Nerve monitoring review

Vaninder K. Dhillon[1], Catherine F. Sinclair[2], Joseph Scharpf[3]

[1]Division of Endocrine Head and Neck Surgery, Department of Otolaryngology, Johns Hopkins University, Bethesda, MD, USA; [2]Division of Head and Neck Surgery, Department of Otolaryngology, Mount Sinai, New York, NY, USA; [3]Head and Neck Institute, Cleveland Clinic Foundation, Cleveland, OH, USA

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Correspondence to: Joseph Scharpf, MD, FACS. Head and Neck Institute, Cleveland Clinic Foundation, 9500 Euclid Ave, Cleveland, OH 44195, USA. Email: SCHARPJ@ccf.org.

Abstract: Intraoperative nerve monitoring (IONM) is a validated and well-recognized adjunct in thyroid and parathyroid surgery. Practice paradigms are changing in the adoption of IONM, in its intermittent and continuous forms. This article explores the current and future trends of nerve monitoring, including guidelines and practice patterns on its use, new technological advancements that inform its progress and the importance of sound surgical decision-making as it relates to prevention of recurrent laryngeal nerve injury with monitoring.

Keywords: Intraoperative nerve monitoring (IONM); thyroid surgery; intermittent; continuous

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Introduction

The role of intraoperative nerve monitoring (IONM) has become increasingly utilized in thyroid and parathyroid surgery as surgeons have recognized that vocal fold paralysis resulting from loss of function of laryngeal nerves can occur with neurophysiologic changes to the nerve that are not visually apparent. Loss of neural functional integrity increases patient morbidity and the risk for vocal fold paralysis. Technical advances and enhanced understanding of laryngeal neurophysiology plus collection of IONM data from different populations of patients and surgeons have been instrumental in the ongoing evolution of monitoring strategies and management algorithms. In turn, this has led to worldwide adoption of the technology for neck endocrine surgeries. This article will discuss the present applications and future directions of neuromonitoring in thyroid and parathyroid surgery.

IONM

The guidelines on the appropriate use, set-up and troubleshooting of IONM have been established by the International Neural Study Monitoring Group (INMSG) (1). IONM is currently done with the use of specialized endotracheal tubes that have surface electrodes embedded on the tube and make direct contact with each true vocal fold. Electromyographic compound muscle action potentials (CMAP) elicited by vocal fold contraction respond to direct nerve stimulation (2). Induction with a short acting non-depolarizing agent is necessary because long-term depolarizing agents cannot be used with nerve monitoring. Proper endotracheal tube placement, and visualization of the electrodes intralaryngeally, taping of the tube, and patient positioning in extension are each components of proper set up. The confirmation of tube position is followed by monitoring the threshold, stimulation current and impedance testing. Surgical field testing is done with stimulation of the ipsilateral vagus nerve in order to confirm the circuit is intact (V1 signal). Stimulation throughout the case is done with a handheld probe in intermittent nerve monitoring and is continuous with the placement of an electrode around the vagus intraoperatively.

Current forms of IONM

Neuromonitoring of laryngeal nerves can be performed using intermittent (IONM) or continuous (CIONM) methodology. Pre- and post-operative laryngoscopic evaluation of the true cords for decreased mobility is recommended when utilizing this technology to confirm function before and after surgery (3,4). Intermittent monitoring involves intermittent stimulation of the nerve using a handheld or instrument mounted probe, which enables a "moment in time" evaluation of neurophysiologic function of the nerve. Continuous nerve monitoring is real-time nerve monitoring of the vagus/recurrent laryngeal nerve (RLN) complex that provides a continuous recording of vocal fold EMG potentials. CIONM has the ability to monitor trends in nerve function over time with the objective of detection of amplitude decline as early as possible, thereby allowing the surgeon to take immediate action to reverse the change (5).

Multiple series have demonstrated that if standard IONM protocols are followed, the negative predictive value of loss of electrical signal is >95% in regards to with vocal cord immobility (6,7). The INMSG has published a protocol by which most neuromonitoring data is collected and this has enabled the mechanisms of RLN injury and definitions of loss of signal (LOS) to be defined (1).

The types of RLN nerve injury that can occur include traction, compression, sharp, or thermal injury, with traction injury being the most common (8). LOS is defined as an amplitude decrease to less than 100 μV on stimulation with 1 to 2 mA. There have been two identifiable LOS types; type I is segmental focal injury and type II is global injury (8). Type I injury occurs by a focal disruption to a segment of nerve conduction on RLN. Positive EMG signal at laryngeal entry point but negative signal at proximal point of exposed RLN or vagus nerve indicates a type I injury. We can detect the injured point by testing the RLN from laryngeal entry point to proximal area. Type II injury is a global injury whereby there is no featured disrupted point of nerve conduction on the entire RLN, but there is a positive response from contralateral vagus nerve stimulation. LOS is confirmed after the troubleshooting algorithm (1) has been checked (to ensure the observed change is real and not artifact) and the nerve amplitude fails to recover to at least 50% of initial baseline (7). If there is a loss of signal, the risk of postoperative vocal cord palsy is about 90% using CIONM and 70% using I-IONM. Signal recovery less than 50% of baseline amplitude indicates postoperative vocal cord palsy in all patients with LOS type 1, and two thirds of patients with LOS type 2 injuries (9). LOS is an important indicator for staging bilateral surgery. If there is an unexpected LOS during dissection of one nerve in bilateral thyroidectomy with strong concern for temporary vocal fold paralysis, the surgeon is advised to postpone contralateral dissection until neural function returns in order to avoid airway compromise from bilateral vocal cord immobility (10).

Current adoption of neuromonitoring

Acceptance and application of IONM in neck endocrine procedures has increased over the past decade, although establishing the true efficacy of neuromonitoring in preventing VFP is difficult due to variability in laryngeal examination practices and low overall rates of vocal fold palsy (11,12). The number of randomized control studies are few and the ability of these trials to demonstrate a clear benefit of IONM over no monitoring is limited by heterogeneity as well as lack of adequate power in study design. Dralle *et al.* have shown that it would be very difficult to have an adequately powered study to differentiate between visual identification alone and IONM, as such a study would require 9 million nerves at risk (NAR) in benign goiter patients and 40,000 NAR in thyroid cancer patients per arm to detect statistical significance (13). A recent Cochrane Review summarizes multiple studies that have demonstrated no significant difference in rates of temporary RLN paralysis between visual identification of the nerve alone versus the use of IONM (14) On the other hand, meta-analyses like Zheng *et al.* demonstrated that within a sample of >36,000 NAR, rates of transient vocal fold paralysis but not permanent vocal fold paralysis was significantly less in the IONM group versus visual identification alone (15). More recently, Bai *et al.* completed a meta-analysis of 34 studies inclusive of 3 randomized controlled trials and 31 non-randomized controlled trials that demonstrated an overall impact of IONM on the rates of temporary and permanent RLN injury. A total of 59,380 NARs were used in the meta-analysis to demonstrate prevention of total, temporary and permanent RLN injury with IONM by reducing the incidence by almost half (16). The study authors go as far to recommend IONM routinely be used in all bilateral thyroidectomies and malignancy operations (16). There is also evidence to suggest that nerve monitoring can improve the outcome results of more inexperienced surgeons to a level that approaches the results of more experienced and higher volume surgeons (17).

Currently, utilization of IONM remains variable around the world although specific indications for its use are mentioned in many thyroid and parathyroid guidelines worldwide. Recent guidelines from the American Academy of Otolaryngology Head and Neck Surgery recommend IONM use in thyroid surgery to improve voice outcomes (18). The German Association of Endocrine Surgeons practice guidelines and the International Neural Monitoring Study Group (INMSG) guidelines both support using IONM in all thyroid surgeries (19), while the American Head and Neck Society endorses its utilization in thyroid cancer cases, especially in patients with preoperative RLN palsy (20). The French Otolaryngology guidelines recommend use of IONM in bilateral dissection of RLN, preoperative RLN paralysis, and cases of previous thyroid surgery (21). The International Neural Monitoring Study Group was established in 2006 as a multidisciplinary collaboration of experts in the field of neck endocrine surgery, laryngology, electromyography, anesthesiology, and neurophysiology to devise standards of practice with the use of neuromonitoring, advance research and data collection and refine, improve and update guidelines on its use (7). The group has published multiple practice guidelines on IONM, CIONM and more recently a two-part consensus guideline discussing nerve monitoring for neck endocrine procedures (10,22,23).

Types of neuromonitoring

As previously mentioned, there are two types of neuromonitoring: intermittent (IONM) and continuous (CIONM). Intermittent IONM utilizes a handheld or instrument-mounted probe to obtain EMG signal from direct RLN and vagus nerve stimulation. The signal obtained by the probe can detect physiologic injury to nerve, and can help predict vocal fold paralysis. CIONM is real-time monitoring of the RLN and vagus nerves. CIONM utilizes an electrode around the vagus nerve which continually stimulates the nerve throughout the surgical procedure, thereby allowing surgeons to obtain EMG continuously throughout dissection. The predictive accuracy is quoted to be up to 99.5%, defined by the low number of false negative and false positives, and allows corrective action which makes it promising in malignant, reoperative cases or when contralateral dissection is planned (24). Disadvantages include circumferential vagal electrode placement during dissection and the possibility of electrode dislodgement, as well as the need for an assistant to monitor the RLN throughout the dissection making it more labor intensive (4,25,26).

Monitoring the superior laryngeal nerve and variations in the RLN

Nerve monitoring of the external branch of the superior laryngeal nerve (EBSLN) and variations in the RLN have proven to be useful, as these nerves are harder to visualize and identify in thyroid and parathyroid surgery. The rate of EBSLN injury may be as high as 50% (27) given the difficulty in its identification during routine superior pole dissection. There is a lack of routine exposure of the EBSLN during thyroidectomy and reports on methods of EBSLN preservation in the literature have thus varied (28-32), although most surgeons tend to avoid rather than routinely expose and identify the EBSLN during thyroidectomy.

The INMSG published a guideline statement on EBSLN monitoring during neck endocrine surgery which introduced standardized procedures for EBSLN identification and stimulation (33). The use of specific endotracheal tubes with larger electrode surface area has allowed improved sensitivity of nerve monitoring in detecting EMG signal for the EBSLN.

While the incidence of non-recurrent laryngeal nerve and extralaryngeal bifurcation of the recurrent laryngeal nerve is less commonly identified, IONM has been shown to prevent injury. The rate of non-recurrent laryngeal nerve is 0.5–3% (34). Donatini *et al.* reported that using a systematic IONM could increase the detection of the non-RLN and decrease the incidence of nerve palsy in cases of the non-RLN (35). Neurophysiological integrity of the vagus nerve can allow for detection of non-recurrent patterns. Kamani *et al.* identified 10 right-sided non-RLNs by application of IONM. They reported that monitoring vagal stimulation at defined points along the vagus provides reliable verification of the presence of the non-RLN (36).

The incidence of extralaryngeal branching of the recurrent laryngeal nerve into motor and sensory branches is 18–65% (37,38). Motor activity of nerve branches can be assessed by IONM and is a widely accepted adjunct to anatomical identification of the RLN (39,40).

New developments in IONM

Future developments in neuromonitoring are exciting and aim to improve the predictability of vocal fold injury, while at the same time advance the technology that exists. Two new developments with early results have been recently published include laryngeal adductor reflex (LAR) and anterior laryngeal electrode (ALE).

In 2017, Sinclair *et al.* described a non-invasive, new method of CIONM utilizing a laryngeal reflex known as the laryngeal adductor reflex (termed LAR-CIONM) (41,42). This technique utilizes electrical stimulation of the laryngeal mucosa on the side contralateral to the operative field and electrodes ipsilateral to the surgical field to continuously monitor RLN function without having to probe or dissect the vagal nerve (41). In addition, sensory vagal nerve fibers can also be monitored continuously for neck surgeries where the internal branch of the superior laryngeal nerve is at risk of injury. Early results of LAR-CIONM have demonstrated a high PPV for vocal fold paralysis (41).

The advantages of this approach include: (I) no additional electrodes or nerve dissection is required other than an EMG endotracheal tube; (II) vagal motor and sensory fibers plus brainstem pathways can be continuously monitored; (III) it elicits bilateral vocal fold contraction such that amplitude decline due to tube rotation can be assessed intraoperatively by checking the contralateral side; (IV) baseline readings can be taken prior to skin incision, before any dissection has occurred; (V) there may be greater sensitivity to detection of nerve stretch / compression than standardized CMAP IONM techniques; (VI) preoperative polyphasic potentials may predict intraoperative nerve irritability (41); and (VII) preliminary data suggests the approach may be able to determine duration of vocal fold paralysis resulting from an intraoperative LOS (permanent versus transient) although this data is not yet published.

As for all IONM techniques, total intravenous anesthesia is required for LAR monitoring. The relative disadvantages of this new neuromonitoring technology is that it relies on the endotracheal tube for both stimulation and recording, and current endotracheal tubes are not adequately designed for these functions. Widespread adoption of the technique would require production of a new endotracheal tube. In addition, because this technique utilizes a reflex pathway to elicit vocal fold contraction, not a CMAP response, it does not conform to published CMAP LOS data and warning criteria for LOS are likely to be different.

Another technology, recently published by Liddy *et al.* describes utilization of ALE on the thyroid cartilage in addition to the standard IONM monitoring (43). This enables greater surgeon control of neuromonitoring, particularly the external branch of superior laryngeal nerve (EBSLN). Feasibility studies have demonstrated that the advantages of this technology are that these anterior electrodes placed on the thyroid cartilage intraoperatively remain in place throughout operative dissection, demonstrating equal sensitivity to standard endotracheal tube (ETT) electrodes in monitoring the RLN (44,45). The problems with misplacement, malrotation and/or manipulation of the ETT electrode during IONM are avoided with ALE as the surgeon has control over the electrode position (43-45).

The disadvantages of this technology are that compared to ETT based surface electrodes, there is a small but significant decrease in EMG amplitude recorded by the ALE with stimulation of the vagus and RLN as there is signal attenuation as it traverses the thyroid cartilage to reach the electrode. This may lead to potentially variable signals based on patient's age and variable ossification of cartilage. This was not shown to confer an increased risk for false negative response in the Liddy *et al.* study, but this is something to consider. The electrodes can potentially move during the surgery and, for minimal access approaches, may be difficult to place and keep correctly positioned. There is also a possibility of tissue reaction to the implantable electrode (43-45).

Other technologies have adapted methods to attach nerve-monitoring devices to instrumentation and energy-based devices that are used in thyroid surgery. Sung *et al.* evaluated the role of a detachable magnetic nerve stimulator in porcine models and a small group of patients who underwent thyroidectomy, and found that EMG amplitudes were equal between the attached nerve monitors and the monopolar nerve probes. Furthermore, the detachable stimulators were simple, convenient, and effective. It provided surgeons with real-time feedback of the EMG response during intermittent IONM (46). Furthermore, Shin *et al.* determined there was no difference in EMG amplitudes when nerve stimulators were attached to energy based devices (EBD) like the Harmonic and Ligasure, and even within 1–3 mm distance from the nerve, the stimulator would allow the surgeon to detect the nerve before use of thermal energy (47).

Surgeon decision-making process

Despite the technical advancements in neuromonitoring with new technologies on the horizon, the success of neuromonitoring depends on the surgeon using the tool at hand. IONM can provide useful intraoperative information but is not a substitute for surgeon experience, nor for a comprehensive understanding of recurrent laryngeal nerve anatomy and ability to visualize and identify the nerve in all cases. Studies have demonstrated lower morbidity in recurrent laryngeal nerve injuries in high volume surgeons as compared to low volume surgeons (48), although among high volume surgeons the risk for complications is not negligible (49). It is important to have knowledge of the common areas for nerve injury, types of injury and use caution to avoid unnecessary risk to the nerve. For example, the suspensory ligament of the thyroid gland (Berry's ligament) is a known area for difficult dissection of the. The nerve can be adherent to embedded within this ligament. The risk/benefit of excision of all thyroid tissue in a total thyroidectomy has to be balanced with the risk for neural injury. The surgeon must also be knowledgeable in the troubleshooting algorithm of the technology at hand. Surgeon decision making is also important in determining whether or not to stage thyroidectomy if concern for neurophysiologic injury is present. Technology does not replace surgeon experience and decision-making.

Development of endoscopic thyroid surgery and nerve monitoring

The advancement of minimally invasive thyroid surgery such as transoral endoscopic thyroid surgery has led to adjustments in practice patterns with neuromonitoring. Neuromonitoring is being incorporated in endoscopic thyroid surgery, with placement of handheld probes for the recurrent nerve through endoscopic ports. The advantages of using IONM in endoscopic cases are that it helps in locating and mapping of the nerve for the endoscopic surgeon, and it can confirm that the nerve is functionally intact after dissection is complete, especially when visualization may be limited in the endoscopic field. The disadvantages of using IONM in endoscopic thyroid surgery may include user error and failure in identifying nerve tissue, ineffective stimulation with interference from electrocautery and injury to the distal RLN which is not fully mapped during endoscopic versus open surgery. The RLN is identified at the suspensory ligament of the thyroid gland (Berry's ligament) in transoral approaches only; theoretically intermittent monitoring of the RLN may not fully occur along the trajectory of the RLN which may not be fully dissected. A review of neuromonitoring in endoscopic and robotic thyroidectomy looked at 522 nerves at risk in nine studies between the years 2009 to 2016. Adherence to the International Monitoring Study Group was low with only 30% of studies performing vagus nerve stimulation (50). Intermittent IONM was the technology used in more than 90% of the studies. The reported rates of temporary RLN injury was in the range of 0 to 3.6% and permanent RLN injury was in the range of 0 to 0.4% (51). CIONM has been used in endoscopic cases as well. The disadvantages of CIONM in endoscopic surgery are that the vagus nerve is not routinely in the operative field and dissection of the nerve may be cumbersome, contributing to an increase in the operative time (52,53). Also, CIONM, as discussed above, may increase the cost.

Sung *et al.* applied the detachable magnetic nerve stimulator to endoscopic instruments in porcine models and determined EMG detection was equivalent to monopolar probes. This technology would provide real-time feedback on neural integrity for surgeons without having to switch instrumentation, as well as improve identification of RLN and EBSLN during the dissection (54).

New, non-invasive continuous IONM technologies such as LAR-CIONM may prove useful in endoscopic procedures in the future as well.

Conclusions

In conclusion, IONM has become an important adjunct to thyroid and parathyroid surgery. Current practice patterns as well as guidelines on the use of IONM in both intermittent and continuous forms continue to evolve. This article reviews those practice models, as well as studies that have evaluated the utility of IONM. This article also frames the future of nerve monitoring and the upcoming technologies. Overall, this review serves to provide the reader a comprehensive evaluation of the present and future of nerve monitoring in endocrine surgery.

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Footnote

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