Review Article

The Role of Intraoperative Neurophysiological Monitoring in Intracranial Cavernous Malformation Surgery: A Narrative Review

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Abstract

Cavernous malformations, also known as cavernous hemangiomas or cavernomas, are abnormal vascular lesions that can occur in various parts of the body, including intracranially. Surgical resection is often the preferred treatment for symptomatic or high-risk lesions located in eloquent or critical brain or spinal cord regions. However, cerebral cavernous malformation surgery presents unique challenges due to the risk of neurological deficits and the proximity of these lesions to vital neural structures. Intraoperative neurophysiological monitoring (IONM) plays a crucial role in enhancing surgical safety, minimizing complications, and optimizing patient outcomes. This review aimed to provide an overview of the various IONM techniques employed during cerebral cavernous malformations resection, particularly the relationship between intraoperative stimulation intensity and distance to fiber tracts or specific brain nuclei as monitored by IONM.

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Keywords ● Hemangioma, cavernous, central nervous system ● Intraoperative neurophysiological monitoring ● Evoked potentials, motor ● Evoked potentials, somatosensory ● Pyramidal tracts

What's Known

- Intraoperative neurophysiological monitoring (IONM) plays a crucial role in enhancing neurosurgical safety, minimizing complications, and optimizing patient outcomes.

What's New

- IONM plays a key role in evaluating the relationship between intraoperative stimulation intensity and the proximity to critical fiber tracts or specific nuclei during surgery.

Introduction

Cavernous malformations (CMs) are abnormal clusters of dilated blood vessels with a characteristic mulberry-like appearance. While these lesions can occur anywhere in the body, those located in the central nervous system (CNS) pose the greatest clinical risk due to their potential to cause hemorrhage, seizures, and neurological deficits.[1, 2] Surgical resection is typically recommended for symptomatic or high-risk cerebral CMs (CCMs), particularly when located in eloquent or critical areas of the brain or spinal cord.[3] However, CCMs surgery presents unique challenges, including intraoperative bleeding risks, proximity to critical neural structures, and potential postoperative neurological deficits.

Intraoperative neurophysiological monitoring (IONM) plays a vital role in enhancing surgical safety, minimizing complications, and optimizing patient outcomes.[4] This review aimed to provide a comprehensive overview of various IONM techniques employed in CCM surgery, including their applications, benefits, and limitations, supported by current literature evidence, as well as future directions in this field.

CCMs, or cavernous hemangiomas, are vascular lesions composed of abnormally dilated blood vessels with no intervening normal neural tissue. These lesions occur throughout the central nervous system and present significant neurosurgical challenges, particularly when located in eloquent regions such as the brainstem.[1] Surgical management aims for complete resection to prevent rehemorrhage and alleviate symptoms, while carefully weighing the risks of new neurological deficits. For brainstem cavernomas, surgical approaches including retrosigmoid or suboccipital techniques are selected to minimize risks and optimize resection outcomes.[5]

Intraoperative neurophysiological monitoring (IONM), particularly motor evoked potentials (MEPs), serves as a crucial surgical guide for preserving motor function. The maintenance of stable MEPs during surgery is associated with better outcomes, highlighting the importance of continuous monitoring.[6] While CCM surgery presents significant challenges, particularly in eloquent brain regions, technological advances in both surgical techniques and neurophysiological monitoring have significantly enhanced patient outcomes. Optimal outcomes require meticulous preoperative planning and individualized surgical strategies to achieve maximum lesion resection while minimizing functional impairment. This review aimed to summarize the different methods of IONM modalities in CCM surgery, with special emphasis on the relationship between stimulation intensity and anatomical proximity to critical white matter tracts or deep nuclei during monitoring.

Principles of Intraoperative Neurophysiological Monitoring (IONM)

IONM encompasses various techniques to evaluate the functional integrity of neural pathways during surgery, providing real-time feedback to surgeons and allowing for immediate surgical adjustments.[4] The primary IONM modalities in CCMs surgery, as shown in table 1, included motor evoked potentials (MEPs), somatosensory evoked potentials (SSEPs), electroencephalography (EEG), brainstem auditory evoked responses (BAERs), visual evoked potentials (VEPs), and electromyography (EMG). Each modality offers unique insights into distinct neural pathways, while their integrated applications enable a comprehensive assessment of neurological function intraoperatively.[7, 8]

Table 1: Comparison of intraoperative neurophysiological monitoring modalities, including their strengths, limitations, and specific applications in surgery for cerebral cavernous malformations

IONM Modality	Strengths	Limitations	Specific Applications in CCM Surgery	References
Motor evoked potentials (MEPs)	- Real-time monitoring of motor pathway integrity - High sensitivity and specificity in forecasting motor outcomes	- Lack of standardized criteria for interpreting changes - Influenced by anesthesia and patient-specific factors	Preservation of motor function in high-risk procedures	9-13
Somatosensory evoked potentials (SSEPs)	- Monitor the integrity of the dorsal column-medial lemniscus pathway - Complements MEPs when motor monitoring fails	- Limited in detecting motor pathway injury. - Influenced by anesthesia, temperature, and blood pressure.	- Complementary to MEPs - Sensory function monitoring, especially in preserving proprioception	14-18
Electroencephalography (EEG)	- Detecting seizure activity - Valuable in surgeries involving the eloquent cortex	- less effective for deep-seated lesions. - Affected by deep anesthesia, limiting utility	Helps prevent postoperative seizures and provides feedback on brain activity	19-22
Brainstem auditory evoked responses (BAERs)	- Vital for auditory pathway integrity monitoring -Effective in preserving hearing function	- Transcranial recordings are less reliable - Susceptible to anesthesia and brain manipulation	Early detection of auditory dysfunction and cochlear nerve integrity in brainstem regions	23-27
Visual evoked potentials (VEPs)	- Real-time information on visual pathway status - Direct cortical recordings linked with outcomes	- Susceptible to anesthesia, craniotomy, and tissue manipulation - Risk of false positives	Used to predict postoperative visual deficits, especially related to homonymous hemianopia	4, 28-32
Electromyography (EMG)	- Real-time detection of cranial nerve and nerve root irritation - Triggered EMG enhances precision in neural structure identification	- Less reliable for slowly developing issues (such as compression or ischemia) - Affected by anesthesia-induced muscle relaxation	- Identifying acute nerve irritation/injury - Precision in surgical intervention	4, 33-38

Motor Evoked Potentials (MEPs)

MEPs have become an indispensable tool in neurosurgery, particularly for real-time monitoring of motor pathway integrity. Their primary advantage is the ability to provide direct intraoperative assessment of the corticospinal tract. A study demonstrated that MEPs significantly enhanced the detection of motor deficits, facilitating immediate surgical intervention that reduced postoperative complication risks.[9] The predictive value of MEPs for motor outcomes is remarkable, with reported sensitivity of 71% and specificity of 94% in predicting postoperative deficits following degenerative cervical myelopathy surgeries.[10] This high diagnostic accuracy highlights the critical role of MEPs in supporting neurosurgeons' intraoperative decision-making processes.

Despite their advantages, MEPs have some limitations. A major challenge is the absence of standardized interpretation criteria for determining significant changes that necessitate surgical intervention. While some institutions employ strict thresholds, such as a 50% reduction in amplitude, others advocate for a more comprehensive approach incorporating trend analysis, anesthesia effects, and patient-specific baseline characteristics.[11-13] This variability highlights the essential role of experienced neurophysiologists capable of contextualizing MEP data within the broader surgical physiological context.

Somatosensory Evoked Potentials (SSEPs)

SSEPs involve the electrical stimulation of peripheral nerves with subsequent recording of the evoked responses along the somatosensory pathway. The primary advantage of SSEPs is their ability to monitor the integrity of the dorsal column-medial lemniscus pathway, thereby providing critical intraoperative assessment of sensory function.[14] Notably, SSEPs could be successfully monitored in cases where MEP recordings failed, demonstrating their complementary value when used in conjunction with other monitoring techniques. Additionally, it might be particularly important for the preservation of the medial lemniscus and proprioceptive function.[15, 16] However, interpreting SSEP changes requires meticulous evaluation of various factors, including anesthesia depth, body temperature, and blood pressure, all of which might significantly influence signal characteristics. While SSEPs demonstrate high negative predictive value (with stable signals reliably indicating intact neurological function), their positive predictive value remains more variable, as SSEP alterations do not consistently correlate with postoperative neurological deficits.[17, 18]

Electroencephalography (EEG)

EEG monitoring provides several potential benefits during cerebral cavernous malformations (CCMs) surgeries, particularly for detecting seizure activity. Continuous EEG enables identification of early electrophysiological changes, permitting immediate surgical modifications to reduce postoperative seizure risk.[19] This modality proves especially valuable for surgeries involving eloquent cortex regions, as it provides real-time feedback on brain activity.[20] When integrated with other modalities, such as MEPs or SSEPs, EEG significantly enhanced a more comprehensive assessment of functional brain integrity throughout the surgical procedure.[21]

However, EEG monitoring demonstrates limited efficacy for deep-seated lesions, such as those in the brainstem or thalamus, due to poor signal resolution from subcortical structures.[21] Its high sensitivity to anesthetic agents diminishes its reliability in procedures requiring deep sedation.[22] While EEG shows utility in preventing postoperative seizures, its predictive value for long-term neurological outcomes remains poorly characterized, generating ongoing debate regarding its optimal role in neurovascular surgery.

Brainstem Auditory Evoked Responses (BAERs)

BAERs are critical for monitoring the auditory pathway during surgeries involving the cerebellopontine angle or brainstem, particularly CCM cases. By analyzing waveforms generated by auditory stimuli, BAERs provide information regarding the cochlear nerve, cochlear nucleus, and the auditory pathways.[23, 24] Early identification of auditory dysfunction alerts the surgical team to potential risks, enabling prompt adjustments.[23, 24] However, interpreting BAERs intraoperatively can be challenging, especially when wave V latency or amplitude changes suggest potential hearing loss.[25, 26] Additionally, individual anatomical and physiological differences might complicate waveform interpretation, while background noise or electrical interference might further compromise results.[27]

Visual Evoked Potentials (VEPs)

VEPs provide real-time information about the functional status of the visual pathway by monitoring the amplitude and latency changes in the P100 wave, a key indicator of visual function impairment.[32] Direct cortical recordings demonstrate stronger correlations with postoperative visual field deficits than transcranial recordings.[28] A 40% decrease in the VEP waveform amplitude during surgery serves as a critical warning sign, correlating with postoperative visual deterioration.[32] Intraoperative VEPs reliably predict postoperative visual field changes, particularly for assessing risks of homonymous hemianopia.[28, 29]

In contrast, transcranial VEPs recording demonstrate lower reliability due to their susceptibility to anesthetic depth, craniotomy effects, and brain tissue manipulation.[30] They also carry a risk of false-positive alerts, where VEP changes might not reflect actual visual field deficits, potentially prompting unnecessary surgical modifications.[4, 31] Therefore, VEP monitoring should be combined with other modalities to optimize surgical outcomes.

Electromyography (EMG)

Continuous EMG monitoring is critical for assessing cranial nerves and spinal nerve roots during neurosurgery.[4] For CCMs located near the brainstem, EMG provides real-time detection of spontaneous activity, alerting surgeons to potential nerve irritation or injury, and facilitating immediate interventions.[33-35] Triggered EMG, which utilizes direct electrical stimulation to identify neural structures, enhances surgical precision and helps differentiate nerves from surrounding tissues, thereby minimizing inadvertent damage.[36]

While effective for detecting acute nerve irritation or injury, EMG is less reliable for identifying slowly progressive issues, such as progressive nerve compression or ischemia.[37] This constraint has prompted consideration of supplementary monitoring techniques to achieve comprehensive intraoperative nerve function assessment. Furthermore, muscle relaxants used during anesthesia might attenuate EMG response, potentially obscuring signs of nerve stress and complicating signal interpretation.[38]

Anesthesia Plan for Intraoperative Neurophysiological Monitoring (IONM) During Brain Surgeries

The anesthetic plan plays a pivotal role in successful IONM during brain surgeries, as anesthetic agents and techniques can significantly impact signal quality. Total intravenous anesthesia (TIVA) with agents such as propofol and remifentanil represents the gold standard for IONM, offering minimal interference with MEPs and SSEPs.[39, 40] Propofol maintains stable signals, while remifentanil provides adequate analgesia without suppressing evoked potentials. In contrast, volatile anesthetics, such as sevoflurane, even in low doses, may suppress IONM signals.[18] Muscle relaxants such as rocuronium require careful titration, as most IONM modalities, including MEPs and EMG, necessitate minimal neuromuscular blockade.[38] Anesthesia depth must be precisely controlled, with bispectral index (BIS) monitoring helping balance between oversedation, which can suppress signals, or undersedation, which increases the risk of patient movement.[41, 42]

Maintaining stable hemodynamics and physiological parameters is essential in anesthetic management for IONM during brain surgeries, as these parameters directly impact monitoring reliability. Factors such as hypothermia, hypotension, or excessive anesthetic depth can significantly attenuate evoked potentials, compromising monitoring sensitivity and accuracy.[43, 44] Individualized hemodynamic management is particularly important for preserving cerebral perfusion during surgeries in eloquent brain regions.[45, 46] Moreover, preventing artifacts caused by anesthesia equipment or patient positioning is essential for minimizing signal interference.[4, 21] A systematic approach involving proper placement of IONM electrodes, noise reduction, and optimal grounding techniques remains critical. The application of advanced filtering algorithms in modern IONM systems has further improved artifact reduction.[47]

Intraoperative Neurophysiological Monitoring (IONM) for Cerebral Cavernous Malformations (CCMs) Surgeries

The primary goal of IONM in CCMs surgeries is real-time detection and prevention of injury to motor, sensory, and cranial nerve pathways, thereby reducing postoperative deficit risks. The process initiates with preoperative planning, where the monitoring team evaluates the cavernoma's anatomical position, particularly when adjacent to eloquent regions, such as the motor/sensory cortex or cranial nerve nuclei.[33] Standard IONM modalities employed here include MEPs for monitoring corticospinal tract integrity, SSEPs for real-time feedback on sensory pathway integrity, BAEPs for brainstem-adjacent lesions, and VEPs for cavernomas near visual pathways.[4] For patients with cavernoma-related seizure history, continuous EEG monitoring proved particularly valuable by detecting cortical irritation during surgery.[33] When cavernomas involve cranial nerve pathways, direct cranial nerve monitoring is essential to prevent permanent nerve injury.[4] Collectively, these IONM techniques enable real-time data-driven surgical decision-making that optimizes the balance between complete lesion resection and functional preservation, ultimately reducing postoperative neurological complications.

IONM modalities for CCMs differ from those used in gliomas due to variations in lesion characteristics involving location, vascular, and neurological risk profiles. In CCM resection, the primary goal involves protecting eloquent brain regions while preserving motor and sensory functions, typically requiring SSEPs, MEPs, and occasionally BAEPs or VEPs. In contrast, glioma surgeries focus on aggressive tumor resection while sparing critical structures, frequently incorporating SSEPs, MEPs, and direct cortical stimulation, particularly during awake craniotomies for low-grade gliomas.[48, 49] Additionally, CCMs' monitoring frequently incorporates BAEPs and cranial nerve assessments, particularly for lesions near vascular structures, while glioma resection, particularly for high-grade tumors, often demands extensive motor cortex monitoring due to their infiltrative growth pattern. A significant distinction involves EEG application: glioma surgeries emphasize eloquent cortex and white matter tract mapping, frequently necessitating awake surgeries and neurocognitive tests.[50] Conversely, EEG monitoring during CCM procedures primarily targets seizure detection, given the association of these lesions with epilepsy.[2] However, the effectiveness of EEG in deep-seated CCMs remains limited by subcortical signal attenuation, heightening the importance of MEP monitoring.[51] Overall, these protocol differences underscore the necessity for tailored IONM strategies to optimize surgical outcomes and minimize neurological deficits.

Advancements in Intraoperative Neurophysiological Monitoring (IONM) Techniques for Nuclei and Fiber Tract Mapping

The corticospinal/corticobulbar (CS/CB) tracts and specific brain nuclei represent critical neural structures requiring precise mapping and continuous monitoring to prevent permanent neurological deficits. Recent advancements in IONM techniques have enabled continuous cortical and subcortical mapping approaches, which provide neurosurgeons with real-time, high-resolution feedback during procedures. These technological developments significantly enhance the accuracy of identifying and preserving these essential neural pathways throughout surgical interventions.

Brain Nuclei Mapping

Mapping of brain nuclei, particularly in the brainstem, is challenging yet remains crucial for preserving neurological function during lesion resection. While traditional techniques, such as anatomical landmarks and preoperative imaging, provide guidance, they lack the precision required to accurately localize these small, yet functionally vital structures. Advanced IONM techniques now enable continuous dynamic mapping, allowing for improved delineation of nuclear topography and boundaries with greater spatial accuracy.

IONM in pediatric neurosurgery demonstrates particular value for brainstem tumor resection, where direct stimulation mapping on the floor of the fourth ventricle could localize cranial nerve nuclei. Clinical studies have successfully identified facial, hypoglossal, and vagal nuclei based on EMG responses in their respective muscle groups, enabling safer resection while preserving functional neural tissue.[52] A recent study emphasized the synergistic use of intraoperative subcortical mapping (ISM) with diffusion tensor imaging (DTI), which compensates for individual anatomical variability and improves the accuracy of neural pathway localization during surgery.[53]

Supratentorial and Infratentorial Fiber Tract Mapping

Mapping corticospinal/corticobulbar (CS/CB) tracts is essential in surgeries near critical pathways. Techniques such as DTI/DTT provide preoperative estimates of tract locations. Combining DTI with intraoperative electrical stimulation improves accuracy and safety during glioma surgery. However, brain shifts can cause discrepancies between preoperative imaging and intraoperative findings, highlighting the necessity for real-time navigation updates.[54]

Intraoperative electrical stimulation provides effective mapping of fiber tracts (figure 1 A-D). Through systematic variation of stimulation intensities and analysis of muscle responses, neurosurgeons can accurately determine the spatial relationship between lesions and CS/CB tracts.[55] A recent review emphasized the efficacy of this technique in preserving corticospinal function during brainstem surgeries, highlighting the importance of continuous monitoring and adaptive surgical strategies based on intraoperative findings.[52] However, the correlation between stimulation thresholds and distance from tracts is under investigation.[7, 55]

Collectively, advanced IONM techniques for intraoperative nuclei and fiber tract mapping enhance both surgical safety and procedural efficacy. The integration of DTI with electrical stimulation offers patient-specific anatomical insights. However, persistent challenges remain in the accurate interpretation of these data, particularly concerning brain shift phenomena and the complex anatomy of the brainstem pathways.

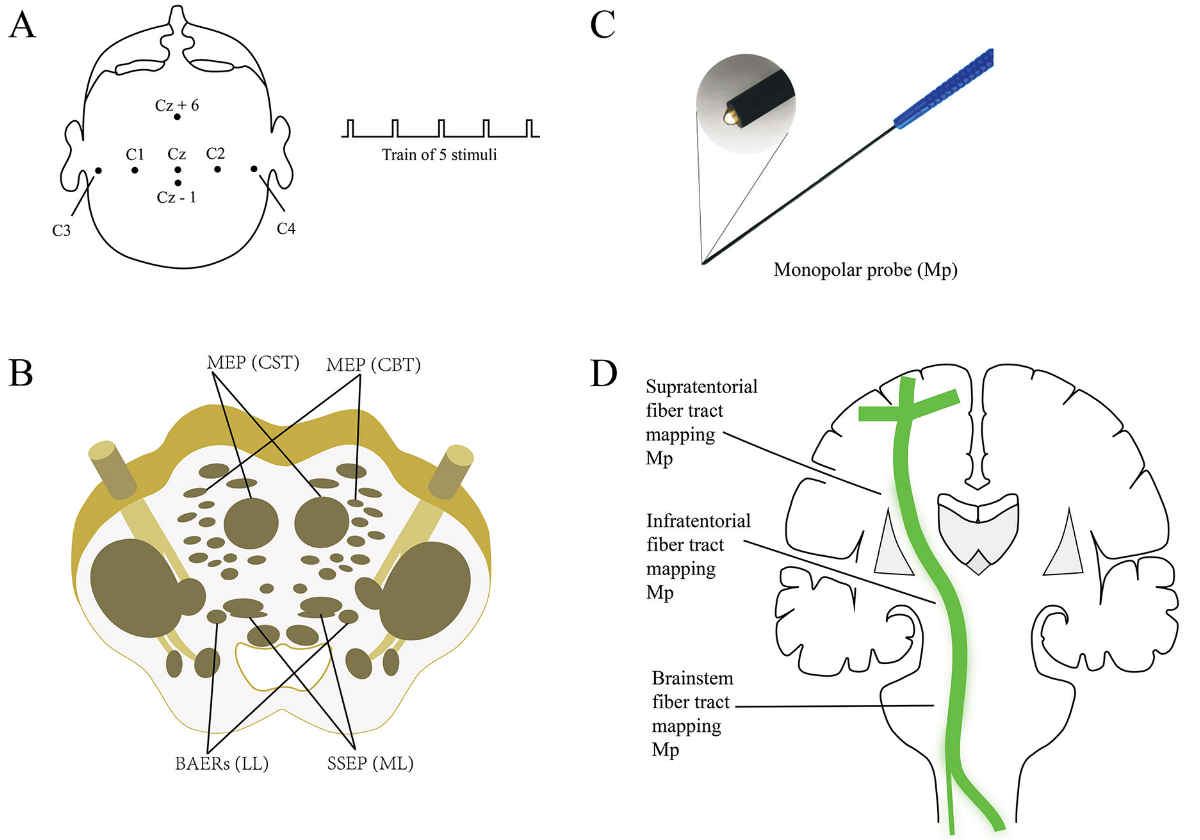

Figure 1: The schematic illustrates classification of intraoperative neurophysiological monitoring (IONM) and fiber tracts mapping through the combination of monopolar stimulation and IONM. (A) Transcranial electric stimulation (TES) array configuration for neurophysiological monitoring, demonstrating the standard train-of-five stimulation paradigm. (B) IONM applications help monitor the functional integrity of neural pathways (motor, sensory, auditory) throughout the CCMs surgeries. (C) The use of monopolar probe technique for direct fiber tract mapping; (D) Combined supratentorial and infratentorial fiber tract mapping with detailed brainstem descending pathway localization; BAERs: Brainstem auditory evoked responses; CBT: Corticobulbar tract; CST: Corticospinal tract; LL: Lateral lemniscus; MEPs: Motor-evoked potentials; ML: Medial lemniscus; SSEPs: Somatosensory-evoked potentials; BAERs: Brainstem auditory-evoked responses

Relationship Between Stimulation Intensity and Distance to Neural Structures

The relationship between stimulation intensity and proximity to corticospinal/corticobulbar (CS/CB) tracts or specific brain nuclei remains an active research focus. A recent study demonstrated the feasibility of using intraoperative stimulation to map the CST during brainstem procedures. By delivering stimuli at various intensities and recording the resulting compound muscle action potentials, they could identify the spatial distribution of the CST, helping prevent motor deficits during demanding neurosurgical procedures on the brainstem.[55]

It is widely accepted that there is a linear relationship between stimulation current and depth of tissue penetration, with a ratio of 1 mA per 1 mm. Consequently, it is recommended that lesion resection be stopped absolutely at a 1-mA MEP-positive site, regardless of how the MEP signal from direct cortical stimulation changes.[56] On the other hand, a study investigated this relationship in the context of subcortical MEP stimulation, reporting a nonlinear correlation between stimulation intensity and the distance to the corticospinal tracts.[8] In their investigation of corticospinal tract mapping using direct brainstem stimulation, Yang and colleagues found that a positive MEP at 2 mA stimulation intensity indicated a distance of less than 4 mm, while 1 mA corresponded to less than 2 mm, with relatively high sensitivity and specificity for this association.[55] Therefore, the relationship between stimulation intensity and distance to critical structures remains an area of ongoing research and debate. Future research should focus on refining our understanding of these relationships and developing more sophisticated algorithms for real-time integration of multimodal data during surgery.

Impact on Surgical Strategy and Outcomes

The use of IONM in CCM surgery has significantly influenced surgical strategies and patient outcomes. Real-time feedback on neural function allows surgeons to adjust resection or approach during surgery to reduce the risk of neurological deficits. Numerous studies demonstrated the positive effect of IONM on outcomes in CCM resection.[49, 57-59] Patients monitored with IONM had fewer postoperative neurological deficits than those without monitoring.[59] IONM is also associated with higher rates of complete resection, particularly for lesions in eloquent brain regions.[59]

Multimodal approaches combining IONM with intraoperative imaging, such as iMRI, iCT, or ultrasound, have enhanced surgical guidance and mapping, while their widespread adoption remains limited by increased procedural complexity and resource requirements.[60-62] Emerging technologies such as intraoperative fMRI, advanced signal processing, and machine learning applications in IONM show, while but require further development, and their clinical value and cost-effectiveness need additional evaluation.[16, 63, 64]

However, multimodal monitoring presents challenges including increased technical complexity, potential data overload, and the need for skilled personnel to interpret diverse signals. Additionally, the long-term impact of IONM on functional outcomes and quality of life requires further investigation. While immediate benefits are well-documented, more research is required to determine whether these short-term improvements lead to sustained functional gains.

Limitations and Future Directions

Despite its benefits, IONM in CCM surgery presents several challenges, including variable sensitivity and specificity, which may yield false positives (causing unnecessary surgical pauses) or false negatives (potentially missing critical neural injuries). Anesthesia management further complicates signal integrity. The technical complexity of the procedure demands advanced equipment and skilled personnel, straining institutional resources and limiting widespread adoption. Additionally, inconsistent interpretation criteria for signal changes among practitioners underscore the need for standardized protocols and specialized training. Cost remains an additional barrier, as IONM requires substantial investment in equipment and personnel, raising cost-effectiveness concerns, particularly in resource-limited settings.

Looking ahead, IONM's future in CCM surgery is promising. Machine learning and AI could enhance real-time signal analysis and surgical decision-making. Advances in high-density electrode arrays could improve spatial mapping of neural functions, particularly in eloquent brain regions. The integration of IONM with functional MRI or diffusion tensor imaging could provide more comprehensive intraoperative guidance. Optogenetic stimulation could offer a less invasive option for neural monitoring, and wireless IONM systems might streamline setup procedures, enhance operational flexibility, and broaden monitoring applications, making IONM more accessible and efficient.

Conclusion

IONM has emerged as an indispensable tool in CCM surgery, delivering real-time intraoperative guidance to maximize lesion resection while minimizing neurological risks. The multimodal monitoring approach enables a comprehensive neural function assessment, allowing surgeons to precisely balance complete tumor removal with the preservation of eloquent structures. While challenges persist regarding standardization, interpretation variability, and resource allocation, IONM's significant contributions to improved patient outcomes are well-established.

Authors' Contribution

M.Sh: Study design and drafting, QY. H: Data collection and drafting; JW. S: Data collection and drafting, FQ.W: Data gathering, drafting and reviewing; YN.L: Data gathering, drafting and reviewing; X.L: Data gathering, drafting and reviewing; FL.W: Study design, supervision, and reviewing the manuscript; All authors have reviewed and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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