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WILEY
Neuromonitored Thyroid Surgery: Optimal Stimulation Based on Intraoperative EMG Response Features

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Objectives: To evaluate/compare normative electrophysiologic electromyography (EMG) response characteristics of recurrent laryngeal, vagus, and external branch of superior laryngeal nerve evoked with different stimulators used in neuromonitored thyroid surgery.

Study Design: Prospective crossover study.

Methods: EMG responses obtained via endotracheal tube surface electrodes in 11 patients undergoing thyroid surgery were recorded when stimulated with four stimulators: two monopolar (Prass standard and ball tip), one bipolar, and one dissecting instrument. Normative mean EMG results including latency, amplitude, threshold, saturation currents, and distance-sensitivity were compared.

Results: The Prass standard stimulator had shorter latency time when nerve was not covered with fascia ($P = .04$). The bipolar, dissecting instrument, and ball tip demonstrated similar latency times with and without nerve fascia. Pooled mean latency increased significantly from 1.66 ms to 2.16 ms when comparing nerves without fascia and nerves with fascia ($P < .05$). The Prass standard monopolar stimulator had the lowest mean threshold at 0.40 mA, with the dissecting instrument having the highest threshold at 0.89 mA for dissected nerve. Pooled mean threshold and saturation increased from 0.6 mA to 1.7 mA ($P < .0001$) and 1.57 mA to 4.15 mA ($P < .001$) with fascia covering nerve, respectively. The mean depolarization rate was 100% for monopolar and bipolar electrodes and 81% for dissecting instrument at 1 mA. Only 9% of monopolar electrodes generated an EMG response when stimulated from 2 mm away.

Conclusion: Monopolar stimulators are more sensitive for neural mapping, whereas bipolar instruments are more specific, thus reducing false positive stimulation. Dissecting instruments share many features of monopolar stimulators while being more specific, and thus are a viable alternative.

Key Words: Thyroid surgery, stimulation, stimulator, EMG, intraoperative neuromonitoring, electrophysiology.

Level of Evidence: 2b

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INTRODUCTION

Thyroidectomy is a commonly performed operation, with almost one hundred thousand operations performed annually, with thyroid cancer incidence rising to 14.42 per 100 thousand person-years. Temporary or permanent injury to the recurrent laryngeal nerve (RLN) has serious laryngeal consequences, including voice change, hoarseness, dysphagia, aspiration, stridor, or even respiratory distress. A meta-analysis of 25 thousand thyroidectomy patients revealed a rate of 9.8% (range 0%–18.6%) postoperative vocal cord paralysis (VCP). Injury prevention is aided with the use of intraoperative neural monitoring (IONM) and has become a useful addition to visual nerve identification, which is the gold standard. Among IONM’s benefits are neural mapping, identification of the external branch of the superior laryngeal nerve (EBSLN), identification anatomic variations of RLN, clarification of mechanism of injury, and prediction of postoperative vocal cord function. IONM in multiple meta-analyses has shown to be protective against transient, permanent, and total RLN injuries. In recent large survey analysis, 85% of North American surgeons utilize IONM, with rates doubling over the last decade with 40% to 60% utilizing the IONM information in the thyroid surgery strategy.

IONM utilizes a stimulation probe that depolarizes the nerve to evoke a laryngeal electromyographic (EMG) response, which can be recorded on a monitoring system through recording electrodes. EMG magnitude correlates to the number of muscle fibers being activated during nerve depolarization, which conveys RLN functionality. This is useful at the end of surgery, where if the EMG response is similar to the initial EMG response at the beginning of surgery, good RLN postoperative functional and voice outcomes can be predicted. Conversely, loss of signal (LOS) at the end of surgery indicate severe RLN...
damage to the point they cannot conduct an action potential, predicting postoperative vocal cord paralysis. Indeed, a range of recent animal and human studies have now defined criteria for EMG changes that are predictive of postoperative paralysis, further codifying the objective analysis of these changes. With complete LOS during a planned total thyroidectomy, the recommendation is to stage the procedure to prevent bilateral RLN injury and VCP.

Additionally, vagus nerve (VN) identification and stimulation have been shown to improve the accuracy of IONM results and are recommended during neuromonitored thyroid surgery.

There are a multitude of IONM probes available for EBSLN, RLN, and VN for intraoperative stimulation and monitoring. Recently, our group has compared different stimulator, dissector, and probe types in a porcine model to identify electrophysiology profiles of various models. However, there is minimal data in humans using various stimulators to corroborate these findings and little is known about different stimulator's electrophysiology responses. Thus, using a validated IONM system, we establish human normative electrophysiologic parameters and compare laryngeal EMG potentials elicited by four different stimulator and dissector types in patients undergoing monitored thyroid surgery.

METHODS

Patients, Operation, and Anesthesia

Patients were consented for IONM use and EMG intraoperative study by the senior author (G.W.R.), which was approved by the Human Studies Committee of the Massachusetts Eye and Ear, Harvard Medical School (Boston, MA). The patients were anesthetized per standard protocol for neuromonitored thyroid surgeries and intubated using video laryngoscope with a nerve integrity monitor (NIM) EMG endotracheal tube (Medtronic TriVantage tube, Medtronic, Jacksonville, FL) size 7 and 8 utilized for women and men, respectively. Following thyroid bag inflation, all positioning was confirmed via visualization on video laryngoscopy and with respiratory variation on EMG monitoring. Neuromuscular blockade was never utilized. Thyroidectomy was performed in standard fashion with EBSLN, RLN, and VN visual localization.

Intraoperative Neural Monitoring Equipment

The IONM equipment, setup, and waveform examination were executed under International Neural Monitoring Study Group guidelines. The four stimulators tested include two monopolar stimulator (Prass standard and ball tip: Medtronic Xomed, Inc, Jacksonville, FL), one bipolar stimulator (Medtronic Xomed), and one dissecting instrument (Stimulus hemostat: Proctor Xomed, Inc, Jacksonville, FL), and one dissecting instrument (Stimulus hemostat: Proctor Xomed, Inc, Jacksonville, FL). The side-by-side bipolar probe (Medtronic Xomed, Inc) consist of both a cathode (−) and an anode (+). Care was made to situate the bipolar probe with the cathode (−) distal on the nerve (i.e., closer to the larynx and vocal cord) with the anode (+) proximal.

Minimal and maximal stimulus levels. The EBSLN, RLN, and VN were initially stimulated with 0.1 mA current with EMG recordings. The current was increased in 0.1 mA intervals until a detectable EMG response (DER), defined as an evoked response with an amplitude >100 μV, was recorded. Current was increased until a maximal EMG response was recorded. EMG response amplitude, latency, and waveforms were recorded. The pulsed stimuli of 100 μs duration was repeated at four pulses per second (4 Hz). The minimal stimulus level was defined as the current that first evoked a DER in mA. Maximal stimulus level was similarly defined as the current that evoked maximal EMG response in mA.

Sensitivity testing for nerve with and without fascia at 1 mA. IONM is usually performed at 1 mA stimulus current; therefore, we tested and compared 1 mA-evoked EMG responses by different stimulators for the EBSLN, RLN, and VN under three situations:

1. Stimulation on a dissected nerve without overlying fascia: This situation mimics direct stimulation during thyroidectomy when the nerve has been completely dissected of its enveloping fascial layers.
2. Stimulation with fascia covering the nerve: This was accomplished by identifying the nerve's path and then stimulating directly over the fascia covering the nerve. This corresponds to a situation in which the nerve path is first encountered, during neural mapping when the nerve is not dissected free of the enveloping fascia. Fascia overlying the nerve is less than 1 mm thick, thus not limiting the ability to identify the nerve.
3. Sensitivity testing of neural distance with 1 mA: Stimulation at varying distances from the nerve. Testing began with direct neural stimulation and then proceeded in 1 mm increments away from the nerve utilizing a surgical flexible plastic ruler. Distance was increased at this 1 mm interval until DER was no longer obtainable.

Data Analysis

All evoked EMG data were compiled, maintained, and graphed within Excel (2010) (Microsoft Corp., Redmond, WA). All statistical
analyses utilized SPSS v25.0.0.1 (SPSS Inc, Armonk, NY). To compare stimulators, one-way analysis of variance with Bonferroni post-test was used. Statistical significance was set at $P < .05$.

**RESULTS**

There were 11 patients (5 total thyroidectomy, 5 hemithyroidectomy [3 right-sided, 2 left-sided], 1 parathyroidectomy) who completed stimulator evoked-EMG response testing. All four stimulators evoked valid EMG waveforms when applied directly to the RLN. Sides stimulated were the same sides for hemithyroidectomy and were three right- and three left-sided stimulations for the total thyroidectomy and parathyroidectomy.

**Latency**

The Prass standard stimulator had significantly shorter latency time when applied to nerve without fascia compared to a fascia covered nerve ($P = .04$). The bipolar, dissecting instrument, and ball tip demonstrated similar latency times with and without fascia covering the nerve. The overall/pooled mean latency was 15% shorter when comparing nerves without fascia and nerve with fascia. Pooled mean latency increased significantly from 1.86 ms to 2.16 ms when comparing nerves without fascia and nerve with fascia ($P < .05$). There was no significant difference of nerve latency between stimulator types. Nerve latency values are listed in Table I and graphically represented in Figure 2.

**Evaluating EMG responses of nerves covered with and without fascia.** Higher amplitudes were encountered without fascia covering the nerve, but none reached significance (Table I) (Fig. 3). The overall/pooled mean amplitude was 23.65% lower when comparing nerves with fascia to nerve without fascia. Pooled mean amplitude decreased from 1412 μV to 1078 μV with fascia, although not significant. There was no difference between stimulators amplitude when compared to each other.

All four stimulators demonstrated lower mean threshold when the nerve was stimulated without fascia, as compared to nerve covered with fascia (Table II) (Fig. 4). The Prass standard monopolar stimulator had the lowest mean threshold at 0.40 mA, with the dissecting instrument having the highest threshold at 0.89 mA for bared nerve. For nerve with fascia, the Prass standard and ball tip probe had the same lowest mean threshold of 1.00 mA, whereas the bipolar stimulator had the highest, at 3.05 mA. The overall/pooled mean threshold was lower when comparing nerves without fascia to nerve with fascia. Pooled mean threshold increased from 0.6 mA to 1.7 mA ($P < .0001$).

All stimulators demonstrated lower mean saturation current when the nerve was stimulated without fascia, as compared to nerve covered with fascia (Table II) (Fig. 5). Pooled mean saturation increased from 1.57 mA to 4.15 mA ($P < .001$) comparing nerve without fascia to nerve with fascia.

**Distance sensitivity testing.** Distance sensitivity testing was then carried out (Table III). The mean depolarization rate at zero mm distance (i.e., stimulators was placed on the nerve) was 100% for the monopolar and bipolar electrodes but dropped to 81% for the dissecting instrument for nerve without fascia. Only 9% (2/22) of monopolar electrodes and none of the bipolar or dissecting instrument were able to generate a robust

![Comparison of Nerve Latency](image1)

**Fig. 2.** Comparison of nerve latencies.

![Comparison of Nerve Amplitude](image2)

**Fig. 3.** Comparison of nerve amplitude at stimulation current 1 mA.
waveform when the nerve was stimulated from a distance of 2 mm. No stimulator was able to successfully generate a satisfactory waveform 4 mm away from the nerve.

**DISCUSSION**

Nerve monitoring provides a unique adjunct by adding functional dynamic during surgery, which provides nerve information beyond visual identification alone. Stimulator-evoked EMG responses allow the surgeon to acquire data on how the nerve is functioning and whether there has been an injury that could not be appreciated with visualization alone. This is an important feedback during bilateral surgery, where true loss of signal should provide an opportunity to the surgeon to prevent bilateral RLN injury and vocal cord paralysis.20–22 In order to interpret evoked EMG responses, surgeons must be familiar with normative electrophysiologic characteristics and the variance of EMG waveforms depending on stimulator type and dissection scenario. These data lay the foundation for expected normative evoked-EMG response characteristics by various stimulator types under various normal settings.

This study confirms that scenario and stimulator type alter evoked EMG response characteristics in humans. Overall latency time increases with fascia overlying the nerve, especially for Prass standard monopolar stimulators. This was different compared to our porcine model, where latency did not differ with fascia, indicating that humans might have thicker fascia or fascia with more resistance. Amplitudes at 1 mA were not significantly different depending on stimulator type or whether nerve was covered with fascia. When fascia was covering nerve from an average of 0.6 mA to 1.7 mA, average EMG response thresholds were all increased. Importantly, both monopolar instruments (Prass standard and Ball tip) could consistently evoke a satisfactory response at currents < 1 mA in nerves without fascia. Monopolar stimulators had lower thresholds than bipolar or dissecting instruments and were not as affected by the presence of fascia. Saturation current was lowest for monopolar electrodes compared to bipolar and dissecting instruments.

Clinically, threshold current is crucial when performing neural mapping before the nerve is identified. The evaluation of fascia and stimulation distance gives us an improved understanding of the stimulators’ performance in surgical fields, where commonly fascia covers the nerve or where stimulation is done close to but not on the nerve. Both monopolar instruments had average
threshold currents of 0.40 mA and 0.52 mA. The lowest recorded threshold current was 0.2 mA for the Prass standard, and the highest was 2.5 mA for the dissecting instrument. Hence, a minimum current of 2 mA should be used during neural mapping. If using the dissecting instrument and there is no response, it may be important to raise the current to 3 mA. Once the nerve is located, all instruments had average thresholds below 1 mA, and thus the current can be turned down to between 0.5 and 1 mA. At this level, monopolar stimulators demonstrated a maximal or near-maximal evoked EMG response, thus not necessitating higher currents. This finding was similarly validated in our porcine model; using a Prass slim stimulator, a 1 mA current has previously been shown to have safe, stable intensity to evoke maximal EMG response. Faden et al. found a current of 0.5 mA optimizes IONM predictive value, but there was no mention of which stimulator was used or if different stimulators were tested.

Stimulation distance is also important when locating the RLN during neural mapping. The maximum distance to stimulate the RLN was 2.0 mm and 3.0 mm for the Prass standard and ball tip stimulators. The bipolar and dissecting instrument needed to be directly placed on the nerve to generate evoked EMG response. All stimulators recorded less robust evoked EMG when the stimulator was away from the nerve. Monopolar electrodes seem to have maximum current spread and thus are most sensitive for nerve mapping. Bipolar and dissecting instruments then are more nerve-specific, potentially more useful during sub-labial dissection such as at the suspensory ligament of the thyroid gland, or ligament of Berry, where the RLN is always located laterodorsally to the ligament.

Although this study provides normative electrophysiologic EMG data for various stimulators during thyroid surgery, there are limitations. For nerves with fascia, we used a thin layer of fascia overlying the nerve, which did not preclude visualization. If there was thick overlying fascia or any surrounding tissue, our data would not apply; future study within this setting is needed. This is particularly important during nerve mapping in the initial dissection phase of finding the RLN. However, this method has been valuable and reliable to analyze electrophysiologic IONM EMG outputs.

Overall, because most surgeons will utilize one type of stimulator during a case, we believe the Prass standard stimulator is the best overall option for two reasons: First, it is the best for neural mapping given its lower threshold, and neural mapping is what is done in the vast majority of the cases. Second, it is has the highest amplitude with fascia covering the nerve, the most common surgical scenario. However, if one wished to have the best, most specific stimulation, for example, the final stimulation at the end of the first side dissection before proceeding to the contralateral side, one would have to consider using a bipolar probe.

CONCLUSION
Knowledge of normative electrophysiologic parameters during neuromonitored thyroid surgery is critical for the interpretation of signal characteristics, including the loss of signal. We demonstrate that monopolar, bipolar, and dissecting instruments can effectively evoke EMG responses. Monopolar stimulators appear to be more sensitive when neural mapping, whereas bipolar instruments are more specific to reduce false positive stimulation. Dissecting instruments share many features of monopolar stimulators. They are slightly less sensitive yet more specific, hence they are a viable alternative. A surgeon can optimize IONM utility by selecting a stimulator based on the intended application of IONM and particular characteristics of the stimulator, as well as by being cognizant of the impact of overlying fascia and distance of stimulation point to the nerve.

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