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#### Safety parameters of Ferromagnetic Device during Thyroid Surgery: Porcine model using continuous neuromonitoring

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### Safety parameters of Ferromagnetic Device during Thyroid Surgery: Porcine model using continuous neuromonitoring

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#### Abstract

**Background** The ferromagnetic (FM) device is a new surgical energy modality. This study investigated dynamic recurrent laryngeal nerve (RLN) electromyographic (EMG) data to define safety parameters for using FM devices in thyroidectomy. **Methods** Real-time EMG tracings obtained under continuous neuromonitoring were recorded from 24 RLNs (12 piglets). In the activation study, FM devices were activated at varying distances from the RLN. In the cooling study, FM devices were cooled for varying time intervals, or muscle touch maneuver was performed, before contact with the RLN.

**Results** During the FMwand/FMsealer activation, no adverse EMG events occurred at distances of 2mm or longer. The cooling study revealed no adverse EMG events after 1-second (FMwand) or 3-second (FMsealer) intervals or after muscle touch maneuver.

**Conclusions** An FM device should be activated at a distance of 2mm from the RLN and should be adequately cooled before further contact with the RLN. Surgeons can avoid RLN injury by observing standard procedures for using FM devices.

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**Key Words:** Recurrent laryngeal nerve, Ferromagnetic device, Continuous intraoperative neuromonitoring, Thyroid surgery, Nerve thermal injury.

#### Main Text Introduction

Surgical management of thyroid disease has evolved considerably in the past several decades. In recent years, research and development of energy-based devices (EBD) have played an important role in improving the overall quality of thyroid surgery. Use of EBDs in thyroid surgery has increased because EBDs increase hemostasis efficiency, decrease operation time, and prevent life-threatening hematoma<sup>1-3</sup>. Some studies indicate that, compared to conventional clamp-and-tie technique, EBDs obtain superior outcomes in thyroid surgery, including pain, hospital stay, blood loss, postoperative drainage, and incidence of postoperative hypocalcemia. <sup>4-7</sup> However, the high temperatures, lateral thermal spread, and the residual heat generated by EBDs can cause unexpected iatrogenic thermal injury to recurrent laryngeal nerves (RLNs).<sup>8,9</sup> Therefore, surgeons should follow standard procedures and understand safety parameters when using EBDs for hemostasis and dissection in thyroid surgery.

Currently, the EBDs most commonly used in thyroid surgery are based on bipolar (Ligasure) and ultrasonic (Harmonic) technology. Each method has inherent advantages and disadvantages resulting from their different mechanisms.<sup>1,3</sup>

Ferromagnetic (FM) technology is a new surgical EBD that could be effective for hemostasis and dissection during thyroid surgery. This device generates high-frequency alternating current and transmits it through the heating elements of the device to create a rapidly alternating magnetic field. The FM alloy responds to the rapidly alternating magnetic field by immediately generating pure thermal energy through a combination of ohmic and hysteresis losses. Contact between the heating element of the FM device and the tissue minimizes lateral thermal spread to surrounding tissue and achieves a hemostatic effect. <sup>10,11</sup> The device reportedly maintains electrical silence in terms of muscle contraction, nerve stimulation and interference with electrically sensitive devices, e.g., pacemakers or automatic internal defibrillators. <sup>12</sup>

The FMwand (Domain Surgical, Salt Lake City, UT, USA) is a commercially available hemostatic dissecting scalpel with a dissecting loop that uses FM heating as an energy source. <sup>13</sup> Radiofrequency current from a generator is conducted through an alloy loop and returned to ground without passing through the patient. The loop has a ferromagnetic coating several microns in thickness and is coupled to the high frequency alternating current. **(Fig. 1A).** 

The FMsealer (Domain Surgical, Salt Lake City, UT, USA) is an open shear consisting of a FM heating element in the jaw of a surgical vessel sealing device. Compressing tissue with the open shear generates thermal energy on the heating

element from the active jaw to the inactive jaw. Thermally, the tissue is relatively inert. Heat transmitted perpendicularly through the compressed tissue seals and divides the tissue and vessels without additional cutting mechanisms. In vitro experiments have confirmed that FMsealer effectively seals arteries and veins with diameters ranging from 1 to 7 mm (as measured in a noncompressed naturally pressurized state) with burst pressures consistent with BP sealers and equivalent reliability of vessel seals. <sup>13</sup> (Fig. 1B)

No studies have published experimental or clinical data regarding the safety of FM device in relation to hemostasis and dissection near the RLN during thyroidectomy. The purpose of this study was to investigate real-time electromyographic (EMG) data for the RLN to define safety parameters for using an FM device in thyroidectomy. For this purpose, we recorded the dynamic evoked laryngeal EMG change under continuous intraoperative neuromonitoring (CIONM) when the FM device was used at various distances from the RLN (activation study). We also evaluated the effects of various cooling durations and cooling by muscle touch maneuver to determine the optimal post-activation parameters for cooling an FM device (cooling study).

#### MATERIALS AND METHODS

#### **Subject Preparation and Anesthesia**

The prospective porcine model used for the CIONM experiments in this study was developed by a research team at Kaohsiung Medical University, Taiwan<sup>14,15</sup>. The animal-use protocol was consistent with national/international regulations and guidelines for animal experiments, including replacement, reduction, and refinement principles, and was approved by the Institutional Animal Care and Use Committee.

General anesthesia in the experiment was induced by intravenous injection of thiopental 15 mg/kg with the animal in a supine position. Endotracheal surface electrodes were intubated to record EMG signals generated by electrical stimulation applied from the RLN to the vocalis muscles. Neuromuscular blockade that might interfere with EMG signals under IONM was avoided by excluding use of muscle relaxants throughout the anesthesia process. After the piglets were intubated, tidal volume was set to 8 mL/kg, and respiratory rate was set to 15 to 20 breaths per minute. General anesthesia was maintained with sevoflurane 1% to 2%.<sup>15</sup>

#### **Equipment Setting and Operation**

All IONM procedures were performed according to International Neural Monitoring Study Group guidelines.<sup>16</sup> A nerve integrity monitor size #6 EMG endotracheal tube (NIM Standard Tube, Medtronic, Jacksonville, FL, USA) was used in the manner routinely applied in humans. The CIONM was performed using the Nerve Integrity Monitoring system (NIM3.0, Medtronic) (**Fig. 1C**). Automatic periodic stimulation (APS) of the vagus nerve (VN) was used for accurate, efficient and real-time recording of dynamic EMG signal changes caused by RLN injury<sup>17-19</sup> (**Fig. 1D**).

A long transverse cervical incision was made, and subcutaneous tissue and muscles were divided and retracted away from midline. The lateral border of the sternocleidomastoid (SCM) muscle was dissected and retracted medially. The thyroid glands, VNs and the RLNs were adequately exposed (Fig. 1D). The VN was explored, dissected laterally, freed from fascia, and kept dry for further experimental stimulation. The APS electrode was placed on the VN at the fifth tracheal ring level with optimal stability. Baseline data for VNs, including amplitude and latency of the evoked response, were calibrated automatically. An adverse EMG change was defined as a 50% amplitude decrease or a 10% latency increase.

#### **Study Design**

The activation study determined the distance from the RLN at which the FM devices can be safely used. The cooling study determined the time intervals and procedures required to cool an FM device before further use in hemostasis and dissection near the RLN. **Figure 1** shows the FMwand, FMsealer and the FMX G1 Generator system (Domain Surgical, Salt Lake City, UT, USA) used in this study. In this experiment, the activation power of FMwand was set at 45, and the activation power of FMsealer was set at 3.-

*Activation study*. Figures 2-3 depict the designs of the FM wand activation study and the FM sealer activation study, respectively. The FM wand and FM sealer were applied to soft tissue in a single activation of 3 seconds and at a distance of 5mm from the RLN. If no adverse EMG event (e.g., significant adverse decrease in amplitude or increase in latency) occurred, the distance was progressively decreased to 2mm and then to 1mm. Tests proceeded from the proximal to the distal part of the RLN. Real-time EMG CIONM information was continuously recorded during each FM device activation. A substantial adverse EMG change was interpreted as an injury on the RLN side. Dynamic EMG changes were continuously recorded for at least 20 minutes to observe any recovery of the electrophysiological response.

*Cooling study*. Figures 4-5 show the designs of the cooling studies for FMwand and FMsealer, respectively. First, the FM devices were applied to the SCM muscle in a

single activation of 3 seconds then allowed to cool at room temperature for 5 seconds. The dissecting loop blade of the FM wand or the open shear of the FM sealer was then applied to the RLN. If no adverse EMG event occurred, cooling time was decreased to 3 seconds and then immediately (estimated 1-second time interval for shifting the device from the muscle to the RLN). To test the cooling effect of the "muscle touch maneuver", the operator activated the FM device on the SCM muscle and then touched another part of the SCM muscle. The operator then allowed the FM device to cool for varying time intervals before touching the RLN. Muscle touch maneuver was performed after a single activation of the FM device on the SCM muscle. With the heating element of the device in full contact with the SCM muscle at another position, the device was immediately withdrawn from the muscle and placed in contact with RLN. Real-time EMG information for each stimulation was recorded and analyzed. When an RLN injury occurred, dynamic EMG changes were continuously recorded for at least 20 minutes to observe any recovery.

#### Results

The animal anesthesia, surgical approach, and CIONM were successfully performed in all experiments. Tables 1-2 summarize the results of the FMwand and FMsealer activation and cooling experiments.

#### **Activation Study**

In tests of FMwand activation at distances of 5 and 2 mm, no adverse effects, including amplitude decreases and prolonged latency, occurred. With the shear activated at a distance of 1 mm, all RLNs of piglets showed loss of signal (LOS) after a 20-minute observation (**Table 1** and **Fig. 2C**). In tests of FMsealer activation at distances of 5 and 2 mm, no adverse effects, including amplitude decreases and prolonged latency, occurred. With the shear activated at distance of 1 mm, all RLNs of piglets showed at least 71.2% LOS within a 20-minute observation period (**Table1**). The left RLN in piglet 6 showed LOS without recovery (**Fig. 3C**).

#### **Cooling Study**

**Table 2** shows the details of the cooling study performed in twelve RLNs of six piglets. After a 3-second activation of FMwand followed by a cooling time of 5 seconds, 3 seconds, or immediately, no piglets showed adverse effects when the RLN was touched with the dissecting loop, regardless of whether muscle touch maneuver was performed (**Table 2** and **Fig. 4C**).

When FMsealer was activated for 3 seconds and then allowed to cool for 5 seconds or for 3 seconds, neither side of the RLN showed adverse EMG events when the RLN

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was touched with the shear (**Table 2**). When FMsealer was activated for 3 seconds and then immediately placed in contact with the RLN, three of six nerves showed at least 58.3% EMG signal loss without recovery over a 20-minute observation time (**Fig. 5C**). In the remaining three RLNs, no adverse effects occurred when the muscle touch maneuver was performed after 3 seconds cooling time or immediately (**Table 2**).

#### Discussion

To our best knowledge, this is the first study offered a standardized manner for surgeons to use FM devices near the RLN in thyroid surgery. In the activation study, there was no adverse EMG events occurred when the FMwand and FMsealer were activated at a distance of 2mm or longer from the RLN. In the cooling study, no adverse EMG events occurred after 1-second (FMwand) and 3-second (FMsealer) time intervals or after cooling by muscle touch maneuver.

A thermal injury to the RLN caused by an EBD is of moderate to high severity because recovery is usually poor and because histological disturbance is usually severe relative to other injuries such as traction injury and mechanical trauma<sup>8</sup>. A thermal injury may be difficult to recognize visually, and lateral thermal spread can occur without direct contact with the heat source. <sup>20,21</sup> Application of spread stimuli over 60°C to the RLN can cause permanent functional damage to the endoneurium <sup>22</sup> whereas traction injury is usually limited to the perineurium and epineurium. <sup>8,17</sup> After activation for use in thyroid surgery, most EBDs can reach temperatures higher than 60°C, which can potentially cause RLN thermal injuries of varying severity. No studies have reported experimental or clinical evidence of the safety of FM devices in terms of hemostasis and dissection near the RLN during thyroidectomy. Hence, this study investigated the thermal effects of FM devices to determine their safety parameters during thyroid surgery.

Intraoperative neural monitoring has gained widespread acceptance as an adjunct to the gold standard of visual identification of the RLN during thyroid surgery<sup>23,24</sup>. Use of CIONM can improve thyroid surgery outcomes by detecting anatomic variations that can cause injuries <sup>25-27</sup> and by detecting the presence and mechanisms of nerve invasion or injuries that are predictive of postoperative vocal fold function.<sup>24,28-31</sup> Use of APS during CIONM provides visual and acoustic feedback that thyroid surgeons can use to evaluate nerve function and to facilitate early identification of nerve injury mechanisms, especially traction injuries. In high-risk procedures, CIONM enables the operator to take corrective action to maximize preservation of nerve function. <sup>18,24</sup> However, thermal injury can occur suddenly and unexpectedly when an EBD is used in thyroid surgery, and recovery from such injuries is often difficult. Therefore, taking precautions to avoid injuries caused by EBDs during surgery is more important than using CIONM to identify thermal injuries.

Recently developed FM devices substantially increase the precision of surgical dissection in thyroid surgery. The FM wand enables rapid and precise control of heating and cooling. The generated heat is restricted to the coating itself and the tissue in contact with the coating. <sup>10,11</sup> Since no electrical energy or magnetic effects are applied to surrounding tissue, the device does not interfere with electrophysiological monitors, pacemakers or automatic internal defibrillators. The FMsealer consists of an FM heating element in the jaw of a surgical vessel sealing device. Chen et al. reported several features of the FMsealer<sup>32</sup>. The authors evaluated the reliability of FMsealer by using it to seal porcine arteries (diameter, 5-7 mm) in a controlled laboratory setting. A 95% success rate was achieved for a burst pressure above 240mg. Each vessel was sealed, divided and pressurized using an automated inflation system until the seal failed. The average burst pressure was 1098mmHg. In a blinded histologic evaluation of 5mm vessel seals in vivo, the distance of lateral thermal spreads for the FM (1678±433 µm) and Ligasure (1796±337 µm) devices were significantly shorter compared to that for the Harmonic device (2032±387 µm), P<0.001.

EBDs significantly improved efficacy in achieving hemostasis and were widely used in thyroid surgery. Several porcine model studies investigated the commonly used hemostatic devices and their safety parameters when dissecting RLN<sup>33</sup>. The safe activation distances and cooling times were 5 mm and 1 second for monopolar electrocautery (15 watts); 3 mm and 1 second for bipolar electrocautery (30 watts)<sup>34</sup>; 2 mm and 2 seconds (or cooled by touch muscle maneuver) for the Ligasure Small Jaw<sup>35</sup>; 1 mm and 2 seconds (or cooled by touch muscle maneuver) for the Ligasure Exact Dissector<sup>36</sup>; 2mm and 10 seconds (or cooled by touch muscle maneuver for 2 seconds) for the Harmonic Focus<sup>37</sup>; 4 mm for the Harmonic ACE, and 1 mm for the Harmonic ACE+<sup>38</sup>; 3 mm for the THUNDERBEAT<sup>3936</sup>. The current study investigates the safety parameters of FMs and confirms the FMs are comparable to those commonly used hemostatic devices, and thus FMs can be a potential alternative EBD to facilitate efficient hemostasis and dissection during thyroid surgery.

Since the FMwand and FMsealer share the same power module, the module can be switched during surgery. Therefore, one power module can be used in different dissection stages in thyroid surgery. The thin non-stick dissection loop of the FMwand (**Figs. 1A, 2B, and 4B**) can simultaneously cut and coagulate soft tissue while minimizing collateral tissue damage. Therefore, the FMwand is useful for skin flap elevation and precise dissection in the Berry ligament region or for

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dissection of the parathyroid glands. The FMsealer Open Shears (**Figs. 1B, 3B, and 5B**) provides reliable vessel sealing and minimal thermal impact on healthy tissue and is effective for hemostasis of thyroid vessels and dissection near the RLN.

This study had the following limitations. First, the data and information obtained from this animal study may require further verification in human surgery. the data and information obtained from a prospective porcine model animal study may not beapplicable to human surgery. Many factors can affect thermal transfer from FM devices to the RLN, such as the surgical environment and the use of different species for animal experiments. However, this model has proven useful and reliable for depicting real-time changes in laryngeal EMG caused by RLN injury.<sup>8,15,17,20-22</sup>. A second limitation is that this study only depicted real-time EMG changes during a 20minute period rather than long-term changes in RLN function. Notably, the use of CIONM data for predicting vocal cord function is well established.<sup>18,40</sup> Finally, when applied to actual human surgery, soft tissue coagulation may shorten the distance from the FM device to the RLN. Therefore, although this study indicates that the minimum safe distance for the FM wand and FM sealer is 2 mm, the tip should always be carefully inspected during activation and RLN dissection should be stopped immediately if soft tissue coagulation tends to draw the nerve toward the tip of the device.

#### CONCLUSION

This study used real-time laryngeal EMG data to define safety parameters for using an FM device near the RLN. Ensuring a sufficient activation distance of FM devices is mandatory. Therefore, whenever the FM devices were activated, the RLN should be clearly visible and maintain a safe distance. After activation, the device should be cooled before further use in any procedure that requires direct contact with the RLN. Knowing their respective safety parameters helps to avoid RLN thermal injury and increases surgical efficiency during thyroid surgery.

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#### **Legends for Figures**

**Figure 1.** Surgical approach and equipment settings. (A) Settings for the FMwand Dissector and the FMX Generator. <u>The activation power was set at 45.</u>– (B) Settings for the FMsealer Open Shears and the FMX Generator. <u>The activation power was set at 3.</u> (C) Setup for continuous intraoperative neuromonitoring system with Nerve Integrity Monitor (NIM 3.0) system. (D) For neck exposure, thyroid glands, vagus nerves, and recurrent laryngeal nerves were adequately exposed. Automated periodic stimulation (APS) electrode is applied on the vagus nerve.

**Figure 2**. Activation study of FMwand. (A) Flowchart of activation study protocols. Single activation was discontinued automatically for 3 seconds. Tests were performed from the proximal to distal segments of the RLN. The distance from the tip of the FMwand to the RLN was measured. In this study, the first test was performed at a distance of 5mm from the fifth tracheal ring. If the EMG remained stable after three tests, another test was performed at a distance of 2 mm. If the EMG remained stable after repeated tests at a distance of 2 mm, safety was tested at a distance of 1 mm. If a substantial EMG change was noted, the RLN experiment was complete, and EMG was continuously monitored for at least 20 minutes. (B) The FMwand was tested at a distance of 5, 2, and 1 mm. After activation at 1mm, real-time EMG showed sudden LOS without recovery during 20 minutes of continuous EMG recording.

**Figure 3.** Activation study of FMsealer. (A) Flowchart of activation study protocols. (B). The FMsealer was tested at a distance of 5mm from the left RLN. (C) Left side of piglet 6. The FMsealer was activated at distances of 5, 2, and 1 mm. After activation at 1mm, real-time EMG showed sudden LOS without recovery during 20 minutes of continuous EMG recording.

**Figure 4.** Cooling study of FMwand. (A) Flowchart of cooling study protocols. The tests were performed on the RLN from the proximal to distal segments. After a single FMwand activation on the SCM muscle (white arrow), the RLN (red arrow) was touched with the tip after varying cooling times. The fifth tracheal ring was touched after a cooling time of 5 seconds. If EMG remained stable in three tests, a 3-second cooling time was tested. If the EMG remained stable after repeated tests, safety was tested immediately (estimated 1 second time interval for shifting the device from muscle to the RLN) after touching the RLN after a single activation, with or without the touch maneuver (star sign, quick touching/cooling with surrounding

tissue). (B) The tip of the FMwand was used to touch the left RLN at the fifth tracheal ring level with 5 seconds lag time after 5 seconds activation on the surrounding muscle (white arrow) (C) Left side of piglet 9. The cooling study was performed with 5 seconds and 3 seconds cooling time and immediately touch RLN without muscle touch maneuver, and after a single activation. The EMG results showed no adverse effects. The EMG signal remained stable in repeated tests.

**Figure 5**. Cooling study of FMsealer. (A) Flowchart of cooling study protocols. (B) The left RLN was touched at the fifth tracheal ring level with the open tip of the FMsealer with a 5-second lag time after 5 seconds activation on the surrounding muscle (white arrow). (C) Left side of piglet 10. The cooling study was performed with cooling times of 5 seconds and 3 seconds after a single activation. No adverse effects on EMG occurred. When the RLN was touched with the FMsealer immediately without muscle touch maneuver and after a single activation, a sudden loss of real-time EMG signal occurred. After 20 minutes of continuous EMG recording, a 58.3% signal loss occurred (from 1137  $\mu$ V to 474  $\mu$ V).



Figure 1. Surgical approach and equipment settings. (A) Settings for the FMwand Dissector and the FMX Generator. The activation power was set at 45. (B) Settings for the FMsealer Open Shears and the FMX Generator. The activation power was set at 3. (C) Setup for continuous intraoperative neuromonitoring system with Nerve Integrity Monitor (NIM 3.0) system. (D) For neck exposure, thyroid glands, vagus nerves, and recurrent laryngeal nerves were adequately exposed. Automated periodic stimulation (APS) electrode is applied on the vagus nerve.



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EMG recording, a 58.3% signal loss occurred (from 1137  $\mu$ V to 474  $\mu$ V).

Medtronic 🖗

5 sec 3 sec Cooling Cooling

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В

Data from Piglet 10 , Left side

Session 1

diately

(no musc) touch ) NIM-Response® 3.0

20 minutes after the test: 474 μV (58.3% Loss)

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**Cooling Study Protocols** 

Lag time 5s (at 5th ring) +

*if no EMG change* Lag time 3s (at 3<sup>rd</sup> ring) †

FMsealer 3 animals (n=6 RLNs) Activation on SCM

Touch RLN with tip for at least 3

if no EMG change Immediately +\*muscle touch

or Immediately (at 1st ring) +

Lag 3s

Lag 5s

†finalize test if any substantial EMG change

1st rin

3rd ring

5<sup>th</sup> ring

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# Table 1. Activation Study: Comparison of Real-TimeEMG Change after Fmwand and FMsealer Activation atVarying Distances to RLN

Animal		Distance (EMG* [times of test])			
No.	Side	5 mm	2 mm	1 mm	
FMwand					
1	L	Stable [3]	Stable [3]	LOS† [1]	
	R	Stable [3]	Stable [3]	LOS† [1]	
2	L	Stable [3]	Stable [3]	LOS† [1]	
R		Stable [3]	Stable [3]	LOS† [1]	
3 L		Stable [3]	Stable [3]	LOS† [1]	
	R	Stable [3]	Stable [3]	LOS† [1]	
FMsealer					
4 L		Stable [3]	Stable [3]	71.2% loss [1]	
R		Stable [3]	Stable [3]	LOS† [1]	
5 L		Stable [3]	Stable [3]	77.4% loss [1]	
R		Stable [3]	Stable [3]	LOS† [1]	
6 L		Stable [3]	Stable [3]	LOS† [1]	
R		Stable [3]	Stable [3]	LOS† [1]	

\* EMG, electromyography, data of unstable column represents the final amplitude after at least 20 minutes of continuously real-time EMG recording.

 $\dagger$  LOS, loss of signal, defined as the evoked EMG amplitude less than  $100\mu V$ 

## Table 2. Cooling Study: Comparison of Real-Time EMG Change whenVarying Cooling Time or Muscle Touch Maneuver was Performedafter Fmwand and FMsealer Activation

Animal		Cooling time or Maneuver, (EMG* [times of test])				
	Side	5 2		Immediately**	Immediately**	
No.		seconds	seconds	(with muscle	(no muscle	
				touch)	touch)	
FMwand						
7	L	Stable [3]	Stable [3]	-	Stable [3]	
	R	Stable [3]	Stable [3]	Stable [3]	-	
8	L	Stable [3]	Stable [3]	Stable [3]	-	
	R	Stable [3]	Stable [3]	-	Stable [3]	
9	L	Stable [3]	Stable [3]	-	Stable [3]	
	R	Stable [3]	Stable [3]	Stable [3]	-	
FMsealer						
10	L	Stable [3]	Stable [3]	-	58.3% loss [1]	
	R	Stable [3]	Stable [3]	Stable [3]	-	
11	L	Stable [3]	Stable [3]	Stable [3]	-	
	R	Stable [3]	Stable [3]	-	LOS† [1]	
12	L	Stable [3]	Stable [3]	-	LOS† [1]	
	R	Stable [3]	Stable [3]	Stable [3]	-	

\* EMG, electromyography, data of unstable column represents the final amplitude after at least 20 minutes of continuously real-time EMG recording.

\*\*Estimate there is a 1-second time interval for shifting the device from muscle to the RLN

 $\dagger$  LOS, loss of signal, defined as the evoked EMG amplitude less than  $100 \mu V$