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ORIGINAL SCIENTIFIC REPORT

Intraoperative Neuromonitoring of Recurrent Laryngeal Nerve During Thyroidectomy with Adhesive Skin Electrodes

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Abstract

Background Alternative methods to overcome limitations of electromyogram (EMG) tube applied for intraoperative neuromonitoring (IONM) of recurrent laryngeal nerve (RLN) during thyroidectomy have been introduced. In this study, we evaluated the feasibility of adhesive skin electrodes for IONM of RLN in patients who underwent thyroidectomy.

Methods A total of 39 nerves at risk were prospectively enrolled in this study. Twenty-five patients with papillary thyroid carcinoma, 3 patients with follicular neoplasm, and 2 patients with Graves' disease underwent thyroidectomy. All patients were intubated with EMG tube, and two disposable pre-gelled surface electrodes were attached to skin at both upper margins of thyroid cartilage. We followed the standard procedure of IONM, and the latency (msec) and amplitude (μV) of each signal were recorded prospectively.

Results Intraoperative neuromonitoring using skin adhesive electrodes was successful in all nerves at risk. Amplitudes of the signals in IONM were significantly lower compared to those from EMG tube at each step of IONM, while no significant difference was identified in latency between two methods. Four nerves at risk (10.3%) showed loss of signal (<100 μV) during the steps of IONM from EMG tube, while all nerves at risk from adhesive skin electrodes showed acceptable biphasic EMG signal.

Conclusion We verified the usefulness of adhesive skin electrodes for IONM of RLN during thyroidectomy. Although lower amplitude remains the major limitation of this technique, adhesive skin electrodes may be considered an alternative method for IONM during thyroidectomy.

Introduction

Intraoperative neuromonitoring (IONM) of recurrent laryngeal nerve (RLN) has been considered to be a useful method to help localize and identify the nerve, facilitate RLN dissection, detect nerve injury, elucidate its mechanism to improve surgical technique, and predict the outcome of vocal cord function during thyroidectomy [1–4]. Recent meta-analysis showed that IONM may help reduce the risk of temporary vocal cord paralysis during thyroidectomy [1]. The intraoperative neuromonitoring system includes a stimulating side and a recording side, which require an electromyogram (EMG) endotracheal tube to

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detect the muscle action potential evoked by the nerve stimulation probe. The EMG tube is integrated with a pair of stainless-steel electrodes, embedded within the surface of the tube or within a thin adhesive pad containing the paired electrodes in order to have contact with both vocal cords. However, a recording side error of IONM has been a barrier for surgeons because of false positive outcomes [5, 6]. Various conditions leading to such outcomes have been introduced by troubleshooting strategies [6]. Malposition or displacement of the EMG tube has been the most frequent cause of false 'loss of signal' (LOS) of IONM of the RLN. Pooled saliva at the level of the vocal cords, where the electrodes of the EMG tube have contact, may also lead to an altered EMG signal [6]. Another limitation of using an EMG tube for IONM during thyroidectomy may be the relatively high cost of the tube, which is about 250 US dollars in South Korea.

Recently, Wu et al. [7] presented an alternative IONM method in a porcine model in which the neck-adhesive skin electrodes were used for transcutaneous EMG recording. The animal study showed that the skin electrodes successfully presented the evoked laryngeal EMG during IONM of RLN, with stability and accuracy. Moreover, they demonstrated that skin electrodes may overcome the limitations of EMG tube displacement caused by surgical maneuvers. However, to our knowledge there have been no clinical studies applying adhesive skin electrodes at anterior neck for IONM during thyroidectomy. This study aimed to evaluate the feasibility and accuracy of this novel IONM technique in patients undergoing monitored thyroidectomy.

Materials and methods

Patients

A total of 30 patients (39 nerves at risk, 24 right nerves, 15 left nerves) were prospectively enrolled in this study from November to December 2018. The patients included 24 female and 6 male patients with a median age of 48.7 years (range 25–71 years). Of the 30 patients, 25 patients with papillary thyroid carcinoma (PTC), 3 patients with follicular adenoma, and 2 patients with Graves' disease underwent thyroidectomy (9 total thyroidectomies and 21 unilateral lobectomies). Exclusion criteria were patients with previous neck surgery or radiation therapy, preoperative vocal cord paralysis, gross extrathyroidal extension, clinically identified central or lateral neck lymph node metastasis, a huge tumor or thyroid gland requiring extensive dissection of thyroid cartilage, and any contraindications for IONM. All patients gave their informed consent for this study and IONM, and the institutional review board of our center admitted this study (IRB No. 2018-11-022).

Preoperative laryngoscopy was conducted in all patients one day before the surgery, and postoperative laryngoscopy was done on the day of or one day after surgery. Clinicopathologic factors of the patients were analyzed, including age, sex, body mass index (Kg/m^2), tumor size, and T classification of PTC.

Setup and procedure of intraoperative neuromonitoring

Equipment setup of IONM and anesthesia was done according to the standard procedure [5].

All patients were intubated with an EMG tube (inner diameter 6.0 mm for female and 7.0 mm for male patients) (Medtronic Xomed, Jacksonville, FL, USA). Two disposable pre-gelled surface electrodes (DSE3125, Medtronic Xomed, Jacksonville, FL, USA), sized 1.5 cm × 2.0 cm × 2.5 cm, were attached to the skin at both upper margins of the thyroid cartilage (Fig. 1). Setup time for the surface electrodes was less than one minute in all cases. EMG signals recorded from the EMG tube were presented on channels 1 and 2, whereas signals from the surface electrodes were demonstrated on channel 3. All patients underwent IONM with both EMG tube and adhesive skin electrodes simultaneously. We followed the standard procedure for IONM [5] from V1-R1-R2-V2, and the latency (msec) and amplitude (μV) of each signal were recorded prospectively. V1 and V2 signals were acquired using a ball-tip stimulator without exposing the vagus nerve. The R2 signal was recorded as R2p signal (proximal RLN) and R2d (distal RLN) as has been described by Wu et al. [4]. In addition to the signals of standard IONM procedure, we defined the signal acquired by stimulation of RLN before visual identification (neural mapping) [6] as the R0 signal, which was taken by stimulating the paratracheal fibrofatty tissues covering the RLN, just lateral to the inferior parathyroid gland.

Statistical analysis

Clinicopathologic factors, including the latency and amplitude of EMG signals in each stage of IONM between the two groups, were compared using Fisher's exact test for categorical variables and Student's t test for continuous variables. All reported p values <0.05 were considered significant. Statistical analysis was performed using the PASW 18 software program (SPSS, Inc., Chicago, IL, USA).

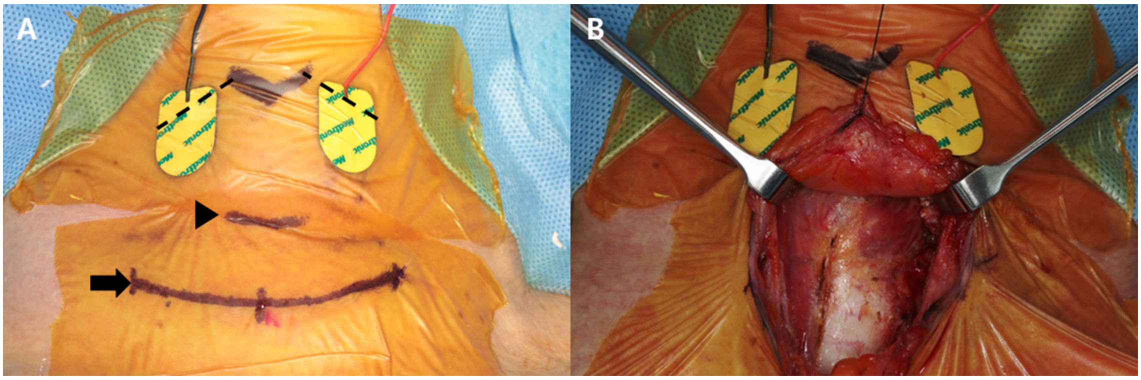

Fig. 1 Setup of adhesive skin electrodes. **a** Electrodes are attached to skin at both upper margins of the thyroid cartilage. Dotted line indicates upper border of thyroid cartilage, arrow head; inferior borer of cricoid cartilage, arrow; skin incision. **b** Completion of total thyroidectomy without exposure of thyroid cartilage

Results

Clinicopathologic factors of enrolled patients are summarized in Table 1. Intraoperative neuromonitoring using adhesive skin electrodes was successful for all nerves at risk. There were no complications or delay of surgery because of the application of adhesive skin electrodes. In all nerves, there was no evidence of nerve injury (positive V2 signal with no weak point of nerve conduction on the exposed RLN) at the end of the operation. Postoperative laryngoscopy showed normal vocal cord mobility in all patients. Biphasic EMG waveforms similar to those from the EMG tube were acquired at every step of IONM with adhesive skin electrodes (V1-R1-R2p-R2d-V2) (Fig. 2). Amplitudes were significantly lower than those from the EMG tube at each step of IONM (Table 2), but no significant difference was identified in latency between the two methods (Table 3). Mean amplitude of the V2 signal from the EMG tube was approximately four times larger than that from the adhesive skin electrodes. The R0 signal before RLN identification presented an acceptable level of amplitude from the adhesive skin electrodes (217 ± 95 μV) although it was also significantly lower ($p < 0.01$) than that from the EMG tube (817 ± 533 μV), but the latency of the R0 signal was comparable between the two groups ($p = 0.907$). Four nerves at risk (10.3%) showed LOS (<100 μV) with loss of the typical biphasic wave during the steps of IONM from the EMG tube, although all EMG signals from these nerves showed an acceptable biphasic wave with amplitude >100 μV from the skin adhesive electrodes (Fig. 3). For the EMG signals from the skin electrodes, an amplitude below 100 μV was identified in 10 nerves (25.6%) from V1 and 3 nerves (7.7%) from V2. However, there were no nerves showing an amplitude below 100 μV in R1, R2p, and R2d, and all EMG signals below 100 μV showed a typical biphasic wave, presenting the integrity of the RLN (Fig. 4).

Table 1 Clinicopathologic factors of the enrolled patients

Clinicopathologic factors	
Age (mean ± SD, years)	48.7 ± 13.7 (25–71)
Gender	Female/male = 24: 6
Body mass index (Kg/cm^2)	23.9 ± 2.9 (19.9–28.5)
Size of tumor (cm)	1.5 ± 1.1 (0.4–3.5)
Pathology	
Papillary thyroid carcinoma	25
T1a	16 (20%)
T1b	1 (1.3%)
T2	1 (1.3%)
T3b	6 (7.5%)
T4a	1 (1.3%)
Follicular adenoma	3
Graves' disease	2

SD standard deviation

Discussion

In this first clinical study of adhesive skin electrodes for IONM, we confirmed the feasibility of applying adhesive skin electrodes attached to the anterior neck skin for IONM during thyroidectomy (Fig. 1). Although the amplitudes of the EMG signal from the adhesive skin electrodes were lower than those from the EMG tube, a biphasic EMG signal with latency similar to that from the EMG tube could be acquired for every nerve at risk (Fig. 2). Regardless of the lower amplitude from the adhesive skin electrodes, neural mapping of RLN before visual identification (R0) was successful for all nerves at risk. IONM using adhesive skin electrodes presented successful and consistent EMG signals even when IONM via EMG tube failed to show any

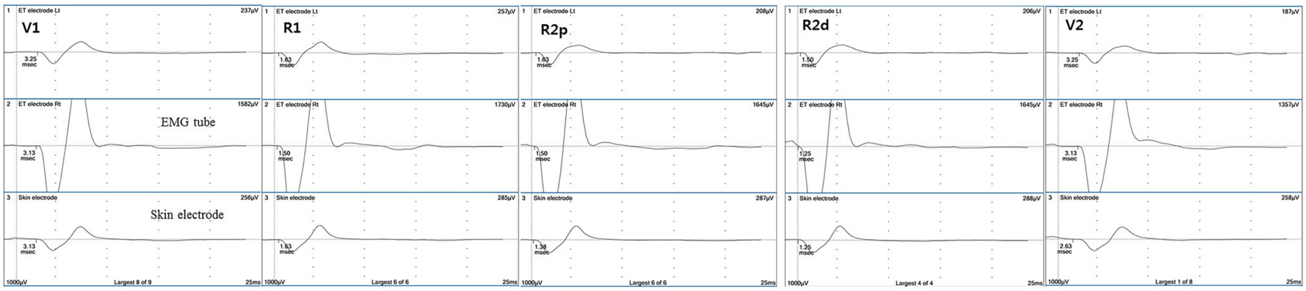

Fig. 2 Electromyogram (EMG) signals at each stage of standard intraoperative neuromonitoring procedure (V1-R1-R2p-R2d-V2). Signals from skin electrodes show biphasic signals similar to those from an endotracheal EMG tube

Table 2 Comparison of amplitudes of EMG signals at each stage of IONM

Stage	Electrode type	Mean ± SD	Min	Max	*p* Value
V1	EMG tube	706.2 ± 435.1	95	1582	< 0.01
	Adhesive skin electrode	186.4 ± 87.04	73	362	
R1	EMG tube	944.7 ± 473.8	146	1730	< 0.01
	Adhesive skin electrode	244.3 ± 103.1	115	463	
R2p	EMG tube	1097 ± 616.5	84	2278	< 0.01
	Adhesive skin electrode	283.6 ± 101.7	116	529	
R2d	EMG tube	1100 ± 606.3	66	2199	< 0.01
	Adhesive skin electrode	282 ± 100.1	149	547	
V2	EMG tube	813.1 ± 515.7	49	1922	< 0.01
	Adhesive skin electrode	203.7 ± 76.67	81	403	

SD standard deviation, *EMG* electromyogram, *Min* minimum, *Max* maximum

Table 3 Comparison of latencies of EMG signals at each stage of IONM

Stage	Electrode type	Mean ± SD	Min	Max	*p* Value
R1	EMG tube	1.94 ± 0.32	1.38	3.00	0.939
	Adhesive skin electrode	1.95 ± 0.3	1.38	3.00	
R2p	EMG tube	1.98 ± 0.3	1.46	2.5	0.326
	Adhesive skin electrode	1.92 ± 0.27	1.25	2.5	
R2d	EMG tube	1.63 ± 0.23	1.25	2.25	0.413
	Adhesive skin electrode	1.59 ± 0.17	1.25	2.00	
V1 Rt	EMG tube	3.36 ± 0.41	2.63	4.35	0.520
	Adhesive skin electrode	3.4 ± 0.37	2.38	4.04	
V1 Lt	EMG tube	6.04 ± 0.72	5.00	7.25	0.770
	Adhesive skin electrode	6.25 ± 0.69	5.00	7.25	
V2 Rt	EMG tube	3.34 ± 0.65	2.00	5.36	0.528
	Adhesive skin electrode	3.29 ± 0.63	2.00	5.16	
V2 Lt	EMG tube	5.90 ± 0.5	5.00	6.63	0.601
	Adhesive skin electrode	5.87 ± 0.5	5.04	6.54	

SD standard deviation, *EMG* electromyogram, *Min* minimum, *Max* maximum

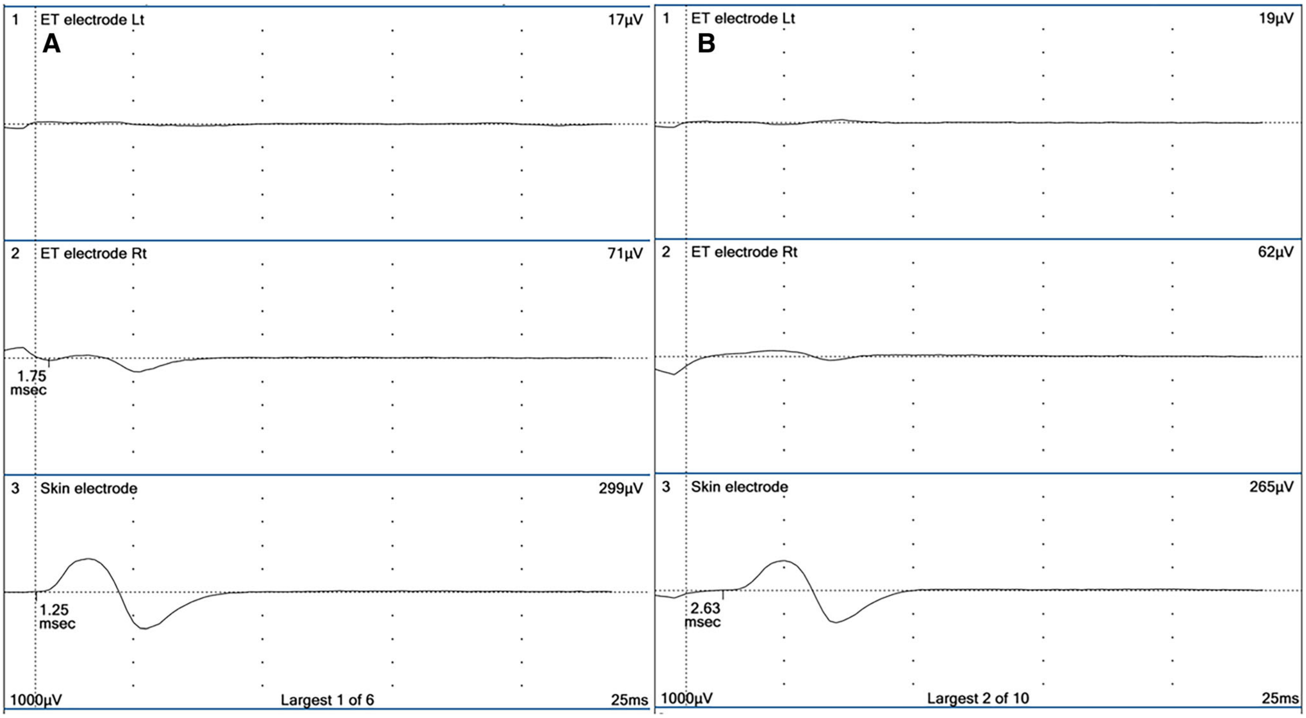

Fig. 3 A right unilateral lobectomy case showing loss of signal from the endotracheal EMG tube and a normal biphasic wave from the adhesive skin electrode. Loss of signal is identified at **a** R2p and **b** V2 from the EMG tube

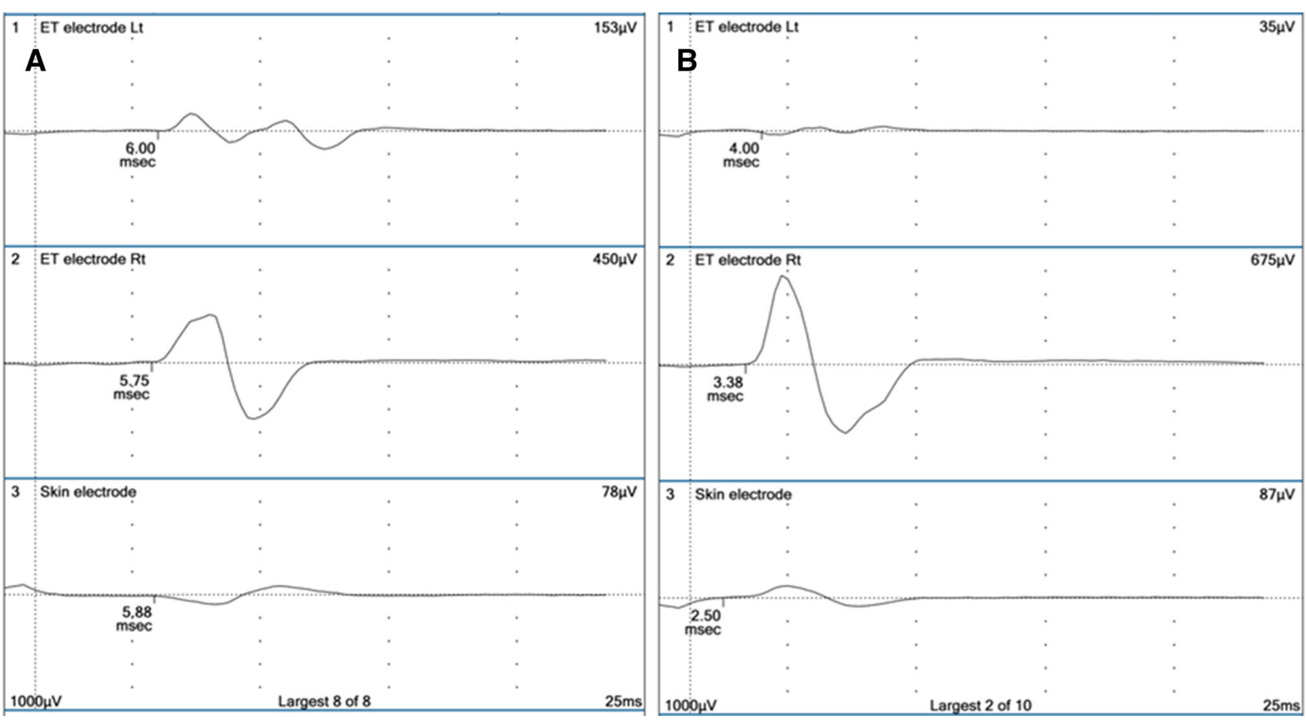

Fig. 4 Electromyogram (EMG) signals showing amplitude lower than 100 uV from the adhesive skin electrodes. The EMG signal still shows biphasic waveforms identical to those from the EMG tube. **a** Left side, V1 signal. **b** Right side, V1 signal

signal or showed a substantial decrease in amplitude because of EMG tube dislocation (Fig. 3).

IONM of RLN during thyroidectomy with an endotracheal EMG tube has been a standard method to identify the nerve or prevent injury by reducing surgical procedures conducted under assumption [5, 6]. As an alternative method to the EMG tube, several studies presented the feasibility of using needle electrodes [8, 9] or adhesive skin electrodes [9–11] on the thyroid cartilage or overlying neck skin. In a comparative clinical study of EMG signals between those from an EMG tube and needle electrodes on the thyroid cartilage, Chiang et al. [9] reported that needle electrodes inserted into the thyroid cartilage are effective and reliable in presenting EMG signals during IONM for thyroidectomy. They demonstrated that EMG amplitudes from needle electrodes were higher and more stable during each stage of standardized IONM than were those from EMG tubes and that needle electrodes could prevent false LOS, which occurred in 15% of IONM cases from the EMG tube. Prevention of false LOS from contact failure of electrodes in the EMG tube may let the surgeon avoid unnecessary intraoperative time delay or misinterpretation of the EMG signal. However, both sides of the thyroid cartilage should be exposed in every case to apply the needle electrodes, which may not be necessary in every case. Although there were no complications because of the electrodes in their series, needle electrodes may not be entirely noninvasive, with potential risk of hematoma, laceration, or endotracheal cuff rupture [11]. In addition, they considered that insertion of needle electrodes into the perichondrium of the thyroid cartilage may be difficult because of calcification in elderly patients.

As an alternative way to apply electrodes to thyroid cartilage, Wu et al. [11] reported the feasibility of applying adhesive pre-gelled electrodes. Although this method could avoid the potential risk of inserting needle electrodes, it still required larger skin incisions to expose the thyroid cartilage. Since the adhesive pre-gelled electrodes are designed for skin attachment, possible dislodging of the electrodes located within the surgical field and covered with body fluid or blood may be limitations of the method. EMG amplitudes were lower than those from the endotracheal EMG tube, since the electrodes had indirect contact with the vocal cord.

As a method to avoid unnecessary exposure of the thyroid cartilage, Wu et al. [7] showed the feasibility of using adhesive skin electrodes on the anterior neck skin to record EMG waveforms from the RLN and vagus nerve. From the animal study, they demonstrated that EMG signals from transcutaneous electrodes had no variations with tracheal displacement, whereas those from the endotracheal EMG tube showed a significant decrease in amplitude or prolongation of latency because of contact failure of the electrodes within the tube. In our series, LOS at the beginning or during the standard procedure of IONM with the EMG tube occurred in four nerves at risk (10.3%). However, it could be interpreted as 'false LOS' with no LOS in the EMG signal from the adhesive skin electrodes. Therefore, adhesive skin electrodes attached to anterior neck skin may prevent false LOS during IONM of thyroidectomy or may be applied when a false LOS from an EMG tube is suspected.

As has been reported by previous studies [9, 11], adhesive skin electrodes present EMG signals with lower amplitudes than from an endotracheal EMG tube or needle electrodes. Such a limitation was also encountered in our series, which may be obvious with indirect delivery of an EMG signal from the vocalis muscle and thyroid cartilage to skin. EMG signals with amplitudes below 100 µV were identified in ten nerves (25.6%) from V1 and three nerves (7.7%) from V2 in the present study and thus demonstrate such limitation. Differences in amount and thickness of undissected fibrofatty tissues overlying the vagus nerve may also have contributed to such outcomes from V1 and V2. Nonetheless, we found that all EMG signals from the adhesive skin electrodes below 100 µV could still be considered as typical biphasic waveforms presenting the integrity of the RLN. However, such limitation may still give confusion to interpretation of standard IONM procedure. Further studies and technical advancement to increase the sensitivity of the surface electrodes and improve the amplitude outcomes will be required. Wu et al. [11] suggested the possibility of applying an electronic skin [12] which may be available commercially in the future. In addition, definition of LOS in IONM using adhesive skin electrodes should be discussed with further studies.

Besides the usefulness of adhesive skin electrodes as a troubleshooting method for false LOS of EMG tube, there are some more advantages. Adhesive skin electrodes may be purchased for 5 US dollars in South Korea and therefore may be more cost-effective than the EMG tube, which is 50 times more expensive [11]. Therefore, it may be relatively easy to apply for patients who cannot afford the high price of an EMG tube. It may also be easy to use when an EMG tube is not covered by the national insurance or when the EMG tube was not prepared before the surgery. In addition, adhesive skin electrodes may be applied for IONM in pediatric thyroidectomy if the conventional EMG tube is hard to use because of size limitation. Patients who need nasal intubation or have a tracheotomy will also be suitable for this technique.

The limitations of this study may be the relatively small number of enrolled patients. Further prospective studies with more patients will be required to verify the usefulness and safety of IONM using adhesive skin electrodes. Since there were no patients with postoperative vocal cord paralysis in our series, efficiency of skin electrodes to present true LOS could not be verified in this study. Future studies including patients with complete or incomplete postoperative vocal cord paralysis or those who underwent RLN shaving due to cancer invasion of the nerve may expand the usefulness of applying adhesive skin electrodes for IONM during thyroidectomy. Such electrodes may not be useful for patients with a huge goiter or thyroid gland requiring extensive skin-flap elevation, including the level above the thyroid cartilage. Care should be taken to avoid detaching electrodes during the surgery, although that was not experienced in this study.

In summary, we verified the usefulness of adhesive skin electrodes for IONM of RLN during thyroidectomy. Although lower amplitude remains the major limitation of this technique, adhesive skin electrodes may be considered as an alternative method for IONM during thyroidectomy.

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Compliance with ethical standards

Conflict of interest The authors have no conflict of interest to declare.

Informed consent All patients gave their informed consent for this study and IONM, and the institutional review board of our center admitted this study (IRB No. 2018–11-022).

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