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Technologically-advanced assessment of upper-limb spasticity: a pilot study

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Abstract

Background

Spasticity is a muscle disorder associated with upper motor neuron syndrome occurring in neurological disorders, such as stroke, multiple sclerosis, spinal cord injury and others. It influences the patient's rehabilitation, interfering with function, limiting independence, causing pain and producing secondary impairments, such as contractures or other complications. Due to the heterogeneity of clinical signs of spasticity, there is no agreement on the most appropriate assessment and measurement modality for the evaluation of treatment outcomes.

Design: Observational pilot study involving five post stroke patients.

Methods: A new robotic device able to automatically assess upper-limb spasticity during passive and active mobilization has been developed. The elbow spasticity of five post stroke patients has been assessed by using the new device and by means of the Modified Ashworth Scale (MAS). After the first assessment, subjects were treated with botulin toxin injections, and then underwent 10 sessions of robotic treatments. After the treatment, subjects spasticity was assessed by using the robotic device and the MAS score.

Results: In four out of five patients, the botulin toxin injection and robotic treatment resulted in the improvement of the MAS score; in three patients the robotic measures were able to detect the MAS changes. In one subject botulin toxin was not effective and the robotic device was able to detect the lack of effectiveness.

Conclusion: By using the robotic device some spasticity parameters can be continuously recorded during the rehabilitation treatment in order to objectively measure the effectiveness of the interventions provided.

Clinical rehabilitation impact: The standardized evaluation parameters recorded using robotic devices may provide several advantages: 1) the measures for spasticity assessment can be monitored during every rehabilitation session (even during each movement), 2) these measurements are able to highlight even small changes, 3) the recovery plateau can be detected early thus avoiding further rehabilitation sessions, and 4) these measurements can reduce the assessment bias in multicenter studies.

Keywords

Rehabilitation, robotics, upper limb, spasticity, assessment.

Introduction

Spasticity is a muscle disorder associated with upper motor neuron syndrome (UMNS) occurring in neurological disorders, such as stroke, multiple sclerosis, and spinal cord injury. This motor disorder influences the patient's rehabilitation, interfering with function, limiting independence, causing pain and producing secondary impairments, such as contractures or other complications due to the immobility. One report estimated that the occurrence of upper limb spasticity after stroke was 50% (33% at three months and 17% later)[1] whilst another study, which evaluated the occurrence of spasticity from the acute stage following stroke, confirmed that spasticity was present in 25% of the patients at day 3 and in 46% at 12 months [2].

It has been demonstrated that spasticity occurs in up to 85% of patients with multiple sclerosis[3] whereas at least seventy-one percent of spinal cord injured patients reported spasticity [4].

From the clinical point of view spasticity may not be considered as a single phenomenon but rather as a concoction of several positive symptoms of the UMNS, such as exaggerated tonic and phasic stretch reflexes, flexor and extensor spasms, associated reaction (synkinesias), spastic dystonia, increased muscles stiffness and contractures. The evaluation of treatment outcomes is a key factor in both clinical rehabilitation practice and research settings, but there is no agreement on the most appropriate outcome measurement selection modality. The main obstacle in adopting a standardized assessment is the aforementioned heterogeneity of clinical symptoms of spasticity, resulting in a large number of instruments and clinical outcome evaluation scales. Instead, in order to evaluate the effectiveness of eventual spasticity treatment, an improved and more specific assessment of all the symptoms of spasticity is needed combining electrophysiological and biomechanical techniques[5].

The selection of the most appropriate outcome parameters to measure for the evaluation of spasticity depends on the definition of this motor disorder even if a definitive agreement on the definition of spasticity is still lacking, probably also due to its underlying pathophysiological mechanisms not yet completely clarified [6].

As the patient's experience of spasticity involve a wide range of unusual sensations, clinical evaluation of spasticity should also include patient's subjective perception of spasticity. The clinical assessment and patient reports may contribute to increase the knowledge on spasticity[7][8].

In a review of the scientific literature related to the upper-limb disorders associated to UMNS, Malhotra and colleagues [9] found that out of a search of 250 references, 31% of the articles did not define spasticity; 31% cited the definition proposed by Lance in 1980 (i.e. "a motor disorder characterized by a velocity dependent increase in stretch reflexes (muscle tone) with exaggerated tendon jerks, as one component of the upper motor neuron syndrome") and 35% equated spasticity

with increased muscle tone but no specific definition of altered muscle tone was provided. Other terms that were used within this context were 'abnormal tone', 'hypertonia' and 'hyperreflexia', however these terms were also not defined explicitly. The remaining 3% of the articles equated spasticity with abnormal and involuntary muscle activity. Other definitions have emerged in the scientific community, such as the one provided by the European SPASM network: here, spasticity is defined as a "disordered sensory-motor control, resulting from an upper motor neuron lesion, presenting as intermittent or sustained involuntary activation of muscles" [10][11] or a "*velocity dependent increase in hypertonia with a catch when a threshold is exceeded*" [12]. These definitions are mainly related to conditions in which the patients joints are passively moved and muscles are stretched. However, the spastic alterations at rest differ considerably from those observed during active movements [6][13][14]. In fact, even if the precise relationship between spasticity, stretch reflex, and the production of active motor performance remains unclear, hyperactive reflexes and changes in the threshold regulation are responsible both for increasing of muscular tone and weakness and abnormal co-contraction between agonists and antagonists muscles during active movement or isometric contractions.

Measuring spasticity during functional activities (such as walking or reaching) can be considered a logical extension of the methods employing execution of voluntary movements. Unfortunately movements used in current state-of-the-art spasticity clinical assessment are less relevant for the patient (also from a psychophysics point of view) than activities of daily living (ADLs). For the clinician it is thus more appropriate to evaluate the patient's spasticity through functional ADLs trials, so-called *functional methods*, and directing the treatment accordingly. These tests provide repeatable and standardized measurements for the clinical experts, but their correlation to the real patient's spasticity, and to its evolution, has yet to be verified [15]. On the other hand, biomechanical evaluation methods are unfortunately often underemployed as for the lack of proper technology or due to uncertainties about what should be measured [16] and to the time demanded for the evaluation.

In order to check which of the above-mentioned measurements for spasticity were mainly used in the past, we searched in the studies published in ten years (from 1st January 2005 to 31st December 2014). The search included databases of MEDLINE, EMBASE, CINALH and Scopus. The following string was used: ab(stroke) AND ab((upper limb OR upper extremity)) AND ab((spasticity evaluation OR spasticity measurement)) AND human(yes) AND la.exact("English") AND mesh.exact(adult OR aged OR "aged,80 and over" OR "middle aged" OR "young adult").

The extraction of measures of spasticity was performed including only scales and other types of assessment able to specifically measure spasticity without considering global functional outcome measures (i.e. Fugl-Meyer, Goal Attainments Scale, Functional Independence Measure, and so on).

A total of 254 papers were analysed: the measures of spasticity which were used as evaluation tools at least twenty times were considered separately whilst the evaluation measures which appeared less

than twenty times were included and classified as “others”. 369 measures were recorded as more than one measure was cited in a lot of papers. The results and the frequency of spasticity measures are reported in the Table 1.

Table 1 HERE

It is noteworthy that more than 50% of the studies considered the evaluation of spasticity by using the Ashworth Scale or the Modified Ashworth Scale only, or in combination with other measures. In particular in 62 articles (about 25%) the Ashworth Scale or the Modified Ashworth Scale were used as the sole evaluation tool and in 68 papers (27%) no specific spasticity evaluation methods were reported.

The aim of this article is to propose the use of new robotic devices for upper-limb spasticity assessment and describe the most relevant measures of spasticity which could be automatically assessed by using a technologically advanced device.

The proposed parameters can be automatically recorded and monitored during the rehabilitation treatment by using the robotic device which is able to provide objective and quantitative data, therefore significantly decreasing the variability introduced by subjective measurements of the effectiveness of the interventions provided. It is obvious that the same parameters cannot be monitored without using technologically-advanced devices but above all they cannot be objectively quantified and continuously recorded.

We conducted a preliminary study involving five post-stroke patients, using a robotic elbow exoskeleton, in order to verify the possibility to extract some spasticity-related parameters.

Methods

Participants

In order to evaluate the effectiveness of our robotic device to detect and measure the changes on spasticity after botulin toxin injection, an observational pilot study has been carried out. When considering that the sample size for a pilot study should be 10% of an hypothetical larger parent study which in our study can be estimated in 50 subjects, five consecutive stroke patients who were eligible for botulin toxin injection in the elbow muscles were recruited.

Inclusion criteria: (i) unilateral right paresis; (ii) ability to understand and follow simple instructions; (iii) Chedoke-McMaster (CM) Stroke Assessment Scale between 1 and 6; (iv) elbow spasticity which needed to be treated by means of botulin toxin injection. Exclusion criteria: (i) bilateral impairment; (ii) severe sensory deficits in the paretic upper limb; (iii) cognitive impairment or behavioural

dysfunction that would influence the ability to comprehend or perform the experiment; (iv) inability to provide informed consent; and (v) other current severe medical problems.

The experimental protocol was approved by the local ethical committee (Azienda Ospedaliera Universitaria of Pisa, reference number 3919, year 2014) and the patients gave their informed consent for participation in the research study.

Five post-stroke patients, age range 19–79 years (mean age 61, standard deviation (S.D.) ± 25) in their chronic phase were treated with the NEEM system on a daily basis. All subjects were right-handed. A physical therapist assessed the participants elbow extension by means of the MAS score before the treatment. In order to assess the level of the upper limb impairment before the treatment, the stage of arm section of the Chedoke-McMaster (CM) Stroke Assessment Scale was scored. After the first assessment was completed, subjects underwent a botulinum toxin injection. Then they started the multi-session treatments based on *isokinetic passive mobilization* consisting in ten daily sessions of 45 minutes of continuous flexion-extension elbow movement provided by the robotic device. Notably the described experimental protocol was focused on the treatment of spasticity in chronic patients with a passive mobilization protocol, thus no active mobilization was needed and no EMG data was recorded. The treatment was provided in a Rehabilitation Centre where the device was located and the subjects were treated in an outpatients setting.

The robotic metrics were extracted from the data of the five participants from each session and validated against the outcomes from the MAS score and the clinical evidence from the state of the art.

Apparatus

The NEUROExos Elbow Module (NEEM) exoskeleton is a prototypical robotic device able to assess clinical signs of elbow spasticity such as an increase in muscular tone, resistance to muscles elongation, stretch reflex threshold, co-contraction, loss of movement fluency, etc. during both passive stretching and active functional flexion-extension movements. The actuated joint allows the elbow flexion-extension movement and employs a passive-degrees-of-freedom mechanism for human-robot joint axis self-alignment. The device lightweight design is due to its remote actuator unit and the carbon-fibre structural frame. Despite its lightness, NEUROExos embeds a custom-designed Series Elastic Actuator (SEA) allowing a fine position and torque control as well as a safe human-robot interaction[17][18]. The device can be controlled in the so-called *robot-in-charge* or *patient-in-charge modes*: in the first mode, the patient movement is passive and robot drives the position of the exoskeleton along a desired reference trajectory and measures at the same time the necessary torque

to overcome the weight of the user's forearm or muscular actions; in the second mode, the subject performs the motion tasks without being resisted and eventually being partially assisted by the robot.

The NEEM has been certified as a class-II medical device for clinical investigation (compliant to certification IEC EN 60601-1:2007 and EN ISO 14971:2012) and used in a clinical study with post-stroke patients in sub-acute phase [19].

Figure 1 HERE

Figure 1 shows the device and the variables measured from the device in flexion/extension cycles executed in the robot-in-charge mode, of a representative patient. The plot shows the outcome of the position and the torque profile of the elbow joint as recorded from the machine; the passive mobilization was realized with a isokinetic extension/flexion motion. From the collected data on each flexion/extension cycle it is possible to extract the following parameters related to the *elbow extension resistance*: (i) the Maximum Extension Torque (MET) is the torque exerted by the NEEM at the fully extended position and (ii) the Zero-Torque Angle (ZTA) is the angle at which the applied torque is zero during the *elbow extension* phase of the cycle. The metrics extracted from the robot are here reported as an example of technologically-advanced assessment of spasticity-related parameters.

Results

Table 2 shows the characteristics of recruited subjects, the CM score before the treatment and the MAS score of five subjects before treatment and after the two weeks of treatment. MAS scores indicate a clinically-assessed improvement in four out of five patients. The CM median score was 4, the mean was 3.6 and standard deviation was ± 1.14 . The MAS median score was 2 before the treatment and 1 after the treatment, whereas the mean and standard deviation were 2.4 and 1.6 the former and ± 1.14 and ± 0.89 the latter, respectively.

Table 2 HERE

Figure 2 shows that the improvements in the MAS scores are captured by the robot metrics. For subject 1, subject 4 and subject 5 the comparison of session 1 and session 10 reveals a clear reduction of the elbow resistance to passive movement (which can be indirectly related to joint spasticity), quantified by reduced ZTA and reduced MET, whereas subject 2 did not show any significant change of the parameters. For subject 3 the data recorded by robotic device were not able to detect the reduction of 1 point in the MAS score at the end of treatment.

In particular for subject 1 the MAS score decreased from 3 to 2, the median value of ZTA moved from 34 degrees at the first session to 28 degrees at the last session and the median value of MET moved

from -1.86 N/m at the first session to -1.54 N/m at the last one. For subject 4 and 5 the same results showed a decrease in the MAS score from 4 to 3, the median value of ZTA changed from 67 to 51 degrees and the median value of MET changed from -5.08 to -3.16 N/m in the former. Between the first and last session, the MAS score decreased from 2 to 1, the median value of ZTA changed from 38 to 22 degrees and the median value of MET changed from -1.70 N/m to -0.93 N/m in the latter. For subject 2 the MAS score did not change after the treatment and the median value of ZTA and MET did not show any significant change after the treatment (ZTA changed from 28 to 25 degrees and MET from -0.63 N/m to 0.69 N/m).

According to the MAS scores, subjects 1, 4 and 5 show a decrease of the joint spasticity: it is clearly visible how the values of torques required to achieve the same Range of Motion decreased from day 1 to day 10.

In fact the mean value of ZTA and MET of subject 1, 4 and 5 changed from 46 (S.D. \pm 18) degrees at the first session to 33 (S.D. \pm 15) degrees, whereas the same mean value of MET changed from -2.88 (S.D. \pm 1.89) N/m to -1.88 (S.D. \pm 1.15) N/m.

This finding can be explained by means of an incremental adaptation of the subjects to the therapy associated to a decrease of involuntary contraction, and to the concurrent effect of the botulinum toxin injection. Furthermore no change in the MAS score has been observed in subject 2 and recorded data by the robot confirm this observation.

Figure 2 HERE

Moreover, the data recorded by the robotic are able to contribute to the clinical assessment by providing a quantitative evaluation of the effectiveness of the treatment at each single session. **Figure 3** shows the comparison of the parameters extracted in the first and last cycles of each session: data reveal a clear reduction of the joint resistance to the passive mobilization in some sessions, which is in line with the clinical evidence reporting a reduced movement resistance after prolonged joint mobilization.

Figure 3 HERE

Discussion

According to the retrieved literature, spasticity is associated with an increase in muscular tone, resistance to muscles elongation, an exaggerated stretch reflex, co-contraction and loss of movement fluency. In order to evaluate these different clinical signs of spasticity a set of objective parameters should be recorded during both passive stretching and active functional movements. Considering the variability in the way spasticity is measured and considering the disagreement on its definition and pathophysiology, an important goal is to select a specific set of parameters that would allow a

quantitative assessment of spasticity using robotic devices that are also a part of the rehabilitation training for patients with UMNS.

Muscle stiffness which encompasses the intrinsic muscle properties and stretch reflex hyper-excitability represent two of the components of spasticity [20]-[24]. Considering these as well as the abovementioned symptoms of spasticity, the following elements should be assessed for an appropriate spasticity evaluation because they cover all signs of the UMNS: increase in muscular tone, resistance to muscle elongation, stretch reflex excitability, co-contraction and the loss of movement fluency. When possible, the measurement should be provided during passive stretching and during active functional movements. Since spasticity presents with various symptoms, it is necessary to quantify several parameters that are specifically designed to target these symptoms while maintaining assessment time and costs low.

Parameters to be recorded during passive stretching should be the follow:

- EMG Burst Duration: percentage of the movement time (MT) during which EMG activity is present [25];
- Position Threshold: joint angle, expressed in degrees, at which the EMG activity is first identified. If the EMG activity is absent for the entire imposed stretch, the position threshold should be reported as 0°;
- Stretch Reflex Onset: this is extrapolated from the EMG envelope, as the first sustained burst that rises and remains above the baseline for at least twice the standard deviation (SD) for at least 50 ms, where the baseline EMG (noise level) is defined as the mean value of the rectified EMG in the 100 ms window prior to the imposed stretch[26]; The velocities of the imposed stretch should be incremented to determine the exact threshold of the stretch reflex[27].
- The tonic Spatial Threshold (ST): this is the threshold angle (R) at which muscles are activated during quasi-static stretching (i.e. when the angular velocity, \dot{x} , is close to zero) [26];
- Passive Range of Motion (ROM);
- Torque: resistance to muscles elongation.

Dynamic assessment during active movements include:

- Active ROM;
- Stretch reflexes in terms of EMG Burst Duration and Stretch Reflex Onset: these parameters can be extrapolated from the EMG envelope, as the first sustained burst that rises and remains above the baseline level of contraction for at least twice the standard deviation (SD) for at least 50 ms, where the baseline level of contraction EMG is defined as the mean value of the rectified EMG in the 100 ms window prior to the imposed stretch [26];
- Stretch reflex threshold: the velocities of the imposed stretch should be incremented to determine the exact threshold of the stretch reflex [27] that is extrapolated from the EMG

envelope, as the first sustained burst that rises and remains above the baseline level of contraction for at least twice the standard deviation (SD) for at least 50 ms, where the baseline level of contraction EMG is defined as the mean value of the rectified EMG in the 100 ms window prior to the imposed stretch [26];

- The dynamic ST: this refers to the angular threshold (R^*) at which muscles are activated during non-zero velocity of muscle stretching. To a first approximation the dynamic ST decreases linearly with increasing angular velocity, \dot{x} , of muscle stretch ($x > 0$ during joint extension, i.e. when flexors are stretched) [26];
- Torque;
- Joint Stiffness;
- Co-contraction as measure of overlapped EMG areas;
- Smoothness defined as minimum jerk (i.e., the third time derivative of position) motion. It is assumed that maximizing the smoothness may be modelled by minimizing the mean-square jerk [28]
- Other kinematic parameters such as measures of the movement fluency.

Norm values in healthy individuals are available in the literature even if a large variability according to sex, age, race, height, weight, etc should be taken into account[29]. In particular normal values for maximal EMG activity of elbow movement according to angular velocity, maximal torque of elbow movement according to angular velocity, joint angle of maximal EMG activity according to angular velocity, joint angle of maximal torque of elbow movement according to angular velocity are reported. Pennati GV et al [30] found the cut off for healthy people for neural component, elastic component, viscous component and resting tension and they showed that the age only correlated with elastic component; elasticity and resting tension were higher in males compared to females and both correlated positively with height.

Many robotic devices for upper-limb rehabilitation have been developed [31] and some of them have been used for the assessment of spasticity.

Some examples from the state of the art are reported hereafter. The Neuroflexor[32][33] is a device able to detect and quantify the neural, elastic and viscous components of spasticity at the wrist and the fingers. The main limitation of this device is that the spasticity is assessed only during passive movements of the wrist and the fingers. The device presented in [34] can capture the difference between healthy people and brain injured patients with MAS equal to 0, by evaluating the velocity-dependent resistance to the movement (using force and position measurements, without any EMG measurement). The device proposed by Prochazka and Kowalczewski[35] can quantify the upper-limb performance when the subject moves his upper limb. The main limitation of this system is that it requires the user to be able to move spontaneously and can not drive the movement itself.

It is noteworthy that in order to assess spasticity robotic devices should have specific features. First of all an exoskeletal approach can provide a continuous recording of kinetic and kinematic variables of the human joints. On the contrary, an end-effector device provides force and motion information for only the distal component of the limb by making it difficult to extract information for each anatomical joint of the entire limb. Moreover external frame-mounted robots can provide measurements affected by the compensatory motions of the subject. To allow the appropriate transfer of all forces to the limb, an exoskeleton must be tightly aligned and compatible in motion with the wearing subject. Such features are hardly manageable within a rigid kinematic architecture, with the added complication that inertia and weight of the wearable parts may heavily disrupt the subject's own motion. In addition a wearable robotic exoskeleton has to comply with safety requirements.

Each robot joint must provide a sensorization for both torque and position, and, in its active role, must be externally controllable through both variables as well. Regarding controllability the robot is required to have a minimum time delay and high compliant interaction with the user.

It is noteworthy that the device properties can influence the measurements: the device should be easy to be donned and doffed, and adjustable according to the anthropometric characteristics of the subjects.

Finally, the robot must be designed by taking into account that in spastic subjects spasms can be rather intense yielding to high forces/torques on muscles/joints. Therefore it needs to be ensured that the robotic structure does not break or cause injuries to the human. The stiffness of mechanical parts must be high, the connection between the mechanical structure and the subject must be tight, any sharp edge at the connection must be avoided, a release mechanism should be able to disengage the subject from the robot.

The NEEM exoskeleton, adopted in this study is an example of a wearable device that can be potentially useful for the measurement of elbow spasticity. The system can be easily synchronized with an EMG acquisition unit and the set of above proposed parameters can be measured during passive stretching (in the robot in charge mode) and active movement (during the patient in charge mode) to assess all signs of the UMNS.

This preliminary study is the first attempt to demonstrate that the NEEM can be safely and effectively used to automatically detect the reduction of muscles hypertonia after botulin toxin injection in patients with very severe spastic conditions.

Although the small sample size may represent a limitation, the results are encouraging. Future larger observational studies will be carried out in order to identify a mathematical relation between the variables including EMG data and some predictive factors for the possible effectiveness of botulin toxin injection.

Conclusions

The NEEM represents an example of a robotic device able to record all parameters needed for a robot-supported spasticity assessment which would significantly decrease the variability introduced by subjective measurement techniques. Moreover our exoskeleton device is also able to capture the changes of spasticity due to botulin toxin treatment and it is much more sensitive compared to clinical subjective evaluation tools. The results reported in this pilot study highlight the high potential of wearable exoskeletons that can measure kinematic and kinetic data for the assessment of spasticity-related parameters. Clearly, the combination of robot data with EMG would allow a more complete description of the patient's motor condition.

As it is well known, spasticity is a frequent impairment in neurological disorders and it is responsible for the appearance of disability both in the upper and lower extremities; a lot of treatments are available and it is a complex phenomenon difficult to be defined. For this reason it needs to be carefully assessed. As described in this paper, the most frequent assessment tools for spasticity are the Ashworth Scale or the Modified Ashworth Scale used alone or associated to other types of measurements. Despite the fact that the reliability, validity and responsiveness of the abovementioned scales is well demonstrated, in order to assess and to compare the effectiveness of the different treatments it would be desirable to use objective and sensitive parameters provided by medical equipments. Such standardized and objective techniques would significantly decrease the variability introduced by subjective measurement techniques. To develop these, the initial step is to provide a standardization of parameters to be recorded.

The standardized robot-supported spasticity assessment described in this article represents a proposal of a set of objective parameters to be recorded in order to evaluate the different clinical signs of spasticity and to recognize how they change when a rehabilitative treatment or other therapeutic procedures (i.e. botulin toxin injection) are delivered and the device described represents the first example of an exoskeleton robot that could be able to record the above mentioned parameters.

In conclusion the standardized evaluation parameters recorded using robotic devices may provide several advantages: the measures for spasticity assessment can be monitored during every rehabilitation session (even during each movement) and the parameters are able to highlight even small changes the recovery plateau can be detected earlier thus avoiding further usefulness rehabilitation sessions and the objective evaluation of parameters can reduce the assessment bias in multicenter studies.

Declaration

Competing interests

The authors declare that they have no competing interests.

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References

- [1] K. H. Kong, J. Lee, K. S. Chua, Occurrence and temporal evolution of upper limb spasticity in stroke patients admitted to a rehabilitation unit. *Arch. Phys. Med. Rehabil.* **93**, 143-148 (2012).
- [2] A. Opheim, A. Danielsson, M. Alt Murphy, H. C. Persson, K. S. Sunnerhagen, Upper-limb spasticity during the first year after stroke: stroke arm longitudinal study at the University of Gothenburg. *Am. J. Phys. Med. Rehabil.* **93**, 884-896 (2014).
- [3] Rizzo MA, Hadjimichael OC, Preiningerova J, Vollmer TL. Prevalence and treatment of spasticity reported by multiple sclerosis patients. *MultScler* 2004;10:589–595
- [4] Andresen SR, Biering-Sørensen F, Hagen EM, Nielsen JF, Bach FW, Finnerup NB. Pain, spasticity and quality of life in individuals with traumatic spinal cord injury in Denmark. *Spinal Cord.* 2016 Apr 12 doi: 10.1038/sc.2016.46
- [5] F. Biering-Sorensen, J. B. Nielsen, K. Klinge, Spasticity-assessment: a review. *Spinal Cord.* **44**, 708-722 (2006).
- [6] D. Burke, J. Wissel, G. A. Donnan, Pathophysiology of spasticity in stroke. *Neurology.* **80**, S20-6 (2013).
- [7] R. H. Bhimani, L. C. Anderson, S. J. Henly, S. A. Stoddard, Clinical measurement of limb spasticity in adults: state of the science. *J. Neurosci. Nurs.* **43**. 104-115 (2011).

- [8] R. H. Bhimani, C. P. McAlpine, S. J. Henly, Understanding spasticity from patients' perspectives over time. *J. Adv. Nurs.* **68**, 2504-2514 (2012).
- [9] S. Malhotra, A. D. Pandyan, C. R. Day, P. W. Jones, H. Hermens, Spasticity, an impairment that is poorly defined and poorly measured. *Clin. Rehabil.* **23**, 651-658 (2009).
- [10] J. H. Burridge, D. E. Wood, H. J. Hermens, G. E. Voerman, G. R. Johnson, F. van Wijck, T. Platz, M. Gregoric, R. Hitchcock, A. D. Pandyan, Theoretical and methodological considerations in the measurement of spasticity. *Disabil. Rehabil.* **27**, 69-80 (2005).
- [11] A. D. Pandyan, M. Gregoric, M. P. Barnes, D. Wood, F. V. Wijck, J. Burridge, H. Hermens, G. R. Johnson, Spasticity: Clinical perceptions, neurological realities and meaningful measurement. *Disabil. Rehabil.* **27**, 2-6 (2005).
- [12] T. D. Sanger, M. R. Delgado, D. Gaebler-Spira, M. Hallett, J. W. Mink, Task Force on Childhood Motor Disorders, Classification and definition of disorders causing hypertonia in childhood. *Pediatrics.* **111**, e89-97 (2003).
- [13] N. K. Musampa, P. A. Mathieu, M. F. Levin, Relationship between stretch reflex thresholds and voluntary arm muscle activation in patients with spasticity. *Exp. Brain Res.* **181**, 579-593 (2007).
- [14] J. F. Fleuren, G. J. Snoek, G. E. Voerman, H. J. Hermens, Muscle activation patterns of knee flexors and extensors during passive and active movement of the spastic lower limb in chronic stroke patients. *J. Electromyogr. Kinesiol.* **19**, e301-10 (2009).
- [15] J. F. Nielsen, T. Sinkjaer, A comparison of clinical and laboratory measures of spasticity. *Mult. Scler.* **1**, 296-301 (1996).
- [16] D. E. Wood, J. H. Burridge, F. M. van Wijck, C. McFadden, R. A. Hitchcock, A. D. Pandyan, A. Haugh, J. J. Salazar-Torres, I. D. Swain, Biomechanical approaches applied to the lower and upper limb for the measurement of spasticity: a systematic review of the literature. *Disabil. Rehabil.* **27**, 19-32 (2005).
- [17] M. Cempini, F. Giovacchini, N. Vitiello, M. Cortese, M. Moise, F. Posteraro, M. C. Carrozza, NEUROExos: A powered elbow orthosis for post-stroke early neurorehabilitation. *Conf. Proc. IEEE Eng. Med. Biol. Soc.* **2013**, 342-345 (2013).
- [18] N. Vitiello, M. Cempini, S. Crea, F. Giovacchini, M. Cortese, M. Moise, F. Posteraro, M. C. Carrozza, Functional Design of a Powered Elbow Orthosis Toward its Clinical Employment. *IEEE/ASME Transactions on Mechatronics*, **2016**, 21(4), 1880-1891.

- [19] S. Crea, M. Cempini, S. Mazzoleni, M. C. Carrozza, F. Posteraro, N. Vitiello. Phase-II clinical validation of a powered exoskeleton for the treatment of elbow spasticity. *Frontiers in Neuroscience*, **2017**, 11, 261.
- [20] G. L. Gottlieb, G. C. Agarwal, R. Penn, Sinusoidal oscillation of the ankle as a means of evaluating the spastic patient. *J. Neurol. Neurosurg. Psychiatry*. **41**, 32-39 (1978).
- [21] T. Sinkjaer, Muscle, reflex and central components in the control of the ankle joint in healthy and spastic man. *Acta Neurol. Scand. Suppl.* **170**, 1-28 (1997).
- [22] T. Sinkjaer, E. Toft, K. Larsen, S. Andreassen, H. J. Hansen, Non-reflex and reflex mediated ankle joint stiffness in multiple sclerosis patients with spasticity. *Muscle Nerve*. **16**, 69-76 (1993).
- [23] V. Dietz, T. Sinkjaer, Spastic movement disorder: impaired reflex function and altered muscle mechanics. *The Lancet Neurology*. **6**, 725-733 (2007).
- [24] M. Willerslev-Olsen, J. B. Andersen, T. Sinkjaer, J. B. Nielsen, Sensory feedback to ankle plantar flexors is not exaggerated during gait in spastic hemiplegic children with cerebral palsy. *J. Neurophysiol.* **111**, 746-754 (2014).
- [25] C. Patten, E. G. Condliffe, C. A. Dairaghi, P. S. Lum, Concurrent neuromechanical and functional gains following upper-extremity power training post-stroke. *J. NeuroengRehabil.* **10**, 1-0003-10-1 (2013).
- [26] A. A. Mullick, N. K. Musampa, A. G. Feldman, M. F. Levin, Stretch reflex spatial threshold measure discriminates between spasticity and rigidity. *Clin. Neurophysiol.* **124**, 740-751 (2013).
- [27] J. Lorentzen, M. J. Grey, C. Crone, D. Mazevet, F. Biering-Sørensen, J. B. Nielsen, Distinguishing active from passive components of ankle plantar flexor stiffness in stroke, spinal cord injury and multiple sclerosis. *Clinical Neurophysiology*. **121**, 1939-1951 (2010).
- [28] Hogan N. An organizing principle for a class of voluntary movements. *J Neurosci*. 1984 Nov;4(11):2745-54
- [29] J. H. Seo, S. W. Yook, C. G. Song, M. H. Ko, S. H. Park, Evaluation of Elbow Stretch Reflex Using a Portable Hand-driven Isokinetic System in Normal Adults. *Ann. Rehabil. Med.* **35**, 529-534 (2011)
- [30] Pennati GV, Plantin J, Borg J, Lindberg PG. Normative NeuroFlexor data for detection of spasticity after stroke: a cross-sectional study. *J NeuroengRehabil*. 2016 Mar 18;13(1):30

- [31] Maciejasz P, Eschweiler J1, Gerlach-Hahn K, Jansen-Troy A, Leonhardt S. A survey on robotic devices for upper limb rehabilitation. *J NeuroengRehabil.* 2014 Jan 9;11:3
- [32] Gäverth J, Sandgren M, Lindberg PG, Forssberg H, Eliasson AC. Test-retest and inter-rater reliability of a method to measure wrist and finger spasticity. *J Rehabil Med.* 2013 Jul;45(7):630-6
- [33] Gäverth J, Eliasson AC, Kullander K, Borg J, Lindberg PG, Forssberg H. Sensitivity of the NeuroFlexor method to measure change in spasticity after treatment with botulinum toxin A in wrist and finger muscles. *J Rehabil Med.* 2014 Jul;46(7):629-34
- [34] Seth N1, Johnson D2, Taylor GW3, Allen OB4, Abdullah HA5. Robotic pilot study for analysing spasticity: clinical data versus healthy controls. *J NeuroengRehabil.* 2015 Dec 2;12:109
- [35] Prochazka A, Kowalczewski J. A fully automated, quantitative test of upper limb function. *J Mot Behav.* 2015;47(1):19-28

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Table 1 Results of literature review

Table 2 Characteristics of the participants

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Figure 1. Left: example of the NEEM worn by a post-stroke subject. Right: torque and position profile of the paretic elbow joint of a post-stroke subject, from repeated exercise cycles. Extracted parameters (i.e. MET, ZTA) in the extension phase.

Figure 2. Overall effects of the treatment. Spasticity-related parameters (ZTA and MET) are reported for all the rehabilitation sessions separately for each subject. The regression line (red) indicates the trend of the parameters over the multi-session rehabilitation.

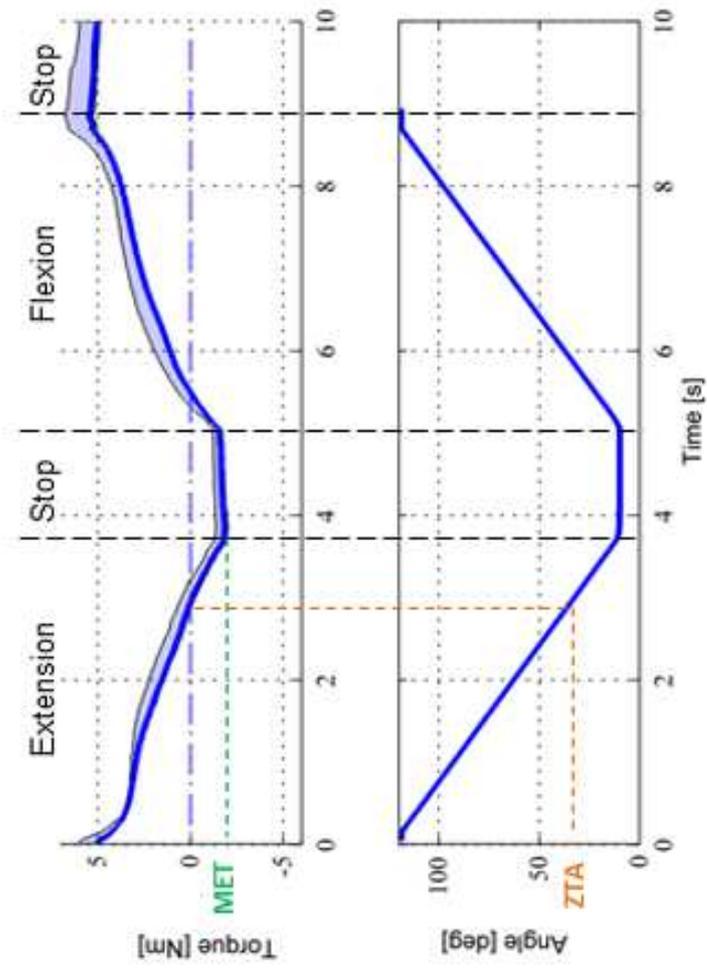
Figure 3. Intra-session effect of the treatment. Spasticity-related parameters (ZTA and MET) are reported for the first (blue) and last (green) cycles of each session and separately for each subject. The corresponding regression lines indicate the trend of the parameters over the multi-session rehabilitation.

Table 1 Results of literature review

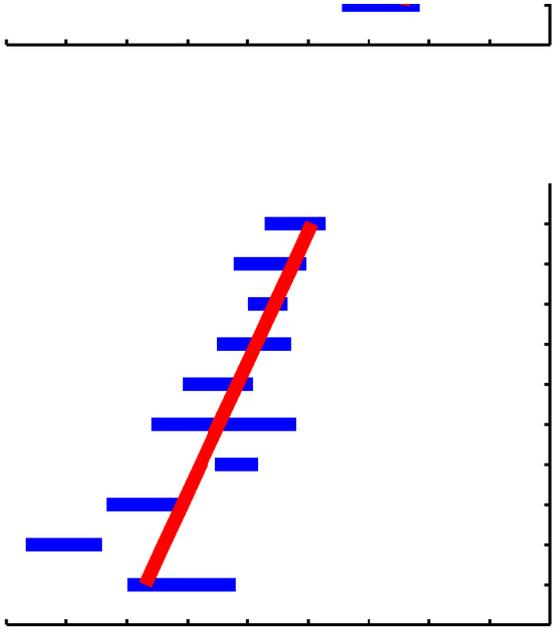
Measure	Number of records	% records	% paper
Ashworth Scale or Modified Ashworth Scale	137	37 %	54 %
Electromyography	50	13,5 %	20 %
Biomechanical parameters	35	9,5 %	14 %
Range of Motion	25	6,5 %	10 %
Tardieu Scale or Modified Tardieu Scale	21	5,5 %	8 %
Clinicalevaluation	20	5,5 %	8 %
Others	13	3,5 %	5 %
No measure	68	18,5 %	27 %

Table 1 Characteristics of the participants

Subject [#]	Age [years]	Gender	Years since acute event	Chedoke	Initial MAS	Final MAS
1	74	M	2 years and 5 months	4	3	2
2	56	F	3 years	5	1	1
3	19	M	1 year and 5 months	4	2	1
4	79	M	5 months	3	4	3
5	78	F	3 years and 10 months	2	2	1

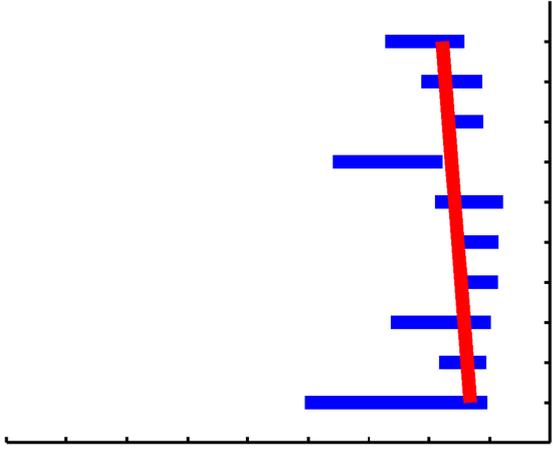


subject 4



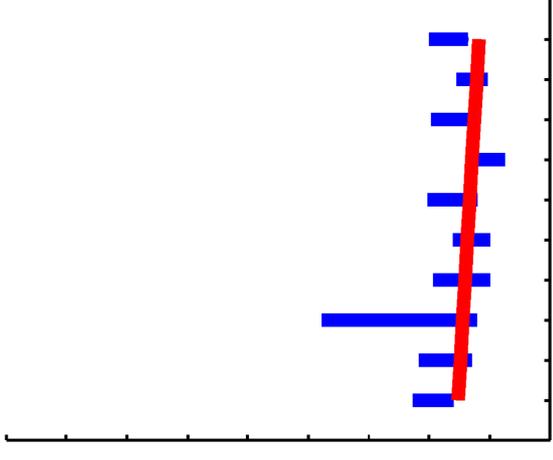
1 2 3 4 5 6 7 8 9 10

subject 3



1 2 3 4 5 6 7 8 9 10

subject 2



1 2 3 4 5 6 7 8 9 10

subject 1



1 2 3 4 5 6 7 8 9 10

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1 2 3 4 5 6 7 8 9 10

1 2 3 4 5 6 7 8 9 10

1 2 3 4 5 6 7 8 9 10

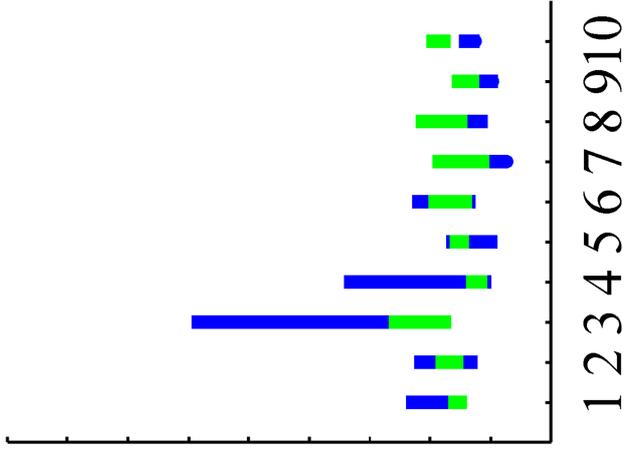
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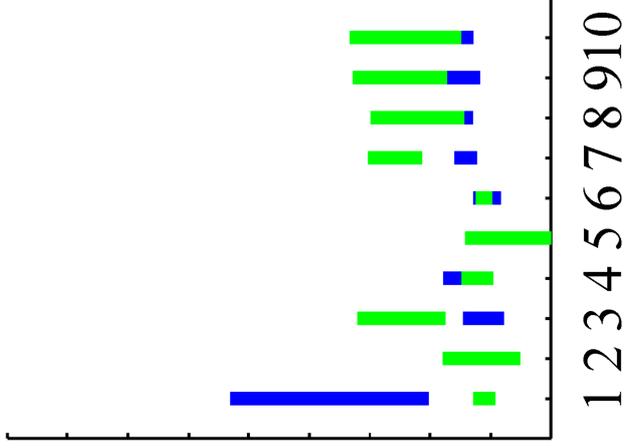
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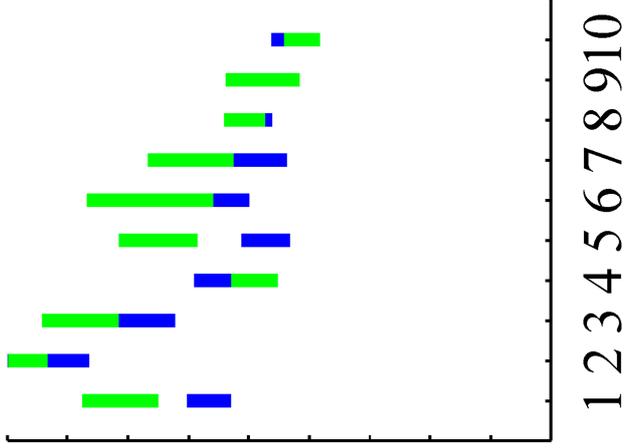
Subject 2



Subject 3



Subject 4



Session 1-10

Session 1-10

Session 1-10

Session 1-10

Session 1-10

Session 1-10

Session 1-10