Peripheral Nerve Localization by Frequency-Based Electrical Stimulation

Dilok Puanhvuan[1], Sorayouth Chumnanvej[1,2], Sarawin Khemmachotikun[1], and Yodchanan Wongsawat[1]

[1] Department of Biomedical Engineering, Faculty of Engineering, Mahidol University, {dilok.ee52,khemmachotikun.s}@gmail.com, yodchanan.won@mahidol.ac.th

[2] Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Thailand sorayouth@gmail.com

Abstract. During surgery, the nervous system is at risk if surgeon could not localize nerve's location. In case of tumor blocked, the surgeon can completely not visualize the nerve due to the tumor. Hence, nerve localization is very important during to operation. Generally, the neurophysiologic intra-operative monitoring (NIOM) has alarming feature, when the surgeon irritated the nerve, they could pre-localize the nerve. However, this alarming is quite sensitive since it sometime alarms even when the surgeon hints other area expected the nerve. This would makes the surgeon qualitative evaluates location of the nerve. This study proposed the new modality of nerve localization. The nature of compound muscle action potential (CMAP) was used in this study. Given a frequency-based electrical stimulation to a targeted area, the CMAP would response if and only if the stimulating electrode was placed directly to the nerve. The results from preliminary study in animal revealed that applying the stimulation at 30Hz and 0.3Volt with 1.5 millimeters width of a bipolar electrode gave highest CMAP detection accuracy (97.5%).

Keywords: Electrical Nerve Stimulation, Nerve Localization, EMG, CMAP.

1 Introduction

Nerve localization during surgery is very important. For example, in the case of vestibular schwannoma, cranial nerve 7th (facial nerve) possibly be damaged by the surgeon due to a blocked tumor. If the facial nerve is permanently damaged, the patient would be facial palsy. Presently, there is a commercialized product available called neurophysiologic intra-operative monitoring (NIOM). The NIOM has a feature that can alarm the surgeon when they are closing to the nerve. When a surgical tool irritates directly to the nerve, there will be a spike and burst of nerve discharge appear on a free running electromyography (EMG). This nerve discharge is then converted to sound which the sound level indicates a level of irritation [1-3]. Therefore, the surgeon can aware of damaging and pre-localize the facial nerve. However, this warning is

M. Lee et al. (Eds.): ICONIP 2013, Part I, LNCS 8226, pp. 352–359, 2013.

quite sensitive. Without directly irritating to the nerve i.e. during tumor removal or dissection, there still is a warning sound the surgeons and makes them qualitative evaluated location of the nerve. The surgeon sometime obsoletes this warning. There is another kind of nerve response called compound muscle action potential (CMAP), it normally uses for facial nerve function preservation [4, 5]. Given an electrical stimulus to the nerve, there will be a pulse response appears at some latency after stimulus. Amplitude of the CMAP response indicates a remaining nerve function. 50% decreasing in amplitude is considered as a safety criteria [4].

This study proposes a new technique of nerve localization that could help the surgeon quantitative localizes the nerve. We employed the nature of the CMAP response that it surely elicits when the stimulating electrode place exactly to the nerve. Instead of using the alarming sound from nerve irritation, this study used stimulating electrodes that contained electrical stimuli. We hypothesized that if we apply an electrical stimulation at some frequency, the CMAP would and would not response at the same frequency after applying the stimulus train to the nerve and other area (i.e. around the nerve and the tumor), respectively. Hence, we could identify whether a current position of a stimulating electrode is the nerve or not.

This work is a preliminary investigation that was studied in animal trials. The sciatic nerve of a rat is used for representing the facial nerve in a human. Agarose gel is use for mimicking a tumor tissue. There are many parameters that need to be figured out for being an optimally frequency-based electrical stimulation i.e. frequency, voltage, pulse duration and the width between anode and cathode.

2 Materials and Methods

2.1 Signal Acquisition and Electrical Nerve Stimulation

The experiment was conducted under animal ethic approval. This study included 4 sciatic nerves of 2 male Sprague-Dawley rats (age, 8 weeks; weight, 300 grams). Fig. 1(a) shows an overview of the signal acquisition and the electrical nerve stimulation systems. Bipolar needle electrodes that placed on the Tibialis anterior, Gastrocnemius, Vastuslateralis and Semimembranosus muscles of the rat's leg are used for EMG signals recording. These EMG signals were sampled at 1 kHz sampling frequency and amplified by 200 gains in the biomedical instrument named "BIOPAC MP35" (BIOPAC systems, Inc., USA). This study used a constant voltage stimulator called "BSLSTMB Stimulator" (BIOPAC systems, Inc., USA) for applying electrical nerve stimulation. The BSLSTMB stimulator generates a defined voltage level and frequency to the sciatic nerve via bipolar needle electrodes as shown (See Fig. 1(b)) and also sent the pulses feedback to the acquisition system.

The "BIOPAC BSL 4.0 MP35"software was used for electrical nerve stimulation and signal recording setups, monitoring and recording all of the acquiring data (EMG, pulses feedback). During the experiment, sound and video were recorded via a webcam synchronously with the signal acquisition time.

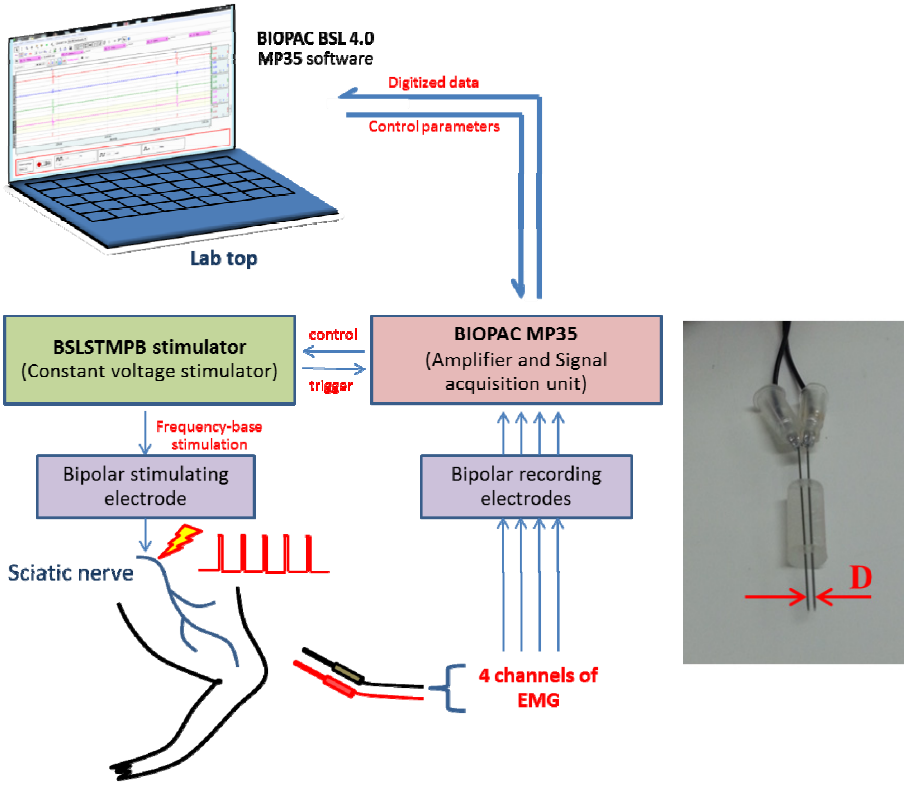


Fig. 1. (a) Block diagram of signal acquisition and frequency based electrical nerve stimulation. (b) The bipolar stimulating electrode was fixed at the width D.

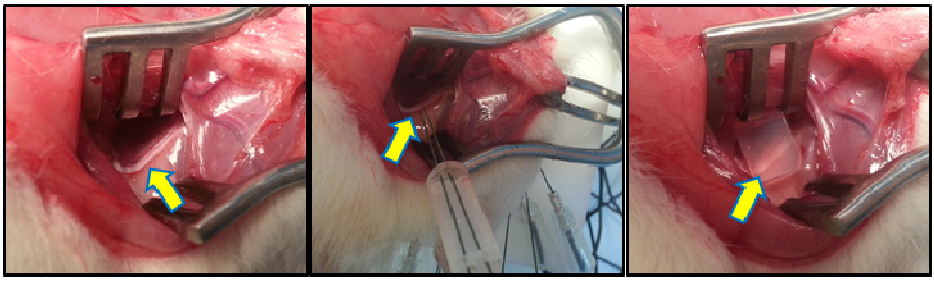
2.2 Experimental Procedure

When all equipment mentioned in the Fig. 1(a) was completely setup, the experiment was first started on the left sciatic nerve by the sequent as follows;

1. Anesthetize the rat by 80 mg/kg ketamine and 10 mg/kg xylazine and wait until the rat was anesthesia [6].
2. Place a needle electrode subdermally to the defined locations on the operating leg. The ground electrode was placed at the anterior part of the higher hind limb.
3. Start surgery to find the sciatic nerve. Fig. 2(a) shows a picture of the sciatic nerve.
4. Perform mind irritation by a pure needle electrode and the forceps direct to nerve and around the nerve.
5. Fix the bipolar stimulating electrodes at 1 mm width by the handmade needle holder as shown in Fig. 1(b). This width would not greater than the targeted nerve (approximately 1.8 mm diameter of facial nerve [7]).

6. Apply the frequency based electrical stimulation directly to the nerve and around the nerve by varying frequency[1] and voltage[2]. Fig. 2(b) was capture during the experiment when applying electrical stimulation directly to the nerve.
7. Repeat the 5th and 6th sequences with 1.5 mm width of the bipolar needle electrode.
8. Place a mimic tumor tissue to the nerve as shown in Fig. 2(c). This tumor phantom is agarose gel that was prepared by mixing agarose powder with PBS (Phosphate Buffer Saline, pH 7.4). 0.65% agarose gel was considered as a realistic brain phantom [8]. However, the density of a tumor mass is higher than brain matter. Hence, this study used 1% agarose gel for mimicking a tumor tissue.
9. Push directly to the mimic tumor tissue by a pure needle electrode and the forceps.
10. Fix the bipolar needle electrodes at 1 mm width.
11. Apply the frequency based electrical stimulation directly to mimic tumor tissue by varying frequency and voltage at 15, 30, 45 Hz and 0.15, 0.20, 0.25 and 0.30 volt, respectively.
12. Repeat the sequent number 2-11 to the right side of the rat's sciatic nerve.

After both sciatic nerves were operated, the rat was terminated by over dosing at three the anesthetic dose [6].



(a) (b) (c)

Fig. 2. Rat's sciatic nerve; (a) the location of the sciatic nerve, (b) the sciatic nerve during stimulation and (c) the mimic tumor (Agarose gel) on the sciatic nerve

2.3 CMAP Responses Detection

The recorded 4 EMG channels were filtered by digital highpass filter at 300 Hz cut off frequency. Given electrical pulse stimulation directly to the nerve, the CMAP response was elicited as shown Fig. 3 (red/thick line). Conversely, applying a stimulus to other area, there was no CMAP response appeared after stimulation (See Fig. 3

[1] The varied frequencies (15, 30, 45 Hz) were assumed which based on refractory period of the neuron (10 ms) [7]. Therefore, maximum frequency should not exceed a half of 100Hz.

[2] The varied voltages (0.15, 0.2, 0.25, 0.3 volt) were assumed according to the voltage different of action potential (depolarization (30mV) – membrane potential (-70mV) = 100 mV) [7]. Therefore, the stimulating voltage should higher than 0.1 volt.

(blue/thin line)). Regarding to the characteristic of the CMAP, it has high variation compared with none CMAP signal. Hence, we could simply detect the CMAP by calculating the variance of the CMAP response comparing with the baseline.

Samples between 1-8 milliseconds after stimulus were segmented according to the feedback stimulation pulse. An array of this sample was used for calculating the variance. If the variance of a target array is greater than **threshold × base line variance**, this response would be considered as CMAP. This base line variance was calculated from a normal condition.

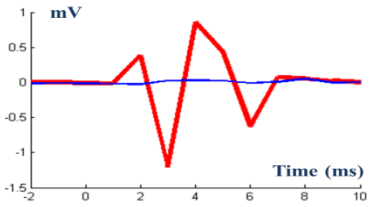


Fig. 3. CMAP (red/thick line) and none CMAP responses (blue/thin line) after given electrical stimulus (at time zero)

3 Results

There was no significant change of EMG signals when irritating direct and indirect to nerve by pure needle electrode. When the nerve was irritated by the forceps (surgical equipment), there was burst and spike of nerve discharge appeared on EMG data as shown in Fig. 4. In addition, irritating around the nerve and onto the mimic tumor also had those nerve discharge appeared on EMG signals.

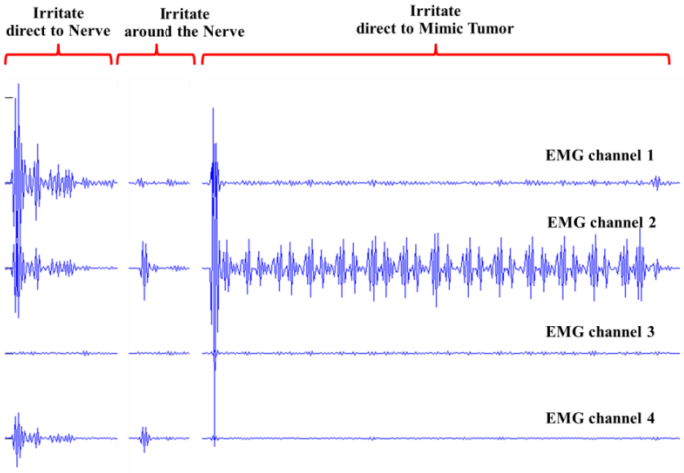


Fig. 4. Burst (a) and spike (b) of nerve discharge on EMG signals after irritated the nerve, around the nerve and onto the mimic tumor by the forceps

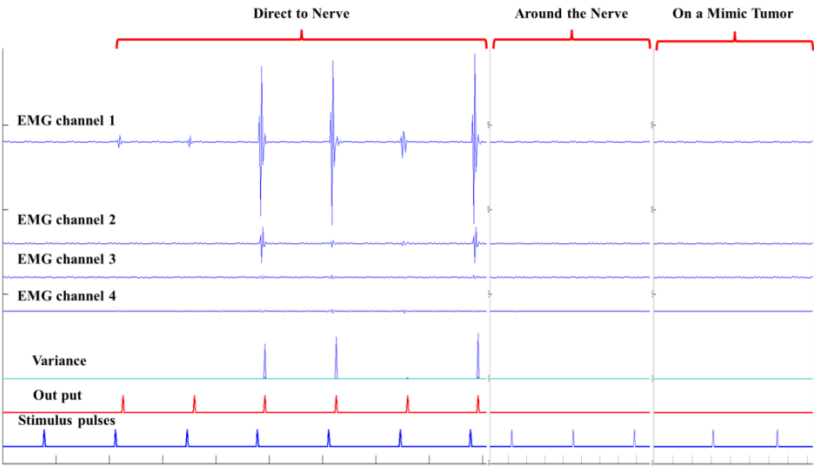


Fig. 5. EMG signal during applying frequency-based electrical stimulation onto the nerve, around the nerve and mimic tumor tissue

Fig. 5 shows the EMG signal during applying frequency-based electrical stimulation onto the nerve, around the nerve and mimic tumor tissue. The results revealed that there was the CMAP response elecited according to the stimulus pulse when the stimulating electrode was place right to the nerve. Conversely, placing the stimulating eletrode to other area could not activate any CMAP response. This information support our hypothesis and it could be used for nerve nerve localization. The EMG channels 1 to 4 were segmented according to the stimulus pulses (see Fig. 5 (bottom line)). The segmented EMG data was calculated variance compared with the base line variance. For offline analysis, this experiment was set the threshold at 100. The classification result was shown in Fig. 5 (red line)) that was able to detect the CMAP response.

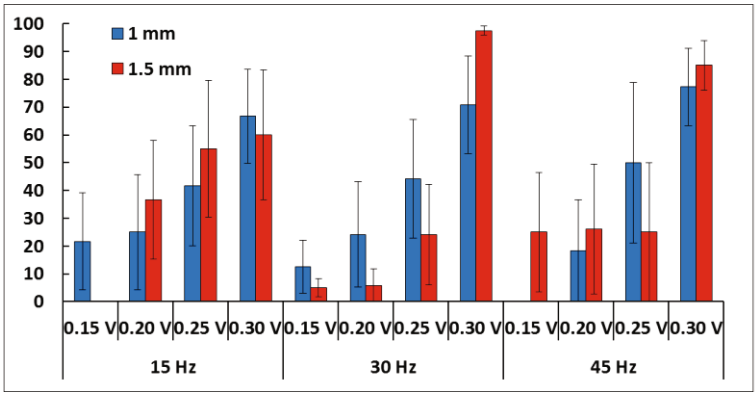


Fig. 6. The averaged CMAP detection accuracy of 4 sciatic nerves (2 rats). Red and blue bars are averaged accuracies of CMAP detection by 1 and 1.5 millimeters width of electrode.

Fig. 6 shows offline CMAP detection accuracy. This accuracy was averaged by 4 sciatic nerves. Red and blue bars are averaged accuracies of CMAP detection by 1 and 1.5 millimeters width of bipolar needle electrode, respectively. The stimulation was applied in 3 frequencies (15, 30 and 45 Hz) and 4 voltage levels (0.15, 0.20, 0.25 and 0.30 volt). The results showed that increasing in voltage level, the accuracy also increased in both 1 and 1.5 millimeters width electrode. 0% detection accuracy could be found at lowest voltage (0.15 volt). If the voltage was high enough (0.3 volt), the CMAP could response to entire stimulus pulse and make CMAP detection accuracy closed to 100%. The stimulation parameters of 30Hz and 0.30 volts showed greatest performance of CMAP detection accuracy.

4 Discussion

Burst and spike EMGs of nerve discharge were occurred when the nerve was irritated. However, this nerve discharge could be seen even when the surgical tool irritated other area for example; around the nerve and onto the tumor (See Fig. 4). This Burst and spike EMGs might be caused by tumor and nerve compression [1-3]. There was no nerve discharge after irritate the nerve by the needle. It might be caused from the small size of the needle electrode compared with the surgical tool.

There was no CMAP response after applied an electrical stimulation pulse to other area excepted for the nerve. This would be the new modality of nerve localization that could make the surgeon precisely and accurately localizing the nerve. The simple CMAP detection algorithm by calculating variance of a small sampling window would make the system rapidly detect the CMAP response in on-line experiment.

Given electrical stimulus at low voltage sometime could not activate the CMAP response and made the CMAP detection algorithm failed to detect. This might be caused by the different impedance in each position of a stimulation point. This problem could be solved by increasing the voltage level. However, applying at high stimulating voltage might damage the nerve. Nevertheless, there is another type of electrical stimulation called constant current stimulator which can regulate a current at the same level even when there is difference in impedance [9]. The problem of varying impedance might be solved by this stimulator. Stimulating frequency at 30 Hz showed a highest CMAP detection accuracy. The wider length between anode and cathode (1.5 mm) of bipolar needle electrode show a better CMAP detection accuracy. However, the width of the bipolar needle electrode should not be wider than the nerve bundle diameter. Otherwise, the nerve could not be stimulated due to the gap.

5 Conclusion

Irritating the nerve by pure needle electrode could not elicit burst or spike EMG. Hence, it was unable to use for nerve localization. The traditional technique of using the burst and spike EMG in NIOM could be used for nerve localization. However, the surgeon needs to have high experience due to the burst and spike EMG were sometime happened when the surgical equipment irritated around the nerve and onto the mimic tumor. This nerve localization method is qualitatively evaluated by the surgeon.

Applying the frequency-based electrical stimulation directly to the nerve could elicit the CMAP response while it could not occur in other areas (around the nerve and onto the mimic tumor tissue). By using this principle, we could then localize the nerve by detecting the CMAP response. The proposed CMAP detection algorithm could be detected CMAP response. The highest CMAP detection accuracy (97.5%) could be found when applying the frequency-based electrical nerve stimulation at 30Hz, 0.3Volt, 1 millisecond of pulse width and 1.5 millimeter width between cathode and anode. The study proposed the new modality of nerve localization. The present study successfully identified and localized position of the sciatic nerve in a rat model. We believe that the proposed method could also be used for nerve localization in the human model. The surgeon could more quantitative localize the nerve by using our proposed technique.

Acknowledgement. This projected is supported in part by Thailand Center of Excellence for Life Sciences (TCELS) and the Government funding of Mahidol University, Thailand.

References

1. Kombos, T., Suess, O., Kern, B.C., Funk, T., Pietilä, T., Brock, M.: Can continuous intraoperative facial electromyography predict facial nerve function following cerebellopontine angle surgery? Neurol Med. Chir (Tokyo) 40, 501–507 (2000)
2. Romstöck, J., Strauss, C., Fahlbusch, R.: Continuous electro-myography monitoring of motor cranial nerves during cerebellopontine angle surgery. J. Neurosurg. 93, 586–593 (2000)
3. Prass, R.L., Lüders, H.: Acoustic (loudspeaker) facial electromyographic monitoring: Part 1. Evoked electromyographic activity during acoustic neuroma resection. Neurosurgery 19, 392–400 (1986)
4. Amano, M., Kohno, M., Nagata, O., Tahiguchi, M., Sora, S., Sato, H.: Intraoperative continuous monitoring of evoked facial nerve electromyograms in acoustic neuroma surgery. Acta Neurochir. 153, 1059–1069 (2011)
5. Silverstein, H., Willcox, T.O., Rosenberg, S.I., Seidman, M.D.: Prediction of facial nerve function following acoustic neurona resection using intraoperative facial nerve stimulation. Laryngoscope 104, 539–544 (1994)
6. Meredith, A., Redrobe, S.: The BSAVA Manual of Exotic Pets, 4th edn. John Wiley & Sons (2002)
7. Chen, Z.J., Gillies, G.T., Broaddus, W.C., Prabhu, S.S., Fillmore, H., Mitchell, R.M., Corwin, F.D., Fatouros, P.: A realistic brain tissue phantom for intraparenchymal infusion studies. J. Neurosurg. 101(2), 314–322 (2004)
8. Marieb, E.N., Hoehn, K.: Human Anatomy & Physiology, 8th edn. Pearson (2010)