PROTOCOL TITLE: THE GENERAL USE OF ROBOTS IN STROKE RECOVERY: THE ANKLE-BOT

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Research Coordinator: Johanna Chang, M.S.

PRODUCT NAME: In-Motion Ankle-bot

INTRODUCTION/BACKGROUND MATERIAL

Cerebral ischemia, stroke, is the 3rd leading cause of death in the U.S. and the leading cause of permanent disability (Amer Heart Assoc 2003). Traditionally, rehabilitation medicine treatment for stroke patients consists of one-on-one treatment and group therapy with physical, occupational and speech therapists who focus their treatment on both compensatory strategies to regain independence and a variety of techniques that can be described as neuromuscular re-education. For example, one learns to brush one's teeth with the non-preferred hand. There are also labor-intensive motor training exercise protocols that focus on the stroke-affected limb using hand-over-hand techniques to move the impaired limb. Prompted by work in non-human primates and other basic experiments, it has become routine in the rehabilitation medicine programs for stroke patients with paralyzed or weakened limb motor function to increase the intensity of activity-based therapy. Recently, the invention of robotic therapy has been investigated as a potentially superior technique to maximize motor recovery after stroke. Interactive motors with low impedance and driven by smart controllers has led to a revolution in treatment of motor impairment. These devices move a patient's limb when the patient cannot move and then as a patient's motor function improves, the device allows the patient to execute voluntary movement. A robot will deliver reproducible movement without tiring and can render the level of training intensity required to alter impairment. A recent multi-center trial that tested the effectiveness of robot treatment compared to standard treatment for motor recovery of the affected upper limb significantly favored robot treatment [1]. There were also significant cost reductions for the robot treated group [2]. These data and other data from our laboratory prompted the American Heart Association and the VA Health System to classify robots treatment as standard of care for post-stroke rehabilitation [3, 4]. The studies proposed here for the use of robots in stroke recovery have the potential to provide significant advancement in the field because they will identify optimal methods to maximize neurological and functional outcome for patients after stroke.

With this protocol we now want to extend robot treatment to the lower limb. We want to initiate a pilot study using a device that has comparable safety features, identical motors that drive the movement of the manipulandum, and identical software programs that record the movement and drive the protocol to the devices that we have used successfully in robots for the upper extremity and in the protocols that have been approved by this IRB. This robot, however, fits around the foot and calf so that ankle flexion and extension can be trained; this device is called an ankle-bot. We want to treat the affected lower limb of patients with chronic stroke. Recent work shows that patients with chronic stroke who are exposed to ankle-bot treatment, first show that the ankle bot does not significantly alter a patient's gait on a treadmill [5]. Moreover, treated chronic stroke patients had decreased ankle stiffness [6] and demonstrated increased walking speed [7], a common measure of training effectiveness.

SPECIFIC AIMS

As part of our continuing effort to achieve a long-term goal of improving motor recovery after stroke, we will determine whether ankle-bot training improves gait speed in patients with chronic stroke. In this pilot study we will expose 55 patients consecutively referred from our referral sources in the department of neurology and physical medicine and rehabilitation to three one hour training periods per week on alternate days for 6 weeks. Prior to training, we will determine baseline gait speed across three measures separated by 2-10 day intervals. We will execute these measures again at the midpoint of training, at the end of training, and 3 months after training has ended.

PRELIMINARY STUDIES AND SIGNIFICANCE

Efforts using robotic devices to train the paretic arm of persons with acute or chronic impairments after stroke have consistently and significantly reduced the motor deficit without untoward side effects [1, 8-16]. Impairment reduction after this class of targeted training agrees with a prominent theme of brain injury recovery, namely, that activity-dependent plasticity underlies neurological recovery.

Recent work by others demonstrates that this ankle-bot is effective in improving gait speed and decreasing ankle stiffness in patients with chronic stroke [6, 7]. The added inertia and friction caused by wearing the ankle-bot device did not alter the gait during overground training or on a treadmill in patients with chronic stroke [5].

Walking speed has been called the sixth vital sign and is crucial to the independence of a post stroke patient [17]. Figure 1. demonstrates a typical scale of walking speeds and shows that independence comes with ambulation speeds of 1.2 – 1.4 m/sec; this means a person can cross the street. Those with walking speeds of 0.8 – 1.2m/s can ambulate in the community, and those with ambulation speeds of less 0.8m/sec can ambulate in the household, but usually need assistance for community ambulation. Several recent studies have not been successful improving the gait speed outcome in patients with chronic stroke on the standard care measures for gait outcomes in patients with stroke [18, 19]. Patients in these studies were stratified into those with severe walking impairment and gait speeds less than 0.4m/s or those with moderate impairment and gait speeds between 0.4 and 0.8 m/s.

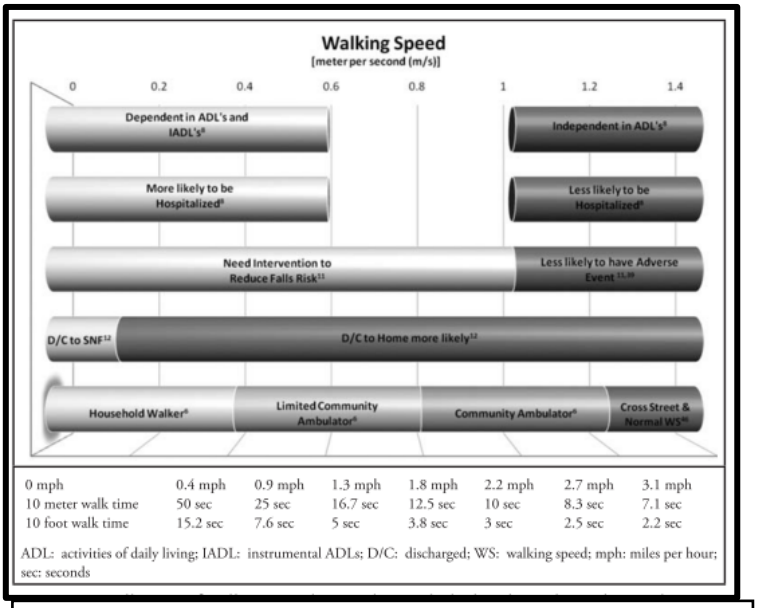

Fig.1. This collection of walking speeds generates ambulation categories that define independence and are linked to rehabilitation needs.

Recently, the invention of robotic therapy has been investigated as a potentially superior technique to maximize motor recovery after stroke. Interactive motors with low impedance and driven by smart controllers has led to a revolution in treatment of motor impairment. These devices move a patient's limb when the patient cannot move and then as a patient's motor function improves, the device allows the patient to execute voluntary movement. A robot delivers reproducible movement without tiring and can render the level of training intensity required to alter impairment.

RESEARCH DESIGN AND METHODS

Inclusion/Exclusion Criteria

Inclusion Criteria:

1. ≥ 18 years of age
2. First single focal unilateral lesion with diagnosis verified by brain imaging (MRI or CT scans) that occurred at least 6 months prior;
3. Cognitive function sufficient to understand the experiments and follow instructions (Mini-Mental Status Score of 24 or higher or interview for aphasic subjects);
4. Some amount of independent ambulation (with orthoses or walker) and a gait speed of at least 0.1m/s.

Exclusion Criteria:

1. Botox treatment within 6-weeks of enrollment;
2. Fixed contraction deformity in the affected limb;
3. Complete and total flaccid paralysis of all lower extremity motor function;
4. Unable to ambulate except with the aid of another person or ambulation speed of <0.4m/s

Visit Schedule

In this pilot study, 55 participants will be accepted from our referral sources in the department of Neurology and Physical Medicine. There will be 3 measurement periods before the training starts, separated by 2-10 days in order to establish a baseline walking speed. Following the lead-in period, each subject will attend eighteen 60-minute sessions (3 visits/week) over a 6-week period (or up to 8-weeks to allow for missed appointments) comprising the training period. Participants will undergo midpoint and discharge outcome measures during training, at sessions nine and eighteen, respectively. Subjects will then return for a final 3-month follow-up visit for further outcome measures. All study procedures will be administered or supervised by the research coordinator, study investigator, or a certified physical or occupational therapist. All visits will be conducted in either the robot suite at the Northwell Health Transitions Outpatient Rehabilitation Center, the robotics suite in the Clinical Research Center at the Feinstein, or at Long Island Pediatric Physical Therapy, which is the rehab office of Philip Koch, PT.

Lead-in Period

- Week 1, Visit 1 (approximately 60 minutes)
    - Clinical outcome measures
    - Medical screening
    - Consent
- Week 2 & 3, Visit 2 & 3 (approximately 60 minutes each)
    - Clinical outcome measures
    - Objective Gait Measures

Training Period

- Week 4-6 Visit 4-11 (approximately 1 hour)
    - Robotic training
- Week 6 Visit 12 (approximately 90 minutes)
    - Robotic training
    - Midpoint Outcome Measures
- Week 7-9 Visit 13-21 (approximately 1 hour)
    - Robotic training
- Week 10, Visit 22 (approximately 1 hour)
    -
    - Discharge Clinical outcome measures
    - Discharge Objective Gait Measures

Final Visit

- Week 22, Visit 23 (approximately 60 minutes)
    - Follow Up clinical outcome measures
    - Follow Up Objective Gait Measures

Clinical Outcome Measures

All outcome measures will be recorded three times prior to the training period separated by 2-10 days to ensure reliability and stability of measures, then again at weeks three (midpoint) and six (discharge) of the training program, and again three months after training has completed (follow up). In general, study visits will take place at the institution of recruitment (e.g. subjects recruited through Feinstein will be treated at Feinstein or Transitions). However, pre and post-study objective gait measures will take place at Long Island Pediatric Physical Therapy, which is the rehab office of Philip Koch, PT.

10 Meter Walking Test (Primary): The 10 Meter Walking Test is a valid and reliable evaluation instrument used for measuring walking speed, which strongly correlates with functional ambulation status in stroke patients [19]. Walking at 1.2-1.4m/s is considered normal, community ambulation pace, and allows a person to perform

activities of daily living independently, including crossing a street. After a stroke, depending on the severity, ambulation speed often varies between 0.2-0.8m/s [18, 19].

6 Minute Walk Test: The 6 Minute Walk Test is a valid a reliable measure of gait speed and aerobic capacity after stroke, in which the participant is asked to walk as fast as safely possible without assistance for 6 minutes and the distance is measured [19].

Berg Balance Scale: The Berg Balance Scale is a valid and reliable measure functional balance abilities after stroke across fourteen simple static and dynamic balance tasks measured on a 0 (unable) to 4 (independent) scale [20].

Stroke Impact Scale (SIS): The SIS is a valid and reliable index that assesses changes in impairments, disabilities and handicaps following a stroke and has internal consistency and established test-retest reliability [21, 22]. We have chosen the Stroke Impact Scale (SIS) Version 3.0 to measure physical abilities, as well as other dimensions that contribute to quality of life and participation in everyday life. This is a 59-item self-reported questionnaire that asks persons with stroke to rate perceived problems in eight domains using a 5-point scale: strength, hand function, mobility, activities of daily living, emotion, memory, communication and social participation. This self-report assessment is unique in that it addresses motor impairments of the paretic limbs in addition to other key variables that are important to patients and their caregivers. This assessment will not only offer data concerning perceived changes in motor abilities following involvement in the planned study, but will also help to identify other incidental changes in emotional status, memory and thinking, or activities of daily living following participation in robot training.

Activities-specific Balance Confidence Scale: The Acitivities-specific Confidence Scale is a valid and reliable 16 point self-report measure of an individual's confidence in performing ambulatory activities after stroke without falling [23].

Objective Gait Measures

Gait analysis measures for fast and comfortable pace will be recorded twice prior to the training period (baseline); measurements will be separated by 2-10 days to ensure reliability and stability of measures. Measures will be taken again at week ten (discharge) of the training program and once more three months following completion of training (follow up). Gait analysis will be performed at the Long Island Pediatric Physical Therapy, which is the rehab office of Philip Koch, PT.

Kinematic Measures will be taken with the Zeno Walkway, which is an electronic floor mat, containing a 16-level pressure sensing pad and circuitry inside a flat, linoleum surfaced walkway. The Kinematic measures will serve to objectively describe the geometry of movement, including step speed, length, power, center of oscillation, and step symmetry. These metrics are valid and reliable objective measures of changes in gait pattern [29-32].

STATISTICAL CONSIDERATION AND DATA ANALYSIS

The primary outcome measure for a robotic trial of the lower extremity is the 10 Meter Walking Test, which is a widely used clinical metric of functional ambulation status post-stroke. Gait speed is the critical measure that tracks functional independence [17]. We will use the accepted post-stroke definitions of impaired ambulation: with severe impairment defined by gait speeds below 0.4m/s, moderate impairment as 0.4-0.8m/s (limited community ambulation ambulation), mild impairment as 0.8-1.2m/s (community ambulation), and functional independence as 1.2-1.4m/s or greater. The reliability and validity of this scale is accepted by clinical researchers as well as clinicians [18, 19].

Secondary outcome measures will include the 6 minute walk test, the Berg Balance Scale, objective gait measures, the Stroke Impact Scale, and the Activities-specific Balanace Confidence Scale, which together

provide valid and reliable measures of aerobic capacity for ambulation, functional balance, objecitve measures of gait pattern, and subjective impression of mobility impairment after stroke.

The clinical evaluations will be administered at baseline, 9 (midpoint) and 18 (discharge) sessions, and 3 months after completion. The paired t-test (and nonparametric Wilcoxon signed-rank test) will be used to evaluate mean score changes for different interventions (i.e., within-group comparisons over time). The independent two-sample t-test (and nonparametric Wilcoxon rank-sum test) will be used to evaluate mean score differences between interventions immediately after treatment and after 3 months. Similar analyses will be repeated for the secondary measures. In our previous studies, randomization has led to comparable groups (baseline) and we expect the same here. We will also perform a repeated measures analysis of variance (RMANOVA) with group as a between-subject factor, and time as a within-subject factor. Because we have repeated measures over time and have two groups to compare at a time, this analysis will allow us to assess potential treatment-by-time interactions more accurately. We will also perform an analysis of covariance (ANCOVA) with treatment protocol as a between-subject factor.

POWER ANALYSIS
The information gained with this study will permit a power analysis so that we can test whether this treatment is more effective than the standard training. The target sample size for this pilot study is 55 patients. We have experienced <5% dropout rate for the treatment, and a 10% drop out rate to complete all measurements, including the 3 month follow up.

DEVICE (ROBOT) INFORMATION

All of the robotic devices that we are proposing to use in patient training trials have been exempt by the FDA. The FDA has ruled that these devices are powered exercise machines. These rulings are provided in the supplementary material. This is also the reason we are filing an expedited review.

Technical Engineering Information

The robot control system is an impedance controller that modulates the way the robot reacts to mechanical perturbation from a patient or clinician and ensures a gentle compliant behavior. Impedance control [24] has been the central contribution of Hogan's engineering research since the early eighties and has been extensively adopted by other robotics researchers concerned with human-machine interaction. At present the MIT-MANUS impedance controller is implemented using coupled nonlinear position and velocity feedback structured to produce a constant isotropic end-point stiffness and damping. High-bandwidth current-controlled amplifiers produce motor output torques directly proportional to commanded input. These facts make the robot a stable device.

For this application, the most important feature of the controller above is that its stability is extremely robust to the uncertainties due to physical contact [25-27] . The stability of most robot controllers is vulnerable when contacting objects with unknown dynamics. In contrast, dynamic interaction with highly variable and poorly characterized objects (to wit, neurologically impaired patients) will not de-stabilize the impedance controller above; even inadvertent contact with points other than the robot end-effector will not de-stabilize the controller. This is essential for safe operation in a clinical context.

The robot control architecture is implemented on a standard personal computer (presently a 66 MHz 486CPU) with 16-bit A/D and D/A I/O cards, as well as a 32-line DIO card. Besides its primary control function, this computer displays the exercise to be performed to both the operator (clinician) and patient via a video-splitter with dedicated monitors. The neuro-rehabilitation workstation also includes a second personal computer (presently a 25 MHz 386CPU) to display on-line video and audio information. Communication between computers is through a serial port at transmission rates that allow video update above 30 frames/sec. Thus important aspects of the patient's sensory and motor experience can be controlled at the same time.

Practical issues regarding the robot control system and patient safety

The software that runs the robot device continuously checks the force, speed and position of the robot armed and on the status of the power. This software can break the robot if the force, speed, or position is beyond set ranges. There are two clearly visible "shut-down" switches that are always in reach of the technician trainer. In the event of software failure, motion beyond the specified range, loss of electrical power, or activation of the "shut-down" switch the device stops (brakes) within 2 milliseconds. The robotic limb will only move the patient's lower limb, and no other body part will be within the active range of this movement. The patients ankle and calf are attached to the robotic limb with a velcro clasp, which can be released with a sudden pull from the patient or therapist. The entire apparatus is ground fault protected to exceed clinical standards.

Finally the PI will be assisted by the other investigators and Research Coordinator Johanna Chang , who collectively have over 20 years of experience using the IMT robotic devices. The robots are distributed world-wide. The ankle-bot is a new device and is installed here at the Feinstein Institute of Medical Research at Northwell Health and in Baltimore at the VA. No one has observed an injury to any subject for the upper extremity robots and for the ankle-bot.

PROTECTION OF HUMAN SUBJECT

RISKS TO SUBJECTS

Human Subject Involvement and Characteristics: We anticipate enrolling 55 human subjects. Inclusion and exclusion criteria are stated above in the Research Design and Methods section.

Sources of Material: Sources of research material will be the hospital records providing demographic and medical information including CT or MRI imaging studies, and clinical examinations performed at outpatient facilities run by the Department of Physical Medicine and Rehabilitation of the North Shore University Hospital (NSUH) and LIJ Medical Center (LIJMC). Additionally, de-identified, objective gait measures will be performed and initially stored at Long Island Pediatric Physical Therapy by Phil Koch, PT.

Potential Risks:
Robot Risks: There are no known risks associated with the use of robotic training for stroke rehabilitation. Some patients who have been trained with the upper extremity robots have pain in the shoulder. Our experience has demonstrated a comparable incidence of shoulder pain in groups that were or were not treated by the robot. No risks or pain have been documented in association with the anklebot device.

Confidentiality Risk: One additional risk concerns the risk to confidentiality incurred with any collection of medical data.

ADEQUACY OF PROTECTION AGAINST RISKS

Recruitment and Informed Consent: Stroke subjects who meet inclusion criteria and do not meet exclusion criteria will be recruited from the Department of Physical Medicine and Rehabilitation and Transitions Outpatient facility of Northwell Health. Recruitment will be done with direct contact, flyers, and letters sent to patients who have been enrolled on other research projects.

Northwell Health physicians and clinicians who have appropriate patient populations will be made aware of the research study protocol and procedures, and given an overview of the study through contacts with the study personnel. The physician or clinician will identify potential study participants. If the patient expresses interest in participation, the physician or clinician will either 1) provide the patient with the study coordinator's contact

information or 2) provide the patient's contact information to study personnel with the patient's permission, which will be documented in the medical record.

After a discussion about the study with a potential subject and a potential subject's spouse or legally authorized representative (LAR/next of kin), interested parties will be given a copy of the consent form by one of the study investigators. The investigator will review and explain the consent form. All information about the study will be provided. Ample time will be given for individuals to ask questions regarding participation and to have questions answered prior to signing the consent form. If so desired, those interested will be given a copy of the consent form so that they may have the opportunity to discuss participation further with family and/or advisors. Only those investigators listed in the study protocol will obtain informed consent. If an individual chooses to enroll, the consent form will be signed before participation begins. Once an individual joins the study and informed consent is obtained, the subject will receive a signed copy of the consent form. The subject may withdraw from the study at any time without repercussions to subsequent care.

If the patient is awake, alert, and oriented to person, place, and time, and demonstrates appropriate cognitive and communicative abilities as determined by the treating clinician, the patient will be deemed to have the appropriate capacity to consent; however, given that borderline cognitive dysfunction and/or aphasia may not be easily distinguishable, the patient's LAR/next of kin will be routinely included when consent to participate is being obtained for all subjects.

If it is determined that a patient is unable to consent for him/herself, due to a lack of capacity or lack of comprehension, consent will be sought from the patient's LAR/next of kin. Assent of the adult subject with the LAR/next of kin will be obtained as appropriate. If such a subject regains his/her ability to make healthcare decisions, he/she will be given the opportunity to provide consent. This consent will be documented using the Addendum to Consent by Research Proxy for Continuing Participation in a Research Study form.

If the patient provides the consent delegate with assent to participate in the research but, due to a physical disability, is unable to sign the consent form, the patient will provide verbal consent and both the patient's LAR/next of kin and a witness will sign the document affirming their presence during the consent process and the patient's physical disability as reason for an absent signature.

A study investigator will obtain informed consent, in person, from interested persons. After a discussion about the study with a potential subject, interested persons will be given a copy of the consent form by one of the study investigators. The investigator will review and explain the consent form to the person. All information about the study will be provided. Ample time will be given for persons to ask questions regarding participation and to have questions answered prior to signing the consent form. If so desired, those interested will be given a copy of the consent form so that they may have the opportunity to discuss participation further with family and/or advisors.

Investigators may contact (or be contacted by) a potential subject's LAR/next-of-kin by telephone to discuss participation in this research protocol. The investigator will provide subject's LAR/next-of-kin with all the information contained in the written consent form. The investigator will answer any questions regarding the research and give the subject's LAR/next-of-kin ample time to consider participation in the study which may require a follow-up phone conversation.

If the subject's LAR/next-of-kin agrees to allow the decisionally incapacitated patient to participate in the research study, the investigator will provide his/her contact information. The investigator will explain (and repeat) the next steps necessary for the LAR/next-of-kin to provide informed consent, which include the following processes. A written consent form will be sent to the LAR/next-of-kin as an email attachment, or left at the nurses' station on the unit where the potential subject is an inpatient or outpatient. The LAR/next-of-kin must read the consent form and call or email the investigator if he/she to discuss research and resolve issues/questions. If subject's LAR/next-of-kin agrees to participation in the protocol, the investigator will direct him/her to sign the consent form and return it to the investigator by mail or fax. Another option would be to scan the signed consent form to a PDF file and return it to the investigator as an email attachment. An

enrollment note must be written by the investigator documenting all phone conversations with the LAR/next-of-kin. Printouts of any email correspondence must be placed in the subject's research chart. After the signed consent form is received, investigator will sign the consent form. A copy will be made and sent to the LAR/next-of-kin for his/her records. In cases where consent is obtained by e-mail/mail, investigators request a waiver for the need for a witness signature.

Only those investigators listed in the study protocol will obtain informed consent. If a person chooses to enroll, the consent form will be signed before participation begins. Once an individual joins the study and informed consent is obtained, the subject will receive a signed copy of the consent form. The subject may withdraw from the study at any time without repercussions to subsequent care.

Protection Against Risk:

Protection against Robot-related risk: The practical issues regarding the robot control system and patient safety include that the software that runs the robot device continuously checks the force, speed and position of the robot armed and on the status of the power. This software can brake the robot if the force, speed, or position is beyond set ranges. There are two clearly visible "shut-down" switches that are always in reach of the technician trainer. In the event of software failure, motion beyond the specified range, loss of electrical power, or activation of the "shut-down" switch the device stops (brakes) within 2 milliseconds. The robotic arm will only move the patient's lower limb, and no other body part will be within the active range of this movement (the head for example is well out of the possible range of the movement of the robotic arm). The patients leg is attached to the robotic arm with a velcro clasp, which can be released with a sudden pull from the patient or therapist. The entire apparatus is ground-fault protected to exceed clinical standards. We will monitor subjects continually during robotic training, and will be in constant contact with the subjects. The study can be immediately stopped at the subject's request.

Protection of Confidentiality: To protect subjects' confidentiality, each subject will be assigned a number, and all data will be stored with the subject number only and not the subject's name. Data will be stored on a password-protected computer with encryption software and on Feinstein's data server, REDcap. The *Feinstein Institute for Medical Research* will be used as a central location for data processing and management. Vanderbilt University, with collaboration from a consortium of institutional partners, has developed a software toolset and workflow methodology for electronic collection and management of research and clinical trial data. REDCap (Research Electronic Data Capture) data collection projects rely on a thorough study-specific data dictionary defined in an iterative self-documenting process by all members of the research team with planning assistance from the Biostatistics Unit of the *Feinstein Institute for Medical Research*. The iterative development and testing process results in a well-planned data collection strategy for individual studies. REDCap servers are housed in a local data center at the Feinstein and all web-based information transmission is encrypted. REDCap was developed specifically around HIPAA-Security guidelines and is recommended to Northwell Health researchers by both our Clinical Research Service, Research Compliance Office and Institutional Review Board. REDCap has been disseminated for use locally at other institutions and currently supports 965 active institutional partners and other institutions in 78 countries (www.project-redcap.org).

Subject charts with medical history and assigned subject numbers will be kept in locked file cabinets in the Feinstein robot suite. Access to charts will be granted only to study investigators. Charts will be kept confidential and will not be shared with any third parties without permission from the subject. Any study data containing PHI that is transferred between investigators at Feinstein and collaborators will be shared via encrypted email or encrypted storage drives.

Of note, Drs. Hogan and Krebs are sub-investigators from MIT and will be assisting in the analysis of data only. Subject data they receive from this research study will be de-identified.

POTENTIAL BENEFIT TO SUBJECTS AND OTHERS

The risk/benefit ratio is very low in the proposed study due to the established safety of the protocol and to the great potential for using the findings to improve rehabilitation methods. Potential benefits include

increasing functional ambulation status of individual participants, and furthering knowledge for improved stroke rehabilitation interventions for the future.

SCIENTIFIC VALUE
The results of this study may help to improve stroke recovery.

DISCONTINUATION OF STUDY/SUBJECT WITHDRAWAL
A patient may withdraw at any time for any personal reason from the study with no effect on his/her treatment at Northwell Health

ADVERSE EVENTS As necessary, adverse events will be immediately reported by the PI to the IRB, according to IRB policy. Adverse events in the combined experience of the PI and sub-investigators (over 20 years and several hundred patients) have been mild and there have been no reports of serious robot-treatment related adverse events (Lo 2010).

Data and Safety Monitoring: To protect both the integrity of the data and the safety of all study participants, study data review in aggregate will occur every 4 months by the Research Coordinator and/or Principal Investigator. Reviews will be documented and retained in the regulator binder accordingly.

DRUG ACCOUNTABILITY
This will not be required for this study.

INSTITUTIONAL REVIEW BOARD (IRB)
We acknowledge the requirement for prior approval of the protocol and the informed consent form from the IRB, as well as the requirement for continued contact between the investigators and the IRB.

CONFIDENTIALITY
Subject confidentiality will be preserved and data will be kept confidential and used only for professional purposes. Clinical and robotic data will be contained on a Northwell Health computer in encrypted files. These data will be stripped of personal identifying information for analysis. Charts will be coded (subject ID will be in sequential numerical order). Data, charts and subject codes will be kept in locked files in the office of the Research Coordinator at the Feinstein institute. Protected health information (PHI) will only be used or shared with study personnel for purposes of the research and will not be disclosed. Objective gait measures will be initially kept in de-identified files on password protected laptop at Long Island Pediatric Physical Therapy and transferred via encrypted email or encrypted storage drive.

DATA DISCLOSURE/PUBLICATION/CONFIDENTIALITY
Data disclosure will occur in the attempt to analyze and publish it with only de-identified information.

SCHEDULE OF EVENTS

	SCREENING1	SCREENING 2	SCREENING 3	MIDPOINT	DISCHARGE	FOLLOWUP
	VISIT 1	VISIT 2	VISIT 3	VISIT 12	VISIT 21	VISIT 22
	DAY 1;SCREENS, 2-10 DAYS, TREATMENT 3X/WEEK FOR 6 WKS, MAXIMUM 147 DAYS					
INFORMED CONSENT	X					
MEDICAL HISTORY	X					
MEDICAL FOLLOWUP		X	X	X	X	X
DEMOGRAPHIC INFORMATION	X					
INCLUSION CRITERIA	X					
NEUROLOGICAL EXAM	X					
GAIT MEASURES	X	X	X	X	X	X
MEDICATION CHECK	X	X	X	X	X	X

A graphic or tabular depiction of the procedures and chronology of the study. See sample schedule of events below:

CREDENTIALS, TRAINING All study personnel have completed CITI Training.

CONFLICT OF INTEREST
The PI has no conflict of interest. As indicated in the individual COI forms, two of the co-PIs are co-inventors of the device.

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