

Single-Isocenter Multiple-Target (SIMT) Technique to Treat Multiple Brain Metastases: A Single Institutional Experience

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ABSTRACT

Background: Brain metastases are the most common Intracranial tumours in adult cancer patients, Stereotactic radiosurgery (SRS) and fractionated stereotactic radiotherapy (FSRT) have become the current standard of care for eligible patients, in addition to avoiding neurocognitive toxicity, they offer the benefit of treatment. Information about single-isocenter multiple-target (SIMT) volumetric-modulated arc therapy (VMAT) in developing country centres is sparse.

Objective: To assess the dosimetric quality, plan conformity and delivery efficiency of VMAT SIMT delivered with LINAC for treatment of multiple brain metastases.

Study Design and Duration: This was a retrospective dosimetric study with 47 consecutive patients with multiple brain metastases who were treated at the Neurospinal and Cancer Care Institute (NCCI), Karachi, between November 2025 and April 2026.

Methodology: The Treatment plans were designed using the Monaco Treatment Planning System (v6.1.3.0) and delivered on Elekta Synergy-P LINAC (Agility head, 6MV). Dosimetric indices analysed were the Paddick Conformity Index (CI), the Gradient Index (GI), the Homogeneity Index (HI), monitor units (MUs), and the Brain – PTV V12Gy. Association between total gross tumour volume (GTV) and each dosimetric parameter was assessed by Spearman's rank correlation.

Results: Median CI was 0.87 (IQR: 0.72–0.96), median GI was 3.62 (IQR: 2.91–4.31), and median HI was 0.11 (IQR: 0.08–0.14). Median total GTV was 13.45 cc (IQR: 6.58–25.12), median Brain-PTV V12Gy was 124.57 cc (IQR: 87.94–174.35), and median MUs were 1678.20 (IQR: 1476.74–1885.48). All dosimetric variables were found to be non-normally distributed (Shapiro–Wilk, all $p < 0.05$). No statistically significant correlations were found between total GTV and CI ($p = -0.239$, $p = 0.106$), GI ($p = 0.047$, $p = 0.752$), HI ($p = 0.174$, $p = 0.242$), or MUs ($p = 0.163$, $p = 0.274$).

Conclusion: It is concluded that SIMT VMAT delivered with LINAC exhibits excellent dosimetric quality and treatment delivery efficiency over the entire range of tumour volume, making it a feasible option in the clinical routine, even in resource-limited radiotherapy centres.

Keywords: Brain Metastases, Single-Isocenter Multiple-Target (SIMT), Stereotactic Radiosurgery (SRS), Volumetric-Modulated Arc Therapy (VMAT), LINAC based Radiotherapy

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INTRODUCTION

Stereotactic radiosurgery (SRS) was first described by Leksell as a method for delivering precisely targeted, high-dose radiation to intracranial lesions in a single treatment session¹. Subsequent dose-escalation trials established the maximum tolerated single-fraction doses according to lesion size, providing the dosimetric foundation for modern radiosurgical practice². Brain metastases (BM) are the most frequently occurring adult malignant intracerebral disease encountered during the course of systemic cancer, affecting 20–40% of all cancer patients at some stage of their disease³. Whole brain radiotherapy (WBRT) was traditionally the preferred treatment for patients with multiple brain metastases; however, a randomized trial demonstrated that SRS alone is associated with significantly less cognitive decline at three months than SRS combined with WBRT in patients with one to three brain metastases, without a difference in overall survival⁴. An individual patient data meta-analysis of phase 3 trials similarly found a survival advantage for SRS alone over SRS plus WBRT in patients aged 50 years or younger with one to four brain metastases, although this benefit was not observed in older patients⁵, and a secondary analysis of this randomized experience further supported omitting WBRT in patients with a more limited burden of intracranial disease⁶. These findings, together with concerns regarding radiation-induced neurocognitive morbidity and the absence of a consistent survival benefit with WBRT, have driven a paradigm shift toward SRS and fractionated stereotactic radiotherapy (FSRT) for appropriate patients^{3,7,8}. Contemporary patient selection increasingly incorporates cumulative intracranial tumour volume, individual lesion size, performance status and estimated prognosis, in addition to the number of lesions³.

The conventional multiple-isocenter method is clinically effective, but the imaging and treatment time is approximately 20 minutes for each lesion, making it operationally inefficient^{7,9,10}. Volumetric-modulated arc therapy (VMAT) has emerged as a considerably more efficient alternative, and one of its most promising implementations is the single-isocenter multiple-target (SIMT) technique^{11,12}. SIMT not only alleviates the burden of patient positioning but also lowers interfraction positioning error, reduces the dose to normal brain parenchyma, and allows simultaneous treatment of multiple lesions in a single session^{12–16}. Preserving target conformity in SIMT planning, however, is

technically difficult because of the sensitivity to rotational setup errors and the steep dose gradients that are inherent to this technique when lesions are widely distributed within the cranial vault^{9,12,15}.

Current literature shows promising dosimetric results, which can be credited to the use of state-of-the-art stereotactic planning systems and accumulating institutional experience^{12,13,17}. However, there is limited clinical experience with institutional SIMT programmes in developing countries, particularly in low-income or resource-poor radiotherapy settings¹⁸. To bridge this gap, the dosimetric accuracy and delivery efficiency of SIMT VMAT using a LINAC are presented in the present study at a tertiary cancer centre in Pakistan.

Thus, the aim of this study was to assess the dosimetric quality, plan conformity and delivery efficiency of VMAT SIMT for treatment of multiple brain metastasis delivered with LINAC at one tertiary centre in Pakistan.

OPERATIONAL DEFINITIONS

SIMT (Single-Isocenter Multiple-Target): A stereotactic radiotherapy (SRT) technique in which a single common isocenter is used to simultaneously treat multiple intracranial metastases^{13,15}.

CI (Paddick Conformity Index): A dosimetric index used to measure the conformity, both in shape and size, of the reference isodose volume to the target volume¹⁹.

GI (Paddick Gradient Index): A parameter reflecting the steepness of the dose fall-off beyond the target volume boundary, characterising normal brain tissue sparing²⁰.

The Homogeneity Index (HI): It is an index of uniformity of dose distribution within the planning target volume^{19,21}.

MATERIAL AND METHODS

The study was a retrospective dosimetric study carried out at Department of Clinical and Radiation Oncology, Neurospinal and Cancer Care Institute (NCCI), Karachi, which is a tertiary cancer centre providing stereotactic radiotherapy services using LINAC in Pakistan.

Study Period: November 2025 – April 2026.

Sample Size: 47 consecutive patients who presented for treatment for multiple brain metastases were included.

Sampling Technique: Non-probability consecutive sampling.

Ethical Approval

This study was done in accordance with the

ethical provisions of the Declaration of Helsinki (2013) and was also approved by the Research and Ethics committee of the Neurospinal and Cancer Care Institute (NCCI), Karachi (IRB Reference: NCCI-IRB-2025-RT-04) before the data collection started. The committee granted waiver of the need for individual informed consent, due to the retrospective nature of the study. All the patient data were anonymised and treated following privacy and data confidentiality institutional procedures. No other intervention was done other than routine clinical management.

Inclusion Criteria:

- Patients aged 18–78 years.
- Patients diagnosed with brain metastasis (radiologically and/or histopathologically) associated with an extra-cranial primary malignancy.
- Patients who were treated by stereotactic radiotherapy with a LINAC-based system.

Exclusion Criteria:

- Patients with widespread Intracranial disease.
- Patients unable to maintain a treatment position due to claustrophobia, pain, or other physical or psychological contraindications
- Patient with a history of acute ischaemic brain injury within the preceding 6 months.

Data Collection: Magnetic resonance imaging (MRI; TOSHIBA 1.5 Tesla) was used with T1-contrast, T2 and FLAIR sequences before treatment and co-registered with planning computed tomography (CT) scans obtained at a slice thickness of 2 mm. The gross tumour volume (GTV) was defined as the lesion that was contrast enhanced on the fused T1c MRI. The planning target volume (PTV) margin was 0-2 mm. The prescribed dose was 25-40 Gy in 3-5 fractions to 95% reference isodose line. All plans were created in the Monaco Treatment Planning System (v6.1.3.0) using either a single arc or multiple full arcs and were delivered on an Elekta Synergy-P LINAC (Agility head, 60 leaf pairs, 5 mm MLC, 6 MV photons).

Data Analysis: The number of brain metastases ranged from 2 to 9 per patient (median of 4, IQR of 3–6). The statistical software SPSS version (26.0) was used for statistical analysis. The Shapiro–Wilk test was used to determine normality of continuous variables. As all dosimetric parameters were found to be non-normally distributed, data are expressed as medians with interquartile ranges

(IQR). The associations between total tumour volume and dosimetric indices were assessed by Spearman's rank correlation. A p value < 0.05 was set as the level of significance.

RESULTS

A total of 47 patients undergoing multiple brain metastases (MBM) therapy with LINAC based SIMT VMAT radiotherapy were selected. The cohort comprised 24 females (51.1%) and 23 males (48.9%), with a mean age of 54.0 years (range: 18–78 years). The number of brain metastases per patient ranged from 2 to 9 (median: 4, IQR: 3–6). Breast carcinoma (27.7%), lung carcinoma (23.4%) and other primary sites were the most common primary malignancies, followed by colorectal carcinoma and melanoma and nasopharyngeal carcinoma.

All dosimetric variables were found to be non-normal (all $p < 0.05$, Table 1) by Shapiro–Wilk tests. Therefore, all continuous variables are given as medians (IQR). The primary dosimetric outcomes are reported as follows: median Paddick CI was 0.87 (IQR: 0.72–0.96), median GI was 3.62 (IQR: 2.91–4.31), and median HI was 0.11 (IQR: 0.08–0.14). Median total GTV was 13.45 cc (IQR: 6.58–25.12), median Brain–PTV V12Gy was 124.57 cc (IQR: 87.94–174.35), and median MUs were 1678.20 (IQR: 1476.74–1885.48).

Spearman's rank correlation analysis revealed no statistically significant association between total GTV and CI ($\rho = -0.239$, $p = 0.106$), GI ($\rho = 0.047$, $p = 0.752$), HI ($\rho = 0.174$, $p = 0.242$), or MUs ($\rho = 0.163$, $p = 0.274$) (Table 2). These results suggest that for this group there was no significant difference between the quality of the plans or the efficiency of their delivery with respect to the total tumour volume.

Table 1: Shapiro–Wilk Test of Normality for Dosimetric Variables

Variable	n	W statistic	p-value	Interpretation
CI (Paddick)	47	0.944	0.024	Non-normal distribution
GI (Paddick)	47	0.399	<0.001	Non-normal distribution
HI	47	0.892	<0.001	Non-normal distribution
Monitor	47	0.730	<0.001	Non-normal

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Variable	n	W statistic	p-value	Interpretation
Units				distribution
Total GTV (cc)	47	0.695	<0.001	Non-normal distribution
Brain-PTV V12Gy (cc)	47	0.883	<0.001	Non-normal distribution

Table 2: Spearman Rank Correlation Total GTV versus Dosimetric Parameters (with Median Primary Outcomes)

Variable Pair	Spearman ρ	p-value	Interpretation
Total GTV vs CI (median 0.87, IQR 0.72–0.96)	-0.239	0.106	No significant correlation
Total GTV vs GI (median 3.62, IQR 2.91–4.31)	0.047	0.752	No significant correlation
Total GTV vs HI (median 0.11, IQR 0.08–0.14)	0.174	0.242	No significant correlation
Total GTV vs Monitor	0.163	0.274	No significant correlation

Variable Pair	Spearman ρ	p-value	Interpretation
Units			

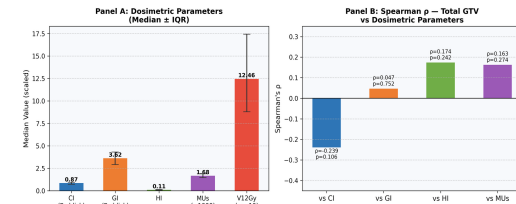


Figure 1. Panel A: Median dosimetric parameters (CI, GI, HI, MUs, V12Gy) with interquartile range error bars. **Panel B:** Spearman correlation coefficients (ρ) between total GTV and each dosimetric parameter. No statistically significant correlation was observed for any parameter (all $p > 0.05$). NCCI, Karachi; $n=47$.

DISCUSSION

In this retrospective dosimetric review of 47 consecutive patients with multiple brain metastases treated using LINAC-based SIMT VMAT at NCCI, Karachi, plan quality was consistently good across a wide range of tumour burden. The median Paddick CI was 0.87 (IQR: 0.72–0.96), median GI was 3.62 (IQR: 2.91–4.31), and median HI was 0.11 (IQR: 0.08–0.14), reflecting favourable target conformity, an acceptable dose gradient, and satisfactory dose homogeneity, respectively. The median total GTV was 13.45 cc (IQR: 6.58–25.12), with a median of 4 lesions per patient (range: 2–9), a median Brain-PTV V12Gy of 124.57 cc (IQR: 87.94–174.35), and a median delivery of 1678.20 MUs (IQR: 1476.74–1885.48). Notably, none of these dosimetric or efficiency parameters correlated significantly with total GTV (CI: $\rho = -0.239$, $p = 0.106$; GI: $\rho = 0.047$, $p = 0.752$; HI: $\rho = 0.174$, $p = 0.242$; MUs: $\rho = 0.163$, $p = 0.274$), indicating that plan quality and delivery efficiency were preserved irrespective of tumour burden in this cohort.

These findings are broadly concordant with the wider SIMT literature. In a multi-institutional evaluation of LINAC-based SIMT platforms, Palmer et al. reported similarly consistent conformity across a range of lesion numbers and volumes¹⁵, supporting the generalisability of SIMT dosimetric performance across differing centres and case-mix. Using an automated planning approach similar to that employed at our institution, Raza et al. likewise found stable dosimetric performance for SIMT¹², consistent with our observation that plan quality did not deteriorate with increasing tumour volume. Hemalatha

Priyadarsini et al. reported consistent plan quality with 5-mm MLC-based SIMT even in patients with 5–10 brain metastases¹³, reinforcing that dosimetric robustness can be maintained as lesion number increases, a pattern our data also support given the median of 4 lesions (range: 2–9) per patient in our cohort.

Ruggieri et al. compared HyperArc-based automated planning with standard manually optimised VMAT for multiple brain metastases and found that HyperArc produced steeper dose gradients and improved conformity relative to standard VMAT.²⁰ Our median GI of 3.62 (IQR: 2.91–4.31), achieved with manually optimised Monaco-based VMAT rather than a dedicated automated single-isocenter module such as HyperArc, compares reasonably with the standard VMAT arm reported in that series, suggesting that careful manual arc and collimator optimisation can narrow the gap with automated platforms where such dedicated software is not available. Not all comparisons were fully concordant, however. Faccenda et al. reported that single-isocenter coplanar arc plans can show suboptimal conformity and gradient metrics for peripherally located lesions because of heightened sensitivity to rotational setup errors,⁹ whereas we did not observe a corresponding decline in conformity or gradient indices with increasing tumour volume or lesion dispersion in our cohort. This difference is most plausibly explained by our arc geometry optimisation and treatment planning approach, informed by the recommendations of Wyatt et al. for improving single-isocenter multi-metastasis delivery efficiency,¹⁰ and by our use of a comparatively tight 0–2 mm PTV margin, which may partly offset the geometric uncertainty associated with rotational setup error. It should nonetheless be acknowledged that we did not perform a formal, quantitative sensitivity analysis of rotational error for peripheral targets, which is discussed further under Limitations.

The median MU value in our series (1678.20; IQR: 1476.74–1885.48) is consistent with the delivery efficiency gains reported for SIMT over multiple-isocenter approaches by Asso et al. and Li et al.^{11,16} Lower MUs and shorter treatment times translate directly into improved patient comfort and higher departmental throughput, an advantage of particular importance in a resource-limited setting such as ours, where LINAC availability is constrained.¹⁸

Kihara et al. demonstrated that SIMT plan quality improves with accumulating

institutional experience.¹⁷ NCCI's SIMT programme is comparatively new in Pakistan, yet the dosimetric results achieved in this cohort were already comparable to those reported by more established international programmes. To our knowledge, this is among the first dosimetric reports of LINAC-based SIMT VMAT from an institution in Pakistan, and one of relatively few such reports from South Asia generally. It therefore adds real-world evidence, currently scarce from developing-country settings, that acceptable SIMT dosimetric quality is achievable early in a programme's experience, and supports the wider and earlier adoption of SIMT-based radiotherapy in similarly resource-limited environments rather than deferring implementation until extensive institutional experience has accrued elsewhere.

Huang et al. developed a voxel-level deep learning model to predict achievable dose distributions for single-isocenter VMAT plans before the actual planning process, allowing clinicians to benchmark plan quality against automatically predicted, achievable dose objectives.¹⁴ The consistent, high-quality plans achieved in our cohort provide a real-world institutional benchmark of the kind such predictive models would need to be validated against, and illustrate the type of dosimetric baseline data that remains scarce from centres without access to commercial automated planning platforms.

Brain-PTV V12Gy is an established surrogate for radionecrosis risk. The median V12Gy in our cohort was 124.57 cc (IQR: 87.94–174.35); however, this population-level, whole-brain aggregate figure cannot be directly compared with the per-lesion V12Gy thresholds (typically <10–20 cc per lesion) reported in the radiosurgery literature^{8,9}, since per-lesion volume and the number of targets treated varied considerably between individual patients in our cohort. Minniti et al. demonstrated that fractionation strategy materially affects this risk-benefit balance for larger metastases, showing that multifraction SRS (3 × 9 Gy) achieved better local control and a lower risk of radionecrosis than single-fraction SRS for lesions larger than 2 cm.²² Given that the prescribed regimens in our cohort spanned 25–40 Gy in 3–5 fractions, fractionation-dependent differences in radionecrosis risk of this kind cannot be excluded by the present dosimetric analysis alone, and prospective correlation of V12Gy with actual toxicity outcomes, stratified by fractionation and per-lesion volume, is recommended as a priority for future work at our centre.

The principal strength of this study is that it represents, to our knowledge, one of the largest single-institution SIMT dosimetric series reported from a developing-country radiotherapy centre, using a consistent planning platform (Monaco TPS) and delivery system (Elekta Synergy-P) across all 47 patients, which minimises inter-platform variability as a confounder and allows a relatively direct assessment of the relationship between tumour burden and dosimetric quality. This study nonetheless has limitations, detailed in the following section, including its retrospective, single-centre design and the absence of prospectively collected clinical outcome data. Building on the present dosimetric findings, future work at our centre should prioritise prospective correlation of these parameters, particularly V12Gy, with clinical toxicity and local control outcomes, formal quantification of rotational-error sensitivity for peripheral lesions, and multivariable analysis incorporating lesion number and inter-target distance alongside total tumour volume, in order to more precisely define the geometric determinants of SIMT plan quality in routine clinical practice.

LIMITATIONS

There are some restrictions that should be recognized. The first is that it is a retrospective study, which does not allow for cause and effect conclusions, and could suffer from selection bias. Second, the single centre experience with a number (n) of 47 patients is adequate for dosimetric correlation analysis but not as generalisable as larger multi-centre trials. Third, this study meant only to assess dosimetric endpoints and the study of clinical endpoints, including local control, radionecrosis incidence, and overall survival, will follow prospective. Fourth, all plans were presented on one LINAC platform (Elekta Synergy-P) which makes it difficult to compare the plans with centres that use different planning software or other LINAC systems. Lastly, no formal sensitivity analysis for rotational errors for peripherally located lesions was undertaken and is a priority for future work.

CONCLUSION

LINAC-based SIMT VMAT provides a consistent dosimetric quality and efficient treatment delivery for multiple brain metastases over a wide range of total tumour volume. The results prove that application of this technique is practicable and valid in clinical routine, even in resource-limited radiotherapy centers. These dosimetric results will be further validated in future prospective

studies and will help to guide optimal patient selection criteria.

CONFLICT OF INTEREST

None

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