The Most Significant Surgical Risk Factors of Giant Intracranial Meningiomas: Localization Matters Much More than Grading and Volume of Peritumoral Brain Edema. A Retrospective Clinical Neuroradiological and Immunohistochemical Study

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Abstract

Background: Giant intracranial meningiomas (GIMs) are extremely rare and are usually considered arduous to resect totally with poorer prognosis. The real mechanisms by which a meningioma can grow to be defined as "giant" are unknown, as well as the real biological , radiological profile and the different outcomes.

Methods: We performed a retrospective review of a consecutive series of surgically-treated patients suffering from intracranial Meningioma. All the patients were assigned on the ground of the preoperative imaging to the Giant and Medium/Large Meningiomas. We investigated whether the presence large diameter on radiological diagnosis is indicative for different mortality rate, grading, characteristic and clinical/neurological outcome.

Results: The study shows that surgically treated giant meningiomas have a higher risk of developing complications in the postoperative phase (Chi square= 11.121, dF=1, p=0.001). The direct proportional relationship between peritumoral brain edema (PBE) volume and tumor volume was present only in the medium/large group and was not present in the giant meningioma group. When comparing the degree of performance there is a statistically significant difference between localization and KPS immediately postoperatively (p=0.04) particularly for sphenopetroclival meningiomas (p=0.071), and partially with GIM of the olfactory groove with arterial encasement. The most frequently encountered complications include the occurrence of ischemia (p=0.049), infection (p=0.03), and the occurrence of postoperative seizures.

Conclusions: We identified that the major surgical risk factor for GIMs is location, where the petro-clival region and, to a lesser extent the anterior basicranium offer a greater risk of neurovascular involvement and arterial encasement. On other hand, the risk correlated with PBE is poorer in GIM although there is a well-noted correlation between the Edema volume and outcome in meningiomas.

Introduction

Meningiomas represent one-third of all are primary central nervous system (CNS) tumors in adults with a female prevalence and median age at diagnosis of 66 years old [1]. They are usually benign, slow-growing tumors that are thought to arise from meningothelial cells. Most meningiomas are slow-growing lesions with a growth rate of approximately 2.4 mm per year [49]. For many patients who present with meningioma, in particular asymptomatic tumors, observation with routine surveillance imaging alone is an acceptable strategy while tumors that are growing or causing symptomatology, maximal safe surgical resection remains the standard of care for therapeutic management of meningioma. The clinical manifestations depend on their location and grade of their mass effect, but some tumors may grow over time without giving any clinical symptoms and therefore arrive at the radiological diagnosis with a considerable size. The so-called giant intracranial meningiomas (GIMs), defined as contrast-enhancing lesions with more than 5cm on the maximum diameter, are extremely rare and are usually considered

arduous to resect totally with a poorer prognosis. Further, GIMs are associated with different degrees of peritumoral brain edema (PBE), despite the usual presentation as benign and extra-axial tumors. PBE is present in 38–67.2 % of cases of all meningiomas [51-54] and is considered as one of the major causes of poor prognosis in meningiomas. It is not unusual to observe GIMs with a large variety of extensions of PBE. Several series of GIMs were reported previously, some reports show considerable series of the case but, many are case reports or small case series. The real mechanisms by which a meningioma can grow to be defined as "giant" are unknown, as well as the real biological and radiological profile and the different outcomes that a patient treated surgically for such an infrequent form may have. We presented a series of 340 cases who underwent surgical management of primary intracranial meningioma analyzing clinical, radiological, and pathological characteristics and we evaluated outcome and risk-rate on the ground of size (117 GIMs and 223 medium/large meningiomas). We focused on the surgical challenges of these rare tumors and highlighted the radiological, histological and, anatomical characteristics, and surgical techniques intending to retrieve the most important risk factors of the outcome.

Materials E Methods

Participants and Eligibility

We performed an Institutional retrospective review of a consecutive series of surgically-treated patients suffering from histologically confirmed intracranial Meningioma, operated on in Sapienza Neurosurgery department of Rome (Italy) and Neurosurgery department of Hospital Spaziani of Frosinone (Italy). We collected a total of 472 patients suffering from Meningioma. Histological diagnoses were performed according to the updated version of the 2021 WHO guidelines [24].

We selected patients affected by newly diagnosed Meningioma who underwent at their first surgery and eventually radiation, and chemotherapy in our Institutions in the period ranging between January 2016 and December 2020 meeting the following inclusion and exclusion criteria:

- Patients were included in the study if their pre- and post- operative magnetic resonance imaging (MRI) was either performed at our institution or available on the picture archiving and communication system (PACS) for review,
- Patients were included if, in the postoperative period, could undergo a standard clinical and radiological follow-up starting from the 30th day after surgery,
- The estimated target of the surgical procedure was the total or subtotal resection of the lesions, No biopsies were included,
- Patients with severe comorbidity such as to compromise evaluation in follow-up (intractable oncological, metabolic or cardiovascular diseases) were excluded,
- Patients were excluded for incomplete or wrong data on clinical, radiological and surgical records and/or lost to follow-up.

All the patients who met the aforementioned inclusion criteria, were assigned on the ground of the preoperative imaging to the following subgroups:

- Tumors classified as Giant Meningiomas (Group A): The contrast-enhancing lesion measure at least 5 cm on major diameter on T1-weighted images on MRI,
- Tumors classified as Medium/Large Meningiomas (Group B): The contrast-enhancing lesion measure less than 5 cm on major diameter on T1-weighted images on MRI,

We investigated whether the presence large diameter on radiological diagnosis is indicative for different OS, grading, immunohistochemical characteristics and clinical/neurological outcome.

For all the included patients we recorded at first: age, sex, time of hospitalization, time of follow-up, clinical onset, presence of smoke habits, hypertension and performance status (measured using Karnofsky performance scale (KPS)) at the moment of radiological diagnosis,

Regarding the clinical onset, we considered as Focal Neurological deficits the focal disorders of body motility and sensitivity, sphincter disorders, and disorders involving cranial nerves including visual disturbances, we considered the presence of dizziness, alteration of mental status and memory loss, the presence of intractable headache, seizure, and the incidental diagnosis.

On radiological evaluation we recorded: location of lesion, tumor major diameter (measured in cm), tumor volumes (measured in cm^3), Edema volume (measured in cm^3 and before anti-edemigen therapy), the presence of multiple meningiomas and or meningiomatosis, the involvement of subtentorial compartment,

On the ground of the histological final diagnoses we recorded: WHO grading with subtypes, mitotic index measured using the count of mitosis on 10 HPF, Immunohistochemistry with ki67 and Progesteron (PR) expression routinely performed in the Department of Neuropathology of our Hospital, Ki67 was applied to frozen sections of fresh tissue using a standard immunoperoxidase technique.

Overall survival (OS) was recorded in months, it was measured from date of diagnosis to date of death or date of last contact if alive. Clinical information were obtained by the digital database of our Institution, whereas OS data, were obtained by telephone-interview. We recorded after surgical procedure the status of performance (using KPS) for each patient at 1 month, 6 month and at last clinical evaluation. A special focus was on the KPS results: such parameter was considered, as previously observed as predictive and associated to survival (methodology described for other studies reported [55]. We evaluated the presence of complicances, recurrence and eventual second treatment recording biological switch.

All the patients included underwent a preoperative brain MRI scan included an high field 3 Tesla volumetric study with the following sequences: T2w, FLAIR, isotropic volumetric T1-weighted magnetization-prepared rapid acquisition gradient echo (MPRAGE) before and after intravenous administration of paramagnetic contrast agent, diffusion tensor sequences (DTI) with 3D tractography

and functional MRI (fMRI) completed our protocol for what concerns gliomas affecting eloquent locations. Volume of the contrast-enhancing lesion and edema were calculated drawing a region of interest (ROI) in a Volumetric enhancing post-contrast study weighted in T1 (a multi-voxel study) and T2, conforming to the margins of the contrast- enhancing lesion with software Horos (**Fig. 1**) [58]. In the first postoperative day, the patients underwent volumetric Brain MRI scan to evaluate the EOR and measuring the Simpson grade.

Surgical treatment

The patients underwent several trans cranial and skull base approaches according to the site of the meningioma. Olfactory groove (OG) and anterior floor lesions were removed through supraorbital, cranioorbital and supraorbital bifrontal approaches, sphenoorbital meningiomas (SOM) were removed via the cranioorbital zygomatic (COZ) approach, temporal floor meningiomas were operated on through the zygomatic and COZ approaches, sphenopetroclival (SPC) meningiomas were removed through the anterior or posterior petrosal approach, and tentorial meningiomas were removed through the suboccipital and retrosigmoid approaches.

Every patients with Simpson grade over I and WHO type II and III was submitted to radiotherapic and oncological evaluation.

Statistical methods

The sample was analyzed with SPSS version 18. Comparison between nominal variables have been made with Chi^2 test. EOR (measured with Simpson Grade) and PFS means were compared with One Way and Multivariate ANOVA analysis along with Contrast analysis and Post-Hoc Tests. Continuous variables correlations have been investigated with Pearson's Bivariate correlation. Threshold of statistical significance was considered $p<.05$.

Potential source of Bias and Study size

We addressed no missing data since incomplete records were an exclusion criteria. A potential source of bias is expected to derive from exiguity of the sample, which nevertheless, in regards to the endpoints selected, presents an excellent post-hoc statistical estimated power (difference between two independent means, $1-\beta = 0.9488$ for α 0.05 and effect size 0.5), thus providing extremely reliable conclusions.

The informed consent were approved by the Institutional Review Board of our Institution. Before surgical procedure, all the patients gave informed written explicit consent after appropriate information. Data reported in the study have been completely anonymized.

For statistical analysis, data collection and analysis of results we have received support from the Neurosurgical department of Turin, Italy directed by Prof. D. Garbossa. No treatment randomization has been performed fo its retrospective nature. This study is perfectly consistent with Helsinki declaration of Ethical principles for medical research to humans.

Results

1. Participants

In the period between between January 2014 and December 2020, 340 patients, matching the inclusion criteria, suffering from intracranial Meningioma underwent surgery in our departments and were retrospectively evaluated for this study.

2. Descriptive data

The final cohort consisted of 340 patients (102 males and 238 females - 70% of the population) respecting the F:M ratio reported in the literature of 2-3:1, and the average age was 60.38±13.56 years (Range 20-90), Smoke habits and Hypertension was revealed at the time of radiological diagnosis respectively in 98 patient (28,8%) and 108 patients (31,8%).

We reported the clinical debut for the population (Table 1), although only symptomatic meningiomas or meningiomas large enough to be evaluated as surgical were considered in this collection, a significant percentage of patients (14 patients, 13.2%) were incidentally diagnosed after investigations for other pathologies.

In a final division in a main subgroup A, Giant meningiomas were 117 (34,4 %) and subgroup B, Medimu/Large meningiomas were 223. All the relevant details with analysis results are included in Table 2.

The two subgroups did not present remarkable differences from the age/sex differences. Clinical debut, presence of seizure, smoke habits and hypertension were not significantly different.

Giant meningiomas did not correlate with known or likely risk factors for meningioma occurrence such as cigarette smoking (Chi-square= 1.362, dF= 1, p=0.243) or high blood pressure (Chi-square= 1.4, dF= 1, p=0.237). Specifically, we compared through contingency analysis (chi-square) whether there was a predominance of seizures at onset in either group obtaining no statistically significant results (p=0.764)

3. Histochemical and Radiological comparison analisys between the two groups

From the histochemical point of view the two subgroups in concerns to the WHO classification group A presented with a higher significant percentage of Grade II (31 patients, 26,5% versus 16 patients, 7,2%, p-value 0,001). There is evidence of a correlation between WHO grade (particularly atypical meningiomas) and tumor size and in general the diagnosis of giant meningiomas (chi-square=24.05, dF= 1, p=0.001), This difference is more evident between WHO grade I and II (in the diagnosis of atypical meningiomas, p=0.001)) than between grade II and grade III (p=0.818).

There is no correlation between the expression of progesteron on immunohistochemical analysis and the size of meningiomas in both groups, this finding is confirmed both when comparing the total volume of the lesion (p=0.847) and the largest diameter of the tumor (p=0.663). On the other hand, there is an independent correlation between ki-67 expression and total tumor volume (p=0.017, as typical for a large number of intracranial lesions [56]).

Interestingly, the direct proportional relationship between edema volume and tumor volume was present only in the medium/large group and was not present in the giant meningioma group with a statistically significant difference in proportionality. (t= -7.611, dF= 215, p<0.01). This finding is confirmed by similarly comparing the ratio of edema volume to lesion volume (t= 2.44, dF= 214, p=0.016). Results are obtained after Turkey and Bonferroni correction methods.

This peculiar feature suggest that giant meningiomas compared with medium and large meningiomas have a less remarkable strong relationship between the volume of the tumor mass and the edema generated around the tumor in the brain tissue. The extent of cerebral edema in relation to tumor size was evaluated. While in lesions under 5 cm there is a stable relationship between the increase in volume of the mass and the simultaneous increase in the volume of edema (Paired sample correlation test, t-student: p= 0.372) this relationship is no longer established in giant meningiomas (Paired sample correlation test, t-student: p<0.001). Analyzing the volume of edema among the different localizations of meningiomas in the whole population shows a strong variability among the different groups of meningiomas (p=0.04), with a greater prevalence of edemigenous lesions in meningiomas of the olfactory shower and sphenoidal plenum, without, however, substantial significance (p= 0.659, group 6, p>1, group 11), therefore there are no significantly edemigenous localizations compared to others. Moreover, while in medium/large meningiomas, as well as in the whole case series, there is no more edemigenous localization than another, in giant meningiomas there is a significant correlation with the site of implantation as far as tumors of the anterior basicranium (olfactory shower and sphenoidal plenum) are concerned.

4. Outcome data and Main Results

Neurological and clinical outcome as measured by KPS is affected by lesion localization, but to a different extent than recovery time. When comparing the degree of performance there is a statistically significant difference between localization and KPS immediately postoperatively (p=0.04) particularly for

sphenopetroclival meningiomas (p=0.071), and partially with GIM of the olfactory groove with arterial encasement (Fig. 2).

This difference is no longer evident in the comparison at the last evaluation where the final KPS has no correlation with the location of the meningioma (p=0.318).

It is found that surgically treated giant meningiomas have a higher risk of developing complications in the postoperative phase (Chi square= 11.121, dF=1, p=0.001, Fig.3).

The most frequently encountered complications include the occurrence of ischemia (p=0.049), infection (p=0.03), and especially the occurrence of postoperative seizures.

Although there is no evidence of a greater presence of epilepsy at diagnosis of a giant meningioma compared to a medium/large meningioma (Chi-square= 0.090, dF= 1, p= 0.764), there is an increased risk of seizures in the postoperative phase (Chi-square= 8.555, dF=1, p=0.003).

On the other hand, there is no significant relationship (Chi-square= 2.189, dF=1, p=0.139) between mortality and the presence at diagnosis of a giant meningioma.

In our case series, the risk of recurrence measured at the last evaluation was superimposable between group A and group B (Chi-square = 2.581, dF = 1, p = 0.108).

Discussion

Although there is no exact definition of GIM in the literature (some authors defined GIM as a tumor of >4.5-5-6 or 7 cm in maximum diameter [7,47,48]), we accepted 5 cm as the lower limit of diameter reported in almost all large series [1-7, 47-52]. While treatment for meningiomas is highly individualized and includes a combination of observation, surgical resection, radiotherapy, and rarely chemotherapy, for GIMs the surgical treatment is considered the primary therapy for their mass effect and neurovascular involvement although it is usually associated with a higher risk of complications [17]. The surgery of GIMs is considered unique due to prominent vascularity, entangling, and limited visualization of various neurovascular structures and, severe cerebral edema [9].

Our series confirms just in part these findings whereas the mortality rate, recurrence rate, Simpson grade, and KPS are comparable between the two groups, but there is a higher rate of complications in the first 30 days after the surgical procedure of GIMs compared with smaller meningiomas, and it has proven more challenging to understand the reasons for this. We also identified infections a higher incidence of postoperative ischemia and seizure in the GIMs group, these findings differ from other studies [48] where complications such as hemorrhage and malignant postoperative edema were more frequently identified with a strong correlation with mortality.

Is well-noted that a variable amount of vasogenic edema is shown in adjacent brain tissue in more than half of meningioma cases [50]. In meningiomas, PBE is considered one of the major factors affecting

surgical prognosis which is found in more than half of all meningioma cases. PBE in meningiomas exacerbates neurological symptoms, increases morbidity and risk of postoperative complications [51, 52].

The cause of the high frequency of cerebral edema in meningiomas has been much discussed because the cerebrospinal fluid space and the structure of the arachnoid membrane are located between the tumor and the brain parenchyma [57]. Electron microscope studies and recent MRI studies have shown that PBE associated with meningiomas is vasogenic, suggesting that meningioma tissue, rather than the brain parenchyma, is the origin of the edema fluid. A variety of causative factors for PBE have been investigated, including tumor volume, location, vascular supply, venous obstruction, microcortical invasion, histology, and sex hormones. However, the exact mechanism of development of PBE remains unclear [51-54].

Finding, in common clinical practice, meningiomas of huge sizes with insignificant amounts of edema is usual (**Fig. 4**). In our collection, we demonstrate that the correlation between tumor volume and edema is valid only up to a certain size and that for GIMs this relationship is no longer evident. Although, the most intuitive hypothesis would be that a larger meningioma with a higher growth velocity (indirectly suggested by the higher number of mitoses per field revealed in the GIMs group) and more frequently higher grade would result in a higher proportion of edema with related symptomatology (therefore, tumors associated with extensive PBE are commonly suspected to be pathologically malignant [54]), yet this does not occur. Such, the reasons for a reduced short-term outcome of GIMs must be investigated in other factors.

Meningiomas are classified into 15 subtypes across 3 grades with survival and recurrence rates worsening as their grade increases [2, 3, 4], and we didn't find a correlation between PBE and grading.

Narayan et al. [7], which is the largest series with 80 cases of GIMs, demonstrated that Regression analysis showed age, sex, location of the tumor, Simpson grade of excision, and histology of tumor were the factors that significantly affected the KPS and recurrence. In our series, we have found a strong correlation with location (in particular with SPC GIMs) and in terms of predicting surgical complications confirming previous data [48], and confirm that a cerebral artery encasement is associated with greater-risk profiles (confirmed with the high risk of olfactory groove GIM) [33].

Limitations and further studies

The main limitation of this study is its retrospective nature, which does not allow for an effective risk study by randomization. In addition, an ad hoc molecular prognostic study should be performed on these types of tumors. Theories on the development of meningiomas and PBE include also multiple molecular factors such production of vascular endothelial growth factor (VEGF), and interleukin-6 expression, but further research need to be done to understand the clinical behavior of these tumors.

Conclusion

GIMs are considered a great challenge for neurosurgeons, their large size, their wide attachment to the dura, their prominent hypervascular nature, and at times the edema, make its treatment more difficult. Surgery of GIMs is complicated for their mass effects that may cause increased intracranial pressure and hemodynamic changes. This study confirms that surgically treated GIMs have a higher risk of developing complications in the postoperative phase. We identified that the major surgical risk factor for GIMs is location, where the petro-clival region and, to a lesser extent the anterior basicranium offer a greater risk of neurovascular involvement and arterial encasement. On other hand, the risk correlated with PBE is poorer in GIM although there is a well-noted correlation between the Edema volume and outcome in meningiomas and preoperative Edema may represent a significant marker of poor functional outcome risk in adults and provides a quantitative measurement to incorporate into surgical decision-making.

Abbreviations

central nervous system (CNS), giant intracranial meningiomas (GIMs), peritumoral brain edema (PBE), Progesteron (PR), magnetic resonance imaging (MRI), Karnofsky performance scale (KPS), Overall survival (OS), magnetization-prepared rapid acquisition gradient echo (MPRAGE), diffusion tensor sequences (DTI), functional MRI (fMRI), region of interest (ROI), Olfactory groove (OG) sphenoorbital meningiomas (SOM) , cranioorbital zygomatic (COZ), sphenopetroclival (SPC)

Declarations

Author contribution

Daniele Armocida: writing, analysis and results

Giuseppina Bevacqua: literature research, discussion

Antonia Catapano: database and interview

Mauro Palmieri: bibliography

Umberto Aldo Arcidiacono: bibliography and design study

Alessandro Pesce: statistical analysis

Fabio Cofano: collection and project design

Veronica Picotti: database and interview

Maurizio Salvati: surgical operator and supervising

Diego Garbossa: project supervising

Giancarlo D'Andrea: surgical operator and supervising

Antonio Santoro: surgical operator and supervising

Alessandro Frati: surgical operator, supervising, project design

Data Availability

The dataset generated and analyses during the current study are not publicly available and is not retrieved for National databases, because it is the result of a institutional internal research of all treated cases of Meningioma in our Hospital (Policlinico Umberto I of Rome and Spaziani Hospital of Frosinone). The original dataset is available from the corrispondi author on reasonable request.

Compliance with ethical standards

Funding: This study was not funded by any association.

Conflict of Interest: We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.We wish to draw the attention of the Editor to the following facts which may be considered as potential conflicts of interest and to significant financial contributions to this work.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

This article does not contain any studies with animals performed by any of the authors.

Informed consent:

Informed consent was obtained from all individual participants included in the study.

The patient has consented to the submission of this review article to the journal.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

We further confirm that any aspect of the work covered in this manuscript that has involved either experimental animals or human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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Tables

Table 1: Population's study

No. 340	Total Meningiomas	
Age	Min: 20 Max: 90	Mean: 60,38 Median: 62 Sd: 13,56
Sex (Female)	F: 238 - 70%	
Smoke	98= 28,8%	
Hypertension	108= 31,8%	
Clinical Debut	Incidental =1 - 45 - 13,2% Dizziness = 2 - 32 - 9,4% Focal deficit = 3 - 80 - 23,5%	Headache = 4 - 46 - 13,5% Seizure = 5 - 88 - 25,9% Mental alteration = 6 - 46 - 13,5%
Hospitalization (330 pts)	Min: 5 Max: 209	Mean: 17,76 Median: 13 Sd: 17,23
Follow-up (months)	Min: 12 Max: 72	Mean: 47,76 Median: 47 Sd: 14,82
WHO Grade	Grade I: 285 - 83,8%. Grade II: 47 - 13,8%. Grade III: 8 - 2,4%	
Hystological type	1 = meningothelial - 205 - 60,3% 2 = Psammomatose - 16 - 4,7% 3 = Transitional - 22 - 6,5% 4 = Microcystic - 8 - 2,4% 5 = Atypic - 40 - 11,8%	6 = Fibrous - 13 - 3,8% 7 = Secretory - 12 - 3,5% 8 = Anaplastic - 7 - 2,1% 9 = Angiomatous - 9 - 2,6% 10 = Lymphoplasmacyte-rich - 1 - 0,3% 11 = Metaplastic - 5 - 1,5%
Switch in a malignant form during follow-up	5 pts/335 - 1,5%	

No. 340	Total Meningiomas	
Multiple/ Meningiomatosis	13 pts - 3,8%	
Location/ position	1 = clinoid - 11 - 3,2%	Sovratentorial - 290 - 85,3%
	2 = APC - 12 - 3,5%	Subtentorial - 26 - 7,6%
	3 = falx - 39 - 11,5%	
	4 = parasagittal parietal - 21 - 6,2%	
	5 = parasagittal frontal - 26 - 7,6%	
	6 = olfactory groove - 14 - 4,1%	
	7 = frontal convexity - 85 - 25%	
	8 = occipital convexity - 12 - 3,5%	
	9 = sphenoid wing - 20 - 5,9%	
	10 = tuberculum sellae - 9 - 2,6%	
	11 = planum sphenoidal - 8 - 2,4%	
	12 = tentorial - 15 - 4,4%	
	13 = temporal convexity - 15 - 4,4%	
	14 = orbital - 3 - 0,9%	
	15 = sphenopetroclival - 12 - 3,5%	
Giant Meningiomas (diameter max >5 cm)	117 pts - 34,4%	

Table 2: The table summarize the main clinical radiological and outcome variables examined in the study comparing giant and Medium/large meningiomas.

	Giant Meningiomas: 117 pts	Medium- Large Meningiomas: 223 pts	P-value
Sex	M: 46 - 39,3%	M: 56 - 25,1%	>1,00
	F: 71 - 60,7%	F: 167 - 74,9%	
Age	Min: 20 Max: 90	Min: 25 Max: 89	>1,00
	Mean: 60,62	Mean: 60,26	
	Median: 64	Median: 60,50	
	SD: 13,99	SD: 13,35	
Smoke	37 = 31,6%	61= 27,4%	>1,00
Hypertension	42= 35,9%	66= 29,6%	0,897
Seizure at onset	24 pts = 20,5%	49 pts = 22%	0,764
WHO Grade	Grade I: 81 - 69,2%.	Grade I: 204 - 91,5%.	
	Grade II: 31 - 26,5%.	Grade II: 16 - 7,2%.	**0,001**
	Grade III: 5 - 4,3%	Grade III: 3 - 1,3%	0,097
Maximum diameter (cm)	Min: 5 Max: 10,5	Min: 0,80 Max: 4,9	
	Mean: 6,26	Mean: 3,3	
	Median: 6	Median: 3,3	
V Edema cm3	Mean: 42,52	Mean: 18,37	**0,001**
	SD: 52,77	SD: 38,59	
V lesion cm3	Mean: 67,32	Mean: 15,79	0,001
	SD: 39,31	SD: 12,59	
Mitotic index/10HPF	Mean: 1,92	Mean: 1,2	0,005
	SD: 2,40	SD: 1,9	
Ki-67 expression	Mean = 7%	Mean = 4,5%	**0,017**
PR+	12 pts	26 pts	0,422
Simpson Grade resection	1 = 51 pts - 43,6%	1 = 102 pts - 45,6%	
	2 = 20 pts - 17,1%	2 = 35 pts - 15,7%	
	3 = 5 pts - 4,3%	3 = 7 pts - 3,1%	
	4 = 1 pts - 0,9%	4 = 1 pts - 0,7%	

	Giant Meningiomas: 117 pts	Medium- Large Meningiomas: 223 pts	P-value
Hospitalization	Mean = 18,71	Mean = 17,27	0,475
Complications	35 pts: 29,9%	33 pts: 14,8%	**0,001**
Complications	Hydrocephalus = 2 pts - 1,7% Hemorrage= 2 pts - 1,7% Infections= 16 pts - 13,7% Intractable seizure = 5 pts - 4,3% Ischemia = 10 pts - 8,5%	Hydrocephalus = 5pts - 2,2% Hemorrage= 4pts - 1,8% Infections= 10 - 4,5% Intractable seizure = 6 - 2,7% Ischemia = 8 - 3,6%	>1 >1 **0,003** >1 **0,049**
Recurrence	17 pts = 14,5%	20 pts = 9%	0,108
Death	14 pts: 12%	16 pts: 7,2%	0,139
KPS at onset	Mean = 70-80 DS= 14,72	Mean = 80 DS = 14	0,569
KPS after procedure	Mean = 80 DS = 20	Mean = 80 DS = 10	>1
KPS last evaluation	Mean = 80	Mean = 80-90	0,123

Figures

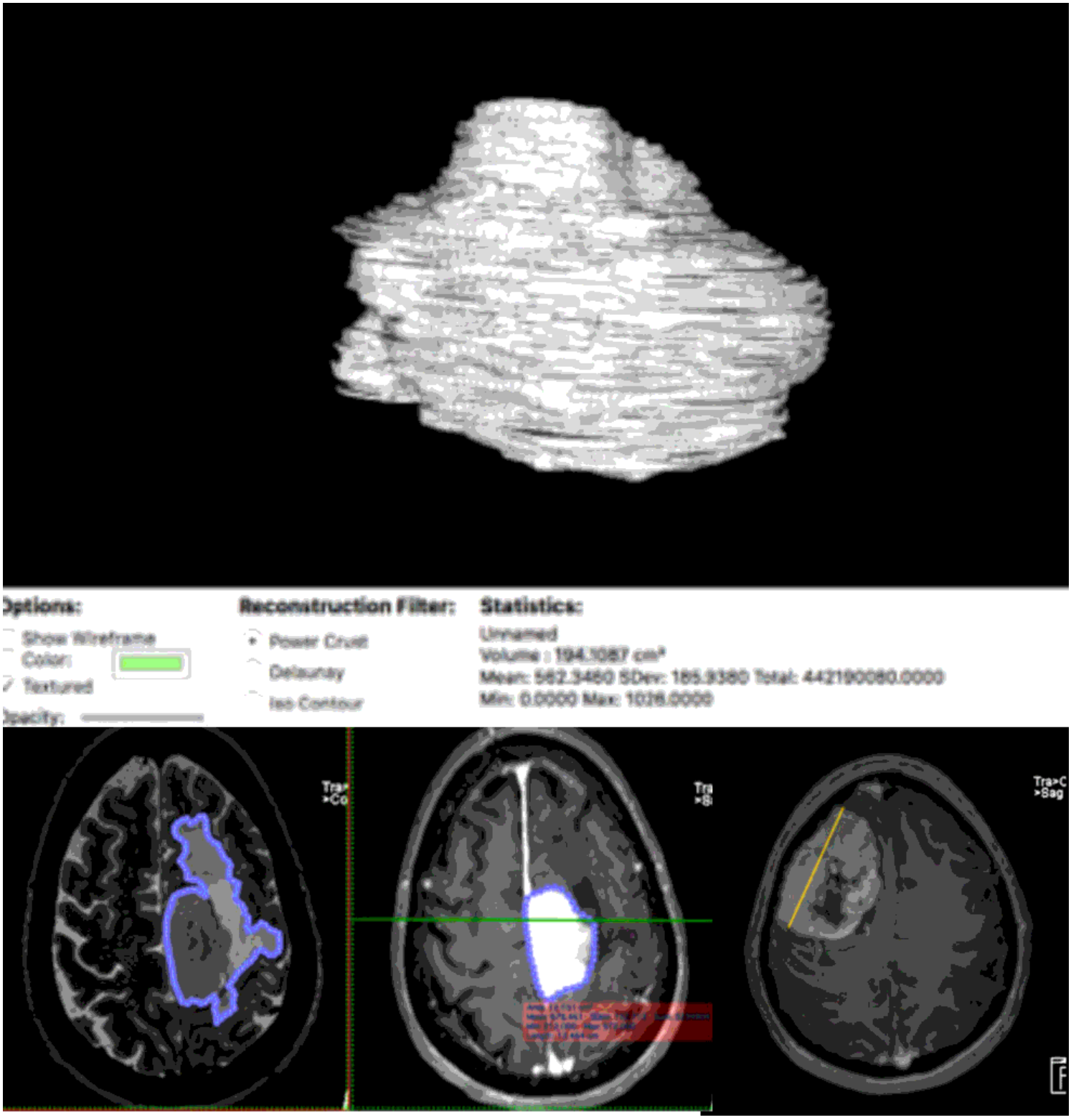


Figure 1

Using Horos software, we measured the largest diameter of each diagnosed meningioma and measured the volume of the contrast-capturing lesion and the relative volume of edema.

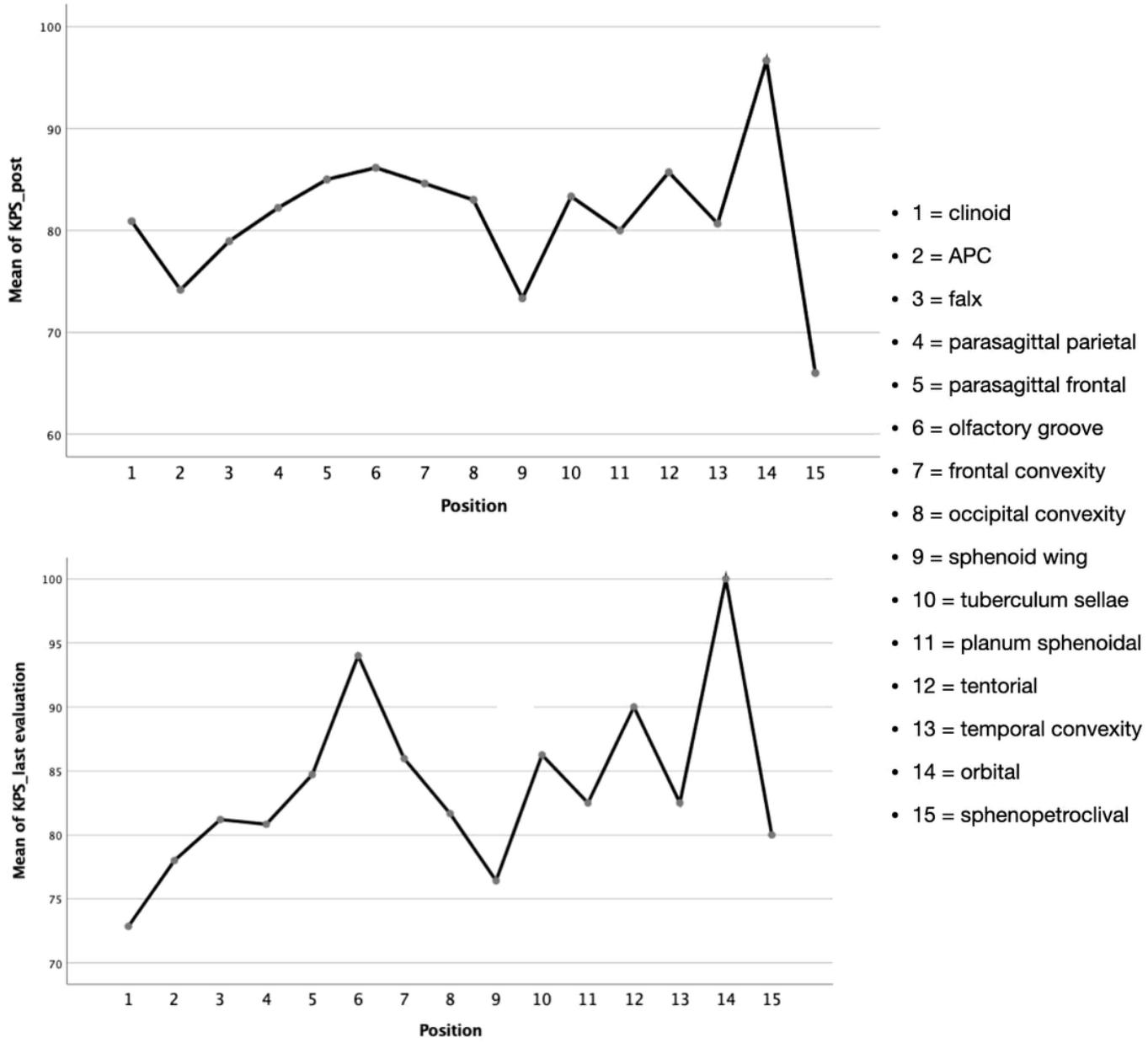
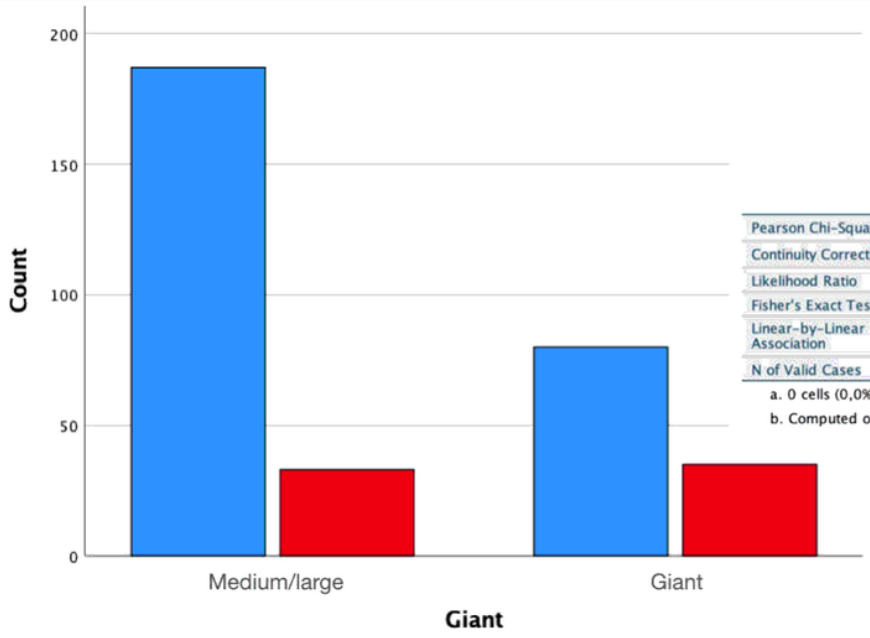


Figure 2

Through an ANOVA study, we found statistically significant differences between the reduction in performance in the postoperative phase and at the last evaluation among the various locations of GIMs.

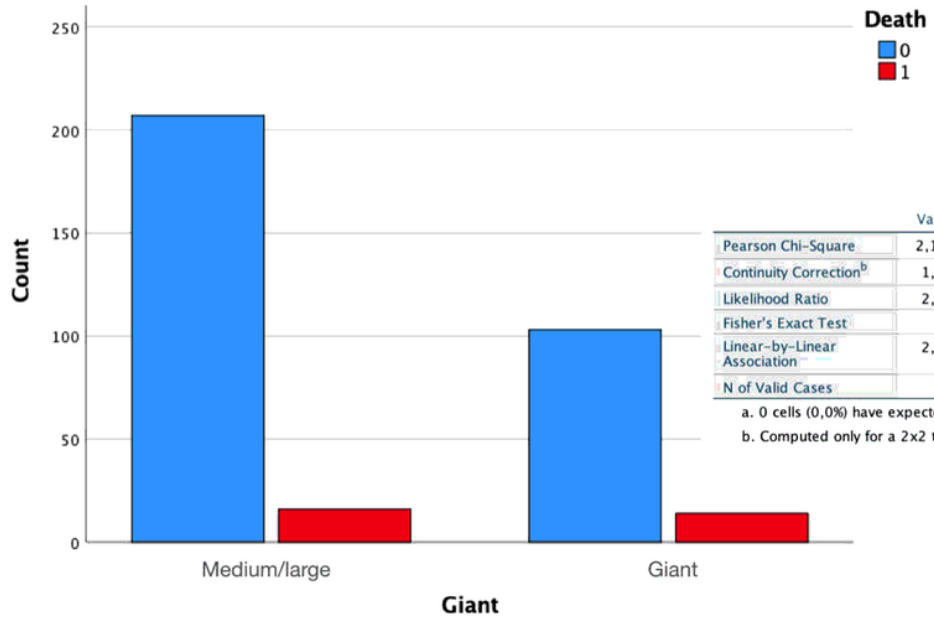


Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	11,121[a]	1	,001		
Continuity Correction[b]	10,187	1	,001		
Likelihood Ratio	10,696	1	,001		
Fisher's Exact Test				,001	,001
Linear-by-Linear Association	11,088	1	,001		
N of Valid Cases	335				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 23,34.

b. Computed only for a 2x2 table



Chi-Square Tests

	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	2,189[a]	1	,139		
Continuity Correction[b]	1,634	1	,201		
Likelihood Ratio	2,105	1	,147		
Fisher's Exact Test				,160	,102
Linear-by-Linear Association	2,183	1	,140		
N of Valid Cases	340				

a. 0 cells (0,0%) have expected count less than 5. The minimum expected count is 10,32.

b. Computed only for a 2x2 table

Figure 3

Chi-square comparison analysis between the two groups analyzed: giant meningiomas were shown to have a higher rate of postoperative complications compared with a comparable mortality rate compared with medium/large meningiomas.

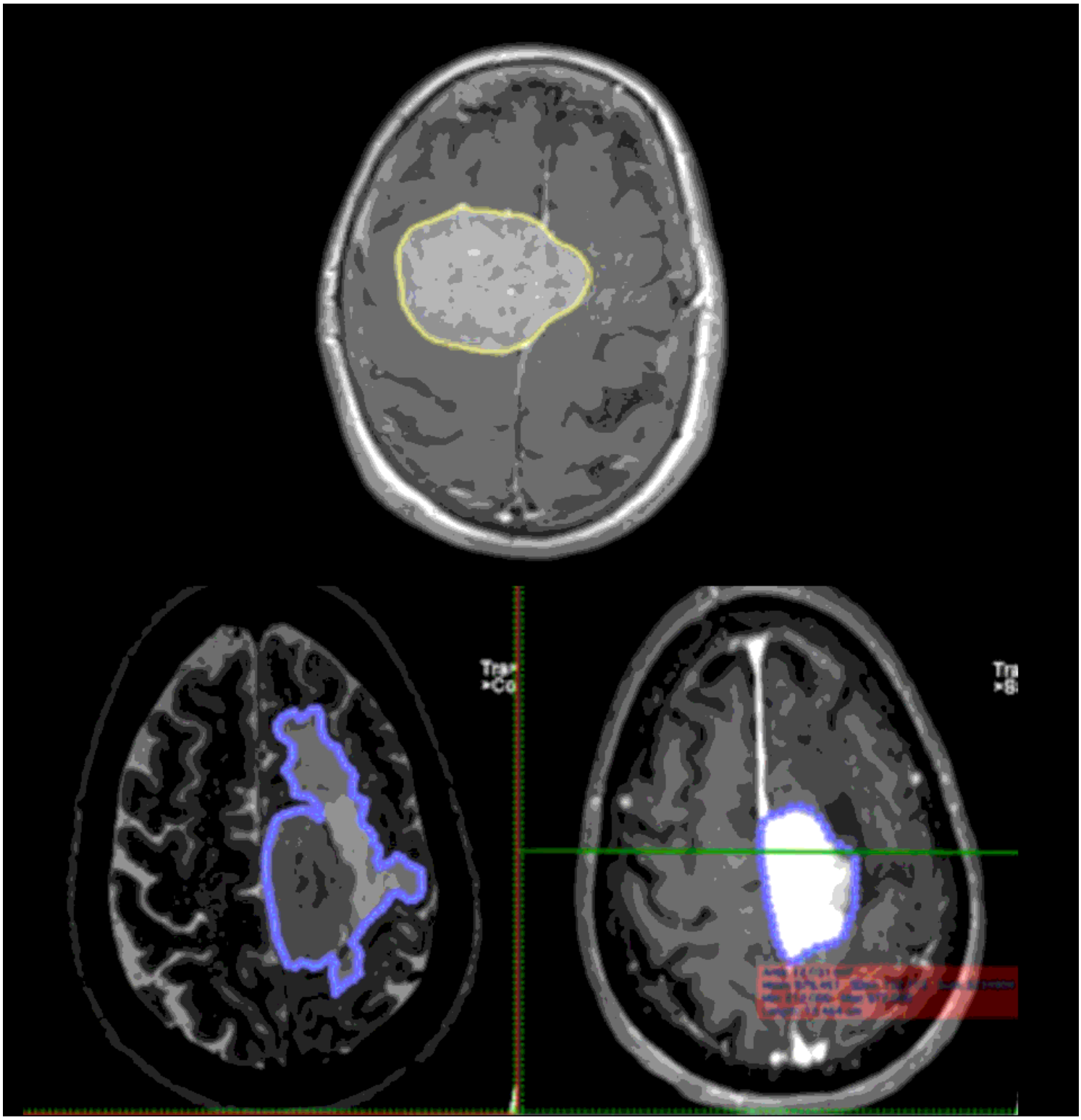


Figure 4

the figure shows a common case of large meningioma with a significant volume of edema compared with a Giant meningioma without edema.