QUANTIFICATION OF SPASTICITY AND RIGIDITY FOR BICEPS AND TRICEPS USING THE PVRM (POSITION, VELOCITY, AND RESISTANCE METER)

BY

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THESIS

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ABSTRACT

Spasticity and rigidity are two common types of abnormal muscle behavior seen among patients with neurological disorders (e.g., stroke, Parkinson's Disease). Clinical assessment of increased muscle resistance during passive movement, or hypertonicity, involves qualitative and subjective scales such as the Modified Ashworth Scale (MAS) for spasticity or the Unified Parkinson's Disease Rating Scale (UPDRS) for rigidity. Inaccurate and inconsistent assessments may occur depending on the rater's level of experience and scale interpretation. Recently, researchers have been developing medical training simulators that mimic hypertonicity to aid the training of these clinician learners. However, there is a lack of quantitative data representing the kinetic and kinematic characteristics of these abnormal muscle behaviors. Thus, we developed a portable measurement device (the PVRM – Position, Velocity, and Resistance Meter) that measures the joint angle, velocity, and muscle resistance of the upper-arm extensor and flexor muscles. In Study 1, the accuracy and reliability of the PVRM was validated by comparing its measurements to a commercial dynamometer (Biodex), a gold standard for measuring biomechanical data. The PVRM measurements were similar to the gold standard Biodex measurements during the passive flexion movement, since the residuals for all measurements were between 1-13%. Therefore, the PVRM was able to quantify behavioral features of spasticity (e.g., catch-release behavior), rigidity (e.g., uniformly elevated muscle tone), and healthy (e.g., no muscle resistance) subjects. In Study 2, we conducted a clinical study of 38 participants using the validated PVRM to establish a database quantifying different levels of spasticity (n=15, MAS 1-4); rigidity (n=11, UPDRS 1-3), and normal healthy (n=12) behavior of the biceps and triceps during passive flexion and extension of the elbow. Spasticity subjects demonstrated stretch speed and MAS score dependent hypertonia marked by a catch-release behavior, resulting in a convex

parabolic stretch speed profile. Rigidity subjects exhibited uniformly increased muscle tone that was dependent on UPDRS score but independent of stretch speed. The PVRM can provide a database for development of physical training simulators to realistically mimic hypertonicity and serve as a clinical measurement tool to reliably quantify the type and degree of hypertonicity.

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CHAPTER 1: INTRODUCTION

1.1 OVERVIEW OF SPASTICITY AND RIGIDITY

1.1.1 SPASTICITY

The physiological definition of spasticity was introduced by Lance et al., who described spasticity as "a motor disorder characterized by a velocity dependent increase in tonic muscle reflexes (TSR) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex" [1]. A spastic muscle exhibits three main behavioral features during passive movement of the associated joint: 1) increased muscle resistance (i.e. hypertonia) due to a decreased threshold of tonic and phasic stretch reflexes [2], 2) catch-release behavior (or clasp-knife phenomenon), manifested by a velocity dependent increase in muscle resistance [3–5], and 3) limited range of motion, a byproduct of prolonged immobilization due to severe spasticity [1]. Therefore, these behavioral features are important signs for distinguishing spasticity from other abnormal muscle behaviors, namely rigidity.

Hypertonia (i.e., abnormally high level of muscle tone or resistance due to spasticity or rigidity) is related to hyper-excitable reflex contractions that resist the passive stretch of the affected muscle [1,6,7]. For healthy individuals, the passive movements of the limbs do not activate TSR or cause reflex muscle contraction below a certain stretch speed threshold (e.g., 200˚/s) [8,9]. However, a spastic muscle's TSR is altered, causing reflex muscle contraction at low stretch speeds (35˚/s) [1,9]. As the stretch speed is increased, the muscle contraction is intensified [10,11]. In addition, these muscle contractions became less sensitive when muscle length is increased [10,12,13]. The degree of muscle tone may vary depending on the severity of spasticity, so understanding the relationship between the magnitude of hypertonia and the

severity of spasticity may be valuable for monitoring changes in spasticity. However, quantification of hypertonia is not well documented. Thus, investigation of hypertonia from different levels of spasticity is needed.

The presence of catch-release behavior is another pathophysiological result of the overactive TSR initiated at fast stretch speed [1]. After the onset of muscle tone due to stretch reflex contractions, the stretch speed decreases below the reflex threshold, reducing the reflex contraction and hypertonia [1]. In clinical practice, catch-release behavior refers to an abrupt increase in muscle tone (i.e. catch) at a certain joint position (i.e., catch angle) followed by a sudden drop of muscle resistance (i.e. release) [1]. For the majority of severe spasticity patients, the catch angle was reported to happen earlier in the range of motion [14–19]. Therefore, catch-release behavior can be a useful feature to not only distinguish spasticity from other types of muscle conditions but also classify different levels of spasticity.

Limited range of motion is another behavioral feature of spasticity. While muscle tone may arise due to a neural component such as the hyperexcitability of the TSR, non-neural components may cause hypertonia due to the loss of compliance of soft tissues (i.e. tendons, ligaments, joints) [1]. Thus, the presence of neural and non-neural components of resistance interfere with a patient's daily movements and activities, causing reduced range of motion and continuous flexion of the affected muscle group for a long time [1]. In addition, certain muscles (e.g., the lower and upper limb flexors) become immobilized in a shortened length due to paresis [25]. This immobilization in a shortened position, seen mainly for severe spasticity patients, is the main reason for developing soft tissue contracture and limited ROM [20–22]. Hence, looking for reduced range of motion can be important to classify severe from mild spasticity patients.

1.1.2 RIGIDITY

Rigidity, characterized by increased stiffness of muscles, is one of the cardinal motor symptoms of Parkinson's disease (PD) along with resting tremor and bradykinesia [23], [24]. Although rigidity may appear in different forms such as cogwheel rigidity (rigidity superimposed by tremor) or lead pipe rigidity (uniform throughout the whole range of motion) stemming from various neurological disorders, we focused on investigating lead pipe rigidity originating from PD (parkinsonian rigidity) in our study due to subject availability. While rigidity may occur during a voluntary movement (i.e. active rigidity), lead pipe rigidity shows symptoms of increased muscle resistance during rest (static component of TSR) and passive stretch (dynamic component of TSR) [24–26]. The degree of muscle resistance in one limb may be further increased through activation, a clinically well-known phenomenon of reinforcing rigidity in one limb by requesting voluntary movements of the contralateral limb [27]. Thus, the main behavioral feature of lead pipe rigidity is uniformly increased resistance that can be enhanced through activation during passive movement.

The underlying pathophysiological mechanism behind rigidity is still unclear [28–31]. Some researchers reported that rigidity, unlike spasticity, does not originate from hyperexcitability of stretch reflexes [30], [34]. The tendon jerks and H-reflexes are almost normal in patients with parkinsonian rigidity [28,30,32–34]. Instead, these researchers found intrinsic changes in muscle properties that caused abnormally high elasticity (stiffness), contributing to hypertonia regardless of stretch speed [35]. However, others claimed that rigidity was affected by velocity-dependent stretch reflexes, causing difficulty in discriminating the physiological mechanisms underlying spasticity and rigidity [28,30,36]. Yet, one common

finding of rigidity is the biomechanical measurement of increased muscle tone across the range of motion [29–31,37,38].

It is still unclear if the increased resistance of rigidity is proportional or even related to stretch speed. Some studies report rigidity is independent of stretch velocity [31,39], while other studies reported there is a dependence in stretch velocity [30,40,41]. Justifying the existence of stretch speed dependency was difficult, since some studies relied purely on subjective clinical evaluation of rigidity while other studies had only a limited number of test subjects [30,31,39–41]. Colin et al. claimed that the stretch speed dependency of stretch reflex and the minimum stretch speed to produce stretch reflex of rigidity change with respect to the progression of PD [26]. For example, the stretch reflex is related to the stretch velocity in the early stages of PD but becomes less so as the disorder progresses [26]. Also, they reported that the velocity dependence of the stretch reflex is more apparent in extensors than flexor muscle groups [26]. With more progression of PD and severe rigidity, the stretch reflex becomes more evident beginning in flexors and later in extensors, most commonly in the most stretched position of biceps, triceps, and quadriceps [26]. Also, patients with more severe rigidity showed a production of stretch reflex electromyographic (EMG) response at low stretch speeds, while patients with mild rigidity were characterized by a high stretch speed for production of stretch reflex EMG response [26]. However, these claims were based on descriptive statistics on limited parameters such as elbow angle and EMG data of rigid muscles. Thus, more in-depth studies involving computation of parameters related to kinetic and kinematic data need to be conducted to verify the stretch speed dependency of muscle resistance for rigid arms.

1.2 CLINICAL ASSESSMENT OF SPASTICITY AND RIGIDITY

1.2.1 MODIFIED ASHWORTH SCALE (MAS), MODIFIED TARDIEU SCALE (MTS), AND UNIFIED PARKINSON'S DISEASE RATING SCALE (UPDRS)

Hypertonicity is clinically assessed using qualitative scales (e.g., the Modified Ashworth Scale (MAS) and Modified Tardieu Scale (MTS) for spasticity and motor section 3 (rigidity) of the Unified Parkinson's Disease Rating Scale (UPDRS)) (Tables 1.1-1.3) [42–44]. During the muscle tone assessment, the clinician examines for the presence of spasticity, rigidity or other abnormalities of tone. To assess for spasticity, the patient is instructed to relax the affected muscle and let the clinician passively stretch (i.e., manually lengthen the muscle when it is not activated) the muscle at multiple speeds. Like the spasticity examination, rigidity is judged on slow passive movement of major joints with the patients in a relaxed position while the examiner manipulates the limbs. However, unlike spasticity, rigidity examination involves two passive stretch tests: a first test without an activation maneuver and, if no rigidity is detected, a second test with activation maneuver (i.e. tapping fingers, fist opening/closing, or foot tapping in the contralateral limb not being tested) [44]. Depending on the level of resistance, the clinician assigns a score that is proportional to the severity of spasticity or rigidity. MAS and MTS are six-point scales starting with a score of 0 (no spasticity) to a score of 5 (severe spasticity), while UPDRS is a five-point scale starting with a score of 0 (no rigidity) to a score of 4 (severe rigidity). Although the MTS is regarded as a more appropriate assessment by some researchers since it considers the stretch speed dependence of muscle tone at various speeds, the MAS is more commonly used due to its simple and straightforward protocol [45–50]. Thus, the remaining thesis will discuss using the MAS for spasticity and UPDRS for rigidity.

Table 1.1. Modified Ashworth Scale (MAS) for assessing spasticity [42]

Score	Description
0 (0)[a]	No increase in muscle tone
1 (1)	Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension
1+ (2)	Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the reminder (less than half) of the range of motion
2 (3)	More marked increase in muscle tone through most of the range of motion, but affected part is easily moved
3 (4)	Considerable increase in muscle tone, passive movement difficult
4 (5)	Affected part is rigid in flexion or extension

[a] Numbers in parenthesis are variants of the Modified Ashworth Scale [51]. This scoring convention is used in this thesis.

Table 1.2. Modified Tardieu Scale (MTS) for assessing spasticity [43].

Score	Description
0	No resistance throughout passive movement
1	Slight resistance throughout, with no clear catch at a precise angle
2	Clear catch at a precise angle followed by release
3	Fatigable clonus (<10 secs) occurring at a precise angle
4	Un-fatigable clonus (>10 secs) occurring at a precise angle
5	Joint immobile

Table 1.3. Section 3 (Rigidity) of the Unified Parkinson's Disease Rating Scale (UPDRS) [44].

Score	Description
0	No rigidity
1	Slight or detectable rigidity only detected with activation maneuver
2	Mild to moderate rigidity detected without the activation maneuver, but full range of motion is easily achieved.
3	Marked rigidity detected without the activation maneuver; full range of motion is achieved with effort.
4	Severe rigidity detected without the activation maneuver and full range of motion not achieved.

1.2.2 PROBLEMS OF CURRENT CLINICAL ASSESSMENT METHODS

The main problem of current clinical examination methods of spasticity and rigidity is the heavy dependence of the assessor's previous training and clinical experience due to the qualitative descriptions of the scales that are open to interpretation (Tables 1.1-1.3) [52–55]. Thus, it is difficult for clinician learners to acquire the skill for reliable and accurate assessment of spasticity or rigidity. Hands-on evaluation experience is required before being able to clinically assess spasticity and rigidity, so current training methods depend on inviting practice patients or asking other students to mimic hypertonicity for each other. This results in inconsistent and inefficient training due to limited availability of practice patients [55]. Therefore, the development of training simulators that can consistently mimic realistic hypertonicity at different levels has recently been explored to aid the current training practices [56–61].

1.3 TRAINING SIMULATORS AND MEASUREMENT DEVICES

1.3.1 TRAINING SIMULATORS

There have been primarily two types of training simulators for replicating hypertonicity: electromechanical training simulators [56–58] and mechanical training simulators [59–61] (Figure 1.1) For the electromechanical designs, brushed or brushless DC motors simulated muscle resistance, and a braking system (e.g., a servo disc brake or magneto-rheological fluid viscous brake) replicated the stretch speed dependency and catch-release phenomenon for spasticity simulation. The advantage of the electromechanical designs was the flexibility of

programming various torque profiles to realistically generate different levels and types of hypertonicity. Various behavioral features (e.g., catch-release behavior, increased muscle tone, and reduced ROM) were easily implemented following a mathematical model built from quantitative data collected from real spasticity/rigidity patients. However, disadvantages of such designs were the use of potentially expensive electrical components and requirement of a power supply, limiting cost efficiency and portability [59]. So, a fully mechanical passive training simulator that utilized viscous hydraulic damper and a mechanical linkage system was developed to provide a stretch speed and position dependent haptic feedback [59–61]. Muscle resistance was created by forcing a viscous fluid to flow through size-adjustable orifices on the damper's piston head, allowing replication of different levels of spasticity and stretch speed dependent tone behavior. Regardless of the type of simulators, there is a definitive need in the research community for a comprehensive database that quantifies the behavioral features of abnormal muscle conditions in order to fine tune the simulators to realistically mimic all levels of hypertonicity [17,19,55–62]. Thus, measurement devices were developed to establish a database quantifying the passive stretch responses of spasticity and rigidity. Research related to developments of exoskeleton, orthosis, and other assistive/rehabilitation devices could also benefit from this database for proper component selection [63–67]. For example, when developing a soft exo-glove, knowing the magnitude of muscle resistance of spastic fingers can be useful for selecting a properly sized motor that is powerful enough to maneuver the spastic fingers for grabbing differently shaped objects while preventing excessive torque applied on the joints [63,66].

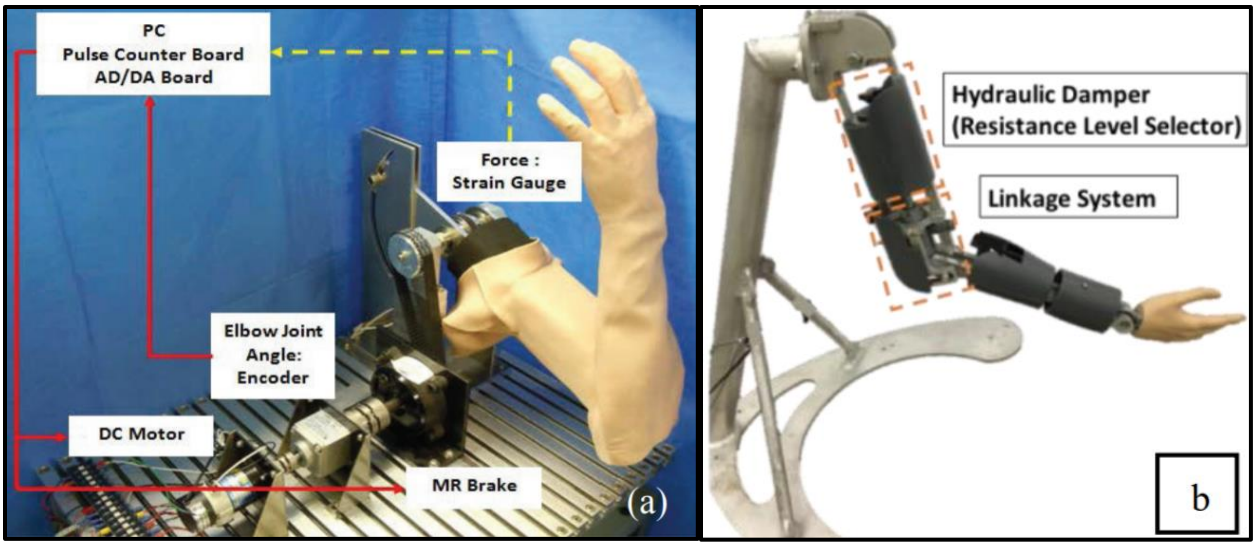

Figure 1.1. (a) Electromechanical training simulator using DC motor and MR fluid system [56] and (b) mechanical training simulators using hydraulic damper and linkage system [59].

1.3.2 MEASUREMENT DEVICES

Different types of measurement devices were developed by researchers to quantify the upper-arm muscle behavior of spasticity and/or rigidity (Figure 1.2) [14,28–30,47]. These devices collected data on one or more of the following measurements: kinetic data relating to increased muscle tone (applied torque, stiffness, and/or energy), kinematic data (angular position and/or angular speed), and electromyographic (EMG) signal data [14,28–30,47]. To collect kinetic data, sensors (e.g., rotational torque sensor, force transducers connected to air pads, or load cells) were used [14,29,30,68]. To collect kinematic data, sensors, namely gyroscopes, potentiometers, and flexible electro-goniometers, were utilized [14,29,30,68]. Finally, non-invasive surface EMG (sEMG) electrodes were used for measuring EMG activity [28]. To manipulate the subject's arm, either an electromechanical actuator (e.g., DC motor) or a clinician stretched the arm. In terms of study design, some studies investigated both spasticity and rigidity population [28,30], while other studies only performed tests on spasticity or rigidity exclusively

[14,29]. The specific hardware design, study design, post processing of data, and limitations of these studies are explained in the next few paragraphs.

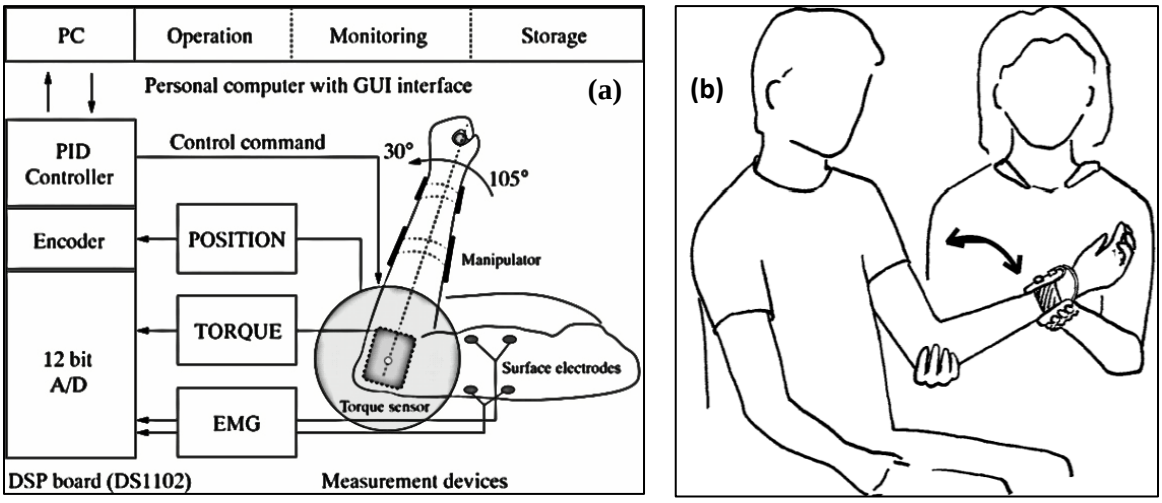

Figure 1.2. (a) Measurement device developed by Lee et al. [30] (b) measurement device developed by Prochazka et al. [29]

Lee et al. developed a motor driven muscle tone measurement system in order to characterize the velocity related properties of hemiparetic spasticity (n=12), parkinsonian rigidity (n=16), and normal (n=12) muscle tone of upper-arm flexor muscle groups [30]. The system included a motor with angular position sensor, torque sensor, and surface EMG electrodes for monitoring muscle activity of biceps. The forearm of the test subject was strapped to the apparatus and stretched at four different speeds (40, 80, 120, and 160 ˚/s). For spasticity and rigidity subjects, the more affected forearm was tested. For controls, the dominant arm side was tested. Three reactive torque parameters (average speed dependent reflex torque (ASRT), velocity sensitivity of ASRT (VASRT), and segmented ASRT (SART)) were proposed by the authors and used to describe the velocity-dependent muscle tone behavior (Figure 1.3). To model the measured torque (T), a linear model that consisted of inertial (I), viscous (B), elastic stiffness (K) components, and constant offset (C) was proposed described in Equation 1 [69].

$$T = I\ddot{\theta} + B\dot{\theta} + K\theta + C \quad (1)$$

To observe only the components relevant to muscle resistance (B – velocity dependent viscous component, K – elastic component in Equation 1), the inertial ($I\ddot{\theta}$) and gravitational effects from the stretched limb and the manipulator (C) were removed. At very slow velocity, the muscle resistance induced by the velocity factor is trivial, but the gravitational effect remained the same as for higher stretch velocities. Essentially, the baseline torque (torque measured at a very slow stretch speed of 5°/s, dashed line in Figure 1.3 (a)) represents the elastic and gravitational parts of the measured torque during stretch. Hence, after subtracting the baseline torque from the high velocity torque, the shaded area during the constant phase can be extracted as the velocity dependent component of reactive torque (Figure 1.3(a)). The normalized area (that is, the averaged amplitude of the shaded area)—defined as averaged speed dependent reflex torque (ASRT)—was used for quantifying the velocity dependent component of increased muscle tone. To analyze the velocity dependent properties of ASRT, the VASRT was compared among the three groups (Figure 1.3(b)). The slope of the regression line represents the averaged VASRT for each group (Figure 1.3(b)). To represent the position related patterns of increased muscle tone, SASRT was derived from the reactive torque as shown in Figure 1.3(c).

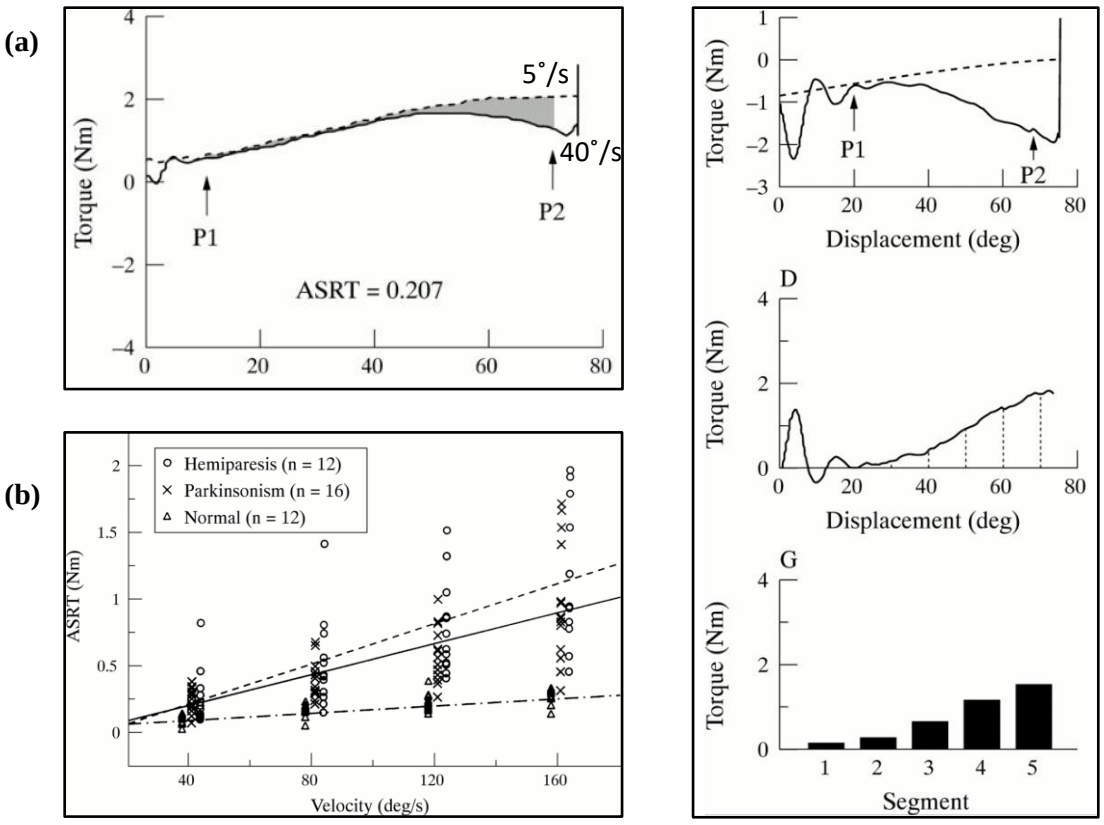

Figure 1.3. Examples of ASRT (a), VASRT (b), and SASRT (c). ASRT is the normalized area of the shaded region. VASRT is the slope of the ASRT at different stretch speeds. SASRT is the segmented torque data between P1 (start of constant stretch speed region and acceleration near zero) and P2 (end of constant stretch speed region). [30]

The results suggested that the apparatus and these metrics were able to differentiate the three subject groups at different stretch speeds. However, there were several limitations to this study. First, the measurement apparatus was bulky and may have involved long setup time due to its large mechanical structure, limiting its usability and practical use in a clinical setting. The test setup required the subject to be supine, which may impose difficulty for severe spasticity and rigidity patients with limited mobility and contractures [22,70–73]. Second, the study only investigated inter-group differences, but no investigation was made on intra-group differences (i.e., severity of hypertonicity within each group). Ambiguities between different MAS levels

were discovered due to unclear description of these scales [17,19,74,75]. Thus, quantifying the differences between various levels of severity of hypertonicity is needed to overcome the limitations of these qualitative scales. Third, the relatively complex definitions of ASRT, VASRT, and SASRT may be difficult for clinicians to understand. In clinical evaluation of spasticity, simple metrics such as range of motion, presence of catch, catch angle, are usually documented. This measurement device and its protocol do not provide the clinician with the metrics that they use commonly during evaluation. Fourth, the study scope was limited since it only focused on upper-arm flexor muscles; spasticity and rigidity are also found in extensor muscles as well.

Pandyan et al. developed a non-invasive biomechanical measuring device, which could be used in clinical practice, to quantify spasticity at the elbow joint [14]. The device utilized a force transducer and an electro-goniometer to measure applied force and passive range of movement, respectively. The resistance to passive movement (defined by them as RPTM), presence of catch, and average stretch speed were computed for 16 subjects with various levels of spasticity. While the device was made to be clinician-friendly and portable, limitations were found in terms of the hardware, testing protocol, test subjects, and data processing. First, there were no surface EMG sensors used to monitor the status of muscle activity. Thus, it was difficult to assess the subject's compliance associated with the inability to relax their muscles. Second, the point of application of force was not standardized, allowing inaccurate readings of muscle resistance. It is critical to standardize the testing protocol and assessment techniques, especially make the direction, magnitude, and location of the applied force consistent [29,75,76]. A simple free body diagram of a passively moving limb with hypertonia reveals that the measured torque is linearly proportional to the distance from the applied force location and rotating axis (i.e.,

elbow joint). An example of a possible scenario is the ambiguity arising from the similar torque measurements between a mildly spastic arm with the force applied close to the elbow joint and a severely spastic arm with the force applied away from the elbow joint. Third, only spasticity subjects from MAS 0 to 2 were recruited in this study, excluding more severe spasticity subjects (MAS 3-4) and rigidity subjects. Thus, comparison between different muscle conditions was not possible. Finally, their definition of the RTPM was inaccurate. Their computation of the muscle resistance did represent spasticity accurately due to the inclusion of inertial effect that varied depending on the subject's arm weight and geometry. Any experimental protocol that involves torque measurement of a moving body should remove the inertial effect when analyzing different components of torque (i.e. muscle resistance) since the product of inertia and acceleration inherently exists. Therefore, the combined torque of inertial effect and muscle resistance is measured by the torque sensor. For example, if one were to measure the muscle resistance of a human forearm during passive movement, any acceleration or deceleration about an axis will naturally induce an inertial term. This inertial term along with muscle resistance will always be coupled regardless of the rotational axis, so it is important to remove the inertial term to analyze the muscle resistance alone.

Prochazka et al. developed a quantification device, consisting of a gyroscope for monitoring stretch speed and a force transducer that read the applied force on the limb, to quantify parkinsonian rigidity at the elbow [29]. Four subjects with idiopathic Parkinson's disease and five normal controls were recruited. The examiner evaluated the UPDRS score of the wrist and elbow with and without activation maneuvers. Mechanical impedance, the vectorial sum of elastic stiffness and viscosity, were computed to quantify different levels of UPDRS scores. The study was able to correlate the UPDRS score to the computed mechanical

impedance, validating the UPDRS scale. However, one limitation was the restricted scope of study since spasticity subjects were excluded. While the calculation of mechanical impedance can distinguish different levels of rigidity, such quantification may not work for differentiating spasticity from rigidity, since spasticity also involves high degree of elastic stiffness and viscosity (i.e., high mechanical impedance) similar to rigidity. Another limitation was the lack of specification of stretch speed. The clinicians involved in the study were not given specific instructions on the stretch speed. It is important to specify and report the stretch speeds because, while rigidity muscle tone has been reported to be less speed dependent than spasticity, numerous reports indicated that rigidity showed observable stretch speed dependency, especially with extensor muscles [40], [41], [30].

Mullick et al. quantified spasticity and rigidity existent in upper-arm flexor and extensor muscle groups using a manipulandum. The study recorded joint angle and velocity and an electromyography (sEMG) signal for spasticity (n=10), rigidity (n=11), and control (n=6) subjects from slow (8˚/s) to fast stretch speeds (160˚/s) [28]. This study primarily focused on computation of three parameters related to tonic and dynamic stretch reflex thresholds (ST): 1) tonic ST, the angle when the muscles are activated during quasi-static stretching (low velocity close to zero); 2) dynamic ST, the angle when the muscles are activated during non-zero velocity of muscle stretching; and 3) sensitivity of dynamic ST, which represents the sensitivity of the stretch reflex activity to different stretch speeds. The study proposed that these metrics could discriminate spasticity from rigidity. However, the tedious setup of sEMG system (e.g., preparation of the skin, and the large size of the manipulandum due to the presence of a motor) can limit its practicality in a clinical environment where reliable evaluation needs to be done in

short time [14]. Also, the differentiating the severity of hypertonicity was not possible using this apparatus and metrics, as the author reported.

1.3.3 QUANTIFICATION OF CATCH-RELEASE BEHAVIOR

To investigate the catch-release behavior of spasticity, a quantitative definition of such behavior had to be defined among researchers [14,47,77]. Different definitions of catch have been introduced by other studies, but most definitions were not comprehensive or accurate enough due to limited number of sensors used in the studies. For example, one study defined catch as an instance during a passive movement when the clinician's stretch speed decreased below 50˚/s due to increased muscle tone [77]. Relying solely on stretch speed is not robust or accurate enough to detect a catch, since other factors can affect the stretch speed: the clinician's preference on stretch speeds or different arm weight. In addition, predefining the speed threshold as 50˚/s was arbitrary and hard to justify, since only four subjects with spasticity were tested. Another study's definition of catch was the instance when the changing rate of resistive torque (i.e., stiffness) was maximum [47]. This definition was too general to characterize catch behavior, since rapid increase in stiffness can be seen in both spasticity and rigidity subjects. Other studies detected catch behavior by relying on the clinician's subjective perception that corresponded to a transient increase of resistance [14]. Thus, a robust quantitative definition of a catch needs to be established that incorporates both kinetic and kinematic data.

1.4 PVRM – POSITION, VELOCITY, AND RESISTANCE METER

To overcome the limitations of the previously mentioned measurement devices, a portable measurement device (the PVRM - Position, Velocity, and Resistance Meter) was developed for objectively quantifying spasticity and rigidity. The PVRM consisted of two modules (moving and main) and three surface electromyographic (sEMG) electrodes (biceps, triceps, and reference). The moving module, containing an IMU and load cell, was placed on the moving body segment (i.e. lower arm), while the main module, which contained another IMU and processed, transmitted, and computed the sensor data, was attached on the adjacent stationary body segment (i.e. upper arm). The goal of the PVRM was to provide a compact and portable device that can accurately and reliably measure the kinetic and kinematic data of spasticity and rigidity in a clinical setting. One design feature of the PVRM was its small size and portability for practical clinical use. The use of small inertial measurement unit sensors and a miniature uniaxial load cell minimized the overall physical size of the PVRM. While motors were used in previously mentioned studies, the drawbacks of motors for stretching the patient's arm (e.g., bulky nature, cost, maintenance, and setup time) motivated the design of the PVRM to exclude these powertrain devices. Rather, we focused on developing a wearable device that allows a clinician to stretch the patient's limb via his or her hands. This reduced the risks of injury and made the patient feel comfortable during assessments by allowing a haptic feedback for the clinician. In addition, a Bluetooth module transmitted the PVRM data wirelessly in order to improve the user-experience and reduce the setup time. Another design feature of the PVRM was its universal application that can be used in not just for the upper-extremity but also for the lower-extremity in both flexion and extension. Spasticity and rigidity can occur in both the upper and lower-extremities, so it is important for the quantification device to be able to accommodate

various muscle geometry. Thus, Velcro straps with adjustable lengths increased the PVRM's adjustability. Also, sEMG electrodes monitored for the passivity of relevant muscles, since the clinical assessment of hypertonicity requires muscles to be fully relaxed. Hence, the PVRM development can be helpful for the researchers and neurologists in the field of spasticity and rigidity by providing useful data explaining spastic and rigid muscle behavior in different muscle groups.

The PVRM data processing involved key outcome parameters that can distinguish not only different types of muscle disorder but also the severity of muscle disorder. Some of these parameters (e.g., catch angle and range of motion) were relatable to clinicians. Other parameters (e.g. stretch speed dependency of hypertonia) were defined to differentiate spasticity from rigidity. Proper filtering of data and removal of gravitational and inertial effect were performed to analyze just the spasticity and rigidity relevant data. Finally, we provided a strict testing protocol for reliable comparison between subjects. The quantification of resistance was computed as applied torque instead of applied force for more accurate representation of resistance. The PVRM moving module was placed at a similar location for all subjects, and the distance between the applied force and the elbow joint was always recorded. Also, the average stretch speed of each assessment was computed to repeat the assessment if the stretch speed was too slow or too fast. In addition, we introduced a more robust quantitative definition of catch-release behavior that involved both kinetic and kinematic data. Therefore, the PVRM data processing aimed to provide accurate database of spasticity and rigidity patient population through rigorous control of testing procedure and computation of clinically relevant metrics.

1.5 THESIS ORGANIZATION

This thesis presents the design, validation, and clinical studies of a portable measurement device (the PVRM – Position, Velocity, and Resistance Meter) that can accurately and reliably quantify muscle behaviors of various levels of spasticity and rigidity during passive stretch about the elbow joint. A validation study was necessary to ensure accurate measurement of muscle behavior. Then, a preliminary clinical study was performed to provide a database for optimizing medical training simulators and quantitatively understanding spasticity and rigidity.

Chapter 1 gives a brief introduction of current understandings and behavioral features of spasticity and rigidity. Also, commonly used clinical scales for assessing hypertonicity and the limitations of these scales were reviewed. Previous developments of medical training simulators and measurement devices that address the drawbacks of the current clinical scales were discussed. To aid the optimization of simulators and understand hypertonicity, the need for a newly developed measurement device (PVRM) that overcomes the limitations of the previous measurement devices was established.

Chapter 2 presents the design and validation of the PVRM used for measuring elbow joint angle and stretch speed, and muscle resistance of the upper-arm extensor and flexor muscles. The PVRM accuracy was validated by comparing the measurements from the PVRM to a gold standard dynamometer (i.e. Biodex System 3). The PVRM data and Biodex data were collected as the Biodex performed a series of passive elbow flexion and extension cycles on test subjects wearing the PVRM. Results indicated that the PVRM can be used to accurately quantify behavioral features of spasticity and rigidity: the catch-release behavior and increased muscle tone during passive stretches.

Chapter 3 presents the results of a preliminary clinical study performed on various levels of spasticity and rigidity subjects using the validated the PVRM to provide a database quantifying hypertonicity. Key outcome parameters were defined and analyzed to quantify the behavioral features of spasticity and rigidity in association to the type and severity of the muscle disorder. A discussion relating the quantifications and the pathophysiology of spasticity and rigidity were made.

Chapter 4 discusses the necessary design improvements of the PVRM for clinical use and gives suggestions of future study designs.

CHAPTER 2: DESIGN AND VALIDATION STUDY OF THE PVRM (POSITION, VELOCITY, AND RESISTANCE METER)

2.1 ABSTRACT

The study goal was to design and validate a wearable and portable measurement device (the PVRM – Position, Velocity, and Resistance Meter) that quantifies unique kinetic and kinematic behavior of hypertonicity (i.e., spasticity and rigidity) during passive joint movement. In this study, the PVRM was used to measure joint angular position, velocity, and muscle resistance during passive flexion of the elbow. The PVRM accuracy was validated by comparing the measurements from the PVRM to a gold standard dynamometer (Biodex System 3). The data from the PVRM and Biodex were collected as the Biodex performed a series of passive elbow flexion cycles on test subjects wearing the PVRM. Five subjects with hypertonicity (n=3 for spasticity, n=2 for rigidity) and five healthy controls were tested. The absolute residual error between the PVRM and the Biodex for joint position, velocity, and resistance were less than 3˚, 5˚/s, and 0.2 Nm, respectively. The PVRM provides a compact, easy to use measurement device to quantify upper-arm hypertonicity. The PVRM can not only help researchers gain additional insight into the quantification of spasticity and rigidity, but also allows clinicians to make more reliable quantitative assessments of their patients.

2.2 INTRODUCTION

Spasticity and rigidity are two common categories of muscle hypertonicity. Spasticity involves a stretch velocity-*dependent* increase in tone, involuntary muscle spasms, and a catch-release behavior (a rapid increase and decrease in muscle tone) [1,78]. This behavior results from

an upper motor neuron lesion and is usually seen in neurological disorders such as stroke, spinal cord injuries, multiple sclerosis, and cerebral palsy [1]. Rigidity involves a stretch velocity-*independent* increase in tone throughout the entire range of motion and loss of motor control and is typically observed with Parkinson's disease [79].

Clinically, accurate assessment of spasticity or rigidity is necessary for effective management and treatment [80–83]. Current clinical assessment of spasticity and rigidity involves categorizing a patient's severity level based on a five- or six-point integer qualitative scale, such as the Modified Ashworth Scale (MAS) [42] or the Modified Tardieu Scale (MTS) [84] for spasticity, and the motor section of the Unified Parkinson's Disease Rating Scale (UPDRS) for rigidity [44]. The assessments involve a clinician performing passive stretches of the patient's affected muscles while the clinician observes and feels for the degree of increase in tone (ranging from "slight", "marked", and "considerable increase" in tone [42]) or presence of catch-release behavior [42,44,84]. For newly trained clinicians, consistent and reliable assessments of spasticity and rigidity may be difficult since these evaluation methods heavily rely on the rater's personal experience and interpretation of the scale. The use of these qualitative scales usually results in poor consistency and low reliability (some reporting as low as 56% [53]) [52,75,85–89]. In addition, training opportunities for new clinicians are limited due to lack of practice patients and practical tools to experience different levels of spasticity and rigidity [53].

A few research groups have developed devices to assess hypertonicity quantitatively [30,43,90–96]. However, there are limitations to these devices: difficulty of practical clinical use due to long setup time and bulky size [97], lack of standardized testing protocol which led to inaccurate measurement [14,29], limited study scope that investigated exclusively only spasticity or rigidity [14,29], or sole reliance on electromyographic (EMG) measures that have a long setup-

time and strict test protocols [28].

To address the limitations of these devices, we present the design and validation testing of a measurement device (the PVRM – Position, Velocity, and Resistance Meter) to quantify spasticity and rigidity. The PVRM consisted of small modules that can be attached to a patient's body segments to measure kinematic and kinetic data, such as angular position and velocity, and the force applied by the clinician to passively stretch the joint. This applied force is interpreted as muscle tone resistance felt by the clinician. The PVRM design goals were to make a compact, light-weight, and portable measurement device that can be attached quickly and with minimum setup requirements. A validation study was conducted to assess the accuracy of the PVRM. The measurements of PVRM accuracy were validated by comparing the values from the PVRM to a gold standard dynamometer (Biodex, System 3, Shirley, New York, USA). The data from the PVRM and Biodex were collected as the Biodex performed a series of passive elbow flexion cycles on a test subject wearing the PVRM modules.

2.3 METHOD

2.3.1 DESIGN

The PVRM was composed of two modules attached to the patient (main and moving), which were wired to a data processing module. To ensure that the muscles were passive during the stretch test, muscle activation status was checked using a commercially-available surface EMG measurement system (Bagnoli, Delsys, Natick, Massachusetts, USA). The data processing module and the Delsys EMG system were connected via USB cables to a computer, where the PVRM and EMG data were processed to calculate the angular position and velocity, and muscle resistance as well as muscle activity (Figure 2.1).

The device used two small commercial inertial measurement unit (IMU) sensors each containing a 3-axis accelerometer and a 3-axis gyroscope (MPU-6050, InvenSense, California, USA), a miniature uniaxial load cell (LCM 300; Futek, California, USA), and a micro controller (Uno; Arduino LLC; Italy). Each IMU measured acceleration and angular velocity about three orthogonal axes (x, y, z) of each module and output a 3D vector parallel to the x, y, z axes in a quaternion form by using an onboard Digital Motion Processing (DMP) algorithm [98].The moving module contained one IMU sensor and the load cell (Figure 2.2). The moving module was attached to the ulnar side of the wrist when assessing elbow flexion and radial side for extension. A load cell cover plate was used to connect the moving module to the Biodex lever arm so that the load was applied only on the cover plate. The main module contained the other IMU and was attached to the midpoint of the upper arm with the module facing laterally (Figure 2.1, 2.2). The positive z-axis of the main module pointed away and normal to the humerus. The data processing module contained the microcontroller, load cell amplifier shield (RB-Onl-38; RobotShop; Vermont, USA), and $I2C$ multiplexer (TCA9548A; Texas Instruments, Texas, USA). The enclosures for these three modules were packaged in polylactic acid 3D printed enclosures. The main and moving modules were designed with built-in slots to accommodate a nylon strap with Velcro to secure the modules to the patient's body segments.

The data processing module sampled the raw IMU and load cell data from the main and moving modules at 100 Hz. For each sampling of the raw data, a 13-component string of data was generated that included: sample number, running time, load cell reading, and IMU data (angular velocity and quaternion vector from each IMU). The Delsys EMG system sampled the EMG signals of biceps and triceps at 1000 Hz.

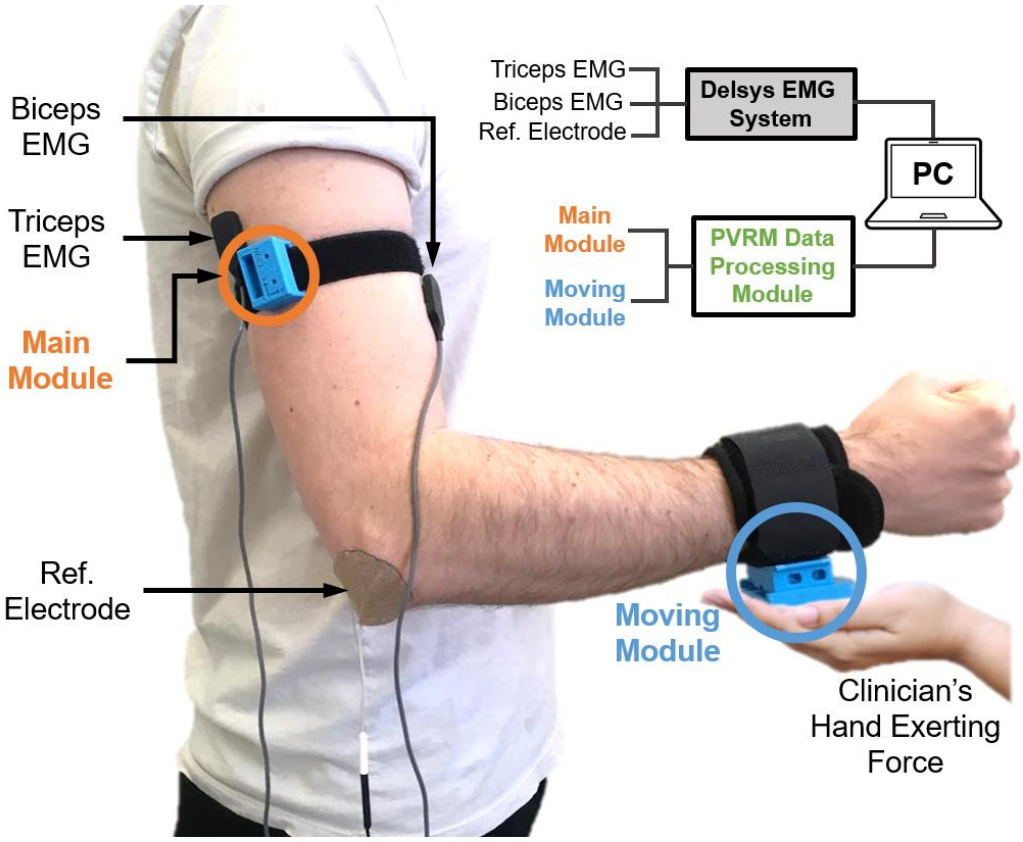

Figure 2.1. The PVRM and Delsys EMG general setup.

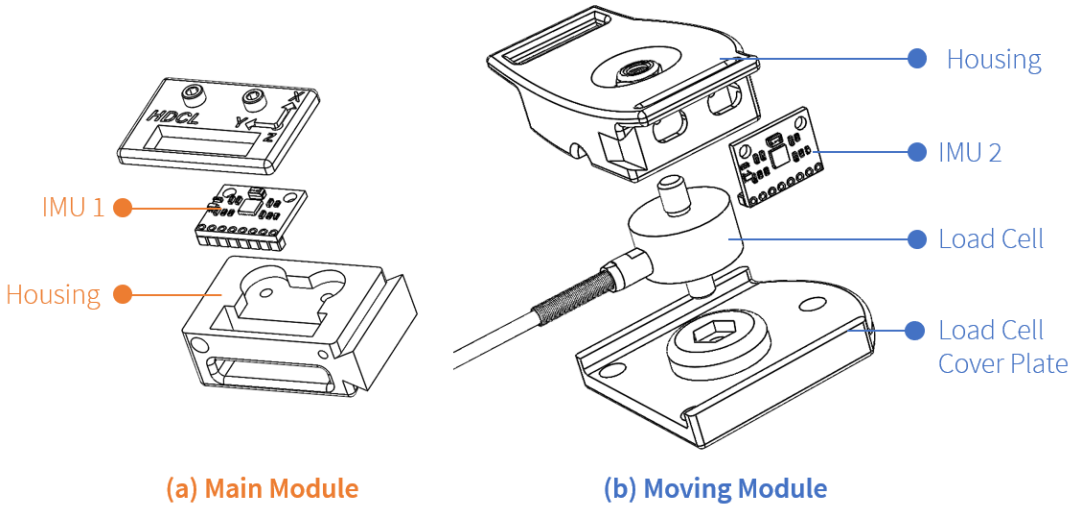

Figure 2.2. The PVRM modules: (a) the main module contained IMU 1, (b) the moving module contained IMU 2 and load cell.

2.3.2 DATA PROCESSING

The joint angular position (θ) and velocity (ω) were computed using the readings of the IMUs of the main module (IMU 1) and moving module (IMU 2). Each IMU outputted four values (a, b, c, d, where a defines the amount of rotation and b, c, d defines the axis of rotation in the 3D Cartesian space) representing a unit quaternion vector to quantify any rotation in 3D space ($\vec{\boldsymbol{q}}$) relative to the initial coordinate frame of the IMU ($\hat{\boldsymbol{\imath}}, \hat{\boldsymbol{\jmath}}, \hat{\boldsymbol{k}}$) (Equation 1).

$$\overrightarrow{\boldsymbol{q_i}} = a + b\hat{\mathbf{i}}_{\mathbf{i}} + c\hat{\mathbf{j}}_{\mathbf{i}} + d\hat{\mathbf{k}}_{\mathbf{i}}\text{, where } i = 1, 2 \qquad (1)$$

Quaternion representation was chosen over Euler angles due to quaternion's simple composition and absence of gimbal lock problems [99]. The rotation matrixes of IMU 1 and 2 ($\boldsymbol{R}_1$ and $\boldsymbol{R}_2$) were derived from the quaternion values of the IMU 1 ($\overrightarrow{\boldsymbol{q_1}}$) and the IMU 2 ($\overrightarrow{\boldsymbol{q_2}}$), respectively, using Equation (2) [100]. Each column of the rotation matrix contained orientations of the local x, y, and z-axes of the rotated IMU relative to its initial coordinate frame (i = 1,2).

$$\boldsymbol{R_i} = [\vec{\boldsymbol{x}}\ \vec{\boldsymbol{y}}\ \vec{\boldsymbol{z}}] = \begin{bmatrix} a^2 + b^2 - c^2 - d^2 & 2bc - 2ad & 2bd + 2ac \\ 2bc + 2ad & a^2 - b^2 + c^2 - d^2 & 2cd - 2ab \\ 2bd - 2ac & 2cd + 2ab & a^2 - b^2 - c^2 + d^2 \end{bmatrix}. \qquad (2)$$

Before any measurement data could be collected from the PVRM, a 5s calibration trial for the IMUs and load cell was required (Figure 2.3 (a)). The calibration was used to 1) zero the load cell readings, and 2) establish the initial coordinate frame for each IMU and also align the local coordinate frames of the IMUs relative to a fixed global coordinate frame, since the two IMUs' coordinate frames were misaligned due to the absence of magnetometers. The fixed global coordinate frame was defined by using the orientation of the initial local coordinate frame of IMU

1 during the 5s calibration. The calibration procedure involved physically attaching the two modules together such that their coordinate frames were aligned parallel for 5s during which IMU and load cell data were collected (Figure 2.3 (a), light grey image). The load cell had no applied load. A calibration matrix ($\boldsymbol{R}^{calib}$) was computed using Equation (3).

$$\boldsymbol{R}^{calib} = \boldsymbol{R}_1\boldsymbol{R}_2^{-1}. \qquad (3)$$

During each calibration trial, the average of the $\boldsymbol{R}^{calib}$ ($\boldsymbol{R}_{avg}^{calib}$) over the 5s of calibration data was computed for obtaining a more accurate calibration matrix. After the calibration, an updated rotation matrix of IMU 2 ($\boldsymbol{R}_{\boldsymbol{2}}^{\boldsymbol{updated}}$) that was referenced from the global frame was computed using Equation (4).

$$\boldsymbol{R}_{\boldsymbol{2}}^{\boldsymbol{updated}} = \boldsymbol{R}_{\boldsymbol{avg}}^{\boldsymbol{calib}}\boldsymbol{R}_{\boldsymbol{2}}. \qquad (4)$$

To obtain θ, the angular difference between the x-axes of IMUs 1 ($\overrightarrow{\boldsymbol{x_1}}$= first column of $\boldsymbol{R_1}$) and 2 ($\overrightarrow{\boldsymbol{x_2}}$= first column of $\boldsymbol{R}_{\boldsymbol{2}}^{\boldsymbol{updated}}$) was computed using the dot product of the two vectors (Equation 5) (Figure 2.3(c)). ω was found by subtracting the gyroscopic readings about the z-axes of IMUs 1 from 2. The angular position and velocity data were filtered via an analog lowpass filter with a cutoff frequency of 50 Hz.

$$\theta = \cos^{-1}\left(\frac{\overrightarrow{\boldsymbol{x_1}}\cdot\overrightarrow{\boldsymbol{x_2}}}{|\overrightarrow{\boldsymbol{x_1}}||\overrightarrow{\boldsymbol{x_2}}|}\right) \qquad (5)$$

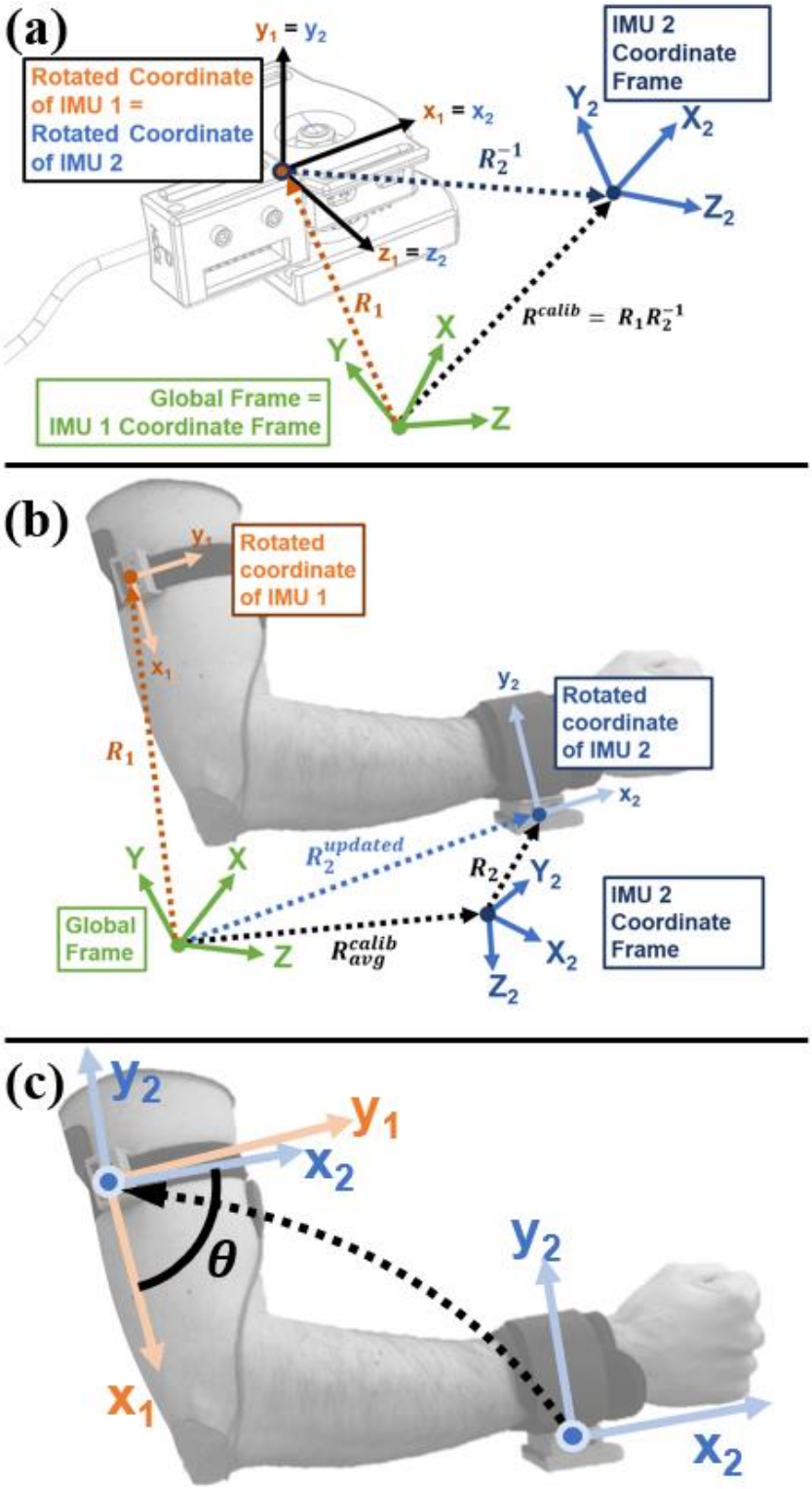

Figure 2.3. (a) The calibration procedure of the PVRM and (b, c) computation of elbow joint angular position (θ).

Calculated muscle resistance (τ) had various contributions: the torque due to the applied force of the clinician ($F_a L_{arm}$), inertial effect ($I_z \alpha$), gravitational effect ($F_g cos(\theta_{hor}) L_{com}$), and unwanted moments (M_{uw}) due to tilting of the load cell (Figure 2.4). Equations (6, 7) show the sum of moment about z-axis (M_z) and rearrangement of this equation for solving τ, respectively. Here, F_a and L_{arm} represents the applied force on the load cell and distance between elbow joint and load cell, respectively. $\alpha, F_g, \theta_{hor}$ are the angular acceleration, force due to gravity, and angle with the global x-axis, respectively. The mass of moving body segment (forearm and hand) (m), distance from the elbow joint to the center of mass (COM) of the moving body segment (L_{com}), and rotational inertia of the moving body segment about the elbow joint or Z-axis (I_z) were estimated using known anthropometric equations given the subject's gender, body mass, and height [101]. A nine-point-moving-average filter was used to filter the calculated τ data after it was calculated.

$$\Sigma M_z = I_z \alpha = F_a L_{arm} - F_g \, cos(\theta_{hor}) \, L_{com} - M_{uw} - \tau. \quad (6)$$

$$\tau = F_a L_{forearm} - F_g \, cos(\theta_{hor}) \, L_{com} - I_z \alpha - M_{uw}. \quad (7)$$

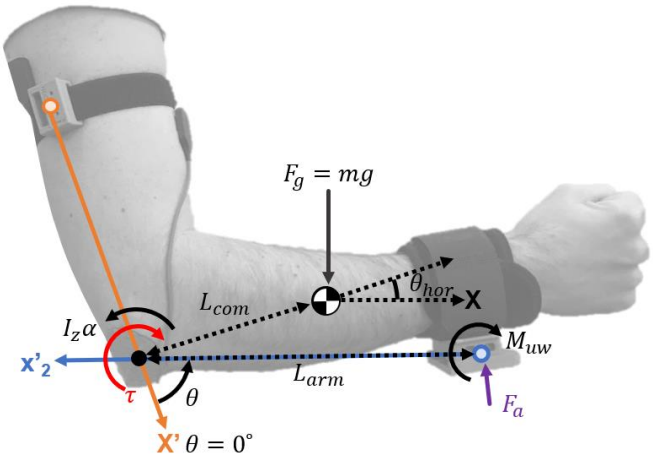

Figure 2.4. Free-body diagram of a subject′s arm during passive movement. $\theta = 0^\circ$ when the forearm was aligned to the upper-arm.

2.3.3 SUBJECT DEMOGRAPHICS

Human subject testing was conducted to validate the accuracy of position, velocity, and resistance measurements of the PVRM during passive arm flexion. The measurements from the PVRM were compared to a gold-standard commercial robotic dynamometer (System 3, Biodex). A total of ten subjects were tested: three subjects with spasticity, two subjects with rigidity and five healthy control subjects (Table 2.1). The inclusion criteria for the spasticity and rigidity patients were: (a) 18-80 years of age, (b) stable neurological condition that causes spasticity or rigidity at the elbow joint, (c) no other significant neurological disorders in addition to the condition that causes spasticity or rigidity, (d) no history of musculoskeletal disorder at the elbow joint, and (e) could consent or be accompanied by someone with a power of attorney and ability to follow commands. The inclusion criteria for the control subjects were: (a) no history of abnormal hypertonic muscle behaviors or any neurological diseases that affect movement of the upper extremity, and (b) able to consent or be accompanied by someone with a power of attorney and

ability to follow commands. The exclusion criteria were: (a) history of paratonia, (b) recent injury to arm in the past 3 months, and (c) presence of tremor during passive stretch. The study was approved by the Institutional Review Boards at the University of Illinois College of Medicine at Peoria, the University of Illinois at Urbana-Champaign, and Bradley University. The human subject testing was conducted at Bradley University and informed consent form was obtained from all participants.

For participants with hypertonicity, a certified clinician (author ST) assessed and recorded the participant's muscle behavior on the Modified Ashworth Scale (MAS) and Modified Tardieu Scale (MTS) for spasticity participants (or Unified Parkinson's Disease Rating Scale (UPDRS) for rigidity participants) immediately before the testing began. For spastic and rigid subjects, the arm side with most affected was tested. For controls, the dominated side was chosen.

Table 2.1. Subject demographics

	Spasticity			Rigidity		Control				
ID	S1	S2	S3	R1	R2	C1	C2	C3	C4	C5
Gender	M	M	M	M	M	M	M	F	M	M
Age (yrs)	33	56	56	71	51	61	56	58	55	25
Tested Arm	R	L	L	R	R	R	R	R	R	R
$L_{forearm}(cm)$	24	23	25	24	24	26	23	22	24	24
Height (cm)	182	175	180	177	178	185	172	165	177	181
Weight (kg)	110	103	95	57	82	90	70	65	72	98
Score [a]	4/2	3/2	3/2	2	2	-	-	-	-	-

[a]The scores for spasticity subjects are expressed in MAS/MTS, and the scores for rigidity subjects are expressed in UPDRS.

2.3.4 EXPERIMENTAL METHODS

The values of θ, ω, τ from the PVRM were compared to those of the Biodex dynamometer. Prior to each test session, the PVRM modules were calibrated, and subject-specific surface EMG thresholds were established to monitor for voluntary biceps or triceps activation during passive movements. To do so, the participant was asked to perform an isometric contraction (70% of maximum voluntary isometric contraction) of biceps for three seconds and then triceps for three seconds while the EMG signals were collected. The skin contacting the sensors and electrodes

were prepared using the appropriate EMG setup guidelines [102] and all data were collected at 1000Hz using the Delsys EMG Acquisition Software (EMGworks). All EMG data were detrended and filtered by (a) subtracting a constant offset (approximately 0.5 mV) of the EMG signals, (b) using a 60 Hz notch filter, (c) using a 4^{th} order Butterworth band-pass filter from 10-400 Hz, and (d) rectifying the EMG signal. The subject-specific EMG thresholds for each muscle group was computed from the averages of these processed EMG data. Voluntary muscle contraction was defined as the instant when the EMG signal collected during a passive stretch test exceeded the thresholds for more than 0.5 seconds.

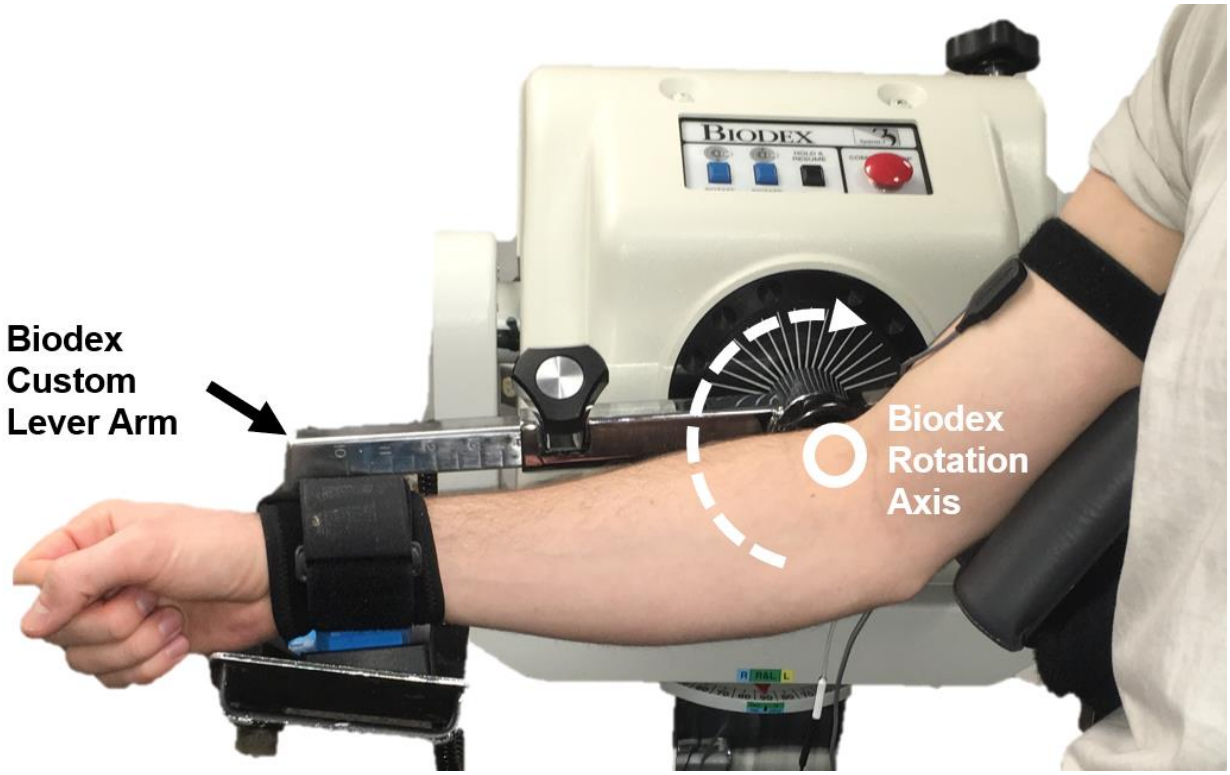

Figure 2.5. Biodex setup for validating the PVRM measurements

The dynamometer would rotate the participant's arm via an adjustable custom-fabricated lever arm (Figure 2.5). The lever arm was used to 1) align the Biodex rotational axis to the elbow joint and 2) transfer all loads from the Biodex to the PVRM load cell. The participant's lateral epicondyle was aligned with the rotating axis of the dynamometer by adjusting the custom lever arm length. The distance ($L_{forearm}$) between elbow epicondyle and the load cell on the moving module was measured and recorded. The PVRM main module was attached on the participant's upper arm, and the moving module was attached via Velcro to the end of the lever arm, allowing the PVRM to measure the same τ measured from the Biodex dynamometer. The PVRM moving module was fastened on the participant's wrist, while the wrist was held in a neutral position (defined as the mid-point between supination and pronation) or as close to the neutral position as possible for participants with wrist contractions. All participants wore a wrist support brace (Yosoo Health Gear, Zhuang Junchao, China) to stabilize against unwanted wrist movements (the support brace was not included in any figures for clarity).

The Biodex dynamometer protocol and hardware were setup to perform passive elbow flexion and extension stretch tests tailored to each subject group. For spasticity and rigidity subjects, the trial started with the arm from the most comfortably flexed position and then passively at a slow speed (10°/sec for the biceps and triceps muscle to relax after the elbow flexion, since the degree of spasticity or rigidity may change after passive muscle movement [30]) to the most extended position comfortably possible. These most extended and flexed positions were determined for each subject by a certified clinician (author ST) prior to the test. Then the arm was flexed back to its determined flexed position at one of the three speeds: 75°/sec, 90°/sec, 120°/sec, which were typical flexion speeds for passive stretch tests of spasticity and rigidity [30]) chosen by a certified clinician (author ST). For spasticity, the flexion speed was chosen prior to the test

such that it was high enough to illicit a catch-release behavior while ensuring subject's safety [103]. For rigidity, the flexion speed was also chosen prior to the test as the highest flexion speed while minimizing discomfort for the subject. Three trials were performed with three minutes of rest between trials to ensure muscle relaxation after each trial. For control subjects, the trial also started with the arm from the most flexed position and moved in extension at 45°/sec to the most comfortably extended position followed by a movement in flexion back to its initially flexed position at the same speed (45°/sec). Three trials were conducted at this speed. One trial at each speed were also performed at 75°/sec and 150°/sec to verify the PVRM's accuracy at high movement speeds.

The dynamometer performed passive movements following the above protocol while the PVRM, Delsys EMG, and Biodex collected data simultaneously. The Biodex sampled a 4-component string of data at 100 Hz that included running time, angular position, angular velocity, and applied torque. The Biodex applied a nine-point moving average filter on the torque data to filter the effect of sudden acceleration or deceleration of the lever arm in the beginning and end of range of motion. For all Biodex torque data, the gravitational and inertial effect of the custom lever arm was removed from all torque readings. If voluntary muscle activation was detected, the trial was repeated. The data from the PVRM, Biodex, and EMG were later processed using MATLAB software (R2016a, MathWorks, Inc., Natick, Massachusetts, USA).

The PVRM and Biodex raw data were processed and analyzed during the subject's arm flexion only, since the load cell cover plate of the moving module was designed for compression only. The PVRM and Biodex data were synchronized by using a cross-correlation between the signals, since a short time delay was observed between the recorded PVRM and Biodex data. Finally, the PVRM and Biodex data were truncated to compare the two data when the flexion

speed was constant. since the non-constant speed region displayed unwanted artifacts (e.g., high magnitudes of torque) of rapid acceleration and deceleration of the dynamometer.

To quantify the differences between the PVRM and Biodex data, the absolute residual as well as the percentage absolute residual between angular position, velocity and torque from the PVRM and Biodex during a given flexion cycle were computed. For each participant, the average and standard deviation of the absolute residual and the percentage absolute residual were computed for subject's entire flexion range of motion. Then, the ensemble average and standard deviation of the absolute residual and of the percentage absolute residual for each test group (spasticity, rigidity, and controls) were computed.

2.4 RESULTS

The PVRM and Biodex captured the joint kinematic and kinetic behavior of each subject group during passive arm movements (Figure 2.6). Spasticity participants displayed expected fluctuating elevated muscle tone marked by a distinct catch-release behavior during passive movement at the tested speeds (Figure 2.6(a,b)). Rigidity participants displayed uniformly elevated muscle tone without a catch-release behavior (Figure 2.6(c,d)). Healthy control participants did not demonstrate any increase in muscle tone even at high flexion speeds; the muscle tone for all control participants remained relatively similar and constantly low (less than 4Nm) during the flexion cycle (Figure 2.6(e,f)). For all subjects and trials, biceps and triceps muscles were inactive. The PVRM and Biodex data at slow and mediums stretch speed for control subject C4 were shown in Appendix A.

The PVRM measurements were similar to the gold standard Biodex measurements during the passive flexion, since the residuals for all measurements were between 1-13%. The error for

angular position and velocity measurements (less than 7 %) were smaller than torque measurements (less than 13%) (Figure 2.6). The torque measurement error was especially high for spasticity subjects. The standard deviation error of angular velocity measurement error was the lowest for all subjects.

Table 2.2. Absolute residuals and percentages of residuals.

		Spasticity	Rigidity	Controls
$\lvert Residuals \rvert$	θ (°)	1.8 (2.7)	1.8 (2.9)	2.6 (2.4)
	ω (°/s)	4.6 (0.6)	1.1 (0.2)	1.0 (0.2)
	τ (Nm)	0.2 (0.1)	0.1 (0.1)	0.2 (0.02)
% $\lvert Residuals \rvert$	θ (%)	3.9 (5.4)	4.7 (6.6)	6.7 (5.0)
	ω (%)	5.8 (0.55)	1.5 (0.23)	1.2 (0.15)
	τ (%)	12.3 (3.0)	6.3 (3.2)	9.8 (1.2)

The average and standard error (in parenthesis) for absolute and percentage residuals are shown above.

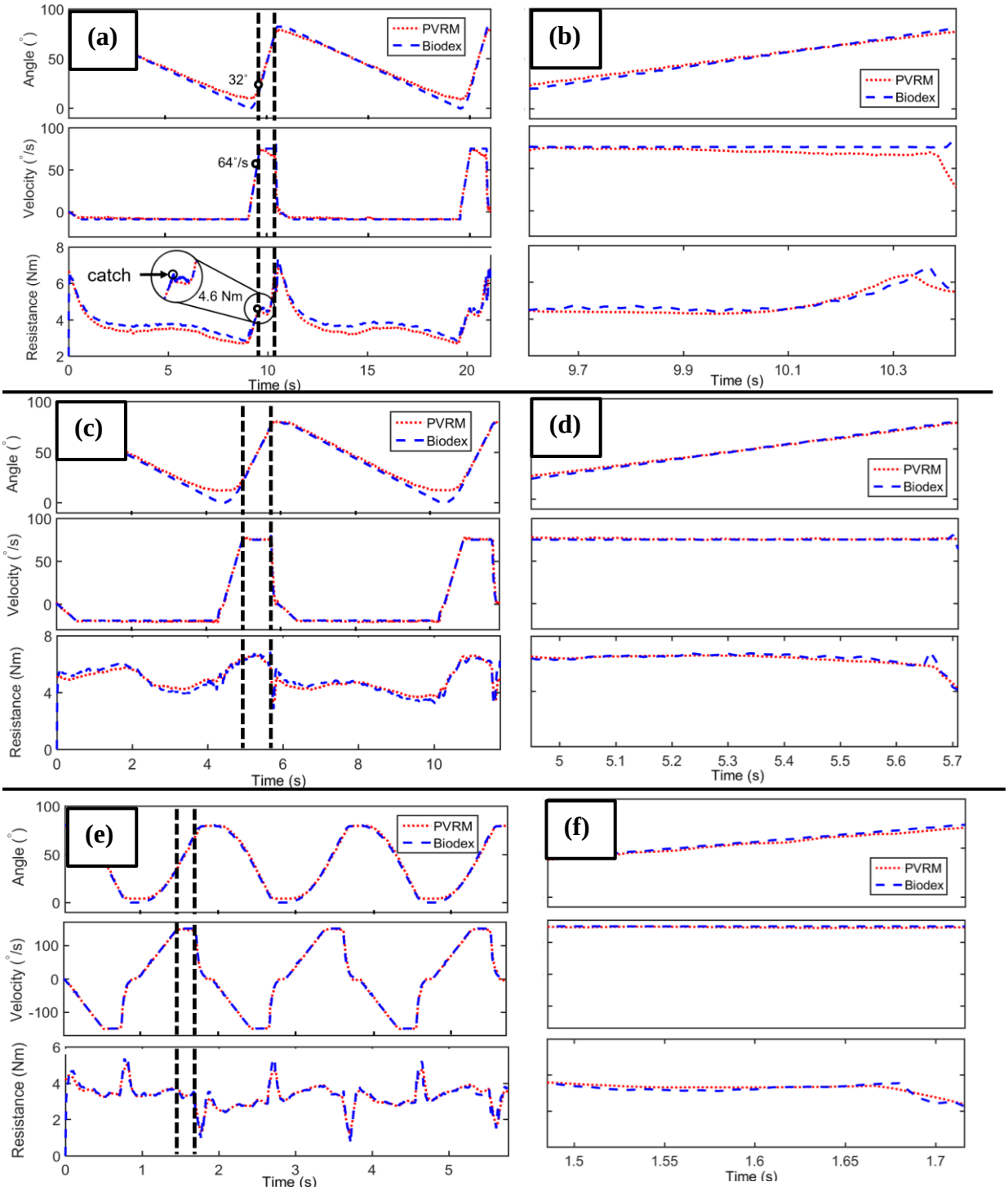

Figure 2.6. Comparison between the PVRM and Biodex data during a full trial (left column) and constant flexion speed (right column) for (a, b) spasticity subject S2, (c, d) rigidity subject R2, and (e, f) control subject C4. The constant flexion-speed-region (vertical dashed lines) in full trial plots was extracted.

2.5 DISCUSSION

The PVRM was able to characterize the arm movement of the three subject groups during passive flexion. The PVRM captured the spasticity patients' catch-release behavior, a unique characteristic of spasticity. For example, a spasticity patient (S2 with MAS and MTS scores of 3 and 2, respectively, demonstrated a distinct catch at a catch angle of 32˚ (t = 9.4 seconds) where the local maximum of torque (τ = 4.6 Nm) was observed during flexion (Figure 2.7 (a)). The torque value at catch and average torque measurements during flexion agreed well with the torque values of spasticity patients with the same MAS and MTS score reported in the literature [43,90]. The catch occurred only when sufficient stretch speed (64˚/s for S2) was reached, since spasticity is stretch speed dependent. After the catch, a sudden drop in torque was observed, which manifested as release. This magnitude of the release was small since the dynamometer continuously exerted force on the subject's arm. The release is more apparent when a clinician moves the patient's arm, since the clinician would "release" or reduce the amount of force exerted on the patient's arm to minimize risks for injury after the clinician feels the catch.

The PVRM quantified expected characteristics of the rigidity patients: uniformly elevated muscle tone during passive arm movement (Figure 2.8 (c, d)). The maximum τ for the rigidity participants (7.2 Nm) was higher than that for the control participants (3.7 Nm) during passive flexion at constant speed. Unlike spasticity participants, the rigidity participants displayed no distinct catch-release behavior. This was expected, since rigidity is stretch velocity independent.

The PVRM accurately quantified the arm movement of the control participants at low, medium, and high flexion/extension speeds (Figure 2.9 (c, d)). Unlike spasticity or rigidity participants, control participants did not show elevated muscle tone or catch-release behavior during flexion even at high flexion/extension speeds (Figure 2.10 (c, d)). Any abrupt increase or

decrease in torque was due to high acceleration or deceleration that resulted from rapid change from flexion to extension or extension to flexion during multiple cycles on the Biodex.

The angular position and velocity measurements of the PVRM were sufficiently accurate for quantifying kinematic behavior of passive arm movement for all subject categories at various stretch speeds. The average absolute residual of angular position and velocity were no more than 2.6˚ and 4.6˚/s, respectively, for all subject groups (Table 2.2). The magnitudes of these residuals are significantly smaller than the total range of motion (approximately 146˚ ~ 152˚ for males and females [104]) and average passive movement velocity during clinical assessments (45˚/s ~ 150˚/s [105]); the angular position and velocity residual was only 1.7% and 1.2% ~ 4%, respectively, of the total ROM and movement speed. These residuals were acceptable to be used in terms of analyzing kinematic behavior of human arm motion, since, even under ideal conditions, unremovable errors from human biomechanics study amount to a few degrees [106]. In addition, the standard deviation of the residuals for angular speed was low compared to angular position. A source of the small residual of angular position and speed was due to the difference of how the PVRM and Biodex measured θ and ω. While the PVRM measured the elbow joint angle and speed by comparing IMU orientations of the forearm and upper arm, the Biodex measured the rotation of the forearm by reading and differentiating values from a rotary potentiometer at the axis of rotation. The PVRM could potentially provide a more accurate elbow joint angle than the Biodex, since the PVRM measured the relative motion of the forearm and upper-arm.

While the torque measurement was the least accurate compared to angular position and speed measurement, the torque measurement can be considered to be accurate enough to be used in quantifying the kinetic behavior of passive arm movement. The PVRM was able to detect catch-release behavior for spasticity, uniformly elevated muscle resistance for rigidity, and low muscle

resistance for controls, despite the relatively high percentage residual (12.3% for spasticity, 6.3% for rigidity, 9.8% for controls) (Table 2.2). Thus, for our purpose of quantifying the characteristics of kinetic behavior of different subject categories, the PVRM provides sufficiently accurate torque measurement. The sources of error for torque measurement were due to 1) the misalignment between the rotational axis of the Biodex dynamometer and the participant's elbow joint, and 2) the abnormal arm posture for spasticity participants. It was critical for the rotational axis of the Biodex dynamometer and the participant elbow joint to be aligned, since any misalignment caused a discrepancy between the trajectory of the subject arm movement and lever arm movement. This trajectory difference could have introduced unwanted moment (M_{uw}) created about the loadcell. The Biodex System 3 did not offer full adjustments of the seat height, making it difficult to align the Biodex rotational axis to the elbow joint. Abnormal arm posture of spasticity patients due to sustained muscle contractions also caused unwanted moment on the load cell. This was particularly evident for spasticity patient S1 with high MAS score, resulting in higher absolute residual for spasticity participants.

Certain limitations of the PVRM existed. The PVRM required a 5s calibration phase to ensure accurate kinematic measurements. The PVRM's angular positional and velocity may be inaccurate at long running times due to the drifting of the IMUs. From our experiences, the drifting does not become an issue until five minutes after the calibration. Therefore, if assessments for multiple joints take longer than five minutes, then the PVRM should be recalibrated before continuing with assessments. Also, the uniaxial load cell could not remove unwanted moments introduced by the misalignment of the elbow joint and Biodex rotation axis.

For future work, a few improvements can be made to the hardware of the PVRM. First, a multi-axial load cell (i.e. 6 axis load cell) should be used to account for loads and moments from

all axes. Second, the ergonomics and user-experience can be improved by reducing the physical size of the PVRM modules for better comfort and reducing the setup time on patients with different arm geometries. With these improvements, the PVRM can be used to quantify various levels of spasticity and rigidity in a larger number of subjects to quantify and investigate biomechanical behavior of spasticity and rigidity during passive arm movement.

2.6 CONCLUSIONS

The PVRM (Position, Velocity, and Resistance Meter) was designed and validated to quantify spasticity and rigidity patients about the elbow joint during passive arm movement. This validation study demonstrated that the PVRM's measurements was able to quantify unique kinematic and kinetic behavior of spasticity and rigidity such as catch-release behavior and uniform elevation in muscle tone. The PVRM can help researchers gain additional insights into the quantification of spasticity and rigidity and allow clinicians to make more reliable assessments of these behaviors and severity levels.

2.7 ACKNOWLEDGEMENTS

We would like to thank Professor Kenneth Wilund and Annabel Biruete from the department of Kinesiology and Community Health at University of Illinois Urbana-Champaign for lending us a Biodex System for pilot work, and Ned Neuhaus for his aid in subject recruitment.

CHAPTER 3: PRELIMINARY CLINICAL STUDY OF SPASTICITY AND RIGIDITY PATIENTS USING THE PVRM

3.1 ABSTRACT

The goal of this study was to quantify and provide a database of joint kinematics and kinetics during passive stretching due to spasticity and rigidity in the upper-arm using a portable and validated measurement device, the PVRM (Position, Velocity, and Resistance Meter). Thirty-eight subjects with different levels of spasticity (n=15, Modified Ashworth Scale (MAS) scores 1-4) and rigidity (n=11, Unified Parkinson's Disease Rating Scale (UPDRS) scores 1-3), as well as healthy age and gender matched controls (n=12) were tested using the PVRM. Key outcome parameters that quantify the joint kinematic and kinetic characteristics of spasticity and rigidity (e.g., increased muscle tone, stretch velocity dependency of muscle tone, presence of catch) were quantitatively defined and analyzed. Spasticity subjects demonstrated stretch velocity and MAS score dependent muscle tone marked by catch-release behavior, resulting in a non-constant torque profile, and a triangular stretch velocity profile across the range of motion. Rigidity subjects exhibited uniformly elevated muscle tone that was dependent on UPDRS score but independent of stretch velocity and showed no catch-release behavior. Healthy control subjects exhibited no increase in muscle tone and no catch-release behavior. While some of these characteristics of spasticity and rigidity have been qualitatively discussed in other literature, our study quantified these characteristics for spasticity and rigidity at different stretch velocities during both flexion and extension of the elbow. This study demonstrated that the PVRM can serve not only as a data collection tool to provide useful data for neuro-rehabilitation related

technologies and medical training simulators, but also as a clinical screening device to differentiate spasticity and rigidity from healthy muscle.

3.2 INTRODUCTION

Hypertonicity is manifested by an abnormal increase in muscle tone (i.e., resistance to movements of relaxed muscles due to an outside force) during rest or passive stretching of the affected muscles [107]. The impaired ability to properly control descending pathways induce disordered spinal reflexes, causing involuntary movement in response to stimulus, and increased activity of muscle spindles, producing incorrect perception of muscle contraction [78].

Spasticity and rigidity are two common types of hypertonicity [107]. Spasticity, caused by damaged motor neurons/descending reflex pathways, is characterized by a catch-release behavior (i.e., a sudden increase in muscle tone ("catch") and a rapid decrease in tone ("release") during passive movement), clonus (i.e., involuntary rhythmic series of muscle contractions and relaxations), and elevated muscle tone that is stretch-velocity *dependent* during passive stretching of the affected muscles [1,78]. Rigidity, caused by damage of basal ganglia/upstream pathways, is marked by a uniformly increased muscle that is stretch-velocity *independent* during passive movement [79][1,78]. There are two types of rigidity: lead-pipe rigidity (i.e., uniformly increased muscle resistance to passive movement throughout the entire range of motion) and cog-wheel rigidity (i.e., muscle resistance superimposed with tremor to passive movement) [107].

The Modified Ashworth Scale (MAS), a six-point scale that rates the degree of spasticity from 0 (healthy) to 5 (severely spastic), and the motor section of Unified Parkinson's Disease Rating Scale (UPDRS), a five-point scale that rates the severity of rigidity from 0 (healthy) to 4

(severely rigid), are the most widely used rating scales for clinically assessing spasticity and rigidity, respectively [42,44]. For our study, we used a variant of MAS that rates from 0 to 5, rather than the original MAS that rates from 0 to 4 [42], These assessments involve a clinician manually moving the patient's affected body segments at various stretch velocities and rating the patient's hypertonicity in the five- or six-point scale. During this process, the clinician would subjectively feel the amount of muscle resistance [42,44]. In particular for spasticity assessment, the clinician would monitor the presence of catch-release behavior [42].

While these rating scales are convenient to use, there are some limitations: 1) inaccurate and unreliable assessments due to heavy reliance on rater's subjective interpretation of the rating scales and past experiences, and 2) difficulty for inexperienced clinicians to learn the rating scales due to lack of practice patients and tools to experience different levels of spasticity and rigidity [53]. The inaccuracy and poor reliability has been reported by many researchers for spasticity and rigidity assessments [52,75,85–89]). Some claim the inter-rater and intra-rater reliability to be as low as 7.0% and 33.3%, respectively, for lower-extremity assessments if subjects with MAS score of 0 were excluded [53]. Interestingly, studies reported high accuracy (as high as 86%) for the upper-extremity assessments [42,108–110]. This dependency on the type of extremity may be due to the effect of limb weight that may affect the rating of the muscle tone [14]. Since the rating scales heavily depend on the assessor's previous training and clinical experience, it is crucial for healthcare professional learners to gain enough hands-on assessment experience before entering the job site [111]. But current training mainly consists of inviting practice patients or asking students to mimic spasticity or rigidity and typically results in poor and inconsistent training outcomes and misrepresentation of true hypertonicity due to limited availability of practice patients [55].

Recently, some researchers have been developing medical training simulators that mimic different levels of spasticity or rigidity of real patients to complement current training practices [17,55–58,60,62,112–114]. However, there is a lack of a comprehensive database that quantifies the kinetic and kinematic behavior of spasticity and rigidity at all levels [17,60,112,113]. Such a database could serve as a valuable reference to fine tune the simulators for more realistic replications of spasticity and rigidity.

Researchers have developed measurement devices that quantify spasticity and rigidity with the intent of providing useful databases and objective assessment of hypertonicity [30,43,90–96]. However, these measurement devices had limitations that include inappropriate design for clinical deployment and narrow study scope. Some measurement devices were too impractical to be deployed in a clinical setting due to long setup time and bulky size [28,97]. Some studies lacked standardized testing protocol which led to inaccurate measurement [14,29]. Other studies had limited study scope that investigated exclusively only spasticity or rigidity, so the investigations of biomechanical differences between spasticity and rigidity were rarely made [14,29]. Even fewer studies quantified the biomechanics of different levels of severity of spasticity or rigidity [96]. Finally, some studies only focused on spasticity in biceps and not in triceps [14,29].

In the current study, we conducted a clinical test on human subjects with mild to severe levels of upper-arm (biceps and triceps) spasticity or rigidity at different stretch velocities using a compact, portable measurement device (the PVRM – Position, Velocity, and Resistance Meter) that can be attached quickly and with minimum setup requirements (Chapter 2). The PVRM consisted of small modules that can be attached to two adjacent body segments to measure kinematic and kinetic data, i.e. angular position and velocity, and the force applied by the

clinician to passively stretch the joint. This applied force is interpreted as muscle tone resistance felt by the clinician. From the PVRM raw data, key parameters that quantify relevant clinical symptoms of spasticity and rigidity, e.g. range of motion, average muscle resistance (tone), presence of catch, were defined and compared among all test subjects at four different stretch speeds (slow, medium, fast, and a velocity preferred by a trained clinician). Different stretch speeds were used to quantify the effect of stretch speed on muscle tone. For this study, a single clinician performed all testing to remove inter-rater variability. We focused on elbow flexion and extension muscle groups, since the MAS was reported to be most reliable for the upper-extremity by others [42,108–110]. The main goal of this study was to develop a preliminary database quantifying kinetic and kinematic muscle behavior during passive elbow flexion and extension for different levels of spasticity and rigidity.

3.3 METHODS

3.3.1 SUBJECT DEMOGRAPHICS

Thirty-eight subjects were tested (15 with spasticity, 11 with rigidity, and 12 age and gender matched healthy controls, Table 3.1). Thirteen spasticity subjects performed both flexion and extension trials. One spasticity subject did only flexion trials, and one spasticity subject did only extension trials. It is important to note that the spasticity subjects (n=13) who performed both movements did not necessarily exhibit the same severity level of spasticity during flexion as during extension (e.g., a subject with score of MAS 3 for extension may have had a score of MAS 2 for flexion). This unidirectional behavior of spasticity may be attributed to the difference of muscle fiber size between extensor and flexor muscles; extensor fiber area is known to be significantly

greater than flexor fiber area for type 2A and type 2B fibers [115], [116]. All spasticity subjects were post-stroke patients with hemiplegia. For rigidity subjects, all participants had rigidity in the flexor and extensor muscles and were diagnosed with Parkinson's Disease. At least three participants were recruited for each level of spasticity (MAS 1-4) and rigidity (UPDRS 1-2). Only two participants were tested for UPDRS 3 due to difficulty of finding subjects with this UPDRS score. Individuals at the most severe levels (MAS 5 and UPDRS 4) were not recruited since they have essentially no movement at the elbow.

Prior to testing, a certified neurologist (CMZ) rated the MAS or UPDRS scores. For spasticity and rigidity subjects, the more affected arm side was tested in this study. The arm with the dominant hand was tested for the healthy control subjects. Also, the clinician determined and noted whether the subject's arm could be passively moved at fast stretch velocities (> 80˚/s). Wrist and arm contraction angles (i.e., contracted wrist pronation/supination angle and contracted elbow joint angle in resting position) were recorded. To note any physical, psychological, or medical effect on the muscle conditions, mental stress and physical fatigue, presence of infections, missed medications or new medications, history of injury on the tested arm in the past two weeks, presence of pain on the tested arm, and history of falls were also recorded.

All subjects satisfied the inclusion-exclusion criteria, and subjects with spasticity or rigidity were assessed using the MAS or motor section of the UPDRS for both arms. The inclusion criteria for the spasticity and rigidity subjects were: (a) 18-80 years of age, (b) in a stable neurological condition that caused spasticity or rigidity at the elbow joint, (c) no other significant neurological disorders in addition to the condition that caused spasticity or rigidity, (d) no history of musculoskeletal disorder at the elbow, and (e) can consent and follow command or be accompanied and consented by someone with a power of attorney. The inclusion criteria for the

healthy control participants were: (a) no history of abnormal hypertonic muscle behaviors or any neurological disease that would affect movement of the upper extremity, and (b) able to consent and follow command or be accompanied and consented by someone with a power of attorney. The exclusion criteria for all groups were: (a) history of paratonia, (b) recent injury to the arm, and (c) presence of tremor during passive stretch. The study was approved by the Institutional Review Boards at the University of Illinois College of Medicine and OSF HealthCare at Peoria and the University of Illinois at Urbana-Champaign. Testing was conducted at the OSF Healthcare Center at the Illinois Neurological Institute, Peoria, IL. Informed consent was obtained from all participants.

Table 3.1. Subject demographics

	Spasticity			Rigidity	Controls
Movement	Bidirectional	Unidirectional (Flexion)	Unidirectional (Extension)	Bidirectional	Bidirectional
Total number of subjects	13	1	1	11	12
Score [a] (number of subjects)	MAS 1 (3) MAS 2 (3) MAS 3* (4) MAS 4* (3)	MAS 4 (1)	MAS 2 (1)	UPDRS 1 (5) UPDRS 2 (4) UPDRS 3 (2)	–
Age ± Stdev (years)	62.6 ± 12.9	74	62	67.2 ± 6.7	60.4 ± 12.9
Male: Female	5:8	0:1	1:0	8:3	5:7

[a] The scores for spasticity subjects are expressed in MAS, and the scores for rigidity subjects are expressed in UPDRS.
* Six out of seven subjects with MAS 3 and 4 could not perform fast passive stretch tests.

3.3.2 PVRM – POSITION, VELOCITY, AND RESISTANCE METER

The PVRM collected kinetic and kinematic movement data (i.e., joint angular position (θ), velocity (ω), and muscle resistance (τ)), as well as monitoring muscle activity during clinical assessments (Figure 3.1). The PVRM consisted of two modules (moving, main) and two surface electromyography (EMG) electrodes for biceps and triceps. The moving module contained an inertial measurement unit (IMU) sensor (MPU-6050, InvenSense, California, USA) and a uniaxial load cell (LCM 300; Futek, California, USA). A wrist support brace (Yosoo Health Gear, Zhuang Junchao, China) was worn to stabilize the wrist. The moving module was strapped over the wrist support brace and was attached to the ulnar side of the wrist when assessing flexion and radial side when assessing extension. A custom cover plate for the load cell, where the clinician applied force, transmitted all of the applied force onto only the load cell. The main module contained a microcontroller (Micro; Arduino LLC; Italy), another IMU (similar as above), and a Bluetooth module (HC-05; Guangzhou HC Information Technology Co., Ltd.; China). The main module was strapped to the midpoint of the upper arm with the module facing laterally and aligned parallel to the humerus. Each EMG electrode was custom-fabricated using a commercially-available bipolar EMG sensor electronics (MyoWare Muscle Sensor; Advancer Technologies; USA) with adjustable gain and two disposable electro-gel type EMG electrode patches (Arbo H124SG; Covidien; United Kingdom). The EMG measurement electrodes were attached to the midpoint of the biceps brachii and the long head of the triceps to ensure passive muscle status during the movement. A reference EMG electrode was attached over the clavicle. The raw PVRM data (i.e., sampled time, IMU data in quaternion form, load cell readings) and EMG data were sampled at 100 Hz and wirelessly transmitted to a tablet (Galaxy Tab E Lite; Samsung; Korea).

Before collecting the data, two calibration phases were needed: 1) a calibration to zero the load cell readings and align the local coordinates of the IMUs, and 2) an EMG calibration to determine the thresholds for voluntary biceps and triceps activation. The kinetic and kinematic calibration involved physically aligning and mating the moving and main modules so that the coordinate frames of IMUs were parallel (following the protocol defined in Chapter 2). The EMG calibration involved computing the EMG thresholds for voluntary muscle activation by recording a volitional degree of isometric contraction of the biceps for 3s and another for the triceps for 3s. The threshold was defined as the average of the recorded EMG signal during the 3s contraction. Voluntary muscle contraction during a passive stretch test assessment was defined as the instance when the EMG signal exceeded these defined thresholds for more than 0.5s.

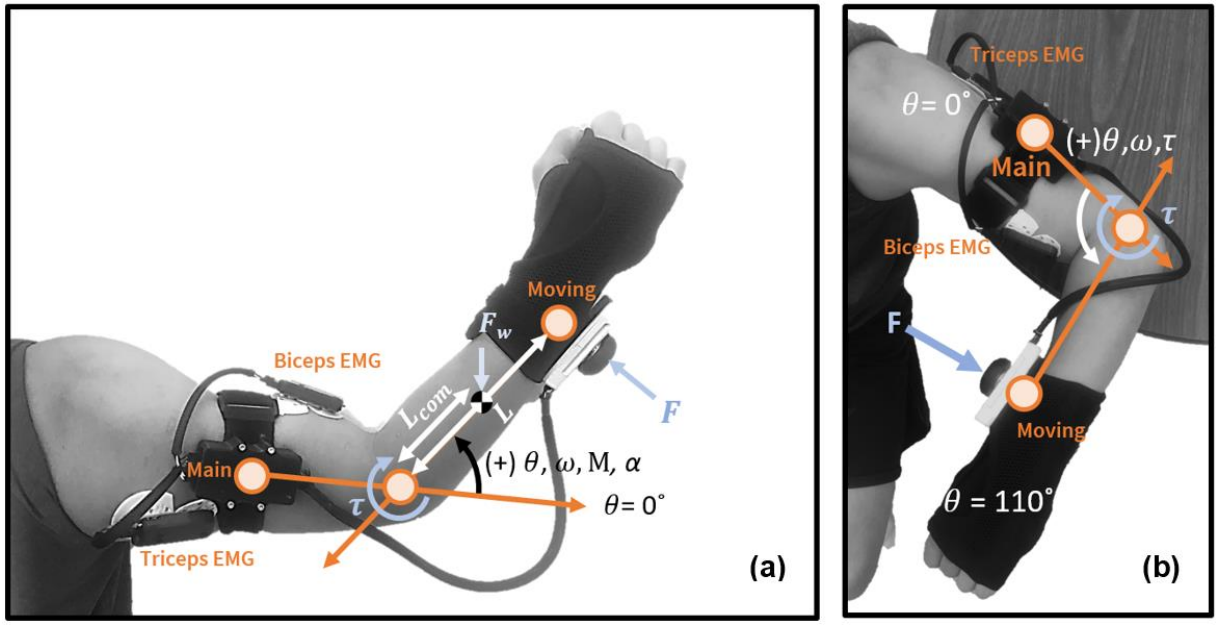

Figure 3.1. The PVRM modules configured for testing (a) flexion and (b) extension.

3.3.3 TESTING PROTOCOL

Two types of passive stretches (flexion and extension) were performed for each subject, except for those indicated in Table 3.1. Passive flexion was performed such that the plane of arm movement was perpendicular to the ground (Figure 3.1). Passive extension was performed with the shoulder abducted close to 90˚ while the elbow rested on a height-adjustable table such that the plane of forearm movement was parallel to the ground (Figure 3.1). This extension arm configuration was necessary to allow the clinician to properly apply force on the PVRM load cell cover plate. Otherwise, gravity would constantly pull the subject's arm away from the clinician's hand, making the exertion of force on the load cell difficult especially for control subjects with no muscle resistance. In addition, the subject's forearm had to be supported to be parallel to the ground. An anatomically neutral wrist position (or a position closest to neutral position) was chosen for the participant since spasticity patients with wrist contractions could not pronate or supinate their forearms.

For each type of passive stretch test, four stretch speeds were tested: slow (5˚/s - 20˚/s), medium (20˚/s - 80˚/s), fast (> 80˚/s), and clinician's preferred speed (> 30˚/s). Preferred speed was the stretch speed at which our clinician-investigator (author CMZ) would typically stretch the subject's arm during a clinical evaluation of spasticity or rigidity. Three trials were performed for each speed. Thus, a total of 24 trials (12 flexion and 12 extension) were performed for all subjects with the following exceptions: two unidirectional spasticity subjects who only performed 12 trials each, and six severely spastic subjects (MAS 3 or 4) who could not perform fast stretch speed trials due to severely increased tone and/or permanent contractures. These six subjects performed only slow, medium, and preferred stretch speeds (a total of 18 trials). For all subjects, flexion trials were performed first starting with slow stretch speed followed by medium,

fast, and preferred stretch speed. Afterwards, extension trials were performed starting with the same stretch speed order as flexion trials. For each trial, the clinician passively stretched the subject's arm until full range of motion was reached. The trial was repeated if the stretch speed was too high or low, or either muscle group was voluntarily activated. After each trial, a rest period of 30-60 seconds was given to ensure muscle relaxation between trials.

3.3.4 DATA PROCESSING

The raw PVRM data from the tablet were later downloaded and post processed in a PC using Python scripts to compute angular position (θ) and velocity (ω), and muscle resistance (τ) data using the same approaches as defined in Chapter 2. To compute θ, the angular difference between the x-axes of IMU 1 (IMU of moving module) and IMU 2 (IMU of main module) was computed using the dot product of the two vectors) (Figure 3.1). ω was found by subtracting gyroscopic readings of IMU 1 from 2. τ was equivalent to the applied torque (exerted by the clinician) with the gravitational and inertial effects of the moving forearm removed. The applied torque was defined as the product of the load cell reading and the distance between elbow joint and the load cell. To remove gravitational and inertial effect of the moving forearm on the torque measurement, the mass of the moving body segment (wrist and forearm), distance from the elbow joint to the center of mass of the moving body segment, and rotational inertia of the moving body segment about the elbow joint or Z-axis were estimated using known anthropometric equations [101] given the subject's gender, body mass, and height. The gravitational effect was only removed for data during passive flexion, since the movement plane during passive extension was parallel to the ground. The PVRM data's accuracy

(% $|Residual|\ of\ \theta, \omega, \tau = 5.1\%, 2.8\%, 9.5\%$) was demonstrated to be sufficient in a validation study where the PVRM values were compared to a gold standard dynamometer (Biodex System 3) in previous studies (Chapter 2, Song et al. 2017, 2018).

The processed PVRM data were filtered and truncated to remove unwanted noise and to analyze the data only relevant to movement. The angular position and velocity data were filtered via an analog lowpass filter with a cutoff frequency of 50 Hz. The torque data from the load cell were filtered using a 4th order Butterworth lowpass filter with a cutoff frequency of 10 Hz. The filtered PVRM data were then truncated. The start of the limb movement (t_{start}) was defined as the time when the movement velocity was above 5˚/s and when the change in torque across a unit sample time ($\frac{\Delta\, Torque}{\Delta\, Time}$) was above 0.1 Nm/s. End of the movement (t_{end}) was defined as the time when the movement velocity was below 5˚/s. Change in torque across unit time was not used for defining t_{end}, since the arm with spasticity or rigidity exhibited changes in torque even at the end of movement.

A robust catch definition was introduced using both kinetic (muscle resistance: τ) and kinematic (angular position, velocity, and acceleration: θ, ω, α, respectively) data to quantify the catch-release behavior of spasticity (Figure 3.2). The quantitative definition of catch was investigated by referring to the clinical definition of a catch: a catch is defined as a sudden appearance of increased muscle activity in response to a fast passive stretch, which leads to an abrupt reduction in velocity (1st criterion) and sudden increased resistance (2nd criterion), at a certain angle before maximum range of motion (ROM) was reached (3rd criterion) [119,120]. Therefore, we defined a catch as the instance when: the forearm was at maximum deceleration (1st criterion), the torque peaked at a local maximum and exceeded a threshold that was trial

specific (threshold = 1.25 × standard error of resistance during one trial) (2nd criterion), and the angular position was below 90% of the subject's maximum ROM (3rd criterion) (Figure 3.2). The release was defined as the instance of the first local minimum of torque after the catch.

To comprehensively characterize each test group, conceptual joint kinetic and kinematic patterns for each group were developed (Figure 3.3(a)). Healthy arms were expected to exhibit low muscle tone at all stretch speeds and a trapezoidal stretch velocity profile that consisted of three regions (acceleration, constant velocity, and deceleration). Rigid arms were expected to demonstrate uniformly elevated muscle tone that was stretch velocity independent and had no catch-release behavior. Also, rigidity would display a trapezoidal stretch velocity profile that resembled the profile of a healthy arm but with smaller velocity magnitude. Spastic arms would display a catch-release behavior and elevated muscle tone especially at fast and clinician's preferred stretch velocities. The presence of a catch-release behavior would cause the muscle tone to vary dramatically across the range of motion. Also, passive stretching of a spastic arm at high stretch speeds would resemble a triangular stretch velocity profile. This was because the clinician would rapidly accelerate the arm to elicit the catch-release behavior and then abruptly decelerate the arm once the end of range of motion was near. It is important to note that, at slow stretch speeds or for mildly spastic arms, spastic behavior would exhibit only small increase in muscle tone without a catch due to the stretch speed dependency of spasticity [103].

A list of outcome parameters that comprehensively quantify passive movement were defined (Table 3.2). To quantify the magnitude of muscle tone, average muscle resistance (τ_{avg}), maximum muscle resistance (τ_{max}), and exerted energy normalized to the range of motion (E_{norm}) were defined. Also, two additional parameters for quantifying kinetic behavior were

defined: i) stiffness (S) and ii) the standard deviation of stiffness (S_{std}). S_{std} could be used to quantify the degree of fluctuations in muscle tone, since the standard deviation (i.e. variations) of the torque change is proportional to fluctuations in muscle resistance. It was hypothesized that S_{std} would be higher for spasticity subjects due to higher degree of torque changes due to presence of catch. To quantify joint kinematic behavior for control and rigidity subjects, the angle at the end of acceleration region (θ_{ω_rise}), angle at the end of constant velocity region (θ_{ω_fall}), and the average velocity at the constant velocity region (ω_{avg}) were introduced to characterize the trapezoidal stretch velocity profile. To quantify joint kinematic behavior for spasticity subjects, maximum stretch velocity (ω_{max}) and angle at maximum stretch velocity (θ_{ω_max}) were defined to characterize the triangular stretch velocity profile and identify the highest velocity point. To evaluate the catch-release behavior of spasticity subjects, parameters relating to catch angle and torque ($\theta_{catch}, \tau_{catch}$), release angle and torque ($\theta_{release}, \tau_{release}$), acceleration at catch ($\alpha_{catch}, \alpha_{release}$), and torque at the end of the post-release region ($\tau_{post-release}$) were established (Figure 3.3(a)). The post-release region started from the onset of release until the end of ROM. Finally, to quantify stretch speed dependent muscle tone, two parameters were developed: difference of muscle resistance between slow and clinician's preferred stretch speed ($\Delta\tau$) and the stretch speed dependency of muscle resistance (SSD). For $\Delta\tau$, muscle resistance at the preferred stretch speed was used due to the six spasticity subjects who could not perform the fast stretch speed trials. SSD was defined to be the slope of the τ_{avg} vs. ω_{avg} plot, where higher SSD indicated greater velocity dependency (Figure 3.3(b)). Seven of the outcome parameters were designated as key outcome parameters that succinctly characterize each subject category was also identified (Table 3.2). These key outcome parameters quantified the range of motion (θ_{ROM}), catch angle (θ_{catch}), average stretch velocity (ω_{avg}), maximum

stretch velocity (ω_{max}), average muscle resistance (τ_{avg}), maximum muscle resistance (τ_{max}), and difference in muscle resistance between preferred and slow test speeds ($\Delta\tau$). Non-key outcome parameters were metrics that were not included in the key outcome parameters. Ensemble sample averages of the outcome parameters of spasticity, rigidity, and control subjects were computed to investigate inter-group and intra-group characteristics.

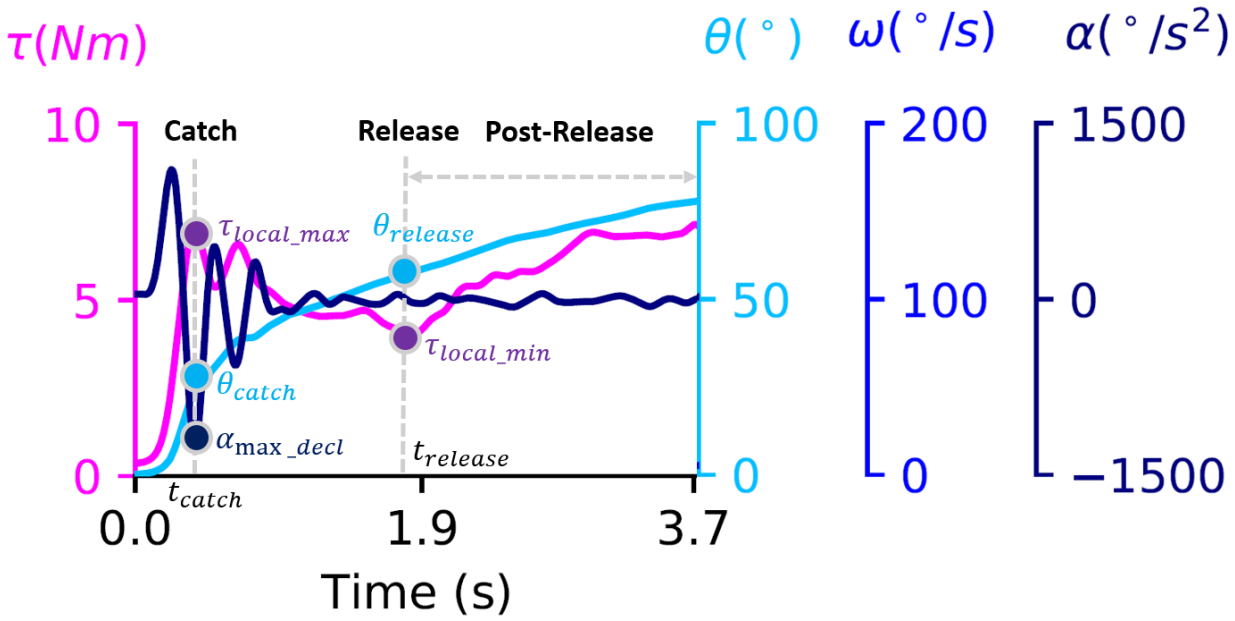

Figure 3.2. Quantitative definition of catch-release behavior.

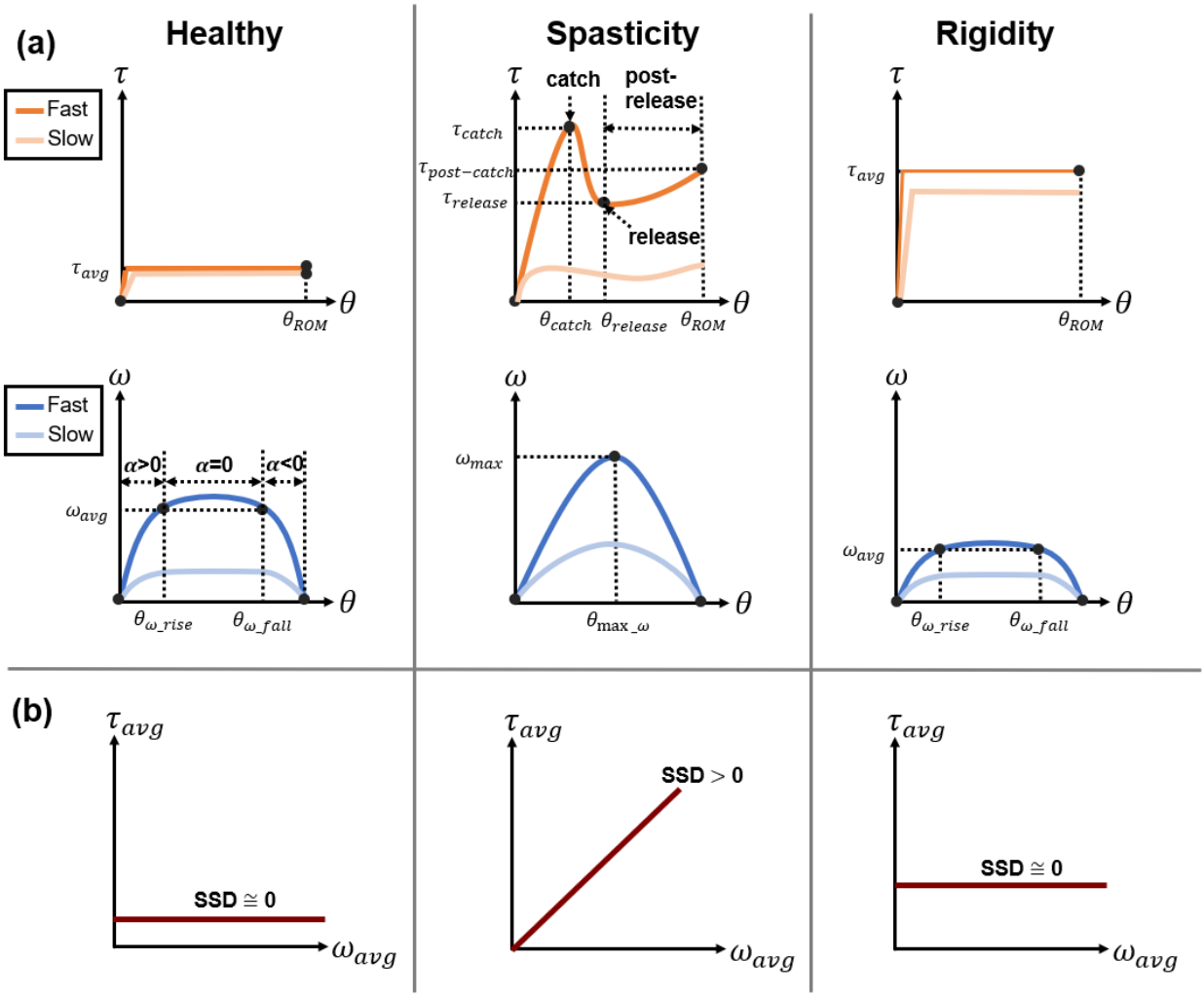

Figure 3.3. Conceptual graphs comparing healthy, spastic, and rigid muscle behavior during passive movement at fast and slow stretch speeds. (a) Muscle resistance (τ) and stretch velocity (ω) profile and (b) stretch speed dependency (SSD) of muscle resistance are shown.

Table 3.2. Definitions and relevant clinical feature of outcome parameters.

	Symbol	Definition	Relevant clinical feature (*subject category*)
Key Outcome Parameters	θ_{ROM} (°)	Range of Motion (ROM)	ROM (*All*)
	θ_{catch} (°/s)	Catch angle	Catch – release behavior (*Spasticity*)
	$\omega_{avg}, \omega_{max}$ (°/s)	Average and maximum velocity for a trial	Trapezoidal (*Control & Rigidity*) and Triangular (*Spasticity*) velocity profile
	τ_{avg}, τ_{max} (Nm)	Average and maximum τ for a trial	Muscle tone (*All*)
	$\Delta\tau$ (Nm)	$\Delta\tau = \tau_{avg}^{preferred} - \tau_{avg}^{slow}$	Velocity dependency of tone (*All*)
Non-Key Outcome Parameters	θ_{ω_rise}(°) θ_{ω_fall} (°)	θ when ω exceeds ω_{avg} for the first time θ when ω is less than ω_{avg} for the last time	Trapezoidal velocity profile (*Control & Rigidity*)
	θ_{max_ω}(°)	θ at ω_{max}	Triangular velocity profile (*Spasticity*)
	$Catch$ %	Catch frequency = $\frac{\#\ of\ catches}{total\ \#\ of\ trials} \times 100$	Catch – release presence (*Spasticity*)
	$\theta_{release}$ (°) $\alpha_{catch}, \alpha_{release}$ (°/s^2) $\tau_{catch}, \tau_{release}$ (Nm)	θ, α, τ at catch and release	Catch – release behavior (*Spasticity*)
	$\tau_{post-release}$ (Nm) $E_{post-release}$ (J)	Average of τ across post-release region. $E_{post-release} = \frac{\int_{\theta=\theta_{release}}^{\theta=ROM} \tau\, d\theta}{(ROM - \theta_{release})}$	Catch – release behavior (*Spasticity*)
	E_{norm} (J)	Applied energy normalized to ROM = $\frac{\text{Area under the } \tau \text{ vs } \theta \text{ (J)}}{ROM\ (in\ rad)} = \frac{\int_{\theta=0}^{\theta=ROM} \tau\, d\theta}{ROM}$	Muscle tone (*All*)
	S $(Nm/°)$	Stiffness	Muscle tone (*All*)
	$S_{avg}, S_{max}(Nm/°)$	Average and maximum of $S = \frac{\Delta\tau}{\Delta\theta}$ for a trial	Muscle tone (*All*)
	S_{std} $(Nm/°)$	Standard deviation of S for a trial	Muscle tone fluctuation (*All*)
	SSD $(Nm/°/s)$	Slope of $\tau_{avg}\ vs\ \omega_{avg}$	Velocity dependency of tone (*All*)

3.4 RESULTS AND DISCUSSIONS

This study quantified the behavioral features of spastic, rigid, and healthy muscles (Figure 3.3) as observed clinically in literature [1,42,44,78,79,84]. The observed characteristics for the rigidity subjects were 1) uniformly elevated muscle tone across the range of motion as compared to healthy controls, 2) muscle tone proportional to UPDRS score with little to no stretch velocity dependency, 3) trapezoidal stretch velocity profiles with lower average stretch velocities than controls, 4) no presence of catch-release behavior, and 5) no significant reduction of range of motion (ROM) (Figures 3.3, 3.4(a), Tables 3.5,3.6). Two cases of anomalous behavior were observed for rigidity trials (Figure 3.5(a): 1) excessive perturbation at the start of range of motion, and 2) increasing resistance across the range of motion). Observed characteristics of the spasticity subjects were 1) varying muscle tone across the range of motion due to presence of catch, 2) increased muscle tone that was stretch velocity dependent, 3) triangular stretch velocity profiles marked by high acceleration and deceleration, 4) occasional presence of catches that occurred at mid-point of ROM and at fast or preferred stretch velocities, and 5) kinetic and kinematic behaviors seen from only severely spastic subjects such as significantly reduced ROM, reduced stretch velocity, and more frequent catch-release behaviors (Figures 3.3, 3.4(b), 3.6, Tables 3.7-3.10). Spasticity without catch presence resembled rigidity especially at slow or medium stretch velocities (Figure 3.5(c,d)). While some of these characteristics of rigidity and spasticity were observed in literature [105,121,122], our study quantified these characteristics from slow to fast stretch speeds for different levels of spasticity and rigidity in extensor and flexor muscle groups.

3.4.1 RIGIDITY

Generally, rigidity subjects exhibited elevated muscle resistance (with minor disturbances) that was constant across the range of motion. Outcome parameters relating to muscle tone ($\tau_{avg}, \tau_{max}, E_{norm}$) were all higher for rigidity subjects than healthy controls at all stretch speeds. For example, subjects with UPDRS score of 1 showed three to five times more average muscle resistance (τ_{avg}), and subjects with UPDRS score of 3 showed seven to ten times more average muscle resistance at all stretch velocities during passive extension and flexion (Table 3.5, 3.6). Most rigidity subjects displayed this increased tone from the beginning of the range of motion, indicating that the muscle tone was present during rest (Figure 3.4(a)). This indirectly confirms literature's findings that elevated tone of rigidity can be attributed to abnormal increase in elasticity and stiffness of muscles that are present during rest [28–31,45,46,123–125]. This increase in elasticity implies that rigidity could originate from changes in intrinsic properties of joints, tendons, and muscles [126]. Thus, based on our results, rigidity may be partially affected from changes in passive properties of joints and soft tissues. Other studies have shown that another contributing factor for rigidity may be hyperexcitability of stretch reflex [126,127].

This muscle tone of rigidity subjects was proportional to the UPDRS score but independent to stretch speed. Severe rigidity subjects (UPDRS 3) displayed almost two to three times as much muscle tone ($\tau_{avg}, \tau_{max}, E_{norm}$) than mild rigidity subjects (UPDRS 1) at all stretch velocities during passive flexion and extension. Also, muscle tone of rigidity subjects was independent of stretch speed (Figure 3.4(a), Tables 3.5, 3.6). The stretch speed dependency of muscle tone (SSD) of rigidity subjects were significantly smaller in magnitude compared to spasticity subjects (Figure 3.6). All rigidity subjects had a small positive value of SSD close to

zero (0.035 - 0.051 Nm/(˚/s)) during extension, indicating only a slightly positive stretch speed dependency (hypersensitivity) of tone (Figure 3.6). Interestingly, flexion test results contained only a small negative value of SSD close to zero (-0.016 - 0.028 Nm/(˚/s)), indicating small negative stretch speed dependency (hyposensitivity) of tone (Figure 3.6). In addition, SSD depended only slightly on UPDRS scores: SSD of higher UPDRS score subjects was more positive during extension but more negative during flexion (Figure 3.6). Other studies also found this directional dependency of rigidity's sensitivity to stretch speed [28,40,41]. Nevertheless, the magnitudes of these SSD were much smaller (175% and 910% smaller during extension and flexion trials, respectively) compared to the spasticity subjects (Figure 3.6). Thus, while a small directional dependency (i.e., hyposensitive velocity dependency during flexion while hypersensitive velocity sensitivity during extension) of muscle tone was observed, the muscle tone dependency on stretch velocity of rigidity was minimal compared to spasticity.

Trapezoidal stretch velocity profiles of rigidity subjects had lower average and maximum stretch velocity (ω_{avg}, ω_{max}) than healthy subjects for fast and preferred stretch velocity trials by approximately 20˚/s during flexion and extension (Figure 3.4(a), Tables 3.5, 3.6). Interestingly, higher UPDRS score did not correlate with lower ω_{avg}, ω_{max}, indicating that the stretch velocity did not reduce significantly due to increased muscle tone (Figure 3.4(a), Tables 3.5, 3.6). In addition, the stretch velocity profiles for the mild rigidity subjects were similar to those for the healthy control subjects (Figure 3.4). Ultimately, the stretch velocity profile of rigid arms resembled that of healthy arms in shape but smaller in magnitude.

No significant reduction of ROM was observed for rigidity subjects since none displayed permanent contractures. The range of motion (ROM) of all rigidity subjects were similar to the

control subjects during extension and flexion (Figure 3.4, Tables 3.5, 3.6). The ROM for all rigidity subjects was only smaller than the controls by 17% during extension and 5% during flexion (Tables 3.5, 3.6). Others have also reported that rigidity subjects did not show significant reduction of ROM [25].

There were two cases of unexpected kinetic behaviors for rigidity subjects: i) excessive perturbations of the muscle resistance, and ii) linearly increasing muscle resistance across range of motion (Figure 3.5(a)). This overshooting of muscle resistance occurred in only 3 % of the total test trials and appeared only in the beginning of ROM (Figure 3.5(a)). These perturbations may be due to excessive tilting action introduced by the clinician, increasing unwanted moments about the load cell. For 13% of all rigidity test trials, resistance was linearly proportional to angular position (Figure 3.5(a)). This linearity may suggest that the changes of elasticity and stiffness is a function of angular position for some rigidity subjects. Other studies have reported similar findings [128]. The changes in intrinsic and passive muscle properties may be more severe towards the end of ranges of motion or longer muscle stretch length. Interestingly, the slope of the best fitting line of muscle resistance increased was proportional to the UDPRS score (Figure 3.5(a)). Apart from these irregular kinetic behaviors, the majority (87% of all rigidity test trials) displayed no major perturbation of resistance or linearly increasing muscle tone across the range of motion.

3.4.2 SPASTICITY

Spasticity subjects demonstrated elevated and varying muscle tone across the range of motion. For example, the average and peak muscle resistance for spasticity subjects at average

stretch velocities were 4.8Nm and 6.8Nm, respectively, higher than control subjects during passive extension (Table 3.7). This elevated muscle tone can be attributed to stretch reflex hyperexcitability and muscle contractures that alter the intrinsic mechanical properties of muscles [1,2,71,73,78,129]. S_{std}, a parameter that describes the degree of muscle tone variation, was greater for spasticity subjects than rigidity and control subjects by almost two to three times, respectively, during passive extension and flexion (Tables 3.7, 3.9). This variation of tone can be attributed to the presence of catch-release behavior, since the catch induces a rapid increase in tone and a sudden drop in tone. Note that the magnitude of release may be dependent on the clinician's stretching technique; the clinician slowed the movement once a sufficient resistance (i.e., catch) was felt. From our previous study (Chapter 2) that elicited a catch-release behavior using a dynamometer (Biodex) that continuously flexed the subject's arm at a constant acceleration until constant speed was reached, we observed that the magnitude of release for a MAS 3 subject was not as severe as the MAS 3 subjects in this study. Thus, if many raters are involved in future studies, consolidating on a uniform rating technique may be important to minimize the inter-rater variability.

Muscle tone of spasticity was stretch speed dependent (Figures 3.4(b), 3.6, Tables 3.7, 3.9). These subjects had positive SSD that was greater than rigidity subjects by 160% during extension and 532% during flexion (Figure 3.6). In literature, this stretch velocity dependency has been found in other joints as well, e.g. knee and ankle [130,131]. Ultimately, spasticity was marked by hypertonia during passive movement and was hypersensitive to changes in stretch velocity. This supports the claim that spasticity can generally be regarded more as a viscous component of muscle tone (artifact of neuromodulated behavior) rather than an elastic component (artifact of intrinsic changes of muscle tissues and tendons) due to its dependency on

stretch velocity rather than position [19,30]. Interestingly, MAS 1 subjects had similar SSD to UPDRS 2 & 3 subjects during extension, suggesting that there is little biomechanical difference between MAS 1 and UPDRS 2-3. Also, the MAS 1 subjects displayed an SSD like the controls during flexion, indicating that very mild spasticity kinetically behaves similarly to healthy controls for extensor muscles. Therefore, stretch speed dependency of muscle resistance may be a valuable differentiating factor to separate spasticity from rigidity and controls except for very mild cases of spasticity.

The stretch velocity profile for spasticity subjects resembled a triangular or a convex parabolic shape, where the maximum stretch velocity (vertex of parabola) had to be achieved as fast as possible to elicit a catch-release behavior (Figure 3.4(b)). The maximum velocity was always reached before the catch occurred for all spasticity subjects. In addition, the stretch velocity profile contained another local maximum after the release for mild spasticity subjects (MAS 1-2), indicating that the stretch velocity increased slightly after the release (Figure 3.4(b)). For severe spasticity subjects (MAS 3-4), the stretch velocity would either not increase at all or increase only slightly (Figure 3.4(b)). This could be due to the clinician's response of accelerating the limb to maintain a constant resistance after the release had occurred. For mild spasticity subjects, the magnitude of resistance during post-release region was lower than severe spasticity subjects, so the clinician was able to increase the stretch velocity more for mildly spastic arms than for severely spastic arms (Figure 3.4(b)). Hence, the stretch velocity profile of spastic arm involved a small increase of stretch velocity after the release, but the overall stretch velocity profile followed a triangular shape.

Another behavior of spasticity was the occasional presence of catch at the mid-point of ROM (Figure 3.4(b), Tables 3.7-3.10). Catches occurred more frequently (26.2% - 57.7% of all

trials) at fast and preferred stretch speeds and none at slow stretch speeds. For medium stretch speed, there was high catch percentage during extension (40%) and none during flexion (Tables 3.7, 3.9). While this intermittent presence of catch-release behavior among spasticity subjects was reported by other researchers as well [132], our study is the first to report the frequency of catch among spasticity subjects. Most of the catches for spasticity subjects occurred approximately at the mid-point of the ROM. While the θ_{catch} was smaller for higher MAS scored subjects, these catches occurred consistently at the mid-point of the range of motion ($\frac{\theta_{catch}}{ROM} \times 100\% \cong 50\%$) for all spasticity subjects (Figure 3.4(b), Tables 3.8, 3.10). θ_{catch} for MAS 4 subjects was 61% of ROM during extension and 53% of ROM during flexion, and θ_{catch} for MAS 2 was 51% of ROM during extension and 53% of ROM during flexion (Tables 3.8, 3.10). While we confirmed the reporting of other studies that catches occur earlier (i.e., smaller catch angle) for more severe spasticity subjects [132], we found that the relative catch location to the total ROM (% ROM) is similar for all spasticity subjects because the severely spastic subjects had less ROM. Catch occurring at half of ROM may be due to the need for clinician to accelerate sufficiently in the beginning to reach the velocity for eliciting catch while decelerating at the end of ROM to minimize risks of injury.

Release occurred immediately after the catch and displayed less muscle resistance, whereas the post-release region contained slightly smaller or larger muscle resistance than resistance at release ($/\tau_{release}$) (Figure 3.4(b), Tables 3.8, 3.10). For all spasticity subjects, the release occurred after catch within 10˚ during extension and 12˚ during flexion (Figure 3.4(b), Table 3.8, 3.10). In addition, the torque at release was significantly lower than torque at catch. For example, $\tau_{release}$ was lower than τ_{catch} for all spasticity subjects by 76 % during extension

and 33% during flexion at preferred stretch speed (Table 3.8, 3.10). Also, the magnitude of deceleration at release was much smaller than that of catch, since only a small amount of resistance prevailed after catch. For example, the magnitude of deceleration was reduced by 105% during extension and 110% during flexion at preferred stretch speed (Tables 3.8, 3.10). After the release, the post-release region contained higher muscle tone than $\tau_{release}$ for the severe spasticity subjects by 19% during extension and 4% during flexion (Figure 3.4(b), Tables 3.8, 3.10). Ultimately, immediately after catch, release was found where the magnitude of deceleration and resistance greatly decreased.

Different kinetic and kinematic characteristics were displayed by severely spastic subjects (MAS 3-4). First, significantly reduced range of motion (ROM) was seen for these subjects (Tables 3.7, 3.9). Also, the ROM of these spasticity subjects was lower in mildly spastic subjects by 32 % during extension and 33 % during flexion. This reduction of ROM was mainly attributed to paresis or permanent muscle contraction while spasticity was an indirect cause. Severe spasticity and prolonged immobility increases the elastic stiffness of muscles by altering the properties of muscles and connective tissues, ultimately causing permanent muscle contraction [22,71–73,83,133]. The muscle tone for MAS 4 subjects who had the most reduction of ROM exhibited less muscle tone than MAS 3 subjects particularly during flexion, since the clinician had difficulty passively flexing the arm and exerting greater torque as the end of range of motion was reached very early. Second, the maximum stretch velocity (ω_{max}) for the severely spastic subjects were lower than mild subjects (Figure 3.4(b), Tables 3.7, 3.9). For example, the ω_{max} of MAS 4 was greater than MAS 1 by +56% during extension and +88% during flexion (Tables 3.7, 3.9). This reduction of stretch velocity is due to the higher degree of muscle tone existent among severely spastic subjects. While it was difficult to reach faster stretch velocities,

nevertheless the clinician was able to elicit a catch from these subjects, which indicated that the dependency of spasticity to stretch velocity becomes significantly more apparent for high MAS subjects. Third, catches were more frequently elicited for severely spastic subjects than mildly spastic subjects during flexion and extension. While the catch percentage was 22% during extension and 12% during flexion for mild spasticity subjects, the catch percentage was 47% during extension and 23% during flexion for severe spasticity subjects (Tables 3.7, 3.9). Again, this may be because severe spasticity was more sensitive to stretch velocity. In addition, for severe spasticity subjects, the muscle resistance increased slightly during the post-release region. This coincides well with the qualitative description for the MAS 3 and 4 grades in the MAS table [42].

Like rigidity, a few cases of irregular behavior were observed for the spasticity subjects (Figure 3.5(b-d)). First, 2% of flexion trials demonstrated signs of excessive releases in which the moving forearm extends by a small amount during release (Figure 3.5(b)). We hypothesize that behavior was due the rater's technique: at the onset of release, the clinician momentarily applies less force. If this reduction of force is too excessive, the moving forearm may drop and extend due to gravity. This anomalous behavior was very rare, and the computation of key outcome parameters were not affected. Second, spasticity kinetic behavior with no catch were similar to rigidity kinetic behavior especially at slow and medium stretch speeds (Figure 3.5(c-d)). These spasticity subjects demonstrated a uniformly elevated muscle resistance, a common behavioral feature of rigidity, (Figure 3.5(c-d)). Since the catch-release behavior was absent for most spasticity subjects at slow and medium stretch speeds, the biomechanical difference between spastic and rigid arm may be only recognized at sufficiently fast stretch speeds. Thus,

reaching large enough stretch speed was very important to differentiate spasticity from rigidity, since the response to high stretch speed distinguished spasticity from rigidity.

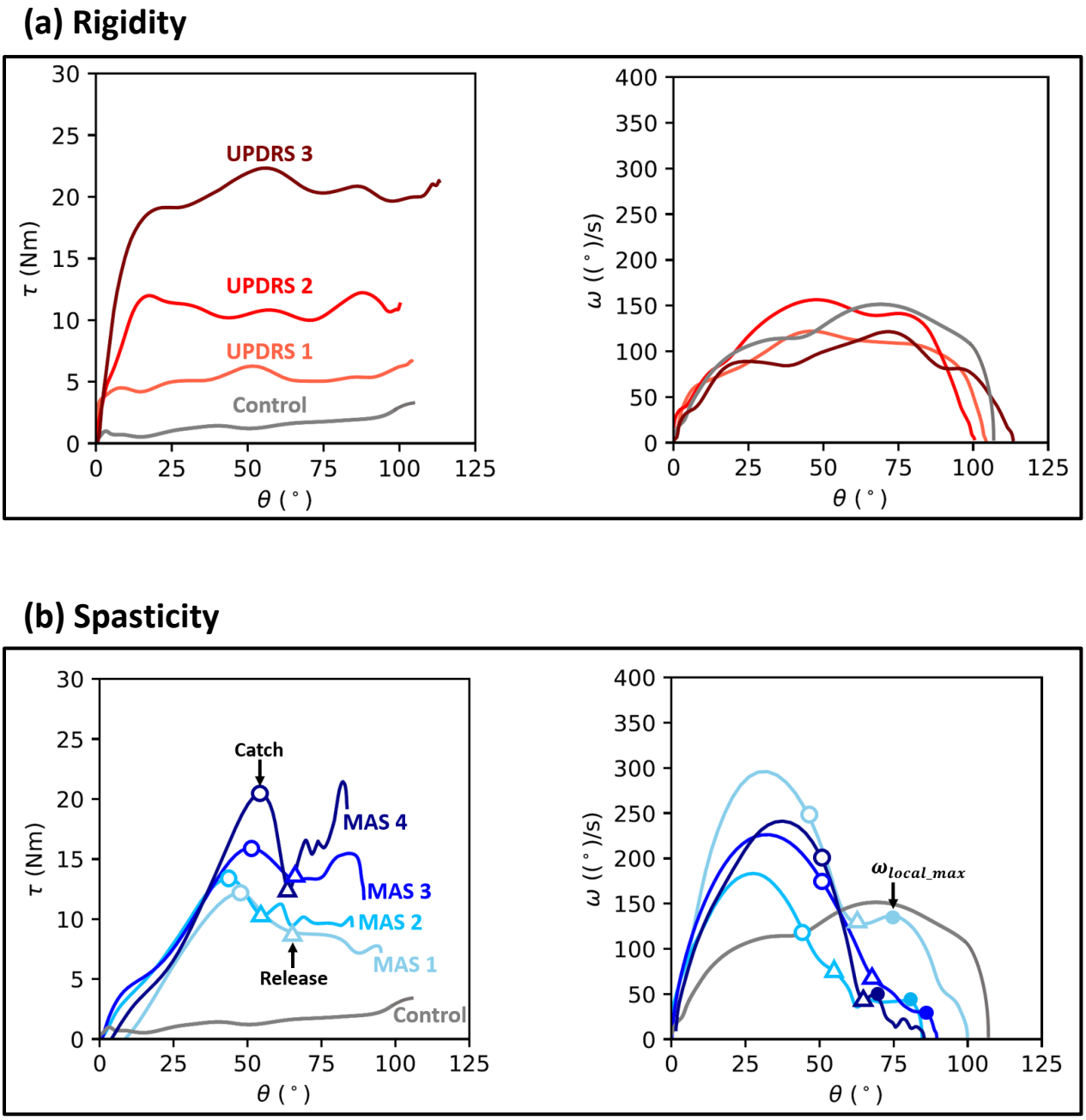

Figure 3.4. Example data of single trial of common kinetic and kinematic behavior during passive extension for various levels of (a) rigidity and (b) spasticity and control participants. For the spasticity data, the locations of catch (open circle), release (open triangle), and local maximum of ω after release (filled circle) are shown. All trials were conducted at preferred stretch speed.

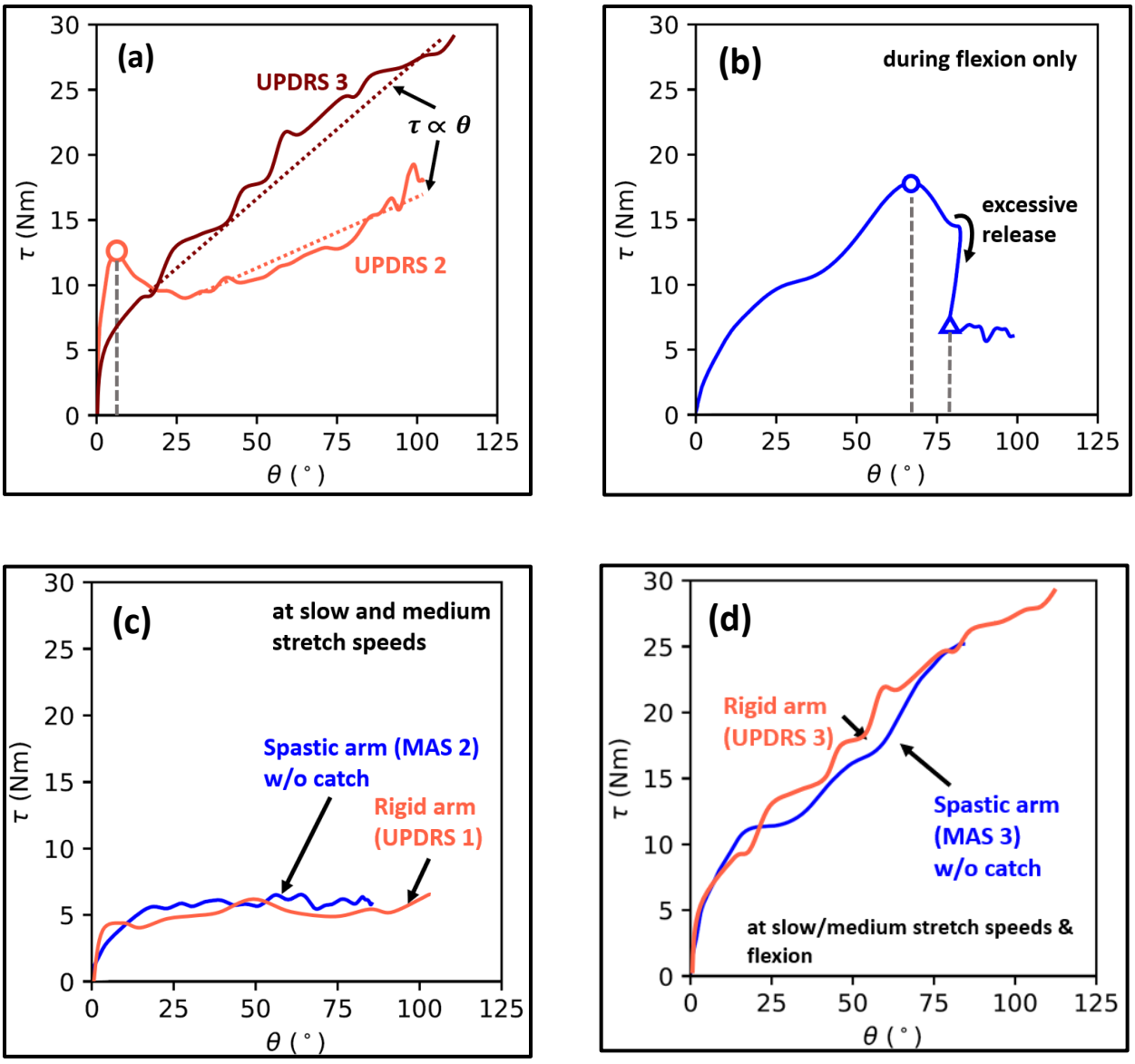

Figure 3.5. Examples of irregular kinetic behavior for the rigidity and spasticity subjects. (a) Excessive torque (open circle) was applied at the beginning of range of motion (ROM), or the resistance continued to increase linearly instead of being constant across the ROM. (b) Spasticity subjects displayed excessive release behavior only during flexion trials. (c, d) The spastic arm without catch resembled a rigid arm.

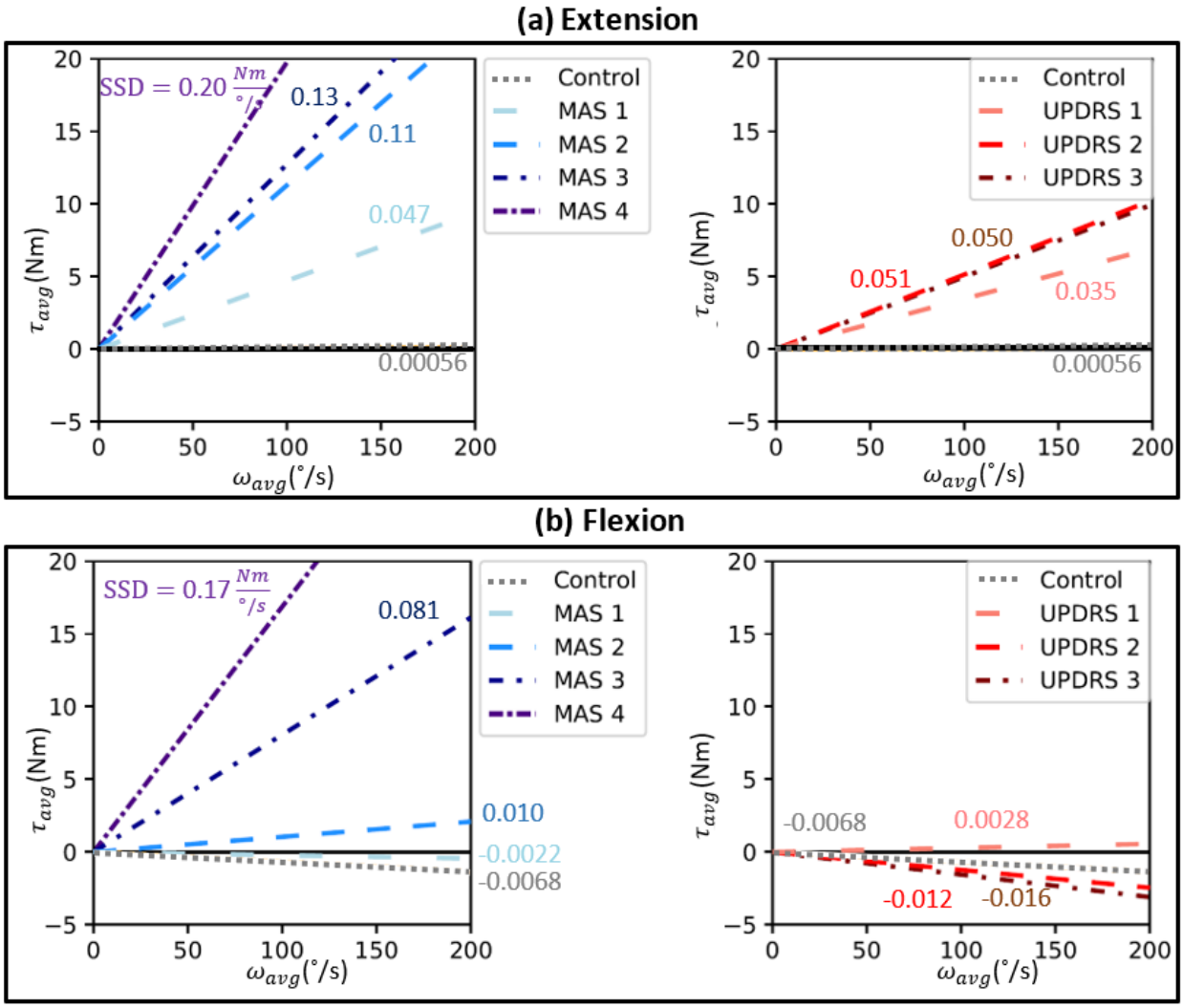

Figure 3.6. Stretch speed dependency of applied torque (SSD) of control, spasticity, and rigidity in (a) extension and (b) flexion.

Table 3.3. Outcome parameters of control subjects during passive extension

CONTROL (n=15) Extension

Stretch Speed	Key Outcome Parameter										Non-Key Outcome Parameter											
	ROM (°)		ω_{avg} (°/s)		ω_{max} (°/s)		τ_{avg} (Nm)		τ_{max} (Nm)		$\Delta\tau$ (Nm)		$\theta_{\omega_{rise}}$ (°)		$\theta_{\omega_{fall}}$ (°)		S_{avg} (Nm/°)		S_{std} (Nm/°)		S_{max} (Nm/°)		E_{norm} (J)		SSD (Nm*s/°)	
	$\bar{x}$*	STD**	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD
Slow	103	8	13	2	23	3	0.9	0.6	2.1	0.9	-	-	16	21	84	19	1.9	0.4	2.4	0.5	7.8	3.4	1.5	1.0	-	
Med	115	7	46	8	82	20	1.0	0.6	2.3	0.9	-	-	11	2	107	9	3.3	1.0	4.2	1.3	11.9	4.3	1.9	1.2	-	
Fast	119	7	82	15	154	35	1.2	0.7	3.3	0.9	-	-	9	2	111	6	6.6	2.0	8.4	2.9	22.3	9.3	2.2	1.5	-	
Pref	121	7	86	11	165	34	1.0	0.5	3.1	0.7	0.1	0.5	9	2	112	7	6.7	2.1	8.5	2.6	21.7	7.2	1.8	0.9	-	
Avg	115	10	57	31	106	63	1.0	0.6	2.7	1.0	-	-	11	11	104	16	4.6	2.6	5.9	3.4	16.0	9.0	1.8	1.2	0.00056	

*$\bar{x}$ is the mean of parameters computed for three trials

**STD is the standard deviation of the mean for three trials

Table 3.4. Outcome parameters of control subjects during passive flexion

CONTROL (n=15) Flexion

Stretch Speed	Key Outcome Parameter										Non-Key Outcome Parameter											
	ROM (°)		ω_{avg} (°/s)		ω_{max} (°/s)		τ_{avg} (Nm)		τ_{max} (Nm)		$\Delta\tau$ (Nm)		$\theta_{\omega_{rise}}$ (°)		$\theta_{\omega_{fall}}$ (°)		S_{avg} (Nm/°)		S_{std} (Nm/°)		S_{max} (Nm/°)		E_{norm} (J)		SSD (Nm*s/°)	
	$\bar{x}$*	STD**	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD
Slow	108	10	12	3	26	8	1.7	1.7	3.6	2.2	-	-	8	12	74	28	1.7	0.5	2.3	0.7	9.4	13.3	2.8	3.0	-	
Med	104	8	50	12	76	18	0.9	1.1	2.6	1.7	-	-	16	14	97	12	3.4	1.0	4.1	1.2	12.0	5.4	1.9	2.2	-	
Fast	108	9	109	26	176	49	1.1	1.3	3.2	1.6	-	-	12	3	102	11	7.7	3.6	9.4	4.9	25.3	11.1	2.2	2.6	-	
Pref	108	10	119	28	188	47	0.8	1.2	2.9	1.7	−0.9	1.4	11	3	103	13	9.1	4.8	11.2	6.1	30.8	15.5	1.6	2.6	-	
Avg	107	9	72	48	117	76	1.1	1.4	3.1	1.9	-	-	12	10	94	21	5.5	4.3	6.7	5.4	19.4	14.9	2.1	2.7	-0.0068	

Table 3.5. Outcome parameters of rigidity subjects during passive extension.

Rigidity (n=11) Extension

Score	Stretch Speed	Key Outcome Parameter												Non-Key Outcome Parameter											
		ROM (°)		ω_{avg}		ω_{max} (°/s)		τ_{avg}		τ_{max}		$\Delta\tau$		θ_{ω_rise}(°)		θ_{ω_fall}(°)		S_{avg} (Nm/°)		S_{std} (Nm/°)		S_{max} (Nm/°)		E_{norm} (J)		SSD	
		$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$
UPDRS-1 (n=3)	S	91	4	14	3	30	7	4.0	1.3	6.2	1.5	-	-	5	4	72	11	2.8	0.4	3.5	0.5	10.3	1.4	6.4	2.1	-
	M	100	7	48	12	85	25	5.4	0.9	7.7	1.7	-	-	11	2	91	9	5.7	1.7	6.7	1.7	19.0	5.6	10.4	1.8	-
	F	106	9	76	10	143	18	6.6	0.7	9.5	1.2	-	-	9	3	99	9	9.9	3.0	10.9	2.4	29.7	4.0	13.2	1.5	-
	P	106	10	79	11	148	14	6.2	1.3	9.5	2.7	2.2	1.0	8	2	98	10	9.5	1.9	10.6	2.0	32.1	9.1	11.9	2.8	-
	Avg	101	10	54	28	101	51	5.5	1.5	8.2	2.3	-	-	8	3	90	14	7.0	3.5	7.9	3.5	22.8	10.5	10.5	3.3	0.035
UPDRS-2 (n=6)	S	87	8	12	3	25	4	5.7	1.6	9.2	3.3	-	-	3	3	70	14	3.5	2.3	4.5	2.9	16.9	9.2	9.2	2.9	-
	M	95	6	36	9	65	14	7.5	2.6	11.6	4.3	-	-	9	10	86	8	6.5	1.9	7.5	2.3	24.4	9.9	14.1	5.2	-
	F	92	24	60	23	121	44	7.6	3.0	12.6	5.5	-	-	6	2	83	24	11.3	4.8	13.3	5.5	40.2	14.6	15.7	7.0	-
	P	95	7	59	13	113	24	8.0	2.4	12.0	4.0	2.3	1.6	6	2	87	7	10.1	2.8	12.4	3.6	38.0	13.2	15.8	5.1	-
	Avg	92	14	42	24	81	47	7.2	2.6	11.3	4.5	-	-	6	6	81	16	7.8	4.4	9.4	5.2	29.9	15.3	13.7	5.9	0.051
UPDRS-3 (n=2)	S	78	20	8	3	18	7	7.7	2.9	11.2	3.7	-	-	16	14	76	18	2.8	0.6	3.6	0.8	13.8	6.1	12.6	5.2	-
	M	102	4	36	3	60	7	7.3	4.9	11.0	6.7	-	-	7	2	93	6	5.7	2.0	6.3	1.9	20.5	7.3	13.4	9.4	-
	F	106	4	71	14	125	16	10.3	4.2	15.1	6.0	-	-	9	3	96	6	13.0	1.9	14.8	2.5	46.9	9.9	20.3	9.8	-
	P	105	7	62	16	117	34	10.3	5.5	16.2	9.1	2.6	2.3	8	2	93	5	11.9	3.3	13.2	2.9	41.1	9.4	18.7	11.8	-
	Avg	98	16	44	27	80	48	8.9	4.7	13.4	7.0	-	-	10	8	89	13	8.3	4.8	9.5	5.1	30.6	16.1	16.3	9.9	0.050
Total (n=11)	S	86	11	12	3	25	7	5.6	2.2	8.8	3.4	-	-	6	8	72	15	3.2	1.8	4.0	2.2	14.5	7.9	9.1	3.9	-
	M	97	7	39	11	69	20	6.9	3.0	10.4	4.7	-	-	9	8	88	8	6.1	1.9	7.1	2.1	22.2	8.8	13.0	5.9	-
	F	98	20	67	20	128	36	7.8	3.2	12.2	5.2	-	-	7	3	90	20	11.2	4.1	12.9	4.6	38.5	13.2	15.9	7.1	-
	P	100	10	65	16	123	29	7.9	3.3	12.1	5.6	2.3	1.6	7	2	91	9	10.3	2.8	12.0	3.3	37.0	12.0	15.3	6.9	-
	Avg	95	14	46	26	86	49	7.1	3.1	10.9	5.0	-	-	8	6	85	16	7.7	4.3	9.0	4.8	28.1	14.7	13.3	6.6	0.045

Table 3.6. Outcome parameters of rigidity subjects during passive flexion

Rigidity (n=11) Flexion

Score	Stretch Speed	Key Outcome Parameter												Non-Key Outcome Parameter											
		ROM (°)		ω_{avg}		ω_{max} (°/s)		τ_{avg}		τ_{max}		$\Delta\tau$		θ_{ω_rise}(°)		θ_{ω_fall}(°)		S_{avg} (Nm/°)		S_{std} (Nm/°)		S_{max} (Nm/°)		E_{norm} (J)		SSD
		$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	ST	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$
UPDRS-1 (n=3)	S	104	7	11	2	27	9	3.2	1.7	5.5	2.1	-	-	15	21	89	12	2.6	0.4	3.3	0.5	11.1	3.1	5.7	2.7	-
	M	104	6	48	9	86	23	3.9	1.7	6.4	2.4	-	-	13	9	97	12	4.9	1.0	5.7	1.5	17.1	3.8	7.8	3.5	-
	F	110	9	81	18	144	37	5.1	1.3	9.3	2.5	-	-	7	5	101	17	9.6	4.2	10.6	5.7	29.7	12.6	10.8	2.7	-
	P	105	9	75	20	136	42	2.9	1.0	6.5	2.1	-0.3	1.5	8	6	96	15	8.6	3.2	9.5	4.4	25.1	8.6	6.4	3.7	-
	Avg	106	8	54	31	98	56	3.8	1.7	6.9	2.7	-	-	11	13	96	15	6.4	3.9	7.3	4.7	20.8	10.8	7.7	3.7	0.0028
UPDRS-2 (n=6)	S	103	14	11	3	24	6	8.2	4.1	12.6	5.8	-	-	9	10	82	23	3.4	1.1	4.3	1.4	15.8	6.8	14.0	7.1	-
	M	99	13	54	15	83	21	7.3	2.8	12.1	4.4	-	-	9	4	93	16	7.8	2.8	7.5	2.9	24.2	9.8	14.2	5.7	-
	F	102	14	101	23	160	29	7.2	3.3	13.3	5.1	-	-	10	5	100	14	15.0	5.8	14.1	7.5	41.4	16.8	15.7	7.7	-
	P	100	13	78	19	126	39	7.1	4.1	11.7	6.2	-1.1	0.9	9	4	92	20	12.9	8.5	14.1	11.2	39.9	31.2	15.1	9.8	-
	Avg	101	14	61	37	98	58	7.4	3.7	12.4	5.5	-	-	10	6	92	20	9.7	7.0	10.0	8.1	30.3	21.6	14.8	7.8	-0.012
UPDRS-3 (n=2)	S	105	5	9	1	24	10	13.2	7.0	18.4	8.4	-	-	10	12	88	15	3.9	1.9	4.9	2.4	16.6	8.4	21.6	11.0	-
	M	93	8	34	4	62	8	9.2	6.1	15.9	10.7	-	-	8	3	85	6	7.0	3.8	6.2	2.5	18.7	8.5	18.1	12.0	-
	F	105	12	97	21	158	22	8.6	6.4	16.8	12.2	-	-	12	7	103	11	15.1	6.6	13.2	3.8	44.7	14.8	20.1	15.7	-
	P	103	3	94	19	156	24	7.6	5.6	14.4	9.9	-5.6	2.1	13	5	95	12	13.8	5.8	11.0	2.8	37.2	9.4	17.3	13.2	-
	Avg	101	9	59	41	100	61	9.7	6.7	16.4	10.5	-	-	11	8	93	13	10.0	6.7	8.8	4.5	29.3	16.0	19.3	13.2	-0.016
Total (n=11)	S	103	11	11	3	25	8	7.8	5.5	11.7	7.2	-	-	11	15	85	20	3.2	1.3	4.1	1.6	14.7	6.8	13.1	8.9	-
	M	100	12	49	14	80	22	6.7	3.9	11.2	6.6	-	-	10	6	93	14	6.9	2.9	6.8	2.7	21.3	8.9	13.2	7.7	-
	F	105	13	95	23	155	31	6.9	3.9	12.8	7.0	-	-	10	6	101	15	13.5	6.1	13.0	6.7	38.8	16.4	15.2	9.4	-
	P	102	11	80	20	134	39	6.0	4.4	10.8	6.9	-1.8	1.5	10	5	94	17	11.9	7.2	12.3	8.9	35.4	24.7	13.1	10.3	-
	Avg	102	12	59	37	98	58	6.8	4.5	11.6	7.0	-	-	10	9	93	18	8.9	6.4	9.0	6.9	27.5	18.7	13.6	9.2	-0.0084

Table 3.7. Outcome parameters of spasticity subjects during passive extension.

Spasticity (n=15) Extension

Score	Stretch Speed	Key Outcome Parameter												Non-Key Outcome Parameter											
		ROM (°)		ω_{avg}		ω_{max} (°/s)		τ_{avg}		τ_{max}		$\Delta\tau$		θ_{ω_max}(°)		S_{avg} (Nm/°)		S_{std} (Nm/°)		S_{max} (Nm/°)		E_{norm} (J)		SSD	Catch
		$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	$\bar{x}$
MAS-1 (n=3)	S	84	11	11	2	24	4	1.5	0.8	2.9	0.8	-	-	33	26	1.8	0.3	2.3	0.4	6.8	1.4	2.4	1.4	-	0.0
	M	92	21	57	13	113	25	3.4	2.1	5.7	2.7	-	-	39	8	6.1	4.0	6.8	4.4	18.7	11.3	5.8	4.0	-	0.0
	F	94	13	100	25	303	52	6.6	2.6	11.4	4.8	-	-	43	6	19.4	8.9	27.6	14.8	78.8	43.0	12.4	6.8	-	22.2
	P	101	13	111	25	311	40	6.4	2.0	11.1	3.6	4.9	1.4	47	7	19.5	8.2	23.3	10.8	60.9	23.6	11.2	4.6	-	22.2
	Avg	93	16	70	43	188	128	4.5	2.9	7.8	4.9	-	-	41	15	11.7	10.1	15.0	14.3	41.3	38.8	7.9	6.2	0.047	10.3
MAS-2 (n=4)	S	89	11	11	2	23	9	2.6	0.8	4.3	1.3	-	-	32	17	2.0	0.8	2.5	0.9	7.3	2.3	4.0	1.3	-	0.0
	M	96	15	35	10	96	26	5.1	1.0	6.9	1.5	-	-	30	17	4.8	1.1	6.5	1.5	22.7	8.8	8.9	1.7	-	33.3
	F	108	15	76	12	203	52	6.4	1.2	11.2	1.8	-	-	41	16	14.9	3.4	20.5	5.6	62.1	18.7	12.0	1.8	-	75.0
	P	104	17	74	25	200	41	6.7	1.7	10.3	2.2	4.1	1.3	45	16	12.9	3.2	17.5	3.6	52.1	7.8	12.7	3.2	-	33.3
	Avg	98	16	45	30	120	83	5.0	2.0	7.8	3.2	-	-	36	18	7.9	5.8	10.7	8.1	33.0	24.3	9.0	4.0	0.11	34.6
MAS-3 (n=4)	S	60	12	8	2	20	8	3.2	1.0	5.1	1.1	-	-	17	12	2.2	0.5	2.7	0.6	9.6	2.4	4.9	1.6	-	0.0
	M	67	10	37	8	137	69	6.7	2.2	12.8	6.8	-	-	28	9	15.5	14.1	26.5	31.2	98.9	127.5	9.9	3.6	-	50.0
	F[a] (n=1)	90	2	66	4	208	20	12.1	0.3	16.5	0.2	-	-	34	2	17.4	2.3	24.4	3.2	85.1	7.9	20.4	1.8	-	16.7
	P	69	11	45	12	193	47	6.5	2.3	14.5	5.5	3.3	1.7	29	8	21.7	13.1	38.2	27.6	133.1	105.9	10.7	4.6	-	91.7
	Avg	67	13	33	20	124	87	6.0	3.0	11.3	6.5	-	-	26	11	13.4	13.3	22.6	27.1	80.9	104.7	9.4	5.3	0.13	44.2
MAS-4 (n=4)	S	75	8	10	2	23	10	2.9	0.8	5.2	1.2	-	-	20	12	2.2	0.6	2.7	0.8	9.4	3.6	4.1	1.3	-	0.0
	M	76	12	34	10	142	30	8.1	3.3	12.2	4.5	-	-	30	6	9.8	4.8	13.5	5.0	44.1	11.8	12.2	4.8	-	66.7
	F[b] (n=2)	83	2	38	17	167	57	10.4	4.9	15.0	8.0	-	-	26	12	15.9	12.0	22.6	16.0	79.6	53.4	14.0	5.9	-	50.0
	P	78	9	42	20	172	28	9.7	5.1	14.2	7.3	6.8	3.0	31	9	14.3	9.5	20.2	10.7	74.4	29.2	14.4	7.0	-	75.0
	Avg	77	9	30	19	120	70	7.4	4.8	11.2	6.8	-	-	27	11	9.8	9.0	13.6	11.6	47.9	38.3	10.8	6.7	0.20	50.0
Total (n=15)	S	77	15	10	3	22	8	2.6	1.1	4.5	1.4	-	-	25	18	2.1	0.6	2.6	0.7	8.3	2.9	3.9	1.7	-	0.0
	M	82	19	40	13	123	47	6.0	2.9	9.7	5.4	-	-	31	12	9.2	9.0	13.8	18.4	47.9	73.9	9.4	4.3	-	40.0
	F[c] (n=12)	96	15	74	29	229	74	8.0	3.6	12.7	5.2	-	-	38	13	16.9	8.1	23.8	12.3	74.1	38.1	13.5	5.6	-	42.2
	P	86	19	64	34	214	65	7.4	3.6	12.8	5.6	4.8	2.4	37	13	17.2	10.2	25.4	18.6	83.5	68.0	12.3	5.4	-	57.8
	Avg	84	19	44	33	136	97	5.8	3.5	9.5	5.8	-	-	32	15	10.6	10.1	15.4	17.3	50.6	62.5	9.3	5.7	0.12	36.4

[a,b,c] Only three subjects (MAS 3,4, n=1,2) could perform fast stretch velocities

Table 3.8. Catch-release parameters of spasticity subjects during passive extension.

Spasticity (n=15) Extension

Score	Stretch Speed	Catch-release Behavior															
		θ_{catch} (°)		α_{catch}(°/s²)		τ_{catch}(Nm)		$\theta_{release}$ (°)		$\alpha_{release}$(°/s²)		$\tau_{release}$(Nm)		$\tau_{post-release}$(Nm)		$E_{post-release}(J)$	
		$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD
MAS-1 (n=3)	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	F	69	20	-1804	662	13.3	0.6	99	15	-689	23	8.3	0.7	7.8	0.7	8.1	2.1
	P	84	7	-1614	438	8.8	4.2	101	13	-296	71	4.9	1.1	6.6	1.4	3.5	1.7
	Avg	77	17	-1709	569	11.0	3.7	100	14	-492	203	6.6	1.9	7.2	1.2	5.8	3.0
MAS-2 (n=4)	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	M	36	23	-611	277	6.4	1.9	42	22	186	186	4.7	2.1	5.9	0.9	5.4	1.1
	F	54	20	-899	384	11.2	1.8	70	22	88	309	7.6	2.0	7.8	1.7	7.1	1.2
	P	54	18	-825	341	11.0	1.7	70	21	-90	226	8.3	1.6	8.3	1.1	7.0	1.4
	Avg	50	22	-814	370	10.0	2.7	63	25	69	283	7.1	2.4	7.5	1.6	6.7	1.4
MAS-3 (n=4)	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	M	46	13	-1278	925	15.8	7.9	52	11	164	264	5.4	3.7	8.7	3.2	3.6	1.7
	F[a] (n=1)	50	1	-727	175	15.2	1.3	63	4	-425	31	13.5	0.4	15.1	0.1	10.0	0.0
	P	46	11	-1275	627	14.6	5.8	54	10	190	186	5.3	3.0	7.4	3.1	3.4	1.9
	Avg	46	11	-1218	728	15.0	6.3	54	11	117	277	6.2	4.0	8.6	3.7	4.2	2.6
MAS-4 (n=4)	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	M	45	9	-846	211	9.4	3.5	53	9	62	137	7.2	2.6	8.0	4.4	4.6	2.6
	F[b] (n=2)	42	20	-1004	580	13.1	7.9	49	20	154	179	9.5	6.7	12.4	6.7	6.6	2.2
	P	48	13	-997	211	12.2	6.5	56	15	47	222	9.7	5.8	10.9	7.4	6.0	3.6
	Avg	45	15	-946	355	11.5	6.2	53	15	80	190	8.8	5.3	10.3	6.5	5.7	3.0
Total (n=15)	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	M	43	15	-938	623	10.9	6.3	50	14	124	206	6.0	3.1	7.8	3.7	4.4	2.1
	F[c] (n=12)	51	21	-1010	553	12.4	4.8	65	24	-27	367	8.9	4.4	10.0	4.8	7.3	1.9
	P	51	16	-1136	512	12.8	5.8	60	19	60	246	7.3	4.5	8.7	5.1	4.9	2.9
	Avg	49	18	-1041	564	12.1	5.7	59	21	52	285	7.4	4.3	8.8	4.7	5.5	2.7

[a,b,c] Only some severely spastic subjects (MAS 3 (n=1), MAS 4 (n=2)) could perform fast stretch velocities

Table 3.9. Outcome parameters of spasticity subjecting during passive flexion.

Spasticity (n=15) Flexion

Score	Stretch Speed	Key Outcome Parameter												Non-Key Outcome Parameter									
		ROM (°)		ω_{avg}		ω_{max}		τ_{avg}		τ_{max}		$\Delta\tau$		θ_{ω_max}(°)		S_{avg}		S_{std}		S_{max}		E_{norm}		SSD	Catc
		$\bar{x}$	ST	$\bar{x}$	ST	$\bar{x}$	STD	$\bar{x}$	ST	$\bar{x}$	ST	$\bar{x}$	ST	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	$\bar{x}$
MAS-1 (n=3)	S	10	5	11	1	22	2	2.7	1.2	4.5	1.2	-	-	38	22	2.1	0.7	2.7	0.9	9.9	3.6	4.6	2.2	-	0.0
	M	91	6	59	15	86	18	2.5	0.8	4.0	0.9	-	-	60	21	4.5	1.6	5.5	2.3	17.4	7.0	4.8	1.6	-	0.0
	F	10	8	16	85	288	129	3.4	1.5	7.4	2.7	-	-	52	13	22.6	9.4	25.7	8.5	56.3	18.0	6.9	3.5	-	11.1
	P	98	9	17	70	298	104	2.9	1.0	7.5	2.3	0.	1.1	51	13	22.8	5.6	24.2	6.6	56.5	19.9	6.1	2.3	-	22.2
	Avg	98	8	10	89	173	148	2.9	1.2	5.9	2.5	-	-	50	19	13.0	11.2	14.5	11.8	35.0	25.7	5.6	2.7	-0.0022	10.3
MAS-2 (n=3)	S	10	14	13	2	26	4	4.6	3.7	7.2	5.7	-	-	34	18	2.1	0.8	2.5	0.8	8.0	2.4	7.4	5.9	-	0.0
	M	10	13	72	23	117	48	4.2	2.0	7.1	3.5	-	-	65	25	6.5	2.8	6.6	2.8	20.6	8.3	8.1	4.4	-	0.0
	F	10	12	15	34	252	35	5.8	2.1	12.	3.4	-	-	51	10	20.2	2.8	18.6	3.8	50.6	8.6	12.	4.8	-	11.1
	P	11	8	14	21	295	43	6.6	2.0	11.	2.9	2.	2.8	46	8	22.8	3.4	25.0	5.4	58.3	16.3	13.	5.2	-	33.3
	Avg	10	12	96	62	172	113	5.3	2.7	9.6	4.7	-	-	49	20	12.9	9.2	13.2	9.7	34.4	23.1	10.	5.7	0.010	12.8
MAS-3 (n=5)	S	87	10	11	3	23	6	8.6	3.4	12.	4.8	-	-	23	15	2.9	0.8	3.4	0.9	12.9	3.4	13.	4.9	-	0.0
	M	88	10	55	9	112	12	9.9	3.2	16.	5.6	-	-	39	10	13.1	4.9	12.4	4.4	39.9	16.2	20.	6.3	-	0.0
	F[a] (n=4)	94	9	62	16	236	25	15.	4.5	26.	7.2	-	-	37	8	28.0	11.6	40.4	17.6	124.8	58.1	30.	8.9	-	60.0
	P	87	7	67	21	215	29	13.	6.7	23.	9.5	5.	3.1	40	10	26.0	13.4	32.4	17.0	96.3	44.7	27.	12.	-	66.7
	Avg	89	10	48	27	142	88	11.	5.5	19.	8.8	-	-	35	13	16.9	13.6	21.2	19.0	65.5	56.6	22.	10.	0.081	35.4
MAS-4 (n=4)	S	72	14	8	2	22	8	8.1	3.3	10.	3.6	-	-	15	6	3.0	0.7	3.7	0.8	12.4	2.0	13.	5.5	-	0.0
	M	71	11	49	19	107	24	8.3	4.1	13.	4.8	-	-	40	22	12.3	3.7	15.3	5.7	56.2	25.6	16.	6.8	-	0.0
	F[b] (n=0)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	P	65	11	64	31	149	25	7.9	4.7	14.	8.1	-	2.8	34	14	16.7	4.7	20.3	8.6	69.0	32.7	16.	8.5	-	33.3
	Avg	69	12	40	32	92	57	8.1	4.1	12.	6.0	-	-	30	19	10.7	6.7	13.1	9.2	45.9	34.1	15.	7.2	0.17	10.3
Total (n=15)	S	91	17	11	3	23	6	6.4	4.0	9.4	5.4	-	-	27	18	2.6	0.9	3.2	1.0	11.1	3.6	10.	6.2	-	0.0
	M	88	15	58	18	106	29	6.7	4.2	11.	6.7	-	-	49	22	9.7	5.2	10.3	5.6	34.4	21.8	13.	8.3	-	0.0
	F[c]	10	11	12	70	256	78	9.1	6.4	16.	9.9	-	-	46	12	24.0	9.7	29.4	15.4	82.0	52.0	18.	12.	-	26.2
	P	90	18	10	61	236	81	8.7	6.3	15.	9.4	1.	2.4	42	13	22.6	9.5	26.4	12.5	73.8	37.2	17.	11.	-	42.9
	Avg	92	16	70	62	148	110	7.6	5.4	12.	8.4	-	-	32	15	14.0	11.4	16.4	14.6	47.9	42.9	14.	10.	0.065	19.8

[a,b,c] Only a few severe spasticity subjects (MAS 3 (n=4), MAS 4 (n=0)) could perform fast stretch velocities.

[d] MAS 4 subjects had severe arm contractions and abnormal resting arm postures that reduced the range of motion during flexion.

Table 3.10. Catch-release parameters of spasticity subjects during passive flexion.

Spasticity (n=15) Flexion

Score	Stretch Speed	Catch-release Behavior															
		θ_{catch} (°)		α_{catch}(°/s²)		τ_{catch}(Nm)		$\theta_{release}$ (°)		$\alpha_{release}$(°/s²)		$\tau_{release}$(Nm)		$\tau_{post-release}$(Nm)		$E_{post-release}(J)$	
		$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD	$\bar{x}$	STD
MAS-1 (n=3)	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	F	71	0	-1811	0	8.0	0.0	88	0	329	0	3.3	0.0	4.7	0.0	2.2	0.0
	P	77	2	-2190	222	8.4	1.0	92	3	675	214	1.7	0.0	4.1	0.5	1.9	0.4
	Avg	75	3	-2063	255	8.3	0.8	91	3	559	239	2.2	0.8	4.3	0.5	2.0	0.3
MAS-2 (n=3)	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	F	51	0	-331	0	9.4	0.0	110	0	-454	0	4.4	0.0	6.2	0.0	7.6	0.0
	P	59	22	-810	326	10.0	1.5	93	19	77	475	5.5	0.9	7.3	0.9	6.5	2.0
	Avg	57	19	-690	350	9.8	1.4	97	18	-55	471	5.2	0.9	7.0	0.9	6.8	1.8
MAS-3 (n=5)	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	F[a] (n=4)	63	6	-1266	419	28.5	6.7	75	8	126	186	18.9	6.5	20.8	6.8	10.6	3.5
	P	61	6	-1184	432	28.8	6.0	69	5	80	237	23.3	5.6	24.4	6.2	10.3	3.4
	Avg	62	6	-1223	428	28.7	6.3	72	7	102	216	21.2	6.4	22.7	6.7	10.4	3.5
MAS-4 [d] (n=4)	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	F[b] (n=0)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	P	34	3	-485	113	25.3	1.9	38	4	-106	111	19.0	3.5	15.6	1.7	6.1	2.9
	Avg	34	3	-485	113	25.3	1.9	38	4	-106	111	19.0	3.5	15.6	1.7	6.1	2.9
Total (n=15)	S	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	F[c] (n=10)	63	7	-1231	499	24.9	9.8	79	13	92	248	16.2	8.3	18.0	8.6	9.6	4.0
	P	58	16	-1117	585	22.8	9.6	71	20	115	346	17.2	9.5	17.8	9.3	8.0	4.1
	Avg	60	13	-1160	556	23.6	9.7	74	18	106	313	16.8	9.1	17.9	9.0	8.6	4.1

[a,b,c] Only a few severe spasticity subjects (MAS 3 (n=4), MAS 4 (n=0)) were able to perform fast stretch velocities. [d] MAS 4 subjects had severe arm contractions and abnormal resting arm postures that reduced the range of motion during flexion.

3.4.3 LIMITATIONS

A limitation of this study was the sole reliance on measuring mechanical responses for investigating spasticity and rigidity. Some argued that these mechanical responses can be less sensitive to changes in motoneuronal excitability and more influenced by factors other than spasticity and rigidity, for example, the rheological changes in muscle properties [28]. Thus, one can argue that measurement of motoneuronal activity such as recordings of electromyographic (EMG) signal is more important than measuring biomechanical responses for accurately understanding the pathophysiology of spasticity and rigidity. While the surface EMG electrodes of the PVRM did not have high enough resolution of muscle activity data to be used for investigation of motoneuronal activity, the use of EMG may not be practical in a clinical setting or even necessary. Incorporation of EMG in a clinical setting can be impractical if not impossible due to the requirements demanded by a clinical setting, that is relatively inexpensive, time-efficient, and simple method for assessing abnormal muscle conditions. For accurate and reliable EMG readings, it is critical to prepare the skin thoroughly to remove dead skin cells to optimize conductivity of the [134–136]. In addition, the surface EMG sensors may not be needed since the clinicians can usually monitor the muscle activation status of the patient from haptic feedback.

3.4.4 TRAINING SIMULATOR DESIGN GUIDELINES

To mimic spasticity and rigidity for medical training purposes, two types of simulators have been developed: 1) an electromechanical simulator that exerts resistive torque from a motor programmed using a closed loop torque control and an angular position sensor feedback [17,58,62], or 2) a mechanical simulator that utilizes a hydraulic damper system to mimic velocity dependent resistance [59,61]. Both types of simulators allowed for adjustments of

different levels of hypertonicity to replicate different muscle behaviors of different severities of hypertonicity (e.g. a mechanical simulator with adjustable setting that replicates MAS 1-4 muscle response) [59,61].

While a mechanical simulator has advantages over an electromechanical simulator, such as requiring no power supply, an electromechanical simulator can be a more promising choice for reproducing different types of hypertonicity. Spasticity and rigidity have very different muscle behavior in terms of stretch velocity dependency and catch presence. This may cause numerous design complications for mechanical simulators, since the mechanical designs that mimic one type of hypertonicity (e.g., spasticity) may contradict other designs that replicate other types of hypertonicity (e.g., rigidity). For example, a robust simulator needs to not only recreate increased muscle resistance with catch-release behavior for spasticity, but also be able to replicate uniformly increased muscle tone without catch-release behavior for rigidity. In addition, the triggering of catch-release behavior needs to be stretch speed dependent and occur intermittently, adding more design complexities. Finally, the reactive torque from the simulator needs to be continuous and smooth for healthy muscle and mild spasticity, requiring tighter tolerances for manufacturing. All these challenges can increase the developmental and manufacturing time and costs. However, an electromechanical simulator can allow for high adjustability of joint kinematic and kinetic behaviors for all levels of rigidity, spasticity, and even other types of hypertonicities such as dystonia with less complications. The occasional presence of catch can be programmed into the controller of an electromechanical simulator by randomizing the occurrence of catch. Higher MAS level can increase the probability of catch occurrence, since severe spasticity subjects displayed more frequent catch-release behavior (Tables 3.7, 3.9). A mechanical simulator can be used to replicate one specific type of

hypertonicity, but an electromechanical simulator may be needed to recreate multiple types of hypertonicity.

3.4.5 POTENTIAL AND FUTURE WORK FOR CLINICAL APPLICATION

The PVRM can be potentially used as a clinical screening tool for evaluating hypertonicity. The key outcome parameters introduced in this study can assist in distinguishing spastic, rigid, and healthy muscles from the PVRM data. Spasticity and rigidity could be differentiated from healthy muscles using parameters related to muscle tone. Range of motion may also differentiate severe spasticity patients, as severely spastic patients demonstrated reduction of range of motion due to permanent contractures (Tables 3.5,3.6,3.7,3.9). To distinguish spasticity from rigidity, one may detect for presence of catch-release behavior. If catch is not present, the stretch speed dependency of muscle tone (SSD) can evaluated, since muscle tone from spasticity was more sensitive to stretch velocity than hypertonia from rigidity (Figure 3.6, Tables 3.5,3.6,3.7,3.9). Through future studies with more comprehensive subject demographics, it may be even possible to distinguish different levels of spasticity and rigidity using SSD and muscle tone related parameters, since these metrics and the MAS/UPDRS scores displayed an ordinal relationship.

Some of the key outcome parameters can differentiate not only the type but also the severity of the hypertonicity. For example, parameters relating to muscle tone ($\tau_{avg}, \tau_{max}, S_{avg}, S_{max}, S_{std}, E_{norm}$) can distinguish spastic and rigid muscles from healthy muscles, and parameters describing the stretch speed dependency of tone (i.e., SSD) can separate

spasticity from rigidity. In addition, the magnitudes of these parameters can classify different levels of hypertonicity. For example, MAS scores are proportional to SSD, and UDPRS scores are proportional to parameters relating to muscle tone. Classifying the type and severity of hypertonicity can be beneficial to clinicians and patients for identifying and monitoring the progression of the underlying neurological disorder. Although qualitative scales such as the Modified Ashworth Scale (MAS) are used currently for this purpose, inexperienced clinicians have difficulty reliably assessing hypertonicity using these scales due to the heavy reliance on the rater's personal experience and interpretation of the scales. Therefore, the key outcome parameters presented in this study can potentially help the medical community by providing a new quantitative scale established from the PVRM data collected in future studies. Also, the PVRM can be optimized to automatically output a MAS or UPDRS score after a clinical assessment, alleviating clinicians from the burden of relying on past training experiences and subjective interpretation of the qualitative scales.

With further development and additional studies, the PVRM can be optimized to automatically output a MAS or UPDRS score after a clinical assessment, alleviating clinicians from the burden of purely relying on past training experiences and subjective interpretation of the qualitative scales. To deploy the PVRM in a clinical environment, the PVRM hardware needs to be optimized for better ergonomics and reduce setup time. The current version of the PVRM uses a uniaxial load cell that cannot monitor unwanted torque from tilting or twisting motion, so the clinician needs to apply the load as perpendicular to the moving module as possible. Hence, the usability of the PVRM can be improved by replacing the uniaxial load cell with a 6-axis load cell sensor that can decouple any unwanted torque applied, allowing the clinician to freely apply the load to the moving module. Alternatively, it may be possible to create a wearable device that

the clinician can done to quantify the applied load, similar to the prototype glove developed by Garudadri et al. [137]. Also, the two PVRM modules and the three surface electromyographic (sEMG) electrodes can be simplified to a single moving module to improve the setup time. While the sEMG electrodes provide information regarding muscle activation status, the EMG electrodes may be omitted in the future versions of the PVRM due to the long setup time such as skin preparation and the calibration process to establish activation thresholds. Clinicians can typically sense voluntary muscle activation during the clinical assessments. The contents of the main module can be moved to the moving module, reducing the overall size and setup time of the PVRM even further. Knowing the relative joint angle from a single inertial measurement unit (IMU) could be enough to assess other key outcome parameters. In addition, the PVRM cover plate design needs revision to allow for the same arm position during flexion and extension assessments. In our study, the arm position during flexion was perpendicular to the ground, while the arm position during extension was parallel to the ground. For practical clinical use and more direct comparison of data, flexion and extension should involve a similar movement plane relative to the ground so that the PVRM can capture data from sequential flexion and extension cycles. Finally, the PVRM design should be revised to allow assessments of hypertonicity about multiple joints in the body such as the wrist, shoulder, hip, knee, and ankle. In particular, PVRM should accommodate assessments for knee and ankles, the two most common joints affected by spasticity, since assessments of these joints have been reported to have the lowest inter-rater reliability [53].

Future studies with more test subjects and raters can be proposed. Additional subjects must be recruited to comprehensively represent the spasticity and rigidity population to perform statistical analysis to quantify inter-group and intra-group differences. More subjects should be

recruited for each MAS and UPDRS level. In addition, more raters with varying level of relevant clinical experience should be involved to investigate the feasibility of PVRM usage in a clinical and even residential setting to determine if the PVRM can reproduce repeatable results regardless of the rater's experience. Ultimately, a new clinical scale can be introduced that is based on quantitative data rather than clinical observations. The currently used clinical scales such as MAS and UPDRS were based on qualitative observations from clinicians that may not fully represent all levels of spasticity and rigidity patient population. Thus, a quantitative scale established from the data such as that collected by the PVRM may allow for an automated classification of different levels of spasticity and rigidity.

The testing protocol of the PVRM also needs revision in the future studies. First, the MAS score should be reported for every trial since a few of the MAS subject's score changed during every test trial. These score changes could be attributed to not only the loosening of muscles due to frequent passive movements, but also other factors such as the stress level of the subject and inherently fluctuating nature of hypertonicity [1,3]. Second, the arm posture during flexion test trials should be similar during extension test trials. In our study, the arm position during flexion was approximately perpendicular to the ground, while the arm position during extension was almost parallel to the ground. For practical clinical use and more direct comparison of data, flexion and extension should involve a similar movement plane relative to the ground. Third, stretch speed for each test trial should be randomized instead of being sequential. Since hypertonia arising from spasticity and rigidity may change after numerous stretches of the muscle, the torque data collected near the end of test trials (i.e. fast and preferred stretch speeds) may be downscaled in our study.

3.5 CONCLUSIONS

The PVRM (Position, Velocity, and Resistance Meter) was used to evaluate the kinetic and kinematic data (angular position, velocity, and muscle resistance) during passive flexion and extension of healthy, spastic (MAS 1-4), and rigid (UPDRS 1-3) biceps and triceps at various stretch speeds. Key outcome parameters (e.g., range of motion, average and max stretch velocity, average and peak muscle resistance, difference in resistance at fast and slow stretch velocity, and catch presence) were computed from the raw PVRM data to provide a preliminary database quantifying spasticity and rigidity. This database can serve as a reference i) for understanding the abnormal muscle behaviors, ii) for optimizing designs of medical devices, and iii) for providing insight into developing algorithms for classifying spastic, rigid, and healthy muscles. Medical simulator development can benefit from this database to fine tune the simulators for more realistic replication of hypertonicity. Most importantly, the PVRM itself can serve as a clinical screening tool to reliably screen for the type and degree of hypertonicity without relying on subjective scales that require extensive training and experience.

3.6 ACKNOWLEDGEMENTS

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CHAPTER 4: CONCLUSIONS

4.1 REVIEW OF FINDINGS

4.1.1 DESIGN AND VALIDATION STUDY OF THE PVRM

In Chapter 2, we present a study where we designed and validated a portable custom measurement device (the PVRM – Position, Velocity, and Resistance Meter) that quantified abnormal muscle behaviors (i.e., spasticity and rigidity) of biceps and triceps in terms of kinetic and kinematic data during passive movement. The PVRM consisted of two modules (main and moving) and three surface electromyographic (sEMG) electrodes (biceps, triceps, and reference). The moving module was fastened on the participant's wrist, while the main module was attached on the upper-arm. As a clinician applied force on the moving module to stretch the subject's arm, the PVRM recorded the biomechanical data (i.e., angular position, speed, and force) during the passive movement. The data processing module computed the sampled time and biomechanical data from the main and moving modules and received the electromyographic (EMG) data from the electrodes.

These PVRM modules were designed with three main design goals: 1) to provide accurate and reliable data describing muscle tone and movement of spastic and rigid arms, 2) to present an ergonomic and patient-friendly device that can be used in a clinical setting, and 3) to accommodate different geometries and sizes of muscles seen in both upper and lower extremities. To achieve the first design goal, we chose small inertial measurement units (IMU) to measure the kinematic data (angular position, speed, and acceleration), uniaxial load cell to evaluate the kinetic data (muscle resistance), and sEMG electrodes to monitor for voluntary muscle activity. For the second goal, miniaturized electronics and customized printed circuit boards were used to make the physical size of the PVRM smaller. In addition, the PVRM

transferred data wirelessly via Bluetooth module, removing the setup necessary for electrical cables. To accomplish the third goal, the main and moving modules of the PVRM contained a Velcro strap that can be easily adjusted to different shapes and sizes of the muscle. Therefore, the PVRM can quantify muscles in not only upper-extremities but also lower-extremities as well. After the development of the PVRM, we conducted a validation study to verify the accuracy and reliability of its measurements and to receive design feedback from the clinicians and patients.

The validation study confirmed the accuracy of the PVRM measurements by comparing it to measurements (angular position, speed, and applied torque) from a commercial dynamometer (i.e., Biodex), a gold standard for quantifying biomechanical data. The study tested subjects with upper-arm spasticity (n=3), rigidity (n=2), and healthy muscles (n=5). The dynamometer stretched the subject's arm via a custom-fabricated lever arm. The moving module of the PVRM was secured to the end of the lever arm, allowing the PVRM to measure the same kinetic and kinematic data measured from the Biodex dynamometer. The PVRM measurements were similar to the gold standard Biodex measurements during the passive flexion movement, since the residuals for all measurements were between 1-13%. The angular position and angular speed measurements of the PVRM were observed to be sufficiently accurate for quantifying kinematic behavior of all subject categories and even at high stretch speeds. While the torque measurement was the least accurate compared to angular position and speed measurement, it was still accurate enough to be used in quantifying unique kinetic behavior of hypertonicity: 1) elevated tone and a distinct increase of muscle tone (i.e., catch) seen from spastic muscle, and 2) uniformly elevated tone without a sharp increase in tone displayed by rigid muscles. Therefore, the PVRM was able to quantify behavioral features of spasticity (e.g., catch-release behavior), rigidity (e.g., uniformly elevated muscle tone), and healthy (e.g., no muscle resistance) subjects.

4.1.2 CLINICAL STUDY USING THE PVRM

In Chapter 3, we present a clinical study using the validated PVRM to establish a preliminary database quantifying different levels of spastic and rigid arms during passive flexion and extension. Thirty-eight subjects with different levels of spasticity (n=15, MAS 1-4), rigidity (n=11, UPDRS 1-3), as well as gender-age matched healthy controls (n=12) were tested. A neurologist (CMZ) performed multiple stretches of the subject arm at four different stretch speeds (slow (5˚/s - 20˚/s), medium (20˚/s - 80˚/s), fast (> 80˚/s), and clinician's preferred speed (> 30˚/s)) while the subject wore the PVRM modules and EMG electrodes.

Key outcome parameters that quantify the unique muscle behaviors of spasticity and rigidity, (e.g., increased muscle tone, stretch speed dependency, presence of catch) were defined and analyzed. Spasticity subjects demonstrated stretch speed and MAS score *dependent* hypertonia marked by catch-release behavior, resulting in a convex parabolic stretch speed profile. Interestingly, catch-release behavior was only observed for approximately half the test trials, and the frequency of catch was higher for more severe spasticity subjects. As expected, catch-release behavior was triggered mostly at fast and preferred stretch speeds. Also, severe spasticity subjects (MAS 3, 4) had permanent muscle contractures that enhanced hypertonia and limited the range of motion. Rigidity subjects exhibited uniformly elevated muscle tone that was dependent on UPDRS score. The stretch speed dependency of rigidity differed based on the type of movement. Rigidity was slightly positively stretch speed dependent during extension, but negatively stretch speed dependent during flexion.

We investigated the underlying pathophysiological mechanisms to explain these behavioral features of spasticity and rigidity by referencing past studies that examined the stretch reflex thresholds of hypertonicity [28,45,46,123–125]. For patients with hypertonicity, the range

of spatial threshold of stretch reflex fell within the biomechanical range of the moving limb, causing a motor deficit. This motor deficit can be identified as spasticity and rigidity. Further studies involving the stretch reflex activity and biomechanical behavior will be necessary to verify the pathophysiological mechanisms of hypertonicity.

For spasticity trials, a few cases of unexpected muscle behavior were observed including 1) excessive releases after catch during flexion trials, and 2) resemblance between spasticity without catch and rigidity in terms of kinetic behavior. For rigidity trials, excessive torque was sometimes applied at the start of the range of motion due to tilting of the load cell. Other times, the resistance increased linearly to joint angle, and the slope of this resistance profile was proportional to the UPDRS score. However, these irregular muscle behaviors happened in only a small percentage of the test trials.

Some of the key outcome parameters can differentiate not only the type but also the severity of the hypertonicity. For example, parameters relating to muscle tone ($\tau_{avg}, \tau_{max}, S_{avg}, S_{max}, S_{std}, E_{norm}$) can distinguish spastic and rigid muscles from healthy muscles, and parameters describing the stretch speed dependency of tone (i.e., SSD) can separate spasticity from rigidity. In addition, the magnitudes of these parameters can classify different levels of hypertonicity. For example, MAS scores are proportional to SSD, and UDPRS scores are proportional to parameters relating to muscle tone. Classifying the type and severity of hypertonicity can be beneficial to clinicians and patients for identifying and monitoring the progression of the underlying neurological disorder. Although qualitative scales such as the Modified Ashworth Scale (MAS) are used currently for this purpose, inexperienced clinicians have difficulty reliably assessing hypertonicity using these scales due to the heavy reliance on

the rater's personal experience and interpretation of the scales. Therefore, the key outcome parameters presented in this study can potentially help the medical community by providing a new quantitative scale established from the PVRM data collected in future studies. Also, the PVRM can be optimized to automatically output a MAS or UPDRS score after a clinical assessment, alleviating clinicians from the burden of relying on past training experiences and subjective interpretation of the qualitative scales.

4.2 FUTURE WORK

The PVRM hardware design needs more iterations to provide better ergonomics and improved user-experience for the clinician and the patient. The usability of the PVRM can be enhanced by changing the uniaxial load cell with a 6-axis load cell sensor that can decouple any unwanted force and torque applied, allowing the rater to freely apply the load in multiple direction to the moving module. Thus, raters can still use their own assessment techniques without significant changes when using the PVRM during assessments of hypertonicity. In addition, the system of the PVRM can be simplified into a single module that collects, processes, stores, and transmits the PVRM and patient data. The EMG electrodes may be omitted in the future versions of the PVRM due to the long setup time for accurate EMG recordings.

The testing protocol of the PVRM also needs revision in the future studies. First, the MAS score should be reported for every trial since a few of the MAS subject's score changed during every test trial. These score changes could be attributed to not only the loosening of muscles due to frequent passive movements, but also other factors such as the stress level of the subject and inherently fluctuating nature of hypertonicity [1,3]. Second, the arm posture during

flexion test trials should be similar during extension test trials. In our study, the arm position during flexion was approximately perpendicular to the ground, while the arm position during extension was almost parallel to the ground. For practical clinical use and more direct comparison of data, flexion and extension should involve a similar movement plane relative to the ground. Third, stretch speed for each test trial should be randomized instead of being sequential. Since hypertonia arising from spasticity and rigidity may change after numerous stretches of the muscle, the torque data collected near the end of test trials (i.e. fast and preferred stretch speeds) may be downscaled in our study.

We still suggest future studies with more test subjects and raters, since we only tested three subjects per level of spasticity and rigidity. Additional subjects must be recruited to comprehensively represent the patient population to perform more reliable statistical analysis on the quantitative differences between spasticity and rigidity. We recommend that at least fifteen subjects be recruited for each level of MAS and UPDRS. In addition, more raters with varying level of relevant clinical experience should be involved to determine if the PVRM can reproduce repeatable results regardless of the rater's previous experience. Another potential future study can be the investigation of hypertonicity for lower extremities, since hypertonicity about the ankles and knees are common [130,131]. After optimizing the PVRM hardware design as mentioned above, the PVRM modules can be easily implemented for various muscle groups. Other possible studies may include quantifying the effect of treatments for spasticity (e.g., baclofen and Botox injections) and rigidity (e.g., deep brain stimulation and levodopa) using the PVRM [138,139]. Selecting the proper dosage and timing for these medications is important to minimize the side effects [138]. For example, too much dosage of baclofen may cause excessive weakening of muscles and tiredness, while too little dosage may not help with reducing

spasticity [138]. The PVRM can help with not only quantifying the efficacy of these treatments, but also providing the clinicians and patients with a proper dosage of medications for effective and safe treatment.

In the long-term future, the author envisions extensive use of technology quantifying the symptoms of neurological disorders in the clinical setting for more accurate and reliable assessments. The two problems faced in the field of neurology are the shortage of neurologists and the difficulty of screening for neurological disorders in the early stages of development. In 2012, the shortage of neurologists was 11% and is expected to grow to 19% by 2025 [140]. According to Vidic et al., "In the absence of efforts to increase the number of neurology professionals and retain the existing workforce, current national and geographic shortfalls of neurologists are likely to worsen, exacerbating long wait times and reducing access to care for Medicaid beneficiaries. Current geographic differences in adequacy of supply likely will persist into the future." [140]. Also, many motor and non-motor symptoms of neurological disorders are often ambiguous, making the screening process difficult and subjective. For example, the motor and non-motor section (e.g., tremor, gait, posture, hand movements, facial expressions, handwriting, motivation, speech, salivation) of the Unified Parkinson's Disease Rating Scale (UPDRS) all rely on subjective interpretation of the scales, since qualitative words such as "mildly affected" and "severely affected" are used to describe different levels of rigidity. With the advent of cost-effective sensors and advanced algorithms, these motor and non-motor symptoms are quantifiable [141,142]. For example, a camera can record the facial expressions, gait, and posture of the PD patients and look for traits of distinct PD [142]. Given a large database of speech patterns from PD patients, machine learning algorithms can be implemented to screen for PD from audio data collected via a microphone [141].

I predict that patients in the future can be diagnosed in a room equipped with quantifying devices (e.g., cameras, microphones, PVRM's) that objectively evaluate patient's behaviors related to motor and non-motor symptoms (e.g., gait, posture, speech, rigidity). The patient will follow a set of instructions (e.g., walking/running on a straight path or reading a sentence displayed on a screen) with a help of a nurse or general practitioner while the devices record the patient's behaviors. If the patient exhibited distinctive signs of PD or other neurological disorders, he or she can be referred to a neurologist nearby. Hence, the patient can not only be screened earlier for neurological disorders but also the chances of misdiagnosis can be reduced with the use of these technologies, alleviating the neurologist's burden while providing the patients with more available and standardized diagnosis [117,141–143]. Developing this technology will require extensive interdisciplinary collaboration including fields such as neurology, computer science, and engineering in order to fuse the ample data collected from various sensors together and process the multidimensional data to accurately diagnose the patient. Thus, the research of the PVRM should be conducted in conjunction with other emerging technologies to strive for convenient but accurate diagnosis that benefit patients and clinicians.

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APPENDIX A: SUPPLEMENTARY FIGURES AND RESULTS FOR VALIDATION STUDY

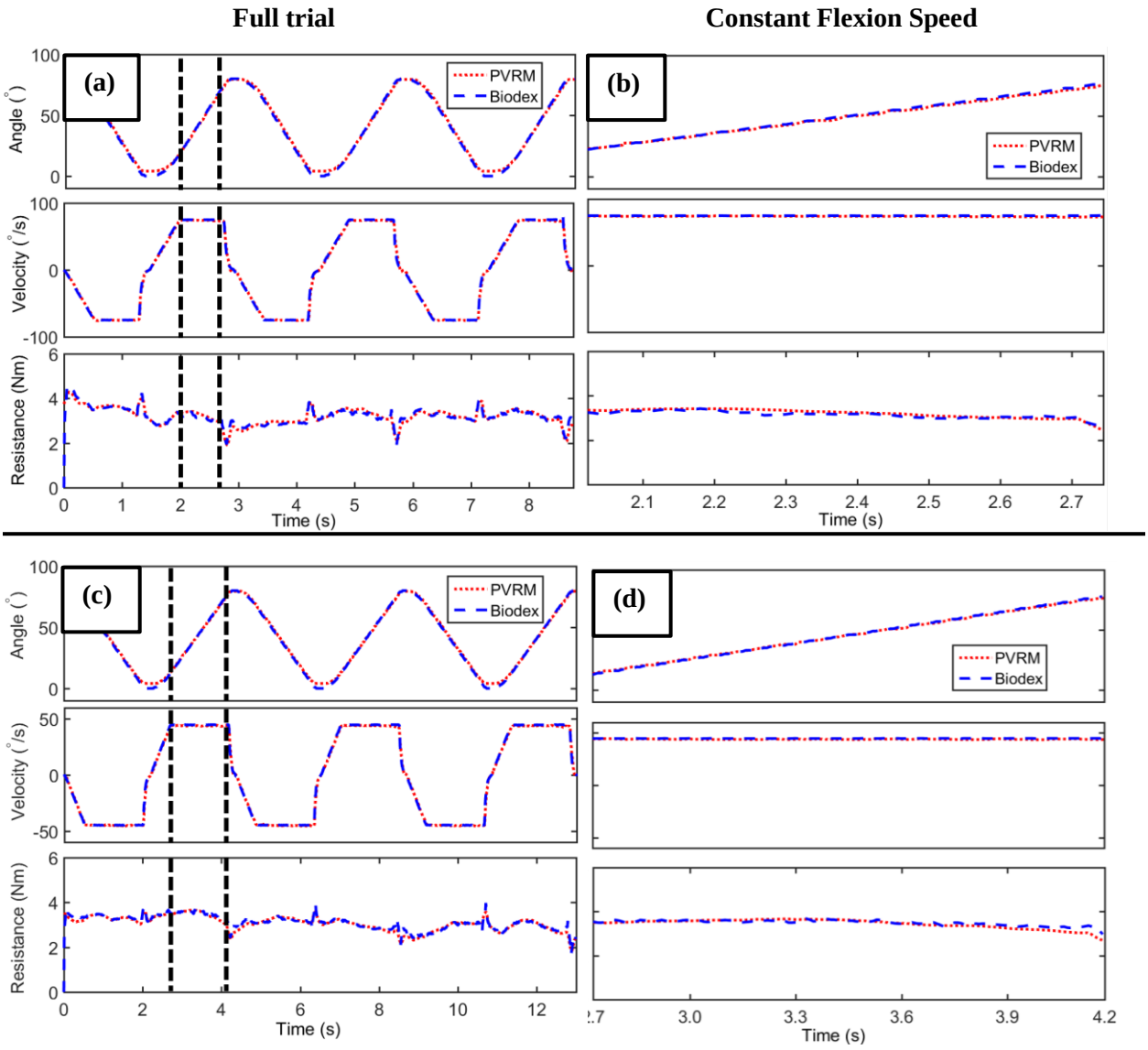

Figure A.1. Comparison between the PVRM and Biodex data during a full trial (left column) and constant flexion speed (right column) for a control subject (C4) during flexion (a, b) at 75˚/s, and (c, d) at 45˚/s. The constant flexion-speed-region (vertical dashed lines) in full trial plots was extracted.

APPENDIX B: ESTIMATING MASS, CENTER OF MASS LOCATION, AND MOMENT OF INERTIA OF LOWER ARM

The effect of gravity and inertia of the lower arm (forearm and wrist) had to be removed from the PVRM torque data to analyze just the muscle resistance due to spasticity or rigidity. To do so, the mass (M), center of mass length (L_{com}), and moment of inertia (I) about the elbow was estimated using empirical anthropometric equations and simple static equations shown below [101].

$$M\ (kg) = body\ mass\ (kg) \times \frac{P_{gender}(\%)}{100} \quad \begin{cases} P_{gender} = 2.52\ , if\ gender = male \\ P_{gender} = 2.07, if\ gender = female \end{cases}$$

$$L_{COM}\ (m) = 0.652 \times forearm\ length(m)$$

COM length was defined as the distance from the elbow epicondyle along the ulna bone.

$$I\ (kg * m^2) = I_{centroid}\ + ML_{COM}^2 = \frac{1}{3} ML_{lower-arm\ length}^2 + ML_{COM}^2$$

Moment of inertia was about the rotation axis of the elbow joint which was obtained through parallel axis theorem. The moment of inertia of the lower-arm (forearm and wrist) about its centroid ($I_{centroid}$) was simplified as a rod with lower-arm length and lower-arm mass, rotating about one end.

APPENDIX C: INSTITUTIONAL REVIEW BOARD (IRB) APPROVAL LETTERS FROM UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN (UIUC) AND UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE AT PEORIA (UICOMP)

UNIVERSITY OF ILLINOIS
AT URBANA-CHAMPAIGN

Office of the Vice Chancellor for Research
Office for the Protection of Research Subjects
805 West Pennsylvania Ave
Urbana, IL 61801

Date: September 12, 2017

Elizabeth Hsiao-Wecksler
Mechanical Science & Engineering
124 MEB
1206 West Green Street
Urbana, IL 61801

RE: *Evaluation of Hypertonic Muscle Behavior Using a Custom-Fabricated Measurement Device*
IRB Protocol Number: 16478

Dear Dr. Hsiao-Wecksler:

Thank you very much for forwarding the modifications to the University of Illinois at Urbana-Champaign Institutional Review Board (IRB) office for your project entitled *Evaluation of Hypertonic Muscle Behavior Using a Custom-Fabricated Measurement Device*. I will officially note for the record that these minor modifications to the original project, as noted in your correspondence received August 16, 2017, updating the research team, changing payment, adding Clark-Lindsey Village as a performance/research site, increasing participant estimates, and adding additional funding have been approved. The expiration date for this protocol, IRB number 16478, is 01/26/2018. The risk designation applied to your project is *no more than minimal risk*.

As your modifications involved changes to consent form(s), I am attaching the revised form(s) with date-stamp approval. Please note that copies of date-stamped consent forms must be used in obtaining informed consent. If modification of the consent form(s) is needed, please submit the revised consent form(s) for IRB review and approval. Upon approval, a date-stamped copy will be returned to you for your use.

Please note that additional modifications to your project need to be submitted to the IRB for review and approval before the modifications are initiated. To submit modifications to your protocol, please complete the IRB Research Amendment Form (see https://www.oprs.research.illinois.edu/forms-templates/forms/protocol-amendment-form). Unless modifications are made to this project, no further submittals are required to the IRB.

We appreciate your conscientious adherence to the requirements of human subjects research. If you have any questions about the IRB process, or if you need assistance at any time, please feel free to contact me at the OPRS office, or visit our website at https://www.oprs.research.illinois.edu.

Sincerely,

Rebecca Miller, MSW
Human Subjects Research Specialist, Office for the Protection of Research Subjects

Attachment(s) Consent documents, Research team application, Collaborating Investigator Agreement

c: Yinan Pei
Seung Yun Song

U of Illinois at Urbana-Champaign • IORG0000014 • FWA #00008584
Telephone (217) 333-2670 • email IRB@illinois.edu

Figure C.1. Institutional Review Board (IRB) approval letter from University of Illinois at Urbana-Champaign (UIUC) IRB

UNIVERSITY OF ILLINOIS
COLLEGE OF MEDICINE AT PEORIA

Institutional Review Board
One Illini Drive
Box 1649
Peoria, Illinois 61656-1649

FWA 00005172

IRB #00000688
IRB #00000689

DATE:	July 18, 2017
TO:	Christopher Zallek, MD
FROM:	University of Illinois College of Medicine at Peoria IRB 1
STUDY TITLE:	[859104-8] Evaluation of Hypertonic Muscle Behavior Using a Custom-Fabricated Measurement Device
IRB REFERENCE #:	
SUBMISSION TYPE:	Continuing Review Response/Follow-Up - Missing HIPAA language added to Informed Consent Forms
ACTION:	APPROVED
APPROVAL DATE:	July 13, 2017
EXPIRATION DATE:	July 12, 2018
REVIEW TYPE:	Expedited Review

Thank you for your submission of Continuing Review Response/Follow-Up materials for this research study. University of Illinois College of Medicine at Peoria IRB 1 has approved your renewal submission for one year of study. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Expedited Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

The University of Illinois College of Medicine at Peoria's (UICOMP) Office of Human Research Oversight (OHRP) will no longer accept local or non-local adverse events or safety reports for IRB review that do not meet the definition of an unanticipated problem involving risks to subjects or others (UPIRSO).

UPIRSOs are any incident, experience, or outcome that meets all of the following criteria:

1. are not expected (in terms of nature, severity or frequency) given (a) the research procedures that are described in the protocol-related documents (such as the research protocol and informed consent document); and (b) the characteristics of the subject population being studied;
2. are related or possibly related to participation in the research; and

3. suggest that the research places subjects or others at greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.

If you have any questions, please contact Deb Wolf at (309) 680-8632 or debwolf@uic.edu. Please include your study title and reference number in all correspondence with this office.

cc:

Figure C.2. Institutional Review Board (IRB) approval letter from University of Illinois College of Medicine at Peoria (UICOMP) IRB. The UICOMP's IRB approval allowed us to conduct testing at Bradley University, Peoria IL.