

Cover Page

Robot-Assisted Therapy and Motor Learning: An Active Learning Program for Stroke

NCT02747433

Study Protocol and Statistical Analysis Plan

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ORGANIZATION AND DETAILED PROTOCOL

Title: Infusing Robot-Assisted Therapy with Motor Learning Principles: An Active Learning Program for Stroke (ALPS)

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I. Background and Significance

Stroke is the leading cause of long-term disability in older adults in the United States. At six months after stroke, up to 65%¹ of the more than 795,000 persons² who experience a stroke each year continue to have upper extremity (UE) impairments that inhibit functional use of the paretic arm during daily activities. Stroke-related motor deficits can persist long term, contributing to loss of independence in activities of daily living (ADL) in more than 70% of stroke survivors³ and negatively impacting quality of life. In order to advance rehabilitative practice and optimize satisfaction and participation after stroke, improved methods are needed to optimize the recovery of UE motor function for home and community activities.

Rehabilitation robots and passive gravity-assist orthoses provide clinicians with new treatment options to improve upper extremity (UE) motor capacity and performance after stroke. Previous studies have shown that robot-assisted therapy is as effective as more labor-intensive interventions at increasing motor capacity, as measured by standardized clinical assessments.⁴ While systematic reviews of robot-assisted therapy for the paretic UE confirm gains in motor capacity as measured by clinical assessments, they provide little evidence of improved UE performance during daily tasks and occupations.^{5,6,7} This disparity between UE motor capacity and daily use of the paretic arm and hand is a significant clinical issue⁸ and critical barrier to the integration of robotic technology into clinical practice. These findings may be attributed to the limited availability of rehabilitation robots to train the paretic hand and a primary focus on intensity of practice with little regard for other *principles of motor learning and experience-dependent neuroplasticity*.^{9,10} These principles, including the salience of training tasks, transfer of acquired skills to similar activities, and active engagement and problem solving, are key to task-oriented training paradigms in stroke (e.g. constraint-induced movement therapy) but have not been well integrated into robot-assisted therapy protocols. The transfer of robot-trained movements to UE activities within the home and community needs further exploration before widespread use in rehabilitation practice is expected.

The purpose of this pilot project is to develop and refine a stroke therapy protocol that infuses robot-assisted therapy with a structured Active Learning Program for Stroke (ALPS) and patient-targeted home action plan for the paretic arm and hand. The intent of this protocol is to teach stroke survivors ways to better use their weaker arm after stroke during daily activities. This project has the potential to improve the effectiveness of robot-assisted therapy by facilitating UE self-management through active problem identification and problem solving, and specifically

addressing the transfer of acquired skills (e.g. UE motor capacity) to the performance of UE tasks during activities of daily living (ADL). The ALPS protocol will be relevant to clinical practice because it will provide clinicians with a structured, patient-centered motor learning approach to facilitate use of the paretic arm and hand. In addition, comparisons between our two intervention groups (robot-assisted therapy vs. robot-assisted therapy [RT] and task-oriented training [RT-TOT]) will add to our scientific knowledge of whether the combination of robot therapy and therapist-directed task-oriented training provides added benefit to RT alone. We will examine participant outcome measures across domains of the International Classification of Functioning (ICF)¹¹ to provide insights regarding mechanisms that underlie the recovery of motor function after stroke.

II. Specific Aims

The specific aims of this pilot study are:

Aim 1: To develop and refine a structured Active Learning Program for Stroke (ALPS) that integrates motor learning strategies with a patient-targeted home action plan to be used with either 1) robot-assisted therapy (RT) or 2) combined robot-assisted therapy and task-oriented training (RT-TOT) for the paretic arm and hand after stroke, in preparation for a larger clinical trial.

Hypothesis 1.1: RT and combined RT-TOT protocols that incorporate ALPS training will be feasible and well-tolerated by participants.

Hypothesis 1.2: After intervention, participants in both treatment groups will identify and implement a greater number of motor learning strategies during UE tasks in clinic and home settings and will report increased self-efficacy as measured by the Confidence in Arm and Hand Movement (CAHM) scale.

Aim 2: To examine effects of ALPS training and a patient-targeted home action plan combined with either 1) RT or 2) RT-TOT on paretic UE motor capacity and performance during daily activities, using *outcome measures across ICF domains*.

Hypothesis 2.1: Compared to RT alone, RT-TOT will yield similar outcomes on clinical measures of UE motor capacity (e.g. Fugl-Meyer Assessment, Wolf Motor Function Test), but greater gains on measures of UE function in the home and community (e.g. Motor Activity Log, UE accelerometry data via wearable sensors).

III. Subject Selection

We will recruit up to 20 adults between the ages of 18 and 82 years and diagnosed with unilateral stroke more than 6 months prior to study enrollment. Stroke type will include both ischemic and hemorrhagic stroke. Eligible participants will be screened and enrolled in the study if they meet all inclusion and exclusion criteria. Protocol approval will be obtained from the SRH Institutional Review Board (IRB) and all participants will provide their informed consent prior to study participation.

Inclusion criteria:

- Moderate UE hemiparesis (i.e. some ability to move shoulder, elbow & hand and initial score on the Fugl-Meyer Assessment (FMA) between 21-50/66)

- Intact cognitive function to understand and actively engage in the ALPS robotic therapy procedures (Montreal Cognitive Assessment Score $\geq 26/30$)¹² during initial evaluation visit

Exclusion criteria:

- No more than moderate impairments in paretic UE sensation, passive range of motion, and pain that would limit ability to engage in therapy
- Increased muscle tone as indicated by score of ≥ 3 on the Modified Ashworth Scale;
- Hemispatial neglect or visual field loss measured by the symbol cancellation subtest on the Cognitive Linguistic Quick Test ¹³
- Aphasia sufficient to limit comprehension and completion of the treatment protocol
- Currently enrolled or has plans to enroll in other upper limb therapy/research during the study period
- Contraindications for robot-assisted therapy including recent fracture or skin lesion of paretic UE

IV. Subject enrollment

Recruitment Methods:

Potential subjects may be identified by the following sources:

- Printed flyers given to rehabilitation departments of local hospitals.
- Flyers posted in the outpatient clinics, therapy gyms and in public spaces inside and outside of the hospital.
- The Partners RSVP for health website.
- Contact with support groups and conferences.
- Research recruitment emails, for example Spaulding Rehabilitation Network Research Recruitment emails, and Social Medias.
- Contact to patients listed in the Partners Research Patient Data Registry (RPDR).
- Stroke Survivors who previously volunteered to be contacted about opportunities to participate in research studies at SRH may be contacted by phone by a study staff.
- Attending physicians and therapists may refer their stroke inpatients/outpatients to the study. We will provide the physicians with study flyers.

Eligible patients will contact or give permission to be contacted by study staff to obtain more information about the study and informed consent.

At the first point of contact (usually a phone call), study staff will administer a phone-screening questionnaire to see if subjects are eligible for the study. Potential subjects who are deemed eligible during this initial contact will be invited to attend an in-person screening to ensure that all inclusion and exclusion criteria are met. If a prospective subject fails this screening, he/she will be excluded from the study.

Informed consent will be obtained by study staff members who have completed the Partners Healthcare System's human subject protection educational requirements, and the CITI Program in Protection of Human Subjects, in compliance with all Federal regulations regarding such training. Prospective subjects will be interviewed to determine preliminary eligibility.

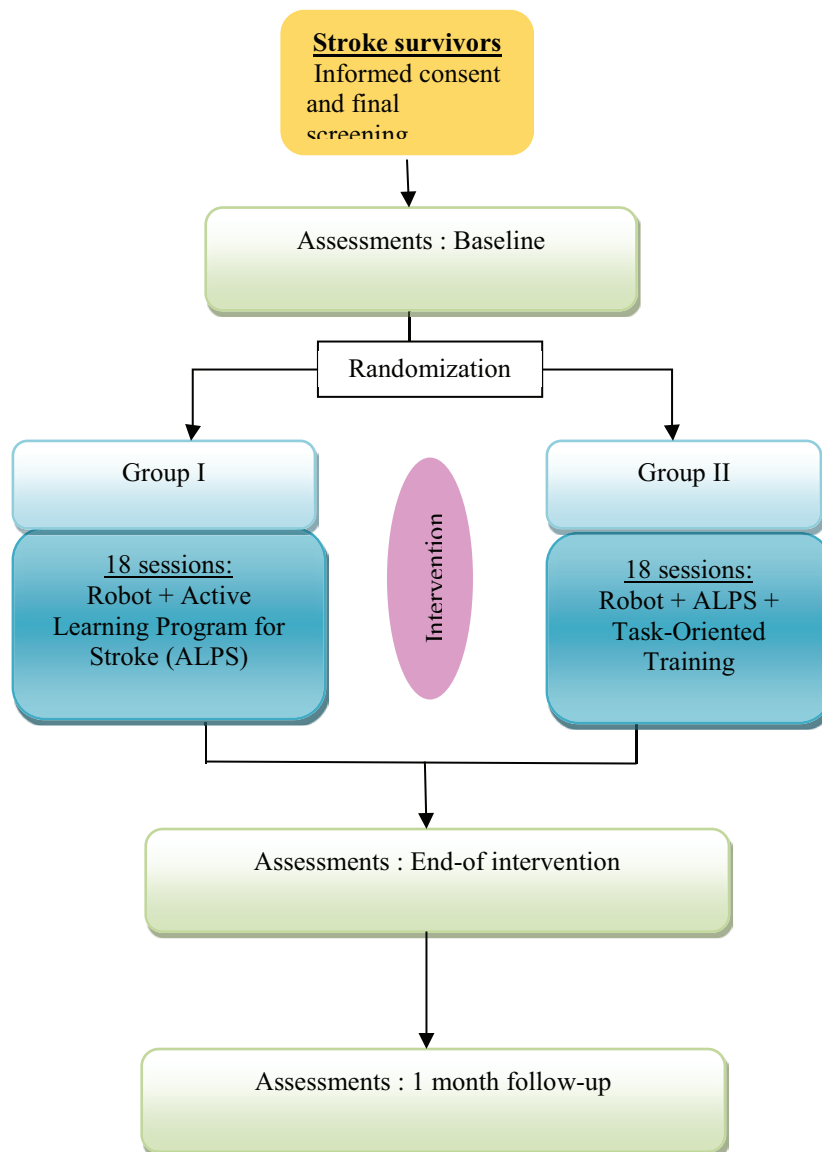
Informed consent will be obtained and subjects will be enrolled in the study prior to any clinical or laboratory testing. Subjects will be given a copy of the IRB approved consent form during the initial interview, and study staff will explain in detail the nature of the informed consent process, study purpose and procedures, time commitments, risks, potential benefits, treatment alternatives, rights as research participants, study staff contact information, confidentiality procedures, and arrangements for medical care provided in case of injury during the study. Subjects will be given adequate time to consider their decision and encouraged to ask questions, both during the initial interview and throughout the study. The subject's decision-making capacity and ability to give consent will be assessed by the PI (Fasoli) or Catherine Adans-Dester, Research Coordinator/Manager in the Motion Analysis Lab at SRH, using the University of California at San Diego (UCSD) Brief Assessment of Capacity for Consent Questionnaire. The subject must demonstrate an understanding of the study, that it is research, and answer questions re: the risks and benefits involved in the procedures.

Specifically, the informed consent will be obtained by the principal investigator (Fasoli) or Catherine Adans-Dester, Research Coordinator/Manager in the Motion Analysis Lab at SRH. The testing and intervention protocol will be described and the research space and equipment will be shown to the subject. Study staff will clearly explain all procedures and risks of the protocol outlined in the informed consent form (ICF). The subject will be given adequate time to consider his/her decision and encouraged to ask questions, both during the initial interview and throughout the study. A member of the study staff will answer any questions regarding the study at the time consent is given. Enrollment will begin when the subject thoroughly understands and signs the informed consent form. Participants will be provided with a signed copy of the completed consent form. Once enrolled, the subject may pause or terminate his/her participation at any time during the study. Participants will be randomized to one of two treatment groups (robot-assisted therapy [RT] or robot-assisted therapy plus task-oriented training [RT-TOT]) according to a randomization sequence prepared by Dr. Fasoli.

V. Study Procedures

Study procedures will occur in the Motion Analysis Lab (MAL). The study involves up to 24 visits in total to be completed within a 16 week period. The total duration may vary within this 16 week period to accommodate missed study visits.

1. MAL Visit Day 1: Screening and enrollment
2. MAL Visit Days 2-3: Baseline outcomes assessment battery. We will equip participants with Actical wearable sensors for home-based accelerometry data collection.
3. MAL Visit Days 4-21: Intervention. We will retrieve Actical wearable sensors at after baseline data collection at the onset of intervention visits.
4. MAL Visit Days 22-23: End-of-intervention outcomes assessment battery. We will equip participants with Actical wearable sensors for home-based accelerometry data collection.
5. MAL Visit Day 24: Follow-up outcomes assessment battery. We will equip participants with Actical wearable sensors for home-based accelerometry data collection.



Schema 1: study procedures flow

- 1) MAL Visit Day 1: Screening and enrollment** (procedures described in section IV)
- 2) MAL Visit Days 2-3: Baseline outcomes assessment battery** (administered within a 2-3 week period before intervention). **Equip with Actical wearable sensors.**

The clinical assessment session will last approximately 1 ½ to 2 hours, and the standardized measures listed in Table 1 will be administered. All are reliable and valid measures of UE motor capacity and function. Minimal detectable change scores have been reported for the FMA,¹⁴ Motor Activity Log,¹⁵ and Stroke Impact Scale.¹⁶ The clinical evaluator will be blinded to the participants' group assignment and study hypotheses.

Kinematic data indicative of movement quality will be collected via 3-D motion capture (Vicon Motion Systems Ltd. UK) in the Motion Analysis Laboratory (MAL) during reach/grasp tasks with the paretic arm. Variables of interest may include index of curvature (IOC) (ratio of actual distance the hand travels to the most direct distance), movement smoothness (number of times hand trajectory = 0 during reach), trunk displacement (degrees of movement in sagittal, planar, and transverse planes), and interjoint coordination (range of angular motion at the shoulder, elbow and wrist).^{17,18} The kinematic testing protocol will be collaboratively developed by Dr. Fasoli and Dr. Bonato and his MAL staff. This may include reach and grasp movements directed toward targets positioned in front of the subject to elicit functional movements, including upward reach, forward reach, shoulder abduction, shoulder rotation, pronation of the forearm, wrist extension, and finger flexion/extension. We anticipate that this quantitative assessment will require an additional 1-1/2 hour/session at baseline and discharge.

Surface electromyographic (SEMG) data may be gathered during the kinematic testing protocol above to study the characteristics of muscle activation patterns in stroke survivors during the performance of arm reaching movements. Data will be collected using Cometa WavePlus wireless surface electrodes with 16 channels (www.cometasystems.com) for the detection of EMG activity from muscles that are involved in the performance of upper extremity movements. We will follow the SENIAM (Surface Electromyography for the Non-Invasive Assessment of Muscles) guidelines to place electrodes on several muscles involved in the performance of the arm reaching movements. Muscles may include the following: rhomboid major, latissimus dorsi, infraspinatus, superior trapezius, deltoid - anterior part, deltoid - medial part, deltoid - posterior part, pectoralis major, clavicular head, triceps brachii, lateral/medial heads, biceps brachii (short heads), biceps brachii (long heads), brachialis, brachioradialis, pronator teres, extensor carpi radialis and extensor carpi ulnaris. The EMG on the back, shoulder, upper arm and forearm will be attached using bio-adhesive double sided tape and secured with Coban.

We may ask permission from study participants to video record them during the performance of the above-described clinical tests and the lab-based assessments.

Home Based Accelerometry – Wearable Sensors: The Actical physical activity monitoring system (<http://www.philips.com>) is a multi-directional, waterproof sensor used to quantitatively measure UE activity during everyday living situations. Sensors will be worn on both wrists during 72-hour periods at each assessment point to allow comparisons between paretic and intact UE activity in the home/community.¹⁹ A single page user guide for the wrist sensors will be provided to participants, and sensors may be removed at any time due to discomfort. There will be no penalty for loss or damage to a wrist sensor, subjects will be given a pre-stamped envelope to return the Actical at the end of the 72-hour period. Staff in Dr. Bonato's Motion Analysis Laboratory (MAL) at SRH have used this device and will analyze de-identified raw data in order to examine changes in arm movement pre- to post-intervention (e.g. the amount and laterality of use).

The proposed assessment timeline is below (Table 1).

ICF Domain/Assessments	Baseline	Discharge	1-month Follow-up
<i>UE Function:</i>			
<i>Fugl-Meyer Assessment – UE, pain, sensation subtests</i> ^{20,21}	X	X	X
<i>Modified Ashworth Scale</i> ²²	X	X	X
<i>MAL: 3-D motion capture/SEMG analysis UE reach/grasp</i>	X	X	
<i>Activities & Participation:</i>			
<i>Wolf Motor Function Test</i> ²³	X	X	X
<i>Motor Activity Log</i> ²⁴	X	X	X
<i>Stroke Impact Scale</i> ²⁵	X	X	X
<i>Confidence in Arm & Hand Movement (CAHM)</i> ²⁶	X	X	X
<i>Home-Based Accelerometry/Wearable Sensors</i>	X	X	X

Table 1. Assessment Timeline.

3) MAL Visit Days 4-21: Intervention. Retrieve Actical wearable sensors.

Participants will be randomly assigned to one of two treatment groups:

- A. Robot-Assisted Therapy (RT) + ALPS protocol to enhance active problem solving, confidence in UE use, and transfer of training to functional UE tasks, and all will be provided a home action plan.
- B. Robot-Assisted Therapy (RT) + Task-Oriented Training (TOT) + ALPS protocol to enhance active problem solving, confidence in UE use, and transfer of training to functional UE tasks, and all will be provided a home action plan.

Robot-Assisted Therapy (RT): Participants will receive robot-assisted UE therapy using two commercially-available rehabilitation devices available for use at SRH: the Armeo@Spring (Hocoma AG, Switzerland) and Amadeo (Tyromotion, Graz, AU)(Figure 1). The Armeo@Spring is a passive exoskeletal spring suspension system that provides repetitive practice of virtual goal-directed reaching tasks for the paretic UE. A distal sensor that detects grasp pressure allows the grasp/release of virtual objects during games. The amount of gravity assist and virtual task demands are adjusted by the clinician to provide challenging yet achievable movement therapy. During the first treatment session, the Armeo@Spring will be adjusted for the participant’s arm size and required angle of suspension (approximately 45° shoulder flexion, 25° elbow flexion) and the workspace will be measured via standard procedures.

The Amadeo robotic system provides position-controlled exercises during computerized games that emphasize grasp and release of the paretic hand. Participants will be seated comfortably with the forearm/wrist strapped to an adjustable splint attached to the robot device with the wrist

in approximately neutral position. A small magnetic disc is secured to the distal phalanx of each



Figure 1. Armeo and Amadeo.

digit for connection to the robotically controlled slide that guides movement. Each one hour session will include visually evoked games that provide active-assistive training of collective, sequential and individual flexion and extension of the digits as well as isometric flexion/extension contractions. Rest periods will be offered between games, as needed. Task challenge for each training device will be incrementally increased or decreased based on participant performance.

All participants will receive 1 hour sessions, 2-3x/week for 6-9 weeks (total 18 sessions), divided into two 9 session treatment blocks. The two treatment blocks will be given in order, with all participants receiving proximal training via Armeo@Spring during the first block followed by Amadeo distal training during block 2. All training sessions for one treatment block will be completed before proceeding to the next. The robot training sessions will follow standard protocols that provide highly repetitive movement training, and the number of games/repetitions completed in each session will be recorded. Participants may miss up to 3 appointments, and we will reschedule the following day or week at a time that is mutually convenient. Participants who miss 4 consecutive appointments may be removed from the study.

Active Learning Program for Stroke (ALPS): ALPS development and implementation will be based upon principles of experience dependent neuroplasticity as described by Kleim & Jones,⁹ empirical evidence from UE motor learning and task-oriented training programs for individuals with stroke,^{10,27,28} and a conceptual framework for integrating skill, capacity and motivation as described in multiple publications by Winstein et al.^{10,29,30} While principles of repetition, intensity, and specificity of training are active ingredients of the RT and RT-TOT protocols to improve motor capacity, other motor learning constructs have not been well-infused into prior robot training programs. These constructs will be implemented during RT and RT-TOT sessions and will be an integral component of the home action plan. Preliminary examples of protocol components are highlighted in Table 3 below.

Motor Learning Principles	Example
<i>Use it or lose it</i> ^{9,10,27}	Identify interfering and changeable impairments Provide targeted UE training based on individual's motor capacity
<i>Saliency of training tasks</i> ^{9,10}	Establish clear patient-centered goals
<i>Transference</i> ^{9,10}	Facilitate UE self-management through active problem identification and problem solving
<i>Feedback</i> ^{28,31}	Provide knowledge of performance Encourage self-assessment and discovery
<i>Motivation</i> ^{10,29,30}	Assure challenging and meaningful practice Address self-efficacy and confidence

Table 3. ALPS Motor Learning Principles.

Task-Oriented Training (TOT): Participants randomized to the robot and task-oriented training (RT-TOT) group will receive therapist-guided task-oriented training in addition to RT during 20-30

minutes of each 1 hour treatment session. The participant's baseline performance on the FMA will be reviewed, and the FMA keyform and patient-targeted treatment activities outlined by Woodbury^{32,33} may aid the selection of UE tasks with greatest potential for improvement during TOT. The treatment dose (duration and frequency of therapy sessions) will be equivalent across RT and RT-TOT groups.

Home Action Plan: All participants in the RT and RT-TOT groups will be provided a home action plan to encourage implementation of ALPS principles during practice of patient-targeted tasks in the home and community.

The tasks selected for the home action plan (HAP) will be based on the participant's identified upper extremity (UE) goals and/or therapist input based on a) the current focus of robot therapy (i.e. shoulder/elbow, hand) and b) scores on the FMA key form. Because of this participant-centered approach there will be no core tasks included in every HAP, however, similarities may be observed across individuals. Participants will identify an UE task to be completed at home and the ALPS strategy or strategies they will use to facilitate performance weekly. A brief self-report questionnaire to collect ordinal data on ALPS strategy use, HAP performance, frequency, & perceived difficulty will be administered by research staff after every 3rd therapy session. Participant's engagement in the home action plan will be rated using a 3 point Likert type scale²⁹ and patient-targeted UE tasks will be updated as needed. A similar questionnaire will be administered during the follow-up assessment to gain information regarding the participant's engagement in home practice after formal therapy has ended. Participants will be instructed that completion of the HAP is voluntary and will not affect their therapy in any way. The intent of the HAP is to provide documentation of home carry-over. It is not designed to be a comprehensive home exercise program.

4) MAL Visit Days 22-23: End-of intervention outcomes assessment battery
(administered at discharge assessment after 18 treatment sessions) **Equip with Actical wearable sensors.**

The same assessment battery as the one performed at baseline will be re-administered.

5) MAL Visit Day 24 (Final Visit): Follow-up outcomes assessment battery
(administered at 1 month post-therapy) **Equip with Actical wearable sensors.**

The same assessment battery as the one performed at baseline will be re-administered, **except for** the Motion Capture and EMG analysis.

VI. Biostatistical Analysis

Separate repeated measures analyses of variance (2 group x 3 time points) will examine changes in scores for each outcome measure across a) baseline, b) discharge and c) follow-up assessments. Descriptive statistics will be used to compare key group characteristics, including age, hand dominance, side of lesion, and years of education. Group comparisons will be assessed by chi-square analyses for categorical data and t-tests for continuous data. The data collected from this pilot study may be used for a power analysis of a larger clinical trial.

VII. Risks and Discomforts

Subjects will not be at higher risk for injury during the research protocol than during their usual daily activities, and they will be supervised by study staff at all times during study assessments and intervention procedures. Staff in Dr. Bonato's MAL and Dr. Fasoli have extensive experience with the measurement tools (e.g. motion capture, wearable sensors) and intervention devices (Armeo & Amadeo) used in this study, and have maintained excellent safety records at SRH and at institutions outside the Partners network. Research staff will be trained in the proper use of all study devices prior to use with participants to assure safety. Potential risks and discomforts are described below:

During the camera-based motion analysis assessments, it is possible that the use of adhesive tape to secure reflective markers or electromyographic sensors to the skin may cause skin irritation. We will minimize this risk by using hypoallergenic adhesive tape approved for medical use.

The Actical wearable sensors used in this study are powered by low voltage batteries and are completely isolated from other electrical sources such as power lines. Black velcro straps from the manufacturer will be used to secure the sensors to the participants' wrists. For persons with sensitive skin, we will modify these straps with Velfoam strapping as needed to increase comfort and prevent skin irritation.

All laboratory equipment meets or exceeds hospital standards for electrical safety. Robot-assisted therapy with the Armeo device is very unlikely to cause injury as the Armeo has no actuated components. The straps of the device may cause redness of the skin. We will assure proper upper limb positioning during intervention and will pad the straps as needed so they are comfortable for the subject.

Unlike the Armeo, the Amadeo is equipped with actuated components (i.e. motors) capable of independent motion. As stated in the manufacturer's instruction manual, risks are minimal when the Amadeo is used according to instructions. Small injuries, such as pinching or bruising can occur in rare cases, however, numerous safety features and procedures have been implemented to minimize risk of injury. These include a system controller designed to avoid excessively fast movements of the fingers/thumb; safety limits set for the estimated interaction forces during finger motions, and two emergency switches to immediately shut off robot power in the event of a malfunction. Height adjustments of the Amadeo will be performed with caution so injury does not occur when lowering the device to ensure proper positioning for therapy. We will ensure that fingers are not in contact with the finger slides during reference runs when initializing the device. During intervention, small magnets are attached to the subject's fingers and thumb via medical tape to provide a safe and easily removed connection to Amadeo's actuated finger slides. This tape can be replaced by custom made velcro or velfoam strips in the event of skin irritation or discomfort. During task-oriented training in which subjects are asked to perform several sets of common, task-oriented movements, it is possible that they will feel discomfort due to fatigue or muscle soreness as they increase their tolerance to exercise. During robot-assisted therapy and task-oriented training, participants may take rest breaks as needed to minimize possible fatigue or muscle soreness following multiple repetitions of upper limb movements.

VIII. Potential Benefits

Potential benefits of robot-assisted therapy for the paretic arm after stroke include reductions of motor impairment however, the transfer of robot-trained movements to UE activities within the home and community has not been well studied. The proposed study aims to develop and refine a stroke therapy protocol that infuses robot-assisted therapy with a structured Active Learning Program for Stroke (ALPS) and patient-targeted home action plan. If successful, it has good potential to improve the effectiveness of robot-assisted therapy by facilitating improved self-management of the paretic arm and specifically addressing the transfer of acquired skills (e.g. UE motor capacity) to everyday UE tasks. These methods could benefit rehabilitation practice by providing clinicians with a structured motor learning approach to enhance recovery of UE function during stroke intervention.

IX. Monitoring and Quality Assurance

Approval of protocol, informed consent procedures, and recruitment will be obtained from the IRB during annual reviews. Because this study's procedures pose relatively low risk to subjects, monthly data and procedural reviews by the PI and/or site responsible investigator (Dr. Bonato) in consultation with study staff will be sufficient to identify and ameliorate any potential safety issues. However, any safety concerns about the exercise equipment or clinical protocol will be brought to the attention of the P.I. at the time they occur, and immediate action will be taken. Dr. Fasoli and Dr. Bonato will be responsible for determining whether the research should be altered or stopped in the event that participant safety is at risk.

Study staff will report any adverse event within 24 hours to the PI. A written report will be submitted to the IRB within 48 hours. Remedial action to prevent reoccurrence of the event will be instituted prior to resumption of study procedures. Compliance with regulatory standards for study documentation will be closely monitored by the PI.

Study staff will conduct quarterly audits to ensure compliance with regulatory standards to assure the integrity of study documentation and adherence to the IRB-approved protocol. Specifically, the accuracy and completeness of case report forms, source documents and informed consent forms will be audited by study staff under direct supervision of the PI (Fasoli). Although the study evaluator (Adans-Dester) is highly experienced with the administration and scoring of the outcome measures used in this study, the PI will review test administration procedures with her at study onset and quarterly thereafter to ensure proper use of standardized testing procedures.

Subjects will be assigned a study number, which will be used for all documentation, except for master lists (electronic and paper) matching subjects' names and study numbers and intake interview forms. The master list and interview forms will be kept in a secure location in locked offices at SRH. No non-study staff will have access to any identifiable patient study data or demographic information. All participants will be informed of their privacy rights and sign a HIPAA-compliant authorization form previously approved by the Spaulding IRB. All videotapes of assessment sessions will be stored securely in the Motion Analysis Laboratory at Spaulding Rehabilitation Hospital; only investigators listed on the study application will have access to them. The videotapes will be stored for the duration required by NIH standards; should NIH standards change prior to destroying the tapes, we will adhere to new regulatory standards.

No personally identifiable data will be sent to or viewed by collaborators outside of SRH or MGH Institute of Health Professions (Dr. Fasoli's home institution). Only co-investigators and study staff will have access to the data from the study. Study data will be maintained on

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computers with password-codes accessible only to study staff, and hard data will be kept in locked cabinets and offices at SRH.

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