

Peer Review File

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Reviewer A

Comment 1: I was really pleased to read this really interesting article. It is a well-structured study on the controversial issue of IONM during thyroid surgery.

The authors wrote an excellent scientific article highlighting all aspects of intraoperative neuromonitoring in thyroid surgery and focused on the application of patch stimulator for IONM in thyroidectomy.

Methods and statistical analysis are well-presented and the discussion is well-written.

The only weakness is the small number of patients.

I would suggest to accept this very interesting article for publication to your distinguished journal.

Reply 1: Thank you for reviewing our manuscript and thank you for your comments. We have acknowledged the small sample size as a limitation of our study in the discussion section, but we believe that it is sufficient for a feasibility study.

Reviewer B:

Many thanks for this interesting manuscript on a clinically relevant topic. Clear, well-conducted study.

Major issue:

Comment 1: Do the authors have any information on latency times? Combined events require latency and amplitude... The study would benefit if latency times could be analyzed as well.

Reply 1: Thank you for this comment. We also recognize that latency time as well as amplitude are important factors of a 'combined event' in IONM. However, because the aim of our study was to assess the feasibility of using the patch stimulator for IONM, we did not measure the latency times associated with RLN injury. Nevertheless, in theory, because the stimulation current is transmitted through the tip of the dissecting instrument to the nerve, and latency is a parameter associated with the conduction of the nerve itself, we suppose that there would be no difference in the latency times between the two stimulators. Further studies are needed on this topic.

Minor issues:

Comment 2: The results in the abstract are almost completely the same as the results in the results section. Please shorten the results section in the abstract.

Reply 2: Thank you for pointing this out, we have shortened and rephrased the results section in the Abstract as follows:

Changes in the text: (See lines 70-74) No statistically significant differences were seen in the mean amplitudes evoked by the patch stimulator and the conventional probe stimulator for the V1 signal ($825.5 \pm 394.6 \mu\text{V}$ vs. $821.8 \pm 360.9 \mu\text{V}$, $p=0.954$), R1 signal ($1044.8 \pm 471.2 \mu\text{V}$ vs. $1039.2 \pm 507.4 \mu\text{V}$, $p=0.898$), R2 signal ($1037.8 \pm 495.0 \mu\text{V}$ vs. $938.2 \pm 415.8 \mu\text{V}$, $p=0.948$), or V2 signal ($812.5 \pm 391.9 \mu\text{V}$ vs. $787.3 \pm 355.7 \mu\text{V}$, $p=0.975$).

Comment 3: Were these 15 patients operated on consecutively?

Reply 3: Yes, these patients were operated on consecutively, and we arranged the cases in chronological order.

Changes in the text: (See line 68) Fifteen consecutive patients
(See 175) A total of 15 consecutive patients

Comment 4: As it is a feasibility study: were there any disturbances in EMG signal when using mono- or bipolar, or energy-based devices if the mosquito is in place (fe burning tissue in between both legs of the instrument while in place?)

Reply 4: This is a very valid question, thank you. Before starting this study, we had the same experience as the reviewer described. When we applied the monopolar device to coagulate tissue between the two legs of a patch stimulator, the fuse blew at the patient interface. Since then, we have not used monopolar devices or energy-based devices in physical contact with the patch stimulator. Therefore, we do not have such a case in this study. We have included this important point as a limitation in the Discussion section as follows:

Changes in the text: (lines 267-270) We took care not to allow the monopolar or energy-based device to make contact with the stimulating dissecting instrument. Doing so could result in a blown fuse in the nerve monitoring system when the electric current is transferred to the system.

Comment 5: Line 207-208: This will never replace c-IONM, as traction injury (fe when retracting the thyroid lobe) will not be excluded. So, I disagree with the fact that it combines both I-IONM and c-IONM. When not used, the stimulating dissecting instruments do not protect against pending nerve injury because of traction.

Reply 5: Thank you for sharing this valid point. We also believe that stimulating dissecting instruments will never replace C-IONM because it does not protect against pending nerve injury by traction. In line 209, we mentioned that C-IONM allows the surgeon “to dissect and stimulate at the same time”, which we see as a strength of C-IONM. Then, in lines 215-216 we stated that stimulating dissecting instruments “combine the strengths of both the tools and techniques of I-IONM and C-IONM”, meaning that they encompass not all but some of the features of both techniques. To clarify what we intend to say, we have revised our manuscript as follows:

Changes in the text: (See lines 215-216) Recently, the use of stimulating dissecting instruments that combine the beneficial features of both I-IONM and C-IONM has been proposed.

Comment 6: Line 97 spelling error ('of perform' → 'to perform')

Reply 6: We have revised our text as advised.

Changes in the text: (See line 100) to perform

Comment 7: Line 173 spelling error ('Grave's disease' → 'Graves' disease')

Reply 7: We have revised our text as advised.

Changes in the text: (See line 181) Graves' disease

Reviewer C

The original article entitled “Application of Patch Stimulator for Intraoperative Neuromonitoring during Thyroid Surgery: Maximizing Surgeon’s Convenience” enrolled 15 patients who underwent thyroidectomy using both conventional stimulator and adhesive patch stimulator for I-IONM, and evaluated the feasibility of the patch stimulator approach.

The followings are my comments:

Comment 1: Although a small case number (n=15) enrolled, this study had new discoveries, and it really offers a novel, cheap, and convenient stimulating dissecting instrument method. Surgeons who read this article will want to try the same method in their operation.

Reply 1: Thank you for your comment.

Comment 2: The author did not describe/evaluate the stimulations when vagus nerve was not exposed or recurrent laryngeal nerve had not been visually identified. It should be mentioned in the discussion/limitation

Reply 2: Thank you for your comment. We completely agree that vagal stimulation without exposing the vagus nerve can minimize the risk of vagus nerve injury and that stimulation before visual identification of the RLN facilitates RLN identification. However, the aim of this study was to assess whether the patch stimulator could obtain comparable responses to those of the conventional stimulator. Because the tip of the conventional stimulator and the tip of the dissecting instrument have different shapes, areas, and properties, we believed that it would be difficult to accurately compare the amplitudes of the two conditions when the nerve is covered. In addition, because the tip of the conventional stimulator used in this study was sharp, and the vagus nerve is often located posterior to the common carotid artery or internal jugular vein, we worried that blind vagal stimulation without carotid sheath dissection would be ineffective and perhaps even dangerous. Thus, in this study, all of the nerves were exposed before nerve stimulations.

Comment 3: Lightweight is one of the major advantages of this method. The author may compare the weight of the probe, the patch, and other attachable stimulators to give readers a reference. The author can also list the advantages/disadvantages of the attachable stimulators such as weight/price/disposable/accessibility in a table to facilitate readers’ understanding.

Reply 3: Thank you for this suggestion. We have added a table to compare the characteristics of the different types of stimulators used for IONM as follows:

Changes in the text: Table 3. Comparison of different types of stimulators (See lines 251-252) A comparison of the different types of stimulators is summarized in Table 3.

Comment 4: Please also provide more details about the patch attachable stimulator,

including the size, thickness, and wire length, etc.

Reply 4: We added more details on the patch stimulator in the introduction and discussion section as follows:

Changes in the text: (See lines 111-112) The adhesive patch electrode is small ($20 \times 15 \times 1$ mm), lightweight (4 grams), inexpensive (US\$ 2.5), disposable, and easily applied onto dissecting instruments.

(See line 244) patch electrodes are small ($20 \times 15 \times 1$ mm), lightweight (4 grams)

Reviewer D

The authors reviewed the medical records of patients who underwent thyroidectomy using both conventional stimulator and adhesive patch stimulator for Intraoperative neuromonitoring (IONM). The EMG amplitudes of the vagal and the RLN before (V1, R1) and after thyroid resection (V2, R2) were alternatively checked with each type of stimulator at the same location of each nerve, and the result show no statistically significant differences were seen in the mean amplitudes between the two groups for the V1 ($p=0.954$), R1 ($p=0.898$), R2 ($p=0.948$), and V2 ($p=0.975$) signals. The authors concluded the patch stimulator was safely and effectively used for intraoperative neuromonitoring during thyroid surgery and provided similar nerve monitoring responses as conventional stimulators. This approach may be used to enhance the surgeon's convenience during thyroid surgery.

Comment 1: IONM is increasingly being used routinely in thyroid surgery, and stimulating dissecting instruments (SDIs) combined functionality were developed with the ability of perform both dissection and nerve stimulation to enhance the surgeon's convenience. In this paper, the authors describe in the title that the application of "adhesive patch electrode" -"Maximizing Surgeon's Convenience!". Although there is paragraph in the discussion describes the different types of SDIs, this paper would be more informative for the readers if the authors can provide a Table that summarize/compare the advantages and disadvantages of different stimulation probes/instruments (monopolar, bipolar, SDIs- wire bounded, attachable ring, detachable magnetic)

Reply 1: We have added a table to compare the different types of stimulators used for IONM as follows:

Changes in the text: Table 3. Comparison of different types of stimulators

(See lines 251-252) A comparison of the different types of stimulators is summarized in Table 3.

Comment 2: Small sample size (15 patients) and lack of detailed stimulus-response & distance-sensitivity data should be mentioned in the discussion section.

Reply 2: We have added the following text in the discussion section as follows:

Changes in the text: (See lines 270-272) Lastly, this study has a small sample size. Nevertheless, we showed the feasibility of the use of patch stimulators for IONM, and anticipate that this study will be a basis for further studies with larger sample size.

Comment 3: Please correct the typo in line 95: problems of I-IONM "monitoring"

Reply 3: Thank you. We have revised our text as advised.

Changes in the text: (See line 98) problems of I-IONM

Comment 4: Table 2. Patient 14. The difference of EMG signal between Patch and Probe in R2 is 777, in V2 is 453. The overall difference between Patch and Probe in R2 is larger than R1. Do you have any comment on this finding? Is this related to patch SDI with current shunting to surrounding structures?

Reply 4: Thank you for your question. There are many factors that influence the EMG amplitudes upon stimulating, including the duration of stimulation, extent of traction, wetness of the field, and shunting. Because we cannot fully control all these factors when stimulating the nerve two times with two different stimulators, shunting may indeed be one of the reasons for the difference between the EMG amplitudes evoked by the two stimulators.