The home stroke rehabilitation and monitoring system trial: a randomized controlled trial

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Abstract

Rationale—Because many individuals post-stroke lack access to the quality and intensity of rehabilitation to improve upper extremity (UE) motor function, a home-based robotic-assisted UE rehabilitation device is being paired with an individualized home exercise program (HEP).

Aims/Hypothesis—The primary aim of this project is to determine the effectiveness of robotic-assisted home therapy compared to a home exercise program on UE motor recovery and health-related quality of life for stroke survivors in rural and underserved locations. The secondary aim is to explore whether initial degree of motor function of the upper limb may be a factor in predicting the extent to which patients with stroke may be responsive to a home therapy approach. The HEP intervention, when enhanced with robotic-assisted therapy will result in significantly better outcomes in motor function and quality of life.

Design—A total of 96 participants within six months of a single, unilateral ischemic or hemorrhagic stroke will be recruited in this prospective, single-blind, multi-site randomized clinical trial.

Study Outcomes—The primary outcome is the change in UE function using the Action Research Arm Test. Secondary outcomes include changes in: UE function (Wolf Motor Function Test), UE impairment (UE portion of the Fugl-Meyer Test), self-reported quality of life (Stroke Impact Scale), and affect (Centers for Epidemiologic Studies Depression Scale).

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Conflict of Interest Statement: Dr. Wolf is Chairman of the Scientific Advisory Board for Kinetic Muscles Inc., and is a paid consultant for Kinetic Muscles Inc. Sharon Buchanan is a paid consultant for Kinetic Muscles Inc. No other authors have any financial relationship with Kinetic Muscles Inc.
**Discussion**—Similar or greater improvements in UE function using the combined robotic-HEP intervention compared to HEP alone will be interpreted as evidence that supports the introduction of in-home technology to augment the recovery of function post-stroke.

**Keywords**
stroke; assistive technology; robotics; telerehabilitation; upper extremity

**Introduction and Rationale**

Stroke is the leading cause of severe, long-term disability among older adults in the United States\(^1\). By six months following a stroke, approximately 65 percent of stroke survivors cannot incorporate the affected hand into daily activities requiring distal control\(^2, 3\). Although the neurophysiological basis for motor recovery after stroke is not completely understood, results from several studies indicate that neuronal cortical connections and cortical representation areas are modifiable by sensory input, experience and learning, resulting in cortical reorganization or plasticity\(^4, 5\). Rehabilitation interventions found to be most effective in facilitating cortical reorganization incorporate principles of motor learning emphasizing *intensive, active* (patient-initiated), *goal-directed repetitive* practice\(^4–7\). These types of interventions are traditionally conducted by a physical therapist (PT) or occupational therapist (OT) using a one-on-one model of delivery in traditional rehabilitation environments. However, many individuals post-stroke, especially those living in underserved urban and rural settings, do not have access to comprehensive stroke rehabilitation programs or teams, thereby limiting functional recovery while contributing to long-term disability\(^8, 9\). Both financial and logistical barriers have been reported as factors limiting access to stroke rehabilitation including lack of insurance, difficulty with transportation, dependence on caregivers, and/or the lack of stroke rehabilitation programs\(^10, 11\). The use of enabling technologies, such as robotic-assisted therapy and web-based telemedicine, have the potential to bridge this gap by providing access to UE rehabilitation overseen remotely by a skilled PT or OT, based on current principles of neurorehabilitation to facilitate motor recovery. The primary aims of this trial are to determine the effectiveness of home-based robotic-assisted therapy on UE motor recovery and health-related quality of life for stroke survivors in rural and underserved locations.

Robotic-assisted devices that make use of motor learning principles can provide valuable repetitive practice to patients who might otherwise not have access to the intensive therapy necessary to elicit neuromotor recovery\(^12\). In general, robotic devices are thought to facilitate motor recovery by providing guided practice, augmenting the patient’s voluntary efforts, during goal-directed, repetitive movements\(^13\). Limitations of robotic-assisted therapy approaches include expense, portability, and their efficacy in transferring acquired movement into meaningful, functional tasks\(^14\). The Hand Mentor Pro robotic device used in this clinical trial is based on principles of motor learning by providing repetitive, goal-directed practice, engaging the participant and offering feedback during the performance of activities that are intended to transfer to functional distal motor activities. Activities prescribed using the robotic device focus on improving active range of motion and control about the wrist and fingers. The robotic-assisted therapy is paired with an individualized
home exercise program (HEP) to facilitate the transfer of newly acquired movement into functional tasks and activities of daily living. To overcome the barrier of access, the device selected for use in this trial is portable, allowing for usage in the home, and has the capability of supporting a telerehabilitation approach via remote monitoring.

Home-based telerehabilitation, in which a health care professional oversees the rehabilitation process from a remote location, has been shown to be a valuable and feasible alternative for patients with limited access to traditional rehabilitation(15). In a recent systematic review, Johansson and Wild(16) found telerehabilitation to be efficacious in improving the health of patients post-stroke, including upper extremity function, while also being supportive of caregivers needs. Piron and colleagues(17) reported improvements in upper extremity function for patients post-stroke using a virtual reality intervention conducted remotely via real-time videoconferencing. Lum and co-workers(18) described a model of remotely supervised constraint-induced (CI) movement therapy utilizing a device designed to automate the intensive training portion of CI therapy, while reducing direct therapist-patient interaction time. This form of telerehabilitation resulted in comparable gains in upper extremity function to directly-supervised use of the device or traditional CI therapy without the device. In our preliminary laboratory studies comparing combined repetitive task practice and robotic-assisted therapy to dose-matched repetitive task practice alone, comparable gains in upper extremity function were shown across interventions(19, 20). These promising results provide a rationale for examining the feasibility of a telerehabilitation program in which this robotic device is paired with an individualized HEP to improve upper extremity function.

We specifically seek to determine the effectiveness of robotic home therapy on UE motor recovery for stroke survivors with limited access to rehabilitation and hypothesize that the robotic-based home therapy intervention will produce significantly greater improvement in UE motor function than usual and customary care enhanced with a non-robotic UE home exercise program. An exploratory aim is to assess whether initial level of upper limb function may be a factor in the identification of patients that could be suitable for a home therapy intervention. In an effort to understand the potential impact of this intervention on quality of life, the Stroke Impact Scale (SIS) will be used for secondary analyses.

**Methods**

**Design**

This prospective, single-blind, multi-site randomized clinical trial investigates the efficacy of home-based robotic-assisted therapy as part of a HEP compared to a dose-matched HEP-only intervention among individuals up to six months post-stroke. A total of 96 patients will be recruited to participate in this trial, with an equal number of patients at two study sites: The Cleveland Clinic in Cleveland, Ohio and Emory University in Atlanta, Georgia. The Institutional Review Boards (IRB) at Cleveland Clinic and Emory University have approved this study.
Patient Population

Inclusion criteria for study participation include the following: age ≥18, unilateral ischemic or hemorrhagic stroke within six months confirmed with neuroimaging, persistent hemiparesis with UE voluntary activity as indicated by a score of 11–55 on the Fugl-Meyer Assessment, limited access to an organized stroke rehabilitation program, preserved cognitive function as indicated by a score of ≤3 on the Short Portable Mental Status Questionnaire, and no UE injury or condition that limited function of the more affected side before the stroke.

Exclusion criteria include: inability to provide informed consent, not independent before the stroke as determined by a score of >1 on the Modified Rankin Scale, sensory loss ≥2 on the sensory item of the National Institutes of Health Stroke Scale, hemispatial neglect as determined by asymmetry > 3 errors on the Star Cancellation Test, spastic hypertonus of hemiparetic hand or wrist musculature ≥3 on Modified Ashworth Scale, Botox injection in hemiparetic upper extremity within 6 months of enrolment, and life expectancy ≤ one year.

Potential participants who meet initial demographic inclusion criteria as assessed during a phone screen are scheduled for an in-home screening examination completed by the study physical or occupational therapist. Informed consent is obtained, followed by an examination which includes past medical history, review of systems, neurological physical exam (vital signs, Fugl-Meyer Assessment, range of motion, strength, spasticity, sensation, vision, pain), and a functional mobility assessment. To further assess criteria for participation, the Short Portable Mental Status Questionnaire and Star Cancellation Test are administered. Standardized forms and an inclusion/exclusion criteria checklist are used by both study sites to ensure uniformity in participant selection procedures. Participants may not receive concurrent rehabilitation therapy for the involved UE while enrolled in the study.

Randomization

To balance critical participant characteristics, an adaptive, stratified, computer-driven minimization procedure will be used for group assignment(21). The goal of this process is to minimize imbalance between groups across four factors: gender, handedness (whether dominant or non-dominant UE was affected), age (<62 or ≥62 years of age), and level of impairment (≤33 or >33 on Fugl-Meyer Assessment). Figure 1 summarizes the recruitment process and study flow for participants over the course of enrolment.

Interventions

Upon completion of baseline testing, participants are randomized into one of two intervention groups: Robotic-assisted therapy with Hand Mentor Pro and HEP (HM+HEP) or HEP only (HEP). Total intervention time for participants in both groups is 120 hours. Participants are asked to complete three hours of the assigned exercise each day, five days per week for an 8-week duration. The rationale for the selection of this dosage was based on previous intervention times of constraint-induced movement therapy, other repetitive task practice interventions, and robotic interventions that have been shown effective in clinical environments(18, 22). The 8-week program is designed to occur without interruption; however, should an individual be unable to complete the intervention as designed due to
reasons other than voluntary non-compliance, the study treatment can be extended by up to four weeks. Examples of lapses in treatment resulting in an extension of participant involvement include vacations, illness, hospitalizations, or device malfunctions.

The study therapist conducts a home visit regardless of group assignment to instruct the patient and available family member(s)/caregiver(s) in the study intervention. This home visit is completed within two weeks of baseline testing, and can last from one to three hours, based largely on the participants’ ability to comprehend and complete the assigned treatment intervention. A standardized home visit checklist is completed by the study therapist at each site to ensure thorough and consistent training, and to document potential barriers to adaptation or the need for a follow-up home visit.

Behavioral techniques to facilitate compliance are utilized uniformly for both intervention groups. As part of the initial home instructional visit, participants receive a written home exercise prescription, are asked to sign a behavioral contract, and maintain a daily exercise log. Participants in both groups are asked to incorporate the involved UE into functional tasks and weekly follow-up phone calls are made to determine exercise compliance and changes in UE movement or motor function, and to guide exercise/activity progression.

**Control Group: Home Exercise Program Only**—The HEP was designed using evidence-based principles consistent with current stroke rehabilitation practice, with the primary purpose of facilitating motor learning and the recovery of UE function\(^\text{23, 24}\). Exercises include preparatory activities to improve range of motion, strength, and coordination of the impaired UE, in addition to functional, task-based activities. The exercise prescription is based on the patient’s available movement, function, and goals; and designed with the intent of challenging the patient sufficiently to elicit gains in motor function without being frustrating. Accordingly, a wide range of exercise type and difficulty have been created to account for the variability of movement and function anticipated in the participant pool. The exercises are organized under the following headings: 1) self-range of motion; 2) weight bearing activities; 3) active-assisted exercises with cane 4) shoulder exercises; 5) elbow/forearm exercises; 6) wrist/hand exercises; 7) functional activities. Each exercise has clearly written instructions for performance, prescribed dosage and is accompanied by a picture, consistent with current clinical practice standards. Each exercise page is labelled to correspond with a diary, which participants use to document the details of their daily exercise routine. As an alternative for patients with difficulty reading or writing due to aphasia, a simpler version of the diary is utilized in which the participant records total time dedicated to UE exercise each day.

Participants are asked to complete a total of three hours of UE exercises/activities each day, five days per week. Functional tasks and activities of daily living can be included in the 3-hour daily intervention, providing that the affected UE is incorporated into the tasks. For example, using a fork and knife while eating can be included, but grooming tasks utilizing the non-affected UE only would not count toward the 3-hour intervention time.

**Treatment Group: Robotic-Assisted Therapy and Home Exercise Program**—Participants in the treatment group are prescribed an identical dose of therapeutic
intervention as the control group; however two hours are using the robotic device while the third hour of therapy is spent performing exercises and functional tasks similar to the control group.

**Robotic Device**—The Hand Mentor Pro robotic device uses a pneumatic artificial muscle to facilitate movement about the wrist and fingers while providing visual biofeedback about the quality and quantity of wrist movements. The device consists of three components: control box, arm unit and data collection and communications module (see Figure 2). The control box houses the electronics of the device (12"W x 12"L x 12"H, 14 lbs.) and has a 10.4" color touch screen to facilitate user interface. The control box is connected to the arm unit by a pneumatic hose and data cable. The pneumatic actuator is the top portion of the arm unit and provides air into and out of the hose to simulate dorsal muscle contraction and relaxation. Voltage changes are detected from a potentiometer that is aligned to the wrist joint. These changes are calibrated to reflect active range of motion. Resistance to force generation into wrist and finger extension is detected by a pressure transducer housed within the arm unit. This quantification of resistance extension is utilized by the various programs when providing passive stretch to the wrist, and to modulate the level of difficulty of each program.

There are four training modules designed to improve active control of the wrist musculature and one spasticity reduction program. In an effort to keep the patient engaged, video gaming design principles were used to create these modules. Figure 3 depicts screen shot examples of two of the games. Two variations of the basic motor control program train flexion and extension or extension-only movement patterns. These programs use function-based games in which the goal is to move the hand to a target (e.g. pick up a barbell, corresponding to wrist flexion) and raise it first to waist height (neutral wrist), then overhead (corresponding to wrist extension) within a time specified by the therapist. The time to reach the target is decreased as the patient experiences success. If the patient does not achieve the goal within the specified time, the air muscle actuates to assist the patient through the desired range of motion (ROM). If the patient is successful in achieving the goal on 80 percent of the trials, difficulty programatically increases by one level (ten levels total for each program), requiring an increase in the distance the wrist must move to achieve the target. Conversely, if the patient is successful less than 20 percent of the trials, the level is decreased. The ROM requirements to achieve the target increase by 1.5° of wrist flexion and 3° of wrist extension for each subsequent level of difficulty.

The advanced motor control programs incorporate timing-based training principles, requiring the patient to lift the hand at a precise time and velocity. In the balloon game (Figure 3, lower), a hot-air balloon moves up and down on the screen corresponding to active wrist extension and flexion, respectively. The participant must avoid objects as they scroll across the screen from right to left. In the second of these games, the patient moves a paddle up and down to bounce a ball back to the other side of the playing field, which is controlled by the computer. As the patient completes successful trials, the active range of motion, timing, velocity, and strategic demands for the motor response are increased. The flexion and extension range of motion requirements for these advanced motor control games
increase by three degrees for each level. There are ten levels, each containing three velocities.

The goal of the Spasticity Reduction program is to decrease flexor tone of the fingers and wrist via visual biofeedback and assistive motion. The initial position of the hand is at approximately 30 degrees of flexion. The air muscle then inflates to bring the wrist to approximately half of the patient’s available passive range of motion. The amount of force necessary to achieve this position is measured while a potentiometer measures wrist position. A thermometer is displayed on the screen with a green line showing the initial resistance; increased resistance is shown as yellow and then red. The line is reduced as flexor stiffness (resistance to passive motion) decreases. Each time a patient completes a program, the summary for that session is displayed on-screen and stored in that patient’s coded electronic database.

Data are stored in non-volatile memory and are encrypted and transmitted from the robotic device to a secured website via a landline telephone, internet, or cellular connection where it is accessible to study therapists to enable remote monitoring. The data collection and communication module records the following variables: overall time of use, time of use in each module, number of attempted and successful repetitions, wrist angle and pneumatic pressure.

The HEP portion of the intervention is designed to incorporate movement acquired through the robotic-assisted exercise into meaningful, functional activities. Additionally, exercises incorporating the proximal UE are included in the HEP, as the robotic device used in this trial addresses mainly the wrist and fingers. With the goal of utilizing comparable adherence strategies with both groups, behavioral contracts, daily exercise logs, and weekly follow-up phone calls are administered uniformly.

**Outcome Measures**

After informed consent is obtained and the telephone screening procedure has verified participant eligibility, a battery of tests evaluating motor function, quality of life, and depression administered by an evaluator blinded to group randomization. The same battery of tests is repeated at the conclusion of the 8-week intervention interval by the same blinded evaluator. The therapist at The Cleveland Clinic was trained and standardized in the testing procedures by the therapist at Emory University who was responsible for training all evaluators from the EXCITE clinical trial(25). The primary outcome measure is the total change in score (from baseline to post-evaluation) of the affected upper extremity on the Action Research Arm Test (ARAT). Secondary outcome measures included the Wolf Motor Function Test (WMFT), the Stroke Impact Scale (SIS), the Fugl-Meyer Assessment (FMA), Centers for Epidemiologic Studies Depression Scale (CES-D) and Modified Ashworth Scale (MAS).

**Primary Outcome Measure**—The ARAT consists of four subscales that address grasp, grip, pinch, and gross motor movements (19 tasks) of both the affected and non-affected upper extremity. Patients are scored with an ordinal scale from 0–3 with a score of 3 indicating normal performance of task within 5 seconds and a score of 0 indicating the
inability to perform any part of the task within 60 seconds. Higher scores indicate better movement capabilities. The ARAT is considered a valid and reliable tool for upper extremity deficits following stroke(26–28). The minimal clinically importance difference (MCID), or the smallest difference in score that a patient perceives as beneficial, is 12 points if the dominant UE is affected and 17 points if the non-dominant UE is affected(29). The minimal detectible change (MDC) is the smallest change in two scores that likely represents a statistically significant change(30). For the ARAT, the inter-rater MDC is 13.1 and test-retest MDC is 3.5(31).

**Secondary Outcome Measures**—The WMFT consists of 15 timed tasks and 2 strength tasks of both the affected and non-affected upper extremities. Tasks progress from proximal to distal, beginning with isolated shoulder movements and progressing to fine-motor tasks of the hand. Patients are encouraged to perform each timed task as quickly as they can. Shorter times reflect better performance. Timed movements are also graded with a functional ability scale for quality of movement. The WMFT has been validated for use with acute to chronic stroke patients(32–34). For the cumulative timed portion of the test, MCID is 19 seconds for the dominant side, while the non-dominant side had no MDIC value due to the very small relationship between test score and subject perceived change rating. The functional ability scale portion of the Wolf Motor Function test has a MCID of 1.0 and 1.2 in the dominant and non-dominant side, respectively(29). The interrater MDC is 20.2 points and the test-retest MDC is 12.0 points(31).

The SIS is a quality of life questionnaire that addresses several domains following stroke including physical impairments, memory and cognition, mood, performance with activities of daily living, mobility, use of affected UE, and return to activities that have meaning to the patient. The SIS has been shown reliable and valid in sub-acute to chronic stroke populations(35). The MDC and MCID for subsets of the test are as follows: Performance of activities of daily living: 17.3 and 5.9 points; strength: 24.0 and 9.2 points; mobility: 15.1 and 4.5 points; and use of affected UE: 25.9 and 17.8 points(30).

The upper extremity Fugl-Meyer Assessment (FMA) is an impairment-based measure for the upper extremity following stroke, consisting of 33 movements with higher scores indicating increased ability of the patient to move out of synergistic patterns toward more isolated movements. Movement quality of the affected UE is compared to the movement quality of the non-affected UE on a 0–2 ordinal scale with 0 indicating no movement at all, 1 indicating partial movement of the affected extremity, and 2 indicating equal movement between affected and non-affected upper extremities. The FMA is a reliable and valid tool for measuring UE impairment following stroke(36, 37). The MDIC for the FMA is 10% of the total possible score, or 6.6 points(37). The inter-rater reliability MDC is 12.9 points and the test retest MDC is 5.2 points (31).

The CES-D is a questionnaire used to screen for depressive symptomology. The test consists of 20 questions that capture how well a patient is coping emotionally. Scores > 16 can indicate the patient is at risk for depression. The CES-D has been found reliable and valid for the subacute stroke population(38, 39).
The MAS is used to assess spastic hypertonus following stroke. Patients are scored on a scale of 0–4 with higher scores indicating more tone. For this case report, wrist flexion, supination, and finger flexion were assessed. The reliability and validity of the MAS is questionable, yet this measure is the most commonly used clinical tool to assess spasticity following stroke. A recent study found the MAS to be moderately reliable for upper and lower extremity muscle groups between raters.

**Data Monitoring Body**

The home stroke rehabilitation and monitoring system trial has been deemed a low risk study by the IRB’s for the study. Kinetic Muscles Incorporated (KMI) is a registered Medical Device Manufacturer and the commercially-available Hand Mentor Pro robotic device used in the study is listed with the Food and Drug Administration. Both the Emory and Cleveland Clinic IRBs approved the study in expedited review. There have been no serious adverse events related to Hand Mentor use since it was introduced in 2003. For these reasons this study qualifies for data and safety monitoring by an Independent Medical Monitor.

The site Principal Investigators (PI) are responsible for monitoring the safety and efficacy of this trial, executing the Safety Monitoring Plan, and complying with the reporting requirements. The study statistician will submit descriptive performance data and safety data to the PIs and the Independent Medical Monitor for their review. The PI will provide a summary of the Safety Monitoring report to National Institute of Neurologic Disorders and Stroke periodically. The Safety Monitoring report will include participants’ socio-demographic characteristics, expected versus actual recruitment rates, treatment retention rates, any quality assurance or regulatory issues that occurred during the past year, summary of adverse events and serious adverse events, and any actions or changes with respect to the protocol. Any serious adverse event, whether or not related to study intervention, will be reported to the IRBs. In the event that a patient either withdraws from the study or the investigator decides to discontinue a patient due to a serious adverse event, the patient will be monitored by the investigator via ongoing status assessment until a resolution is reached (i.e.: the problem requiring hospitalization has resolved or stabilized with no further changes expected), the serious adverse event is determined to be clearly unrelated to the study intervention, or the serious adverse event results in death.

The Independent Medical Monitor reviews the research protocol and ongoing study activities with emphasis on data integrity and study participant safety issues, including: review of adverse events; recommendations to the National Institute of Neurologic Disorders and Stroke and PI concerning continuation or conclusion of the trial(s); protection of the confidentiality of the trial data and the results of monitoring; and Review of data and study quality.

**Data Collection and Entry**—Data will be collected using standardized paper forms and will only be identified with the study ID of the participant. The codes that link the name of the participant and the study ID will be kept confidential by the Principal Investigators in a secured cabinet. Data will be entered into a secure, customized Microsoft Access database.
independently by two teams of trained data entry staff at each study site. The two sets of data will be sent to the study statistician for comparison via secure file transfer protocol, and discrepancies will be corrected by an investigator, based on source documents. Data from the robotic device are encrypted and transmitted to a secure database via a landline telephone, internet, or cellular connection. The quality of the data will be monitored once per month by the Independent Medical Monitor for the first three months, then, if satisfactory performance is noted, once every three months. There are no interim analyses planned, but rather the entire trial will be completed prior to unblinding and data analysis. The study’s statistician will analyze the data, using the SPSS® version 18 software (SPSS Inc, Chicago).

**Intervention Integrity Monitoring**—To monitor subject compliance, a physical or occupational therapist will perform weekly follow up phone calls to both the HM+HEP and HEP only groups. During these phone calls, the therapist can modify home exercise programs as the subject progresses, discuss any barriers to intervention adherence, and encourage compliance. To facilitate accurate self-reporting, subjects are provided with a daily activity diary where they record time spent engaged in exercise or functional activity with their affected UE. For those participants randomized to the robotic group, study personnel monitor compliance via the secured website, comparing data transmitted from the device to self-reported time of use.

**Sample Size**

Based on previous experience, we expect an effect size of 0.75 if the intervention with the Mentor is to be of clinical significance in a mild to moderate stroke impaired group. Given that many patients recruited for this study will be more impaired, thus approaching the moderate to severe range, generating an effect size approximating .50 is reasonable. This effect size or greater can be observed at 90% statistical power for the primary aim if 40 subjects in each of the two groups complete the trial, assuming a 15% dropout rate.

**Statistical Analysis**

This analysis will be conducted using an intent-to-treat framework, including all subjects randomized. The primary outcome variable is the change in ARAT in the more affected arm from baseline to end of treatment. Secondary outcomes include the WMFT and FMA. We hypothesize that the HM+HEP intervention will produce significantly more improvement in upper extremity motor function than a self-administered HEP. A repeated-measures analysis of variance model will be fit with group assignment (HM+HEP or HEP-only) as the between-patient factor and time as the within-patient factor. If baseline data are determined to be unbalanced across groups on potentially prognostic factors, and this imbalance influences the outcome measure, variables may be added as covariates or additional factors. The group-by-time interaction will be tested to determine if the HM+HEP intervention produces significantly more improvement in upper extremity motor function than the self-administered HEP. A secondary analysis will be performed to evaluate the impact of initial level of upper extremity functioning on degree of improvement over the course of the trial(41). To address this secondary goal, patients scoring ≤33 on the Fugl-Meyer Assessment are classified as “low functioning” and those scoring >33 are classified as “high
functioning”. This analysis will be augmented to test for the possibility of a triple interaction, group by time by function level (high vs. low).

**Study Organization and Funding**

The leadership team that will oversee this clinical trial is comprised of three co-principal investigators. Dr. Koeneman, founder of Kinetic Muscles, Inc., is a bioengineer who has 40 years’ experience in developing medical devices. He developed the robotic device used in this study. Dr. Alberts is a neuroscientist who also has more than 10 years’ experience in conducting motor control studies in patient populations such as Parkinson’s disease, stroke and dystonia. Dr. Wolf is a rehabilitation scientist and physical therapist with a 35-year funding history during which time he has studied neuromuscular and musculoskeletal disorders, especially all aspects of restoration of upper extremity function following stroke. Dr. Alberts was the PI on a preliminary feasibility study, R21 HD045514, designed to provide preliminary data for a larger trial and refine the utilization of the device in clinical practice.

Dr. Koeneman also provides the monitoring services that are used in the study. To control for conflict of interest, the study utilizes a multiple PI approach where the clinic sites have independent PI’s who have complete control over conducting the trial at their site. The Cleveland Clinic and Emory University School of Medicine have contracts with KMI that specify they are free to present and publish information without the approval of KMI, although KMI may request manuscripts prior to publication. In addition, data analysis will be done by an outside contractor to control conflict of interest.

**Discussion**

Several barriers have been identified which limit patients post-stroke from achieving their potential for motor recovery. The barriers this telerehabilitation study is designed to overcome include limited access to stroke rehabilitation programs, limitations in receiving the quality and intensity of rehabilitation thought to optimize motor recovery, and difficulty with patient adherence to home exercise programs. Specifically, this trial is designed to determine the efficacy of an in-home therapeutic intervention combining robotic-assisted therapy with a customized HEP overseen remotely by a skilled physical or occupational therapist to improve UE function for individuals who otherwise lack access to traditional stroke rehabilitation.

Barriers of accessibility to stroke rehabilitation can potentially be overcome by providing an in-home intervention using a telerehabilitation model, thus bypassing the need for the patient to attend therapy in an outpatient clinical setting. In this trial, a skilled physical or occupational therapist conducts a home visit to instruct the patient and available caregiver(s) in the home-based, self-administered intervention. However, unlike a traditional HEP in which the patient is expected to complete the intervention independently without the guidance of a physical or occupational therapist, the prescribed intervention is monitored and advanced weekly by the study therapist. Because poor adherence to HEP’s has been identified as a factor which may contribute to disability in patients post-stroke(42), this study is designed to provide guidance to the patient and a sense of accountability toward the
expectation of compliance with the rehabilitation program. In addition to the weekly follow-up phone calls, the use of a behavioral contract and exercise logs are incorporated into the study design to further improve adherence to this self-administered rehabilitation program.

Both the robotic and HEP interventions are based on motor learning principles thought to optimize neuroplasticity and motor recovery post-stroke. Although repetitive, goal-directed practice appears to be important in fostering neuroplastic change post-stroke; such repetition should include functionally based training that embraces task-specific practice to foster motor recovery\(^2\). This consideration is not embedded within the application of robotic devices. To facilitate transfer from movement to function and to overcome this limitation, the current approach relies heavily on the inclusion of a focused HEP in which a broad spectrum of appropriately challenging functional tasks is prescribed to the patient. Incorporating the involved UE into daily tasks appears instrumental in optimizing functional recovery\(^{23, 44}\). Finally, although the exact dosage of therapy necessary to elicit neuroplastic change post-stroke is not precisely known, the intensity of exercise prescribed for both groups is based on previous clinic-based trials that have demonstrated efficacy in motor recovery \(^{18, 22, 25, 45}\).

Another significant gap addressed by this study design is the investigation of the efficacy of either intervention in improving UE function in patients with significant paresis post-stroke. While most UE rehabilitation interventions investigated in large-scale randomized controlled trials that have been found to be efficacious following stroke have had stringent movement requirements\(^{25, 45, 46}\), the proposed study includes individuals with a score as low as 11 on the FMA. Systematically investigating the effect of these home-based interventions on the recovery of motor function in patients with very low functioning upper extremities will provide valuable information in directing rehabilitative care for this population.

Conclusion

Results from this trial will provide insights into the feasibility and efficacy of using a robotic device to augment a HEP designed to improve UE function post-stroke. Behavioral components surrounding compliance with a self-administered rehabilitation program that includes robotic-assisted therapy will be determined. Finally, we will explore whether this approach may exhibit different effects as a function of the participant’s initial level of UE motor function. The identification of participants that are responsive to this intervention approach may increase access to rehabilitative care for a population traditionally excluded from large-scale stroke trials.

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References


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23. Weinstein, CJWS. Chapter 17: Task oriented training to promote upper extremity recovery. In: Stein, JZR.; Harvey, RF.; Macho, RV.; Weinstein, CJ., editors. Stroke Recovery and Rehabilitation. Woodbridge, CT: Demos Publishing; 2009.


Figure 1.
Diagram depicting expected recruitment numbers and study flow during participants’ course of enrolment
Figure 2a

Control box and touch-screen display

Pneumatic hose and data cable

Arm unit with pneumatic actuator

Figure 2b

Mentor Pro™ Controller Box

Figure 2.
Illustration of the Hand Mentor Pro robotic device: a) control box b) arm unit
Figure 3.
Sample screen shots of two of the motor control programs: a) strongman b) balloon game