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Prospective evaluation of the utility of routine neuromonitoring for an established thyroid surgical practice

Jane Lee,* Sheila Fraser,* Anthony Glover*† and Stan Sidhu*†

*The University of Sydney Endocrine Surgery Unit, Royal North Shore Hospital, St Leonards, New South Wales, Australia and
†Sydney Medical School Northern, Royal North Shore Hospital, The University of Sydney, Sydney, New South Wales, Australia

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Correspondence
Professor Stan Sidhu, The University of Sydney Endocrine Surgery Unit, Level 3, Royal North Shore Hospital, St Leonards, NSW 2065, Australia.
Email: stansidhu@nebsc.com.au

J. Lee MD, FACS; **S. Fraser** FRCS; **A. Glover** PhD, FRACS; **S. Sidhu** PhD, FRACS.

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Abstract

Background: The use of routine intraoperative neuromonitoring (IONM) is controversial in thyroid surgery. Guidelines have been published to standardize IONM. This study examines the impact of routine IONM on a high-volume thyroid surgeon.

Methods: A prospective study was conducted using IONM between May 2013 and December 2014. Demographics, type of operation, pathology, recurrent laryngeal nerve (RLN) and external branch of the superior laryngeal nerve (EBSLN) visualization and subtype classification, cricothyroid or cricopharyngeal twitch/electrode depolarization were obtained, and complications were recorded. Outcomes were compared with 500 thyroidectomies performed by the same surgeon without neuromonitoring.

Results: Two hundred and ninety-nine total thyroidectomies and 191 hemithyroidectomies were performed with IONM resulting in 789 RLN and 789 EBSLN at risk of injury. Demographics, indication, pathology and complications were similar between the two groups. IONM provided additional information for 58 RLN dissections (7.4%) stratifying surgical decision-making. Loss of signal was detected in 1.8% of nerves at risk. IONM assisted in identification of 109 (13.8%, $P < 0.0001$) EBSLN, including a 15.8% improvement in identifying type 2b EBSLN. Utility of IONM was not predicted by surgery indication; however, multinodular goitre was a significant predictor of IONM assisted identification of type 2b EBSLN (OR = 2.24, $P = 0.01$).

Conclusion: Routine IONM provides intraoperative information to a high-volume thyroid surgeon regarding the recurrent and external nerves over and above direct visualization alone, and its utility could not be predicted by operative indication.

Introduction

Routine intraoperative neuromonitoring (IONM) in thyroid surgery has been a topic of controversy. From the descriptions of thyroidectomy by Theodore Kocher leading to his Nobel Prize in 1909, surgeons have striven to improve outcomes and reduce morbidity. One of the significant complications is vocal cord paralysis (VCP) from recurrent laryngeal nerve (RLN) injury. The gold standard to avoid VCP is direct visualization, dissection and protection of RLN.[1] Using this technique, nerve injury rates have been low, with reported temporary RLN palsy of 3–8% and permanent RLN palsy (PLNP) of 0.3–3%.[2]

With the introduction of IONM, it was hoped that VCP would become even more rare. However, the rate of PLNP has not been shown to decrease in a number of studies despite the use of IONM.[3–7] It has been demonstrated in one randomized control study to decrease the rate of temporary RLNP.[8] Due to the low RLN injury rate, most studies are underpowered to detect statistically significant differences. However, Chung *et al.*, using a large database of 243 527 thyroidectomies, found that IONM was associated with a higher rate of VCP.[9] In this study, IONM was used for <10% of cases, and it was noted that in hospitals that used IONM for more than half of thyroidectomies, a lower rate of VCP (1.1%) was observed compared to cases without IONM (1.4%).[9] Despite the controversy, IONM has entered clinical practice with routine use for some surgeons, while others have adopted selective use of IONM, reserving its use for potentially difficult cases including cancers and reoperations. In response to the variations in practice and conflicting data, a consensus statement by the International Neural Monitoring Study Group in 2011 emphasized the importance of standardizing the use of IONM in RLN identification as an adjunct to visualization.[10]

The use of IONM for identification of external branch of the superior laryngeal nerve (EBSLN) has become a more recent focus of investigation. EBSLN injury rates have been reported to be as high as 58%.[5] In 2013, a guideline statement was published to address the use of neuromonitoring for EBSLN.[11] In a recent study, we demonstrated that the use of IONM as an adjunct to visualization improved the rate of EBSLN identification from 85.7% by visualization alone to 97.2% with IONM.[12]

Most studies on IONM focus on detecting differences in RLN palsy rates for IONM groups versus direct visualization. To our knowledge, no study has prospectively evaluated the utility of the introduction of routine IONM for the established, high-volume thyroid surgeon. Therefore, the primary aim of this study was to prospectively evaluate the utility of routine IONM for the established thyroid surgeon. Secondary aims were to examine outcomes for cases utilizing IONM and identification of preoperative factors which could predict utility for IONM.

Methods

Study design and patient selection

All routine thyroidectomies with neuromonitoring available performed by one primary surgeon were prospectively evaluated from 20 May 2013 to 31 December 2014. Prior to this period, IONM was not routinely utilized. Data were collected and stored in a database approved by the Northern Sydney Area ethics committee. The study included 299 total thyroidectomies and 191 hemithyroidectomies resulting in 789 RLN and 789 EBSLN potentially at risk of injury. Preoperative and postoperative laryngoscopy was performed to assess position and mobility of vocal cords. Demographics, type of operation, pathology, visualization of EBSLN and RLN, observation of cricothyroid twitch or cricopharyngeal twitch/electrode depolarization, EBSLN sub-type classification (as defined by Cernea *et al.*[13]) and complications were recorded. The role of neuromonitoring in providing additional information to routine RLN and EBSLN identification was also recorded for each case. The study group baseline characteristics were compared with 500 consecutive patients who underwent thyroid surgery from October 2011 to May 2013 without IONM.

Surgical technique

Thyroidectomy was performed in a standard fashion under general anaesthesia with division of the strap muscles preserving the innervation by the ansa cervicalis, use of the LigaSure thermal sealing system, NIM 2.0/3.0 system (Medtronic, Jacksonville, FL, USA) and the NIM TriVantage EMG endotracheal tube. Vagal response was tested at the beginning and end of each operation, ensuring proper function.

Identification of the EBSLN was carried out in a systemic manner as previously reported.[12] Following identification, electrical stimulation with the NIM probe was performed. A positive result was recorded if strong and simultaneous contraction of the pars recta and pars oblique components of the cricothyroid muscle was observed. If no cricothyroid twitch was found, visual identification was recorded as negative and further dissection was undertaken to locate the EBSLN. If no cricothyroid twitch was found on stimulation after further dissection, any nerve-like structures were preserved, and NIM-guided identification was recorded as negative. Following division of the superior thyroid vessels, repeated nerve conduction was performed stimulating the nerve proximal to the point of the nearest thermal seal.

The RLN was also identified and dissection was carried out following the course of the nerve. NIM stimulation was also performed to confirm nerve function. All loss of signal (LOS) cases were verified by contralateral stimulation of the vagus nerve to exclude equipment failure and palpation for a cricothyroid twitch on ipsilateral stimulation of the RLN and vagus nerve. If the RLN was not confidently identified and the NIM assisted identification, this was recorded.

Statistical analysis

Data were analysed using SPSS Statistics, release 21 (IBM Corp, Armonk, NY, USA) and Prism Version 6.0 (GraphPad, La Jolla, CA, USA). Categorical variables were compared using Fisher's exact test. Continuous variables were compared using Student's *t*-test. Statistical significance was set at $P < 0.05$.

Results

Patient demographics

Four hundred and ninety thyroidectomies (299 total and 191 hemithyroidectomies) were performed using IONM from May 2013 to December 2014, resulting in 789 RLN and 789 EBSLN at risk of injury. The patient demographics of this study group were similar to 500 thyroidectomy cases (294 total and 206 hemithyroidectomies) performed without IONM by the same surgeon from October 2011 to May 2013 (Table 1). Eighty percent of patients were females with mean age of 56 years for both groups. Most cases were primary thyroid operations. About 6.7% of cases in the

Table 1 Patient demographics

	NIM assisted (n = 490)	No NIM (n = 500)	P-value
Female	393 (80.2%)	401 (80.2%)	0.99
Mean age (years)	56	56	0.50
Type of surgery			
Total thyroidectomy	299 (61%)	294 (59%)	0.52
Hemithyroidectomy	191 (39%)	206 (41%)	
Indication for surgery			
Risk of malignancy	170 (35%)	156 (31%)	0.24
MNG	208 (42%)	223 (45%)	0.50
Thyrotoxicosis	63 (13%)	70 (14%)	0.60
Other	49 (10%)	51 (10%)	0.92
Histopathology			
MNG	240 (49%)	249 (50%)	0.80
Graves' disease	30 (6%)	31 (6%)	0.96
Other benign	123 (25%)	139 (28%)	0.34
Carcinoma	97 (20%)	81 (16%)	0.14

IONM group and 8.6% of cases in the control group were reoperations.

Identification of RLN

All 789 RLNs at risk were identified by dissection, and nerve function was confirmed using IONM. Information obtained from IONM that assisted in RLN dissection was recorded (Table 2). IONM provided additional information for 58 RLN dissections (7.4%). IONM assisted in confirming function in 25 nerves at risk (3.2%) especially after difficult dissection and possible stretching of the nerve or extensive dissection around the nerve (Table 2). These 25 nerves at risk included a number of thyroid cancer dissections where the nerve was adherent to the thyroid, and IONM assisted in the careful dissection of the nerve and confirmed function after dissection.

IONM was also valuable in cases with aberrant anatomy, including identification and confirmation of two nonrecurrent laryngeal nerves (Table 2). IONM also proved useful in eight cases (1.6%) with a small RLN or fine anterior branch of the RLN, which appeared visually similar to the inferior thyroid artery or its branches.

Temporary LOS was observed in 12 cases (1.5%) with recovery of signal at the end of the case (Table 2). Fourteen nerves (1.8%) with no visual evidence of nerve damage had persistent LOS at the end of the case, possibly due to heat or traction injuries (Table 2). Four cases involved focal injuries (NIM signal obtained distal to the site of injury) with minimal effect on postoperative voice. Ten cases involved global LOS. In five planned bilateral thyroidectomy cases for large goitre, management was staged due to global LOS on the initial side to prevent possible bilateral RLN palsy (Table 2).

Identification of EBSLN

A total of 789 EBSLN were at risk (388 right and 401 left), of which 668 (84.7%; 95% CI = 82.1–87.2) were identified by visual identification alone with IONM confirmation, while 777 nerves were identified with the use of visual identification and IONM-assisted dissection (98.5%; 95% CI = 97.6–99.3). IONM assisted in identification of 109 (13.8%; 95% CI = 1.1–16.5; $P < 0.0001$) nerves above visual identification alone. Thirty-four (4.3%) nerves were sub-fascial/intramuscular and required neural stimulation of the cricothyroid muscle for identification. Three nerves could not be confirmed with IONM due to technical problems with conduction of the NIM circuit, and nine nerves were not visualized despite careful dissection possibly due to the high location of the nerve.

Data for Cernea sub-type of EBSLN was available for 686 of the EBSLN nerves. Table S1 shows the incidence of each sub-type and the results of identification by dissection. Use of IONM improved identification of the at-risk type 2b EBSLN by 15.9% (95% CI = 8.2–23.7; $P < 0.0001$).

To assess whether preoperative indication for surgery could be used to predict whether IONM could aid in identification of type 2b EBSLN, regression analysis was performed. On univariate logistic regression, a preoperative indication of multinodular goitre was associated with IONM-assisted identification of a type 2b EBSLN (OR = 2.7; 95% CI = 1.5–4.8; $P = 0.001$). A preoperative indication of toxicity or cancer was not associated with IONM assisted identification of a type 2b EBSLN (OR = 1.1; 95% CI = 0.5–2.5; $P = 0.74$ for toxicity and OR = 0.3; 95% CI = 0.1–0.8; $P = 0.2$ for cancer). On multivariate logistic regression, a preoperative indication of multinodular goitre remained a significant predictor of IONM assisted identification of a type 2b nerve (Table S2).

Table 2 Information obtained from IONM

RLN	Number (%)
Loss of signal	14 (1.8%)
Loss of signal (temporary)	12 (1.5%)
Confirmed identification and function	25 (3.2%)
Identified aberrant anatomy	6 (0.8%)
Assisted dissection in cancer	6 (0.8%)
Change in surgical strategy (staged)	5 (1% of cases)

Loss of signal (temporary) refers to cases where IONM signal returned during operation. IONM, intraoperative nerve monitoring; RLN, recurrent laryngeal nerve.

Complications

The complication profiles for the two groups showed no difference in incidence of haematoma, temporary RLN palsy, permanent hypoparathyroidism and PLNP (Table S3).

Utility of IONM cannot be predicted by indication for surgery

To assess whether the use of IONM could be predicted by indication for surgery, logistic regression analysis was performed. No significant prediction of IONM changing operative management could be shown by surgical indication of multinodular goitre (OR = 0.95; 95% CI = 0.65–1.39; $P = 0.81$), toxicity (OR = 1.3; 95% CI = 0.73–2.23; $P = 0.38$) or cancer (OR = 0.86; 95% CI = 0.52–1.43; $P = 0.57$). Similarly, the indication for surgery was not associated with IONM LOS of the recurrent nerve, with an indication of multinodular goitre (OR = 0.74; 95% CI = 0.34–1.62; $P = 0.46$), toxicity (OR = 2.2; 95% CI = 0.83–5.56; $P = 0.13$) or cancer (OR 1.02; 95% CI 0.38–2.77, $P = 0.97$) not associated with LOS.

Discussion

As far as is known, this is the first study that prospectively examines the utility of IONM for an experienced thyroid surgeon. The study was undertaken to revisit IONM in light of new technology and recent guidelines to evaluate if there was any benefit to be derived from routine implementation above the standard practice of visual identification and preservation of the RLN and EBSLN. The 'internal control' for the study was the practitioner experienced in the art of thyroidectomy prospectively documenting if the scientific adjunct of IONM provided any intraoperative benefit.

Through this prospective study, we found that IONM provided additional information in 7.4% of RLN dissections. IONM provided information to distinguish a small, anterior branch of the RLN from a branch of the inferior thyroid artery. IONM also aided in cases with aberrant anatomy including a nonrecurrent laryngeal nerve, extensive scar tissue, adhesion of the nerve to malignant tissue and overlying blood vessels. In cases with extensive dissection and possible stretch injury, IONM was valuable in confirming function of the nerve. Additionally, IONM provided prognostic information regarding RLN function and potential recovery. In five planned bilateral thyroidectomy cases with global LOS of the RLN, surgical strategy was modified to a staged procedure to prevent the possibility of bilateral RLN palsy.

The value of IONM in thyroid surgery has been an ongoing topic of debate since the introduction of IONM technology. A few randomized control trials have been published comparing the use of IONM to direct visualization of the RLN. Barczynski *et al.* conducted a prospective randomized trial on 1000 patients with 2000 nerves at risk and concluded that there was a reduction in temporary RLN palsy with the use of IONM.[8] Sari *et al.* studied 237 patients undergoing thyroidectomy with 409 nerves at risk and examined operating time with IONM.[14] The identification time and operating time were significantly shortened with the use of IONM (4 and 65 min in the IONM group versus 11 and 79 min without IONM, respectively).

Although a clear benefit has not been demonstrated in preventing RLN palsy rates with IONM, other benefits of IONM have been studied including prognosis of postoperative nerve function,[8] aid in preventing bilateral RLN injury,[15,16] assistance in identification and preservation of EBSLN[17–19] and decreased risk of temporary EBSLN injury.[20] Our prospective study adds to this body of knowledge, demonstrating the information gained by IONM in each case.

In addition, IONM improved identification of EBSLN, especially in multinodular goitre. Interestingly, we observed a correlation between multinodular goitre and the use of IONM in identifying type 2b EBSLN. Cernea *et al.* have shown that in large goitres, the probability of a high-risk type 2b nerve increases. This has also been reported by Glover *et al.*[12,21] In these cases, IONM may increase identification and prevent injury of the type 2b EBSLN.

However, other preoperative indications that have been suggested for selective use of IONM such as malignancy and reoperation did not predict the utility of IONM. These results support the routine use of IONM as the surgeon cannot predict which cases will benefit from its use.

The benefits of IONM in EBSLN monitoring have been demonstrated by several studies. Lifante *et al.* published a small prospective, randomized trial of IONM use for EBSLN in 47 patients showing increased rate of visualization and improved voice quality.[19] Barczynski *et al.* conducted a randomized control trial of 210 total thyroidectomy patients demonstrating improved identification rate of EBSLN (34.3% in no IONM group versus 83.8% in the IONM group) and reduced the risk of early voice changes with IONM.[22] A meta-analysis by Sanabria *et al.* examined six randomized control trials with 1602 patients and 3064 nerves at risk and demonstrated that the IONM group had a decreased risk of temporary EBSLN injury.[20]

No tangible difference was observed in PLNP rates in this prospective study as demonstrated by other studies. Several retrospective studies have been published showing no difference in RLN injury rates with IONM. Shindo *et al.* conducted a retrospective study of 684 patients with 1043 nerves at risk and studied the incidence of VCP with and without neuromonitoring showing no statistically significant difference.[3] Atallah *et al.* evaluated the role of IONM in high-risk thyroid surgery including surgery for thyroid cancer, Graves' disease and recurrent goitre with 421 nerves at risk and demonstrated no difference.[4] Calo *et al.* also conducted a retrospective study of 2034 consecutive patients and concluded that the RLN palsy rate did not differ with IONM.[5]

A meta-analysis of one randomized clinical trial, seven comparative trials and 34 case series with 64 699 nerves at risk by Higgins *et al*. demonstrated no statistically significant difference in the incidence of true vocal cord palsy with IONM.[6] Pisanu *et al*. also conducted a meta-analysis of three prospective randomized trials, seven prospective trials and 10 retrospective observational studies including 23 512 patients with 35 513 nerves at risk showing no difference.[7]

Limitations of our study include the cohort design and the lack of randomization. However, our groups were closely matched in gender, age, indication and pathology, allowing comparison of the two groups. Complications between both groups were similar.

This study examined the potential benefits of routine IONM use in a high-volume endocrine surgery practice. In conclusion, our prospective study shows that routine use of IONM provides additional information to assist in identification and functional preservation of the RLN and EBSLN during thyroidectomy.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Table S1. External branch of the superior laryngeal nerve identification.

Table S2. Predictors of intraoperative neuromonitoring-assisted identification of type 2b external branch of the superior laryngeal nerve.

Table S3. Complication profiles.