

Volumetric measurement of intracranial meningiomas: a comparison between linear, planimetric, and machine learning with multiparametric voxel-based morphometry methods

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Abstract

Purpose

To compare the accuracy of three volumetric methods in the radiological assessment of meningiomas: linear (ABC/2), planimetric, and multiparametric machine learning-based semiautomated voxel-based morphometry (VBM), and to investigate the relevance of tumor shape in volumetric error.

Methods

Retrospective imaging database analysis at the authors' institutions. We included patients with a confirmed diagnosis of meningioma and a volumetric acquired cranial magnetic resonance imaging. After tumor segmentation, images underwent automated computation of shape properties such as sphericity, roundness, flatness, and elongation.

Results

Sixty-nine patients (85 tumors) were included. Tumor volumes were significantly different using linear (13.82 cm³ [range: 0.13–163.74 cm³]), planimetric (11.66 cm³ [range: 0.17–196.2 cm³]) and VBM methods (10.24 cm³ [range: 0.17–190.32 cm³]) ($p < 0.001$). Median volume and percentage errors between the planimetric and linear methods and the VBM method were 1.08 cm³ and 11.61%, and 0.23 cm³ and 5.5%, respectively. Planimetry and linear methods overestimated the actual volume in 79% and 63% of the patients, respectively. Correlation studies showed excellent reliability and volumetric agreement between manual- and computer-based methods. Larger and flatter tumors had greater accuracy on planimetry, whereas less rounded tumors contributed negatively to the accuracy of the linear method.

Conclusion

Semiautomated VBM volumetry for meningiomas is not influenced by tumor shape properties, whereas planimetry and linear methods tend to overestimate tumor volume. Furthermore, it is necessary to consider tumor roundness prior to linear measurement so as to choose the most appropriate method for each patient on an individual basis.

Introduction

Meningiomas are the most common intracranial and central nervous system (CNS) tumors, which are mostly slow-growing, benign tumors that can be cured with complete surgical resection [1]. Symptoms are usually nonspecific and may result from neurovascular structure compression and brain tissue displacement [2].

Monitoring the growth of meningiomas has important therapeutic and prognostic implications since it helps in the decision-making for clinical or surgical management [3], suggests higher histological grades in rapidly-growing tumors, and provides image-based criteria for disease progression [4–6].

In clinical practice, the most commonly used method for volumetric measurement of intracranial lesions is the modified ellipsoid formula ($ABC/2$), also known as the linear method, where A, B, and C correspond to the largest perpendicular diameters of the lesion measured on imaging examinations [7]. Comparative analysis between different volumetric methods for intracerebral hematomas indicated that the linear method tends to overestimate the hematoma volume in 45% of patients, much due to the irregular shape of these lesions [7].

Concerning the volumetric measurement of meningiomas, the literature is relatively sparse. Previous studies indicate that, although volumetry has a positive correlation between the linear (manual) and the planimetric (edge-contouring) methods, volumetric estimation based on the linear method underestimates tumor growth [3, 8, 9]. Voxel-based morphometry (VBM) is an otherwise powerful computational tool to quantify the volume of three-dimensional structures. VBM has the assumption to substitute manually-based volumetry [10]. Although there are several VBM modalities, reliable tumor volume quantification can be achieved using semiautomated tissue classification, in which tissues (tumor, white matter, gray matter, cerebrospinal fluid, bone) are classified by the user through manual tissue sampling.

Since meningiomas exhibit different growth rates and irregular shapes, high volume accuracy is essential in clinical practice [6]. Therefore, we aimed to compare the accuracy of the following volumetric methods: linear, planimetric, and multiparametric machine learning-based semiautomated VBM. We hypothesized that meningioma shape features are related to the error obtained among volumetric measurement techniques.

Methods

Study Design

Institutional review board (IRB) approval was obtained for a retrospective analysis of a prospectively collected database at the University of Indiana, USA (between November 2010 and April 2021 [IRB #10174]) and Fluminense Federal University, Brazil (between January 2012 and April 2019 [IRB CAAE 03206718.5.0000.5243/2019]). No patient consent was required according to the study design.

Patient population

Patients were selected according to the following inclusion criteria: (a) tumors diagnosed as meningiomas by histological examination, and (b) patients with cranial magnetic resonance imaging (MRI) with a volumetric acquisition. Patients with inadequate or incomplete imaging for one of the volumetric methods or with extracranial meningioma extension were excluded. T1-weighted, T1-weighted

with contrast enhancement (T1CE), T2-weighted, and FLAIR (fluid-attenuated inversion recovery) images were retrieved for this study. Tumor characteristics (number and location) were collected from all patients. Demographic variables were not recorded for this evaluation.

Linear tumor volume estimation

Three-dimensional T1CE images were reconstructed in axial, sagittal, and coronal planes, and the lesions were measured along their largest diameter on each plane on RadiAnt DICOM Viewer (Medixant, New York) (Fig. 1a). The volume of each tumor was estimated by the simplified ellipsoid equation ($ABC/2$).

Planimetric tumor volume measurement

T1CE images were used for layer-by-layer tumor contouring on OsiriX DICOM Viewer (Pixmeo, Switzerland). The software automatically estimated the volume by superposing the contoured layers and rendering the tumor spatially (Fig. 1b).

Voxel-based morphometry of tumors

MRI volumes for T1-weighted, T1CE, T2-weighted, and FLAIR images were preprocessed with bias-field inhomogeneities correction and denoising using Advanced Normalization Tools (ANTs) [11]. Subjects' images underwent skull stripping and linear coregistration using the FSL tool *flirt* (Analysis Group, FMRIB, Oxford, UK). Tumor segmentation was carried out in the ITK-Snap with a multiparametric machine learning-based semiautomated method using tissue classification, distinguishing the tumor from the surrounding tissue types based on the multiple acquisition sequences for each segmentation session in the software (Fig. 1c) [12]. Tumors were classified as small or large using the threshold of 10 cm³.

Tumor shape features

The previously generated tumor segmentation files were imported to 3D Slicer (version 4.13.0; <http://www.slicer.org>) for automated computation of shape properties such as roundness, flatness, and elongation using the Segment Statistics tool. Sphericity (Ψ), which is defined as the ratio of the surface area of a sphere having the same volume as the tumor over the tumor surface area, can be derived from the variables flatness (p) and elongation (q), as in Eq. 1 [13].

(Eq. 1)

$$\Psi = \frac{12.8 \left(\sqrt[3]{p^2 q} \right)}{1 + p(1 + q) + 6(\sqrt{1 + p^2(1 + q^2)})}$$

Statistical analyses

SPSS Statistics for Windows (Version 26.0. Armonk, NY: IBM Corp.) was used for statistical analyses and figure plotting. The Shapiro-Wilk test was used to determine the normality of continuous variables. Tumor characteristics were analyzed using descriptive statistics. Friedman test was performed to compare median volumes estimated by the three methods, with posthoc analysis to compare the methods pair by pair. A two-way random-effect intraclass correlation coefficient (ICC) analysis was run to calculate the level of agreement between each method. An ICC value of 0 indicates a lack of reliability, and a value of 1 indicates perfect reliability. The degree of interrater intraclass correlation is classified as the following: poor (0–0.2), fair (0.2–0.4), moderate (0.4–0.6), good (0.6–0.8), and excellent (0.8–1). The error indices for the linear and planimetric methods were calculated using VBM as the reference standard, and we used a multifactorial general linear model to investigate whether tumor shape features could explain the error magnitude for each method. Receiver operating characteristic (ROC) curve analyses were performed to compare the diagnostic performance of the linear method based on tumor geometry.

Results

A total of 129 patients were eligible for this study. After analysis of the images, 59 patients were excluded for not having imaging scans with the necessary acquisition sequences and slice thickness for VBM, and one for having an extracranial extension of the meningioma, resulting in a sample of 69 patients affected by 85 tumors.

Tumors were mostly located in the frontal lobe, on the right side, and 87% of the patients were affected by only one tumor. The epidemiological characteristics of the tumors are summarized in Table 1.

Table 1
Study population characteristics.*

Number of patients	69
Number of tumors	85
Tumor per patient, n (%)	
1	60 (86.9%)
2	6 (8.8%)
3 or more	3 (4.3%)
Tumor location, n (%)	
<i>Frontal</i>	34 (40%)
<i>Parietal</i>	24 (28.2%)
<i>Occipital</i>	1 (1.2%)
<i>Temporal</i>	4 (4.7%)
<i>Skull base</i>	12 (14.1%)
<i>Infratentorial</i>	10 (11.8%)
Tumor side, n (%)	
<i>Left</i>	34 (40%)
<i>Right</i>	40 (47%)
<i>Midline</i>	11 (13%)
Roundness	0.8 (0.45–0.96)
Sphericity	0.92 (0.73–0.95)
Flatness	0.77 (0.36–0.99)
Elongation	0.83 (0.35–0.96)
* n = number	

The three measurement methods provide significantly different results

Shapiro-Wilk test for the continuous variables analyzed showed a significant deviation from normality (all $P < 0.05$). Tumor volumes were calculated using linear (13.82 cm³ [range: 0.13–163.74 cm³], planimetric (11.66 cm³ [range: 0.17–196.2 cm³]) and VBM methods (10.24 cm³ [range: 0.17–190.32 cm³]). Three-sample Friedman test showed a statistically significant difference between methods ($P < 0.001$).

Wilcoxon signed-rank posthoc analysis was conducted with a Bonferroni correction for multiple comparisons, resulting in a significance level set at $P < 0.017$. Significant difference was found between planimetric and VBM ($P < 0.001$), linear and VBM ($P = 0.015$), and planimetric and linear methods ($P = 0.005$).

Linear and planimetric methods have overall high reliability with VBM

Intraclass correlation coefficient analysis demonstrated excellent overall reliability between linear and VBM methods (ICC 0.987, 95% CI [0.980–0.992]). Similarly, the agreement between the planimetric and VBM methods was also excellent (ICC 0.996, 95% CI [0.988–0.998]). Stratified ICC analysis revealed preserved agreement between the linear and VBM methods for small (ICC 0.912, 95% CI [0.815–0.957]) and large tumors (ICC 0.955, 95% CI [0.919–0.975]). Agreement was also preserved between planimetry and VBM for small (ICC 0.912, 95% CI [0.802–0.957]) and large tumors (ICC 0.987, 95% CI [0.894–0.996]).

Linear and planimetric methods overestimate the actual volume

Median volume error and percentage error between the planimetric and VBM methods were 1.08 cm³ (range: -3.68–16.71 cm³) and 11.61% (range: -62% – 234%), respectively. Whereas the median volume error and percentage error between the linear and VBM methods were 0.23 cm³ (range: -31.91–36.77 cm³) and 5.5% (range: -54% – 154%), respectively (Table 2). Planimetry and linear methods overestimated the actual value in 79% and 63% of the patients, respectively. Although greater median volume was found for ABC/2 compared to planimetry, overall, the latter yielded greater volume in 70% of the cases.

In terms of error magnitude, without taking into consideration whether there was an overestimation or underestimation of tumor volume, the median absolute error for the planimetric method was 14.14% (range, 0.46–233.88%), while the median absolute error for the linear method was 13.04% (range, 0.05–153.93%).

Table 2
Volumetric differences between the linear, planimetric, and semi-automated methods.*

		Methods		
	VBM	Planimetric	Linear	<i>P</i> -value
Volume (cm ³), median (range)	10.24 (0.17-190.32)	11.66 (0.17–196.2)	13.82 (0.13–163.74)	< 0.001
Error (cm ³), median (range)	-	1.08 (-3.68–16.71)	0.23 (-31.91–36.77)	0.005
Error (%), median (range)	-	11.61 (-62–234)	5.5 (-54–154)	< 0.001
Absolute error (%), median (range)	-	14.14 (0.46–233.88)	13.04 (0.05–153.93)	0.291

* Error (cm³) is the difference between the volume estimated by the planimetric or linear methods in cm³, taking VBM as the reference. Error (%) is the difference between the VBM and the other two methods in percentage. Absolute error is the same difference, without taking into consideration if the error was positive or negative. VBM: voxel-based morphometry.

Proportional error is greater in smaller tumors in planimetry but not in ABC/2

Small tumors (< 10 cm³) corresponded to 46.9% (n = 38) of our sample. Absolute measurement error was associated with tumor volume for both methods (planimetric, $\rho = .752$, $P < .001$; linear, $\rho = .738$, $P < .001$), that is, greater tumors tend to have greater absolute errors. Nevertheless, absolute percentage volume difference only held a negative correlation with tumor volume in planimetry ($\rho = -.577$, $P < .001$), meaning that smaller tumors are more prone to a greater percentage error through this technique. This association was not present in ABC/2 measurements.

Meningioma shape features

Tumors generally presented with high median roundness (0.80; range, 0.45–0.96) and high median sphericity (0.92; range, 0.73–0.95). Tumors varied greatly in flatness (median 0.77; range, 0.36–0.99) and elongation (median 0.83; range, 0.35–0.96). Convexity meningiomas were associated with high sphericity ($P = .032$), and smaller tumors tended to be more rounded ($\rho = -.309$, $P = .004$).

Tumor shape influences volumetric measurements

A multifactorial general linear model was developed to investigate the influence of tumor shape features (roundness, sphericity, flatness, and elongation) on the error observed in volume estimation. For the planimetric method, flatness showed an inverse effect on the measurement error ($F = 4.46$, $P = .038$),

meaning that the flatter the tumor, the lower the percentage error in volume estimation (Fig. 2a). A second multifactorial general linear model was run for the linear method with the same variables. In this model, roundness affected the measurement error ($F = 6.67$, $P = .012$), with less rounded tumors having greater linear error indices (Fig. 2b).

Linear measurement is suitable for tumors with roundness greater than 0.6

Given that the linear method is currently the most used in clinical practice and knowing that tumor roundness influences the error in linear measurements, we performed a series of ROC curve analyses to determine the best cutoff point for tumor roundness to reach minimal error. Threshold values were determined according to the distribution of roundness, from 0.50 to 0.85 (Fig. 2c). The best performance was obtained with a threshold greater than 0.60 ($AUC = 0.849$, $P = 0.001$). The error in linear measurement analysis was indeed higher in tumors with roundness smaller than 0.60 ($P = .001$) (Fig. 3).

Discussion

Key Results

Using a large population base from two institutions with homogeneous tumors, i.e., without bone hyperostosis or extracranial extension, our results indicated that both manual methods (linear and planimetric) overestimated tumor volume, being planimetry the most susceptible to this extrapolation, on the order of 12%. Median error (in cm^3) was small, while the absolute mean error (%) was expressive, considering the current standards for diagnosing progressing brain tumors [14, 15]. Large and flatter tumors had greater accuracy on planimetry, whereas less rounded tumors contributed negatively to the accuracy of the linear method.

Interpretation and generalizability

Compared to VBM, the ABC/2 formula overestimated volumes in 63% of cases. Similarly, in a study on the natural history of petroclival meningiomas, the volume estimated by the linear method was on average 1.6 times larger than that estimated using ROI and threshold-based VBM segmentation. The authors suggested that the irregular shape of meningiomas, which often differs from the shape of an ellipsoid, a characteristic necessary for accurate estimation by the ABC/2 formula, would be responsible for the overestimation [16].

Semiautomated segmentation is considered more reliable than other volumetric methods to assess tumor growth since meningiomas may present areas with higher growth rates than the rest of the tumor, resulting in an irregular shape [6]. Besides, the volumetric criterion of tumor progression, given by the volume calculated using semiautomated segmentation, strongly correlates with overall survival compared to 1D and 2D volumetric approaches, although the difference was modest [6].

Although error percentage had no association with linear volume estimation, smaller tumors exhibited greater error indices in planimetry. This is partly due to surrounding voxels included when manually contouring the tumor edges, making small lesions proportionally more affected by the inclusion of nearby tissue. This effect is corrected for in multiparametric segmentation. In T1CE images, the interface between the tumor and surrounding structures may become slightly broader to the naked eye due to signal interpolation on the DICOM viewer software. For this reason, signal intensity fades at the tumor-parenchyma interface, making it difficult to define the limits precisely. Multiparametric VBM is not susceptible to this pitfall for two main reasons: (1) segmentation is based on voxel numerical signal intensity, eliminating the susceptibility to visual artifacts, such as blurring, and (2) tissue segmentation is based on the voxel-by-voxel signal intensity from multiple acquisition sequences, removing the hypersignal bias from a T1CE-only border definition.

In our cohort, planimetry revealed larger volume than linear measurements in 70% of cases. Contrarily, a previous study reported a larger volume in ABC/2 compared to planimetry in 76% of cases [3]. Tumor shape heterogeneities may also explain such discrepancies between samples since ABC/2 does not account for tumor surface irregularities.

Linear measurement error correlated only with tumor roundness, regardless of tumor size. In linear estimations, roundness increased measurement accuracy because the method used to determine tumor volume is based on the assumption of tumor sphericity, intrinsic to the ABC/2 formula. Thus, the closer to a sphere or ellipsoid shape, the greater the estimation accuracy. In this regard, we have found that roundness needs to be greater than 0.6 for an adequate assessment using the linear method. However, deciphering the roundness in clinical practice may be a challenge. For this purpose, Krumbein's chart for visual determination of roundness might be used to predetermine eligible tumors (Fig. 3) [17]. With regards to flatness, it was shown to reduce planimetric error. When manually drawing along the tumor edges, this effect may also be explained by the overinclusion of surrounding voxels. Considering tumor volume as the sum of each layer's ROI, flat tumors end up including fewer surrounding voxels as fewer layers are drawn during segmentation.

From a clinical standpoint, meningioma growth rate is crucial for therapeutic decisions. Therefore, a practical and accurate volume measurement method is valuable for neurosurgeons and neuro-oncologists. Chang et al. [8] identified that the modified ellipsoid formula produced lower tumor growth rates, detecting significant tumor growth in 12 of 29 patients. In comparison, the planimetric method detected 19 patients with significant growth, meaning that planimetry is more sensitive than ABC/2 in detecting tumor growth for follow-up purposes. Notably, the planimetric method is much more time-consuming than the ABC/2 method and can exhibit considerable inter-rater variability due to the difficulty in distinguishing tumor margins with bone involvement and skull base tumors.[6, 18, 19] In addition to the volume measurement methods cited above, fully automated volumetric models for meningioma segmentation have recently been developed, with high accuracy and reliability [18, 19].

The best volumetric assessment for meningiomas is yet to be defined. Response assessment criteria for meningioma are still in progress by the Response Assessment in Neuro-oncology (RANO) committee [20]. However, considering previous RANO criteria for progressive high-grade gliomas [15] and brain metastases [14], which used bi- and unidimensional measurements, respectively, the role of our tridimensional findings in terms of the median absolute error obtained by manually-based methods (up to 14%) is highly relevant and should be included in the discussion. Even though its use in clinical practice is not yet widespread, VBM has become more accessible and more straightforward by using MRI straight from a hospital Picture Archiving and Communication System (PACS).

Planimetry is time-consuming, especially for the layer-by-layer contouring of large and irregular tumors. On the other hand, linear measurements can be done in minutes, but it ends up oversimplifying tumors' sometimes complex and irregular shape. Furthermore, considering that meningiomas cause symptoms by compression of nearby neurovascular structures, and that larger tumors tend to be less rounded, it is essential to ponder the advantages and limitations of this method. VBM merges the benefits of a relatively fast segmentation, taking about 5–10 minutes by tumor, and a machine learning-aided accurate measurement. In this sense, considering the available options and choosing the most adequate method have become the two most important tasks when dealing with patients with meningiomas, especially when the growth rate needs to be closely monitored.

Limitations

First, the retrospective study design is not bias-free. Second, the absence of demographic information, especially clinical and histopathological, does not allow for a correlation between tumor growth rate and shape with its aggressiveness profile and behavior. Third, the lack of follow-up of these patients does not allow us to infer the clinical impact of the volumetric overestimation of the linear and planimetric methods. Fourth, methodological issues can interfere with VBM results, as demonstrated by the exclusion of 59 of our eligible patients because of the nonstandardized protocol for MRI acquisition. Despite these limitations, our study allows for greater generalizability of the results because of the large population base used, in addition to the inclusion of a large proportion of infratentorial and skull-base tumors. Additionally, our results shed light on the basic tumor shape properties that enable higher accuracy across the volumetric methods.

Conclusions

Correlation studies showed excellent volumetric agreement between manual- and computer-based methods. Multiparametric machine learning-based semiautomated VBM volumetry for meningiomas is highly accurate and produces reliable results that are not influenced by tumor shape compared to manual methods. Large and flatter tumors had greater accuracy on planimetry, whereas less rounded tumors contributed negatively to the accuracy of the linear method. Our results should be considered for response assessment criteria for meningioma progression and detection of tumor growth on follow-up for incidental meningiomas due to the relevant median absolute error in manual volumetric measurement

methods. VBM could replace manually-based volumetric assessment in the future, especially for research purposes, and could have a complementary role for clinical purposes.

Declarations

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Author contributions: Study conception and design were performed by Jonadab dos Santos Silva, Lázaro de Lima, Cristopher D. Wilson, Marcus André Acioly, and Aaron Cohen-Gadol. Material preparation and data collection were performed by Jonadab dos Santos Silva, Lázaro de Lima, Cristopher D. Wilson, Luke McVeigh, Joseph Acchiardo, and Marcus André Acioly. Data analysis was performed by Jonadab dos Santos Silva, Cláudia Abib Schreiner, Lázaro de Lima, and Carlos Eduardo Pinheiro Leal Brigido. Statistical analyses were performed by Jonadab dos Santos Silva, Cláudia Abib Schreiner, and Marcus André Acioly. The first draft of the manuscript was written by Jonadab dos Santos Silva and Cláudia Abib Schreiner, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data Availability: The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figures

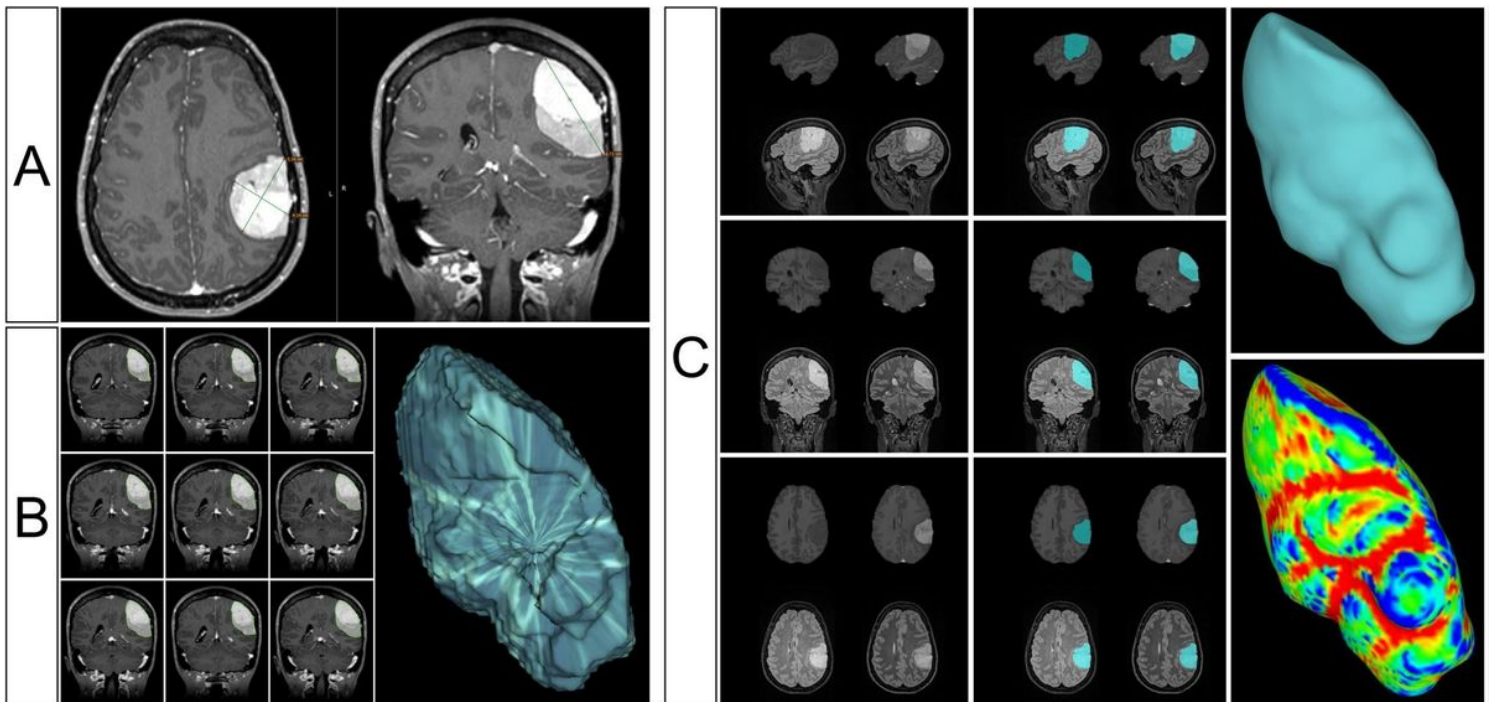


Figure 1

(A) T1-weighted gadolinium enhanced images in the axial and coronal planes demonstrating how to measure A, B, and C diameters. “A” is the longest diameter in the axial plane, while “B” is the longest perpendicular dimension in the same axial section. “C” is the longest dimension in the coronal plane. **(B)** Sequential T1-weighted gadolinium enhanced images demonstrating tumor measurement using the planimetric method, with a spatial rendering of tumor shape. **(C)** Multiparametric MRI of a convexity meningioma before (first column) and after (second column) semiautomated segmentation with the VBM method. Tumor spatial rendering could be obtained for shape (blue) and depth complexity (color-coded).

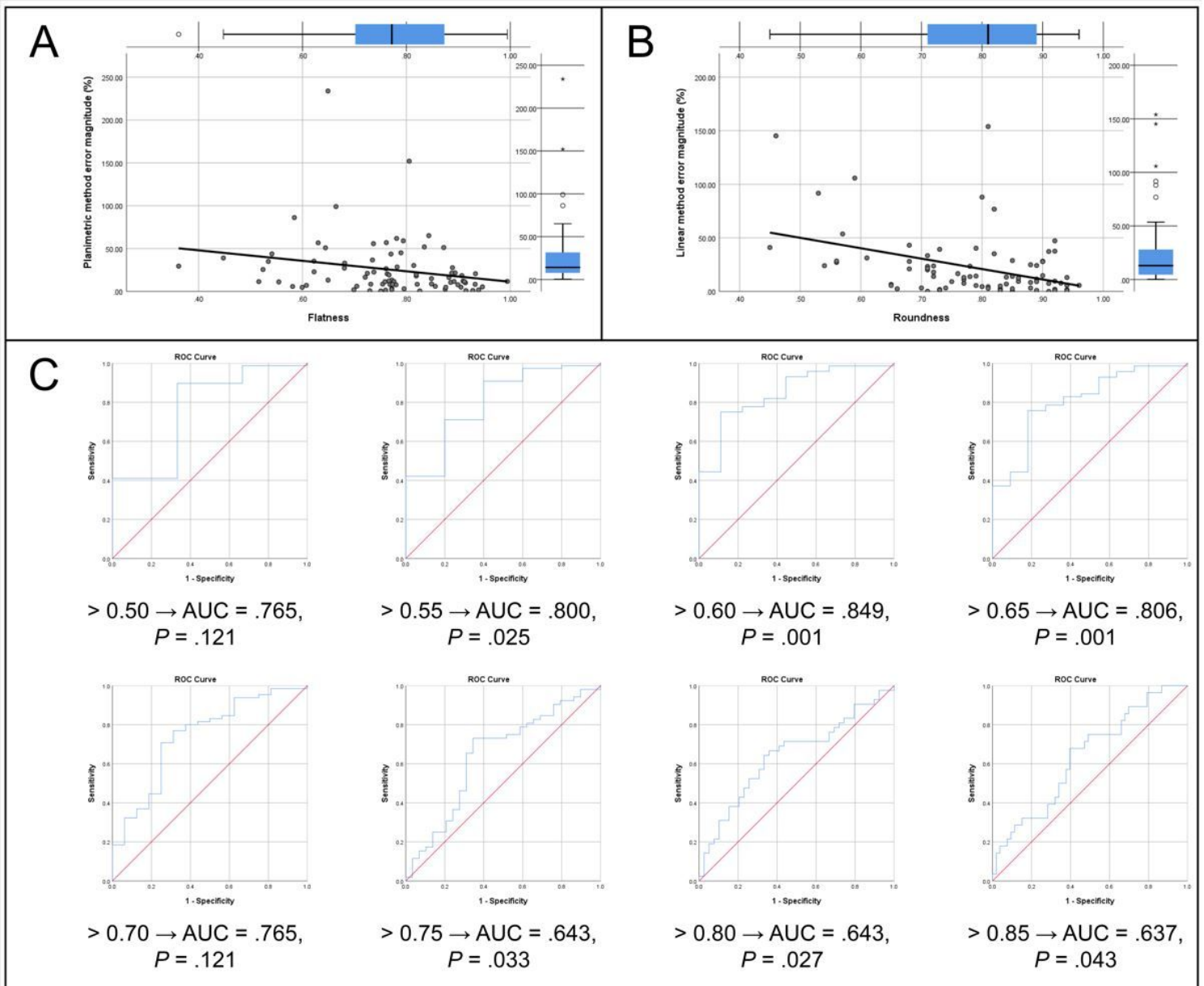


Figure 2

Plotting tumor shape influence on volumetric measurements (A and B). In **A**, flatter tumors were associated with lower proportional errors in the planimetric method, while in **B**, rounded tumors indicated lower proportional errors in the linear method. **(C)** Illustrations of the distribution of curves to classify the error in the volumetric assessment of the linear method by tumor roundness. The best overall performance was obtained for the > 0.60 threshold. AUC – area under the curve.

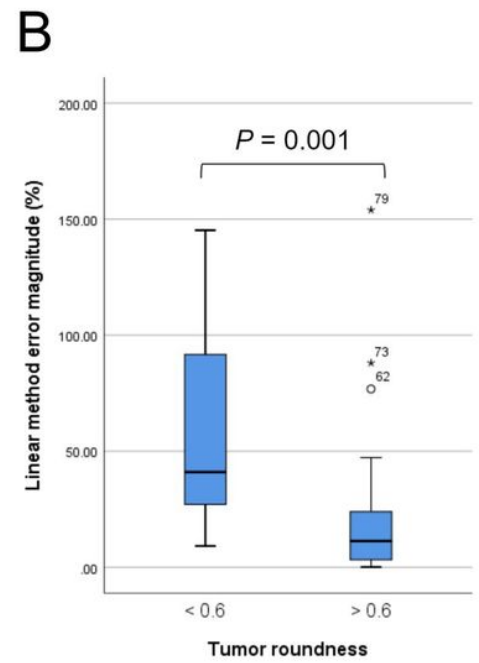
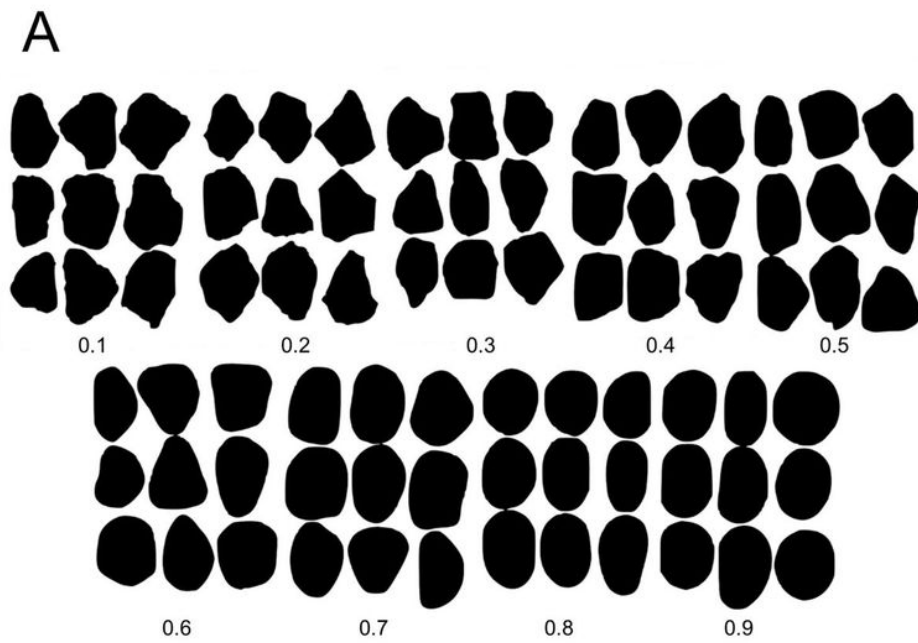


Figure 3

(A) Krumbein's chart for visual determination of roundness, adapted from Krumbein [17]. **(B)** Boxplot chart representing the difference in error between tumors classified according to a roundness threshold of 0.6.