

Safety of LigaSure in Recurrent Laryngeal Nerve Dissection-Porcine Model Using Continuous Monitoring

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Objectives/Hypothesis: This study investigated recurrent laryngeal nerve (RLN) real-time electromyography (EMG) data to define optimal safety parameters of the LigaSure Small Jaw (LSJ) instrument during thyroidectomy.

Study Design: Prospective animal model.

Methods: Dynamic EMG tracings were recorded from 32 RLNs (16 piglets) during various applications of LSJ around using continuous electrophysiologic monitoring. At varying distances from the RLN, the LSJ was activated (activation study). The LSJ was also applied to the RLN at timed intervals after activation and after a cooling maneuver through placement on the sternocleidomastoid muscle (cooling study).

Results: In the activation study, there was no adverse EMG event at 2 to 5 mm distance (16 RLNs, 96 tests). In the cooling study, there was no adverse EMG event after 2-second cooling time (16 RLNs, 96 tests) or after the LSJ cooling maneuver on the surrounding muscle before reaching the RLNs (8 RLNs, 24 tests).

Conclusion: Based on EMG functional assessment, the safe distance for LSJ activation was 2 mm. Further LSJ-RLN contact was safe if the LSJ was cooled for more than 2 seconds or cooled by touch muscle maneuver. The LSJ should be used with these distance and time parameters in mind to avoid RLN injury.

Key Words: Recurrent laryngeal nerve, electromyography, LigaSure, thyroidectomy, intraoperative neuromonitoring.

Level of Evidence: N/A.

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INTRODUCTION

Energy-based surgical devices (EBD) have been increasingly applied in thyroid surgery due to attractive combined dissection and hemostatic properties. Two instruments that have gained increasing acceptance over the past

decade for use in thyroidectomy are the electrothermal bipolar vessel sealing system, or LigaSure (LF1212 Europe, LF1212A USA; Medtronic, Covidien products, Minneapolis, MN), and the Harmonic scalpel (Ethicon, Cincinnati, OH).^{1–4} These two instruments have been described in terms of reduction of procedure time, incision length, operative blood loss, postoperative pain, hospital stay, and usefulness in endoscopic procedures.^{1–12}

Following traction injury, thermal injury is the most common mechanisms of recurrent laryngeal nerve (RLN) injury during thyroid surgery.^{13,14} EBDs are widely used for hemostasis and dissection; thus, their safety must be studied—especially as it relates to the RLN. In our previous animal study,¹⁵ we evaluated the safety parameters of the Harmonic scalpel during thyroid surgery and realized that the EBDs may cause unexpected iatrogenic RLN injury and its use should be standardized. However, there is no published experimental evidence for the safety issue of Ligasure as it relates to RLN dissection.

LigaSure Small Jaw (LSJ) instrument (LF1212 Europe, LF1212A USA; Medtronic) is an FDA-approved electrothermal bipolar vessel sealing system for thyroid surgery; recent randomized controlled trials^{5,6} have supported its safety to be equivalent to the Harmonic scalpel. The LSJ provides thermal sealing with a tissue divider and is designed for hemostasis and dissection in thyroid surgery. It seals vessels up to 7 mm in diameter by denaturing collagen and elastin within the vessel wall and surrounding connective tissue.⁵ The aim of this experimental

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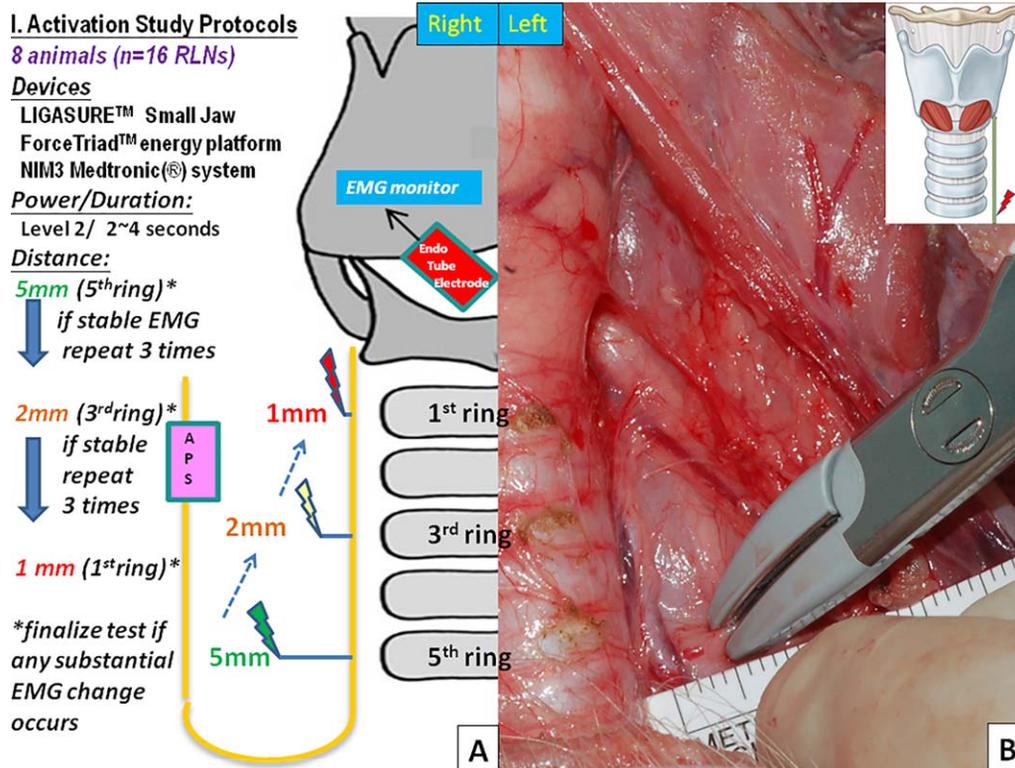


Fig. 1. Activation study details. (A). The flow chart is illustrated. LigaSure Small Jaw (Medtronic, Covidien products, Minneapolis, MN) with the energy from the ForceTriad (Medtronic, Covidien products, Minneapolis, MN) energy platform is used to test the safety, and the real-time evoked EMG changes is recorded by NIM EMG tube and analyzed by the NIM3 system (Medtronic, Minneapolis, MN). The power is set at level 2, and the energy discontinues automatically by 2 to 4 seconds. Distance range of LSJ application from RLN was set at 5, 2, and 1 mm distance. For 1-mm distance determinations, the tip of the LSJ is placed 0 mm from the nerve because the LSJ tip coating is 1 mm thickness. If any substantial EMG change occurs after the test (star sign), the experiment of the RLN is finalized. (B). Test the LSJ by the 5 mm distance near to the left RLN. EMG = electromyography; LSJ = LigaSure Small Jaw; RLN = recurrent laryngeal nerve. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

study is to investigate how LSJ can be safely utilized near the RLN during thyroidectomy in porcine model using continuous intraoperative neuromonitoring (CIONM) to monitor real-time electromyography (EMG) changes during the application of LSJ near the RLN at various distances from the nerve (activation study). We also evaluated the cooling time and muscle cooling maneuver to determine postactivation optimal LSJ cooling parameters (cooling study).

MATERIALS AND METHODS

Animal, Anesthesia, and Equipments

This study was designed and started during the International Course of Intraoperative Neuromonitoring in Thyroid Surgery and Animal Experiment, Kaohsiung Medical University, Kaohsiung, Taiwan, December 2–5, 2013 (IACUC protocol No. 100097, 102100). A prospective porcine model¹⁶ was used to study the electrically evoked EMG recorded from the vocalis muscles via endotracheal surface electrodes. The EMG parameters of this model, including the threshold, latency, amplitude, and evoked potentials, have been demonstrated to be comparable to reported human data.¹⁷ Sixteen piglets (18–25 kg) (n = 36 RLNs) underwent general anesthesia induction via intravenous thiopental 15 mg/kg, and then a size #6 EMG endotracheal tube (NIM

Standard EMG Tube, Medtronic, Minneapolis, MN) was inserted by an anesthesiologist without administration of a neuromuscular blocking agent. The tube was placed with the middle of the exposed electrodes, in good contact with the true vocal cords, under a direct laryngoscope. General anesthesia was maintained with sevoflurane (1%–2%).

The CIONM via vagus nerve (VN) stimulation was performed, and animals had their EMG tracings continuously recorded during LSJ–RLN testing. The monitor was set with a response threshold of 150 μ V, stimulation rejection artifact at 2.6 ms, and rectangular pulse negative stimulus of 100 μ s duration at 4Hz. Proper EMG tube position was verified by laryngoscope and by obtaining first vagal nerve V1 stimulation value and baseline > 500 μ V.¹⁸

Operation and Experimental Design

A long transverse cervical incision was made, and the strap muscles were divided and retracted from midline to expose the thyroid gland and the bilateral RLNs. Continuous intraoperative neuromonitoring was achieved by means of the Automatic Periodic Stimulating (APS, Medtronic) accessory.¹⁹ Access to the carotid sheath and VN for APS position was performed with a lateral approach behind the sternocleidomastoid (SCM) muscle to provide for optimal APS electrode stability. After connecting the APS electrode with the Nerve Integrity Monitor system (NIM3.0, Medtronic), baselines for the latency

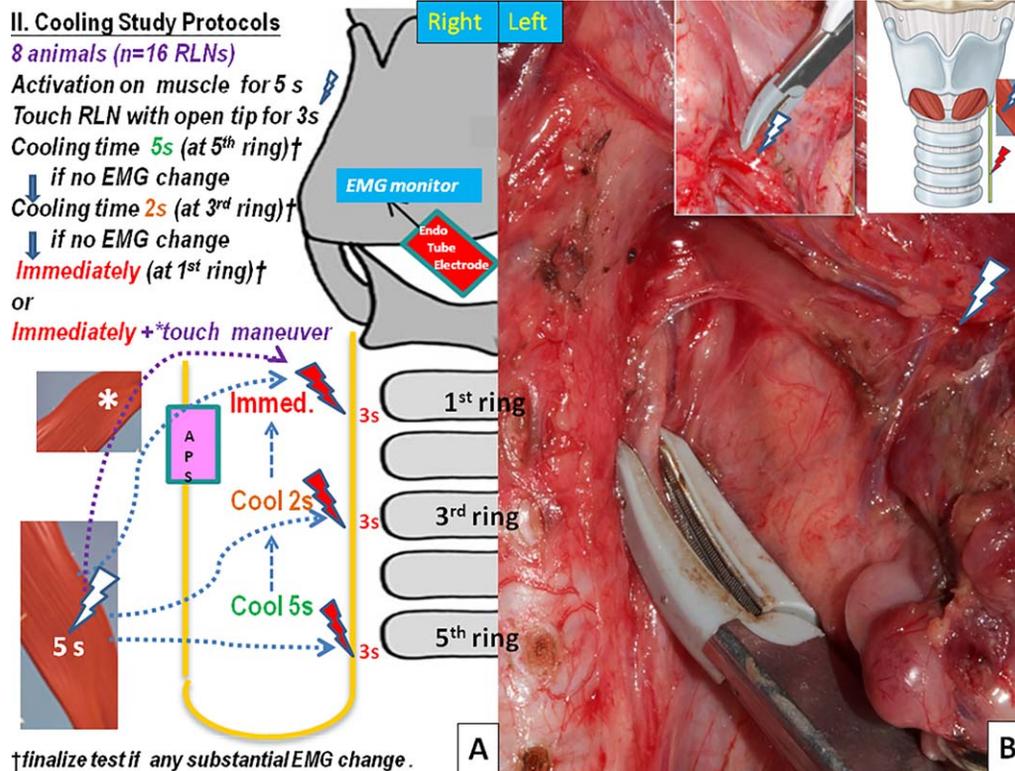


Fig. 2. Cooling study details. (A) The flow chart is illustrated. The devices and power used are the same with the activation study. The LSJ (Medtronic, Minneapolis, MN) is firstly activated on the surrounding muscle for 5 seconds (white arrow), and the open tip will be used to touch the RLN (red arrow) after 5- and 2-second cooling period (cool). If the EMG remains stable after repeated 5- and 2-second cooling time tests, we test the safety when immediately touching the RLN after activation (Immed.) with or without the muscle touch maneuver (star sign; cooling by quick touch of the surrounding muscle). (B). Use the open tip of LSJ touch the left RLN at the first tracheal ring level immediately after activation the on the surrounding muscle for 5 seconds (white arrow). EMG = electromyography; Immed. = immediately; LSJ = LigaSure Small Jaw; RLN = recurrent laryngeal nerve. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

and amplitude of the evoked response were calibrated automatically. Stimulation frequency for CIONM was set once per second, thus evaluating the RLN and VN continuously.

The study protocol included two phases:

1. Activation Study.

Eight animals (16 RLNs) were used to investigate the safe distance of LSJ application near the RLN. Figure 1 summarizes the scheme for activation study protocol. The LSJ was used with ForceTriad energy platform (Medtronic, Covidien products, Minneapolis, MN) with power setting at second level. The average seal cycle of LSJ is 2 to 4 seconds when used with the ForceTriad energy platform. The tests are performed on the RLN from the proximal to distal segment. The distance is measured from the tip of LSJ to the RLN, including the coating (1 mm thickness). We firstly test the 5 mm distance at the fifth tracheal ring. If EMG shows stable after three times repeated tests, we further test the 2 mm distance. If the EMG remains stable after repeated 2-mm distance tests, we test the safety when directly touching the coating of tip on the RLN. If any substantial EMG change occurs after the test, the experiment of the RLN is finalized, and we keep the real-time EMG evolution for at least 25 minutes on record.

2. Cooling Study.

Another eight animals (16 RLNs) were used to evaluate the cooling time, as well as the muscle-touch cooling maneuver associated with safe LSJ-RLN contact after prior activation. Figure 2 summarizes the scheme for cooling study

protocol. The LSJ is firstly activated on the surrounding muscle for 5 seconds, and the open tip will be used to touch the RLN directly after a different cooling period. We firstly test the 5-second cooling time at the fifth tracheal ring; if EMG shows stable after three repeated tests, we further test the 2-second cooling time at the third tracheal ring. If the EMG remains stable after repeated 2-second cooling time tests, we test the safety when immediately touching the RLN at the first tracheal ring after activation, with or without the muscle touch maneuver. During the experiment, the stimulated EMG signals were registered continuously. The amplitude and latency waveforms were displayed separately, and an upper limit threshold for the latency (+10%) and a lower limit threshold for amplitude (-50%) were depicted as separate alarm lines.¹⁹ Acoustic and optical signals alerted the surgeon when a preset threshold had been crossed or when the electrode had become dislodged. To minimize the potential bias, all of the testing was conducted without any manipulation or traction on the trachea to avoid changes to the contact area of the electrodes. Additionally, the surgical field was maintained dry with a swab to avoid any artifacts and/or signal shunting or dispersion.

RESULTS

Baseline amplitude signal was $1,229 \pm 292 \mu\text{V}$ (range 754–1,751). No differences in terms of baselines

TABLE I.

Activation Study: Comparison of Real-Time EMG Change When LSJ Activation Is Close to RLN at Varying Distances.

No.	Animal Side	Distance (EMG* [times of test])		
		5 mm	2 mm	1 mm
1	R	Stable [3]	Stable [3]	87% loss [1]
	L	Stable [3]	Stable [3]	LOS [†] [1]
2	R	Stable [3]	Stable [3]	66% loss [1]
	L	Stable [3]	Stable [3]	55% loss [1]
3	R	Stable [3]	Stable [3]	60% loss [1]
	L	Stable [3]	Stable [3]	50% loss [1]
4	R	Stable [3]	Stable [3]	LOS [†] [1]
	L	Stable [3]	Stable [3]	70% loss [1]
5	R	Stable [3]	Stable [3]	74% loss [1]
	L	Stable [3]	Stable [3]	LOS [†] [1]
6	R	Stable [3]	Stable [3]	67% loss [1]
	L	Stable [3]	Stable [3]	72% loss [1]
7	R	Stable [3]	Stable [3]	68% loss [1]
	L	Stable [3]	Stable [3]	74% loss [1]
8	R	Stable [3]	Stable [3]	LOS [†] [1]
	L	Stable [3]	Stable [3]	78% loss [1]

*EMG data of unstable column represents the final amplitude after at least 25 minutes of continuously real-time EMG recording.

[†]LOS defined as the evoked EMG amplitude less than 100 μ V.

EMG = electromyography; L = left; LOS = loss of signal; LSJ = LigaSure Small Jaw; R = right; RLN = recurrent laryngeal nerve.

amplitudes were noted between the right and left side. Median values for the right VN and left VN showed latency 5.5 ms and 7.7 ms, respectively.

1. Activation Study.

Table I summarizes and compares the real-time EMG profiles with LSJ activation at different RLN distances. The EMG remains stable at 2- to 5-mm distance test (totally 96 tests). Using LSJ (Medtronic) at 1 mm distance resulted in immediate complete EMG loss in four RLNs and partial reduction of amplitude between 50% to 87% in 12 RLNs.

2. Cooling Study.

Table II summarizes and compares the real-time EMG profiles when touching the RLN with the activated LSJ after different cooling times or after the muscle touch maneuver. The EMG remained stable if the cooling time was at least 2 seconds (totally 96 tests). Touching the RLN immediately after LSJ (Medtronic) was activated determined EMG complete loss in three RLNs and partial amplitude reduction 48% to 70% in four RLNs. Electromyography remained stable if LSJ touched SCM muscle tissue before reaching the other eight RLNs.

In both the activation and cooling studies, none of the injured RLN's EMG showed progressive recovery after at least 25 minutes of observation. Overall, latency of the LSJ thermal-injured RLN became elevated but was less consistent than amplitude. Of note, all of the injured segments of the RLN could not be well visualized despite being accurately mapped by distal to proximal segmental probe nerve-mapping stimulation in all RLNs (Fig. 3).

DISCUSSION

Elucidating the mechanism of RLN injury helps surgeons better refine their techniques, and may serve to reduce RLN palsy rates.^{13,14,20,21} Given the wide availability of EBDs during thyroid surgery, it is expected that many nerve injuries may be caused by thermal injury.¹⁰ The study confirms that LSJ can be safely applied near the RLN in a standardized manner. In the activation study (Fig. 1), there was no adverse EMG event at 2 mm or more distance (Table I). In the cooling study (Fig. 2), there was no adverse EMG event after 2-second cooling time or after the LSJ was quickly touched on the surrounding muscle before contacting the RLNs (Table II). To our best knowledge, this is the first experimental model to evaluate the RLN safety parameters and elucidate injury mechanism of application of LSJ during thyroid operation utilizing real-time EMG to determine physiologic significant injury.

Our previous study using the same animal and CIONM model demonstrated that the critical temperature to cause RLN thermal injury is approximately 60 °C.²² Two independent experimental studies using infrared thermal imaging demonstrated that the temperature of the LigaSure device can rise up to 96 °C,^{23,24} and the mean lateral thermal spread above 60 °C is about 1.376 \pm 0.27 mm with activation on thyroid parenchyma.²³ According to this literature and our current experimental findings (Table I), we recommend that a safe distance of 2 mm is required to avoid RLN thermal injury by the lateral thermal spread. In addition, it is important not to use the

TABLE II.

Cooling Study: Comparison of Real-Time EMG Change When Touching RLN With Activated LSJ After Different Cooling Time or Maneuver.

No.	Animal Side	Cooling Time or Maneuver, (EMG* [times of test])			
		5 Seconds	2 Seconds	Immediately	Immediately + Touch Maneuver
9	R	Stable [3]	Stable [3]	LOS [†] [1]	-
	L	Stable [3]	Stable [3]	LOS [†] [1]	-
10	R	Stable [3]	Stable [3]	-	Stable [3]
	L	Stable [3]	Stable [3]	-	Stable [3]
11	R	Stable [3]	Stable [3]	70% loss [1]	-
	L	Stable [3]	Stable [3]	-	Stable [3]
12	R	Stable [3]	Stable [3]	-	Stable [3]
	L	Stable [3]	Stable [3]	48% loss [1]	-
13	R	Stable [3]	Stable [3]	LOS [†] [1]	-
	L	Stable [3]	Stable [3]	-	Stable [3]
14	R	Stable [3]	Stable [3]	-	Stable [3]
	L	Stable [3]	Stable [3]	61% loss [1]	-
15	R	Stable [3]	Stable [3]	-	Stable [3]
	L	Stable [3]	Stable [3]	62% loss [1]	-
16	R	Stable [3]	Stable [3]	LOS [†] [1]	-
	L	Stable [3]	Stable [3]	-	Stable [3]

*EMG data of unstable column represents the final amplitude after at least 25 minutes of continuously real-time EMG recording.

[†]LOS defined as the evoked EMG amplitude less than 100 μ V.

EMG = electromyography; L = left; LOS = loss of signal; LSJ = LigaSure Small Jaw; R = right; RLN = recurrent laryngeal nerve.

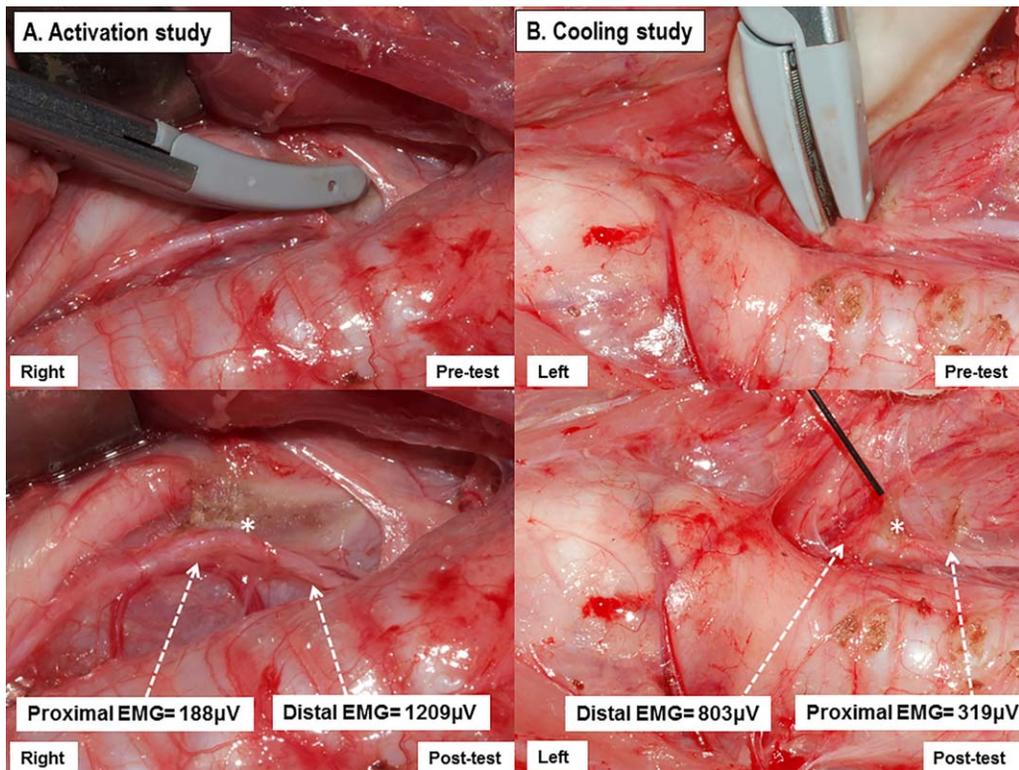


Fig. 3. Physical and EMG changes of experimental RLN injury after being directly touched with the LSJ (Medtronic, Covidien products, Minneapolis, MN) during or immediate after the activation. (A) Activation study: LSJ activation when directly touching the tip on the RLN (data from pig no. 1 right-side test: < 1 mm, first round). (B). Cooling study: Open tip of LSJ was used to touch the left side RLN immediately after activation (data from pig no. 15; left-side test: immediately and without touch maneuver, first round). After both experiments, only mild redness at the nerve sheath was grossly identifiable, but the real-time EMG showed substantial decreased waveform and a weakened point (star sign) of nerve conduction can be detected and pinpointed on the RLN. EMG = electromyography; LSJ = LigaSure Small Jaw; RLN = recurrent laryngeal nerve. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

uncooled LSJ for blunt dissection around the RLN. The device can be cooled in the room air for 2 seconds or by touching surrounding muscle tissue. In this study, we noted that the muscle touch maneuver is useful to cool down the LSJ quickly in order to subsequently be applied safely near the RLN (Table II).

In this study, we noted that the LSJ nerve injuries are not easy to identify visually (Fig. 3). Therefore, the LSJ should be used in a standardized manner to avoid unexpected iatrogenic RLN injury. This finding correlates to previous clinical observations that RLN insults due to thermal as well as traction, compression, contusion, or pressure are often undetected by the surgeon's eye, and IONM aids demonstration of impaired RLN function and in fact accurately maps out the specific segment affected intraoperatively, even when the nerve is still visually intact.^{13,14,20,21,25,26} The CIONM is useful in order to provide real-time data about the nerve function.¹⁹ In this study, we noted that the CIONM depicts a single, rapid acute amplitude-decrease profile, and thus the amplitude reduction and latency increase are sensitive parameters for diagnosing LSJ thermal nerve injury. A pilot study on RLN traction injury described a different EMG profile with a slow, progressive partial amplitude decrease under RLN tractions with different tension.²⁷ Thus, the surgeon

can react promptly to nerve traction stress but cannot react and avoid it when LSJ thermal nerve injury occur. Although RLN injury has already occurred when these adverse electrophysiologic findings are noted, the real-time EMG profile provided by CIONM is reported to be helpful for detecting some forms of injury in its earliest phases,²² and for avoiding the continued or repeated RLN damage to reduce risk of permanent vocal cord palsy.¹³

There are limitations in the present study. Firstly, this study is to investigate how LSJ can be safely utilized near the RLN; thus, the findings apply only for use of the LSJ. Secondly, this is an animal model with median sample size, and caution must be taken in translating these data into clinical context. The RLN physiopathology in porcine may be different from the human. Porcine anatomy may have different tissue composition. Nevertheless, this model has been previously proven as a useful and reliable model to investigate the laryngeal EMG changes during IONM,^{16,22,27} and there was a certain level of reproducibility in each datum.

CONCLUSION

Based on EMG functional assessment, the safe distance for LSJ activation was 2 mm. Further LSJ-RLN contact was safe if the LSJ was cooled for more than 2

seconds or cooled by touch muscle maneuver. The LSJ should be used with these distance and time parameters in mind to avoid RLN injury.

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