

# MUNE over the past 30 years : a personal experience

*F. Wang (Liège, Belgique)*

Dear Alain,



# MUNE over the past 30 years : a personal experience

*F. Wang (Liège, Belgique)*




**But, without all these people, I wouldn't have been able to achieve it**


In 1991

**CHU Liège**

**Neurology  
Citadelle**



**Neurology  
Sart Tilman**

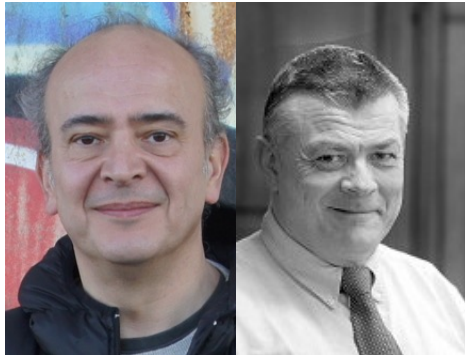


**PRM  
Sart Tilman**



**CHU  
de Liège**

**In 1991**



**It was one of the best decisions in my life !**

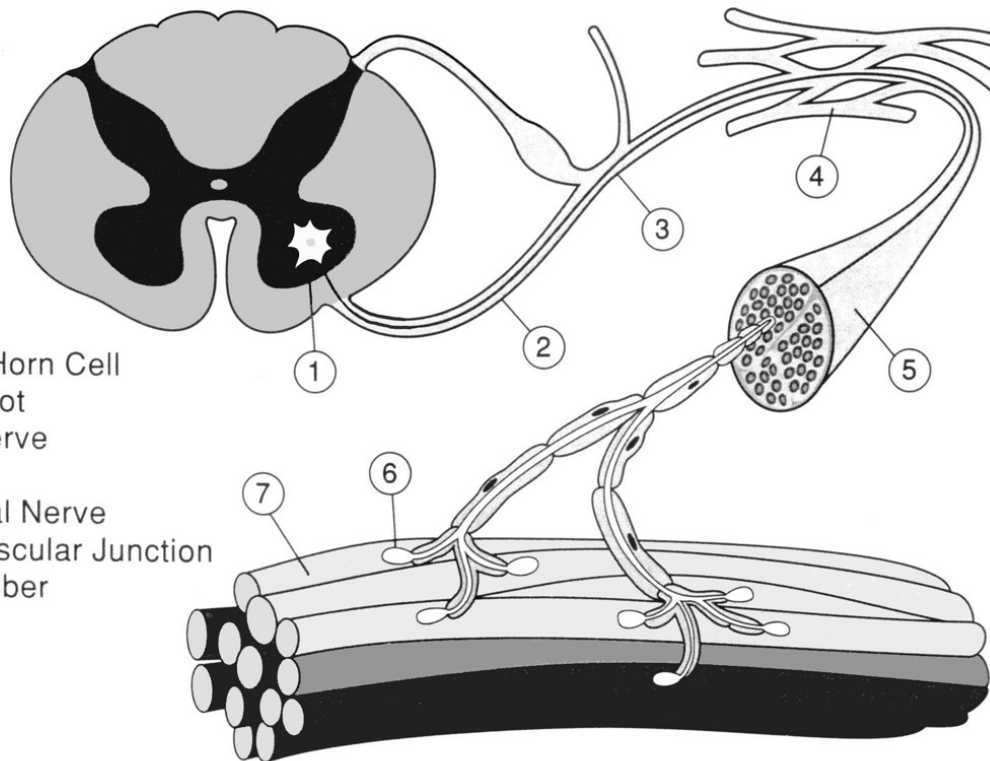
## Motor unit

### Motor unit potential

### Motor Unit Number Estimate

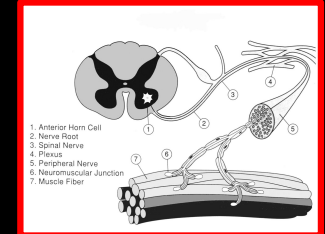
Renewed interest  
in the early 1990s

1. Anterior Horn Cell
2. Nerve Root
3. Spinal Nerve
4. Plexus
5. Peripheral Nerve
6. Neuromuscular Junction
7. Muscle Fiber



- Initial MUNE : **McComas** *et al* , 1971
- **Macro EMG** : de Koning *et al* , 1988
- **Statistical method** : Daube, 1988
- **Computer MUNE** : Galea *et al* , 1991
- **MPS** : Doherty *et al* , 1993
- **STA** : Bomberg, 1993
- **F-response** : Stashuk *et al* , 1994

# General principle in 2 steps



## 1. Average MU size estimation

from a 10-20 MU sample



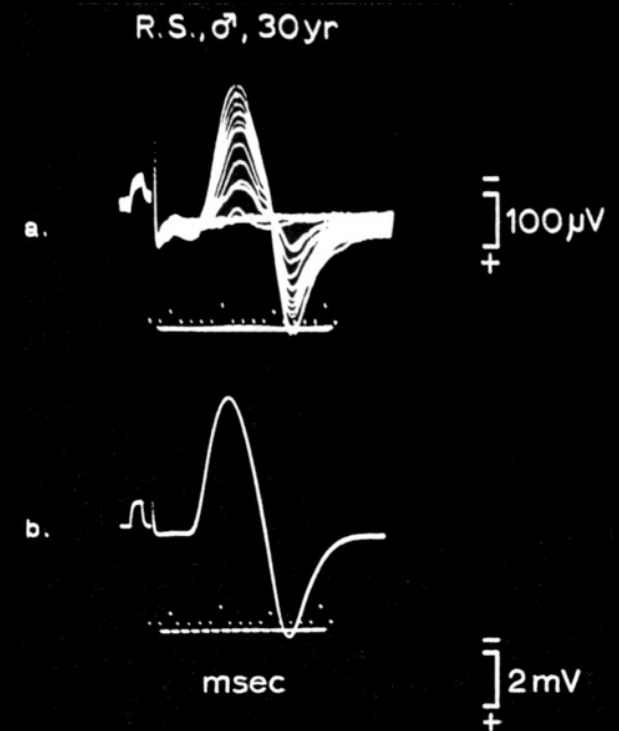
*Twitch*



MUP

## 2. Supramaximal Twitch or CMAP size measurement

$$\text{MUNE} = \frac{2}{1}$$





Alan McComas

## Fundamental principle in 2 steps

### Incremental stimulation

- percutaneous nerve stimulation
- short stimulation duration : 0.05 ms
- increased by 0.1 mA increment

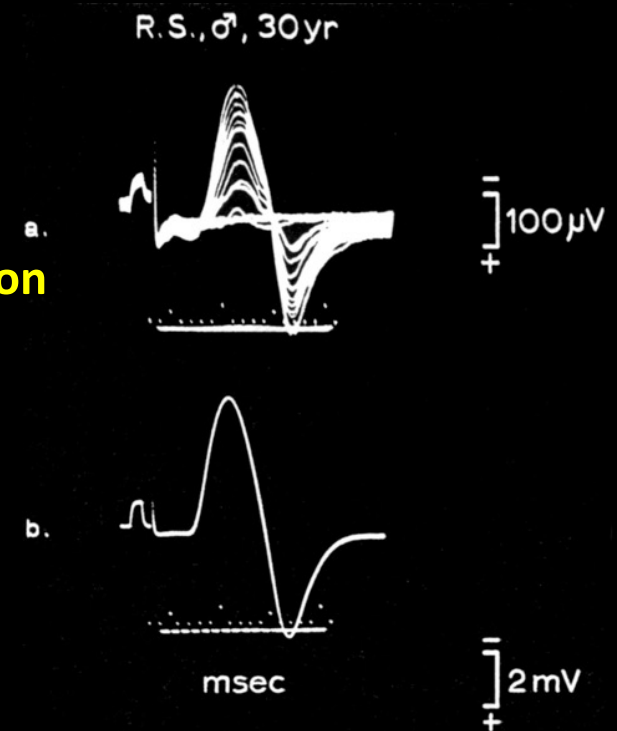
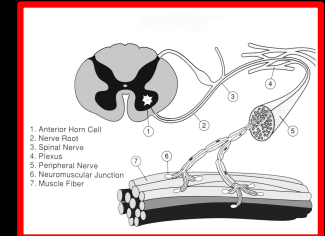
=> individual & sequential motor axon activation

### Initial MUNE technique based on incremental stimulation

- only 1 stimulation site/point
- 10 successive increments

=> average MUP size

=> supramaximal CMAP size/average MUP size = MUNE

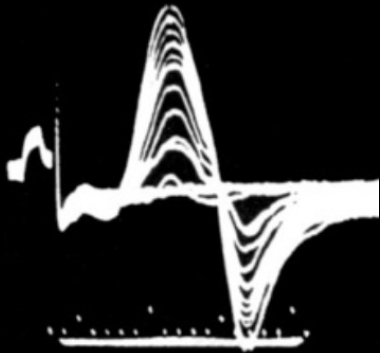






Alan McComas

R.S., ♂, 30 yr



Niagara falls (Canada)

McMaster  
University



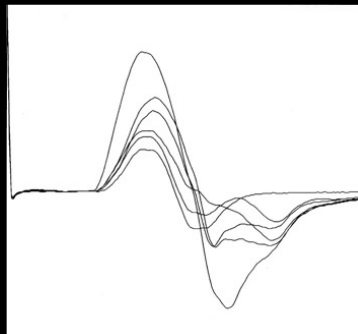
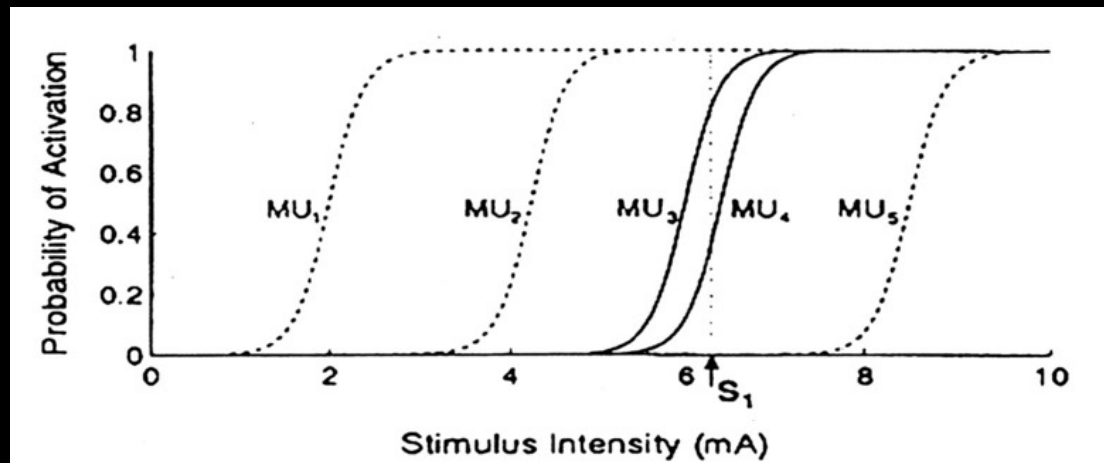
**Motor unit number estimate**



# Alternation



Alan McComas

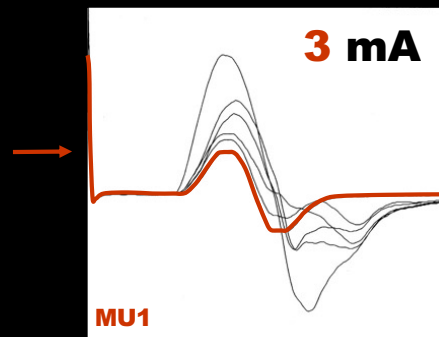
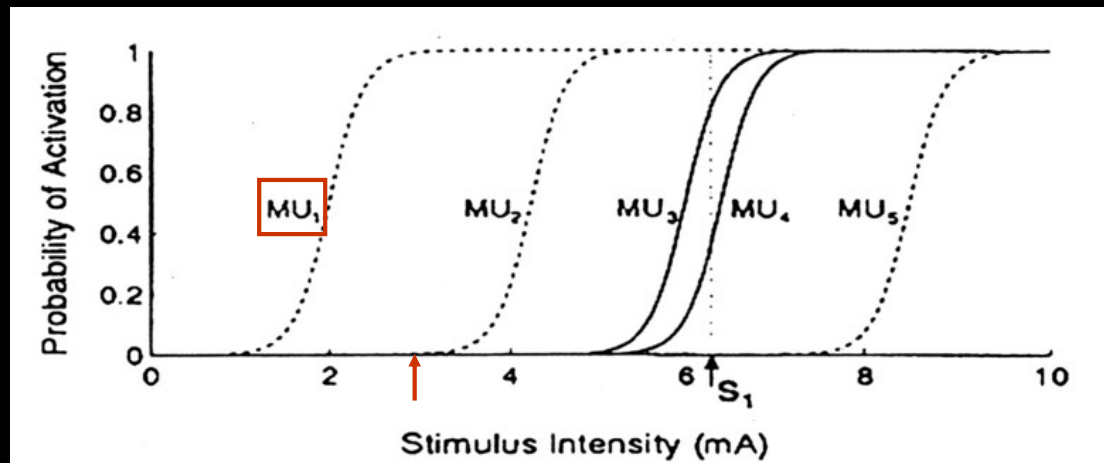


- The activation of MU does not occur in an all-or-nothing manner
- It occurs with a probability ranging from 0 to 100% based on the intensity of the stimulus

# Alternation



Alan McComas

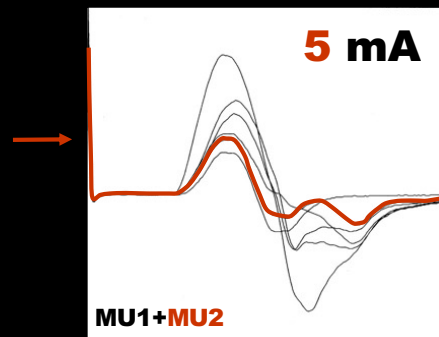
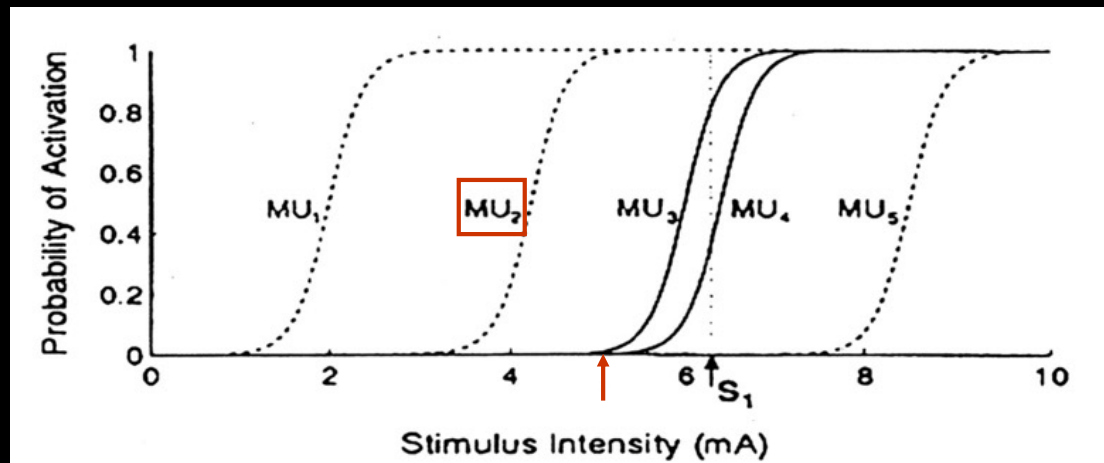


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Alan McComas

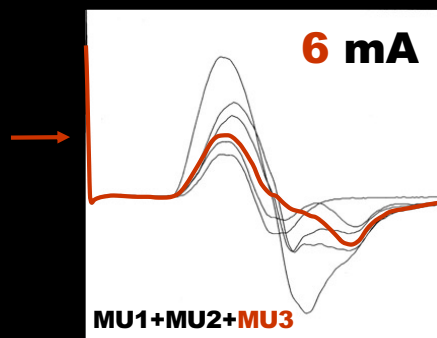
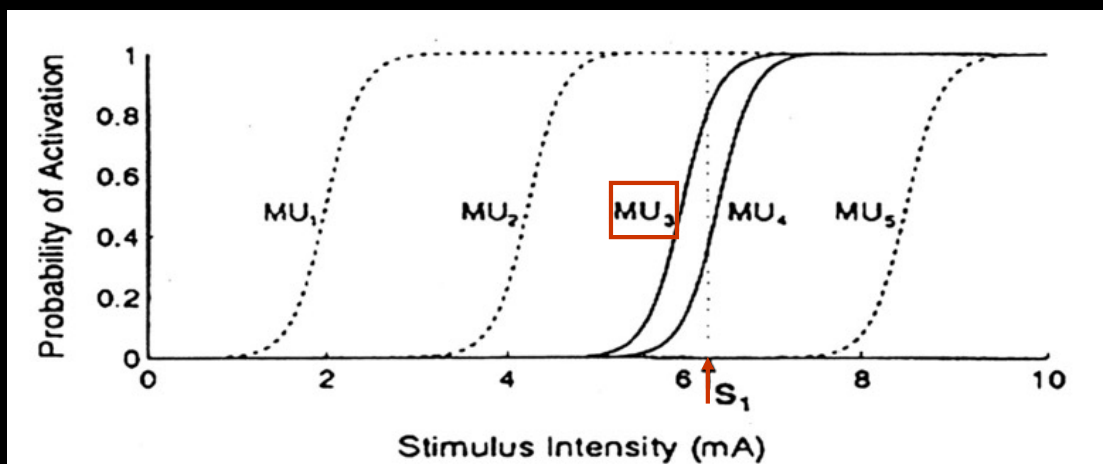


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Alan McComas

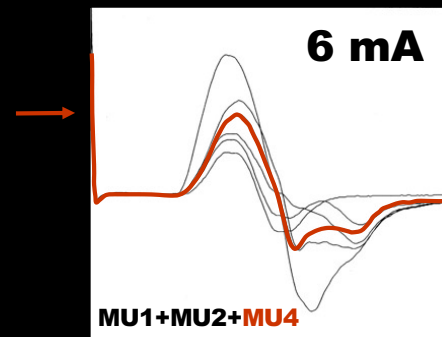
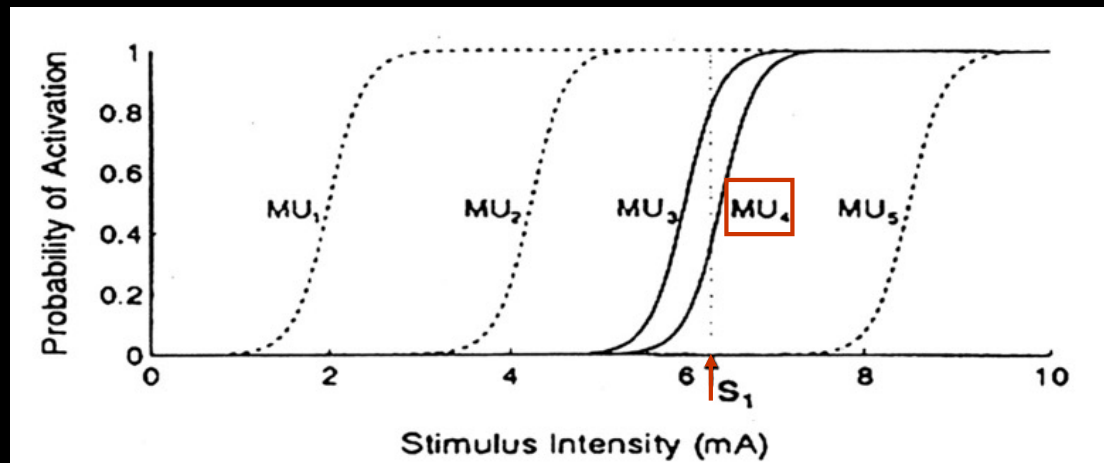


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Alan McComas

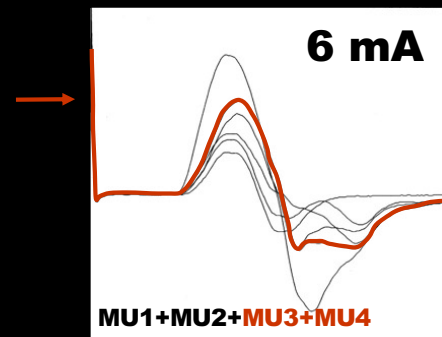
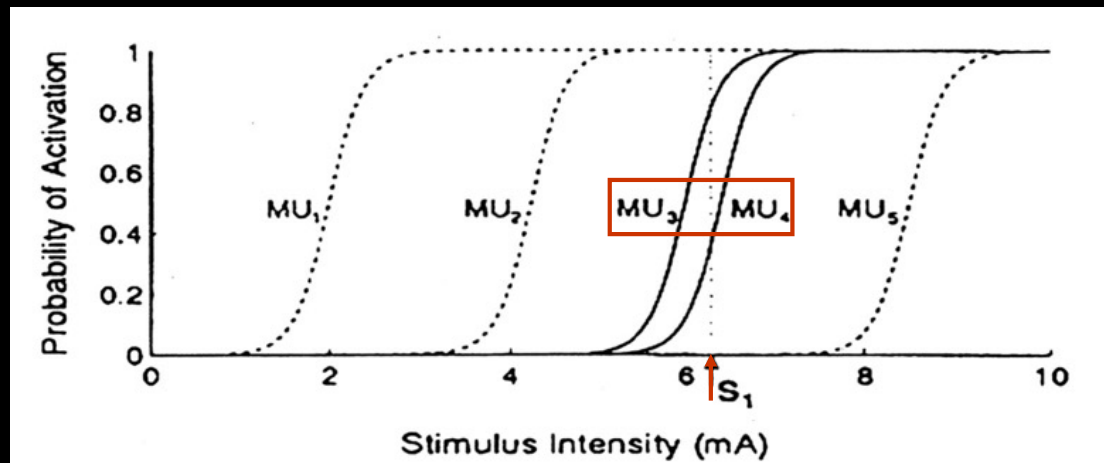


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Alan McComas



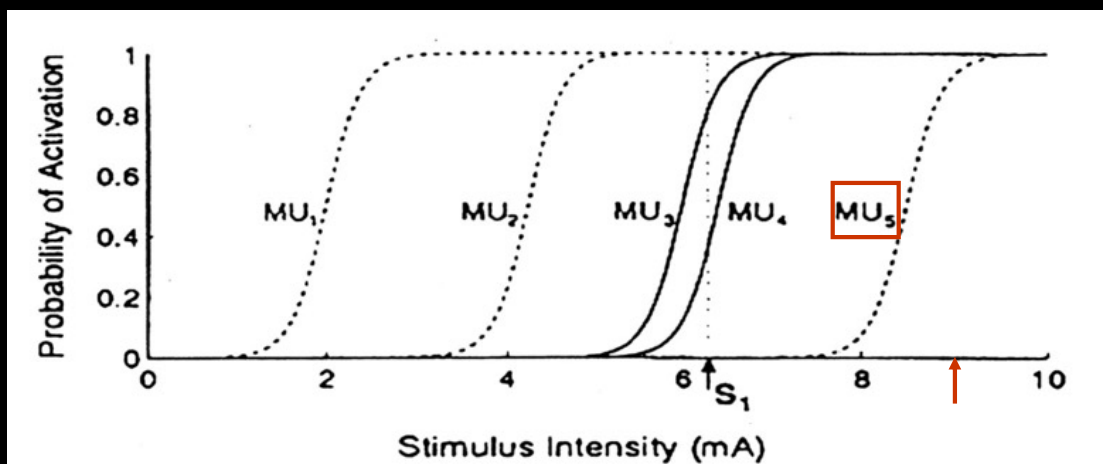
- The activation of MU does not occur in an all-or-nothing manner
- It occurs with a probability ranging from 0 to 100% based on the intensity of the stimulus



# Alternation

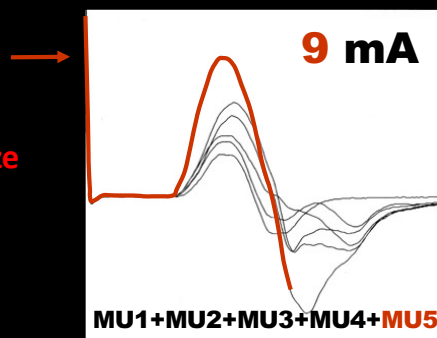


Alan McComas



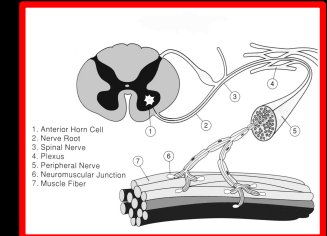
- 5 MU activated
- 6 distinct motor responses

=> underestimation of average MUP size  
=> overestimation of MUNE



- The activation of MU does not occur in an all-or-nothing manner
- It occurs with a probability ranging from 0 to 100% based on the intensity of the stimulus

## MPS -> AMPS



### Incremental stimulation

- percutaneous nerve stimulation
- short stimulation duration : 0.05 ms
- increased by 0.1 mA increment

### Multiple point stimulation method (Brown & Milner-Brown, 1976; Doherty et al, 1993)

- 10 stimulation sites/points along the course of the nerve
- only 1 increment at each site
- Often difficult to evoke 10 distinct motor units at 10 different stimulation sites, particularly when the number of motor units is low =>

### Adapted multiple point stimulation method

(Kadrie et al, 1976; validated by Wang & Delwaide, 1995)

- 4-5 stimulation sites/point along the course of the nerve
- 2-3 increments at each site, free of alternation (criteria)

MUP activated in an all-or-nothing manner  
Motor axons recruited

- with distinct thresholds,
- in an orderly and reproducible manner
- without any fractionation of the motor response to successive stimuli.

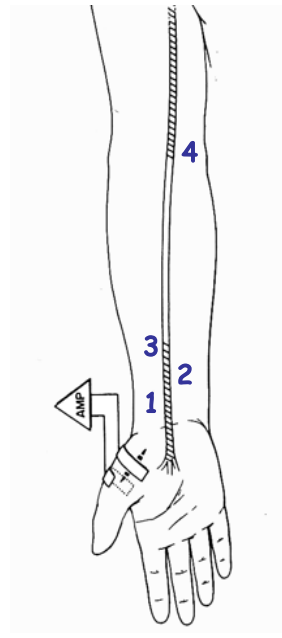
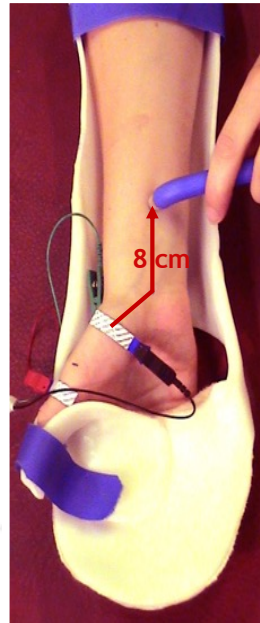
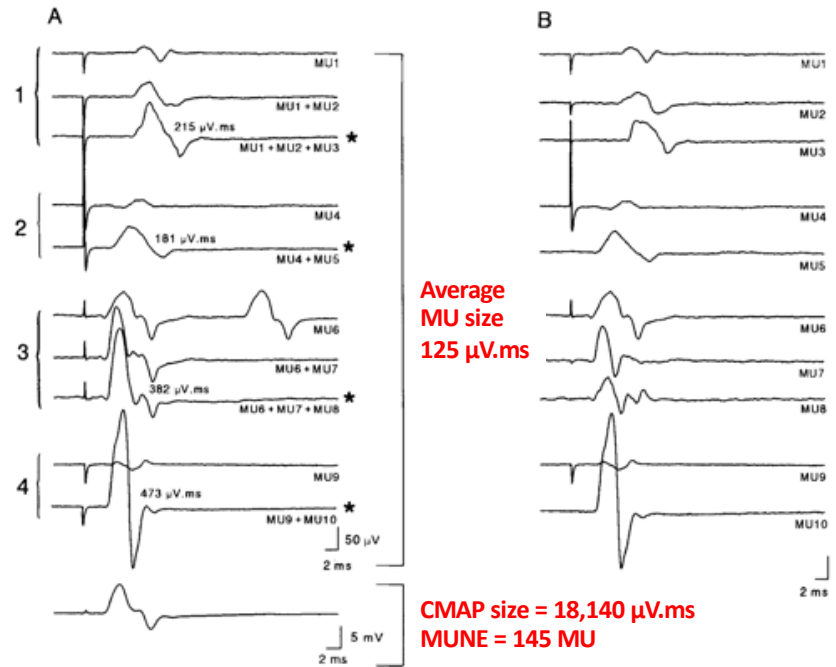
# NUMBER AND RELATIVE SIZE OF THENAR MOTOR UNITS ESTIMATED BY AN ADAPTED MULTIPLE POINT STIMULATION METHOD

FRANÇOIS-CHARLES WANG, MD, and PAUL J. DELWAIDE, MD, PhD

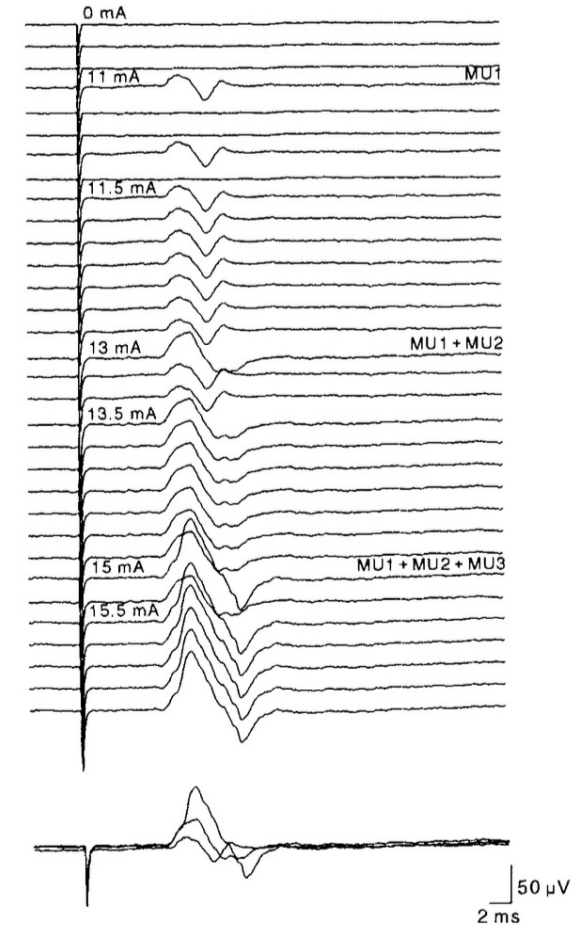


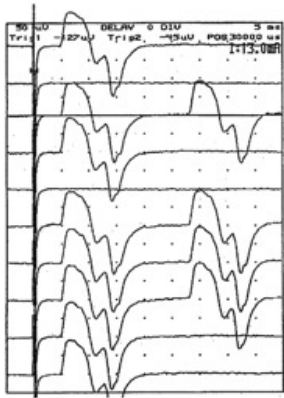
To ensure that the motor units activated at different stimulation points are distinct from each other, the morphology of each motor unit potential is reconstructed using a trace subtraction program

## AMPS method



## Incremental stimulation





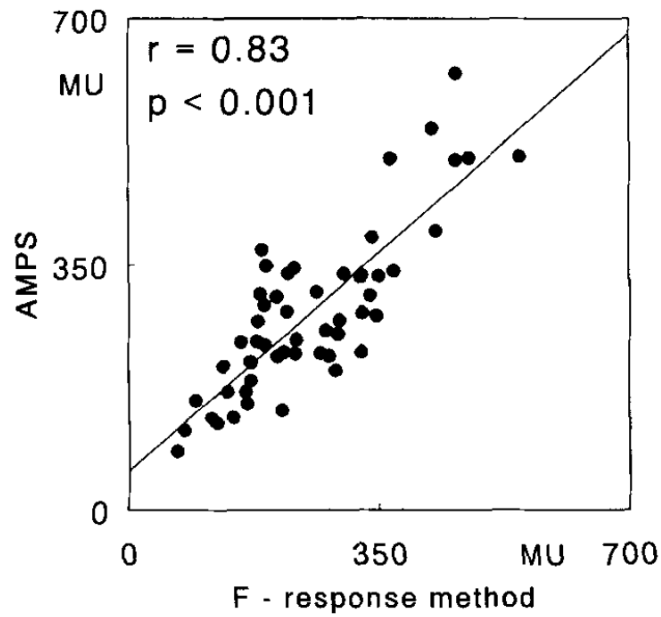
Single MU  
F-wave

### NUMBER AND RELATIVE SIZE OF THENAR MOTOR UNITS ESTIMATED BY AN ADAPTED MULTIPLE POINT STIMULATION METHOD

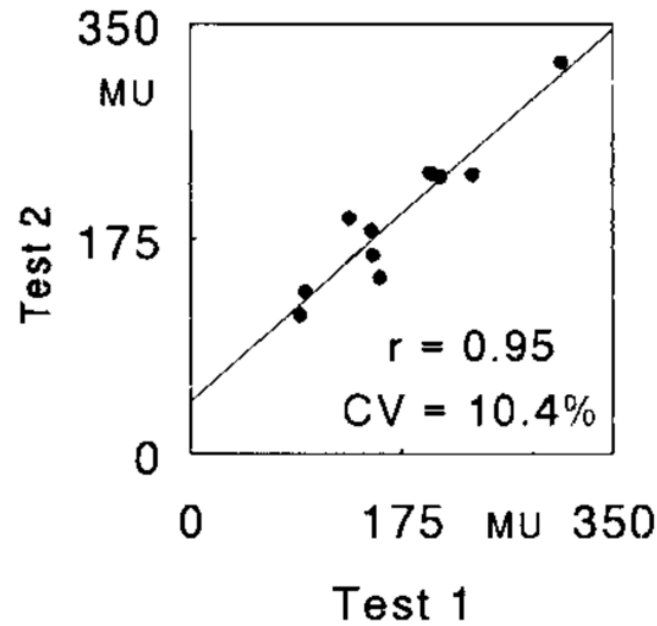
FRANÇOIS-CHARLES WANG, MD, and PAUL J. DELWAIDE, MD, PhD



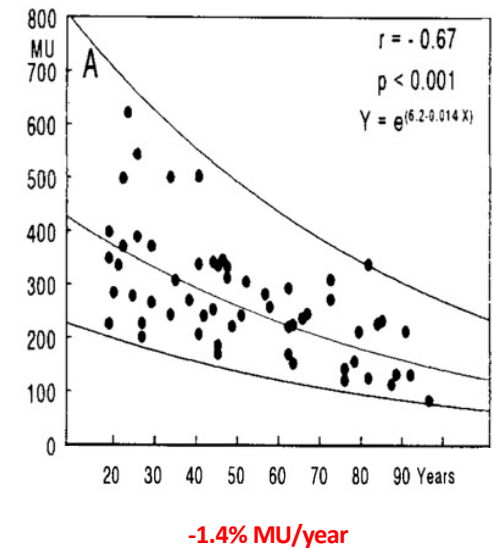
Convergent validity (n = 54)



Test-retest reliability (n = 10)



MUNE vs Age (n = 59)



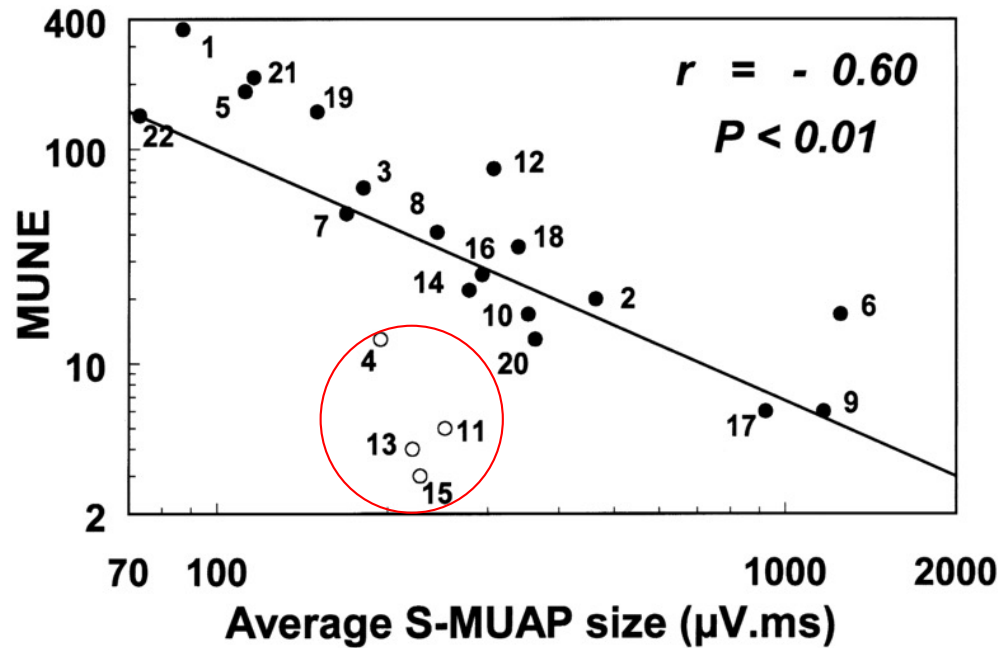
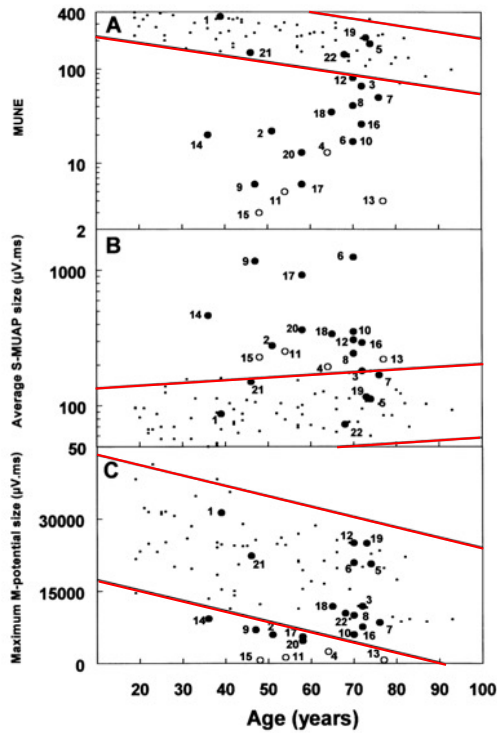


## Number and relative size of thenar motor units in ALS patients: application of the adapted multiple point stimulation method

### MUNE, MUP & CMAP size in ALS patients (n = 22)

F.C. Wang, P.J. Delwaide\*

### MUNE vs MUP size in ALS patients (n = 22)

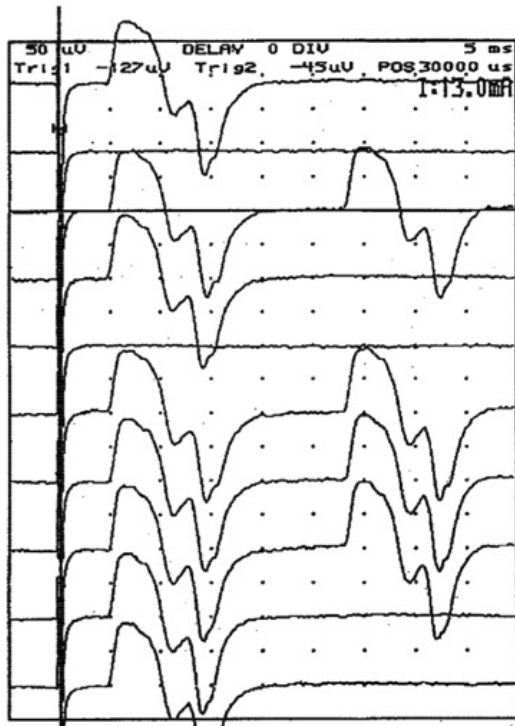


## AGE-RELATED CHANGES IN FASTEST AND SLOWEST CONDUCTING AXONS OF THENAR MOTOR UNITS

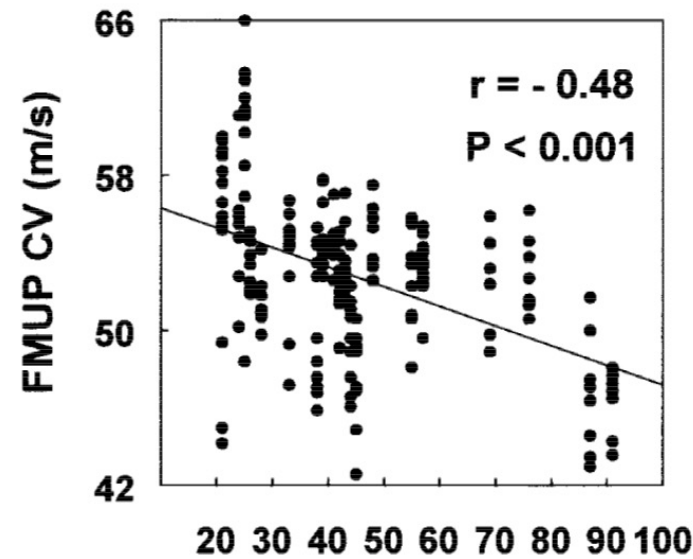
FRANÇOIS-CHARLES WANG, MD, VICTOR DE PASQUA, and  
PAUL J. DELWAIDE, MD, PhD



### Single MU F-wave



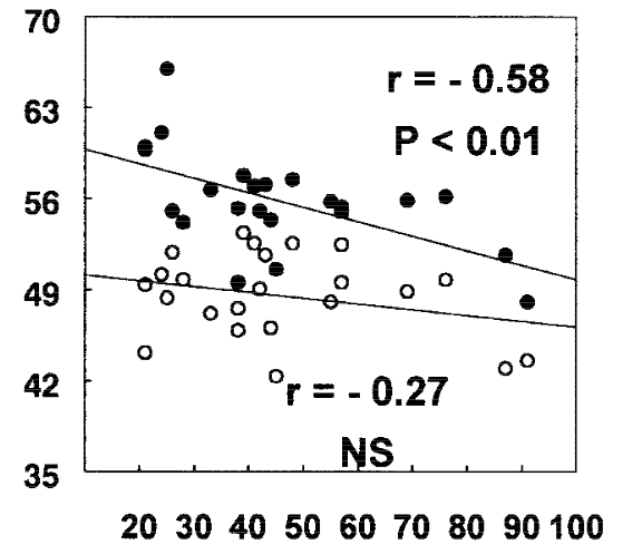
### Single MU F-wave CV vs Age



The conduction velocity of motor units decreased significantly with age

Age (years)

Prominent loss with age of the largest and fastest conducting MU







## Single motor axon conduction velocities of human upper and lower limb motor units. A study with transcranial electrical stimulation

Francesca Dalpozzo, Pascale Gérard, Victor De Pasqua,  
François Wang, Alain Maertens de Noordhout\*

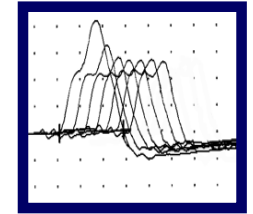
**Conclusions:** Compared with previously published values, the present method gives better access to slow-conducting units, first recruited by transcranial stimulation and voluntary effort. The spectrum of individual CV was much broader for EIP and TA than for FDI. A linear decline of maximal CV with age was observed, while minimal CV were not affected, suggesting that aging causes a selective loss of the fastest-conducting units. © 2002 Elsevier Science Ireland Ltd. All rights reserved.



## Prognostic value of decremental responses to repetitive nerve stimulation in ALS patients

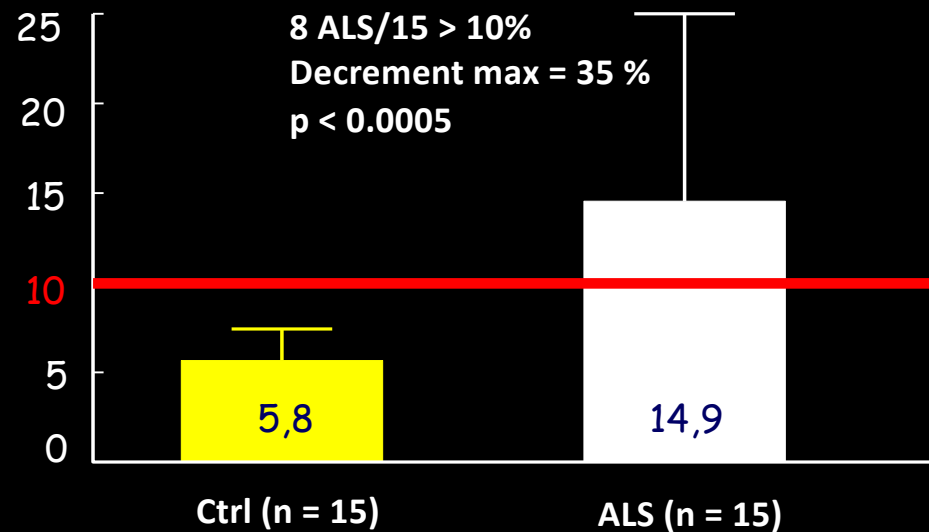
**Article abstract**—Decrement of the thenar compound muscle action potentials (CMAP), after repetitive nerve stimulation (RNS) of the median nerve at 3 Hz, was evaluated in patients with ALS before riluzole therapy. CMAP size as well as motor unit number and size estimates were evaluated twice before and after 1 year of riluzole therapy. The correlation between decrement and CMAP size reduction per year was highly significant ( $r = 0.77$ ), but no relationship could be demonstrated between decrement and other variables. The authors thus propose that decrement after RNS may be used as a predictor of further drop in CMAP size.

NEUROLOGY 2001;57:897–899

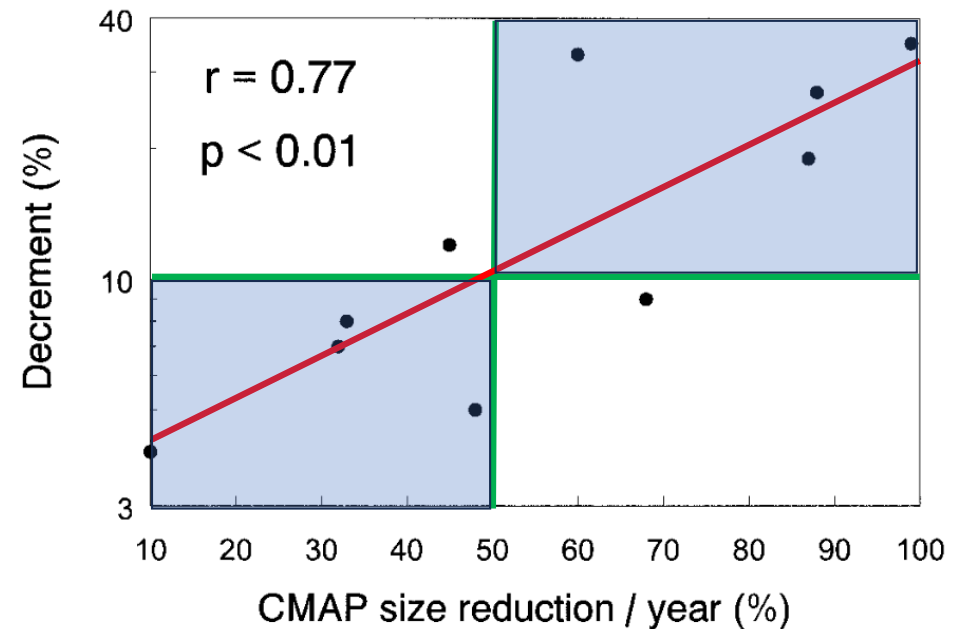


F.C. Wang, MD; V. De Pasqua, Phys; P. Gérard, Phys; and P.J. Delwaide, PhD

### Decrements at the beginning of the study (median nerve at the wrist)



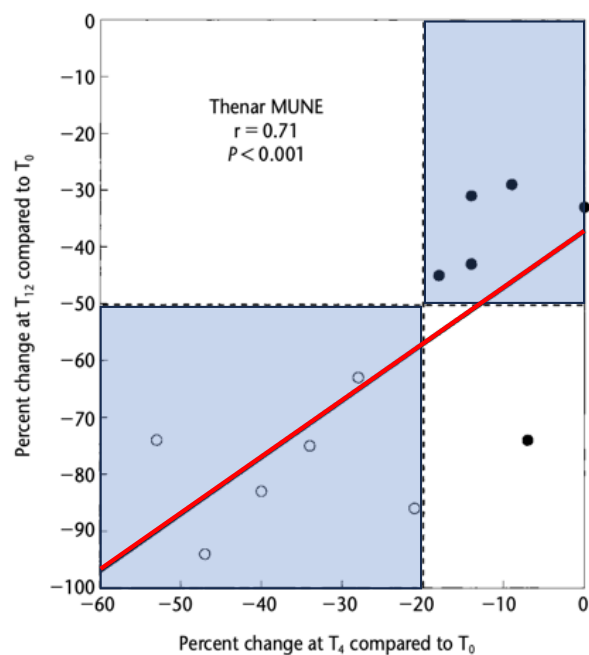
### Decrement may be used as predictor of further drop in CMAP size



## Changes in motor unit numbers in patients with ALS: a longitudinal study using the adapted multiple point stimulation method\*



FC Wang<sup>1</sup>, O Bouquiaux<sup>1</sup>, V De Pasqua<sup>1</sup> and PJ Delwaide<sup>2</sup>



Still among patients with ALS :

Percent change of MUNE at T<sub>4</sub>, compared to T<sub>0</sub> may be used as predictor of percent change of MUNE at T<sub>12</sub>, compared to T<sub>0</sub>

If percent change of MUNE at T<sub>4</sub>, compared to T<sub>0</sub> is > 20%

=> percent change of MUNE at T<sub>12</sub>, compared to T<sub>0</sub> will be > 50%

# Liège convention center



**2004**

*Sous la direction de*

*Alain Maertens de Noordhout et François Wang*



*E.A.*

# Analyse critique des techniques d'estimation du nombre d'unités motrices

F.C. WANG (\*), P. GÉRARD (\*\*), O. BOUQUIAUX (\*)

TABLEAU II : AVANTAGES ET LIMITES DES MÉTHODES DE COMPTAGE D'UNITÉS MOTRICES

	Technique Incrémentale (manuelle) (2)	SPM (manuelle) (7-9)	TASPM (10-11)	STA (14-16)	Réponses-F (manuelle) (12)	Méthode Statistique (20-21)
<b>Biais lié à l'alternation</b>	+++	0	+	0	0	0
<b>Biais de sélection</b>	Axones moteurs les plus excitables	Axones moteurs les plus excitables	Axones moteurs les plus excitables	Première UM recrutées par la contraction volontaire  Grandes UM	?	Pré-requis discutable : toutes les UM sont de taille identique  Ignore les UM de grande et de petite taille
<b>Applicable dans toutes circonstances</b>	Oui	Non	Oui	Oui	Non	Non
<b>Applicable aux muscles proximaux</b>	Oui	Non	Non	Oui	Non	Oui
<b>Coefficient de variation des E<sub>i</sub> UM</b>	± 15 %	± 10 %	± 10 %	> 20 %	± 10 %	< 10 % (moyenne de 2 ENUM)
<b>Rapidité de réalisation</b>	± 10'	> 20'	< 20'	± 45'	> 30'	< 20'
<b>Confort</b>	+++	+++	+++	Invasif	++	Grand nombre de stimulations à intensité élevée
<b>Disponibilité des logiciels</b>	+++	+++	+++	++	+++	Un seul fabricant

ENUM : estimation du nombre d'unités motrices, SPM : stimulation en des points multiples, STA : *Spike-Triggered Averaging*, TASPM : technique adaptée de stimulation en des points multiples, UM : unité motrice.

Critical analysis of various counting methods

Chapter 5



Adapted multiple point stimulation MUNE technique



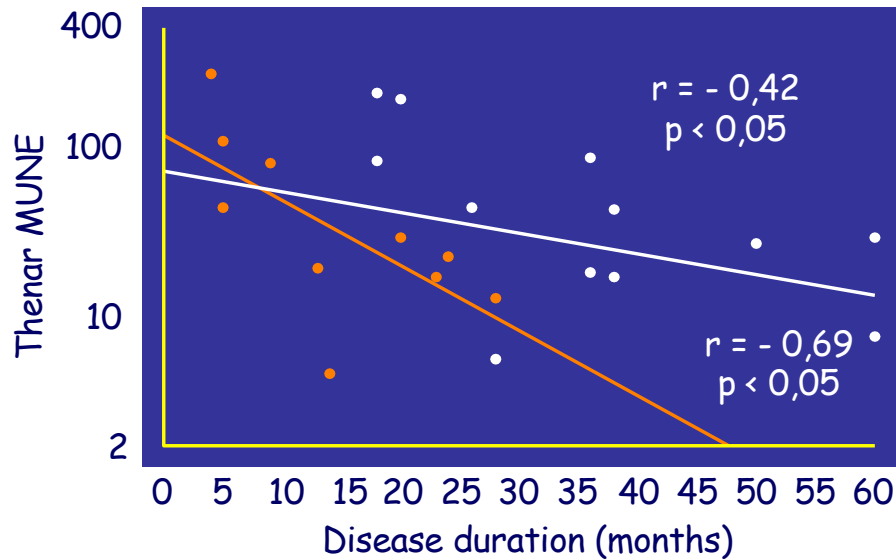
F.C. Wang<sup>a,\*</sup>, O. Bouquiaux<sup>a</sup>, V. De Pasqua<sup>a</sup>,  
 A. Maertens de Noordhout<sup>b</sup> and P.J. Delwaide<sup>b</sup>



Survival (n = 22)

> 3 ans

< 3 ans



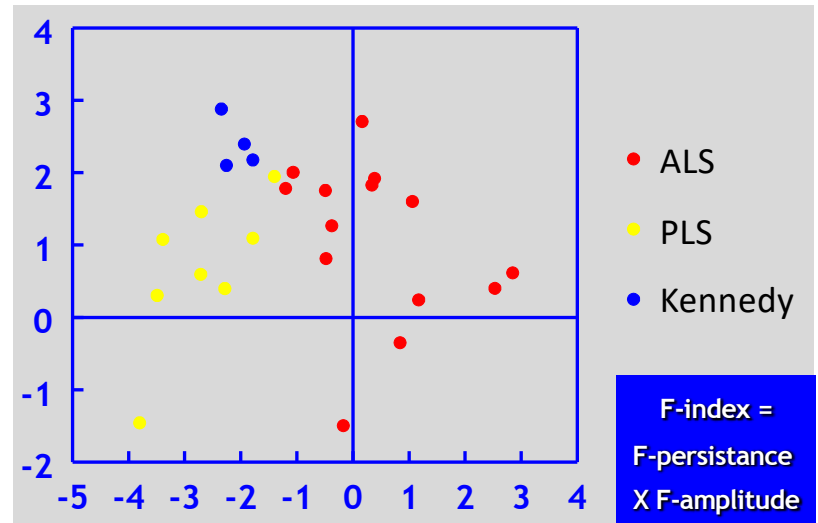
Chapter 14

Motor neuron disorders: novel electrophysiologic approach (MUFDEC protocol)

F.C. Wang<sup>a,\*</sup>, N. Le Forestier<sup>b</sup>, P. Gérard<sup>a</sup>, J.C. Willer<sup>b</sup>, V. Meininger<sup>b</sup>,  
 D. Dive<sup>a</sup>, A. Maertens de Noordhout<sup>a</sup> and P. Bouche<sup>b</sup>

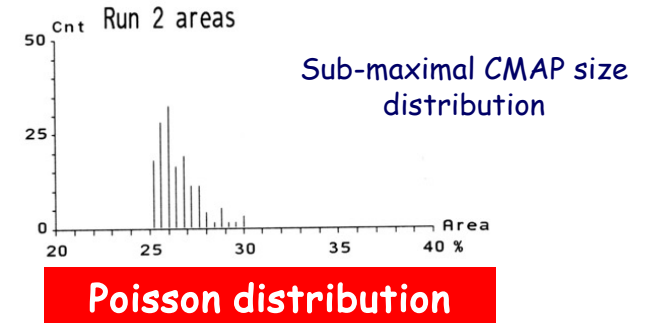
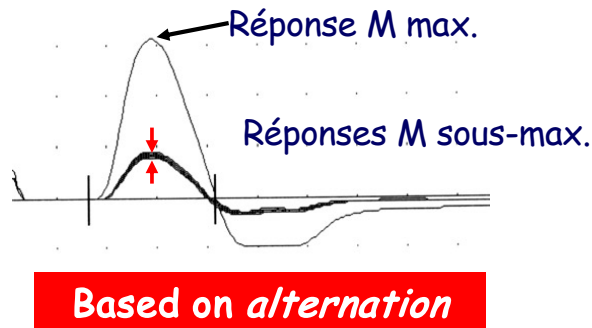
Canonical discriminant analysis

CAN2 =  $\text{Dex} \times 0.04 - (\text{CMAP/DD}) \times 0.00006 + \text{rightTAarea} \times 0.00005 - \text{F-index} \times 0.0061$

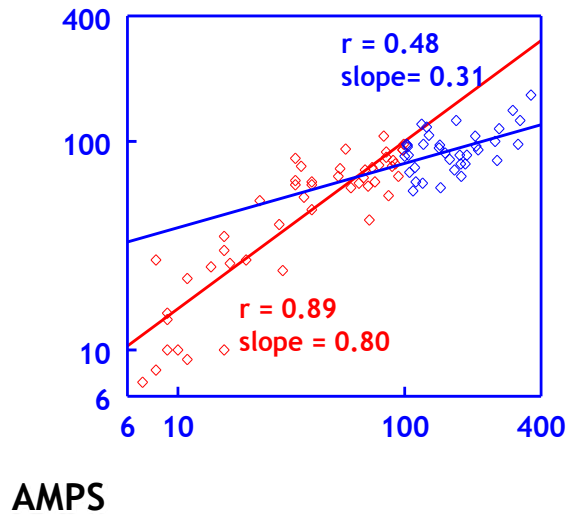
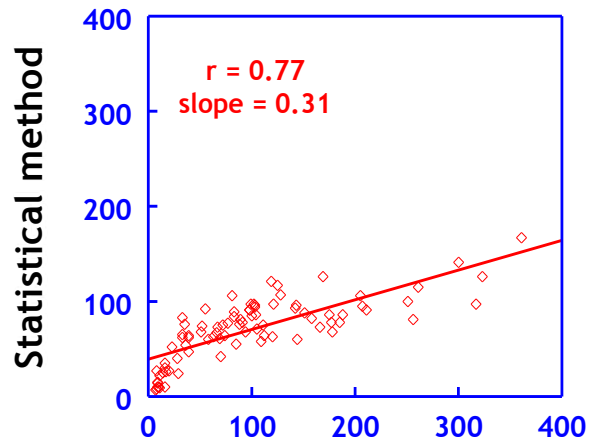


CAN1 =  $\text{Dex} \times 0.15 + (\text{CMAP/DD}) \times 0.0003 - \text{rightTAarea} \times 0.00006 - \text{F-index} \times 0.0064$





### AMPS vs Statistical method (n = 100)



- 120-300 sub-maximal stimuli
- If: - sub-maximal CMAP size distribution is Poisson  
- all MUP are identical in size
- Variance = Mean

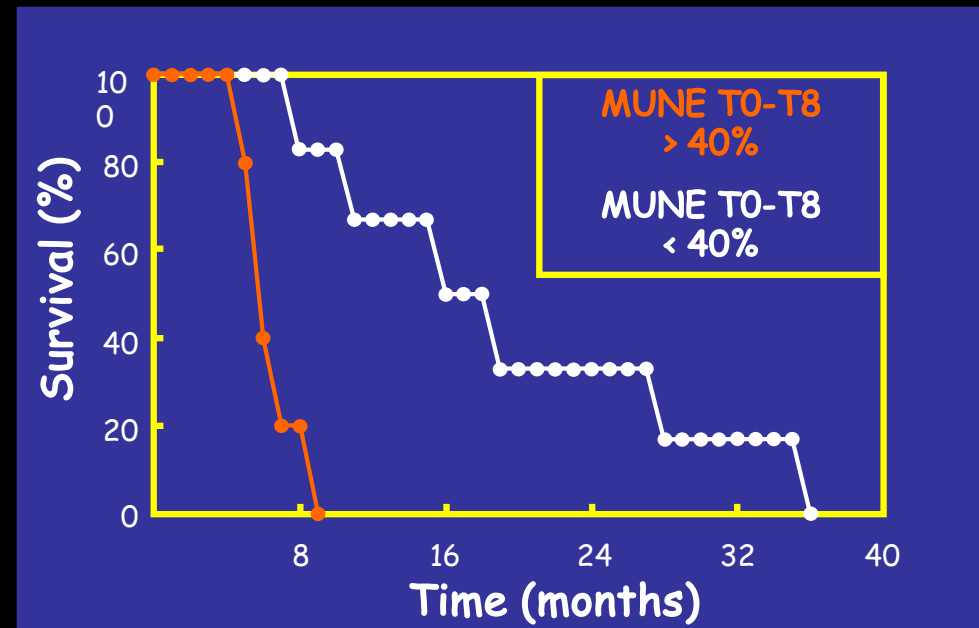
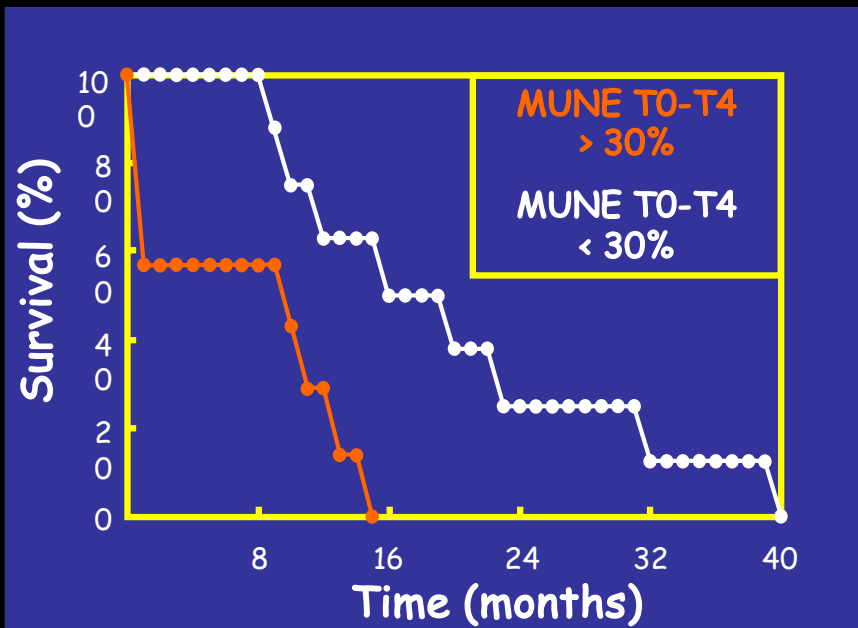
$$\text{PUM size} = \frac{\text{sub-maximal CMAP size variance}}{\text{mean - minimal (CMAP size)}}$$

Dropouts by AMPS: 0%  
Dropouts by the statistical method: **15%**



# Unpublished data

Patients with a small reduction in MUNE between the 4<sup>th</sup> or 8<sup>th</sup> month and the baseline evaluation had significantly longer survival than patients with a MUNE reduction exceeding 30% at the 4th month or exceeding 40% at the 8th month



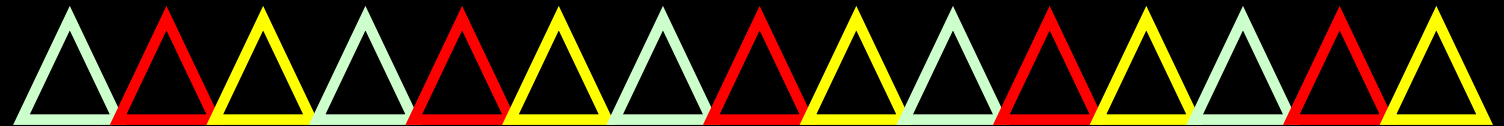
The Kaplan-Meier survival analysis

# MUNIX

CMAP (percutaneous  
nerve stimulation)

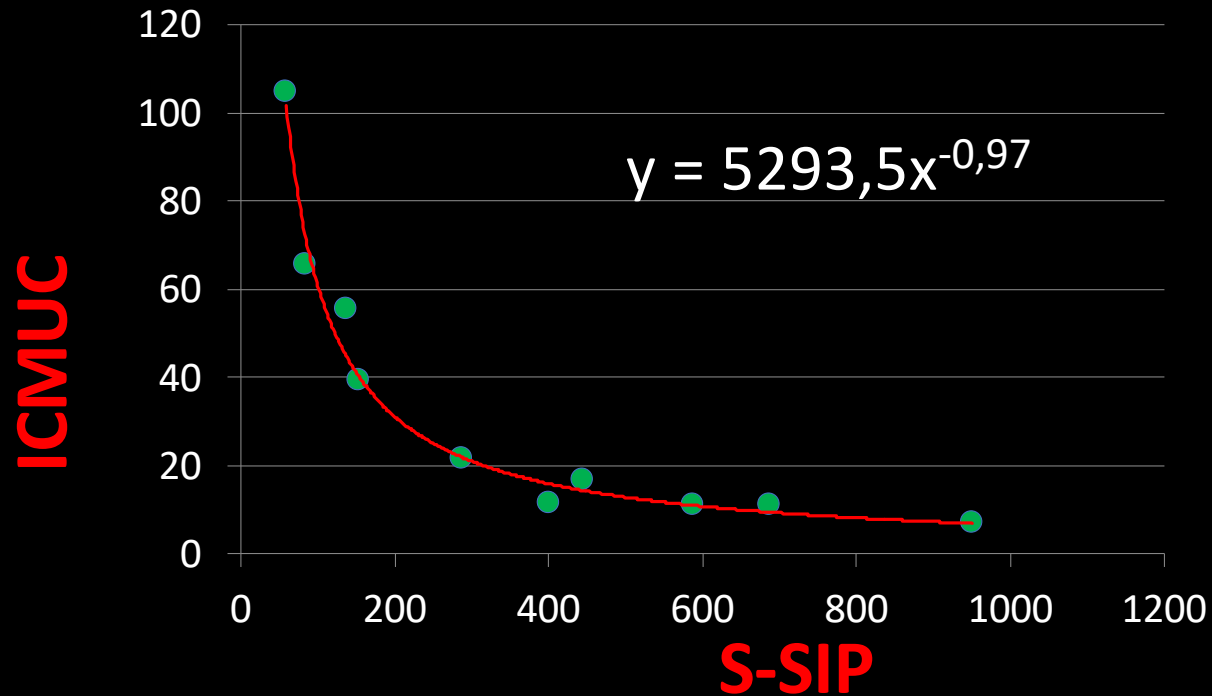


Interference pattern by surface EMG (S-SIP)



MUP number: **N**  
MUP amplitude: **A-PUM** (mV)  
MUP area: **S-PUM** (ms.mV)  
MUP power: **P-PUM** (ms.mV<sup>2</sup>)

# MUNIX



MUNIX = ICMUC when S-SIP (x) = 20 ms.mV

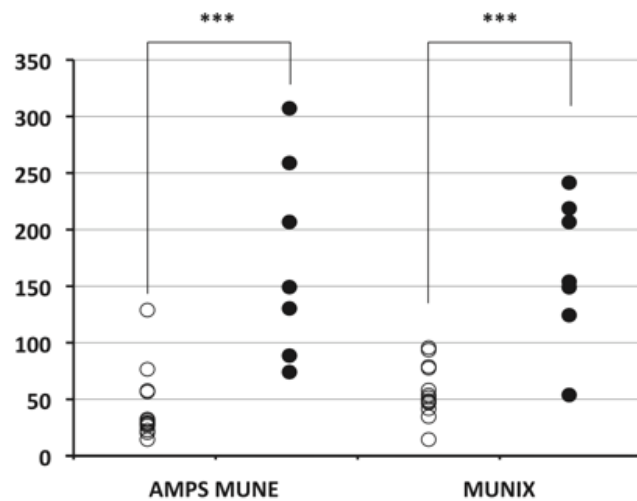
**MUNIX = 290**

## Correlations between MUNIX and adapted multiple point stimulation MUNE methods

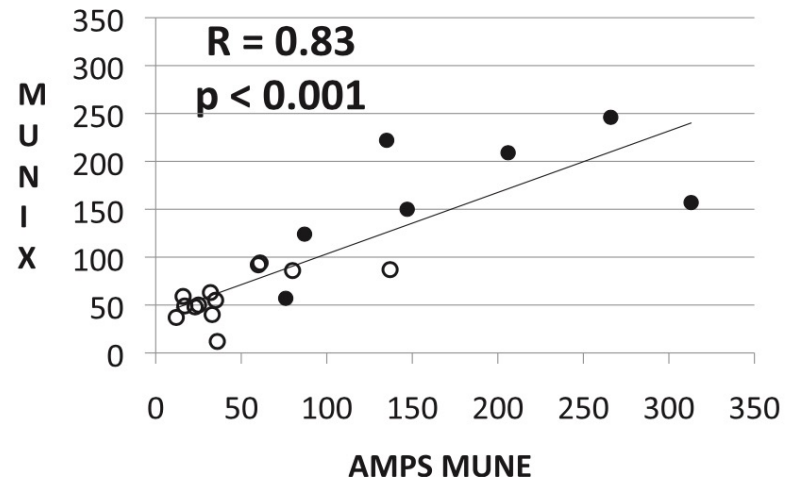
Karim Benmouna, Christophe Milants, François Charles Wang\*

Comparative study between our counting method and the MUNIX procedure, both in healthy subjects and patients with motor neuron degeneration

Comparison



Correlation

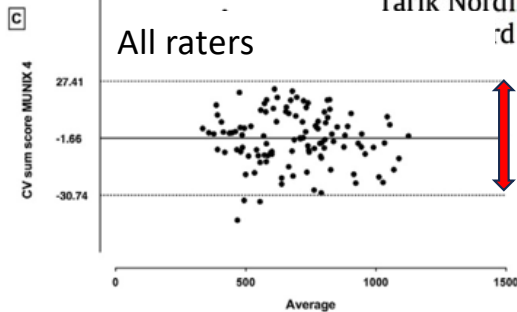




## Motor unit number index as an individual biomarker: Reference limits of intra-individual variability over time in healthy subjects



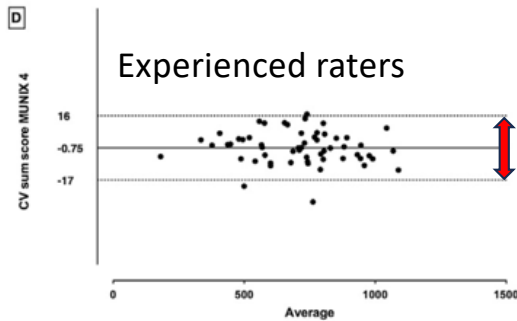
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### 11 university departments

Five operators were considered experienced because they had been practicing the MUNIX technique several times a month for more than 3 years

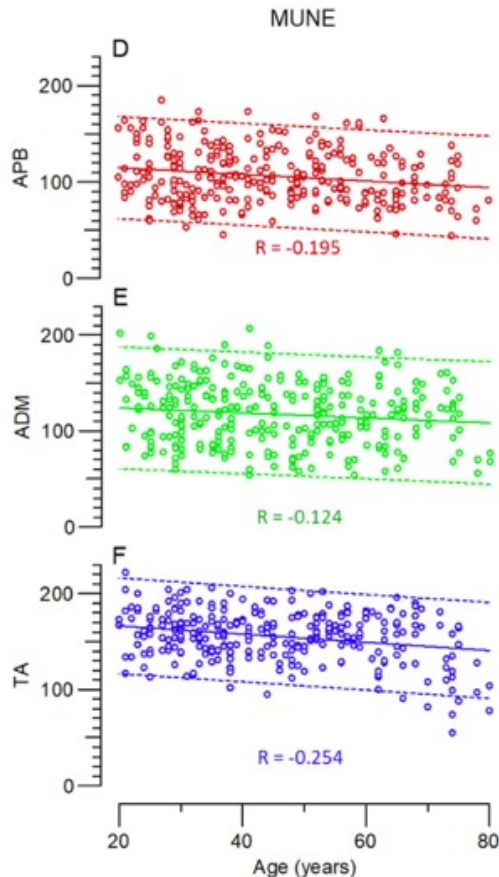
**Sum score = TA + ADM + APB + deltoid results**



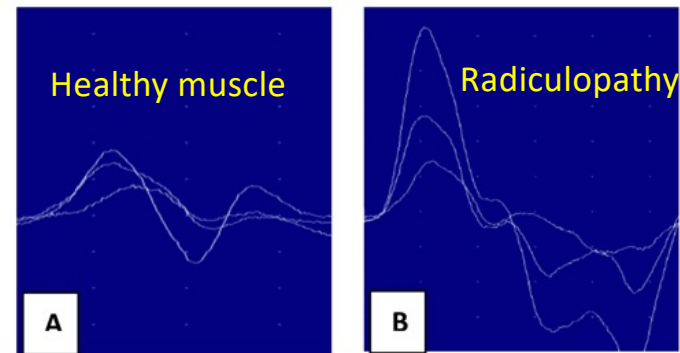
### For the purpose of longitudinal patient follow-up

**A change in the MUNIX sum score more than 20% could be interpreted as a significant change of muscle innervation.**

# Conclusions



(Sørensen *et al*, 2023)



**Figure 5.** Examples of incremental stimulation in modified MPS MUNE. (A) 3 incremental stimulations in a healthy ADM. (B) 3 incremental stimulations in an ADM affected by radiculopathy. The larger steps in B will result in a larger mean SMUP and lower MUNE overall. MPS: multipoint stimulation. MUNE: motor unit number estimate. ADM: abductor digiti minimi. Scale: 20 ms per horizontal division and 100uV per vertical division.

(Mandeville *et al*, 2023)

- MUNE is always a relevant parameter, for instance for assessing the effectiveness of new treatments in spinal muscular atrophy
- AMPS is non-invasive, reliable and fast MUNE technique, applicable to any patient regardless of the reduction in number of motor units
- MUNIX : offers many benefits, may best be applied for tracking over time (Mandeville *et al*, 2023), but perhaps not enough benefits, as its primary developer continues to propose new procedures as STEPIX & AMPIX (Nandedkar *et al*, 2022)
- High- density S-EMG (van Dijk *et al*, 2008)
- MScanFit MUNE (Bostock, 2016)



**CHU ST**



**CHR**

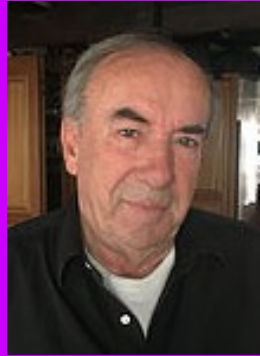




**My Masters !**



**My Masters !**



**My Masters !**



**Pascale**



**Minh**



**Li**



**Alain !**





**Amicalement vôtre**



**Amicalement vôtre**