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The Current State of Recurrent Laryngeal Nerve Monitoring for Thyroid Surgery

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Abstract There is an increasing interest in intraoperative nerve monitoring (IONM), and numerous institutions have begun to perform monitored thyroidectomies. Attitudes have changed with the introduction of non-invasive devices, the publication of trials and guidelines defining standards, structured courses and descriptions of legal implications. The use of IONM helps to identify the nerve and give an objective evaluation of its function during the dissection. Recently, continuous IONM was introduced; it is a promising tool for early recognition of recurrent laryngeal nerve stress. This paper describes current issues in IONM.

Keywords Recurrent laryngeal nerve · Nerve monitoring · Guidelines · Research · Stage thyroidectomy · Informed consent

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Introduction: State of the Art

Intraoperative neuromonitoring (IONM) has been applied as an adjunct to standard visual identification of the recurrent laryngeal nerve (RLN) to help prevent nerve paralysis [1••, 2••, 3]. In the last decade, IONM has gained widespread acceptance among surgeons (Fig. 1), and much research has been conducted to solve common pitfalls and investigate implications and new applications of IONM [2••, 3–15] (Fig. 2).

De facto, as correctly noted in recent publications [2••, 4–15], the main aims of IONM are as follows:

(1) Early definitive localization of the nerve, thus avoiding excessive manipulation and damage to RLN and possible extralaryngeal branch(es) or anatomic variants (i.e. the nonrecurrent laryngeal nerve);
(2) Confirmation of RLN visual identification (preventing visual RLN misidentification);
(3) Evaluation of the laryngeal nerve function before, during and after dissection, with objective confirmation of the neurophysiological integrity on the first side before approaching the contralateral side.

Most of the existing studies have shown that although there is a reduction in the rate of RLN paralysis with the use of standardized IONM compared with the gold standard of nerve visualization alone, the difference between the two methods is not statistically significant [3, 16••]. Only one prospective randomized study has shown significant benefit for the reduction of the temporary palsy rate with IONM [17••].

The uncertainty in the literature concerning the merit of IONM to reduce overall RLN paralysis led to the analysis of other possible benefits; for example, in the case of an inexperienced surgeon, type\risk of thyroid disease treated,

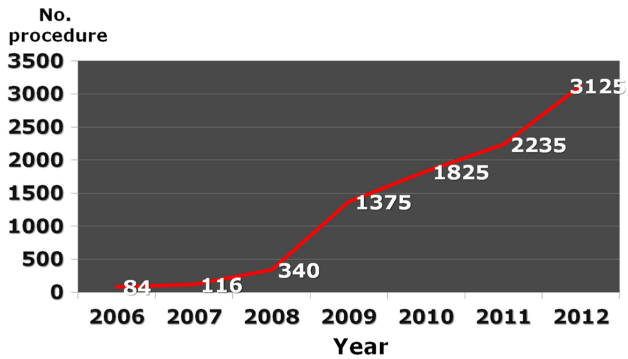

Fig. 1 Increasing prevalence of use of intraoperative neuromonitoring (IONM) in Italy. *Source data*: Inomed, Langer, Medtronic, Italy manufacturers' sales data

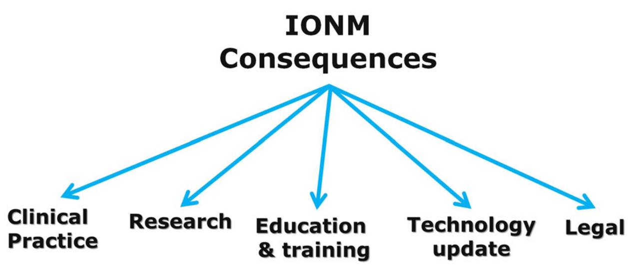

Fig. 2 Implications and consequences of IONM

surgical procedure and strategy (i.e. central compartment neck dissection (CCND) and to prevent bilateral RLN injury).

Dralle et al. [3, 18] demonstrated that the rates of nerve paralysis correlate with the surgical experience, and that a minor surgical experience is associated with a lower rate of paralysis when the nerve is identified both visually and with the aid of IONM.

Because both reoperation and first thyroid operations with an atypical course and anatomy of the recurrent nerve are associated with an increased risk of paralysis [3, 19••], it must be assumed that even in situations of this type, neuromonitoring presents an advantage because it allows a better representation of the course of nerve. The experienced surgeon must remember that some surgeries are difficult not only because of the thyroid disease being treated (e.g. high-risk procedures such as Graves' disease, cancer and re-do surgery), but also because of atypical anatomy of the neck and the RLN (non-RLN, RLN ramification, relationship with the inferior thyroid artery, Berry's ligament and Zuckerkandl tubercle and nerve dislocation) [3, 19••]. These situations cannot be identified beforehand, preoperatively.

In a recent study by Barczynski, IONM decreased the incidence of transient RLN paresis in repeat thyroid operations compared with nerve visualization alone [20••]. In detail, transient and permanent RLN injuries were found respectively in 2.6 and 1.4 % nerves with IONM, versus 6.3 and 2.4 % nerves without IONM ($p = 0.003$ and $p = 0.202$, respectively) [20••].

A more recent retrospective study of a large cohort of patients demonstrated that adding CCND to total thyroidectomy does not increase the risk of transient or permanent RLN palsy [21]. Moreover, Chiang et al. [22] reported that in 101 patients, extensive RLN dissection did not result in a decrement of neurotransmission. Therefore, the role of IONM during primary CCND, either elective or therapeutic, remains controversial; nevertheless, the possibility of better identification of the nerve, especially in the presence of the aforementioned anatomic variants, and objective evaluation of the nerve's status before approaching the contralateral site that minimizes the risk of bilateral nerve palsy, remain two important factors that cannot be neglected. In contrast, when performing a revisional CCND, IONM can be extremely useful, because it may ease the identification of the RLN in a surgical field that lacks anatomic landmarks and may have abundant scar tissue. In this scenario, the mapping of the area where the nerve is supposed to be may avoid a dangerous "blind" dissection [23]. As for CCND, once thyroidectomy has been completed, all the important anatomic structures, including the RLN, should have been clearly identified and preserved; thus, CCND should not entail an increased risk of misidentification of the nerve per se. In contrast, the increased manipulation of the RLN associated with CCND could be expected to compromise its function (Fig. 3).

Technology Perspectives

Continuous IONM (*C*-IONM)

Currently, the intermittent IONM (*I*-IONM) mode of application presents relevant limits (Table 1) [24]. With *I*-IONM, the functional integrity of the RLN is limited to the short interval of direct nerve stimulation [24]. Via *I*-IONM, the wholeness of the laryngeal nerve is limited merely to the site of direct nerve stimulation: in proximal neurogenic lesions of the RLN, distal stimulation near the larynx may produce a false negative "normal" IONM signal [24]. Thus, the RLN is still at risk for damage during thyroidectomy (*a*) proximal to the site of the surgeons' stimulation and/or (*b*) during the time gap between two nerve stimulations. De facto, *I*-IONM tests the integrity of the RLN just *following* a thyroid dissection, allows the evaluation of the RLN solely *at the moment* of stimulation, and detects RLN injury merely *after* insult occurs [24].

To overcome these *I*-IONM limits, a *C*-IONM technology has been proposed. [25–28] *C*-IONM represents an

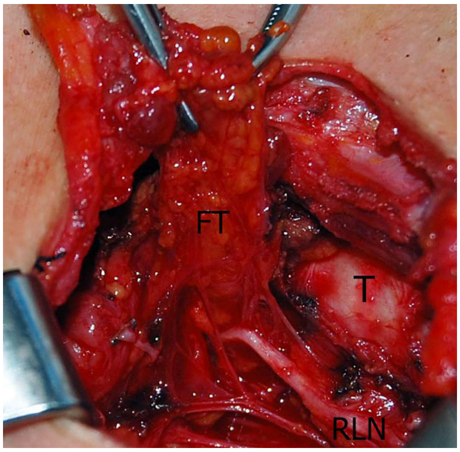

Fig. 3 Central compartment neck dissection (CCND) on the left side. The dissection of the recurrent laryngeal nerve (RLN) should be performed with blunt instruments, trying to exert a minimal traction on the fibro-adipose tissue (FT). (T: trachea). IONM is useful to test the function of RLN during and after CCND

Table 1 Limits of intermittent IONM

1. RLN palsy still occurs
2. Need for standardized and well-trained use to avoid pitfalls
3. Knowledge of most-common pitfalls
4. Ability to use troubleshooting algorithms
5. IONM does not replace clinical judgment
6. Relatively low positive predictive value
7. Cost-effectiveness is still not evaluated
8. Need for further research focused on neurophysiology of the RLNs
9. IONM of the external branch of the superior laryngeal nerve
10. Assessment of posterior branch of RLN
11. Thyroidectomy in local anesthesia

automatic stimulation of the vagus nerve (VN) using a software-based reassessment of the change in electromyographic endotracheal (EMG) amplitude and latency during surgery. According to preliminary observations, this mode of IONM application provides the surgeon with real-time visual and acoustic feedback about the current RLN conductivity, allows testing for the integrity of the RLN throughout the dissection, and allows *steady* evaluation of the RLN [25–28].

The recent introduction of *C*-IONM includes several considerations.

C-IONM might perceive imminent and/or increasing RLN risk intraoperatively. In principle, in cases of weak and decreased EMG signal, the surgeon may react early intraoperatively to RLN stress, and RLN injury may be reversible. Theoretically, the surgeon may avoid eventual further injury to the RLN, and the nerve will be restored by the early relief of trauma. This may occur in neuropraxia, but not in the case of a more significant disruption, acute, or complete division of a nerve, as in cases of neurotmesis or axonotmesis (i.e. RLN section or in case of thermal injury). According to recent observation [25–28], RLN traction injury is still the most common cause of RLN injury. *C*-IONM is useful for preventing imminent traction injury by detecting progressive decreases in EMG amplitude combined with progressive latency increases. As recently described by Schneider et al. [27], to facilitate the interpretation of clinically relevant quantitative EMG signals, adverse EMG events should be categorized based both (combined and multiple) on changes of evoked signal amplitude and latency, consisting of a >50 % decrease in amplitude paralleled by a >10 % increase in latency.

Further clinical research, especially in neurophysiology and neuropathology, is necessary for qualitative and quantitative *analyses* and *interpretations* of the change in signal obtained with *C*-IONM before the procedure can be widely used on patients [24]. These data are essential to the surgeon’s intraoperative decision-making process.

The quality of the EMG signal is fundamental. A critical evaluation of the currently available neuromonitoring devices is essential for the development and introduction of this new IONM application method. Moreover, under EMG endotracheal surface electrodes, it is difficult to tell whether the change in EMG amplitude is caused by the change in contact between the electrodes and vocal cords or by true nerve injury. In addition, an EMG signal from *C*-IONM application might be limited by the type of anesthesia, the manipulation of the trachea and the vagal nerve electrode dislocation (acute signal loss = electrode dislocation) [24]. The stimulating electrodes must be configured in a manner that protects against dislocation and changes in their distance from the nerve during surgical manipulation within the surgical site.

The VN electrode for *C*-IONM should be versatile [4, 6]. The location of the VN in relation to the common carotid artery (CCA) and internal jugular vein (IJV) is classified as *A* (anterior), *P* (posterior), *PJ* (posterior to IJV), or *PC* (posterior to the CCA) [6]. Most vagal nerves lay in the posterior region of the carotid sheath, in the groove between these two vessels (95 %) [6]. The *P* location of the VN is the most common configuration observed on either side, followed by the *PC* (15 %) and *PJ* (8 %) locations. Overall, less than 5 % of *A* location cases are observed [4, 6]. Moreover, the medial location of the CCA and the anterolateral or lateral location of the IJV are the most common configurations in the carotid sheath. Few cases of medial IJV position are observed. Tortuosity, kinking, or coiling of the extracranial carotid arteries may be observed with advancing age [4, 6].

It is equally essential that the safety of a new procedure is established before it is widely used on patients. With

I-IONM, a lesser and partial dissection of the carotid sheath and VN is used: the VN is exposed by dissecting the carotid sheath from just a 1-cm pouch; thus, not all of the carotid sheath is completely or routinely dissected. Moreover, when *I*-IONM is used to expedite VN identification or when the surgeon is not confident about carotid sheath dissection (in case of fatty areolar tissue, reoperative surgery, large goiter, hostile neck, endoscopic thyroidectomy or gross lateral metastatic lymph nodes that may displace the VN), VN identification and stimulation may be facilitated simply by increasing the amplitude to 2–3 mA with the probe on the carotid sheath *without* dissecting the neck vessel sheath [4]. Nevertheless, most *C*-IONM methods require dissecting the VN circumferentially (360°) to place the VN electrode on it. This procedure can be difficult, time-consuming, or even harmful to the VN and carotid sheath while the electrode is positioned during surgery and when it is removed. The electrode placement should be tension-free. Experimental histologic evaluation on the VN after probe positioning and repeated stimulation is necessary. The systemic safety of *C*-IONM has been already evaluated [4].

Finally, we would like to again emphasize the importance of *I*-IONM: traditional manual stimulation should still be used in combination with *C*-IONM. *C*-IONM seems to be a technological improvement. Likely, *C*-IONM via vagal nerve stimulation should enhance the standardization process, intraoperative RLN information, documentation, protection, training, and research in modern thyroid surgery.

IONM in Endoscopic Thyroidectomy

There have been four reports describing the efficacy of IONM in endoscopic thyroidectomy [29, 30••, 31, 32]. Kandil et al. [29] first reported the retrospective data for IONM use in minimally invasive video-assisted thyroidectomy, and concluded that IONM could be a very useful adjunct for RLN identification during endoscopic thyroid surgery. However, their method of IONM is not limited to the standardized IONM technique, in which the essential IONM procedure is vagal stimulation prior to the direct identification of RLN [1••, 9, 29]. The standardization of the IONM technique covers a fundamental technical aspect of thyroid surgery and endoscopic thyroidectomy. In 2012, Dionigi et al. [30••] reported a study of RLN injury during video-assisted thyroidectomy (VAT). They described the standardized IONM technique used in VAT surgery. The technique is composed of six steps [30••]: (1) preoperative laryngoscopy; (2) VN stimulation before thyroidectomy; (3) RLN stimulation upon initial identification; (4) RLN stimulation at the end of thyroid dissection and complete hemostasis; (5) VN stimulation after complete thyroidectomy and hemostasis; and (6) Postoperative laryngoscopy [1••, 9, 30••]. The fundamental steps of IONM during endoscopic thyroidectomy are the same as those used during conventional open surgery, and this technique should not be different in other approaches to endoscopic thyroidectomy.

Lang et al. [31] reported a retrospective study of IONM during gasless transaxillary endoscopic thyroidectomy and robotic-assisted thyroidectomy. This study demonstrated the technical feasibility of using a conventional open-nerve stimulator probe in both gasless transaxillary endoscopic thyroidectomy and robotic-assisted thyroidectomy [31]. They also compared two nerve stimulation techniques: direct RLN stimulation and indirect stimulation via the VN [31]. The result of this study showed that indirect stimulation via the VN produced more reliable and accurate IONM results than direct RLN stimulation [31]. This result supports the assertion that the standardized IONM technique is essential.

In endoscopic or robotic surgery, the electromyographic endotracheal (EMG) tube is identical to that used in conventional open thyroidectomy. However, a conventional probe cannot be used. Instead, there are two alternative methods for stimulating nerves. First, some hospitals use a flex wire stim probe (Fig. 4). This wire goes between the cannula and skin to access the vagus or laryngeal nerves. The wire probe stimulates the nerve via an endoscopic or robotic grasper. Generally, the NIM stimulation unit (NIM Response 3.0 System®, Medtronic Xomed, Jacksonville, FL, USA) is linked to a conventional probe or wire probe. In our hospital, we connect the NIM stimulation unit to the endoscopic monopolar electrocauterization hook. This second method is convenient because it allows the operator to stimulate the nerve without grasping the wire probe, and this procedure makes it easy to switch between cauterization and stimulation.

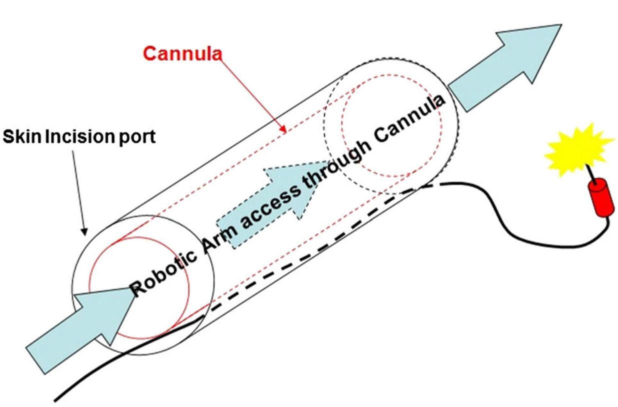

Fig. 4 Diagram of flex wire stim probe. The probe is connected with electronic stimulator through flexible wire and goes between the cannula and skin

In 2009, Dionigi et al. [32] reported a prospective, randomized case–control study of neuromonitoring in video-assisted thyroidectomy using a standardized IONM technique. To our knowledge, this is the only randomized controlled study of IONM in endoscopic thyroidectomy. The authors successfully showed the technical feasibility and safety of IONM in VAT [32]. The incidences of temporary RLN injury were 2.7 and 8.3 % in the IONM and control group, respectively [32]. The authors concluded that IONM enables surgeons to feel more comfortable with their approach to VAT [29, 30••, 31, 32]; however, they did not show a significant reduction in postoperative complications among the IONM group [32]. Thus, larger series with prospective, randomized, controlled studies will be needed to prove the benefit of IONM for RLN injury prevention.

In endoscopic thyroidectomy, standardized IONM is as feasible and safe as conventional open thyroidectomy.

Issues Surrounding IONM

The introduction of IONM has implications for preoperative and postoperative patient management.

Preoperative Management

Preoperative management may include adequate patient information and a specific informed consent. Thus, a proposed informed consent may describe the possible consequences of thyroidectomy, the risk of the operation and the *consequences* of IONM. Therefore, the patient must be informed preoperatively of the possibility of undergoing thyroidectomy in two phases if loss of signal (LOS) to the first side occurs. If a total thyroidectomy is planned, the possibility of learning intraoperatively that one nerve is injured aids in the decision about whether to go to the other side. IONM allows the surgeon to stage contralateral surgery if RLN damage is diagnosed, thereby avoiding the potential for bilateral vocal cord paralysis [33].

De facto, possible consequences of a LOS of the RLN on the first side is helpful in considering optimal contralateral surgery timing. With LOS, the surgeon must consider that the ipsilateral nerve is injured at least temporarily, and can determine whether it is important enough and in the patient's best interest to perform surgery on the contralateral side that day, given the new intraoperative information about ipsilateral paralysis [33]. According to the Goretzki group [34••], a failed IONM stimulation of RLN after resection of the first thyroid lobe is specific enough to reconsider the surgical strategy in patients with bilateral thyroid disease to confidently prevent bilateral RLN palsy. In fact, in 85 % with known nerve injury and in 56 % with negative IONM stimulation on the first side of dissection, the surgical strategy was changed with no resulting postoperative bilateral RLN palsy. This was in contrast to the 17 % of patients with bilateral RLN palsy ($p < 0.05$) that occurred when surgeons were not aware of a preexisting or highly likely nerve injury on the first side of thyroid dissection [34••, 35].

Dralle et al. noticed that the growing appreciation that standardized IONM can prevent bilateral RLN palsies after signal loss on the initial side of resection may become increasingly relevant to malpractice litigation. Among German surgeons, 93.5 % were willing to change their surgical strategy to prevent bilateral RLN palsy when unilateral LOS was present: 84.7 % by discontinuing bilateral surgery and 8.8 % by reducing the planned extent of surgery [36••].

According to Sadowski, even patients understand perfectly the benefit of staging thyroidectomy [37].

In view of the worldwide proliferation of IONM, it may become harder to defend future malpractice claims regarding bilateral RLN palsies, unless IONM was conducted on the initial side of resection according to international standards [33, 38, 39••].

If the surgeon, despite the LOS to the first side, decides to continue to operate on the opposite side, he must justify the reason and clearly describe it in the medical records [33, 38, 39••].

Postoperative Management

The position of the surgeon in cases of RLN damage is not easy to evaluate, because the correct analysis of the case requires precise assessment of the entire set of variables, including (a) evaluation of the individual case (i.e. thyroid disease); (b) the procedure (i.e. the fact that it is a high-risk operation); (c) the surgeon's position (experience, training, volume); (d) the surgeon's experience with IONM (standardized methodology); (e) the comprehensive description of the surgical procedure; and (f) traceability of the use of IONM in the specific case. The neurostimulation electromyographic documentation is essential to draw surgical conclusions that justify any intraoperative surgical deliberation and for forensic issues [39••].

The postoperative management of the patient undergoing thyroidectomy should include proper EMG documentation in the medical records. IONM converts muscle activity into recordable EMG signals that can be printed out. Documentation of the normal neurophysiologic signals of the RLNs may have a forensic function, permitting early differentiation between RLN-related and unrelated voice changes.

Proper IONM documentation includes the printed or digital time traceable *V*1, *R*1, *R*2, *V*2 stimulations per side according to IONM international standards, together with preoperative and postoperative laryngoscopy findings (Table 2) [1••, 9].

Research

Currently, IONM research can be classified into two categories: (a) animal experimental models and (b) clinical observational studies.

Animal Experimental Models

Translation of scientific discoveries into meaningful human applications, particularly novel surgical technologies such as IONM, requires development of suitable animal models. Experimental approaches can be used to test different anesthetic drugs, equipment settings, surgical procedures, new devices, and most importantly, the nerve injury models during IONM.

Several animal models, such as porcine/mini-pig [7, 25, 40–42, 43••, 44, 45], canine/dog [46, 47] and rabbit [48], have been used in recent IONM research. The porcine model is the most commonly used model, because pigs and humans have anatomical and physiological similarities, especially in the neck and larynx (Fig. 5). In addition, the use of the mini-pig is economical and does not raise the public concerns associated with the experimental use of primates, cats, and dogs, thus providing a cost-effective research model.

The current animal IONM research can be subdivided into four categories:

1. Safety and normative EMG data

Wu et al. [12] conducted a prospective porcine model (Fig. 5) evaluation to confirm the safety and investigate the optimal intensity of electrical VN and RLN stimulation during IONM. They found no unusual electrophysiological or cardiopulmonary effects after continuous pulsatile VN and RLN stimulations for 10 min.

2. Anesthetic perspective

Neuromuscular blocking agents (NMBAs) might diminish the EMG signal of the vocalis muscles during IONM. Lu [7, 41] conducted a porcine study to investigate the effects of NMBAs on IONM. They also compared the recovery profile of the laryngeal muscles between different agents and dosages, and translated the information into clinical applications.

3. Feasibility study of new approach or device

Witzel K et al. [42] used a porcine model to test the feasibility of IONM during transoral thyroid resection; Schneider et al. [25] used a pig model to test and confirm the feasibility of using a new vagal anchor electrode for continuous IONM (*C*-IONM).

4. Nerve injury study

Different models of RLN injury during IONM, including transection [43••, 44], clamping or crush [43••, 45–47], traction or compression [25, 43••], and thermal injury [25, 43••, 48], have been studied, and their EMG tracings were recorded and correlated with the nerve injury.

Table 2 Standardized IONM

Preoperative	
	Structured informed consent (discuss staging thyroidectomy)
	*L*1: preoperative laryngoscope
Intraoperative	
	*V*1: stimulation of the VN before dissection
	*R*1: stimulation of the RLN at first identification
	*R*2: stimulation of the RLN after complete hemostasis
	*V*2: stimulation of the VN at complete hemostasis
Postoperative	
	*L*2: postoperative laryngoscope
	EMG documentation. Printed or digital time traceable *V*1, *R*1, *R*2, *V*2 stimulations, including waveform morphology, amplitude and latency

Clinical Observational Studies

The current clinical IONM research can be subdivided into three categories:

1. Anesthetic perspectives

IONM requires good cooperation with the anesthesiologist. The following two issues are current areas of research interest.

The Use of Muscle Relaxants (Neuromuscular Blocking Agents, NMBAs)

The use of NMBAs in general anesthesia is essential for achieving clinically acceptable tracheal intubating conditions and preventing laryngeal trauma. NMBAs, however, can be a potential cause of false-negative responses during IONM. In the past 5 years, Chiang's study group has determined the feasibility of IONM after the administration of a nondepolarizing NMBA (a single dose of either rocuronium or atracurium) [49, 50]. They also confirmed that a total of 1 ED95 of rocuronium (0.3 mg/kg) is an optimal dose for IONM [51].

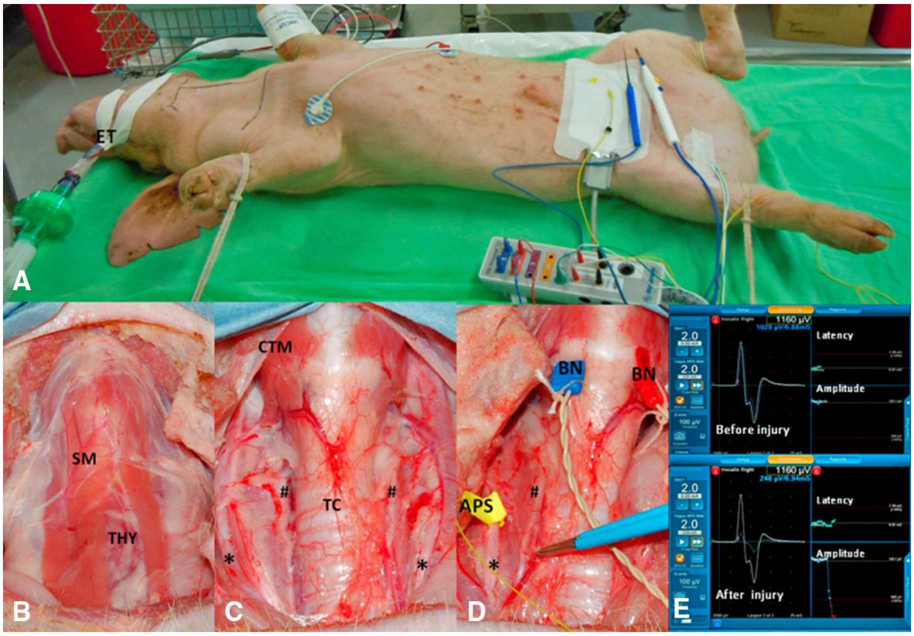

Fig. 5 Example of porcine animal model for IONM research. **a** A mini-pig was intubated with EMG endotracheal tube (ET) and prepared for IONM research. **b** Neck was opened. **c** Strap muscles (SC) and thyroid (THY) were removed to expose the trachea cartilage (TC), cricothyroid muscle (CTM), as well as the bilateral VNs (*) and RLNs (#). **d** Bipolar needle (BN) electrodes can be inserted to vocalis muscles for additional recording. Automated periodic stimulation (APS) electrode was put on the VN for CIONM. Various experiments can be tested on the RLN (in this photo, the thermal effect and injury on the RLN by bipolar cauterization was evaluated). **e** Real-time EMG tracings were recorded and correlated with the nerve experiments. (Photos from Dr. Chiang and Dr. Wu's animal Lab in Taiwan)

The Placement of an EMG Endotracheal Tube

Malposition of the endotracheal surface electrodes can result in equipment failure or unsuccessful monitoring, which could potentially give misleading information that might increase the risk of RLN injury. Chiang's study group [52] conducted a study to investigate the optimal depth of the EMG tube and concluded that the information would be a useful reference value for detecting the malposition of electrodes and adjusting the depth of the tube during the operation. Another study [8] found that the electrodes can be severely displaced when the patient's head position is changed from the neutral position for tracheal intubation to full extension for thyroid surgery. Therefore, the authors suggested checking the final electrode position routinely with laryngoscopy after patient positioning.

2. Innovative application

Many studies of innovative IONM applications have been published recently, including: (a) elucidation of surgical pitfalls and the mechanism of RLN injury [53••, 54]; (b) VN stimulation techniques for technical problem solving, recognizing any RLN lesions, precisely predicting RLN postoperative function [5, 6, 9, 55], and detecting a nonrecurrent laryngeal nerve [56–58]; (c) techniques for early RLN localization and identification (neural mapping) [59], identifying and handling the anatomical variations [60, 61••], and extensive RLN dissection [62]; (d) techniques for monitoring the external branch of the superior laryngeal nerve (EBSLN) [2••]; and (e) feasibility and devices for CIONM [25].

3. Normative Electrophysiological Data and Standardized Techniques

Normative intraoperative electrophysiological data for VN/RLN and EBSLN [63, 64] have been reported recently. "Normal" parameters are prerequisite for the interpretation of quantitative changes of intraoperative neuromonitoring during thyroid surgery to enable interpretation of influence on surgical strategy and prediction of postoperative vocal cord function [1••, 63, 64, 65••]. Lorenz [65••] analyzed systematic data of multicenter evaluation on quantitative intraoperative neuromonitoring parameters (amplitude, latency) of a total of 1,996 nerves. Median amplitude was significantly larger for the right versus left vagal nerve, latency was significantly longer for the left versus right vagal nerve, and duration of the left versus right vagal nerve was significantly longer. Age disparities were only present in the form of significantly higher amplitude in patients below 40 years of age. Regarding gender, there was significantly higher amplitude and smaller latency in women compared to men. Duration of surgery revealed a reduction of amplitude with operative time; contrarily, latency and signal duration remained stable. The type of underlying thyroid disease showed no influence on quantitative parameters of intraoperative neuromonitoring [65••].

Conclusion

High quality IONM is fundamental to optimizing surgical strategy that will yield the best patient outcomes as it relates to laryngeal function. The role of the surgeon is critical in obtaining an excellent quality of IONM. The surgeon, together with the anesthesiologist, should optimize the EMG signal, and in particular the *V*1 signal, by means of appropriate verification of electrode materials and stimulation protocols, correct EMG tube position and proper use of induction and maintenance of anesthesia drugs. Members of the IONM Study Group have proposed a proper definition\level for *V*1 amplitude >500 mcV [1••, 65••]. *V*1 signal is the prerequisite for the correct interpretation, diagnosis and verification of a functional intact RLN, for definition of a "significant" reduction of signal, "re-entry" signal (i.e. subsequent intraoperative EMG signal recovery and normal postoperative vocal cord function), LOS and again for the correct evaluation of the results. An unequivocal definition of normative EMG data is mandatory.

Conventional IONM is used to evaluate the function of RLN only at the moment of stimulation; using this technique, the nerve is still at risk of injury between two intermittent stimulations. When LOS is detected, the nerve has been injured. This leaves the surgeon without the opportunity to react immediately before LOS.

Consequently, several varieties of electrodes for VN stimulation have been designed for *C*-IONM, and they offer more seamless monitoring of the nerve's functional integrity along its entire course during surgery [25–28]. Some studies have reported that *C*-IONM is useful for detecting adverse EMG changes and preventing imminent RLN injury during the operation [25–28].

In an animal experiment [43••], *C*-IONM is actually a useful and objective tool to investigate the mechanism of RLN injury, particularly for thermal and traction injuries. The information of characteristic graded partial EMG change during acute RLN traction could be translated to clinical practice, and the substantial EMG decrease could be used as a warning criterion that would alert surgeons to immediately correct the surgical maneuver to prevent progressive nerve damage [43••].

Currently, conventional intermittent IONM remains more popular than *C*-IONM in clinical use; future studies are also needed to continuously develop innovative applications to make IONM a simple, safe, and surgeon-friendly procedure during thyroid and parathyroid operations.

Compliance with Ethics Guidelines

Conflict of Interest Gianlorenzo Dionigi, Che-Wei Wu, Davide Lombardi, Remo Accorona, Anna Bozzola, Hoon Yub Kim, Feng-Yu Chiang, Maurizio Bignami, Paolo Castelnuovo, and Piero Nicolai declare that they have no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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Papers of particular interest, published recently, have been highlighted as follows:
•• Of major importance

1. •• Randolph GW, Dralle H, Abdullah H, et al. Electrophysiologic recurrent laryngeal nerve monitoring during thyroid and parathyroid surgery: international standards guideline statement. Laryngoscope. 2013;121 Suppl 1:S1–6. *These guidelines are intended to improve the practice of neural monitoring of the inferior laryngeal nerve during thyroidectomy or parathyroidectomy, and to optimize clinical utility of this technique based on available evidence and consensus of experts.*
2. •• Barczyński M, Randolph GW, Cernea CR, et al. External branch of the superior laryngeal nerve monitoring during thyroid and parathyroid surgery: International Neural Monitoring Study Group standards guideline statement. Laryngoscope. 2013;123 Suppl 4:S1–14. *These guidelines are intended to improve the practice of neural monitoring of the external branch of the superior laryngeal nerve during thyroidectomy or parathyroidectomy, and to optimize clinical utility of this technique based on available evidence and consensus of experts.*
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disease showed no significant influence on quantitative parameters of intraoperative neuromonitoring. This study presents for the first time collective data of a large series of nerves at risk in a multicenter setting. It seems that definitions of "normal" parameters are prerequisite for the interpretation of quantitative changes of intraoperative neuromonitoring during thyroid surgery, to enable interpretation of influence on surgical strategy and prediction of postoperative vocal cord function.