Correlation-based Method for Measuring the Duration of Motor Unit Action Potentials

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Abstract: We present a novel automatic method for measuring the duration of motor unit action potentials (MUAPs) and compare it with two state-of-the-art automatic duration methods on normal and pathological MUAPs. To this end we analyzed 313 EMG recordings from normal and pathological muscles during slight contractions. A "gold standard" of the duration positions (start and end markers) was obtained for each MUAP from the manual measurements determined by two expert electromyographists. The results of the novel method were compared to those obtained by the two automatic methods using the "gold standard" duration measures for the different groups of normal and pathological MUAPs. Several statistical tests were applied and showed that the novel method provided closer duration positions to the "gold standard" and fewer gross aberrant errors than those obtained by the two other methods in the four MUAP groups, being significantly different in many of the cases.

1 INTRODUCTION

The motor unit (MU) is the functional unit for the voluntary activation of the muscle. It comprises a motor-neuron and the muscle fibres (MFs) innervated by it. The order for contraction of these MFs comes from the spinal cord and ultimately from the brain as a train of action potentials traveling along the motor unit. When they reach the muscle fibres highly synchronized action potentials are generated in these fibres and they travel towards the tendons producing the contraction of the fibres. The potential wave observed by an electrode near the MU is called motor unit action potential (MUAP) and is dependent of the structure and function of the whole MU. Analysis of the MUAP is a central aspect of needle EMG studies and is applied for diagnosis in clinical neurophysiology practice.

The MUAP waveform is quantitatively characterized by several parameters of which duration is an essential one, as the rest of parameters are measured within the MUAP time span defined by its duration (Stalberg et al., 1986). MUAP duration is related to the number of muscle fibres in the MU and to the temporal dispersion of the activation times of the fibres and their conduction velocities (Stalberg et al., 1996).

The MUAP onset is usually an abrupt takeoff due to the muscle fibre depolarization. However the offset is more difficult to determine as the final phase of the potential returns to the baseline (BL) very slowly and asymptotically without a distinct end point (Sonoo and Stalberg, 1993). It has been demonstrated in real electromyographic (EMG) recordings and simulation studies that the extinction of the action potentials continues for over 20 ms after the main spike of the MUAP (Lateva and McGill, 1998; Dumitru and King, 1999; Dumitru et al., 1999). Real routine EMG signals almost invariably show slow baseline (BL) fluctuations and other noise such that it is very difficult to distinguish the full extension of the final portion of the MUAP. This work is devoted to the "clinical MUAP duration", i.e., that which can be observed in routine neurophysiological practice and which has clinical meaning, as opposed to the "physiologic MUAP duration" (Dumitru and King, 1999; Dumitru et al., 1999), which lasts until the repolarization is entirely completed.

Measuring MUAP duration presents hard intrinsic difficulties, so much that manual duration

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measurement has been previously described as "an arbitrary task" (Sonoo, 2002) and low degrees of reliability of manual duration markers have been reported (Stalberg et al. 1986; Nandedkar et al., 1988; Chu et al., 2003; Takehara et al., 2004b; Rodríguez et al., 2007a). A number of automatic algorithms have been designed to overcome the limitations of the subjective assessment of MUAP duration (Stalberg et al., 1986; Nandedkar et al., 1995). These were eventually implemented in available commercial EMG acquisition systems. But, as reported by several authors (Bischoff et al., 1994; Stalberg et al., 1995; Takehara et al., 2004a), conventional automatic algorithms imply the necessity of continuous visual supervision and frequent manual readjustments of the duration markers. These methods fail to estimate correctly the duration measurement mainly because of the presence of noise and fluctuations in the BL and other potentials, all of them being unfortunately common in routine EMG signals.

Apart from the previous (conventional) approaches, a different automatic duration measurement method based on the wavelet transforms was presented more recently (Rodríguez et al., 2010; Rodríguez et al., 2012). In a comparative study, this duration algorithm outperformed the results of conventional methods over normal and pathological signals. However, recent works are still using conventional methods to measure MUAP duration (Ghosh et al., 2014; Matur et al., 2014), sometimes applying manual corrections (Jian et al., 2015).

In this paper we present a novel duration algorithm based on correlation. In biological systems some physiological situations generate a train of potentials or a quasi-periodic repetition of certain waveforms. This is the case of MUAP trains in voluntary or artificially-induced contractions of skeletal muscles, the P, QRS and T complexes in the ECG, the S1 and S2 sounds in the phonocardiogram, or the spike-and-wave complexes in the EEG of epileptic patients. If the physiological and recording conditions stay stable during a certain period of time in these situations, the potentials that can be recorded will include a deterministic component, that can be considered basically unaltered throughout this time, and a stochastic component, i.e., noise and artifacts of different origins which may include biological potentials from other sources different from the ones of interest. According to this, the correlation between two waveforms of a train will be high. Moreover the correlation between corresponding segments (i.e., the initial upraise, the central spike, the final portion, etc.), of two different waveforms of the train will also be large.

On the other hand, the correlation between signal periods in which these repetitive waveforms are absent will be much lower. This is the central idea behind our new MUAP duration estimation method: to determine the potential duration regarding the time extension in which it presents high correlation with other potentials in the train.

In this work we present this novel algorithm, and compare it to a well-known conventional automatic duration method and to the more recent wavelet-based approach over signals extracted from normal and pathological muscles.

2 MATERIAL

We analyzed 313 recordings containing a 5 seconds long EMG signal during slight voluntary contractions: 68 signals from 14 normal deltoid muscles, 105 from muscles with myopathies, 27 from chronic neurogenic muscles, and 72 from subacute neurogenic muscles. All these signals were recorded from eight different muscles and exhibited definite changes of characteristic pathologies. These signals were acquired with a Medelec Synergy Mobile electromyograph (Oxford Instruments Medical, Inc.), using concentric needle electrodes (type DCN37; diameter = 0.46 mm, recording area = 0.07 mm2; Medtronic). The filter setting was 3 Hz to 10 kHz with a sampling rate of 20 kHz and 16-bit analogue-to-digital conversion. The digitized signals were stored on the hard disk of a PC computer and further analysis was performed off-line.

The multi-MUAP procedure of an automatic decomposition method was used to extract MUAPs from the continuous EMG signals (Florestal et al., 2006). Epochs of 50 or 100 ms containing discharges (potentials) of the same MUAP train were obtained. The maximal negative peak of the MUAP was centred on 40% of the length of the window epoch (at 20 or 40 ms corresponding to 50 or 100 ms epoch window). A 100 ms epoch window was only used in 8 MUAPs from chronic and subacute neurogenic muscles, as in these cases a 50 ms epoch was not sufficient to visualize the whole MUAP.

Next, the waveforms of the isolated discharges of each MUAP train were aligned in the time axis by maximum correlation (Proakis and Manolakis, 1996; Campos et al., 2000) and in the voltage axis by euclidean distance minimization (the MUAP discharges are ordered in accordance to their euclidean distance to the average of MUAP discharges) (Navallas et al., 2006). Besides,

interactive tools were implemented to visualize the set of the extracted discharges in raster and superimposed modes in order to discard manually undesirable ones. The MUAP waveform was finally obtained using a novel method of sample estimation based on a sliding window algorithm (Malanda et al., 2008).

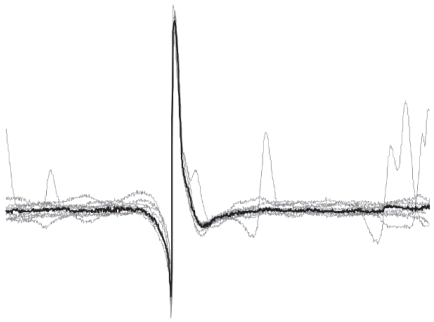

Figure 1: MUAP discharges (grey) and MUAP representative waveform (black) obtained using a sliding window algorithm.

This method optimizes the MUAP waveform extraction procedure and can be applied in the presence of low or high superposition of discharges from other MUs (Fig. 1).

Well defined waveforms (avoiding superimpositions, gross baseline fluctuations and secondary potentials) of 3 to 10 (mean 9.9 and standard deviation (SD) 0.7) discharges were selected for each studied MUAP. All the selected MUAP waveforms were well-defined above baseline (BL) activity and had a "rise-time" < 1 ms (most of them less than 500 μs). A total of 295 MUAPs were accepted for analysis: 68 from normal deltoid muscles, 124 from myopathic muscles, 20 from chronic neurogenic muscles and 83 from subacute neurogenic muscles.

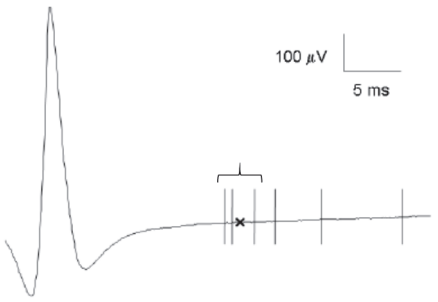

Figure 2: Example of determination of the gold standard of the duration markers positions (GSP) from six manual marker positions for the end point (continuous vertical lines). The GSP (x) is calculated as the mean position of the three closest manual marker positions.

Notice that in relation to the number of analyzed signals, the number of extracted MUAPs is reduced. One of the reasons of this reduction is related to the extraction process. In spite of the efficiency of the described automatic methods for selection, alignment and cleaning of the discharges, all the processes were supervised and final selection were carried out manually for ensuring the acceptation of representative and distortion free MUAP waveforms.

3 METHODS

3.1 Determination of the Gold Standard Duration Marker Positions

The high variability in the manual placement of duration markers requires first to define the best manual position among a set of several measurements. Therefore, a method was devised by the authors to find the "most likely" MUAP start and end points. Over the whole set of MUAPs extracted from the 313 recordings, two experienced electromyographists (LGU and IGG) made each of them three measurements of the duration, each measurement separated by at least two weeks. To perform this task they were provided with a software interactive tool (designed in *Matlab*^{TM}) that showed the MUAP waveform and the set of the extracted discharges in raster and superimposed modes. The sensitivity scale was fixed at 100 μV/cm and the sweep speed at 10 ms/cm to place the duration markers. From the six manually marked positions for the start or end markers, the "most likely" placement was the mean point of the three closest positions using a probabilistic procedure (Fig. 2) as explained on a previous paper (Rodríguez et al., 2007a). This was considered our gold standard position (GSP).

Among all the MUAPs extracted from the 313 recordings, we decided to select those MUAPs with a high degree of agreement in the duration markers manually placed. Therefore, MUAPs with a maximum range of variation of 1 ms among all the six manual placements for the start and also for the end markers were selected. The mean and SD obtained from the range of the three closest markers were 0.02 and 0.05 ms for the start marker and 0.1 and 0.1 ms for the end marker. This confirms the GSP markers as consistent estimates of the MUAP start and end points. Fig. 2 illustrates the GSP determination procedure.

3.2 Automatic Methods for the Measurement of MUAP Duration

Our proposed based-correlation method (CM) was compared with two automatic methods for the measurement of MUAP duration were used: a well-known conventional method (Nandedkar et al., 1995), and the wavelet-based method (WM) previously mentioned (Rodríguez et al., 2010). The conventional method and the WM were directly applied to the representative MUAP waveforms (only 1 potential), while the CM used the whole set of discharges of the MUAP train (from 3 to 10 discharges).

3.2.1 Conventional Automatic Method

The conventional automatic method is detailed in (Nandedkar et al., 1995), and we call it Nandedkar's method, NM. In NM, MUAPs are automatically isolated, identified and classified using a multi-MUAP system. In the referenced work from 50 to 65 discharges are extracted for each MUAP and its representative waveform is obtained using median averaging. To find the MUAP start and end markers NM calculates the BL first, as the average of the first 5 ms of the window epoch. Once the BL is subtracted, NM begins its search from the maximum MUAP peak. From this point, the start and end markers are calculated using thresholds related to the area under the MUAP and to the amplitude sample values.

3.2.2 Wavelet Method

This MUAP duration estimation method was based on the discrete wavelet transform (DWT) (Rodríguez et al., 2007a; Rodríguez et al., 2007b; Rodríguez et al., 2010; Rodríguez et al., 2012). In the DWT scales, the peaks related to MUAP peaks are identified and amplitude and slope thresholds are used to determine MUAP start and end points. Besides, high frequency noise and BL fluctuations can be put aside, so that BL estimation is not necessary.

3.2.3 Correlation Method

As explained before, the time span of a set of discharges from a MUAP train will be obtained so that different segments of the potentials in the set will be highly correlated to the corresponding segments in other discharges in the set. The first thing to do is to align the set of potentials in the time and amplitude axes. Each potential in the train is time aligned to the average potential by use of the standard technique of cross correlation maximization (Proakis and Manolakis, 1996). As for the amplitude alignment, we simply add a constant amplitude to each potential so that its Euclidean distance to the mean (i.e. the average of all the potentials in the MUAP train) is minimized. After this, a sliding window of a certain length (Lw) is moved along the complete length of these discharges (50 or 100 ms in our case), with hops of a given time length (Δh). We will call x_{ij} to the i-th discharges in the set as seen by the sliding window in its j-th hop (Fig. 3).

The correlation coefficient (CC) between every pair of segments in a given hop will be computed (Matlab *corrcoef* function, which implements the standard algorithm was used) and the average among the CC of the different pairs will be obtained. This will be repeated for every j-th hop, yielding a curve of segment correlation along the complete interval under study (50 or 100 ms in our case) (Fig. 4). This curve usually has its maximum near the time occurrence of the MUAP central spike, around which a 'plateau' appears. Some ms at either side of the maximum point, the curve normally declines rapidly. To search the MUAP start marker, we will set a threshold (Th1) and find the time instant when, moving from the maximum peak to the left (towards the initial part of the discharges), the correlation curve goes below this threshold. This is tentatively our MUAP start marker. To make the detection more robust we will still move further to the left inspecting if there is a second peak higher than Th2, in which case, from this point we repeat again the search of the point where the curves goes down below Th1 and finally set there the MUAP start marker (Fig 4). To obtain the MUAP end marker we repeat all this operation, but moving from the maximum peak to the right (towards the final part of the potentials). To increase flexibility, different sets of parameters (Th1, Th2, Lw and Δh) can be used for the detection of the initial and the marker.

In our study, for the start marker we empirically set Th1 and Th2 to 0.06 and 0.5, respectively, and Lw and Δh to 1 and 0.1 ms, respectively. For the end marker, Th1 and Th2 were set to 0.05 and 0.5, respectively, and Lw and Δh to 2.5 and 0.25 ms, respectively. Those values were set by visual inspection, not by computer simulations.

3.2.4 Statistical Analysis

To assess the accuracy of the automatic methods for MUAP duration measurement three statistical comparative tests were performed for each method:

(a) Comparison of bias and precision. To measure the performance of both methods, the mean and the SD of the relative differences to the GSP were computed

for the start and end markers. The mean is related to the bias of a method around the GSP and the SD is related to its precision. The results of the methods in each group of MUAPs were compared using a Student's t test.

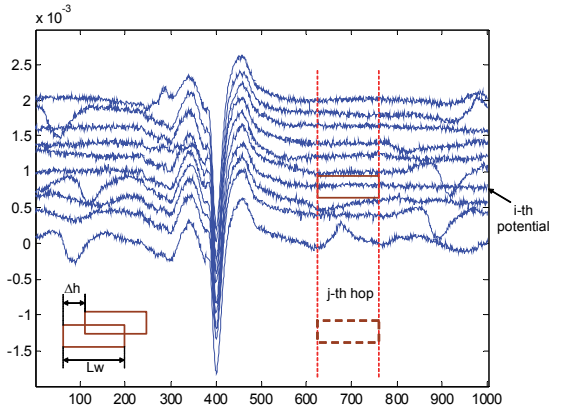

Figure 3: MUAP potentials presented in raster mode. Sliding window for selection is shown. (Time axis is given in samples and amplitude axis in Volts).

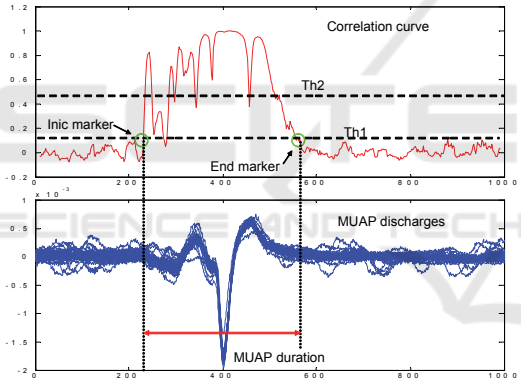

Figure 4: shows how the CM calculates the start and end markers. (Time axis is given in samples and amplitude axis in Volts).

(b) Calculation of the EMSE values. The mean of the differences between the automatic marker position (considering both start and end markers) and the GSP (i.e., the bias of each method) and the standard deviation (SD) of such differences (the precision) were calculated. Then we calculated the estimated mean square error (EMSE) of the differences as follows:

$$EMSE = mean^2_{d,start} + \mathrm{var}_{d,start} + mean^2_{d,end} + \mathrm{var}_{d,end} \quad (1)$$

with $mean^2_{d,start}$ and $var_{d,start}$ being the square mean and the variance, respectively, of the differences between the start marker position of the method and the start GSP for each MUAP group; and $mean^2_{d,end}$ and $var_{d,end}$ are equivalent measures for the end marker. We also obtained the global EMSE value for all the different MUAP groups using the next equation:

$$EMSE_G = (EMSE_N \cdot N_N + EMSE_M \cdot N_M + EMSE_C \cdot N_C + EMSE_S \cdot N_S)/N_T \quad (2)$$

where $EMSE_N$, $EMSE_M$, $EMSE_C$ and $EMSE_S$ are the results for the normal, myopathic, chronic neurogenic and subacute neurogenic potentials, respectively, and N_N, N_M, N_C and N_S are the number of MUAPs of the four different groups considered for the study, and N_T is the total number of MUAPs from all the groups put together.

(c) Rate of gross errors. The number of cases in which the absolute difference between the GSP and the automatic marker position was greater than 5 ms was counted for each method. Such cases can be generally considered as gross errors. The proportions of gross errors corresponding to each method were compared using the Chi-square test.

4 RESULTS

4.1 Comparison of Bias and Precision

The mean and the SD of the differences (bias and precision, respectively) between the start and end marker positions and GSPs of the three automatic methods are respectively given in Tables 1 and 2. Asterisks are shown to indicate significant differences between any method and the CM.

Table 1: Differences between GSP and the start marker positions assigned by NM and CM for the different MUAP groups. Mean/SD (ms).* = p<0.05 (Student's t test). Chr=Chronic. Subac=Subacute.

MUAPs/Method	NM	WM	CM
Normal	-1.4/1.2*	-0.3/1.3	-0.1/0.8
Myopathic	-1.2/1.0*	-0.5/1.1*	0.0/0.5
Chr. neurogenic	1.6/6.7	0.7/2.3*	0.0/0.5
Subac. neurogenic	-1.3/1.4*	-0.4/1.6	-0.1/0.9

Table 1 shows the results for the start marker positions. It can be appreciated that the CM is the less biased and the most precise method placing the start marker, as it has simultaneously the lowest mean and the lowest SD of differences to the GSP for all the five MUAP groups. The CM presents significant differences against NM in all the MUAP groups

except for the chronic neurogenic MUAPs. On the other hand, the CM shows significant differences against the WM in myopathic and chronic neurogenic MUAPs.

Table 2: Differences between GSP and the end marker positions assigned by NM and CM for the different MUAP groups. Mean/SD (ms).* = p<0.05 (Student's t test). Chr=Chronic. Subac=Subacute.

MUAPs/Method	NM	WM	CM
Normal	3.1/3.1*	-0.1/3.5	-0.7/2.4
Myopathic	4.4/2.9*	0.6/2.6*	-0.7/1.9
Chr. neurogenic	6.5/10.6*	1.4/7.6	-3.5/7.5
Subac. neurogenic	4..3/4.2*	0.8/4.0*	-0.7/3.3

In Table 2, the results for the end marker positions are shown. It can be appreciated that the CM presents significant differences against the NM in all the MUAP groups. Comparing to the WM, the CM exhibits significant differences in myopathic and subacute neurogenic MUAPs, with more precision (lower SD).

From inspection of the two tables, we can notice that in chronic neurogenic MUAPs, the bias of the methods is higher and the precision is lower than in other groups. This is probably a consequence of the rare characteristics of the analysed signals, which are the longest MUAPs and frequently present polyphasia.

It can also be appreciated from these tables that end marker placements present higher mean and SD in absolute value than the start markers, which indicates that it is more difficult for the automatic methods to place the end markers than the start markers.

4.2 Calculation of the EMSE Values

Table 3 shows the EMSE values of the three methods for the four different MUAP groups and the global EMSE. As it can be appreciated, the CM presents the lowest EMSE in all the cases, except for the chronic neurogenic MUAPs.

Table 3: EMSE values of NM and CM for the different MUAP groups and $EMSE_G$. Chr=Chronic. Subac=Subacute.

MUAPs/Method	NM	WM	CM
Normal	10.4	12.4	3.4
Myopathic	15.3	4.2	2.1
Chr. neurogenic	98.5	32.1	33.1
Subac. neurogenic	19.9	9.5	5.9
Total ($EMSE_G$)	21.5	8.6	5.0

4.3 Rate of Gross Errors

The rate of gross errors for the start and end markers of the three duration methods for the four different MUAP groups are shown in Tables 4 and 5, respectively.

For the start and end markers, the CM presents the lowest rate of gross errors in all cases. Significant differences were found between CM and the rest in chronic neurogenic MUAPs for the start marker. For the end marker, the CM showed significant differences in normal, myopathic and subacute neurogenic MUAPs against the NM, and in myopathic MUAPs against the WM.

Table 4: Rate of automatic start marker placements in % with differences to the GSP greater than 5 ms for NM and CM and different MUAP groups.* = p<0.01 (Chi-square test) Chr=Chronic. Subac=Subacute.

MUAPs/Method	NM	WM	CM
Normal	0.0	2.9	0.0
Myopathic	1.6	0.8	0.0
Chr. neurogenic	6.9*	10.3*	0.0
Subac. neurogenic	3.6	3.6	1.2

Table 5: Rate of automatic end marker placements with differences to the GSP greater than 5 ms for NM and CM and different MUAP groups.* = p<0.01 (Chi-square test) Chr=Chronic. Subac=Subacute.

MUAPs/Method	NM	WM	CM
Normal	29.4*	11.8	7.4
Myopathic	39.5*	9.7*	3.2
Chr. neurogenic	37.9	27.6	13.8
Subac. neurogenic	42.2*	9.6	9.6

4.4 Visual Assessment

Some examples of the NM and the CM over normal and the different pathological MUAP groups are shown in Figure 5.

Normal MUAPs can have small or medium amplitude (Fig. 5.a). Polyphasic serrated myopathic MUAP is more difficult to measure (Fig. 5.b). Chronic poten tials can have great amplitude and also large duration (Fig. 5.c).

Finally, subacute neurogenic MUAPs can have multiple turns and be polyphasic too (Fig. 5.d). In all these cases the CM achieves the best results.

4.5 Computational Cost

The CPU times in ms (mean/SD) for the Matlab implementation of the three algorithms (NM, WM and CM) were 0.26/0.6, 5.1/2.4 and 513.3/101.4 ms,

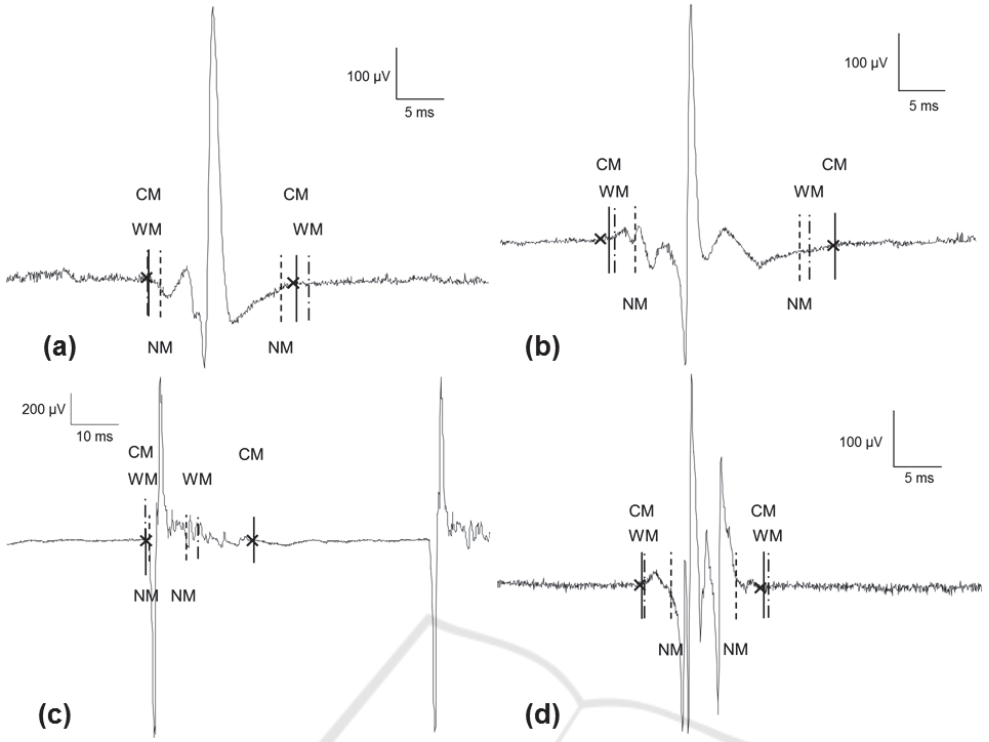

Figure 5: Examples of duration measurements of NM and CM on normal (a), myopathic (b), chronic neurogenic (c) and subacute neurogenic (d) MUAPs. GSP are in crosses.

respectively. Therefore they are all fast enough for any real-time application.

5 DISCUSSION

MUAP duration is a very important, yet elusive, parameter in quantitative EMG, as it gives relevant information about the MU generating the MUAP (the number of fibres) and is also critical for the estimation of other MUAP waveform parameters. In this paper we have presented an automatic procedure to obtain MUAP duration markers with high agreement with the markers obtained by expert neurophysiologists in normal and pathological signals.

The novel approach provides more accurate duration marker placements and fewer gross aberrant errors for normal and pathological MUAPs than the other two tested methods. This, together with its simplicity and low computational cost makes it a very valuable tool for quantitative analysis of MUAPs, reducing the requirement for electromyographists' manual intervention. Moreover, real-time implementations in a clinical setting could reduce exploration time and patient discomfort.

Future works will focus on computational approaches aimed to obtain optimum values for the CM parameters.

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