Loss of Signal in IONM and Staged Thyroid Surgery

18

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Abstract

Intraoperative neuromonitoring (IONM) through vagus nerve (VN) stimulation in thyroid surgery provides indisputable recurrent laryngeal nerve (RLN) identification and comprehensive functional assessment of neural integrity during the process of thyroid resection. Neurostimulation of the RLN and VN generates an electromyogram with audio-tone. Relevant information regarding neural integrity using IONM is gained by observing the EMG parameters of amplitude, latency, and signal configuration. Relevant changes and corresponding surgical maneuvers must be considered to react timely and thereby possibly prevent neural injury. The hallmark of neural injury that corresponds with postoperative vocal cord dysfunction is the loss of signal (LOS) without recovery during IONM-guided thyroid surgery. Therefore, after LOS on the first side operated, staging of the planned bilateral surgery by postponing the second side until RLN function is restored is recommended. In this chapter, detailed definitions of the relevant IONM parameters and LOS are provided, and a description of IONM application with procedural recommendations is presented.

Keywords

Intraoperative neuromonitoring • Loss of signal • EMG • Signal recovery • Bilateral vocal cord palsy • Staged thyroidectomy

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Introduction

Intraoperative neuromonitoring (IONM), when used in a standardized fashion as provided by the International Neural Monitoring Study Group (INMSG), gives a competitive edge over mere visual identification of the inferior recurrent laryngeal nerve (RLN) by faster identification of the nerve along with any co-existing extralaryngeal branches and by continual confirmation of the nerve's functional integrity as the dissection moves forward [1–5]. Comprehensive functional assessment of the complete RLN, from its separation off the vagus nerve (VN) to its laryngeal entry point, is dependent on stimulation of the ipsilateral VN.

Although gross anatomic injury to the RLN typically results in RLN dysfunction and vocal cord palsy (VCP), the converse does not necessarily hold true: gross morphological nerve integrity is not definitively correlated with functional nerve integrity. Only IONM, affording almost real-time monitoring of RLN function, can give reasonable assurance of intact postoperative vocal cord function [1–7]. Prevention of bilateral VCP with the potential of permanent tracheostomy remains a key priority of surgical strategy in the neck. The success of that strategy hinges on the reliability of intraoperative information about the functional status of the RLN on the first side of resection before embarking on completion of the other side.

Reliability of IONM

The reliability of IONM signals is only assured when the L1, V1, R1, R2, V2, L2 approach published by INMSG is strictly adhered to [1–12]:

1. Determination of baseline vocal cord function on preoperative laryngoscopy (L1).
2. Stimulation of the VN and RLN before (V1, R1) and during/after (R2, V2) resection to confirm the functional integrity of the VN–RLN axis, using the troubleshooting algorithm in the event of loss of signal (LOS).
3. Confirmation of vocal cord function on postoperative laryngoscopy (L2).

Strict observation of these conditions is set to improve the reliability of IONM, the positive predictive value (PPV) of which ranges from 62.5 % to 77.8 % (intermittent IONM) and 88.2 % (continuous IONM) in the most current literature [5] (Table 18.1).

Definition of LOS

Based on current literature and the international standards guideline statement published by the INMSG [1], LOS is defined as loss of the audiotone and/or decrease of the nerve amplitude to below 100 μV on stimulation with 1–2 mA in the corresponding electromyogram. To make that determination, vocal cord function must be normal on preoperative laryngoscopy, and the baseline amplitude of the RLN should not be lower than 500 μV (and in no event lower than 300 μV) with normal nerve latency [8, 10, 13–18].

The severity of nerve damage is reflected by the rapidity of onset of LOS and fall of nerve amplitude. Unfolding damage can be picked up faster with continuous IONM, rather than intermittent IONM. Structural injury is caused by transection, clamping, or thermal injury to the nerve, whereas traction and stretch of the RLN tends to produce a more slowly evolving and perhaps more subtle nerve injury.

Solitary or serial increases in nerve latency or decreases in nerve amplitude, even when they surpass thresholds of 10 % and 50 % relative to baseline, respectively, are considered mild events. Combined events (the joint occurrence of increases in latency and decreases in nerve amplitude) qualify as severe events because they may develop into LOS after exceeding the above thresholds of 10 % increase in latency and 50 % decrease in amplitude [7]. Decreases in nerve amplitude, in isolation, are clinically less relevant

Table 18.1 Prediction of transient and permanent postoperative vocal cord palsy by intermittent and continuous intraoperative neuromonitoring

Author	Year	NAR	Sensitivity	Specificity	PPV (%)	NPV (%)	Transient VCP (%)	Permanent VCP (%)
IIONM								
Hamelmann et al. [34]	2002	428	23.5	98.5	40.0	96.8	19 (4.4)	1 (0.2)
Thomusch et al. [35]	2004	12,486	33.0	98.3	36.7	97.9	413 (2.7)[a]	104 (0.7)[b]
Beldi et al. [36]	2004	429	40	98	67	91	37 (8.7)	6 (1.4)
Hermann et al. [37]	2004	475	57.1	99.3	87.0	96.6	43 (8.9)[c]	15 (3.1)[c]
Chan et al. [38]	2006	271	53	94	35	97	15 (5.5)	2 (0.7)
Tomoda et al. [39]	2006	2197	69.3	99.7	92.1	98.5	80 (3.6)	21 (1.0)
Barczynski et al. [40]	2009	1000	63.0	97.1	37.8	98.9	27 (2.7)	8 (0.8)
Melin et al. [41]	2014	3426	85.4	99.0	68.0	99.6	82 (2.4)	N/A
Calò et al. [42]	2014	2068	91.3	99.4	77.8	99.8	23 (1.1)	6 (0.3)
De Falco et al. [43]	2014	600	83.3	99.5	62.5	99.8	5 (0.8)	4 (0.7)
Schneider et al. [5]	2015	965	73.9	99.5	77.3	99.4	23 (2.4)	4 (0.4)
CIONM								
Schneider et al. [5]	2015	1314	90.9	99.7	88.2	99.8	33 (2.5)	0 (0)

CIONM continuous intraoperative neuromonitoring, *IIONM* intermittent intraoperative neuromonitoring, *N/A* not available, *NAR* nerves at risk, *NPV* negative predictive value, *PPV* positive predictive value, *VCP* vocal cord palsy

[a] Based on 15,403 nerves at risk with follow-up information

[b] Based on 15,340 nerves at risk with follow-up information

[c] Based on 481 nerves at risk with follow-up information

Based on data from [5]

than decreases in amplitude with concordant increases in latency and often may be caused by dislocation of the endotracheal tube during the operation [19].

LOS comes in two varieties: segmental LOS type 1 and global LOS type 2.

Segmental LOS Type 1

Segmental LOS type 1 is defined by loss of nerve function downstream of, distal to, or towards the larynx from a point of damage, regardless of the level of upstream (proximal) nerve stimulation (Fig. 18.1). A handheld stimulation probe can help pinpoint the location of injury, below which regular electromyographical (EMG) signals can be elicited [19]. In this setting, stimulation of the VN failing to produce a response signal below the level of nerve injury quickly clarifies the situation.

This point of damage can be located anywhere along the course of the RLN. The nerve segments at risk of injury are listed below in descending frequency:

1. Between the intersection of the RLN with the inferior thyroid artery (ITA) and the entry of the RLN into the larynx (P1; encompassing the ligament of Berry).
2. Around the intersection of the RLN with the ITA (P2).
3. Below the intersection of the RLN with the ITA (P3).

The most common mechanism of injury underlying segmental LOS type 1 is direct trauma, as a result of pinching, clamping, clipping, or thermal injury to the nerve. Such trauma may strike instantly, in which case LOS type 1 is not heralded by premonitory EMG signals. LOS type 1 typically happens all of a sudden, with a plunge of the nerve amplitude that leaves little, if any, room for corrective action (even if continuous IONM was employed). When segmental LOS type 1 has manifested on the first side of

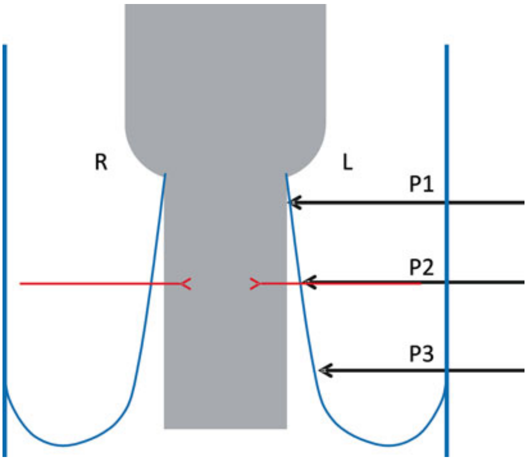


Fig. 18.1 Location of type 1 (segmental) loss of signal anatomical localization. P1: neural lesion superior to the intersection of the RLN with the inferior thyroid artery (ITA). P2: neural lesion at the level of RLN/ITA intersection. P3: neural lesion inferior to the intersection of the RLN with the ITA

resection and fails to resolve during the operation, a staged thyroidectomy needs to be considered.

Global LOS Type 2

Global LOS type 2 denotes a complete loss of the audio-tone, often with a progressive decline in nerve amplitude, in the absence of an identifiable point of damage and is associated with LOS along the VN–RLN axis. Global LOS type 2 may reflect more indirect mechanisms of injury, typically secondary to traction on the nerve through more distant maneuvers. This type of LOS tends to unfold more gradually and most of the time is preceded by the mild or severe events as previously defined. Although intermittent IONM is usually spaced out too much to allow for immediate corrective action in the event of imminent LOS type 2, continuous IONM frequently gives sufficient lead time to release a distressed nerve before the damage has become permanent. This is why global LOS type 2, by and large, has a better clinical outcome than segmental LOS type 1.

Troubleshooting Algorithm for LOS

Dislocation of the endotracheal tube, technical failures (e.g., defective hardware, disconnection of cables, impedance issues as a result of salivary pooling), and the use of muscle relaxants can mimic LOS even though nerve function is perfectly normal. Because they may trigger unnecessary actions, false-positive findings must be uncovered. A troubleshooting algorithm has been published by the INMSG (Fig. 18.2) to aid in this endeavor.

If stimulation of the contralateral VN fails to return normal EMG signals, it is crucial to exclude the intraoperative use of muscle relaxants, double-check the position of the endotracheal tube, and check the connections of the stimulation device. If contralateral VN stimulation elicits normal electrophysiological responses, injury to the ipsilateral VN–RLN axis is a reasonable possibility necessitating further work-up. Absence of a laryngeal twitch on palpation supports a diagnosis of LOS.

Intraoperative Recovery of Nerve Function after LOS

Once LOS has occurred, intraoperative recovery of nerve amplitude to >50 % of its baseline, also referred to as “complete recovery” [20], is hard to predict but should be given a mandatory waiting time after initial LOS. During the intraoperative wait (usually for a minimum of 20 min), all surgical activity must cease, and traction on the RLN, ligament of Berry, and trachea (in addition to any lifting of the thyroid lobe on the side of LOS) is to be avoided [20, 21].

Corrective action depends on the type of LOS. In segmental LOS type 1, care must be taken to quickly identify and remove any clips or ligatures that impinge on the RLN near the point of damage. In the event of thermal injury, no effective remedy may be available because the damage has already been done. In global LOS type 2, the gradual decrease of the nerve amplitude calls for interruption of the underlying surgical maneuver.

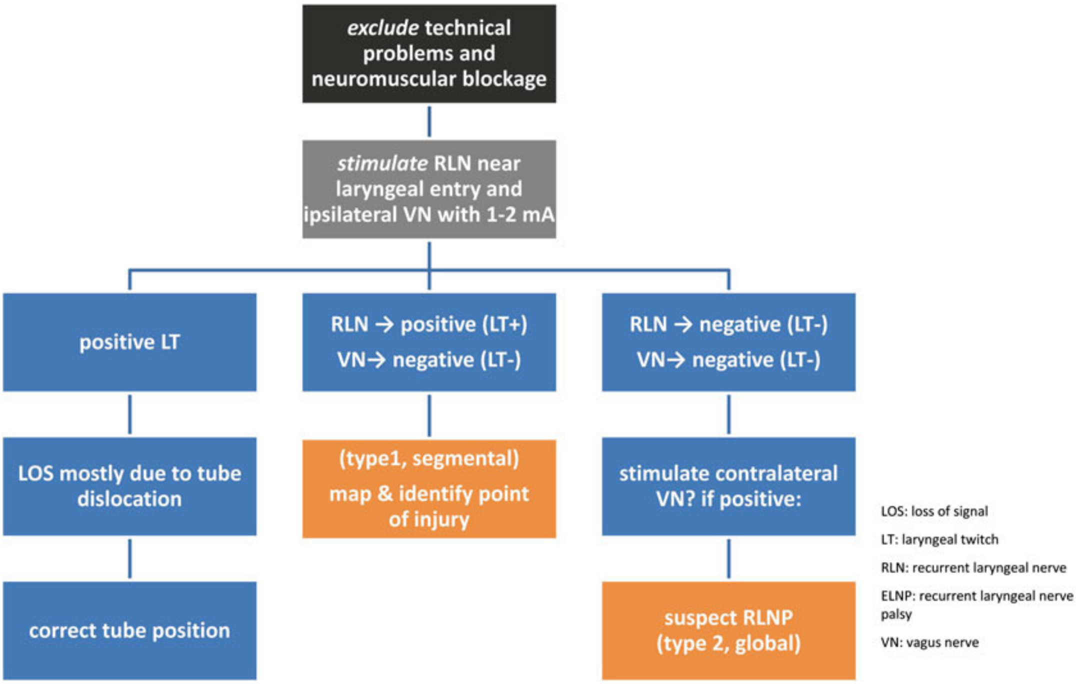


Fig. 18.2 LOS troubleshooting algorithm. [Based on data from 3, 45]

Using continuous IONM (C-IONM), recovery of nerve amplitude can be monitored almost in real time. After expectant observation for 20 min, during which all surgical activity is stopped, complete recovery of the nerve becomes increasingly unlikely. Incomplete recovery (failure of the nerve amplitude to recoup more than 50 % of its baseline), unlike complete recovery, carries a high risk of postoperative VCP. To date, there is little evidence to suggest that intravenous steroids or calcium channel blockers are effective in restoring RLN function once LOS has taken place [22–24]. In a double-blind, placebo-controlled, randomized study, however, preoperative administration of 8 mg of dexamethasone was reported to reduce transient RLN palsies from 8.4 to 4.9 % ($P = 0.04$) [25].

Modification of the Surgical Plan after LOS

For safety reasons, surgery should start on the most severely affected side, leaving the surgeon and patient with more options after LOS on the first side of resection [26]. Modifications of the surgical plan, in the event of LOS or invasion of the RLN by tumor, should be anticipated and discussed with the patient during the informed consent process.

When LOS has been confirmed after checking the troubleshooting algorithm, and the nerve amplitude fails to recover at least 50 % of its preoperative baseline during the operation, there is a 62.5 %–77.8 % (intermittent IONM) to 88.2 % (C-IONM) risk of postoperative VCP [2, 19, 22, 26–28] (Table 18.2; Fig. 18.3).

These data mandate a reconsideration of the surgical plan especially when LOS has happened on the first side of resection or involves the only intact RLN. Depending on clinical circumstances (type of thyroid disease, related urgency of surgical intervention, and surgeon skill and experience), options include:

1. Postponement of completion surgery (staged thyroidectomy) until the RLN has made a full recovery [8, 14, 26, 29].
2. Contralateral subtotal (rather than total) completion lobectomy during the same surgical

session, staying as far away from the contralateral RLN as possible [26, 30–33].

3. In exceptional circumstances (high-risk approach; not generally recommended), continuation of completion surgery exercising utmost diligence to protect the contralateral RLN. This should be engaged only in the most experienced settings.

Postoperative Airway Management After LOS

Prediction of postoperative vocal fold function is also beneficial in unilateral thyroid surgery. Because this information has immediate bearing on the patient's postoperative airway management, close collaboration between surgeons and anesthesiologists is pivotal. In addition to enforcing modifications to the surgical plan, evidence of LOS warrants careful monitoring of the patient, with the anesthesiologist being present during extubation [8, 29].

Postoperative Recovery of Nerve Function

Because voice changes also reflect laryngeal inflammation and swelling after tracheal intubation, postoperative laryngoscopy (L2) is mandatory to determine postoperative vocal cord function. Determination of postoperative vocal cord function on the day of surgery may be disadvantageous because the patient may not be fully awake and cooperative and laryngeal swelling may compromise the examination [11, 15, 29]. This examination is frequently performed on the second postoperative day because the VCP rate on that day is not higher than that on the day of surgery [31]. In the event of early postoperative VCP, serial laryngoscopies are scheduled to monitor restitution of RLN function. Occasionally, vocal cord function is normal in the face of intraoperative LOS confirmed after troubleshooting. This unusual finding may represent a defect of intraoperative troubleshooting or recovery of an injured nerve in the early postoperative phase.

Because the repair mechanisms of a nerve are typically activated within a few days of injury, nerve function is usually restored within a few weeks' time. Randolph and Dralle [1] found that "mild cases" of vocal cord dysfunction revert to the previous functional state 6–8 weeks after LOS. Although VCPs lasting for more than 6 months are generally considered permanent, 91 % of injured nerves make a full recovery within 6 months after LOS [31]. Infrequently, injured nerves can make a full recovery 12 months or later [32].

Staged Thyroid Surgery

As a matter of principle, completion thyroidectomy on the non-injured side is contingent on prior restitution of RLN function on the injured side, as documented by normal vocal cord function on laryngoscopy. Because scar formation sets in one week after surgery, completion thyroid surgery is best carried out within the first week of surgery or 3 months later.

Rarely, the thyroid disease may dictate completion thyroid surgery on the uninjured side in the presence of VCP on the other side of the neck. The decision to complete the non-injured side, jeopardizing the only fully functional nerve, should be based on broad interdisciplinary consensus and should include the patient's explicit acceptance of the risk of bilateral VCP and its ramifications (e.g., permanent tracheostomy).

These high-risk patients should be referred to expert surgical centers well experienced in advanced neck surgery. Risk minimization measures, including the use of C-IONM, should also be implemented.

Medicolegal Considerations

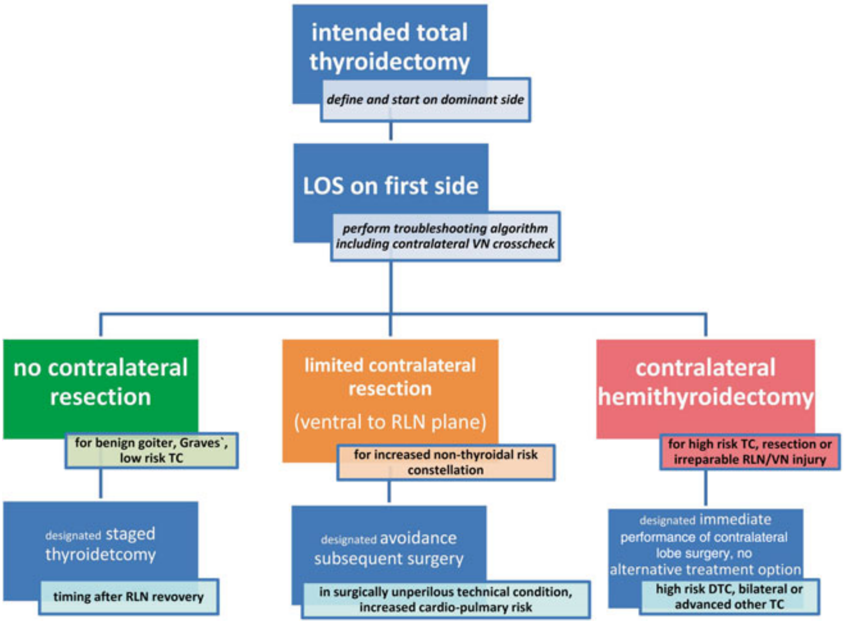
In order to have several options to choose from when LOS occurs on the first side of resection, the thyroid operation must tackle the most severely affected side first [26]. For determination of that side, criteria such as volume of the

Table 18.2 Synopsis of published data on intraoperative change of surgical strategy in LOS at first side in intended bilateral thyroid resection and outcome

Author	Intended bilateral thyroidectomy	LOS on first side	Type of LOS 1 = segmental 2 = global	Intraoperative strategy after LOS on first side, *n*			Staged procedures	Unilateral VCP	Bilateral VCP	FN	FP	Time to completion thyroidectomy
	n/NAR	n/%		No contralateral resection	Limited contralateral resection	Contralateral hemithyroidectomy	n	Trans/perm, *n* (%)	Trans/perm, *n* (%)	*n*	*n*	
Goretzki et al. [30]	1321/2642	36/2.7	n.a.	15	5	16	9	32 (2.4)/4 (0.3)	3 (0.2)/0 (0)	2	n.a.	po day 1–po 4 months
Melin et al. [41]	2546/4012	98/3.8	n.a.	40	–	24	18	119 (2.9)/ 15 (0.37)	4 (0.1)/6 (0.2)	22	47	po day 1–po > 24 months
Périé et al. [13]	100/200	4/4.0	n.a.	4	0	0	3	9 (9.6)/2 (2.0)	2 (2.0)/0 (0)	2	n.a.	2–6 po months
Sadowski et al. [25]	220/440	9/4.1	n.a.	9	0	0	8	7 (3.2)/	0 (0)/0 (0)	0	2	po day 3–po 6 months
Sitges-Serra et al. [20]	290/580	16/5.5	1:11 2:5	0	4	14	0	10 (3.4)/n.a.	0 (0)/0 (0)	3	0	–
Schneider et al. [44]	1049/2086	27/2.6	1:11 2:16	12	4	11	9	26 (2.5)/4 (0.4)	0 (0)/0 (0)	5	6	n.a.
Fontenot et al. [9]	206/412		n.a.	10	–	–	10	8 (1.9)/1 (0.5)	0 (0)/0 (0)	0	2	14.1 ± 11.7 mean po weeks

[a] Partial overlap with duplicate data compilation in Goretzki et al.

FN false negative (intact intraoperative IONM with postoperative vocal cord palsy), *FP* false positive (loss of signal in intraoperative IONM with intact postoperative vocal cord mobility), *n.a.* not assessed



LOS: loss of signal
RLN: recurrent laryngeal nerve
VN: vagal nerve
TC: thyroid carcinoma

Fig. 18.3 Change of strategy and surgical options in intraoperative LOS at first side of resection for intended bilateral thyroidectomy. [Based on data from 44]

thyroid mass, risk of malignancy, and difficulty of resection need to be considered [30].

Changes of strategy that may become necessary during the operation, such as staged thyroid surgery after LOS on the first side of resection, should be anticipated and fully covered by the patient's informed consent. It is also important to detail to the patient the residual risk

1. that staged thyroid surgery, requiring an additional operation, may turn out unnecessary in hindsight because of a false-positive IONM result.
2. that RLN palsies can get missed owing to a false-negative IONM result [4, 20].

There is overwhelming evidence to suggest that IONM and staged thyroid surgery after LOS on the first side of resection prevent bilateral VCP [3, 5, 9, 25, 27, 30]. Accordingly, the surgeon's adaptation of the intended type and extent of thyroid resection due to IONM events increases. In a recent survey among thyroid surgeons in Germany, overall more than 90 % of IONM users expressed compliance to IONM events and either stopped surgery after resection of the first side or limited the intended resection of the contralateral side in occurrence of LOS [29] (Table 18.3). It is of note that particularly high-volume thyroid surgeons with >200 thyroid procedures per year with routine IONM utilization expressed a willingness to stop surgery in the event of LOS on the first side of resection. Whenever IONM is widely available as a risk minimization tool, the failure to use it becomes hard to defend, even more so in the event of bilateral VCP. There is increasing awareness regarding the medicolegal implications of the widespread utilization of IONM in Germany, as it may be perceived as standard of care just by the high prevalence of application. Moreover, the indication, correct use, and documentation of IONM can become the subject matter of heightened medicolegal scrutiny as is evidenced in recent legal decisions in court or conciliation committees.

Conclusion

Since its advent as a fledgling new technology, IONM has come a long way in maturing into a valuable risk minimization tool. Intermittent IONM, characterized by unsupervised dissection

Table 18.3 Surgeons' choice of preferred procedure after LOS in intended bilateral goiter surgery in German IONM users

		Surgical strategy after LOS at first side operated		
Hospital volume TT/year	IONM with IONM RLN[a]	Termination after LOS (%)	Limited contralateral resection (%)	Unlimited contralateral resection (%)
<50	3400	70.7	20.4	8.9
50–99	12,800	73.6	18.3	8.1
100–199	1600	75.7	14.9	9.4
≥200	44,200	92.3	3.0	4.7
Total	76,400	84.7	8.8	6.4

[a] Total numbers rounded to nearest 100 as numbers of thyroidectomies multiplied by IONM of RLN (owing to rounding not all numbers add up)

[Based on data from 29]

IONM intraoperative neuromonitoring, *LOS* loss of signal, *TT* bilateral thyroid lobectomy

periods between two stimulation cycles, displays LOS typically only after RLN injury has happened. In contrast, C-IONM can monitor RLN injury almost in real time, providing the surgeon with the opportunity to immediately release a distressed nerve. As a step in innovation, C-IONM enables earlier corrective action than intermittent IONM before the palsy becomes irreversible.

Recent achievements include the distinction between segmental LOS type 1 and global LOS type 2, reflecting different modes of RLN injury (acute and direct vs. gradual and indirect) and clinical outcome (worse vs. better). To make best use of that information, it is critical to heed the INMSG's troubleshooting algorithm.

Once LOS has been confirmed, a 20-minute wait period will allow the surgeon to know whether the affected nerve will recover fully or not and whether a staged thyroid surgery needs to be considered after the first side of resection is completed. This surgical strategy is widely accepted and has become part of the informed consent process in Germany [30], but this strategy is not yet implemented all around the globe [33].

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