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Simulation Study on the Effect of Fiber Loss to the Compound Action Potential of a Sural Nerve

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Abstract— **This paper reports the result of computer simulation about compound action potential of a sural nerve with and without fiber loss. A compound action potential is a wave of electric potential detectable on the skin after electric stimulation of a peripheral nerve. The loss of nerve fibers, which is observed in some neuropathies, is considered as the cause of low amplitude and slow conduction of the wave. To quantify the relationship between fiber loss and compound action potential, computer simulation of the stimulation of a human sural nerve was executed. As a result, the conduction velocity of the first negative peak of the compound action potential was substantially reduced in case of thick fiber loss, and was slightly enlarged in case of thin fiber loss. However the amplitude of the peak was not always reduced. The effect of thin fiber loss was observed in the amplitude of the second positive peak and the second negative peak.**

I. Introduction

Measurement of skin potential over a peripheral nerve after electric stimulation of the nerve is a common method for diagnosis of any malfunction of peripheral nerves. This method, generally called a nerve conduction test, is both practical and noninvasive. Reductions of amplitude and delay of the conduction velocity of the measured waveform obtained by a nerve conduction test are recognized as typical signs of nerve damage.

The degree of damage to a sural nerve is a possible factor for estimating the condition of various nervous diseases, especially diabetes mellitus, because the distal nerve tends to be affective first in metabolic disorders. Also, a biopsy can be performed as it does not include motor nerve fibers. Morphological research has revealed that a decrease in the number of nerve fibers and demyelination are often seen in the nerves of diabetic patients [1]–[5]. However, it is quite difficult to estimate the amount of nerve fibers that have disappeared or the extent of the damage to myelin sheaths. To find the relationship between the condition of a damaged nerve and the measured potential, computer simulation seems an efficient methodology.

As the sources of the potential are the axonal currents of each fiber inside the nerve, it appears important to consider and compare the distribution of the axonal current of normal nerves and injured ones . Therefore, in this paper, we introduce an electric current model of an active nerve after electric stimulation to ascertain electric features of degenerated sural nerves.

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II. Methods

A. Fiber model

Each fiber was modeled as a cable of a Ranvier's node [6]. Although the original was a model of a myelinated nerve fiber of an amphibian, the magnitude of each elements was changed to conform with a fiber of a human being. The correlation between the fiber diameter D [m] and axonal diameter d [m] was formulated with the following equation as:

$$d = 0.76D + 1.37 \times 10^{-7}. \tag{1}$$

The internodal length L [m] was also formulated as a function of D as:

$$L = \begin{cases} 102D + 7.15 \times 10^{-5} \\ \quad (D \leq 1.2 \times 10^{-5}) \\ \\ 4.68 \times 10^{-4} \ln(D/9.74 \times 10^{-7}) \\ \quad (D > 1.2 \times 10^{-5}) \end{cases} . \tag{2}$$

These equations were obtained by fitting a curve to an anatomical data [7]. The other parameters to define the characteristics of the ion dynamics of the membrane were obtained in accord with experimental data of human sural nerves [8].

B. Maximum excitable distance

The equivalent circuit during stimulation of a nerve fiber can be drawn as Fig. 1. Where G_e denotes the conductance generated by the external medium causing the current flow between the electrode and Ranvier's node or the myelin sheath. G_e may be described as:

$$G_e(n) = \frac{1}{4\pi r(n)\rho_e} \tag{3}$$

where $r(n)$ is the distance between the electrode and the nth node, and ρ_e denotes the conductivity of the external medium. The excitation of a nerve fiber was defined by the existence of increase of the electric potential at the Ranvier's node nearest to the stimulating electrode after 100 μsec from the stimulation ceasing. The threshold distance l_e to make the fiber excitable was found for every fibers with different diameters.

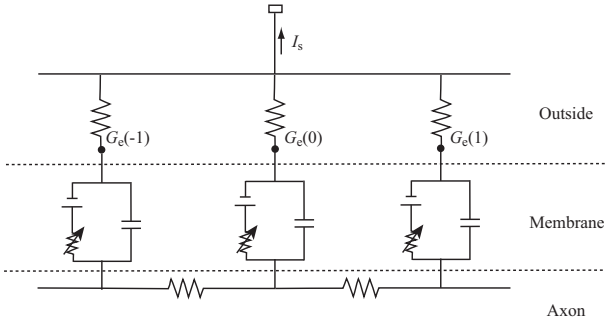

Fig. 1. An equivalent circuit of a nerve fiber under stimulation. I_s: stimulus current, G_e: conductance between each node and the cathode.

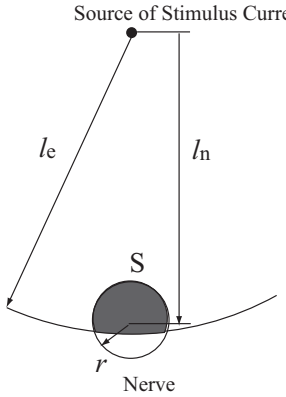

Fig. 2. The principle for the approximation of the sum of the axonal currents of nerve fibers inside a nerve.l_n: the distance between the cathode and the core of the nerve, r: the radius of the nerve, l_e: the threshold distance to make a fiber having the same property excite.

C. Total axonal current

Nerve fibers with a specific diameter inside a nerve were assumed to have uniform distribution in a cross section. For n threads of nerve fibers of diameter D, the sum of the axonal current at the position x can be described as $i_D(x)$. If the rate of the number of excitable nerve fibers of diameter D were to be $e(D)$, then the total amount of the axonal currents $I_n(D)$ can be described as:

$$I_{n,D}(x) = n(D)e(D)i_D(x). \tag{4}$$

Here $e(D)$ is the rate of the common area S to the cross section of the nerve and a circle with its center located at the electrode for stimulation, having a radius l_e, to the area of the cross section of the nerve (Fig.2). It can be described as:

$$e = \frac{S}{\pi r^2} \tag{5}$$

where r denotes the radius of the nerve. Therefore, the total axonal current I_n would be expressed as:

$$I_n(x) = \int n(D)e(D)i_D(x)dD. \tag{6}$$

D. Compound action potential

The compound action potential produced by the activity of the nerve was calculated on the assumption of quasistatic

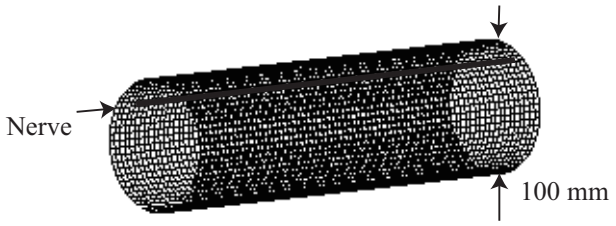

Fig. 3. A cylindrical boundary of conductor used in this simulation. A straight nerve was located 10 mm in depth from the surface of the boundary.

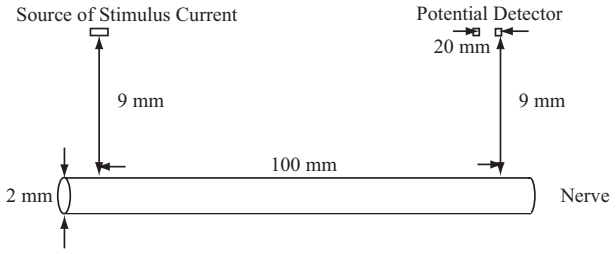

Fig. 4. The assumed location of the electrodes. An electric current stimulator and a potential detector were located 10 mm apart from the core of the nerve.

condition. After quantizing I_n into an array of electric current dipoles at intervals of 1 mm, The electric potential on the surface of the boundary was calculated with boundary element method [9].

III. Condition of the Simulation

A. Conductor and nerve model

The nerve was laid in a cylinder 350mm long at the depth of 10 mm from the surface. The nerve was assumed as a straight, 2 mm diameter (Fig. 4). It was constructed as a bundle of myelinated nerve fibers with diameters ranging from 1 to 17 mm. The number of fibers of each diameter was as in an earlier anatomical study of human sural nerves [7]. The cylinder was filled with homogeneous conductor of 20 S/m. The outside of the cylinder was assumed as a complete insulator.

As the distribution of nerve fiber diameter, histograms shown in Fig.5 were assumed. (a) is the distribution of a normal sural nerve obtained by Behse [7]. To investigate the effect of diameter dependent fiber loss to the electric potentials, the histograms (b)-(j) were assumed. Different stages of progress of large fiber loss ((b)-(e)) and small fiber loss ((f)-(j)) were simulated.

B. Stimulation model

A rectangle current pulse of 100 mA amplitude and 100 μsec duration was given at a point 10 mm away from the core of the nerve. A semi-infinite homogeneous conductor was assumed between each fiber and the point of the current injection. Mutual electrical interaction between fibers was neglected.

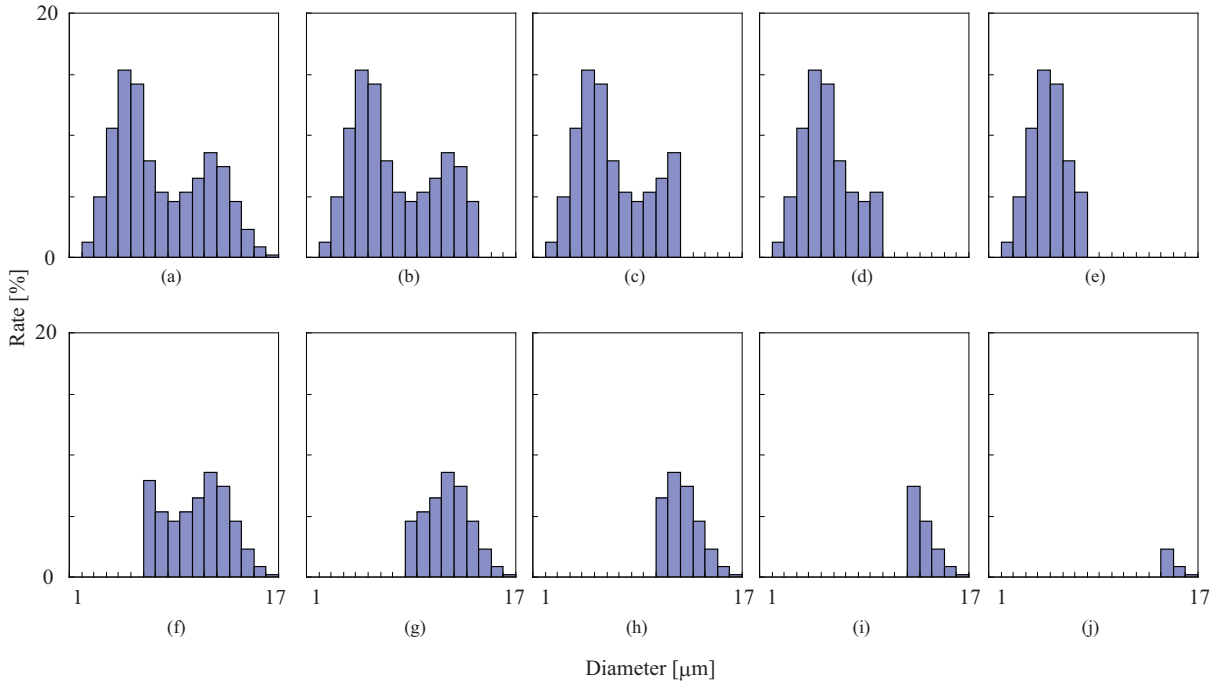

Fig. 5. The assumed histograms of fiber diameter inside a nerve. (a): normal distribution, (b)-(e): large fiber loss from slight to severe cases, (f)-(j): small fiber loss from slight to severe cases.

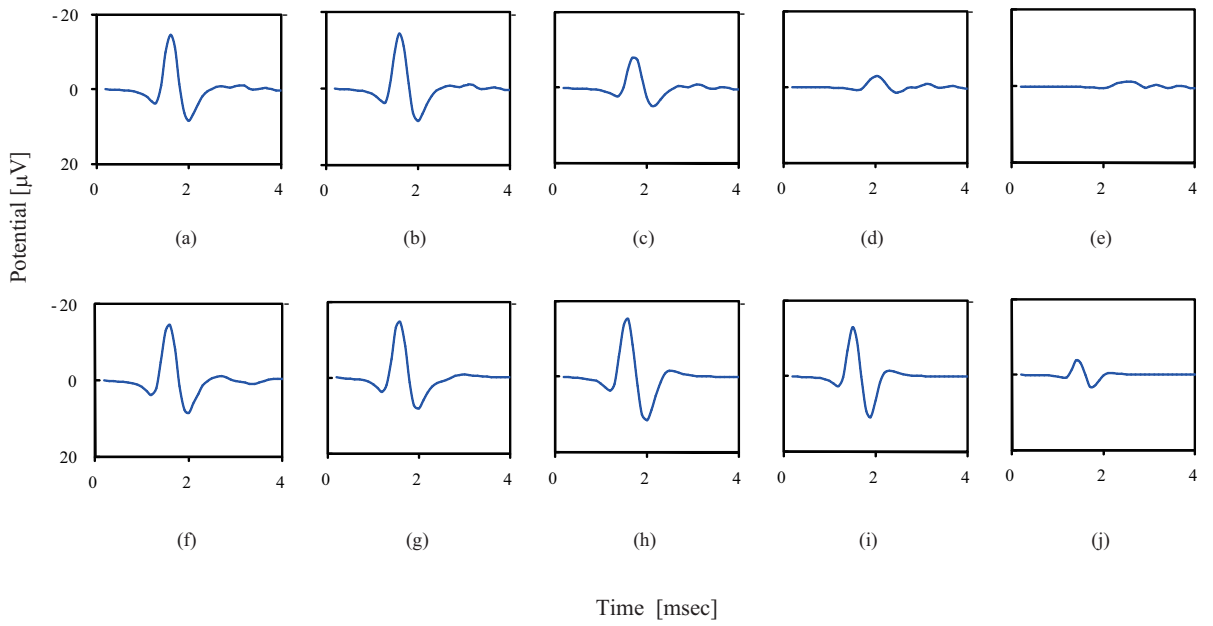

Fig. 6. Simulated timecourses of the compound action potential. Each plot is correspond to the histograms in Fig.5.

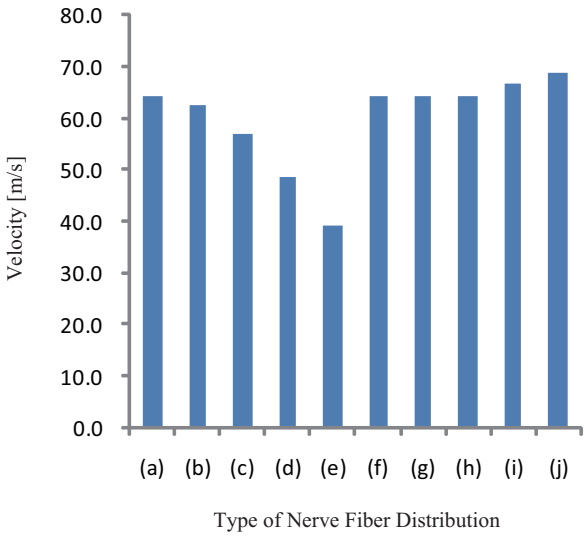

Fig. 7. Conduction velocity of the first negative peak of the compound action potentials (a)-(j) in Fig.6. Thick fiber loss decreased the velocity, and thin fiber loss increased it. The amount of increase was not prominent to that of decrease.

IV. Result

Fig. 6 shows the obtained potential wave. The amplitude of the negative peak in the plots (c), (d), (e), (i) and (j) was smaller than the peak of the normal case (a). This is consistent with the common knowledge that the decrease of the amplitude reflects the loss of large nerve fibers. As in the distribution (c) nerve fibers thicker than 12 μm diameter are lost and in the distribution (i) nerve fibers thinner than 12 μm diameter are lost, the loss of nerve fibers larger than about 10 μm seems to make the peak smaller. However in cases of (b), (g) and (h), slightly larger wave was observed. In (h) and (i), large second positive peak was also observed.

The loss of thick fibers made the conduction velocity of the first negative peak slow, whereas the loss of thin fibers made it fast. (Fig.7)

V. Discussion

The reduction of the amplitude and the conduction velocity of the first negative peak of the compound action potential are considered as a sign of neuropathy. Even in recent reports, evaluation of these parameters was carried out experimentally. [10]–[12] This means that these measures are correlative to neuropathy, however the result of this study showed that the relationship is not always sure. At the early phase of diabetic neuropathy or in arsenic intoxication, fiber loss is limited to thin fibers. The typical histogram of nerve fiber diameter in this case may be drawn as from (f) to (j) in Fig.5. In a common knowledge, nerve conduction study cannot detect the loss of thin fibers. As shown in Fig.7, in our simulation, the effect of small fiber loss to the velocity of the first negative peak was observed, but rather small in comparison with the effect of large fiber loss to the velocity of the peak. However our result also showed that the shape of the second positive peak and the second negative peak reflects it. Although it is difficult to analyze these components as their amplitude is small in comparison with the first nagative peak in practice, it may be possible to detect the loss of thin fibers by focusing these components of the potential wave.

VI. Conclusion

The compound action potential of a sural nerve with fiber loss was simulated. The result showed that thick fiber loss caused slow conduction velocity of the first negative peak of the potential wave, which is consistent to the common knowledge. However in case of thin fiber loss, the velocity slightly increased, and the amplitude of the second positive peak increased in spetial cases of nerve fiber distribution. Measuring these components may be significant to estimate the loss of thin nerve fibers.

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