## Quantitative neuromuscular monitoring Now way around?



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Head of Division of Anesthesiology

Ospedale Regionale di Lugano and Director of Department of Anesthesiology EOC Consultant physician HUG









### Poison discovered by the Amazonian Indians







## Neuromuscular blocking agents (NMBA) in modern clinical practice: the benefits

General anaesthesia: 400 million/year worldwide

✓ NMBA: **70%** of elective surgeries

Intensive care:

✓ NMBA: 30 to 60% of patients

## Thus, the safe use of muscle relaxants has become a public health issue.

Intercontinental Marketing Services (IMS) Health, Multinational Integrated Data Analysis System (MIDAS), September 2010











**400 MILLION!** 



Facilitates intubation conditions, reduces risks Improves conditions for robotic, laparascopic surgery Allows ENT operations on vocal cords, trachea Facilitates mask ventilation, Lung protective ventilation, Jet ventilation Critical care: ARDS

Czarnetzki C , Rehberg B, Walder B, Moderne Anästhesie, Therapeutische Umschau, 2017,
 deBacker J, Hart N, Fan E. Neuromuscular Blockade in the 21st Century, Management of the Critically III Patient. Chest, 2017







A STUDY OF THE DEATHS ASSOCIATED WITH ANESTHESIA AND SURGERY\* based on a study of 599,548 anesthesias in ten institutions 1948–1952, inclusive Henry K. Beecher, M.D., and Donald P. Todd, M.D.

> Annals of Surgery July, 1954

TABLE XIII. Total Incidence of "Curare" Use and Associated Death.

Total Number Anesthesias. Number Anesthesias in which "Curare" Used (1 Frequency of Death Related to Anesthesia Anesthesias Which Did Not Include "Curare" (66) 1 : 2100 Anesthesias Which Included "Curare" (118). 1 : 370















Christie and Churchill-Davidson, Lancet 1958







## SINGLE TWITCH



















## TRAIN DE QUATTRE









## DOUBLE BURST ET TRAIN DE QUATRE (TOF)









## **CLINICAL SIGNS**



## PERIPHAL NERVE STIMULATOR (PNS)









## PERIPHAL NERVE STIMULATOR (PNS)





Baurain et al Anesth & Analg 1998





## PERIPHAL NERVE STIMULATOR (PNS)





Baurain et al Anesth & Analg 1998





## **CLINICAL SIGNS OR PNS**



Genève

FACULTÉ DE MÉDECINE





Upper airway permeability

Eikermann et al Am J Respir Crit Care Med 2007







eoc

## TOF-RATIO $\geq 0.9$ ?



no RP

TOF-ratio: 0.8

Upper airway permeability

Eikermann et al Am J Respir Crit Care Med 2007









## TOF-RATIO $\geq 0.9$ ?

#### Tabelle 1

Quantifizierung klinisch relevanter Effekte einer partiellen neuromuskulären Blockade mit der TOF-Ratio des M. adductor pollicis

Monitoring M. adductor pollicis	TOF-Ratio			
	0,5	0,8	1	
Tidalvolumen	Normal	Normal	Normal	
Forcierte Vitalkapazität	Häufig beeinträchtigt	Häufig normal	Normal	
Pharyngeale Funktion (Schluckakt)	Sicher beeinträchtigt	Meist beeinträchtigt	Meist normal	
Integrität des oberen Atemwegs	Sicher be inträchti jt	Meist bee ntra chtig	Meist normal	
Hypoxische Atemantwort	Häufig beeint ächtigt	Häufig norma	Normal	

Die Angaben basieren auf Ergebnissen von Untersuchungen zweier Arbeitsgruppen (Eikermann et al. [17, 18, 21] und Eriksson [22] sowie Eriksson et al. [23]) an wachen, gesunden Probanden während partieller neuromuskulärer Blockade.

Fuchs-Buder et al, Anaesthesist 2006







## CLINICAL CONSEQUENCES OF RESIDUAL PARALYSIS

#### Residual Neuromuscular Blockade and Critical Respiratory Events in the Postanesthesia Care Unit

- clinical evaluation of CRE s during 15 min after arrival in the PACU
- CRE: hypoxia, VAS obstruction, dyspnea, deglutition disorders, reintubation, etc;
- if CRE: measurement of T4/T1 (case) and matched patients (control)
- 7459 patients included, 61 (0.8%) with CRE in PACU (neostigmine!)
- analyzed: 2 x 42 patients

Murphy et al, Anesth & Analg 2008





## CLINICAL CONSEQUENCES OF RESIDUAL PARALYSIS

#### **Residual Neuromuscular Blockade and Critical Respiratory Events in the Postanesthesia Care Unit**

n: 2 x 42	Residual Paralisis	Control
T4/T1 (%)	$0,62 \pm 0,2$	0,98 0.07
> 0,9 (n)	4 (9,5%)	38 (95%)
< 0.7 (n)	31 (73,8%)	0
0.7 - 0.9 (n)	7 (16,4%)	4 (90,5%)
Severe hypoxia	22 (52,4%)	-
Moderate hypoxia	10 (23,8%)	-
Upper airway obstruction	15 (35,7%)	-

Murphy et al, Anesth & Analg 2008







Anaesthesia 2017, 72 (Suppl. 1), 16-37

Table 2 Selected reports of postoperative residual paralysis, 2006–2016.

	Study	Intermediate-acting NMBA	Reversal	TOF Threshold	Monitoring modality	Residual paralysis	Comments
	Cammu et al. [26]	Atrac/Cis/Miv/Roc Outpatients Inpatients	In 26% In 25%	0.9	Clinical (49% of cases)	38% 47%	One of 320 inpatients required re-intubation in PACU; Subjective assessment did not decrease incidence of recidual paralysis
	Maybauer et al [88]	Cis	None	0.9	AMG	57%	Variability in duration
	Waybauer et al. [00]	Roc	None	0.9	AMG	44%	of action of Roc greater
							than Cisatrac
	Murphy et al. [89]	Roc	Yes	0.9	AMG	5%	AMG lowers RNMB risk
					Subjective	30%	
	Butterly et al. [14]	Vec/Cis	Yes	0.9	Subjective	22%	Less RNMB with Cis
	Yip et al. [90]	Atrac/Vec/Roc	In 65%	0.9	Not reported	31%	21% of patients with RNMB required airway support
	Murphy et al. [7]	Roc	Yes	0.9	AMG	15%	AMG monitoring lowers
		enance et C		0.9	Subjective	50%	RNMB
	Cammu et al. [91]	Atrac/Roc/Miv		0.9	Subjective		Body mass index we an
			None	1000 TO 100	(38% of cases)	15%	independent predictor
			Neo			15%	of desaturation in PACU
			SGX			2%	
	Kumar et al. [92]		Yes in 100%	0.9	Not performed		RNMB resulted in
		Vec				66%	reductions in forced
		Atrac				60%	vital capacity and peak
		Roc				46%	expiratory flow
	Norton et al. [93]			0.9		30%	CRE present in 51% with RNMB
	Esteves et al. [94]	Atrac/Cis/Roc/Vec	Yes (67% of patients)	0.9	Subjective	26%	Incomplete recovery more frequent after reversal than no reversal (31% vs. 17%)
	Kotake et al. [17]	Roc		0.9	Clinical		RNMB as high as 9%
			None			13%	with SGX without
			Neo			24%	monitoring
			SGX	0.0		4%	1.11
	Pietraszewski et al. [95]	Roc	None	0.9	Not used	44%	Incidence of RNMB was 44% in elderly and 20% in young patients
	Fortier et al. [96]	Roc	Yes	0.9	Optional	64%	Incidence of RNMB was 56% on PACU arrival
	Xara et al. [97]	NMBAs used in 66% of patients	Yes	0.9	Optional	18%	CRE more common (46%) in patients with RNMB
	Ledowski et al. [98]	Atrac/Roc/Vec	Yes (48% of patients)	0.9	Optional (used in 23% of patients)	28%	RNMB after neo reversal was twice as high as no reversal in paediatric
al Anaesthesia 2017	Pruckmann et al	Por			Subjective		OR discharge shorter in
, , , , , , , , , , , , , , , , , , , ,	fueckmann et al.	KOC	Voc Noo	0.0	Subjective	120/	SCX-treated patients
	[23]		VesSGX	0.9		45%	sov-reated patients
	Batistaki et al. [18]	Roc/Cis	163-307	0.9	Clinical	0 70	Female gender and
	satistant et al. [10]		Yes-Neo	0.9		14.6%	co-morbidities increased
Ποριται			Yes-SGX	0.9		9.5%	incidence of RNMB



NMBA, neuromuscular blocking agent; TOF, train-of-four; RNMB, residual neuromuscular block; Atrac, atracurium; Cis, cisatracurium; Vec, vecuronium; Roc, rocuronium; Miv, mivacurium; PACU, post-anaesthesia care unit; AMG, acceleromyography; CRE, critical respiratory events; SGX, sugammadex; OR, operating room.

#### Post-anaesthesia pulmonary complications after use of muscle relaxants (POPULAR): a multicentre, prospective observational study



- data from 211 hospitals in 28 European Countries
- 17150 patients received a NMBA
- 10282 had no neuromuscular monitoring (59.9%!)
- 8355 received no reversal agent (47.8%)
- *extubation based of clinical criteria: 11789 (68.7%)*
- *only* 4182 were monitored with objective neuromuscular monitoring (24.3%)
- 1343 of them were extubated before reaching a  $TOFR \ge 0.9$  (32.1%)
- *just 2839 patients extubated with a documented TOFR* ≥ 0.9 (16.5% of those *exposed to NMBA*)

Lancet Respir Med Sept 2018





Table 3 Incidences and ORs<sub>adj</sub> of postoperative pulmonary complications according to seven key factors in neuromuscular management

	Postoperative pulmonary co	OR <sub>adj</sub> (95% CI)	p values	
	Key factor does not apply Key factor applies			
Use of any NMBA	131/4001 (3·3%)	1527/17 693 (8.6%)	1.86 (1.53–2.26)	<0.0001
High dose of NMBA	936/13 697 (6·8%)	505/3453 (14·6%)	1.03 (0.88–1.20)	0.75
NMM used	676/9927 (6·8%)	765/7223 (10·6%)	1·31 (1·15–1·49)	<0.0001
Reversal agent given	645/8223 (7·8%)	796/8927 (8·9%)	1.23 (1.07–1.41)	0.0028
Quantitative ( <i>vs</i> qualitative) NMM	292/2686 (10·9%)	441/4182 (10.5%)	1.07 (0.90–1.29)	0.44
Extubated at TOFR ≥0.9	157/1343 (11·7%)	284/2839 (10.0%)	1.03 (0.82–1.31)	0.78
Sugammadex ( <i>vs</i> neostigmine)	567/6805 (8·3%)	213/1990 (10.7%)	1.03 (0.85–1.25)	0.74

Data are n/N (%), unless otherwise specified. OR<sub>adj</sub>=adjusted odds ratio. NMBA=neuromuscular blocking agent. NMM=neuromuscular monitoring. TOFR=train-of-four ratio.

\* Defined as a dose of an expected duration of 159 min or more (5th quintile of dose).









## Use of a train-of-four ratio of 0.95 *versus* 0.9 for tracheal extubation: an exploratory analysis of POPULAR data

Manfred Blobner<sup>1,\*</sup>, Jennifer M. Hunter<sup>2</sup>, Claude Meistelman<sup>3</sup>, Andreas Hoeft<sup>4</sup>, Markus W. Hollmann<sup>5</sup>, Eva Kirmeier<sup>1</sup>, Heidrun Lewald<sup>1</sup> and Kurt Ulm<sup>6</sup>



British Journal of Anaesthesia, 124 (1): 63e72 (2020)







#### Absolute risk reduction by 4.9% (1.2 - 8.5%) when patients extubated at TOFR > 0.95 compared to 0.9 and 0.95.



87% acceleromyographs



Blobner et al. BJA 2020





## MECANOMYOGRAPHY



#### Brull SJ, Anesthesiology 2010







© C. Czarnetzki

## SITES OF STIMULATION







## MONITORING AU NIVEAU DU VISAGE



#### Donati F, Anesthesiology 2001





## CONTROL TOF > 100%



#### Kopman AF, Anesthesiology 2002





## NORMALISATION

- TOF ratio during recovery is referred to the control TOF ratio
- E.g. control TOF value is 1.20
- A TOF 0.9 during recovery corresponds to a normalized TOF ratio of 0.75 (90% of 1.20)

Kopman AF, Anesthesiology 2002





## Increasing precision of AMG

- Hand Adapter applied to AMG increases the precision
- However, the TOF ratio is increased as well



Claudius C. et al: Is the performance of acceleromyography improved with preload and normalization? A comparison with mechanomyography. Anesthesiology 2009; 110: 1261-70







# Simultaneously obtained AMG TOF and MMG TOF data in one patient



# If control TOF is not available ensure TOF is 1.00 before tracheal extubation



Claudius C. et al: Anesthesiology 2009





## Comparison of the TOFscan and the TOF-Watch SX during Recovery of Neuromuscular Function

Glenn S. Murphy, M.D., Joseph W. Szokol, M.D., Michael J. Avram, Ph.D., Steven B. Greenberg, M.D., Torin D. Shear, M.D., Mark Deshur, M.D., Jessica Benson, B.S., Rebecca L. Newmark, B.A., Colleen E. Maher, B.S.



« Conclusions: Good agreement between the TOF-Watch SX with calibration and preload application and the uncalibrated TOFscan was observed throughout all stages of neuromuscular recovery. »









The Future is back!

MIPM präsentiert den TOF<sup>3D</sup>®

Von den Machern des TOF-Watch<sup>\*</sup>.









 Received: 13 March 2019
 Revised: 5 September 2019
 Accepted: 22 September 2019

 DOI: 10.1111/aas.13487

#### ORIGINAL ARTICLE

### Assessment of spontaneous neuromuscular recovery: A comparison of the TOF-Cuff $^{\ensuremath{\mathbb{R}}}$ with the TOF Watch SX $^{\ensuremath{\mathbb{R}}}$

Eve Sfeir Machado<sup>1</sup> | Gleicy Keli-Barcelos<sup>1</sup> | Elise Dupuis-Lozeron<sup>2</sup> | Martin R. Tramèr<sup>1,3</sup> | Christoph Czarnetzki<sup>1,3</sup>



- The primary outcome was total recovery time (time in minutes from the injection of rocuronium to a normalized TOF ratio of 90%).
- Agreement between the two devices was calculated using mean difference and limits of agreement.

#### Acta Anaesthesiol Scand. 2019;00:1–7





### Results

- The primary outcome could be **analysed in 27 patients** because of 13 exclusions due to neuromuscular block reversal for shorter procedure surgical time, necessity of reinjection of rocuronium or technical failures of one of the two devices.
- Median total recovery time:
  - test device: 45 minutes (interquartile range [IQR] 38.5-61.5)
  - reference device: 63 minutes (IQR 51.1-74.5).
- Total recovery time with the test device was on average 16.4 minutes shorter (limits of agreement, -6.1 to 39)
  - increasing total recovery time was associated with increasing difference.

Sfeir et al. Acta Anaesthesiol Scand. 2019;00:1-7





#### Results



Hôpitaux Universitaires Genève



#### Results

FIGURE 2 Bland and Altman plot showing the degree of agreement between TOF Watch SX<sup>®</sup> and TOF-Cuff<sup>®</sup> regarding total recovery times in minutes from the injection of rocuronium to a normalised TOF ratio of 90% (n = 27). Recovery times were on average 16.4 min shorter with the TOF-Cuff<sup>®</sup> compared with the TOF Watch SX<sup>®</sup> (dashed line). Lower and upper limits of agreement (95% confidence interval [CI]; dotted lines) were -6.1 and +39.0 min. TOF = train of four



Sfeir et al. Acta Anaesthesiol Scand. 2019;00:1–7





#### Least sensitive

#### Diaphragm

- Corrugator supercilii muscle
- Laryngel muscles
- Orbicularis oculi muscle
  - Abdominal muscles

#### **Adductor pollicis**



- Genioglossus muscle
- Geniohyoideus muscle
- Masseter muscle



Upper oesophagel sphincter

Most sensitive





#### **Standard monitoring**

#### The validity and tolerability of awake calibration of the TOF Watch SX® monitor:

#### An interventional prospective multicenter study

Silvia Pozza M.D.; Daniele Speciale M.D.; Sina Grape M.D.; Sander MJ van Kuijk, Ph.D.;

Sorin J Brull M.D.; Christoph Czarnetzki, M.D., M.B.A.









#### 9/21/2022

**Results:** The primary outcome was total recovery time (time in minutes from the injection of rocuronium to a normalized TOF ratio of 90%). It could be analyzed in 33 patients due to a monitoring failure in one patient. Mean total recovery time with awake calibration was 51 min (standard deviation (SD) 14) and with the asleep calibration 51 min (SD 14). There was no systematic difference (-0.37, 95% CI: -1.88; 1.14, p = 0.624). The intraclass correlation between both measures was 0.96 (95% CI: 0.92; 0.98). The mean pain rated during the awake calibration on a 0 to 10 NRS was 3.2 (SD 1.9), range: 0 to 8.

**Conclusions:** Awake calibration of the TOF Watch SX is in general well tolerated and produces valid results. It might be used before rapid sequence induction.

Future studies should be designed to document the feasibility of performing an automated monitor calibration and selection of maximal stimulating current in the clinical setting of rapid induction of anesthesia and intubation.











### MagNeoSug study

Interaction entre le sulfate de magnésium intraveineux et la néostigmine ou le sugammadex

pour l'antagonisation d'un bloc neuromusculaire induit par le rocuronium - Une étude

électrophysiologique randomisée double aveugle





Sina Grape, Hôpital du Valais Sion





UNIVERSITÉ 8 patients à randomiser. DE GENÈVE FACULTÉ DE MÉDE DE ÉDUT prévu 1.2018



#### **Clinical Study Protocol**

#### Interaction between intravenous magnesium sulfate and volatile anesthetics compared to propofol. A multi-center prospective randomized single-blinded electrophysiological study





Lugano – Sion









## ELECTROMYOGRAPHIE



#### Brull SJ, Anesthesiology 2010





## ELECTROMYOGRAPHIE















## ANESTHESIOLOGY

#### Ipsilateral and Simultaneous Comparison of Responses from Acceleromyography- and Electromyography-based Neuromuscular Monitors

Réka Nemes, M.D., Szabolcs Lengyel, Ph.D., D.Sci., György Nagy, M.D., David R. Hampton, Ph.D., Martyn Gray, B.Eng. (Hons), C.Eng. M.I.E.T., J. Ross Renew, M.D., Edömér Tassonyi, M.D., Ph.D., D.Sci., Béla Fülesdi, M.D., Ph.D., D.Sci., Sorin J. Brull, M.D., F.C.A.R.C.S.I. (Hon)

ANESTHESIOLOGY 2021; 135:597-611











**Conclusions:** Bias was lower than in previous studies. Limits of agreement were wider than expected because acceleromyography readings varied more than EMG both at baseline and during recovery. The EMG-based monitor had higher precision and greater repeatability than acceleromyography. This difference between monitors was even greater when EMG data were compared to raw (nonnormalized) acceleromyography measurements. The EMG monitor is a better indicator of adequate recovery from neuromuscular block and readiness for safe tracheal extubation than the acceleromyography monitor.





# Incidence of residual neuromuscular block at tracheal extubation



Saager L, et al. J Clin Anesth. 2019 Aug;55:33-41







#### **Consensus Statement on Perioperative Use of Neuromuscular Monitoring**

Mohamed Naguib, MB BCh, MSc, FCARCSI, MD,\* Sorin J. Brull, MD, FCARCSI (Hon),† Aaron F. Kopman, MD,‡ Jennifer M. Hunter, MBE, MB ChB, PhD, FRCA, FCARCSI (Hon),§ Béla Fülesdi, MD, PhD, DSci, II Hal R. Arkes, BA, PhD,¶ Arthur Elstein, PhD,# Michael M. Todd, MD,\*\* and Ken B. Johnson, MD††

The panel believes that whenever a neuromuscular blocker is administered, neuromuscular function must be monitored by observing the evoked muscular response to peripheral nerve stimulation. Ideally, this should be done at the hand muscles (not the facial muscles) with a quantitative (objective) monitor. Objective monitoring (documentation of train-of-four ratio ≥0.90) is the only method of assuring that satisfactory recovery of neuromuscular function has taken place. The panel acknowledges that publishing this statement per se will not result in its spontaneous acceptance, adherence to its recommendations, or change in routine practice. Implementation of objective monitoring will likely require professional societies and anesthesia department leadership to champion its use to change anesthesia practitioner behavior.

Anesth Analg 2018;127:71-80







6

7

Processed

#### Guidelines

#### Recommenda anaesthesia a

Guideline from the /

#### A. A. Klein<sup>1</sup> T. Meek<sup>2</sup> J. J. Pandit,<sup>8</sup> A. Pawa,

1 Consultant, Department of Association of Anaesthetists 2 Consultant, Department o Association of Anaesthetists 3 Consultant, Department o 4 Consultant, Royal United F 5 Consultant, Department o 6 Consultant, Royal Derby H 7 Consultant, Department o 8 Professor, University of Ox 9 Consultant, Department o Regional Anaesthesia UK (R/ 10 Consultant, Department 11 Consultant, Department

#### Summary

This guideline updates a of this document is to proanaesthesia or sedation anaesthetists practising i other areas of the world. phase are included. The There are new sections sp indications for processed doi:10.1111/anae.15501

## Quantitative neuromuscular monitoring should be

used whenever neuromuscular blocking (NMB) drugs are administered, throughout all phases of anaesthesia from before initiation of neuromuscular blockade until recovery of the train-of-four ratio to > 0.9 has been confirmed.

#### electroencephalogram

monitoring should be used when total intravenous anaesthesia (TIVA) is administered together with a NMB drug. It should start before induction and continue at least until full recovery from the effects of the neuromuscular blockade has been confirmed. It should be considered anaesthetic during other techniques including inhalational anaesthesia and for the high-risk patient.

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### Raccomandazioni per la curarizzazione e "antagonizzazione"

	Suxamethonium		Rocuroniu	im	Atracurium
Monitoraggio	<b>Ogni curarizzazione necessita di un monitoraggio quantitativo.</b> Per una misura con accelerometrica affidabile, il pollice deve essere libero di mu (Non necessario Con electromyografia)				oversi.
D E C	No antagonizzazione		*		Blocco superficiale TOF = 4
U R A	Blocco profondo TOF=0 PTC=1 a 5	Blocco moderato TOF =1 a 3	Blocco superficiale TOF = 4	<b>Rescue inhibition</b>	Neostigmina 0,04 mg/kg peso reale
R I Z 7	Sugammadex 4mg/kg peso reale	Sugammadex 2mg/kg peso reale	Neostigmina 0,04 mg/kg peso reale	- Can't intubate, can't ventilate (dopo Rocuronium)	
A Z I O N E	<ul> <li>Al termine di un aspettare la dee</li> <li>Obesità con BMI</li> <li>Patologie neuron</li> <li>Necessità operat intervento)</li> </ul>	a chirurgia elettiva, conviene sempre surarizzazione spontanea salvo nelle seguenti situazioni: ≥ 35 nuscolari orie (es: curarizzazione profonda fino a fine		- Shock anafilattico presunto (al Rocuronium) Sugammadex 16 mg/kg peso reale	
Estubazione		FSTUR	A7IONE appen	a T4/T1 > 1	

#### ESTUBAZIONE appena $14/11 \ge 1$

#### 1. A systematic review of sugammadex vs neostigmine for reversal of neuromuscular blockade. Abad-Gurumeta A, et al. Anaesthesia review group. 2015;70:1441-52 **References:**

- Secondo la Conferenza di attualizzazione 
  <sup>®</sup> 2018 Sfar (Società francese d'anestesia e reanimazione) https://sfar.org/wp-content/uploads/2018/10/2 RFE-CURARE-3.pdf 2.
- Thèse de Privat docent Christoph Czarnetzki 2017 Drug interactions in the context of neuromuscular blockade: clinical implications and safety issues З. https://archive-ouverte.unige.ch/unige:100276

Redazione:

Modificato dal Originale linea guida HUG Ginevra Marzo 2017. Tradotto dal francese: I. Baudracco, Agosto 2019. Modificazioni C. Czarnetzki settembre 2019

## Thanks for your attention



