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ORIGINAL RESEARCH

Mindray 3-directional NMT Module (a new generation "Tri-axial" neuromuscular monitor) versus the Relaxometer mechanomyograph and versus the TOF-Watch SX acceleromyograph

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Abstract
Recently introduced Mindray "3-directional" neuromuscular transmission transducer (NMT, Shenzhen, China) acceleromyograph) claim to monitor thumb movement in 3 different directions. We compared NMT with the gold standard Relaxometer® mechanomyograph (MMG, Groningen University, Netherlands) in Study-1 and with TOF-Watch SX™ (WTCH) acceleromyograph from which it was developed in Study-2. We used first twitch (T_1%) and train-of-four (TOF) ratio rocuronium 0.6 mg kg^{-1} neuromuscular block to evaluate NMT diagnostic accuracy in indicating 3 clinically relevant time points namely; MMG T_1 5% (95% twitch depression) for tracheal intubation, MMG T_1 25% for repeat neuromuscular blocking agents (NMBAs) administration, and MMG 0.9 TOF ratio full neuromuscular block recovery. We compared onset time (time from beginning of rocuronium administration until maximal depression), Dur_{25} (time until T_1 25% recovery) and $Dur_{0.9}$ (time until 0.9 TOF ratio recovery). In Study-1, NMT showed low sensitivity in indicating MMG time for tracheal intubation, repeat NMBAs administration and full neuromuscular block recovery (6.25%, 38.9% and 38.9% respectively). NMT onset time, Dur_{25} and $Dur_{0.9}$ (2:51 ± 00:57, 36:50 ± 24:25, 70:08 ± 25:27 min:s) were significantly longer than MMG (1:56 ± 00:46, 30:26 ± 20:24, 62:03 ± 20:01). In Study-2, NMT onset time, Dur_{25} and $Dur_{0.9}$ (02:37 ± 00:53, 35:38 ± 11:54, 53:40 ± 13:49) were not significantly different than WTCH (02:23 ± 00:45, 33:27 ± 12:51, 53:57 ± 12:47). NMT could not efficaciously detect MMG time for tracheal intubation; NMBAs repeat dose administration or full neuromuscular block recovery. Data from NMT cannot be used interchangeably with MMG. Our study revealed that NMT Tri-axial acceleromyography seems to offer no advantage over the MMG gold standard or the classic Mono-axial TOF-Watch SX monitor.

Keywords Neuromuscular block · Monitoring · Neuromuscular function · Equipment · Mechanomyograph · Diagnostic accuracy

1 Introduction

Neuromuscular monitors are often replaced with new devices claimed to better perform the currently available devices. New devices might obtain Food and Drug Administration (FDA) or Certificate European (CE) lengthy 9–18 months approval without a keen objective appraisal of their efficacy compared with the gold standard devices or compared with the devices they are replacing. Conventional mechanomyography (MMG) is regarded by the Stockholm revision consensus conference [1] as the gold standard for precise quantification of neuromuscular block. MMG quantifies force displacement isometric muscle contraction of a preload restrained thumb in response to electric stimulation at the ulnar nerve [1]. The main obstacle facing their wide clinical use is being rather bulky and taking time to set up.

There are numerous stand-alone or modular-integrated neuromuscular monitoring devices that quantify the neuromuscular function on the basis of physiological phenomena that are closely related to force displacement. The first commercially available one-directional Mono-axial acceleromyograph (AMG); the TOF-GUARD™ (Organon Teknika, Oss, Netherlands) [2] and its simplified version the TOF-Watch™ (MIPM, Mammendorf, Germany) [3] both quantify acceleration of a piezo-sensor attached to a freely moving

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thumb. Instead of measuring the evoked force, according to Newton's second law, thumb acceleration can be measured and quantified. However a major impediment of AMGs, among other numerous methodological problems [3]; is the piezo-sensor being not always "properly aligned" to the optimal plane of thumb movement [3].

The discontinuation of the TOF-Watch series gave way to a new generation of Tri-axial AMGs using 3 perpendicularly placed piezo sensors to measure acceleration. These include Stimpod NMS 450 (Xavant, South Africa), TOFscan (Dräger, Lübeck, Germany) and the modular neuromuscular transducer NMT (Mindray, Shenzhen, China). The primary objective of our study was to compare the new Tri-axial NMT monitor with MMG for diagnostic accuracy at three clinically relevant time points, and to evaluate the new monitor based on an improvement of a previous technology (Mono-axial acceleromyography). To the best of our knowledge this is the first study comparing one of the new Tri-axial generation with the gold standard MMG and with the one-directional AMG TOF-Watch SX from which the NMT was developed.

2 Methods

Our clinical trial was registered prior to patient enrollment by principal investigator: AD at Food and Drug Administration (http://www.ClinicalTrials.gov); trial registration number: NCT02892045. Protocol NMT1; record released and made public on 8th September 2016. We conducted 2 separate clinical trials in Sarajevo Medical University, Bosnia Herzegovina and in Dalian Emergency Department, People's Republic of China in accordance with the Stockholm revision of the guidelines of "Good Clinical Research Practice (GCRP) in Pharmacodynamic Studies of Neuromuscular Blocking Agents II" [1], and "Standards for Reporting of Diagnostic Accuracy" (STARD) [4]. After Sarajevo Medical University ethics committee approval (0406-19256 at 5th May 2016 meeting chaired by Doc. Dr. Sci. Med Jasmina Krehic) and Dalian University Second affiliated Hospital ethics committee approval (2015-106 at 14th January 2016 meeting chaired by Prof Dr. Ren Ping) all patients who agreed to participate in the 2 studies gave a written informed consent. Between September 2016 and September 2017 we recruited 24 patients in Study-1 (NMT vs. MMG Relaxometer, Groningen University, The Netherlands) and another 24 patients in Study-2 (NMT vs. WTCH TOF-Watch) with body mass index 20–35 kg m^{-2}, aged 18–75 year, undergoing an orthopedic procedure under general anesthesia for an approximate 1 h duration in the supine position. This was slightly different than the Stockholm revision GCRP consensus conference recommendations of 18–65 year and BMI 18.5–24.9 [1], as we wanted to include a broader patient population that is more representative of daily anesthesia practice. Because we were comparing neuromuscular monitoring on both arms of the same patient; age and BMI did not confound our results. Exclusion criteria included history of neuromuscular disease, small joint arthritis or patients on treatment with drugs thought to interfere with neuromuscular transmission.

We warmed patients using a forced-hot-air-blanket to maintain core temperature > 36 °C and skin temperature > 32 °C. We comfortably positioned, rigidly supported both arms on arm-boards and fastened both hands to the arm-boards with palmer straps. The stimulating electrodes of the NMT module were placed on the area above the ulnar nerve at the wrist and the NMT piezo-sensor was attached to the thumb of one hand. To level out the effect of dominance of one hand, the NMT piezo-sensor was randomly allocated to the dominant and non-dominant hands. On the other hand, we attached the MMG force transducer in Study-1, or TOF-Watch piezo-sensor in Study-2. The MMG preload on the thumb was maintained within 200–400 g throughout the whole procedure [5]. No preloads were applied to NMT or WTCH. After entering patients' anthropometric data to Orchestra® Base Primea (Fresenius Kabi, Brezins, France), we set propofol target controlled infusion (TCI) plasma concentration (C_p) to reach 4 μg mL^{-1} and remifentanil C_p to reach 4 ng mL^{-1}. We inserted a ProSeal Laryngeal Mask Airway [6], and after capnographic confirmation of correct positioning we ventilated the lungs mechanically with 40% oxygen in air, adjusted to maintain 4.0–4.6 kPa end-tidal carbon dioxide.

2.1 Tetanic stimulation, calibration and stabilization periods

2.1.1 Tetanic stimulation

Following anesthesia induction and prior to data collection, we applied a short (3–5 s) 50-Hz tetanic stimulation to MMG, NMT and WTCH to diminish post-recovery drift [7].

2.1.2 Calibration period

We administered 1-Hz single-twitch electric stimuli (pulse width 200 μs, square wave) to MMG, NMT and WTCH in an ascending sequence starting with 10 mA. Supramaximal current was then set as the maximal response + 20%. After calibration, the ulnar nerves at the wrist of both arms were stimulated with train-of-four (TOF) stimuli (2-Hz, pulse width 200 μs, square wave for 2 s) at 12-s intervals. First twitch (T_1%) before neuromuscular blocking agents (NMBAs) administration (T_0) and TOF ratio (T_4:T_1) were used to evaluate the neuromuscular block.

2.1.3 Stabilization period

As recommended by Stockholm revision GCRP consensus conference [1], to ensure a fairly stable T_1% and TOF ratio as well as reliable time-course-of-action parameters [1]; monitoring of MMG, NMT and WTCH continued until a "stable control response" defined as variation of less than ± 2% for the last 3 min [1] was reached.

After stabilization, rocuronium 0.6 mg kg^{-1} (twice the 95% effective dose, ED_{95}) was administered; lag and onset times (time from beginning of NMBA administration until the first decline and until maximal depression) were recorded. We adjusted propofol C_p to maintain deep anesthesia, and we adjusted remifentanil C_p to maintain hemodynamic stability. Patients were allowed to recover spontaneously from the neuromuscular block; Dur_{25} and $Dur_{0.9}$ (time until T_1 25% and 0.9 TOF ratio recoveries) were recorded [1].

In Study-1 the MMG and NMT data were simultaneously collected and stored on a lap top computer using MMG AZG-Relaxometer 5.0 program and Mindray Data management and Review software. In Study-2, NMT and WTCH data were simultaneously collected and stored using Database Export for TOF-Watch® SX Monitor, version 2.3.

2.2 Statistical analysis

2.2.1 Definition of endpoints

Our primary objective was to evaluate the new NMT for diagnostic accuracy at 3 clinically relevant time points namely [8]; MMG T_1 5% (95% twitch depression) for tracheal intubation [1, 9], T_1 25% for repeat NMBAs administration, and 0.9 TOF ratio for full neuromuscular block recovery [1], NMT sensitivity, specificity and positive/negative predictive values (PPV/NPV):

1. At MMG T_1 5% for tracheal intubation: NMT $T_1 > 15\%$ (false negative) and NMT $T_1 < 3$ twitches (false positive).
2. At MMG T_1 25% for repeat NMBAs: NMT $T_1 < 15\%$ (false negative) and $T_1 > 35\%$ (false positive).
3. At MMG 0.9 TOF ratio for full recovery: <0.8 TOF ratio (false negative) and 1.0 TOF ratio (false positive).

For our primary objective a-priori power analysis ($\alpha = 0.05$ with > 90% power) we considered a 20% difference between the 2 monitors as a clinically significant difference based upon previously published study [10]; where MMG onset time of 1.8 ± 0.6 min compared with M/E-NMT (GE, Helsinki, Finland) 1.5 ± 0.3 min [10] showed that a sample size of 12 patients would be required to reveal a statistically significant difference between the two monitors. MMG Dur_{25} of 20.2 ± 6.3 min compared with M/E-NMT 25.6 ± 8.0 min [10] showed that a sample size of 9 patients is required. MMG $Dur_{25\text{-}0.8}$ of 30.3 ± 19.0 min compared with M/E-NMT 23.1 ± 15.1 min [10] showed that a sample size of 8 patients is required. The sample size was then increased to 24 patients (twice the highest sample size).

Additionally to validate a new monitor Bland and Altman [11] scatterplots should be created. Bias is the difference between the 2 monitors. Limits of agreement (LOA) are bias ± 1.96 SD in which 95% of the differences are expected to lie [11]. We further used Myles and Cui [12] "random effects model" within-subject variance estimated by a random effects model that only includes individual patient's mean measurements and not all recorded measurements [12].

We used Student-*t* test to compare NMT variables (lag time, onset time, Dur_{25} and $Dur_{0.9}$) with MMG in Study-1, and to compare NMT with WTCH in Study-2. We implemented no statistical significance threshold adjustments as we did not perform repeated measures on these time-course-of-action parameters. Data were expressed as mean ± SD. $P < 0.05$ was considered statistically significant.

3 Results

Patients' characteristics are presented in Table 1.

3.1 Induction Period and time-course-of-action parameters

Before rocuronium administration, NMT T_4 exceeded T_1 (pre-relaxation reverse fade) in 13/24 Study-1 patients (1.19 ± 0.18) and in 17/24 Study-2 patients (1.21 ± 0.20) before finally stabilizing. In Study-1, NMT lag time, onset time, Dur_{25} and $Dur_{0.9}$ were significantly longer than MMG. In Study-2, there was no significant difference between NMT and WTCH lag time, onset time, Dur_{25} and $Dur_{0.9}$ (Table 2). After recovery from neuromuscular block, NMT T_1 exceeded 100% (post-recovery drift) in 13/24 Study-1 patients (143.1 ± 35.0) and in 11/24 Study-2 patients (114.5 ± 12.1).

3.2 Primary objective NMT sensitivity, specificity at 3 clinically relevant time points

NMT demonstrated very low sensitivity (6.25%) in indicating MMG T_1 5% for tracheal intubation. NMT showed low sensitivity (38.9%) in indicating both MMG T_1 25% for repeat NMBAs administration and MMG 0.9 TOF ratio full neuromuscular block recovery (Table 1). Mean NMT was 40% ±24 at MMG T_1 5% for tracheal intubation, NMT was 13% ±15 at T_1 25% recovery, and NMT TOF ratio was

Table 1 Patients' characteristics

Study 1 NMT versus MMG				
Male/female				7/17
Age (years)				58.0 ± 10.2
Height (cm)				172.5 ± 9.4
Weight (kg)				79.9 ± 14.7
BMI (kg m^{-2})				26.8 ± 3.6
Study 2 NMT versus WTCH				
Male/female				5/19
Age (years)				53.0 ± 15.6
Height (cm)				169.6 ± 6.3
Weight (kg)				77.2 ± 14.8
BMI (kg m^{-2})				26.2 ± 4.2
Study 1 NMT versus MMG	**Sensitivity (%)**	**Specificity (%)**	**PPV (%)**	**NPV (%)**
NMT at MMG 5% T_1 induction	6.25	87.5	50	31.8
NMT at MMG 25% T_1 recovery	38.9	66.7	77.8	26.7
NMT at MMG 0.9 TOF ratio recovery	38.9	100	100	35.3

Primary objective NMT sensitivity, specificity, positive and negative predictive (PPV, NPV) values

Means ± SD, n = 24, *BMI* body mass index, *MMG* Mechanomyograph, *NMT* neuromuscular transmission module, *WTCH* TOF-Watch SX, *PPV* positive predictive value, *NPV* negative predictive value, T_1 first response of train-of-four, *TOF* train-of-four

Table 2 Rocuronium time-course-of-action parameters

Study 1 NMT versus MMG			
	NMT	**MMG**	**P value**
Lag time (min:s)	01:37 ± 00:33	00:46 ± 00:26	< 0.001
Onset time (min:s)	02:51 ± 00:57	01:56 ± 00:46	0.002
Dur_{25} (min:s)	36:50 ± 24:25	30:26 ± 20:24	0.033
$Dur_{0.9}$ (min:s)	70:08 ± 25:27	62:03 ± 20:01	0.024
Study 2 NMT versus WTCH			
	NMT	**WTCH**	**P value**
Lag time (min:s)	01:41 ± 00:47	01:33 ± 00:39	0.420
Onset time (min:s)	02:37 ± 00:53	02:23 ± 00:45	0.318
Dur_{25} (min:s)	35:38 ± 11:54	33:27 ± 12:51	0.586
$Dur_{0.9}$ (min:s)	53:40 ± 13:49	53:57 ± 12:47	0.945

Means ± SD, n = 24, *MMG* Mechanomyograph, NMT Neuromuscular Transmission Module, *WTCH* TOF-Watch SX, *lag time* time from beginning of rocuronium administration until first measurable effect of neuromuscular block, *onset time* time from beginning of rocuronium administration until maximal depression of first response (T_1), Dur_{25} time from beginning of rocuronium administration until 25% T_1 recovery, $Dur_{0.9}$ time from beginning of rocuronium administration until 0.9 train-of-four (TOF) ratio recovery

0.64 ± 0.17 at MMG 0.9 TOF ratio neuromuscular block recovery.

3.3 Bland and Altman/regression plots

In Study-1, NMT versus MMG T_1% (Fig. 1a, b) and TOF ratio (Fig. 2a, b) revealed considerably wide LOA. Study-2 NMT versus WTCH (Fig. 3a, b) revealed relatively narrower LOA. Myles and Cui [12] (Table 3) that only includes patient's mean values revealed considerably narrower LOA than the classical Bland and Altman [11].

4 Discussion

The main finding of Study-1 was NMT very low 6.25% sensitivity in indicating MMG tracheal intubation that manifested as significantly longer NMT lag and onset

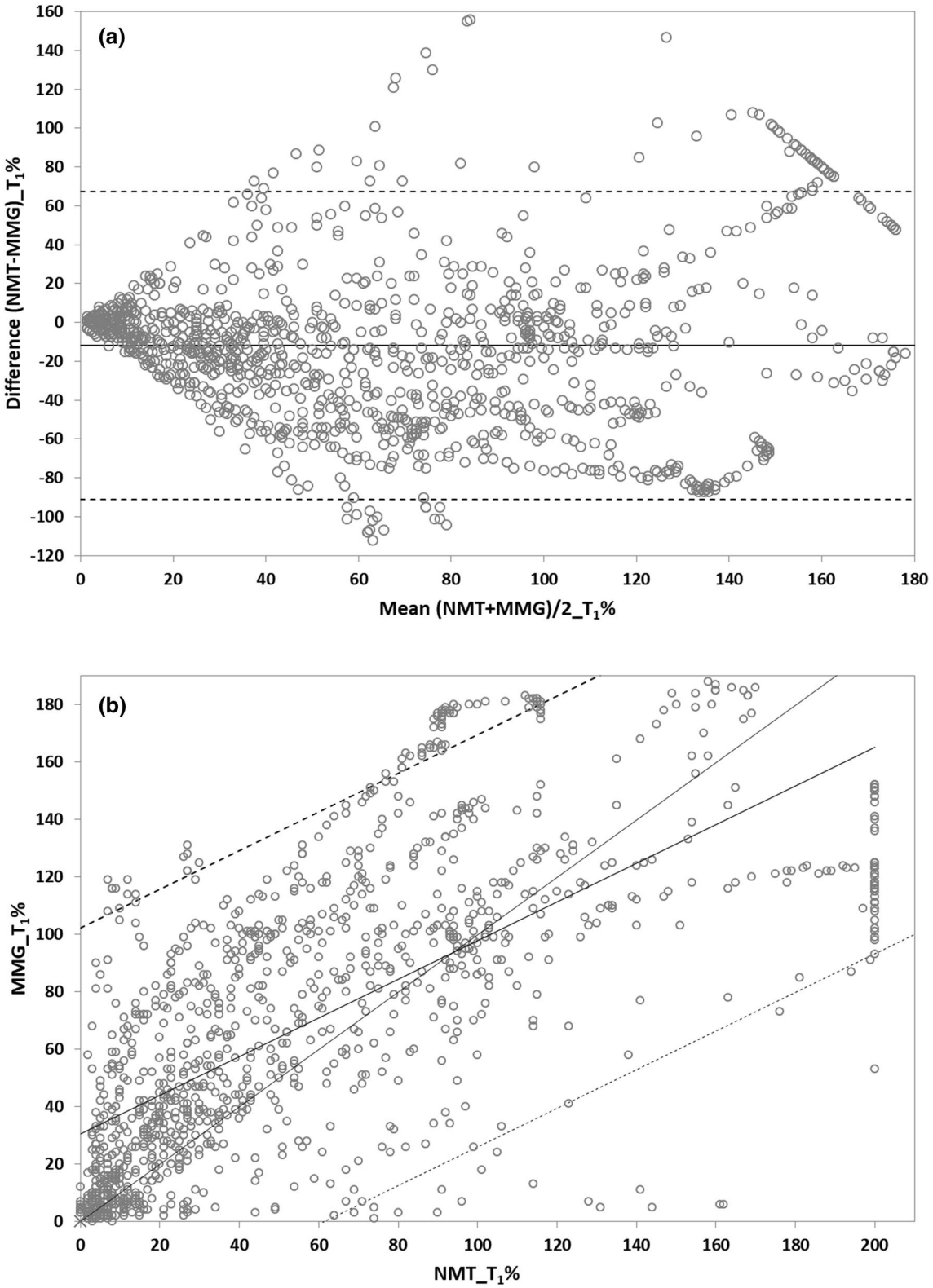
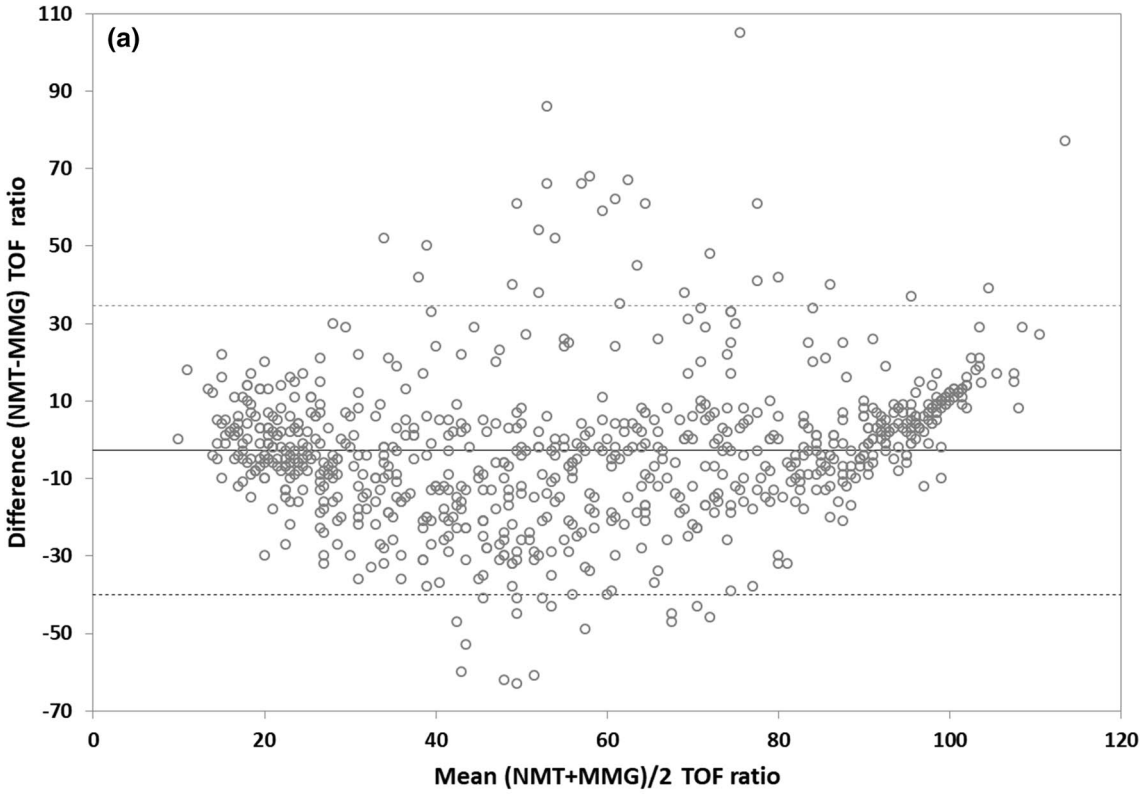
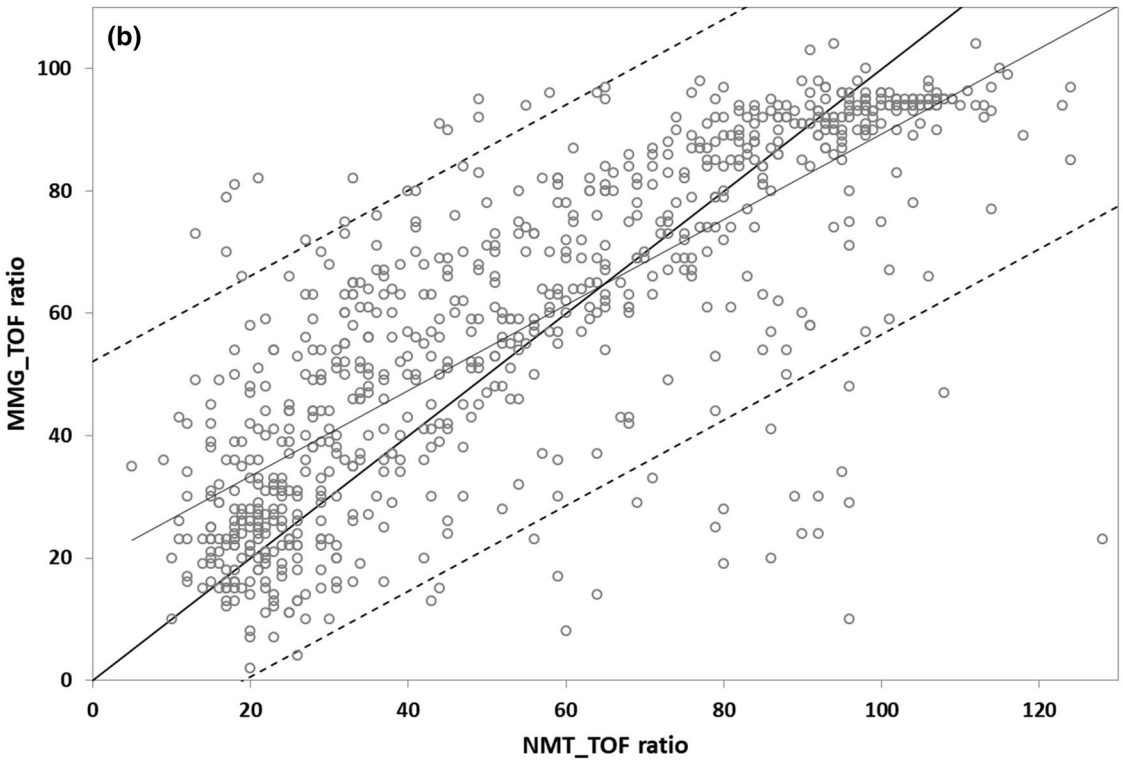


Fig. 1 **a** Study-1 Bland and Altman scatter plot of the first twitch (T_1%) difference between the Neuromuscular Transmission Module (NMT) and the mechanomyograph (MMG) against the mean of the two measurements. The middle dotted line represents the bias. Upper and lower dotted lines represent the limits of agreement between the two monitors. **b** Study-1 regression plot of the first twitch (T_1%) of the Neuromuscular Transmission Module (NMT) and mechanomyograph (MMG). The middle dotted line represents the line of identity. The upper and lower dotted lines represent 95% confidence intervals


(a)
Difference (NMT-MMG) TOF ratio
Mean (NMT+MMG)/2 TOF ratio
110
90
70
50
30
10
-10
-30
-50
-70
0
20
40
60
80
100
120


(b)
MMG_TOF ratio
NMT_TOF ratio
100
80
60
40
20
0
0
20
40
60
80
100
120

◂**Fig. 2** **a** Study-1 Bland and Altman scatter plot of the Train-of-Four ratio (TOF) difference between the Neuromuscular Transmission Module (NMT) and the mechanomyograph (MMG) against the mean of the two measurements. The middle dotted line represents the bias. The upper and lower dotted lines represent the limits of agreement between the two monitors. **b** Study-1 regression plot of the Train-of-Four ratio (TOF) of the Neuromuscular Transmission Module (NMT) and mechanomyograph (MMG). The middle dotted line represents the line of identity. The upper and lower dotted lines represent 95% confidence intervals

times compared with MMG. Whereas NMT 38.9% low sensitivity in indicating MMG full neuromuscular block recovery resulted in NMT Dur_{25} and $Dur_{0.9}$ recovery parameters both lagging 7–8 min behind MMG.

4.1 Primary objective: how would NMT diagnostic accuracy affect anesthesiologists in their routine clinical practice

Different muscle groups are sequentially curarization; as laryngeal adductor muscles and diaphragm are the first to be paralyzed and first to recover; the superciliary arch (corrugator supercilii) and the eyelid (orbicularis oculi) follow; the thumb (adductor pollicis muscle) is the last to be paralyzed and last to recover [13]. Based on our study results, NMT lag behind MMG could be a major impediment for NMT diagnostic accuracy; as this will further confound an already existing problem facing all neuromuscular monitoring devices, including MMG, that monitor the adductor pollicis muscle. At induction, the displayed adductor pollicis paralysis is already physiologically 1–2 min lagging behind the more sensitive laryngeal muscles paralysis [13]. This means that for few minutes at induction, the further lagging NMT is indicating that patients' upper airway reflexes are still fully intact when in fact laryngeal muscles are long deeply paralyzed and totally unprotected.

On the other hand, NMT lagging 7–8 min behind MMG at neuromuscular block recovery diagnostic accuracy will similarly confound the considerably longer adductor pollicis 11–12 min physiological lag behind upper airway laryngeal muscles recovery [13], resulting in a total lag of 18–20 min in displayed values.

4.2 Stabilization period

Despite meticulous arm-board fixation and straps; NMT T_4 exceeded T_1 before rocuronium administration in Study-1 (1.19) and in Study-2 (1.21). Historically Viby-Mogensen [14] reported 1.16 T_4 exceeding T_1 with the first prototype Acceleration Transducer, so did Harper [15] with the Mini-Accelograph and Loan [12] with the TOF-Guard. We reported 1.08 T_4 exceeding T_1 with the TOF-Guard in a previous study [16]. The Copenhagen GCRP Conference acknowledged the fact that AMGs are highly prone to errors resulting from movements [1], including those caused inadvertently by surgeons or other operating room personnel [17], as the free-moving thumb does not necessarily always return after each stimulation to the exact original position before stimulation [2]. "Staircase phenomenon" has no effect on the TOF ratio; because with repetitive stimulations T_1% increases whereas the TOF ratio does not change [7].

4.3 Bland and Altman

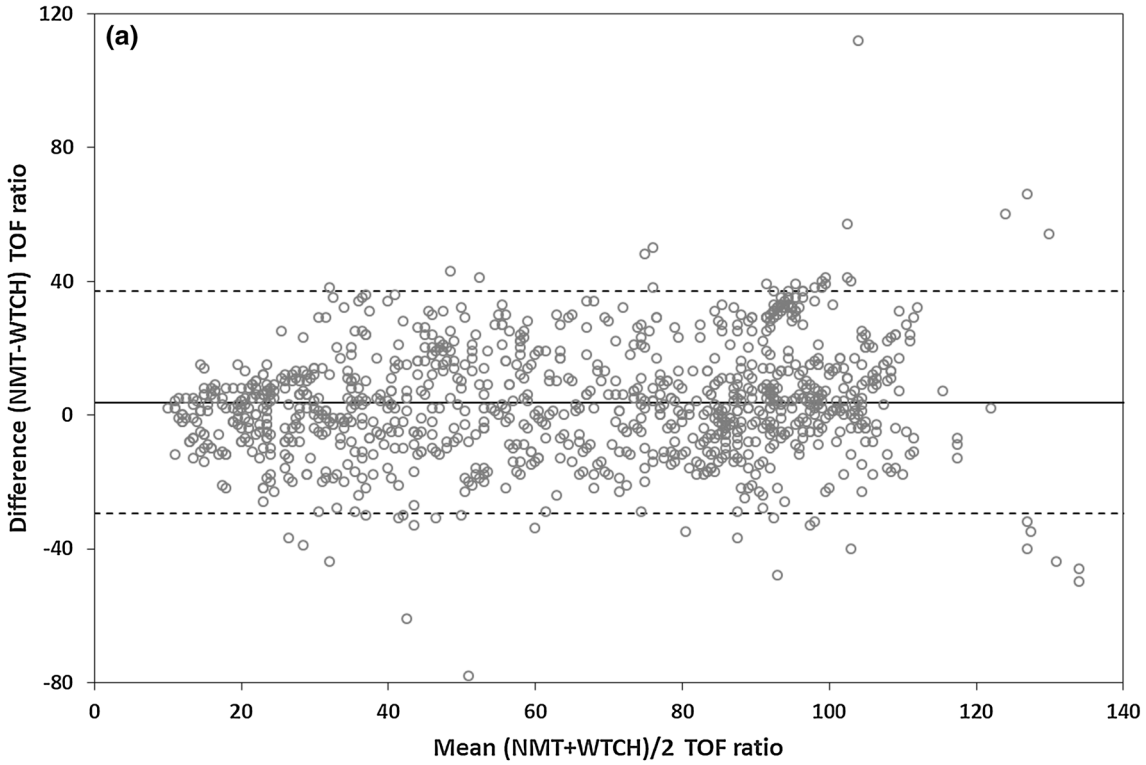
Our NMT versus MMG Bland and Altman schematic presentation revealed considerably wide T_1% bias (LOA) to allow values given by NMT to be used interchangeably with MMG. Furthermore NMT is not better performing other types of neuromuscular monitors such as kinemyographic monitors; as NMT bias (LOA) was considerably wider than the ParaGraph + 5.5 (+54, −43) [18] or M/E-NMT − 15.9 (+8.9, −40.8) [10] versus MMG.

Furthermore, when it was designed to better perform other Mono-axial AMG monitors with its 3-directional piezo sensors; our NMT TOF ratio versus MMG and versus WTCH LOA, apparently are not better performing other published AMG monitors versus MMG LOAs; such as the piezoelectric sensor (0.28, −0.24) [19], or TOF-Guard (0.30, −0.30) [2] LOAs. The fact that NMT performed worse than other AMG monitors published data [2, 19] could indicate a serious flaw in the basic fundamental Tri-axial concept design.

Our Table 3 Myles and Cui [12] approach revealed considerably narrower LOA, clearly due to narrower Standard Deviation when taking mean values of each patient and not taking all recorded measurements. With the narrow Myles and Cui [12] LOA; NMT could still be considered by some as effectively interchangeable. Despite the fact that NMT was not interchangeable with MMG [3]; historically this did not impair AMG wide use in the operating room mainly due to its portability and ease of use.

4.4 Post-recovery drift

In our study baseline TOF ratios measured by NMT were usually more than 1.0 and varied widely among patients. According to Suzuki et al. [20] a TOF ratio of 0.9 displayed post-operatively by AMGs does not always indicate adequate recovery of neuromuscular function and should be normalized to baseline value to reliably detect residual paralysis [20]. In our 2 studies we did not normalize NMT TOF ratio to baseline value because our aim was to compare the real-time displayed NMT post-operative TOF ratio value with MMG or WTCH also not normalized real-time displayed values.



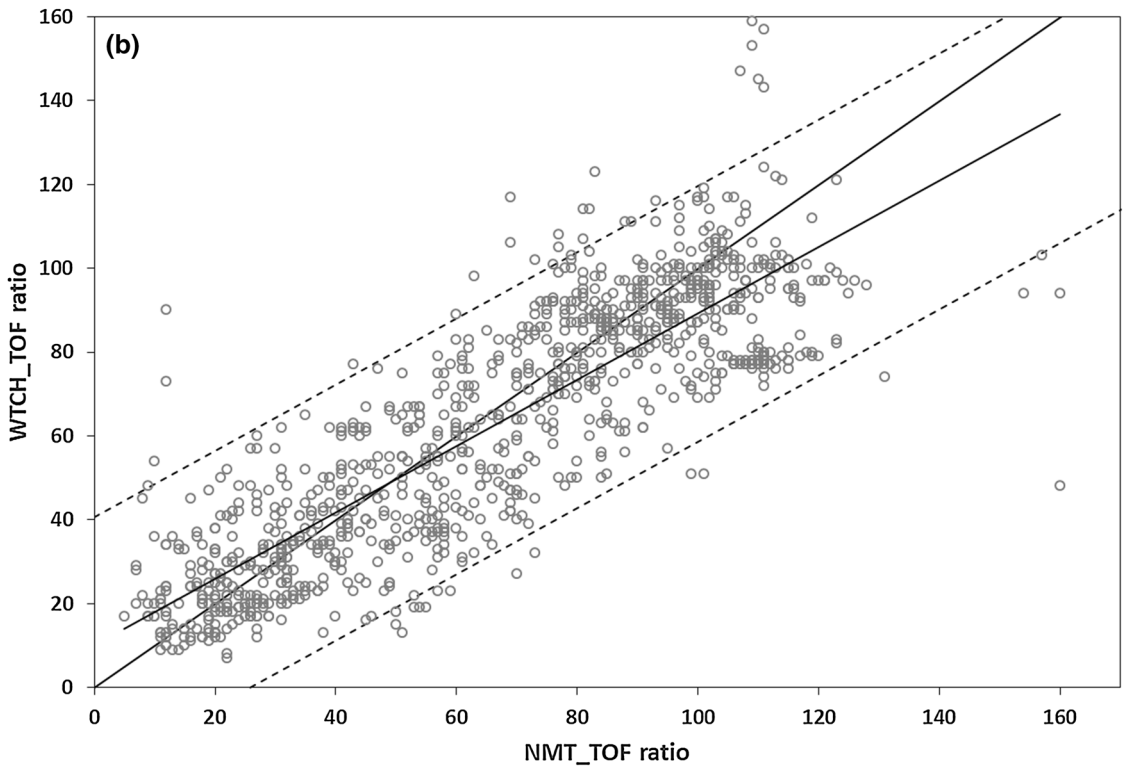


Fig. 3 **a** Study-2 Bland and Altman scatter plot of the Train-of-Four ratio (TOF) difference between the Neuromuscular Transmission Module (NMT) and the TOF-Watch SX (WTCH) against the mean of the two measurements. The middle dotted line represents the bias. The upper and lower dotted lines represent the limits of agreement between the two monitors. **b** Study-2 regression plot of the Train-of-Four ratio (TOF) of the Neuromuscular Transmission Module (NMT) and the TOF-Watch SX (WTCH). The middle dotted line represents the line of identity. The upper and lower dotted lines represent 95% confidence intervals

Table 3 Bland and Altman/Myles and Cui approach

	Bias	Upper LOA	Lower LOA
Study 1 Bland and Altman			
NMT versus MMG T1%	–11.8	+67.2	– 90.9
NMT versus MMG TOF ratio	–0.03	+0.35	– 0.40
Study 1 Myles and Cui NMT versus MMG			
NMT versus MMG T1%	–11.8	+20.9	– 44.5
NMT versus MMG TOF ratio	– 0.03	+0.22	– 0.28
Study 2 Bland and Altman			
NMT versus WTCH TOF ratio	+0.04	+0.37	– 0.30
Study 2 Myles and Cui NMT versus WTCH			
NMT versus WTCH TOF ratio	+0.04	+0.28	– 0.20

n = 24, *MMG* Mechanomyograph, *NMT* Neuromuscular Transmission Module, T_1 first response of train-of-four, *TOF* train-of-four. *Bias* is the difference between the 2 monitors, *LOA* limits of agreement define the bias ± 1.96 SD in which 95% of the differences between the two monitors are expected to lie, Myles and Cui approach = within-subject variance which includes the mean measurements of the two methods

After full recovery from neuromuscular block, NMT was prone to the post-recovery "drift" phenomenon of T_1 exceeding 100% in Study-1 and Study-2 patients. T_1% "drift" phenomenon was previously reported in the majority of AMG Mini-Accelerograph patients (120.6%) [15]. One possible explanation [2] is the "Staircase phenomenon" when repetitive stimulation of a motor nerve evokes muscle contractions of increasing amplitudes due to a significant increase in regulatory myosin phosphorylation [7, 21]. T_1% values of > 130 should not occur if a proper stabilization period has taken place. Our NMT post-recovery 143.1% T_1% drift might imply less than ideal stabilization although we have meticulously implemented GCP recommendations of a 3-min stable period [1]. In our opinion this is a major limitation compromising NMT external validity. Copenhagen GCRP consensus Conference [1] acknowledged that the TOF-Watch monitor should not be taken as a true representation of neuromuscular block recovery as it does not display actual readings; rather a special algorithm is used to calculate the TOF ratio at recovery [22].

5 Conclusions

In Study-1 we demonstrated that Mindray NMT could not efficaciously detect MMG time for tracheal intubation, NMBAs repeat dose administration or full neuromuscular block recovery. The NMT data cannot be used interchangeably with MMG. In Study-2 the new generation NMT Tri-axial AMG does not produce results significantly different than those obtained with the classic TOF-Watch SX Mono-axial AMG. The Tri-axial AMeGs have yet to prove that this technology has any clinical advantage over traditional one-directional AMG monitors and transducers. In fact its pre-induction reverse fade and post-recovery drift appear to be more prominent.

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Clinical trial registry numbers Our clinical trial was registered by Primary Investigator: Ashraf Dahaba prior to patient enrollment at Food and Drug Administration Clinical Trials Database www.ClinicalTrials.gov; trial Registration Number: NCT02892045. Date of registration: protocol record NMT1 released and made public on 8th September 2016 on www.ClinicalTrials.gov. Sarajevo Medical University, Sarajevo Bosnia and Herzegovina ethics committee approval (0406-19256 at 5th May 2016 meeting chaired by Doc. Dr. Sci. Med Jasmina Krehic), and Dalian University Second affiliated Hospital ethics committee Dalian, People's Republic of China (2015-106 at 14th January 2016 meeting chaired by Prof Dr. Ren Ping), Dalian, People's Republic of China.

Author contributions Primary investigator AAD conducted the study,participated in data collection, data analysis and manuscript writing. IS participated in perioperative anesthesia management,conducting the study, data collection, data analysis and manuscript writing. ZX participated in perioperative anesthesia management,conducting the study, data collection, data analysis and manuscript writing. KW is the statistician who designed the Bland and Altman scatterplots and regression plots as well as statistical analysis.

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Compliance with ethical standards

Conflict of interest All authors attest to the validity and legitimacy of the data and its interpretation, and agree to its submission. All authors have significantly contributed to the manuscript and no person or group of persons who actively contributed were excluded from the study. All authors confirm that they have read and approved the paper, have met the criteria for authorship as established by the International Committee of Medical Journals Editors, believe that the paper represents honest work, and are able to verify the validity of the results reported. All authors state that we have absolutely no conflicts of interest (including financial, consultant, institutional and other relationships that might lead to bias or a conflict of interest). None of the authors received honoraria from a company or were on the speaker's bureau for any Organization, and there were no sources of financial support, corporate involvement or patent holdings other than above mentioned grants from the Scientific Research Fund of Ministry of Health - Major Plan of Science and from above mentioned departmental sources. There was no support whatsoever from a pharmaceutical company or a manufacturer in any role whatsoever such as editing of the protocol, financial support, drug supply, data analysis or writing of the paper.

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