THE FEASIBILITY OF MEASURING REHABILITATION-INDUCED CHANGES IN UPPER LIMB MOVEMENT AND COGNITION USING ROBOTIC KINEMATICS IN CHRONIC STROKE

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Abstract

Background: Robotic measurement of kinematics is a potential method to detect precise rehabilitation-induced changes in upper limb movement and cognition post-stroke. To what degree robot-derived data aligns with other gold-standard upper limb measurement tools has yet to be described. Such comparisons would be important for translating such tools to research and clinical practice.

Methods: Using the Kinesiological Instrument for Normal and Altered Reaching Movement (Kinarm), we compared the relationship between robot-derived values and gold-standard clinical tests of upper limb performance and cognitive function before and after a rehabilitation intervention in patients with chronic stroke. The intervention involved 10 sessions of pairing aerobic exercise with skilled motor and cognitive practice. Participants underwent motor performance and cognitive function assessments using the Kinarm endpoint robot and standardized measurement scales at baseline, after the 10 intervention sessions and 30 days later.

Results: Ten participants with chronic upper limb impairment due to stroke (69.4 ± 12.9 years old: 7 males, 3 females) completed the intervention sessions. There were no significant improvements in upper limb recovery when measured using the clinical gold-standard tests. However, robotic kinematics variables showed significant changes in motor performance at follow-up. There were no significant changes in cognitive measures pre- and post-rehabilitation intervention.

Conclusion: Rehabilitation-induced changes in upper limb performance and cognitive changes may be effectively detected and quantified using robotic kinematics measures.

Keywords: Aerobic Exercise, Kinarm, Clinical tests, Stroke Recovery.

General Summary

This study investigated the effectiveness of using robotic measurements to detect and quantify changes in upper limb movement and cognitive function following a rehabilitation intervention for stroke patients. The research compared robot-derived data from the Kinesiological Instrument for Normal and Altered Reaching Movement (Kinarm) with gold-standard clinical tests. Ten participants with chronic upper limb impairment due to stroke underwent 10 sessions of aerobic exercise combined with skilled motor and cognitive practice. The results showed no significant improvements in upper limb recovery according to the clinical tests, but the robot-derived kinematics variables demonstrated significant changes in motor performance after the intervention. However, there were no significant changes in cognitive measures before and after the rehabilitation intervention. These findings suggest that robotic measurements may detect and quantify improvements in upper limb performance resulting from rehabilitation, providing valuable insights for research and clinical practice.

Keywords: Stroke recovery, aerobic exercise, Kinarm, clinical tests

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Co-Authorship Statement

This thesis represents original research conducted by Michael Babalola under the supervision of Dr. Michelle Ploughman. While collaboration and assistance were sought from various individuals, this co-authorship statement clarifies the contributions made by each party involved.

First and foremost, I would like to acknowledge the invaluable guidance and support my supervisor, Dr. Michelle Ploughman, provided. Her expertise and insightful suggestions significantly influenced the direction and quality of this research. Her input during the conceptualization, methodology development, and data analysis stages played a vital role in shaping the overall outcomes of this thesis.

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LIST OF ABBREVIATIONS AND SYMBOLS

Symbol/ Abbreviation	Meaning
ANOVA	Analysis of variance
cm	Centimeter
e.g.,	For example
FMA-UE	Fugl Meyer Assessment-Upper Extremity
FOLLOW-UP	Follow-up assessment
hrs	Hours
KINARM	Kinesiological Instrument for Normal and Altered Reaching Movement
MOCA	Montreal Cognitive Assessment
NL	Newfoundland and Labrador
OH	Object Hit
OHA	Object Hit & Avoid
OH_AffectedHandspeed	Object Hit AffectedHandspeed variable
OHA_Distractor_Hit_Total	Object Hit & Avoid Distractor Hit Total variable
PRE	Pre-intervention assessment
POST	Post-intervention assessment
SD	Standard deviation
WHO	World Health Organization
WMFT	Wolf Motor Function Test
±	Plus, or minus
%	Percentage
=	Equal

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1 CHAPTER ONE

1.1 OVERVIEW

Stroke incidence has increased significantly globally, making it an important area for research and intervention. Stroke ranks as the second leading cause of death worldwide, with an annual mortality rate of about 5.5 million and over 13 million new cases reported [1].

In Canada, stroke ranks third, after cancer and heart disease, as the leading cause of death[2]. Importantly, stroke results in severe and prolonged physical and cognitive disability, affecting individuals and their families for their lifetimes. Every year, approximately 62,000 people with stroke receive treatment in Canadian hospitals, with over 400,000 people living with its effects [3].Stroke has devastating consequences: approximately 66% of people who have a stroke will be left with some forms of disability [4]. Stroke costs the Canadian economy 3.6 billion dollars per year in lost wages, long-term disability, and patient-related health care costs [5].

The acute management of stroke involves a complex and time-sensitive process of evaluation, diagnosis, and treatment [6]. Despite advancements in medical technology and best practice guidelines, there are still gaps in the stroke management system that result in suboptimal patient outcomes. Two common treatments for acute ischemic stroke are tissue plasminogen activator and endovascular thrombectomy [7]. Although effective, only about 10% of patients receive these treatments. Limited access to facilities that provide tissue plasminogen activator and endovascular thrombectomy, inability to meet inclusion criteria, and a lack of trained medical personnel are all factors that impede timely access [8].

While tissue plasminogen activator and endovascular thrombectomy have been shown to be effective in improving outcomes, they may not provide complete recovery for all patients [9]. Rehabilitation, on the other hand, can play a crucial role in further improvement of functional outcomes and quality of life for stroke survivors [10], [11]. Rehabilitation programs should be individualized to address each patient's specific needs and should be started as soon as possible after the stroke event [12].

Effective stroke management requires a multidisciplinary approach that includes nurses, doctors, physical therapists, occupational therapists, psychologists and social workers [13]. Improving access to rehabilitation services, providing individualized treatment plans, and training healthcare professionals can improve patient outcomes and reduce the associated impairment due to stroke and its impact on patients and their families [14], [15].

Stroke-related impairments can vary greatly depending on the location and extent of the brain injury, but they often include physical, cognitive, and emotional difficulties, see Figure 1.1. Physical/Motor impairments can range from weakness or paralysis on one side of the body, to difficulty with fine motor skills, balance, and coordination. In severe cases, patients may need help with basic daily activities such as bathing, dressing, and eating [16]. Sensory impairments are also one of the most common impairments post-stroke, including loss of sensation in the face or limbs, difficulty with spatial awareness, or problems with the perception of objects [17], [18]. About 50%-80% of stroke survivors experience sensory abnormalities in tactile sensation (touch) or proprioception (awareness of body position), which may require sensory-specific training [19] [20].

Cognitive impairments after a stroke can include memory loss, difficulty with problem-solving and decision-making, and language and communication difficulties [21], [22]. These can

significantly impact a person's ability to perform daily tasks, including work, and may also lead to emotional challenges such as depression, anxiety, and frustration [23], [24]. Emotional impairments after a stroke can include changes in mood, such as depression and anxiety, and emotional lability (i.e., sudden and unpredictable changes in mood) [25]. These emotional changes can be particularly challenging for patients and their loved ones and may require additional support from mental health professionals.

The most noticeable deficit following a stroke is motor impairment. These impairments are extremely debilitating because they impair people's ability to perform daily tasks. The severity of the impairment can vary greatly depending on the extent of the damage in brain areas responsible for controlling movement and sensation in the arm, hand, and fingers, also an individual's age, general health, and prior level of physical function [26], [27]. Motor impairments significantly impact stroke survivors' functional activities, especially regarding the upper limb disability [28].

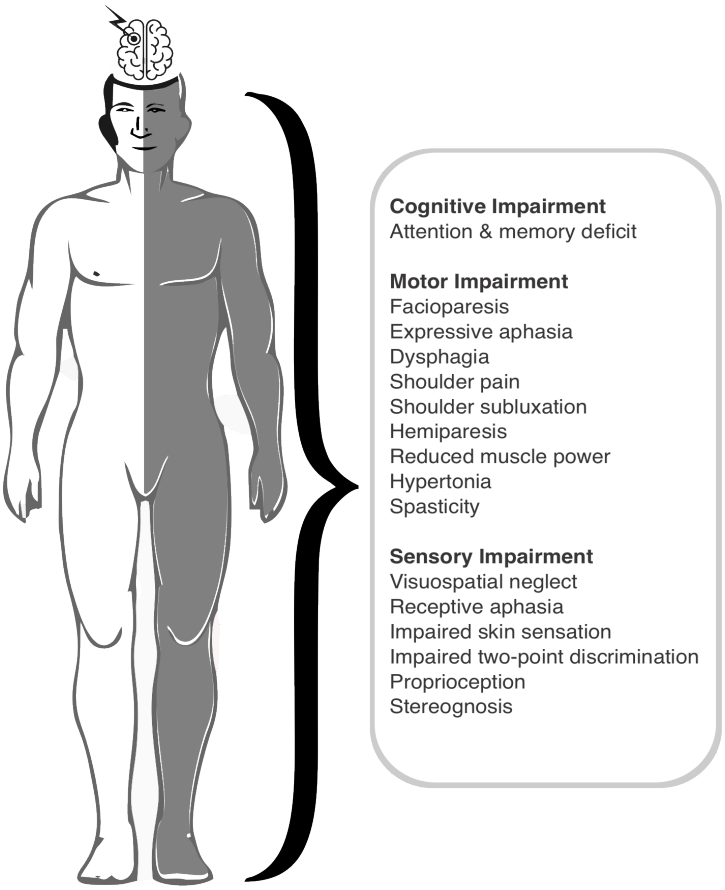


Figure 1.1 Stroke-related impairments. (Original Illustration by MB). The Grey area in the figure represents the affected side of the body contralateral to the stroke. Examples of the three main domains of stroke-related impairment, cognitive, motor, and sensory, are provided.

Neuroplasticity is the basic mechanism underlying improvement in functional outcome after stroke [29]. Therefore, one important goal of rehabilitating stroke patients is the effective use of neuroplasticity for functional recovery. A key principle of neuroplasticity is providing a high volume and intensity of task-specific training [30]. Therefore, high-dose intensive training and repetitive practice of specific functional tasks are important for recovery after stroke [30]. These requirements make stroke rehabilitation a labor-intensive process. Innovative methods to deliver and measure the effects of rehabilitation using robotics, are showing great promise [31], [32].

Robotic technology has advanced significantly in recent years, with new computing techniques, faster and more potent processors, and more sophisticated electro-mechanical components [33]. Robotics are now available for functional evaluation and as a therapy tool for rehabilitation intervention because of these technological breakthroughs. A robot is a programmable, multi-functional system created to move objects, parts, or specialized devices according to a set of predetermined movements [34]. The ability to offer high-dosage, high-intensity training and to quantitatively assess performance is one of the main benefits of adopting robot technology in rehabilitation interventions [35], [36]. Research into robotic rehabilitation and its usage, particularly in stroke rehabilitation, has significantly increased over the years [37]–[39]. The use of robotic technology in stroke rehabilitation helps to provide more accurate quantitative measures of participant performance and monitor, and carefully control, the dosage of therapy while providing consistent and engaging feedback to help stroke survivors comply with rehabilitation therapy.

The purpose of this study was to pilot the use of robotic outcome measures within an existing rehabilitation research intervention study. The first aim was to understand the feasibility of measuring rehabilitation-induced changes in upper limb movement and cognition using robotics kinematics in chronic stroke patients. The second aim was to determine the relationships between robot-derived upper limb performance outcomes and the gold standard clinical outcome measures.

This thesis contains three chapters. Chapter One is a literature review that introduces important concepts related to the current understanding of stroke and the physiological impact of the event. Chapter Two examines the feasibility of measuring rehabilitation-induced changes in upper limb movement and cognition using robotics kinematics in chronic stroke patients and determining the relationships between robot-derived upper limb performance outcomes and the

gold standard clinical outcome measures. Lastly, Chapter Three provides an in-depth discussion of the results expanding upon how these results answered the primary research questions and addressing potential study limitations and future research directions.

1.2 STROKE

1.2.1 The Etiology of Stroke

Stroke is a medical emergency that occurs when blood flow is disrupted to the central nervous system, which results in cell death and is associated with a focal loss of neurological function and may even cause loss of life [33], [34]. Stroke is classified into two types: ischemic and hemorrhagic. Ischemic stroke occurs in 80% of cases and is caused by insufficient blood supply to certain parts of the brain [33]. Hemorrhagic stroke occurs in 20% of cases and is caused by spontaneous hemorrhage, an uncontrolled leaking of blood into surrounding brain tissue or on the brain's surface [34], [35].

Stroke can occur for a variety of reasons, both in young adults and older populations [36]. Individuals with a greater number of associated risk factors such as persistent hypertension, vasculitis, coronary heart disease, obesity, poor cardiorespiratory fitness, cigarette smoking, diabetes, and other comorbid conditions have a high chance of experiencing a stroke [37], [38]. Some risk factors are modifiable and can be addressed with increased fitness, proper diet and nutrition, and identifying and treating medical conditions that increase stroke risk [39], [40].

1.2.2 Population Impact of Stroke

Stroke is the second leading cause of death in the world and the leading cause of disability-adjusted life years [41], [42], a measure used to quantify burden in terms of years lost due to disease. Recent global estimates show that 101.5 million people experienced a stroke in 2019, and 3.3 million people died [43], which is 6 times higher than the recorded estimate of 16.9 million people with stroke in 2010 [44]. In Canada, over 800,000 new cases of stroke have been recorded [45], with Newfoundland and Labrador having the highest rates [46], making the issue particularly

important for this country and province. These statistics show that there is an urgent need to address primary and secondary stroke prevention and treatment through research and intervention.

1.2.3 Trajectory of recovery after stroke

According to the Stroke Roundtable Consortium's proposed categorization, the post-stroke period is commonly divided into several phases. The hyperacute phase refers to the first 24 hours after a stroke, followed by the acute phase lasting up to 7 days, the early sub-acute phase spanning the initial 3 months, the late sub-acute phase occurring between months 4 and 6, and finally, the chronic phase extending beyond 6 months [47], [48]. This distinction is based on the time-dependent nature of recovery processes following a stroke. Shortly after cerebral ischemia, a series of mechanisms that enhance plasticity is triggered, resulting in the growth of dendrites, the sprouting of axons, and the formation of new synaptic connections [49], [50]

The recovery trajectory after a stroke varies depending on the individual's age, the severity of the stroke, and the location of the brain affected [51]. Recovery can be influenced by various factors such as capacity for neuroplasticity, the intensity of rehabilitation received, and social support [52]. The recovery trajectory after a stroke typically follows a pattern, with the most significant recovery occurring in the first few weeks to months after the stroke. This initial recovery period is followed by a slower phase of recovery, which can last several years. After this phase, some individuals may reach a plateau in their recovery, while others may continue to make progress [47], [53].

Neuroplasticity refers to the brain's ability to adapt and reorganize itself, especially after injury, and is crucial in recovery after a stroke. Rehabilitation, including physical therapy, occupational therapy, and speech therapy, can help individuals regain lost function and improve

their quality of life. Social support, including family and community support, can also aid recovery. Various challenges associated with stroke recovery include fatigue, depression, and cognitive impairments. These challenges can affect an individual's ability to participate in rehabilitation and impact their overall recovery trajectory [54].

1.2.4 Impact of Stroke on the Individual

Stroke can affect four major brain areas (cortical, subcortical, cerebellar, and brainstem), each with a distinct set of clinical symptoms depending on the level and brain regions affected. A variety of clinical symptoms and deficits emerge, including language impairments, somatosensory impairments, cognitive impairments, and motor impairments [55]. Language deficit can impair an individual's ability to engage in communication during daily activities [56]. Somatosensory impairment affects the ability to effectively process sensory information received by sensory receptors on the skin. It can include a reduced ability to feel touch, discomfort, warmth, position, or the ability to identify items in your hands [57]. Cognitive impairment and memory loss are common post-stroke with up to fifty percent of stroke survivors estimated to develop neurocognitive disorder [58], [59]. These deficits persist in 40% to 60% of stroke patients in the chronic stage [60], thereby increasing the challenges of motor recovery by making it more difficult to relearn lost skills.

1.3 MOTOR IMPAIRMENTS IN STROKE

1.3.1 Motor consequences of stroke

Following a stroke, the high prevalence of motor impairments may be due to its tendency to damage motor regions of the cortex coordinating movement and function [61], [62]. Motor impairment frequently affects the upper limb, making it difficult to use hands and fingers and limiting the ability to perform routine tasks like cooking and cleaning. Motor deficits post-stroke are characterized by weakness, decreased muscle activation, abnormal muscle co-activation, and other impairments that reduce movement capacity and alter spatiotemporal coordination of movements. Spasticity is a condition defined by an abnormal increase in muscular tone or stiffness, which may interfere with movement or be accompanied by discomfort or pain [63]. As a result of spasticity, movements are slower and more irregular, with limb reach trajectories that are less precise and more extraneous.

1.3.2 Motor impairment classification and measurement

The classification of motor impairment in stroke is based on the severity, location, and type of motor deficit. The National Institutes of Health Stroke Scale is one of the most used measures for classifying stroke severity. The National Institutes of Health Stroke Scale (NIHSS) measures the degree of impairment in consciousness, language, neglect, visual field loss, motor function, ataxia, sensory loss, and dysarthria. A study by Kasner et al. (1999, 2006) found that the NIHSS is reliable for assessing stroke severity and can predict long-term outcomes [64], [65]. Although useful, the outcome tool combines all impairments' ratings into one score, so it is difficult to discern changes in a specific domain, such as the upper extremity. Limb-specific standardized measures have been developed to measure motor impairment in stroke, including the Fugl-Meyer

Assessment for both the arm and leg and the Wolf Motor Function Test (WMFT) for the upper limb.

The Fugl-Meyer Assessment involves asking the patient to attempt to move the affected limb joint by joint, comparing the quality of movement to the less affected side. It is a commonly used measure for assessing motor impairment in stroke survivors. Hernandez et al. (2019) reported strong validity and reliability of the Fugl-Meyer Assessment in measuring motor impairment in stroke survivors (see Appendix A) [66].

The WMFT is a standardized clinical assessment tool used to evaluate upper extremity motor function in people who have had a stroke or other neurological conditions. The test consists of 17 tasks designed to assess the upper extremities' speed, strength, and dexterity, such as picking up small objects, turning a key in a lock, and manipulating objects. The test measures both the time to complete tasks and the quality of movement. It is frequently used in clinical and research settings to evaluate treatment outcomes and plan rehabilitation interventions [67]. Beverly et al. (2020) reported the graded WMFT's reliability in measuring upper limb function post-stroke (see Appendix F) [68].

1.4 COGNITIVE IMPAIRMENT IN STROKE

1.4.1 Cognitive impairment and assessment

Cognitive impairment is a common consequence of stroke that can significantly impact a person's quality of life [69]. The degree and type of cognitive impairment vary depending on the location and severity of the stroke. The impairments can affect various cognitive domains such as attention, memory, language, executive function, and visuospatial abilities [70].

Recent research has shown that cognitive impairment significantly predicts long-term functional disability, mortality, and quality of life after stroke [71]–[74]. Therefore, it is essential to identify and treat cognitive impairment in stroke patients to improve their outcomes.

Various approaches to assessing cognitive impairment after stroke include neuropsychological assessments, cognitive screening tools, and brain imaging [75], [76]. Rehabilitation interventions such as cognitive training, occupational therapy, speech therapy, and exercise can effectively improve cognitive function in stroke patients [77]–[80].

Cognitive measurements are essential tools clinicians and researchers use to evaluate various aspects of an individual's cognitive functioning [81]. The Montreal Cognitive Assessment (MOCA: see Appendix B) and the Raven's Standard Progressive Matrices Test (Raven's; see Appendix C) are commonly used cognitive measurements.

The MOCA is a 30-point test that measures various domains of cognitive function, including attention, memory, language, visuospatial abilities, and executive functions. It is a screening tool for mild cognitive impairment and dementia. The test takes approximately 10 to 15 minutes to administer and is more sensitive than other cognitive screening tools in detecting early cognitive changes [82].

The Raven's Standard Progressive Matrices Test (Raven's), on the other hand, is a nonverbal test of abstract reasoning and problem-solving skills. It consists of 60 items that require participants to complete a series of matrices by identifying the missing piece that completes the pattern. The test measures fluid intelligence, which refers to reasoning, solving problems, and thinking abstractly [52]. The test takes approximately 40 to 60 minutes and has no time limit. The Raven's test has been shown to be a reliable and valid measure of fluid intelligence and has been used extensively in research settings [83].

The MOCA and Raven's tests are widely used and validated cognitive assessment tools, but they measure different aspects of cognitive function. The MOCA is a comprehensive test that assesses multiple domains of cognition, while Raven's test precisely measures abstract reasoning ability. These tools can be used together or separately to provide a complete picture of an individual's cognitive function.

1.5 PERFORMANCE ASSESSMENT MEASURES

1.5.1 Characteristics of outcome measures

An outcome measure is used to evaluate a patient's condition. An outcome measure may offer a score, an explanation of the findings, and occasionally a patient risk classification. An outcome measure offers baseline information before any intervention is given. The results from the measures might be used to guide treatment decision-making. The same tool used to evaluate a patient's condition may be utilized in subsequent assessments after treatment to determine whether the patient has shown change [84].

Outcome measures used in clinical practice can be classified into two types: (1) measures based on self-report (subjective) and (2) measures based on performance (usually objective). Self-report measures are typically collected using a questionnaire. The questionnaires are graded using a predetermined point system based on the patient's responses. Performance-based measures require that the patient perform a series of movements or tasks. Performance-based measures can have scores based on either an objective measurement (e.g., time to complete a task) or a qualitative assessment that is assigned a score (e.g., normal, or abnormal mechanics for a given task). Using technology to measure human performance is considered to be more objective and sensitive compared to observer-reported measures [85]–[88].

The psychometric properties of an outcome measure are important features to consider. Psychometric properties are key characteristics of an outcome measure. These properties include reliability, validity, sensitivity, responsiveness, feasibility, floor and ceiling effects, content and construct validity, clinical relevance, and utility [84], [89]. Reliability refers to the degree to which the measure produces consistent results over time and across different raters. Validity is the degree to which the measure accurately measures what it is intended to measure. Sensitivity is the ability of the measure to detect change over time [90]. Responsiveness is the ability of the measure to detect a clinically meaningful change in response to an intervention. An outcome measure should also be feasible regarding the ease of use and practicality of the measure in a clinical setting. Floor and ceiling effects refer to the degree to which the measure can detect change at the lower and upper limits of function. Clinical relevance is the extent to which the measure is meaningful and relevant to the patient and clinician. Finally, it must be useful to guide clinical decision-making and improve patient outcomes.

1.6 ROBOTICS IN STROKE REHABILITATION

1.6.1 Importance of rehabilitation interventions in stroke recovery

Rehabilitation interventions play a vital role in the recovery of stroke survivors by improving their functional outcomes and reducing the burden on caregivers [91]. Rehabilitation interventions are tailored to the individual's specific impairments and may include physical therapy, occupational therapy, speech and language therapy, and cognitive rehabilitation. Research has demonstrated that early intervention in stroke recovery is crucial, and rehabilitation should begin as soon as possible after a stroke [91]. Evidence suggests that intensive rehabilitation in the early stages of stroke recovery leads to better outcomes, including improved mobility, reduced

spasticity, improved cognition, and enhanced activities of daily living [92]. However, rehabilitation should be continued throughout the recovery process, as the brain can adapt and rewire even years after a stroke [93].

In addition to traditional rehabilitation interventions, emerging technologies, such as virtual reality and robotics, show promise in stroke rehabilitation. These technologies can provide a more engaging and immersive rehabilitation experience, leading to better outcomes [94]. Robotics can be used to deliver high volumes of limb motor practice that would otherwise require a high degree of costly human effort. Robotics can also help to measure, more sensitively, the motor and cognitive changes that occur during rehabilitation which can determine whether the rehabilitation approach is working or not.

1.6.2 The use of robotics in stroke rehabilitation for motor function

Robotic-assisted therapy has been shown to have several benefits in stroke rehabilitation [95]. Firstly, it allows for repetitive and consistent movements, which are essential for relearning motor skills. Also, robotics provide real-time feedback, which helps patients improve their movement accuracy and speed. Secondly, using robotics provides a safe and controlled environment for patients to practice their movements, which can help prevent secondary injuries. Finally, robotics allow for individualized therapy, as the devices can be customized to meet each patient's specific needs [96], [97]. Studies have shown that robotic-assisted therapy could be more effective, in contrast to traditional rehabilitation methods, in improving motor function and reducing disability. For example, a systematic review of the effect of robot-aided therapy on recovery of the hemiparetic arm after stroke found that robotic-assisted therapy was associated with significant improvements in upper limb function, muscle strength, and activities of daily

living [98]. Another study found that using robotics in stroke rehabilitation improved motor function and decreased muscle tone in the upper extremities [99].

The use of robotics in rehabilitation has led to significant improvements in motor outcomes, including motor strength, coordination, and dexterity [100]–[103]. A study by Susan S. Conroy et al. 2019 investigated the effectiveness of two robot-assisted interventions on motor outcomes in stroke patients with chronic upper extremity motor deficits. The study included 45 participants assigned to either 60 minutes of robot therapy or 45 minutes of robot therapy combined with 15 minutes of therapist-assisted transition-to-task training. The study found that chronic upper extremity motor deficits were responsive to intensive robot-assisted therapy of 45 or 60 minutes per session. Individuals with stroke with moderate to severe levels of arm disability can benefit from high-intensity robot-mediated repetitive task practice with or without real-world task-specific training [103].

Another study by Hung et al. 2016 compared the efficacy of two robot-assisted interventions on motor function and quality of life in patients with chronic stroke. The study included 21 participants who were randomized into either robot therapy combined with task-specific training or robot therapy combined with impairment-oriented training. The study showed significant within-group improvements in motor function, muscle power, and quality of life [102].

Rachele Bertani et al., 2017, in a systematic review, assessed the effectiveness of different robotic devices compared to other interventions for stroke rehabilitation. Compared to conventional therapy, the review found that robot-assisted rehabilitation improves upper limb motor function recovery, especially in chronic stroke patients. The primary outcomes measured were motor function and muscle tone, using the Fugl-Meyer Assessment and modified Ashworth

scale. Secondary outcomes were measured using the functional independence measure and motor activity log for activities of daily living [100].

In summary, these studies suggest that robot-assisted interventions, whether combined with task-specific or impairment-oriented training, can effectively improve motor function and quality of life in patients with chronic upper extremity motor deficits due to stroke. Robot-assisted rehabilitation is also found to be more effective than conventional therapy in improving upper limb motor function recovery, especially in chronic stroke patients. However, there is limited evidence regarding the benefits of robotics rehabilitation therapy on cognitive function in stroke patients. While some studies have suggested potential cognitive benefits, such as improved attention, memory, and executive functions, however the efficacy of a robotic intervention in improving cognitive function still needs to be explored [104], [105].

In a pilot study conducted by Aprile et al. 2020, the impact of a technological rehabilitation intervention on cognitive functions in patients with stroke was explored using three robots and one sensor-based device for upper limb rehabilitation. The study included 51 patients enrolled within 6 months post-stroke who underwent 30 rehabilitation sessions. The intervention included motor/cognitive exercises selected to train cognitive functions. The study found that a significant percentage of impaired patients exhibited cognitive deficits. After the treatment, patients improved in all the investigated cognitive domains, as measured by selected cognitive assessment scales. However, the long-term benefits of the improvement were not tracked in this study [104].

Another recent study by Bui et al. 2023 aimed to investigate the relationship between cognitive and motor performance on a robotic rehabilitation system in individuals with stroke. The study included 31 participants with a stroke who completed a trajectory-tracking task using the Haptic Thera Drive rehabilitation robot system. The study found that visuospatial and executive

function significantly impacted motor performance on the robot-based task, with differences emerging between different functional groups on various robot-based metrics. The study suggests that cognitive domains involved in the visuomotor tracking task can significantly predict motor performance on the robot-based task and that impairment in these domains results in worse motor performance than subjects with no cognitive impairment. These studies suggest that robotic interventions have the potential to improve cognitive function in individuals with stroke, further research is needed to understand better the potential benefits of robotic rehabilitation therapy on cognitive outcomes in stroke patients and to optimize the use of robotic devices to maximize the overall efficacy of stroke rehabilitation programs.

The use of robotics in stroke rehabilitation is becoming increasingly important due to key factors. Firstly, the aging population is increasing, and stroke is more prevalent in older adults. As a result, the demand for effective stroke rehabilitation methods is growing. Secondly, there is a need for more trained healthcare professionals, particularly in low-income countries. Robotics can help address this shortage by providing an automated and standardized rehabilitation process. Finally, robotics can help reduce healthcare costs by decreasing the length of hospital stays and the need for multiple healthcare professionals [106].

Using robotics as an outcome measure is a newer approach [107], [108] and data is emerging suggesting it could be useful to detect therapy-induced changes during stroke rehabilitation [109]–[111]. However, further research is needed to optimize the use of robotics in stroke rehabilitation and to determine the most effective ways to incorporate it into clinical practice.

1.6.3 Kinematic measures of upper limb behavioral tasks

Kinematic measures of upper limb behavioral tasks include joint angles, movement time, and movement velocity, which help researchers to understand the subtle aspects of motor behavior [112]. Kinematics were traditionally measured using motion capture systems. Motion capture systems usually involve placing reflective markers on the body while multiple cameras around a room record walking or reaching movements. The technique is challenging because it requires multiple specially trained personnel, and the participant will usually have to disrobe in order that the markers can be applied.

Recent studies have shown that kinematic measures, such as movement time, velocity, and smoothness, can be used to assess upper limb deficits in stroke patients [113], [114]. These measures have also been shown to be sensitive to changes in upper limb function following rehabilitation [115], [116]. Furthermore, kinematic measures have been used to identify cognitive changes in individuals with Parkinson's disease [117], [118] and traumatic brain injury [119].

Despite the promising findings, several gaps exist in using kinematic measures for upper limb deficits and cognitive changes. One of the challenges is the need for more standardization in selecting kinematic measures and protocols across studies [120]. Lack of standardization makes it difficult to compare results across studies and limits the ability to establish clear guidelines for clinical use.

Another gap in the literature is the limited use of kinematic measures in individuals with more severe neurological conditions or cognitive impairments [121]. However, some studies have included individuals with severe impairments [122], and kinematic measures in this population still need to be explored. This is particularly relevant as these measures may be more challenging for individuals with severe deficits and require additional technological resources. While some

measures may be sensitive to certain impairments, others may be less informative. Therefore, kinematic measures should be tailored to the specific deficits being assessed and the populations being studied.

1.6.4 Using Robotics to measure motor and cognitive impairment in stroke

Robotics can provide objective and quantitative measures of motor and cognitive impairments in stroke patients [123]–[125]. A review of hand rehabilitation robotic technology showed that several robotic devices, including exoskeletons, end-effectors, and robotic arms, have been used to assess motor functions such as muscle strength, coordination, and range of motion [126]. For instance, a study by Ortmann et al. (2020) used a robotic exoskeleton to measure hand grip strength in stroke patients [127]. They found that the robotic device provided more accurate, reliable, and precise measurements than traditional manual tests.

Despite the promising results of using robotics to measure motor and cognitive impairments in stroke patients, several gaps in knowledge still exist. Most studies have focused on using robotics to measure upper limb function, with limited studies on lower limb function and cognition. Secondly, the optimal robotic devices and protocols for measuring motor and cognitive functions in stroke patients still need to be clarified. Thirdly, whether robots can sensitively track meaningful improvements over time is not known. Using robotics to measure motor and cognitive impairments in stroke patients is a promising area of research that can potentially improve the assessment and rehabilitation of stroke patients.

1.6.5 Using the Kinarm to measure motor and cognitive impairment in stroke

The Kinesiological Instrument for Normal and Altered Reaching Movement (Kinarm) is a robotic device that allows for interactive assessment of sensorimotor and cognitive brain function using behavioral tasks involving the upper limb using a suite of behavioral tasks called Kinarm Standard Tests ™ (KSTs) (BKIN Technologies Ltd., Kingston, ON, Canada) [128], [129]. There are two types of Kinarm robotic devices; the Kinarm Exoskeleton Lab which permits arm flexion and extension in the horizontal plane to support the upper limb of users (particularly individuals with severe musculoskeletal dysfunction) while attempting the KSTs, and the other type is the Kinarm Endpoint Lab, which requires individuals to grasp a handle attached to the end of a robotic arm [130], [131]. The endpoint bimanual robotic device permits free movement of the upper extremities in the horizontal plane while seated. The key difference between the two robots is that the Exoskeleton cradles the arm such that hand grip is not required to operate the machine while the Endpoint permits more natural movement but requires hand grip. See **Figure 1.2** for the depiction of the two types of Kinarm robotic devices that display the virtual reality system in which the visual targets appear in the same plane as the arms, and **Table 1.1** for a detailed description of KSTs [132].

Figure 1.2 Kinarm Exoskeleton (Left side), Kinarm Endpoint (Right side). The images above depict two types of Kinarm robot devices. On the left is the exoskeleton type, while on the right side is the endpoint type. © Copyright BKIN Technologies 2023. All Rights Reserved (Received Permission to use).

Kinarm Standard Tasks ™		
Test	**Brain Function**	**Duration**
Motor		
Object Hit	Rapid visuomotor skills, spatial skills	2.5 min
Visually Guided Reaching	Visuomotor skills multi-joint coordination	2 min/arm
Ball on Bar	Bimanual coordination visuomotor skills	3.5 min
Arm Posture Perturbation	Goal-directed motor corrections	2 min/arm
Elbow Stretch	Assess presence of spasticity and high tone	5 min/arm
Cognitive		
Object Hit & Avoid	Rapid motor decisions, Inhibitory control Spatial attention	2.5 min
Reverse Visually Guided Reaching	Cognitive control of visuomotor skills, Inhibitory control attention	3.5 min/arm
Trails A & B	Executive function; task switching	2.5 min
Spatial Span	Visuospatial working memory	5.5 min
Paired Associated Learning	Visuospatial working memory	5 min
Sensory		
Arm Position Matching	Somatosensation: position sense	3 min/arm
Arm Movement Matching	Somatosensation: kinesthesia	3 min/arm

Table 1.1 A detailed description of KSTs

The table provides a detailed description of all the Kinarm Standard Tasks, including the ones used in the study, the name of the tasks, the specific motor function assessed, and any additional relevant details for each task.

The Kinarm is a cutting-edge robotic device that has gained attention as a promising tool for measuring motor and cognitive function in stroke survivors [133]. However, there is a need to understand further the relevance and application of this robotic device in clinical research, particularly stroke.

A key consideration in using Kinarm for measuring motor and cognitive impairments in stroke patients is its feasibility across patients with varying severities of impairment. Several recent studies have examined the feasibility of using Kinarm in stroke patients with different levels of impairment. For example, a study by Mochizuki et al. (2019) investigated the feasibility of using Kinarm Exoskeleton to measure motor function in chronic stroke patients with mild to severe motor impairments. Seventy individuals over 18 years of age in Canada with stroke were divided into Spasticity (n=35) and No Spasticity groups (n=35). Upper limb function was characterized using two tasks using the Kinarm robot: Visually Guided Reaching, in which participants moved the limb from a central target to 1 of 4 or 1 of 8 outer targets when cued (measuring reaching function), and Arm Position Matching, in which participants moved the less-affected arm to mirror-match the position of the affected arm (measuring proprioception), which was passively moved to 1 of 4 or 1 of 9 different positions. The results showed that Kinarm measures were feasible in patients with a wide range of motor impairments, indicating its potential as a tool for assessing motor function in stroke patients with varying levels of severity [134]. Similarly, another study by Lowrey et al. (2022) evaluated the feasibility of quantifying impairments in cognitive-motor integration following stroke. Fifty-nine participants with subacute stroke (occurs 7 days to 6 months post-stroke) were recruited to perform two tasks using the Kinarm Exoskeleton: Reverse Visually Guided Reaching and Visually Guided Reaching. Impairments in Reverse Visually Guided Reaching improved over time, but 71% of participants tested longitudinally were still

impaired with the affected arm ~6 months post-stroke and 57% were impaired with the less affected arm at 6 months. These individuals were not impaired in visually guided reaching. Individuals with stroke were impaired in reverse reaching tasks, but many did not show similar impairments in a standard reaching task, highlighting selective impairment in cognitive-motor integration. The study suggested that Kinarm could detect cognitive impairments across a wide range of severities, suggesting that it may be a viable tool for assessing cognitive function in stroke patients with diverse cognitive deficits. These findings collectively suggest that Kinarm is feasible for use in stroke patients with different severities of impairments. However, further research is needed to validate its reliability and validity in these populations, especially using the Kinarm Endpoint, and whether it detects change as a result of an intervention [135].

An essential aspect of assessing the effectiveness of Kinarm as a tool for measuring motor and cognitive impairments in stroke patients is its sensitivity to change which refers to its ability to detect meaningful changes in motor and cognitive function over time. Some studies have reported promising results in detecting motor and cognitive performance changes using the Kinarm robot in other neurological disorders. For example, a study by Simmatis et al. (2017) explored the effectiveness of the Kinarm Exoskeleton robot in measuring changes in hand dexterity in patients with Transient Ischemic Attacks over 1 year of follow-up. They recruited 48 individuals to the cohort and 28 to the migraine cohort. Individuals in both groups displayed impairments on robotic tasks within 2 weeks of symptom cessation and approximately 1 year after symptom cessation, most commonly in tests of cognitive-motor integration. The Transient Ischemic Attack cohort participants were assessed at 2, 6, 12, and 52 weeks after symptom resolution. Migraineurs were assessed at 2 and 52 weeks after symptom resolution. The study showed that up to 51.3% of people in the Transient Ischemic Attack cohort demonstrated an impairment on a given task within 2

weeks of symptom resolution, and up to 27.3% had an impairment after 1 year. In the migraine group, these numbers were 37.5% and 31.6%, respectively [136]. Similarly, Andrushko et al. examined the effectiveness of Kinarm Endpoint in measuring changes in cognitive-motor function in patients with chronic stroke at a one-time point (24 hrs.) post-rehabilitation. The study found that Kinarm could detect significant improvements in cognitive function in rehabilitation patients, suggesting that the device was sensitive to change, however, it is worth noting that participants had high scores (average of 52) on the Fugl-Meyer Upper Limb Assessment so had very mild impairment [137]. Longitudinal studies are needed to determine the sensitivity of Kinarm in detecting changes in motor and cognitive function over time post-rehabilitation and responsiveness to treatment especially among patients with a wide range of motor impairment [138]. Additionally, research comparing Kinarm outcomes with other established motor and cognitive function measures would further validate its sensitivity to change and enhance its clinical utility.

Another critical aspect of evaluating the use of Kinarm for measuring motor and cognitive impairments in stroke patients is its alignment with gold-standard clinical measures. Clinical measures such as the Fugl-Meyer Assessment and Wolf Motor Function Test to assess motor function and the Mini-Mental State Examination, Montreal Cognitive Assessment, and Standard Raven's Progressive Matrices for cognitive function are commonly used as standard assessments in stroke research and clinical practice (outcome measures in stroke rehabilitation). While Kinarm has shown promising results in measuring motor and cognitive impairment in stroke survivors, limited research has examined its alignment with established clinical measures commonly used in stroke rehabilitation. A study by Otaka et al. (2015) compared Kinarm Exoskeleton outcomes with clinical assessment of the upper limb in hemiparetic stroke patients. Fifty-six participants with a hemiparetic arm due to chronic stroke were recruited. Participants used the paretic and non-

paretic arms to complete clinical and robotics assessments. They found that the robot-derived measures could successfully differentiate between the paretic and non-paretic arm performances and were valid compared to the well-established clinical scales [139].

Despite the promising results from studies investigating the effectiveness of the Kinarm robot in measuring impairments, there is still a need for further research to establish its effectiveness compared to traditional clinical assessments and its sensitivity to detect recovery changes after rehabilitation interventions. Specifically, more studies are needed to fully validate the use of the Kinarm robot as a reliable and valid tool for assessing upper limb function in clinical practice and in people with a broad range of impairments. Furthermore, there is much less data available using the Kinarm Endpoint robot which requires functional grasp yet provides more natural movement trajectories than the Exoskeleton. Therefore, additional research is necessary to provide further evidence of the benefits and limitations of using the Kinarm robot in assessing and treating patients with neurological conditions.

Hence, the primary objective of this research is to investigate and elucidate the extent to which the Kinarm Endpoint robotic device can accurately detect improvements in motor function following skill training and exercise-based rehabilitation interventions in individuals with chronic stroke. This study also aims to ascertain to what degree the Kinarm robotic device outcomes correlate with established clinical measures widely regarded as gold standards in evaluating stroke recovery.

Research Questions

The primary research questions addressed in this thesis are:

1. How feasible is Kinarm to use to measure motor and cognitive impairment in people with varying severities of stroke?
2. What are the relationships between robot-derived upper limb performance outcomes and gold-standard tests of the upper limb and cognitive function (Fugl-Meyer Assessment-Upper Extremity /WMFT /Raven's)?

2 CHAPTER TWO

2.1 INTRODUCTION

Stroke is a leading cause of long-term disability, and upper limb impairment is a common consequence of stroke, significantly affecting an individual's quality of life [140]. Rehabilitation interventions that target upper limb motor function effectively promote recovery after stroke [141]. In recent years, there has been increasing interest in utilizing technology, such as robotics and virtual reality, to enhance stroke rehabilitation outcomes [142]. Robotics can be used as an intervention, permitting high volumes of task-specific practice, or as a tool to measure severity of impairment and the effects of rehabilitation interventions. Robotics mimic real-world environments in which attention, cognitive processing and sensorimotor ability are required to complete tasks. Assessing upper limb kinematic function and cognition using robotics and evaluating the efficacy of motor-cognitive robotics in chronic stroke remains a complex and evolving area of research.

Kinematic Assessment for Normal Altered Reaching Movement (Kinarm) is a type of robotic technology used to evaluate motor function and cognitive performance using upper limbs. The system consists of a robotic actuators, motion-tracking cameras, and virtual reality software that allows for precise and objective measurements of upper limb function. The Kinarm has been used in mainly research settings to assess motor deficits and monitor recovery following stroke [143].

The Kinarm assessment involves a set of tasks designed to evaluate motor, sensory and cognitive function in form of reaching, proprioceptive and visuospatial processing tasks respectively. Reaching tasks involve reaching movements of the upper limbs towards targets

presented on a screen. Visuospatial processing tasks involve perceiving and interpreting visual information [144].

Visually guided reaching is a fundamental component of the Kinarm assessment and is widely recognized as one of the most frequently utilized reaching tasks. This task strongly emphasizes the patient's ability to reach toward targets on a screen. The target's position continuously varies throughout the task, adding complexity to the patient's reaching movements. By requiring the patient to adapt and respond to the changing target positions, the visually guided reaching task effectively evaluates their capacity to control the trajectory of their arm movements. It assesses their ability to make precise adjustments and corrections in real-time based on the dynamic visual information provided by the target's varying position. Consequently, the task provides valuable data and insights into the patient's visual-motor coordination, ability to integrate visual feedback into motor planning, and overall reaching proficiency. The visually guided reaching task is pivotal in assessing the patient's reaching abilities and ability to execute accurate and adaptable movements in response to changing visual stimuli [145].

Another commonly used task is the object hit task, which measures the patient's ability to control reaching movements to contact a moving target. In this task, the target moves in a unpredictable pattern and the patient must make adjustments to reach the target [146], [147].

The use of robotics to assess upper limb function in stroke patients, particularly the Kinarm robot, has increased interest in recent years. Bourke et al. (2016) conducted a study using the Kinarm Exoskeleton robot, a device that provides maximal external support to the upper limbs, to evaluate impairments in rapid motor decisions and actions with stroke patients. The study recruited 157 stroke subjects with mild upper limb impairment and 309 control subjects, and most stroke subjects were assessed within 28 days of their stroke. The authors found that most subjects with

stroke were impaired when performing the Kinarm motor tasks, particularly those with visuospatial neglect. The study concluded that many parameters had high inter-rater reliability and correlated with various clinical measures of impairments and the ability to perform daily activities [11].

Overall, the study by Bourke et al. (2016) provides evidence for the feasibility of using robotic assessments to measure stroke-related upper limb function. The study's findings suggest that the Kinarm Exoskeleton robot can be useful for quantifying impairment in rapid motor decisions and actions, especially for those with neglect. The high inter-rater reliability and correlation with clinical measures of impairments and daily activities also suggest that the Kinarm robot can provide reliable and valid measures of upper limb function in stroke patients.

However, some gaps in the study need to be addressed. One important gap is the lack of longitudinal measures of impairment. The study by Bourke et al. (2016) only assessed subjects at a single time point, and studies need to track changes in upper limb function over time. Longitudinal measures would help to identify the trajectory of recovery and provide valuable information about the effectiveness of rehabilitation interventions. While the study provides evidence for the feasibility and validity of robotic assessments, study participants were prescreened such that they had mild arm impairments. The Kinarm Exoskeleton cradles the arms such that hand and grip control is not required. The more recent version of the Kinarm, the Endpoint robot, provides more natural movement with no support to the shoulder or elbow while requiring functional grasp. The research examining the Kinarm Endpoint robot is much more sparse.

Tyryshkink et al. (2014) demonstrated the potential of the Kinarm Exoskeleton platform for assessing upper limb motor function following a stroke. The object hit task they developed required participants to hit virtual balls moving toward them in the workspace with virtual paddles

attached to each hand. The task difficulty increased over time, making it more challenging as the participant progressed. The study found that stroke participants performed the task with lower accuracy than healthy controls, with most stroke participants hitting fewer balls than 95% of controls. The task was also sensitive to visuospatial neglect, as nearly all participants with this condition hit fewer balls than healthy controls [148]. Once again, the study took place using the Kinarm Exoskeleton, proving full support, rather than the Kinarm Endpoint robot, so the validity of these tests in the more naturalistic Endpoint has not been determined.

Overall, the literature suggests that tasks requiring cognitive and motor ability that mimic real-world tasks can provide a valuable tool for assessing motor and cognitive function more ecologically valid than traditional assessments [149], [150]. Robotic platforms, such as the Kinarm Exoskeleton, have provided a way to objectively quantify sensorimotor impairments. While the system has been used extensively in research, there still needs to be more investigation regarding the feasibility of measuring impairments in a range of severities, correlation with other gold standard measures, and sensitivity to change over time especially using the Kinarm Endpoint. The current research on the Kinarm system demonstrates its efficacy in evaluating motor and cognitive impairments among stroke survivors with mild to moderate deficits. However, a critical knowledge gap exists regarding the potential existence of a severity threshold, commonly referred to as a "floor effect," beyond which the applicability of the Kinarm system is uncertain. Further investigation is needed to determine whether there are limitations in utilizing the Kinarm system for individuals with more severe impairments, thereby establishing the extent of its effectiveness across a broader range of stroke severity.

In order to establish the clinical utility of Kinarm, its validity needs to be evaluated by comparing it to established measures like the Fugl-Meyer Assessment for Upper Extremity, Wolf Motor Function Test, and Montreal Cognitive Assessment. Additionally, for Kinarm to be employed as an outcome measure in clinical trials, it is essential to assess its sensitivity in detecting changes resulting from rehabilitation interventions over time.

The primary objective of this study was to conduct a pilot investigation on the use of robotic outcome measures in an existing rehabilitation research intervention study, focusing on a longitudinal assessment of recovery changes following the rehabilitation intervention. The study aimed to assess the sensitivity of the robotic outcome measures in detecting these changes, with the goal of determining the feasibility and potential utility of robotics as an outcome measure in future stroke rehabilitation trials. The findings from this study are expected to provide valuable insights into the use of robotics in stroke rehabilitation research and guide the development of future clinical trials using this technology as an outcome measure.

Based on recommendations for pilot and feasibility studies outlined by Thebane et al. (2010) [151], we considered two key domains of feasibility:

1. Process: The time taken to complete the assessments, training required for administrators and participants and whether participants having different levels of abilities would be able to complete the tests (which would inform eligibility criteria).
2. Validity and Responsiveness: Whether the robotic outcomes were correlated with other gold standard measures before and after the rehabilitation research intervention (validity) and to what extent there was a change (improvement) in robotic measures after the intervention (responsiveness).

Therefore, the primary research questions addressed in this thesis are:

1. How feasible is Kinarm Endpoint robot to use to measure motor and cognitive impairment in people with varying severities of stroke?
2. What are the relationships between robot-derived upper limb performance outcomes and gold-standard tests of the upper limb and cognitive function (FMA-UE /WMFT/Raven's)?

2.2 METHODS

2.2.1 Participants

Participants with chronic (> 6 months) stroke were recruited from the provincial tertiary rehabilitation hospital in St. John's, Newfoundland and Labrador, Canada. They were recruited as part of an ongoing interventional study with its own specific inclusion/exclusion criteria. The participants' clinical characteristics are reported in **Table 2.1.** Participants were included if they, 1) were between the ages of 40-95, 2) had upper limb movement-related deficits (left or right-hand dominant) following a first, middle cerebral artery stroke, and 3) were in the chronic phase of recovery (stroke >6 months). The exclusion criteria were 1) severe motor deficits in the upper limb such that they would be unable to participate in arm rehabilitation therapy and 2) severe cognitive and aphasic deficits such that they could not follow directions, and 3) other neurological and psychological diagnoses. This study and testing procedures were approved by the provincial Health Research Ethics Board (HREB # 2020.273) in accordance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans, 2014, and the principles outlined in the Declaration of Helsinki. This study conforms to the Consolidated Standards of Reporting Trials statement extension for feasibility studies [152]. All participants provided signed informed consent prior to participation in the study and data collection.

2.2.2 Sample Size Estimation

The sample size for this study was estimated based on feasibility factors. The intended sample size was between 10 and 15 participants, which is deemed sufficient for research addressing feasibility challenges in a single group of participants [153].

2.2.3 Experimental Design

Participants were required to visit the laboratory for three two-hour data collection sessions, before the intervention (PRE), 24 hours after the last session of the ten-day intervention (POST) and 30 days later (FOLLOW-UP). After completing the baseline assessment (Table 2.1), those participants who could grasp the hand enough to hold a robotic device participated in ten days of exercise rehabilitation intervention paired with skilled arm practice (Table 2.2, Figure 2.1). An overview of the assessments, sessions and study schematic is provided in **Table 2.1, Table 2.2, and Figure 2.1,** respectively.

Table 2.1 - Overview of Assessments

Clinical Assessments			**Robotic Assessments**	
Demographics	**Motor**	**Cognition**	**Motor**	**Cognition**
1. Age 2. Sex 3. Stroke Stage 4. Stroke Location 5. Affected Hand	1. Wolf Motor Function Test 2. Fugl Meyer Assessment for Upper Extremity	1.Montreal Cognitive Assessment 2. Raven's Standard Progressive Matrices Test of Fluid Intelligence	1. Object Hit Task	1.Object Hit & Avoid Task

The table presents an overview of assessments used in the study, including the assessment measures employed, such as the Kinarm Robotic Device and Gold-Standard Clinical Measures, along with the demographics of the study participants.

Table 2.2 - Overview of Sessions

Sessions 1&2		Sessions 3-12	Sessions 13&14	
Eligibility Criteria	**Baseline Assessments**	**Intervention**	**24 Hours Post**	**30 Days Follow-Up**
1. Inclusion 2. Exclusion	1. Clinical Assessments 2. Robotic Assessments	Ten days (separated by at least 48 hours) of exercise paired with skilled motor practice on the Kinarm robot	1. Clinical Assessments 2. Robotic Assessments	1. Clinical Assessments 2. Robotic Assessments

The table provides an overview of the research study sessions, outlining the different sessions conducted during the study, including the specific interventions and assessments administered in each session.

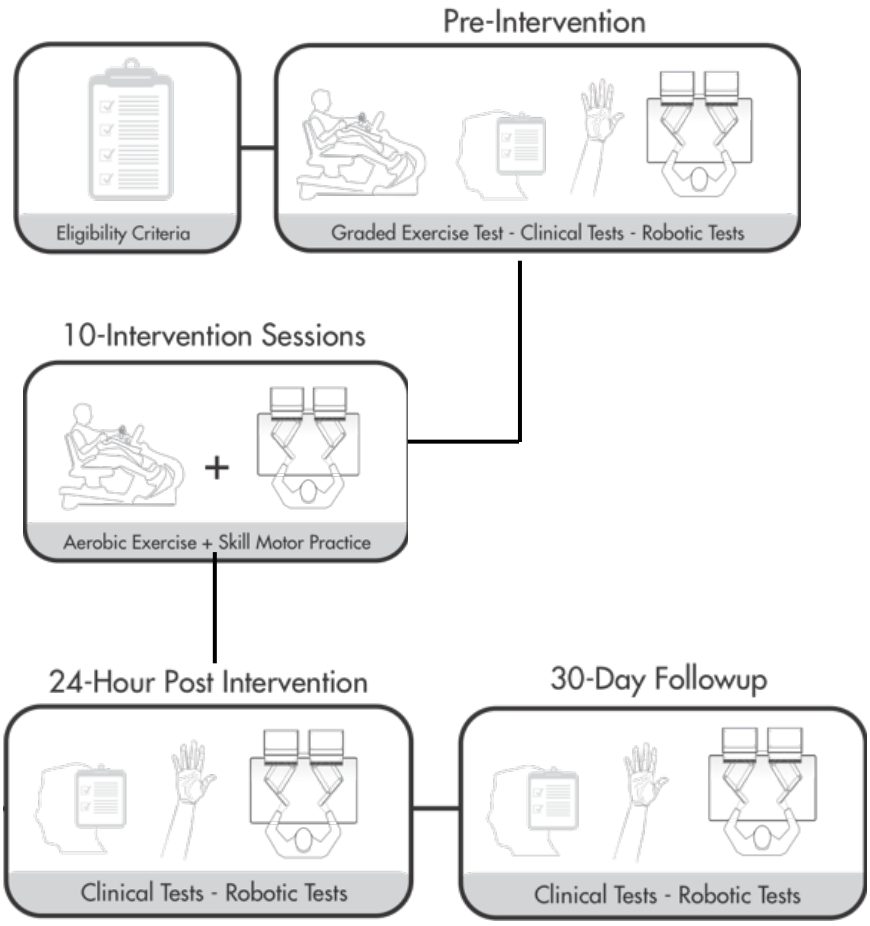


Figure 2.1- Study Schematic. A schematic representation of the research design, illustrating the flow of interventions and assessments conducted throughout the study, providing a visual overview of the study's experimental timeline, and highlighting the sequence and relationship between various research components. (Original Illustration by MB)

2.2.4 Clinical Assessments

Participants in the study underwent a series of standardized clinical measures that examined disease severity, performance-based impairment, and motor recovery according to the International Classification of Functioning and Disability (ICF) [154], [155].

Hand and arm impairment were assessed using the Fugl-Meyer Assessment for Upper Extremity (FMA-UE). It is a performance-based stroke impairment index developed by Fugl-Meyer AR et. al (1975) to assess motor function of the upper extremities (shoulder, elbow, forearm, wrist, and hand), sensory, and joint function in patients with post-stroke hemiplegia [156], [157]. The FMA-UE consists of a standardized set of 33 tasks that evaluate motor function, sensation, range of motion, and joint pain.

The five domains of the FMA-UE include reflex activity, flexor synergy, extensor synergy, movement coordination, and sensation. The tasks include movements controlled by different muscle groups in the upper extremity and the ability to perform coordinated movements. Each task is scored on a 3-point ordinal scale, with higher scores indicating better motor function. The total possible score is 66 points, and the individual's score on each task is summed to produce a total score. The assessment typically takes about 45-60 minutes to complete.

A study by Hernández et al. (2019) evaluated the inter-rater reliability of the FMA-UE and found high agreement among raters, indicating the tool's reliability for clinical and research use [66]. Physical therapists and other healthcare professionals widely use the FMA-UE to evaluate the degree of impairment and recovery in patients with upper limb deficits [158].

Hand and arm function post-stroke in real world tasks was assessed using the Wolf Motor Function Test (WMFT) - a widely used standardized assessment tool for evaluating upper extremity motor function in individuals with neurological impairments as shown in **Figure 2.2**.

[159]. The WMFT instrument has high interrater reliability, internal consistency, test-retest reliability, and adequate stability [160]–[162]. It assesses both gross and fine motor abilities and evaluates functional movements related to activities of daily living.

The procedure for administering the WMFT involves having the patient perform a set of 15 timed functional tasks using their affected arm or hand, as shown in **Figure 2.2** These tasks include opening and closing a door, turning a key in a lock, picking up and manipulating small objects, and lifting a weighted can. The test is usually completed within 20-30 minutes.

During the test, a trained evaluator scores the patient's performance on each task using a 5-point ordinal scale that ranges from 0 (no movement) to 5 (normal movement). The evaluator also records the time taken to complete each task. A task received a zero score if no repetitions were finished within 120 seconds. Higher rates indicate faster movements and better motor function. Each task was classified by rate calculation (repetitions/60 seconds) [159], [163].

The WMFT encompasses various measures to evaluate upper extremity function comprehensively, the overall performance score, and task completion time. These specific measures include the Functional Ability Scale, which employs a 5-point scale to assess the patient's level of independence during task completion, ranging from total dependence to complete independence. Strength is measured using a handheld dynamometer to evaluate the patient's hand force generation ability. The grasp component evaluates the patient's capability to hold objects of different sizes and weights, while the release component assesses their ability to release objects in a controlled manner. Dexterity is evaluated by examining the patient's proficiency in manipulating small objects, such as picking up pegs or coins. Range of Motion (ROM) assessment involves gauging the patient's arm or hand movement capability throughout the full range of motion. Together, these measures comprehensively evaluate upper extremity function in the WMFT.

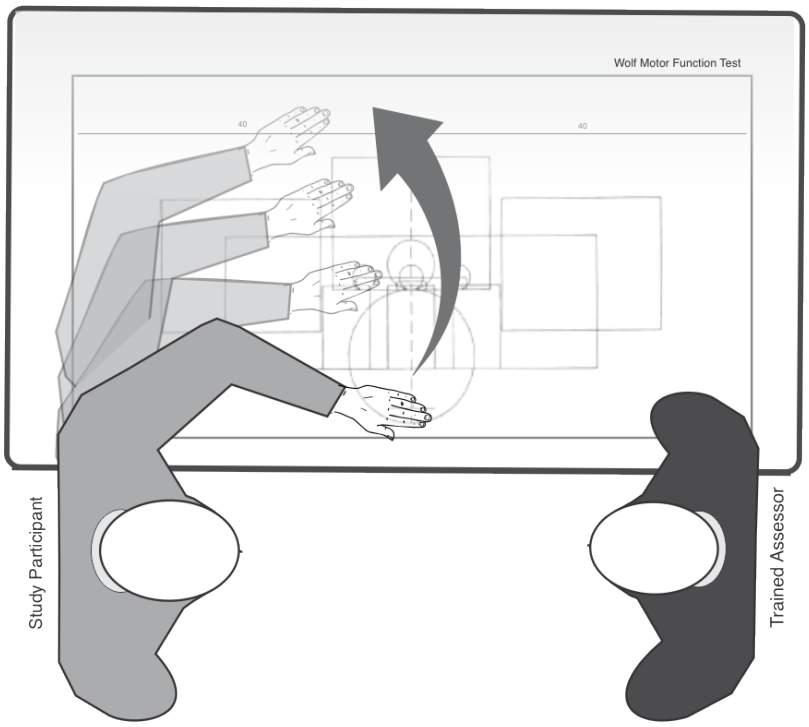


Figure 2.2- Participant performing functional tasks on the WMFT Card.

This figure depicts a participant engaging in a functional task called Extend elbow (to the side) as part of the Wolf Motor Function Test. In this task, the participant attempts to reach across the template's 40-cm line by extending the elbow (to the side). Shoulders should be kept level to prevent leaning with the trunk. The time elapsed from the starting point to when the thumb crosses the line is recorded. (Original Illustration by MB)

Cognitive function was assessed using the Montreal Cognitive Assessment (MOCA) [164] and also Raven's Standard Progressive Matrices Test [165]. The MOCA is a widely used screening tool for detecting cognitive impairment. The test is administered one-on-one and takes approximately 10-15 minutes. The MOCA consists of several tests that assess different cognitive

domains, including visuospatial abilities, attention, language, memory, and executive function. Some of the specific tests included in the MOCA are:

1. Visuospatial/executive: Clock Drawing Test, Cube Copy, Trail Making Test
2. Naming: Animal Naming and Phonemic Fluency
3. Attention: Sustained Attention to Response Task (SART) and Digit Span.
4. Language: Sentence Repetition and Verbal Fluency
5. Memory: Short-term memory recall and Delayed Recall.

The MOCA is scored out of 30 points, with a score of 26 or higher generally considered within the normal range. However, the interpretation of MOCA scores should be based on various factors, including age, education level, and cultural background, as well as the specific purpose of the assessment [164].

The Raven's Standard Progressive Matrices Test has been widely used in research and clinical settings to assess cognitive ability and potential for academic and occupational success [52], [166]–[168]. The procedure for administering the Raven's Standard Progressive Matrices test involves presenting a series of matrices or patterns with a missing piece or pieces. The task is to select the missing piece from a set of options. The Raven's Standard Progressive Matrices test consists of 60 items, presented in sets of 12, arranged in increasing order of difficulty, and takes approximately 40-60 minutes to complete.

A new study led by University College London Queen Square Institute of Neurology and National Hospital for Neurology and Neurosurgery researchers published in Brain examined 227 patients who had either a brain tumor or a stroke. Using the Raven's Standard Progressive Matrices test, they concluded that it is the best-established test of fluid intelligence [169]. The Raven's Standard Progressive Matrices test does not evaluate upper extremity function or motor skills.

Rather, it assesses cognitive abilities unrelated to motor function. The Raven's Standard Progressive Matrices test is a nonverbal measure of cognitive ability that assesses individuals' fluid intelligence, i.e., their ability to identify abstract patterns and solve problems through reasoning[170]. It does not require verbal or numerical skills and can be used to assess individuals across ages and educational backgrounds.

The test is usually administered individually, and the examiner provides instructions and demonstrations before each item. The test-taker is not allowed to use external aids or tools and is required to solve the problems mentally. The Raven's Standard Progressive Matrices test measures several specific cognitive abilities, including:

(1) Perceptual speed: The ability to quickly identify and discriminate visual stimuli.

(2) Figural analogy: The ability to identify relationships between visual patterns and use that information to solve problems.

(3) Spatial visualization: The ability to mentally manipulate objects and visualize their spatial relationships.

(4) Inductive reasoning: Inferring general rules or principles from specific examples.

(5) Abstract reasoning: The ability to understand and manipulate abstract concepts.

The test provides a score derived by adding up the number of correctly solved items. The maximum score is 60, and the interpretation of scores can vary depending on the purpose of the assessment and the characteristics of the population being tested. A score below 30 on the Raven's Standard Progressive Matrices test generally indicates impaired cognitive function. However, the interpretation of scores should consider various factors, including age, education level, cultural background, and the specific purpose of the assessment. The Raven's Standard Progressive

Matrices test provides a single score compared to normative data to determine the test-takers relative cognitive ability [171].

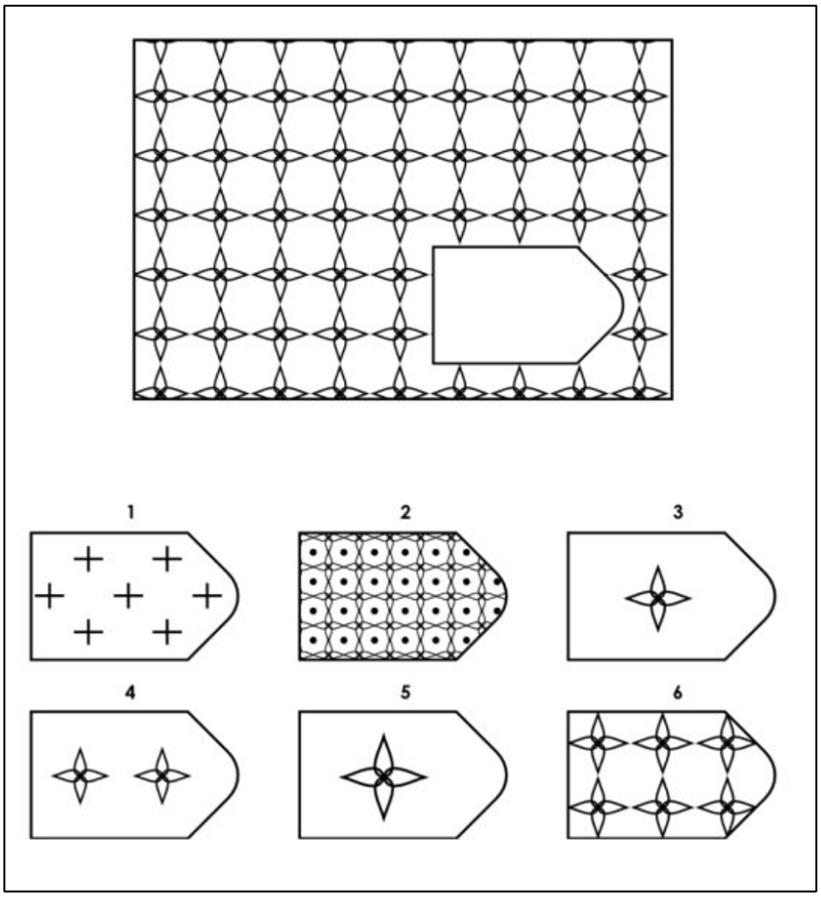


Figure 2.3 Raven's Standard Progressive Matrices test (J.C Raven's 2003).

The figure above displays Raven's Standard Progressive Matrices test, a widely used non-verbal cognitive assessment tool. This page of the Raven's test presents a series of patterned designs or shapes arranged in a particular order, with one pattern that completes the missing piece. Option 6 is the pattern that completes the missing piece in the figure above.

2.2.5 Robotic Assessments

Skilled arm practice and motor and cognitive assessments were performed using a robotic device called Kinarm. For this study, the robotic assessment was completed using the Kinarm Endpoint bimanual robotic device and software version Dexterit-E 3.8.2-8570 (**Figure 2.4**).

The Kinarm robot is a highly sophisticated and advanced device used to study the motor and sensory systems of the brain. The validity and reliability of this robot have been tested and documented in preliminary studies [124], [136], [138], [172]. Validity refers to the extent to which a measurement tool accurately measures what it is intended to measure [139]. In the case of the Kinarm robot, the larger Exoskeleton version has been studied the most. The Kinarm Exoskeleton Robot (not the Endpoint Robot) has been shown to have high validity for assessing motor and sensory function in both healthy individuals and those with neurological disorders such as stroke, multiple sclerosis, and cerebral palsy [134], [173]–[175]. The Exoskeleton robot has been validated against other commonly-used motor and sensory function measures, such as the Fugl-Meyer Assessment and the Action Research Arm Test. [11], [108]. Reliability refers to the consistency of the measurements taken by a tool over time and across different evaluators [148]. The Kinarm Exoskeleton robot has been shown to have high reliability in multiple studies. For example, in one study, different evaluators using the Kinarm robot to assess motor function in stroke patients achieved high inter-rater reliability, indicating that the robot can produce consistent results even when used by different evaluators [176].

Participants first attempted to hold onto the handle with their affected hand and then try to move the robot. Those participants who could not hold, did not proceed. If the participant could hold the robot, they completed the tasks by moving their arms, held onto the handles linked to the robot, in the horizontal plane underneath a semitransparent mirror. To support the palm of the

hands while holding the handle during assessments, the handle had a 7 cm-diameter circular base. Torque sensors incorporated with the handle accurately assessed users' hand position, movement, and grasp range. Kinarm Standard Tasks were projected downward onto this mirror screen by the custom-built screen above, while the direct vision of the participant's arms was occluded. Upon holding the robot handle, a white cursor dot appeared on the screen to indicate hand position. Participants also experienced a force feedback mechanism (like the feeling of hitting a squash ball) while hitting the target shapes with the robot handles during specific tasks. Setting up and calibrating a subject in the robotic system took 5 to 10 minutes. Operators received 15 hours of formal training on utilizing the software, setting up subjects, and operating the device.

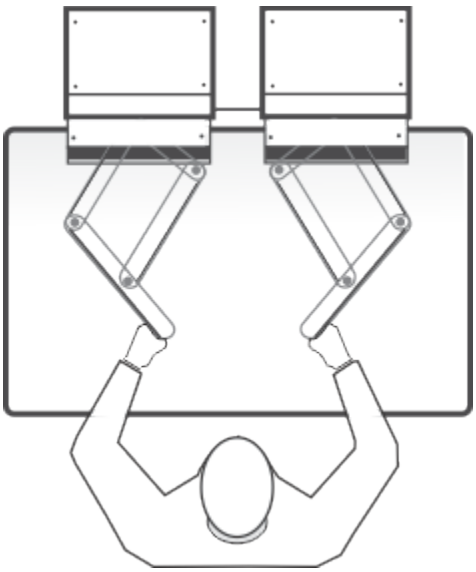


Figure 2.4 Kinarm Endpoint Robot (Superior View). (Original Illustration by MB). The above illustration provides a top-down view of an individual utilizing the Kinarm Endpoint Robot.

A total of two tasks were collected. Object Hit task, a sensorimotor task, and Object Hit & Avoid task, a visuospatial task, were chosen on the Kinarm Endpoint robot with both hands

(affected and unaffected). These are described below. The relationships between the clinical and robotic assessment and the variables used in this study are shown in **Table 2.3** below.

Table 2.3 Relationship between the clinical and robotic assessments

Standard Clinical Tests	Kinarm Standard Tests/Variables
Motor Performance	
1. Wolf Motor Function Test 2. Fugl Meyer Assessment for Upper Extremity	Object Hit Task - Object Hit-AffectedHand-Speed
Cognitive Performance	
1. Raven's Standard Progressive Matrices Test 2. Montreal Cognitive Assessment	Object Hit & Avoid Task - Object Hit and Avoid-Distractor-Hit-Total

2.2.5.1 Object Hit Task

Object Hit (OH) is a sensorimotor task that assesses rapid visuomotor skills, bi-manual motor planning, and spatial attention [177]. Participants were instructed to hit the target (red circles), dropping into the virtual environment with the two visually displayed green paddles as their hands. Hand motion matched that of the paddle, as shown in **Figures 2.5a and 2.5b**. As the task proceeds, the balls fall randomly with an initial slow speed and then at greater speeds (10-50 cm/s), increasing the difficulty. The virtual environment consists of 10 distinct invisible bins at the top, each 8 cm apart, from which 30 red circles randomly fall. A total of 300 targets were randomly presented in 2 minutes 30 seconds.

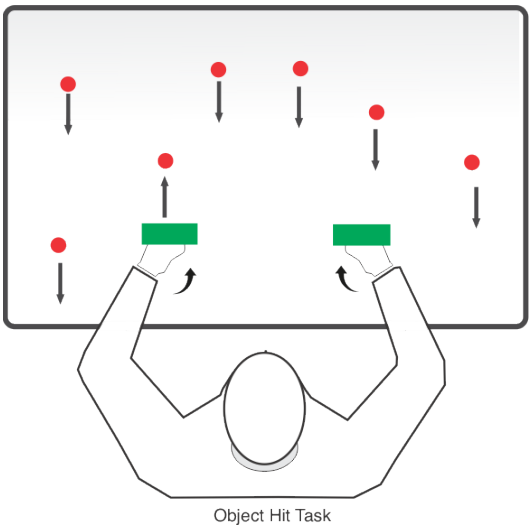


Figure 2.5a Object Hit Task

(Original Illustration by MB). The illustration above showcases the superior (top) view of the participant's interaction with the robot, depicting their arm movements and positioning while using the device. (view task here: https://shorturl.at/fjvIP)

Figure 2.5b Example of subject positioning using adjustable Kinarm electronic chair while performing Object Hit and Avoid Tasks. (Original Image by MB).

2.2.5.2 Object Hit Task Variables

Although there are multiple variables that can be extracted from the Kinarm tasks, we focused on only one for the purpose of this study (Table 2.3). Overall Task Score (performed with both hands) was derived and compared to percentile ranks derived from performance in a large cohort of healthy controls [136]. It provides a global measure of a subject's performance. Specifically, it measures how far from the best performance was the subject's performance. Task Scores are always positive; a score of 0 denotes the best performance, and increasing values represent poorer performance. Task Scores follow the same percentiles as ±1SD of a normal distribution (i.e., 1 = 68.3%, 2 = 95.4%). Task Scores > 1.96 indicated impaired performance on the task [177].

Also, the other variable, Hand_Speed, consists of the Right- and Left-hand speed measured in meters per second (m/s) maintained throughout the entire task. It is calculated by joint velocities measured by the Kinarm robot and the length of the arm segments. Hand speed measures of both

arms are independent, as each measure can be used for analysis separately. We considered only the OH_AffectedHand_Speed. We also looked at the Target Hit Total Variable in this same task, which is the number of balls hit off the screen in the opposite direction from its original path. The total number of balls is 300. There is a value of target hits for each hand; however, for the purpose of this study, we only considered the values recorded for the affected hand; hence the variable is Target_Hit_Affected Hand.

2.2.5.3 Object Hit & Avoid Task

Object Hit and Avoid is a visuomotor task that assesses rapid bimanual motor decision-making, spatial attention, and inhibitory control [147]. Participants were asked to hit two red targets (e.g., oval and square) and avoid distractions as objects dropped at an increasing rate (from a single slow 10cm/s stimulus to a maximum of 16 fast 50 cm/s stimuli) shown in **Figure 2.6**. A total of 300 stimuli (200 targets and 100 distractors) were randomly presented for two minutes and thirty seconds. The total number of target hits and distractor hits for each hand served as the dependent variables **(Table 2.3)**.

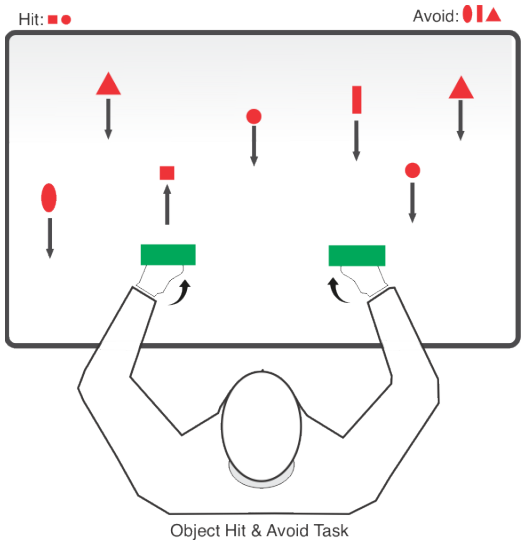


Figure 2.6 Object Hit & Avoid Task (Original Illustration by MB). The illustration above showcases the superior (top) view of the participant's interaction with the robot, depicting their arm movements and positioning while using the device. Participant is asked to hit only squares and circles.

2.2.5.4 Object Hit & Avoid Task Variables

Task Scores, Target Hit Total, and Hand speed variable(s), similar to the Object Hit task, were also measured in this task. The distractor hit total variable, which is the total number of distractor objects (out of 100) that the subject hit, is reported as the % of total distractors dropped, higher values indicate lower attention and greater distraction. The distractor hit total variable was the only assessment variable for change in cognitive performance.

2.3 FEASIBILITY ASSESSMENT

Feasibility of measuring rehabilitation-induced changes in upper limb movement and cognition using robotic kinematics in chronic stroke was assessed using a checklist that included logistical challenges and safety hazards during clinical assessments (difficulty performing the upper-limb tasks in the assessment, difficulty switching between sitting and standing positions), hand use during robotic assessments (difficulty in grasping the robotic handle to perform the standard tasks, difficulty in body position on the robotic chair).

2.4 STATISTICAL ANALYSIS

Aspects of feasibility were reported descriptively. Only participants (n=10) who were able to complete the Kinarm, FMA-UE, WMFT, and Raven's were included in longitudinal data analysis. All statistical analyses were completed using SPSS software (SPSS 27.0; IBM Corporation, Chicago, IL, USA). Data were tested for normality with the Shapiro-Wilk test with $\alpha = .005$. A Spearman's correlation (Bivariate) was used to compare the associations between the clinical variables and robotic variables at baseline (Pre-Intervention) and after the intervention (POST, FOLLOW_UP). To examine responsiveness to change due to the study intervention, a one-way ANOVA was used to assess whether there was a significant difference in scores over time (PRE, POST, FOLLOW-UP), and pairwise comparison was used to determine which group differences were statistically significant ($p < 0.05$). All descriptive statistics are reported as mean (SD) unless otherwise indicated. The significance level for all tests was $p \leq 0.05$.

2.5 RESULTS

2.5.1 Feasibility of recruitment, attendance, and retention

2.5.1.1 Recruitment

Fifty-eight patients with chronic stroke (>6 months) were contacted to determine their willingness to participate. Twenty-seven stroke patients did not meet the inclusion criteria (due to other medical pathologies, spasticity, travel distance, age, and type of stroke). Seven were not contactable, and six declined to participate (see Flow Chart in Appendix E). Out of eighteen stroke patients who agreed to participate, ten met the eligibility criteria for the main intervention study. Eight patients did not meet the eligibility criteria and were excluded from the main intervention study (Table 2.4). Their data was included in the feasibility assessment. The 10 participants who proceeded to the intervention (7 males and 3 females; **Table 2.4**) were aged 53 to 93, and ten participants completed the 10-day rehabilitation intervention. All 10 participants completed the assessments immediately after the rehabilitation intervention sessions. Thirty days later, nine participants (2 females) returned to complete the follow-up assessments.

2.5.2 Demographics and Baseline Characteristics

Considering all 18 participants, including the eight that did not proceed to the intervention, (14 males, 4 females), the right hand was affected in 10 participants and the left hand in eight participants. Participants are listed in **Table 2.4** according to the FMA-UE from most impaired to least impaired. Four participants could not complete the FMA-UE and eight participants could not grasp the Kinarm robot handle due to severe spasticity.

On average, the intervention group (n=10) were 64.9 years of age (±12.9), of which 70% were males and 30% were females with stroke (> 6 months) (Table 2.6). 50% of the participants

had a stroke to the left middle cerebral artery with the right hand affected, while the other 50% had a stroke to the right middle cerebral artery with the left hand affected (Table 2.4). On average, FMA-UE was 47.2 (±12.2), and MOCA was 22.5 (±2.9). None of the participants required additional assistance from the physical therapist during upper-limb motor assessments.

Table 2.4: Participant Demographics (ALL)

Participant (Completed intervention?)	Age	Sex	Stroke side/Type	Participant (Hold the Kinarm handle?)	WMFT Score	FMA-UE Score	MOCA Score
1. NO	63	M	RMCA	NO	-	CNC	-
2. NO	71	M	LMCA	NO	-	CNC	-
3. NO	78	M	LMCA	NO	-	CNC	-
4. NO	49	M	LMCA	NO	-	CNC	-
5. NO	69	F	RMCA	NO	-	17	-
6. NO	70	M	RMCA	NO	-	21	-
7. YES	53	M	LMCA	YES	37	23	16
8. NO	27	M	LMCA	YES	-	32	-
9. YES	76	M	RMCA	YES	14	39	25
10. YES	55	M	LMAC	YES	19	39	22
11. YES	68	M	LMCA	YES	15	45	23
12. YES	69	F	RMCA	YES	14	46	23
13. YES	71	M	RMCA	YES	15	48	26
14. YES	53	M	LMCA	YES	58	50	25
15. YES	79	F	RMCA	YES	25	54	23
16. YES	77	M	RMCA	YES	33	63	20
17. NO	74	M	RMCA	YES	-	64	-
18. YES	93	F	LMCA	YES	31	65	22

Participants are in order of upper limb severity, from most severely involved to less severely involved. Abbreviations: M, Male; F, Female; L, Left; R, Right; FMA-UE, The Fugl-Meyer Upper Extremity; WMFT; Wolf Motor Function Test; MOCA; Montreal Cognitive Assessment; CNC; Could Not Complete.

Table 2.5 The attendance rates of participants with chronic stroke in the intervention

S/N Participant(s)	Total number of visits attended	Total number of missed appointments	Stroke Stage	Discontinued intervention (Yes/No)
1	12	2	Chronic	NO
2	14	0	Chronic	NO
3	13	1	Chronic	NO
4	14	0	Chronic	NO
5	14	0	Chronic	NO
6	14	0	Chronic	NO
7	12	2	Chronic	NO
8	11	3	Chronic	NO
9	14	0	Chronic	NO
10	6	8	Chronic	NO

This table presents the attendance rates of participants with chronic stroke who were enrolled in the study. It provides an overview of the participant's adherence to the intervention or assessment sessions throughout the study.

Table 2.6 Participant Demographics (Intervention Group).

Demographic Variable(s)	Participants (n=10)
Sex (M/F)	7/3
Age [mean, years] (SD)	64.9(12.9)
FMA-UE [mean] (SD)	47.2(12.2)
MOCA [mean] (SD)	22.5 (2.9)

M; Male, F; Female, SD; Standard Deviation, MOCA; Montreal Cognitive Assessment, FMA-UE; Fugl Meyer Assessment-Upper Extremity

2.5.3 Feasibility of using the Kinarm

2.5.3.1 Adverse events and safety

For better ergonomic adaptation for participants with relatively more severe motor deficits (Fugl-Meyer Score Upper Extremity between 15-35), we worked with a local 3D printing company (Polyunity, St. John's NL Canada)) to custom-build 3D-printed paddle to extend the supportive base for the hand on the handle of the robot (Figure 2.7). The hand support worked well to support the hand and prevent it from slipping off however the torque sensor of the robot showed an error message. After consultation with Kinarm manufacturer, we were advised to discontinue use of the additional hand support because of potential damage to the robot. All participants independently utilized the electric-powered chair of the robot without any assistance from the assessor for positioning.

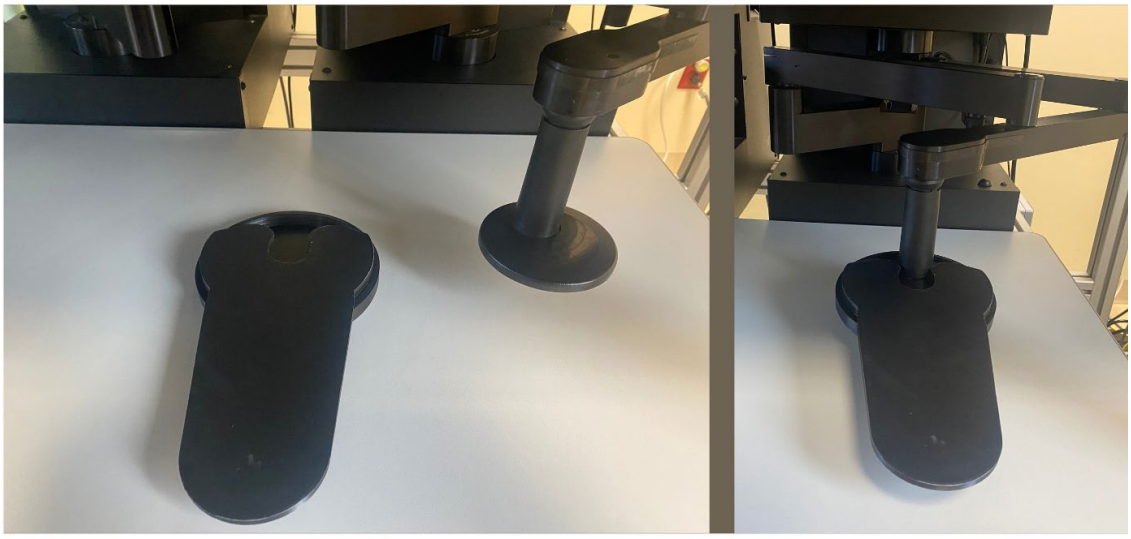


Figure 2.7 3D-Printed Handle. This figure shows the 3D-printed handle designed specifically for the Kinarm paddle used in the study. The handle, which was custom built using advanced 3D printing technology, offered participants an ergonomic and customized grip. Its design considers the comfort and stability required during motor tasks using the Kinarm system.

2.5.3.2 Tests administration time

The clinical assessments which included, Raven's test, Wolf Motor Function Test and Fugl Meyer Assessment for Upper limb Extremity, each took about 60 mins to complete, while it took five minutes to complete both Object Hit and Object & Avoid tasks in the Kinarm Endpoint robot. The Kinarm Endpoint setup involved positioning the participant in the robot's electric-powered chair. During the assessment, instructions were given to the participant to perform the Object Hit and Object Hit and Avoid tasks, guiding task-specific goals and performance expectations.

2.5.3.3 Relationship between clinical outcome measures and robotic measures at baseline

Low, moderate, and high correlations refer to the strength and direction of the relationship between two variables. A low correlation (<0.30) indicates a weak association between the variables, meaning that changes in one variable are not consistently related to changes in the other. A moderate correlation (0.3-0.7) suggests a moderate level of association, where changes in one variable correspond to some extent with changes in the other. A high correlation (>0.7) signifies a strong relationship, with changes in one variable reliably and consistently coinciding with changes in the other. The sign of the correlation (+ or -) indicates the direction of the relationship, whereas positive correlations indicate that the variables move in the same direction. In contrast, negative correlations indicate that the variables move in opposite directions. There was a moderate significant positive correlation between the clinical variable, FMA_UE and the Kinarm variable, OH_AffectedHand_Speed (Table 2.7. Spearman's rank correlation coefficient, rs=0.650, p=0.04) which are a measure of motor performance. There was no significant association between the clinical variables Raven's or MOCA and the Kinarm variable, OHA_Distractor_Hit_Total for cognitive performance measure. However, there was a moderate significant positive correlation (Spearman's rank correlation coefficient, rs=0.689 p=0.04) between the clinical motor performance measure FMA-UE and the Kinarm cognitive performance measure OHA_Distractor_Hit_Total. This association likely links the role of arm function in executing cognitive tasks. (Table 2.8) (Figure 2.8)

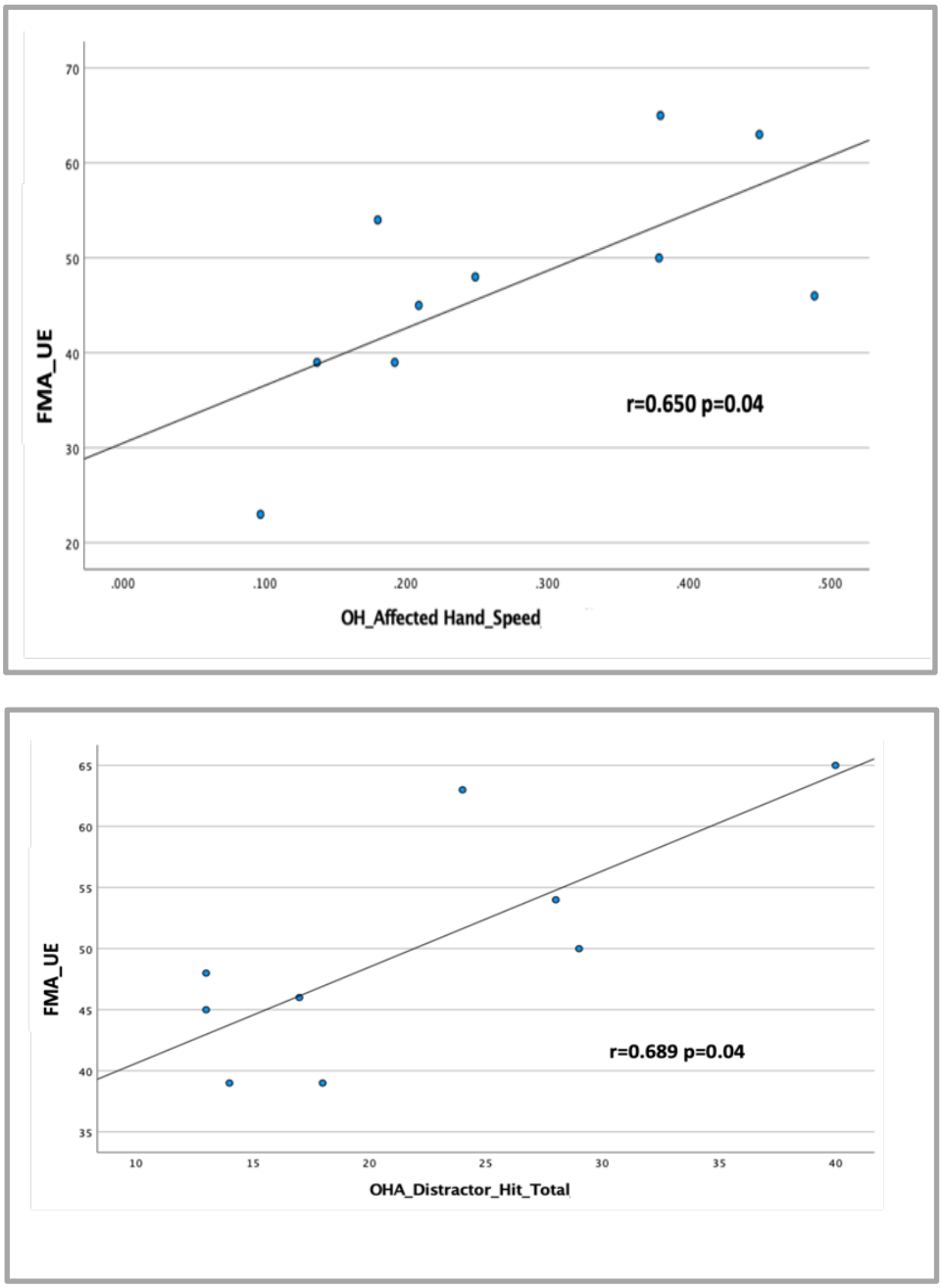


Figure 2.8 A graphical representation showing baseline correlations between clinical and robotic outcome measures. Data are presented as individual values. a; Fugl-Meyer Assessment for Upper Extremity (Score total-66) b; Object Hit_AffectedHand_Speed (in m/s), c; Object Hit and Avoid_Distractor_Hit_Total (out of 100). All variables are measured at baseline before rehabilitation intervention.

Table 2.7 The relationship between clinical outcome measures and robotic measures before rehabilitation intervention.

Variables at Baseline (n=10)	FMA-UE r/pvalue	WMFT r/p value)	Raven's r/pvalue	MOCA r/pvalue
OH_AffectedHand_Speed	**0.650/0.04**	-0.424/0.91	0.012/0.97	0.037/0.92
OHA_Distractor_Hit_Total	**0.689/0.04**	0.644/0.06	-0.046/0.91	-0.266/0.49

Abbreviations: *FM-UE, Fugl Meyer Assessment Upper Extremity scale; WMFT, Wolf Motor Function Test; OH, Object Hit; OHA, Object Hit & Avoid. Bolded text indicates statistically significant relationship.*

2.5.3.4 Change in clinical measures after intervention

The results in **Table 2.8** represent changes in the clinical variables before (PRE), after (POST), and follow-up (FOLLOW-UP) intervention. Pairwise comparison ANOVA demonstrated that there was no significant change in the clinical variables measuring recovery changes in motor and cognitive function PRE, POST rehabilitation intervention and at FOLLOW-UP.

2.5.3.5 Change in robotic measures after intervention

Pairwise comparison ANOVA demonstrated that there was a significant decline in the robotic variable OH_AffectedHand_Speed measuring recovery changes in motor performance from Pre rehabilitation intervention to Follow-up (t=1.438; p=0.004). There was no significant change in OHA_Distractor_Hit_Total which measured cognitive function using the Kinarm robot during the study periods (Table 2.8). Figure 2.9 shows the individual data.

Table 2.8 shows changes in outcomes from motor and cognition performance measured with clinical and robotics measurements at PRE, POST, and FOLLOW-UP

Variables at Baseline (n=10)	Pre (M±SD)	Post (M±SD)	Follow-up (M±SD)	Pre vs Post	Pre vs Follow-up	Post vs Follow-up
WMFT	26.03±14.11	30.9±12.42	28.66±14.98	-1.650; p=0.146	-1.250; p=0.576	0.400; p=0.371
Raven's	27.8±8.89	27.6±8.37	28±8.28	0.056; p=0.906	-0.111; p=0.814	-0.056; p=0.906
OH_AffectedHand_Speed	0.28±0.14	0.24±0.12	0.21±0.09	0.813; p=0.104	**1.438; p=0.004**	0.625; p=0.211
OHA_Distractor_Hit_Total	21.78±9.22	21.13±16.64	17.88±10.34	0.857; p=0.109	0.857; p=0.109	0.000; p=1.000

Abbreviations: **, p-value was set at 0.05 significance level; (M ± SD), Values from Mean and Standard Deviation; BL, Baseline Results; PI, 24 hours Post Intervention Results; FU, 30 Days follow-up results, vs, versus; WMFT, Wolf Motor Function Test. Bolded text indicates statistically significant (p<0.05),*

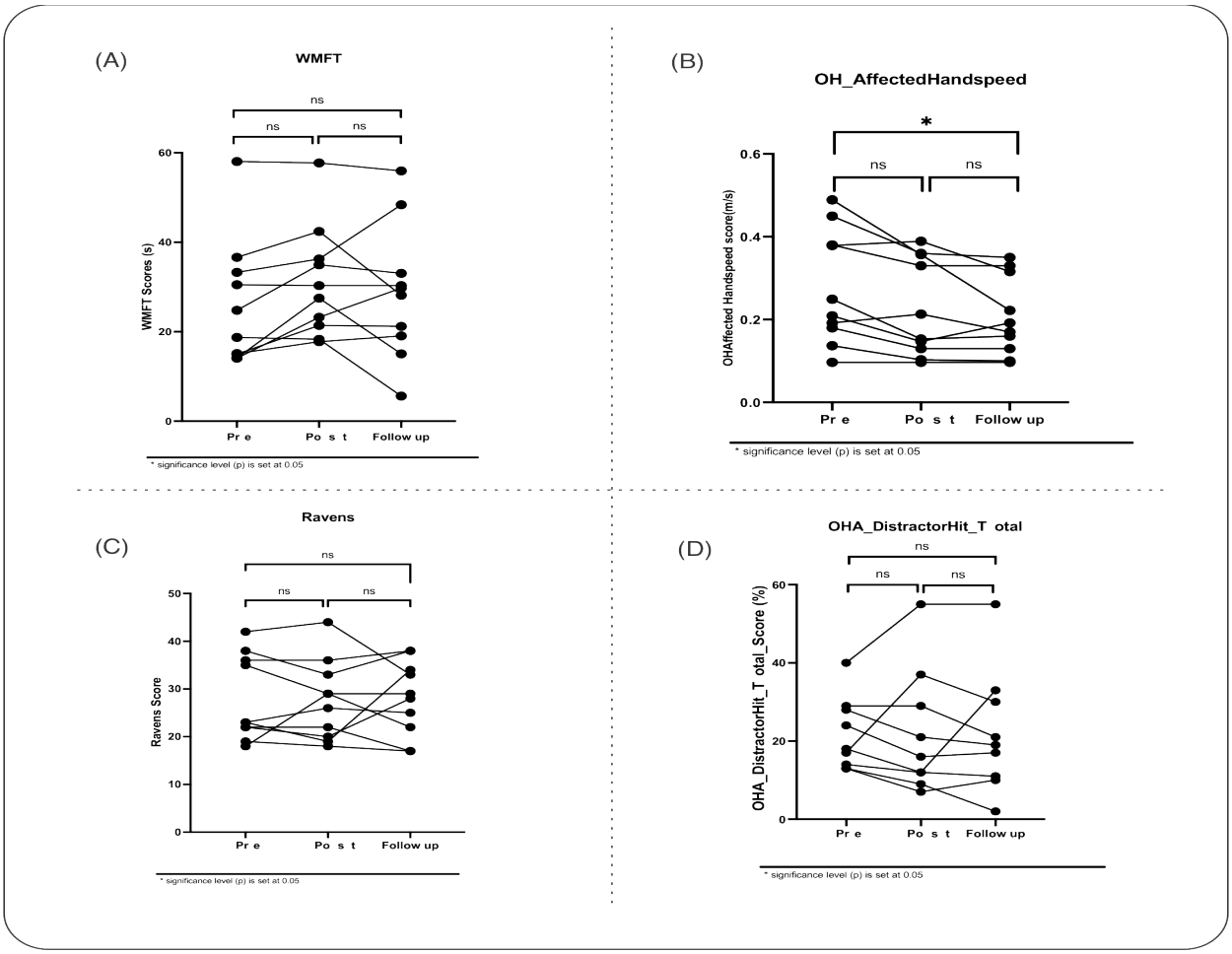


Figure 2.9 The figure above is a graphical representation showing individual changes in motor and cognition performance. Data are presented as individual values. a; Wolf Motor Function Test (in seconds) b; Object Hit_AffectedHand_Speed (in m/s), c; Raven's (out of 60) d; Object Hit and Avoid_Distractor_Hit_Total (out of 100). All variables are measured at PRE, POST, and FOLLOW-UP, respectively. *indicates statistically significant decline from PRE to FOLLOW-UP. ns indicates not statistically significant.

2.6 DISCUSSION

We undertook this study to examine the feasibility and reliability of using robotics as an outcome measure in a clinical trial. We report four main findings. First of all, although robotic assessment was efficient and safe, six out of 18 participants with stroke were unable to grasp the robot securely enough to be tested. The attempt to build a custom-designed 3D-printed hand support failed because of system incompatibility. Based on the FMA-UE, those that could not grasp the robot scored lower than 21. This is preliminary support for the concept that patients must meet a threshold of function before they can proceed to robotic assessment and that there is a floor-effect to consider when employing robotics. Secondly, affected hand speed during the robotic test correlated with FMA-UE but not WMFT, suggesting that robotics align better with tests of impairment (FMA-UE) than real-world function (WMFT). Third, the distractor hit variable in the Object Hit and Avoid Task did not correlate with either of the cognitive measures, MOCA (overall cognition) and Raven's (fluid intelligence), suggesting that it may not measure cognition specifically. Finally, robotics was more sensitive than FMA-UE or WMFT in measuring changes during the treatment, although after this intervention, hand speed worsened rather than improved.

2.6.1 Feasibility of robotic training post-stroke

The Fugl-Meyer scale is widely recognized as a reliable tool for measuring motor recovery after stroke, demonstrating excellent reliability and construct validity [157]. It is responsive to changes in motor performance, although limitations such as a ceiling effect (patients scoring high do not have complete recovery) and disproportionate weighting of the arm exist [157]. Studies have reported the high reliability of the Fugl-Meyer scale in assessing motor performance in stroke patients, including inter-rater and test-retest reliability[178], [179]. Platz et. al (2005) also

validated its use in evaluating arm function in patients with other neurological conditions, such as multiple sclerosis and traumatic brain injury. The hierarchical properties of the Fugl-Meyer motor scale support its use as a stagewise and subsection-wise hierarchical assessment, even in very impaired individuals, enabling a shortened administration method and appropriate scoring for untested items [180]. However, its predictive ability regarding functional outcomes has not been directly addressed in the literature. Woodbury et. al (2008) proposed an optimal cut-off point of approximately 19±2 points on the Fugl-Meyer Assessment for Upper Extremity (FMA-UE) to differentiate severe and moderate impairment of hand function. Cut-off scores are commonly employed in prognostic studies to identify patients likely to regain some upper-limb capacity. Nevertheless, there is a lack of consensus on the specific cut-off scores [181].

In our study, we explored the use of robotic assessment in stroke participants and found it to be efficient (modest set up and testing time) and safe (no adverse events). However, a significant proportion of participants (6 out of 18) could not securely grasp the robot for testing. Notably, those unable to grasp scored below a cut-off of 21 on the Fugl-Meyer Assessment for Upper Extremity. Additionally, a custom-designed 3D-printed hand support extension intended to provide ergonomic support and leverage to those unable to use the robot proved effective but had the potential to damage the robotic actuators. While no specific papers directly address the relationship between the Fugl-Meyer Assessment score and the inability to grasp the Kinarm Endpoint robot handle securely, some studies provide information on the Fugl-Meyer Assessment's association with upper limb capacity and dexterity [181], [182]. Previous studies examining the validity of the Kinarm, either employed the Exoskeleton [172], [173], which does not require grasping, or excluded subjects with severe arm impairment. Here we show novel findings that the Kinarm Endpoint has clear limitations for use in clinical and research

environments. Wider use among patients with varying degrees of hand impairment could be facilitated by permitting hand support on the robotic handles.

2.6.2 Object Hit affected hand speed is related to FMA-UE but not with WMFT

We observed that the affected hand speed variable for the object hit task using the Kinarm Endpoint robot correlated with the FMA-UE, which measures impairment, but not WMFT, which evaluates functional performance in real world tasks, such as turning a key and picking up objects. Studies have explored the correlation between robotic and clinical measures, indicating that robotic assessments are valid and reliable for evaluating motor function in stroke patients and exhibit a strong association with the WMFT, FMA-UE and other clinical measures [139], [183], [184].

A study by Otaka et al. (2015) on 56 hemiparetic patients with chronic stroke compared the relationship between robotic and clinical measures in differentiating the paretic arm from the non-paretic arm. The robotic measures were performed using the Visually Guided Reaching (VGR) task in the Kinarm Exoskeleton, while clinical measures were administered using FMA-UE, WMFT, and Motor Assessment Scale. They found that robotic measures of reaching movement, particularly for the Visually guided reaching task, were valid and significantly correlated with the Functional Ability Scale of the WMFT and the FMA-UE and could successfully differentiate between the paretic and non-paretic arms [139]. The Otaka sample are similar to ours in that they also recruited participants with chronic stroke. However, the previous study used the Kinarm Exoskeleton, in which grasping is not required and participants place their hand to shoulder level into the arm support extension of the robot to perform the robotic tasks. Task choice is an important consideration. Otaka and group used a visually guided reaching task, in which accuracy was the main outcome, while our study used the Object Hit task, a task that is more sensitive to speed. The Kinarm standard tasks include five motor, five cognitive and one

sensory task, using either the Exoskeleton or the Endpoint robots. In order to translate the Kinarm robotic tool into clinical trials and practice, future research should recruit a large sample of people with stroke, with wide range of impairment levels, and test all standard tasks in both robots.

The study findings indicate that the robotic task (Object Hit task) used in the research may better assess impairment-based measures like FMA-UE rather than comprehensive evaluations of functional abilities like WMFT. Although this task correlates well with impairment-based measures, additional measures or tasks from the Kinarm robot's standard task list may be needed to capture real-world functional performance and other motor changes fully [173], [174].

2.6.3 No Relationship between Clinical and Robotic Cognitive Measures

The Montreal Cognitive Assessment (MOCA) is widely recognized as a screening instrument for cognitive impairment [164]. It evaluates various cognitive domains, including executive functioning, visuospatial abilities, attention, concentration, working memory, language, abstract reasoning, memory, and orientation[185]. Similarly, Raven's Standard Progressive Matrices test has been established as a reliable measure of cognitive functioning and fluid intelligence, particularly in individuals with motor and speech impairments [69], [171], [186]. The MOCA and Raven's tests have proven to be valuable and valid traditional clinical measures for assessing cognitive impairment and attention[185]. Previous studies have examined the relevance of utilizing MOCA and Raven's test as valid measures of cognitive impairment and fluid intelligence, respectively, in people with neurological diseases [17], [52], [167], [187], [188].

In a recent study by Wu et al. (2019), the psychometric and clinimetric properties of the MOCA were explored in stroke survivors undergoing rehabilitative therapy. The MOCA and Stroke Impact Scale were administered to 65 stroke survivors before and after a 4 to 5-week therapy period. The study assessed the responsiveness of the MOCA by calculating the effect size

and standardized response mean (SRM). The minimal clinically important difference (MCID) was estimated using anchor- and distribution-based methods. Criterion validity was measured using the Spearman correlation coefficient. The findings indicated that the MOCA demonstrated satisfactory predictive validity, responsiveness, and minimal clinically important difference in stroke populations[187]. Another study by Ploughman et al. 2019 used both MOCA and Ravens' tests to determine the synergistic benefits of combined aerobic and cognitive training on fluid intelligence and the role of IGF-1 in chronic stroke. These measures were assessed at baseline, post-training and 3-month follow-up. They found significant improvement in fluid intelligence as measured by Ravens' in the groups that combined aerobic exercise and physical activity with cognitive training [52].

Although clinical measures are considered valid for assessing impairments in neurological diseases, they have inherent limitations. Subjectivity, susceptibility to patient bias, variability among clinicians, and the inability to capture cognitive nuances challenge their reliability[187], [189]. Robotic technologies offer promising solutions by objectively capturing precise data and enabling quantitative assessment of cognitive domains. These technologies have the potential to bridge the disparity between subjective observations and objective measurements, ultimately enhancing understanding and accuracy in stroke populations [174], [190]. However, a research gap exists regarding integrating robotics into cognitive assessment. While the potential benefits of robotics are recognized, further investigation is necessary to explore how they can be effectively integrated into cognitive assessments [191].

In our study, we examined the relationship between robotic measures and clinical measures for cognition in people with stroke; we found no correlation between distraction during the Object Hit and Avoid task (errors) and the two standard clinical measures we used to assess cognition.

This is similar to the findings of Simmatis et. al. (2020) which looked at the feasibility of using robotics to assess various sensorimotor and cognitive functions in people with epilepsy. Forty-six individuals with epilepsy and 92 control participants were involved in the study. Participants underwent cognitive screening using MOCA and then performed a battery of 8 robotic behavioral tasks that tested upper-limb motor and sensory performance and cognition. The study tested the correlations between participants' total scores on the MOCA and their performance on individual robotic tasks. The three tasks, Arm position matching, Object Hit and Avoid, and Trail Making Test, had correlation p-values less than 0.05. However, after multiple comparisons using the Bonferroni method for adjusting the family-wise error rate, which reduces the α value from 0.05 to 0.05/11 = 0.0045, only the Trail Making Test remained significant with MOCA. Furthermore, the study identified that many of the study individuals with epilepsy had abnormal motor task performance while performing the robotic behavioral task. The Object Hit and Avoid task requires both motor and cognitive abilities, as participants must scan the visual field, avoid distractions, and accurately hit specific targets. However, due to the task's overlapping motor and cognitive requirements, it is limited in its ability to differentiate between these two aspects. Instead, the scores from the Object Hit and Avoid task are more likely to be closely related to functional scores in tasks such as driving simulation, which were not measured in this study, rather than specific cognitive domains. This task primarily assesses motor response and visuospatial processing, as participants must move their hands to hit shapes while dealing with increasing speed within a short time interval. The distractor hit variable measures the capacity to avoid irrelevant stimuli and maintain attention on task-relevant objects[174][192]. Our study findings could suggest that the Object Hit and Avoid task may not specifically measure cognitive abilities while attention is a cognitive process, it is mediated by complex neural networks involving various brain regions,

including the prefrontal cortex, parietal cortex, and subcortical structures [193], [194]. The specific cognitive measures used in this study, MOCA and Ravens', may not capture the attentional aspects that the distractor hit variable the task assesses. Cognitive abilities are multifaceted and involve diverse cognitive domains, such as memory, executive functions, and language [52]. The Object Hit and Avoid Task may only comprehensively evaluate some of these cognitive domains, leading to no correlation with the chosen cognitive measures.

2.6.4 Robotics detected an unexpected slowing of hand speed at follow-up

Our study focused on comparing the sensitivity of robotics measures to traditional clinical measures, specifically the FMA-UE and the WMFT in measuring changes during and after a rehabilitation intervention. We were surprised to observe a significant decline in affected hand speed during the Object Hit task after the study intervention at FOLLOW-UP. Visual inspection of WMFT scores in Figure 2.8A suggest there was a trend towards worsening of hand function in individual participants. However, because the WMFT relies on observer scoring, it is likely less sensitive that robotics which can measure performance in small units such as milliseconds.

Krebs et al. (2014) examined the responsiveness of robotic assessments and clinical measures in individuals with stroke. The study involved 90 stroke survivors who underwent an assessment of motor function using clinical scales and robotic devices to measure arm movement 7, 14, 21, 30, and 90 days after their stroke event at 2 clinical sites. They found that robotic measures demonstrated higher sensitivity and responsiveness in capturing motor recovery changes compared to clinical measures. In contrast, Logan et al. (2017) compared the effectiveness of robotics and the FMA-UE and other clinical measures in assessing motor recovery in individuals with traumatic brain injury. The study involved 23 subjects with first-time traumatic brain injury in the subacute and chronic phase, and their data was matched with 275 to 497 healthy control

subjects. They reported that both the robotics measures and the FMA-UE showed similar sensitivity and responsiveness in measuring motor and cognitive performance changes. Although there are variations in the specific populations and interventions across these studies, our findings are consistent with previous research suggesting that robotics measures are generally more sensitive in capturing recovering (or declining) changes compared to traditional clinical measures such as the FMA-UE or WMFT[126], [195].

The observed decline in motor performance at 30day follow-up is surprising and worth discussing. In Figure 2.9, showing individual motor and cognitive data, there is stability in scores from PRE to POST with an observable decline at Follow-Up. This post-intervention decline may be because of the short intervention (15 session) and likely short-lived effects. Alternately, participants experienced a high degree of social interaction and coaching during the intervention which was halted once the intervention ceased. The attention of the investigators during the study intervention could have created a Hawthorne Effect that wore off over time. Notably there was a statistically significant decline in affected hand speed scores from PRE to Follow Up but not from POST to Follow Up which was interesting. Regardless, the robotic assessment detected this unexpected finding when the other standard clinical test (WMFT) did not. There is a limited number of published papers specifically examining the sensitivity of robotics measures compared to clinical assessments. Our findings add to an emerging body of research examining the sensitivity and responsivity of robotic outcome measurement in various neurological conditions[172], [190], [190], [191].

2.6.5 Limitations

One limitation of our study is that we could only complete longitudinal assessments on those participants who could use the Kinarm Endpoint robot. Some participants who initially met our inclusion criteria were later excluded due to hand spasticity and inability to use the Kinarm robotic device. This exclusion may limit the generalizability of our sensitivity/responsivity findings to stroke patients with only mild to moderate motor deficits who could use the Kinarm robotic device. Additionally, we observed a floor effect with the Kinarm robotic device, as participants scoring below 21 on the FMA-UE assessment could not use the device. This limited our study's range of motor deficits, making it difficult to include all stroke participants with severe motor deficits. The device manufacturer should consider adaptive modifications to permit grasping of the robot handle even among people with weak grip.

Another limitation is the small sample size. The study included a limited number of participants, which may not represent the broader population of individuals with chronic stroke. This small sample size may limit the generalizability of our findings, as well as the statistical power to detect significant changes in upper limb movement and cognition following rehabilitation. Additionally, the study was conducted at a single center, which may limit the external validity of the findings to other clinical settings. Further studies with larger sample sizes and conducted at multiple centers are necessary to confirm the feasibility of using robotic kinematics to measure rehabilitation-induced changes in upper limb movement and cognition in individuals with chronic stroke.

2.7 CONCLUSION

The use of the Kinarm Endpoint robot for robotic assessment proved to be efficient and safe, although certain stroke participants encountered difficulty in securely grasping the robot during testing. This underscores the necessity for adaptive grip support to accommodate individuals with severe hand weakness. Regarding the data obtained from the Object Hit task, particularly the Affected Hand Speed, it exhibited a correlation with impairments in the hand and arm (FMA-UE). However, no correlation was found with everyday hand function (WMFT), suggesting that the task might not effectively measure functional abilities in daily life. Analysis of the Object Hit and Avoid Task revealed no significant correlations with cognitive measures. This implies that the task primarily focuses on motor aspects, such as hand-eye coordination and response speed, rather than specifically assessing cognitive functions. An unexpected decline in affected hand speed over time was identified through robotics during the object hit and avoid task. This discovery provides evidence supporting the sensitivity of the robotic tool in capturing changes in motor performance over a period of time. In conclusion, although the robotic assessment displayed promise in evaluating motor impairments, further enhancements are required to address grip support for individuals with severe hand weakness. The Object Hit and Avoid task is more suitable for assessing motor abilities rather than cognitive functions, and the robotic tool demonstrates sensitivity in detecting changes in motor performance over time.

3 CHAPTER THREE

The aftermath of stroke often results in a wide range of physical and cognitive deficits, which can significantly impact the quality of life of the affected individuals [196]. Therefore, it is essential to accurately assess stroke patients' motor and cognitive changes to tailor rehabilitation programs and improve their functional outcomes. Traditionally, clinical assessments such as the Fugl-Meyer Assessment and the Modified Rankin Scale have been used to measure motor and cognitive changes in stroke patients, respectively [197][198]. However, these assessments have several limitations, such as the inability to capture subtle changes in stroke patients' motor and cognitive abilities and the reliance on subjective ratings by clinicians[199]. Recent advancements in robotics technology have enabled the development of objective and quantitative assessments of motor and cognitive function in stroke patients [200]. These assessments have shown promise in accurately measuring the functional outcomes of stroke rehabilitation programs. The primary purpose of this pilot study was to evaluate the feasibility of measuring motor and cognitive changes in chronic stroke patients using robotics assessments against traditional clinical assessments. We hypothesized that robotics assessments would provide more objective and accurate motor and cognitive function measures than traditional clinical assessments. This chapter will focus on aspects of the study not previously discussed in other chapters.

3.1 DISCUSSION OF RESULTS

3.1.1 Robotics as a measurement method or as a therapy:

The Kinarm robot is a sophisticated robotic device used to assess motor function and rehabilitation progress in individuals with stroke. The robot can measure a range of movement

parameters, such as speed, accuracy, and precision, with high precision and reliability. However, the robot was also used as a therapeutic tool in this study. Participants completed aerobic exercise paired with a motor learning task on the Kinarm system. Although the assessment task and the therapeutic tasks were different, there were some common elements such as learning to interact with the virtual reality environment and the joint angles required to manipulate the endpoint effectors. It is possible that participants simply learned to use the robot better; which may not be related to 'recovery' of lost movement per se. Ideally, the robotic outcome assessment should take place on a different platform to remove the effects of practice.

3.1.2 The robotic interface was enjoyable and engaging for participants:

Although the study did not involve obtaining feedback from participants on the acceptability of the Kinarm device, anecdotal evidence gathered over the approximately 150 sessions of robotic training and assessments supports that participants with stroke enjoyed using the platform. Several participants felt that the robotic training was helpful to them and requested to continue the robotic training after the study was completed. Future work examining the feasibility and acceptability of the robotic platform should engage with patient users to gather their perspectives.

3.1.3 Exoskeleton versus Endpoint Kinarm Robot:

The current study employed the Endpoint version of Kinarm robot. Of the two systems, Endpoint is considered the 'second' and least expensive version of the Kinarm. However, the Endpoint provides more naturalistic movement of the arms than the Exoskeleton version. In the Endpoint, the arms are oriented near the waist in a "sawing wood" position, whereas in the Exoskeleton, the elbows are raised laterally to shoulder height, which will likely become

uncomfortable with repeated movement practice and could create shoulder pain. Future work should compare the effects of robotic training in the two configurations on musculoskeletal pain.

3.1.4 Kinarm Standard Tests:

If one were to complete the entire suite of Kinarm Standard Tests for sensory, motor and cognitive functions, testing would take more than 60min, which is not practical within a clinical trial and would likely be fatiguing for participants. The study outlined in this thesis examined two specific tests but, at this time, it is not clear which of the Kinarm Standard Tests are the most suitable as a outcomes for clinical trials. Future work should undertake a head-to-head comparison of the Kinarm Standard Tests, helping to prioritize those that are most sensitive and reliable.

3.2 LIMITATIONS

The current study has limitations, which have been previously acknowledged. One limitation pertains to the inability to utilize the Kinarm robot in individuals with severe motor impairments due to stroke severity, particularly spasticity in the affected arm(s). Moreover, three additional limitations are worth noting: sample size, sample population, result generalization, the limited scope of assessment, learning time, and purchasing costs.

Firstly, the sample size of this study was small, consisting of only ten participants, and lacked a control group. This limited sample size adversely affected the study's statistical power and hindered the ability to draw robust conclusions regarding the effectiveness of the Kinarm robot in stroke rehabilitation.

Secondly, the sample population may introduce limitations. Individuals with severe motor impairments or cognitive deficits may not be suitable candidates for the Kinarm robot, as they may need help to adhere to the instructions or successfully complete the required tasks. Consequently,

this could result in a biased sample that may not represent the broader stroke rehabilitation population.

Thirdly, the Kinarm robot's assessment capabilities may have a restricted scope. Although the robot excels in measuring specific movements, it may not be as suitable for evaluating other aspects of rehabilitation, such as balance or gait. Consequently, the use of the Kinarm robot may need to be supplemented with additional measures to obtain a comprehensive evaluation of rehabilitation progress.

Another potential limitation lies in the generalizability of the findings. The Kinarm robot is a specialized tool typically employed in research and clinical settings, and its availability and feasibility may vary across different rehabilitation programs and populations. Thus, caution must be exercised when generalizing the results to contexts beyond those utilizing the Kinarm robot.

Additionally, a learning curve associated with using the Kinarm robot may impact the study outcomes. Participants may require an adjustment period to acclimate to the robot and develop proficiency in its use, potentially influencing the measurements' reliability.

Finally, the cost of the Kinarm robot may pose a limiting factor for certain rehabilitation programs or research studies. The high financial investment required to acquire the device may hinder its widespread adoption, particularly in resource-limited settings.

Despite these limitations, this study has provided promising evidence for the potential of the Kinarm robot as a valuable tool for measuring rehabilitation-induced changes in the stroke population. However, further research is necessary to address these limitations and provide a more comprehensive understanding of the role and effectiveness of the Kinarm robot in stroke rehabilitation.

3.3 RECOMMENDATION

Based on the research conducted in this study, several key observations, and recommendations regarding the Kinarm robotic system have been identified. The focus of the study was primarily on participants' performance during the completion of the Kinarm Standard Test and the Serial Reaction Time Task, both of which were carried out using the Kinarm platform while participating in the rehabilitation intervention. We observed that despite the participants' extensive practice with the Kinarm system, their performance on the tasks did not show the expected improvement. This raises the question of why participants did not perform better despite the ample practice. Could it be that participants intentionally compromised speed to achieve better accuracy? Additionally, exploring participants' enjoyment of using the Kinarm system and their comprehension of its operation would provide valuable insights, as we noticed that all participants were excited each time of their study visits to use the Kinarm robotic device and overall gave us great user experience feedback. All participants understood the instructions for using the device and performed the assigned tasks with no difficulty.

Furthermore, although the Kinarm robot is a 2D virtual reality/Augmented device, which is a common technology amongst gamers in the younger populations, we noticed that the older participants we recruited into the study did not have much trouble understanding the use of the system effectively as we provided the information on how to use the device comprehensively. Another important consideration is the difference in arm positioning between the Exoskeleton and Endpoint models of the Kinarm system. The Endpoint model we used in our study has a movement pattern that is presumed to be more natural, which could benefit individuals experiencing post-stroke shoulder pain, unlike the Exoskeleton model that requires the arm to be abducted to shoulder height while some arm movement tasks, which may pose difficulties for individuals with post-stroke shoulder pain.

Another observation was time constraints associated with completing assessments using the Kinarm system. Completing all the KSTs would take approximately two hours, so it is advisable to develop an evidence-based algorithm that guides the selection of the most suitable KST for a specific impairment. Such

an algorithm would enable researchers and clinicians to choose the optimal test based on their specific requirements and time limitations. Also based on our observations, participants with moderate or severe upper limb impairments that could not grasp the paddle encountered a limitation with the Kinarm Endpoint system. The custom 3D hand extension we designed proved incompatible, risking damage to the torque sensor. To address this, we recommend incorporating an improved handle and extension for the paddle, providing better support, preventing hand slippage, and eliminating elbow dragging on the table surface. In order to further enhance the usability and effectiveness of the Kinarm system, especially for individuals with moderate or severe upper limb impairments, we propose exploring potential improvements in the handhold design of the Endpoint model. Developing and implementing a more effective handhold design can reduce hand slippage and minimize the risk of elbow dragging, significantly enhancing overall usability and effectiveness. This would ultimately offer greater utility for patients with these specific impairments.

3.4 FUTURE RESEARCH

Throughout this study, it became clear that some areas require additional research. Future research on the role of the Kinarm Robot in stroke rehabilitation could explore several areas, including: (1) Long-term outcomes: Studies could investigate the long-term effects of Kinarm Robot-assisted therapy on stroke patients. This could include assessing the durability of functional gains achieved with the Kinarm Robot and the impact of therapy on quality of life and participation in daily activities. (2) Individualized therapy: Research could explore ways to tailor Kinarm Robot-assisted therapy to individual patient needs. This could include developing personalized therapy protocols based on patient-specific impairments or using machine learning algorithms to adapt the therapy to the patient's progress over time. (3) Comparison to other interventions: Studies could compare the effectiveness of Kinarm Robot-assisted therapy to other forms of stroke rehabilitation, such as traditional physical therapy or virtual reality-based interventions. This could help identify

which interventions are most effective for different patient populations and which therapy components are most important for achieving functional gains. (4) Mechanisms of action: Research could investigate the underlying neural mechanisms by Kinarm Robot-assisted therapy that leads to functional improvements in stroke patients. This could include using neuroimaging techniques to study changes in brain activity or connectivity following therapy. (5) Cost-effectiveness: Finally, studies could assess the cost-effectiveness of Kinarm Robot-assisted therapy compared to other forms of stroke rehabilitation. This could include analyzing the direct costs of therapy and the potential cost savings associated with improved functional outcomes and reduced healthcare utilization.

3.5 CONCLUSION

Our study findings suggest that using the Kinarm robotic assessment in individuals with chronic stroke could be feasible and may be capable of effectively identifying a broad range of upper-limb motor and cognitive impairments. Furthermore, we may have observed that the Kinarm robot might complement existing clinical rating scales by providing valuable insights into evaluating disability resulting from stroke. The results of our study may suggest that the Kinarm robot might be a sensitive, reliable, and practical tool that could potentially surpass standard clinical assessments in detecting changes induced by rehabilitation in chronic stroke patients.

Consistent with prior research, our study confirms the efficacy of the Kinarm robot in detecting motor impairments and monitoring alterations in motor performance among patients with neurological disorders. By offering precise and quantitative measurements of critical movement parameters, including speed, accuracy, and real-time feedback, the Kinarm robot enables a comprehensive assessment and continuous monitoring of rehabilitation progress. Moreover, the

controlled and standardized testing environment of the Kinarm robot minimizes the influence of confounding variables such as fatigue and motivation.

The objective and quantitative measurements provided by the Kinarm robot hold substantial promise in aiding clinicians to identify specific deficits and tailor treatment interventions accordingly. Our study highlights the potential of the Kinarm robot as a valuable tool for assessing and monitoring the rehabilitation progress of individuals with chronic neurological disorders. Additionally, it offers valuable insights into the effectiveness of various treatment interventions. These findings contribute significantly to the growing body of evidence supporting the integration of the Kinarm robot into clinical practice, ultimately leading to improved quality of care and rehabilitation outcomes for individuals with chronic stroke and other neurological conditions.

REFERENCES

[1] V. L. Feigin *et al.*, "World Stroke Organization (WSO): Global Stroke Fact Sheet 2022," *International Journal of Stroke*, vol. 17, no. 1, pp. 18–29, Jan. 2022, doi: 10.1177/17474930211065917.

[2] J. Boulanger *et al.*, "Canadian Stroke Best Practice Recommendations for Acute Stroke Management: Prehospital, Emergency Department, and Acute Inpatient Stroke Care, 6th Edition, Update 2018," *International Journal of Stroke*, vol. 13, no. 9, pp. 949–984, Dec. 2018, doi: 10.1177/1747493018786616.

[3] K. L. Lanctôt *et al.*, "Canadian Stroke Best Practice Recommendations: Mood, Cognition and Fatigue following Stroke, 6th edition update 2019," *International Journal of Stroke*, vol. 15, no. 6, pp. 668–688, Aug. 2020, doi: 10.1177/1747493019847334.

[4] S. M, "Portrait of caregivers. 2012. Statistics Canada.," Mar. 09, 2017.

[5] "Connected by the numbers," *Heart and Stroke Foundation of Canada*. https://www.heartandstroke.ca/en/articles/connected-by-the-numbers/ (accessed Dec. 21, 2022).

[6] C. S. Mang, K. L. Campbell, C. J. D. Ross, and L. A. Boyd, "Promoting Neuroplasticity for Motor Rehabilitation After Stroke: Considering the Effects of Aerobic Exercise and Genetic Variation on Brain-Derived Neurotrophic Factor," *Physical Therapy*, vol. 93, no. 12, pp. 1707–1716, Dec. 2013, doi: 10.2522/ptj.20130053.

[7] L. P, B. J, and K. G, "Stroke rehabilitation," *Lancet (London, England)*, vol. 377, no. 9778, May 2011, doi: 10.1016/S0140-6736(11)60325-5.

[8] X. Wang *et al.*, "Endovascular thrombectomy with or without intravenous alteplase for acute ischemic stroke due to large vessel occlusion: a systematic review and meta-analysis

of randomized trials," *Stroke Vasc Neurol*, vol. 7, no. 6, Dec. 2022, doi: 10.1136/svn-2022-001547.

[9] European Stroke Organisation (ESO) Executive Committee and ESO Writing Committee, "Guidelines for management of ischaemic stroke and transient ischaemic attack 2008," *Cerebrovasc Dis*, vol. 25, no. 5, pp. 457–507, 2008, doi: 10.1159/000131083.

[10] A. Esquenazi and A. Packel, "Robotic-assisted gait training and restoration," *Am J Phys Med Rehabil*, vol. 91, no. 11 Suppl 3, pp. S217-227; quiz S228-231, Nov. 2012, doi: 10.1097/PHM.0b013e31826bce18.

[11] T. C. Bourke, C. R. Lowrey, S. P. Dukelow, S. D. Bagg, K. E. Norman, and S. H. Scott, "A robot-based behavioural task to quantify impairments in rapid motor decisions and actions after stroke," *J Neuroeng Rehabil*, vol. 13, p. 91, Oct. 2016, doi: 10.1186/s12984-016-0201-2.

[12] K. J. Pascual, E. Vlasova, K. J. Lockett, J. Richardson, and M. Yochelson, "Evaluating the Impact of Personalized Stroke Management Tool Kits on Patient Experience and Stroke Recovery," *J Patient Exp*, vol. 5, no. 4, pp. 244–249, Dec. 2018, doi: 10.1177/2374373517750416.

[13] A. Frisoli, M. Barsotti, E. Sotgiu, G. Lamola, C. Procopio, and C. Chisari, "A randomized clinical control study on the efficacy of three-dimensional upper limb robotic exoskeleton training in chronic stroke," *Journal of NeuroEngineering and Rehabilitation*, vol. 19, no. 1, p. 14, Feb. 2022, doi: 10.1186/s12984-022-00991-y.

[14] C. Langstaff *et al.*, "Enhancing Community-Based Rehabilitation for Stroke Survivors: Creating a Discharge Link," *Topics in Stroke Rehabilitation*, vol. 21, no. 6, pp. 510–519, Nov. 2014, doi: 10.1310/tsr2106-510.

[15] C. M. Stinear, C. E. Lang, S. Zeiler, and W. D. Byblow, “Advances and challenges in stroke rehabilitation,” *The Lancet Neurology*, vol. 19, no. 4, pp. 348–360, Apr. 2020, doi: 10.1016/S1474-4422(19)30415-6.

[16] P. Raghavan, “Upper Limb Motor Impairment After Stroke,” *Physical Medicine and Rehabilitation Clinics of North America*, vol. 26, no. 4, pp. 599–610, Nov. 2015, doi: 10.1016/j.pmr.2015.06.008.

[17] P. Aqueveque *et al.*, *After Stroke Movement Impairments: A Review of Current Technologies for Rehabilitation*. IntechOpen, 2017. doi: 10.5772/67577.

[18] “NINDS | Post-Stroke Rehabilitation.” https://www.stroke.nih.gov/materials/rehabilitation.htm (accessed Apr. 02, 2023).

[19] S. Masiero *et al.*, “The value of robotic systems in stroke rehabilitation,” *Expert review of medical devices*, vol. 11, Jan. 2014, doi: 10.1586/17434440.2014.882766.

[20] N. Norouzi-Gheidari *et al.*, “Feasibility and preliminary efficacy of a combined virtual reality, robotics and electrical stimulation intervention in upper extremity stroke rehabilitation,” *Journal of NeuroEngineering and Rehabilitation*, vol. 18, no. 1, p. 61, Apr. 2021, doi: 10.1186/s12984-021-00851-1.

[21] H. Jokinen *et al.*, “Post-stroke cognitive impairment is common even after successful clinical recovery,” *European Journal of Neurology*, vol. 22, no. 9, pp. 1288–1294, 2015, doi: 10.1111/ene.12743.

[22] B. Patel and J. Birns, “Post-Stroke Cognitive Impairment,” in *Management of Post-Stroke Complications*, A. Bhalla and J. Birns, Eds., Cham: Springer International Publishing, 2015, pp. 277–306. doi: 10.1007/978-3-319-17855-4_12.

[23] L. Terroni *et al.*, "Association among depression, cognitive impairment and executive dysfunction after stroke," *Dement Neuropsychol*, vol. 6, no. 3, pp. 152–157, 2012, doi: 10.1590/S1980-57642012DN06030007.

[24] S. Hama *et al.*, "Relationships between motor and cognitive functions and subsequent post-stroke mood disorders revealed by machine learning analysis," *Sci Rep*, vol. 10, p. 19571, Nov. 2020, doi: 10.1038/s41598-020-76429-z.

[25] J. M. Ferro, L. Caeiro, and C. Santos, "Poststroke emotional and behavior impairment: a narrative review," *Cerebrovasc Dis*, vol. 27 Suppl 1, pp. 197–203, 2009, doi: 10.1159/000200460.

[26] D. H. Saunders, C. A. Greig, and G. E. Mead, "Physical Activity and Exercise After Stroke," *Stroke*, vol. 45, no. 12, pp. 3742–3747, Dec. 2014, doi: 10.1161/STROKEAHA.114.004311.

[27] E. S. Lawrence *et al.*, "Estimates of the Prevalence of Acute Stroke Impairments and Disability in a Multiethnic Population," *Stroke*, vol. 32, no. 6, pp. 1279–1284, Jun. 2001, doi: 10.1161/01.STR.32.6.1279.

[28] Y. W. Kim, "Update on Stroke Rehabilitation in Motor Impairment," *Brain Neurorehabil*, vol. 15, no. 2, p. e12, Jul. 2022, doi: 10.12786/bn.2022.15.e12.

[29] C. Liu, J. Lu, H. Yang, and K. Guo, "Current State of Robotics in Hand Rehabilitation after Stroke: A Systematic Review," *Applied Sciences*, vol. 12, no. 9, Art. no. 9, Jan. 2022, doi: 10.3390/app12094540.

[30] X. Xue *et al.*, "Global Trends and Hotspots in Research on Rehabilitation Robots: A Bibliometric Analysis From 2010 to 2020," *Frontiers in Public Health*, vol. 9, 2022,

Accessed: Dec. 21, 2022. [Online]. Available: https://www.frontiersin.org/articles/10.3389/fpubh.2021.806723

[31] S. P. Dukelow, "The potential power of robotics for upper extremity stroke rehabilitation," *International Journal of Stroke*, vol. 12, no. 1, pp. 7–8, Jan. 2017, doi: 10.1177/1747493016654483.

[32] C. B. C. News ·, "Robot helps measure stroke effects | CBC News," *CBC*, Apr. 14, 2010. https://www.cbc.ca/news/canada/calgary/robot-helps-measure-stroke-effects-1.884495 (accessed Apr. 03, 2023).

[33] P. Tadi and F. Lui, *Acute Stroke*. StatPearls Publishing, 2022. Accessed: Nov. 06, 2022. [Online]. Available: https://www.ncbi.nlm.nih.gov/books/NBK535369/

[34] A. P. Coupland, A. Thapar, M. I. Qureshi, H. Jenkins, and A. H. Davies, "The definition of stroke," *J R Soc Med*, vol. 110, no. 1, pp. 9–12, Jan. 2017, doi: 10.1177/0141076816680121.

[35] G. J. Hankey and D. J. Blacker, "Is it a stroke?," *BMJ*, vol. 350, p. h56, Jan. 2015, doi: 10.1136/bmj.h56.

[36] M. S. Elkind and R. L. Sacco, "Stroke Risk Factors and Stroke Prevention," *Semin Neurol*, vol. 18, no. 4, pp. 429–440, 1998, doi: 10.1055/s-2008-1040896.

[37] A. Sabih, P. Tadi, and A. Kumar, *Stroke Prevention*. StatPearls Publishing, 2022. Accessed: Jan. 05, 2023. [Online]. Available: https://www.ncbi.nlm.nih.gov/books/NBK470234/

[38] A. Hussain, M. Lee, J. Rana, and S. S. Virani, "Epidemiology and risk factors for stroke in young individuals: implications for prevention," *Current Opinion in Cardiology*, vol. 36, no. 5, p. 565, Sep. 2021, doi: 10.1097/HCO.0000000000000894.

[39] C. Isabel, D. Calvet, and J.-L. Mas, “Stroke prevention,” *La Presse Médicale*, vol. 45, no. 12, Part 2, pp. e457–e471, Dec. 2016, doi: 10.1016/j.lpm.2016.10.009.

[40] A. K. Boehme, C. Esenwa, and M. S. V. Elkind, “Stroke Risk Factors, Genetics, and Prevention,” *Circulation Research*, vol. 120, no. 3, pp. 472–495, Feb. 2017, doi: 10.1161/CIRCRESAHA.116.308398.

[41] N. Goljar *et al.*, “Functioning and disability in stroke,” *Disability and Rehabilitation*, vol. 32, no. sup1, pp. S50–S58, Jan. 2010, doi: 10.3109/09638288.2010.517598.

[42] S. S. Virani *et al.*, “Heart Disease and Stroke Statistics—2020 Update: A Report From the American Heart Association,” *Circulation*, vol. 141, no. 9, pp. e139–e596, Mar. 2020, doi: 10.1161/CIR.0000000000000757.

[43] S. S. Virani *et al.*, “Heart Disease and Stroke Statistics—2021 Update: A Report From the American Heart Association,” *Circulation*, vol. 143, no. 8, Feb. 2021, doi: 10.1161/CIR.0000000000000950.

[44] V. L. Feigin *et al.*, “Global and regional burden of stroke during 1990–2010: findings from the Global Burden of Disease Study 2010,” *The Lancet*, vol. 383, no. 9913, pp. 245–255, Jan. 2014, doi: 10.1016/S0140-6736(13)61953-4.

[45] P. H. A. of Canada, “Canadian Chronic Disease Surveillance System (CCDSS).” https://health-infobase.canada.ca/ccdss/data-tool/#wb-cont (accessed Nov. 06, 2022).

[46] “Our province. Our health. Our Future. A 10-Year Health Transformation: The Report”.

[47] J. Bernhardt *et al.*, “Agreed definitions and a shared vision for new standards in stroke recovery research: The Stroke Recovery and Rehabilitation Roundtable taskforce,” *Int J Stroke*, vol. 12, no. 5, pp. 444–450, Jul. 2017, doi: 10.1177/1747493017711816.

[48] C. Grefkes and G. R. Fink, “Recovery from stroke: current concepts and future perspectives,” *Neurological Research and Practice*, vol. 2, no. 1, p. 17, Jun. 2020, doi: 10.1186/s42466-020-00060-6.

[49] S. T. Carmichael, L. Wei, C. M. Rovainen, and T. A. Woolsey, “New patterns of intracortical projections after focal cortical stroke,” *Neurobiol Dis*, vol. 8, no. 5, pp. 910–922, Oct. 2001, doi: 10.1006/nbdi.2001.0425.

[50] S. T. Carmichael, B. Kathirvelu, C. A. Schweppe, and E. H. Nie, “Molecular, cellular and functional events in axonal sprouting after stroke,” *Exp Neurol*, vol. 287, no. Pt 3, pp. 384–394, Jan. 2017, doi: 10.1016/j.expneurol.2016.02.007.

[51] A. Alawieh, J. Zhao, and W. Feng, “Factors affecting post-stroke motor recovery: Implications on neurotherapy after brain injury,” *Behav Brain Res*, vol. 340, pp. 94–101, Mar. 2018, doi: 10.1016/j.bbr.2016.08.029.

[52] M. Ploughman *et al.*, “Synergistic Benefits of Combined Aerobic and Cognitive Training on Fluid Intelligence and the Role of IGF-1 in Chronic Stroke,” *Neurorehabil Neural Repair*, vol. 33, no. 3, pp. 199–212, Mar. 2019, doi: 10.1177/1545968319832605.

[53] N. F. Horgan, M. O’Regan, C. J. Cunningham, and A. M. Finn, “Recovery after stroke: a 1-year profile,” *Disabil Rehabil*, vol. 31, no. 10, pp. 831–839, 2009, doi: 10.1080/09638280802355072.

[54] A. M. Ch’Ng, D. French, and N. Mclean, “Coping with the Challenges of Recovery from Stroke: Long Term Perspectives of Stroke Support Group Members,” *J Health Psychol*, vol. 13, no. 8, pp. 1136–1146, Nov. 2008, doi: 10.1177/1359105308095967.

[55] S. A. Chohan, P. K. Venkatesh, and C. H. How, “Long-term complications of stroke and secondary prevention: an overview for primary care physicians,” *Singapore Med J*, vol. 60, no. 12, pp. 616–620, Dec. 2019, doi: 10.11622/smedj.2019158.

[56] M. J. M. Ramos-Lima, I. de C. Brasileiro, T. L. de Lima, and P. Braga-Neto, “Quality of life after stroke: impact of clinical and sociodemographic factors,” *Clinics*, vol. 73, p. e418, Jan. 2018, doi: 10.6061/clinics/2017/e418.

[57] “Post-stroke sensory deficits and re-education,” *Cambridge University Hospitals*. https://www.cuh.nhs.uk/patient-information/post-stroke-sensory-deficits-and-re-education/ (accessed Jan. 06, 2023).

[58] J. W. Lo *et al.*, “Long-Term Cognitive Decline After Stroke: An Individual Participant Data Meta-Analysis,” *Stroke*, vol. 53, no. 4, pp. 1318–1327, Apr. 2022, doi: 10.1161/STROKEAHA.121.035796.

[59] M. Barbay, M. Diouf, M. Roussel, O. Godefroy, and G. Study Group, “Systematic Review and Meta-Analysis of Prevalence in Post-Stroke Neurocognitive Disorders in Hospital-Based Studies,” *DEM*, vol. 46, no. 5–6, pp. 322–334, 2018, doi: 10.1159/000492920.

[60] M. Marendic *et al.*, “Categorization of Ischemic Stroke Patients Compared with National Institutes of Health Stroke Scale,” *Med Arch*, vol. 70, no. 2, pp. 119–122, Apr. 2016, doi: 10.5455/medarh.2016.70.119-122.

[61] J. Puig *et al.*, “Decreased Corticospinal Tract Fractional Anisotropy Predicts Long-term Motor Outcome After Stroke,” *Stroke*, vol. 44, no. 7, pp. 2016–2018, Jul. 2013, doi: 10.1161/STROKEAHA.111.000382.

[62] T. A. Jones, “Motor compensation and its effects on neural reorganization after stroke,” *Nat Rev Neurosci*, vol. 18, no. 5, pp. 267–280, May 2017, doi: 10.1038/nrn.2017.26.

[63] "Post-stroke Spasticity: A Review of Epidemiology, Pathophysiology, and Treatments | Elsevier Enhanced Reader." https://reader.elsevier.com/reader/sd/pii/S1873959818300073?token=436E3DFBCF14DAA85CE239DF969A0F92D4CDA92718399E82610574E2EFA8B39EA2DE6038411E6A1C90C08A815524A754&originRegion=us-east-1&originCreation=20230109194035 (accessed Jan. 09, 2023).

[64] S. E. Kasner, "Clinical interpretation and use of stroke scales," *Lancet Neurol*, vol. 5, no. 7, pp. 603–612, Jul. 2006, doi: 10.1016/S1474-4422(06)70495-1.

[65] S. E. Kasner *et al.*, "Reliability and Validity of Estimating the NIH Stroke Scale Score from Medical Records," *Stroke*, vol. 30, no. 8, pp. 1534–1537, Aug. 1999, doi: 10.1161/01.STR.30.8.1534.

[66] H. Ed *et al.*, "Intra- and inter-rater reliability of Fugl-Meyer Assessment of Upper Extremity in stroke," *Journal of rehabilitation medicine*, vol. 51, no. 9, Apr. 2019, doi: 10.2340/16501977-2590.

[67] J.-H. Lin *et al.*, "Psychometric comparisons of 4 measures for assessing upper-extremity function in people with stroke," *Phys Ther*, vol. 89, no. 8, pp. 840–850, Aug. 2009, doi: 10.2522/ptj.20080285.

[68] B. Turtle, A. Porter-Armstrong, and M. Stinson, "The reliability of the graded Wolf Motor Function Test for stroke," *British Journal of Occupational Therapy*, vol. 83, no. 9, pp. 585–594, Sep. 2020, doi: 10.1177/0308022620902697.

[69] T. B. Cumming, A. Brodtmann, D. Darby, and J. Bernhardt, "The importance of cognition to quality of life after stroke," *Journal of Psychosomatic Research*, vol. 77, no. 5, pp. 374–379, Nov. 2014, doi: 10.1016/j.jpsychores.2014.08.009.

[70] P. D. Harvey, “Domains of cognition and their assessment,” *Dialogues Clin Neurosci*, vol. 21, no. 3, pp. 227–237, Sep. 2019, doi: 10.31887/DCNS.2019.21.3/pharvey.

[71] V. I. H. Kwa, M. Limburg, and R. J. de Haan, “The role of cognitive impairment in the quality of life after ischaemic stroke,” *J Neurol*, vol. 243, no. 8, pp. 599–604, Aug. 1996, doi: 10.1007/BF00900948.

[72] N. K. J. Oksala *et al.*, “Cognitive impairment predicts poststroke death in long-term follow-up,” *Journal of Neurology, Neurosurgery & Psychiatry*, vol. 80, no. 11, pp. 1230–1235, Nov. 2009, doi: 10.1136/jnnp.2009.174573.

[73] D. Rohde *et al.*, “The Impact of Cognitive Impairment on Poststroke Outcomes: A 5-Year Follow-Up,” *J Geriatr Psychiatry Neurol*, vol. 32, no. 5, pp. 275–281, Sep. 2019, doi: 10.1177/0891988719853044.

[74] M. D. Patel, C. Coshall, A. G. Rudd, and C. D. A. Wolfe, “Cognitive Impairment after Stroke: Clinical Determinants and Its Associations with Long-Term Stroke Outcomes,” *Journal of the American Geriatrics Society*, vol. 50, no. 4, pp. 700–706, 2002, doi: 10.1046/j.1532-5415.2002.50165.x.

[75] T. J. Quinn, E. Elliott, and P. Langhorne, “Cognitive and Mood Assessment Tools for Use in Stroke,” *Stroke*, vol. 49, no. 2, pp. 483–490, Feb. 2018, doi: 10.1161/STROKEAHA.117.016994.

[76] “Evaluation of cognitive assessment in stroke rehabilitation - M McKinney, H Blake, K A Treece, N B Lincoln, E D Playfordand, J RF Gladman, 2002.” https://journals.sagepub.com/doi/10.1191/0269215502cr479oa (accessed Mar. 24, 2023).

[77] M. N. McDonnell, J. Bryan, A. E. Smith, and A. J. Esterman, “Assessing cognitive impairment following stroke,” *Journal of Clinical and Experimental Neuropsychology*, vol. 33, no. 9, pp. 945–953, Nov. 2011, doi: 10.1080/13803395.2011.575769.

[78] X. Li, D. Geng, S. Wang, and G. Sun, “Aerobic exercises and cognitive function in post-stroke patients: A systematic review with meta-analysis,” *Medicine (Baltimore)*, vol. 101, no. 41, p. e31121, Oct. 2022, doi: 10.1097/MD.0000000000031121.

[79] L. Xuefang, W. Guihua, and M. Fengru, “The effect of early cognitive training and rehabilitation for patients with cognitive dysfunction in stroke,” *Int J Methods Psychiatr Res*, vol. 30, no. 3, p. e1882, Jun. 2021, doi: 10.1002/mpr.1882.

[80] L. E. Oberlin, A. M. Waiwood, T. B. Cumming, A. L. Marsland, J. Bernhardt, and K. I. Erickson, “Effects of physical activity on post-stroke cognitive function: a meta-analysis of randomized controlled trials,” *Stroke*, vol. 48, no. 11, pp. 3093–3100, Nov. 2017, doi: 10.1161/STROKEAHA.117.017319.

[81] G. P. Wagner, S. E. MacPherson, M. A. M. P. Parente, and C. M. Trentini, “Cognitive estimation abilities in healthy and clinical populations: the use of the Cognitive Estimation Test,” *Neurol Sci*, vol. 32, no. 2, pp. 203–210, Apr. 2011, doi: 10.1007/s10072-010-0449-4.

[82] P. Julayanont, N. Phillips, H. Chertkow, and Z. S. Nasreddine, “Montreal Cognitive Assessment (MoCA): Concept and Clinical Review,” in *Cognitive Screening Instruments: A Practical Approach*, A. J. Larner, Ed., London: Springer, 2013, pp. 111–151. doi: 10.1007/978-1-4471-2452-8_6.

[83] Dr. Nurhudaya, A. Taufik, E. Sakti Yudha, and D. Suryana, “The Raven’s Advanced Progressive Matrices in Education Assessment with a Rasch Analysis,” *ujer*, vol. 7, no. 9, pp. 1996–2002, Sep. 2019, doi: 10.13189/ujer.2019.070921.

[84] L. Fetters and J. Tilson, *Evidence Based Physical Therapy*. in bookid=1917&sectionid=139054429. Philadelphia, PA 19103: F. A. Davis Company, 2012. [Online]. Available: https://www.fadavis.com/product/physical-therapy-practical-guide-evidence-based-practice-fetters-tilson

[85] “Guide to Selecting Outcome Measures,” *Physiopedia*. https://www.physio-pedia.com/Guide_to_Selecting_Outcome_Measures (accessed Nov. 10, 2022).

[86] J. F. Bean, D. D. Ölveczky, D. K. Kiely, S. I. LaRose, and A. M. Jette, “Performance-Based Versus Patient-Reported Physical Function: What Are the Underlying Predictors?,” *Phys Ther*, vol. 91, no. 12, pp. 1804–1811, Dec. 2011, doi: 10.2522/ptj.20100417.

[87] C. Hefford, J. H. Abbott, G. D. Baxter, and R. Arnold, “Outcome measurement in clinical practice: practical and theoretical issues for health related quality of life (HRQOL) questionnaires,” *Physical Therapy Reviews*, vol. 16, no. 3, pp. 155–167, Jun. 2011, doi: 10.1179/1743288X11Y.0000000004.

[88] N. Black, “Patient reported outcome measures could help transform healthcare,” *BMJ*, vol. 346, p. f167, Jan. 2013, doi: 10.1136/bmj.f167.

[89] “Clinical Meaningfulness of an Outcome Measure,” *Physiopedia*. https://www.physio-pedia.com/Clinical_Meaningfulness_of_an_Outcome_Measure (accessed Mar. 24, 2023).

[90] P. Asunta, H. Viholainen, T. Ahonen, and P. Rintala, “Psychometric properties of observational tools for identifying motor difficulties – a systematic review,” *BMC Pediatrics*, vol. 19, no. 1, p. 322, Sep. 2019, doi: 10.1186/s12887-019-1657-6.

[91] C. J. Winstein *et al.*, "Guidelines for Adult Stroke Rehabilitation and Recovery: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association," *Stroke*, vol. 47, no. 6, pp. e98–e169, Jun. 2016, doi: 10.1161/STR.0000000000000098.

[92] A. Pollock *et al.*, "Interventions for improving upper limb function after stroke," *Cochrane Database Syst Rev*, vol. 2014, no. 11, p. CD010820, Nov. 2014, doi: 10.1002/14651858.CD010820.pub2.

[93] G. Kwakkel *et al.*, "Standardized measurement of sensorimotor recovery in stroke trials: Consensus-based core recommendations from the Stroke Recovery and Rehabilitation Roundtable," *Int J Stroke*, vol. 12, no. 5, pp. 451–461, Jul. 2017, doi: 10.1177/1747493017711813.

[94] K. E. Laver, B. Lange, S. George, J. E. Deutsch, G. Saposnik, and M. Crotty, "Virtual reality for stroke rehabilitation," *Cochrane Database Syst Rev*, vol. 11, no. 11, p. CD008349, Nov. 2017, doi: 10.1002/14651858.CD008349.pub4.

[95] N. Norouzi-Gheidari, P. S. Archambault, and J. Fung, "Effects of robot-assisted therapy on stroke rehabilitation in upper limbs: Systematic review and meta-analysis of the literature," *JRRD*, vol. 49, no. 4, p. 479, 2012, doi: 10.1682/JRRD.2010.10.0210.

[96] J. Mehrholz, M. Pohl, T. Platz, J. Kugler, and B. Elsner, "Electromechanical and robot-assisted arm training for improving activities of daily living, arm function, and arm muscle strength after stroke," *Cochrane Database Syst Rev*, vol. 2015, no. 11, p. CD006876, Nov. 2015, doi: 10.1002/14651858.CD006876.pub4.

[97] J. Mehrholz, M. Pohl, T. Platz, J. Kugler, and B. Elsner, "Electromechanical and robot-assisted arm training for improving activities of daily living, arm function, and arm muscle

strength after stroke," *Cochrane Database of Systematic Reviews*, no. 9, 2018, doi: 10.1002/14651858.CD006876.pub5.

[98] G. B. Prange, M. J. A. Jannink, C. G. M. Groothuis-Oudshoorn, H. J. Hermens, and M. J. IJzerman, "Systematic review of the effect of robot-aided therapy on recovery of the hemiparetic arm after stroke," *JRRD*, vol. 43, no. 2, p. 171, 2006, doi: 10.1682/JRRD.2005.04.0076.

[99] C. Duret, A.-G. Grosmaire, and H. I. Krebs, "Robot-Assisted Therapy in Upper Extremity Hemiparesis: Overview of an Evidence-Based Approach," *Frontiers in Neurology*, vol. 10, 2019, Accessed: Mar. 25, 2023. [Online]. Available: https://www.frontiersin.org/articles/10.3389/fneur.2019.00412

[100] R. Bertani, C. Melegari, M. C. De Cola, A. Bramanti, P. Bramanti, and R. S. Calabrò, "Effects of robot-assisted upper limb rehabilitation in stroke patients: a systematic review with meta-analysis," *Neurol Sci*, vol. 38, no. 9, pp. 1561–1569, Sep. 2017, doi: 10.1007/s10072-017-2995-5.

[101] M. J. Johnson, "Recent trends in robot-assisted therapy environments to improve real-life functional performance after stroke," *Journal of NeuroEngineering and Rehabilitation*, vol. 3, no. 1, p. 29, Dec. 2006, doi: 10.1186/1743-0003-3-29.

[102] C. Hung, Y. Hsieh, C. Wu, Y. Lin, K. Lin, and C. Chen, "The Effects of Combination of Robot-Assisted Therapy With Task-Specific or Impairment-Oriented Training on Motor Function and Quality of Life in Chronic Stroke," *PM&R*, vol. 8, no. 8, pp. 721–729, 2016, doi: 10.1016/j.pmrj.2016.01.008.

[103] S. S. Conroy, G. F. Wittenberg, H. I. Krebs, M. Zhan, C. T. Bever, and J. Whitall, "Robot-Assisted Arm Training in Chronic Stroke: Addition of Transition-to-Task Practice,"

Neurorehabil Neural Repair, vol. 33, no. 9, pp. 751–761, Sep. 2019, doi: 10.1177/1545968319862558.

[104] I. Aprile *et al.*, "Robotic Rehabilitation: An Opportunity to Improve Cognitive Functions in Subjects With Stroke. An Explorative Study," *Front Neurol*, vol. 11, p. 588285, Nov. 2020, doi: 10.3389/fneur.2020.588285.

[105] K. D. Bui, B. Lyn, M. Roland, C. A. Wamsley, R. Mendonca, and M. J. Johnson, "The Impact of Cognitive Impairment on Robot-Based Upper-Limb Motor Assessment in Chronic Stroke," *Neurorehabil Neural Repair*, vol. 36, no. 9, pp. 587–595, Sep. 2022, doi: 10.1177/15459683221110892.

[106] I. Jakob *et al.*, "Robotic and Sensor Technology for Upper Limb Rehabilitation," *PM&R*, vol. 10, no. 9S2, pp. S189–S197, 2018, doi: 10.1016/j.pmrj.2018.07.011.

[107] B. T. Volpe, M. Ferraro, H. I. Krebs, and N. Hogan, "Robotics in the rehabilitation treatment of patients with stroke," *Curr Atheroscler Rep*, vol. 4, no. 4, pp. 270–276, Jul. 2002, doi: 10.1007/s11883-002-0005-7.

[108] A. B. Keeling, M. Piitz, J. A. Semrau, M. D. Hill, S. H. Scott, and S. P. Dukelow, "Robot enhanced stroke therapy optimizes rehabilitation (RESTORE): a pilot study," *J Neuroeng Rehabil*, vol. 18, p. 10, Jan. 2021, doi: 10.1186/s12984-021-00804-8.

[109] T. Takebayashi, K. Takahashi, Y. Okita, H. Kubo, K. Hachisuka, and K. Domen, "Impact of the robotic-assistance level on upper extremity function in stroke patients receiving adjunct robotic rehabilitation: sub-analysis of a randomized clinical trial," *Journal of NeuroEngineering and Rehabilitation*, vol. 19, no. 1, p. 25, Feb. 2022, doi: 10.1186/s12984-022-00986-9.

[110] A. A. Blank, J. A. French, A. U. Pehlivan, and M. K. O'Malley, "Current Trends in Robot-Assisted Upper-Limb Stroke Rehabilitation: Promoting Patient Engagement in Therapy," *Curr Phys Med Rehabil Rep*, vol. 2, no. 3, pp. 184–195, Sep. 2014, doi: 10.1007/s40141-014-0056-z.

[111] W. H. Chang and Y.-H. Kim, "Robot-assisted Therapy in Stroke Rehabilitation," *J Stroke*, vol. 15, no. 3, pp. 174–181, Sep. 2013, doi: 10.5853/jos.2013.15.3.174.

[112] H. Chen, K. Lin, R. Liing, C. Wu, and C. Chen, "Kinematic measures of Arm-trunk movements during unilateral and bilateral reaching predict clinically important change in perceived arm use in daily activities after intensive stroke rehabilitation," *Journal of NeuroEngineering and Rehabilitation*, vol. 12, no. 1, p. 84, Sep. 2015, doi: 10.1186/s12984-015-0075-8.

[113] N. Hussain, K. S. Sunnerhagen, and M. Alt Murphy, "End-point kinematics using virtual reality explaining upper limb impairment and activity capacity in stroke," *Journal of NeuroEngineering and Rehabilitation*, vol. 16, no. 1, p. 82, Jul. 2019, doi: 10.1186/s12984-019-0551-7.

[114] M. A. Murphy, C. Willén, and K. S. Sunnerhagen, "Kinematic Variables Quantifying Upper-Extremity Performance After Stroke During Reaching and Drinking From a Glass," *Neurorehabil Neural Repair*, vol. 25, no. 1, pp. 71–80, Jan. 2011, doi: 10.1177/1545968310370748.

[115] N. Nordin, S. Q. Xie, and B. Wünsche, "Assessment of movement quality in robot-assisted upper limb rehabilitation after stroke: a review," *Journal of NeuroEngineering and Rehabilitation*, vol. 11, no. 1, p. 137, Sep. 2014, doi: 10.1186/1743-0003-11-137.

[116] A. Schwarz, M. M. C. Bhagubai, G. Wolterink, J. P. O. Held, A. R. Luft, and P. H. Veltink, “Assessment of Upper Limb Movement Impairments after Stroke Using Wearable Inertial Sensing,” *Sensors*, vol. 20, no. 17, Art. no. 17, Jan. 2020, doi: 10.3390/s20174770.

[117] R. Bouça-Machado *et al.*, “Kinematic and Clinical Outcomes to Evaluate the Efficacy of a Multidisciplinary Intervention on Functional Mobility in Parkinson’s Disease,” *Frontiers in Neurology*, vol. 12, 2021, Accessed: Apr. 09, 2023. [Online]. Available: https://www.frontiersin.org/articles/10.3389/fneur.2021.637620

[118] P. Zham *et al.*, “A Kinematic Study of Progressive Micrographia in Parkinson’s Disease,” *Front Neurol*, vol. 10, p. 403, Apr. 2019, doi: 10.3389/fneur.2019.00403.

[119] R. W. Carlsen, A. L. Fawzi, Y. Wan, H. Kesari, and C. Franck, “A quantitative relationship between rotational head kinematics and brain tissue strain from a 2-D parametric finite element analysis,” *Brain Multiphysics*, vol. 2, p. 100024, Jan. 2021, doi: 10.1016/j.brain.2021.100024.

[120] A. Hussain *et al.*, “Quantitative assessment of motor functions post-stroke: Responsiveness of upper-extremity robotic measures and its task dependence,” *2017 International Conference on Rehabilitation Robotics (ICORR)*, pp. 1037–1042, Jul. 2017, doi: 10.1109/ICORR.2017.8009386.

[121] G. Kwakkel *et al.*, “Standardized measurement of quality of upper limb movement after stroke: Consensus-based core recommendations from the Second Stroke Recovery and Rehabilitation Roundtable,” *International Journal of Stroke*, vol. 14, no. 8, pp. 783–791, Oct. 2019, doi: 10.1177/1747493019873519.

[122] A. Schwarz, C. M. Kanzler, O. Lambercy, A. R. Luft, and J. M. Veerbeek, "Systematic Review on Kinematic Assessments of Upper Limb Movements After Stroke," *Stroke*, vol. 50, no. 3, pp. 718–727, Mar. 2019, doi: 10.1161/STROKEAHA.118.023531.

[123] R. Colombo *et al.*, "Robotic techniques for upper limb evaluation and rehabilitation of stroke patients," *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, vol. 13, no. 3, pp. 311–324, Sep. 2005, doi: 10.1109/TNSRE.2005.848352.

[124] J. A. Semrau, T. M. Herter, S. H. Scott, and S. P. Dukelow, "Robotic Identification of Kinesthetic Deficits After Stroke," *Stroke*, vol. 44, no. 12, pp. 3414–3421, Dec. 2013, doi: 10.1161/STROKEAHA.113.002058.

[125] M. Gilliaux *et al.*, "Using the robotic device REAplan as a valid, reliable, and sensitive tool to quantify upper limb impairments in stroke patients," *Journal of rehabilitation medicine : official journal of the UEMS European Board of Physical and Rehabilitation Medicine*, vol. 46, Nov. 2013, doi: 10.2340/16501977-1245.

[126] F. Aggogeri, T. Mikolajczyk, and J. O'Kane, "Robotics for rehabilitation of hand movement in stroke survivors," *Advances in Mechanical Engineering*, vol. 11, no. 4, p. 1687814019841921, Apr. 2019, doi: 10.1177/1687814019841921.

[127] S. J. Ortmann, J. Kesselring, and J. Kool, "Reliability and validity of measuring grip strength with a robotic-assisted device in patients after stroke," *International Journal of Therapy and Rehabilitation*, vol. 27, no. 3, pp. 1–10, Mar. 2020, doi: 10.12968/ijtr.2019.0018.

[128] "Kinarm Standard Tests." https://kinarm.com/kinarm-products/kinarm-standard-tests/ (accessed Mar. 23, 2023).

[129] M. D. Wood, L. E. R. Simmatis, J. Gordon Boyd, S. H. Scott, and J. A. Jacobson, "Using principal component analysis to reduce complex datasets produced by robotic technology in healthy participants," *Journal of NeuroEngineering and Rehabilitation*, vol. 15, no. 1, p. 71, Jul. 2018, doi: 10.1186/s12984-018-0416-5.

[130] "(104) KINARM Exoskeleton Lab by BKIN Technologies - YouTube." https://www.youtube.com/watch?v=M7psCB0ZOx0&ab_channel=Kinarm (accessed Mar. 23, 2023).

[131] "Kinarm End-Point Lab." https://kinarm.com/kinarm-products/kinarm-end-point-lab/ (accessed Mar. 23, 2023).

[132] "Kinarm Standard Tests." https://kinarm.com/kinarm-products/kinarm-standard-tests/ (accessed Mar. 23, 2023).

[133] "Exoskeleton robot helps researchers shed new light on learning and stroke recovery," *News*, May 30, 2022. https://ucalgary.ca/news/exoskeleton-robot-helps-researchers-shed-new-light-learning-and-stroke-recovery (accessed Apr. 13, 2023).

[134] G. Mochizuki, A. Centen, M. Resnick, C. Lowrey, S. P. Dukelow, and S. H. Scott, "Movement kinematics and proprioception in post-stroke spasticity: assessment using the Kinarm robotic exoskeleton," *Journal of NeuroEngineering and Rehabilitation*, vol. 16, no. 1, p. 146, Nov. 2019, doi: 10.1186/s12984-019-0618-5.

[135] C. R. Lowrey, S. P. Dukelow, S. D. Bagg, B. Ritsma, and S. H. Scott, "Impairments in Cognitive Control Using a Reverse Visually Guided Reaching Task Following Stroke," *Neurorehabil Neural Repair*, vol. 36, no. 7, pp. 449–460, Jul. 2022, doi: 10.1177/15459683221100510.

[136] L. Simmatis, J. Krett, S. H. Scott, and A. Y. Jin, "Robotic exoskeleton assessment of transient ischemic attack," *PLoS One*, vol. 12, no. 12, p. e0188786, Dec. 2017, doi: 10.1371/journal.pone.0188786.

[137] J. W. Andrushko *et al.*, "Improved cognitive-motor processing speed and decreased functional connectivity after high intensity aerobic exercise in individuals with chronic stroke." bioRxiv, p. 2023.01.15.523513, Feb. 11, 2023. doi: 10.1101/2023.01.15.523513.

[138] C. Little *et al.*, "Test-retest reliability of KINARM robot sensorimotor and cognitive assessment: In pediatric ice hockey players," *Journal of neuroengineering and rehabilitation*, vol. 12, p. 78, Sep. 2015, doi: 10.1186/s12984-015-0070-0.

[139] E. Otaka *et al.*, "Clinical usefulness and validity of robotic measures of reaching movement in hemiparetic stroke patients," *J Neuroeng Rehabil*, vol. 12, p. 66, Aug. 2015, doi: 10.1186/s12984-015-0059-8.

[140] L. M. Weber and J. Stein, "The use of robots in stroke rehabilitation: A narrative review," *NeuroRehabilitation*, vol. 43, no. 1, pp. 99–110, Jan. 2018, doi: 10.3233/NRE-172408.

[141] S. M. Hatem *et al.*, "Rehabilitation of Motor Function after Stroke: A Multiple Systematic Review Focused on Techniques to Stimulate Upper Extremity Recovery," *Frontiers in Human Neuroscience*, vol. 10, 2016, Accessed: Apr. 13, 2023. [Online]. Available: https://www.frontiersin.org/articles/10.3389/fnhum.2016.00442

[142] M. M. Carbajal-Galarza, N. O. Chinchihualpa-Paredes, S. A. Abanto-Perez, and M. Lazo-Porras, "Effectiveness of technological interventions to improve upper limb motor function in people with stroke in low- and middle-income countries: Protocol for a systematic review and meta-analysis." Nov. 13, 2020. doi: 10.1101/2020.11.10.20209197.

[143] Jumphost, “Prof invents first ever objective brain function assessment tool,” *The Queen’s Journal*, Dec. 02, 2010. https://www.queensjournal.ca/prof-invents-first-ever-objective-brain-function-assessment-tool/ (accessed May 07, 2023).

[144] “Kinarm | Interactive Robotics Brain Injury Research.” https://kinarm.com/ (accessed May 07, 2023).

[145] S. H. Scott, “Apparatus for measuring and perturbing shoulder and elbow joint positions and torques during reaching,” *Journal of Neuroscience Methods*, vol. 89, no. 2, pp. 119–127, Jul. 1999, doi: 10.1016/S0165-0270(99)00053-9.

[146] L. E. Simmatis, A. Y. Jin, S. W. Taylor, E. J. Bisson, S. H. Scott, and M. Baharnoori, “The feasibility of assessing cognitive and motor function in multiple sclerosis patients using robotics,” *Mult Scler J Exp Transl Clin*, vol. 6, no. 4, p. 2055217320964940, 2020, doi: 10.1177/2055217320964940.

[147] *KST: Object Hit and Avoid, Subject with TBI*, (Aug. 14, 2018). Accessed: Mar. 23, 2023. [Online Video]. Available: https://www.youtube.com/watch?v=VpiN6hTqgMc

[148] K. Tyryshkin *et al.*, “A robotic object hitting task to quantify sensorimotor impairments in participants with stroke,” *J Neuroeng Rehabil*, vol. 11, p. 47, Apr. 2014, doi: 10.1186/1743-0003-11-47.

[149] C. Janouch, U. Drescher, K. Wechsler, M. Haeger, O. Bock, and C. Voelcker-Rehage, “Cognitive—Motor Interference in an Ecologically Valid Street Crossing Scenario,” *Front Psychol*, vol. 9, p. 602, May 2018, doi: 10.3389/fpsyg.2018.00602.

[150] B. Sokołowska, “Impact of Virtual Reality Cognitive and Motor Exercises on Brain Health,” *Int J Environ Res Public Health*, vol. 20, no. 5, p. 4150, Feb. 2023, doi: 10.3390/ijerph20054150.

[151] L. Thabane *et al.*, "A tutorial on pilot studies: the what, why and how," *BMC Medical Research Methodology*, vol. 10, no. 1, p. 1, Jan. 2010, doi: 10.1186/1471-2288-10-1.

[152] S. M. Eldridge *et al.*, "CONSORT 2010 statement: extension to randomised pilot and feasibility trials," *BMJ*, vol. 355, p. i5239, Oct. 2016, doi: 10.1136/bmj.i5239.

[153] M. A. Hertzog, "Considerations in determining sample size for pilot studies," *Res Nurs Health*, vol. 31, no. 2, pp. 180–191, Apr. 2008, doi: 10.1002/nur.20247.

[154] C. Metcalf, J. Adams, J. Burridge, V. Yule, and P. Chappell, "A review of clinical upper limb assessments within the framework of the WHO ICF," *Musculoskeletal Care*, vol. 5, no. 3, pp. 160–173, 2007, doi: 10.1002/msc.108.

[155] H. O. World Health Organization, "International classification of functioning," *Disability and Health (ICF)*, vol. 28, p. 66, 2001.

[156] A. R. Fugl-Meyer, L. Jääskö, I. Leyman, S. Olsson, and S. Steglind, "The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance," *Scand J Rehabil Med*, vol. 7, no. 1, pp. 13–31, 1975.

[157] D. J. Gladstone, C. J. Danells, and S. E. Black, "The Fugl-Meyer Assessment of Motor Recovery after Stroke: A Critical Review of Its Measurement Properties," *Neurorehabil Neural Repair*, vol. 16, no. 3, pp. 232–240, Sep. 2002, doi: 10.1177/154596802401105171.

[158] K. D. Rech, A. P. Salazar, R. R. Marchese, G. Schifino, V. Cimolin, and A. S. Pagnussat, "Fugl-Meyer Assessment Scores Are Related With Kinematic Measures in People with Chronic Hemiparesis after Stroke," *Journal of Stroke and Cerebrovascular Diseases*, vol. 29, no. 1, Jan. 2020, doi: 10.1016/j.jstrokecerebrovasdis.2019.104463.

[159] S. L. Wolf, P. A. Catlin, M. Ellis, A. L. Archer, B. Morgan, and A. Piacentino, "Assessing Wolf Motor Function Test as Outcome Measure for Research in Patients After Stroke," *Stroke*, vol. 32, no. 7, pp. 1635–1639, Jul. 2001, doi: 10.1161/01.STR.32.7.1635.

[160] D. M. Morris, G. Uswatte, J. E. Crago, E. W. Cook, and E. Taub, "The reliability of the wolf motor function test for assessing upper extremity function after stroke," *Arch Phys Med Rehabil*, vol. 82, no. 6, pp. 750–755, Jun. 2001, doi: 10.1053/apmr.2001.23183.

[161] S. L. Wolf *et al.*, "The EXCITE trial: attributes of the Wolf Motor Function Test in patients with subacute stroke," *Neurorehabil Neural Repair*, vol. 19, no. 3, pp. 194–205, Sep. 2005, doi: 10.1177/1545968305276663.

[162] D. F. Edwards, C. E. Lang, J. M. Wagner, R. Birkenmeier, and A. W. Dromerick, "An evaluation of the Wolf Motor Function Test in motor trials early after stroke," *Arch Phys Med Rehabil*, vol. 93, no. 4, pp. 660–668, Apr. 2012, doi: 10.1016/j.apmr.2011.10.005.

[163] T. M. Hodics, K. Nakatsuka, B. Upreti, A. Alex, P. S. Smith, and J. C. Pezzullo, "Wolf Motor Function Test for Characterizing Moderate to Severe Hemiparesis in Stroke Patients," *Archives of Physical Medicine and Rehabilitation*, vol. 93, no. 11, pp. 1963–1967, Nov. 2012, doi: 10.1016/j.apmr.2012.05.002.

[164] Z. S. Nasreddine *et al.*, "The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool For Mild Cognitive Impairment," *Journal of the American Geriatrics Society*, vol. 53, no. 4, pp. 695–699, 2005, doi: 10.1111/j.1532-5415.2005.53221.x.

[165] J. E. Nickols, "Insight, superior intelligence, and the Raven Progressive Matrices, set E," *J Clin Psychol*, vol. 18, p. 351, Jul. 1962, doi: 10.1002/1097-4679(196207)18:3<351::aid-jclp2270180336>3.0.co;2-s.

[166] W. Arthur and D. V. Day, “Development of a short form for the Raven Advanced Progressive Matrices Test,” *Educational and Psychological Measurement*, vol. 54, pp. 394–403, 1994, doi: 10.1177/0013164494054002013.

[167] J. Duncan, D. Chylinski, D. J. Mitchell, and A. Bhandari, “Complexity and compositionality in fluid intelligence,” *Proceedings of the National Academy of Sciences*, vol. 114, no. 20, pp. 5295–5299, May 2017, doi: 10.1073/pnas.1621147114.

[168] L. Cipolotti *et al.*, “Graph lesion-deficit mapping of fluid intelligence,” *Brain*, vol. 146, no. 1, pp. 167–181, Jan. 2023, doi: 10.1093/brain/awac304.

[169] “Brain area necessary for fluid intelligence identified,” *ScienceDaily*. https://www.sciencedaily.com/releases/2022/12/221228092247.htm (accessed Mar. 18, 2023).

[170] John and J. Raven, “Raven Progressive Matrices,” in *Handbook of Nonverbal Assessment*, R. S. McCallum, Ed., Boston, MA: Springer US, 2003, pp. 223–237. doi: 10.1007/978-1-4615-0153-4_11.

[171] A. Basso, E. Capitani, and M. Laiacona, “Raven’s coloured progressive matrices: normative values on 305 adult normal controls,” *Funct Neurol*, vol. 2, no. 2, pp. 189–194, 1987.

[172] B. W. Benson, M. Cosh, C. S. Mang, S. H. Scott, C. Debert, and S. Dukelow, “Test-retest reliability of the kinarm end-point robot for assessment of sensory, motor and neurocognitive function in athletes,” *Br J Sports Med*, vol. 51, no. 11, pp. A11–A11, Jun. 2017, doi: 10.1136/bjsports-2016-097270.26.

[173] C. S. Mang *et al.*, "Test-retest reliability of the KINARM end-point robot for assessment of sensory, motor and neurocognitive function in young adult athletes," *PLoS One*, vol. 13, no. 4, p. e0196205, Apr. 2018, doi: 10.1371/journal.pone.0196205.

[174] L. E. Simmatis, A. Y. Jin, S. W. Taylor, E. J. Bisson, S. H. Scott, and M. Baharnoori, "The feasibility of assessing cognitive and motor function in multiple sclerosis patients using robotics," *Mult Scler J Exp Transl Clin*, vol. 6, no. 4, p. 2055217320964940, Oct. 2020, doi: 10.1177/2055217320964940.

[175] L. Saenen, J.-J. Orban de Xivry, and G. Verheyden, "Development and Validation of a Novel Robot-Based Assessment of Upper Limb Sensory Processing in Chronic Stroke," *Brain Sciences*, vol. 12, no. 8, Art. no. 8, Aug. 2022, doi: 10.3390/brainsci12081005.

[176] J. A. Semrau, T. M. Herter, S. H. Scott, and S. P. Dukelow, "Inter-rater reliability of kinesthetic measurements with the KINARM robotic exoskeleton," *J Neuroeng Rehabil*, vol. 14, p. 42, May 2017, doi: 10.1186/s12984-017-0260-z.

[177] "KST Summary (analysis version 3.8)." https://kinarm.com/download/kst-summary-analysis-version-3-8/ (accessed Feb. 24, 2023).

[178] C. Gowland *et al.*, "Measuring physical impairment and disability with the Chedoke-McMaster Stroke Assessment.," *Stroke*, vol. 24, no. 1, pp. 58–63, Jan. 1993, doi: 10.1161/01.STR.24.1.58.

[179] T. Platz, C. Pinkowski, F. van Wijck, I.-H. Kim, P. di Bella, and G. Johnson, "Reliability and validity of arm function assessment with standardized guidelines for the Fugl-Meyer Test, Action Research Arm Test and Box and Block Test: a multicentre study," *Clin Rehabil*, vol. 19, no. 4, pp. 404–411, Jun. 2005, doi: 10.1191/0269215505cr832oa.

[180] J. L. Crow and B. C. Harmeling-van Der Wel, “Hierarchical Properties of the Motor Function Sections of the Fugl-Meyer Assessment Scale for People After Stroke: A Retrospective Study,” *Physical Therapy*, vol. 88, no. 12, pp. 1554–1567, Dec. 2008, doi: 10.2522/ptj.20070186.

[181] M. L. Woodbury, C. A. Velozo, L. G. Richards, P. W. Duncan, S. Studenski, and S.-M. Lai, “Longitudinal Stability of the Fugl-Meyer Assessment of the Upper Extremity,” *Archives of Physical Medicine and Rehabilitation*, vol. 89, no. 8, pp. 1563–1569, Aug. 2008, doi: 10.1016/j.apmr.2007.12.041.

[182] M. H. Hoonhorst, R. H. Nijland, J. S. van den Berg, C. H. Emmelot, B. J. Kollen, and G. Kwakkel, “How Do Fugl-Meyer Arm Motor Scores Relate to Dexterity According to the Action Research Arm Test at 6 Months Poststroke?,” *Archives of Physical Medicine and Rehabilitation*, vol. 96, no. 10, pp. 1845–1849, Oct. 2015, doi: 10.1016/j.apmr.2015.06.009.

[183] H. I. Krebs *et al.*, “Robotic measurement of arm movements after stroke establishes biomarkers of motor recovery,” *Stroke*, vol. 45, no. 1, pp. 200–204, Jan. 2014, doi: 10.1161/STROKEAHA.113.002296.

[184] C. B. Moretti *et al.*, “Robotic Kinematic measures of the arm in chronic Stroke: part 2 - strong correlation with clinical outcome measures,” *Bioelectron Med*, vol. 7, no. 1, p. 21, Dec. 2021, doi: 10.1186/s42234-021-00082-8.

[185] P. van Gils, C. van Heugten, J. Hofmeijer, H. Keijzer, S. Nutma, and A. Duits, “The Montreal Cognitive Assessment is a valid cognitive screening tool for cardiac arrest survivors,” *Resuscitation*, vol. 172, pp. 130–136, Mar. 2022, doi: 10.1016/j.resuscitation.2021.12.024.

[186] R. Pueyo, C. Junqué, P. Vendrell, A. Narberhaus, and D. Segarra, “Raven’s Coloured Progressive Matrices as a measure of cognitive functioning in Cerebral Palsy,” *J Intellect Disabil Res*, vol. 52, no. Pt 5, pp. 437–445, May 2008, doi: 10.1111/j.1365-2788.2008.01045.x.

[187] C.-Y. Wu, S.-J. Hung, K. Lin, K.-H. Chen, P. Chen, and P.-K. Tsay, “Responsiveness, Minimal Clinically Important Difference, and Validity of the MoCA in Stroke Rehabilitation,” *Occupational Therapy International*, vol. 2019, p. e2517658, Apr. 2019, doi: 10.1155/2019/2517658.

[188] H. H. Tan *et al.*, “Decline in changing Montreal Cognitive Assessment (MoCA) scores is associated with post-stroke cognitive decline determined by a formal neuropsychological evaluation,” *PLoS ONE*, vol. 12, no. 3, p. e0173291, Mar. 2017, doi: 10.1371/journal.pone.0173291.

[189] J. Zariffa, M. Myers, M. Coahran, and R. H. Wang, “Smallest real differences for robotic measures of upper extremity function after stroke: Implications for tracking recovery,” *J Rehabil Assist Technol Eng*, vol. 5, p. 2055668318788036, Sep. 2018, doi: 10.1177/2055668318788036.

[190] L. Simmatis, G. Atallah, S. H. Scott, and S. Taylor, “The feasibility of using robotic technology to quantify sensory, motor, and cognitive impairments associated with ALS,” *Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration*, vol. 20, no. 1–2, pp. 43–52, Jan. 2019, doi: 10.1080/21678421.2018.1550515.

[191] S. H. Scott and S. P. Dukelow, “Potential of robots as next-generation technology for clinical assessment of neurological disorders and upper-limb therapy,” *JRRD*, vol. 48, no. 4, p. 335, 2011, doi: 10.1682/JRRD.2010.04.0057.

[192] "Assessing various sensorimotor and cognitive functions in people with epilepsy is feasible with robotics - Epilepsy & Behavior." https://www.epilepsybehavior.com/article/S1525-5050(19)31100-X/fulltext (accessed Apr. 13, 2023).

[193] S. E. Fasoli, H. I. Krebs, J. Stein, W. R. Frontera, and N. Hogan, "Effects of robotic therapy on motor impairment and recovery in chronic stroke," *Archives of Physical Medicine and Rehabilitation*, vol. 84, no. 4, pp. 477–482, Apr. 2003, doi: 10.1053/apmr.2003.50110.

[194] F. Bressi *et al.*, "Effects of robotic upper limb treatment after stroke on cognitive patterns: A systematic review," *NeuroRehabilitation*, vol. 51, no. 4, pp. 541–558, doi: 10.3233/NRE-220149.

[195] S. Balasubramanian, R. Colombo, I. Sterpi, V. Sanguineti, and E. Burdet, "Robotic assessment of upper limb motor function after stroke," *Am J Phys Med Rehabil*, vol. 91, no. 11 Suppl 3, pp. S255-269, Nov. 2012, doi: 10.1097/PHM.0b013e31826bcdc1.

[196] A. Bhalla, C. D. A. Wolfe, and A. G. Rudd, "Management of acute physiological parameters after stroke," *QJM: An International Journal of Medicine*, vol. 94, no. 3, pp. 167–172, Mar. 2001, doi: 10.1093/qjmed/94.3.167.

[197] "Stroke Outcome Measures Overview," *Physiopedia*. https://www.physio-pedia.com/Stroke_Outcome_Measures_Overview (accessed Apr. 13, 2023).

[198] J. L. Banks and C. A. Marotta, "Outcomes Validity and Reliability of the Modified Rankin Scale: Implications for Stroke Clinical Trials," *Stroke*, vol. 38, no. 3, pp. 1091–1096, Mar. 2007, doi: 10.1161/01.STR.0000258355.23810.c6.

[199] J. K. Harrison, K. S. McArthur, and T. J. Quinn, “Assessment scales in stroke: clinimetric and clinical considerations,” *Clin Interv Aging*, vol. 8, pp. 201–211, 2013, doi: 10.2147/CIA.S32405.

[200] R. Mendonca, K. Sheehy, E. Freedman, and N. Grampurohit, “Effectiveness of Robotic Therapy on Upper-Extremity Function and Pain in Adults With Chronic Stroke: A Systematic Review,” *The American Journal of Occupational Therapy*, vol. 73, no. 4_Supplement_1, p. 7311520384p1, Aug. 2019, doi: 10.5014/ajot.2019.73S1-PO2024.

LIST OF APPENDICES

Subject ID:_____ Date:_____ Completed By (initials): _____

Fugl-Meyer (Upper Extremity Motor Impairment) (Enter to REDCap)

Test the wrist and hand function independently of the arm. During the wrist tests (items 7a-e), support under the elbow may be provided to decrease demand at the shoulder; however, the subject should be activating the elbow flexors during the elbow at 90 degree tests and activating the elbow extensors during the elbow at 0 degree tests. In contrast, assistance can be provided to the arm at the elbow and just proximal to the wrist in order to position the arm during the hand tests (items 8a-g).

Item	Instructions	Scoring
I. Reflex Activity	- Patient is sitting. "Relax your arm as I support it and test your reflexes." - Attempt to elicit the biceps (or finger flexor) and triceps reflexes. Can tap over assessor's finger if you like. - Test reflexes on unaffected side first. - Test affected side.	**Maximum possible score = 4** - (0) No reflex activity can be elicited. - (2) Reflex activity can be elicited (visual or palpatable). **Items to be scored are:** 1. Biceps or finger flex_____/2 2. Triceps _____/2
II. Flexor synergy	- Patient is sitting. The starting position should be arm at side, shoulder neutral, elbow extended in comfortable position. Have patient perform movement with unaffected side first. "Raise your hand toward your ear, bring your elbow up to shoulder height, and keep your thumb pointed up toward the ceiling, like you are answering the telephone, like this" End position: The starting position should be that of full extensor synergy. If the patient cannot actively achieve the starting position, the limb may be passively placed extended towards opposite knee in shoulder adduction/internal rotation, elbow extension, and forearm pronation.	**Maximum possible score = 12** - (0) Cannot be performed at all (for scapular movements, no scapular movement visualized or palpated). - (1) Performed partly (any degree less than non-affected side). - (2) Equal or greater than non-affected side **Items to be scored are:** 3. Scapular retraction _____/2 4. Scapula elevation _____/2 5. Shoulder abduction (at least 90°)____/2 6. Shoulder external rotation _____/2 7. Elbow flexion _____/2 8. Forearm supination _____/2
III. Extensor synergy	Patient is sitting. Start position (can passively place): Shoulder girdle fully elevated and retracted with shoulder abducted ≥ 90. Shoulder ext rotation, elbow flexion, and forearm supination to touch same ear with thumb up. Fingers flexed or extended. Knees should be apart. "Raise your hand toward your ear, bring your elbow up to shoulder height, and keep your thumb pointed up toward the ceiling. Then fully straighten your elbow while reaching across your body toward your opposite knee, turning your palm down, like this. End position: Shoulder adduction across midline and elbow extension to 0. Shoulder internal rotation and forearm pronation must be sufficient to touch contralateral knee with entire palmar surface of hand. Fingers can be flexed or extended.	**Maximum possible score = 6** - (0) Cannot be performed at all - (1) Performed partly (less than non-affected side). - (2) Equal to or greater than non-affected side **Items to be scored are:** 9. Shoulder adduction/int rotation____/2 10. Elbow extension /2 11. Forearm pronation /2 (note #11 can be 2 only if #9 and #10 are 2)

Subject ID:_____ Date:_____ Completed By (initials): _____

IV. Movement combining synergies The patient is asked to perform 3 separate movements (a, b, c)	**a. Hand to lumbar spine:** Seated toward front of chair before performing the task, hand on lap. "Place the back of your hand to your low back, like this". End position: Shoulder extension and internal rotation, and elbow flexion to touch lumbar spine with dorsum of hand, and ≥1 interphalangeal (IP) joint must pass the line created when connecting lumbar spinous processes.	**Maximum possible score = 2** - (0) No IP joint passes frontal plane defined by ASIS - (1) at least 1 IP joint) passes ASIS - (2) Dorsal hand actively reached lumbar spine with at least 1 IP joint passing line connecting lumbar spinous processes; full elbow extension is not required to score a 2). _____/2
	b. Shoulder flexion to 90°, elbow extended, midposition between supination/pronation Start: Shoulder neutral, elbow extended to 0°, forearm neutral. "Fully straighten your elbow at your side and point your thumb forward. Keep your elbow straight and raise your arm up to shoulder height. Do not bend your elbow as you are moving, like this." End position: Shoulder flexed to 90°, elbow extended to 0°, forearm neutral. May assist to starting position, but subject must be able to maintain shoulder/elbow extension in 0˚to begin task.	**Maximum possible score = 2** (0) subject cannot achieve the starting position, **or** deviation from starting position occurs at onset of shoulder flexion (eg, abduction or elbow flexion) **or** no shoulder flexion occurs. (1) while actively maintaining starting position, shoulder flexion does not reach 90°, **or** any deviation from starting position occurs following the onset of shoulder flexion. (2) actively maintains starting position, and shoulder flexes to 90°, with elbow extended. _____/2
	c. Pronation/supination of forearm, elbow at 90°, shoulder at 0°: Start shoulder neutral, elbow flexed to 90, forearm in resting position. "Place your arm at your side in the shape of an "L", like this (demonstrate), and without moving the rest of your arm, turn your palm up and down as far as you can go, like this". End position: Shoulder neutral, elbow flexed to 90, forearm completed supination-pronation cycle. Elbow flexion must be actively achieved and maintained. Elbow flexion to 90 may be approximate; allow up to 10 degrees deviation	**Maximum possible score = 2** (0) subject cannot achieve the starting position, or deviation from starting position occurs at the onset of pronation or supination, or no pronation or supination occurs. (1) while actively maintaining position, any degree of supination or pronation that is less than unaffected side, or any deviation from starting position occurs after the onset of pronation or supination. (2) achieves and maintains starting position, and pronation and supination is equal to or greater than the unaffected side. _____/2

Subject ID:_____ Date:_____ Completed By (initials): _____

V. Movement out of synergy **The patient is asked to perform three separate movements (5a, 5b, 5c).**	**5a. Shoulder abduction to 90°, elbow extended, and forearm neutral:** Start with shoulder neutral, elbow extended to 0, forearm neutral. "Rest your arm at your side, fully straighten your elbow, bring your arm out toward the side to shoulder height, keeping your palm facing the floor, like this". End position: shoulder abducted to 90, elbow extended to 0, forearm neutral. May assist to starting position, but subject must be able to maintain shoulder/elbow extension in 0˚ to begin task -	**Maximum possible score = 2** - (0) subject cannot achieve starting position, or deviation from starting position occurs at onset of abduction, or no shoulder abduction occurs. - (1) while actively maintaining starting position, abduction does not reach 90, or any deviation from starting position occurs following the onset of abduction - (2) actively maintains starting position, and shoulder abducts to 90 (no elbow flexion) _____/2
	5b. Shoulder flexion from 90°-180°, elbow at 0°, and forearm in mid-position: Start with shoulder flexed to 90, elbow extended to 0, forearm neutral. "Hold your arm straight out in front of your body, straighten your elbow, point your thumb up toward the ceiling. Bring your arm up as far as you can, like this". End position: shoulder flexed to 180, elbow extended to 0, forearm neutral. May assist to starting position, but subject must be able to maintain shoulder in 90˚ of flexion to begin task	**Maximum possible score = 2** - (0) subject cannot maintain the starting position, or deviation from starting position occurs at onset of shoulder flexion > 90, or no shoulder flexion >90 occurs. - (1) while actively maintaining starting position, shoulder flexion does not reach 180, or any deviation from starting position occurs following the onset of shoulder flexion > 90. - (2) actively maintains starting position, and shoulder flexes from 90 to 180. _____/2

Subject ID:_____ Date:_____ Completed By (initials): _____

V. Movement out of synergy **The patient is asked to perform three separate movements (5a, 5b, 5c).**	**5c. Pronation/supination of forearm, elbow at 0°, and shoulder at 30°-90° of flexion:** Start: Shoulder flexed between 30-90, elbow extended to 0, forearm in resting position. "Straighten your arm in front of your body, keep your elbow straight and turn your palm up and down as far as you can go, like this". End position: Shoulder flexed between 30-90, elbow extended to 0, forearm completed pronation-supination cycle. May assist to starting position by stretching elbow to extended position, but subject must be able to maintain shoulder flexion 30-90 with elbow extended to 0˚to begin task. Do not allow shoulder joint rotation to compensate for pronation/supination.	**Maximum possible score = 2** - (0) subject cannot maintain the starting position, or deviation from starting position occurs at the onset of pronation/supination, or no pronation or supination occurs (1) while maintaining starting position, any degree of pronation or supination is less than the unaffected side, or deviation from starting position occurs following the onset of pronation or supination - (2) maintains starting position, and pronation and supination is equal to or greater than the unaffected side. _____/2
VI. Normal Reflexes (sitting)	- This item is only included if the patient achieves a maximum score on all previous upper extremity items (6/6), otherwise score 0. - The examiner shall elicit biceps, triceps and finger flexors and note if the reflexes are hyperactive or not.	**Maximum possible score = 2** - (0) At least 2 of the 3 phasic reflexes are markedly hyperactive. - (1) One reflex is markedly hyperactive - (2) all 3 reflexes are present, none is hyperactive _____/2
VII. Wrist During the wrist tests, support under the elbow may be provided to decrease demand at the shoulder; however, the patient should be activating the elbow flexors during the elbow at 90 degree tests and activating the elbow extensors during the elbow at 0 degree tests. The patient is asked to perform five separate movements (7a, 7b, 7c, 7d, 7e).	**7a. Wrist stability, elbow at 90°, forearm pronation and shoulder at 0°:** Start with shoulder neutral, elbow flexed to 90, forearm pronated, wrist in resting position. "Place your arm at your side in the shape of an "L", palm facing down; without moving the rest of your arm, extend and hold your wrist upwards, like this". End position: wrist extended ≥ 15° past neutral plane and maintained against force applied by assessor. Only when 15° is achieved, then assess applies force to across metacarpals against wrist extension (3+ to 5 strength). May assist subject in maintaining starting position by supporting the proximal forearm. Do not support wrist.	**Maximum possible score = 2** - (0) subject cannot achieve the starting position even with support provided to the proximal forearm or deviation from starting position occurs at the onset of wrist extension, or cannot achieve wrist extension to 15°. - (1) achieves 15° wrist extension but with attempt to take resistance, subject deviates from starting position, or subject cannot maintain 15° wrist extension. - (2) Position15° can be maintained with some (slight) resistance. _____/2

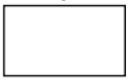
Subject ID:_____ Date:_____ Completed By (initials): _____

VII. Wrist During the wrist tests, support under the elbow may be provided to decrease demand at the shoulder; however, the patient should be activating the elbow flexors during the elbow at 90 degree tests and activating the elbow extensors during the elbow at 0 degree tests. The patient is asked to perform five separate movements (7a, 7b, 7c, 7d, 7e).	**7b. Wrist flexion/extension, elbow at 90°, forearm pronation and shoulder at 0°:** Same start as above. "Without moving the rest of your arm, extend your wrist all the way up and down, like this". May assist subject in maintaining starting position by supporting the proximal forearm. Do not support wrist. 1 complete flexion/extension cycle is required to score a 2. Fingers may be somewhat flexed during wrist extension.	**Maximum possible score = 2** - (0) subject cannot achieve the starting position even with support provided to the proximal forearm or deviation from starting position occurs at the onset of wrist movement, or no wrist movement occurs. - (1) any degree of wrist movement that is less than subject's passive wrist range of motion in flexion or extension, or deviation from starting position occurs following the onset of wrist movement. - (2) maintains starting position, and wrist flexion and extension is equal to passive range of motion during 1 full flex/extension cycle. _____/2
	7c. Wrist stability, elbow at 0°, and shoulder at 30° flexion: Start with shoulder flexed between 30°-90°, slight abduction permitted, elbow extended to 0, forearm pronated, and wrist in resting position. "Straighten your arm in front of your body; keep your elbow straight, extend and hold your wrist upwards, like this". Only when 15° wrist extension is achieved, assessor applies force to dorsal hand across metacarpals against extension. May assist subject in maintaining starting position by supporting the proximal forearm. Do not support wrist. Elbow extension must be actively maintained by subject.	**Maximum possible score = 2** - (0) subject cannot achieve the starting position even with support provided to the proximal forearm or deviation from starting position occurs at the onset of wrist extension, or cannot achieve wrist extension to 15°. - (1) with attempt to take resistance, subject deviates from starting position, or subject cannot maintain 15° wrist extension. - (2) maintains starting position while wrist is extended to 15° and resistance is taken. _____/2

Subject ID:_____ Date:_____ Completed By (initials): _____

VII. Wrist During the wrist tests, support under the elbow may be provided to decrease demand at the shoulder; however, the patient should be activating the elbow flexors during the elbow at 90 degree tests and activating the elbow extensors during the elbow at 0 degree tests. The patient is asked to perform five separate movements (7a, 7b, 7c, 7d, 7e).	**7d. Wrist flexion/extension, elbow at 0°, and shoulder at 30° flexion:** Same start as above. "Straighten your arm in front of your body; keep your elbow straight, bend your wrist all the way up and down, like this". Do not allow shoulder joint rotation to compensate for pronation/supination. May assist subject in maintaining starting position by supporting the proximal forearm. Do not support wrist.	**Maximum possible score = 2** - (0) subject cannot achieve the starting position even with support provided to the proximal forearm or deviation from starting position occurs at the onset of wrist movement, or no wrist movement occurs - (1) any degree of wrist movement that is less than subject's passive wrist range of motion in flexion or extension, or deviation from starting position occurs following the onset of wrist movement. - (2) maintains starting position, and wrist flexion and extension is equal to passive range of motion during 1 full flexion/extension cycle. _____/2
	7e. Circumduction: Same start as above. "Straighten your arm in front of your body; keep your elbow straight, move your wrist in a circle, like this. May assist subject in maintaining starting position by supporting the proximal forearm. Do not support wrist. Elbow extension must be actively maintained by subject. Do not allow forearm, elbow or shoulder movements to compensate for wrist movements.	**Maximum possible score = 2** - (0) subject cannot achieve the starting position even with support provided to the proximal forearm or deviation from starting position occurs at the onset of wrist movement, or no circumduction is possible (no movement at the more proximal joints, movement must be combination of wrist flexion/extension and ulnar/radial deviation) - (1) maintains starting position, any degree of wrist circumduction that is less than the unaffected side (is jerky or incomplete), or deviation from starting position occurs following the onset of wrist movement. - (2) maintains starting position, and wrist circumduction is equal to the unaffected side, complete and is performed smoothly. _____/2

Subject ID:_____ Date:_____ Completed By (initials): _____

VIII. Hand Subject must sufficiently extend fingers enough to achieve grasp when object is directly in front of their hand. If necessary, the assessor may stretch the hand into a pre-grasp position, allow 1 second of rest prior to initiating movement or presenting object to subject. Assessor may support forearm in 90° elbow flexion, however, MAY NOT support the wrist. Do not mistake tone related movements for volitional movements.	**8a. Finger mass flexion:**  - Start with shoulder approximately neutral, elbow flexed at 90°, forearm and wrist/fingers in resting position. "Make a strong fist, like this".	**Maximum possible score = 2** - (0) No MCP or IP flexion - (1) any degree of MCP or IP flexion in any finger that < 90° (2) MCP and IP flexion equal or greater to non-affected side _____/2
	8b. Finger mass extension:  - Start with shoulder approximately neutral, elbow flexed at 90°, forearm and wrist in comfortable position, fingers fully extended so that MCP's and IP's of digits 1-5 in 0°."Open your hand as much as you can, like this".	**Maximum possible score = 2** - (0) No MCP or IP extension - (1) any degree of MCP or IP extension in any finger that does not reach 0° - (2) MCP and IP extension equal or greater to non-affected side. _____/2
	8c. Grasp I: Hook/Claw  - Shoulder approximately neutral, elbow flexed at 90, forearm and wrist/fingers in resting position. "Make your hand look like a hook or claw; don't let me pull your fingers straight, like this". MCP's extended to 0 with PIP's and DIP's of digits 2-5 actively flexed at least 45°. Apply resistance (4/5 force) to subject's fingers in a pulling motion, only after the subject actively achieves the correct joint position	**Maximum possible score = 2** - (0) Starting position cannot be attained. - (1) maintains starting position, but grasp cannot withstand resistance - (2) maintains starting position, and holds grasp against great resistance _____/2
	8d. Grasp II: Thumb Adduction   Start with shoulder approximately neutral, elbow flexed at 90, forearm, wrist and fingers in resting position, thumb abducted sufficiently to admit a piece of paper to be grasped between thumb and 2nd metacarpal with 1st CMC, MCP and IP extended to 0. Hold this paper between your thumb and index finger keeping them both straight; don't let me pull it away, like this". Assessor applies resistance with a sudden tug (4/5 force) of a single sheet of paper in the direction away from subject. Subject should be warned of sudden movement.	**Maximum possible score = 2** - (0) subject cannot achieve the starting position or cannot grasp paper - (1) maintains starting position, and grasps paper but cannot withstand resistance - (2) maintains starting position and paper is held against great resistance _____/2

	8e. Grasp III: Pincer  Start with shoulder approximately neutral, elbow flexed at 90, forearm and wrist in resting position, thumb and index finger extended and non-opposed sufficiently to admit placement of pencil. "Take the pencil from me with the pads of your thumb and index finger; don't let me pull it away, like this". Assessor presents pencil in a vertical manner and applies resistance (4/5 force) with a sudden tug of the pencil in the direction away from subject. Ensure subject uses ONLY pads of digits 1-2. Do not allow digits 3-5 to assist holding the pencil.	**Maximum possible score = 2** - (0) subject cannot achieve starting position or cannot grasp pencil - (1) maintains starting position and pencil is kept in place but not against resistance - (2) maintains starting position and pencil is held against great resistance. _____/2
	8f. Grasp IV: Cylinder  - Start with shoulder approximately neutral, elbow flexed at 90, forearm and wrist in resting position, thumb and index finger extended sufficiently to admit placement of can. "Take the can from me with your thumb and index fingers wrapped around it; don't let me pull it away, like this". Use a Campbell soup can. Assessor presents can to subject's finger tips and once grasped, assessor applies resistance (4/5 force) with a sudden tug of the can in an upward direction. Subject should be warned of sudden movement.	**Maximum possible score = 2** - (0) subject cannot achieve starting position or cannot grasp can - (1) maintains starting position and can is kept in place but not against resistance - (2) maintains starting position and can is held against great resistance **NOTE:** the hand must open and close on the can; it is not acceptable to have the patient grasp top of the can. _____/2
	8g. Grasp V:  - Start with shoulder approximately neutral, elbow flexed at 90, forearm and wrist in resting position, thumb and fingers abducted with MCP's extended, IP's 2-5 extended sufficiently to admit placement of tennis ball. "Take this tennis ball from my hand with your fingers; don't let me pull it out of your hand, like this. Assessor presents tennis ball on their open palm to subject's finger tips and once grasped, assessor applies resistance with a sudden tug (4/5 force) of the ball in an anti- palmar direction. Subject should be warned of sudden movement. Do not mistake flexor tone for active grasping.	**30. Maximum possible score = 2** - (0) subject cannot achieve starting position or cannot grasp ball volitionally - (1) maintains starting position and ball is kept in place but not against resistance - (2) maintains starting position and ball is held against great resistance _____/2

Subject ID:_____ Date:_____ Completed By (initials): _____

IX. Coordination and speed - Sitting: Finger to nose (5 repetitions in rapid succession)	Start with elbow extended, hand on ipsilateral knee. "While keeping your eyes closed (or blindfolded), bring your finger (or 1st knuckle) from your knee to your nose as rapidly as possible 5 times, like this. Start when I say 'Go'." Begin timing with stop watch when subject's hand leaves knee and stop timing when hand reaches nose for 5th time. For efficiency, the maximum time allowed for stroke-affected side performance will be equal to the time taken on the unaffected side plus 6 seconds. If more time is needed, tell subject to stop, and score 0 for speed task. Do not allow forward flexion of head or trunk to compensate for arm flexion toward nose. If subject cannot assume the starting position, or cannot complete hand to nose task 5 times, then score 0 for speed subtest. Score dysmetria and tremor separately, even if subject does not complete 5 hand to nose cycles. For tremor subtest, resting tremor alone does not contribute to scoring. In order to score tremor attributable to stroke effects, and not other processes such as essential tremor, features of tremor are only scored when greater than anything seen in the non-stroke hand.Tremor and dysmetria scores are 2's when tremor and dysmetria are absent during movement,and are considered absent if unable to move arm.	**31. Maximum tremor score = 2** - (0) Marked tremor which substantially interferes with coordination - (1) Slight tremor which mildly interferes with coordination - (2) No tremor _____/2 **32. Maximum dysmetria = 2** - (0) Pronounced or unsystematic dysmetria - (1) Slight or systematic dysmetria (same error of size and direction) - (2) No dysmetria (finger tip or MCP lands within 1 cm to nose tip) _____/2 **33. Maximum speed score = 2** - (0) – Activity is more than 6 seconds longer than unaffected hand - (1) – 2-5 seconds longer than unaffected side - (2) – less than 2 seconds difference _____/2

Total Fugl-Meyer Upper Extremity Motor Score: _____/66

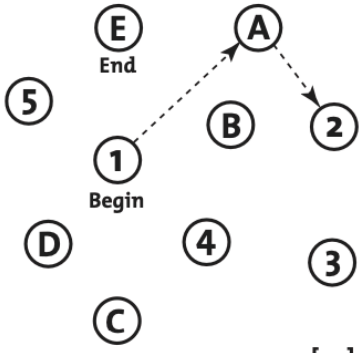
See SAFE Score on Next Page.

Appendix B: Montreal Cognitive Assessment sheet

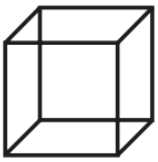
MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE — POINTS



Copy cube



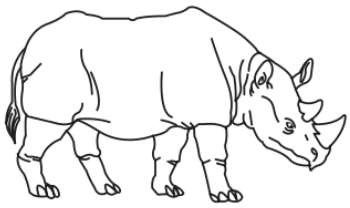
[ ] [ ]

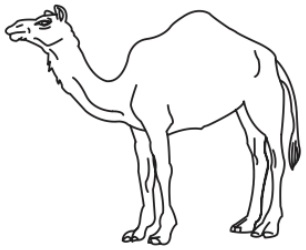
Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

__/5

NAMING





[ ] [ ] [ ]

__/3

MEMORY — Read list of words, subject must repeat them. Do 2 trials. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION — Read list of digits (1 digit/ sec.).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

__/3

LANGUAGE — Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] ____ (N ≥ 11 words)

__/1

ABSTRACTION — Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

__/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
		[ ]	[ ]	[ ]	[ ]	[ ]	
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

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Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Appendix C: Raven's Progressive Matrices Score Sheet

Standard Progressive Matrices
J.C. Raven
Sets A, B, C, D, E

Participant Code:

Date:

Assessor:

Time Test Begun: Time Test Ended: Total Time:

A			B			C			D			E		
1			1			1			1			1		
2			2			2			2			2		
3			3			3			3			3		
4			4			4			4			4		
5			5			5			5			5		
6			6			6			6			6		
7			7			7			7			7		
8			8			8			8			8		
9			9			9			9			9		
10			10			10			10			10		
11			11			11			11			11		
12			12			12			12			12		

Total Score:

Percentile:

Appendix D: Kinarm Task Sheet

kinarm

Recovery & Performance LABORATORY

KINARM SHEET - STT

Visit: [___]

Participant Number: _____ **Study**: _____ Date: _____

*Gender: [_] Male [_] Female [_] other *Date of Birth:_____ *Age:_____

*Height (cm) _____ *Weight (kg) _____

*Handedness [_] Left [_] Right *Affected arm [_] Left [_] Right [_] Nil

*Degree of arm mobility [_] Mild [_] Moderate [_] Severe [_] No report

Pathology			
Stroke	[_]	Multiple Sclerosis	[_]
Concussion	[_]	Movement disorder	[_]
Cerebral palsy	[_]	Traumatic Brain Injury	[_]
Healthy Control	[_]	Fetal alcohol spectrum disorder	[_]

KINARM Tasks			
Object hit	[_]	STT Reverse	[_]
Ball on bar	[_]	STT Retention	[_]
Spatial span	[_]	STT Recognition	[_]
Trail making	[_]	STT Recognition Reverse	[_]
Object hit & avoid	[_]	Visually guided reaching adult	[_]
Arm position matching	[_]	Reversed visually guided reaching adult	[_]
STT Practice	[_]		

Key:
*d- dominant hand
*nd- non-dominant hand

Time started: _____
Time ended: _____

Comments: _____

_____

Researcher initials_____ Date completed_____

Version 2: 16 July 2021

Recovery and Performance Laboratory
Room 400; 100 Forest Rd.
St. John's NL

KINARM- Serial Targeting Task

DAY 1 | **Date:**

Task	Pre-Test	Block 1	Block 2	Block 3	Block 4
STT					

DAY 2 | **Date:**

Task	Block 1	Block 2	Block 3	Block 4
STT				

DAY 3 | **Date:**

Task	Block 1	Block 2	Block 3	Block 4
STT				

DAY 4 | **Date:**

Task	Block 1	Block 2	Block 3	Block 4
STT				

DAY 5 | **Date:**

Task	Block 1	Block 2	Block 3	Block 4
STT				

DAY6 | **Date:**

Task	Block 1	Block 2	Block 3	Block 4
STT				

Recovery and Performance Laboratory
Room 400; 100 Forest Rd.
St. John's NL

DAY 7 | **Date:**

Task	Block 1	Block 2	Block 3	Block 4
STT				

DAY 8 | **Date:**_____

Task	Block 1	Block 2	Block 3	Block 4
STT				

DAY 9 | **Date:**_____

Task	Block 1	Block 2	Block 3	Block 4
STT				

DAY 10 | **Date:**

Task	Block 1	Block 2	Block 3	Block 4
STT				

24HR POST | **Date:**_____

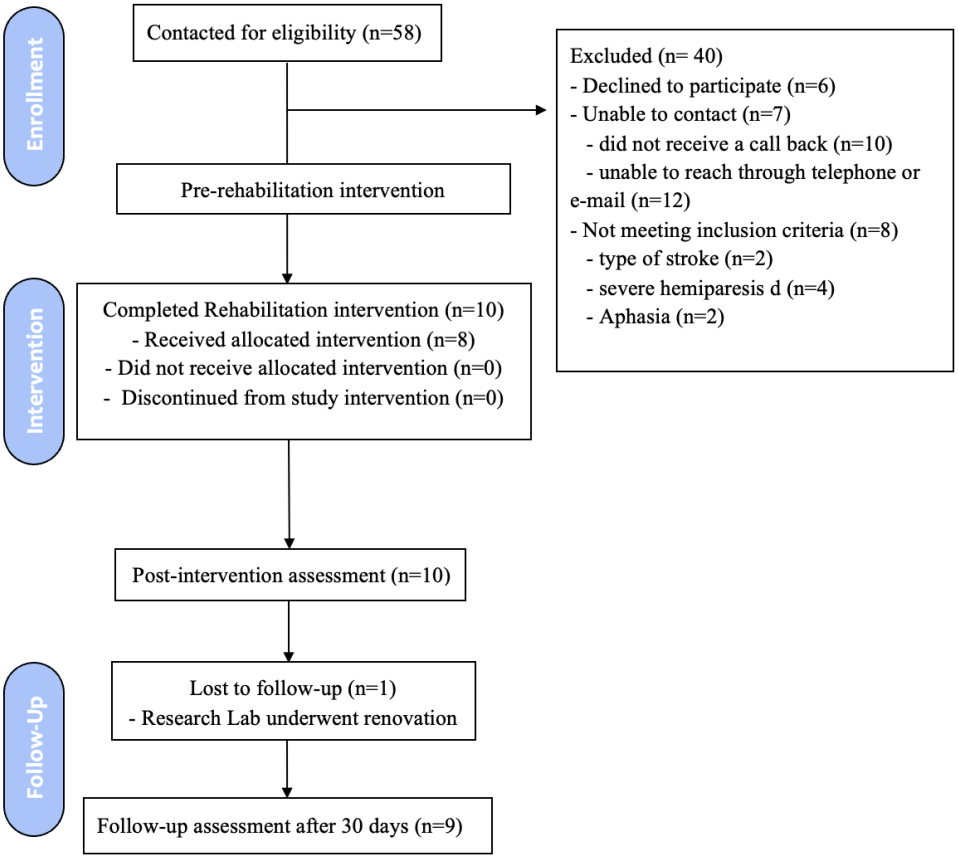
Task	Retention Block
STT	

30 DAYS FOLLOW UP | **Date:**_____

Task	Retention Block
STT	

Please note: Participant would only take this task with their affected limb

Appendix E: Study recruitment flowchart diagram



Appendix D: Study recruitment flow diagram

Appendix F: Wolf Motor Function Test

WOLF MOTOR FUNCTION TEST
DATA COLLECTION FORM

Subject's Name: _____ Date: _____

Test (check one): Pre-treatment _____ Post-treatment _____ Follow-up ____

Arm tested (check one): More-affected _____ Less-affected _____

	Task	Time	Functional Ability	Comment
1.	Forearm to table (side)		0 1 2 3 4 5	
2.	Forearm to box (side)		0 1 2 3 4 5	
3.	Extend elbow (side)		0 1 2 3 4 5	
4.	Extend elbow (weight)		0 1 2 3 4 5	
5.	Hand to table (front)		0 1 2 3 4 5	
6.	Hand to box (front)		0 1 2 3 4 5	
7.	Weight to box	_____lbs.		
8.	Reach and retrieve		0 1 2 3 4 5	
9.	Lift can		0 1 2 3 4 5	
10.	Lift pencil		0 1 2 3 4 5	
11.	Lift paper clip		0 1 2 3 4 5	
12.	Stack checkers		0 1 2 3 4 5	
13.	Flip cards		0 1 2 3 4 5	
14.	Grip strength	_____kgs.		
15.	Turn key in lock		0 1 2 3 4 5	
16.	Fold towel		0 1 2 3 4 5	
17.	Lift basket		0 1 2 3 4 5	

Appendix G: HREB Ethics approval letter

HREB - Approval of Ethics Renewal
administrator@hrea.ca
Sent: Friday, December 09, 2022 1:06 PM
To: Ploughman Michelle(Principal Investigator) [mploughm@mun.ca]
Cc: Boyd Lara(Co-Principal Investigator) [lara.boyd@ubc.ca]; Hreaadministrator

Researcher Portal File #: 20210906

Dear Dr. Michelle Ploughman:

This e-mail serves as notification that your ethics renewal for study HREB # 2020.273 – Optimizing the timing of priming exercise to boost motor learning and enhance motor and cognitive recovery from stroke - CPSR Exercise – has been **approved**. Please log in to the Researcher Portal to view the approved event.

Ethics approval for this project has been granted for a period of twelve months effective from November 25, 2022 to November 25, 2023.

Please note, it is the responsibility of the Principal Investigator (PI) to ensure that the Ethics Renewal form is submitted prior to the renewal date each year. Though the Research Ethics Office makes every effort to remind the PI of this responsibility, the PI may not receive a reminder. The Ethics Renewal form can be found on the Researcher Portal as an "Event".

The ethics renewal will be reported to the Health Research Ethics Board at their meeting dated December 15, 2022.

Thank you,

Research Ethics Office

(e) info@hrea.ca
(t) 709-777-6974
(f) 709-777-8776
(w) www.hrea.ca
Office Hours: 8:30 a.m. – 4:30 p.m. (NL TIME) Monday-Friday