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Intramedullary spinal cord tumors: the value of intraoperative neurophysiological monitoring in a series of 57 cases from two Italian Centres.

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ABSTRACT

Background: Intramedullary spinal cord tumors are rare lesions of the central nervous system. Anatomical, molecular and radiological features are well defined, but correct management is still matter of debate. Pertinent literature has reported conflicting opinions regarding the use of intraoperative electrophysiological monitoring (IONM) in the surgical treatment of this kind of lesions, recently. We report a retrospective study from two Italian centres, in order to highlight the usefulness of IONM in the management of intramedullary lesions.

Methods: We performed a retrospective review of patients with intramedullary spinal tumor who underwent surgical resection from February 2011 to February 2018 in two different institutions. Clinical and radiological data, lesion features, timing of symptom onset and IONM findings were recorded. The IONM included somatosensory-evoked potentials(SSEP), motor-evoked potentials(MEP) and D-Wave whenever possible. We evaluated the outcome according to the Modified McCormick scale. We also evaluated the accuracy and relevance of surgical outcomes for each evoked potential(SSEP, MEP, D-Wave).

Results: A total of 57 patients were included. A gross total removal was achieved in 46 cases. Neurological follow-up was assessment at 3 days, and 3 and 6 months after surgery. Comparing the preoperative status and 6 months follow-up: the M-McCormick scale showed a neurological stability for 30 patients (52.63%), a worsening of neurological status for 7 patients (12.28%) and an improvement for 20 patients (35.08%). IONM presented high accuracy (sensibility of 100% and specificity of 95.65%) and significantly predicted postoperative permanent motor deficits

(P<0.0001; AUC=0.978). D-Wave appeared to have significant greater predictive value than MEP and especially SSEP alone(0.967 vs 0.722 vs 0.542; P = 0.044 and P<0.001 respectively).

Conclusions: The gold standard in the intramedullary lesion treatment is maximal safe resection with good neurological outcome, as shown in our patients. The use of IONM is helpful in intramedullary tumors resection in order to minimize postoperative neurological deficits and our analysis suggests that the use of D-Wave presents a statistically significant higher accuracy for predicting postoperative deficits than SSEP and MEP alone.

Keywords: spinal tumor; intraoperative monitoring; intramedullary tumors; D-wave; motor evoked potentials; somatosensory evoked potentials.

Abbreviations

MEPs: Motor evoked potentials

SSEPs: Somatosensory evoked potentials

IONM: Multimodal intraoperative monitoring

NCCN: National Comprehensive Cancer Network

Introduction:

Intramedullary spinal cord tumors (IMSCT) comprise 2 – 8.5% of central nervous system neoplasms in adults (1). The most common type of IMSCT is ependymoma, followed by astrocytoma (1).

Microsurgical resection with gross-total removal of IMSCT is considered the primary treatment modality, followed by adjuvant radiotherapy, especially for high grade tumors (2).

The surgical option should take into account the risk-benefit ratio due to the high possibility of postoperative neurological deficits. Despite recent advantages, surgery for IMSCTs is still very challenging and may carry significant morbidity.

Intraoperative neuro-electrophysiological monitoring (IONM) has been shown to play an important role in IMSCT surgery but recently their role has been debated (3-7).

Multimodality IONM includes somatosensory evoked potentials (SSEPs), motor evoked potentials (MEPs), D-waves, and electromyography. D-waves are generated via transcranial stimulation and monitored directly at the spinal cord level via placement of an epidural/subdural recording electrode caudal to the region at risk. D-waves are relatively resistant to anesthetic effects and permit the use of neuromuscular blockade for paralysis (8). D-waves can only be used above D10 since its recording is generated in the spinal cord. In general, a 20% decrease in D-wave amplitude is considered to be a preliminary warning, whereas a 50% reduction in amplitude is considered indicative of potential neurological injury. Combining the use of these multiple IONM modalities could improve clinical outcomes by maximizing surgical manipulations to pathologies while minimizing damage to normal structures.

The purpose of this study was to investigate: 1) preoperative clinical status, tumor features and timing of clinical onset as predicting factors in postoperative neurological outcomes, 2) the usefulness of IONM in the management of IMSCT, 3) the accuracy of IONM (SSEPs, MEPs, and D-waves) in predicting new postoperative neurological deficits

Methods

Study population

The authors retrospectively reviewed the surgical/clinical database and 300 cases of spinal tumor were extracted, from which 57 patients affected by spinal intramedullary lesion were selected (Tab 1). The patients were treated by senior spinal surgeons (M.F, F.S., R.G) in two institutions (Humanitas Research Hospital, Milan, and Santa Maria Hospital, Reggio Emilia) between February 2011 and February 2018. The two institutions basically shared the same indications for surgery and the same intraoperative monitoring.

Eligibility criteria included:

-Pre- and postoperative imaging accessible;

-Clinical/demographic/follow-up data available;

-Complete histo-pathological and molecular information;

-Use of intraoperative monitoring during the surgical removal procedure.

Exclusion criteria:

-Incomplete radiological/clinical/demographic/follow-up data;

-Metastasis;

-Cauda equine ependymoma.

Informed consent was signed before each surgical procedure in according to IBC guidelines.

Pre operative - clinical and radiological data

A careful neurological clinical examination was performed in the preoperative phase. An MRI was performed with and without gadolinium to define characteristics of the tumors and identify any multiple locations if present. We reviewed the preoperative images to calculate the diameter, length and volume of the lesion, to consider any possible association between preoperative clinical status and lesion characteristics. Moreover, we reported the time between the onset of symptoms and surgical treatment.

Surgical management

All patients underwent a dedicated anesthetic protocol for interventions with IONM including orotracheal intubation without pancuronium and induction of anesthesia with propofol and remifentanil without halogenated anesthetics. Anesthesia was then maintained with propofol (100–150 g/kg/min) and fentanyl (1 g/kg/hr) infusions, avoiding bolus doses. This protocol minimizes the interaction of drugs with IONM and facilitates a rapid awakening with the possibility of early neurological assessment. Sphinteric function was monitored in cases of lesions involving the lower thoracic cord. Patients were placed in prone position. A Mayfield clamp was used for cervical surgeries. A standard laminectomy was performed for all patients. IONM was used. Baseline SSEP and MEP, epidural electrodes were placed above and below the levels of the durotomy to monitor D-Wave, whenever possible. Posterior median sulcus was then identified and gently opened to access the tumor. Ultrasound examination was useful in some selected cases to confirm the position of the tumor (10) as well as an intraoperative image fusion between intraoperative CT and preoperative NMR (11).

A myelotomy was performed with continuous electrophysiological monitoring (dorsal column mapping) to reach the lesion through a safe entry zone. We preferred not use coagulation and remained within the limits of the tumor, performing internal debulking with the help of dissector and tumor forceps, and an ultrasonic surgical aspirator. (Fig 1)

Postoperative deficit and follow-up

Clinical/neurological examination was performed immediately after surgery. A postoperative MRI was performed within 7 days following surgery. The postoperative modified McCormick Scale (Tab 2) grade was assigned at day 3 after surgery and at the 3 and 6-month follow-up. We consider improvement of neurological outcome a decrease of almost 1 point in McCormick scale and worsening of neurological outcome an increase of almost 1 point in McCormick scale. All changes in IONM were correlated with postoperative and follow-up neurological status. All new motor deficits were defined as permanent or transitory if present or not at 6-month follow-up.

Statistical analysis

Categorical variables were compared using the chi square test. The analysis was performed to evaluate key predictors of postoperative functional outcomes.

The Kruskal-Wallis H test, a rank-based nonparametric test, was used to determine if there were statistically significant differences between two or more groups of an independent variable on a continuous or ordinal dependent variable.

Each IONM modality accuracy was determined by comparing intraoperative evoked potential changes to the presence of new persistent motor post-operative deficits via receiver operating characteristic (ROC) curves. A Pairwise t test was then used to compare the ROC curves of the SEPs, MEPs and D-Wave.

Results

Baseline characteristics

A total of 57 patients (30 M, 27 F, mean age 49.9 yr) were included. Results of baseline characteristics including sex, age, predominant spinal level of operation, histology, modified

McCormick Scale grade on admission and at follow-up, neurophysiological evaluation with SSEPs and MEPs, are summarized in Table 1.

Ependymomas were the most frequent subtype of tumors with 37 cases (64.91%), 6 hemangioblastomas (10.52%), 4 astrocytomas (7.01%, grade III), 5 cavernous malformation (8.77%) and 5 other tumors: 1 melanocytoma (1.75%), 1 solitary fibrous tumor (1.75%), 1 granulocytome (1.75%), 1 mesenchymal tumor (1.75%) and 1 capillary hemangioma (1.75%) .

The lesion was located in: the cervical spine in 20 cases, the cervico-thoracic spine in 10, the thoracic spine in 25, the lumbar spine in 1 case, and at the bulbomedullary junction in 1 case. (Table 3) An associated syringomielia was present in 12 patients.

Clinical symptoms were nonspecific with, the predominant being: pain (17.54%), paraparesis (24.56%), monoparesis (14.03%), tetraparesis (10.53%), hemiparesis (12.28%), bladder dysfunction (7.02%), ataxia (8.78%), and sensory deficits (5.26%). The diagnosis was incidental only for 6 patients but in the wait-and-see period we observed a significant increase in tumor size. The clinical data were classified in a standardized scale and, after careful neurological examination, all patients were evaluated according to the modified McCormick Scale.

Preoperative M-Mc grade was I for 17 patients, II for 18 patents, III for 16 patients, and IV for 6 patients. (Tab 3)

The mean time between signs or symptom onset and surgery was 16.7 months (7 days to 228 months). A gross total removal was obtained in 46 cases (80.70%) and a subtotal removal in 11 (19.30%). For those cases the histological diagnosis was: 3 astrocytoma, 5 ependymoma, 1 melanocytoma, 1 mesenchymal tumor and 1 granuloma. The reasons for the subtotal removal were: persistent variations in IONM in 6 cases, intraoperative histological report in 3 cases and in 2 cases the tumor tissue was not easily dissectible from nervous tissue. For two of these patients the D-wave had not been positioned since the tumor was located in D12.

IONM changes and clinical correlations

Overall significant IONM changes were registered in 33 patients out of 57 (57.89%). In 17 cases (51.51%), the presence of a stable caudal D-wave was predictive of a favorable long-term motor outcome even when the MEP and/or SEP were reduced or lost and allowed us to proceed with complete tumor resection. To the contrary, in 7 cases (21.21%) the D-wave amplitude dropped by 50% ore more and we chose to stop tumor resection due to the high risk of permanent paraplegia. In 5 cases (15.15%) the D-wave was reduced of less than 50% at the end of the surgery, allowing us to complete the procedure. In 3 cases (9.09%) the D-wave recording resulted difficult and unstable during the surgical procedure and at the end of tumor resection the D-wave was diminished over 50%, while MEP and SSEP remained stable or slightly changed. All of these patients emerged from surgery without any deficit and we considered the results of registration of D-Wave as a false positive. Finally, in 1 case (3.03%) the D-wave was not used because of the lesion site (D12) and we recorded a reduction of SSEPs.

Postoperative complications were observed in 13 patients (22.8%): 10 cases of CSF leaks, 1 case of CSF leak and meningitis, 1 intramedullary hematoma, 1 venous thrombosis of the legs and meningitis. The CSF leaks were treated with external spinal drainage and antibiotic therapy in 7 cases, while 4 cases required surgical revision. The meningitis was treated with antibiotic therapy, the intramedullary hematoma was re-operated, and the venous thrombosis of the legs was treated with anticoagulant therapy.

Postoperative 3-day M-Mc grade was I for 17 patients, II for 14 patients, III for 11 patients, IV for 13 patients, V for 2 patient. At 3-day postoperative evaluation, compared to the preoperative status, 29 patients (50.87%) remained stable, 9 cases (15.78%) improved and 19 patients (33.3%) worsened after the surgical procedure. At 6-month follow-up the M-McCormick scale showed a neurological stability for 30 patients (52.63%) compared to the preoperative status, for 7 patients (12.28%) a worsening of neurological status and an improvement for 20 patients (35.08%) with a clear improvement of the neurological status as compared to the immediate postoperative period. (Tab 4)

Table 2 shows the M-McCormick postoperative and during follow-up, in detail.

Statistical analysis of results

Our series showed no significant difference in age (p=0.953) or sex (p=1.000) or the timing of onset of symptoms (p=0.681) in predicting a good 6-month outcome. The only associated predictor seems to be patient preoperative neurological status (P<0.001).

We analyzed the correlation between preoperative clinical status and the diameter of the tumor (p= 0.4951), the length (p= 0.5053) and the volume (p= 0.1857) of the lesion but there was no statistically significant relationship between tumor size and symptoms.

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratio positive (LH+) and likelihood ratio negative (LH-) analysis of each evoked potential are shown in Table 5.

In our series, multimodal IONM (SSEP+, MEP+, D-wave) presented high accuracy (sensibility of 100% and specificity of 95.65%) and significantly predicted postoperative permanent motor deficits (P<0.0001; AUC=0.978). Comparing the area under ROC curves (AUC) of these tests, D-Wave appeared to have significant greater predictive value than MEP and especially SSEP alone (0.967 vs 0.722 vs 0.542; P = 0.044 and P<0.001 respectively). The ROC curves were displayed in Figure 2 and these results were summarized in Table 5.

Discussion

The golden standard of treatment for intramedullary spinal cord tumors should be maximal safe resection avoiding, whenever possible, the worsening of neurological symptoms. This goal can be achieved better if the lesions are treated by an experienced neurosurgeon in a highly specialized center with all the latest technological tools available.

Excellent results have been reported in both pediatric and adult patients (12, 13). Additionally, as surgical techniques continue to advance, patient outcome is expected to improve with a decrease in risks associated with resection (13, 14).

Postoperative outcome is determined by many factors. The preoperative neurological status, the time of postoperative hospitalization, as well as the time between the onset of symptoms and the surgical procedure, impact on the postoperative outcome. (15)

Our statistical data suggest that the volume, diameter and length of the tumor do not influence the postoperative outcome of patients. It is therefore essential to proceed with the surgical removal of an intramedullary lesion at the onset of symptoms. In accordance with recent literature, early surgical intervention (in the presence of symptoms) is recommended since it minimizes the risk of postoperative complications, thus reducing hospitalization time and improving the clinical outcome of patients (16, 17).

The histology of the tumor is another important predictive factor of good outcome.

Astrocytomas and ependymomas represent the most common intramedullary neoplasms (18).

Ependymomas usually require gross total removal without any postoperative treatment (19).

Early diagnosis and surgery, before severe paralysis, are important to obtain good functional outcomes.

Subtotal resection may be necessary in some cases, particularly in patients with encapsulated tumors (15, 20). There are no randomized trials addressing the role of postoperative radiation therapy and it appears to offer no advantages over gross total removal (21). Most observational studies have found that postoperative RT is associated with improved local control and progression-free survival, but the effect on overall survival is less clear (15, 22). There is a proposal that higher doses of RT (50.4 to 54 Gy) are more effective than lower doses (20). Nevertheless, consensus-based guidelines reported by the National Comprehensive Cancer Network (NCCN) suggest postoperative RT only for patients who have undergone subtotal resection or biopsy of a

myxopapillary ependymoma. In our series, only 5 patients with ependymoma underwent subtotal resection. We chose not to perform any adjuvant therapy and to follow the patients with periodic MRI scans.

Regarding astrocytomas, the best management strategy remains controversial. Some studies recommend aggressive resection, while others conclude that biopsy alone yields a better prognosis (23, 24). In general, it is our opinion that the resection of spinal cord astrocytomas should be reserved for selected cases. We treated 4 astrocytomas: 1 underwent gross total removal and 3 subtotal.

We clinically and radiologically followed these patients up to 12 months following the surgical procedure. All of them underwent adjuvant radiotherapy, and none of them had a recurrence

The value of IONM

The use of intraoperative electrophysiology techniques including SSEP, MEP, D-wave and dorsal column mapping have been advocated to modify surgical strategy, in order to preserve the patient's neurological function after surgery that, along with excision of the entire tumor, is the aim in most procedures (25, 26).

As surgical removal, with possible GTR, represents the standard of care in the management of these tumors, different tools are described in literature for this purpose. Ultrasonography helps to determine tumor margins (10), the presence of cysts and the location of the tumor; another option is represented by the use of intraoperative fluorescein (27, 28) and /or intraoperative navigation by merging CT scan and MRI. (11)

The results of our study suggest that the most important tool for this kind of surgery is the use of IONM. The aim of neurophysiological intraoperative monitoring is to identify a spinal cord injury at a reversible stage and to modify surgical strategy according to that data. Loss of MEPs and/or a decrease in the D-wave amplitude should be a warning to the surgeon of a motor pathway injury.

Together with SSEPs, MEPs may totally disappear during surgery. In these cases, if the D-wave amplitude is either stable or decreased by less than 50%, the possible postoperative motor deficits will recover after surgery in a few days or months, as shown in our cases. We had an intraoperative reduction of the D-wave < 50% with an important reduction or disappearance of the MEPs in 5 cases and those patients had a transient deficit. Seven patients had a permanent neurological deficit with reduction of the D-wave ≥ 50%. The D-wave has more specificity and sensibility in detecting motor deficit (29) compared to MEPs. This phenomenon can be due to the reversible inactivation of noncorticospinal descending tracts and the propriospinal system, whilst fast-conducting corticospinal fibers are mostly preserved (29). Use of dorsal column mapping is essential because a delicate myelotomy incision is required to reach intramedullary tumors. (Fig 1) The midline in a normal cord is the dorsal median sulcus, located between the elevated posterior columns, midway between the root entry zones. The midline can also be identified by following the dorsal median sulcal vein. However, in the presence of intramedullary tumors the surface anatomy may be altered significantly, from cord edema or the tumor itself, and the use of dorsal column mapping becomes necessary in locating a safe entry zone. Many symptoms such as generalized numbness, painful dysesthesias below the surgical level, proprioceptive loss, and gait dysfunction are due to dorsal column dysfunction. These deficits can be very disabling, even with good postoperative motor function. It was possible to reduce the surgical morbidity in IMSCT surgery through the combined use of somatosensory evoked potential, motor evoked potential, and D-wave recordings (30-32).

IONM accuracy in the IMSCT surgery

D-Wave monitoring is actually considered the golden standard for assessing the integrity of CT in spinal monitoring, the real accuracy of D-Wave in comparison with the other evoked potentials is not well investigated (33-36).

In our study, comparing the area under ROC curves (AUC) of each evoked potential, D-Wave appeared to have greater predictive value than MEP and especially SEP. (Figure 2)

Based on these results, the recording of D-Wave significantly increased the accuracy of neurophysiological monitoring in intramedullary tumors (34) and also in extramedullary tumors (37).

After more than 10 years of experience in the treatment of intramedullary tumors with IONM these are our remarks:

- often, during surgery, the MEPs response is recorded in an on-off fashion; on the contrary, D-wave deterioration usually occurs gradually so there is time to take corrective measures (29, 30).

- the D-wave allows a continuous monitoring of the function of the cortico-spinal tract without the need to interrupt surgery for elicitation of the MEPs; this real-time continuous monitoring is important mostly during dissection of a tumor with less well-defined border between lesion and healthy spinal cord tissue (33, 34).

- A stable D-Wave amplitude allows proceeding with tumor resection even in the case of MEP/SSEP loss because the deficit expected is transitory (34).

Despite our positive experience, there are still controversial views about the usefulness of IONM during intramedullary spinal cord tumors surgery.

The authors of a recent American Guideline (35) recommended the use of IONM during spinal cord/spinal column surgery only as a diagnostic adjunct to assess spinal cord integrity (level I), while the use of the same monitoring is not recommended as a therapeutic tool during intramedullary tumor resection procedures (level II) or other spinal cord/spinal column surgery (level III). Finally, the authors concluded that IONM can only document a neurological deficit but does not prevent it and, for this reason, the use of IONM during spinal surgery cannot be considered a "standard of care." (36)

These guidelines have been developed also with the purpose (fully acceptable) of protection from medico-legal complaints based on the "mandatory" use of a technique with limited evidence.

A recent review (38) also failed to show benefit from IONM in spinal tumors surgery but out 15 examined papers only 2 reported the recording of the D-wave which in our experience is the most important monitoring tool.

Many letters were written in response to these guidelines (4-7, 33). Furthermore, other important reviews reached different conclusions (36, 39). This make us aware that the effectiveness of the IONM is still a debated question and a worldwide consensus is far off.

It is our opinion that the use of IONM in defining the correct myelotomy point is undoubtedly useful. (Fig 1) Moreover, even if the IONM cannot prevent neurological damage, they can warn the surgeon in order to prevent further surgical manipulation of a sensitive or already injured anatomical region.

This warning is useful in the clinical outcome only if the surgeon takes care of it (40).

Limits:

The limitations of our study include its retrospective nature, lack of randomization, and no comparison patient group who underwent tumor removal without IONM. However, monitoring was performed by the same team throughout the study, and all operations were performed by senior surgeons (M.F, R.G. and F.S.), thus limiting a possible source of bias. Hence, the results of this study may warrant larger prospective studies on a multicenter basis to further elucidate its diagnostic and therapeutic value and cost-effectiveness in patient care involving IMST.

Conclusion:

Our case series of intramedullary tumors leads us to conclude that these tumors should be treated whenever the patient becomes symptomatic. The probability of a good clinical outcome is closely

related to the patient's preoperative neurological status and to the timing between the onset of symptoms and surgical treatment while there is no significant relationship with volume, length or diameter of the tumor. The gold standard should be maximal safe tumor resection. The use of D-wave presented statistically significant higher accuracy to predicting postoperative deficits than SSEP and MEP alone. Furthermore, the use of multimodal IONM, including D-Wave, represents an important tool to avoid neurological injury during surgery, allowing a modification of the surgical strategy and subsequent prevention or mitigation of postoperative deficits.

Delia Cannizzaro and Cristina Mancarella contributed equally to the drafting of this manuscript.

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Figure legends

Figure 1. A, B and C show intraoperative monitoring in order to define the entry zone and the myelotomy. Preoperative cervical MRI, (D) axial and (E) sagittal images show a big cervical intramedullary lesion.

Figure 2. The ROC curve compares the accuracy of diagnostic tests. In our analysis, it shows that D-Wave appeared to have significant greater predictive value than MEP and SSEP alone.

Tables

N	Age	Sex	Site	Histology	Syrinx	Removal	Complication	Timing from diagnosis (months)	MMC before surgery	MMC Postop			SSEP changes	MEP changes	D-Wave changes
										3 days	3 months	6 months			
1	55	M	D2-D3	hemangioblastoma	Y	total	intramedullar hemorrage	3	II	IV	IV	IV	N	Y	Y
2	51	M	D5-D7	ependymoma	Y	subtotal	N	48	III	IV	IV	III	N	Y	Y
3	35	M	D4	ependymoma	Y	total	N	3	I	I	I	I	N	N	N
4	37	M	D11-D12	ependymoma	N	total	N	6	I	I	I	I	N	N	N/A
5	52	M	C5	Cavernous angioma	N	total	N	12	I	I	I	I	N	N	N
6	51	F	C6	Cavernoma	N	total	N	6	III	III	II	II	N	Y	N
7	46	M	D11-D12	ependymoma	N	subtotal	N	2	I	I	I	I	N	N	N/A
8	47	M	D2	Solitary fibrous tumor	N	total	N	30	II	II	II	I	N	N	N
9	55	M	D3-D4	astrocytoma	N	subtotal	CSF-leak	14	I	I	I	I	N	N	N
10	17	F	C3-C5	hemangioblastoma	N	total	CSF-leak	3	III	II	II	II	Y	N	N
11	49	M	C4C5	ependymoma	N	total	N	3	I	I	I	I	N	N	N
12	59	F	C7-D1	ependymoma	N	total	N	6	II	III	III	II	Y	N	N
13	74	M	D8-D9	Capillary hemangioma	N	total	N	4	IV	III	III	III	N	N	N
14	51	F	C4C6	ependymoma	N	total	CSF-leak	3	I	II	I	I	N	Y	N
15	62	M	C3-C7	ependymoma	N	total	CSF-leak	10	II	II	II	II	Y	N	N
16	41	F	C6-D2	ependymoma	N	total	N	4	II	III	II	II	Y	N	N
17	43	M	C3C7	ependymoma	N	subtotal	CSF-leak/meningitis	9	II	II	II	I	N	N	N
18	30	F	D4	ependymoma	N	total	N	1	I	I	I	I	Y	N	N
19	48	F	C7-D1	ependymoma	Y	total	CSF-leak	36	II	II	II	II	N	N	N
20	21	F	D12-L1	ependymoma	N	total	N	12	II	II	II	II	N	N	N/A
21	51	F	D8-D10	granuloma	N	subtotal	N	24	IV	IV	IV	IV	N	Y	Y
22	28	F	C5-C7	ependymoma	N	total	N	2	I	I	I	I	N	N	N
23	56	M	C7-D3	ependymoma	Y	total	CSF-leak	36	III	III	II	II	N	Y	Y
24	70	M	C3-D4	ependymoma	N	Total	CSF-leak	36	IV	III	IV	IV	N	Y	Y
25	48	F	C2-C4	hemangioblastoma	Y	total	N	101	II	II	II	II	N	N	N
26	54	F	C3-C5	ependymoma	N	total	N	11	II	I	I	I	N	N	N
27	46	M	D1-D2	astrocytoma	N	total	N	2	II	II	II	I	N	Y	Y
28	43	F	C5C7	ependymoma	Y	total	N	3	I	II	II	I	N	N	N
29	50	F	C4-D2	ependymoma	N	total	N	228	III	II	II	II	N	Y	N
30	52	F	C3C6	ependymoma	N	total	CSF-leak	84	II	IV	III	III	Y	Y	Y
31	52	M	D7	ependymoma	Y	total	N	0,25	III	V	IV	IV	N	Y	Y
32	56	F	C7-D1	ependymoma	N	total	N	3	I	I	I	I	N	N	N
33	18	M	D9-D11	ependymoma	Y	total	N	7	I	I	I	I	N	N	N
34	38	F	D10-D12	astrocytoma	N	subtotal	N	2	III	III	III	III	Y	N	N/A
35	52	M	D9	ependymoma	N	total	N	12	IV	V	IV	IV	Y	Y	Y
36	67	M	C3-C5	ependymoma	N	total	N	10	I	I	I	I	N	N	N
37	49	M	D11	melanocitoma	N	subtotal	meningitis/PTV	6	II	IV	IV	IV	Y	Y	Y
38	67	M	C7-D1	astrocytoma	N	subtotal	N	4	I	I	I	I	N	N	N
39	79	F	D3D5	mesenchymal	N	subtotal	N	1	III	IV	IV	IV	N	Y	Y
40	31	F	C4C5	ependymoma	N	total	N	3	I	III	II	II	Y	Y	N
41	35	F	C4-C6	hemangioblastoma	N	total	csf-leak	5	I	I	I	I	N	N	N
42	49	M	D1-D2	Cavernous hemangioma	N	total	N	2	II	III	II	II	Y	Y	Y
43	47	F	medulla	ependymoma	N	total	N	60	III	IV	III	II	Y	Y	Y
44	74	F	D2	ependymoma	N	total	N	10	IV	IV	IV	IV	N	N	N
45	60	M	C4C5	ependymoma	N	total	N	5	IV	IV	III	II	N	N	N
46	77	M	C5-D1	ependymoma	N	subtotal	CSF-leak	18	III	IV	IV	IV	Y	Y	Y
47	36	M	D3-D5	ependymoma	Y	total	N	4	III	IV	III	II	Y	Y	N
48	65	M	D4-D7	ependymoma	N	total	N	4	II	II	I	I	N	N	N
49	52	M	D7-D11	ependymoma	N	total	N	6	III	III	II	II	Y	Y	N
50	57	M	C5	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	Y	Y
51	60	F	D4	Cavernous angioma	N	total	N	6	II	I	I	I	Y	N	N
52	46	F	D2-D3	cavernous angioma	N	total	N	6	II	I	I	I	Y	N	N
53	46	F	C4-C5	cavernous	N	total	N	5	III	II	I	I	Y	N	N

				angioma											
54	24	M	C4.C7	ependymroma	Y	total	N	6	II	III	II	I	Y	Y	N
55	56	M	C6-D1	hemangioblastoma	N	total	N	9	III	IV	III	II	N	Y	N
56	65	F	C6-C7	ependymroma	N	total	N	7	I	I	I	I	N	N	N
57	66	F	D7	hemangioblastoma	N	total	N	2	III	II	II	I	Y	Y	N

Table 1 Clinical and radiological data summary

Grade	Modified McCormick scale
I	Intact neurologically, normal deambulation, minimal dysesthesia
II	Mild motor or sensory deficit, functional independence
III	Moderate deficit, limitation of function, independent with external aid
IV	Severe motor or sensory deficit, limited function, dependent
V	Paraplegia or quadriplegia, even with flickering movement

Table 2 Modified McCormick scale

N	57
Gender (M)	30 (52.6%)
(F)	27 (47.4%)
Age (years)	49.9 ± 14.1

Predominant spinal level of operation	
Cervical	20 (35.1%)
Cervico-thoracic	10 (17.5%)
Thoracic	25 (43.9%)
Lumbar	1 (1.75%)
Bulbomedulary junction	1 (1.75%)
Histology	
Ependymoma	37 (64.9%)
Hemangioblastoma	6 (10.5%)
Cavernous malformation	5 (8.8%)
Astrocytoma	4 (7.0%)
Melanocytoma	1 (1.75%)
Solitary fibrous tumor	1 (1.75%)
Granulocytoma	1 (1.75%)
Mesenchymal tumor	1 (1.75%)
Capillary hemangioma	1 (1.75%)
Modified McCormick scale grade	
At admission	
I	17 (29.8%)
II	18 (31.6%)

III	16 (28.1%)
IV	6 (10.5%)

Table 3 Histology, localization, clinical and neurological data

N	57
Modified McCormick scale grade	
3 days follow up	
I	17 (29.8%)
II	14 (24.6%)
III	11 (19.3%)
IV	13 (22.8%)
V	2 (3.5%)
3 months follow up	
I	19 (33.3%)
II	19 (33.3%)
III	9 (15.8%)
IV	10 (17.5%)
V	0
6 months follow up	
I	26 (45.6%)

II	17 (29.8%)
III	5 (8.8%)
IV	9 (15.8%)
V	0

Table 4 Clinical follow-up: Modified McCormick scale grade

	Multimodal IONM (SSEP+MEP+ D-Wave)	**SSEP**	**MEP**	**D-Wave**
Truenegative	44	29	27	43
Truepositive	7	2	6	7*
Falsenegative	0	5	1	0
Falsepositive	2	17	19	3
Sensitivity	100%	28,6%	85,71%	100%
Specificity	95,65%	63%	58,7%	93,48%
Positivepredictive value	77,7%	11,1%	24%	70%
Negativepredictive value	100%	85,71%	96,4%	100%
Likelihoodratio+	23	1,13	2,08	15,33
Likelihoodratio-	0	0,77	0,24	0
AUC	0.978	0.542	0.722	0.967
95%CI	0.894-0.997	0,399–0,68	0,5820–0.836	0.878 - 0.996
P Value	**0.0001**	0.71	0.002	**0.0001**

Table 5 Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), likelihood ratio positive (LH+) and likelihood ratio negative (LH-), area under the curve (AUC) and statistical analysis of IONM.

Four patients without D-wave recording have not been included in the statistical analysis.

* Patients with postoperative permanent motor deficit and D-wave amplitude reduced of 50% or more.