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Relaxofon: A Neuromuscular Blockade Monitor for Patients Under General Anesthesia

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Abstract— **Anesthesia consists of three components: unconsciousness, analgesia and neuromuscular blockade (NMB). A specific drug is administered by the anesthesiologist to control these different components. In this paper we propose a new system for monitoring the neuromuscular blockade in anesthesized patients during surgery. Neuromuscular blockade drugs are used routinely by clinicians to induce muscle relaxation in patients. However, the use of these drugs has some risks, so an adequate monitoring of the effects of these drugs is essential. This paper describes the Relaxofon, a NMB monitoring device based on phonomyography. The Relaxofon is composed of a hardware subsystem that records muscle sounds using microphones and a special circuit to filter out the noise and amplify the signal, and a software subsystem that analyses the acquired signal. We tested the ability of the system to record phonomyographic signals from the adductor pollicis and the corrugator supercilii muscles. We then performed the Bland-Altman test to compare the manual Train-of-Four ratio (a measure of the depth of muscle relaxation) calculation against the one performed by the Relaxofon. Finally, we calculated the Pearson correlation coefficient to measure the linear dependence between the two methods. Automatic Train-of-Four ratio calculations using this system showed very good agreement with manual calculations. Results from this work may ultimately lead to integration of NMB monitoring to an automated closed-loop anesthesia system.**

I. INTRODUCTION

GENERAL anesthesia consists of inducing loss of consciousness and sensation during a surgical procedure. It comports three components: hypnosis, analgesia and muscle relaxation.

This paper focuses on muscle relaxation, also known as neuromuscular blockade (NMB). Muscle relaxants allow anesthesiologists to induce NMB, and are used routinely for many procedures in modern anesthetic practices. They are often used to ensure patient immobility and facilitate surgical exposure in select procedures [1]. They are also given to facilitate tracheal intubation, and adequate relaxation of the vocal cords is one of their desired effects [2]. However, the use of neuromuscular blockade drugs (NMBD) is not without risk. An overdose might lead to postoperative pulmonary complications [1]. It is therefore essential to monitor the effect of NMDBs on patients. This is done by stimulating a motor nerve and analysing the evoked muscle response. Several methods of NMB monitoring are used to detect and analyse the induced muscle response [3].

Mechanomyography (MMG) measures the actual force developed by the muscle [3]. However, MMG requires meticulous preparations and precautions, and can only be used to measure the response at the adductor pollicis (AP) muscle located in the hand [3]. Electromyography (EMG) measures the action potential after muscle contraction. It is less cumbersome than MMG, and could be used on most muscle sites of interest in clinical practices [3], [4], [5], [6]. Nevertheless, EMG of smaller muscles is difficult because of the small action potential created [3], and EMG is sensitive to electromagnetic interferences. Acceleromyography (AMG) measures the acceleration produced by a contracting muscle, and is based on Newton's second law of motion given by the following equation: $Force = mass \times acceleration$. The use of AMG, however, is limited, and is difficult with muscles that do not create a distinctive movement [3]. Despite their reliability, the aforementioned methods are not perfect. They are not always easy to use, they do not allow the study of all the muscles sites, and they are high-priced.

Phonomyography (PMG) is another method of NMB monitoring and is the basis of the Relaxofon, a NMB monitoring device described in this paper. The Relaxofon is an instrument that measures the low frequency sounds emitted by contracting muscles. It is composed of a hardware subsystem that records the muscle sounds, and a software subsystem that analyses the signals.

This paper is organized as follows. In section II we give a little background about the project. In section III we describe the developed system discussing the different modules it is constituted of. Results are given in section IV. Finally, section V concludes the paper.

II. BACKGROUND

A. Phonomyography

Phonomyography is based on the fact that low frequency sounds are emitted by contracting muscles. Grimaldi first described muscle sounds in 1665 [7]. The most frequently used transducers to record muscle sound are microphones and capacitive accelerometers [8]. The signal can be recorded at the skin surface, and frequencies below 50 Hz represent about 90% of the signal power spectrum [9], so it is important to have adequate sensitivity to record low frequency signals. The recorded signal is biphasic as shown in Fig. 1, and its most useful characteristic is the peak-to-peak amplitude.

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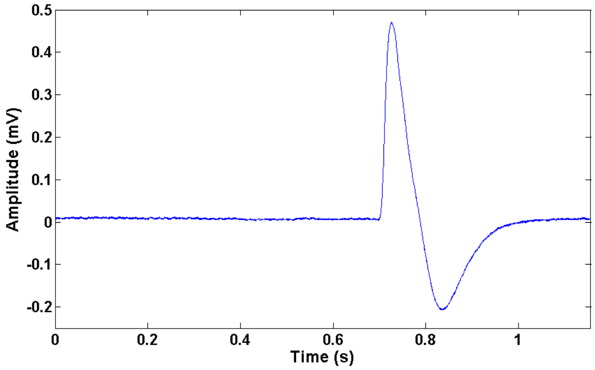


Fig. 1. Muscle sound signal shape.

When compared to other techniques such as the AMG and MMG, PMG showed good to very good agreement [2], [3]. One of the advantages of PMG is that it is an easy-to-apply, non-invasive technique. PMG has been tested in several research centers, but is still not available commercially.

B. Train-of-Four Stimulation

Train-of-four (TOF) stimulation is one of the most widely used patterns for monitoring neuromuscular functions [10], [11]. It consists of a delivery of a square wave stimulus of 0.2 msec duration at a frequency of 0.5 Hz using a peripheral nerve stimulator. TOF monitoring is very useful in evaluating the level of intra-operative relaxation, using what is known as a TOF-ratio. The TOF-ratio is obtained by dividing the peak-to-peak amplitude of the fourth muscle twitch by the peak-to-peak amplitude of the first muscle twitch. It is a dimensionless value, ranging from 0 to 1. Fig. 2 shows the evoked response after a TOF stimulation.

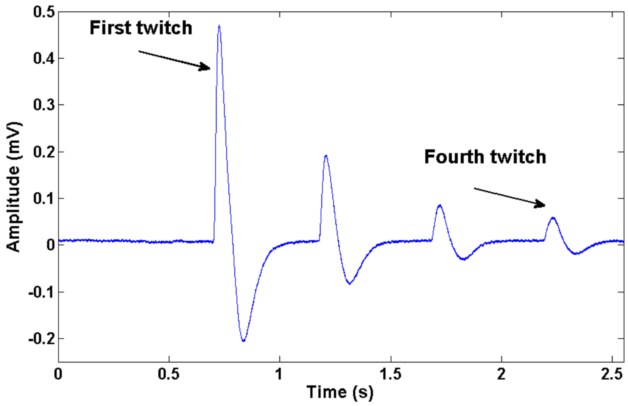


Fig. 2. The evoked response due to a train-of-four stimulation of a partially relaxed muscle.

A TOF-ratio between 0.15 and 0.25 usually indicate an adequate surgical relaxation [3]. A TOF-ratio greater than 0.9 indicates a sufficient recovery of neuromuscular transmission for safe extubation following surgery [12].

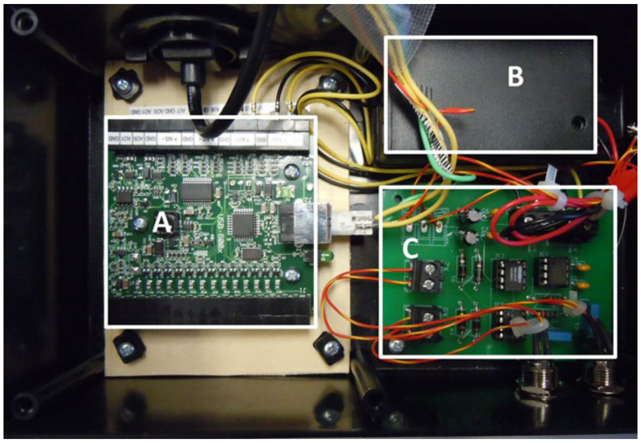


Fig. 3. Hardware subsystem of the Relaxofon: A) USB data acquisition system, B) battery compartment and C) signal acquisition circuit.

III. RELAXOFON

The hardware subsystem of the Relaxofon is detailed in Fig. 3. It is composed of three components: a USB data acquisition system (NI USB-6009, National Instruments, Austin, TX, USA), a battery compartment and a dual channel signal acquisition circuit.

Two piezoelectric microphones, model UFI 1010 (UFI, Morro Bay, CA, USA), were used as input of the dual channel acquisition circuit due to their small size and high output. The microphones are connected to a precision instrumentation amplifier (INA114, Texas Instruments, Dallas, TX, USA) that creates an impedance matching with a unity gain, and reduces the microphone's sensitivity to electromagnetic noise. Following that, we employed a passive low-pass filter (LPF) with a cut-off frequency of 70 Hz corresponding to the frequency domain of the acoustic signals in question. Finally, at the output of the LPF, a voltage follower was implemented in order to make the filter more robust and less sensitive to parasitic variations at its output. Fig. 4 details the schematic of the dual channel acquisition circuit.

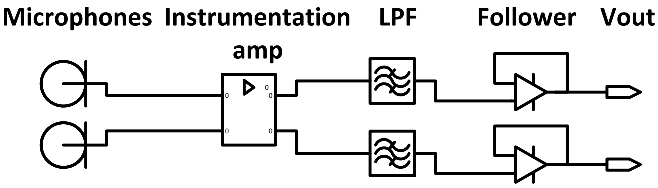


Fig. 4. Schematic of the dual channel acquisition system.

After testing the circuit on a breadboard, a double layer layout was drawn using EAGLE 6.1 (Cadsoft, Pembroke Pines, FL, USA) and printed (Fig. 3 C) to reduce the electromagnetic noise caused by connection wires. There are no metallic parts on the microphones in contact with the test subjects. In this prototype, the front-end is not isolated; however, this will be addressed in future iterations of the design.

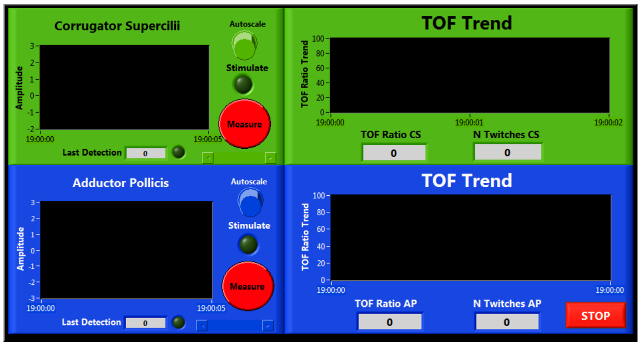
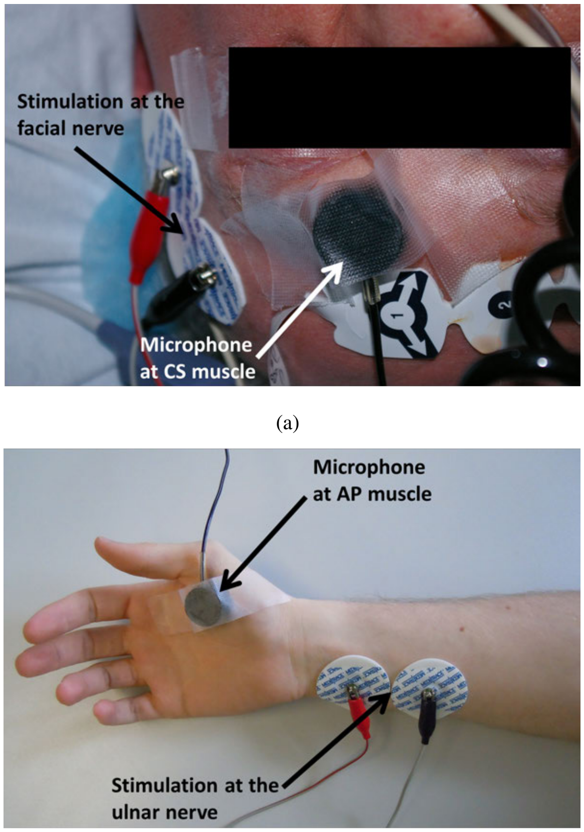


Fig. 5. The Relaxofon user interface.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(a)

(b)

Fig. 6. Microphone and peripheral nerve stimulator electrode positioning: (a) for the corrugator supercilii muscle and (b) for the the adductor pollicis muscle.

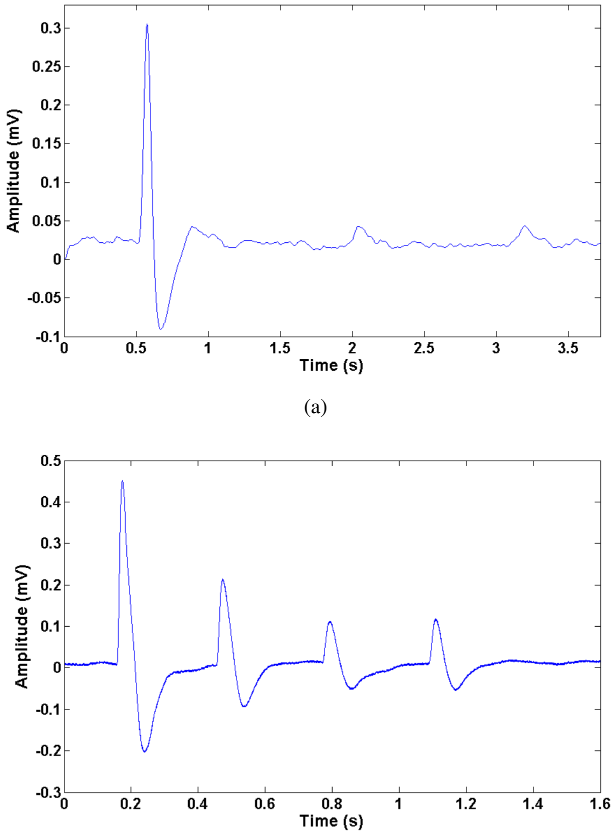
The signals are transferred to a computer via the USB data acquisition system where a program is used to analyze and calculate the TOF-ratios. The program is written in LabVIEW 2010 (National Instruments, Austin, TX, USA), and the user interface (UI) is shown in Fig. 5.

The UI is divided into two parts for the muscles we are studying, the corrugator supercilii muscle (CS) (in green) located at the medial end of the eyebrow (Fig. 6(a)), and the adductor pollicis muscle (AP) (blue) located in the hand (Fig. 6(b)). For each muscle, the system plots the raw phonomyographic signal recorded at the muscle's site, and a history of the calculated TOF ratio for each measurement.

Once the microphones and electrodes are properly positioned on the patient as shown in Fig. 6, we start the data acquisition and give a train-of-four stimulation to the muscle of interest, using an external peripheral nerve stimulator (Innervator NS 252, Fisher & Paykel, Auckland, New Zealand). The acquisition will automatically stop after 3 seconds, since the duration of the stimulation is only 2 seconds. When the acquisition stops, the program will analyze the signal: it will detect the maxima and minima, count the number of twitches (equals to the number of maxima), calculate the peak-to-peak amplitude of every twitch, and if four twitches are detected, calculate the TOF-ratio by dividing the fourth twitch by the first twitch. The number of twitches and the TOF-ratio are prominently displayed on the program's interface for both muscles as shown in Fig. 5.

IV. RESULTS

The system was tested on an anesthetized patient during surgery. The Relaxofon successfully recorded the phonomyographic signals at the CS and AP muscle sites as illustrated in Fig. 7. Following signal recording, the system was able to calculate the TOF-ratio after each stimulation. We then calculated the TOF-ratio manually to test the precision of



(a)

(b)

Fig. 7. The recorded phonomyographic signals using the Relaxofon: 7(a) at the corrugator supercilii muscle site and 7(b) at the adductor pollicis muscle site.

our system. We studied the agreement between Relaxofon calculated TOF-ratios and manually calculated TOF-ratios. Results are tabulated in Table I and are partitioned into two groups by their TOF-ratio ranges: from 0 to 30% and from 70 to 100%. The mean difference of TOF-ratios determined using the Relaxofon and manually and the limits of agreement between the two methods were analyzed using the Bland-Altman test [13]. For TOF-ratios ranging between 0 and 30%, the mean bias was -0.26% with limits of agreement of -1.17 to 0.65% and a precision of 0.91%. For TOF-ratios ranging between 70 and 100% the mean bias was 3.7% with limits of agreement of -6.2 to 14% and precision of 9.87%. For the two groups combined, the mean bias was 1.7% with limits of agreement of -6.33% to 9.73% and a precision of 8.03%.

TABLE I

TOF-RATIOS: RELAXOFON VS. MANUAL CALCULATION

	From 0% to 30%		From 70% to 100%	
Measurement	Relaxofon	Manual	Relaxofon	Manual
1	11.8%	12.0%	75.8%	76.0%
2	15.0%	15.2%	99.6%	85.9%
3	18.0%	17.4%	85.1%	84.9%
4	18.0%	18.0%	99.6%	95.5%
5	17.7%	17.9%	90.8%	90.0%
6	17.0%	18.0%	89.0%	90.1%
7	18.2%	19.0%	100%	90.5%
8	26.7%	27.0%	100%	97.7%

The bias is calculated by taking the average of the differences between the two methods ($\bar{d}$). The limits of agreement represent a confidence interval (CI), and we are 95% confident that the difference between Relaxofon and manual calculation will lie between these limits. This interval is calculated using the following formula: $\bar{d} \pm 2s$, where s is the standard deviation of the difference between the two methods [13]. The precision is calculated as $2s$.

These results show excellent agreement for clinical purposes. The calculated precision varies from 1% to 10%, showing that even on the most pessimistic interpretation there is not a clinically significant difference between the two methods.

To further illustrate the agreement between Relaxofon and manual calculations, we calculated the Pearson correlation coefficient. The correlation coefficient was 0.996 (significance of $P < 0.0001$). This correlation coefficient indicates an excellent relationship between the two methods [14], [15].

V. CONCLUSION

This paper describes a perioperative neuromuscular blockade monitoring system for general anesthesia. The Relaxofon is able to record the phonomyographic signal of stimulated muscles in real-time, and calculate the TOF-ratio to inform anesthesiologists of the depth of relaxation of patients. The Relaxofon has an intuitive, user-friendly interface that provides the clinician with parameters pertaining to patients' neuromuscular blockade. The preliminary results show that the Relaxofon is a reliable device for perioperative neuromuscular blockade monitoring. Future plans include integrating this device to an automated closed-loop anesthesia system developed in our research laboratory [16]. Future plans also include integrating a peripheral nerve stimulator to the Relaxofon, to reduce the number of devices needed for the monitoring.

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