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## Quantifying neural and non-neural components of wrist hyper-resistance after stroke: Comparing two instrumented assessment methods

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### ABSTRACT

Patients with poor upper limb motor recovery after stroke are likely to develop increased resistance to passive wrist extension, i.e., wrist hyper-resistance. Quantification of the underlying neural and non-neural elastic components is of clinical interest. This cross-sectional study compared two methods: a commercially available device (NeuroFlexor®) with an experimental EMG-based device (Wristalyzer) in 43 patients with chronic stroke. Spearman's rank correlation coefficients ( $r$ ) between components, modified Ashworth scale (MAS) and range of passive wrist extension (PRoM) were calculated with 95% confidence intervals. Neural as well as elastic components assessed by both devices were associated ( $r = 0.61$ , 95%CI: 0.38–0.77 and  $r = 0.53$ , 95%CI: 0.28–0.72, respectively). The neural component assessed by the NeuroFlexor® associated significantly with the elastic components of NeuroFlexor® ( $r = 0.46$ , 95%CI: 0.18–0.67) and Wristalyzer ( $r = 0.36$ , 95%CI: 0.06–0.59). The neural component assessed by the Wristalyzer was not associated with the elastic components of both devices. Neural and elastic components of both devices associated similarly with the MAS ( $r = 0.58$ , 95%CI: 0.34–0.75 vs. 0.49, 95%CI: 0.22–0.69 and  $r = 0.51$ , 95%CI: 0.25–0.70 vs. 0.30, 95%CI: 0.00–0.55); elastic components associated with PRoM ( $r = -0.44$ , 95%CI: -0.65– -0.16 vs. -0.74, 95%CI: -0.85– -0.57 for NeuroFlexor® and Wristalyzer respectively). Results demonstrate that both methods perform similarly regarding the quantification of neural and elastic wrist hyper-resistance components and have an added value when compared to clinical assessment with the MAS alone. The added value of EMG in the discrimination between neural and non-neural components requires further investigation.

### List of abbreviations

EC	elastic component of wrist hyper-resistance
ECR	extensor carpi radialis muscle
EMG	electromyography
FCR	flexor carpi radialis muscle
MAS	modified Ashworth scale
NC	neural component of wrist hyper-resistance
NF	NeuroFlexor®
PRoM	range of passive wrist extension

WA Wristalyzer

### 1. Introduction

Worldwide, 15 million people suffer a stroke each year [1], of which about 80% initially experience upper limb motor deficits [2]. More than half of these patients show poor to moderate upper limb motor recovery in the first six months post stroke [3] and experience long-term upper limb impairments that severely affect their daily activities and quality of life [4,5]. Patients showing limited upper limb motor recovery are likely

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to develop increased resistance to passive wrist extension, i.e. wrist hyper-resistance, in weeks to months post stroke [6,7]. This hyper-resistance of the wrist joint is hypothesized to originate from a complex interaction between impaired neuromuscular activation and altered tissue properties of the muscles spanning the joint [8,9]. Impaired neuromuscular activation includes spasticity, defined as velocity-dependent stretch hyperreflexia [10], and involuntary background activation [11]. Altered tissue properties comprise changes in elasticity, viscosity, and muscle shortening [12]. The distribution and level of aforementioned neural and non-neural tissue property-related components may change over time post stroke [13–15] and may differ between individual patients [16]. Accurate discrimination between the components is important to understand their influence on post-stroke motor recovery and may help to optimize individual treatment decisions [17]. However, this is not possible by manual assessment of joint resistance, which is the current clinical standard [18,19]. There is a need for a valid and reliable non-invasive assessment method that is easy to apply in clinical practice [19,20].

Various instrumented assessment methods have been developed that differ in setup and neuromuscular modelling [16,21–23]. The commercially available medical device NeuroFlexor® (Aggero MedTech AB, Älta, Sweden) [21] derives the neural and non-neural elastic components from resistance to a passive wrist extension movement. Construct validity [21,24,25], good to excellent test-retest reliability [25,26], and good responsiveness [27] of this device were shown. The experimental Wristalyzer [16] uses measured joint torque during an imposed perturbation of the wrist in combination with electromyography (EMG) of wrist flexor and extensor muscle activity to estimate neural and elastic components using a neuromuscular model including wrist mechanics and muscle properties. Similar instrumented assessment methods for the wrist and ankle joint have shown to be valid in patients with acute [13] and chronic [16,28] stroke and have shown moderate to good test-retest reliability [29,30]. However, as far as we know, a head-to-head comparison of methods within the same patient sample has not been done.

The aim of the present study was to compare the NeuroFlexor® with the EMG-based Wristalyzer for the quantification of neural and non-neural elastic components of wrist hyper-resistance in patients with chronic stroke. Additionally, we compared the outcomes of both devices with the modified Ashworth scale (MAS) and range of passive wrist extension, obtained by goniometry and the Wristalyzer. We hypothesized similarity between both devices in the quantification of the neural as well as elastic components. Additionally, we expected similar discriminative validity of both devices compared to the clinical MAS [16,25] and similar association strength between the elastic components of both devices and range of passive wrist extension.

## 2. Methods

### 2.1. Participants

For this study, patients with chronic stroke and initial upper limb paresis were recruited. Inclusion criteria were: (1) ischemic or haemorrhagic stroke at least six months prior to inclusion; (2) initial upper limb paresis as defined by the National Institutes of Health Stroke Scale (NIHSS) item 5 a/b-score > 0 (i.e. not able to hold the affected arm at a 90° angle for at least 10 s); (3) age 18 years or older, and (4) sufficient cognitive ability to follow test instructions (mini-mental state examination > 17) [31]. Exclusion criteria were: (1) limitations of the arm-hand function of the affected side other than due to stroke; (2) less than 40° of passive wrist extension with extended fingers in order to comply with the NeuroFlexor® protocol and (3) botulinum toxin injections in the affected arm in the previous three months which may have affected wrist hyper-resistance components. Ethical approval was obtained from the Medical Ethics Committee of the VU University medical centre, Amsterdam, The Netherlands (NL47079.029.14). In

accordance with the Declaration of Helsinki [32], all participants gave written informed consent.

### 2.2. Experimental design

In this cross-sectional study, demographic data, stroke characteristics, neurological status (NIHSS and Fugl-Meyer motor assessment of the upper extremity), and medical history were collected. NeuroFlexor® (NF), Wristalyzer (WA), and clinical assessments were performed in an arbitrary sequence on the same day, with at least 10 min in between, or, for practical reasons, on two separate days with a maximum of one day in between. When performed on two separate days, the MAS was performed on the same day as the NF assessment. All assessments were performed on the patients' impaired arm by a team of five trained researchers according to a standardized protocol.

### 2.3. NeuroFlexor®

#### 2.3.1. Instrumentation and measurement protocol

The NeuroFlexor® [21], is a motor-driven device which applies isokinetic positional perturbations to the wrist with extended fingers from 20° flexion towards 30° extension at two controlled velocities (5 and 236°/s), see Table 1 for characteristics. Resistance during passive wrist extension is measured in Newton [N] using a force sensor mounted underneath the moveable hand platform. The patient was seated comfortably beside the device with the shoulder in 45° of abduction, 0° of flexion, the elbow in 90° of flexion, with the forearm fastened to the device in pronation, and the hand pronated (facing down) with extended fingers fastened to the movable platform. The axis of the wrist joint was visually aligned with the rotation axis of the device. One measurement consisted of five slow movements, followed by ten fast movements. The first movement at both velocities was excluded from the analysis to avoid bias from startle reflexes and mechanical hysteresis. Two NeuroFlexor® measurements were performed at least 15 min apart and mean values were used for further analysis.

#### 2.3.2. Model description and component calculation



Wrist hyper-resistance components were derived from a unidirectional biomechanical model [21,33] based on the force-time traces during passive wrist extension (software program NeuroFlexor Scientific v0.06, Supplementary file 1) The neural component (NF-NC, in Newton) is defined as the immediate resisting force at the end of the fast passive wrist extension movement (i.e., 30° wrist extension) minus the non-neural elastic and viscous components. The elastic component (NF-EC, in Newton) is the length-dependent resisting force recorded 1 s after stopping the slow movement (i.e., 30° wrist extension). The viscous component is the velocity-dependent resisting force of soft tissues to stretch.

### 2.4. Wristalyzer

#### 2.4.1. Instrumentation and measurement protocol

The Wristalyzer is a one degree-of-freedom haptic manipulator (MOOG, Nieuw Vennep, The Netherlands) [34] rotating a custom-made handle (Meester Techniek, Leiden, The Netherlands) by a vertically positioned servo motor (Parker SMH100 series, Parker Hannifin, Charlotte, NC, USA), see Table 1 for characteristics. Patients were seated comfortably with the shoulder slightly abducted and elbow in 90° flexion. The forearm was strapped in a lower arm cuff in a neutral position between pronation and supination with the hand in the neutral (parasagittal) plane with extended fingers fixated to the handle. The axis of the wrist joint was visually aligned with the vertical rotation axis of the haptic manipulator. Muscle activity of the flexor carpi radialis (FCR) and extensor carpi radialis (ECR) muscles was measured by EMG using pairs of unipolar electrodes (Blue Sensor N, Ambu, Ballerup, Denmark) placed on the muscle belly [16]. Maximal passive range of wrist

**Table 1**  
Comparison of characteristics of the NeuroFlexor® versus Wristalyzer.

	NeuroFlexor®	Wristalyzer
		
Device:	NeuroFlexor®	Wristalyzer
Range wrist perturbation:	20° flexion to 30° extension	max flexion to max extension and back
Movement in:	vertical plane (rotation axis horizontal)	horizontal plane (rotation axis vertical)
Position forearm:	pronation	neutral position in between pronation and supination
Modelling:	unidirectional biomechanical model based on signal analysis	bi-directional EMG-based optimization model
Input parameters:	wrist angle force	wrist angle torque EMG FCR and ECR
Outcome parameters:	neural force [N]* elastic force [N]* viscous force [N]	neural torque of FCR&ECR [Nm] elastic stiffness of FCR&ECR [Nm/rad]*

\* Determined at 30° wrist extension. EMG: electromyography; FCR: flexor carpi radialis muscle; ECR: extensor carpi radialis muscle. Detailed information about the models and the model parameters is described in *Supplementary files 1 and 2*.

extension and flexion was determined by applying a slow increasing torque with a duration of 15 s up to a maximal torque of 2 Nm in both flexion and extension direction. Subsequently, the wrist was passively extended and flexed over the full recorded passive range of motion (PRoM) minus one degree in both the maximal flexion and extension direction (sweep), including two slow sweep trials at 5°/s, two sweeps at PRoM/s, and two fast sweep trials at 236°/s. Each sweep trial contained a preparatory movement from neutral wrist angle position towards maximal flexion, followed by a sweep towards maximal extension, returning to maximal flexion, and ending towards neutral position respectively.

Wrist angle, torque, and EMG signals of the FCR and ECR were recorded simultaneously at 2048 Hz using a Refa amplifier (TMSi, Oldenzaal, The Netherlands). Matlab R2017b (The Mathworks, Inc., Natick, MA, USA) was subsequently used for offline data analysis. Wrist angle and torque signals were low-pass filtered at 20 Hz (3rd-order Butterworth). EMG signals were band-pass filtered at 20–450 Hz (3rd-order Butterworth), full-wave rectified, and subsequently low-pass filtered at 20 Hz (3rd-order Butterworth), to obtain the EMG envelope. Finally, the minimal EMG value, determined with steps of 8 ms during the total time window, was subtracted from the total EMG to reduce the influence of noise and offset muscle activation.

#### 2.4.2. Model description and component calculation

An EMG-based antagonistic optimization wrist model was used based on a bidirectional wrist model [16] which is derived from an ankle model [28]. Wrist angle, torque, and EMG of the FCR and ECR were used to estimate 12 parameters by a nonlinear least squares optimization algorithm and minimizing the error function, i.e. the difference between the measured torque and predicted torque. The model optimized the parameters over the full duration of the sweep protocol with different joint velocities in both extension and flexion direction. Detailed information about the optimization model is described in *Supplementary file 2*. After parameter optimization, the neural component induced by the velocity-dependent stretch reflex of the FCR during passive wrist extension (WA-NC, in Newton • meter [Nm]) was calculated based on root mean square values of the modelled variant active torque within the time window of the fast (236°/s) extension sweeps and the elastic tissue component of the FCR during passive wrist extension (WA-EC, in

Nm/rad) was taken at 30° wrist extension at a velocity of 5°/s.

#### 2.5. Clinical assessment

Resistance to manually applied passive wrist extension movement with extended fingers was measured using the modified Ashworth scale [35], an ordinal scale with scores ranging from 0 (no increased tone) to 4 (the joint is rigid). The maximal range of passive wrist extension with extended fingers was determined using a goniometer. Mean values of three extension movements were used for further analysis.

#### 2.6. Statistical analysis

In the absence of a gold standard, a priori assumptions for the similarity between outcomes of the NeuroFlexor® and Wristalyzer were formulated [36]. Correlation coefficients above 0.50 were considered as similar constructs, between 0.30–0.50 as related, but distinct constructs, and below 0.30 as unrelated constructs [37]. We expected 1<sub>a,b</sub>) correlation coefficients above 0.50 between the corresponding components of both devices (convergent validity); 2<sub>a,b</sub>) correlation coefficients below 0.30 between the different components of both devices (discriminant validity); 3<sub>a,b</sub>) both devices to separate wrist hyper-resistance in two different components ( $r < 0.30$ ) (discriminant validity); 4) similar individual ranking of the wrist hyper-resistance components of both devices; 5<sub>a,b</sub>) neural and elastic components of both devices to relate in the same way to the clinical MAS ( $0.30 < r < 0.50$ ); 6) higher neural and elastic components in patients with higher MAS scores for both devices (discriminative validity), and 7<sub>a,b</sub>) the elastic component of both devices to relate in the same way to the range of passive wrist extension, obtained by goniometry and the Wristalyzer respectively ( $0.30 < r < 0.50$ ).

Study data were analysed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used for demographic and clinical characteristics. Correlation coefficients between components, and with the MAS and range of passive wrist extension, were calculated using Spearman's rank correlation coefficients to address assumptions 1, 2, 3, 5, and 7, respectively. A Fisher's z transformation was used to calculate 95% confidence intervals of the correlation coefficients [38]. To test whether components relate in the same way to the MAS and the range of passive wrist extension, 95%

confidence intervals were compared (assumption 5 and 7). Overlapping confidence intervals were considered similar. Percentage explained variance was calculated by  $r^2 \times 100\%$ .

To deal with the differences in metric units used by both devices, outcomes of each component were ranked in order from the lowest to the highest value (rank 1 to 43 respectively). Wilcoxon signed-ranks tests were used to test the differences between the individual ranks of the neural and elastic components of both devices (assumption 4). In addition, for both components of both devices, patients' scores were classified into quartiles. The quartile classifications of the two devices were compared at individual level for both the neural and elastic components. A difference of more than one quartile between the two devices for the same component within one patient was classified as divergent.

Patients were classified according to their MAS score. Patients with a MAS score of 1 and 1+ were both classified as MAS<sub>1</sub>. The between MAS group differences in neural and elastic components for both devices were assessed by the Kruskal-Wallis analysis, with Mann-Whitney U *post-hoc* analyses (assumption 6). The level of significance was set two-tailed at 0.05. To correct for multiple testing in the *post-hoc* analyses, a Bonferroni correction was applied.

### 3. Results

Of the 46 patients in the study, data of 43 patients were included in the analysis. Two patients could not perform the measurements due to pain during passive wrist extension movement and data of one patient was excluded from analysis due to a technical problem of the NF during wrist extension. For three patients, the second NF measurement was missing and data of one measurement was used for analysis. The main demographic and clinical characteristics of the patient population are summarized in Table 2.

Table 3 shows an overview of the pre-determined assumptions and the results of the similarity between the outcomes of the NF and WA, and their relation with the MAS and range of passive wrist extension.

**Table 2**  
Demographic and clinical characteristics of the study population, stratified by modified Ashworth scale.

	Overall	MAS <sub>0</sub>	MAS <sub>1</sub>	MAS <sub>2</sub>	MAS <sub>3</sub>
	<i>n</i> = 43	<i>n</i> = 8	<i>n</i> = 24	<i>n</i> = 7	<i>n</i> = 4
Age, years (mean ± SD)	60.1 ± 10.0	65.5 ± 7.2	59.3 ± 10.4	56.9 ± 11.8	60.3 ± 8.5
Gender, male/female ( <i>n</i> )	29/14	4/4	18/6	5/2	2/2
Stroke type, iCVA/hCVA ( <i>n</i> )	37/6	7/1	22/2	5/2	3/1
Time post stroke, months (mean ± SD)	61.1 ± 78.4	33.9 ± 48.0	68.5 ± 93.2	78.3 ± 65.3	41.0 ± 44.7
Affected side, left/right ( <i>n</i> )	23/20	3/5	14/10	3/4	3/1
NIHSS score (mean ± SD)	4.7 ± 3.2	4.3 ± 3.9	3.9 ± 2.3	6.6 ± 4.0	6.8 ± 4.3
FM-UE (mean ± SD (min; max))	34.0 ± 18.4 (6; 64)	53.1 ± 11.0 (33; 64)	33.5 ± 16.6 (9; 63)	24.6 ± 17.6 (7; 56)	15.0 ± 6.2 (6; 19)
Passive wrist extension <sub>gonio</sub> , ° (mean ± SD)	73.2 ± 14.3	82.9 ± 13.8	71.7 ± 14.0	68.6 ± 14.1	71.0 ± 13.8
Passive wrist extension <sub>wa</sub> , ° (mean ± SD)	56.4 ± 18.1	65.0 ± 13.5	57.4 ± 16.7	51.2 ± 23.9	42.5 ± 18.9
MAS (median [25 <sup>th</sup> -75 <sup>th</sup> percentile])	1.5 [1 to 2]				

iCVA: ischemic stroke; hCVA: haemorrhagic stroke; NIHSS: National Institutes of Health Stroke Scale [range: 0–42]; FM-UE: Fugl-Meyer motor assessment of the upper extremity [range: 0–66]; passive wrist extension<sub>gonio</sub>: obtained by goniometry; passive wrist extension<sub>wa</sub>: obtained by the Wristalyzer using 2 Nm; MAS: modified Ashworth scale [range 0–4].

Corresponding scatterplots of the correlations are presented in *Supplementary file 3*. NF-NC showed a significant correlation coefficient with WA-NC (0.61, 95% CI: 0.38 to 0.77) and NF-EC showed a significant correlation coefficient with WA-EC (0.53, 95% CI: 0.28 to 0.72). NF-NC showed significant correlation coefficients with WA-EC (0.36, 95% CI: 0.06 to 0.59) and with NF-EC (0.46, 95% CI: 0.18 to 0.67). WA-NC showed non-significant correlation coefficients with NF-EC (0.15, 95% CI: -0.16 to 0.43) and with WA-EC (0.16, 95% CI: -0.15 to 0.44).

Fig. 1 presents an overview of the rank numbers for each component of both devices per patient, ordered by NF-NC. Wilcoxon signed-ranks tests did not show a difference in individual ranks on the NC and EC between the two devices ( $P = 0.57$  and  $P = 0.87$ , respectively). As illustrated in Fig. 2, for the neural component, 20 of the 43 patients (47%) were categorized into equal quartiles by both devices. Nineteen patients (44%) were categorized into different, but adjacent, quartiles, while four patients (9%) were categorized into divergent quartiles. For the elastic component, 17 of the 43 patients (40%) were categorized into equal quartiles. Nineteen patients (44%) were categorized into adjacent quartiles, while seven patients (16%) were categorized into divergent quartiles.

The neural components of both devices, i.e. NF-NC and WA-NC, showed significant correlation coefficients with overlapping confidence intervals with the MAS (0.58, 95% CI: 0.34 to 0.75 and 0.49, 95% CI: 0.22 to 0.69, respectively) (Table 3). The elastic components NF-EC and WA-EC also showed correlation coefficients with overlapping confidence intervals with the MAS (0.51, 95% CI: 0.25 to 0.70 and 0.30, 95% CI: 0.00 to 0.55, respectively). All components showed a gradual increment with MAS category (Table 4). Kruskal-Wallis analysis revealed a significant difference between the MAS categories for NF-NC ( $P = 0.005$ ), NF-EC ( $P = 0.014$ ), and WA-NC ( $P = 0.010$ ). *Post-hoc* Mann-Whitney U analyses showed a significantly higher NF-EC for patients with MAS<sub>1</sub> and MAS<sub>2</sub> compared to MAS<sub>0</sub> ( $P \leq 0.008$ ). WA-NC for patients with MAS<sub>3</sub> was significantly higher compared to MAS<sub>0</sub> and MAS<sub>1</sub> ( $P \leq 0.008$ ).

The elastic components of both devices, i.e. NF-EC and WA-EC, showed significant negative correlation coefficients with overlapping confidence intervals with the range of passive wrist extension, as obtained by goniometry (-0.44, 95% CI: -0.65 to -0.16 and -0.74, 95% CI: -0.85 to -0.57, respectively). Significant negative correlation coefficients with non-overlapping confidence intervals were found with the range of passive wrist extension, as obtained by the WA at 2 Nm (-0.54, 95% CI: -0.72 to -0.28 and -0.87, 95% CI: -0.93 to -0.78, respectively) (Table 3).

### 4. Discussion

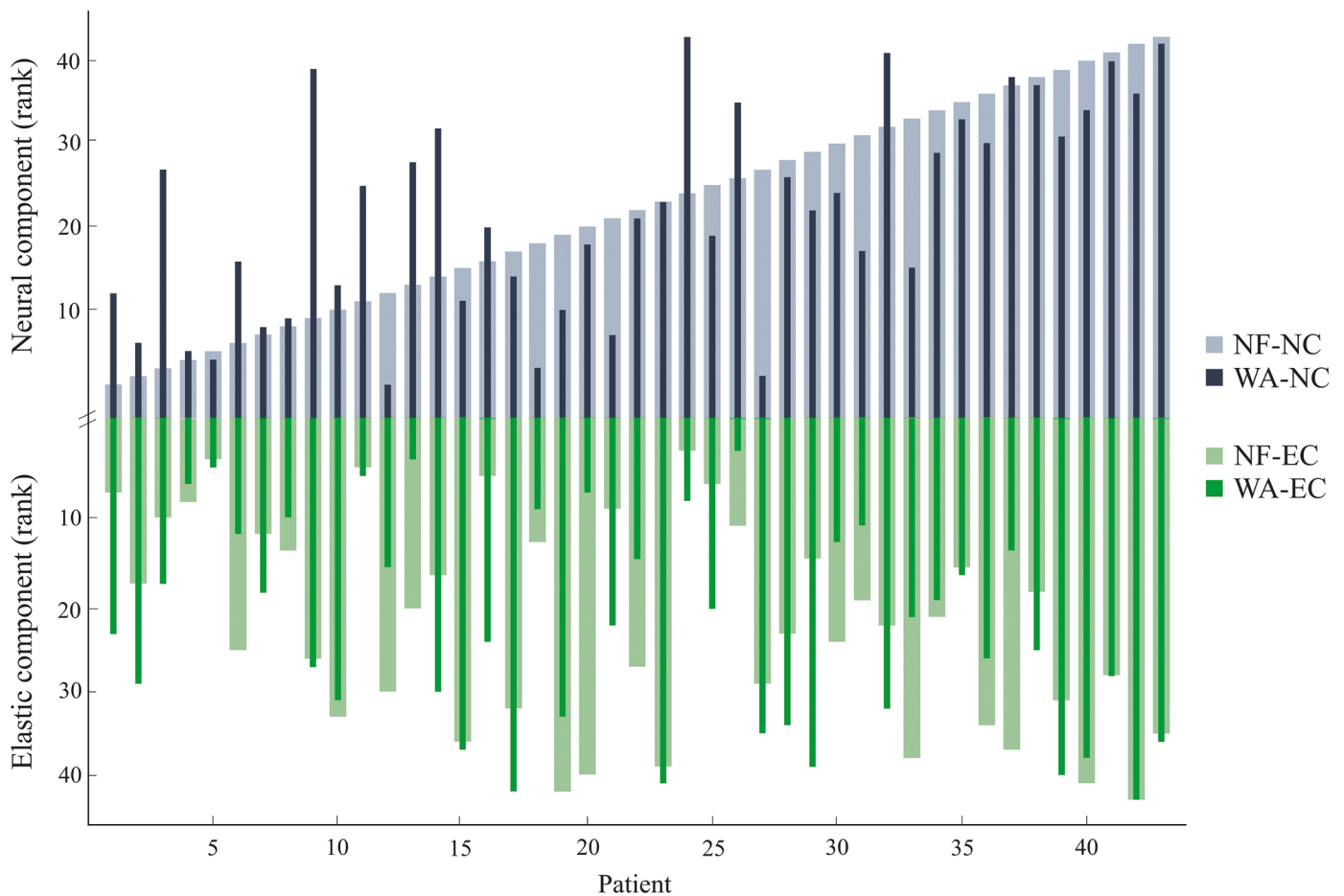
We performed a head-to-head comparison of the NeuroFlexor® (NF) with the EMG-based Wristalyzer (WA) for the quantification of neural and non-neural elastic components of resistance to passive wrist extension in 43 patients with chronic ischemic or haemorrhagic stroke with initial upper limb paresis. The majority (9/12) of our pre-determined assumptions were confirmed by this study, which supports the similarity between the two instrumented assessment methods.

Significant associations above 0.50 between the neural components as well as between the elastic components obtained by the two devices were as expected, suggesting that the components measured by both devices represent similar constructs. The remaining unexplained variance (i.e., 63% for the neural components and 72% for the elastic components) is substantial and may evolve from differences in measurement setup and protocol, including the presence or absence of direct determination of muscle activity, the different modelling methods in deriving the components and/or the different states at which both components are determined. In comparison, the NF uses a fixed position of 30° wrist extension after a fast wrist extension movement over a fixed 50-degree perturbation range to obtain the neural component, regardless of the patients' passive range of motion, whereas the WA estimates the neural component over the patients' full passive range of motion at a

**Table 3**  
Overview of pre-determined assumptions and their results for similarity between the outcomes of the NeuroFlexor® and Wristalyzer.

Pre-determined assumptions for similarity		Expected correlation	Results Correlation coefficients (95% CI)	Explained variance	Assumption confirmed?
1	a NF-NC vs. WA-NC	$r > 0.50$	0.61 (0.38 to 0.77)	37%	✓
	b NF-EC vs. WA-EC	$r > 0.50$	0.53 (0.28 to 0.72)	28%	✓
2	a NF-NC vs. WA-EC	$r < 0.30$	0.36 (0.06 to 0.59)	13%	x
	b WA-NC vs. NF-EC	$r < 0.30$	0.15 (-0.16 to 0.43)	2%	✓
3	a NF-NC vs. NF-EC	$r < 0.30$	0.46 (0.18 to 0.67)	21%	x
	b WA-NC vs. WA-EC	$r < 0.30$	0.16 (-0.15 to 0.44)	3%	✓
4	Ranking of components per individual is similar in both devices				
5	a NF-NC vs. MAS ( $r_1$ ) is equal to WA-NC vs. MAS ( $r_2$ )	$r_1 = r_2$	$r_1 = 0.58$ (0.34 to 0.75) $r_2 = 0.49$ (0.22 to 0.69)		✓
	b NF-EC vs. MAS ( $r_3$ ) is equal to WA-EC vs. MAS ( $r_4$ )	$r_3 = r_4$	$r_3 = 0.51$ (0.25 to 0.70) $r_4 = 0.30$ (0.00 to 0.55)		✓
6	NC's and EC's measured by devices are higher in patients with higher MAS scores				
7	a NF-EC vs. passive wrist extension <sub>gonio</sub> ( $r_1$ ) is equal to WA-EC vs. passive wrist extension <sub>gonio</sub> ( $r_2$ )	$r_1 = r_2$	$r_1 = -0.44$ (-0.65 to -0.16) $r_2 = -0.74$ (-0.85 to -0.57)		✓
	b NF-EC vs. passive wrist extension <sub>wa</sub> ( $r_3$ ) is equal to WA-EC vs. passive wrist extension <sub>wa</sub> ( $r_4$ )	$r_3 = r_4$	$r_3 = -0.54$ (-0.72 to -0.28) $r_4 = -0.87$ (-0.93 to -0.78)		x

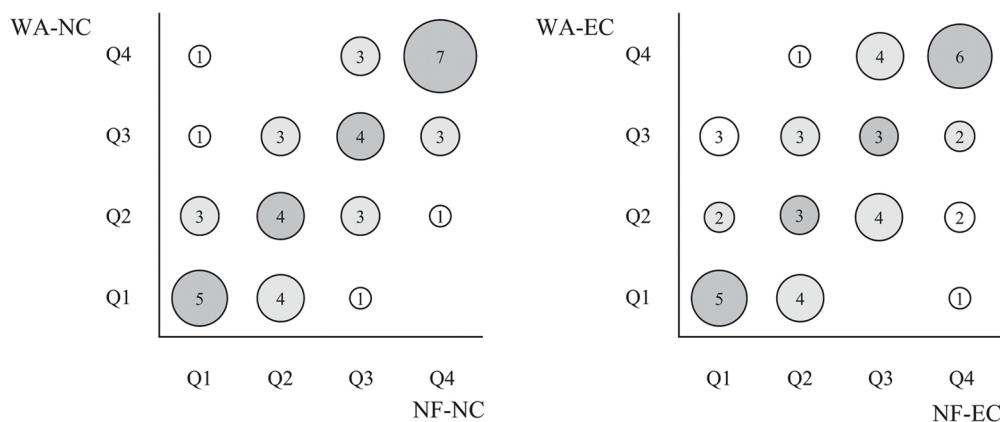
✓, assumption confirmed; x, assumption not confirmed; NF-NC: NeuroFlexor®, neural component [N]; NF-EC: NeuroFlexor®, elastic component [N]; WA-NC: Wristalyzer, neural component [Nm]; WA-EC: Wristalyzer, elastic component [Nm/rad]; MAS: modified Ashworth scale [-]; passive wrist extension<sub>gonio</sub>: obtained by goniometry [°]; passive wrist extension<sub>wa</sub>: obtained by the Wristalyzer using 2 Nm [°]. Values are Spearman's rank correlation coefficients ( $r$ ) with 95% confidence intervals.



**Fig. 1.** Overview of the ranking of neural and elastic components of both devices per patient, with patients ordered according to the neural component assessed by the NeuroFlexor®. The outcomes of each component were ranked in order from the lowest to the highest value (rank 1 to 43 respectively). NF-NC: NeuroFlexor®, neural component; WA-NC: Wristalyzer, neural component; NF-EC: NeuroFlexor®, elastic component; WA-EC: Wristalyzer, elastic component.

velocity of 236°/s, using EMG, which will affect the estimate of the reflexive response of muscle activity. Furthermore, the position of the forearm in which the wrist is moved differs per device. In the wrist

extension movement in the vertical plane, which is imposed by the NF, the gravitational component of the mass of the hand may influence the exerted force from which the neural and elastic components are



**Fig. 2.** Comparison of the NeuroFlexor® (NF) and Wristalyzer (WA) for the classification into quartiles at the individual level for the neural component (NC) and the elastic component (EC). The numbers in the circles represent the number of patients categorized according to the quartile classification of the two devices. Q: quartile.

**Table 4**

Neural and elastic components of wrist hyper-resistance as obtained by the NeuroFlexor® and Wristalyzer, stratified by modified Ashworth scale.

	Overall <i>n</i> = 43	MAS <sub>0</sub> <i>n</i> = 8	MAS <sub>1</sub> <i>n</i> = 24	MAS <sub>2</sub> <i>n</i> = 7	MAS <sub>3</sub> <i>n</i> = 4	<i>P</i> Kruskal-Wallis
<b>NeuroFlexor®</b>						
NF-NC [N]	10.01 [5.02 to 22.47]	1.87 [1.45 to 10.93]	9.29 [5.16 to 21.57]	12.57 [7.75 to 22.73]	37.11 [17.81 to 42.68]	0.005
NF-EC [N]	4.88 [3.01 to 7.03]	2.63 [2.46 to 3.70]	4.93 <sup>a</sup> [3.35 to 7.29]	5.85 <sup>a</sup> [4.85 to 7.40]	7.96 [2.89 to 15.44]	0.014
<b>Wristalyzer</b>						
WA-NC [Nm]	0.42 [0.08 to 0.95]	0.20 [0.02 to 0.43]	0.32 [0.08 to 0.85]	0.68 [0.17 to 2.07]	1.53 <sup>a,b</sup> [1.04 to 2.27]	0.010
WA-EC [Nm/rad]	1.26 [0.62 to 2.30]	1.01 [0.40 to 1.38]	1.23 [0.61 to 2.22]	2.26 [0.82 to 3.39]	2.54 [0.79 to 7.11]	0.333

Values are median [25<sup>th</sup> and 75<sup>th</sup> percentile]. *n*, number of patients; NF-NC: NeuroFlexor®, neural component; NF-EC: NeuroFlexor®, elastic component; WA-NC: Wristalyzer, neural component; WA-EC: Wristalyzer, elastic component; MAS: modified Ashworth scale.

Mann-Whitney *U* post-hoc analysis: <sup>a</sup> significantly different from MAS<sub>0</sub> (*P* ≤ 0.008); <sup>b</sup> significantly different from MAS<sub>1</sub> (*P* ≤ 0.008)

obtained. Additionally, the NF, unlike the WA, uses a unidirectional (i. e., extension) biomechanical modelling method based on the force-time traces only, without taking muscle activity and tissue properties of the extensor muscle into account. Despite the possible limitations of the NF, this portable device, which determines the components immediately after the measurement, may be more practical for clinical use. The WA, on the other hand, uses a more extensive EMG-based optimization model, including all contributing factors, supported by literature. However, the clinical applicability of this experimental method is currently still limited as the offline signal analysis is yet complex and computationally intensive.

NF-NC showed unexpectedly high associations with the elastic components of both devices, while WA-NC showed no association with both elastic components, which may be explained in two ways. First, the discrimination between the neural and elastic component in the NF is less adequate in absence of a direct measurement of muscle activity. Second, NF-NC may have been influenced by other factors that are not included in the unidirectional biomechanical model. This can be due to either a non-neural component, such as viscosity, or other neural factors, such as involuntary background activation. Our findings suggest that the WA, using input from EMG, provides better discrimination between the neural and elastic component of wrist hyper-resistance. Our findings are consistent with previous studies that suggest that assessments using biomechanical parameters, such as joint angle and resistance, alone may be less valid to describe neural components than measurements using EMG-related parameters [39,40]. In contrast, EMG-based instrumented assessment of the neural component previously showed poorer reliability in terms of intraclass correlation coefficients and smallest

detectable change [16,29,30,41] compared to the NF [25]. Further investigations are required to assess whether muscle activity measurements by EMG are needed to gain a valid, reliable, and accurate discrimination between the neural and non-neural tissue property-related components.

The overall results of our study indicate comparable outcomes for the NF and WA at group level, however, there is misclassification at the individual level given the values seen in Fig. 2. This may lead to different treatment decisions in clinical practice at the individual level. The responsiveness of the neural and non-neural components to different treatments, such as botulinum toxin and orthotics, should be evaluated in future studies to gain insight into treatment options for patients with increased neural and/or non-neural components of wrist hyper-resistance and the associated cut-off values that can be used for patient selection.

As expected, components of both devices were moderately associated with the MAS, and the elastic components of both devices showed negative associations with the range of passive wrist extension, suggesting construct validity of both devices for quantification of neural and elastic components of wrist hyper-resistance in patients with chronic stroke. However, these assessment methods that are able to discriminate between components of wrist hyper-resistance have an added value compared to clinical assessment with the MAS alone.

#### 4.1. Study limitations

Differences in metric units prevented the assessment of absolute agreement. Patients with passive wrist extension of less than 40° had to

be excluded due to the NF protocol, which may have affected the variance in the passive tissue properties of the wrist flexor muscle in the included group of patients. Due to pragmatic reasons, the NF and WA assessments were performed in a semi-randomized order and, in thirteen patients, on different days. As the neural drive can vary from day-to-day and even within a day, these fluctuations could have influenced the variance in the neural component between the devices.

## 5. Conclusions

The current study shows similarity between two instrumented assessment methods, i.e. NeuroFlexor® and the EMG-based Wristalyzer, for the quantification of neural and non-neural elastic components of wrist hyper-resistance in patients with chronic stroke. The NeuroFlexor® is easier for clinical use, while the EMG-based Wristalyzer may provide a better distinction between the independent components of wrist hyper-resistance. The possible added value of EMG in the discrimination between the neural and non-neural components, as well as the improvement of the classification of wrist hyper-resistance components at the individual level, requires further investigation.

## CRedit authorship contribution statement

**Aukje Andringa:** Visualization, Formal analysis, Writing – original draft, Investigation. **Carel Meskers:** Conceptualization, Supervision, Writing – review & editing. **Ingrid van de Port:** Writing – review & editing. **Sarah Zandvliet:** Software, Investigation, Writing – review & editing. **Larissa Scholte:** Data curation, Software, Formal analysis, Writing – review & editing. **Jurriaan de Groot:** Software, Data curation, Writing – review & editing. **Gert Kwakkel:** Conceptualization, Supervision, Writing – review & editing. **Erwin van Wegen:** Conceptualization, Supervision, Writing – review & editing.

## Declaration of Competing Interest

None declared.

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## Ethical approval

Ethical approval was obtained from the Medical Ethics Committee of the VU University medical centre, Amsterdam, The Netherlands (NL47079.029.14).

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.medengphy.2021.10.009](https://doi.org/10.1016/j.medengphy.2021.10.009).

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