Original Article

# Brief Insight About Management Of Meningioma

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## Abstract

**Background:** Meningiomas account for approximately 1/3 of primary intracranial tumours in adults, with an age-adjusted incidence rate of approximately 7 per 100,000 person-years. meningiomas comprises 37.6% of all primary CNS tumors and 53.3% of all benign CNS tumors. Meningiomas arise from meningothelial (arachnoid) cells (MECs). These cells are a cellular component of the pia mater, arachnoid mater, and the trabeculae and septae of the subarachnoidal space. Arachnoid cap cells make up the outer layer of the arachnoid mater and arachnoid villi and with cytological similarities to meningiomas cells, it is likely their cell of origin. Meningiomas are most commonly seen in the following areas: convexity (lateral hemisphere) (20–37%); parasagittal (medial area of hemispheres) (13–22%) (includes falcine meningiomas (5%)); spinal (7–12%); skull base (43–51%); frontobasal (10–20%); sphenoid and middle cranial fossa (9–36%); posterior fossa (6–15%); tentorium cerebelli (2–4%); cerebellar convexity (5%); cerebellopontine angle (2–11%); foramen magnum (3%); and petroclival (<1–9%); intraventricular (1–5%); orbital (<1–2%); and ectopic locations (<1%). The presentation of meningiomas are often non-specific, but location and compression of adjacent brain and vascular structures can lead to focal neurologic deficits (including cranial nerve deficits) [54]. Symptoms that are commonly seen are as follows: headache (33.3–36.7%), focal cranial nerve deficit (28.8–31.3%), seizure (16.9–24.6%), cognitive change (14.4%), weakness (11.1%), vertigo/dizziness (9.8%), ataxia/gait change (6.3%), pain/sensory change (5.6%), proptosis (2.1%), syncope (1.0%), and asymptomatic (9.4%). management for meningiomas is highly individualized and includes a combination of observation, surgical resection, radiotherapy, and rarely chemotherapy. The potential consequences of different treatments can vary greatly. Through recent advances in neurosurgery, neuroimaging, and neuroanesthesia, patients are experiencing better long-term outcomes, retreatment free survival, and overall survival. Surgical resection is the primary choice for symptomatic, observation failure meningiomas, or large tumors that are anticipated to causes symptoms soon. gross total resection (GTR) can cure the majority (70–80%) of patients. Radiation therapy (RT) has become a first-line treatment for unresectable meningiomas, such as certain skull base meningiomas that have encased neurovascular structures. Patients who develop recurrent or progressive meningiomas that no longer respond to surgery or radiotherapy are treated with salvage systemic therapy. The National Comprehensive Cancer Network (NCCN) recommends the use of α-IFN, somatostatin receptor agonists, and vascular endothelial growth factor (VEGF) inhibitors for the treatment of meningioma.

**Keywords:** Meningioma

## INTRODUCTION

Meningiomas account for approximately 1/3 of primary intracranial tumours in adults, with an age-adjusted incidence rate of approximately 7 per 100,000 person-years [1]. meningiomas comprises 37.6% of all primary CNS tumors and 53.3% of all benign CNS tumors. The incidence of meningiomas increases with age, with the median age at diagnosis being 66 years old [2]. The incidence rate in patients age 40+ years is 18.69/100,000 and in age 0–19 years it is 0.16/100,000 [2]. In patients age 40+ years, age 15–39 years, and age 0–14 years, meningiomas make up 43.6%, 15.6%, and 1.7% of all CNS tumors, respectively [2].
Benign and malignant meningiomas are more common in females versus males, with incidence rate ratios of 2.33 and 1.12, respectively [2]. Females and males in the age 0–19 year range had similar incidence ratios of meningiomas [2]. Children most often have higher grade meningioma with a higher risk of recurrence and decreased overall mortality [4][5].

Benign and malignant meningiomas were also more common in Black people versus Whites people, with incidence ratios of 1.18 and 1.52, respectively [2]. At autopsy, incidental meningiomas were found in 2–3% of patients [6].

Understanding the natural history of meningiomas is imperative for clinicians with a growing amount of incidental meningiomas now detected secondary to advanced imaging studies. meningiomas are generally slow growing lesions with a linear growth rate of 2–4 mm/year for asymptomatic meningiomas [7]. In a retrospective study in which incidental meningiomas were followed by imaging, approximately a third of the tumors did not grow at all. However, of those that grew, nearly 25% grew

exponentially, further underscoring the importance of surveillance imaging in untreated patients [7]. The natural course of symptomatic larger lesions is deemed anecdotally to be a more aggressive growth pattern, but these lesions are rarely left untreated, and therefore, their true natural history remains ill-defined [8].

Recurrence is a function of surgical resection, location and the histological grade of the meningioma, although location and surgical resection are somewhat interlinked [9].

In terms of recurrence differences with grade, the five-year progression free survival (PFS) for a WHO grade I tumors is ~90% after gross total resection (GTR), Grade II are ~ 60%–90%, whereas grade III PFS after GTR is 28% [10]. These recurrences translate into meningioma-specific mortality in these patients, with 10-year overall survival rates of 53% for grade II patients and 0% for grade III patients, despite aggressive therapeutic efforts [11].

**Meningioma Cell of Origin:**

Meningiomas arise from meningothelial (arachnoid) cells (MECs). These cells are a cellular component of the pia mater, arachnoid mater, and the trabeculae and septae of the subarachnoidal space. Arachnoid cap cells make up the outer layer of the arachnoid mater and arachnoid villi and with cytological similarities to meningiomas cells, it is likely their cell of origin [12]. Meningiomas are tumors of the meninges but they also occur rarely as primary tumors in the ventricles of the CNS and extracranial organs such as the lungs, presumably from aberrant MECs. They make up a monolayer covering of the meninges and are connected via tight junctions, gap junctions, and desmosomes, providing an interface between neuronal tissue and the cerebrospinal fluid (CSF) [12]. Aside from providing a physical barrier to the CNS and protecting it from mechanical damage, MECs also play a significant role in immunological processes and the maintenance of homeostasis and host defense in the CSF [13]. Through secretion of pro- and anti-inflammatory chemokines and cytokines, MECs are able to initiate and quench immune reactions [14]. MECs also protect against infection and neurodegeneration via phagocytosis of bacteria and apoptotic bodies, as well as macropinocytosis of neurotoxic peptides and proteins, respectively [14] [13]. MECs have different embryologic origins depending on their anatomic locations. MECs found at the skull base and cerebral convexity have mesoderm and neural crest origins, respectively. This difference affects the predominating histological subtypes of meningiomas that arise from these cells and the distribution of recurrent somatic mutations [12].

**Historical Overview of Meningioma classification :**

The earliest known attempt to classify dural tumors was that of Virchow in 1863, followed by Engert in 1900 who described four types: fibromatous, cellular, sarcomatous, and angiomatous. Cushing and Bailey in 1920 approached the classification of meningiomas in terms of their anatomic location (frontal, paracentral, parietal, occipital, and temporal) as well as histopathologic features (meningothelial, fibroblastic, angioblastic, and osteoblastic). The latter four histological categories were expanded by Bailey and Bucy in 1931 to include nine histological subtypes. In 1938, Cushing and Eisenhardt distinguished 9 main types and 20 subtypes of meningioma based on anatomical sites and histological characteristics, later simplified by a working classification in 1941 to five major types: syncytial, fibroblastic, transitional, angioblastic, and mixed patterns [15].

The first World Health Organization (**WHO**) classification of CNS tumors, published under the "Histologic Typing of tumors of the Central Nervous System" or the "Blue book" in 1979 described six subtypes of Grade I meningiomas, including hemangioblastic and hemangiopericytic subtypes. This classification also included papillary and anaplastic meningioma, which corresponded to either Grade II or III [16]. Its revision in 1993 went on to include 11 subtypes of benign meningiomas in addition to papillary, atypical, and anaplastic meningiomas while also recognizing hemangiopericytoma as a class of mesenchymal/non-meningothelial tumors [17]. However, it continued to be plagued by the use of imprecise terminology, such as "increased" cellularity and "frequent" mitoses in defining various grades of meningioma. The 2000 and 2007 revisions to the WHO classification did not greatly enhance our understanding of the genetic basis of these tumors, and merely served to add a category of rhabdoid meningiomas, based on histology, while refining the histological criteria used in the diagnosis of atypical and anaplastic meningiomas[15].

The 2016 classification was heralded as the first to break with the principle of diagnosis based entirely on microscopy, integrating molecular parameters into the classification of CNS tumor entities. Due to the lack of broad availability of genotype testing at the time, the classification relied on "integrated diagnoses" combining genotypic and phenotypic features and set the stage for a paradigm shift to solely genotype-based classification with minimal reliance on histologic features [16-18]. While previously ambiguous histological categories, such as the oligoastrocytoma benefitted from the increased objectivity afforded by the use of molecular markers, and ependymomas, gliomas and medulloblastomas were effectively prognosticated based on genotype [19], meningiomas continued to be classified purely on the basis of histology. The major change in their grading was the introduction of brain invasion as a histological criterion for the diagnosis of atypical WHO Grade II meningioma, before which it was included as a "staging" factor that predicted recurrence and higher mortality rates regardless of grade [18]. The WHO Grade of II was assigned to atypical meningiomas and meningiomas with chordoid or clear cell morphology, whereas the WHO Grade of III was assigned to anaplastic, papillary, and rhabdoid meningiomas.

While the current WHO grades appear to have a significant bearing on the prognosis of meningiomas, they suffer from suboptimal reproducibility as demonstrated by the NRG Oncology Radiation Therapy Oncology Group **(**RTOG) Trial 0539, which reported a concordance rate for tumor Grade of 87.2% in a series of 172 patients. They concluded that the development of biomarkers was a more promising strategy than the clarification of subjective histologic criteria [19,20]. The 2021 WHO

CNS5 classification apart from the introduction of Arabic numerals for the different grades, incorporated a change in terminology, classifying all meningiomas as a single "type" and all 15 histologic entities as "subtypes." This amendment maintained the grading of meningiomas as before, with clear cell, chordoid, and atypical morphology assigned to WHO Grade 2 and papillary, rhabdoid, and anaplastic assigned to WHO Grade 3 [21]. The WHO CNS5 however advises that the WHO Grade of 2 and 3 should be assigned not solely on the basis of the histological subtype but with applying the histological criteria for WHO grade 2 and 3 [21].

Several molecular biomarkers have also been introduced, that serve an adjunctive role in classification and grading, such as *SMARCE1* for clear cell subtype, *BAP1* for rhabdoid subtype, *KLF4/TRAF7* for secretory subtype, *TERT* promoter mutations, and/or homozygous deletion of *CDKN2A/B* for WHO Grade 3, and loss of nuclear expression of *H3K27me3* signaling worse prognosis and methylome profiling for prognostic subtyping [15].

**Meningiomas grading**

The WHO grade system is based on the histological features of meningioma.

Grade 1 constitutes more than 80% of meningiomas, includes nine histological variants, and lacks anaplastic features that can be seen in other grades. These variants include meningothelial, fibroblastic, transitional or mixed, psammomatous, angiomatous, microcystic, secretory, lymphoplasmacyte-rich, and metaplastic subtypes. More than 70% of meningiomas are positive for progesterone receptors. One of the histopathological characteristics of meningiomas is the growth of meningothelial cells that eventually mineralize to form psammoma bodies. Hyperostosis of the bone adjacent to the tumor can sometimes be identified [22].

Grade 2 are atypical lesions characterized by three or more of the following: necrosis, sheet-like growth, prominent nuclei, increased cellularity, or high nucleus/cytoplasm ratio. An increased mitotic activity (4-19 mitoses per 10 high-power fields), will also indicate an atypical tumor. The histological variations included in this grade include atypical, clear, and chordoid cell subtypes. A meningioma with brain invasion is now considered a grade 2 tumor [22] [18].

Grade 3 are anaplastic, malignant lesions that can be similar to high-grade sarcomas, carcinoma, or melanomas with a high rate of distant metastases. A high mitotic activity (20 or more mitoses per 10 high-power fields) will also indicate a grade 3 lesion. The histological variations of this grade include papillary and rhabdoid subtypes [22-26].

Cystic meningioma represents a meningioma with intratumoral or peritumoral cysts. It accounts for about 4 to 7% of meningiomas. A cystic meningioma might be challenging to differentiate from an intra-axial glial or metastatic tumor. There are several hypotheses postulated on how cystic meningiomas are formed [23-29]. Tumor degeneration or necrosis explains that the cystic formation is due to the macro-cavitation. This phenomenon results from the molecular pathogenesis of the tumor due to an intracellular regressive process. Oasis phenomenon is another explanation that occurs due to the development of an arteriolar hyalinization in the intratumoral cavity leading to ischemic necrosis. Other hypotheses include that the cystic formation might be secreted directly from the meningioma or originating from a peripheral arachnoid cyst containing CSF. Intracranial cystic meningiomas are classified into four types, according to Nauta classification [30-36]

**Molecular markers in Meningiomas :**

The genetic profiles of meningiomas have been the focus of a great deal of work between the 2016 and 2021 editions of the WHO classification. This work has resulted in the association of specific mutations with particular morphological subtypes or locations (for example, BAP1 mutations in rhabdoid meningiomas, SMO mutations in olfactory groove meningiomas, and KLF4 and TRAF7 mutations in secretory meningiomas). However, unlike the gliomas and embryonal tumours, none of the gene-specific molecular alterations drive prognosis, with two exceptions — TERT promoter mutations and homozygous CDKN2A/B deletion [37]. When either of these lesions is encountered, the meningioma is grade 3, even if it does not quite meet the histopathological criteria for a grade 3 meningioma [38]. Although most individual gene alterations do not seem to be prognostically important, evidence indicates that larger chromosomal alterations (such as chromosome 1p loss) and methylation subclusters might provide better outcome stratification when incorporated into multivariable algorithms alongside histopathology, TERT and CDKN2A/B [39-44]. Another important change in the 2021 WHO scheme is that meningiomas that have rhabdoid or papillary patterns by histology are no longer automatically considered WHO grade 3 tumours, as long as other histopathological and/or molecular features of grade 3 tumours are absent [45-50].

From a clinical perspective, the 2021 WHO classification scheme does not substantially change how meningiomas are managed. Patients with complete resection of grade 1 and grade 2 meningiomas can be observed, although adjuvant radiation therapy is an option for patients with grade 2 meningiomas [38]. Whether grade 1 and grade 2 meningiomas that are completely resected but have molecular alterations associated with worse prognosis (such as specific chromosomal copy number alterations) should be treated with adjuvant radiation therapy is an evolving area of research that requires more definitive studies [50-55]. Patients with incompletely resected grade 2 meningioma, and all patients with grade 3 meningioma, require postoperative radiation therapy. This includes meningiomas that appear low-grade when assessed by light microscopy but have a TERT promoter mutation and/or CDKN2A/B deletion. However, as described above, emerging data suggest that more extensive revisions to the classification of meningiomas are likely to occur in the next edition of the WHO scheme, informed by ongoing clinical trials such as RTOG 0539. Future revisions to meningioma classification should help determine which patients require more aggressive postsurgical adjuvant therapy, as well as select patients for specific clinical trials [38].

**Presenting Locations**

Meningiomas are most commonly seen in the following areas: convexity (lateral hemisphere) (20–37%); parasagittal (medial area of hemispheres) (13–22%) (includes falcine meningiomas (5%)); spinal (7–12%); skull base (43–51%); frontobasal (10–20%); sphenoid and middle cranial fossa (9–36%); posterior fossa (6–15%); tentorium cerebelli (2–4%); cerebellar convexity (5%); cerebellopontine angle (2–11%); foramen magnum (3%); and petroclival (<1–9%); intraventricular (1–5%); orbital (<1–2%); and ectopic locations (<1%) [52].

Grade I meningiomas are more likely to be found at the skull base, whereas higher grade meningiomas are more likely to be found at the convexity, parasagittal, falcine, torcular, and intraventricular regions [53]. Multiple meningiomas with and without NF2 alterations are present in 1% and 4% of patients, respectively. Because of these characteristic locations for meningiomas, imaging can often be sufficient in the diagnosis[43].

**Signs and Symptoms**

The presentation of meningiomas are often non-specific, but location and compression of adjacent brain and vascular structures can lead to focal neurologic deficits (including cranial nerve deficits) [54]. Symptoms that are commonly seen are as follows: headache (33.3–36.7%), focal cranial nerve deficit (28.8–31.3%), seizure (16.9–24.6%), cognitive change (14.4%), weakness (11.1%), vertigo/dizziness (9.8%), ataxia/gait change (6.3%), pain/sensory change (5.6%), proptosis (2.1%), syncope (1.0%), and asymptomatic (9.4%) [52].

Skull base meningiomas present more often with neurological deficits and non-skull base meningiomas are more likely to present with seizures [55]. Anterior cranial fossa meningiomas (anterior falcine, olfactory groove, or orbitofrontal) are often large at presentation and present with impaired vision (54%), headache (48%), anosmia (40%), seizure (20%), psychomotor symptoms, and behavioral disturbance with personality disintegration [43]. Along with gradual personality changes with apathy and dementia, anterior falx meningiomas often present with a long history of headache and optic atrophy. Parasagittal meningiomas can grow to considerable size before presenting with symptoms. They mostly present with Jacksonian seizures of the lower limbs or headache and advanced anterior parasagittal meningiomas, which are characteristically present with papilledema and homonymous hemianopia. Tuberculum sellae meningiomas usually present with insidious unilateral visual loss, followed by scotomatous defects in the other eye [43].

Suprasellar meningiomas may present with only minor hormonal abnormalities. Lateral sphenoid wing meningiomas often present with painless unilateral exophthalmos, followed by unilateral loss of vision. Temporal lobe meningiomas frequently presented with seizures [43]. Petroclival meningiomas can present with ataxia and cranial nerve neuropathies such as trigeminal nerve impairment [56]. Clinoidal meningiomas often present with a wide variety of visual impairment, cranial nerve palsies, and exophthalmos [43].

Posterior cranial fossa meningiomas can develop obstructive hydrocephalus and present with papilledema and early-morning headache. Peritorcular meningiomas symptoms are commonly caused by compression of the occipital lobe or the cerebellum and present with a headache with occipital localized pain, papilledema, and homonymous field deficits, as well as ataxia, dysmetria, hypotonia, and nystagmus. Spinal meningiomas, which are most common in the thoracic spine, present with slowly progressive spastic paresis with or without radicular or nocturnal pain. Cervical spine and craniocervical junction are the second most common sites of spinal meningiomas and present with spastic quadriparesis with or without low bulbar signs. Meningiomas close to the bone can cause focal hyperostosis and is almost invariably a sign of bone invasion by meningioma cells and can cause bulging of bones and localized pain [43].

Spontaneous bleeding rarely occurs and are seen more in patients less than 30 and older than 70 years old [57]. Spontaneous bleeding has an overall mortality rate of 21% and patients with spontaneous bleeding who are unable to regain consciousness before surgical intervention has an overall mortality rate of 75% [58]. Elderly patients 70+ years old are more likely to present with sensory-motor deficits (38.3%) and cognitive impairments (28.8%) [59].

**Diagnostics**

The initial tentative diagnosis of meningiomas can be made via magnetic resonance imaging (MRI) or contrast-enhanced computed tomography (CT) in patients with contraindications to MRI (e.g., pacemaker) [60]. With high expression of somatostatin receptor 2 (SSTR2) on meningioma cells, positron emission tomography (PET) imaging using SSTR ligands such as 68Ga-DOTATOC and 68Ga DOTATATE has been used as a diagnostic tool and to help delineate healthy tissue from meningiomas [61]. Meningiomas on MRI are usually hypo- to isointense relative to the cerebral cortex on T1-weighted sequences and iso- to hyperintense on T2-weighted sequences, displaying strong homogeneous enhancement following administration of gadolinium contrast. Although not specific and demonstrated in other dural neoplasms, a dural tail can be seen in 72% of meningiomas on postcontrast imaging and can help differentiate meningiomas from other extra-axial tumors such as schwannomas and pituitary adenomas. Heterogenous appearance can be caused by the presence of intratumoral cysts, hemorrhage, or necrosis and may be associated with more aggressive behavior of the tumor [62]. Meningiomas on CT usually appear isodense relative to cerebral cortex but can occasionally be hyperdense or slightly hypodense [60]. Meningiomas usually present as a sharply circumscribed lobular mass with a broad-based dural attachment and demonstrate homogenous enhancement following iodine contrast administration [62]. CT is more sensitive than MRI in detecting hyperostosis, intratumoral calcifications, and interosseous tumor growth [61].

Histological verification helps rule out other diagnosis such as metastasis [61]. Often inconspicuous or absent, meningiomas can present with histologic features such as pathognomonic whorls, and intranuclear cytoplasmic pseudoinclusions and psammoma bodies [11]. Many other dural masses including primary neoplastic processes, metastases, granulomatous diseases and infections can mimic meningiomas [63]. Meningioma mimics presented in the convexity (40%), parafalcine (24%), and skull base (24%). The most common meningioma mimics were hemangiopericytoma/solitary fibrous tumor (HPC/SFT),

followed by metastatic lesions and schwannomas [64].

**Management of meningiomas**

management for meningiomas is highly individualized and includes a combination of observation, surgical resection, radiotherapy, and rarely chemotherapy. The potential consequences of different treatments can vary greatly [61]. Through recent advances in advancements in neurosurgery, neuroimaging, and neuroanesthesia, patients are experiencing better long-term outcomes, retreatment free survival, and overall survival [65].

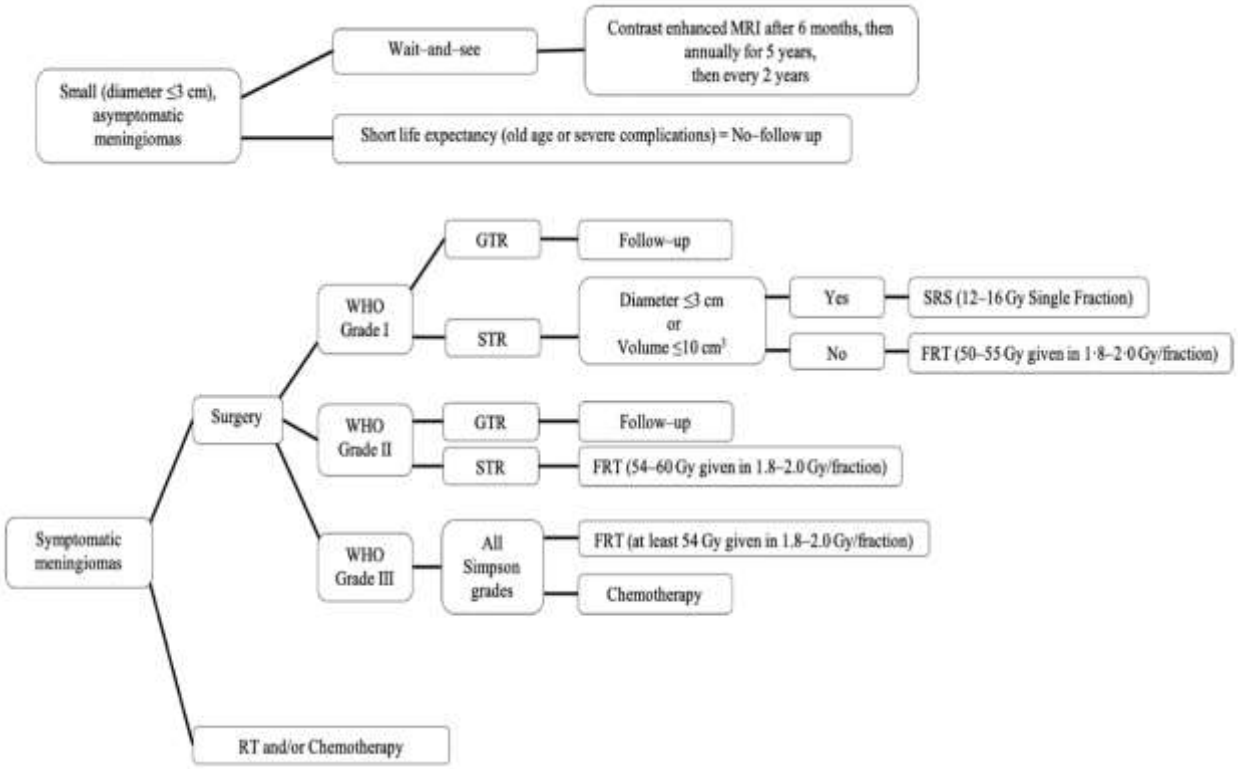


**Figure 1.** Summary of recommended management of meningiomas. SRS, stereotactic radiosurgery; FRT, fractionated radiotherapy; GTR, gross total resection; STR, subtotal resection.

**Observation and symptomatic treatments:**

The "wait-and-see" observation approach is a common strategy used for patients with incidentally diagnosed meningiomas that are small (tumor diameter ≤3 cm) and asymptomatic. Most definitions were based on a certain extent of growth, such as an increase in the maximal diameter > 2 mm/year or an increase in volume > 15% from the previous value/year [12].

Asymptomatic meningioma may remain undiscovered because of the tumor's slow growth. In such cases, conservative follow-up is apparently a better choice than an operation because it avoids postsurgical complications. The key to a conservative treatment decision is the careful evaluation of the growth possibilities of the meningioma that can be predicted using a patient's clinicoradiologic factors such as age, gender, tumor location, calcification, MRI T2 signal intensity, and peritumoral brain edema. However, so far the associations between tumor growth and the parameters just listed have not always been consistent [66].

A number of radiological features have been consistently linked to growth potential: peritumoral edema and hyperintense signal on T2W-MRI have been associated with rapid tumor growth, whereas the presence of calcification and hypointense signal on T2W-MRI tend to be associated with low growth potential. These results are supported by pathological examination [67],

Two factors, tumor calcification and low MRI T2 signal intensity, indicate slow growth or even no growth of meningioma. In such cases of asymptomatic meningioma, a follow-up strategy can be preferentially considered [66].

For instance, if a patient has tumor calcification or a low signal in the MRI T2 sequence, a follow-up observation with neuroimaging and clinical monitoring can be preferentially considered. The follow-up interval can be as long as 6 months or 1 year. However, if the imaging examination does not find calcification or low signal in the MRI T2 sequence, the possibility of rapid growth exists within such tumors. However, because the patient manifests no symptoms, follow-up imaging could still be suggested at the early stage, and the follow-up interval should be shorter. As suggested by several studies, the reexamination of imaging should be done 3 months after diagnosis to exclude atypical or malignant meningioma or other non-meningioma lesions [66].

These patients are observed and followed with MRI scans until they become symptomatic or until their tumors are considered large enough to treat in order to prevent future symptoms [73]. Some tumors will not progress. According to the European Association of Neuro-Oncology (EANO), after initial diagnosis they suggest performing a contrast enhanced MRI 6 months

later to evaluate for tumor changes [61]. If the patient remains asymptomatic, he can be followed up annually for 5 years and then every 2 years thereafter . Patients that have a clear radiological diagnosis of benign meningioma with shorter life expectancy due to old age or severe complications do not need to be observed [61].

Symptomatic treatments include oral or intravenous steroids, that may help improve the mass effect by reducing peripheral edema to temporarily relieve the symptoms, for instance before surgery. Antiepileptic drugs are introduced only in epileptic patients, and preventive treatment is not recommended. Surgical removal helps achieving seizure freedom in 70% of preoperatively epileptic patients, but it can also induce epilepsy, in 12% of the preoperatively non-epileptic patients [74].

**Surgery:**

Surgical resection is the primary choice for symptomatic, observation failure meningiomas, or large tumors that are anticipated to causes symptoms soon. GTR can cure the majority (70–80%) of patients [75]. The goal for surgery is Gross Total Resection GTR (Simpson I, GTR); however, the ability to achieve this may be limited by various factors, including tumor location, involvement of venous sinuses and neurovascular tissue, and other patient factors affecting safety of surgery in general. These factors influence the decision to pursue surgery, the surgical approach, and the extent of resection [11]. The extent of resection, defined by the Simpson grade, heavily impacts the rates of recurrence for surgically treated meningioma of all WHO grades [61]. The Simpson grade is defined by postoperative imaging and the neurosurgeon's assessment [11]. Over time, there has been an increase in the rate of GTR achieved [65]; however, most neurosurgeons focus on a better functional outcome over tumor resection outcome. functional outcome of patients with tumors of the cerebral convexity have significantly better outcomes, and those with petroclival meningiomas and meningiomas of the foramen magnum have relatively adverse outcomes. Additional significant outcome predictors in the univariate analysis included patient age, tumor size, and the degree of resection [76].

**Table 1: Simpson grades of meningioma resection.**

| Extent of Resection | Simpson Grade | Description |
|---|---|---|
| Gross Total Resection (GTR) | Grade 1 | Gross total resection of tumor, dural attachment, and involved bone (extradural extension) |
| | Grade 2 | Gross total resection of tumor, coagulation of dural attachment |
| | Grade 3 | Gross total resection of tumor without resection or coagulation of dural and extradural components |
| Subtotal Resection (STR) | Grade 4 | Partial (subtotal) resection of tumor |
| -- | Grade 5 | Biopsy only |

Intracranial meningiomas can be completely removed with a morbidity and mortality risk within acceptable limits. The location of the tumor has an impact on the extent of resection, as tumors were completely removed in the majority of patients with convexity meningiomas, while incomplete removal of the tumors was observed mostly in cases of skull base meningiomas. The only risk factor for perioperative neurological deterioration was a critical tumor location such as localization at the skull base or in an eloquent area, as well as large vessels involvement by tumor [77].

**Radiation**

Radiation therapy (RT) has become a first-line treatment for unresectable meningiomas, such as certain skull base meningiomas that have encased neurovascular structures [75]. With a lack of data from randomized controlled clinical trials comparing different RT for meningiomas, most RT data is based on retrospective studies [11]. In WHO grade I, meningiomas after subtotal resection (Simpson IV, STR) or in the setting of recurrence of previously resected meningiomas, stereotactic radiosurgery (SRS), or fractionated radiotherapy (FRT) can be offered. SRS (12–16 Gy single fraction) is used in small tumors (<3 cm in diameter) and FRT (50–55 Gy given in 1.8–2.0 Gy per fraction) is used when the tumor volume cannot be treated with a single fraction [43]. Even after Simpson I resection, WHO grades II and III meningiomas have a high risk of recurrence (30–40% and 50–80% after 5 years, respectively) [75]. Therefore, adjuvant RT is often apart of initial treatment after surgery in WHO grades II and III meningiomas, with FRT being preferred over SRS. Data for RT in WHO grade II meningiomas after GTR remains unclear but it is recommended that WHO grade II STR receive adjuvant FRT (54–60 Gy given in 1.8–2.0 Gy per fraction) and WHO grade III receive adjuvant FRT (at least 54 Gy given in 1.8–2.0 Gy per fraction), regardless of GTR or STR [43].

Patients who develop recurrent or progressive meningiomas that no longer respond to surgery or radiotherapy are treated with salvage systemic therapy [75]. The EANO considers the use of systemic therapy to be experimental with only level C evidence,

thus no specific recommendations are given [61]. The National Comprehensive Cancer Network (NCCN) recommends the use of α-IFN, somatostatin receptor agonists, and vascular endothelial growth factor (VEGF) inhibitors for the treatment of meningioma [78]; however, efficacy is greatly limited.

**Outcomes and Natural History of Meningioma**

Meningiomas are typically slow growing, with a linear growth rate of 2–4 mm/year for asymptomatic meningiomas. However, a third of all meningiomas experience no growth and of the meningiomas that grow, 25% experience exponential growth [43]. The most reliable prognostic factors of meningiomas are the histological grade (WHO grade) and the extent of tumor resection (Simpson grade) [79]. A number of radiological features have been consistently linked to growth potential: peritumoral edema and hyperintense signal on T2W-MRI have been associated with rapid tumor growth and may suggest a higher-grade meningioma, whereas the presence of calcification and hypointense signal on T2W-MRI tend to be associated with low growth potential and lower-grade meningioma. These results are supported by pathological examination [67].

Overall survival (OS) as a metric is strongly dependent upon the WHO grade classification. The 10-year overall survival rate of WHO grades 1, 2, and 3 tumors are 83.7%, 53%, and 0%, respectively, despite aggressive therapy effort [43]. Grade I meningiomas have the best survival outcomes, as compared to those of higher grades. A meta-analysis of asymptomatic, untreated meningiomas smaller than 3 cm in diameter revealed no tumor growth for a period of 5 years after radiological diagnosis. Grade 1 meningiomas have a reported mean OS of over 10 years [80] [81]. Patient outcome for grade 2 meningiomas is largely infuenced by the extent of resection and subsequent treatment. The 5-year OS for grade 2 meningiomas is between 80 and 100% [80]. Patients with grade III meningiomas unfortunately have worse outcomes. Median OS of patients with grade III meningiomas is 2–3 years [82].

Benign and malignant spinal meningiomas had a higher 10 year survival rate of 95.6% and 73.4%, respectively, than benign and malignant cerebral meningiomas of 83.2% and 55.7%, respectively [2].

The 5-year recurrence rates of WHO grades 1, 2, and 3 tumors after Simpson grade 1 GTR are 7–23%, 50–55%, and 72–78%, respectively [7]. After 15 years, almost all STR patients relapse, 60% of which died, and most occurred within 10 years [75].

Metastasis is an exceedingly rare complication, estimated to occur in ~0.1% of meningiomas and most of which are WHO grade 3. The most common sites of metastasis are lung (60%) and pleura, followed by the bone, liver, lymph nodes, and kidneys. In rare cases, WHO grade 1 meningiomas may metastasize to the lung, though the prognosis is surprisingly good. Of the patients that received surgery, 12.3% developed new postoperative seizures and 40% developed cognitive or emotional problems (e.g., anxiety or depressive symptoms) [43].

**At The End**

Meningiomas are usually benign, WHO grade 1, slow growing neoplasms with a linear growth rate of 2–4 mm/year. Third of all meningiomas experience no growth and of the meningiomas that grow, 25% experience exponential growth. Intracranial meningiomas increases with age each decade of life and peaks in the 60-69 year age, so conservative management can be used specially in asymptomatic cases with small lesion**.** Surgical resection is the primary choice for symptomatic, observation failure meningiomas, or large tumors that are anticipated to causes symptoms soon. Gross Total Resection GTR can cure the majority (70–80%) of patients. The goal for surgery is Gross Total Resection GTR (Simpson I, GTR). A number of radiological features have been consistently linked to growth potential: peritumoral edema and hyperintense signal on T2W-MRI have been associated with rapid tumor growth and may suggest a higher-grade meningioma, whereas the presence of calcification and hypointense signal on T2W-MRI tend to be associated with low growth potential and lower-grade meningioma**.**

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