Neurosurgical Subspecialties **2026** vol. 2(1) | 15–21
DOI: 10.14218/NSSS.2025.00036

Original Article

Evaluation of Target Irregularity as a Potential Parameter in Gamma Knife Treatment Planning: A Retrospective Cross-sectional Study in Vestibular Schwannoma

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Received: July 22, 2025 | **Revised:** October 09, 2025 | **Accepted:** February 16, 2026 | **Published online:** March 04, 2026

Abstract

Background and objectives: Fast inverse planning in radiosurgery planning is limited by an excessive number of isocenters, which is clinically hypothesized to be driven by the morphological irregularity of the target volume. This retrospective cross-sectional study aimed to empirically evaluate this hypothesis in vestibular schwannoma cases.

Methods: Consecutive patients diagnosed with vestibular schwannoma and receiving Gamma Knife radiosurgery in 2023 were included, and their treatment plans designed using the GammaPlan planning system were collected. Morphological irregularity–related parameters, including standard sphericity (SS), volume ratio sphericity (VRS), and the coefficient of variance of diameters (DCV), were calculated based on parameters provided by the system. Basic demographic and clinical data were collected to evaluate their impact on sphericity. The effects of different sphericity assessment methods on common treatment plan parameters were analyzed.

Results: Treatment plans of 280 patients with vestibular schwannoma were collected. The SS, VRS, and DCV of the tumors were 0.85 (0.77–0.91), 0.46 ± 0.16, and 0.22 (0.14–0.34), respectively. Multivariate analysis showed that lesion volume, acoustic neuroma consensus on systems for reporting results grade, and age were significant factors influencing sphericity. All other planning parameters, except prescription dose and homogeneity index, were significantly correlated with sphericity. DCV was more closely correlated with SS than with VRS.

Conclusions: DCV may serve as a simple quantitative metric of target morphological irregularity, showing strong consistency with SS. Incorporating morphological irregularity into Gamma Knife treatment plan evaluation may help improve future planning strategies and support optimization of isocenter utilization.

Introduction

Fast inverse planning (FIP) is a recently developed optimization system for Gamma Knife treatment planning.[1–3] Advances in GammaPlan workstation hardware have enabled the computationally intensive, convex optimization–based FIP to be executed within clinically feasible timeframes.[1] The introduction of FIP has significantly lowered the technical barrier to generating high-quality treatment plans and markedly improved inter-planner consistency.[3] Nevertheless, a well-recognized limitation of FIP is its tendency to generate an excessive number of isocenters—often several times more than those used in manually optimized plans.[2–4]

With growing insights into the radiobiology of stereotactic radiosurgery, it has become evident that a higher isocenter count may alter the biologically effective dose even at identical physical dose levels,[5] potentially influencing clinical outcomes.[6] Current FIP systems operate purely through constraint-driven algorithms without integrating expert knowledge or adaptive learning mechanisms, thus lacking true artificial intelligence capabilities. In contrast, manual planning, refined through extensive clinical experience, offers valuable heuristic guidance that should inform the development of future intelligent planning systems. Clinicians

Keywords: Gamma Knife; Coefficient of variance of diameters; Vestibular schwannoma; Sphericity; Treatment planning; Irregularity.

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How to cite this article: Wu H, Chen J. Evaluation of Target Irregularity as a Potential Parameter in Gamma Knife Treatment Planning: A Retrospective Cross-sectional Study in Vestibular Schwannoma. *Neurosurg Subspec* 2026;2(1):15–21. doi: 10.14218/NSSS.2025.00036.

commonly observe that target volume complexity correlates with increased isocenter requirements, with non-spherical, irregularly shaped targets typically demanding more isocenters.[7]

In this study, target irregularity refers to the geometric deviation of a lesion from a perfect sphere. This deviation was quantitatively assessed using three measurable parameters: standard sphericity (SS), volume ratio sphericity (VRS), and the coefficient of variance of diameters (DCV). Lower sphericity or a higher DCV indicates greater geometric irregularity. We aimed to preliminarily identify factors that may influence target geometric irregularity and further investigate whether such irregularity affects treatment planning parameters. This analysis will provide foundational data for future optimization of isocenter quantity in AI-assisted FIP.

Materials and methods

Participants

This retrospective cross-sectional study was conducted in 2025 using treatment plans from patients with vestibular schwannoma who underwent Gamma Knife radiosurgery at Shanghai Gamma Hospital in 2023. Consecutive eligible cases were included for analysis. All cases met the following criteria: (1) treatment plans were formulated within the same cobalt source replacement cycle; (2) classic single-session Gamma Knife treatment; (3) newly diagnosed cases; (4) cases with residual tumors more than three months after surgery; (5) all patient records were anonymized by replacing names with coded identifiers before being transferred to the research-dedicated treatment planning workstation. To evaluate whether the novel parameter could approximate the commonly used standard, the sample size was estimated based on detecting a clinically meaningful correlation between the two parameters using regression analysis. Assuming a moderate Pearson correlation coefficient of 0.5, with a significance level (α) of 0.05 and 80% statistical power, a minimum of 26 subjects was required. To ensure adequate power even for weaker correlations (e.g., r = 0.3), and to allow for potential subgroup analyses, a target sample size of at least 80–100 retrospective cases was considered appropriate.

This study was carried out in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments. The protocol was approved by the Ethics Committee of Shanghai Gamma Hospital (Approval No. 2025-011-02).

Collection of general data

General data of the subjects were collected, including patient age, gender, surgical history (yes/no), presence of hearing loss or significant impairment on the affected side (yes/no), facial paralysis on the affected side (no severity classification; yes/no), presence of vertigo (yes/no), gross target volume (GTV, unit: cm^3), and acoustic neuroma consensus on systems for reporting results (ANCSRR) size classification.[8]

Collection of planning system–related parameters

Treatment plan parameters were collected based on data provided by the GammaPlan Gamma Knife treatment planning system (ELEKTA AB, version 11.0), including: prescription dose (PD, unit: Gy), isodose line (IDL, expressed directly as a decimal), planning target volume (PTV, unit: cm^3), number of shots, number of shots required to cover 1 cm^3 of PTV (Sh/PTV), homogeneity index (HI, calculated as [dose covering 2% volume − dose covering 98% volume] divided by dose covering 50% volume), coverage index (CI, expressed directly as a decimal), selectivity index (SI, expressed directly as a decimal), Paddick's conformity index (PCI, equal to CI × SI, not exceeding 1), gradient index (GI), and the maximum diameter of GTV on the cross-section with the largest area, the maximum vertical diameter on the same cross-section, and the maximum vertical diameter in the z-direction (D1, D2, D3; unit: mm). The maximum value among D1–D3 was defined as Dmax.

Sphericity calculation

SS was calculated using Krumbein's approximate surface area sphericity formula; the closer SS was to 1, the closer the lesion was to a sphere. VRS was calculated as: VRS = GTV / (π × $Dmax^3$ / 6).[7] The closer VRS was to 1, the closer the lesion was to a sphere. The relative standard deviation was calculated based on D1, D2, and D3 as follows: $SQRT(\Sigma(Di - D)^2 / 3)$, where D was the average of D1–D3, and i = 1–3. The DCV was obtained by dividing the standard deviation by the average diameter; the closer DCV was to 0, the closer the lesion was to a sphere. Using SS as the standard, the correlations between VRS and SS, and between DCV and SS, were compared.

Statistical analysis

Quantitative data were tested for normal distribution. If normally distributed, they were expressed as mean ± standard deviation; otherwise, they were expressed as median (lower quartile–upper quartile). Categorical data were presented as counts. For comparative analysis of quantitative data between groups, a variance homogeneity test was first performed; if the *P*-value of the variance homogeneity test exceeded 0.05, a t-test was used; otherwise, a corrected t-test was used. Correlation analysis was performed for quantitative data, and r-values were calculated. For multivariate analysis, all influencing factors were initially included, and factors with no statistical significance were removed one by one in descending order of their LogWorth values. Subsequently, the impact of irregularity on the planning-related parameters was analyzed. After correlation analysis of statistical relationships between quantitative data, if scatter plots suggested an obvious linear correlation, linear fitting was performed for regression analysis to calculate R^2 and corresponding *P*-values. Statistical significance was set at $\alpha < 0.05$. Statistical analyses were conducted using JMP software (SAS Institute Inc., version 17.0).

Results

Participants

Given the availability of a substantial research data pool, we meticulously selected all data meeting the inclusion criteria from this pool to ensure that the case volume was at least tenfold the number required for the study. A total of 280 patients' treatment plans were included (Fig. 1).

Descriptive data

The median SS of the tumors was 0.85 (0.77–0.91); the VRS was 0.46 ± 0.16; the DCV was 0.22 (0.14–0.34). Multivariate analysis showed that lesion volume, ANCSRR grade, and age were statistically significant factors. Regarding the correlation between sphericity and other planning parameters, all parameters except PD and HI showed statistical significance. The DCV appeared to have a better statistical correlation with SS than VRS.

The relationship between patient-related factors and different

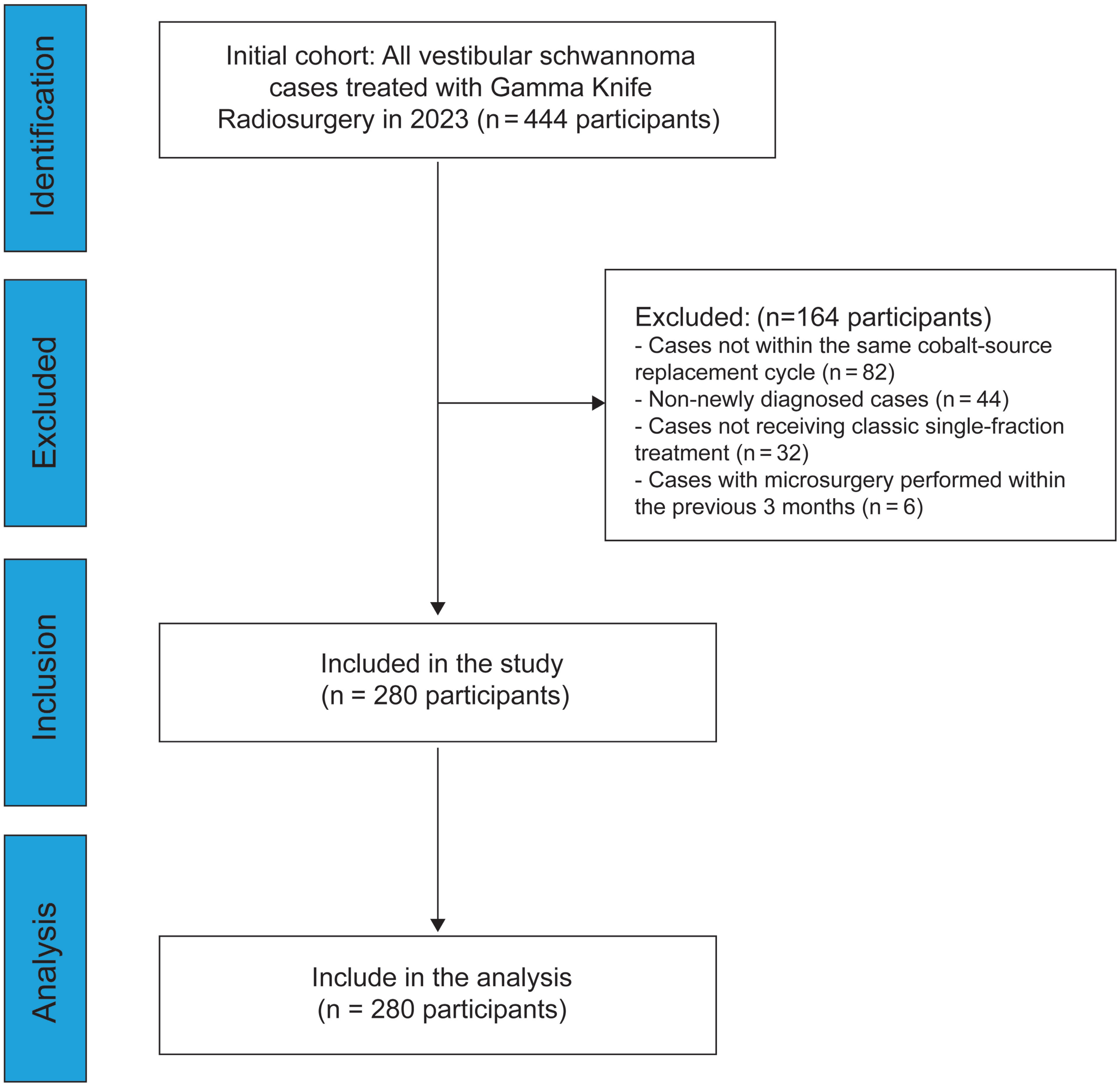

Fig. 1. The STROBE flow diagram of the study.

sphericity calculation methods is shown in Table 1. Further analysis of the relationship between surgical history and other factors revealed that surgical history was only statistically significantly related to patient age: the average age of the surgical group was 48.6 ± 1.6 years, while that of the non-surgical group was 56.3 ± 0.8 years ($P < 0.01$).

Regression model between the new and old indices

The impact of sphericity on Gamma Knife treatment plan parameters is shown in Table 2. Except for PD, CI, and HI, other parameters showed good consistency among SS, VRS, and DCV. In addition, the correlations between VRS and SS, and between DCV and SS, were analyzed by fitting, and it was found that: SS = 0.61 + 0.49 × VRS ($R^2 = 0.74$, $P < 0.01$); SS = 0.99 − 1.06 × DCV ($R^2 = 0.97$, $P < 0.01$) (Figs. 2 and 3).

Discussion

Currently, there are few studies on lesion irregularity and its relationship with Gamma Knife treatment.[7,9] Some of these studies focus on extracranial tumors rather than intracranial tumors.[10,11] Irregularity in these studies is measured by sphericity. Some studies have found that sphericity is related to therapeutic effect,[10,12] while others believe it is not.[9,11] Sphericity has also been used to compare dose distributions between different treatment plans and to study influencing factors of Gamma Knife radiosurgical treatment plan parameters.[7,9,13] The aforementioned studies predominantly utilized acoustic neuromas as research subjects, likely due to their well-defined boundaries and minimal adhesion to surrounding tissues, which facilitates unambiguous boundary identification.

For the measurement standard of morphological irregularity, all

Table 1. Factors that may affect sphericity

Factors	Mean or ratio	SS	SS	VRS	VRS	DCV	DCV
		R value	*P*-value	R value	*P*-value	R value	*P*-value
Age (years)	56 (46–64)	0.21	<0.01	0.15	0.01	−0.23	<0.01
Gender	Male:Female = 95:185	–	0.55	–	0.83	–	0.54
Surgical history	Yes:No = 63:217	–	0.01	–	0.06	–	<0.01
Hearing impairment	Yes:No = 251:29	–	0.84	–	0.44	–	0.59
Facial paralysis	Yes:No = 42:238	–	0.58	–	0.38	–	0.43
Vestibular symptoms	Yes:No = 75:205	–	0.07	–	0.11	–	0.08
GTV	2.60 (1.30–4.66)	0.30	<0.01	0.36	<0.01	−0.29	<0.01
ANCSRR	Grade 0:15; Grade 1:110; Grade 2:128; Grade 3:27	–	0.18	–	0.06	–	0.24

ANCSRR, acoustic neuroma consensus on systems for reporting results; DCV, coefficient of variance of diameters; GTV, gross target volume; SS, standard sphericity; VRS, volume ratio sphericity.

Table 2. Factors that may be affected by sphericity

Factors	Mean* or ratio	SS	SS	VRS	VRS	DCV	DCV
		R value	*P*-value	R value	*P*-value	R value	*P*-value
GI	2.82 (2.72–3.01)	−0.15	<0.01	−0.18	<0.01	0.18	<0.01
Sh	9 (6–13)	0.32	<0.01	0.34	<0.01	−0.31	<0.01
IDL	0.50±0.02	−0.22	<0.01	−0.17	<0.01	0.21	<0.01
PD	12.5±1.5	−0.10	0.10	−0.15	0.01	0.10	0.11
CI	0.99 (0.98–1.0)	0.15	0.01	0.06	0.33	−0.15	<0.01
SI	0.81 (0.74–0.86)	0.21	<0.01	0.47	<0.01	−0.21	<0.01
PCI	0.80 (0.73–0.85)	0.22	<0.01	0.48	<0.01	−0.23	<0.01
HI	0.60±0.07	0.11	0.07	0.22	<0.01	−0.10	0.11
Sh/PTV	2.6 (2.0–4.2)	−0.31	<0.01	−0.34	<0.01	0.32	<0.01

CI, coverage index; DCV, coefficient of variance of diameters; GI, gradient index; HI, homogeneity index; IDL, isodose line; PCI, Paddick's conformity index; PD, prescription dose; PTV, planning target volume; Sh, number of shots; SI, selectivity index; SS, standard sphericity; VRS, volume ratio sphericity.

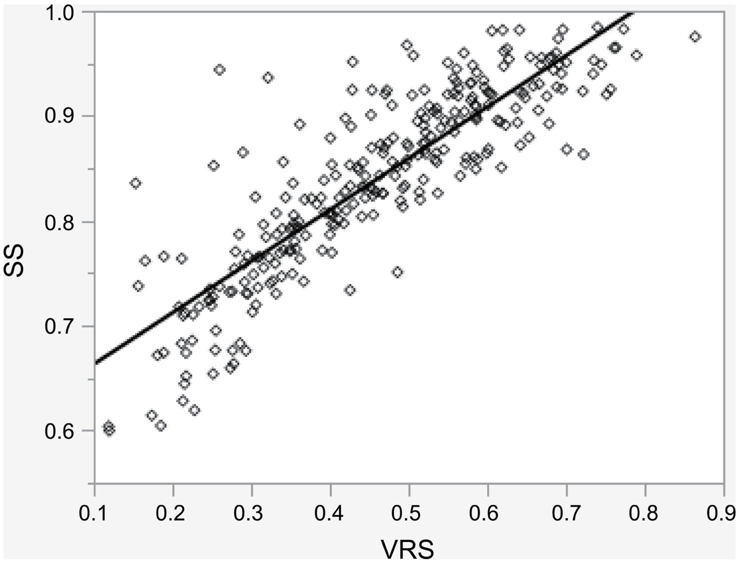

Fig. 2. The scatter plot of VRS and SS with the regression model line. The regression equation: SS = 0.61 + 0.49×VRS (R^2 = 0.74, P < 0.01). SS, standard sphericity; VRS, volume ratio sphericity.

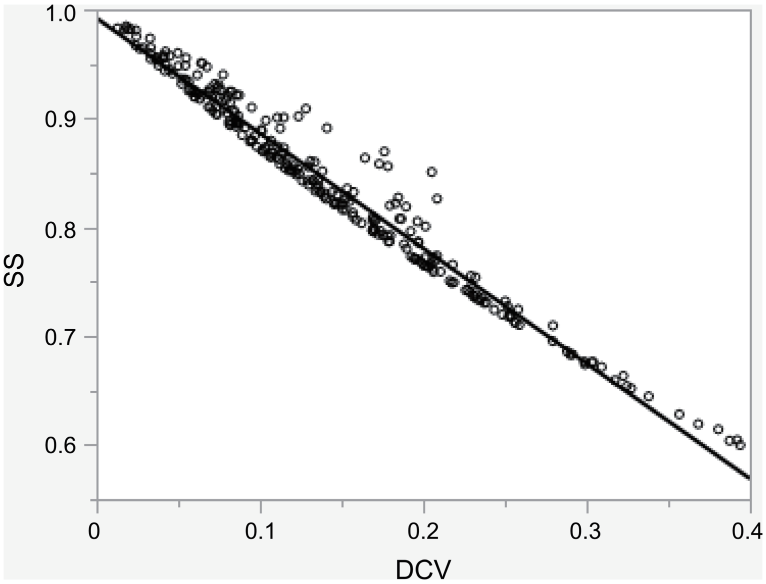

Fig. 3. The scatter plot of DCV and SS with the regression model line. The regression model can be quantified as SS = 0.99 − 1.06×DCV ($R^2 = 0.97$, $P < 0.01$). DCV, coefficient of variance of diameters; SS, standard sphericity.

the studies used sphericity.[7,9] However, there are various methods for calculating sphericity.[9] According to studies by experts in other fields, sphericity should be calculated as the surface area of the lesion's volume-equivalent sphere divided by the actual surface area of the lesion. This method was first proposed by geologist Wadell in his study on rock irregularity and later applied to other fields such as concrete particles.[14] Experts in other fields have also recognized the difficulty in directly calculating the surface area of particles; thus, Krumbein proposed a simpler alternative calculation method.[14] In medical morphology research, Wadell's original surface area–based definition is often referred to as the theoretical formulation of sphericity, although practical implementations vary across fields. However, unlike radiotherapy planning systems, the current version of GammaPlan still does not support surface area calculation. If the Wadell sphericity calculation is to be carried out, other software (*i.e.*, MATLAB) needs to be used, which is not convenient for clinical application. Therefore, Chagas Saraiva et al. improved this method by using volume to calculate sphericity, but this study did not verify the reliability and rationality of volume-based sphericity calculation and directly introduced this concept.[7] Since most current studies on intracranial and extracranial lesions still use the classic surface area calculation method, this study used a simplified approximate method for surface area–based sphericity calculation as the standard area method (two-dimensional method) and compared it with three-dimensional and one-dimensional (three diameters) methods. The study showed that Saraiva's method had a linear correlation with SS (Fig. 2) with a high R^2 value; however, it did not show more advantages compared with one-dimensional DCV. Although DCV was negatively correlated with SS, the R^2 value was close to 1, indicating an obvious linear relationship between the two, which deserves further verification through algorithmic derivation. In addition, Saraiva's study found that the average sphericity value calculated by their method was 0.69 (0.50–0.91), while this study found that the average sphericity of the treated lesions was 0.46 (95% confidence interval: 0.44–0.48), with no overlap with Saraiva's results. Differences may partly arise from variations in measurement methodology or tumor size distribution between cohorts. Since the number of cases in this study was much larger than that reported in Saraiva's study, the mean sphericity might not be as high as reported in Saraiva's study. According to the simplified surface area method, the average SS was 0.85, and the average DCV was 0.22, suggesting a small deviation from a spherical shape; however, based on Saraiva's method,[7] the sphericity value was only 0.46, indicating a large deviation from a spherical shape. Therefore, whether volume-based sphericity can be used as an indicator for measuring irregularity requires further research.

The basic assumption of this study is that the morphological irregularity of tumors is determined by various pre-treatment factors, which may affect the formulation of treatment plans. Univariate analysis of irregularity based on SS showed that age, surgical history, and GTV had statistical significance for sphericity; multivariate statistical analysis showed that age, ANCSRR grade, and GTV were statistically significant related factors. This may be because all postoperative patients included in this study were more than three months post-surgery, and residual tumors may tend to shrink due to changes in intracranial pressure; it may also be because patients with surgical history were relatively younger.[15] This study found that the average age of the surgical group was nearly eight years lower than that of the non-surgical group, which may be one of the reasons why surgery was not an influencing factor in multivariate analysis. The more definite factors are age and pre-treatment tumor volume/grade. Univariate analysis showed that the sphericity of tumors increased with patient age; although the linear relationship was weak, there was a positive correlation trend. This may be because older patients with vestibular schwannomas pay less attention to hearing loss, and the interval from onset to lesion detection may be longer. As the lesion grows sufficiently and slowly, its growth morphology becomes closer to a sphere; it may also be because as the volume of the extratubal segment tumor increases, the proportion of the intratubal segment tumor volume to the total volume becomes smaller. Moreover, according to follow-up studies on tumor growth, some tumors may not grow significantly over a long period,[15] which may cause older patients to pay more attention to the tumor. Different from Koos grading, ANCSRR is a semi-quantitative grading method,[8] considering both tumor distribution and size; most vestibular schwannomas, unlike metastases, are not regular spheres. Although there is a certain correlation between ANCSRR grade and GTV, they independently affect sphericity.

In terms of the impact of sphericity on treatment plans, all planning parameters except PD and HI showed statistically significant correlations with SS. PD is a relatively fixed parameter in vestibular schwannoma treatment with a limited range of variation; it may be more meaningful to study other tumors with a relatively larger range of PD variation.[16,17] HI is an important parameter in radiotherapy, but Gamma Knife treatment plans inherently have low IDL and cannot achieve the same HI level as radiotherapy. In clinical practice, since HI needs to be calculated manually using dose–volume histograms, and real-time HI information cannot be obtained in the planning system, planners usually do not pay special attention to HI. The method to improve dose uniformity in Gamma Knife treatment plans is usually to set some small-weight fine-tuning shots with small collimators evenly in the target area, which usually prolongs the treatment time. Clinically, this is rarely used unless for special reasons (such as increasing the local dose at the tumor base).

SS was positively correlated with shots, CI, SI, and PCI. This finding is partially consistent with the findings of previous studies by other scholars.[9] Since PCI is the product of CI and SI, the positive correlation of PCI is easy to understand. The higher the sphericity, the closer the lesion is to a sphere, and the dose distribution of a single shot in Gamma Knife is also close to a sphere, making it easier to formulate a plan with complete coverage, thus resulting in a higher CI; similarly, it may be easier to cover GTV in the plan, thus resulting in a higher SI. Theoretically, sphericity should be negatively correlated with the number of shots, i.e., the higher the sphericity, the closer the lesion is to a sphere, and fewer shots are needed. However, this study found a positive correlation between SS and shots, which can be explained by the relationship between Sh/PTV and SS. Due to tumor volume, covering a larger volume may require more shots, and covering unit PTV (per cm^3) can measure shot distribution well, excluding the impact of target volume. This study found a negative correlation between Sh/PTV and SS, i.e., the higher the sphericity, the fewer shots needed to cover unit PTV, which is consistent with clinical practice.

Sphericity was negatively correlated with GI, i.e., the higher the sphericity, the lower the GI. This may be because for nearly spherical tumors, there is no need to place shots at the tumor boundary to improve conformality during treatment planning, and only IDL or the weight of virtual shots need to be adjusted. Plans with lower GI may also have lower IDL, which has been confirmed in other related studies.[18] For example, this study found that reducing IDL from 70% to 30% can significantly reduce GI and improve dose distribution outside the prescription IDL. Since Gamma Knife customarily uses 50% IDL as the PD line, adjustments to IDL in clinical practice are mainly based on the consideration of complete tumor coverage rather than tumor shape. Therefore, the impact of SS on IDL is more likely mediated by GI, which needs further research to confirm.

This study has several limitations. First, data from other tumor types were not included in the analysis, limiting the generalizability of our findings. Second, owing to software limitations, the Wadell method was not utilized for sphericity calculation. Third, a multicenter collaborative study was not undertaken to maintain result consistency. Fourth, given that manual diameter measurements may introduce certain degrees of error, the authors and their research team are currently conducting further investigations into this issue. Finally, the study did not explore the potential relationship between tumor morphological irregularity and clinical follow-up outcomes.

Conclusions

DCV may serve as a simple indicator of tumor shape irregularity. Incorporating morphological irregularity into future Gamma Knife planning evaluation parameters may be necessary to further optimize treatment planning. The irregularity of vestibular schwannomas may be affected by lesion volume, ANCSRR grade, and age, which may be connected to surgical choices; sphericity has direct or indirect impacts on other planning parameters. The rationality of using volume ratio as a substitute method for sphericity calculation needs further verification, while the substitute method using the DCV for sphericity calculation has good consistency with the classic calculation method.

Acknowledgments

This study employed an AI-based translation tool developed by DeepSeek to translate the original Chinese text. The scientific content and manuscript preparation were performed by the authors.

Funding

None.

Conflict of interest

HW has been an editorial board member of *Neurosurgical Subspecialties* since November 2024 and was not involved in the peer review or editorial decision-making process for this submission. All authors declare that they have no other competing interests to report.

Author contributions

Study concept and design (HW), acquisition of data (JC), analysis and interpretation of data (HW), drafting of the manuscript (HW), critical revision of the manuscript for important intellectual content (HW, JC), administrative, technical, or material support (JC), and study supervision (HW). Both authors have made significant contributions to this study and have approved the final manuscript.

Ethical statement

This study was carried out in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments. The protocol was approved by the Ethics Committee of Shanghai Gamma Hospital (Approval No. 2025-011-02). The requirement for individual informed consent was waived due to the retrospective nature of the analysis utilizing anonymized data.

Data sharing statement

The dataset used in support of the findings of this study is available from the corresponding author.

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