Neuro-Oncology Advances
6(S3), iii73–iii82, 2024 | https://doi.org/10.1093/noajnl/vdae123 | Advance Access date 31 August 2024

Clinical, molecular, and genetic features of spinal meningiomas

Dylan Deska-Gauthier[†], Laureen D. Hachem[†], Justin Z. Wang, Alex P. Landry, Leeor Yefet, Chloe Gui, Yosef Ellengbogen, Jetan Badhiwala, Gelareh Zadeh, and Farshad Nassiri

All author affiliations are listed at the end of the article.
[†]These authors contributed equally as first authors.

Corresponding Authors: Farshad Nassiri, MD, PhD, 101 College St 4th floor, Room #601, Toronto, ON M5G 1L7, Canada (farshad.nassiri@mail.utoronto.ca); Gelareh Zadeh (neuro.onc.advances@gmail.com).

Abstract

Spinal meningiomas comprise 25%–46% of all primary spinal tumors. While the majority are benign and slow-growing, when left untreated, they can result in significant neurological decline. Emerging clinical, imaging, and molecular data have begun to reveal spinal meningiomas as distinct tumor subtypes compared to their intracranial counterparts. Moreover, recent studies indicate molecular and genetic subtype heterogeneity of spinal meningiomas both within and across the classically defined WHO grades. In the current review, we focus on recent advances highlighting the epidemiological, pathological, molecular/genetic, and clinical characteristics of spinal meningiomas. Furthermore, we explore patient and tumor-specific factors that predict prognosis and postoperative outcomes. We highlight areas that require further investigation, specifically efforts aimed at linking unique molecular, genetic, and imaging characteristics to distinct clinical presentations to better predict and manage patient outcomes.

Keywords:

genomics | meningioma | molecular | oncology | spine

Spinal meningiomas arise from arachnoid cap cells and account for approximately 25%–46% of primary spinal tumors.[1] While the majority are benign and slow growing,[2–5] when left untreated, spinal meningiomas can result in significant spinal cord compression and progressive neurological decline. A small subset of patients can present with more aggressive disease courses, often associated with tumors displaying distinct histopathological and molecular characteristics.

Recent studies have begun to shed light on the molecular and genetic heterogeneity across spinal meningioma subtypes that may correlate with clinical presentations and prognosis.[6–9] Furthermore, emerging evidence suggests distinct genetic profiles between meningiomas of spinal and cranial origin.[8,10–12] Understanding the clinical and biological landscape of these tumors may facilitate the development of prognostication tools and enable a more personalized approach to patient management.[13]

In the current review, we focus on recent advances highlighting the epidemiological, pathological, molecular/genetic, and clinical characteristics of spinal meningiomas. Moreover, we present emerging insights into predictive factors for postoperative functional outcomes and tumor recurrence. Moving forward, advances in imaging and genetic/molecular studies present promising avenues for enhancing our understanding of the pathophysiological underpinnings and clinical presentations of spinal meningioma subtypes.

Epidemiology

Demographics and Risk Factors

The incidence of spinal meningiomas has remained stable in recent years,[14] however, incidence rates are expected to

increase as populations grow in the coming decades. In the United States between 1997 and 2016, benign spinal meningiomas (WHO grade I) had an incidence of 0.62 per 100 000 while atypical/malignant spinal meningiomas (WHO grade II/III) had an incidence of 0.056 per 100 000.[4] Grade II/III meningiomas are typically less common to occur in the spine (2.4%) compared to the cranium (12.8%).[5]

Spinal meningiomas are most commonly diagnosed in the sixth decade of life.[3,15,16] Females are approximately 3 times more likely to be diagnosed than males,[2–4,15,16] although sex ratios are skewed at both age extremes. For elderly patients (>70 years of age), the female to male ratio is approximately 4.4:1.[3] In contrast, for pediatric patients (<18 years of age), males are more likely to be diagnosed with a female to male ratio of 1:1.6.[3] Males are also more likely to be diagnosed with higher grade (WHO grade II/III) spinal meningiomas compared to females.[2,4] A recent U.S. epidemiological study further identified higher rates of spinal meningiomas in middle/high-income individuals as well as White and Asian/Pacific Islanders.[4] These results are consistent with previous work that identified Hispanic ethnicity as a risk factor for spinal meningiomas.[15]

Additional risk factors have been identified for spinal meningiomas beyond demographic factors. Increased height was recently found to be positively associated with a risk for spinal meningioma.[17] Additionally, female breast cancer patients may be at a higher risk of developing a spinal meningioma compared to the general population. A recent study by Wang et al.[18] found that of 55 female spinal meningioma patients in the United Kingdom, 16.4% had a preceding breast cancer diagnosis—a significantly higher frequency than the general U.K. population. This association is also substantially greater than previous associations reported between breast cancer and intracranial meningiomas.[19,20] While these differences may be attributed to differential expression of hormone receptors between the brain and spinal cord (see section: Receptor expression profiles of spinal meningiomas), further work is required to validate these findings and elucidate the potential underlying mechanism.

Spinal Regions

The majority of spinal meningiomas are present in the thoracic spinal cord (approximately 70%), followed by cervical (25%), lumbar (4%), and sacral (<1%) regions.[3] Emerging evidence suggests that thoracic and cervical spinal meningiomas may represent distinct molecular subtypes (see section: Molecular subtypes of spinal meningiomas). The majority of spinal meningiomas are intradural (approximately 80%), followed by extradural (5%–15%), with a small subset being both intradural and extradural (5%).[16,21]

Genetic Predisposition

While spinal meningiomas are most commonly single tumors, underlying genetic syndromes can often present with multiple spinal lesions. Spinal meningiomas resulting from underlying genetic syndromes are more commonly present in younger patients. Neurofibromatosis 2 (NF-2) is a genetic disorder associated with bilateral vestibular schwannomas and ependymomas in addition to spinal and intracranial meningiomas.[22] The overall prevalence of NF2 in spinal meningioma patients is approximately 3%, though, the prevalence is much higher (approximately 40%) in younger patients.[3] Thus, genetic testing should be considered in patients presenting at younger ages, with multiple meningioma lesions, or with additional tumor types.

Pathology

Grade

A recent metanalysis including 5 641 spinal meningiomas across 44 studies reported that 95.5% of diagnosed lesions were WHO grade I.[3] Approximately 4% of spinal meningiomas were WHO grade II and less than 0.5% WHO grade III.[3] Higher grader (WHO grade II/III) spinal meningiomas are on average diagnosed at younger ages and are associated with worse post-operative outcomes and increased tumor recurrence rates.[23,24] Currently, the extent of surgical resection combined with tumor grade is the best predictor of recurrence.

Histology

The WHO classification further distinguishes meningiomas into 15 histopathological subtypes. The most common histopathological subtypes for WHO grade I tumors include psammomatous (~40%), meningothelial (~34%), transitional (~14%), and fibrous (~9%). Common WHO grade II histopathological subtypes include atypical (~67%) and clear cell (~29%) while WHO grade III includes anaplastic (~70%) and papillary (~30%).[3]

While spinal and intracranial meningiomas display overlapping histopathological subtypes, spinal meningiomas present with different frequencies of psammomatous, transitional, and meningothelial subtypes.[11,25] Psammomatous and transitional subtypes are more common in spinal meningiomas while meningothelial subtypes are less common. Spinal meningiomas also display less aggressive clinical presentations compared to their intracranial counterparts. Specifically, spinal meningiomas are on average diagnosed at older ages, display lower mitotic counts, lower MIB-1 indices, less macrophage infiltration, and longer periods of progression-free survival.[12]

Recent studies have begun to investigate links between molecular and histopathological spinal meningioma subtypes. Molecularly distinct WHO grade I spinal meningiomas—NF2 and AKT1 subtypes—present with different histopathological patterns. Hua et al.,[8] found that while NF2 mutant meningiomas displayed variable histology (meningothelial, psammomatous, transitional, and fibrous), 93.3% of AKT1-mutant meningiomas displayed a meningothelial histology. Furthermore, SMARCE1 mutations have been specifically associated with WHO grade II

clear-cell meningiomas across both spinal and intracranial locations.[26,27]

Calcification

While varying frequencies of calcified spinal meningiomas have been reported in the literature (5%[28]; 51%[29]; and 75%[30]), the presence of calcification has been associated with worse clinical outcomes,[31,32] in part due to increased adherence to surrounding tissues which can complicate surgical resection.[33,34] The majority of calcified spinal meningiomas are benign WHO grade I (97.4%) and of the psammomatous histological subtype (50.7%).[34]

Molecular and Genetic Features of Spinal Meningiomas

Molecular Subtypes of Spinal Meningiomas

Emerging evidence has begun to reveal chromosomal abnormalities, genetic mutations, and receptor expression profiles associated with spinal meningiomas. Early work by Arslantas et al.[6] demonstrated that spinal meningiomas are commonly associated with either partial or complete loss of several chromosomal locations. Among 16 spinal meningiomas, chromosomal changes were observed in 11 of the samples, with the most common abnormality being the complete or partial loss of chromosome 22—a chromosomal feature also common to intracranial meningiomas. Chromosome 22q12.2 harbors the tumor suppressor gene, Neurofibromatosis type 2 (NF-2). NF-2 inactivation (via mutation or chromosomal deletion) has been associated with both sporadic and NF-2 syndrome spinal and intracranial meningiomas. NF-2 encodes the cytoskeletal protein, Merlin, which is involved in several intracellular signaling pathways including those involved in proliferation suppression.[22] Chromosomal losses on 1p, 9p, and 10q and chromosomal gains on 5p and 17q were also observed.[6]

Beyond chromosomal abnormalities, several single gene alterations associated with spinal meningiomas have been described (Table 1). Hua et al.,[8] performed targeted next-generation sequencing of 50 WHO grade I spinal meningiomas and uncovered 2 clinical cohorts of mutually exclusive WHO grade I genetic mutations: (1) NF2 mutants; and (2) AKT1 mutants. These 2 molecular subtypes displayed distinct epidemiological, clinical, histopathological, and epigenetic characteristics. NF2 subtypes compared to AKT1 mutants were diagnosed at significantly younger ages (65 vs 71 years of age) and were more frequently seen in females (94% vs 48% female). Furthermore, NF2 subtypes most frequently occurred in the thoracic spine (75%) with dorsal/dorsolateral positioning (59.3%) while AKT1 subtypes most frequently occurred in the cervical spinal (73.3%) with ventral/ventrolateral positioning (87%). NF2 subtypes also displayed more variable histopathologies with meningothelial, psammomatous, transitional, and fibrous subtypes identified. In contrast, 93.3% of AKT1 subtypes were meningothelial. An independent investigation by Ricklefs et al.[9] found that DNA methylation arrays also separated spinal meningiomas into 2 distinct clusters which corresponded to either NF2 or AKT1 subtypes. Thus, epigenetic regulation may further separate spinal meningiomas into discrete subtypes aligned with their gene-specific mutations, regional locations, and clinical presentations.

Tate et al.,[35] also performed whole exome sequencing of a non-NF2 42-year-old spinal meningioma patient uncovering a mutation in the FAT atypical cadherin 2 (FAT2) gene. FAT2 is involved in planar cell polarity, tumor suppression, and Hippo signaling in arachnoid cells. Of note, Hippo signaling is also downstream of Merlin, indicating that the shared downstream Hippo signaling pathway may be important for both NF2 and non-NF2 spinal meningioma pathogenesis.

Distinct gene mutations have also been described for rarer WHO grade II spinal meningiomas. Smith et al.,[26] performed exome sequencing in individuals with multiple spinal meningiomas that were non-NF2. They identified SMARCE1 mutations on chromosome 17q21.2 to be associated with the clear cell subtype. Clear cell meningiomas are a histological subtype of WHO grade II that are diagnosed at younger ages (mean age of resection, 24 years old), often display multiple lesions, and have high recurrence rates.[36] A review of the literature (234 patients across 65 studies and case reports) revealed that 45% of patients with clear cell meningioma had tumor recurrence with a mean follow-up of 45 months.[27] Local recurrence occurred in 84% of cases, local and distant recurrence in 11% of cases, and distant recurrence in 5% of cases. SMARCE1 functions as a transcriptional activator of genes repressed by chromatin mutations and is associated with clear cell meningiomas across spinal and cranial locations.[26,37] Furthermore, a retrospective multicenter study (26 patients with intracranial and spinal meningiomas) demonstrated that the loss of SMARCE1 immunostaining was sensitive and specific for the clear cell meningioma subtype across both intracranial and spinal tumors.[27] Thus, SMARCE1 serves as a strong diagnostic and prognostic molecular marker for clear cell meningiomas.

Molecular Distinctions Between Spinal and Intracranial Meningiomas

While molecular similarities between spinal and intracranial meningiomas have been described, several distinctions have also been uncovered. Wach et al.[12] recently conducted a retrospective analysis of 541 adult patients with non-NF2 meningiomas who underwent a Simpson grade I or II resection. It was found that spinal meningiomas were diagnosed at significantly older ages, had lower rates of WHO grade II tumors, fewer mitotic cells (MIB-1 index), fewer CD68+ macrophage infiltrations, and longer progression-free survival times compared to intracranial tumors.

Molecular differences likely play a key role underlying the clinical presentation of spinal meningiomas. Indeed, several groups have revealed distinct gene expression profiles between spinal and intracranial meningiomas. Sayagués et al.[11] employed in situ hybridization and microarray analyses of spinal and intracranial meningiomas to examine differential expression of 1 555 genes. Thirty-five genes were identified that

Table 1. Identified Molecular Subtypes Of Spinal Meningiomas

Gene mutation	Chromosome location	Protein function	Histology	WHO grade	Clinical features	References
Neurofibromatosis type 2 (NF2)	22q12.2	Encodes Merlin, a tumor suppressor protein, upstream of mTOR and other signaling pathways	Variable: meningothelial, psammomatous, transitional, and fibrous identified	I	Frequently in the thoracic spine (75%) with dorsal/ dorsolateral positioning (59.3%). Associated NF-2 syndrome: may have multiple meningiomas, schwannomas, ependymomas. Often presents in younger patients.	3,8,9,22
AKT Serine/ Threonine Kinase 1 (AKT1)	14q32.33	Oncogene involved in cellular proliferation	Majority are meningothelial	I	Frequently in the cervical spine (73.3%) with ventral/ ventrolateral positioning (87%).	8,9
FAT atypical cadherin 2 (FAT2)	5q33.1	Tumor suppression gene involved in Hippo signaling and planar cell polarity of arachnoid cells.	N/A	I	Described in non-NF2 42-year-old.	35
SMARCE1	17q21.2	SWI/SNF-related matrix-associated actin-dependent regulator of chromatin subfamily E member 1	Clear cell meningioma	II	Associated with multiple meningiomas and higher post-operative recurrence rates.	26,27,36,37

together enabled distinction between spinal and intracranial tumors. Specifically, 30 genes were distinctly upregulated in spinal meningiomas and 5 were distinctly downregulated. Upregulated genes included those involved in transcription regulation as well as intracellular and extracellular signaling (cytokine and cell–cell adhesion protein expression). The AKT1 spinal subtype may also be molecularly distinct from AKT1-mutant meningiomas in the cranium. In the cranium, Clark et al.[10] reported that 75% of AKT1-mutant meningiomas displayed TRAF7 co-mutations. In contrast, Hua et al.[8] reported that only 3% of AKT1 spinal meningiomal subtype cases displayed a TRAF7 co-mutation. Thus, combinatorial gene expression analyses may further reveal genetic patterns that underlie subtype diversity between intracranial and spinal meningiomas.

Intracranial meningiomas may further possess more complex chromosomal abnormalities contributing to their more aggressive progressions. Sayagués et al.[11] found that intracranial meningiomas, and not spinal meningiomas, often presented with more than 1 tumor cell clone.

Receptor Expression Profiles of Spinal Meningiomas

Meningiomas, including spinal meningiomas, can be differentiated into subtypes by distinct receptor expression profiles. Differences in the expression of somatostatin receptor subtypes (SSTR) 1-5 were recently found between spinal and cranial meningiomas. Spinal meningiomas displayed elevated SSTR1,4,5 and diminished SSTR2A expression compared to skull base meningiomas.[38] Moreover, distinct combinations of SSTR1-5 expression profiles corresponded to different frequencies in sex, age of diagnosis, anatomical location, recurrence, NF2 status, grade, and histological subtype.[38]

Hormone receptor expression may also distinguish meningiomas into clinically relevant subtypes. Portet et al.[39] evaluated androgen receptor (AR), estrogen receptor (ER), and progesterone receptor (PR) expressions across 30 intracranial and 30 spinal meningiomas. This study found that spinal meningiomas had higher expression rates of AR (spinal, 100%; intracranial, 73%) and ER (spinal, 30%; intracranial, 7%), while both intracranial and spinal meningiomas displayed equivalent PR (spinal, 87%; intracranial, 90%) expression levels. Similarly, an analysis of 300 patients found that PR expression levels were increased at spine and medial skull base locations compared with lateral skull base meningiomas.[40] It was also found that PR-expressing tumors were associated with lower WHO grade and proliferative index (Ki-67 labeling index). In a cohort of 58 spinal meningiomas, Barresi et al.[41] reported that 86% expressed PR and displayed a low Ki-67 labeling index (1%–5%). This low-grade nature of PR-expressing spinal meningiomas was demonstrated despite high co-expression levels of matrix-metalloproteinase-9 (MMP-9)—a marker typically associated with more aggressive tumor subtypes in the cranium.[41,42] Thus, MMP-9 may be expressed in distinct intracranial and spinal PR-positive meningioma subtypes. Taken together, a significant portion of low-grade spinal meningiomas appear to express a combination of sex hormone receptors raising the possibility of hormone-altering risk factors for meningioma growth. Given this link, hormonal therapies have been investigated as potential meningioma risk factors. Samoyeau et al.[43] conducted a prospective cohort study screening for meningiomas using MRI in 250 patients

exposed to consecutive progestin therapies (cyproterone). Patients exposed to cyproterone displayed higher rates of meningiomas compared to the general population. Furthermore, discontinuation of cyproterone in patients with meningiomas resulted in tumor size reduction, suggesting a dose-dependent response to progestin therapies. These results are consistent with a study in 30 patients diagnosed with meningiomas while on cyproterone acetate, reporting that 97% expressed PRs and 87% expressed ARs.[39]

Further work is required to better elucidate the unique receptor expression profiles of spinal meningiomas. Uncovering the molecular underpinnings of differential receptor expression profiles may inform risk prevention strategies and enhance prognostication. Moreover, identification of unique receptor expressions may provide potential therapeutic targets for recurrent tumors and patients contraindicated for surgery.

Clinical Presentation

Spinal meningiomas are slow-growing tumors that typically present with gradual symptoms. The average duration from symptom onset to diagnosis and treatment is approximately 13 months.[44] However, higher-grade spinal meningiomas typically have shorter time periods from symptom onset to diagnosis due to their accelerated growth patterns.[45] To date, no clear association between spinal segment tumor location and time to diagnosis has been established.[46]

Clinical symptoms arising from spinal meningiomas are most commonly secondary to mass effect. Pressure on the spinal cord from tumor growth results in compression of descending and ascending spinal tracts. Corticospinal tract compression may lead to gait impairment, hyperreflexia, and discoordination caudal to the lesion. Brown-Sequard syndrome may also result from unilateral cord compression.[47] Vascular compromise due to spinal artery compression may further contribute to functional deficits at and remote to the primary tumor location.[48] Moreover, compression of the epidural venous plexus can impair venous drainage resulting in vasogenic edema and additional functional decline.[48]

Across all spinal meningioma types, motor dysfunction, sensory dysfunction, and back pain have been reported to be the most common initial presenting symptoms.[44] Gait and balance disturbances, bladder and bowel dysfunction, and radicular pain have also been reported.[44] Both age and rostrocaudal tumor locations have shown moderate correlations with clinical symptoms. Schwake et al.[49] observed that older age at time of diagnosis positively correlated with motor symptoms, sensory symptoms, and incontinence, but negatively correlated with the presence of radicular pain. Yamaguhi et al.[50] also observed that pain symptoms were significantly more common with cervical lesions while motor and sensory symptoms were significantly more common with thoracic lesions.

Several studies have also focused on the unique symptomologies of higher-grade (WHO grade II/III) spinal meningiomas. Han et al.[51] reported on the clinical features of 19 high-grade spinal meningioma patients. Low-back pain was the most common symptom presenting in 78.9% of patients. They also found that most lesions were localized to the lumbosacral segments (30%), which stands in contrast to what has been reported for WHO grade I spinal meningiomas (predominantly located in the thoracic spine). This was further supported by Li et al.,[45] who observed that out of 12 WHO grade II clear cell meningiomas, 58% of lesions were located in the lumbar spine. Motor and sensory symptoms each presented in approximately 50% of WHO grade II/III patients.[51]

While the majority of spinal meningiomas are diagnosed secondary to neurological symptoms, a proportion are diagnosed in asymptomatic patients. Recent work from Corell et al.[52] aimed to determine MRI imaging cutoffs to predict symptomatic onset to help guide treatment decision-making in asymptomatic patients. In a cohort of 111 patients, they determined that patients with a tumor occupancy >65% were most likely to experience motor deficits. This is supported by a subsequent study reporting a tumor occupancy of >64% as the threshold for development of motor symptoms.[50] Despite these findings, other studies have found no correlation between tumor occupancy and pre-operative functional status.[53,54] Thus, while surgical resection may be considered in asymptomatic patients approaching 65% tumor occupancy, the natural history of patients may vary despite similar tumor characteristics. Further work is required to identify patient-specific factors that contribute to the onset and degree of functional impairment to properly guide treatment decisions for asymptomatic and symptomatic patients.

Imaging Characteristics

Magnetic resonance imaging (MRI) is the gold standard for diagnosing spinal meningiomas in both symptomatic and asymptomatic patients. Spinal meningiomas are commonly isointense on T1-weighted MRI, either isointense or hypointense on T2-weighted MRI and characteristically present with homogenous enhancement on gadolinium-enhanced MRI (Figure 1).[55,56] Spinal meningiomas can also present with characteristic morphologies on MRI. The presence of a fan-shaped spinal cord with an intratumoral streak has been suggested to be indicative of meningioma tumors.[57] Meningiomas may also present on contrast-enhanced MRI with the characteristic dural tail sign. This imaging marker results from dural thickening manifesting as clear signal enhancement adjacent to the meningioma. Lee et al.[58] reported that within a cohort of 59 meningioma tumors, 64% presented with a dural tail sign, in contrast to 1% of schwannomas presenting with this sign.

While the majority of meningiomas display characteristic imaging findings, distinct imaging subtypes have also been identified. A study investigating the MRI characteristics of 105 adult spinal meningiomas classified tumors into 4 subtypes.[29] Type A displayed characteristic dural tail signs and intense homogenous enhancement (77%). Other subtypes included tumors that were oval-shaped with internal hypointensities (type B, 17%), en plaque tumors (type C, 3%), and tumors with heterogeneous features (type D, 3%).

On average, type C and D tumors were larger in size and were more frequent in the cervical spine. Furthermore, type D tumors presented in younger patients compared to the other subtypes.

Calcified meningiomas can be readily detected by computed tomography (CT). Yeo et al.[29] reported 51% of 105 meningiomas displayed internal calcifications while a more recent study reported that 75% of 53 meningiomas were calcified.[31] Kobayashi et al.[31] categorized meningiomas as calcified on CT imaging using a Hounsfield unit (HU) value greater than 60HU. The authors found that HU values positively correlated with symptom duration (R = 0.59). Additionally, when comparing the 2 most frequent histopathological subtypes, psammamatous tumors on average had significantly higher HU values relative to meningothelial tumors. Calcified tumors also displayed longer operative times, higher estimated blood losses, and modestly lower functional improvements post-operatively. This is likely due to the added surgical challenge of resecting more rigid tumor masses resulting in increased mechanical irritation of the underlying spinal cord. Thus, CT-based HU quantification of meningioma calcification may aid in prognosticating surgical outcomes and functional improvements following resection.

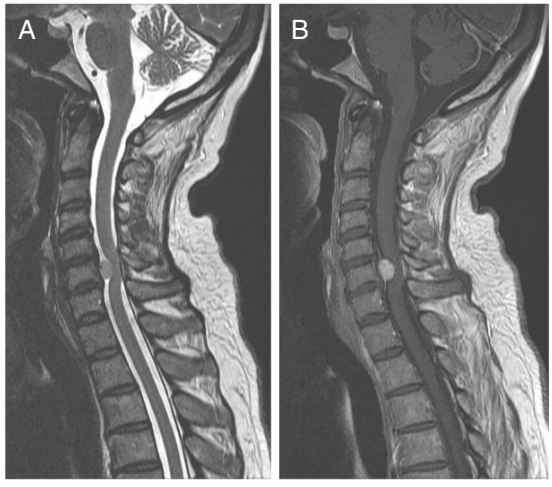

Figure 1. MRI demonstrating a ventral cervical spinal meningioma. (**A**) Sagittal T2-weighted, (**B**) sagittal contrast enhanced T1-weighted images. *Modified from Hachem* et al *2023.*[7]

In addition to distinguishing meningioma subtypes, several groups have attempted to establish clear criteria to differentiate meningiomas from other intradural extramedullary lesions. In addition to the dural tail sign, other key imaging and clinical features have been directly compared between meningiomas and schwannomas (Table 2). Meningiomas and schwannomas display distinct MRI signal intensities compared to one another as well as relative to surrounding tissues. Indeed, the signal intensity ratio between tumor and subcutaneous fat is significantly higher in spinal schwannomas compared to meningiomas (cutoff of 0.42, sensitivity 80%, specificity 70%–75%).[61] More recently, Hung et al.[60] demonstrated that quantitative signal intensity measurements of MR images can distinguish spinal meningiomas from schwannomas. Specifically, T2max, T2min, T2mean, T1CEmax, and rTF were all significantly higher in schwannomas compared to meningiomas. With contrast-enhanced MRI, schwannomas displayed intense heterogenous enhancement[59] as well as rim enhancement[56] compared to more moderate and homogeneous enhancement exhibited by meningiomas.[56,59]

Meningiomas and schwannomas may also be differentiated based on their anatomical and morphological characteristics. On average, Zhai et al.[56] reported that schwannomas were significantly larger than meningiomas. Schwannomas were also most frequently located in dorsolateral regions of the thoracic and lumbar spine while meningiomas were most frequently located in ventral and ventrolateral regions of the thoracic spine. Schwannomas more commonly displayed a dumbbell-shaped appearance with intervertebral foramen widening compared to meningiomas.[56] Additionally, Lee et al.[58] found that schwannomas presented with a significantly higher frequency of cystic changes (schwannoma, 96%; meningioma, 24%) and neural foramen extension (schwannoma, 29%; meningioma, 3%).

Finally, deep learning algorithms have recently been explored for differentiating intradural extramedullary lesions. Maki et al.[62] conducted a retrospective analysis employing a convolutional neural network to classify pre-operative MRI images (T2-weighted and contrast-enhanced T1-weighted) as spinal meningiomas or schwannomas ($n = 50$ schwannoma patients, $n = 32$ meningioma patients). The algorithm was able to accurately classify tumor classes with an area under the curve of

Table 2. Imaging Features Differentiating Meningiomas and Schwannomas

	Meningioma	Schwannoma	References
Dural tail sign	Common	Uncommon	29,58
Fan-shaped spinal cord with intra-tumoral streak	Common	Uncommon	57
Foraminal widening	Uncommon	Common	56
Cystic changes	Uncommon	Common	58
T1W-MRI with Gadolinium	Moderate homogeneous enhancement	Intense heterogenous enhancement	29,55,56,59
T2W-MRI: T2max, T2min, T2mean	Lower	Higher	60

0.876 and a receiver operating characteristic of 0.87. This work presents promising new avenues for deep learning networks to help differentiate between key tumor features on preoperative MRI images.

Management and Prognosis

Surgical resection is the mainstay treatment for spinal meningiomas with the goal of achieving a complete resection (Simpson grades I and II).[23] While most spinal meningiomas present as single lesions, in rare cases there may be multiplicity. When evaluating multiple lesions, it is important to identify and surgically target the lesions most responsible for a patient's symptoms. The surgical approach for spinal meningiomas is largely guided by tumor location, size, and patient characteristics. In general, targeted hemilaminectomy should be favored wherever possible to avoid biomechanical instability and limit the need for instrumentation.

Improved or stabilized neurological function is often achieved following surgical resection of a spinal meningioma.[44,63,64] A recent systematic review examining postoperative outcomes across 42 studies found that 65.2% of patients displayed improved neurological status while 28.8% remained unchanged following surgical resection.[44] In a cohort of 131 patients surgically treated for spinal meningiomas, morbidity, and mortality rates were 3.0% and 0.8%, respectively.[64] Despite generally favorable results following surgical resection, a subset of patients can exhibit peri-operative complications and long-term neurological deterioration. Thus, several groups have attempted to identify prognostic factors for outcomes following surgical resection of spinal meningiomas.

Patient-related factors that have been shown to be predictive of neurological outcomes include preoperative neurological status[24,30,65] and sphincter dysfunction.[23,65] Evidence on the potential impact of patient age on surgical outcomes has been conflicting.[66,67] Tumor factors such as invasion of arachnoid/pia mater,[24] anterior tumor location,[23,65,68,69] tumor size,[67,69] WHO grade II/III,[23,68,70] tumor calcification,[1] mitotic Ki-67 index,[70] and recurrent lesions[64–66] may portend a worse outcome following resection. Furthermore, pre-operative presentation times (time from diagnosis to surgery)[23,30,67] and higher Simpson grade III/IV resections[23] were identified as significant predictive factors of neurological outcomes postoperatively.

While intra-operative neuromonitoring (somatosensory-evoked potentials and motor-evoked potentials) has been proposed as a potential tool to improve functional outcomes, the evidence remains inconclusive. In a retrospective study of 100 intradural-extramedullary spinal tumor resections (including meningioma resections), Korn et al.[71] demonstrated that intraoperative neuromonitoring to be highly sensitive (0.82) and specific (0.95) for identifying iatrogenic injury to the spinal cord during surgery. Hohenberger et al.[72] also suggested intra-operative neuromonitoring may improve functional outcomes for spinal meningioma resection patients. In contrast, Harel et al.[73] did not observe significant differences in postoperative outcomes with intra-operative neuromonitoring. Thus, while further studies are required, intra-operative neuromonitoring may be useful for surgically complex cases.

Taken together, a multitude of factors may be associated with clinical recovery and prognosis following spinal meningioma resection. Attempts to incorporate these factors into a prognostic tool have resulted in the development of a spinal meningioma prognostic evaluation score (SPES) that utilized 4 variables: anterior lesion position, preoperative sphincter impairment, recurrent lesion, and preoperative functional status.[65] Pre-operative SPES scores were correlated to postoperative Frankel and McCormick scores. Future work is necessary to further incorporate molecular and genetic factors into a comprehensive prognostic tool for spinal meningioma patients.

Several studies have examined predictive factors for postoperative tumor recurrence. The extent of surgical resection is a key predictor for tumor recurrence with complete resections (Simpson grade I or II) displaying low recurrence rates (0%–13%).[1,40,74] Nakamura et al.[74] performed a long-term follow-up study (mean postoperative follow-up time of 12 years) of 68 spinal meningioma patients. Patients who received complete resection (Simpson grade I or II) had a recurrence rate of 9.7% while patients with an incomplete resection (Simpson grade III or IV, 6 patients total) had a recurrence rate of 100%. While there is a clear distinction in spinal meningioma recurrence rates between Simpson grade I/II and Simpson grade III/IV resections, differences in recurrence risk between Simpson grade I and II resections remain less clear. Both Barber et al.[75] and Kobayashi et al.[30] reported no significant difference in spinal meningioma recurrence rates between Simpson grade I and II resections. In contrast, Volrich et al.[76] reported that Simpson grade II recurrence rates may be underestimated in the literature due to inadequate follow-up times. Specific challenges can arise when attempting a conventional Simpson I resection of spinal meningiomas. Specifically, complete resection of the involved dura and subsequent need for duroplasty, particularly in ventral lesions, can involve significant spinal cord manipulation and carry a higher rate of CSF leaks. As such, it may be preferred to resect the inner dural attachment layer alone and preserve the outer dural layer to limit the need for complex dural reconstruction.[77] Indeed, resections using this strategy have resulted in no recurrence at a median follow-up of 132 months in a series of 10 patients with spinal meningiomas.[78] Higher WHO grade and invasion of the arachnoid/pia are additional predictors of postoperative tumor recurrence.[24,44,70] Moreover, en plaque lesions,[79] tumor calcification,[66] foraminal location,[79] radiographic evidence of a dural tail sign,[30,69] male sex,[30,69,70,80] younger age,[30,79] and pre-existing bladder and bowel symptoms[80] have also been associated with increased spinal meningioma recurrence rates across studies.

Evidence for the use of adjuvant therapy is limited for spinal meningiomas. Adjuvant radiation may be considered in patients contraindicated for surgery or for cases of atypical or malignant lesions when subtotal resection is achieved.[81,82] Yolcu et al.[83] reported that adjuvant radiation for malignant lesions was associated with decreased mortality. Furthermore, other select studies

suggest that when dosed appropriately, radiation therapy may present a safe and effective alternative treatment when surgical resection is not available for higher-grade tumors.[81,84,85]

Conclusion

Spinal meningiomas comprise a significant proportion of primary spinal tumors. While the majority are benign, spinal meningiomas can result in permanent neurological damage and impaired quality of life. Increasing work has begun to reveal significant heterogeneity of spinal meningiomas with differing epidemiological, pathological, and prognostic characteristics. Emerging insight from molecular and genetic investigations has led to the identification of distinct signatures differentiating spinal meningioma subtypes. Furthermore, these subtypes appear distinct from their intracranial meningioma counterparts underscoring the need for further work focused on this unique entity. Better understanding of the molecular and genomic landscape of spinal meningiomas may help more accurately predict clinical outcomes, recurrence rates, and management decisions. In the future, continued study into the molecular and genetic underpinnings of spinal meningiomas will likely further define distinct subtypes with clinical and prognostic relevance, moving in parallel to the progress seen with intracranial meningiomas.

Funding

None.

Conflict of interest statement

None declared.

Affiliations

Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada (D.D.-G.); Division of Neurosurgery, Department of Surgery, University of Toronto, Toronto, Ontario, Canada (L.D.H., J.W., A.L., L.Y., C.G., Y.E., J.B., G.Z., F.N.); Princess Margaret Cancer Center, University Health Network, Toronto, Ontario, Canada (G.Z., F.N.)

References

1. Roux FX, Nataf F, Pinaudeau M, et al. Intraspinal meningiomas: review of 54 cases with discussion of poor prognosis factors and modern therapeutic management. *Surg Neurol.* 1996;46(5):458–63; discussion 463.
2. Cao Y, Jiang Y, Liu C, et al. Epidemiology and survival of patients with spinal meningiomas: a SEER analysis. *Eur J Surg Oncol.* 2021;47(9):2340–2345.
3. El-Hajj VG, Pettersson Segerlind J, Burstrom G, Edstrom E, Elmi-Terander A. Current knowledge on spinal meningiomas: a systematic review protocol. *BMJ Open.* 2022;12(6):e061614.
4. Ghaffari-Rafi A, Mehdizadeh R, Ghaffari-Rafi S, Leon-Rojas J. Demographic and socioeconomic disparities of benign and malignant spinal meningiomas in the United States. *Neurochirurgie.* 2021;67(2):112–118.
5. Shin HK, Park JH, Cho YH, et al. Risk factors for high-grade meningioma in brain and spine: systematic review and meta-analysis. *World Neurosurg.* 2021;151:e718–e730.
6. Arslantas A, Artan S, Oner U, et al. Detection of chromosomal imbalances in spinal meningiomas by comparative genomic hybridization. *Neurol Med Chir (Tokyo).* 2003;43(1):12–8; discussion 19.
7. Hachem LD, Nater A, Fehlings MG. Spinal Meningiomas. *Adv Exp Med Biol.* 2023;1416:69–78.
8. Hua L, Alkhatib M, Podlesek D, et al. Two predominant molecular subtypes of spinal meningioma: thoracic NF2-mutant tumors strongly associated with female sex, and cervical AKT1-mutant tumors originating ventral to the spinal cord. *Acta Neuropathol.* 2022;144(5):1053–1055.
9. Ricklefs FL, Fita KD, Mohme M, et al. Genetic and epigenetic profiling identifies two distinct classes of spinal meningiomas. *Acta Neuropathol.* 2022;144(5):1057–1059.
10. Clark VE, Erson-Omay EZ, Serin A, et al. Genomic analysis of non-NF2 meningiomas reveals mutations in TRAF7, KLF4, AKT1, and SMO. *Science.* 2013;339(6123):1077–1080.
11. Sayagues JM, Tabernero MD, Maillo A, et al. Microarray-based analysis of spinal versus intracranial meningiomas: different clinical, biological, and genetic characteristics associated with distinct patterns of gene expression. *J Neuropathol Exp Neurol.* 2006;65(5):445–454.
12. Wach J, Lampmann T, Guresir A, et al. Proliferative potential, and inflammatory tumor microenvironment in meningioma correlate with neurological function at presentation and anatomical location-from convexity to skull base and spine. *Cancers (Basel).* 2022;14(4):1033.
13. Nassiri F, Liu J, Patil V, et al. A clinically applicable integrative molecular classification of meningiomas. *Nature.* 2021;597(7874):119–125.
14. Dolecek TA, Dressler EV, Thakkar JP, et al. Epidemiology of meningiomas post-public law 107-206: the benign brain tumor cancer registries amendment act. *Cancer.* 2015;121(14):2400–2410.
15. Kshettry VR, Hsieh JK, Ostrom QT, et al. Descriptive epidemiology of spinal meningiomas in the United States. *Spine.* 2015;40(15):E886–E889.
16. Levy WJ, Jr, Bay J, Dohn D. Spinal cord meningioma. *J Neurosurg.* 1982;57(6):804–812.
17. Gheorghiu A, Brunborg C, Johannesen TB, et al. The impact of body mass index and height on risk for primary tumours of the spinal cord, spinal meninges, spinal and peripheral nerves in 1.7 million norwegian women and men: a prospective cohort study. *Acta Oncol.* 2022;61(1):1–6.
18. Wang D, Sadek AR, Vaseeharan S, et al. Presentation and management of spinal meningioma and its association with breast carcinoma-case series and systematic review. *Br J Neurosurg.* 2022;1:1–6.
19. Custer BS, Koepsell TD, Mueller BA. The association between breast carcinoma and meningioma in women. *Cancer.* 2002;94(6):1626–1635.
20. Rao G, Giordano SH, Liu J, McCutcheon IE. The association of breast cancer and meningioma in men and women. *Neurosurgery.* 2009;65(3):483–489; discussion 489. discussion 89.
21. Cohen-Gadol AA, Zikel OM, Koch CA, Scheithauer BW, Krauss WE. Spinal meningiomas in patients younger than 50 years of age: a 21-year experience. *J Neurosurg.* 2003;98(3 Suppl):258–263.

22. Coy S, Rashid R, Stemmer-Rachamimov A, Santagata S. An update on the CNS manifestations of neurofibromatosis type 2. *Acta Neuropathol.* 2020;139(4):643–665.
23. Raco A, Pesce A, Toccaceli G, et al. Factors leading to a poor functional outcome in spinal meningioma surgery: remarks on 173 cases. *Neurosurgery.* 2017;80(4):602–609.
24. Setzer M, Vatter H, Marquardt G, Seifert V, Vrionis FD. Management of spinal meningiomas: surgical results and a review of the literature. *Neurosurg Focus.* 2007;23(4):E14.
25. Foda AAM, Rafi S, Ikram N, Alam MS, Ayesha S. Spinal versus intracranial meningioma: aberrant expression of CD10 and inhibin with relation to clinicopathological features and prognosis. *Pathol Oncol Res.* 2020;26(2):1313–1318.
26. Smith MJ, O'Sullivan J, Bhaskar SS, et al. Loss-of-function mutations in SMARCE1 cause an inherited disorder of multiple spinal meningiomas. *Nat Genet.* 2013;45(3):295–298.
27. Tauziede-Espariat A, Parfait B, Besnard A, et al. Loss of SMARCE1 expression is a specific diagnostic marker of clear cell meningioma: a comprehensive immunophenotypical and molecular analysis. *Brain Pathol.* 2018;28(4):466–474.
28. Doita M, Harada T, Nishida K, et al. Recurrent calcified spinal meningioma detected by plain radiograph. *Spine.* 2001;26(11):E249–E252.
29. Yeo Y, Park C, Lee JW, et al. Magnetic resonance imaging spectrum of spinal meningioma. *Clin Imaging.* 2019;55:100–106.
30. Kobayashi K, Ando K, Matsumoto T, et al. Clinical features and prognostic factors in spinal meningioma surgery from a multicenter study. *Sci Rep.* 2021;11(1):11630.
31. Kobayashi K, Ando K, Nakashima H, et al. Characteristics of cases with and without calcification in spinal meningiomas. *J Clin Neurosci.* 2021;89:20–25.
32. Ruggeri AG, Fazzolari B, Colistra D, et al. Calcified spinal meningiomas. *World Neurosurg.* 2017;102:406–412.
33. Alafaci C, Grasso G, Granata F, Salpietro FM, Tomasello F. Ossified spinal meningiomas: clinical and surgical features. *Clin Neurol Neurosurg.* 2016;142:93–97.
34. Shah DS, Reddy RV, Dogruel Y, et al. Calcified spinal meningiomas: a systematic review of clinical characteristics, treatment strategies, and outcomes. *J Neurooncol.* 2023;162(2):295–305.
35. Tate G, Kishimoto K, Mitsuya T. A novel mutation of the FAT2 gene in spinal meningioma. *Oncol Lett.* 2016;12(5):3393–3396.
36. Zhang H, Ma L, Shu C, et al. Spinal clear cell meningiomas: clinical features and factors predicting recurrence. *World Neurosurg.* 2020;134:e1062–e1076.
37. Smith MJ, Wallace AJ, Bennett C, et al. Germline SMARCE1 mutations predispose to both spinal and cranial clear cell meningiomas. *J Pathol.* 2014;234(4):436–440.
38. Behling F, Fodi C, Skardelly M, et al. Differences in the expression of SSTR1-5 in meningiomas and its therapeutic potential. *Neurosurg Rev.* 2022;45(1):467–478.
39. Portet S, Banor T, Bousquet J, et al. New insights into expression of hormonal receptors by meningiomas. *World Neurosurg.* 2020;140:e87–e96.
40. Maiuri F, Mariniello G, Guadagno E, et al. WHO grade, proliferation index, and progesterone receptor expression are different according to the location of meningioma. *Acta Neurochir (Wien).* 2019;161(12):2553–2561.
41. Barresi V, Alafaci C, Caffo M, Barresi G, Tuccari G. Clinicopathological characteristics, hormone receptor status and matrix metalloproteinase-9 (MMP-9) immunohistochemical expression in spinal meningiomas. *Pathol Res Pract.* 2012;208(6):350–355.
42. Barresi V, Vitarelli E, Tuccari G, Barresi G. MMP-9 expression in meningiomas: a prognostic marker for recurrence risk? *J Neurooncol.* 2011;102(2):189–196.
43. Samoyeau T, Provost C, Roux A, et al. Meningioma in patients exposed to progestin drugs: results from a real-life screening program. *J Neurooncol.* 2022;160(1):127–136.
44. El-Hajj VG, Pettersson-Segerlind J, Fletcher-Sandersjoo A, Edstrom E, Elmi-Terander A. Current knowledge on spinal meningiomas-surgical treatment, complications, and outcomes: a systematic review and meta-analysis (part 2). *Cancers (Basel).* 2022;14(24):6251.
45. Li J, Zhang S, Wang Q, et al. Spinal clear cell meningioma: clinical study with long-term follow-up in 12 patients. *World Neurosurg.* 2019;122:e415–e426.
46. Onken J, Obermuller K, Staub-Bartelt F, et al. Surgical management of spinal meningiomas: focus on unilateral posterior approach and anterior localization. *J Neurosurg Spine.* 2018;30(3):308–313.
47. Breuer AC, Kneisley LW, Fischer EG. Treatable extramedullary cord compression. Meningioma as a cause of the Brown-Sequard syndrome. *Spine.* 1980;5(1):19–22.
48. Ikeda H, Ushio Y, Hayakawa T, Mogami H. Edema and circulatory disturbance in the spinal cord compressed by epidural neoplasms in rabbits. *J Neurosurg.* 1980;52(2):203–209.
49. Schwake M, Adeli A, Sporns P, et al. Spinal meningiomas - Risks and potential of an increasing age at the time of surgery. *J Clin Neurosci.* 2018;57:86–92.
50. Yamaguchi S, Menezes AH, Shimizu K, et al. Differences and characteristics of symptoms by tumor location, size, and degree of spinal cord compression: a retrospective study on 53 surgically treated, symptomatic spinal meningiomas. *J Neurosurg Spine.* 2020;32:931–940.
51. Han B, Zhang L, Jia W, Yang J. Clinical features and surgical outcomes of high-grade spinal meningiomas: report of 19 cases and literature review. *J Clin Neurosci.* 2020;72:264–269.
52. Corell A, Cerbach C, Hoefling N, Bjorkman-Burtscher IM, Jakola AS. Spinal cord compression in relation to clinical symptoms in patients with spinal meningiomas. *Clin Neurol Neurosurg.* 2021;211:107018.
53. Ahn DK, Park HS, Choi DJ, et al. The surgical treatment for spinal intradural extramedullary tumors. *Clin Orthop Surg.* 2009;1(3):165–172.
54. Davies S, Gregson B, Mitchell P. Spinal meningioma: relationship between degree of cord compression and outcome. *Br J Neurosurg.* 2017;31(2):209–211.
55. Chung JY, Lee JJ, Kim HJ, Seo HY. Characterization of magnetic resonance images for spinal cord tumors. *Asian Spine J.* 2008;2(1):15–21.
56. Zhai X, Zhou M, Chen H, et al. Differentiation between intraspinal schwannoma and meningioma by MR characteristics and clinic features. *Radiol Med.* 2019;124(6):510–521.
57. Yamaguchi S, Takeda M, Takahashi T, et al. Ginkgo leaf sign: a highly predictive imaging feature of spinal meningioma. *J Neurosurg Spine.* 2015;23(5):642–646.
58. Lee JH, Kim HS, Yoon YC, et al. Differentiating between spinal schwannomas and meningiomas using MRI: a focus on cystic change. *PLoS One.* 2020;15(5):e0233623.
59. De Verdelhan O, Haegelen C, Carsin-Nicol B, et al. MR imaging features of spinal schwannomas and meningiomas. *J Neuroradiol/Journal de Neuroradiologie.* 2005;32(1):42–49.
60. Hung ND, Dung LT, Huyen DK, et al. The value of quantitative magnetic resonance imaging signal intensity in distinguishing between spinal meningiomas and schwannomas. *Int J Med Sci.* 2022;19(7):1110–1117.
61. Takashima H, Takebayashi T, Yoshimoto M, et al. Differentiating spinal intradural-extramedullary schwannoma from meningioma using MRI T(2) weighted images. *Br J Radiol.* 2018;91(1092):20180262.
62. Maki S, Furuya T, Horikoshi T, et al. A deep convolutional neural network with performance comparable to radiologists for differentiating between spinal schwannoma and meningioma. *Spine (Phila Pa 1976).* 2020;45(10):694–700.

63. Jecko V, Loit MP, Houston D, Champeaux-Depond C. Functional outcome after spinal meningioma surgery. *Asian Spine J.* 2022;16(5):692–701.
64. Sandalcioglu IE, Hunold A, Muller O, et al. Spinal meningiomas: critical review of 131 surgically treated patients. *Eur Spine J.* 2008;17(8):1035–1041.
65. Frati A, Pesce A, Toccaceli G, et al. Spinal meningiomas prognostic evaluation score (SPES): predicting the neurological outcomes in spinal meningioma surgery. *Neurosurg Rev.* 2019;42(1):115–125.
66. Kilinc F, Setzer M, Marquardt G, et al. Functional outcome and morbidity after microsurgical resection of spinal meningiomas. *Neurosurg Focus.* 2021;50(5):E20.
67. Pettersson-Segerlind J, Mathiesen T, Elmi-Terander A, et al. The risk of developing a meningioma during and after pregnancy. *Sci Rep.* 2021;11(1):9153.
68. Gilard V, Goia A, Ferracci FX, et al. Spinal meningioma and factors predictive of post-operative deterioration. *J Neurooncol.* 2018;140(1):49–54.
69. Maiti TK, Bir SC, Patra DP, et al. Spinal meningiomas: clinicoradiological factors predicting recurrence and functional outcome. *Neurosurg Focus.* 2016;41(2):E6.
70. Hua L, Zhu H, Deng J, et al. Clinical and prognostic features of spinal meningioma: a thorough analysis from a single neurosurgical center. *J Neurooncol.* 2018;140(3):639–647.
71. Korn A, Halevi D, Lidar Z, et al. Intraoperative neurophysiological monitoring during resection of intradural extramedullary spinal cord tumors: experience with 100 cases. *Acta Neurochir (Wien).* 2015;157(5):819–830.
72. Hohenberger C, Gugg C, Schmidt NO, Zeman F, Schebesch KM. Functional outcome after surgical treatment of spinal meningioma. *J Clin Neurosci.* 2020;77:62–66.
73. Harel R, Schleifer D, Appel S, et al. Spinal intradural extramedullary tumors: the value of intraoperative neurophysiologic monitoring on surgical outcome. *Neurosurg Rev.* 2017;40(4):613–619.
74. Nakamura M, Tsuji O, Fujiyoshi K, et al. Long-term surgical outcomes of spinal meningiomas. *Spine.* 2012;37(10):E617–E623.
75. Barber SM, Konakondla S, Nakhla J, et al. Oncologic benefits of dural resection in spinal meningiomas: a meta-analysis of Simpson grades and recurrence rates. *J Neurosurg Spine.* 2019;32:441–451.
76. Voldrich R, Netuka D, Benes V. Spinal meningiomas: is Simpson grade II resection radical enough? *Acta Neurochir (Wien).* 2020;162(6):1401–1408.
77. Saito T, Arizono T, Maeda T, Terada K, Iwamoto Y. A novel technique for surgical resection of spinal meningioma. *Spine.* 2001;26(16):1805–1808.
78. Tominaga H, Kawamura I, Ijiri K, Yone K, Taniguchi N. Surgical results of the resection of spinal meningioma with the inner layer of dura more than 10 years after surgery. *Sci Rep.* 2021;11(1):4050.
79. Park BJ, Dougherty MC, Noeller J, et al. Spinal meningioma in adults: imaging characteristics, surgical outcomes, and risk factors for recurrence. *World Neurosurg.* 2022;164:e852–e860.
80. Kwee LE, Harhangi BS, Ponne GA, et al. Spinal meningiomas: treatment outcome and long-term follow-up. *Clin Neurol Neurosurg.* 2020;198:106238.
81. Meola A, Soltys S, Schmitt A, Gerszten PC, Chang SD. stereotactic radiosurgery for benign spinal tumors. *Neurosurg Clin N Am.* 2020;31(2):231–235.
82. Noh SH, Kim KH, Shin DA, et al. Treatment outcomes of 17 patients with atypical spinal meningioma, including 4 with metastases: a retrospective observational study. *Spine J Official J North Am Spine Soc.* 2019;19(2):276–284.
83. Yolcu YU, Goyal A, Alvi MA, Moinuddin FM, Bydon M. Trends in the utilization of radiotherapy for spinal meningiomas: insights from the 2004-2015 National Cancer Database. *Neurosurg Focus.* 2019;46(6):E6.
84. Gerszten PC, Quader M, Novotny J, Jr, Flickinger JC. Radiosurgery for benign tumors of the spine: clinical experience and current trends. *Technol Cancer Res Treat.* 2012;11(2):133–139.
85. Hwang L, Okoye CC, Patel RB, et al. Stereotactic body radiotherapy for benign spinal tumors: meningiomas, schwannomas, and neurofibromas. *J Radiosurg SBRT.* 2019;6(3):167–177.