

## Review Article



# Future Directions of Neural Monitoring in Thyroid Surgery

Hoon Yub Kim <sup>1</sup>, Xiaoli Liu<sup>2</sup>, Che-Wei Wu<sup>3</sup>, Young Jun Chai <sup>4</sup>, Gianlorenzo Dionigi <sup>5</sup>

<sup>1</sup>Korea University Medical Center (KUMC) Thyroid Center, Korea University Anam Hospital, Korea University College of Medicine, Seoul, Korea

<sup>2</sup>Division of Thyroid Surgery, Jilin Provincial Key Laboratory of Surgical Translational Medicine, China-Japan Union Hospital of Jilin University, Changchun, China

<sup>3</sup>Department of Otolaryngology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan

<sup>4</sup>Department of Surgery, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Seoul, Korea

<sup>5</sup>1st Division of General Surgery, Research Center for Endocrine Surgery, Department of Medicine and Surgery, ASST dei Sette Laghi Ospedale di Circolo e Fondazione Macchi, Polo Universitario, University of Insubria (Varese-Como), Varese, Italy

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### Correspondence to

Gianlorenzo Dionigi

Division of Endocrine Surgery, Department of Human Pathology in Adulthood and Childhood "G. Barresi", University Hospital G. Martino, University of Messina, Via C. Valeria 1, Messina 98125, Italy.

Tel: +39-090-2212637

Fax: +39-090-2212611

E-mail: gdionigi@unime.it

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### ORCID iDs

Hoon Yub Kim

<https://orcid.org/0000-0002-6731-3912>

Young Jun Chai

<https://orcid.org/0000-0001-8830-3433>

Gianlorenzo Dionigi

<https://orcid.org/0000-0003-0864-6087>

### Author Contributions

Conceptualization: Hoon Yub Kim, Xiaoli Liu, Che-Wei Wu, Young Jun Chai, Gianlorenzo Dionigi; Data curation: Hoon Yub Kim, Xiaoli Liu, Che-Wei Wu, Young Jun Chai, Gianlorenzo Dionigi; Formal analysis: Hoon Yub Kim, Xiaoli Liu, Che-Wei Wu, Young Jun Chai, Gianlorenzo

## ABSTRACT

Dissecting and identifying the recurrent laryngeal nerve (RLN) are considered routine procedures now that safe and effective methods have been established. Preventing RLN injury during thyroid surgery requires good visualization and exposure of the RLN, adequate knowledge of RLN anatomy, adequate surgical experience and training, and pre- and post-operative laryngoscopy. Whereas these requirements are widely accepted for routine thyroid surgery, new technical developments have emerged in the past 15 years. Literature show that both intermittent intraoperative neural monitoring (I-IONM) and continuous IONM (C-IONM) are recognized as effective techniques for RLN. The aim of this paper is to discuss advantages, limits and possible future directions for use of IONM and C-IONM in thyroid and parathyroid surgery.

**Keywords:** Thyroid gland; Recurrent laryngeal nerve; Intraoperative neurophysiological monitoring; Endoscopic; Thyroidectomy; Standards

## INTRODUCTION

In 1970, Riddell (1) stated that, in a bilateral procedure, the secondary lobe should not be resected until integrity of the recurrent laryngeal nerve (RLN) has been confirmed by stimulation with an electrical current. Electrical stimulation can also reveal whether or not an unidentified strand of tissue is RLN tissue.

Dissecting and identifying the RLN are considered routine procedures now that safe and effective methods have been established (2,3). Preventing RLN injury during thyroid surgery requires good visualization and exposure of the RLN, adequate knowledge of RLN anatomy, adequate surgical experience and training, and pre- and post-operative laryngoscopy (**Table 1**) (2,3).

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**Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

**Table 1.** Standards for RLN management in thyroid and parathyroid surgery

<b>Standards</b>
Comprehensive knowledge of nerve anatomy
Visual identification of RLN
Exposure of RLN
Adequate surgical experience and training
Pre- and post-operative laryngeal examination
RLN = recurrent laryngeal nerve.

**Table 2.** Reasons for increased use of IONM

<b>Reasons</b>
Development of non-invasive devices
Development of user-friendly systems
Data from randomized trials
Establishment of guidelines and standard procedures
Establishment of KINMOS define courses and training programs
Medico legal issues
Research
Recommendations of professional organizations and societies (e.g., KINMOS)
Commercial effort
IONM = intraoperative neural monitoring; KINMOS = Korean Intraoperative Neural Monitoring Society.

Whereas these requirements are widely accepted for routine thyroid surgery, new technical developments have emerged in the past 15 years. Specifically, intraoperative neural monitoring (IONM) has been widely adopted by thyroid surgeons, by general practitioners, and by specialists in endocrine medicine, head and neck cancer, and ear, nose and throat medicine (**Table 2**). For example, IONM is now used in 90% and 70% of all thyroid procedures performed in the USA and in Germany, respectively (4,5).

Currently, both intermittent IONM (I-IONM) (2,3) and continuous IONM (C-IONM) (7,8) are recognized as effective techniques for RLN management. Studies also show that IONM can facilitate functional preservation of the external branch of the superior laryngeal nerve (SLN) (6). Specific advantages of IONM include the following:

- Avoidance of excessive or unnecessary traction by early and definite RLN localization (including extra-laryngeal branches, anatomical variation, distortion, and non-RLN tissues).
- Superior accuracy in confirming the RLN compared to visual identification.
- Significantly reduced rate of temporary palsy in high risk procedures (I-IONM) (9) and significantly reduced risk of permanent injury (C-IONM) (10).
- Reduced risk of bilateral injury. Specifically, use of IONM in staged thyroidectomy procedures reduces the risk of bilateral RLN palsy at the first dominant side in thyroid surgery procedures.

Below we discuss possible future directions for use of IONM in thyroid and parathyroid surgery (**Table 3**).

**Table 3.** Future directions of neural monitoring in thyroid surgery

Future directions
Enhanced continuous monitoring of the RLN via VN stimulation
Clarification of current limitations of neural monitoring technology
Improved stability of EMG signals
Simplified application of technology
Increased clinical use of monitoring in endoscopic thyroidectomy
Updated monitoring guidelines

RLN = recurrent laryngeal nerve; VN = vagal nerve; EMG = electromyography.

## MAJOR LIMITATIONS OF IONM

Notwithstanding these advantages, surgeons must be aware that current IONM technology has several important limitations (**Table 4**). First, currently available IONM techniques (including both neurosurgical and orthopedic techniques) cannot provide class I evidence. Using IONM for class II and class III studies also has major limitations (8,11) (**Table 5**). Ideally, IONM should provide the level of evidence needed for the thyroid surgery procedures most commonly performed in clinical practice. Outcomes of IONM applied in evidence based medicine are no worse than those obtained by conventional thyroid surgery. Class I evidence is rarely obtained by IONM because IONM is rarely used to prevent RLN deficit and because the incidence of permanent RLN complications is low (8,11). **Table 4** shows the future directions of IONM research that are needed to improve its outcomes.

## C-IONM OF THE RLN VIA VAGAL NERVE (VN) STIMULATION: A PROMISING ADVANCE IN MONITORING TECHNOLOGY

Currently, C-IONM procedures are performed more frequently than I-IONM procedures. One reason for the relatively greater use of C-IONM is that it enables continuous VN monitoring.

**Table 4.** Limits of IONM

Limits
Continued occurrence of RLN palsy
Need for training and standardization to avoid pitfalls
Knowledge of most common pitfalls
Need for skill in applying troubleshooting algorithms
Continued reliance on clinical judgment of IONM operator
Relatively low positive predictive value
Need for further research in RLN neurophysiology
Thyroidectomy in local anesthesia
Ineffectiveness/inapplicability of C-IONM in some injury types
High complexity of C-IONM probe installation and application procedures

IONM = intraoperative neural monitoring; RLN = recurrent laryngeal nerve; C-IONM = continuous IONM.

**Table 5.** Levels of evidence

Levels	Evidences
I	Systematic reviews, meta-analyses, randomized controlled trials
II	Two groups, non-randomized studies (e.g., cohort, case-control)
III	One group, non-randomized (e.g., before and after pre-test and post-test)
IV	Descriptive studies that include analysis of outcomes (single-subject design, case series)
V	Case reports and expert opinion that include narrative literature reviews and consensus statements

**Table 6.** mCEs and sCEs detected by C-IONM

Variables	Descriptions
mCE	Amplitude decrease of 50%–70% with a concordant latency increase of 5%–10%
sCE	Amplitude decrease of 70% with a concordant latency increase of 10%

C-IONM = continuous intraoperative nerve monitoring; mCE = mild combined event; sCE = severe combined event.

That is, function can be monitored throughout the entire RLN. Additionally, C-IONM provides comprehensive electromyography (EMG) documentation, detects imminent RLN failure, and reveals RLN stress mechanisms. Finally, C-IONM can reveal malposition of an EMG tube (7,8,12).

A major advantage of C-IONM is that, by alerting the surgeon to the potential for irreversible neural damage, it can reduce the risk of permanent RLN injury (7,8). For example, C-IONM can provide an early warning of impending neural injury by revealing adverse changes in EMG. Nerve function can then be preserved by taking appropriate corrective action and by aborting maneuvers that can potentially cause adverse EMG changes and permanent vocal cord paralysis (VCP) (7,8). However, thyroid surgeons require effective methods for identifying important adverse events and for differentiating between true adverse events and artifacts (7,8,12). Additionally, amplitude reductions and latency increases detected by C-IONM can reveal a mild combined events (mCEs) or severe combined events (sCEs) (Table 6). Notably, mCEs and isolated amplitude or latency changes are not associated with VCP whereas sCEs denote electrophysiologic events that can be reversed by aborting the related surgical maneuver. However, both mCEs and sCEs can cause a loss of signal (LOS), which typically has much lower reversibility, and postoperative VCP (7,8). Thus, modification of a surgical maneuver associated with sCEs can prevent subsequent neural injury leading to postoperative VCP. However, surgeons should consider that any IONM modality is more effective for preventing impending neural damage secondary to a stretch or compression injury than for preventing neural damage caused by inadvertent neural transection or thermal injury.

For the above reasons, C-IONM performed via continuous permanent stimulation of the RLN via the VN is clearly an important future direction of IONM. That is, C-IONM is likely to become a standard procedure in monitored thyroidectomy.

## IMPROVING EMG SIGNAL STABILITY AND SIMPLIFICATION OF TECHNOLOGY

### 1. Endotracheal EMG tube

A high-quality EMG signal is essential for effective IONM. A baseline V1 amplitude of >500  $\mu$ V indicates a functionally intact RLN and is considered a prerequisite for RLN diagnosis and for further interpretation of reduction of signal, recovery signal, LOS, preoperative VCP (nerve conduction\EMG signal preserved) (7,8,12).

A strong and stable EMG signal is essential for effective IONM of the RLN, particularly in C-IONM. Recording methods used for IONM should be reliable, applicable in all patients, and simple and easy to perform.

A thorough introduction to C-IONM requires a critical evaluation of neuromonitoring devices available in the near future (7,8,12). Moreover, when using EMG endotracheal

surface electrodes, a difference in EMG amplitude caused by a change in electrode-vocal cord contact may be difficult to distinguish from a change caused by a true nerve injury. The EMG signal detected by C-IONM can also be affected by the anesthesia type, by manipulation of the trachea, and by dislocation of the VN electrode (acute LOS indicates electrode dislocation) (12).

Finally, the EMG endotracheal tube must be easy to position. A simple, comprehensive, and continuous intraoperative surveillance system is needed to confirm the correct positioning of the EMG tube.

Further studies are needed to develop methods of detecting EMG signals that clearly and accurately indicate the status of the VN, RLN, and SLN and are not highly susceptible to interference.

## 2. Stimulation probes for I-IONM

The technology for I-IONM stimulation probes has not been perfected. Ideally, the probe should be wireless and long enough for simultaneous stimulation of vagal and laryngeal nerves during conventional and/or endoscopic remote access procedures. For flexible and versatile application in bilateral procedures in all nerves (VN, RLN, and SLN), the stimulation probe should enable contemporaneous application with a dissecting instrument or coagulating device and with a console for remote control of software. Ideally, the probe should deliver low intensity stimulation and should be reusable and ergonomic for either endoscopic or robotic use (13). During IONM of RLN in thyroid surgery, the need for frequent shifting between dissecting instruments and stimulation probes can be troublesome and time-consuming. Therefore, support for simultaneous use of 2 instruments is an important area for further research (14).

Further prospective studies are needed to identify the optimal dissection and stimulation instruments for both conventional and endoscopic procedures. Specifically, additional studies are needed to determine the optimal current, threshold, and stimulation intensity as well as the optimal characteristics of the dissecting instrument (e.g., shape, length, exposed vs. covered tips, and materials, etc.) (13-16).

## 3. Stimulation probes for C-IONM

The C-IONM stimulating electrodes must be configured to protect against dislocation and against variations in their distance from the nerve during manipulation within the surgical site. Currently available C-IONM probes differ in their size, their design/geometry (closed vs. open), their installation procedure (e.g., need for VN dissection), their stimulation mode, their adaptability and versatility, and their safety (**Table 7**). Studies show that, compared to electrodes with open designs/geometries, those with closed designs/geometries are generally preferable because of their lower displacement rate, lower stimulation current, higher EMG amplitude, and higher signal stability (7,8).

Although the C-IONM probe is considered an important technological improvement, further simplification is needed. For example, some surgeons avoid routine application of C-IONM because use of the probe requires additional procedures (opening the carotid sheath and VN dissection) that are not required in routine surgery for benign thyroid disease (7,8). Surgeons require C-IONM probes that are easy to apply. Given the varying position of the VN, the C-IONM probe must also be highly versatile. The location of the VN in relation to the common carotid artery and internal jugular vein can be classified as anterior (A), posterior

**Table 7.** Summary of available C-IONM probes

Variables	S-shaped	Anchor	V3	Delta	Saxophone	APS
Design						
	Open	Open	Open	Partially closed	Partially closed	Closed
VN dissection	Partial	Partial	Partial	<360°	<360°	360°
Installation	+	+	+	+	+	+
Size (mm)	54×8×0.8	25×0.8×18	20.8×4.8	18.05×5×7	17.6×different	2–3
Adaptability	+	+	+	++	++	+++
Versatility	+	+	+	++	++	+++
Flexibility	+++	+	+	++	++	+++
Hindrance	+	+	+	++	++	+++
Stimulation mode	Tripolar	Bipolar	Tripolar	Bipolar	Tripolar	Monopolar
Safety	+	+	+	+	+	+
Manufacturer	Dr. Langer Medical GmbH, Waldkirch, Germany	Dr. Langer Medical GmbH, Waldkirch, Germany	Inomed Medizintechnik GmbH, Emmendingen, Germany	Inomed Medizintechnik GmbH, Emmendingen, Germany	Dr. Langer Medical GmbH, Waldkirch, Germany	Medtronic, Minneapolis, MN, USA
CE market	2010	2009	2008	2013	2013	2011
Type	Reusable	Reusable	-	Disposable	Disposable	Disposable
Pulse width (mcs)	200	200	200	200	200	200
Stimulation intensity	1–2.5	1–2.5	3–5	1	1–2.5	1

C-IONM = continuous intraoperative nerve monitoring; APS = automatic periodic stimulation; VN = vagal nerve; CE market = Conformité Européenne market.

(P), posterior to the internal jugular vein (PJ), or posterior to the common carotid artery (PC) (17). Most (90%) VNs lie in the posterior region of the carotid sheath in the groove between these 2 vessels. On both sides, the most common location of the VN is the P location followed by the PC (15%) and PJ (8%) locations (17). The highly variable location of the VN is yet another reason why a simpler C-IONM probe is needed (17).

#### 4. Console and monitor

The major benefit of IONM is that it enables a multidisciplinary cooperative effort. However, further simplification of the IONM console and monitor is needed to support collaborative efforts by surgeons, anesthesiologists, and nurses. An easy setup procedure and support is also needed for reading, online tutoring, remote control, wireless, IONM integration with the operating room and offices. Finally, the IONM console and monitor should integrate data for anesthesia and EMG tube intubation to enable continuous assessment and verification of EMG position and displacement.

## DEVELOPMENTS IN MONITORING TECHNOLOGY FOR ENDOSCOPIC THYROIDECTOMY

Endoscopic thyroidectomy is a new and increasingly adaptive technique that demands full control of nerve function. Surgeons cannot apply new endoscopic approaches without full control of the laryngeal nerves. This would be in contrast with commonly performed routine open surgery. It would be a step back. Endoscopic thyroidectomy has to be in the same security area of open procedure for RLN management. To achieve a net benefit, all new approaches to remote thyroidectomy require an effective method of nerve monitoring.

In comparison to open procedures, acceptance of endoscopic thyroidectomy monitoring has been relatively slow (13). Some studies of monitoring methods for endoscopic or robotic procedures indicate that standard I-IONM (V1, R1, R2, and V2) is feasible and effective (13). In comparison, the use of C-IONM in endoscopic or robotic thyroidectomy is not well reported. One reason is the difficulty of using currently available C-IONM probe electrodes during endoscopic or robotic thyroidectomies.

Similarly, the ideal stimulating probes for I-IONM in endoscopic/robotic thyroidectomy have not yet been identified. I-IONM probes can be percutaneous using conventional open probes, or long probe (from spinal surgery), adapting dissecting endoscopic instruments to the IONM monitor, flexible wires electrodes, or integrating neural monitoring features with energy based devices (EBDs).

Technological developments in endoscopic thyroidectomy present an exciting opportunity to improve IONM outcomes and to simplify IONM techniques and accessories.

## UPDATING GUIDELINES

The first guidelines for neural monitoring of the RLN were published in 2010 (3). Guidelines for SLN monitoring were published in 2012 (6). The tremendous advances in IONM technologies and techniques in the past 5 years include new monitoring equipment, EMG tubes, intermittent and continuous probe stimulators, and software. New clinical evidence and outcomes have also been reported. Therefore, current guidelines must be updated. In addition to the updated guidelines required by health professionals, patients require updated information about monitored procedures, including technological failure rates and staged procedures.

Furthermore, with the introduction of IONM in endoscopic thyroidectomy, troubleshooting algorithms must also be reassessed because laryngeal twitch is difficult to assess by endoscopy. The same is true for contralateral VN stimulation, which are essential in the problem-solving moment. Based on the clinical experience of endoscopic thyroid surgeons, professional organizations (e.g., The American Society of Neurophysiological Monitoring) must clarify and refine guidelines for monitored endoscopic and robotic approaches, identify and prioritize important areas of research and technological development (e.g., further simplification of monitoring technology, use of SLN monitoring technology, use of C-IONM technology, and nerve injury mechanisms), explore the full utility of monitoring in endoscopic surgery, refine standards for equipment set up (e.g., endotracheal tube placement), refine standards for evaluating LOS events, and refine intraoperative problem-solving algorithms.

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