Original Article

Reliability of the Size Evaluation Method for Meningiomas: Maximum Diameter, ABC/2 Formula, and Planimetry Method

Yukitomo Ishi MD, nekozamurai@me.com

Shunsuke Terasaka MD, terasas@med.hokudai.ac.jp

Shigeru Yamaguchi MD, syamama1945@gmail.com

Michiharu Yoshida MD, michi511leo@yahoo.co.jp

Shogo Endo MD, du_en03_05@yahoo.co.jp

Hiroyuki Kobayashi MD, hiro-ko@med.hokudai.ac.jp

Kiyohiro Houkin MD, houkin@med.hokudai.ac.jp

Department of Neurosurgery, Hokkaido University Graduate School of Medicine

Corresponding Author:

Shigeru Yamaguchi MD

Department of Neurosurgery,

Hokkaido University Graduate School of Medicine,

North 15 West 7, Kita-ku, Sapporo 060-8638, Japan

Phone: (+81)11-706-5987

Fax: (+81)11-708-7737

syamama1945@gmail.com

Key words: meningioma, maximum diameter, ABC/2 formula, planimetry method, volumetric analysis

Abbreviations in this paper: ANOVA = analysis of variance; CISS = constructive interference steady state; FF = form factor; ICH = intracerebral hemorrhage; MRI = magnetic resonance imaging; Gd-T1WI = gadolinium-enhanced T1 weighted image

Abstract

BACKGROUND: To evaluate the accuracy of tumor size by the maximum diameter, ABC/2 formula, and planimetry method using thick and thin slice magnetic resonance imaging (MRI).

METHODS: Maximum diameter and tumor volume calculated using the ABC/2 formula (V1) and planimetry method with thick slice (V2) and thin slice (V3) MRI were examined in 83 meningiomas. Form factor (FF) analysis was performed to assess irregularity of the tumor. V3 values were considered as real tumor volumes. The accuracy of V1 and V2 was evaluated using ratio and difference from V3. Meningiomas were categorized by tumor locations: skull base (anterior, middle, and posterior) and non-skull base (calvarium and other sites).

RESULTS: Correlation between maximum diameter and V3 was statistically significant (r = 0.91), but the error was significant in tumors with longer maximum diameters. Correlation between V1 and V3 was significant (r = 0.97). However, V1 tended to be larger in middle skull base meningiomas or in tumors with low FF values (R^2 = 0.21). V2 represented relatively accurate

volumes in both groups, except in the case of small size meningiomas. When tumors presented within three fractions in thick slice MRI, the ratio of V2 to V3 showed significant variability.

CONCLUSIONS: Using the ABC/2 formula, the volume of meningiomas in the middle skull base or those with low FF value might be calculated larger than the real tumor volume. The planimetry method with thick slice MRI presented relatively accurate volumes if the tumor was fractionated in more than four slices.

(248/250)

Introduction

The tumor size of meningiomas is an important issue in clinical practice. The size of the meningioma as well as the clinical symptoms are significant factors to discuss the treatment strategy (1), natural history (2-15), postoperative course, or growth control after radiosurgery (16-19). However, in previous studies, the method used to evaluate tumor size has not been standardized.

Among the several methods that have been previously used to evaluate the size of meningiomas by computed tomography (CT) or magnetic resonance imaging (MRI), the maximum diameter has been used to analyze the natural history of meningiomas (5-9). It is the simplest procedure; however, it is uncertain whether the maximum diameter accurately reflects the real volume of the tumor. The ABC/2 formula is frequently used to calculate the volume of intracerebral hemorrhage (ICH) because of its simplicity and quickness; however, the accuracy of the ABC/2 formula has been previously debated (20-24). Although some studies have used the ABC/2 formula (2,25,26) or the original ellipsoid volume (10,19,27) to measure the volume of intracranial tumors, including meningiomas, few studies have evaluated the accuracy of ABC/2 formula for intracranial

tumors. The planimetry method presents a more approximate volume for the real tumor and has been applied in many studies (3,4,11-15); however, this method is more cumbersome than the ABC/2 method. In addition, the thickness of MRI used to calculate tumor volume differs between each investigator. The aim of this study was to evaluate the accuracy of maximum diameter and volume calculated by the ABC/2 formula and the planimetry method using thick slice MRI compared with calculations using thin slice MRI in order to clarify the optimal method for evaluating the size of meningiomas.

Materials and Methods

Patient population and imaging

This study included meningioma patients who underwent tumor resection surgery and were pathologically diagnosed as meningioma in Hokkaido University Hospital from 2002 to 2015. Patients who underwent following preoperative MRI in 2 different sequences were included in this study and were radiologically analyzed: conventional thick slice (4.0–5.0 mm thickness and 0.5–2.0 mm slice space) gadolinium-enhanced T1 weighted imaging (Gd-T1WI) and thin slice (0.9–1.5 mm thickness) 3-dimensional constructive interference steady state (CISS) imaging. According to the tumor location, the meningiomas were divided into skull base meningiomas and non-skull base meningiomas. Skull base meningiomas included the anterior skull base, middle skull base, and posterior skull base. Non-skull base meningiomas included the calvarium and other sites. Anterior skull base meningiomas included olfactory groove, planum sphenoidale, and tuberculum sellae meningiomas. Middle skull base meningiomas included sphenoid ridge, clinoid, cavernous sinus, and middle fossa meningiomas. Posterior skull base meningiomas included petrosal, clival, and petroclival meningiomas. Calvarium meningiomas included cerebral convexity, cerebellar convexity, and parasagittal meningiomas. Meningiomas in other sites included falx, tentorial, or

lateral ventricle meningiomas that had no or lesser attachment to the skull. MRIs of the patients included in this study were retrospectively analyzed by the following procedures using the Osirix software package (Pixmeo, Geneva, Switzerland). The tumors with massive perifocal edema were excluded in this study, because the real tumor volume could not be evaluated for the obscure boundary line of tumor on CISS imaging. The patients with multiple meningiomas and obvious bone infiltration of tumors were also excluded. Bone CT was used to distinguish tumors from hyperosteosis, wherever required.

Form factor analysis

To approximately evaluate the configuration of tumor, form factor (FF) analysis was performed on each tumor. Among the CISS images that contained attachment with the dura mater, the maximum area and perimeter at the same slice were measured. FF was calculated as $(4\pi \times \text{area})/\text{perimeter}^2$, where FF = 1 indicates a perfect circle and FF = 0 indicates a straight line (28). For meningiomas without attachment to the dura mater (i.e., intraventricular meningiomas), FF was calculated at the slice with the maximum area among all the slices.

Measurement of maximum diameter and calculation of tumor volume

The maximum diameter of the tumor was measured among axial, coronal, and sagittal views of the CISS imaging. For calculating tumor volume, 3 methods were applied for each tumor. V1 was defined as the volume calculated by the ABC/2 method using axial images on thick slice Gd-T1WI. The ABC/2 calculation was conducted as follows: A, maximum tumor diameter; B, diameter of the tumor perpendicular to A (Figure 1A); and C, maximum height of the tumor acquired on the browser of the picture archiving and communication system. V2 was defined as the volume calculated by the planimetry method using axial images on thick slice Gd-T1WI (Figure 1B). For

measurements in Gd-T1WI, enhancement of dural tail was excluded from the tumor. V3 was defined as the volume calculated by the planimetry method using axial images on thin slice CISS imaging (Figure 1C). For the planimetry method, regions of interest were set by tracing the boundary of the tumor manually. Among these methods, V3 (calculated by the planimetry method with thin slice MRI) was presumed to be closest to the actual volume of the tumor (3,25) and was considered as the real volume in this study. The accuracy of the ABC/2 and planimetry methods using thick slice MRI was assessed by the ratio of V1 to V3 (V1/V3) and V2 to V3 (V2/V3) and the difference of V1 from V3 (V1-V3) and V2 from V3 (V2-V3), respectively. Because V1/V3 = 1.0 and V2/V3 = 1.0 would indicate equality between V1, V2, and V3, respectively, the absolute value of (1–V1/V3) and (1-V2/V3) was calculated to evaluate the variability of V1 and V2 from the real tumor volume (referred to as |1-V1/V3| and |1-V2/V3|, respectively).

Statistical analysis

Tumor maximum diameter and calculated tumor volume are represented as mean ± standard deviation. Pearson correlation was used to appraise the relationship between V1, V2, and V3 (r = coefficient of correlation). Student's *t*-test was used to assess between-group differences. Between-group differences in tumor sizes according to five sub-locations were assessed on one-way analysis of variance (ANOVA) followed by the Tukey–Kramer test as post hoc analysis. Regression analysis was performed to assess the correlation between FF and V1/V3. A difference with a probability value of <0.05 was considered to be statistically significant.

Results

Eighty-three meningiomas from 83 patients were analyzed. The location of the meningiomas was calvarium in 22 tumors, anterior skull base in 8 tumors, middle skull base in 19 tumors,

posterior skull base in 21 tumors, and other sites in 13 tumors. Among all the tumors in this study, the V1 values were 0.5–138.9 (33.1 ± 35.3, mean ± standard deviation) cm^3, the V2 values were 0.5–134.5 (28.4 ± 29.1) cm^3, and the V3 values were 0.4–128.6 (28.2 ± 28.6) cm^3. Details of the results are summarized in Table 1.

FF analysis

FF of the non-skull base meningiomas was statistically higher than that of the skull base meningiomas ($p < 0.01$, Figure 2A). This indicates that the meningiomas in the skull base tended to be more irregular in shape compared with the meningiomas in the calvarium or other sites. Among the 3 groups of skull base meningiomas, the difference in FF was not statistically significant.

The correlation between tumor maximum diameter and tumor volume

The correlation between tumor maximum diameter and V3 was significant ($r = 0.91$, Figure 2B). However, the calculated tumor volume differed in each case despite the tumors presenting comparable maximum diameter (Figure 2C). This trend became more significant as the tumor diameter became larger.

Accuracy of the ABC/2 formula compared with the planimetry method with thin slice MRI

The correlation between V1 and V3 was statistically significant among all the meningiomas ($r = 0.97$, Figure 3A). In the non-skull base meningiomas, V1/V3 were 0.89–1.40 (1.07 ± 0.11, Figure 3B, C). In the skull base meningiomas, V1/V3 were 0.86–1.93 (1.22 ± 0.24, Figure 3B, C). These results indicate that V1 in both skull base and non-skull base meningiomas tend to be higher than V3. The V1/V3 values of skull base meningiomas were statistically higher than that of non-

skull base meningiomas (Figure 3C). One-way ANOVA of V1/V3 among the five locations showed significant between-group differences ($p < 0.01$); Tukey–Kramer test demonstrated significant differences between meningiomas in calvarium and middle skull base ($p < 0.05$), and between other sites and middle skull base ($p < 0.05$). Among the 3 groups of skull base meningiomas, the mean V1/V3 was highest in the middle skull base meningiomas followed by the posterior skull base meningiomas (Figure 3C). This result indicates that the ABC/2 formula tended to overestimate the tumor volume, particularly in the middle skull base. The value of |1-V1/V3|, indicating inaccuracy of the ABC/2 formula, was statistically higher in skull base meningiomas than in non-skull base meningiomas (Figure 3D).

Correlation between FF and V1 was not significant ($r = -0.1$, Figure 4A). On comparing FF and V1/V3, 33 of 34 (97.1%) tumors with FF $\geq$ 0.85 presented V1 within 20% of difference from V3 (Figure 4B). Additionally, regression analysis revealed linear regression between FF and V1/V3 ($R^2 = 0.21$, Figure 4B).

Accuracy of the planimetry method with thick slice MRI compared with thin slice MRI

The correlation between V2 and V3 was statistically significant in all the meningiomas ($r > 0.99$, Figure 5A). V2/V3 were 0.75–1.12 (0.98 ± 0.09, Figure 5B, C) in the non-skull base meningiomas and 0.60–1.25 (0.99 ± 0.09, Figure 5B, C) in the skull base meningiomas. The difference between V2 and V3 was not statistically significant (Figure 5C). In each of the 3 groups of skull base meningiomas, the mean error from the real volume was within 10% (Figure 5C). The value of |1-V2/V3| presented no significant difference between non-skull base and skull base meningiomas (Figure 5D), which indicated the utility of the planimetry method using thick slice MRI regardless of the tumor location. The accuracy of the planimetry method using thick slice MRI compared with the ABC/2 method was also indicated by the significantly smaller difference between V2 and V3 (Figure 6A). However, in non-skull base and skull base meningiomas, tumors

with small V3 tended to present variability of V2/V3 regardless of their location (Figure 5B). This indicated that the planimetry method with thick slice MRI could over- or underestimate tumor volume when the tumor was small. We further analyzed the correlation between the accuracy of the planimetry method with thick slice MRI and its number of fractions in MRI slices. In thick slice MRI, the number of MRI slices that presented tumor was 2 in 1 case, 3 in 10 cases, 4 in 14 cases, 5 in 11 cases, 6 in 15 cases, 7 in 12 cases, 8 in 8 cases, 9 in 7 cases, 10 in 3 cases, and 11 in 2 cases. V1/V3 and V2/V3 in each group according to MRI slices are summarized in Table 2. Although accuracy of the tumor volume tended to be superior with the planimetry method by thick slice MRI compared with the ABC/2 formula, V2/V3 varied more widely in tumors within 3 slices than tumors of more than 4 slices in thick slice MRI, with a mean V2/V3 of 0.89 ± 0.17 and 1.00 ± 0.06, respectively (Figure 6B). This variability of V2/V3 in small tumors was also indicated by the |1-V2/V3| values (Figure 6C). Therefore, the planimetry method with thick slice MRI tended to over- or underestimate the volume of small meningiomas within 3 slices, while in most of the meningiomas of more than 4 slices in thick slice MRI, tumor volume could be calculated by the planimetry method with thick slice MRI within 10% error compared with thin slice MRI (Figure 6B).

Discussion

Although maximum diameter has been used to evaluate the natural history of meningiomas (5-9), our results indicate intercase differences in tumor volumes even for tumors with comparable maximum diameters. Therefore, maximum diameter of the tumor should be used exclusively for the assessment of the same tumor, such as for the evaluation of the natural history, and is not adequate for the comparison of different cases. We adopted FF analysis to quantify the irregularity of tumors because the assessment of tumor shape largely depends on subjective view of examiner. To our knowledge, FF analysis is a clinically available method to assess the irregularity of tumor, and we

consider that it is a helpful and a simple procedure. However, not all cases with high FF presented accurate V1 in this study, which would be a limitation of this method because FF is calculated only by one slice with maximum cross-section.

Because the ABC/2 formula can provide the volume of a lesion easily and within short time, it is useful in clinical practice for cerebrovascular disorders, such as ICH (20-24,29) or cerebral infarction (30), that require rapid decision-making. However, the accuracy of the ABC/2 formula has been previously debated in these fields, particularly in ICH. This is because the ABC/2 formula tends to overestimate volume if the hematoma is of an irregular shape (21,24,29). Because the ABC/2 formula is calculated on the presumption that the lesion is ellipsoid in shape, the calculated volume tends to differ from the exact volume if the form of the lesion differs from ellipsoid.

The accuracy of the ABC/2 formula for intracranial tumors has not been debated. In previous studies, the ABC/2 formula has been reported as a calculable method for acoustic neuromas (25) and pituitary adenomas (26). These tumors arise at specific locations, and variations in tumor shape are limited. However, meningiomas arise in various intracranial sites, and the shape of the tumor can present in various patterns. In this study, parameters of skull base meningiomas calculated with ABC/2 formula showed a tendency for overestimation as compared to that in case of non-skull base meningiomas. This is most likely because meningiomas in these regions tend to have relatively irregular shapes that are dependent on the anatomy of the skull base as presented by FF analysis. Although meningiomas in other locations tended to have relatively accurate volumes with the ABC/2 formula, a proportion of the tumors in these locations also had overestimated volumes (Figure 3B). We consider that this discrepancy is because of the lobular shape of the meningiomas. Because the ABC/2 formula calculates the volume of an ellipsoid based on the maximum diameter of the tumor, such lobular-shaped tumors would be overestimated by the ABC/2 formula similar to the previous studies on ICH (21,24,29). According to the results of this study, the use of the ABC/2 formula should be limited to non-skull base meningiomas with regular and round or ellipsoid

shapes. To obtain a more accurate tumor volume using the ABC/2 formula, Dirks et al. have recommended using the ABC/2 formula by dividing the tumor into compartments for multilobulated tumors (2). Although the ABC/2 formula appears to be useful for calculating the growth rate of a tumor rather than quantification of tumor volume, this has been reported as an underestimation (1).

The planimetry method has been widely used to calculate the volume of meningiomas in previous studies (3,4,11-15); however, the details of the procedure depend on each investigator. The thickness of MRI used in the planimetry method is often not regarded in the study. It is obvious that the planimetry method with thin slice MRI can demonstrate volume more accurately compared with thick slice MRI (3); however, the use of thin slice MRI is more cumbersome for the examiner if the tumor has a large volume. Hashiba et al. (3) validated the accuracy of the planimetry method with thick slice MRI in 10 cases of meningioma. This small series is the largest case series that compared thick and thin slice MRI for the planimetry method in meningiomas. We found that the planimetry method with thick slice MRI was not inferior to thin slice MRI if the thick slice MRI fractionated the tumor for 4 or more slices. However, the reliability of the planimetry method with thick slice MRI was significantly inferior to thin slice MRI if the thick slice MRI fractionated the tumor for 3 or less slices. Therefore, there is inaccuracy because of the thickness of slices at the reconstruction of 3-dimensional images. According to this study, we recommend the use of the planimetry method with thin slice MRI if the tumor is small, i.e., within 3 slices in thick slice MRI. Moreover, in clinical practice, such discrepancy between thick and thin slices should be considered particularly in serial follow-up or case-to-case comparison of small tumors.

Although tumor volume influences the planning of treatment, the degree of accuracy of tumor volume required for this purpose is not clear. Correlation between accuracy in calculation of tumor volume and treatment outcomes is yet to be reported. However, considering that previous reports have used different methods to calculate volume of meningiomas, a standardized method for

calculation is required for discussion and standardized treatment of meningiomas.

Conclusions

Maximum diameter is known to be associated with the volume of meningiomas; however, the error becomes significant in tumors with longer maximum diameters. The ABC/2 formula tended to present relatively larger volume of meningiomas located in middle skull base or those with low FF value. The planimetry method with thick slice MRI was not inferior to thin slice MRI if the number of fractions in thick slice MRI was 4 or more. While the planimetry method with thin slice MRI is recommended for small tumors within 3 fractions in thick slice MRI so as not to overlook the signs of tumor growth.

References

Uncategorized References

1. Chang V., Narang J., Schultz L., Issawi A., Jain R., Rock J. and Rosenblum M. Computer-aided volumetric analysis as a sensitive tool for the management of incidental meningiomas. Acta Neurochir (Wien). 2012;154:589-597; discussion 597
2. Dirks M. S., Butman J. A., Kim H. J., Wu T., Morgan K., Tran A. P., Lonser R. R. and Asthagiri A. R. Long-term natural history of neurofibromatosis Type 2-associated intracranial tumors. J Neurosurg. 2012;117:109-117
3. Hashiba T., Hashimoto N., Izumoto S., Suzuki T., Kagawa N., Maruno M., Kato A. and Yoshimine T. Serial volumetric assessment of the natural history and growth pattern of incidentally discovered meningiomas. J Neurosurg. 2009;110:675-684
4. Hashimoto N., Rabo C. S., Okita Y., Kinoshita M., Kagawa N., Fujimoto Y., Morii E., Kishima H., Maruno M., Kato A. and Yoshimine T. Slower growth of skull base meningiomas compared with non-skull base meningiomas based on volumetric and biological studies. J Neurosurg. 2012;116:574-580
5. Olivero W. C., Lister J. R. and Elwood P. W. The natural history and growth rate of asymptomatic meningiomas: a review of 60 patients. J Neurosurg. 1995;83:222-224
6. Go R. S., Taylor B. V. and Kimmel D. W. The natural history of asymptomatic meningiomas in Olmsted County, Minnesota. Neurology. 1998;51:1718-1720
7. Niiro M., Yatsushiro K., Nakamura K., Kawahara Y. and Kuratsu J. Natural history of elderly patients with asymptomatic meningiomas. J Neurol Neurosurg Psychiatry. 2000;68:25-28
8. Herscovici Z., Rappaport Z., Sulkes J., Danaila L. and Rubin G. Natural history of conservatively treated meningiomas. Neurology. 2004;63:1133-1134
9. Yano S., Kuratsu J. and Kumamoto Brain Tumor Research G. Indications for surgery in patients

with asymptomatic meningiomas based on an extensive experience. J Neurosurg. 2006;105:538-543
10. Kuratsu J., Kochi M. and Ushio Y. Incidence and clinical features of asymptomatic meningiomas. J Neurosurg. 2000;92:766-770
11. Firsching R. P., Fischer A., Peters R., Thun F. and Klug N. Growth rate of incidental meningiomas. J Neurosurg. 1990;73:545-547
12. Yoneoka Y., Fujii Y. and Tanaka R. Growth of incidental meningiomas. Acta Neurochir (Wien). 2000;142:507-511
13. Nakamura M., Roser F., Michel J., Jacobs C. and Samii M. The natural history of incidental meningiomas. Neurosurgery. 2003;53:62-70; discussion 70-61
14. Zeidman L. A., Ankenbrandt W. J., Du H., Paleologos N. and Vick N. A. Growth rate of non-operated meningiomas. J Neurol. 2008;255:891-895
15. Oya S., Kim S. H., Sade B. and Lee J. H. The natural history of intracranial meningiomas. J Neurosurg. 2011;114:1250-1256
16. Harrison G., Kano H., Lunsford L. D., Flickinger J. C. and Kondziolka D. Quantitative tumor volumetric responses after Gamma Knife radiosurgery for meningiomas. J Neurosurg. 2015;1-9
17. Feigl G. C., Bundschuh O., Gharabaghi A., Samii M. and Horstmann G. A. Volume reduction in meningiomas after gamma knife surgery. J Neurosurg. 2005;102 Suppl:189-194
18. Starke R. M., Przybylowski C. J., Sugoto M., Fezeu F., Awad A. J., Ding D., Nguyen J. H. and Sheehan J. P. Gamma Knife radiosurgery of large skull base meningiomas. J Neurosurg. 2015;122:363-372
19. Ichinose T., Goto T., Ishibashi K., Takami T. and Ohata K. The role of radical microsurgical resection in multimodal treatment for skull base meningioma. J Neurosurg. 2010;113:1072-1078
20. Divani A. A., Majidi S., Luo X., Souslian F. G., Zhang J., Abosch A. and Tummala R. P. The ABCs of accurate volumetric measurement of cerebral hematoma. Stroke. 2011;42:1569-1574
21. Huttner H. B., Steiner T., Hartmann M., Kohrmann M., Juettler E., Mueller S., Wikner J., Meyding-Lamade U., Schramm P., Schwab S. and Schellinger P. D. Comparison of ABC/2 estimation technique to computer-assisted planimetric analysis in warfarin-related intracerebral parenchymal hemorrhage. Stroke. 2006;37:404-408
22. Sheth K. N., Cushing T. A., Wendell L., Lev M. H., Romero J. M., Schwab K., Smith E. E., Greenberg S. M., Rosand J. and Goldstein J. N. Comparison of hematoma shape and volume estimates in warfarin versus non-warfarin-related intracerebral hemorrhage. Neurocrit Care. 2010;12:30-34
23. Maeda A. K., Aguiar L. R., Martins C., Bichinho G. L. and Gariba M. A. Hematoma volumes of spontaneous intracerebral hemorrhage: the ellipse (ABC/2) method yielded volumes smaller than those measured using the planimetric method. Arq Neuropsiquiatr. 2013;71:540-544
24. Wang C. W., Juan C. J., Liu Y. J., Hsu H. H., Liu H. S., Chen C. Y., Hsueh C. J., Lo C. P., Kao H. W. and Huang G. S. Volume-dependent overestimation of spontaneous intracerebral hematoma volume by the ABC/2 formula. Acta Radiol. 2009;50:306-311
25. Yu Y. L., Lee M. S., Juan C. J. and Hueng D. Y. Calculating the tumor volume of acoustic neuromas: comparison of ABC/2 formula with planimetry method. Clin Neurol Neurosurg. 2013;115:1371-1374
26. Lundin P. and Pedersen F. Volume of pituitary macroadenomas: assessment by MRI. J Comput Assist Tomogr. 1992;16:519-528
27. Sekhar L. N., Swamy N. K., Jaiswal V., Rubinstein E., Hirsch W. E., Jr. and Wright D. C. Surgical excision of meningiomas involving the clivus: preoperative and intraoperative features as predictors of postoperative functional deterioration. J Neurosurg. 1994;81:860-868
28. Huang L., Holtzinger A., Jagan I., BeGora M., Lohse I., Ngai N., Nostro C., Wang R., Muthuswamy L. B., Crawford H. C., Arrowsmith C., Kalloger S. E., Renouf D. J., Connor A. A., Cleary S., Schaeffer D. F., Roehrl M., Tsao M. S., Gallinger S., Keller G. and Muthuswamy S. K. Ductal pancreatic cancer modeling and drug screening using human pluripotent stem cell- and

patient-derived tumor organoids. Nat Med. 2015;21:1364-1371
29. Xu X., Chen X., Zhang J., Zheng Y., Sun G., Yu X. and Xu B. Comparison of the Tada formula with software slicer: precise and low-cost method for volume assessment of intracerebral hematoma. Stroke. 2014;45:3433-3435
30. Sims J. R., Gharai L. R., Schaefer P. W., Vangel M., Rosenthal E. S., Lev M. H. and Schwamm L. H. ABC/2 for rapid clinical estimate of infarct, perfusion, and mismatch volumes. Neurology. 2009;72:2104-2110

Figure Captions

Figure 1

A representative case of a convex meningioma. Tumor volume was calculated by 3 different methods.

A: ABC/2 formula with thick slice Gd-T1WI. A = maximal tumor diameter and B = diameter of the tumor perpendicular to A.

B: Planimetry method with thick slice Gd-T1WI.

C: Planimetry method with thin slice CISS.

Figure 2

FF analysis and correlation between maximum diameter and V3.

A: FF of skull base meningiomas was significantly lower than that of non-skull base meningiomas (left). Among the skull base meningiomas, the difference of FF was not statistically significant between each location (right) (*; $p < 0.01$, N.S; not significant).

B-C: Comparison between maximum diameter and V3 (planimetry method with thin slice CISS). Horizontal axis, maximum diameter (mm); Vertical axis, V3 (cm^3)

B: The correlation between the maximum diameter and V3 was significant ($r = 0.91$).

C: Tumors classified according to the maximum length (every 10 mm). Longer maximum length

was related to variability in tumor volume.

Figure 3

Evaluation of the accuracy of V1 (ABC/2 formula) for V3 (planimetry method with thin slice CISS).

A: Correlations between V1 and V3 were statistically significant among all meningiomas ($r > 0.96$). Horizontal axis, V3 (cm^3); Vertical axis, V1 (cm^3)

B: Correlation between V3 and V1/V3. Skull base meningiomas (left) had greater and wider variability of V1/V3 than non-skull base meningiomas regardless of the real volume (right).

C: Correlation between V1/V3 and the location of the meningiomas. V1/V3 of skull base meningiomas was statistically higher than that of non-skull base meningiomas (left) (*; $p < 0.01$). This trend was particularly seen in the middle skull base meningiomas followed by the posterior skull base meningiomas (right).

D: Variability of V1/V3 as assessed by |1-V1/V3|. This value was statistically higher in skull base meningiomas than in non-skull base meningiomas (*; $p < 0.01$).

Figure 4

Correlation between form factor analysis and ABC/2 formula

A: Correlation between FF and V1 in all meningiomas was not statistically significant ($r = -0.10$).

B: Correlation between FF and V1/V3 presenting that 33 of 34 (97.1%) tumors with FF $\geq$ 0.85 presented V1 within 20% of difference from V3. Linear regression between FF and V1/V3 was also presented ($R^2 = 0.21$).

Figure 5

Evaluation of the accuracy of V2 (planimetry method using thick slice MRI) for V3 (thin slice MRI).

A: Correlation between V2 and V3 was statistically significant among all the meningiomas ($r > 0.99$). Horizontal axis, V3 (cm^3); Vertical axis, V2 (cm^3)

B: Correlation between V3 and V2/V3. Both non-skull base meningiomas (left) and skull base meningiomas (right) presented mean V2/V3 values that approximated to 1.0 except for meningiomas with a small real volume.

C: The differences of V2/V3 between non-skull base meningiomas and skull base meningiomas were not statistically significant (left) (N.S; not significant). Among the skull base meningiomas, the mean V2/V3 represented an accurate calculation of tumor volume in middle and posterior skull base meningiomas (right).

D: Variability of V2/V3 as assessed by |1-V2/V3|. The difference of this value was not statistically significant between non-skull base and skull base meningiomas (N.S; not significant).

Figure 6

The planimetry method using thick slice MRI presented relatively accurate volumes of the meningiomas; however, inaccurate volumes were calculated when the tumor was fractionated less than 3 slices.

A: Accuracy of the ABC/2 method as assessed by the difference between V1 and V3 [left, horizontal axis, V3 (cm^3); vertical axis, V1–V3 (cm^3)] and the planimetry method using thick slice MRI as assessed by the difference between V2 and V3 [right, horizontal axis, V3 (cm^3); vertical

axis, V2–V3 (cm^3)]. The planimetry method presented a more accurate and less varied volume of the tumor than the ABC/2 method.

B: Comparison between V2/3 and the number of fractions in thick slice Gd-T1WI (horizontal axis, number of MRI slices; vertical axis, V2/V3). The accuracy of V2 correlated with the number of MRI fractions (left). Tumors within 3 fractions in thick slice Gd-T1WI tended to present with an over- or underestimated volume, and tumors of more than 4 fractions tended to present with relatively approximate volumes with the planimetry method (right).

C: Variability of V2/V3 as assessed by |1-V2/V3|. This value was statistically higher in meningiomas within 3 fractions in thick slice Gd-T1WI than in tumors of more than 4 fractions (*; $p < 0.01$).

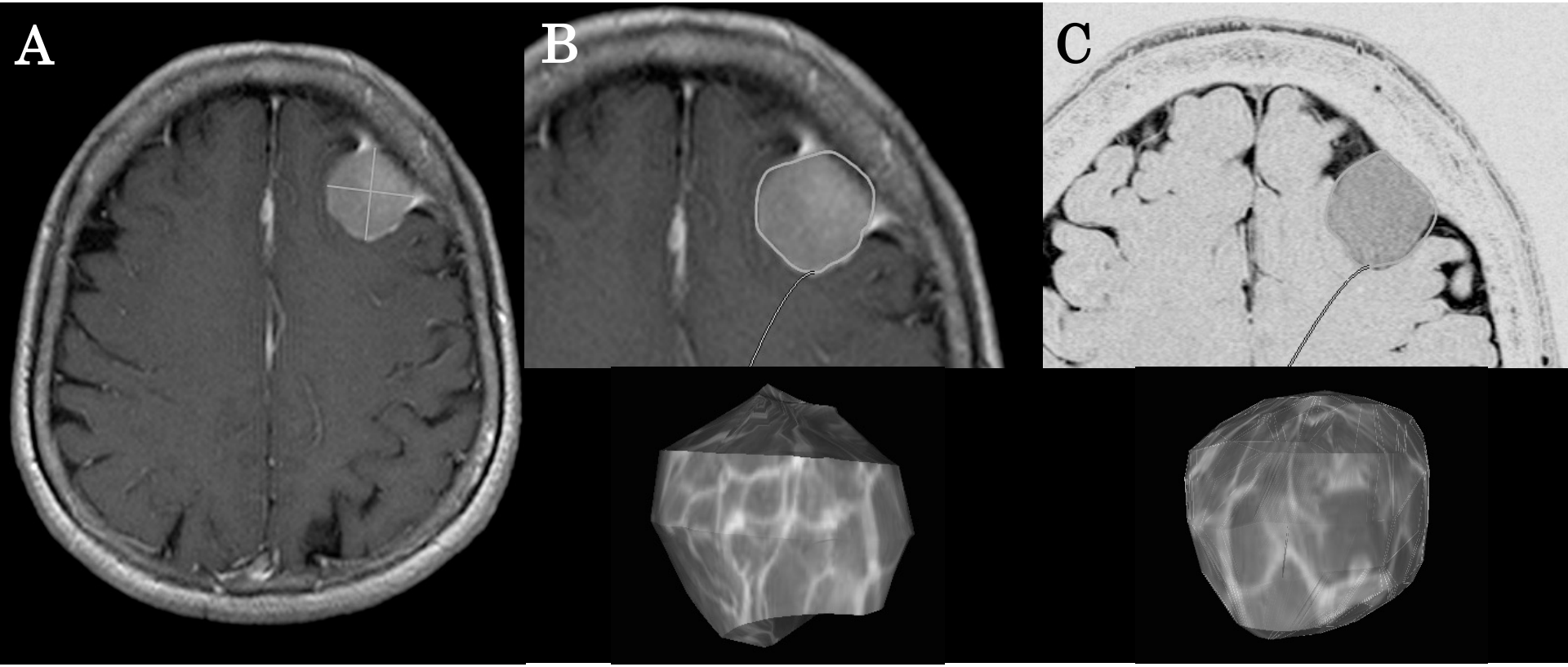

Fig. 1

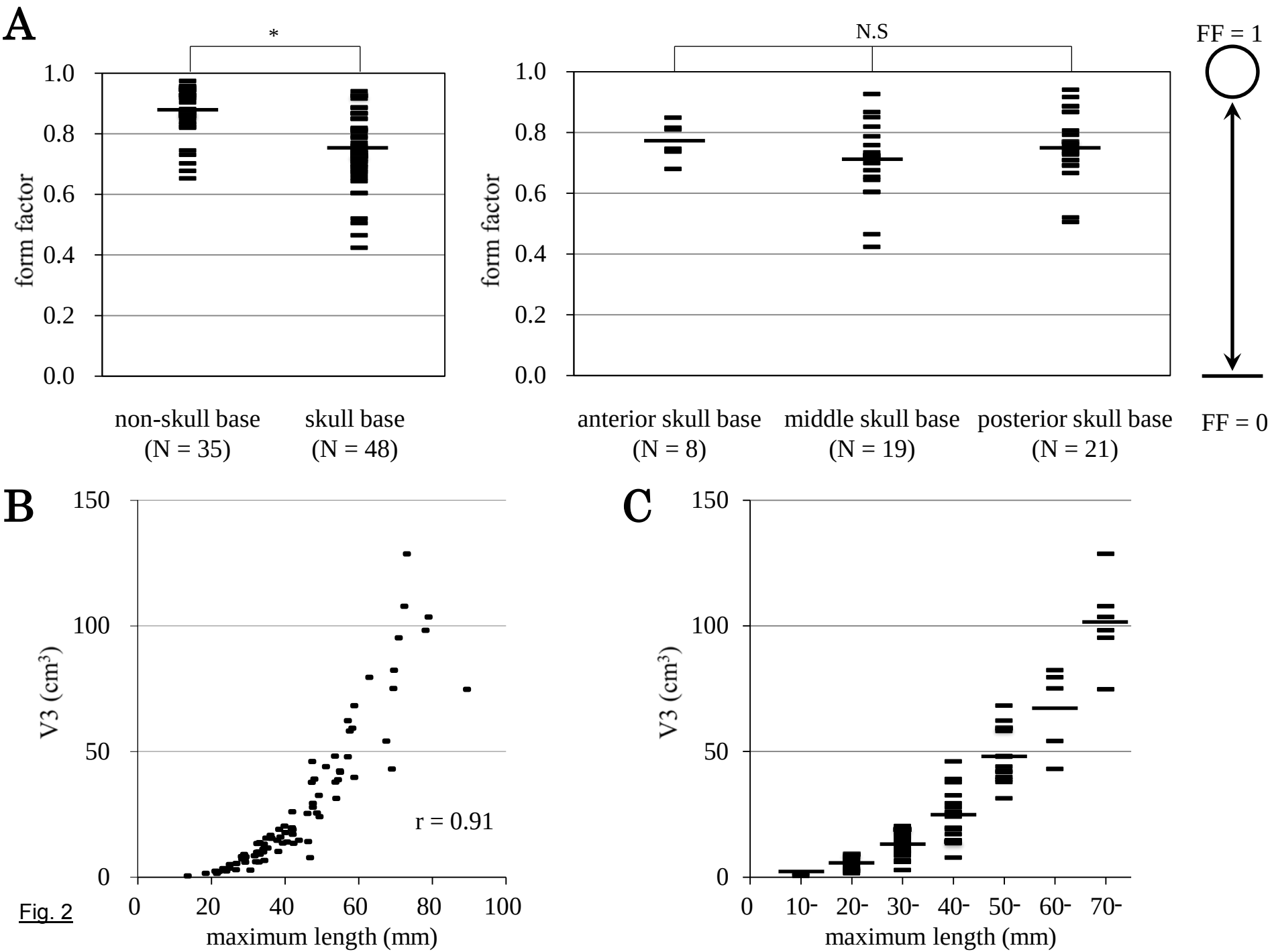
A
*
N.S
FF = 1
FF = 0
form factor
1.0
0.8
0.6
0.4
0.2
0.0
non-skull base
(N = 35)
skull base
(N = 48)
anterior skull base
(N = 8)
middle skull base
(N = 19)
posterior skull base
(N = 21)
B
C
V3 (cm³)
150
100
50
0
r = 0.91
0
20
40
60
80
100
maximum length (mm)
10-
20-
30-
40-
50-
60-
70-

Fig. 2

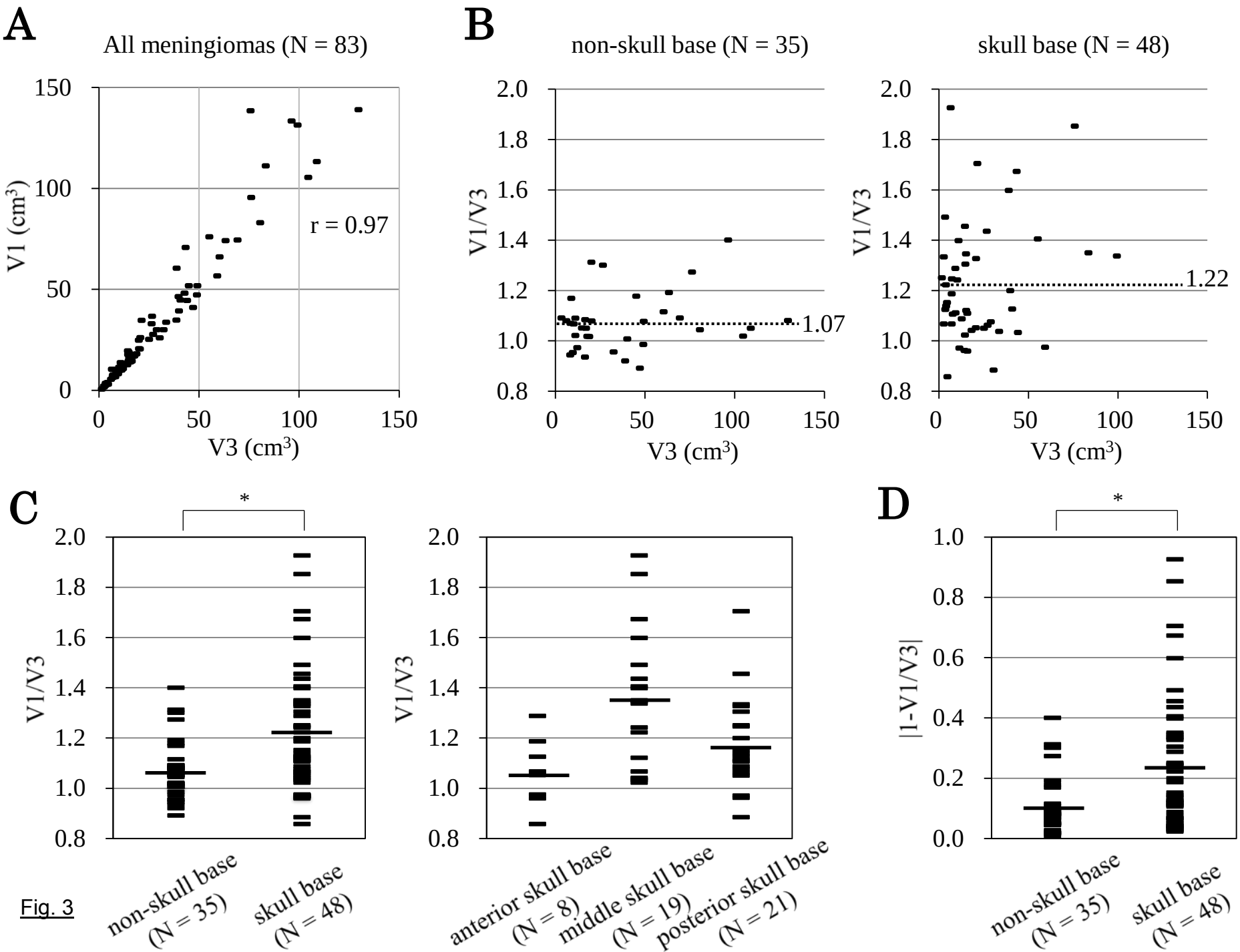
A
All meningiomas (N = 83)
V1 (cm3)
V3 (cm3)
r = 0.97
B
non-skull base (N = 35)
skull base (N = 48)
V1/V3
V3 (cm3)
1.07
1.22
C
*
V1/V3
non-skull base (N = 35)
skull base (N = 48)
anterior skull base (N = 8)
middle skull base (N = 19)
posterior skull base (N = 21)
D
*
|1-V1/V3|
non-skull base (N = 35)
skull base (N = 48)

Fig. 3

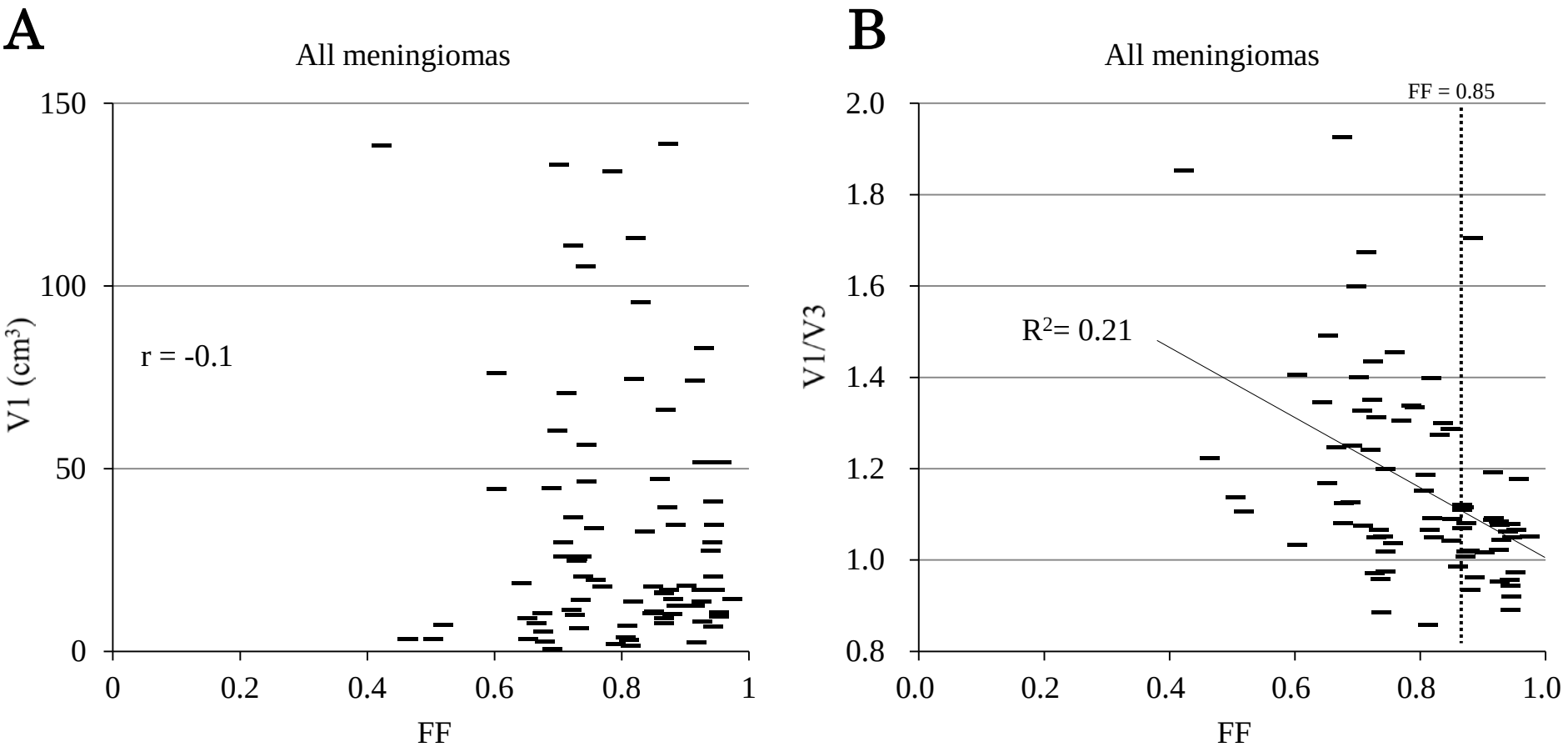
A
All meningiomas
150
100
50
0
V1 (cm3)
r = -0.1
0
0.2
0.4
0.6
0.8
1
FF
B
All meningiomas
FF = 0.85
2.0
1.8
1.6
1.4
1.2
1.0
0.8
V1/V3
R2= 0.21
0.0
0.2
0.4
0.6
0.8
1.0
FF

Fig. 4

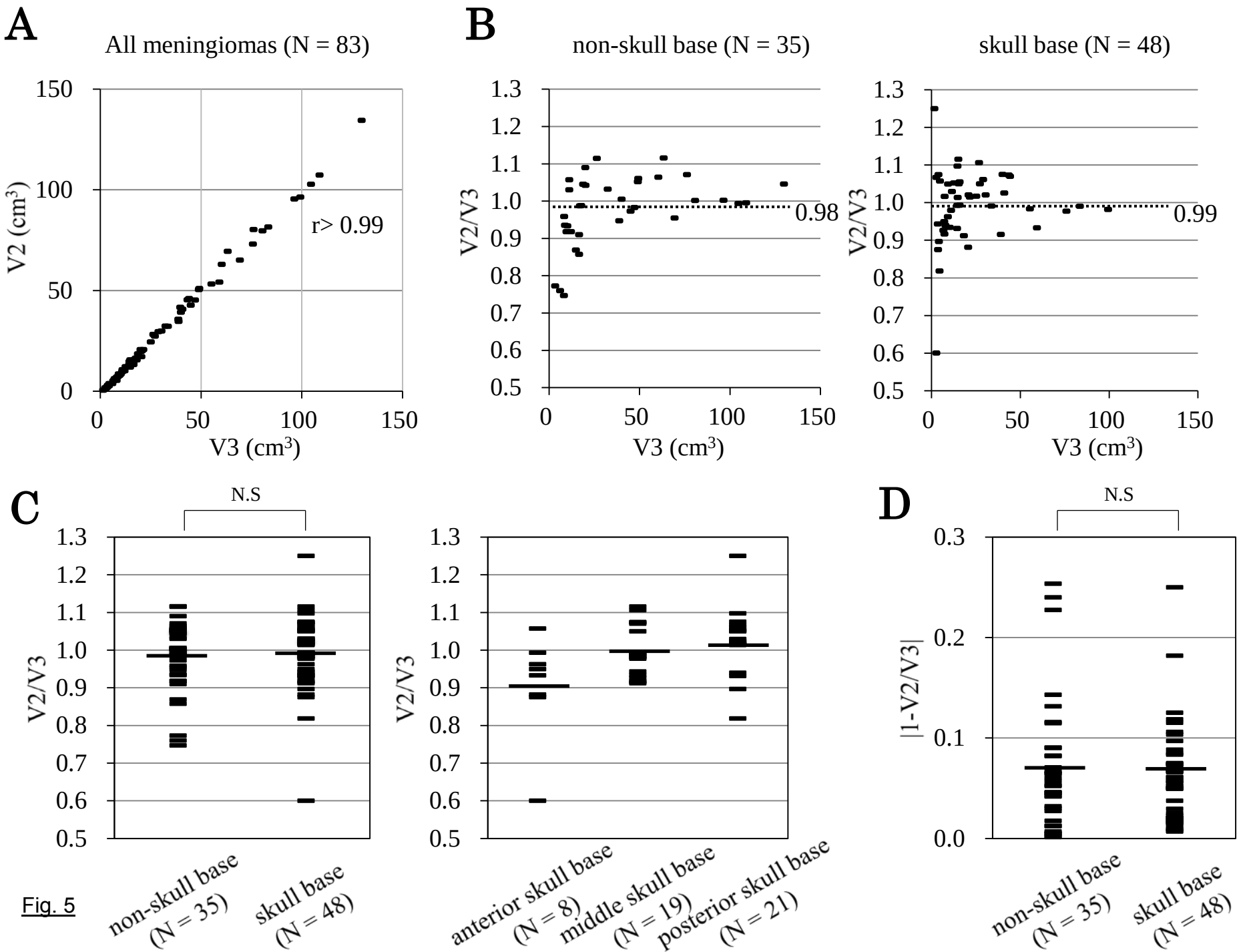
A
All meningiomas (N = 83)
V2 (cm3)
V3 (cm3)
r> 0.99
B
non-skull base (N = 35)
skull base (N = 48)
V2/V3
V3 (cm3)
0.98
0.99
C
N.S
V2/V3
non-skull base (N = 35)
skull base (N = 48)
anterior skull base (N = 8)
middle skull base (N = 19)
posterior skull base (N = 21)
D
N.S
|1-V2/V3|
non-skull base (N = 35)
skull base (N = 48)

Fig. 5

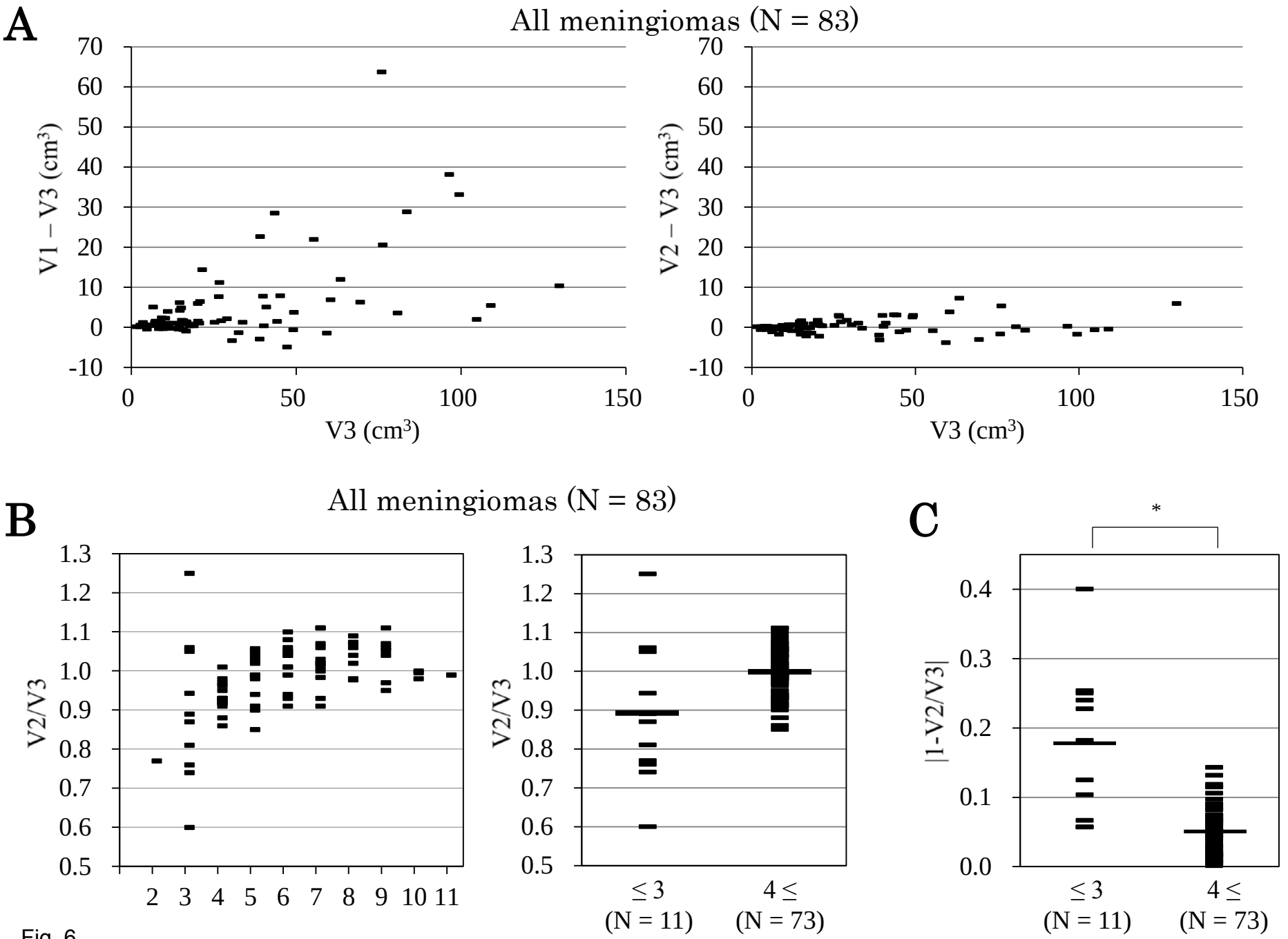
A
All meningiomas (N = 83)
V1 – V3 (cm3)
V2 – V3 (cm3)
V3 (cm3)
V3 (cm3)
B
All meningiomas (N = 83)
V2/V3
V2/V3
≤ 3 (N = 11)
4 ≤ (N = 73)
C
*
|1-V2/V3|
≤ 3 (N = 11)
4 ≤ (N = 73)
Number of fractions in thick slice MRI

Fig. 6

Table 1

Summary of form factor and tumor volumes calculated by ABC/2 formula (V1) and the planimetry method with thick (V2) and thin (V3) slice MRI.

Location	Number of cases	Form factor	V1 (cm^3)	V2 (cm^3)	V3 (cm^3)	V1/V3 ratio	V2/V3 ratio
non-skull base	35	0.87 ± 0.08	41.0 ± 38.1	37.8 ± 34.4	37.4 ± 33.4	1.07 ± 0.11	0.98 ± 0.09
calvarium	22	0.87 ± 0.09	33.4 ± 35.4	31.6 ± 34.2	31.3 ± 33.0	1.07 ± 0.11	0.96 ± 0.11
other sites	13	0.87 ± 0.07	54.0 ± 39.0	48.5 ± 32.1	47.7 ± 31.6	1.09 ± 0.12	1.01 ± 0.04
skull base	48	0.74 ± 0.11	27.4 ± 31.5	21.5 ± 21.6	21.4 ± 21.8	1.22 ± 0.24	0.99 ± 0.09
anterior skull base	8	0.77 ± 0.05	14.5 ± 17.0	13.2 ± 16.4	14.2 ± 17.6	1.06 ± 0.13	0.91 ± 0.13
middle skull base	19	0.70 ± 0.12	43.0 ± 42.3	30.7 ± 27.6	30.7 ± 28.0	1.35 ± 0.27	1.00 ± 0.06
posterior skull base	21	0.76 ± 0.11	18.2 ± 13.1	16.2 ± 12.0	15.7 ± 11.3	1.17 ± 0.18	1.02 ± 0.08
Total	83	0.80 ± 0.12	33.1 ± 35.3	28.4 ± 29.1	28.2 ± 28.6	1.16 ± 0.21	0.99 ± 0.09

mean ± standard deviation

Table 2

Summary of V3 and V1/V3 and V2/3 ratios according to the number of MRI slices that fractionates the tumor.

Number of MRI slices	Number of cases	V3 (cm^3)	V1/V3 ratio	V2/V3 ratio
2	1	2.2 ± 0.0	1.09 ± 0.00	0.77 ± 0.00
3	10	3.0 ± 1.8	1.14 ± 0.17	0.90 ± 0.18
4	14	10.3 ± 4.0	1.17 ± 0.25	0.94 ± 0.04
5	11	11.2 ± 3.5	1.05 ± 0.07	0.99 ± 0.06
6	15	26.7 ± 12.5	1.09 ± 0.14	1.02 ± 0.05
7	12	29.1 ± 20.0	1.25 ± 0.24	1.02 ± 0.06
8	8	39.6 ± 18.3	1.30 ± 0.31	1.04 ± 0.04
9	7	69.3 ± 26.2	1.13 ± 0.09	1.04 ± 0.05
10	3	100.4 ± 5.4	1.26 ± 0.15	0.99 ± 0.01
11	2	92.9 ± 10.6	1.18 ± 0.17	0.99 ± 0.01

mean ± standard deviation

Highlights

- Reliability of the four size evaluation methods for meningiomas was analyzed.
- Error of maximum diameter was significant in tumors with longer maximum diameters.
- ABC/2 formula tended to overestimate the volume of the skull base meningiomas.
- Planimetry method with thick slice MRI presented accurate volume in most tumors.
- Planimetry method with thin slice MRI was recommended for small tumors.