**Sporadic Multiple Intracranial Meningioma Does Not Infer Worse Patient Outcomes – Results from A Case Control Study**

**Authors:**

Abdurrahman I. Islim1,2, Jing X. Lee3, Mohammad A. Mustafa1,2, Christopher P. Millward1,2, Conor S. Gillespie1,2, George E. Richardson1,2, Basel A. Taweel1,2, Emmanuel Chavredakis1,2, Samantha J. Mills4, Andrew R. Brodbelt1,2 & Michael D. Jenkinson1,2.

**Affiliations**

1. Institute of Systems, Molecular and Integrative Biology, University of Liverpool, Liverpool, UK
2. Department of Neurosurgery, The Walton Centre NHS Foundation Trust, Liverpool, UK
3. Department of Clinical Neurosciences, Salford Royal Hospital NHS Foundation Trust, Manchester, UK
4. Department of Neuroradiology, The Walton Centre NHS Foundation Trust, Liverpool, UK

**Corresponding author**

Dr Abdurrahman I Islim

Institute of Systems, Molecular and Integrative Biology, University of Liverpool

Crown street, Liverpool, UK, L69 7BE

Email: a.islim@doctors.org.uk

Telephone: +44 (0)151 795 4400

**Conflicts of interest**

The authors report no conflicts of interest in relationship to this work.

**Funding**

The authors have not received any funding to complete this study.

**Word count**

2586 words

# **ABSTRACT**

## Background

Sporadic multiple meningioma are uncommon. Population-based data suggests that these patients have a reduced overall survival when compared to patients with solitary meningioma. The aim of this study was to investigate the clinical outcomes in multiple and solitary meningioma.

## Methods

A single-centre matched cohort study (2008-2018) was performed. Patients with synchronous multiple meningioma at presentation, with no history of prior intracranial radiation, concurrent hormone replacement therapy or features of NF2-schwannomatosis were included. Eligible patients were matched 1:1 to patients with solitary meningioma. Outcomes of interest were occurrence of an intervention, recurrence, new meningioma development and mortality.

## Results

Thirty-four patients harboring 76 meningioma at presentation were included. Mean age was 59.3 years (SD=13.5). Thirty-one (91.2%) were female. The median number of meningioma per patient was 2 (range 2-6). Eighteen patients (52.9%) were symptomatic at presentation. Median overall follow-up was 80.6 months (IQR 44.1-99.6). Compared to patients with a sporadic meningioma, there was no difference in intervention rates (67.6% vs 70.6%, P=0.792). Eight patients (34.8%) with a multiple meningioma had a WHO grade 2 meningioma compared to 7 (29.2%) with a solitary meningioma (P=0.679). Median recurrence-free survival was 89 months (95% CI 76-104) with no difference between the two groups (P=0.209). Mean overall survival was 132 months (95% CI 127-138) with no difference between the two groups (P=0.860). One patient with multiple meningioma developed two further new meningioma 36 months following diagnosis.

## Conclusion

Sporadic multiple meningioma may not have worse clinical outcomes. Management of patients with sporadic multiple meningioma should be tailored towards the symptomatic meningioma or high-risk asymptomatic meningioma.

# **INTRODUCTION**

Meningioma are the most common primary non-malignant brain tumors, with incidence rates of 5-6 cases per 100 000 males and 11-12 cases per 100 000 females per year.1 The mainstay of treatment is surgical resection. Radiation therapy may be used in the adjuvant setting or at recurrence (1). The World Health Organisation (WHO) classifies meningioma into grade 1 (non-malignant) and grades 2 and 3 which are more aggressive. The ten-year relative survival rates for non-malignant meningioma are around 81-87% and 60-70% for higher grade meningioma (2,3). Approximately1-9% of meningioma patients present with multiple tumors which are defined as the presence of ≥2 spatially separated synchronous lesions (4). Risk factors for this include previous intracranial radiation, NF2-schwannomatosis (NF2) and exposure to high doses of exogenous hormones such as cyproterone acetate (5–7). A recent large population-based study found that in general, patients with multiple meningioma have a worse overall survival, in comparison to patients with a solitary meningioma (8). However, it is uncertain if patients with sporadic synchronous multiple meningioma also share the same outcome.

# **OBJECTIVE**

The aim of the study was to assess the clinical outcomes of patients with sporadic synchronous multiple meningioma compared to a matched cohort of patients with solitary meningioma.

# **METHODS**

## Study design and patient selection

This is a retrospective case control study of a cohort of patients diagnosed with sporadic synchronous multiple meningioma at presentation, matched with a cohort of patients diagnosed with solitary meningioma. Patients were diagnosed at The Walton Centre NHS Foundation Trust, Liverpool, UK, between January 2008 and December 2018. Follow-up was through to July 2021. Inclusion criteria were adult patients (≥ 18 years) with ≥2 meningioma at presentation. Exclusion criteria were patients who had previous intracranial radiation therapy (radiation induced meningioma), had a diagnosis of NF2 or had/were at the time of diagnosis on hormonal therapy. Data were collected on demographics, symptoms, neuroimaging features, treatment, outcomes and histopathological features. Data were anonymised and recorded into an encrypted Excel® database (Microsoft, Redmond, WA, USA). Local intuitional approval was obtained.

## Study outcomes

The outcomes of interest were intervention-free survival, recurrence-free survival following an intervention, new meningioma development and overall survival.

## Study variables and definitions

Clinical characteristics were collected and recorded at the time of diagnosis. Patient sex, age, presenting clinical features (asymptomatic vs symptomatic), WHO performance status, and age-Adjusted Charlson comorbidity index (ACCI) were included. The radiological features of the meningioma were recorded. The tumor location was defined according to the International Consortium on Meningioma (ICOM) classification system (9). The meningioma volume was calculated using the simplified ellipsoid formula (ABC/2) and reported in centimeters cubed (cm3). Meningioma signal intensity was categorized into hyperintense and iso/hypointense, in relation to the contralateral gray matter, on T2 weighted or fluid-attenuated inversion recovery (FLAIR) magnetic resonance imaging (MRI). The presence of peri-tumoral signal change was determined from T2 weighted or FLAIR MRI. Proximity to major dural venous sinuses or critical neurovascular structures (e.g, optic apparatus) was noted. The primary intervention was categorised as surgery, stereotactic radiosurgery (SRS) or fractionated radiotherapy (*f*RT). Surgical extent of resection was defined using the Simpson grading Scale (gross total resection [Simpson 1-3] and subtotal resection [Simpson 4-5]). Radiotherapy dose and fractionation were recorded. Adjuvant treatment was defined as additional radiotherapy given within six months of an operation. Salvage treatment was defined as treatment delivered due to meningioma recurrence/growth.

## Statistical analysis and matching process

Data are presented as count (%), mean (standard deviation [SD]), or median (interquartile range [IQR]), as appropriate. For all patients, matching was performed for ACCI (≥6 [older patients with comorbidities] vs remainder), performance status (0-2 vs 3-4) and duration of follow-up. For patients who were asymptomatic, matching was also based on the meningioma with higher risk features, determined using the IMPACT score, which is a prognostic tool used to evaluate the risk of incidental meningioma progression (10). IMPACT classifies a meningioma based on four MRI parameters - volume, tumor signal intensity, peri-tumoral signal intensity and proximity to critical neurovascular structures - into low- (<1), medium- (1-3) and high-risk (≥3). For each patient, the meningioma with a higher score was designated as the index meningioma and used for the purpose of matching to a patient with a solitary meningioma. For patients who were symptomatic, matching was based on the meningioma causing symptoms. The characteristics that were matched for included meningioma location (skull base vs non skull base) and volume. Cohorts were matched without replacement in a 1:1 ratio using a tolerance level of 10 units for tumor volume, and duration of follow-up. Exact matching was performed for categorical variables. Across outcome groups, categorical variables were analysed using χ2 test. Continuous variables were analysed using either the unpaired t- test or Mann-Whitney U test. A p value <0.05 was considered significant. Life table statistics and Kaplan Meier analyses were used to assess intervention-survival, recurrence-free and overall survival. Multivariable analyses, using backward stepwise Cox regression analysis, were constructed to assess factors associated with each outcome in the joint cohort. All statistical tests and matching were performed using SPSS® Statistics 25 (IBM Corp., Armonk, NY, USA).

# **RESULTS**

## Study population and baseline demographics

There were 34 patients with multiple meningioma, who were matched to 34 patients with solitary meningioma. The mean age of the whole study cohort was 58.3 years (SD=13.7). Fifty-four (79.4%) were female. More females were present in the multiple meningioma group (91.2 vs 67.6%, P=0.36). Thirty-six patients (52.9%) were symptomatic at presentation. Baseline clinical characteristics are detailed in Table 1. In patients with multiple meningioma, the median number of meningioma per patient was 2 (range 2-6). Twenty-nine (85.3%) patients had 2 meningioma, 4 (11.8%) had 3 and 1 (2.9%) had 6. Sixteen patients (47.1%) had their multiple meningioma in non-skull base locations, 5 (14.7%) in skull base locations and 13 (38.2%) had a mix of both. Baseline imaging characteristics, per patient and meningioma, are detailed in Table 1. Overall median follow-up was 85.9 months (IQR 47.6-105.8), with no difference between the two cohorts (P=0.454).

## Requirement for primary intervention

Treatment details are presented in Table 2. In total, 26 primary interventions (26/76, 24.2%) were performed in 23 (67.6%) patients with multiple meningioma (Figure 1). These were predominately for the index meningioma (n=22, 84.6%) and were surgery (n=21) and *f*RT (n=1). Four patients underwent treatment for a meningioma other than the index tumor; 3 after surgery for their index tumors (surgery, n=1; SRS, n=1; *f*RT, n=1) and 1 patient underwent SRS with no previous interventions. The rates of undergoing a primary intervention per patient did not differ between patients with multiple and solitary meningioma (67.6 vs 70.6%, P=0.792). Meningioma growth was the indication for treatment in 19.2% (5/26) of patients with multiple meningioma, compared to 16.7% (4/24) of patients with a solitary meningioma (P=0.816). The remainder underwent an intervention for a symptomatic meningioma. The median intervention-free survival was 3.4 months (95% CI 0-18.0) in patients with multiple meningioma compared to 8.3 (95% CI 0-87.1) in patients with solitary meningioma (P=0.918). The 5-year intervention free survival was 42% (95% CI 24.4-59.6) in patients with multiple meningioma compared to 34% (95% CI 18.3-49.7) in patients with solitary meningioma. In multivariable analysis, factors associated with an intervention were a symptomatic presentation (HR 14.7 [95% CI 6.1-35.7], P<0.001) and volume of index meningioma (HR 1.02 [95% CI 1.01-1.03], P<0.001) (Supplementary Table 1).

## Intervention outcome - surgery and adjuvant radiation

Treatment details for the cohort are presented in Table 2. Twenty-one patients (61.8%) with multiple meningioma underwent 22 primary surgical interventions, compared to 24 patients with a solitary meningioma (70.6%). Gross total resection (GTR) was achieved for 18 multiple meningioma (81.8%). Sixteen patients (66.7%) with a solitary meningioma had GTR. Histology revealed a WHO grade 2 tumor in 7 patients (31.8%) with multiple meningioma, and 7 (29.2%) with solitary meningioma (P=0.679). There were no cases of *de novo* WHO grade 3 tumors. After surgery, adjuvant radiation was administered to 1 patient with multiple meningioma (STR + WHO grade 1) and 8 patients with a solitary meningioma (P=0.013) (Figure 2). There were 8 recurrences in patients with multiple meningioma (36.4%) and 6 in patients with solitary meningioma (25.0%) (P=0.402). The overall median recurrence-free survival was 89 months (95% CI 76-104). The median recurrence-free survival was 73.5 months (95% CI 44.3-102.7) in the multiple meningioma group compared to 123.9 months (95% CI NA) in the solitary meningioma group, however this did not reach statistical significance (P=0.209) (Figure 3). In multivariable analysis, factors which were associated with recurrence were a higher WHO grade (HR 6.26 [95% CI 1.66-23.57], P=0.007) and adjuvant radiotherapy (HR 0.08 [95% CI 0.01-0.78], P=0.029) (Supplementary Table 2). Three recurrences in each group (multiple meningioma, 37.5%; solitary meningioma, 50%) were managed with salvage *f*RT/SRS with no further regrowth afterwards whilst the remainder continued to be actively monitored (P=0.639).

## Intervention outcome – primary SRS and *f*RT

Two meningioma received SRS (12.5Gy) and two had *f*RT (54Gy, 30 fractions). Indication for treatment was growth. Median follow-up duration after treatment was 42.9 months (IQR 15.6-83.4). Thirty-three months following surgery for an index convexity meningioma (WHO grade 1), one patient received SRS for a growing parafalcine meningioma. Twenty-six months later the patient developed leg weakness with further growth of the parafalcine meningioma and underwent surgery (GTR), which revealed a WHO grade 2 tumor. Thirty-seven months later, they underwent a reoperation for a recurrence with worsening leg weakness and the meningioma had undergone malignant transformation to grade 3. The patient remains alive 89 months following diagnosis with no further recurrences. There were no other incidences of regrowth.

## Overall survival and development of new meningioma

There was one meningioma-related death (2.9%) due to a hospital acquired pneumonia 28 days after surgery for a parafalcine meningioma. There were 5 other unrelated deaths (multiple meningioma, n=3, 8.8%; solitary meningioma, n=2, 5.9%). Mean overall survival was 132 months (95% CI 127-138) with no difference between multiple and solitary meningioma (P=0.860) (Figure 3). One patient with multiple meningioma developed two further new meningioma 36 months following diagnosis.

# **DISCUSSION**

In this single centre, retrospective matched cohort study, the outcomes of patients with sporadic multiple and solitary meningioma were investigated. Matching was based on the clinical characteristics of patients and the radiological features of the symptomatic meningioma or asymptomatic meningioma at higher risk of progression. Intervention-free survival, recurrence-free survival and overall survival did not differ between patients with sporadic multiple and solitary meningioma. These results suggest that sporadic multiple meningioma do not incur an increased risk of recurrence and worse overall survival, and that clinical management should be determined by the clinical characteristics and imaging features of the index tumor.

## Rate of intervention and outcomes following surgery and radiotherapy

The rate of intervention in this study was like other recent single-centre studies of patients with multiple meningioma. In a study of 133 patients, of whom half were asymptomatic at presentation, 64% of patients had received a primary treatment for 33% of meningioma by the end of the study period. Indications for treatment were similar to our practice including a symptomatic or growing asymptomatic meningioma (11). However, in a meta-analysis of studies of multiple meningioma, the rate of intervention was higher, with 44% of tumors having received an intervention by the end of follow-up. This was skewed by inclusion of studies which focused solely on treated multiple meningioma (12). Studies of intracranial meningioma on the whole demonstrated no association between meningioma multiplicity and patient outcomes. In a study assessing the prognostic relevance of multiple imaging and clinical features in 303 patients who underwent surgery, multiple meningioma were not associated with recurrence or overall survival (13). Likewise, in a study of 128 patients who underwent surgical resection of a meningioma, assessment of radiomic features demonstrated no relationship between recurrence and number of meningioma per patient (14). With regards to meningioma subject to conservative management, a study of 441 patients demonstrated no relationship between growth of tumor necessitating intervention and having multiple meningioma (10). Imaging features such as meningioma volume, peri-tumoral oedema and apparent diffusion coefficient values have been consistently shown to be associated with patient outcomes and we therefore matched for these in our study (10,13–15). Recent studies which did not match or adjust for these characteristics demonstrated that multiple meningioma were associated with worse recurrence-free and overall survival (8,16), which contrasts with our study and others (10,13–15). In our study, of the four patients who received radiation treatment, one continued to have meningioma growth requiring salvage surgery and eventually transforming into a WHO grade 3 meningioma. The patient also had another meningioma resected which was grade 1. This highlights that some sporadic multiple meningioma can have a more aggressive clinical course, and be of different grades and with different genomic changes (17).

## Role of genetic testing in patients with multiple meningioma

The patients with multiple meningioma in our study did not have other syndromic features (e.g., NF2-schwannomatosis) and therefore genetic testing was not performed. A recent study of 152 patients with multiple meningioma alone, reported that 7% and 5% had pathogenic variants in the *NF2* and *SMARCB1* genes, respectively (18)*.* These finding are of importance as they would implicate family members and likely influence the development of further meningioma and intracranial tumors such as vestibular schwannoma. In the aforementioned study, *SMARCB1* was found mostly in patients with both cranial and spinal meningioma (18). Moreover, their population was younger (median age 46 vs 58 years) and therefore more likely to have a tumor predisposition syndrome (18,19). Finally, approximately 40% of patients with NF2-schwannoamtosis develop *de novo* meningioma during follow-up (20). In our study, the rate of this was substantially lower - only 1 (2.9%) patient with multiple meningioma developed further tumors within the follow-up period. The current diagnostic criteria for NF2-schwannomatosis does not recognise the presence of multiple meningioma alone as a diagnostic feature (7). Further work is required to define the clinical features of patients with multiple meningioma and no other syndromic manifestations, but who may nevertheless harbor these genetic changes.

## Suggested management strategies

Our suggested management strategy for patients with multiple meningioma is presented in Figure 4. For patients who present with a symptomatic meningioma, this is defined as the ‘index meningioma’ and management may be tailored based on this. Upfront treatment for other meningioma is not recommended and these should be monitored with interval MRI, alongside monitoring for recurrence or regrowth of the treated meningioma. In patients with asymptomatic meningioma, the risk of each meningioma growth can be estimated using a prognostic tool such as IMPACT (10), and the highest-risk tumor should be defined as the ‘index meningioma’ and MRI follow-up should be tailored to this.

## Study limitations

Some limitations of the study should be noted. First, this was a single centre retrospective study, with a small sample size limited by treatment selection bias. However, all patients with multiple meningioma at presentation were analysed with no restriction based on initial treatment decision. Second, assessment of study outcomes was based on clinical notes and images with possible recall bias, and the use of intervention as an outcome was limited by patient and clinician biases. Third, the cohorts weren’t balanced for characteristics such as sex, meningioma location subclass, peri-tumoral signal intensity, extent of surgical resection and utility of adjuvant *f*RT/SRS. These variables however, apart from adjuvant *f*RT, were not associated with outcomes in multivariable analyses. Conversely, recurrence-free survival in patients with multiple meningioma was non statistically shorter than in patients with solitary meningioma and this may be attributed to the lower use rate of adjuvant *f*RT/SRS. Fourth, most patients had 2 meningioma: a large index lesion with 1 other much smaller meningioma. This mode of presentation for sporadic multiple meningioma is the most common, previously described as the “mother-son tumor” phenomenon (21). The study findings therefore may not be applicable to the rarer scenario of patients with ≥2 large meningioma. Fifth, assessment of quality of life was not possible with the data available.

**CONCLUSIONS**

Sporadic multiple meningioma may not have worse recurrence-free and overall survival compared to solitary meningioma. Management of patients should be tailored to the symptomatic meningioma or higher risk asymptomatic meningioma – the so-called ‘index meningioma’.

# **FIGURES**



Figure 1. A bar plot presenting the number of interventions in patients with solitary and multiple meningioma



Figure 2. Extent of resection and utility of adjuvant treatment with recurrence rates stratified by each



Figure 3. A) Recurrence-free survival and B) overall survival stratified by multiplicity of meningioma



Figure 4. Recommended management strategies for the management of patients with multiple meningioma at presentation

|  |
| --- |
| **TABLES**  |
| **Table 1. Baseline characteristics of the study cohort as a whole and by matched groups** |
| Patient Characteristics | Overall (n=68) | Multiple meningioma (n=34) | Solitary meningioma (n=34) | P-value |
| Age, mean (SD) | 58.3 (13.7) | 59.3 (13.5) | 57.3 (14.0) | 0.557 |
| Female sex, count (%) | 54 (79.4) | 31 (91.2) | 23 (67.6) | 0.036 |
| Performance Status 0-2, count (%) | 68 (100) | 34 (100) | 34 (100) | 0.999 |
| Incidental diagnosis, count (%) | 32 (47.1) | 16 (47.1) | 16 (47.1) | 0.999 |
| Duration of follow-up, median (IQR) | 85.9 (47.6-105.8) | 80.6 (43.7-100.9) | 91.1 (53.1-107-8) | 0.454 |
| **For index tumour** |
| Meningioma location, count (%) |  |  |  | 0.213 |
| Non-skull base | 44 (64.7) | 22 (64.7) | 22 (64.7) |  |
| Convexity | 18 (26.5) | 12 (35.3) | 6 (17.6) |  |
| Parasagittal | 9 (13.2) | 3 (8.8) | 6 (17.6) |  |
| Parafalcine | 10 (14.7) | 3 (8.8) | 7 (20.6) |  |
| Intraventricular | 3 (4.4) | 0 | 3 (8.8) |  |
| Tentorial | 3 (4.4) | 3 (8.8) | 0 |  |
| Pineal | 1 (1.5) | 1 (2.9) | 0 |  |
| Skull base | 24 (35.3) | 12 (35.3) | 12 (35.3) |  |
| Sphenoid wing | 15 (22.1) | 8 (23.5) | 7 (20.6) |  |
| Anterior midline | 4 (5.9) | 2 (5.9) | 2 (5.9) |  |
| Posterior fossa – lateral and posterior | 3 (4.4) | 1 (2.9) | 5 (5.9) |  |
| Posterior fossa – Midline | 2 (2.9) | 1 (2.9) | 1 (2.9) |  |
| Meningioma volume, median (IQR) | 9.0 (3.0-35.2) | 8.3 (2.0-30.7) | 10.1 (3.3-36.5) | 0.364 |
| Peri-tumoural signal intensity, count (%) | 24 (35.3) | 9 (26.5) | 15 (44.1) | 0.102 |
| Proximity to critical neurovascular structures, count (%) | 51 (75) | 25 (73.5) | 26 (76.5) | 0.779 |
| IMPACT score, median (IQR)\* | 2.3 (1.4-3.6) | 2.3 (1.2-3.9) | 2.3 (1.5-3.6) | 0.880 |
| **For all meningioma** |
| Number of meningioma, (range) | 110 (1-6) | 76 (2-6) | 34 (1-1) | - |
| Meningioma location, count (%) |  |  |  | 0.131 |
| Non-skull base | 72 (65.4) | 50 (65.8) | 22 (64.7) |  |
| Convexity | 34 (30.9)  | 28 (36.8) | 6 (17.6) |  |
| Parasagittal | 12 (10.9) | 6 (7.9) | 6 (17.6) |  |
| Parafalcine | 19 (17.3) | 12 (15.8) | 7 (20.6) |  |
| Intraventricular | 3 (2.7) | 0 | 3 (8.8) |  |
| Tentorial | 3 (2.7) | 3 (3.9) | 0 |  |
| Pineal | 1 (0.9) | 1 (1.3) | 0 |  |
| Skull base | 38 (34.5) | 26 (34.2) | 12 (35.3) |  |
| Sphenoid wing | 21 (19.1) | 14 (18.4) | 7 (20.6) |  |
| Anterior midline | 7 (6.4) | 5 (6.6) | 2 (5.9) |  |
| Posterior fossa – lateral and posterior | 7 (6.4) | 5 (6.6) | 2 (5.9) |  |
| Posterior fossa – Midline | 3 (2.7) | 2 (2.6) | 1 (2.9) |  |
| Total meningioma volume per patient, median (IQR) | 11.1 (3.3-34.3) | 12.9 (3.3-39.4) | 10.1 (3.3-36.5) | 0.904 |
| Meningioma volume, median (IQR) | 3.3 (0.7-12.7) | 1.4 (0.4-8.1) | 10.1 (3.3-36.5) | 0.001 |
| Peri-tumoural signal intensity, count (%) | 24 (21.8) | 9 (11.8) | 15 (44.1) | 0.001 |
| Proximity to critical neurovascular structures, count (%) | 73 (66.3) | 47 (61.8) | 26 (76.5) | 0.133 |
| IMPACT score, median (IQR)\* | 1.3 (-0.2-2.6) | 0.9 (-0.7-3.6) | 2.3 (1.5-3.6) | 0.001 |
| \* For asymptomatic tumours |

|  |
| --- |
| **Table 2. Treatment details for the study cohort** |
|  | Overall (n=68) | Multiple meningioma (n=34) | Solitary meningioma (n=34) |
| **For index tumour** |
| Surgery, count (%) |  |  |  |
| Primary | 45 (66.2) | 21 (61.2) | 24 (70.6) |
| *Simpson 1* | *15 (33.3)* | *9 (42.9)* | *6 (25.0)* |
| *Simpson 2* | *15 (33.3)* | *6 (28.6)* | *9 (37.5)* |
| *Simpson 3* | *3 (6.7)* | *2 (9.5)* | *1 (4.2)* |
| *Simpson 4* | *12 (26.7)* | *4 (19.0)* | *8 (33.3)* |
| Salvage | 0 | 0 | 0 |
| SRS, count (%)  |  |  |  |
| Primary | 0 | 0 | 0 |
| Adjuvant | 1 (1.6) | 0 | 1 (2.9) |
| Salvage | 2 (2.9) | 1 (2.9) | 1 (2.9) |
| *f*RT, count (%) |  |  |  |
| Primary | 1 (1.6) | 1 (2.9) | 0 |
| Adjuvant  | 8 (11.8) | 1 (2.9) | 7 (20.6) |
| Salvage | 4 (5.9) | 2 (5.9) | 2 (5.9) |
| **Due to other meningioma** |
| Surgery, count (%) |  |  |  |
| Primary | 1 (1.6) | 1 (2.9) | - |
| *Simpson 1* | *1 (100)* | *1 (100)* | *-* |
| Salvage | 1 (1.6) | 1 (2.9) | - |
| *Simpson 2* | *1 (100)* | *1 (100)* | *-* |
| SRS, count (%) |  |  |  |
| Primary | 2 (2.9) | 2 (5.9) | - |
| Adjuvant | 0 | 0 | - |
| Salvage | 0 | 0 | - |
| *f*RT, count (%) |  |  |  |
| Primary | 1 (1.6) | 1 (2.9) | - |
| Adjuvant  | 0 | 0 | - |
| Salvage | 0 | 0 | - |
| The percentages between brackets for Simpson’s grade of resection = the number of patients who underwent said extent of resection/number of patients who underwent surgery. Otherwise, the percentages between brackets are in relation to the overall number of patients or the number of patients with multiple or solitary meningioma  |

# **REFERENCES**

1. Goldbrunner R, Stavrinou P, Jenkinson MD, Sahm F, Mawrin C, Weber DC, et al. EANO guideline on the diagnosis and management of meningiomas. Neuro-Oncology. 2021 Nov 1;23(11):1821–34.

2. Ostrom QT, Patil N, Cioffi G, Waite K, Kruchko C, Barnholtz-Sloan JS. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2013–2017. Neuro-Oncology. 2020 Oct 30;22(Supplement\_1):iv1–96.

3. Brodbelt AR, Barclay ME, Greenberg D, Williams M, Jenkinson MD, Karabatsou K. The outcome of patients with surgically treated meningioma in England: 1999–2013. A cancer registry data analysis. British Journal of Neurosurgery. 2019 Nov 2;33(6):641–7.

4. Lusins JO, Nakagawa H. Multiple Meningiomas Evaluated by Computed Tomography. Neurosurgery. 1981 Aug 1;9(2):137–41.

5. Weill A, Nguyen P, Labidi M, Cadier B, Passeri T, Duranteau L, et al. Use of high dose cyproterone acetate and risk of intracranial meningioma in women: cohort study. BMJ. 2021 Feb 3;372:n37.

6. Gillespie CS, Islim AI, Taweel BA, Millward CP, Kumar S, Rathi N, et al. The growth rate and clinical outcomes of radiation induced meningioma undergoing treatment or active monitoring. J Neurooncol. 2021;153(2):239–49.

7. Plotkin SR, Messiaen L, Legius E, Pancza P, Avery RA, Blakeley JO, et al. Updated diagnostic criteria and nomenclature for neurofibromatosis type 2 and schwannomatosis: An international consensus recommendation. Genetics in Medicine [Internet]. 2022 Jun 8 [cited 2022 Aug 26];0(0). Available from: https://www.gimjournal.org/article/S1098-3600(22)00773-0/fulltext

8. Ramos-Fresnedo A, Domingo RA, Vivas-Buitrago T, Lundy L, Trifiletti DM, Jentoft ME, et al. Multiple meningiomas: does quantity matter? a population-based survival analysis with underlined age and sex differences. J Neurooncol. 2020 Sep;149(3):413–20.

9. Nassiri F, Wang JZ, Au K, Barnholtz-Sloan J, Jenkinson MD, Drummond K, et al. Consensus core clinical data elements for meningiomas (v2021.1). Neuro-Oncology. 2022 May 1;24(5):683–93.

10. Islim AI, Kolamunnage-Dona R, Mohan M, Moon RDC, Crofton A, Haylock BJ, et al. A prognostic model to personalize monitoring regimes for patients with incidental asymptomatic meningiomas. Neuro-Oncology. 2020 Feb 20;22(2):278–89.

11. Tsermoulas G, Turel MK, Wilcox JT, Shultz D, Farb R, Zadeh G, et al. Management of multiple meningiomas. Journal of Neurosurgery. 2017 Jul 21;128(5):1403–9.

12. Araújo Pereira BJ, Nogueira de Almeida A, Pires de Aguiar PH, Paiva WS, Teixeira MJ, Nagahashi Marie SK. Multiple Intracranial Meningiomas: A Case Series and Review of the Literature. World Neurosurgery. 2019 Feb 1;122:e1536–41.

13. Morin O, Chen WC, Nassiri F, Susko M, Magill ST, Vasudevan HN, et al. Integrated models incorporating radiologic and radiomic features predict meningioma grade, local failure, and overall survival. Neurooncol Adv. 2019 Dec;1(1):vdz011.

14. Ko CC, Zhang Y, Chen JH, Chang KT, Chen TY, Lim SW, et al. Pre-operative MRI Radiomics for the Prediction of Progression and Recurrence in Meningiomas. Front Neurol. 2021 May 14;12:636235.

15. Hwang WL, Marciscano AE, Niemierko A, Kim DW, Stemmer-Rachamimov AO, Curry WT, et al. Imaging and extent of surgical resection predict risk of meningioma recurrence better than WHO histopathological grade. Neuro-Oncology. 2016 Jun 1;18(6):863–72.

16. Ramos-Fresnedo A, Domingo RA, Sanchez-Garavito JE, Perez-Vega C, Akinduro OO, Jentoft ME, et al. The impact of multiple lesions on progression-free survival of meningiomas: a 10-year multicenter experience. Journal of Neurosurgery. 2021 Nov 19;137(1):9–17.

17. Juratli TA, Prilop I, Saalfeld FC, Herold S, Meinhardt M, Wenzel C, et al. Sporadic multiple meningiomas harbor distinct driver mutations. acta neuropathol commun. 2021 Jan 6;9(1):8.

18. Hannan CJ, Hammerbeck-Ward C, Pathmanaban ON, Smith MJ, Rutherford SA, Lloyd SK, et al. Multiple Meningiomas as a Criterion for the Diagnosis of Neurofibromatosis Type 2 and Other Tumor Predisposition Syndromes. Neurosurgery. 2022 Jun;90(6):793–9.

19. Pathmanaban ON, Sadler KV, Kamaly-Asl ID, King AT, Rutherford SA, Hammerbeck-Ward C, et al. Association of Genetic Predisposition With Solitary Schwannoma or Meningioma in Children and Young Adults. JAMA Neurol. 2017 Sep 1;74(9):1123–9.

20. Jaoude SA, Peyre M, Degos V, Goutagny S, Parfait B, Kalamarides M. Validation of a scoring system to evaluate the risk of rapid growth of intracranial meningiomas in neurofibromatosis type 2 patients. Journal of Neurosurgery. 2020 May 22;134(5):1377–85.

21. Wang L, Chen W, Liu F, Zhang LF, Chen J. Letter to the Editor. Multiple meningiomas. Journal of Neurosurgery. 2018 May 1;128(5):1593–4.