.34 ± 0.42 for 15 VMAT plans with 1–5 targets with size range from 0.67–44.68 cm³. In our study, the GI range is 3.65–9.46 with a mean of 5. Ballangrud et al. published GI is reduced with increasing target size. Therefore, our results agreed with the study by Ballangrud et al. The larger volume of targets was generated low dose received to normal brain. Therefore, 6-Gy received to normal brain (315.70 and 322.30 cm³) appeared the highest in large target volume (TV = 23.6 and 25.8 cm³). CI and HI value are not significant different for all patients. Thus, our studies recommend using noncoplanar single isocentre technique the patient of 2–5 brain metastases. The results of our studies for plan qualities shows the similar result of Clark et al. study. Phongprapun W also describes that conformity of plan quality in single isocentre was more improved the patient in three lesions of brain metastases and the size and location of the lesions affect the dose conformity. Patient 8 results describes lesser conformity (CI = 0.59) than the other (CI = 0.69 to 0.79). Audet et al. also revealed a worse conformity index for smaller lesions than larger lesions, our clinical results confirmed this study.

5. Conclusion

The single isocentre with non-coplanar arc is equivalent dose fall off and conformity to double isocentres (NC) VMAT and it is optimal technique for treating multiple lesions of brain metastases. Therefore, non-coplanar single isocentre VMAT technique is recommended for 2–5 lesions metastases SRT.

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