Chapter

Examination of New Parameters from F-Wave Waveform Using Addition Averaging Method

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Abstract

To evaluate the excitability of the spinal motor neural function, F wave in evoked electromyogram is often used. As the dominant nerve to the muscle was electrically stimulated, retrograde action potentials are transmitted from the stimulation point to the anterior horn cells of the spinal cord. Action potentials that are regenerated in the anterior horn cells of the spinal cord are transmitted to the muscle in an anterograde manner, which are recorded at the muscle. From this route, because F wave can be measured from the whole body nerve, it has been used in various situations. Usually, it is characteristic that the waveform of F wave appears in variety. In other words, the same waveform does not appear in healthy people. However, the same waveform may appear when a certain disease occurs. It has been reported that the same waveform called “repeater F” appears in patients with neurological diseases. However, techniques and experience are required to analyze the waveform, and it is not widely used in clinical practice. This article will explain the F waves in terms of neurophysiology and investigate whether the averaging method can be applied to F-wave waveform analysis.

Keywords: F-wave waveform, usefulness of the addition averaging method, correlation coefficient, same waveform, F-wave parameters

1. Introduction

When we move, the electrical signals are generated in the brain through the spinal cord, and muscles contract, which causes movement. In the electrical signal transmission, although the function of the spinal cord is important, there is no consensus on the function (i.e., spinal cord excitability). The F wave which is an evoked electromyogram is one of the means to reflect the excitability of the spinal cord. Although the generation mechanism of the F wave will be described later, the F wave is characterized by various waveform shapes that can be usually recorded. On the one hand, in cases of spinal cord disease and cerebral infarction, the F wave with same shape may be recorded. Recently, due to these characteristics of the F wave, the excitability of the spinal cord has been utilized for grasping the pathological condition of neurological disorders. On the other hand, the analysis for the waveform of the F wave varies depending of the researcher, and the F wave appears in various ways; it has not yet been established as one evaluation. Hence, the ultimate objective is to establish an analysis method of waveform with low cost.
and effort and to improve the versatility of the analysis method in clinical setting. I will explain the F waves in terms of neurophysiology and investigated whether the averaging method can be applied to F-wave waveform analysis. In this article, we will explain with a brief reference to the physiological aspects of the F-wave generation mechanism in order to understand waveform analysis more deeply. The same waveform appears in motor nerve demyelinating diseases and diseases involving degeneration of spinal anterior horn cells. However, the same criterion for waveforms may differ from each researcher. Therefore, we found the same criterion using the correlation coefficient. The usefulness of the addition averaging method in waveform analysis was examined using the reference value of the same waveform and will be introduced here.

2. Outbreak mechanism and characteristics of F wave

F waves conduct retrogradely toward the center when a certain electrical stimulus is afforded to the α motor neuron (hereinafter αMN). Originally, the axon does not reach the cell body due to impedance mismatch (resistance $\Omega = V/I$) at the axon hillock. Therefore, the spinal cord anterior horn cells do not fire and do not generate F waves. However, when spikes cross the axon hillock and reach the anterior horn cells of the spinal cord due to some effect, they propagate to the dendrites and generate SD (soma-dendritic) spikes there. This spike reaches the axon hillock that has escaped from the absolute refractory period and conducts the axon antegrade from there, resulting in compound muscle action potential (CMAP) evoked from the governing muscle [1]. Nerve fibers have an absolute refractory period of 1 ms, and if the spike returns during the period corresponding to the refractory period of the axon hillock, no F waves can be generated because they cannot be conducted antegrade. Also, αMN has a structure of antidromic inhibition via Renshaw cells. Antidromic inhibition takes 2 ms, and it takes 1 ms to return from the axon hillock to the spinal cord anterior horn cells. In other words, in order to generate the F wave, the spinal cord anterior horn cells must reignite and conduct to the periphery between 1 ms after the absolute refractory period of the axon hillock has ended and 2 ms before antidromic inhibition of Renshaw cells. Whether or not the axon hillock is out of the absolute refractory period is determined by slight timing differences, and this is thought to significantly affect the incidence of F waves [1, 2]. In addition, the following three conditions are considered in which the F wave is likely to occur: (1) the hyperpolarized state in the cells increases the time required for conduction to the dendrites, which makes it easier to avoid the absolute refractory period of the axon hillock; (2) reduction of the absolute refractory period; and (3) excessive depolarization of the axon lowers the threshold level, making spikes more likely to occur with small stimuli [1] (Figure 1).

![Figure 1.](image)

F-wave generation mechanism.
Although the F wave is conducted antegrade by refiring of the spinal cord horn cells and can be recorded, refiring does not occur in all neurons. Furthermore, the probability of firing the same cell with each electrical stimulation is usually low, and re-excitation occurs only once every 10–100 times [1]. Komori et al. reported that 1406 F waves were evoked by a total of 1957 electrical stimuli in 10 cases, which consisted of 1160 waveforms, of which 1033 (89.1%) had only 1 occurrence [3]. F waves can be evoked from most motor nerves, but the nerves used mainly for examination are the median nerve, ulnar nerve, and tibial nerve. Among these nerves, the ulnar and tibial nerves have a persistence close to 100%. In addition, the normal value of the F-wave persistence varies among researchers. For the median nerve, Komori and Suzuki et al. reported more than 40%, and Fisher et al. reported 79–100%, but if too high, they may suspect spasticity, a disorder of upper motor neurons. There are reports of peroneal nerves in the nerves targeted for F-wave tests, but it is said that there are cases of difficulties in Japanese people even in healthy subjects [4, 5]. In the background, Japanese people are suspected of having a potential peroneal neuropathy due to the unique Japanese culture such as sitting straight custom. Hirashima et al. reported that CMAP (M-wave) amplitude increased by peroneal nerve stimulation since 1995 [6] and examination of the peroneal nerve is now being examined.

3. Relationship between F wave and motor unit

In the anterior horn of the spinal cord, there are neurons of various motor units (motor neuron pool). A motor unit is a unit composed of motor neurons, and the muscle fibers are governed by the neurons. One F wave appears due to the combination of refiring motor units. The F-wave waveforms are different due to the combination of the motor units and the timing shift; therefore, the F wave has a feature in which its waveforms appear in a variety. There are three types of motor units. The S type (slow-twitch type) is small in size and slow in contraction speed. The FF type (fast-twitch fatigable type) is large in size and fast in contraction speed but is easily fatigued. The FR type has characteristic between S type and FF type. When a person exerts, it depends on the number of motor units activated (recruitment) and the frequency of firing of motor neurons (rate coding) [7].

Henneman reports that there is a strong correlation between motor neuron size and recruitment order [8]. When exercising, there are rules that are mobilized in order from smaller motor units to larger motor units (size principle) [1, 2, 7]. Small motor neurons have a low stimulus threshold and are easy to fire even with weak input. The percentage of motor units varies from muscle to muscle. Enoka reported that 92.5% of S-type motor neurons and 7.5% of FR-type motor neurons dominated in gastrocnemius muscles. Similarly, the musculus interossei dorsales pedis and triceps brachii muscle were dominated mostly by small motor neurons [9].

When humans exert their power, fluctuations in rate coding, in addition to recruitment of motor units, have a great effect, too [10, 11]. For example, in a study by Moritz et al., as the muscle contraction strength of the musculus interossei dorsales pedis of the hand was gradually increased, the rate coding of firing and the number of motor units increased, and the contraction strength reached 60% or more (against maximum contraction strength). At 60% or more contraction, most of the work was done only by increasing the rate coding. In the case of F wave, it has no effect on one waveform, but F wave treats the average value of the waveform obtained by 16 or more stimuli. At that time, the rate coding of the same motor unit with respect to the number of stimulations is reflected [12].
From the above, it is necessary to adjust the rate coding of firing of units of various sizes according to the scene. When various units fire, they appear in the waveform of the F wave, and the rate coding is directly reflected in the persistence of the F wave. In other words, it can be said that the waveform and appearance persistence of the F wave reflect the motor unit. However, it has been reported that when the number of anterior horn cells decreases or degenerates due to spinal cord anterior horn cell disease or motor neuron damage, the firing of the same unit is biased and the F wave shows the same waveform. Evaluation the F wave reflecting the unit this way has the potential to lead to an objective evaluation of muscle output and voluntary motion.

4. F-wave parameters

4.1 Latency (ms)

Latency is the time taken of an electrical stimulation conduction to reach the spinal cord anterior horn cells and return to the dominant muscle. This parameter is most commonly used in clinical practice and is a highly reproducible index. In addition, the shortest rise latency in the recorded F wave is called the minimum latency, which reflects motor fibers with fast conduction time. Conversely, the longest rise latency is called the maximum latency, which reflects motor fibers with slow conduction times (Figure 2). The speed of conduction is said to be affected by height, limb length, and skin temperature. Speed of conduction is particularly reduced in diseases that affect the myelin of peripheral nerves (e.g., Guillain-Barre syndrome, Charcot-Marie-Tooth disease, etc.) [1].

4.2 Amplitude (μV)

Amplitude represents the magnitude of the waveform. There are two types of measurement methods. The first is the baseline to peak amplitude. The second is the peak-to-peak amplitude of the negative and positive vertices (Figure 3). We used
the second peak-to-peak amplitude this time to analyze the waveform, including
the positive wave. To normalize the amplitude of the F wave, the amplitude F/M
ratio is expressed by the ratio divided by the peak-to-peak amplitude of the M
wave when the maximal stimulation is given to the motor nerve. It is said that if the
amplitude F/M ratio shows a value of 5% or more, the possibility of upper motor
neuropathy is suspected [13].

4.3 Duration (ms)

Duration indicates the time from the rise of the amplitude of the F wave to its
return to the baseline. However, depending on the waveform, the position to return
to the baseline is unclear, and care must be taken when using this index because it
may be affected by the experience value of the measurer. In the case of the median
nerve, the location where the F wave is generated is on the baseline after the genera-
tion of the M wave, so it is difficult to define the baseline (Figure 4).

4.4 Persistence (%)

Persistence indicates the ratio of the appearance of the F wave to the total
number of stimulations. Analysis of only one waveform is not sufficient because
the F wave has different waveforms at each stimulus. Komori et al. reported that sufficient reproducibility was obtained with more than 50 stimuli [14]. Currently, Kimura et al. have generally analyzed using the average value of F waves obtained at least 16–30 times or more stimuli.

Others analyze the number of negative vertices of the waveform. There is also an index called Fchronodispersion which indicates the variation of latency from the difference between the minimum latency and the maximum latency.

5. Characteristics of disease and F-wave waveform

Among peripheral neuropathies (neuropathies), abnormalities of F-wave waveform due to motor nerve disorders have been reported mainly by Kimura et al. [1, 15–19]. There are reports of Guillain-Barre syndrome [15–17], Charcot-Marie-Tooth disease [19], and diabetic neuropathy [20, 21], which are diseases in which motor nerves are predominantly impaired. There are reports related to spasticity, one of the pyramidal tract disorders [22–25]. In recent years, there have been many reports of amyotrophic lateral sclerosis that is an intractable disease in which both upper and lower motor neurons are degenerated [1, 2]. In neuropathy, demyelination of axon myelin sheaths inhibits jump conduction and slows the conduction speed. As a result, it is easy to obtain a result such as a delay in the rise latency and a decrease in the persistence of the F wave. These diagnoses can be determined by latency which has high reproducibility among F-wave parameters.

The authors focused on abnormal F waveforms in disorders involving upper motor neuron disorders and spinal cord anterior horn cell degeneration. In cases of spasticity among stroke, Suzuki et al. report that as the electrical stimulation intensity is increased, the waveform of the F wave appears more like the H wave as the degree of muscle tone and tendon reflex increases [26]. In addition, Suzuki et al. measured F waves obtained from the abductor of the thumb by median nerve stimulation in one case of cerebrovascular disease and compared the disease duration at 9 months, 52 months, and 70 months later. Meanwhile, physical therapy was given. As a result, they reported that as the duration of physiotherapy increased, the amplitude of F waves decreased, and the waveforms varied. In addition, improved hand muscle tone and voluntary motion. Komori et al. also reported that the amplitude of F waves increased with spasticity [25]. However, other researchers measured F waves when median nerve stimulation was applied to 14 stroke patients, and the latency and persistence were not significantly different between the non-paralyzed side and the paralyzed side. The persistence of motor unit has been reported to decrease significantly on the paralyzed side regardless of the degree of muscle tone [23, 27]. In the case of amyotrophic lateral sclerosis, atrophy of the anterior horn cells of the spinal cord reduces the number of motor units and the number of firing anterior horn cells, so the persistence decreases significantly, and the same waveform begins to appear [27]. Similarly, spinal and bulbar muscular atrophy (SBMA) has been reported to produce F-wave waveform with similar characteristics [28–30].

6. Regulation of the same waveform

F waves with matching latency and amplitude values may appear when spasticity due to stroke or when atrophy of the spinal cord horn cells occurs, such as in ALS and SBMA. This is known as “repeater F.” This repeater F is reported
to significantly appear more in patients with diabetic polyneuropathy, ALS, carpal tunnel syndrome, ulnar neuropathy, and L5 radiculopathy than in healthy subjects [1, 2, 31, 32].

The authors wondered how it is difficult to determine the consistency of the waveforms using only the amplitude value or the latency and how to judge the waveforms to be the same. Some studies report the same waveform as an analysis item, but few describe the judgment method in detail. Some of the methods described for determining the same waveform include the following: (1) a method of visual judging by superimposing recorded waveforms [3, 33], (2) a method of determining the correlation coefficient between waveforms at a value of 1.00 [34, 35], and (3) in recent years, some researchers have decided to develop their own analysis software [36]. There is a risk that the evaluation method can be used only by those who are familiar with F waves when using the visual observation to determine the same waveform, because the degree of match defined as the same waveform includes individual differences.

6.1 Regulation of the same waveform using correlation coefficient

The authors examined the relationship between the results that three researchers familiar with F waves judged visually the same waveform and the results of the correlation coefficient calculated from the data [37]. The target waveform is a waveform of 30 shots derived from the musculus abductor pollicis brevis by median nerve stimulation of a healthy person for 5 trials. A total of 150 waveforms were prepared. We asked each researcher to select the same waveform in a separate room to avoid interference. The data processing method of the F wave was a moving average of three terms using Microsoft Excel. The correlation between the waveform after the moving average and the raw waveform was an extremely high value of R = 0.9963, which sufficiently reflects the raw waveform. Next, the correlation coefficients of all combinations of waveforms evoked by applying 30 electrical stimuli per trial were calculated. The waveforms visually judged the same waveforms selected by two or more out of three people.

The results showed that the same waveform was selected by the 2 individuals as 10 waveforms, of which 9 (90%) showed a correlation coefficient of 0.95 or more. Next, the waveforms selected by the three persons had two waveforms, and both waveforms showed a correlation coefficient of 0.95 or more. It was suggested that the number of correlation coefficients R = 0.95 may be one index of the same waveform when analyzing the waveform of the F wave (Table 1).

However, one waveform judged to be the same waveform was recognized, although the correlation coefficient was 0.71. They were similar in waveform

| Correlation coefficient | Total number checks |
|-------------------------|---------------------|
| 0.95 or more             | 9 (90%)             |
| 0.95–0.90                | 0 (0%)              |
| 0.89–0.85                | 0 (0%)              |
| 0.85 or less             | 1 (10%)             |
| **Total**                | **10**              |

Table 1.
Results of the selection of the same waveform.
but slightly different in latency when the actual raw waveforms were checked. Therefore, the latency was shifted by 0.625 ms until the negative peak matches with the visual confirmation; as a result the waveform showing a correlation coefficient of 0.71 showed a correlation coefficient of 0.96.

Although the waveforms were the same in this study, the different latencies suggested that the correlation coefficient was low. We thought that the slight shift in the rise latency was affected the time it took for the spike to occur in the spinal cord anterior horn excitation threshold. This time the evoked musculus abductor pollicis brevis is composed of 115–171 motor units, considering the possibility that the rise latency could be shifted due to the spatial relationship of the cell bodies when cells are similar in size during refiring. Komori et al. allow for differences in negative peak latencies up to 1 ms when comparing the reproducibility of F waves [38]. It may be necessary to consider such differences in latency when analyzing the same waveform.

7. Research using the addition averaging method

An analysis method that takes into account the F wave, in which various waveforms appear, has not yet been established. In addition, there is a report on the F-wave method (F-MUNE) for estimating motor units using F waves. However, analysis requires time and effort, and versatility is poor at present [27, 39, 40]. Therefore, as stated in this introduction, we examined whether the averaging method is applicable to F waves to increase versatility by establishing simple analysis methods. The averaging method approaches 0 by averaging the waveforms that appeared in diversity with repeated stimuli. On the other hand, a waveform that appears at a fixed latency also appears as a waveform after overlapping and addition averaging [1]. In the case F wave appears in the diversification, the value become close to 0 when the addition averaging process is performed. The wave remains after the addition averaging process when the same waveform appears repeatedly. It may be possible to distinguish the same or similar waveforms if the addition averaging method is used to analyze the waveform of the F wave. However, there is a risk that the waveform may disappear due to a slight difference in latency when applying this addition averaging method to the analysis of the waveform of the F wave. Furthermore, meaning is still unclear what waveform is calculated by the addition averaging method, so we first examined the relationship between the averaging waveform and the raw waveform.

7.1 Previous research on waveform analysis using the addition averaging method

Eisen et al. [13] first studied F waves using the addition averaging method. They addition averaged the F waves obtained by giving 32 electrical stimulations into the tibial nerve of cerebrovascular patients and compared them with that of the healthy subjects. The waveform after addition averaging reported that the duration and amplitude could be reproduced in both cerebrovascular and healthy subjects [13]. In Japan, Komori et al. focused on the latency of the negative peak in order to pursue an evaluation method that combines reproducibility and simplicity in order to promote clinical application of F wave. The waveform after adding the negative peaks manually (addition method) showed that the reproducibility of the waveform was 86.7% for the median nerve and 73.3% for the tibial nerve, even when measured on another day [38]. Next, they reported that the waveform obtained by the addition averaging method sufficiently reflected the waveform of the proven addition method [41]. Sakamaki et al. point out that such as F waves, when negative waves
and positive waves appear at the same latency, may be offset when the addition averaging method is used for waveforms that appear in diversity [42]. Hiratsuka et al.’s research also tried to use the addition averaging method, but the amplitude was significantly reduced, making analysis difficult [43]. There have been fewer studies using the addition averaging method for F-wave analysis since the first half of 1988 from this background. There are other reports that use the addition averaging method for the F-wave analysis items [44–46], but only the latency and duration reflect the raw waveform, and it is a difficult situation to establish these as parameters.

7.2 Relationship between F-wave persistence and addition averaging waveform

We reexamined the usefulness of the addition averaging method, taking into contents what Sakamaki pointed out. First, we examined whether the persistence of F waves needs to be considered for the median nerve since the persistence of F waves differs for each nerve to be affected.

The method measured the F wave at rest and calculated the coincidence rate between addition averaging waveform for all waveforms and averaging waveform reflecting only F-wave appearance waveform. Subjects were 99 healthy volunteers (55 males and 45 females) who agreed to the study with an average age of 23.3 ± 5.3 years. The F wave was obtained by electrically stimulating the median nerve of the non-dominant upper limb. From the measured F waves, the waveform after addition average of the “waveform data of 1 trial (30 shots) (thereafter, TW)” and “waveform data of only the F-wave appearance waveform (thereafter, AW)” was obtained using Microsoft Excel. Next, the correlation coefficient between the two waveforms after addition average values was calculated using CORREL function. This correlation coefficient indicates the coincidence rate. The reference value of the same waveform used the correlation coefficient of 0.95 from previous studies. Next, a scatter diagram from the data of the F-wave persistence of each subject is created, and the coincidence rate is calculated using single regression analysis. The coefficient of determination (R2) is calculated, and the variation is obtained. It is examined whether the coincidence rate depends on the persistence of F wave. 80/99 subjects had a correlation coefficient between TW and AW of 0.95 or more, accounting for 80% of the total. Among them 38 subjects showed a correlation coefficient of 1.00, representing 38% of the total. 19/99 subjects showed a correlation coefficient of

Figure 5.
A circle graph showing the correlation coefficient of two addition averaging waveforms.
0.95 or less, accounting for 20% of the total (Figure 5). A scatter plot showing the persistence of F wave and the coincidence rate is presented in Figure 6.

The coefficient determination (R) was 0.53, indicating “somewhat correlated.” The highest F-wave persistence was 60%, and the lowest value was 10% in the group that showed a concordance rate of 0.95 or less (thereafter, group A). The highest F-wave persistence was 100%, and the lowest value was 23% in the group that showed a concordance rate of 0.95 or higher (thereafter, group B) (Figure 6). The result we expected was that the higher the persistence of F waves, the higher the coincidence rate. However, those with a high coincidence rate and those with a low coincidence rate were recognized despite low persistence of F wave in group A and group B. Therefore, we confirmed the raw waveform of those with low persistence of F wave in both groups. Then, there were two factors that reduced the coincidence rate in Group A.

The first factor is that the persistence of F waves is significantly lower. The amplitude could be confirmed visually because the fewer the number of waveforms that appeared, the smaller the value to be divided. On the other hand, the amplitude value was lost because the denominator to be divided was large. From the above, it is considered that the coincidence rate of the two waveforms has a low value. This result is similar to the reported study of Hiratsuka et al. [43].

The second factor is that high-amplitude waveforms appear localized. It was considered that the addition averaging waveform of AW had a higher amplitude value and a lower coincidence rate because of appearing several high-amplitude waveforms. In group B, there were also two possible factors for the high coincidence rate despite the low persistence of F-wave appearance as in group A. The first factor is that the persistence of the F wave is around 50%, and the appearing waveform shows almost a similar waveform. The second factor is, even though the number of appearing waveforms was few, they were canceled out by the appearance of diversity which is also a characteristic of the F wave. As a result, we thought that the matching rate approached the baseline and showed a high value. We think that the tasks of making the persistence of F waves approach 100% using muscle contraction or evoked from tibial nerve are suitable when using addition averaging method to analyze F-wave waveform.

### 7.3 Method of addition averaging

#### 7.3.1 Normal or match of negative peak or match of rise latency

Compared with the commonly used amplitude F/M ratio, the amplitude value of after addition averaging waveform showed about 1/2 of the value [41]. It is
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considered to be the result of the overlap between the negative and positive waves as reported by Sakamaki and Takasu [42]. To avoid the reverse winding proposal, averaging was performed in three ways, and the ratio of amplitudes of addition averaging and the average of the values obtained for each stimulus were compared. The three ways of performing the averaging method are described below:

1. A method of addition averaging the recorded F wave as it is (normal).
2. A method of addition averaging after the match of negative peak.
3. A method of addition averaging after the match of rise latency.

Subjects picked up and analyzed one subject who showed 100% persistence of F wave. The results are shown in Table 2. The error amplitude F/M ratio was 2.0%, and the measured value was 25.79 μV during normal addition averaging. Next, the error when matching the negative peak was 0.43%, and the measured value was 39.59 μV. Finally, the error when the rise latency was matched was 0.67%, and the measured value was 62.05 μV. From the above, in the case of one subject this time, the average is usually the closest to the raw data, but it is necessary to increase the number of subjects and pursue it because it is the result of only one subject.

8. Conclusions

At the present time, when using the addition averaging method for the F-wave waveform analysis, (1) the constant criterion of the same waveform using the correlation coefficient should be 0.95, (2) the persistence of F waves when using the addition averaging method is at least 60% or more and (3) the normal addition averaging method has less error in the amplitude value compared to the raw data.

However, all the contents described this time are the analysis results of F waves evoked by electrically stimulating “median nerve.” Therefore, we will analyze the ulnar nerve, the tibial nerve, and the peroneal nerve in the same way as described at the beginning and examine the innervated nerves to which the addition averaging method is applicable. In addition, “cluster analysis” will be introduced to avoid pointing out the content of Sakamaki et al. In this analysis method, similar waveforms are collected to create a cluster. By carrying out the cluster analysis before the addition averaging, the similar waveforms can be classified, and the cancelation of the positive wave and the negative wave due to the variation in the latency can be avoided. In addition, you can see how many F-wave clusters make up one trial.

| Addition averaging | Common values | Normal | Match of negative peak | Match of rise latency |
|--------------------|---------------|--------|------------------------|-----------------------|
| Measured value (μV) | 185.97        | 160.18 | 146.38                 | 123.92                |
|                    |               | (-25.79)| (-39.59)              | (-62.05)              |
| F/M amplitude ratio (%) | 2.00       | 1.7    | 1.57                   | 1.33                  |
|                    |               | (-0.3) | (-0.43)               | (-0.67)              |

( ): Error value from common values

Table 2. Comparison of three addition averaging methods and average data.
during a case characteristic of F-wave waveform such as stroke with spasticity or ALS with atrophy of spinal cord horn cells.

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Conflict of interest

Nothing.

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