Laryngeal Nerves Monitoring in Thyroid Surgery

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12.1 Introduction

In recent years, intraoperative neuromonitoring (IONM) has been gaining more and more acceptance in thyroid and parathyroid surgery as a method complementing the standard of visual identification of the recurrent laryngeal nerve (RLN) and allowing for assessing preservation of its functional integrity during the procedure. The percentage of thyroid surgeries with neuromonitoring varies from country to country. The highest percentage of thyroid surgeries with neuromonitoring occurs in Germany, where over 95% of the nearly 80,000 thyroid surgeries performed annually are monitored in this way. In Europe, according to data from the EUROCRINE registry from 2022, approximately 84% of thyroid surgeries are monitored, of which 86% with intermittent neuromonitoring (i-IONM), and 14% with continuous neuromonitoring (c-IONM) (www.eurocrine.eu). Barczyński et al. confirmed in a randomized trial involving 2000 nerves at risk of injury that the prevalence of early RLN injury (mainly transient) more often (about 5–7%) than permanent lesions (0.5–2%), it is significantly lower in the group of patients operated on with IONM compared to operations with visual visualization of the nerve, but without neuromonitoring (respectively: 3.8% vs. 1.9%, p = 0.011) [1].

12.2 Standardization of Intraoperative Neuromonitoring

The International Neural Monitoring Study Group (INMSG) in Thyroid and Parathyroid Surgery published guidelines for recommended standards for the application of IONM of the RLN in 2011, and in 2013 also for neuromonitoring of the

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external branch of the superior laryngeal nerve (EBSLN) [2, 3]. These recommendations were based on many years of multicenter experience of the research group members and focused on two essential aspects: standardization of equipment preparation for the procedure and assessment of the correct placement of surface electrodes on the endotracheal tube, as well as standardization of the procedure algorithm in cases of intraoperative signal loss, enabling precise differentiation of true loss of signal allowing prediction of RLN damage from the loss of a false signal resulting from various technical errors in the method application. In 2018, the INMSG published another two guidelines on staging bilateral thyroid surgery with monitoring loss of signal and on optimal RLN management for invasive thyroid cancer-incorporation of surgical, laryngeal, and neural electrophysiologic data [4, 5]. These guidelines are envisioned to assist the clinical decision-making process involved in RLN management during thyroid surgery by incorporating the important information domains of not only gross surgical findings but also intraoperative RLN functional status and preoperative laryngoscopy findings. The above-mentioned guideline statements are empowered by the most recently published recommendations on the desired informed consent for IONM in thyroid and parathyroid surgery and required format for the training courses in laryngeal nerve monitoring in thyroid and parathyroid surgery [6, 7].

Intraoperative laryngeal nerve monitoring currently comes in three formats:

1. intermittent neuromonitoring (i-IONM) of the RLN, including NerveTrend mode
2. continuous neuromonitoring (c-IONM) of the RLN
3. neuromonitoring of the external branch of the superior laryngeal nerve (EBSLN).

12.3 Intermittent Intraoperative Neuromonitoring

The i-IONM technique is useful in thyroid surgery in three main areas:

1. In aiding identification of the RLN (which includes both confirmation of the accuracy of the visual identification of RLN, as well as the use of the RLN neuromapping technique in the peritracheal area to identify the nerve before it is exposed in the operating field),
2. During tissue preparation, because after the identification of the RLN, repeated stimulation of the surrounding tissues and the nerve itself allows for the location of the further course of the nerve in the operating field, which is particularly important in cases of reoperation in a scarred operative field or operations in an altered field (e.g., advanced thyroid cancer),
3. In the intraoperative assessment of RLN activity and prognosis of postoperative nerve function and, in cases of loss of signal (LOS), also the identification of the nature of the damage (anatomical vs. functional while maintaining the anatomical integrity of the nerve), differentiating segmental (type I) from global (type II) lesions, and in cases of segmental (type I) lesions also locating the damage site and explaining the mechanism of RLN damage.

In practice, the very high negative predictive value of IONM method, exceeding 99.8%, allows for the safe continuation of the planned bilateral thyroidectomy if the correct neuromonitoring signal is maintained after the first lobe excision, practically eliminating the possibility of bilateral damage to the RLN. Hence, many authors believe that neuromonitoring is a tool that allows the risk of bilateral damage to the vocal folds to be reduced to zero, provided that the tactics of surgical treatment include the concept of staged thyroidectomy, in cases of neuromonitoring LOS on the first operated side.

12.4 NerveTrend Mode of Intermittent Intraoperative Neuromonitoring

The fourth generation of nerve integrity monitoring (NIM) systems introduced on the market in 2020 (NIM Vital) expanded the i-IONM format by adding a new NerveTrend mode in which electromyography (EMG) reporting – from vagus nerve (VN), RLN, or EBSLN – enables nerve condition tracking throughout a procedure, even when using intermittent nerve monitoring. After an initial probe stimulated EMG baseline trended readings at the same location on the nerve, NIM NerveTrend EMG reporting can enable comparisons of EMG amplitude and latency trends relative to the subsequent probe measurements manually captured throughout the case. A significant decrease in amplitude and/or increase in latency can signal degradation of the nerve condition. In addition, green, yellow and red color-coded EMG reporting and associated audible tones can help to understand when significant EMG changes occur and can help inform surgical strategy (Fig. 12.1). Potential benefits of NIM NerveTrend mode are: no additional cost over i-IONM, it is easy to use, it provides almost real-time feedback, it tracks functional status of the nerve, it is a step forward in prognostic calculation of the EMG tracings, its intuitive display is easy to follow even during challenging operations. Potential limitations of this mode are: it is an operator-dependent technique (manual trending); potential variability of stimulation site – VN vs. RLN – may occur; it may be more challenging to stimulate the VN in obese patients and in patients with a large thyroid volume; clinical evidence of its accuracy is in progress, as a randomized controlled trial (RCT) is ongoing (see details on: www.clinicaltrials.gov, NCT04794257). However, data recently presented by Barczyński et al. in Vienna during the International Association of Endocrine Surgeons (IAES) 2022 meeting which were based on the interim safety analysis of the ongoing RCT were favorable for the NerveTrend mode when compared to the i-IONM mode (personal communication; data not published). Of 132 nerves at risk in each group (NerveTrend vs. i-IONM), transient and permanent RLN injuries were found respectively in 1 (0.76%) vs. 7 (5.30%) nerves ($p = 0.03$) and 0 (0%) vs. 2 (1.51%) nerves (non-significant difference). Severe combined events occurred in 12 (9.0%) nerves at risk operated on with NerveTrend but were reversible in 11 of 12 cases (91.66%). Hence, the system seems to alert the surgeon to the imminent nerve injury in time as the majority of intraoperative nerve events were reversible. This initial observation needs to be validated further in an ongoing RCT until a designated power of the study is reached.

Fig. 12.1 NerveTrend mode allows for tracking the electromyographic (*EMG*) signals from the vocalis muscles and warns the surgeon on the impending nerve injury with severe combined events (*sCEs*) or loss of signal (*LOS*). EMG recovery allows for safe continuation of the surgical plan

12.5 Continuous Intraoperative Neuromonitoring

The c-IONM technique is based on the use of an electrode placed on the VN, through which the neuromonitor continuously and automatically checks the activity of the RLN by analyzing the EMG recordings from the vocal muscles, comparing the instantaneous parameters during the procedure with the initial baseline parameters at the beginning of the procedure.

In the event of repeated EMG phenomena forecasting nerve damage (reduction of the signal amplitude by more than 50% and extension of the EMG signal latency by more than 10%), which are mostly reversible, the device warns the surgeon with an acoustic signal, allowing for corrective action to avoid complete LOS, which is synonymous with functional damage to the nerve (Fig. 12.2).

Taking into consideration that the majority of RLN injuries occur in a time-dissociated manner, as an accumulation of microinjuries to the nerve deriving from surgical manipulations (traction, pulling, pressure), a temporary cessation of tissue preparation until the EMG recording improves enables the occurrence of RLN damage to be prevented. Hence, c-IONM is a technology that allows the surgeon to: recognize impending RLN injury during thyroidectomy; correct surgical maneuvers so that RLN damage does not occur; and verify the return of RLN function after intraoperative EMG LOS.

Recently, it was shown in 788 patients (1314 nerves at risk) that immediate reaction by withdrawing nerve tension prevented progression to LOS in 80% (63/77 patients) of combined events [8]. More recently, a study of 455 continuously stimulated nerves at risk revealed that the immediate release of retraction successfully preserved the nerve function in all cases with impending injury [9].

As shown by an international multicenter study of 115 LOS cases at the end of surgery, 80% (92/115 patients) of LOS are caused by traction of the RLN [10]. It was established in an international multicenter study of 68 patients (68 nerves at risk) that amplitude recovery ≥50% relative to baseline reliably predicted normal early postoperative vocal cord function in all patients after transient segmental LOS or global LOS [11]. On receiver-operating characteristics analysis, relative and absolute amplitude recovery of 49% and 455 μV (both $p < 0.001$) after segmental LOS type 1 and 44% ($p = 0.01$) or 253 μV ($p = 0.15$) after global LOS type 2 differentiated best between normal and impaired early postoperative vocal cord function. Practically then it may be justifiable to use one amplitude recovery threshold of ≥50% for both types of LOS. This single threshold accurately predicts normal early postoperative vocal cord function after segmental LOS, but may slightly underestimate normal early postoperative vocal cord function after global LOS (the less serious form of nerve injury).

Hence, the c-IONM technique has a potential of preventing unilateral RLN injury, which is not the case for the i-IONM technique. As shown by data published by Schneider et al. based on a total of 6029 patients, of whom 3139 underwent continuous and 2890 intermittent IONM (5208 vs. 5024 nerves at risk, respectively), c-IONM had a 1.7-fold lower early postoperative vocal cord palsy rate than i-IONM (1.5% vs. 2.5%). This translated into a 30-fold lower permanent vocal cord palsy

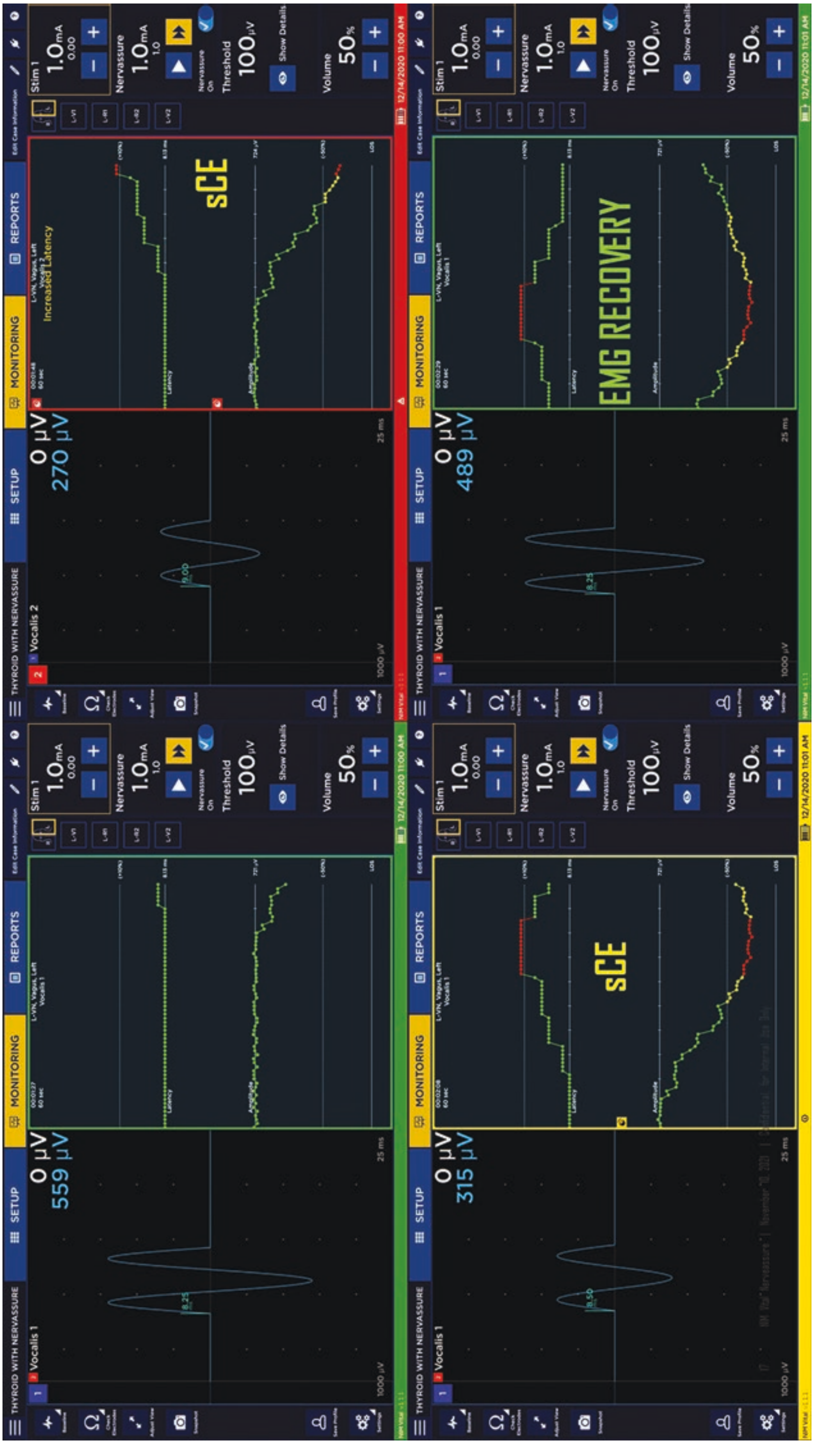

Fig. 12.2 NerveAssure mode (*c-IONM*) allows for tracking the electromyographic (*EMG*) signals from the vocalis muscles and warns the surgeon on the impending nerve injury with severe combined events (*sCEs*), or loss of signal (*LOS*). EMG recovery allows for safe continuation of the surgical plan

rate (0.02% vs. 0.6%). In multivariable logistic regression analysis, c-IONM independently reduced early postoperative vocal cord palsy 1.8-fold (odds ratio [OR] 0.56) and permanent vocal cord palsy 29.4-fold (OR 0.034) compared with i-IONM. One permanent vocal cord palsy per 75.0 early vocal cord palsies was observed with c-IONM, compared with one per 4.2 after i-IONM. Early postoperative vocal cord palsies were 17.9-fold less likely to become permanent with c-IONM than with i-IONM [12]. These data have clearly demonstrated that c-IONM is superior to i-IONM in preventing vocal cord palsy. Similar conclusions were drawn based on the meta-analysis of recently published data in the field [13].

12.6 Monitoring of the External Branch of the Superior Laryngeal Nerve

When using the IONM method, one should not forget about the usefulness of this technique in identifying and maintaining EBSLN functional integrity.

The prevalence of EBSLN injury is underestimated and, according to many authors, reaches 20%. This injury causes paralysis of the cricothyroid muscle impairing the production of high tones, and altering the voice's fundamental frequency, which may be especially problematic for women and voice professionals. The EBSLN has a close anatomical relationship with the superior thyroid pedicle and is at risk of injury during dissection of these vessels in approximately one-third of patients.

In patients with a large goiter, a thyroid tumor localized within the upper thyroid pole or in patients with a short neck, the anatomical relationship between the nerve and the superior thyroid pole vessel can be much more intimate, making the EBSLN particularly prone to inadvertent injury. The most widely recognized surgical classification of the EBSLN was proposed in 1992 by Cernea et al.

The Cernea EBSLN classification scheme identifies three types of anatomical relationship:

- Type 1 nerve crosses the superior thyroid vessels more than 1 cm above the upper edge of the thyroid superior pole and occurs in 68% of patients with small goiter and in 23% of patients with large goiter.
- Type 2A nerve crosses the vessels less than 1 cm above the upper edge of the superior pole and occurs in 18% of patients with small goiter and 15% of patients with large goiter.
- Type 2B nerve crosses the superior thyroid pedicle below the upper border of the superior thyroid pole and occurs in 14% of patients with small goiters and 54% of patients with large goiters.

Types 2A and 2B are particularly prone to injury during dissection and ligation of the superior thyroid vessels due to their low-lying course.

The use of tissue stimulation in the area of the upper pole of the thyroid gland before ligating these vessels allows for reliable identification of the EBSLN, as it results in an easy to observe contraction of the cricothyroid muscle. Nevertheless, in contrast to RLN monitoring, EBSLN monitoring is based on two distinct outcome measures following the stimulation of the EBSLN: evaluation of cricothyroid twitch (present in all patients) and EMG glottis response of vocal cord depolarization identified on surface endotracheal tube electrode arrays in approximately 70–80% of patients when using standard EMG tubes. However, a novel EMG tube with additional and more proximally located anterior surface electrodes allowed for identification of EMG response after stimulation of the EBSLN in all (100%) patients.

Visual identification of the EBSLN can be confirmed by applying the stimulation probe directly to the nerve (if seen) above the entry point into the cricothyroid muscle (Fig. 12.3). To facilitate localization of the EBSLN it is recommended to stimulate tissues parallel and underneath the laryngeal head of the sternothyroid muscle which can be regarded as a highly reliable landmark for the identification of the EBSLN in its distal course before termination within the cricothyroid muscle (Fig. 12.4). A technique of togging the stimulator probe between the tissue of the superior thyroid pole vessels (with negative stimulation) and the region of the laryngeal head of the sternothyroid muscle (with positive stimulation) is recommended to assure preservation of the EBSLN. The role of measuring the waveform amplitude in prognostication of EBSLN function is yet to be determined.

In conclusion, monitoring of the EBSLN is of enormous importance in improving the quality of life of patients undergoing surgery for various thyroid diseases, including thyroid cancer, as it increases the chances of preserving the timbre and voice register after surgery.

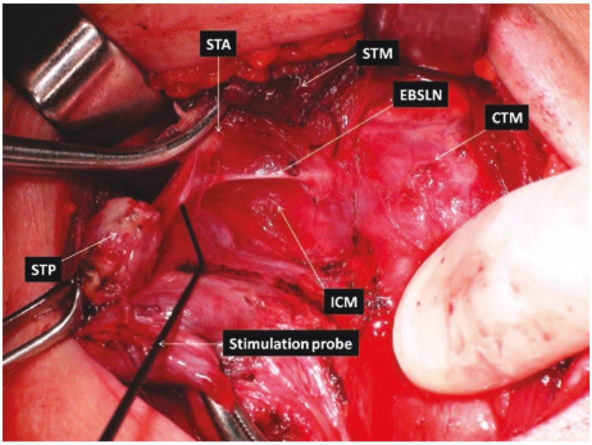

Fig. 12.3 The right-sided intraoperative view: step by step ligation of individual branches of the superior thyroid artery can be undertaken under both visual control and stimulation of the external branch of the superior laryngeal nerve (*EBSLN*) to assure not only anatomical but also functional preservation of the nerve which can be documented as a positive cricothyroid twitch. *CTM* cricothyroid muscle, *ICM* inferior constrictor muscle, *STA* superior thyroid artery, *STM* sternothyroid muscle, *STP* superior thyroid pole

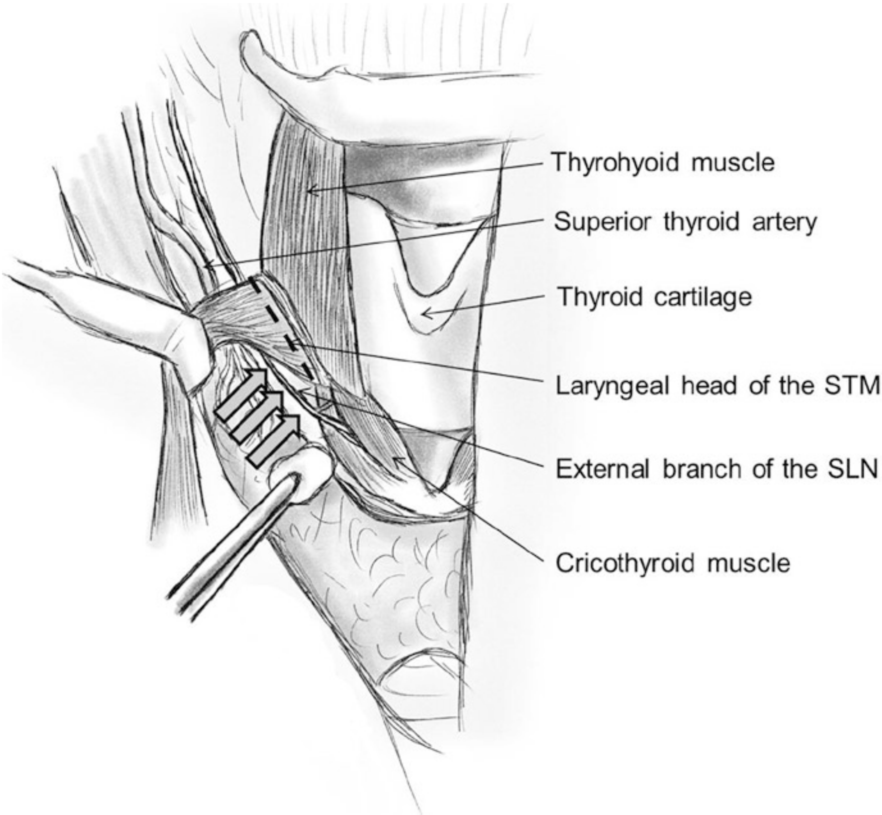

Fig. 12.4 Stimulation of tissues parallel and underneath the laryngeal head of the sternothyroid muscle (marked with the dashed line) allows for the identification of the external branch of the superior laryngeal nerve in its distal course (*large arrows*) before entering the cricothyroid muscle. *STM* sternothyroid muscle, *SLN* superior laryngeal nerve

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