



Enhancing the Effectiveness of Monitoring the Robust Bulbocavernosus Reflex in Cauda Equina Surgeries: Harnessing Machine Learning to Decode the Complexity of Stimulation Parameters

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ABSTRACT

Cauda equina surgeries present significant challenges due to pathological diversity and anatomical variability, particularly in pediatric cases involving tethered spinal cord syndrome, lumbosacral spinal tumors, and congenital deformities. The Bulbocavernosus Reflex (BCR), mediated by the S2–S4 sacral segments, is an efficient multimodality intraoperative neurophysiological monitoring (IONM) tool for preserving sacral neural pathways during these complex procedures. Since its introduction in the IONM arena in the late 1990s, the efficacy of BCR in preventing pelvic neural deficits was gradually established. At the same time, advancements in IONM technology over the decades fostered its widespread and reliable utility. Despite evidence-based advantages, achieving robust BCR monitorability remains challenging due to highly variable stimulation parameters. Standardized protocols can provide a pathway to enhance its potential by enabling widespread adaptability and ensuring consistent neuromonitoring outcomes. A systematic meta-analysis was performed across relevant databases, focusing on studies utilizing BCR as a multimodality IONM during spinal surgeries. The analysis primarily aimed to establish a feasible set of BCR stimulation parameters to enhance monitorability alongside an evaluation of the sensitivity and specificity of BCR in preventing genitourinary postoperative deficits. AI machine learning tools were also employed to determine stimulation parameter combinations associated with 100% monitorability, providing insights into optimal protocols. Optimal BCR monitorability (100%) was consistently achieved with stimulation intensity of 40–50 mA, pulse counts of 4–8, pulse durations between 0.1–0.5 ms, and interstimulus intervals (ISI) of 2–3 ms, reflecting the critical role of not only stimulation intensity but also the synergistically interdependent dynamics of involved parameters, including temporal dynamics. Broad intensity ranges paired with shorter pulse durations and higher pulse counts effectively enhanced neural activation, underscoring the craft of devising a precise set of stimulation parameters essential for achieving reliable monitorability. Machine learning analysis identified stimulation intensity and pulse count as the most influential predictors of monitorability, explaining 69.25% of the variance and providing key insights for optimizing stimulation protocols. BCR monitoring is pivotal in preserving sacral nerve integrity and minimizing postoperative deficits. Advancing parameter optimization within IONM protocols ensures improved monitorability, enhancing surgical precision and patient outcomes.

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INTRODUCTION

Cauda equina surgeries rank among the most complex neurosurgical procedures due to the pathological diversity and congenital anomalies that lead to highly variable and atypical anatomical presentations [1]. These surgeries encompass conditions such as tethered spinal cord syndrome, spinal dysraphism, and lumbosacral lipomas, each posing distinct challenges in surgical management [2,3]. In pediatric cases, these complexities are further compounded by a high prevalence of conditions such as thick filum terminale, diastematomyelia, and tumors, including myxopapillary ependymomas, astrocytoma, and lipomas, along with cerebral palsy cases requiring rhizotomy, which amplify the risks of intraoperative neural injury [4,5]. Preserving sacral neural pathway integrity remains the cornerstone of these surgeries, employing intraoperative neurophysiological neuromonitoring (IONM) techniques such as bulbocavernosus reflex (BCR), Pudendal somatosensory evoked potentials (pSEPs), pudendal dorsal root action potentials (DRAPs), and anal motor evoked potentials (MEPs). Distinguished among these, BCR offers a holistic and efficient means to assess sacral sensory and motor nerve function, proving pivotal in mitigating the risks of nerve injury and ensuring postoperative recovery [1,4].

BCR is an oligosynaptic spinal reflex arc mediated by the S2–S4 sacral segments. It is elicited by stimulating the dorsal nerve of the penis or clitoris and recorded from the external anal sphincter (EAS) using electromyography. The afferent pathway synapses at Onuf's nucleus, with efferent activation of the bulbocavernosus muscle as a primary effector, making BCR a reliable indicator of sacral neural integrity [2]. Its integration into multimodal IONM enables real-time monitoring of sacral pathways, helping preserve urogenital and anal sphincter function during surgeries involving the conus medullaris and cauda equina [6]. This utility is particularly evident in intradural surgeries for schwannomas, ependymomas, and meningiomas, where BCR monitoring minimizes nerve injury risk and improves outcomes [7]. A positive BCR in the presence of a complete lesion suggests that the sacral reflex pathways are intact. However, supraspinal inhibition is lost, indicating an upper motor neuron lesion. Conversely, an absent BCR, often associated with urogenital deficits, indicates a lower motor neuron lesion characterized by disruption of the sacral reflex pathways, resulting from damage to the pudendal nerve or its neural connections [8]. BCR's feasibility allows neurophysiologists to independently perform stimulation and detection without disrupting the surgical workflow. It makes it indispensable in complex procedures like posterior lumbar fusion and deformity corrections for spinal stenosis, kyphosis, and scoliosis [9].

The evolution of BCR monitoring reflects decades of refinement in neurophysiology. Introduced experimentally in the 1970s, BCR became a valuable IONM tool for sacral nerve preservation in 1997, pioneered by Deletis and Vodusek [10,11]. They developed double-pulse stimulation at a 3.0 ms interval to improve intraoperative response detection. However, early adoption faced challenges, including low success rates (approximately 59%), particularly in females, due to anatomical differences, moisture

interference, and electrode placement issues [1,10]. These limitations initially restricted its broader application, but foundational research laid the groundwork for subsequent advancements.

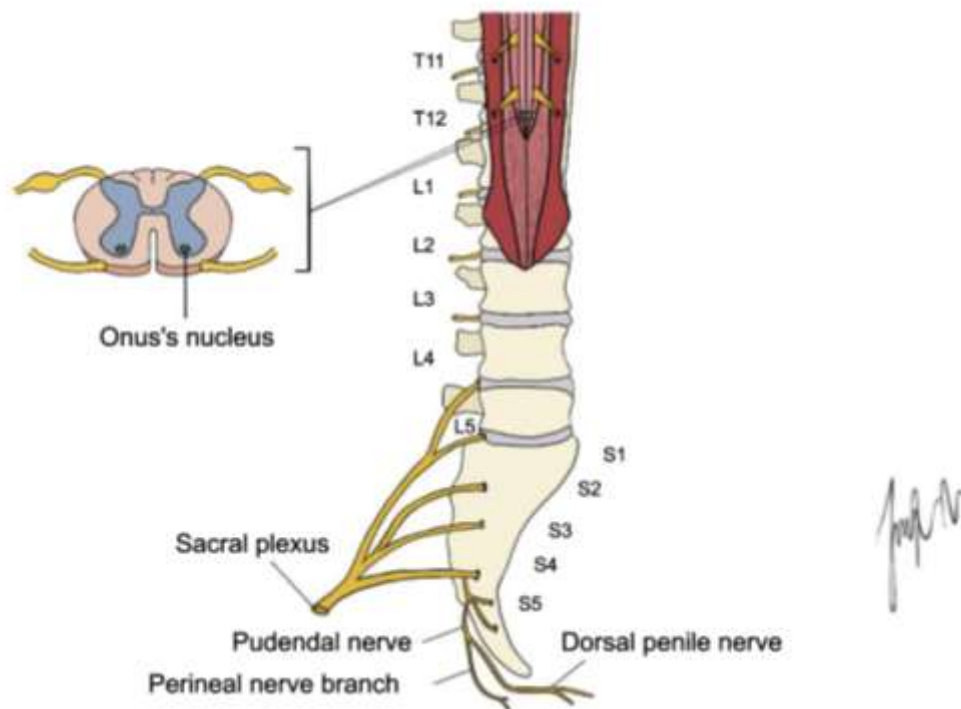


Figure 1. The Bulbocavernosus reflex mediates at the S2-S4 sacral segments through Onuf's nucleus (created by Lily Nguyen).

During the 2000s, BCR monitoring gained clinical validation as a predictive tool for postoperative outcomes, especially in surgeries involving the conus medullaris and cauda equina. Studies demonstrated its utility in maintaining sacral nerve function, though amplitude variability and the polysynaptic nature of the reflex posed interpretive challenges [12]. The 2010s saw further refinements, such as double-train stimulation and optimized electrode placement, leading to success rates exceeding 90% in pediatric cases [13]. A landmark study by Morota et al. (2019) reported a 100% positive predictive value (PPV) for favorable urinary outcomes, with Seungwoo Cha (2018) highlighting 93.4% specificity of BCR in predicting urinary complications in patients with lipomyelomeningocele [14,15].

Despite the widespread adoption of BCR and gradual advancements in monitoring techniques, achieving consistent monitorability remains challenging. Factors such as baseline abnormalities, variability in the reflex response, and patient-specific variables, including pre-existing neural dysfunction, continue to impact monitorability and persistent signal reliability [13,14]. Inconsistent stimulation parameters and the absence of standardized protocols remain critical barriers. Addressing these issues through parameter

standardization and developing reliable warning criteria is essential for ensuring consistent BCR applications across diverse surgical contexts [3].

Bulbocavernosus Reflex (BCR) Monitoring Techniques and Clinical Neurophysiology

Currently, no universally standardized approach for intraoperative BCR monitoring exists. Foundational contributions by Vodušek (1996), Deletis and Vodušek (1997), and Rodi and Vodušek (2001) provide practical methodologies for its neuromonitoring application, offering a framework to address technical challenges and improve monitorability outcomes in caudal spinal surgeries [10,12].

Anesthesia

The BCR, an oligosynaptic reflex, is highly sensitive to general anesthesia, particularly volatile agents, which initially limited its neuromonitoring application. Muscle relaxants, restricted to tracheal intubation, inhibit the reflex [4]. In 1997, Deletis and Vodušek monitored BCR intraoperatively using propofol, fentanyl, and nitrous oxide, limiting vecuronium bromide to intubation. They noted that nitrous oxide and isoflurane suppressed or abolished the reflex when muscle relaxants were used. Rodi and Vodušek later enhanced reliability with continuous propofol and fentanyl infusions [10]. Recently, Choi et al. achieved 100% monitorability with target-controlled infusions (TCI) of propofol and remifentanyl using a single rocuronium dose during intubation [9]. These findings underscore the importance of tailored anesthesia protocols for effective BCR monitoring.

Electrodes Placement

Electrode placement is critical for effective stimulation and recording. For stimulation, silver/silver chloride disc electrodes are positioned on the dorsal penis (2–3 cm apart) in males, with the cathode proximal and the anode distal. In females, the cathode is placed on the dorsal clitoris and the anode on the adjacent labia [10]. Conductive paste and adhesive tape (or Tegaderm) ensure stable fixation. Needle or wire electrodes are preferred for recording due to their precision, particularly in small muscles like the anal sphincter. Teflon-coated wires (76 mm diameter, 2 mm bare tip) are inserted approximately 1.0 cm lateral to the anal orifice at a depth of 2.5 cm. Proper positioning is confirmed by observing muscle twitches in response to low-intensity stimuli. Adjustments are made if no response is detected [10].

Stimulation

BCR stimulation involves applying electrical stimuli to the glans penis or clitoris, eliciting anal sphincter contraction. Supramaximal stimulation is ideal, ensuring all motor units are activated. A 50–60 mA current typically achieves this in anesthetized patients [10]. Stimulation parameters should account for variability in electrode conditions and tissue conductivity. Rodi and Vodušek utilized rectangular pulses of 0.5 ms duration, 40 mA intensity, and an interstimulus interval (ISI) of 3 ms, delivered at 1.0 Hz in trains of four

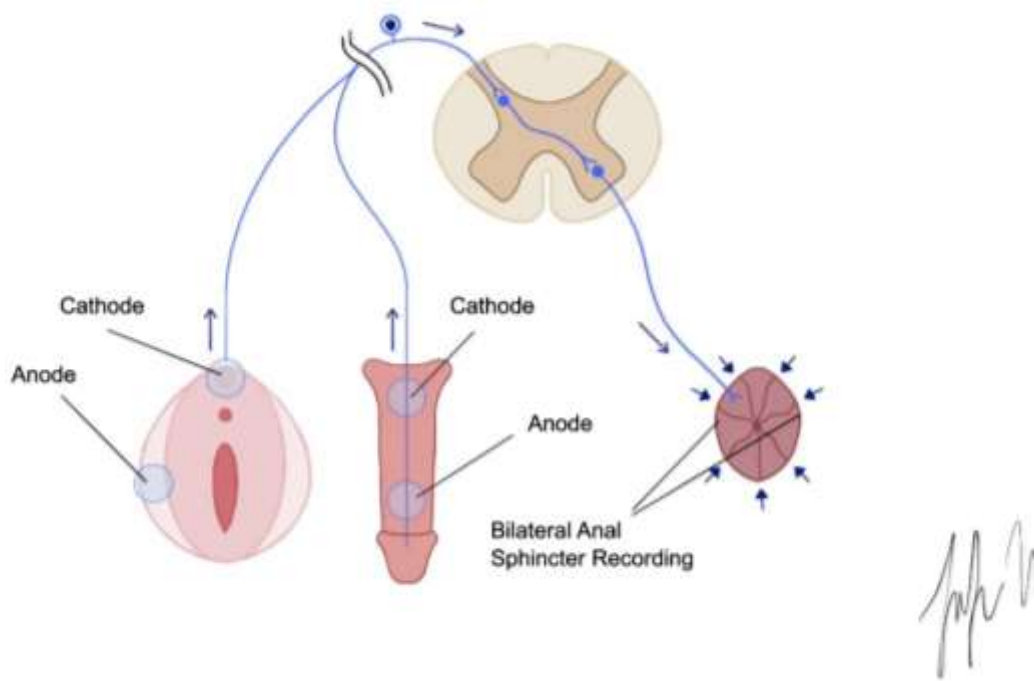


Figure 2. Electrode placement in males and females: In men, the cathode is positioned proximally and the anode distally on the penis. In women, the cathode is placed on the dorsal surface of the clitoris, with the anode positioned on the adjacent labia (*created by Lily Nguyen*).

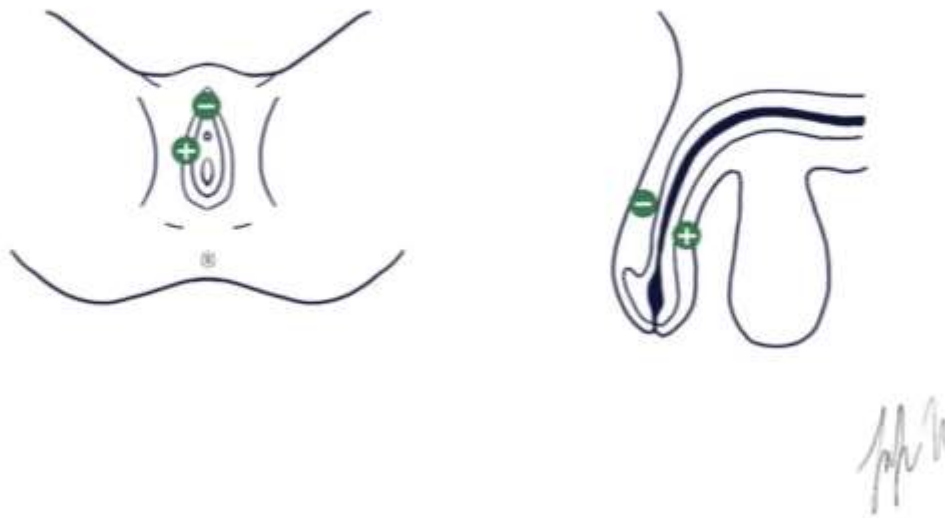


Figure 3. Diagram illustrating the placement of stimulating and recording electrodes in both males and females (*created by Lily Nguyen*).

stimuli. While double-pulse stimulation can enhance reflex responses in patients with partial denervation, trains of 4–5 pulses are more effective for consistent intraoperative BCR monitoring [10].

Recordings

BCR presence is confirmed when 10 consecutive, time-locked, reproducible responses are observed at a sensitivity of 100 μ V. Needle electrodes are preferred for recording sphincter muscle activity with high precision. Reflex acquisition begins 100 minutes post-anesthesia induction to minimize the influence of residual muscle relaxants [10].

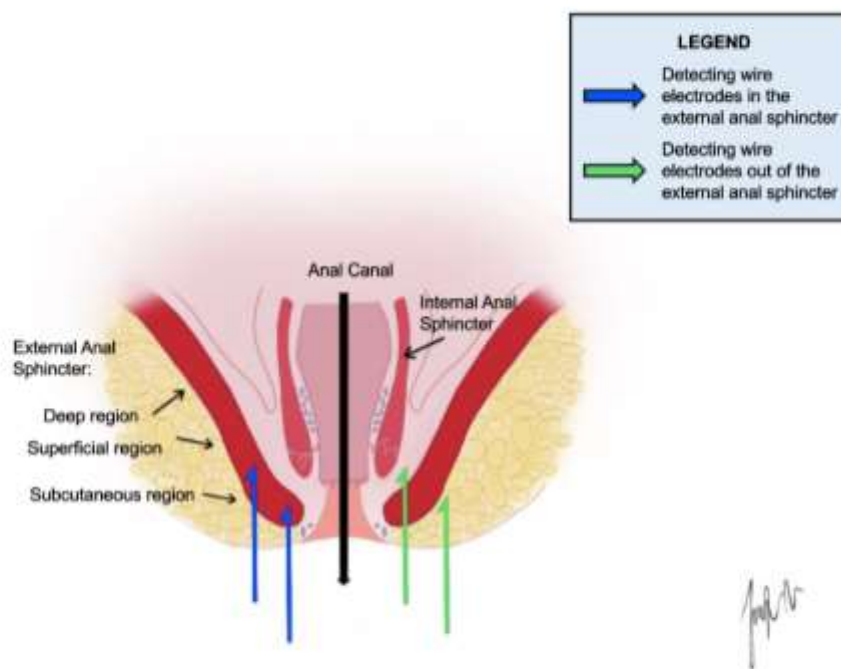


Figure 4. Detecting wire electrode placements at the anal sphincter (created by Lily Nguyen).

Alerts and Warning Criteria

The BCR circuit comprises two components: the oligosynaptic (R1) pathway, characterized by shorter latency and greater anesthetic resilience, and the polysynaptic (R2) pathway, which is more variable under anesthesia [16]. While no universal protocol defines surgical alarms, Morota et al. (2019) proposed thresholds based on amplitude reduction ($\geq 50\%$, 25–50%, and $< 25\%$). Significant amplitude reduction, particularly $< 25\%$, or a complete loss of BCR response strongly correlates with postoperative neurological deficits. Clear criteria are critical for enhancing surgical safety and efficacy [12,6].

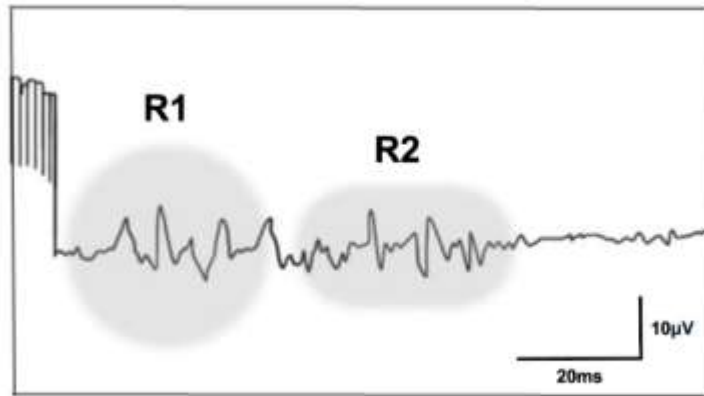


Figure 5. Observed responses from the Bulbocavernosus reflex of the oligosynaptic response (R1) and the polysynaptic response (R2) (created by Lily Nguyen).

Optimal Parameters

In 1997, Deletis and Vodusek described the optimal stimulating parameters as double pulses of 0.5 ms duration, stimulation intensity of 20 mA, with an ISI of 3 ms and a stimulation frequency of 2.3 Hz. With these parameters, the authors elicited BCR in all their patients [2, 10]. However, later studies found that 4 and 5 pulse trains are more effective for intraoperative monitoring [10]. The authors initially used nitrous oxide (NO) for anesthesia, but NO was later determined to depress BCR responses significantly. In 2014, Skinner and Vodusek proposed a refined protocol comprising trains of 4 stimulations with a 0.5 ms pulse duration, 40 mA stimulation intensity, ISI of 3 ms, and a frequency of 1 Hz, which enhanced reliability in anesthetized patients [6]. While no single parameter is universally accepted as “optimal,” a combination of appropriate anesthesia and stimulation parameters has improved monitorability rates during intraoperative BCR monitoring.

Optimal Parameters for Women: Transurethral vs. Conventional BCR Monitoring

Gender-specific challenges, such as clitoral moisture causing electrode displacement, limit conventional BCR (c-BCR) success rates in females to 13%, compared to 81% in males [10]. Hayashi et al. introduced transurethral BCR monitoring (tu-BCR), employing urethral catheter electrodes for stable contact and low resistance. Tu-BCR achieved an 87.5% success rate in producing waveforms versus 66.7% with c-BCR and demonstrated superior specificity for postoperative dysfunction detection (100% vs. 87.2%) [12]. Overzet and Jahangiri (2020) further illustrated the value of multimodality approaches in complex procedures, incorporating BCR and urethral sphincter monitoring to enhance intraoperative reliability and safeguard bowel and bladder function. These findings underscore the importance of adapting BCR techniques to

anatomical differences while leveraging multimodal neurophysiological monitoring for optimal surgical outcomes [16].

Optimal Parameters for Infants

Hwang et al. (2017) identified biphasic 8-pulse stimulation with a 2 ms ISI as optimal for infants under 24 months. This approach produced the largest reflex responses and minimized response overlap, ensuring reliable monitoring in this population [11].

Multimodality Intraoperative Neurophysiological Monitoring (mIONM)

Multimodality monitoring enhances diagnostic accuracy and preserves neural function by integrating techniques like electromyography (EMG), somatosensory evoked potentials (SSEP), and motor evoked potentials (MEP). Combining these modalities with BCR provides higher specificity in detecting neural integrity and minimizing postoperative deficits [5].

Electromyography (EMG)

Electromyography (EMG) records skeletal muscle electrical activity in response to nerve stimulation and is crucial in intraoperative neuromonitoring (IONM) for assessing nerve root function and identifying neuromuscular abnormalities [17]. It is particularly valuable in cauda equina surgeries, where nerve root damage risk is high. Subdermal or intramuscular needle electrodes capture signals, while bipolar probes stimulate specific muscles, with synchronized audio feedback aiding real-time detection of nerve irritation or injury [18]. This capability minimizes neural damage during complex procedures like tethered cord release or tumor resection [5,16]. EMG is also vital in monitoring motor nerve integrity, such as during rhizotomy for spasticity management, where selective nerve root evaluation is essential [4,5]. Its continuous feedback during surgery prevents permanent postoperative deficits [19].

Somatosensory Evoked Potentials (SSEP)

Somatosensory evoked potentials (SSEP) assess sensory pathway integrity by recording neural responses to tactile or electrical stimulation of peripheral nerves. Electrodes placed on the scalp or spine capture signals reflecting the functional status of ascending sensory tracts, particularly in the spinal cord's posterior columns [20]. SSEP is widely used in surgeries involving the conus medullaris and cauda equina to detect ischemic or mechanical sensory pathway injuries [21]. Cortical recordings use CPz or midline scalp electrodes for lower extremity monitoring, with stimulation at tibial or pudendal nerves via adhesive or subdermal electrodes [22]. SSEP latency and amplitude changes are early indicators of nerve compromise in cauda equina surgeries, aiding surgical adjustments to prevent irreversible damage. Studies highlight its predictive value for postoperative sensory preservation, even in high-risk spinal deformity surgeries [23]. However, SSEP is sensitive to anesthesia and may require technique adjustments to ensure signal stability during prolonged procedures [12].

Motor Evoked Potentials (MEP)

Motor evoked potentials (MEP) assess motor pathway integrity by stimulating the motor cortex and recording muscle responses, allowing real-time detection of motor deficits [24]. Scalp electrodes at C1, C2, C3, and C4 facilitate transcranial electrical stimulation [25]. In cauda equina surgeries, lower limb muscle MEP recordings provide critical insights into motor function, preventing paralysis or weakness. MEP is highly effective in deformity corrections, such as scoliosis surgeries, where motor tract injury risks are significant [26]. Anesthesia protocols favor total intravenous anesthesia (TIVA) with propofol and remifentanyl to ensure reliable signals, as halogenated agents impair MEP monitoring [13]. Studies confirm that MEP monitoring reduces motor deficits by enabling timely intraoperative interventions [13,26]. Innovations like transurethral MEP (tu-MEP) have enhanced pelvic floor and bladder function monitoring, reducing complications such as urinary incontinence and retention [27]. Triggered EMG (t-EMG) further supports nerve root mapping, improving bladder control and reducing urinary retention, expanding MEP's role in preserving neurological and urological functions during spinal surgeries [28].

METHODS

Study Search

This systematic review and meta-analysis followed PRISMA guidelines. A comprehensive search of PubMed, Google Scholar, PROSPERO, and ClinicalTrials.gov was conducted for studies on BCR in intraoperative neurophysiological monitoring (IONM) published between April 1996 and June 2023. Priority was given to papers from randomized controlled trials, observational studies and others with comprehensive data on BCR monitorability parameters and those reporting sensitivity and specificity in predicting postoperative deficits. Keywords included BCR, multimodality IONM, monitoring techniques, stimulation parameters, and efficacy. Boolean operators and truncations were used to ensure thorough and efficient coverage.

Study Selection & Eligibility Criteria

Studies were systematically organized and screened using the Rayyan database for record management and deduplication. Screening involved a two-step process: an initial blinded review by independent team members and a non-blinded review to resolve disagreements. The analysis included systematic reviews, retrospective cohort studies, case series, prospective observational, and experimental studies on BCR monitoring during spinal surgeries. Eligibility required multi-modality IONM emphasizing BCR's role in preventing postoperative deficits. Only English-language studies on human subjects were included—exclusions covered duplicates, non-English publications, conference abstracts, single-case reports, and irrelevant studies. Full-text reviews ensured that inclusion criteria were met, and data on study design,

IONM modalities, BCR parameters, and postoperative outcomes were systematically categorized for analysis.

Data Extraction

Data extraction was performed manually and organized using Excel for accuracy. Emphasis was placed on extracting parameters related to BCR monitorability, including stimulation techniques, recording protocols, monitoring outcomes, and anesthesia approaches. Data on true positives, false positives, true negatives, and false negatives were used to calculate sensitivity and specificity. Variations in monitoring protocols and outcomes were thoroughly extracted to evaluate BCR monitorability across studies.

Data Analysis

A comprehensive descriptive comparative analysis was performed using combination charts and visual trend analyses to evaluate BCR monitorability across studies. Patterns and correlations were examined between stimulation parameters such as intensity, number of pulses, pulse duration, and ISI and monitorability outcomes. Studies with 100 percent monitorability were analyzed to identify optimal parameter sets, while those with poor outcomes highlighted limiting factors. Parameters were assessed individually and cumulatively to summarize trends, determining optimal ranges or thresholds for successful BCR. Comparative insights contrasted the highest and lowest monitorability values, identifying parameters linked to improved outcomes.

Machine learning-assisted Analysis

We employed a structured, methodical approach to predict monitorability outcomes and analyze its relationships with stimulation parameters, utilizing various machine learning-assisted models. First, Linear Regression was applied to examine direct linear relationships between stimulation parameters and monitorability. Building on these findings, Polynomial Regression was used to explore non-linear trends suggested by initial observations. Next, Logistic Regression classified monitorability into high and low categories based on predefined thresholds, offering a categorical perspective. The Random Forest Regressor was employed to handle complex, non-linear interactions among variables and identify feature importance, providing valuable insights into parameter significance. For dimensionality reduction, Principal Component Analysis (PCA) was conducted to simplify the dataset while retaining critical variance and facilitating streamlined analysis. Finally, the Partial Dependence Plot (PDP) for Gradient Boosting was employed to visualize the marginal effects of individual stimulation parameters on monitorability while holding other factors constant, enabling a deeper understanding of the independent contributions of each parameter. This stepwise methodology ensured a comprehensive and systematic analysis of stimulation parameters influencing BCR monitorability outcomes.

RESULTS

Our Literature search process yielded 61 studies. After removing 14 duplicates using automated Rayyan screening, 47 studies underwent screening, with 13 excluded for irrelevant focus and non-human subjects. Of the 31 full-text articles retrieved and assessed for eligibility, 14 were excluded due to the absence of BCR monitoring, unavailable monitorability data, or lack of postoperative deficit reduction outcomes. Ultimately, 19 studies met the inclusion criteria and were included in the meta-analysis (Figure 6).

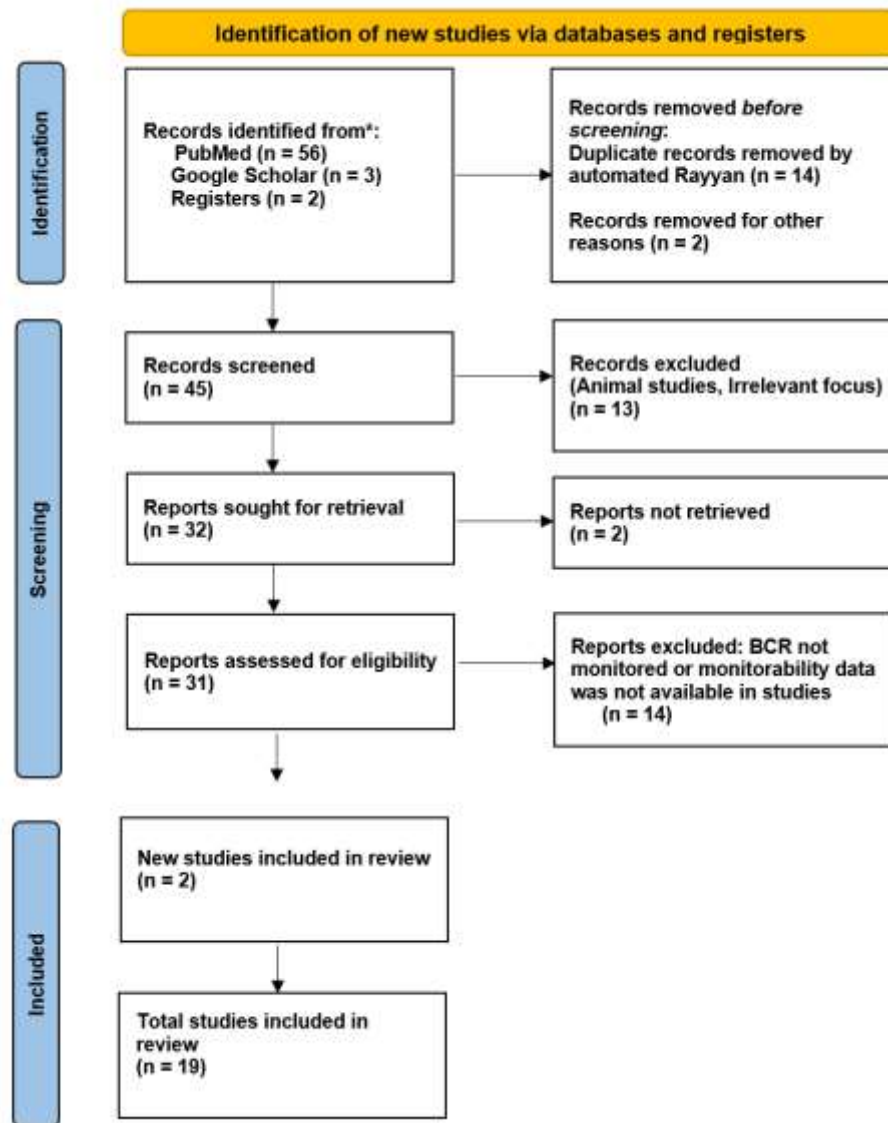


Figure 6. PRISMA Flow Diagram of the study selection. The identification, screening, and inclusion of studies in the review.

The studies included in this meta-analysis encompass a range of study designs, including retrospective cohort studies, prospective observational studies, and case series. These studies provide detailed insights into BCR monitoring during spinal surgeries, focusing on methodological approaches of multimodality neuromonitoring, patient demographics, and monitorability outcomes. Characteristics of the included studies are summarized in Table 1, with extended data and supplementary details available in the appendices.

STUDIES	Study Design	IONM Multimodalities	Sample Size	Ages (yr)	BCR Monitorability
Morota, 2019	Retrospective Cohort Study	S.EMG, SSEP, MEP, BCR	164	0.42	91%
Choi et al., 2022	Retrospective Cohort Study	EMG, SSEP, MEP, BCR	153	68	100%
Cha et al., 2018	Retrospective Cohort Study	EMG, SSEP, MEP, BCR	152	3.3	70%
Deletis and Vodusek, 1997	Prospective Observational Study	EMG, SSEP, MEP, BCR	119	22	100%
Skinner and Vodusek, 2014	Review Article	EMG, SSEP, MEP, EAS MEP, BCR	100	44	94%
Niu et al., 2010	Retrospective Case-Control Study	SSEP, BCR	89	51	48%
Rodi and Vodusek, 2001	Prospective Observational Study	EMG, Pudental SSEP, BCR	65	39	64%
Choi et al., 2021	Retrospective Cohort Study	MEP, SSEP, EMG, BCR	63	50	95%
Sala et al., 2013	Retrospective Case Series	EMG, SSEP, Tc MEP, BCR	33	7.4	59%
Hayashi et al., 2022	Prospective Observational Study	BCR	24	63	67%
Shinjo et al., 2019	Retrospective Cohort Study	S.EMG, SSEP, MEP, BCR	22	2.7	91%
Nonaka et al., 2023	Retrospective Cohort Study	EMG, SSEP, MEP, CMAP, BCR	20	0.37	100%
Taskiran et al., 2019	Retrospective Cohort Study	T.EMG, SSEP, MEP, BCR	16	44	88%
Aydinlar et al., 2019	Prospective Cohort Study	EMG, SSEP, TCeMEP, BCR	15	0.49	90%
Hwang et al., 2017	Retrospective Observational Study	EMG, SSEP, MEP, BCR	12	0.54	100%
Fekete et al., 2020	Retrospective Observational Study	EMG, SSEP, MEP, BCR	8	3.4	63%
Kim et al., 2022	Review Article	EMG, SSEP, TCeMEP, BCR	7	0.42	100%
Crocoli et al., 2022	Retrospective Observational Study	EMG, SSEP, TCeMEP, BCR	6	4	58%
Skinner et al., 2007	Prospective Pilot Study	EMG, SSEP, TCeMEP, TOF, BCR	5	40	100%

Table 1. Overview of studies included in the meta-analysis of BCR monitorability.

This meta-analysis evaluated key parameters influencing BCR monitorability, including stimulation intensity, number of stimulation pulses, pulse duration, interstimulus intervals (ISI), and mean latency.

While Table 2 summarizes the critical findings, supplementary extensive monitorability data is provided in the appendices.

STUDY	Monitorability	Stimulation Intensity (mA)	Number of Pulses	Pulse Duration	ISI (ms)
Niu et al., 2010	0.48	35			
Crocoli et al., 2022	0.58	40			3.0
Hayashi et al., 2022	0.67	50	4	0.500	2.0
Sala et al., 2013	0.59	40	3	0.200	
Fekete et al., 2020	0.63	24	1	0.200	
Rodi and Vodusek, 2001	0.64	40	4	0.500	3.0
Cha et al., 2018	0.70		8	0.075	2.0
Taskiran et al., 2019	0.88	40	5		2.5
Aydinlar et al., 2019	0.90		6	0.500	
Shinjo et al., 2019	0.91	40	4	0.500	2.0
Morota, 2019	0.91	40	5	0.500	2.0
Skinner and Vodusek, 2014	0.94	50	4	0.500	3.0
Choi et al., 2021	0.95	80	8	0.100	2.0
Deletis and Vodusek, 1997	1.00	40	2	0.500	3.0
Skinner et al., 2007	1.00	50	4	0.500	3.0
Choi et al., 2022	1.00	80	8	0.100	2.0
Nonaka et al., 2023	1.00	60	4	0.200	2.0
Kim et al., 2022	1.00	40	8	0.100	2.0
Hwang et al., 2017	1.00	50	8	0.075	5.0

Table 2. The data set of monitorability and stimulation parameters.

Data Analysis: Descriptive and Analytical Interpretations

The cumulative analysis of stimulation parameters revealed their interdependency and the non-linear correlation between these parameters and BCR monitorability outcomes. This combination chart highlighted the complex interplay of pulse count, ISI, pulse duration, and other stimulation parameters in optimizing monitorability across diverse surgical settings.

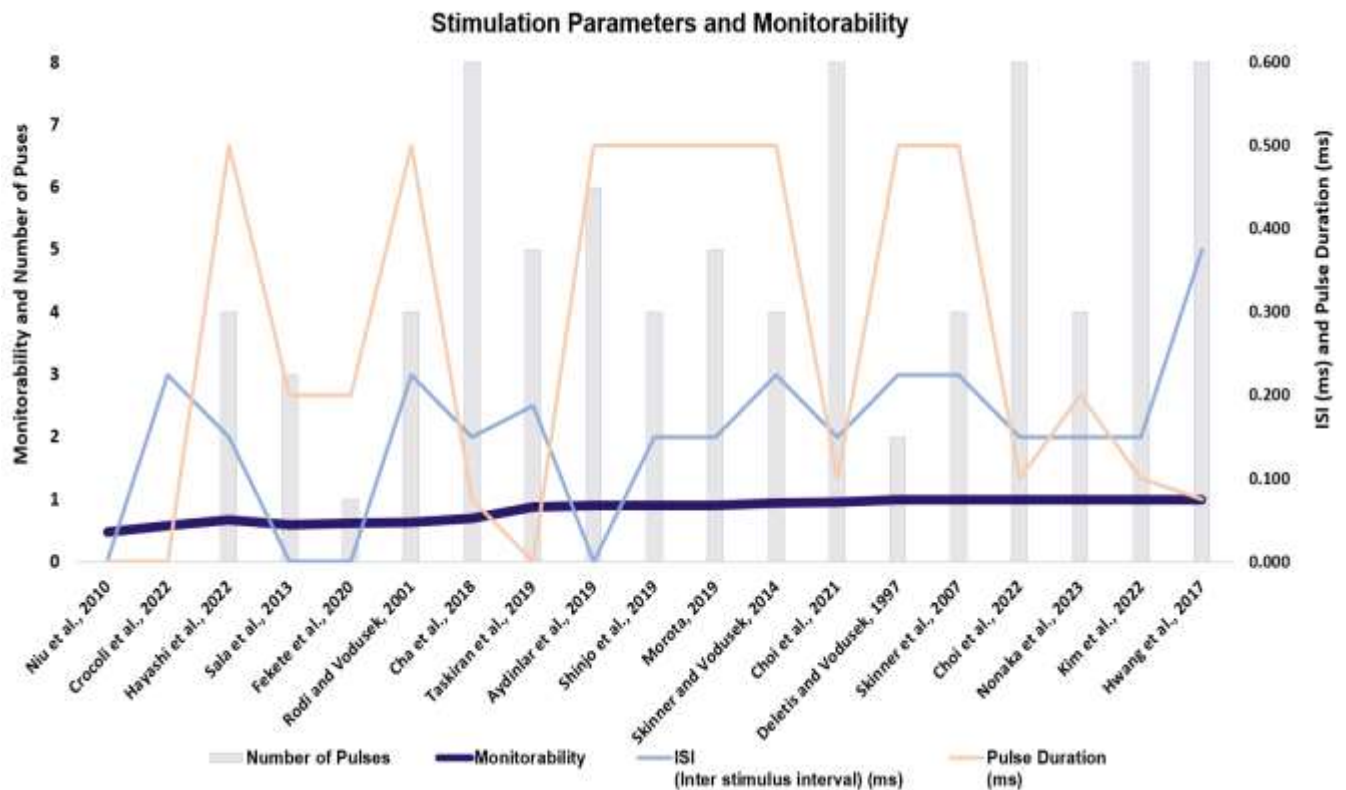


Figure 7. Stimulation Parameters and Monitorability Cumulative. This combination graph illustrates the relationship between independent variables (number of pulses, interstimulus interval, and pulse duration) and the dependent variable (monitorability). Stimulation parameter combinations from included studies are analyzed, showcasing their impact on monitorability outcomes and variations across different sets of parameters.

Monitorability values from included studies ranged across the broad spectrum, from lower (48) to highest (100) percentages. The number of pulses varied between 1 and 8, representing the breadth of pulse counts utilized in stimulation setups, with 4 pulses being the most frequently employed. The inter-stimulus interval (ISI) ranged from 2 ms to 5 ms, with 2 ms as the most used value. The pulse duration spanned 0.075 ms to 0.5 ms, with the most frequent value being 0.5 ms (Figure 1).

Monitorability of 100% was achieved with varying combinations of stimulation parameters, including 2 or 4 pulses with ISI of 3 ms and pulse duration of 0.5 ms, 8 pulses with ISI of 2 ms and pulse duration of 0.1 ms, 4 pulses with ISI of 2 ms and pulse duration of 0.2 ms, and 8 pulses with ISI of 5 ms and pulse duration of 0.075 ms. Four pulses with an ISI of 3 ms and a pulse duration of 0.5 ms yielded 64% monitorability, four pulses with an ISI of 2 ms and a pulse duration of 0.5 ms yielded 67% monitorability, while eight pulses with an ISI of 2 ms and a pulse duration of 0.075 ms yielded 70% monitorability (Figure 7).

Stimulation intensity ranges encompassed values from the lowest range of 0-50 mA to the highest range of 10-80 mA, with the most frequently used range being 20-40 mA. The highest monitorability of 100% was achieved across several stimulation intensity ranges, including 0-50 mA, 10-80 mA, 20-40 mA, 25-60 mA, and 20-50 mA. The lowest value, 48% monitorability, was observed with a stimulation intensity range of 20-35 mA. Monitorability values between 60% and 95% were associated with various stimulation intensity ranges: 67% with a range of 20-40 mA, 63% with a range of 20-30 mA, 91% with a range of 20-40 mA (observed twice), 94% with a range of 10-80 mA, and 95% with a range of 10-80 mA (Figure 2).

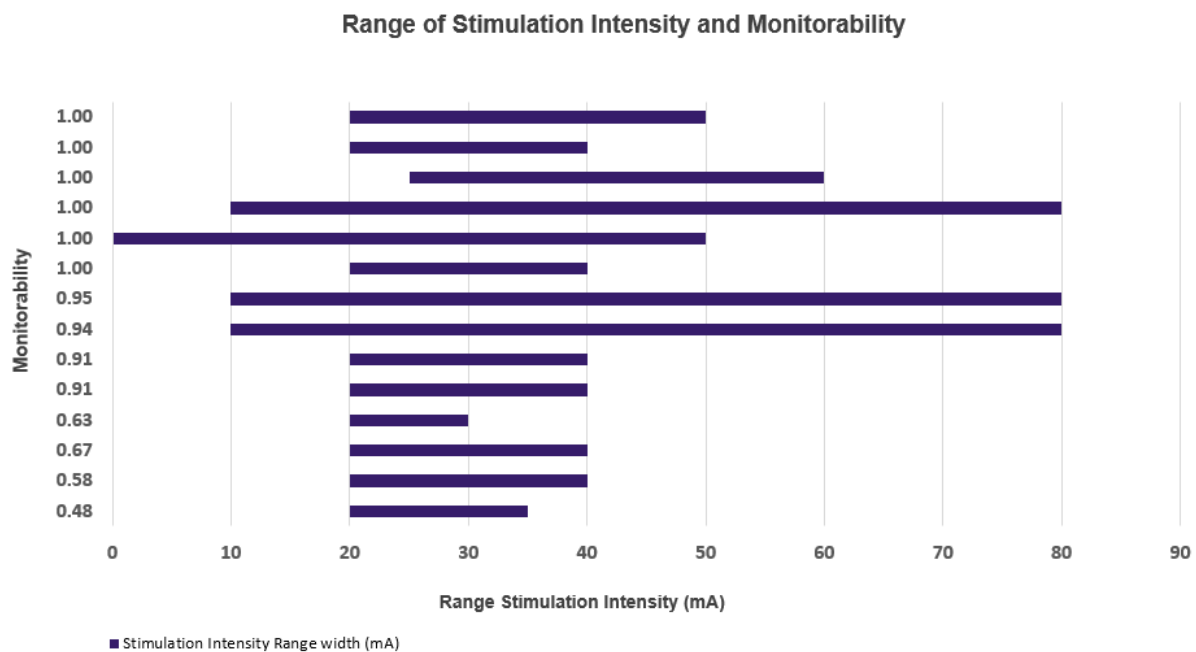


Figure 8. Stimulation Intensity Range and Monitorability. This horizontal bar graph illustrates the relationship between stimulation intensity ranges (mA) and monitorability, highlighting how variations in intensity range influence monitorability outcomes across included studies.

The stimulation intensity range of 20-40 mA appeared across multiple monitorability levels (67%, 91%, and 100%), indicating its potential as a critical and widely applied range in various stimulation parameter sets. Moreover, wider stimulation intensity ranges, such as 10-80 mA and 0-50 mA, were associated with higher monitorability, while narrower ranges, like 20-35 mA and 20-30 mA, corresponded to lower monitorability (Figure 8).

Mean latency values ranged from 32 ms to 48 ms, with corresponding monitorability ranging from 48% to 100%. The optimal range of mean latency, associated with 100% monitorability, was identified as 33 ms to 36 ms, with a plateau observed across this range. In contrast, the highest value of 48 ms yielded a suboptimal monitorability of 48% (Figure 3).

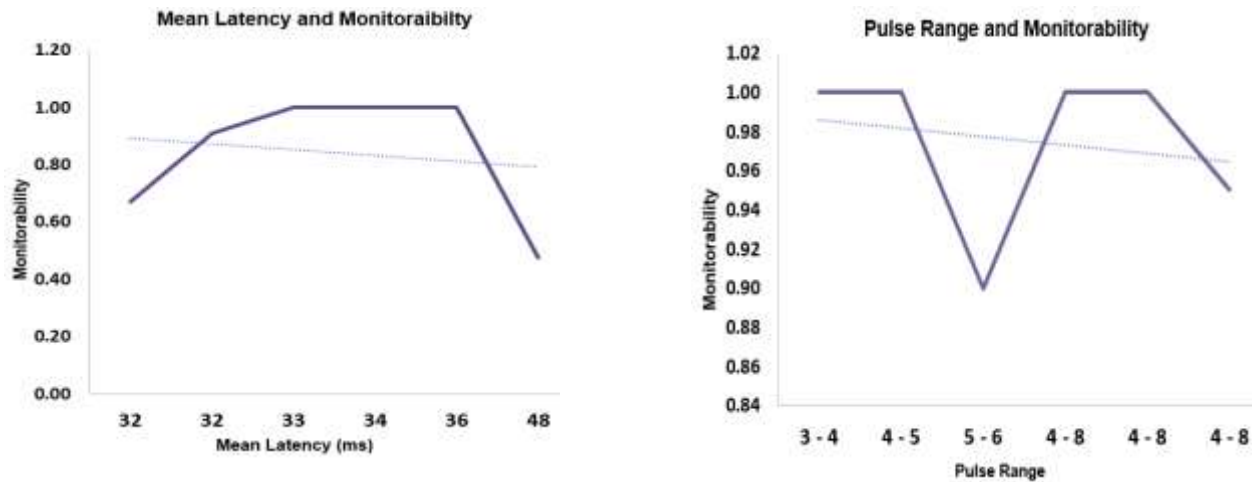


Figure 9. Mean Latency, Pulse number range, and Monitorability. The left graph depicts the relationship between mean latency (ms) and monitorability, highlighting how variations in latency affect monitorability outcomes. The right graph shows the correlation between pulse range and monitorability, demonstrating changes across different pulse range intervals. Only studies reporting the respective parameters (mean latency, pulse range) are included.

Pulse ranges analyzed included 3-4, 4-5, 5-6, and 4-8 pulses, with corresponding monitorability values ranging from 90% to 100%. The pulse range of 4-8 pulses was the most frequently employed, appeared in three instances, and was associated with monitorability values of 95% to 100%. An optimal monitorability of 100% was observed with pulse ranges 3-4, 4-5, and 4-8 pulses, while the pulse range 5-6 pulses yielded a lower monitorability of 90% (Figure 9).

We analyzed the correlation of BCR stimulation intensity with sensitivity, defined as the ability of intraoperative neuromonitoring (IONM) techniques to detect true positives (TP), offering insights into BCR intraoperative changes as predictors of postoperative urinary deficits caused by neurological damage. Moreover, we explored the correlation of BCR stimulation intensity with specificity, emphasizing its role in minimizing false positives (FP) and confirming true negatives (TN) for cases without postoperative urinary deficits. Our analysis revealed that medium stimulation intensity (31-50 mA) demonstrated the highest sensitivity at 45%. In contrast, high stimulation intensity (>50 mA) and low stimulation intensity (0-30 mA) exhibited reduced sensitivities of 10% and 8%, respectively (Figure 10).

Our analysis of stimulation intensity and specificity showed that high stimulation intensity achieved 100% specificity, demonstrating its exceptional ability to minimize false positives during intraoperative BCR monitoring. Medium stimulation intensity exhibited a specificity of 94%, reflecting its optimal reliability in this context (Figure 11).

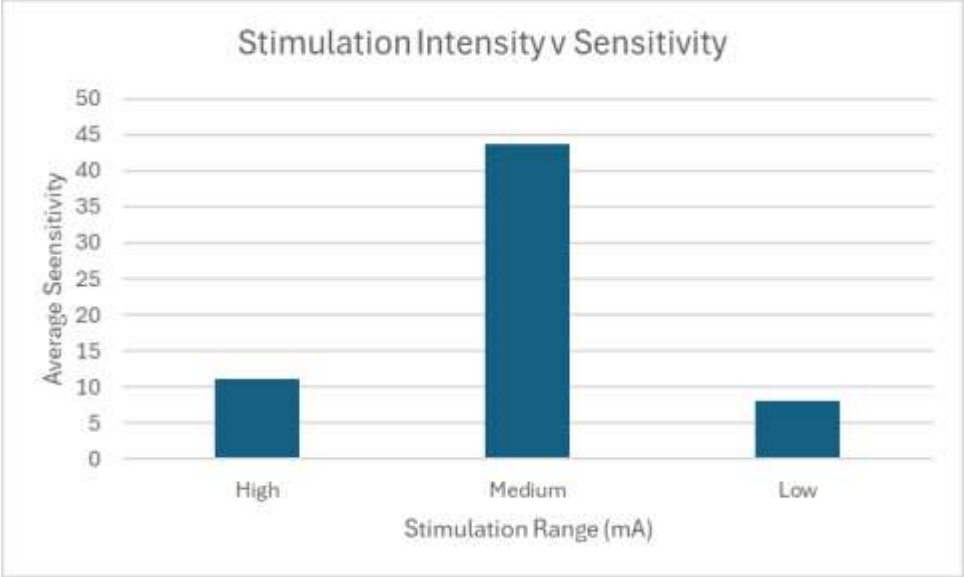


Figure 10. The graph shows the various groups of stimulation intensity (mA) and the sensitivity values. Medium stimulation intensity shows a high sensitivity value, which indicates early detection rates for nerve damage and a high rate of detecting true positives.

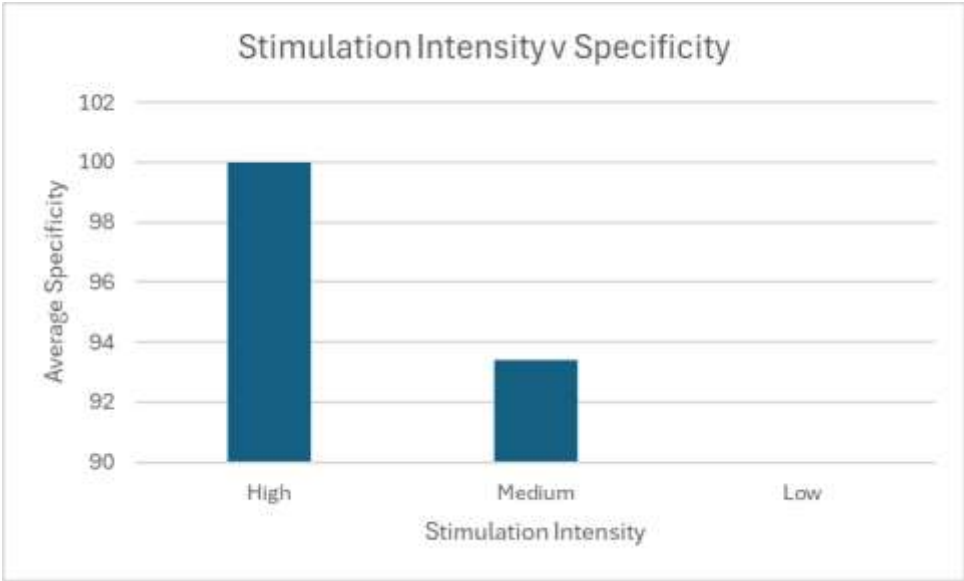


Figure 11. The graph shows the various groups of stimulation intensity (mA) and the specificity values. High stimulation intensity shows a high specificity value, indicating a low false positive result.

Quality of Assessment

The included studies exhibited methodological rigor with a low risk of bias, employing randomized or prospective selection methods. This breadth of data allowed for a comprehensive evaluation of BCR

monitorability across age groups, ensuring that the analysis captures diverse surgical contexts in both adult and pediatric. However, some studies were limited to small sample sizes. Transparent reporting and disclosed limitations across studies further supported the reliability of findings.

Machine Learning Models for Statistical Analysis of BCR Monitorability

Linear regression analysis revealed an R-squared value of 0.5895, indicating that the model explains 58.9% of the variance in monitorability. Stimulation Intensity demonstrated a small positive coefficient (0.007), suggesting a marginal increase in monitorability with higher intensity, while Pulse Duration showed a strong negative coefficient (-0.506), indicating that longer durations reduce monitorability. Although the model captured moderate variance, it was limited in accounting for the non-linear relationships between the stimulation parameters and monitorability outcomes. Polynomial regression demonstrated an R-squared value of 0.8325, capturing 83.25% of the variance in monitorability outcomes. This result highlights non-linear relationships among stimulation parameters, making polynomial regression a more robust model for understanding the complex interplay between these variables compared to linear regression. Logistic regression demonstrated an accuracy of 91.67%, effectively classifying monitorability into high and low categories. The coefficients revealed that stimulation intensity had a positive impact (0.407), increasing the likelihood of achieving high monitorability (>0.8). This model provided reliable categorical predictions, offering insights into the variables most associated with successful BCR monitoring.

The Random Forest Regressor revealed that Stimulation Intensity and Number of Pulses were the most influential factors for predicting monitorability, with feature importance scores of 0.2873 and 0.2450, respectively. Additional parameters, such as Pulse Duration (0.2025), Intensity Range (0.1498), and ISI (0.1154), contributed less significantly. The model achieved an R-squared value of 0.6925, explaining 69.25% of the variance in monitorability. This performance underscores the model's ability to effectively manage non-linear interactions and provide valuable insights into the relative importance of stimulation parameters. Principal Component Analysis (PCA) demonstrated that the first principal component (PC1) captured 84.13% of the variance, primarily reflecting dominant patterns in Stimulation Intensity, Pulse Duration, and Number of Pulses. The second principal component (PC2) accounted for an additional 14.32% of the variance, highlighting subtler interactions among these parameters. PC1 and PC2 explained over 98% of the total variance, simplifying the dataset while retaining essential information for analyzing monitorability trends.

The Partial Dependence Plot (PDP) analysis provided detailed insights into the independent effects of stimulation parameters on monitorability outcomes (Figure 12). Stimulation Intensity demonstrated a positive impact, with monitorability improving as the intensity increased to approximately 50 mA, after which it plateaued, suggesting an optimal range around this value. Pulse Duration displayed a clear inverse relationship, where longer durations negatively impacted monitorability, emphasizing the importance of shorter durations for achieving optimal outcomes. ISI (Inter-Stimulus Interval) showed a mild positive impact, with monitorability increasing slightly up to 3 ms before stabilizing, indicating a limited but

measurable influence. The Number of Pulses revealed a non-linear relationship, with monitorability peaking at lower and higher pulse counts. At the same time, a noticeable dip occurred around five pulses, underscoring the need for carefully selected pulse counts. Larger Stimulation Intensity Ranges were associated with decreased monitorability, while narrower, more focused ranges proved more favorable, highlighting the critical role of precision in parameter settings.

Influence of Stimulation Parameters on Monitorability: Partial Dependence Plot using Gradient Boosting

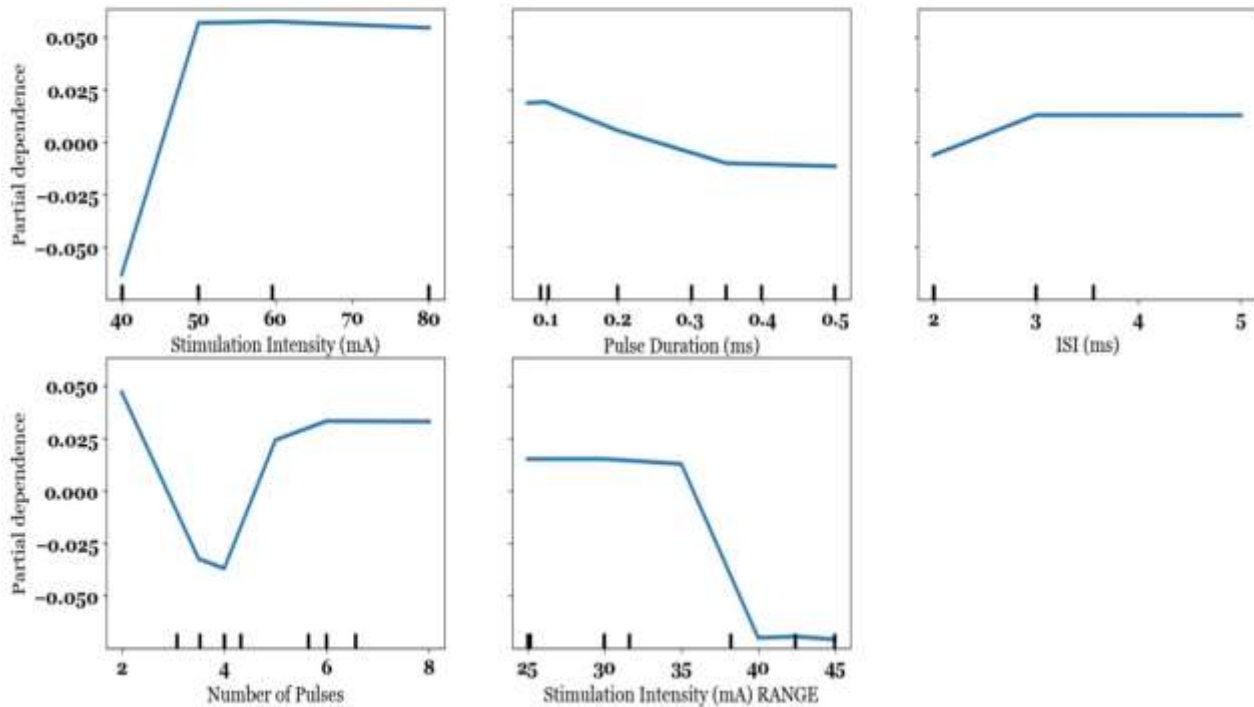


Figure 12. Partial dependence plots show the relationship of individual stimulation parameters with BCR monitorability outcomes while controlling for other variables.

DISCUSSION

Combined parameter impacts on monitorability are complex and challenging to interpret, as changes in one stimulation parameter can alter the effects of other parameter on the monitorability outcome, resulting in a non-linear relationship. Even a slight shift in one parameter not only impacts monitorability directly but also obscures the influence of other parameters. This adds to the complexity of interpreting their combined, non-linear effects on monitorability. A detailed comparative analysis was performed on six key studies that achieved 100% BCR monitorability: Skinner et al., 2007; Choi et al., 2022; Hwang et al., 2017; Deletis and Vodusek, 1997; Nonaka et al., 2023; and Kim et al., 2022. Comprehensive datasets for these

studies are provided in the appendices, offering a thorough exploration of parameters associated with optimal outcomes.

Optimal monitorability is achieved through a dynamic interplay among stimulation intensity, pulse duration, ISI, pulse count, and mean latency. The analysis revealed that 100% monitorability can be attained across various stimulation intensity ranges, from narrower ranges like 20-40 mA (Kim et al., 2022) to broader ranges such as 0-50 mA (Skinner et al., 2007) and 10-80 mA (Choi et al., 2022). Skinner et al. (2007) paired a broad intensity range (0-50 mA) with longer pulse durations (0.5 ms), moderate pulse counts (4 pulses), and an ISI of 3 ms, while Choi et al. (2022) employed an even broader range (10-80 mA) with shorter pulse durations (0.1 ms), higher pulse counts (4-8 pulses), and an ISI of 2 ms. These examples highlight compensatory trends where broader ranges favor shorter durations and higher pulse counts, whereas narrower ranges align with longer durations and fewer pulses. Compensatory relationships were also observed between ISI and pulse duration. Shorter durations, such as 0.075 ms in Hwang et al. (2017), required longer ISI values (5 ms) to ensure neural recovery, while longer durations, like 0.5 ms in Skinner et al. (2007), paired with shorter ISI values (3 ms) to enhance cumulative stimulation. Similarly, mean latencies of 33-34 ms (e.g., Choi et al., 2022; Skinner et al., 2007) were linked to higher pulse counts (4-8 pulses) and moderate intensity ranges, while longer latencies (36 ms in Hwang et al., 2017) were associated with lower pulse counts (3-4 pulses) and broader ranges (25-60 mA).

The optimal stimulation parameters for achieving 100% monitorability include a stimulation intensity range of 40-50 mA, pulse counts of 4-8 pulses, and pulse durations between 0.1-0.2 ms. An ISI of 2-3 ms and mean latencies of 33-34 ms further enhance outcomes. Broader intensity ranges (e.g., 10-80 mA) require shorter durations (0.1 ms) and ISI values (2 ms), while narrower ranges (e.g., 20-40 mA) accommodate longer durations (0.5 ms) and fewer pulses (4-5). The above analytic insights facilitated the identification of a proposed standardized optimal set of stimulation parameters essential for achieving consistent and successful BCR outcomes.

To delve into the challenges of suboptimal monitorability, we focused on studies with monitorability scores between 48% and 70%, analyzing interplay of stimulation parameters to uncover patterns and factors that may impede successful BCR monitoring. Niu et al. (2010) reported a monitorability of 48%, utilizing a stimulation intensity range of 20-35 mA, with a mean latency of 48 ms. Crocoli et al. (2022) achieved a monitorability of 58%, utilizing a stimulation intensity range of 20-40 mA with an inter-stimulus interval (ISI) of 3.0 ms. A stimulation intensity of 40 mA, combined with a pulse duration of 0.200 ms and 3 pulses, resulted in a monitorability of 59% in the study by Sala et al. (2013). Whereas a stimulation intensity range of 20-30 mA, combined with a pulse duration of 0.200 ms and 1 pulse, resulted in a monitorability of 63% in the study by Fekete et al. (2020). Rodi and Vodusek (2001) employed a stimulation intensity of 40 mA, a pulse duration of 0.500 ms, an inter-stimulus interval of 3.0 ms, and 4-8 pulses, achieving a monitorability of 64%. Hayashi et al. (2022) utilized stimulation intensity of 50 mA, a pulse duration of 0.2-0.5 ms, an inter-stimulus interval of 2.0 ms, 4 pulses, and mean latency of 32ms for achieving a

monitorability of 67%. Cha et al. (2018) employed pulse duration of 0.075 ms, an inter-stimulus interval of 2.0 ms, and 8 pulses, achieving a monitorability of 70%.

Evident from the analytic interpretation drawn from Sala et al. (2013) and Fekete et al. (2020), insufficient cumulative stimulation resulted from inadequately balanced combinations of stimulation parameters. In Sala et al., the use of a low pulse count (3 pulses) and moderate pulse duration (0.2 ms) failed to elicit adequate neural activation. Similarly, in Fekete et al., the combination of a limited stimulation intensity range (20-30 mA), a very low pulse count (1 pulse), and a moderate pulse duration (0.2 ms) further impaired monitorability outcomes. In both cases, increasing the pulse count to 4-8 pulses or extending the pulse duration to ~0.5 ms would likely have mitigated these limitations, enhanced cumulative stimulation and improved monitorability. In Rodi and Vodusek (2001), despite optimal pulse count (4-8 pulses) and stimulation intensity (40 mA), the longer pulse duration (0.500 ms) and moderate ISI (3.0 ms) likely restricted monitorability to 64%. Shortening the pulse duration and ISI could have plausibly improved outcomes.

The comparison between Cha et al. (2018) and Hayashi et al. (2022) highlights a critical trend in cumulative stimulation efficiency. Cha's use of a higher pulse count (8 pulses) combined with a shorter, consistent pulse duration (0.075 ms) effectively optimized neural activation, achieving a higher monitorability (70%) compared to Hayashi (67%). In contrast, Hayashi's parameters, including a lower pulse count (4 pulses) and variability in pulse duration (0.2-0.5 ms), likely disrupted cumulative stimulation, despite favorable elements such as a short ISI (2.0 ms) and high stimulation intensity (50 mA). To further improve monitorability, Hayashi's parameters could be refined by increasing the pulse count to 6-8 pulses and standardizing or slightly decreasing the pulse duration to 0.2 ms or less. These adjustments would reduce variability, enhance stimulation precision, and align with the cumulative efficiency demonstrated in Cha et al., leading to better outcomes.

BCR monitoring plays a critical role in preventing postoperative genitourinary deficits by enabling accurate intraoperative assessment of sacral nerve function. Our sensitivity and specificity findings emphasize medium stimulation intensity (31-50 mA) as the optimal range for predicting these outcomes, effectively balancing both measures. High stimulation intensity, while achieving 100% specificity, is less practical due to reduced sensitivity. These results highlight the need to tailor stimulation intensity, as it is not a standalone measure; instead, it must be considered alongside other parameters, such as pulse duration, interstimulus intervals, and the number of pulses, to enhance BCR reliability in specific surgical contexts.

The comparative analysis revealed that optimal BCR monitorability is influenced by the interplay of multiple stimulation parameters rather than any single factor. Stimulation intensity consistently showed strong contributions to monitorability, with ranges such as 40-50 mA and broader intervals (e.g., 10-80 mA) achieving 100% monitorability across studies. Pulse duration, inter-stimulus interval (ISI), and pulse count demonstrated compensatory relationships, with shorter pulse durations (0.1-0.2 ms) paired with higher ISI values (e.g., 3-5 ms) and moderate-to-high pulse counts (4-8) yielding optimal outcomes. Mean

latency values between 33-36 ms were associated with high monitorability, reflecting efficient neural responses. Conversely, suboptimal monitorability outcomes (48-70%) were linked to inadequate combinations, such as low pulse counts or excessive pulse durations. The optimal parameters for achieving 100% monitorability include a stimulation intensity of 40-50 mA, pulse durations of 0.1-0.2 ms, ISI of 2-3 ms, pulse counts of 4-8, and mean latencies of 33-36 ms. These results emphasize the need to tailor parameter combinations to specific surgical contexts, ensuring precise and consistent intraoperative monitoring.

The machine learning analysis, leveraging Random Forest for feature importance, Polynomial Regression for capturing non-linear trends, and Partial Dependence Plots for visualizing marginal effects, identified distinct relationships among stimulation parameters. Stimulation Intensity was highlighted as the most significant factor, with Random Forest and PDPs identifying an optimal range of 40-50 mA, where monitorability consistently improved before plateauing. Pulse Duration in the range of 0.1-0.2 ms was determined through PDP analysis, revealing a clear inverse relationship where shorter durations were more favorable. Inter-Stimulus Intervals (ISI) of 2-3 ms emerged as critical contributors, identified through Polynomial Regression and PDPs, which showed slight positive impacts stabilizing beyond 3 ms. Pulse Count, ranging from 4-8 pulses, demonstrated robust performance across models, with Random Forest emphasizing its importance and PDPs showing its non-linear effect on monitorability. Mean Latencies of 33-36 ms were consistently associated with high monitorability outcomes, as captured in Polynomial Regression trends and PCA analysis.

There is a dire need for standardized parameters for BCR monitoring within multimodality IONM frameworks, particularly in complex spinal surgeries. Previous studies, including those supporting BCR's efficacy in enhancing multimodality monitoring setups, have demonstrated its reliability in preserving sacral nerve function and predicting postoperative outcomes [5, 34]. Numerous studies have also highlighted BCR's complementary role in improving the sensitivity and reliability of multimodal neurophysiological monitoring, which is crucial for detecting intraoperative neural damage [3, 8, 35]. Variability in stimulation protocols and interpretation challenges further underscores the necessity for standardized monitoring techniques [3, 36]. Implementing unified BCR parameters would ensure intraoperative reliability, streamline multimodal IONM applications, and drive consistent improvements in surgical outcomes.

CONCLUSION

This meta-analysis underscores the pivotal role of meticulously optimized stimulation parameters in achieving reliable BCR monitorability during intraoperative neurophysiological monitoring. The study elucidates the intricate yet cohesive, non-linear interplay among BCR stimulation parameters through

comparative and machine learning analyses. Both analyses fostered the identification of a consistent set of optimal stimulation parameters, including a stimulation intensity of 40-50 mA, pulse durations of 0.1-0.2 ms, ISI of 2-3 ms, pulse counts of 4-8, and mean latencies of 33-36 ms, reinforcing the reliability and validity of these findings. These parameters were consistently supported across diverse methodological approaches, emphasizing their reliability for precise and standardized intraoperative BCR monitoring. Incorporating these standardized parameters into intraoperative neuromonitoring protocols is crucial for complex spinal surgeries. Robust sensitivity and specificity of BCR monitoring highlight its effectiveness in predicting postoperative genitourinary deficits. BCR is an indispensable and highly efficient neuromonitoring tool in mitigating postoperative genitourinary deficits, improving the quality of healthcare provision, and enhancing the generalized well-being of patients undergoing complex spinal surgeries.

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