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Electrode Design for High Frequency Block: Effect of Bipolar Separation on Block Thresholds and the Onset Response

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Abstract— **The delivery of high frequency alternating currents (HFAC) to peripheral nerves has been shown to produce a rapid and reversible nerve conduction block at the site of the electrode, and holds therapeutic promise for diseases associated with undesired or pathological neural activity. It has been known since 1939 that the configuration of an electrode used for nerve block can impact the quality of the block, but to date no formal study of the impact of electrode design on high frequency nerve block has been performed. Using a mammalian small animal model, it is demonstrated that the contact separation distance for a bipolar nerve cuff electrode can impact two important factors related to high frequency nerve block: the amplitude of HFAC required to block the nerve (block threshold), and the degree to which the transient "onset response" which always occurs when HFAC is first applied to peripheral nerves, is present. This study suggests that a bipolar electrode with a separation distance of 1.0 mm minimizes current delivery while producing high frequency block with a minimal onset response in the rat sciatic nerve.**

I. Introduction

THE delivery of high frequency alternating currents (HFAC) to peripheral nerves has been shown to produce a rapid and reversible nerve conduction block at the site of the electrode [1]. This technique holds therapeutic promise for diseases and disorders associated with undesired neural activity including spasticity, peripheral pain and autonomic disorders such as hyperhydrosis, which are treated by neuro-destructive techniques in treatment resistant cases [2], [3].

It has been known since 1939 that the configuration of an electrode used for nerve block can impact the quality of the block [4], but to date no formal study of the impact of electrode design on high frequency nerve block has been performed. With few exceptions, high frequency nerve block studies have used multipolar nerve cuff electrodes for delivering HFAC to nerves [4]-[14]. This study focuses on a bipolar nerve cuff design, and evaluates the effect of the separation distance (SD) between the bipolar electrode contacts on two important factors related to high frequency nerve block: the amplitude of HFAC required to block the nerve (block threshold [12]), and the degree to which the transient "onset response" which always occurs when HFAC is first applied to peripheral nerves, is present. Achieving nerve block using the lowest possible amplitudes would be important for conserving power in an implantable nerve block system, and could prove to be important for maximizing nerve safety and electrode integrity during HFAC delivery [15]. Minimizing the degree of transient hyperactivity in the nerve seen at the onset of HFAC delivery (onset response) would be important for minimizing muscle contractions and afferent fiber activation in a clinical HFAC nerve block system.

This study shows that the block threshold amplitude and onset response do not trend together, and that a range of bipolar separation values exists where there is a tradeoff between lower current amplitudes and minimal onset responses.

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II. Methods

Experiments were performed using five adult Sprague-Dawley rats under institutional approval. The experimental setup was similar to that used by Bhadra and Kilgore 2005 [12]. The sciatic nerve was exposed by dissecting the posterior aspect of the leg and biceps femoris muscle. The common peroneal and sural nerves were severed. The

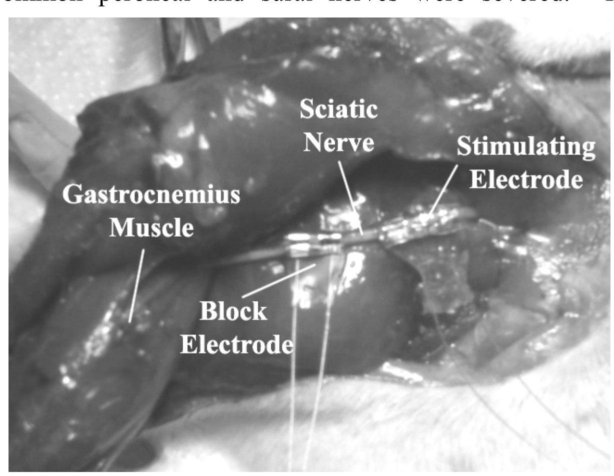

Fig. 1. Photo of experimental preparation in rat, showing proximal stimulating electrode and distal blocking electrode on the sciatic nerve. The gastrocnemius-soleus muscle complex is shown on the left of the figure.

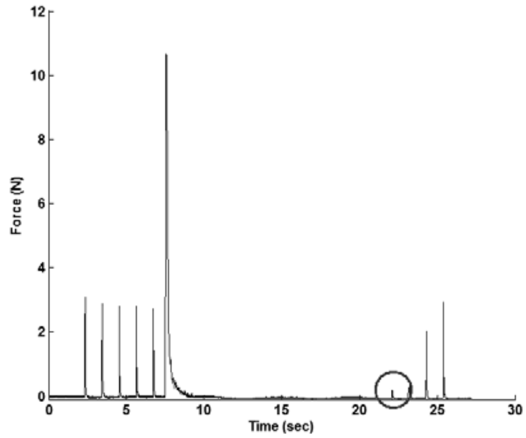

Fig. 2. Recorded force of the gastrocnemius muscle during HFAC nerve block threshold trial. The amplitude of the 40kHz sinusoidal waveform is decremented in 0.1mA steps until nerve conduction is partially restored (as indicated by the bold circle).

gastrocnemius-soleus muscle complex was dissected. The tibia was fixed to the experimental rig using a clamp, and the calcaneal tendon was attached to a force transducer using a toothed clamp. Two electrodes were placed on the nerve: a proximal tripolar stimulating cuff electrode was placed ~1 cm distal to the spinal column, and a distal bipolar blocking cuff electrode was placed just proximal to the branch point for the common peroneal nerve. The proximal electrode was used to deliver 1 Hz supramaximal 20 uSec pulses (Model S88, Grass Technologies), resulting in corresponding 1 Hz muscle twitches in the gastrocnemius-soleus muscle complex. The absence of the muscle twitches was an indicator of nerve block. For each trial, the distal blocking cuff electrode was placed on the nerve near the branch point for the common peroneal nerve. Bipolar electrodes with the following SD were used: 0.5 mm, 1.0 mm, 2.0 mm, 3.0 mm and 4.0 mm. Four bipolar SD were tested in each animal: 1.0 mm, 2.0 mm, 3.0 mm and 4.0 mm were tested in two of the animals, and 0.5 mm, 1.0 mm, 2.0 mm and 4.0 mm were tested in three of the animals. Each electrode had 1.0 mm of silastic between the edge of the platinum contact and the edge of the cuff. The order in which the electrodes were placed on the nerve was block randomized for each animal with three repeats. Two types of trials were performed: block threshold trials and onset response trials. For both types of trials a 40kHz zero-mean sinusoidal blocking current-controlled waveform was used (Model 6221, Keithley Instruments).

Block thresholds were measured using a procedure similar to that described by Bhadra and Kilgore 2005 [12]. For each trial the HFAC amplitude was initially 9.0 mA_{peak}, and after approximately 5 seconds (to ensure that the onset response had subsided) the amplitude was decremented by 0.1 mA per second until muscle twitches were detected. The lowest amplitude at which no muscle twitches were present was determined to be the block threshold for the trial. For the trials in which 9.0 mA was not sufficient to block the nerve, the trial was repeated starting at 11.0 mA. For one trial 11.0 mA was not sufficient to block the nerve, and the block threshold was measured using a starting amplitude of 13.0 mA.

Each block threshold trial was followed by an onset response trial. These trials were performed by delivering a six second burst of HFAC to the nerve. The timing of these trials was under computer control. Two parameters were extracted from the gastrocnemius force recordings for each six second burst. The peak force, which occurs at the beginning of each burst, and the "onset area": the integral of the gastrocnemius force over the first five seconds of HFAC delivery.

III. Results

Figure 2 shows an example trial of a block threshold trial performed for this study. This data is typical of complete HFAC motor block [12], and shows a trial in which the block threshold was found by decreasing the blocking current amplitude until partial block results in small amplitude muscle twitches (as indicated by the bold circle). The 1 Hz muscle twitches are the result of the proximal stimulation. HFAC was delivered with an amplitude of 9.0 mA from approximately 7.5 until 12.5 seconds in Figure 2 and was decremented in 0.1 mA/sec steps until approximately 22 seconds into the trial. The proximally generated nerve impulses are completely blocked by the HFAC (as indicated by the absence of twitches) until the HFAC amplitude was decreased to below block threshold, where partial conduction block occurs at approximately 22 seconds. After the termination of the blocking current at approximately 24 seconds, the proximally generated twitches return as full nerve conduction is restored.

Figure 3 shows the experimentally measured block threshold as a function of the bipolar SD. In the figure, solid diamonds represent the mean for all trials and the error bars represent the standard error of the mean. Thresholds showed a non-monotonic trend with bipolar SD. Thresholds were highest for an electrode SD of 0.5 mm, reached a minima for SD in the range of 1-2 mm, and increased with SD beyond 2 mm. The error bars in Figure 3 represent the standard error of the mean.

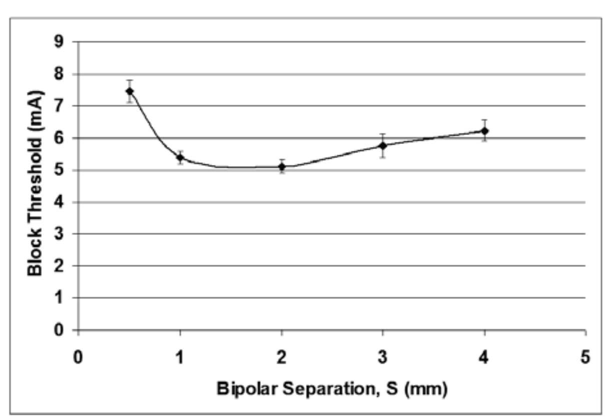

Fig. 3. Experimentally measured block thresholds (mA) with different bipolar contact separations (SD). Solid diamonds represent the mean block threshold for all experiments, error bars represent standard error of the mean.

Figure 4 shows the experimentally measured block onset area as a function of the bipolar SD. In the figure, solid diamonds represent the mean for all trials, and the error bars represent the standard error of the mean. Small onset areas were measured for bipolar SD of 0.5 mm and 1.0 mm. There is a trend of increasing onset area with increasing SD, with the largest onset areas measured for a SD of 4.0 mm.

As shown in Figure 5, changes in bipolar SD resulted in no substantial reduction in the Phase I onset response as measured by peak force. In the figure, solid diamonds represent the mean for all trials and the error bars represent the standard error of the mean.

IV. Discussion

The results presented in this study demonstrate that the bipolar electrode contact SD affects both the amount of current required to achieve complete neural conduction block and the size of the onset response. The trends in these responses however do not move in the same directions. This suggests that different mechanisms may be responsible for the observed phenomena. Modeling of the neuronal dynamics of single axons subjected to high frequency currents has been performed for monopolar point source electrodes using several axon models [7], [8], [16], [17]. Similar models simulating multipolar electrodes may prove useful for elucidating a biophysical explanation for the trends presented in this study.

This study has demonstrated that, over the range of values tested, the optimal SD for reducing the amount of current required to achieve complete high frequency conduction block in the rat sciatic nerve is 1.0 – 2.0 mm. This study has also shown that the optimal SD for reducing the onset area is 0.5 - 1.0 mm over the range tested.

Although the bipolar SD had a significant effect on the onset area, it resulted in no substantial reduction in peak force of the onset response. This also suggests that there may be at least two mechanisms responsible for the onset response. In many trials, particularly for an SD of 0.5 mm, the duration of the onset response was only approximately 100 ms and had a shape similar to a single muscle twitch. We postulate that for nerves of larger diameter these distances will scale up but will still retain a similar relationship.

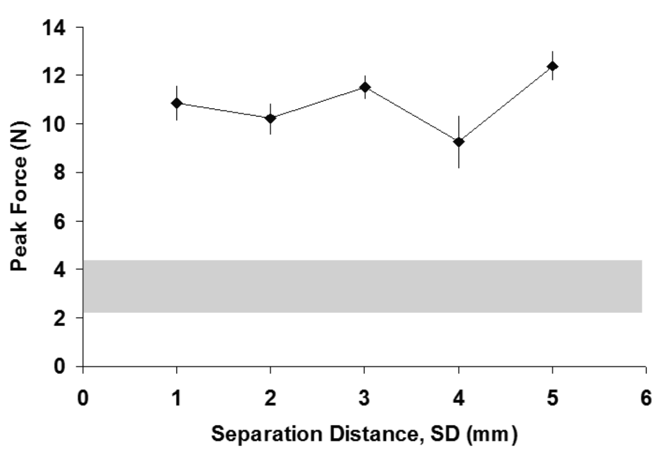

Fig. 5. Experimentally measured peak force (N) with bipolar contact separation (SD). Solid diamonds represent the mean peak force for all experiments, error bars represent standard error of the mean. The shaded region represents the force range for a proximally generated muscle twitch.

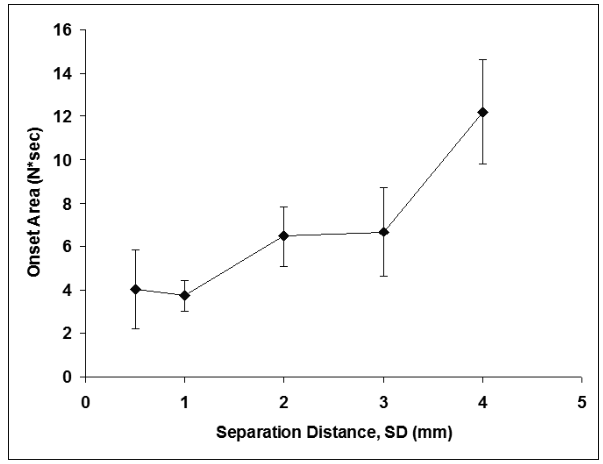

Fig. 4. Experimentally measured onset area (N*sec) with bipolar contact separation (SD). Solid diamonds represent the mean block threshold for all experiments, error bars represent standard error of the mean.

When selecting an electrode design for a clinical high frequency peripheral nerve block application, factors such as the tolerable degree of the onset response, safe levels of current delivery (yet to be formally studied) and minimizing power consumption will be considered. This study shows how the contact separation distance of a multipolar electrode can be used to affect total current delivery and the degree of the onset response.

For the rat sciatic nerve, a bipolar electrode with a separation distance of 1.0 mm seems to provide a solution with minimal current delivery and minimal onset. If minimizing the onset response is a priority, then a separation distance of 0.5 mm could be used at the expense of a higher block threshold. It could also be possible to make use of both portions of this design space by using an electrode with four contacts. The inner pair with SD of 0.5 mm could be used for the initial current delivery to generate a conduction block with minimal onset. After establishing conduction block, the outer pair with SD of 2.0 mm could be used to maintain the block with a lower current amplitude.

V. Conclusion

We have shown through whole nerve animal experiments that block thresholds have a non-linear relationship with bipolar electrode contact separation distance, and that there is a narrow range of bipolar separations for which the block threshold has a minima. We have also demonstrated that the onset response area increases with bipolar separation distance. For the rat sciatic nerve, a bipolar electrode with a separation distance of 1.0 mm seems to provide a solution with minimal current delivery and minimal onset. Computer models simulating multipolar electrodes may prove useful for elucidating a biophysical explanation for the trends presented in this study.

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