Muscle velocity recovery cycles: comparison between surface and needle recordings

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**Abstract** 

**Introduction:** Recording of muscle velocity recovery cycles (MVRCs) has been developed as a technique to investigate the pathophysiology of muscle diseases. MVRCs have been measured by direct muscle stimulation and concentric EMG needle recording. This study was undertaken to determine if recordings can be made with surface electrodes.

**Methods:** MVRCs with 1 and 2 conditioning stimuli were recorded simultaneously with concentric needle and surface electrodes from the brachioradialis muscle in 12 healthy volunteers. Muscle relative refractory period, early and late supernormality, and extra late supernormality were compared between the recording techniques.

**Results:** Surface recordings were possible in all subjects. The multi-fiber action potentials recorded with surface electrodes were smaller than those recorded with needles, but there was no significant difference between any of their MVRC properties.

**Discussion:** MVRCs can be recorded with surface electrodes in healthy subjects. The use of surface electrodes may facilitate the technique of recording MVRCs.

**Key words** 

muscle, myopathy, membrane potential, excitability measurements, surface EMG, characterization of muscle disease

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# **Abbreviations**

MAP = muscle action potential

ESN = early supernormality

ISI = inter-stimulus interval

LSN = late supernormality

MRRP = muscle relative refractory period

MVRC = muscle velocity recovery cycles

SEM = standard error of the mean

XLSN = extra late supernormality

## Introduction

The technique of recording muscle velocity recovery cycles (MVRCs) is based on the principle that an evoked muscle action potential is followed by early and late depolarizing afterpotentials<sup>1,2</sup>. Both influence the propagation velocity of a consecutively evoked muscle action potential as a function of inter-stimulus interval (ISI). By recording MVRCs the following parameters can be assessed: (i) muscle relative refractory period (MRRP), (ii) early supernormality (ESN, the maximal increase of conduction velocity due to the early afterpotential at about 8 ms ISI), (iii) late supernormality (LSN, the increase of conduction velocity at an ISI of about 100 ms related to late afterpotential), and (iv) extra late supernormality (XLSN, augmentation of LSN by additional conditioning stimulus)<sup>2,3</sup>. In previous studies, MVRC recordings have been used to demonstrate distinct changes of muscle membrane properties in vivo. The method has been shown to have a high repeatability<sup>4</sup>, no investigator dependency<sup>5</sup>, and to be applicable to different muscles<sup>5</sup>. In disease, the technique has demonstrated reversible ischemic membrane depolarization in trapezius muscles in patients with postural hypotension during standing<sup>6</sup>, hyperkalemic membrane depolarization in renal failure<sup>7</sup>, membrane depolarization or sodium channel inactivation in critical illness myopathy<sup>8</sup> and in the very early phase of septic myopathy<sup>9</sup>, and membrane depolarization due to inward rectifier dysfunction in Andersen-Tawil syndrome<sup>10</sup>. In myotonia congenita and the myotonic dystrophies characteristic alterations due to chloride channel dysfunction could be demonstrated<sup>11</sup>.

For measurement of MVRCs direct muscle stimulation with a monopolar needle electrode is used to excite a column of muscle fibers. To record the multi-fiber action potentials, a concentric EMG electrode is inserted in the muscle and placed in the vicinity of the activated fibers<sup>2</sup>. Placement of this recording needle can sometimes be difficult and time consuming. The aim of this study was to test whether surface electrode recordings can substitute for concentric EMG needle recordings, which might facilitate recordings.

### **Materials and Methods**

Twelve healthy subjects (5 women and 7 men; ages 23–27 years, mean 23.5 years) participated in this study. Approval was obtained from the local ethics committee (Kantonale Ethikkommission, Bern, Switzerland) and conformed to the Declaration of Helsinki. All participants provided written informed consent.

### Stimulation

Stimulation was performed as described earlier in detail<sup>2,3</sup>. In brief, subjects rested comfortably on a bed in a warm room. An insulated monopolar needle electrode (TECA, Viasys Healthcare, Madison, Wisconsin, USA) served as cathode and was inserted perpendicularly into the brachioradialis muscle of the non-dominant arm to a depth of about 1 to 1.5 cm. The insertion site was about 25% of the distance from the lateral epicondyle of the humerus to the styloid process of the radius (Figure 1). A non-polarizable, self-adhesive surface electrode (Red Dot, 3M Health Care, D-46325 Borken, Germany) served as anode and was placed on the skin just distal to the cathode. An isolated constant-current stimulator (DS7, Digitimer Ltd., Welwyn Garden City, Hertfordshire, UK) was used for stimulation. Stimulus duration was set at 0.05ms.

### Recording

Two recording techniques were used simultaneously: (i) concentric EMG needle electrode and (ii) surface electrode recordings. Concentric EMG needle electrode recordings were performed as described earlier<sup>2,3</sup>. A concentric 30G EMG electrode (Medtronic, Skovlunde, Denmark) was inserted slightly oblique into the brachioradialis muscle about 20 to 25 mm proximal to the cathode. Small position changes were made until a stable monophasic response could be recorded with stimulus intensity of less than 6 mA (Figure 1). After positioning of the needle EMG electrode, surface electrodes were taped on the skin (diameter

0.8cm, Medtronic, Skovlunde, Denmark). The active electrode was placed on the skin just above the tip of the concentric EMG needle electrode. Two anodes were placed adjacent proximal and distal to the cathode. A surface electrode served as ground and was taped on the dorsum of the hand. Signals were amplified (gain 1000, bandwidth 1.6 Hz to 2 kHz) and digitized (National Instruments NI DAQCARD-6062E, National Instruments Europe Corp., Debrecen, Hungary) using a sampling rate of 20 kHz. Stimulation and recording were controlled by QTRAC software (written by H. Bostock, copyright Institute of Neurology, London, UK), using the menu-driven recording protocol 1200RCM2B.QRP.

## Stimulation protocol

Multi-fiber MVRCs with single and paired conditioning stimuli (10 ms apart) were recorded as described earlier<sup>2,3</sup>. The test stimuli were delivered every 2 seconds. The interval between single or paired conditioning stimulus and the test stimulus was decreased in 34 steps from 1000 ms to 2 ms in an approximately geometric series

# Data analysis and statistics

Data analysis was performed using the QTRAC software as described earlier in detail<sup>3</sup>. The waveforms were transformed with forward-reverse digital filters (500 Hz high pass, 100 Hz low pass) to provide baseline stabilization and smoothing without time displacement<sup>3</sup>. For both recording techniques the following measurements were made:

- 1) amplitude of the muscle action potential (MAP);
- 2) from recordings with 1 conditioning stimulus:
  - a) MRRP (interpolated ISI at which velocity first reached its unconditioned value)
  - b) ESN (peak percentage reduction in latency at ISIs shorter than 15 ms)
  - c) Time to peak ESN (ISI at which reduction in latency was maximal)

- d) LSN (peak percentage reduction in latency at ISIs longer than 50 ms and shorter than 150 ms)
- e) Residual supernormality at an ISI of 950 ms
- 3) from recordings with 2 conditioning stimuli:
  - a) XLSN (peak percentage increase in velocity at ISIs longer than 50 ms and shorter than 150 ms due to a second conditioning stimulus)

Statistical computations were performed by the QTRAC data analysis software. Parameters of needle and surface recordings were compared using the Student paired t-test. Data are presented as mean  $\pm$  standard error of the mean (SEM).

### **Results**

All subjects tolerated the examination well, and needle and surface MAPs of good quality could be recorded from all subjects. Figure 2 shows original multi-fiber MAPs from a single subject recorded simultaneously with surface and needle electrodes. Figure 3 displays the averaged MVRC latency changes of all 12 subjects for both recording techniques, for recordings with 1 conditioning stimulus and also the differences in latency change between recordings with 1 and 2 conditioning stimuli. Means and standard errors for peak amplitude, peak variability, and the MVRC measures for the 2 recording methods are compared in Table 1. For all measurements no statistical difference was found between recordings with surface and needle electrodes, except that the surface action potentials were on average less than half the size of those recorded with needles. Figure 4 shows the individual values for both recording techniques for MRRP, ESN, time to peak ESN, and LSN. Table 1 also shows the correlation coefficient between surface and needle measurements across the 12 subjects. Correlation was very high for the early components, but relatively weak for the later components of the recovery cycle..

### Discussion

This study demonstrates that MVRCs with 1 and 2 conditioning stimuli, which previously have only been reported for recordings with concentric needle electrodes, can also be recorded with surface electrodes in healthy subjects. The surface MAPs were smaller than those recorded with needles, but the MVRC measurements did not differ in any statistically significant respect between the 2 recording methods.

Although the MVRC averages were similar for surface and needle recordings, it was noticeable that only the early parts of the recovery cycle (refractoriness and early supernormality) showed a very strong correlation between surface and needle measurements across the 12 subjects (Table 1). Inter-subject differences in the later parts of the recovery cycle appear to be masked partly by the intrinsic variability of those measurements. A similar finding was noted in an earlier study of the repeatability of MVRCs; the intraclass correlation coefficient between 2 MVRC recordings from the same subjects made a week apart was much higher for early than for late supernormality<sup>4</sup>. We conclude that although the later parts of the recovery cycle can be useful to detect membrane abnormalities in groups of patients, such as XLSN in Andersen-Tawil syndrome<sup>10</sup>, they are likely to be of limited diagnostic value for individual patients.

The method of measuring MVRCs was developed to investigate changes of muscle membrane properties independent of nerve function<sup>1,2</sup>. To achieve this goal a column of muscle fibers is stimulated via a monopolar needle electrode, and evoked MAPs are recorded with a concentric needle electrode. Positioning of the recording needle electrode can sometimes be difficult, since it must be positioned in the vicinity of the activated muscle fibers, particularly if these fibers are located in the depth of the muscle and are therefore not

palpable. Furthermore, this method suffers from a slight risk that the recording needle can be displaced as a consequence of the muscle fiber twitches. Hence, the use of surface electrodes could facilitate recordings. In this study, we positioned the active electrode on the skin overlying the tip of the concentric needle electrode between 2 reference electrodes. This tripolar electrode arrangement was used to get a well-defined maximal negative peak of the MAP for accurate latency measurements, and it enabled us to record MAPs of good quality in all subjects. We had expected that the surface recordings might be more stable, because the risk of movement of the concentric needle electrode was avoided, but in fact the variability of the peak MAPs during the recording period of 5-6 minutes was similar for the 2 methods (Table 1). This implies that much of the variability with the conventional method arises from movement of the stimulating rather than the recording needle electrode.

In this study only 12 healthy young volunteers were examined. The data show that MVRCs can be recorded in this population with surface as well as with needle electrodes, which may facilitate the recording procedure. However, it should be noted that we have not yet made any surface recordings in patients with muscle disease, and in some muscle pathologies MAPs are typically of reduced amplitude, which might make the smaller surface recordings more difficult because of a borderline signal-to-noise ratio.

## References

- 1. Mihelin M, Trontelj JV, Stålberg E. Muscle fiber recovery functions studied with double pulse stimulation. Muscle Nerve 1991; 14:739-747.
- 2. Z'Graggen WJ, Bostock H. Velocity recovery cycles of human muscle action potentials and their sensitivity to ischemia. Muscle Nerve 2009; 39:616-626.
- 3. Bostock H, Tan SV, Boërio D, Z'Graggen WJ. Validity of multi-fiber muscle velocity recovery cycles recorded at a single site using submaximal stimuli. Clin Neurophysiol 2012; 123:2296-2305.
- 4. Z'Graggen WJ, Troller R, Ackermann KA, Humm AM, Bostock H. Velocity recovery cycles of human muscle action potentials: Repeatability and variability. Clin Neurophysiol 2011; 122:2294-2299.
- 5. Boërio D, Z'Graggen WJ, Tan SV, Guetg A, Ackermann K, Bostock H. Muscle velocity recovery cycles: effects of repetitive stimulation on two muscles. Muscle Nerve 2012; 46:102-111.
- Humm AM, Bostock H, Troller R, Z'Graggen WJ. Muscle ischaemia in patients with orthostatic hypotension assessed by velocity recovery cycles. J Neurol Neurosurg Psychiatry 2011; 82:1394-1398.
- 7. Z'Graggen WJ, Aregger F, Farese S, Humm AM, Baumann C, Uehlinger DE, Bostock H. Velocity recovery cycles of human muscle action potentials in chronic renal failure. Clin Neurophysiol 2010; 121:874-881.
- 8. Z'Graggen WJ, Brander L, Tuchscherer D, Scheidegger O, Takala J, Bostock H. Muscle membrane dysfunction in critical illness myopathy assessed by velocity recovery cycles. Clin Neurophysiol 2011; 122:834-841.
- Ackermann KA, Bostock H, Brander L, Schröder R, Djafarzadeh S, Tuchscherer D, Jakob SM, Takala J, Z'Graggen WJ. Early changes of muscle membrane properties in porcine faecal peritonitis. Crit Care 2014; 18:484.

- Tan SV, Z'graggen WJ, Boërio D, Rayan DL, Howard R, Hanna MG, Bostock H.
  Membrane dysfunction in Andersen-Tawil syndrome assessed by velocity recovery cycles. Muscle Nerve 2012; 46:193-203.
- 11. Tan SV, Z'Graggen WJ, Boërio D, Rayan DR, Norwood F, Ruddy D, Howard R, Hanna MG, Bostock H. Chloride channels in myotonia congenita assessed by velocity recovery cycles. Muscle Nerve 2014; 49:845-857.

## Figure legends

Figure 1: Electrode arrangement for measurement of MVRCs. Stimulation: A monopolar insulated needle electrode was inserted perpendicularly into the brachioradialis muscle at about 25% of the distance from the lateral epicondyle of the humerus to the styloid process of the radius. A surface electrode served as anode and was attached distal to the cathode. Recordings were made simultaneously with a concentric EMG electrode and surface electrodes. The concentric EMG electrode was inserted slightly oblique into the brachioradialis muscle about 20 to 25 mm proximal to the cathode. The active surface electrode was placed on the skin above the tip of the concentric EMG electrode. Two surface anodes were placed adjacent proximal and distal to the cathode.

**Figure 2:** Multi-fiber CMAP recorded from a subject with 1 conditioning stimulus. The left column shows the inter-stimulus intervals between the conditioning and test stimuli (logarithmic scale). The middle column shows CMAPs evoked by the test stimulus and recorded with surface electrodes, and the right column shows the CMAPs recorded with a needle electrode.

**Figure 3:** Mean muscle velocity recovery cycles (MVRCs) recorded with surface electrodes (A) and needle electrodes (B). The dashed lines indicated the standard errors of the mean. The upper panel shows MVRCs recorded with 1 conditioning stimulus. The lower panels display the differences in latency between recordings with 1 and 2 conditioning stimuli. C) Superimposition of averaged surface and needle recordings.

**Figure 4:** Individual comparisons of the most important MVRC parameters for both recording techniques. A) MRRP, B) Time to peak supernormality, C) ESN, and D) LSN. For

all parameters, no statistical differences were found between recordings with surface and needle electrodes.

	Surface (mean ± SE)	Needle (mean ± SE)	Difference (mean ± SE)	P (paired <i>t</i> -test)	R
Peak amplitude (mV)	0.64 ± 0.15	1.50 ± 0.24	-0.86 ± 0.29	0.012*	-0.038
Peak variability (CV, %)	7.7 ± 1.1	7.0 ± 1.7	0.7 ± 1.8	0.71	0.200
Relative refractory period (ms)	3.23 ± 0.13	3.24 ± 0.12	0.01 ± 0.02	0.70	0.983****
Time to peak supernormality (ms)	6.91 ± 0.28	6.89 ± 0.30	-0.02 ± 0.11	0.81	0.935****
Early supernormality (< 15 ms, %)	10.21 ± 0.79	10.19 ± 0.96	-0.02 ± 0.36	0.92	0.932****
Late supernormality (50-150 ms, %)	4.16 ± 0.37	4.65 ± 0.44	0.49 ± 0.38	0.22	0.572
Extra late supernormality (2-1 cond. Stim, %)	2.84 ± 0.44	3.52 ± 0.56	0.69 ± 0.40	0.11	0.701*
Residual supernormality (950 ms, %)	0.30 ± 0.14	0.20 ± 0.17	-0.10 ± 0.11	0.42	0.742**

Table 1 Comparison between MVRCs recorded simultaneously from the surface and from a concentric needle in 12 normal subjects. Peak amplitudes are the submaximal peaks of the filtered multi-unit waveforms used for the MVRC measurements. The peak variability is expressed as the coefficient of variation of the control peak amplitudes over the 5-6 minutes of the recordings. Only the peak amplitudes showed a significant difference between surface and needle recordings. The last column shows the correlation coefficient between surface and needle measurements over the 12 subjects, with P values indicated by asterisks only (\* = P < 0.05, \*\* = P < 0.01, \*\*\*\* = P < 0.0001).

Figure 1

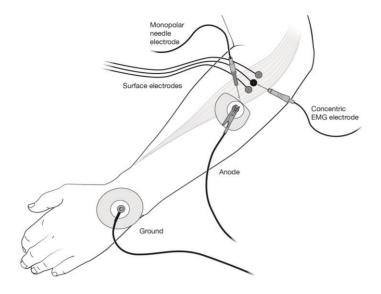


Figure 2

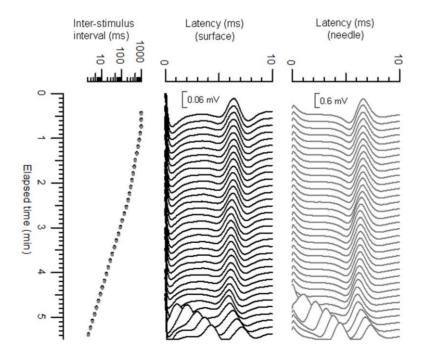


Figure 3

