PROTOCOL

Background

1. Provide the scientific background, rationale and relevance of this project.

INSTRUCTIONS

- This should include a referenced systematic evidenced-based review when possible.
- If this study involves qualitative research explain the major constructs of your study.
- Do not state in this section what you plan to do in this study. This information should be entered later under "What will be done in this protocol?"
- Do not include the bibliography in this section.
- For studies submitted under the Expedited review criteria, this section need not be more than a few paragraphs.
- For those studies where data will be analyzed collaboratively by multiple sites doing a similar study for which there is no common protocol (Collaborative Site Analysis Study) include a description of the common scientific goals/ procedures/data points.
- If this is an update to current templates from Protocol Builder make sure the information throughout the protocol includes the most current information.

Answer/Response:

- includes the most current information.

The scope of the healthcare challenge posed by stroke is massive, both in the number of affected persons and the related cost burden. There were an estimated 892,300 stroke-related hospitalizations in the U.S. in 2005, representing 77.3 stays per 10,000 persons over 45 years of age [1]. Approximately 50% of these individuals suffer from chronic deficits in UE function [2]. As the leading cause of disability in the U.S., the long-term financial impact of stroke is exorbitant. From 2005 to 2050, the total stroke-related burden on the U.S. economy is expected to exceed $2 trillion, including costs due to hospitalization, rehabilitation, nursing home stays, outpatient care, medications, and lost earnings [3].

Modern stroke rehabilitation practice is based on the principle of brain plasticity – the formation of new circuits and changes to internal structures that remap existing synapses to perform functions previously accomplished by injured cortical tissue [4]. Plasticity may strengthen redundant pathways to restore lost functionality, in effect remodeling the lesioned brain [5]. This process requires that the affected neurological pathways be exercised through interactions that involve the stroke-impacted functions [6], [7]. Consequently, research suggests that intensive, repetitive, task-directed therapy can encourage the desired cortical plasticity [8], [9], [10]. Training specificity is also an important component, whether targeting specific functional movements (e.g. squeezing a tube of toothpaste) or an integrated skill (e.g. self-grooming) [11], [12]. Repetitive ADL practice, by definition, satisfies these critical requirements for brain plasticity supporting UE recovery.

Weakness in grip strength and finger extension are leading causes of hand motor control deficits following stroke [13]. In particular, a loss of ability to extend the fingers is a key indicator for poor grasping performance [14]. Additionally, an inability to bring the hand and wrist into a neutral pose can

prevent participation in the task-directed functional practice necessary for neuroplasticity to occur. A common technique to enable stroke patients to achieve a functional hand pose (and thus participate in rehabilitation) is a dynamic splint that supports finger and/or wrist extension. When larger forces are necessary (i.e. to overcome abnormal muscle tone), an outrigger-type splint may be employed. One example is the spring-based SaeboFlex system [15]. For patients lacking finger extension due to weakness or mild hypertonicity, a low profile device such as the SaeboGlove [16] is preferable. SaeboGlove () is a commercially-available, passive glove orthosis that employs a plastic splint to support the wrist and a rubber band-based tensioner system to support finger extension and enable patients to engage in task-specific training. These Saebo products are used in over 2,000 clinics and hospitals (and by 10,000 trained clinicians) worldwide.

Numerous past efforts to apply technology to hand therapy have focused on the use of active assistance including cables, pneumatics, and robotics [17], [18], [19], [20], [21], [22],[23] [24]. The cost of these complex systems is typically very high, and many never find application beyond the research laboratory. On the other end of the spectrum are adaptations of hand tracking systems for therapy that do not provide any assistance to the wrist, hand, or fingers [25] [26] [27]. Hand movements elicited by these tracking system games are not ADL-oriented and experiences do not correlate to real-world tasks, which is a central tenet of brain plasticity In summary, previous systems are limited by: (1) not providing the finger extension and wrist support necessary to enable a stroke patient to bring the hand and wrist into the neutral position required for functional tasks; (2) limitations of sensor and software design that do not permit hand or arm involvement in virtual practice of ADLs; and (3) childish arcade-type user experiences do not involve mental imagery and cognitive challenges that are representative of real-world activities.

Although there is substantial literature on adaptations of "virtual reality" for rehabilitation [28], low-cost commercial sensors and commercial game engine technology have only very recently enabled the development of sophisticated systems at a price point that is compatible with at-home use. Moreover, it is also only recently that researchers have begun to unravel the relationship between game design and patient motivation. Adherence is an essential aspect of any treatment program. A perhaps-obvious, but often-overlooked, reality is that to realize gains through rehabilitation, a patient must accept and adhere to the prescribed treatment regime. The challenge of adherence is compounded by the fact that the intensive, repetitive, task-directed therapies associated with brain plasticity can be mundane, fatiguing, and even painful for stroke patients. Without the direct encouragement of a therapist, adherence is a particular challenge for home-based therapy.

The effectiveness of stroke therapy may be further bolstered by incorporating mental practice of relevant activities [33]. During mental practice of UE motor tasks, neural activation patterns may occur as if the impaired limb were actually performing the intended action [34], [35]. One approach to promoting this effect is by use of a mirror to present the image of an unaffected hand as if it were the paretic one [36]. The resulting enhancement in cortical representation of the impaired extremity appears to lead to tangible improvement in motor function. Empirical evidence of the benefit of mental imagery can, in part, be explained by a

model of cognitive psychology in which subliminal activation of the motor system is embedded in "covert" stages of action that precede actual motor response [37]. These precursor stages encompass visualization of intended outcomes, recognition of environmental factors, and learning by observation – elements that are directly facilitated by task-oriented virtual world-based ADL training. In the virtual world, limitations of impairment can be artificially mitigated, permitting the patients to visualize task completion in the appropriate environmental context, with meaningful tasks that map to real-world experience.

The purpose of this research study is to assess the effectiveness of a novel ADL-centered virtual reality system that is able to incorporate tracking and assistance to the hand for the purposes of stroke rehabilitation. The Glove Rehabilitation Application for Stroke Patients (GRASP) system enhances a commercial glove orthosis, the SaeboGlove (see Figure 1), with finger tracking sensors to enable a patient to manually interact with a virtual environment for UE motor practice.

Figure 1. GRASP sensors on SaeboGlove orthosis

The GRASP system, developed by Barron Associates, Inc., comprises the sensor-enhanced glove orthosis, a Kinect sensor, a Windows 10 computer, and software for virtual world-based practice of activities of daily living. Using the Kinect and the glove sensors, GRASP software tracks a patient's UE movements and translates them into equivalent movements of a graphical avatar that represents the patient in a virtual environment rendered on the computer display monitor. Figure 2 shows examples of virtual activities provided by GRASP software.

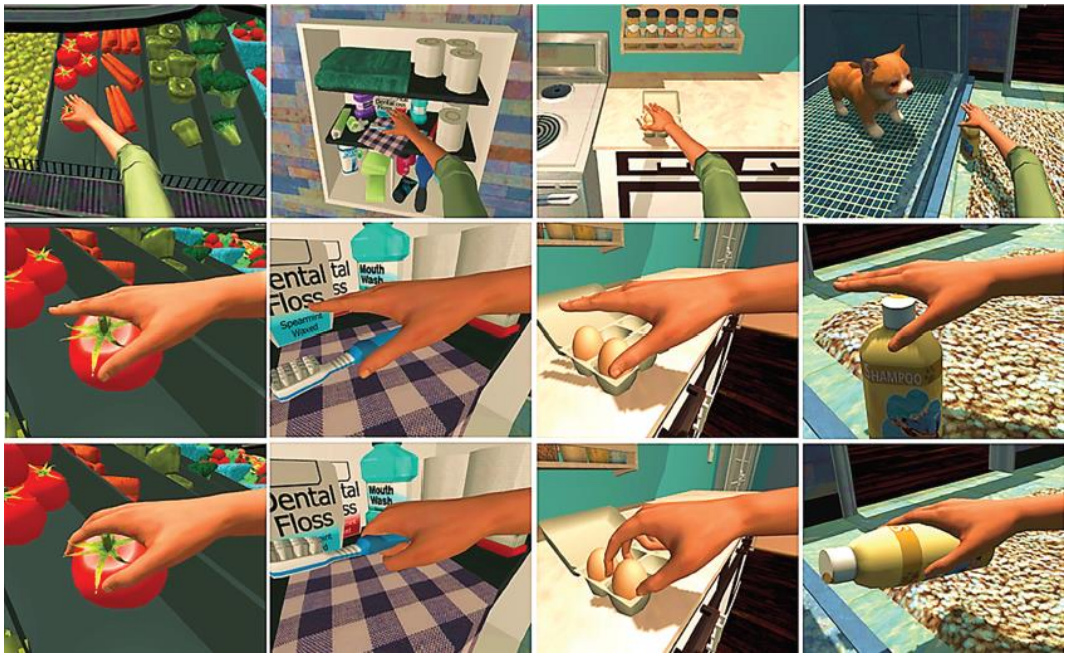


Figure 2. Virtual Activities of Daily Living (ADLs)

A completed GRASP Phase I study (IRB-HSR 19952) involving use of the GRASP device by 15 stroke patients demonstrated the criterion validity of UE performance measures derived from the system, as well as the usability of the device by the targeted patient population. The results of the completed GRASP Phase I study are documented in the following journal paper.

> **Adams, R. J., Ellington, A. L., Armstead, K., Sheffield, K., Patrie, J. T., & Diamond, P. T. (2019). Upper Extremity Function Assessment Using a Glove Orthosis and Virtual Reality System. OTJR: Occupation, Participation and Health, 39(2), 81–89. https://doi.org/10.1177/1539449219829862**

The GRASP Phase II study builds on the Phase I results, targeting demonstration of efficacy of a home exercise program (HEP) for UE stroke therapy employing the GRASP system. The GRASP Phase II device has been improved to address lessons learned in the Phase I study. Notably, the glove sensor system is now wireless (Bluetooth) and the GRASP software incorporates a wider range of virtual activities to support practice over an 8-week intervention.

Objectives/Hypothesis

INSTRUCTIONS:
If this study involves biomedical research clearly state the objectives and hypotheses and clearly define the primary and any secondary outcome measures. If this study involves qualitative research clearly state your research hypothesis or question.

This section should not include information already included in other sections such as background information or information from the procedures section.

Answer/Response:

Objectives:

- **Investigate the efficacy of GRASP therapy for recovery of hand function**
- **Acquire evidence of system usability and user acceptance**

Hypotheses

- **Use of GRASP for UE practice in a Home Exercise Program (HEP) will improve motor function in a cohort of adult stroke patients**
- **Subjects assigned to the GRASP HEP will experience improved motor function compared to those assigned to a Usual Care Treatment (UCT) group**
- **GRASP will be found to be usable and well-accepted by participants who have sustained a stroke.**

Study Design: Biomedical

1. Will controls be used?

Answer/Response:

YES

►IF YES, explain the kind of controls to be used.

Answer/Response:

Half of subjects will be randomized to a UCT group.
Half of subjects will be randomized to a GRASP HEP group.

2. What is the study design?

Example: case series, case control study, cohort study, randomized control study, single-blind, double-blind, met-analysis, systematic reviews, other. You may also view the IRB-HSR Learning Shot on this topic to help you answer this question.
https://hrpp.irb.virginia.edu/learningshots/Writing_protocol_June09/player.html

Answer/Response:

Rater-blinded randomized control study

3. Does the study involve a placebo?

Answer/Response:

NO

►IF YES, provide a justification for the use of a placebo

Answer/Response:

Human Participants

Ages: 18 years or greater
Sex: Any
Race: Any

Subjects- see below

INSTRUCTIONS: For question 1-4 below insert an exact #. Ranges or OPEN is not allowed. This # should be the maximum # you expect to need to enroll (i.e. sign consent) If you are only collecting specimens the number of participants should equate to the # of specimens you need. If you are collecting only data from a chart review the number should designate the number of subjects whose medical records you plan to review. Age/ Sex/Race criteria should designate the demographics of participants from whom you will obtain the specimen/data.

1. **Provide target # of subjects (at all sites) needed to complete protocol.**

INSTRUCTIONS: If this is NOT a database protocol, this number should be the same as the number of subjects needed to obtain statistically significant results.

Answer/Response:
40

2. **Describe expected rate of screen failure/ dropouts/withdrawals from all sites.**

Answer/Response:
20%

3. **How many subjects will be enrolled at all sites?**

INSTRUCTIONS: This number must be the same or higher than the # from question # 1 in order to account for the # of screen failures, dropouts, withdrawals described in question # 2.

Answer/Response:
40

4. **How many subjects will sign a consent form under this UVA protocol?**

INSTRUCTIONS: If the protocol does not have a consent form- the number listed here should reflect such things as the number of subjects from whom specimens will be obtained, the number of charts to be reviewed etc.

Answer/Response:
40

Inclusion/Exclusion Criteria

INSTRUCTIONS:

- The inclusion and exclusion criteria should be written in bullet format.
- *This item applicable if the study will require consent (verbal or written).* Unless there is a scientific reason for not recruiting a certain type of vulnerable population(e.g. not enrolling fetuses, neonates or children in a study regarding Alzheimer's) list the following vulnerable populations under either Inclusion or Exclusion criteria below:

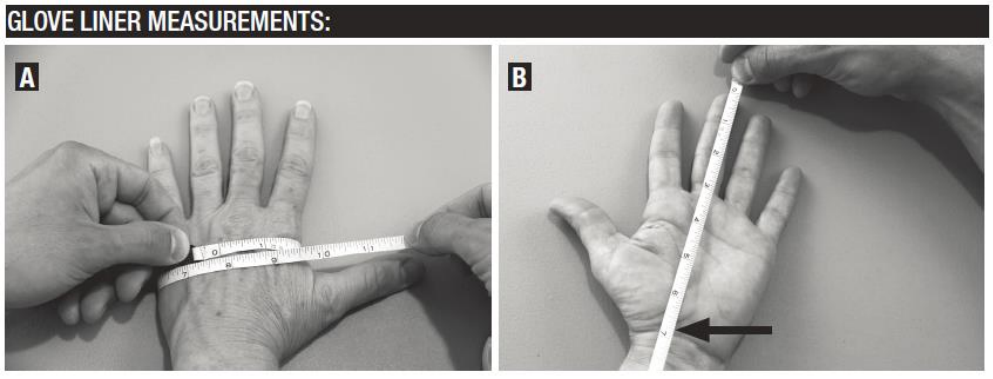
pregnant women, fetuses, neonates, children, prisoners, cognitively impaired, educational or economically disadvantage, non- English speaking subjects .

- If you will not enroll subjects who do not speak English because certain procedures cannot be carried out if the subject does not speak English (e.g. a survey is not validated in other languages) insert the following as an Inclusion Criteria: Willingness and ability to comply with scheduled visits and study procedures.
- If this is a collection of only retrospective* specimens or data, the inclusion criteria must include a start and stop date for when specimens/ data will be collected.
- The stop date must be prior to the version date of this protocol.
- *Retrospective: all specimens are in a lab at the time this protocol is approved by the IRB. All data exists in medical records or records from previous studies at the time this protocol is approved by the IRB.

1. List the criteria for inclusion

Answer/Response:

1. **Participant has had a right or left hemispheric stroke affecting normal hand function**
2. **Participant has sufficient active finger flexion at the MCP joint in at least one finger to be detected by visual observation by a study therapist.**
3. **Participant has visual acuity with corrective lenses of 20/50 or better.**
4. **Participant's affected hand fits within sizing available in the SaeboGlove (see Figure 2).**
5. **Participant must have active movement against gravity of at least 30 degrees shoulder flexion, 45 degrees elbow flexion, elbow extension to within 30 degrees of full extension, and 15 degrees shoulder internal and external rotation.**
6. **In the opinion of a study therapist, participant can independently and safely use the system at home or has an at-home caregiver who is willing and able to assist.**
7. **In the opinion of a study therapist, participant has a suitable and safe space in their home for using the GRASP system.**
8. **Participant is willing and able to provide informed consent.**



A.) **Hand Circumference:** measure hand circumference by wrapping tape circumferentially around hand: _____
B.) **3rd Finger Length:** measure from tip of 3rd digit to the most distal wrist crease: _____

(B) 3RD FINGER LENGTH	(A) HAND CIRCUMFERENCE					
	4-5.5.5	5.5-6.5	6.5-7.5	7.5-8.5	8.5-9.5	9.5-10.5
6.0-6.5	XS	XS	XS			
6.5-7.0	XS	XS	XS	S		
7.0-7.5		S	S	S	M	
7.5-8.0			M	M	L	XL
>8.0				L	XL	XL

Figure 3. Hand measurement procedure and available sizes for SaeboGlove.

2. List the criteria for exclusion

Answer/Response:

1. **Withholding or withdrawal of consent by the participant;**
2. **Inability to understand and follow verbal directions;**
3. **Determination by the Principal Investigator that participation would result in overexertion or significant discomfort or pain;**
4. **A psychological diagnosis that in the determination of the Principal Investigator could significantly impact subject's participation or that could be aggravated by study participation (Principal Investigator will consult with candidate's personal physician as appropriate);**
5. **Determination by the Principal Investigator that participation would result in significant agitation or elevated stress;**
6. **Visual field deficit in either eye that impairs the ability to view the computer monitor;**
7. **Significant stiffness or contractures of the muscles, joints, tendons, ligaments, or skin that restricts normal upper extremity movement;**
8. **More than mild tone/spasticity (measured on modified Ashworth, 5-point scale);**
9. **Severe contractures or joint deformities in the fingers;**
10. **Open wound or infection, severe edema, or excessive swelling which might interfere with wearing the glove;**
11. **Severe pre-stroke co-morbidities, such as cardiovascular, neurological, orthopedic, or rheumatoid impairments before stroke that may interfere with task performance;**
12. **Severe sensory deficits from the involved UE; or**
13. **Hemispatial neglect that impairs the ability to process and perceive visual stimuli provided through the computer monitor.**

3. List any restrictions on use of other drugs or treatments.

INSTRUCTIONS: List only those drugs or treatments that are prohibited while on study, not those listed as an exclusion criteria.

Answer/Response:

NA

Statistical Considerations

1. Is stratification/randomization involved?

Answer/Response:

YES

►IF YES, describe the stratification/ randomization scheme.

INSTRUCTIONS:
The stratification factors and/or the randomization plan should be identified. If there is no randomization component or important patient characteristics that will be used in treatment allocation or data analysis, a statement to this effect should be included.

Stratification factors: These are pretreatment patient characteristics which could be balanced across treatment arms by design or may be used to determine starting dose or treatment allocation.

If randomization is going to be used, the details of the randomization plan should be described.

The description should include:
--the method and timing of randomization
--the type of randomization scheme that will be used in the study
--whether or not the randomization masked/blinded/if so, then to whom is it masked/blinded
--who has access to the randomization scheme

Answer/Response:

To ensure that an approximately equal number of subjects are randomized to the GRASP HEP and UCT groups throughout the Phase II enrollment period, we will randomly assign the patients to the two study-groups in accordance with a permuted block randomization scheme. The randomization list will be generated by PLAN procedure of SAS (SAS Institute Inc., Cary, NC).

The group assignment will be blinded to the therapists (raters) who perform the pre- and post-assessments. The group assignment will be not be blinded to the participants.

The non-rater members of the IRB-approved study team will have access to the randomization list.

►IF YES, who will generate the randomization scheme?

_____ Sponsor
__X__ UVA Statistician. Insert name Answer/Response: Mr. Jim Patrie
_____ UVA Investigational Drug Service (IDS)
_____ Other: Specify Answer/Response:

2. What are the statistical considerations for the protocol?

The objectives section and the statistical section should correspond, and any objective for which analysis is unfeasible should be deleted. Also, the estimates and non-statistical assumptions of the statistical section should be supported by discussion in the background section.

The answer to this question should include:
--Study Design/Endpoints
--Recap of study objectives and endpoint definitions. An assessment of how study objectives will be assessed by identifying & defining which endpoints will be used to assess each component of the study objectives.
--The study design should include contingencies for early stopping, interim analyses, stratification factors (If applicable), and any characteristics to be incorporated in analyses.
--The power/precision of the study to address the major study endpoint(s), the assumptions involved in the determination of power/precision.
--If statistical hypothesis testing is included then specify the null and alternative hypotheses, the test statistic, and the type I and II error rates
--If precision of an estimate, then provide a definition for precision
--If other, then specify

Answer/Response:

Following an initial visit (in outpatient clinic) for consent administration and screening, participants will be asked to return for a pre-assessment visit involving a battery of gold-standard UE function tests including: the Fugl-Meyer assessment of UE motor function (FMUE); the Wolf Motor Function Test (WMFT) assessment of UE motor function; the Box and Blocks Test; and the Motor Activity Log (MAL). Permuted block randomization will be employed. Subjects assigned to GRASP HEP will be asked to employ the GRASP system for UE practice at home over an 8-week period. Patients in the UCT group will not receive any treatment through the study and will continue to receive any previously prescribed therapy services. After 8 weeks, all participants will be asked to return for a post-assessment visit repeating the same battery of tests. Additionally, subjects will be asked to respond to a set of questionnaire-based instruments including the System Usability Scale (SUS); a technology acceptance model (TAM) questionnaire; and a Player Experience of Needs Satisfaction (PENS) questionnaire; and participate in a structured interview.

The pre- to post-intervention change in the composite assessment scores will be the primary endpoint for the GRASP Phase II study. Pre-intervention scores will be subtracted from post-intervention scores to produce a set of delta values which will be analyzed via Analysis of Covariance. One null hypothesis will test if the mean pre- to post-intervention change in scores is equal to zero, while the second null hypothesis will test if the mean pre- to post-intervention change in scores is the same between groups. For both null hypotheses, a $p \leq 0.05$ decision rule will be utilized as the rejection criterion.

3. Provide a justification for the sample size used in this protocol.

Include sample size calculations or statistical power estimation. If not applicable, please provide explanation.

Also include the anticipated accrual rate, the accrual goal for the study, including accrual goals by strata if appropriate, adjustments for drop-outs etc. and study duration.

Answer/Response:

The first row of Table 1 provides the minimum detectable within-intervention changes in the composite Fugl-Meyer Upper Extremity (FMUE) scores that would lead 80% of the time to rejecting the null hypothesis, listed according to patient retention rate. The second row of Table 1 provides the minimum detectable between-intervention difference. Note that accounting for a 20% dropout rate, recruitment of a total of 40 subjects provides sufficient power to detect a pre- to post-intervention change of 2.4 units, a value that is consistent with previous studies of hand therapy interventions [60].

Table 1. Phase II power analysis

comparison type	Phase II Study Patient Retention Rate % (n)				
	100% (20)	95% (19)	90% (18)	85% (17)	80% (16)
within-intervention	1.5	1.5	1.6	1.6	1.7
between-intervention	2.1	2.2	2.2	2.3	2.4

4. What is your plan for primary variable analysis?

Include primary outcome(s)/predictor variable(s), statistical methods/models/tests to be employed, or descriptive summaries as appropriate. If not applicable, please provide explanation.

Answer/Response:

The pre- to post-intervention change in the composite FMUE score will be the primary endpoint for the Phase II efficacy study. Each of the seven tasks in the hand portion of the FMUE will be scored on a scale of 0 to 2 [53] and summed to produce a composite score. The pre-intervention scores will be subtracted from the post-intervention scores to produce a set of delta values. These delta values scores (Δ) will be analyzed via Analysis of Covariance (ANCOVA). One null hypothesis will test if the mean pre- to post-intervention change in the composite FMUE score is equal to zero, while the second null hypothesis will test if the mean pre- to post-intervention change in the composite FMUE score is the same for patients who undergo 8-weeks of GRASP therapy and patients who undergo 8 weeks of intensity-balanced standard care. For both null hypotheses, a $p \leq 0.05$ decision rule will be utilized as the rejection criterion.

5. What is your plan for secondary variable analysis?

Include the following:
--Secondary outcome(s)/predictor variables, statistical methods/models/tests to be employed, or descriptive summaries as appropriate. If not applicable, please provide explanation.
--For phase III studies, the power/precision of the study to address the secondary objective(s).

Answer/Response:

The pre- to post intervention changes in the composite Wolf Motor Function Test (WMFT) scores will be analyzed in exactly the same way as the pre to post-intervention change in the

composite FMUE scores, and the same method of analysis will be used to analyze the pre- to post-intervention changes in Box and Blocks Test scores, and the pre- to post-intervention changes in the Motor Activity Log (MAL) scores.

6. Have you been working with a statistician in designing this protocol?

Consultation with a professional statistician is highly recommended to ensure good science of the study and facilitate the review process.

Answer/Response:

YES

IF YES, what is their name?

Answer/Response:

Mr. James Patrie

7. Will data from multiple sites be combined during analysis?

Answer/Response:

INSTRUCTIONS: IF YES, answer the following questions

NA

Study Procedures-Biomedical Research

1. What will be done in this protocol?

INSTRUCTIONS:
This should include everything that will be done as part of this protocol. Do not repeat information that is included in other sections such as Background or Hypothesis sections.
This section should include an indication of which research interventions if any offer a prospect for direct benefit and which interventions (invasive measurements, collection of blood, tissue, data, surveys, etc.) are being done solely to answer a research question and generate generalizable knowledge. If the interventions done solely for research purposes are associated with greater than minimal risk they need to be justified. Describe and justify any control and experimental arm and include method, dose, and duration of drug administration. Reference any claim of clinical equipoise if applicable.

If you are obtaining specimens or data, provide information regarding the type of specimen/data, amount of specimen needed and how the specimen/data will be obtained and what analysis will be done with the specimen/data.

Special note for studies with waiver of consent/waiver of documentation of consent:
Include a statement regarding how subjects will be recruited. For other studies this information is captured in Recruitment does not need to be duplicated in this section.

Answer/Response:

Participants meeting study criteria will be recruited from the population of current and former stroke patients of the University of Virginia Health System.

Prior to consent, potential candidates will be contacted by phone and asked to respond to questions pertaining to eligibility (inclusion/exclusion criteria). For example:

- **Do you continue to experience weakness or impaired function in your stroke affected hand?**
- **Are you able to bend your fingers partially on your stroke affected hand?**
- **Are you able to move your stroke affected arm and flex your elbow about halfway?**
- **Is your corrected vision good enough to comfortably watch a TV show for 30 minutes?**

The final list of questions will be included in a telephone recruitment scripts that will be submitted for IRB approval prior to use. After pre-screening using the IRB-approved script, candidates will be scheduled for a remotely-administered consent and screening telehealth visit and for a pre-assessment visit at UVA.

ALL – Remotely-administered consent visit (will last about 45 minutes)

- **Participant will take part in remotely-administered telehealth visit with a study coordinator or a study therapist by phone or HIPAA compliant video conferencing (e.g. a Zoom Health account through UVA).**
- **Participant will be asked pre-screening questions to verify inclusion and exclusion criteria**
- **Participant will complete informed consent process and, if consent is provided, sign using DocuSign or alternative institutionally -approved method.**

ALL - Outpatient Visit 1 at UVA: Pre-Assessment (will last about 90 minutes)

- **Blinded study therapist will review consent and re-verify inclusion and exclusion criteria**
- **Blinded study therapist will administer a battery of hand function tests including: the Fugl-Meyer assessment of UE function (FMUE), the Wolf Motor Function Test (WMFT), the Box and Blocks Test, and the Motor Activity Log (MAL).**
- **If administration of the test instruments cannot be completed for any reason (e.g. subject becomes fatigued), the participant may be asked to return for an additional visit to complete the procedures. The participant will be provided the normal per-visit stipend for the additional visit.**
- **Study therapist will take hand measurements for SaeboGlove fitting.**
- **Subject will be assigned to either the GRASP HEP or the UCT group employing the study randomization procedure and scheduled for remaining visits.**

GROUP 1: GRASP HEP GROUP

GRASP HEP Home Visit 1 (will last about 90 minutes)

- **A non-blinded study therapist will conduct a home visit at the patient's residence.**
- **The therapist will set up the GRASP system and verify the patient's ability to safely and successfully use the system at home.**
- **The therapist will provide the patient with an appropriately sized SaeboGlove.**
- **The therapist will assist the patient in learning to don and doff the SaeboGlove with GRASP sensors.**
- **The patient will practice using the GRASP system for virtual world practice of ADLs and IADLs.**

GRASP HEP Home Visit 2 (will last about 60 minutes)

- **A non-blinded study therapist will conduct a second home visit at the patient's residence.**
- **The therapist will verify safety of the system setup in the patient's home.**
- **The therapist will assist the patient in learning to don and doff the SaeboGlove with GRASP sensors.**

- **The patient will practice using the GRASP system for virtual world practice of ADLs and IADLs.**
- **If on the study therapist's recommendation, the study PI determines an additional visit is warranted to ensure a patient can safely and successfully use the system at home, an additional home visit will be conducted.**

GRASP HEP Independent Practice at Home

- **Participants will be asked to employ the GRASP system for UE practice at home 45 minutes/session, 4 sessions/week over an 8-week period.**
- **Patients will continue to perform any previously prescribed therapy.**
- **Once per week during this period, non-blinded study staff will employ an authorized web application on a UVA computing system to remotely monitor de-identified participant data (see Data Security Plan for details) that includes exercise adherence (duration performed), movement repetitions accomplished (exercise reps), and exercise intensity (speed).**
- **At least once every two weeks, non-blinded study staff will contact the participant by phone or HIPAA compliant video conferencing to collect self-reported adherence data and confirm that no change in medical status has occurred that would impact continued participation.**

GRASP HEP Home Visit 3 (will last about 90 minutes)

- **At the end of the 8-week HEP period, a non-blinded study therapist will conduct a home visit at the patient's residence to observe patients' independent use of the system and recover the system hardware.**
- **Participants will respond to questionnaire-based instruments including the System Usability Scale (SUS), a technology acceptance model (TAM) questionnaire, and a Player Experience of Needs Satisfaction (PENS) questionnaire, as well as participate in a structured interview. These assessments will be audiotaped.**

The participant will be encouraged to invite his or her home care provider (e.g. spouse or family member, if applicable) to attend the GRASP HEP visits, so that this individual is able to assist the patient during independent practice.

GROUP 2: UCT GROUP:

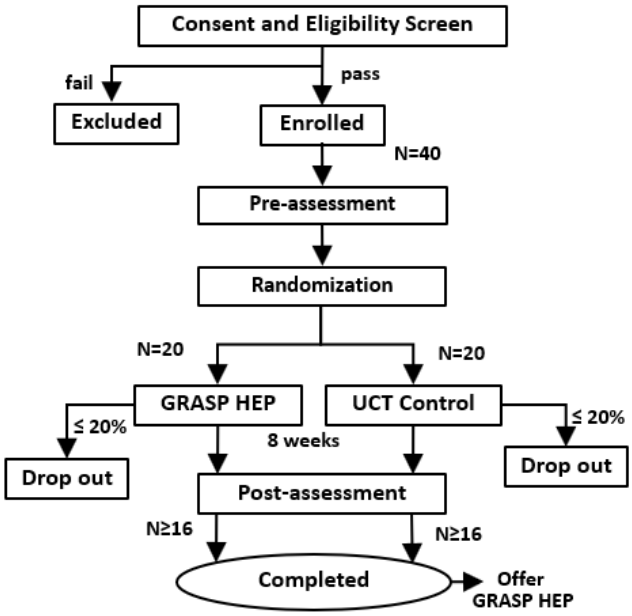
- **Participants in the control group will continue to receive any previously prescribed therapy services. These patients will not receive any treatment services through the study as UCT group participants.**
- **At least once every two weeks during the 8 week period, non-blinded study staff will contact the participant by phone or HIPAA compliant video conferencing to collect self-reported adherence data and confirm that no change in medical status has occurred that would impact continued participation.**

ALL – Final Outpatient Visit at UVA: Post-Assessment (will last about 90 minutes)

- **Study therapist will administer the same battery of tests used in pre-assessment.**
- **If administration of the test instruments cannot be completed for any reason (e.g. subject becomes fatigued), the participant may be asked to return for an**

additional visit to complete the procedures. The participant will be provided the normal per-visit stipend for the additional visit.

A graphical summary of the GRASP Phase II study is provided below.



Assessments

Rater-blinded measures (pre- and post-)

- Fugl-Meyer UE function (FMUE)
- Wolf Motor Function Test (WMFT)
- Box and Blocks Test
- Motor Activity Log (MAL)

Usability assessment (post GRASP HEP)

- System Usability Scale (SUS)
- Technology Acceptance Model (TAM)
- Player Experience of Needs Satisfaction (PENS)
- Free-response interview

Treatments

GRASP HEP

- 3 total therapist home visits for setup and safety eval, observation, and system recovery
- GRASP practice 45 min/day, 4 days/week
- Therapist remote monitoring 1x/week using GRASP web application
- Study coordinator or therapist phone check-in every other week to collect adherence data
- Continue any previously prescribed therapy

UCT Control

- Continue previously prescribed therapy
- Therapist phone check-in every other week

2. If this protocol involves study treatment, explain how a subject will be transitioned from study treatment when they have completed their participation in the study.

Example: If the subject will be taking an investigational drug, will they need to be put back on an approved drug when they have completed the study? If yes, explain how this will be accomplished and who will cover the cost. If the subject has a device implanted will it be removed? Again- who will cover the cost of the removal?
Instructions: Answer NA if this study does not involve a study treatment.

Answer/Response:

At the conclusion of this study, participants assigned to the GRASP HEP group will stop using the GRASP system. No further transition is needed.

To promote equipoise, participants in the UCT group will be offered free access to the GRASP software system following completion of the study. The GRASP systems will be made available to UCT participants for 8 weeks, once the units are no longer needed for the GRASP HEP-assigned participants.

If the UCT participant wishes to take advantage of this offer, when a system becomes available, a study therapist will conduct a home visit at the participant's residence to assist in system setup and training to safely and successfully use the system at home. A study staff member will recover the system after an 8 week period.

If on the study therapist's recommendation, the study PI determines an additional visit is warranted to ensure a patient can safely and successfully use the system at home, an additional home visit will be conducted.

All participants (both GRASP HEP and UCT) will be able to keep the SaeboGlove (without the GRASP system) following completion of the protocol. (https://www.saebo.com/shop/saeboglove/)

Bibliography

INSTRUCTIONS: Provide a current bibliography supporting the hypothesis, background and methodology including references to papers and abstracts that have resulted from previous work by the investigator and references to the work of others.

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APPENDIX: Non- UVa Personnel

Instructions: This section is NOT required if the researcher will be on UVa grounds and has completed a "SOM Volunteer in Research Form". Return to Protocol Builder and answer YES to the question: *Are all personnel listed on this study UVA employees or students?*

1. **Explain the duties of non-UVA personnel on this protocol.**
   Answer/Response:

   Dr. Ellington (OTR/L, DOT) will serve as non-blinded study staff providing remote monitoring and remote check-ins with patients as described in Study Procedures:

- **Once per week during this period, non-blinded study staff will employ an authorized web application on a UVA computing system to remotely monitor de-identified participant data that includes exercise adherence (duration performed), movement repetitions accomplished (exercise reps), and exercise intensity (speed).**
- **At least once every two weeks, non-blinded study staff will contact the participant by phone or HIPAA compliant video conferencing to collect self-reported adherence data and confirm that no change in medical status has occurred that would impact continued participation.**

2. Explain your plans for training and oversight of these personnel.

Answer/Response:

For the purposes of this study, Dr. Ellington (OTR/L, DOT) will fall under the supervision of the GRASP Phase II PI, Dr. Regan Royer, UVA PM&R.

In supporting the above described role of remote monitoring and remote check-ins with study participants, Dr. Ellington will closely coordinate with the GRASP study coordinator and the non-blinded study therapist conducting the GRASP HEP home visits.

Dr. Ellington is highly experienced in conducting IRB-supervised research, having served as study staff on multiple previous UVA IRB-HSR protocols of similar scope (notably 16117 and 17591). She is very well-versed in the details and procedures of the GRASP Phase II protocol, and in human subject protections.

3. How do you plan to access any study records the non-UVA personnel might maintain?

Answer/Response:

Self-reported adherence data collected during remote check-ins will be documented on a printed form and stored in a locking document bag. The adherence data forms will be transferred to the study coordinator approximately once every 2-3 weeks.

4. Will the non- UVA personnel be exposed to any additional risk while working on this protocol?

Answer/Response:

No. All interaction with patients will be remote.

5. List name of any other institution with which they have an affiliation.

Answer/Response:

Mary Baldwin University (Program Director of the Doctor of Occupational Therapy Program)
Barron Associates, Inc. (Consultant on the NIH-funded GRASP Phase II program)

6. Will the non- UVa personnel have access to UVa patients or their health information along with any HIPAA identifiers prior to consent?

Answer/Response:
Answer is NO to all for "prior to consent"

►IF YES, check the HIPAA identifiers below they will have access to:

YES	NO	
	X	1. Name
	X	2. All geographic subdivisions smaller than a state, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of the zip code if, according to the current publicly available data from the Bureau of the Census: (1) The geographic unit formed by combining all zip codes with the same 3 initial digits contains more than 20,000 people and (2) The initial 3 digits of a zip code for all such geographic units containing 20,000 is changed to 000.
	X	3. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older. *[This means you may record the year but not record the month or day of any date related to the subject if the subject is under the age of 89. In addition if the subject is over the age of 89 you may not record their age and you may not record the month, day or year of any date related to the subject]*
	X	4. Telephone numbers
	X	5. Fax numbers
	X	6. Electronic mail addresses
	X	7. Social Security number
	X	8. Medical Record number
	X	9. Health plan beneficiary numbers
	X	10. Account numbers
	X	11. Certificate/license numbers
	X	12. Vehicle identifiers and serial numbers, including license plate numbers
	X	13. Device identifiers and serial numbers
	X	14. Web Universal Resource Locators (URLs)
	X	15. Internet Protocol (IP) address numbers
	X	16. Biometric identifiers, including finger and voice prints

	X	17. Full face photographic images and any comparable images
	X	18. Any other unique identifying number, characteristic, code that is derived from or related to information about the individual (e.g. initials, last 4 digits of Social Security #, mother's maiden name, first 3 letters of last name.)
	X	19. Any other information that could be used alone or in combination with other information to identify an individual. (*e.g. rare disease, study team or company has access to the health information and a HIPAA identifier or the key to the code* .)

7. If any items above are checked YES, list names of non- UVa affiliated individuals who will have access.

Answer/Response:

NA

NOTE:

- If any item other than 2 or 3 is checked in the Table under Question # 6 and the individual listed under # 7 tracking of the disclosure by the study team will be required via EPIC.
- If only item 2 or 3 is noted a HIPAA Data Use Agreement will be required in a contract/ agreement between the unaffiliated investigator and UVa.