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Plan Quality and Optimized Treatment Planning Technique for Single-Isocenter VMAT Brain Stereotactic Radiosurgery/Radiotherapy Using Photon Optimizer

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ABSTRACT

Introduction: This study aims to analyze different dosimetric indices using various formulae in cranial Stereotactic Radiosurgery/Radiotherapy treatment planning.

Material and Methods: 42 targets were constructed from 23 patients with brain metastases (≤30 cc) treated at our institution, selected for this study. The PTVs were generated using a 3.0 mm isotropic margin from the CTV. Sequential boost prescriptions of 5-15 Gy were delivered using 6 MV FFF beams with full, partial, and non-coplanar arcs. The Acuros XB algorithm with a 1.25 mm grid size was optimized to calculate the dose distribution. The Conformity Index Homogeneity Index, and Gradient Index were evaluated using a DVH with different mathematical formulae.

Results: RTOG, Van't Riet, and Paddick, and the Inverse of RTOG values were close to 1.0. Whereas Lomax & Scheib and SALT were 0.92 ± 0.06, 0.94±0.05, respectively, they achieved lower than 1.0. The results of different types of HI values achieved similar ideal values. For GI data scored, each target is in the case of multiple lesions. The effective radius and modified GI results for the dose GI are 4.61 ± 1.12 and 4.28 ± 1.24, respectively.

Conclusion: This study analyzed various CI, HI, and GI definitions to assess dose distribution quality in brain SRS/SRT plans. CI, HI, and GI are valuable tools for evaluating treatment plans by quantifying conformity, dose uniformity, and dose gradient. However, these indices have limitations. Future research should investigate these correlations, linking CI, HI, and GI with local control rates and toxicity outcomes.

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Introduction

Brain metastases are the most common type of intracranial tumor, occurring in 25-50% of all cancer patients. The prognosis for individuals with brain metastases is typically unfavorable. Therapeutic options for brain metastases include surgery, whole brain radiation therapy (WBRT), stereotactic radiosurgery/ radiotherapy (SRS/ SRT), and chemotherapy and targeted therapy in selected patients. Without aggressive treatment, median survival is often limited to 1-2 months [1-2, 4]. Even with standard treatments like WBRT, the median survival time typically extends to around 6 months [2-4].

While whole-brain radiotherapy has historically been the standard treatment for brain metastases, SRS or SRT have emerged as a valuable alternative due to their minimally invasive nature and shorter treatment course [4]. Key treatment options for brain metastases include surgery, whole-brain radiotherapy, chemotherapy, and SRS. However, the introduction of SRS transformed clinical practice, offering a valuable alternative due to its minimally invasive nature and shorter treatment course. Pioneered by neurosurgeon Lars Leksell, SRS utilizes external beam radiation to deliver highly precise, high-dose radiation to the target volume while sparing surrounding healthy tissue. Since introducing the Gamma Knife (GK), SRS has become a widely used treatment for brain metastases [5]. Technological advancements have enabled the use of linear accelerator (LINAC)-based systems, such as volumetric modulated arc therapy (VMAT), to achieve treatment outcomes comparable to GK SRS [6-8]. The single-isocenter VMAT process for treating multiple brain metastases provides high-

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conformity dose distributions, an overall high quality of plans, and reduces treatment delivery time. In the RTOG 9005 trial, dose limits in SRS were determined based on the tumor size. The Maximal tolerated dose was measured as 24 Gy for tumors ≤ 2.0 cm in diameter, 18 Gy for tumors 2.1 to 3.0 cm in diameter, and 15 Gy for tumors 3.1 to 4.0 cm in diameter [4].

SRS treatment plans necessitate high conformity to minimize collateral damage to surrounding tissues [4]. Clinically, plan quality is assessed through visual inspection and analysis of dose-volume histograms (DVH) [8-10]. However, these methods provide qualitative information that is difficult to quantify for objective plan comparisons or clinical trial compliance. To address this, several quantitative plan quality metrics have been developed. Geometry-based metrics, which consider factors such as target volume overlap and dose volume size, are one such category.

Various quantitative indices have been developed for treatment plan evaluation to optimize dose distributions. While DVHs are valuable tools for extracting key dose parameters such as maximum, minimum, and mean dose, they inherently reduce the three-dimensional spatial complexity of the dose distribution to a one-dimensional representation, leading to a loss of crucial spatial information [8, 9]. To overcome this limitation, several indices have been proposed to quantitatively assess dose distribution, including conformity index (CI), homogeneity index (HI), and gradient index (GI). These indices provide a concise means to evaluate the conformity between the prescribed dose area and the planning target volume (PTV), the uniformity of dose within the target, and the rate of dose fall-off outside the target [11-14] (Reference number 10 used above paragraph).

While the assessment of treatment plan quality using quantitative metrics such as CI, HI, and GI is well-established in the field of stereotactic radiosurgery and radiotherapy [9, 11-14], and similar studies have investigated single-isocenter VMAT techniques for brain metastases [7-8], there remains variability in the specific formulations and definitions used for these indices across different studies and clinical practices [13-15]. A main challenge in comparing plan quality results across the literature lies in the lack of a universally adopted standard for calculating these metrics. Many similar works have explored plan quality with VMAT, employing a subset of these indices. However, a comprehensive comparison of the performance and interpretation of multiple distinct formulations of CI, HI, and GI within the context of single-isocenter VMAT brain SRS/SRT optimized with a modern algorithm like Photon Optimizer (PO) on a TrueBeam platform has not been extensively documented. This study aims to address this gap by rigorously evaluating and comparing a wide range of commonly cited CI, HI, and GI definitions when applied to treatment plans generated with this specific technique and optimization algorithm for multiple brain metastases.

The Conformity Index was introduced by the Radiation Therapy Oncology Group (RTOG) in 1993 and subsequently elaborated upon in ICRU Report 62 [9, 15]. The CI has gained significant importance with the advent of conformal radiotherapy techniques in assessing treatment plan quality [15]. According to RTOG Report 63, CI is the reference isodose volume (V_{RI}) ratio to the Target Volume (TV). However, this definition has limitations as it does not account for the shape of the target and reference isodose, nor the degree of spatial overlap between the two volumes [15-17]. Alternative CI approaches have been proposed. The Saint-Anne, Lariboisiere, and Tenon (SALT) group introduced a CI based on standard deviation derived from the differential dose-volume histogram (dDVH) for individual vascular lesions, alongside a geometric CI that quantifies the prescription isodose coverage of the lesion [18, 19]. Lomax & Scheib proposed two CI, considering both the TV covered by the prescribed dose and the volume of adjacent normal tissues [20]. A significant limitation of these early CI is the potential misinterpretation of a CI value of 1. While it may indicate complete target coverage by the reference isodose, it does not guarantee that the entire TV receives the prescribed dose [13]. To address these limitations, Van't Riet et al. introduced the Conformity Number (CN), which incorporates target coverage and normal tissue sparing [21]. Wu et al. investigated the influence of target shape complexity and size on CI. They proposed the Conformity Distance Index, which quantifies the average distance between the prescription isodose and the TV boundary [22]. Park et al. further refined CI by introducing a metric based on the distance between the surfaces of the TV and the reference dose volume, thus considering both the shape of the prescription isodose and the extent of target coverage [23]. Van't Riet et al. [21] pioneered using the Conformation Number (CN) to quantify treatment plan conformity in prostate cancer radiotherapy, encompassing both external beam and interstitial brachytherapy. The CN calculation incorporates PTV coverage and the volume of healthy tissue receiving doses exceeding the prescription. Knoos et al. [17] gave attention to the dose conformity of the PTV during conformal treatments, which is defined as the ratio of the PTV volume to the treated volume, known as the Conformity Index. The ICRU Report 62 [9] also introduced the CI concept, which can be defined as the ratio of the volume of the PTV to the volume of the treated, which is slightly different from the definition of Knoos et al. The so-called 'treated volume' here is the volume of tissues to which the dose given by the oncologist is applied to reach the desired treatment objectives.

The Homogeneity Index is a crucial metric for evaluating the uniformity of dose distribution within the Planning Target Volume [9, 11, 15]. Traditionally, HI is defined as the ratio of the maximum dose (D_{max}) to the minimum dose (D_{min}) or prescription dose (D_p) in PTV, from which CI equals 1 indicates the ideal homogeneity [11]. Alternative definitions have been proposed to mitigate the influence of grid size on point dose estimations, D_{max} and D_{min}. $D_{5\%}$ (the dose covers 5% of the PTV) was suggested to alternate D_{max}, and $D_{95\%}$ (the dose covers 95% of the PTV) to replace D_{min} [24]. Another commonly used HI formulation is HI = ($D_{2\%}$ – $D_{98\%}$) / $D_{p,}$ in which $D_{2\%}$ and $D_{98\%}$ were applied to represent the D_{max} and D_{min}, respectively, and this formulation exhibits greater sensitivity to point dose variations influenced by grid size and placement [22]. Lower HI values generally indicate more homogeneous dose distributions within the PTV. Yoon et al. introduced a new HI based on a statistical analysis of the dose-volume histogram (DVH). This approach defines HI as the standard deviation of the differential DVH curve within the PTV [25].

The GI is another objective metric to evaluate the steepness of dose falloff outside the Planning Target Volume in radiotherapy plans. A standard definition of GI is the ratio of the volume receiving 50% of the prescribed dose to the volume receiving the prescribed dose [26]. This index assesses the rate of dose decline beyond the target, with lower GI values indicating a steeper dose gradient and, consequently, improved sparing of normal tissues [26]. Ohtakara et al. modified the GI by incorporating a factor representing the degree of dose conformity, multiplying the original ratio by the ratio of the prescribed dose volume to the PTV volume [27]. Agostinelli et al. proposed the effective radius as an alternative metric to characterize the dose gradient, aiming to better quantify the impact of dose "splash" beyond the target [28].

This study aimed to evaluate and compare the impact of various dosimetric indices on the quality of cranial SRS and SRT treatment plans generated using single-isocenter VMAT. Specifically, the study investigated the influence of different CI, HI, and GI formulations on treatment plans created on a Truebeam LINAC system (Varian Medical Systems, Palo Alto, CA, USA) for cranial SRS and SRT.

Materials and Methods

Patient selection

Because this study did not involve any direct research on human participants or animals and utilized only existing non-identifiable data, ethical approval was not required. Twenty-three patients with brain metastasis who presented at the outpatient department of radiation oncology in our institute were prospectively enrolled in the study from year of 2022 to 2023. Target volumes were chosen up to 30 cc. Patients were immobilized using a double shell positioning system and underwent computed tomography (CT) imaging in the treatment position. The patients were scanned in a head-first supine position with a 1.0 mm slice thickness for simulation. The acquired CT scans were then imported into the Eclipse treatment planning platform (version 15.6, Varian Medical Systems, Palo Alto, CA) for subsequent fusion with diagnostic T1-weighted, post-contrast magnetic resonance imaging (MRI).

Target volumes were then delineated on the MRI fused scans; PTV was delineated by expanding from gross tumor volume (GTV) with a 3.0 mm isotropic margin uniformly for all cases. 42 target volumes were defined for 23 patients. Organs at risk (OAR) were delineated on the co-registered T1 MRI images. They consisted of the following structures: optic apparatus (optic chiasm and bilateral optic nerves), lenses, temporal lobe of the brain, brainstem, and eyes. For patients with more than one lesion, Boolean operators were used to group individual PTVs into a single conglomerate of one PTV, designated as “PTV_total.” Post WBRT, the prescription dose is delivered as a sequential boost dose of 5 to 15 Gy [4] in single or multiple fractions to 80%–90% isodose line, such that at least 99% of each PTV receives the prescription dose.

Stereotactic Treatment Planning

For all 23 patients, clinical treatment plans were developed in the Eclipse Treatment Planning System for delivery on a TrueBeam LINAC V2.7, employing Millennium 120 Multi leaf collimator (MLC). The PO VMAT optimizer in Eclipse Version 15.6 was used to optimize these SRS VMAT plans. A single isocenter was established for each patient, positioned approximately equidistant from the multiple brain metastases. Treatment plans were generated using two full coplanar arcs combined with two non-coplanar partial arcs. The treatment couch angle individualized for each patient, ranging from ±15° to ±30° based on patient specific geometry and available treatment clearance. The medical physicist determined the number of arcs employed, with the primary goal of achieving optimal dose distribution while minimizing the total number of arcs utilized. When multiple arcs were necessary, non-coplanar arcs were incorporated by adjusting the couch angles. Manual optimization techniques were implemented to minimize MLC tongue-and-groove leakage throughout the arc rotation. Additionally, jaw tracking was enabled during plan optimization to reduce the out-of-field dose. The optimal collimator angles and jaw-tracking settings were selected to minimize MLC leakage and transmission between each arc on the TrueBeam LINAC.

The optimization and normalization of all plans were performed to deliver 100% of the prescribed dose to 99%-100% of the target volume. Each target was treated to the same dose of 5 to 15 Gy as per plan. All SRS/SRT plans were limited to doses conforming to the requirements of both the RTOG-9508 and AAPM TG-101 guidelines [29]. The areas outside the PTV were not supposed to have hot spots. Dose control tuning structures around targets were designed to produce maximum conformity and dose gradient. In addition to optimizing ring structures, the generalized normal tissue objective (NTO) parameters were removed. The Clark et al. [30] planning methodology was adhered to in the development of our dose control tuning structures, which were incorporated in our optimization to control three dose-level areas. The Boltzmann-transport-based AcurosXB dose engine, with heterogeneity corrections (dose calculation grid size: 1.25 mm) and dose-to-medium reporting mode, was used to calculate the dose [31].

Figure 1 presents the isodose color wash 50 percent dose distribution with four multiple mets plans done with Truebeam VMAT SRS plan prescribed 8 Gy/fraction with 85 % prescription isodose line (left panel) with 100% target coverage for all targets. The left panel displays representative beam geometry for VMAT treatment, with the crosshair indicating the isocenter location. Beam angles were 30°, 60°, 300°, and 330° for a full coplanar arc combined with a non-coplanar partial arc. The center panel shows a dose-volume histogram (DVH) representative of multi-target VMAT SRS plans. The right panel illustrates an isodose distribution (50% dose level) for a clinical case with five brain metastases, demonstrating 100% target coverage. Collimator positions were optimized for each arc to prevent situations where multiple targets aligned within the same MLC track, thereby reducing unnecessary dose to surrounding brain tissue.

Photon optimizer (PO) optimization algorithm

At the beginning of the optimization process, the MLC apertures are first shaped to match the target volume, and a uniform dose rate is assigned to all calculation segments. As optimization proceeds, both the MLC leaf positions and the dose rates at each control point within the VMAT arc are refined. In the early stages of this process, larger modifications are typically applied to the leaf sequencing to establish an effective foundation for plan quality. PO optimizes the VMAT plans. A key distinction between the PO algorithm and its predecessors (DVO and PRO) lies in its utilization of a point cloud model to define structures, contrasting with the earlier algorithms. The PO algorithm utilizes a new model of structure, where a unified model is spatially defined using a single matrix over the image, encompassing structures, DVH calculations, and dose sampling. This matrix utilizes a fixed voxel resolution of 1.25 mm, 2.5 mm, or 5 mm. This resolution is determined by the planar X and Y slices. The Z resolution perpendicular to the slices is dependent on both the resolution selected and the slice spacing. For example, an original image with a slice resolution of 1 mm x 1 mm and a slice spacing of 8 mm is assumed; suppose the user chooses an optimization resolution of 2.5 mm. In that instance, a 2.5 mm x 2.5 mm x 4 mm matrix is used by the optimizer. This matrix determines the positions of the structures and the dose sampling, replacing the previously employed point clouds. These samples are also used to present the locations where each field is summed up to define the total dose [32].

The structure volume weights are determined based on volume weights per voxel to determine the DVH of the structure. The volume weight of the voxel determines the ratio of the original structure in a voxel. For small structures, the DVH is super-sampled on the dose matrix to provide a smoother appearance. Repeated adjustments of the optimal field shape and strength are made to achieve the desired dose distribution, and an optimal solution is reached. The Multi-Resolution Dose Calculation algorithm (MRDC) allows the quick dose estimation within the PO of the VMAT and IMRT plan calculation using the CPU. In defining the structures and spatial dose at PO, a point dose cloud model is sparsely sampled with a single matrix across the image [33].

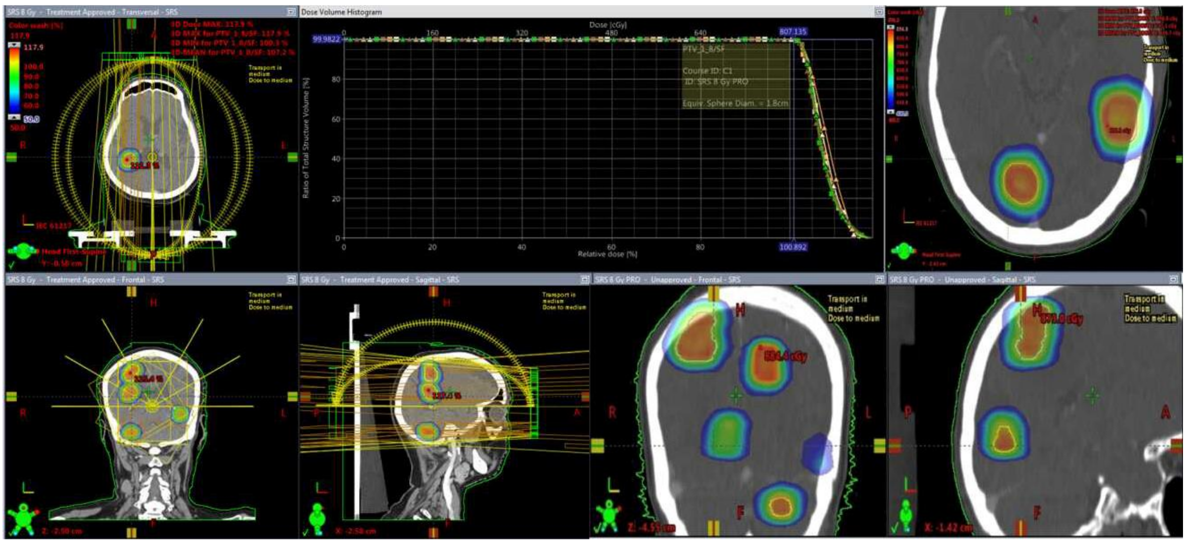

Figure 1. shows the truebeam VMAT SRS plan prescribed 8 Gy/fraction with 85 % prescription isodose line with 100% target coverage for all targets. The isodose color wash 50 percent dose distribution for multiples mets

Table 1. The formula for the plan quality metrics used for clinical plan evaluation analyzed for CI & HI

S.No	Formula	Description	Ideal value	References
1	RTOG conformity index (CI_{RTOG}); $CI_{RTOG} = \frac{V_{RI}}{TV}$	V_{RI}: The volume of the covered by prescription isodose; TV: the target volume;	1.0	Shaw et al. [15]
2	Lomax and Scheib (CI_{Lomax}); $CI_{Lomax} = \frac{TV_{RI}}{V_{RI}}$	TV_{RI}: The target volume covered by prescribed dose;. V_{RI}: The volume of the covered by prescription isodose;	1.0	Lomax et al. [15, 18]
3	SALT (CI_{SALT}); $CI_{SALT} = \frac{TV_{RI}}{TV}$	TV_{RI}: The target volume covered by prescribed dose;. TV: the target volume;	1.0	Lomax et al. [20]
4	Paddick and Van't Riet ($CN_{Paddick}$); $CN_{Paddick} = \frac{TV_{PIV}{}^2}{TV \times V_{RI}}$	CN – Conformity number; TV_{PIV} – the target volume covered by the prescription dose; TV – the target volume; V_{RI} – The volume of the covered by prescription isodose;	1.0	Paddick et al. [21]
5	Inverse of RTOG; $RTOG_{Inverse} = \frac{1}{\frac{V_{RI}}{TV}}$	V_{RI}: The volume of the covered by prescription isodose; TV: the target volume;	1.0	Shaw et al. [15]
6	ICRU 83 HI; $HI = \frac{(D_{2\%} - D_{98\%})}{(D_{50\%})}$	HI: Homogeneity Index; $D_{2\%}$:Target Volume covering 2% of the prescribed dose; $D_{5\%}$:Target Volume covering 5% of the prescribed dose; $D_{95\%}$:Target Volume covering 95% of the prescribed dose; $D_{98\%}$:Target Volume covering 98% of the prescribed dose; D_{max} :Target Volume getting highest dose; D_{min} :Target Volume getting minimal dose ; D_{mean} :Target Volume getting mean dose ; D_p: Target Volume getting the prescribed dose.	0.0	ICRU 83 [11]
7	Knoos et al., HI; $HI = \frac{D_{max}}{D_{min}}$		1.0	Knoos et al. [17]
8	RTOG HI; $HI = \frac{D_{max}}{D_{pres}}$		1.0	Shaw et al. [13]
9	Wu et. al. HI; $HI = \frac{(D_{2\%} - D_{98\%})}{(D_{pres})}$		0.0	Wu et al. [22]
10	Semenenko et al. HI; $HI = \frac{(D_{5\%} - D_{95\%})}{(D_{pres})}$		0.0	Semenenko et al. [24]

Table 2. Various formula for the plan quality metrics of analyzed for GI

S.No	Formula	Description	Ideal value	References
1	Conventional Paddick's gradient index (GI); $GI = \frac{V_{50\%}}{V_{100\%}}$	GI: Gradient Index; $V_{50\%}$: Volume irradiated by 50% of the prescribed dose; $V_{100\%}$: Volume irradiated by 100% of the prescribed dose;	3.0 to 5.0	Paddick et al. [26]
2	Modified GI (mGI); $mGI = \frac{V_{50\%}}{V_{100\%}} \times \frac{V_{RI}}{TV}$	V_{RI} : The volume covered by prescribed dose; TV: Target volume;	3.0 to 5.0	UK SABR Consortium [34]
3	DGI (Dose Gradient Index); $DGI = 100 - \{100 \times ((Reff, 50\%Rx - Reff, 100\%Rx) - 0.3cm)\}$ $Reff = \sqrt[3]{\frac{3V}{4\pi}}$ Reff, 50%Rx: Effective radius 50% isodose line that is equal to one half of the Rx volume. The effective radius of a volume is the radius of a sphere of equal volume. Reff, 100%Rx : is the effective radius of the 100% isodose volume.		Depends on target volume's	Reynolds et al. [35]

Clinical SRS delivery process

A quality assurance check of kilovoltage to megavoltage imaging isocentric coincidence was performed before every SRS treatment, with a Winston-Lutz test conducted to ensure accuracy and precision in target localization. SRS procedures were performed in accordance with all quality assurance procedures that adhered to SRS treatment plans and delivery protocols. A daily QA measurement of kilovoltage to megavoltage imaging isocenter coincidence, including IsoCalc, was conducted before administering every VMAT cranial SRS/SRT treatment to accurately and precisely localize the target. We achieved an IsoCalc localization accuracy of TrueBeam that was less than 0.5 mm.

Tools for plan evaluation

This study employed three different categories of objective assessment formulas: the CI, the HI, and the GI. CI was defined as a ratio of the prescriptive dose volume to the target volume (TV) and the overlap volume. To select the CI definition, five CI definitions were chosen as shown in Table 1. The traditional CI computation approach, which the RTOG or the SALT group can offer, fails to address the shape of the TV or the isodose volume [15, 18-19]. According to the work of the SALT group, Lomax and Scheib, Van t Riet et al., and Paddick, both CN and SALT definitions include the volume of healthy tissue irradiated by the prescribed dose. This definition provides a more accurate representation of dose conformity compared to the other definitions [21].

To assess dose uniformity within the target volume (TV), the homogeneity index was utilized. Five distinct definitions for calculating HI within stereotactic radiation therapy plans were evaluated, as presented in Table 1. The ideal value for the first four definitions is 1, indicating uniform dose delivery to each voxel within the TV. As defined by Paddick, the conventional gradient index (GI) quantifies the dose fall-off rate outside the target. Vx% represents the volume receiving x% of the prescribed dose. A lower GI value indicates a steeper dose gradient, which is desirable as it suggests better sparing of surrounding normal tissue [26]. A modified GI (mGI) was developed to incorporate TV coverage. This metric evaluates the dose gradient based on the TV, incorporating the influence of dose conformity. A lower mGI value signifies a steeper dose fall-off [27, 34].

The dose gradient index (DGI) quantifies the dose fall-off outside the target volume. A DGI value greater than or equal to 100 corresponds to a dose gradient of 0.3 cm or less. This 0.3 cm gradient was empirically determined to be the optimal achievable gradient in SRS planning using linear accelerators based on cases involving non-coplanar arcs. A significant advantage of the DGI is its ease of calculation, requiring only the conversion of Rx and 50% Rx isodose lines into corresponding volumes and the subsequent application of a simple formula [35]. Three distinct GI definitions were selected, as outlined in Table 2.

Results

Conformity Index (CI)

A graph of conformity indexes (CI), PTV target volume versus RTOG, SALT, Lomax & Scheib, and Paddick was constructed for the 42 brain metastases. Generally, plans with smaller target volumes had more significant conformity indexes, whereas the conformity indexes were relatively constant for plans with larger target volumes. The maximum similar conformity index value for RTOG and Paddick 1.37 occurred for a plan with a target volume of 2.7 cc. For the target volume of 1.7 cm^3, the conformation number value was 1.83 for Van't Riet and Paddick CN. Figure 2 shows the individual targets for the patients and individual graph plots.

The CIs are evaluated for each target individually. The mean±SD for CI RTOG, Lomax & Scheib, SALT, Van't Riet & Paddick, and Inverse of RTOG is 1.02 ± 0.11, 0.92 ± 0.06, 0.94 ± 0.05, 1.11 ± 0.21, and 0.98 ± 0.11, respectively. A comparable evaluation of the CI value was found between Lomax & Scheib and SALT. The average values of CIs are listed in Table 3. For CI values RTOG, Van't Riet & Paddick, the Inverse of RTOG values were close to 1.0. Lomax & Scheib and SALT were 0.92 ± 0.06 and 0.94 ± 0.05, respectively, and achieved lower than 1.0. All the plans had better conformity for the prescribed dose and TV.

Pairwise comparisons were performed to investigate the relationships between different CI metrics. The RTOG conformity index was compared to the Lomax & Scheib, Van't Riet & Paddick, and SALT indexes. Scatter plots were generated for each comparison, with RTOG conformity index values plotted against the corresponding values of the other indices (Figures 3a-c). Linear regression analysis was performed on each dataset, yielding the following equations:

1. Lomax & Scheib: CI_Lomax & Scheib = -0.4999 / CI_RTOG ($R^2 = 0.8976$)
2. Van't Riet & Paddick: CI_Paddick = 1.7893 / CI_RTOG ($R^2 = 0.9668$)
3. SALT: CI_SALT = 0.373 / CI_RTOG ($R^2 = 0.7319$)

Additionally, the Lomax & Scheib and the SALT indexes were compared to the Inverse RTOG indexes. Scatter plots were generated for these comparisons (Figures 3d-e), and linear regression analysis revealed the following relationships:

1. Lomax & Inverse RTOG: CI_Inverse RTOG = 1.6364 / CI_Lomax ($R^2 = 0.8231$)
2. SALT & Inverse RTOG: CI_Inverse RTOG = -1.9857 / CI_SALT ($R^2 = 0.8276$)

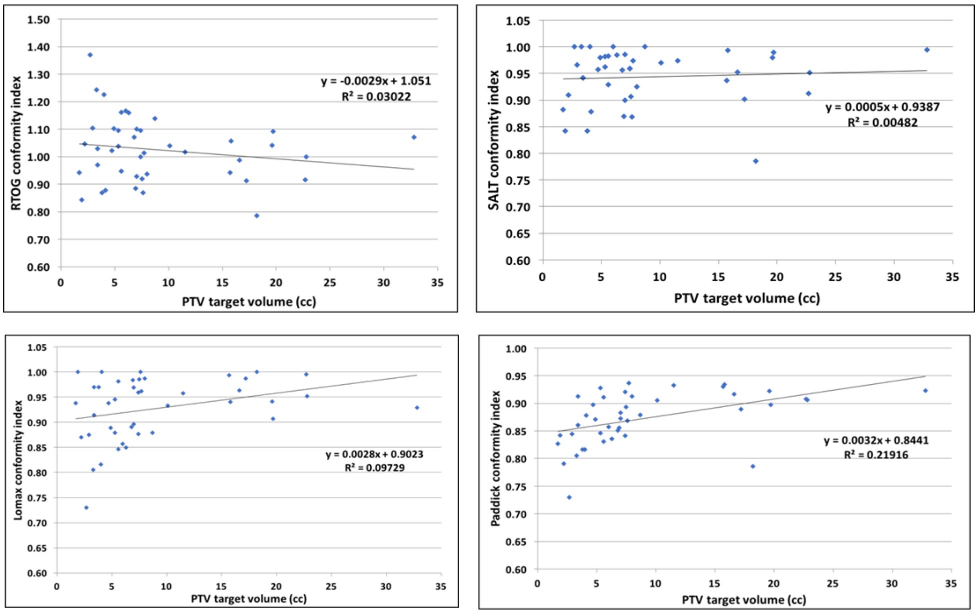

Figure 2. Distributions of Conformity Index of PTV volume versus RTOG, SALT, Lomax & Scheib and Paddick for individual targets.

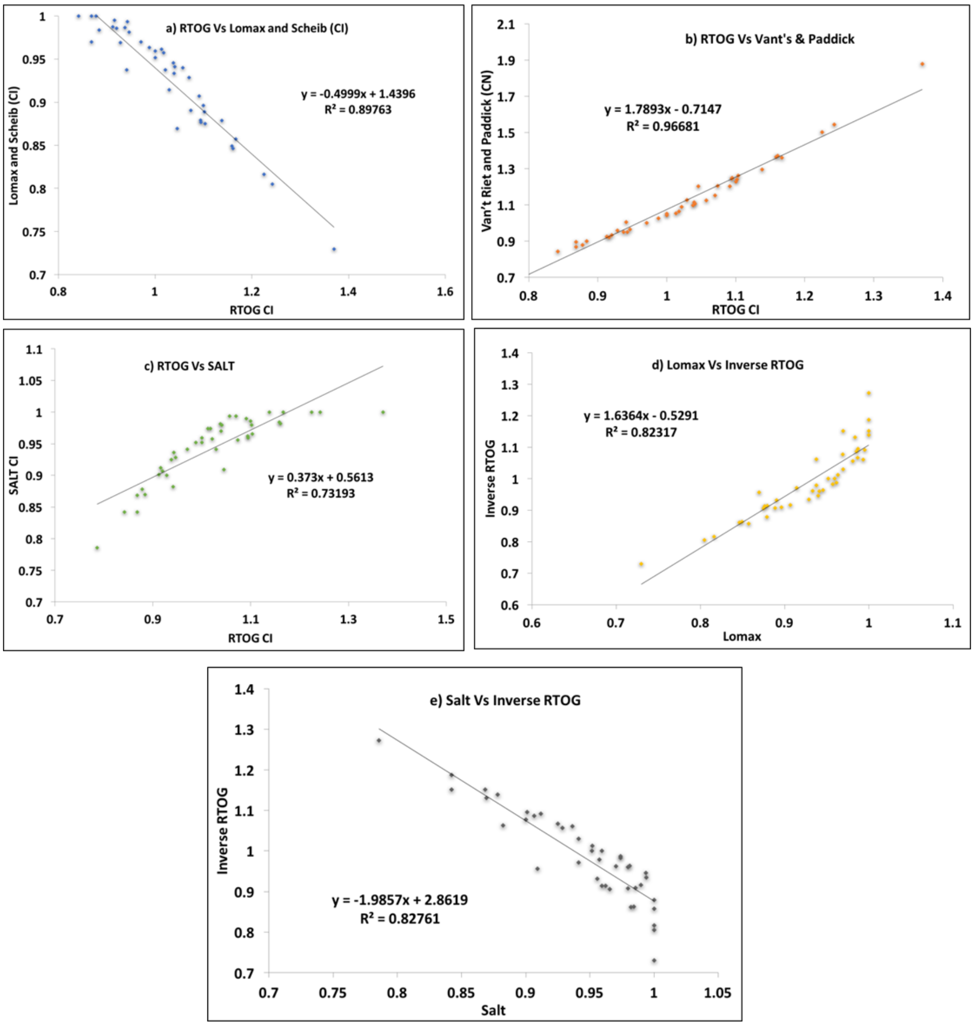

Figure 3. Distributions of Conformity Indexes (CI) RTOG versus a) Lomax and Scheib, b) Van't Riet and Paddick, c) SALT, d) Inverse of RTOG versus Lomax and e) SALT for individual targets.

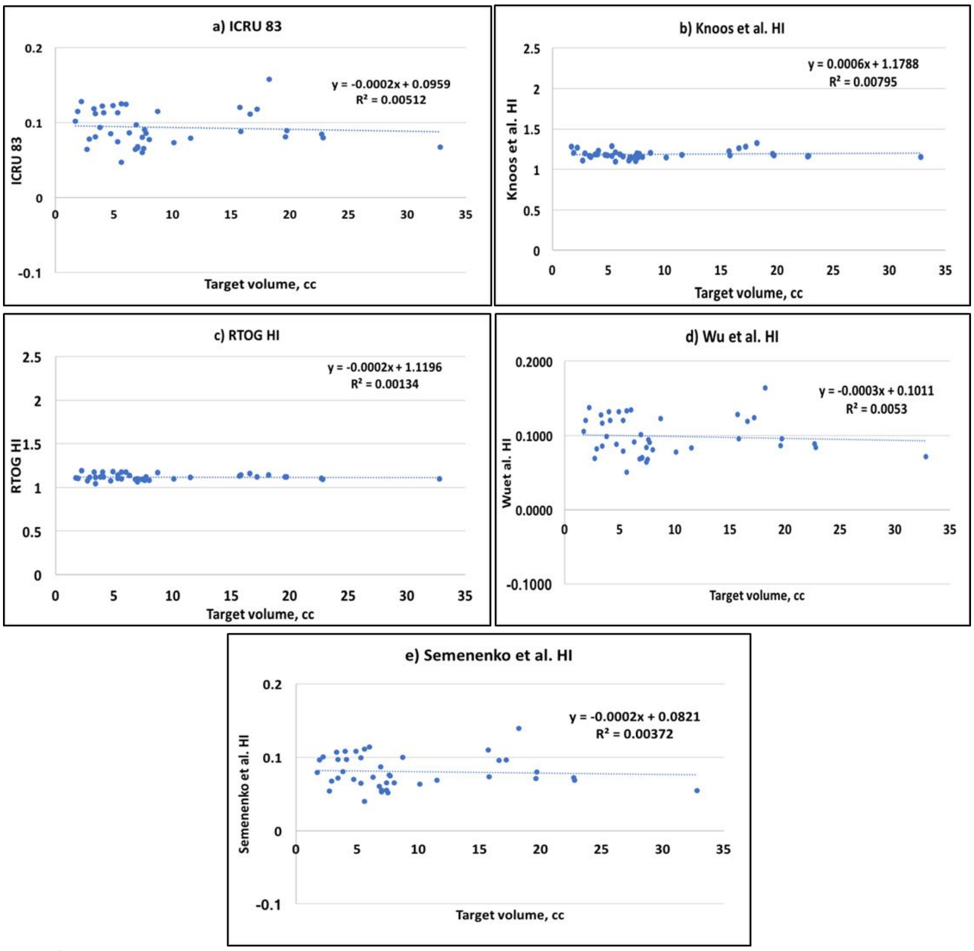

Figure 4. Distributions of Homogeneity indexes (HI) PTV target volume versus a) ICRU 83, b) Knoos et al, c) RTOG, d) Wu et al, e) Semenenko et al for individual targets.

sHomogeneity Index (HI)

A plot of the HI versus PTV target volume is shown in Figure 4 (a-e) for different formulas. All 42 targets had a HI that was well within protocol values. The HI is calculated based on the parameters $D_{98\%}$, $D_{95\%}$, $D_{50\%}$, $D_{2\%}$, $D_{5\%}$, D_{max}, D_{min}, D_{mean} and D_p. The results of different HI values achieved similar ideal values—the HI value calculated by Knoos et al. HI and RTOG HI were all ＞1, whereas 0 was calculated by the ICRU 83, RTOG, and Wu et al. The HI is evaluated for each target individually. The Mean ± SD for HI ICRU 83, Knoos et al., RTOG, Wu et al., and Semenenko et al. is 0.094 ± 0.024, 1.185 ± 0.052, 1.118 ± 0.036, 0.099 ± 0.026, and 0.080 ± 0.022, respectively. A comparable evaluation of the HI value was found between ICRU 83, Wu et al., and Semenenko et al. Also, comparable HI values were achieved between Knoos et al. and RTOG. The average values of CIs are listed in Table 3.

Pairwise comparisons were performed to investigate the relationships between different HI metrics. The Knoos et al. HI was compared to the RTOG index, while the Semenenko et al. and Wu et al. indices were compared to the ICRU 83 index. For each comparison, scatter plots were generated, depicting the values of one index against the corresponding values of the other shown in Figure 5. Linear regression analysis was performed on each dataset, yielding the following relationships:

1. Knoos et al. vs. RTOG: HI_Knoos et al. = 0.3528 / HI_RTOG (R^2 = 0.2604)
2. Semenenko et al. vs. ICRU 83: HI_Semenenko et al. = 0.8964 / HI_ICRU 83 (R^2 = 0.9742)
3. Wu et al. vs. ICRU 83: HI_Wu et al. = 1.0722 / HI_ICRU 83 (R^2 = 0.9974)

Gradient Index (GI)

The results of the GI values calculated from Table 2 are shown in Figures 6 and 7 and Table 3. The Mean ± SD for GI Conventional GI (Paddick and Lippitz), Modified GI (mGI), and DGI (Dose Gradient Index) is 4.618 ± 1.121, 4.289 ± 1.248, and 59.352 ± 9.645, respectively. The average values calculated by the Reff 50% Effective radius 50% PIV and Reff R100 Effective radius PIV were 1.934 ± 0.350 and 1.228 ± 0.297, respectively. In addition, there was likely to be a steeper fall-off of all plans according to the results of Conventional GI, Modified GI (mGI), and DGI.

Table 3. Shows Comparison the different plan evaluation indexes for brain

Comparison the different evaluation indexes for brain			
S.No	Conformity Index (CI)	Mean ± SD	Ideal value
1	CI RTOG	1.024 ± 0.118	1
2	Lomax and Scheib	0.928 ± 0.062	1
3	SALT	0.943 ± 0.052	1
4	Van't Riet and Paddick	1.118 ± 0.215	1
5	Inverse of RTOG	0.989 ± 0.113	1
Homogeneity Index (HI)			
1	HI ICRU 83	0.094 ± 0.024	0
2	Knoos et al. HI	1.185 ± 0.052	1
3	RTOG HI	1.118 ± 0.036	1
4	Wuet al. HI	0.099 ± 0.026	0
5	Semenenko et al. HI	0.080 ± 0.022	0
Gradient Index (GI)			
1	Conventional GI (Paddick and lippitz)	4.618 ± 1.121	3 to 5
2	Modified GI (mGI)	4.289 ± 1.248	3 to 5
3	DGI (Dose Gradient Index)	59.352 ± 9.645	Depends on target volume's

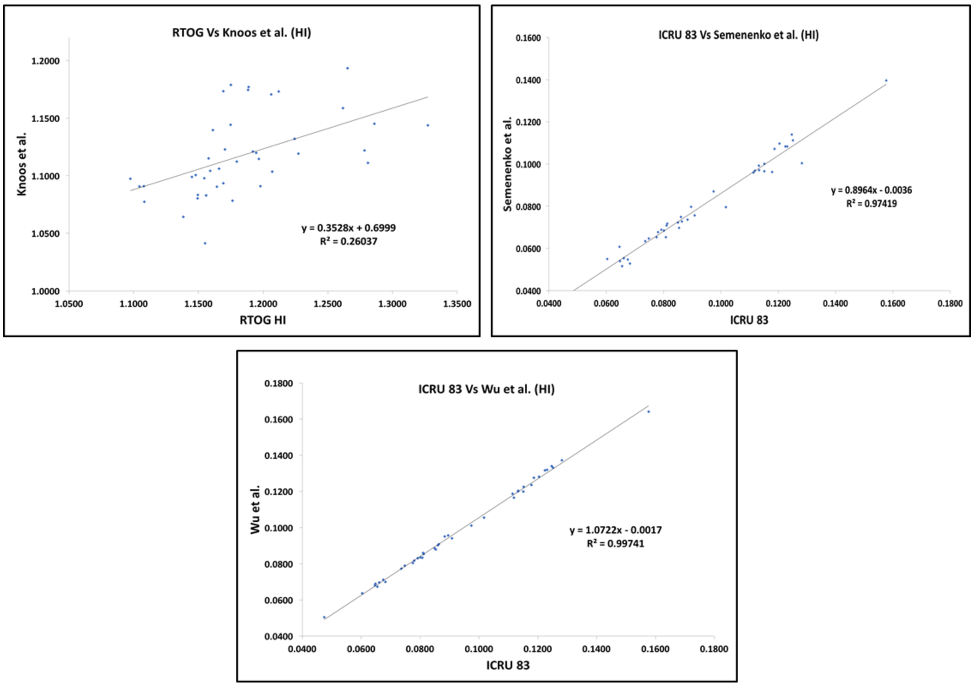

Figure 5. Distributions of Homogeneity indexes (HI) RTOG versus Knoos et al, and ICRU 83 versus Semenenko et al, and Wu et al for individual targets.

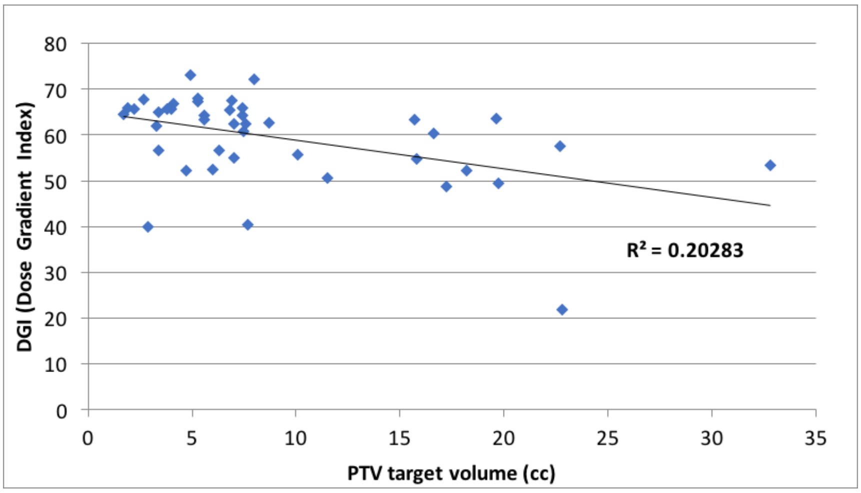

Figure 6. Distribution of Gradient index for PTV target volume versus Dose gradient index for individual targets.

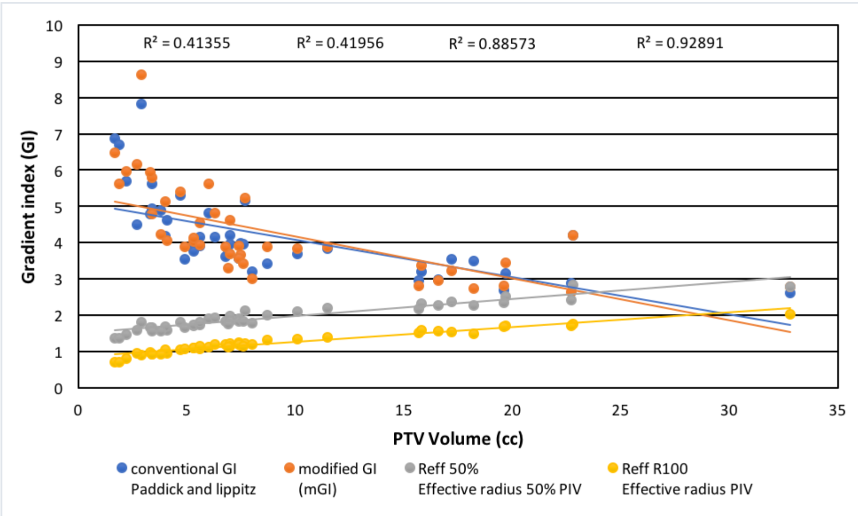

Figure 7. Distribution of Gradient index for PTV target volume versus Conventional GI (Paddick and lippitz), modified GI (mGI), Reff 50% Effective radius 50% PIV and Reff R100 Effective radius PIV for individual targets.

Discussion

Analysis of conformity index (CI) values revealed that the Van't Riet and Paddick method yielded values >1, while the Lomax & Scheib, SALT, and Inverse RTOG methods consistently produced values <1 (Table 1). The RTOG method yielded values closest to 1. For the homogeneity index (HI), the ICRU 83, Wu et al., and Semenenko et al. methods yielded values of 0, indicating ideal homogeneity. In contrast, the Knoos et al. and RTOG methods yielded values greater than 1. The calculated values for conventional gradient index (GI), modified GI (mGI), and dose gradient index (DGI) were consistent with the ideal values as defined in published guidelines.

The CI has been suggested in the correlation of the TV and V_{RI} [9, 15-16]. In the RTOG guideline, the CI RTOG equal to 1 represents the optimum conformity. CI RTOG below 1 indicates that the TV is not completely irradiated. Still, CI RTOG above 1 indicates that the irradiated volume is greater than the TV, and normal tissue is also contained. The CI RTOG values in the current study were 1 each, indicating that the volume of the prescribed dose was similar to the PTV. In the definition of CI RTOG, the TV falls under the recommended dose. In the meantime, it is not entirely clear that the two volumes align with one another when CI RTOG equals 1 [13, 15].

Lomax & Scheib, and the SALT group, were determined as the ratio of PTV covered by the prescribed dose (TV_{RI}) to V_{RI} and TV_{RI} to TV, respectively. Both the SALT CI and the Lomax & Scheib are to take into account the irradiated PTV. But in SALT CI, the amount of healthy tissue surrounding the target is not taken into account. The similar value achieved by Lomax & Scheib was 0.928. These findings suggest that, although the RTOG conformity index is independent of target volume for larger target volumes, it depends on target volume for smaller volumes (less than 1 cm^3) [20]. Even with Lomax & Scheib = 0.5, though V_{RI} was used to replace the TV in the definition of Lomax & Scheib, it is hard to interpret it as whether the total target was entirely covered with the same volume of healthy tissue being irradiated, or TV and V_{RI} were the same in volume, but half volume contact [13, 18-20].

The influence of target size, as studied by Knoos et al. [17], is that when the target size is small, a significant relative change will occur due to a slight shift in absolute volume. The CN suggested by Van't Riet & Paddick was to add the Lomax & Scheib index and the SALT index. Therefore, the TV and the amount of healthy tissue that is irradiated around it may be taken into account [21]. The current research indicated that Van't Riet & Paddick values were evidently superior to other CIs and close to 1.

Although Lomax & Scheib and SALT values were not above 1 in our study, inaccurate information may still exist due to the limitations. The usual issue with these CIs, as applied in the current study, is that the influence of the shape of the prescribed isodose volume and PTV was not considered. The study by Wu et al. indicated that the volume of the prescribed dose around the TV could be influenced by the complexity of the TV, resulting in an impoverished conformity. Wu et al. also observed that the Paddick conformity index behaved similarly to the RTOG conformity index under small target volumes [22].

Five distinct definitions of the HI were employed in this study. For SRS/SRT plans, Knoos et al. and RTOG HI calculated by the ratio of D_{max} to D_{min} or D_p were likely inaccurate because the constraint of D_{max} was not strict in the optimization process. This is attributed to the potential lack of stringent constraints on D_{max} during optimization. Meanwhile, few studies pointed out that D_{max} or D_{min} may be influenced by a single voxel, rendering them highly sensitive to variations in dose calculation parameters, such as grid size and placement [24, 36].

As shown in Figures 4a, d, and e, and Table 3, ICRU 83, Wu et al., and Semenenko et al. HI achieved an ideal value of 0. D2 (D5) and D98 (D95) were used as substitutes for maximum and minimum, respectively, as expressed in equations (Table 1) of Sr. No. 6, 9, and 10 as a way of overcoming the effect of grid size and grid position. We found in our studies that the outcomes of HIs revealed that all the plans offered more homogeneous dose distributions within the PTV. Figure 5 shows a highly correlated graph plot of Wu et al. versus ICRU 83 HI.

The dose of GI provides a method for evaluating the degree of steepness of dose falloff beyond the PTV [26-27, 35]. Our study evaluated conventional Paddick's GI, mGI, and DGI. Conventional GI and mGI were all based on the volume of 50% and 100% prescribed dose, whereas mGI was considered to consider the TV coverage. This equation analyzes the dose gradient based on the TV, which considers the effect of dose conformity as well. The lower mGI value means a steeper dose fall-off [27, 34]. When conventional Paddick's GI and modified GI are used to evaluate the dose falloff for SRS/SRT plans, they perfectly align with ideal values by the recommended criteria shown in Table 2. The equation of mGI was used to replace the denominator in the traditional GI with the PTV to determine the dose gradient using the TV. Meanwhile, mGI was also viewed as mGI = GI × VRI / TV = GI × RTOG CI, primarily in terms of the level of conformity [27, 34].

Tatsiana A. Reynolds et al. investigated the DGI, a metric quantifying radiation dose fall-off beyond the target volume, for intracranial SRS/SRT. Their group developed it as a quantitative metric for characterizing radiation dose fall-off concerning distance away from the outer surface of a target volume [35]. DGI was determined for various tumor sizes and shapes, establishing ideal and minimally acceptable values. The higher the DGI of the plans, the lower the volume of irradiated normal tissues. DGI is linearly proportional to the effective radius of the Rx isodose volume. Each increase in effective radius of one millimeter over 0.3 cm volume is a loss of 10 DGI points. This optimum gradient of 0.3 cm was empirically determined in SRS planning cases as the lowest gradient achievable with a linear accelerator SRS using non-coplanar arcs. Its simple derivation with Rx and 50% Rx isodose volume (i.e., not dependent on dose fall-off) makes the DGI a valuable formula for assessing the quality of a plan, guaranteeing optimal dose fall-off outside the target area to supplement conformity indices. Our findings were similar to those released by Reynolds et al. [35].

Various research groups have evaluated plan qualities compared to those of the LINAC-based SRS/SRT for the brain [27, 30, 35, 37-42]. Our findings align with those reported by G.M. Clark et al. [30], who observed favorable dosimetric indices, CI, HI, and GI, for various target sizes and treatment plans planned and done with multiple brain metastases in 15 consecutive patients with Varian TrueBeam STx LINAC brain metastases. Our results demonstrate that VMAT can achieve excellent dosimetric outcomes for single and multiple intracranial targets, with high conformity and homogeneity indices across a range of target volumes.

Recently, Tingting Cao et al. [42] reported the results of an analysis of different definitions of the CI, HI, and GI used to evaluate prostate cancer SBRT. A total of ten patients with localized prostate cancer staged T1-T2a were randomly selected, for which two SBRT plans were designed for each patient using CyberKnife and EDGE systems, respectively, based on the same images and contours. CI, HI, and GI were calculated for each plan based on different definitions using dose-volume histograms. Their analysis concluded that these indices can evaluate plan quality objectively. They observed better dose distribution and dose gradient conformity for EDGE plans, while CyberKnife plans demonstrated better uniformity. Our conclusions from the present study align with the findings of Tingting Cao et al.

The study by Stanley et al. [41] found a significant difference in CI values between smaller targets (<1 cm^3) and larger targets (>1 cm^3), with smaller targets demonstrating higher CI values on average. This finding is supported by our analysis, which also showed a trend towards higher CI values for smaller targets. However, our study utilized a different set of CI definitions (RTOG, Lomax & Scheib, SALT, Van't Riet & Paddick) compared to Stanley et al. (RTOG and Paddick). Furthermore, our study explored the relationship between different CI metrics through pairwise comparisons and linear regression analysis, providing insights into the correlations between these indices. These analyses revealed significant relationships between the various CI metrics, suggesting they provide complementary information regarding plan quality.

Evan M. Thomas et al. [6-7] compared the quality of plans using TrueBeam STx and Gamma Knife, as well as single-isocenter VMAT plans simulated by delivery with the TrueBeam STx (Varian) in high-intensity FFF mode. They compared the distribution of RTOG and the Paddick conformity index of individual targets and overall plans. In the current study, we find that our results align with those of Evan M. Thomas et al. [6, 7]. Nonetheless, we have also demonstrated evidence of possible dosimetric benefits from using multiple non-coplanar volumetric arcs to address challenging treatment plans.

Recently, Varian introduced Hyperarc [43-44] automatic planning and delivery treatment features with SRS NTO in Photon Optimizer (PO), which activates the HyperArc-SRS NTO instead of the standard NTOs. This specialized NTO is designed to optimize dose distributions for HyperArc treatments. This technique utilizes non-coplanar arcs with varying gantry speeds and modulation to deliver highly conformal radiation doses. For plan evaluation, the following quality metrics are readily available for all targets: Paddick CI, RTOG CI, ICRU83 HI, and Paddick GI.

Clark et al. [30] investigated the impact of treatment planning technique on plan quality for cranial radiosurgery using a Varian linear accelerator equipped with the Varian High Definition 120 MLC. For three simulated metastasis patient scenarios, they formulated three distinct treatment plans: single-arc/single-isocenter (SASI), triple-arc/single-isocenter (TASI), and triple-arc/triple-isocenter (TATI). Plan quality was assessed using the Paddick and RTOG CI, the Paddick GI. They reported slightly higher mean conformity indices for the TASI plans (Paddick CI, 0.761; RTOG CI, 1.33) compared to both the SASI plans (Paddick CI, 0.699; RTOG CI, 1.45) and the TATI plans (Paddick CI, 0.713; RTOG CI, 1.44). Our study demonstrated equivalent or superior dosimetric parameters. Regarding specific metrics, the CN proposed by Van't Riet et al. may offer advantages over other CI definitions by incorporating target volume, prescription isodose volume, and irradiated target volume. The ICRU 83, Wu et al., and Semenenko et al. indices are recommended for HI assessment due to their reduced sensitivity to dose calculation grid size. Concerning dose gradient evaluation, the mGI and DGI demonstrated slightly superior performance to the conventional GI in this study.

Conclusion

This study analyzed various CI, HI, and GI definitions to assess dose distribution quality in brain SRS/SRT plans. The CI, HI, and GI are valuable tools for evaluating treatment plans by quantifying conformity, dose uniformity, and dose gradient. However, these indices have limitations. CI calculations often do not incorporate information regarding target location and shape. Furthermore, the relationships between these dosimetric parameters and clinical outcomes remain unclear. Future research should investigate these correlations, linking CI, HI, and GI with local control rates and complication incidence to determine if improved conformity, homogeneity, and dose fall-off are associated with better clinical results.

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