



Scandinavia goes St. Gallen

Techniques for Motor Unit Number Estimation: MUNIX

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Motor Unit Number Index (MUNIX) as a neurophysiological biomarker for the number of motor neurons

Several different electrodiagnostic biomarkers have been described during the last decades

MUNIX has been reported for the first time in 2004 by Sanjeev Nandedkar and Erik Stålberg

- *Nandedkar SD, Nandedkar DS, Barkhaus PE, Stalberg EV. Motor unit number index (MUNIX). IEEE Trans Biomed Eng 2004*

Since 2010, a growing literature about its application in several diseases have been described as a biomarker for disease progression

Motor Unit Number Index (MUNIX) as a neurophysiological biomarker for the number of motor neurons

Reliability of MUNIX has been evaluated and compared to other motor unit number estimation (MUNE) techniques by several groups

- Multipoint MUNE
- HD MUNE
- MScan-fit MUNE
- Neurophysiological Index

- *Boekestein WA, Schelhaas HJ, et al.. Motor unit number index (MUNIX) versus motor unit number estimation (MUNE): a direct comparison in a longitudinal study of ALS patients. Clin Neurophysiol 2012*

- *Higashihara M, Menon P, et al. Reproducibility of motor unit number index and MScanFit motor unit number estimation across intrinsic hand muscles. Muscle Nerve. 2020*

- *Neuwirth C, Nandedkar S, Stalberg E, et al. Motor Unit Number Index (MUNIX): a novel neurophysiological marker for neuromuscular disorders; test-retest reliability in healthy volunteers. Clin Neurophysiol 2011*

Motor Unit Number Index (MUNIX) as a neurophysiological biomarker for the number of motor neurons

Meanwhile, MUNIX is the most intensively investigated MUNE-method available with standardization and published guidelines

- *Nandedkar SD, Barkhaus PE, Stålberg EV, Neuwirth C, Weber M. Motor unit number index: Guidelines for recording signals and their analysis. Muscle Nerve. 2018*
- https://www.encals.eu/wp-content/uploads/2017/12/MUNIX-Protocol_v1.0_Dec2017.pdf

MUNIX is currently used as an outcome measure in several ongoing clinical trials

Head-to-head analysis of different biomarker in a natural history trial in ALS (Biogen, Methodology Study) is in preparation

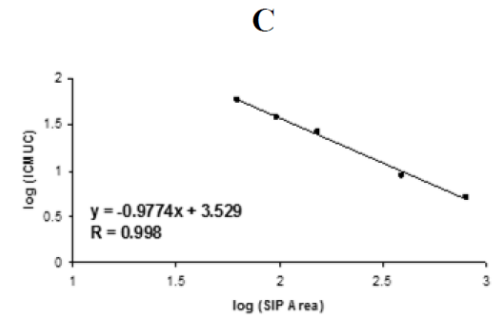
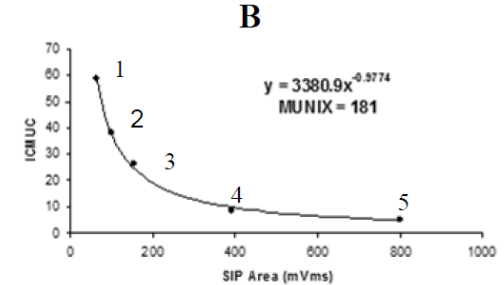
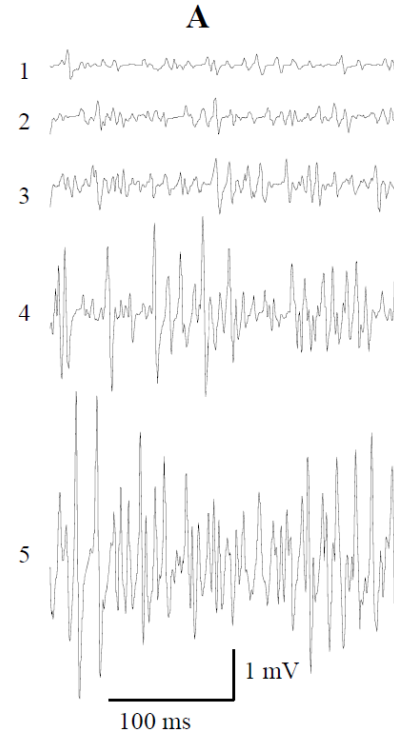
Method: How MUNIX works

- MUNIX provides an estimate of the number of functioning motor units in a given muscle

- MUNIX is a 2 step process:
 1. Recording the compound muscle action potential (CAMP) with optimized amplitude
 2. Recording of surface EMGs at various voluntary isometric force levels (SIPs, **A**)

→ MUNIX is computed using the area and power of the CMAP and SIPs (**B**)

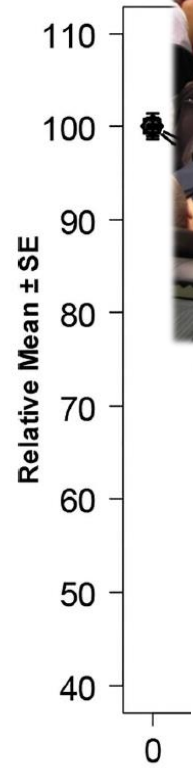
- In average < 5 minutes/muscle
- Can be recorded from any muscle in which CMAP can be elicited



Evolution of



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Application of MUNIX in different neuromuscular diseases and ALS



In spinal muscular atrophy MUNIX has been applied and was feasible in children >4 years of age
Verma S, Forte J, Ritchey M, Shah D. Motor unit number index in children with later-onset spinal muscular atrophy. Muscle Nerve. 2020

In inflammatory neuropathies, MUNIX has been used as an outcome measure for treatment response
- *Lawley A, Seri S, Rajabally YA. Motor unit number index (MUNIX) in chronic inflammatory demyelinating polyneuropathy: A potential role in monitoring response to intravenous immunoglobulins. Clin Neurophysiol. 2019*
- *Philibert M, Grapperon AM, Delmont E, Attarian S. Monitoring the short-term effect of intravenous immunoglobulins in multifocal motor neuropathy using motor unit number index. Clin Neurophysiol. 2017 Jan;128(1):235-240. doi: 10.1016/j.clinph.2016.11.012. Epub 2016 Dec 1. PMID: 27988478.*

MUNIX has been successfully trained and established in 27 centres in an international observational trial (North America, Europe), showing a superior reliability after hands-on-training
Neuwirth C, Braun N, Claeys KG, Bucelli R, Fournier C, Bromberg M, Petri S, Goedee S, Lenglet T, Leppanen R, Canosa A, Goodman I, Al-Lozi M, Ohkubo T, Hübers A, Atassi N, Abrahao A, Funke A, Appelfeller M, Tümmler A, Finegan E, Glass JD, Babu S, Ladha SS, Kwast-Rabben O, Juntas-Morales R, Coffey A, Chaudhry V, Vu T, Saepanh C, Newhard C, Zakrzewski M, Rosier E, Hamel N, Raheja D, Raaijman J, Ferguson T, Weber M. Implementing Motor Unit Number Index (MUNIX) in a large clinical trial: Real world experience from 27 centres. Clin Neurophysiol. 2018

MUNIX compared to MUNE: pro and contra

PRO:

- MUNIX is fast < 5min/muscle
- Proximal muscles feasible (biceps, tibial ant., deltoid)
- Multiple muscles in limbs can be measured
- Non-invasive, few electric stimulations needed
- Feasible even in children
- Good reliability, trainable
- No sophisticated hardware needed, but special software

CONTRA:

- MUNIX needs active cooperation of patients
- unsuitable in animal models
- some MUNIX measurements are technically challenging (e.g. biceps)
- Giving maximal manual resistance in MUNIX can be challenging (e.g. tibial ant, biceps)



MUNIX: things to keep in mind...

MUNIX uses the maximal (!) CMAP amplitude as a fundamental basis

→ Achieving a maximal CMAP amplitude is not as easy as generally assumed

→ Replace the recording electrode several times to track the spot with the highest CMAP
(up to 70% interrater-variability of CMAP amplitude)

Bromberg MB, Spiegelberg T. The influence of active electrode placement on CMAP amplitude. Electroencephalogr Clin Neurophysiol. 1997 Oct

MUNIX is not complicated to perform, but reliability is improvable and trainable even for experienced electrophysiologists and common pitfalls can be avoided

→ Use the opportunity to attend trainings (Email: christoph.neuwirth@kssg.ch)

MUNIX is intended to be a sensitive and reliable biomarker of early disease progression

→ sensitivity as a diagnostic marker is probably limited and should not replace clinical expertise

The MUNIX program is available on several EMG systems

MUNIX video example– Synergy



The screenshot displays the Synergy software interface for a patient named christoph gh, with a visit on 2/9/2017 at 9:10:18 AM. The test performed is MUNIX. The interface is divided into several panels:

- Stores:** Shows a CMAP trace for L Median - APB with a 5mV scale and 30ms duration.
- LongTrace:** Shows a long trace for L Median - APB with a 500µV scale and 500ms duration. A site labeled SIP-1 is marked with a 500ms and 500µV scale.
- Results Table:** A table titled "L Median - APB" showing parameters for various sites. The Beta parameter is 0.4. The table includes columns for # SIP, A, Alpha, MUNIX, MUSIX, Beta, AltMUNIX, and AltMUSIX.
- Results Graphs:** A graph titled "ICMUC v SIP Area (mVms)" showing a plot of ICMUC values against SIP Area (mVms). The x-axis ranges from 0 to 500, and the y-axis ranges from 0 to 200.
- Monitor:** Shows a real-time monitor for L Median - APB with a 2mV scale and 30ms duration.

The bottom of the interface features a toolbar with function keys (F1-F11) and their corresponding actions:

- F1: New Nerve
- F2: Exit Test
- F3: Fwave
- F4: Sensory NCV
- F5: Needle EMG
- F6: Results
- F7: Comments
- F8: S. Impose
- F9: Erase
- F10: Transfer
- F11: Change Focus

The Windows taskbar at the bottom shows the system time as 9:11 AM on 2/9/2017.

Comments? Suggestions? Questions...?

