PROTOCOL TITLE: Comparison of two high-intensity gait training interventions on contraversive pushing behaviors in individuals poststroke

PRINCIPAL INVESTIGATOR (PI):
Arun Jayaraman, PT, PhD
Department of Physical Medicine and Rehabilitation
Northwestern University
Shirley Ryan AbilityLab
355 East Erie Street
Chicago, IL 60611
Phone: (312) 238–6875
Fax: (312) 238–2081
ajayaraman@sralab.org

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STUDY SUMMARY:

Investigational Agent(s) (Drugs or Devices)	N/A
IND / IDE / HDE #	N/A
Indicate Special Population(s)	☐ Children ☐ Children who are wards of the state ☒ Adults Unable to Consent ☐ Cognitively Impaired Adults ☐ Neonates of Uncertain Viability ☐ Pregnant Women ☐ Prisoners (or other detained/paroled individuals) ☐ Students/Employees
Sample Size	30 participants
Funding Source	Shirley Ryan AbilityLab: Brown Fellowship Grant
Indicate the type of consent to be obtained	☒ Written ☐ Verbal/Waiver of Documentation of Informed Consent ☐ Waiver of HIPAA Authorization ☐ Waiver/Alteration of Consent Process
Site	☐ Lead Site (For A Multiple Site Research Study) ☐ Data Coordinating Center (DCC)
Research Related Radiation Exposure	☐ Yes ☒ No
DSMB / DMC / IDMC	☐ Yes ☒ No

OBJECTIVES
The purpose of this study is to investigate the effect of two high-intensity gait training interventions on contraversive pushing behaviors (CPB) in individuals poststroke in the acute inpatient rehabilitation setting. We will also evaluate the effect of these interventions on functional mobility, strength, balance, and endurance. Furthermore, we intend to measure therapist burden when mobilizing individuals with CPB.

BACKGROUND

High-intensity gait training is strongly supported in individuals poststroke to facilitate neuroplastic changes in the brain in order to maximize the recovery of functional independence.[1] In the acute inpatient rehabilitation setting, therapists utilize safety equipment, rehabilitation technicians, and assistive devices to implement high-intensity gait training as soon as possible; however, individuals with CPB exhibit significant postural control deficits, making this feat difficult. Contraversive pushing is characterized by three clinical features: (1) contralesional tilted posture with significant balance impairments, (2) tendency to push with non-affected extremities into abduction and extension toward the hemiparetic side, and (3) resistance to external correction [Refer to Figure 1.A].[2,3] It is hypothesized that this phenomenon occurs due to impaired awareness of midline where individuals perceive their body as "upright" when it is actually tilted up to 18 degrees towards the brain lesion [Refer to Figure 1.B].[3] CPB has been reported in 12-18% of individuals receiving stroke rehabilitation and often leads to longer lengths of stay, poorer functional outcomes, and institutionalized discharge locations compared to individuals with stroke diagnoses without CPB.[2,4,5] At times, these deficits can be accompanied by neglect, sensory deficits, and cognitive deficits, making ambulation overground at high intensities extremely difficult without heavy physical assistance.[3]

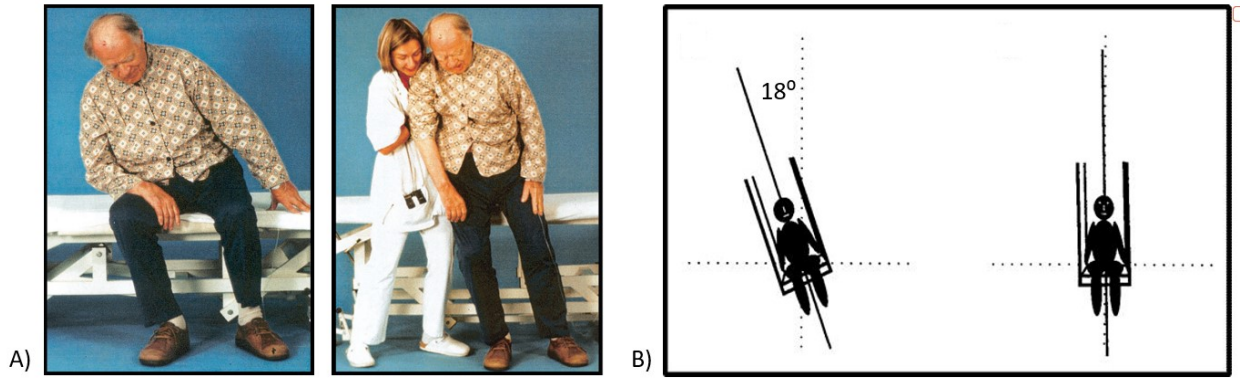

Figure 1. A) An individual demonstrating CPB in sitting and standing.[3] B) Visual representation of perceived midline orientation in individuals with CPB.[3]

There is little research on the utilization of overground-based robotic exoskeletons like the EksoNR to train and ambulate individuals with acute and chronic stroke diagnoses. In addition, high quality evidence guiding physical therapy intervention, specifically gait training, in individuals with CPB is scarce. Robotic assisted gait training utilizing the Lokomat system over a treadmill has been effective in reducing CPB.[4,6,7] However, no studies have assessed the efficacy of gait training with an exoskeleton robotic suit overground as we are proposing to do. Traditional therapeutic interventions in individuals with CPB typically consists of progressing functional mobility while orienting to midline with various forms of visual and tactile feedback.[4,5,8-13] It is hypothesized that the EksoNR will be an efficacious intervention for this population because of its ability to position and orient an individual to midline while simultaneously working on gait training and decreasing the physical burden on clinicians. Unquestionably, there is a demand for research to support appropriate interventions, guide best physical therapy practice, and promote ways to safely maximize high-intensity gait training within this specific population.

This study will include two interventional groups. Intervention for group one will consist of body-weight-supported treadmill training + overground gait training. Intervention for group two will consist of gait training in the EksoNR exoskeleton + overground gait training. We will enroll 5-10 participants in each intervention group with the goal of 10 participants completing the study.

Since participants are inpatients on an acute rehabilitation unit, they will simultaneously be receiving intensive physical, occupational, and speech therapies outside of our research study as part of the standard of care at Shirley Ryan AbilityLab.

Intervention Delivery Systems:
Woodway PPS Medical Series + Body Weight Support LokoStation 55/70
The commercially available Woodway + LokoStation [Refer to Figure 2.A] is intended to assist an individual when performing locomotor therapy under the supervision of a trained physical therapist. The purpose of the body weight support system is to facilitate ambulation for participants with walking difficulties due to cerebral, spinal, neurogenic, muscular, or osseous causes. See attached user manual.

EksoNR Exoskeleton
The commercially available EksoNR [Refer to Figure 2.B] is intended to assist an individual when performing ambulatory functions under the supervision of a physical therapist who has completed formalized training. It is approved by the FDA for use in individuals with stroke diagnoses. The EksoNR is an under-actuated lower extremity exoskeleton with actuation at the knee and hip joints and a passive ankle. The device enables individuals with any amount of lower extremity strength to stand up and walk overground with a natural, weight bearing, reciprocal gait pattern. The EksoNR utilizes cooperative gait rehabilitation algorithms to vary the amount of assistance provided to each user for an individualized therapy experience. This method allows the exoskeleton to work with a user's existing strength and provide only the extra effort required to complete a maneuver correctly and safely. Walking is achieved by shifts in the wearer's weight, which activate sensors in the footplate and initiate steps. See attached user manual.

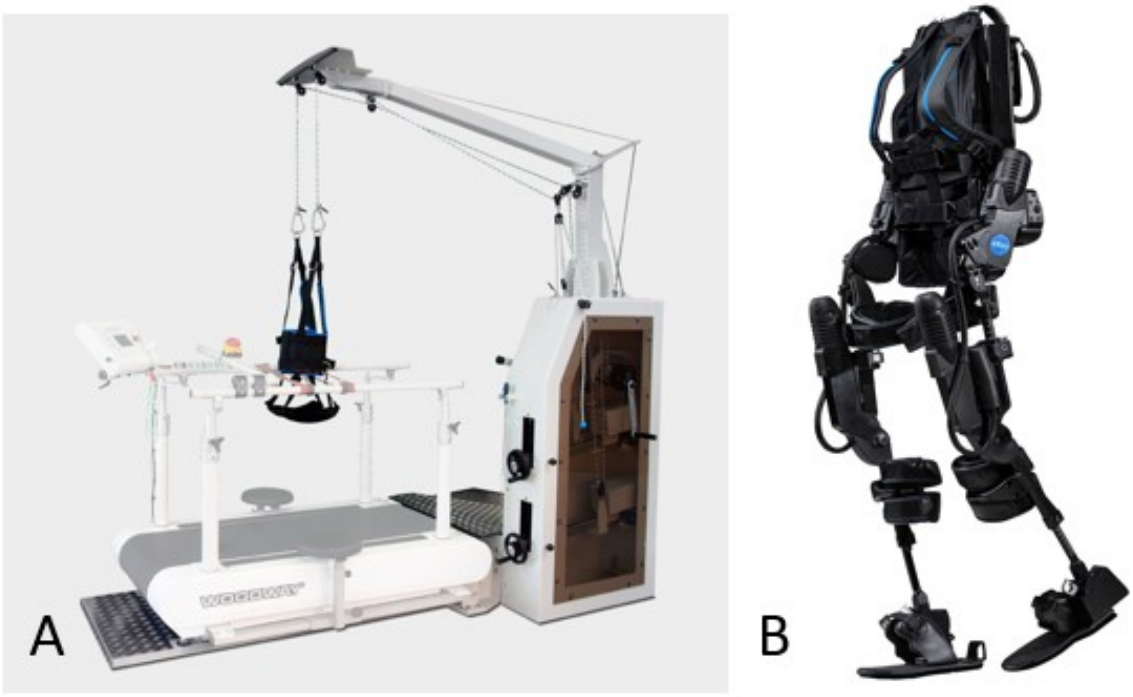

Figure 2. Gait intervention systems. A) Woodway Treadmill System. B) EksoNR Exoskeleton.

STUDY ENDPOINTS

Study endpoints:
The study ends when the participant completes the intervention protocol and outcomes assessment and when data has been collected and analyzed. The study may also end if the participant discharges from the inpatient setting prior to completing the intervention protocol. The participant may choose to withdraw from the study at any time.

Safety endpoints:
Participant enrollment in this study will be terminated if the research or medical team determine that the participant is no longer medically stable to continue participation. Any adverse events will be documented thoroughly.

PROCEDURES INVOLVED

Screening, enrollment, and baseline procedures:
Individuals with stroke admitted as inpatients to the Shirley Ryan AbilityLab will be asked to potentially enroll in the study. A thorough review of the participant's medical history will be completed by licensed physical therapists, and medical clearance will be obtained from the individual's medical team. The study coordinators will assess eligibility based on inclusion criteria, obtain informed consent, and answer any questions from the participant and/or his/her power of attorney (POA). If the participant is deemed unable to consent by the primary medical team, consent will be obtained from the individual's power of attorney (POA). Following informed consent, participants will undergo a physical evaluation and screening exam by a licensed physical therapist. Once they are enrolled, baseline outcome measures will be assessed by a physical therapist [See Clinical Assessments section].

If a participant is placed in the intervention group receiving gait training via the EksoNR exoskeleton, additional steps will be taken during baseline assessments to ensure the participant is appropriate for use of the EksoNR. These measures include upper and lower extremity range of motion, upper and lower extremity strength, spasticity, transfer status, skin integrity, and then three specific body measurements to assist with setting up the EksoNR exoskeleton. The three body measurements include hip width measured in sitting, upper leg lengths measured supine on a mat table, and lower leg lengths measured sitting on the edge of the mat table with feet supported on a step. Measurements are compared bilaterally and then converted to EksoNR values using a chart from Ekso Bionics (See User Manual). All assessments will be completed by a trained physical therapist to ensure standardization and safety of the participant.

Procedures during treatment:
After the baseline testing is completed, participants will complete between 9-24 training sessions dependent on their length of stay. These training sessions will occur in the inpatient Legs + Walking Lab with a licensed physical therapist and will last up to 90 minutes. Each session will be customized based on the participant's functional capacity with the goal of maximizing stepping practice.

Body-weight-supported treadmill + overground gait training group:
Upon arrival to the session, a Polar OH1 Optical Heart Rate Sensor and an ActiGraph GT9X Link will be placed on the participant. Vitals including heart rate, blood pressure, oxygen saturation, and rating of perceived exertion (RPE) will be assessed at the beginning, during walking, and at the end of the session. The physical therapist will then assist with donning a walking harness with padding (as needed) in sitting or standing based on the participant's current functional capacity. The participant will be assisted onto the Woodway treadmill via ramp

while seated in a wheelchair. The participant will be clipped into the body weight support system, assisted into standing, and provided the appropriate amount of body weight support to allow for successful stepping practice. During walking, the physical therapist and a rehabilitation technician will provide physical assistance as necessary to advance the participant's limbs. The participant will be instructed to maximize the number of steps during gait training for up to 60 minutes total with a targeted intensity of 70-85% of age-predicted heart rate maximum. The participant's response to exercise will be continuously monitored via vital monitoring and the participant's subjective report. The participant can request standing or seated rest breaks during session as needed. If, at any time, the participant's heart rate exceeds 90% of age-predicted heart rate maximum, a seated rest break will be initiated by the therapist to allow the heart rate to return to baseline levels prior to returning to the walking protocol. The physical therapist may modify training parameters including: treadmill speed, incline, direction (forward, backward), and amount of body weight support in order to provide the appropriate amount of challenge. Upon completion of each session, the harness will be doffed in standing or sitting, and the participant's skin will be thoroughly assessed. Some sessions may include additional overground gait training to assess carry-over of learning. In this case, the physical therapist will provide the appropriate physical assistance, assistive device, and bracing based on current functional level.

EksoNR gait training + overground gait training group:
Upon arrival to the session, a Polar OH1 Optical Heart Rate Sensor and an ActiGraph GT9X Link will be placed on the participant. Vitals including heart rate, blood pressure, oxygen saturation, and rating of perceived exertion (RPE) will be assessed at the beginning, during walking, and at the end of the session. The physical therapist will then assist with transferring the participant into the EksoNR exoskeleton while in sitting, adding wedges and/or padding as needed. Multiple straps will be applied bilaterally at the shoulders, across the abdomen, mid-thighs, below the knees, and around the shoes. Once the participant is safely secured into the EksoNR exoskeleton, they will be assisted into standing to begin gait training. The physical therapist will encourage them to maximize the number of steps during gait training for up to 60 minutes total with a targeted intensity of 70-85% of age-predicted heart rate maximum. The participant's response to exercise will be continuously monitored via vital monitoring and the participant's subjective report. Therapist will also utilize feedback from the EksoNR to guide the treatment session. The participant can request standing or seated rest breaks during the session as needed. If, at any time, the participant's heart rate exceeds 90% of age-predicted heart rate maximum, a seated rest break will be initiated by the therapist to allow the heart rate to return to baseline levels prior to returning to the walking protocol. The physical therapist may modify the EksoNR programming parameters to provide the appropriate challenge. Upon completion of each session, the EksoNR exoskeleton will be doffed in sitting, and the participant's skin will be thoroughly assessed. Some sessions may include additional overground gait training to assess the carry-over of learning. In this case, the physical therapist will provide the appropriate physical assistance, assistive device, and bracing based on current functional level.

Clinical assessments:
All assessments will be performed by a licensed physical therapist as per the standard of care at the Shirley Ryan AbilityLab. The participant will be given rest breaks as needed between tests to minimize fatigue. The physical therapist will provide the appropriate physical assistance, assistive device, and bracing based on current functional level.

Clinical assessments performed at enrollment and weekly

1. Scale for Contraversive Pushing (SCP)

2. Burke Lateropulsion Scale (BLS)
3. 10 Meter Walk Test (10MWT)
4. 6 Minute Walk Test (6MWT)
5. Berg Balance Scale (BBS)
6. Function in Sitting Test (FIST)
7. Functional Independence Measure (FIM)
8. Quality Indicators (QI)
9. Manual Muscle Test (MMT)
10. Range of Motion (ROM)
11. Modified Ashworth Scale (MAS)

Clinical assessments performed each session

1. Step count
2. Time spent in 70-85% of age-predicted maximum target heart rate zone
3. Rating of perceived exertion (RPE)
4. Therapist heart rate
5. Therapist RPE
6. Therapist Numerical Rating Pain Scale

Description of clinical assessments:

1. Scale for Contraversive Pushing (SCP): The SCP is a three-item test used to measure lateropulsion, scored on a three point ordinal scale. It rates a participant's action/reaction of maintaining or changing a position in both sitting and standing. A score >0 indicates the presence of CPB.
2. Burke Lateropulsion Scale (BLS): The BLS is a five-item test used to measure lateropulsion, scored on a four to five point ordinal scale. It rates a participant's action/reaction of keeping or changing a position in sitting, standing, rolling in supine, transfers, and walking.
3. 10 Meter Walk Test (10MWT): The 10MWT is a common clinical measure of gait speed. Participants will be directed to walk at their comfortable, self-selected speed. Participants will be positioned at the start line and instructed to walk the entire 10 meter distance while the therapist times the middle six meters. The distance before and after the timed course are meant to minimize the effect of acceleration and deceleration. Time will be recorded using a stopwatch and recorded to the one hundredth of a second (ex: 2.46 sec). The test will be performed two times at self-selected speed with adequate rest in between. The average of the two times should be recorded. The test will then be repeated with the participants directed to walk at their fast but safe speed. Appropriate assistive devices, bracing, and the minimal amount of physical assistance from the physical therapist will be applied.
4. 6 Minute Walk Test (6MWT): The 6MWT measures the distance a participant can walk indoors on a flat, hard surface in a period of six minutes. The test is a reliable and valid evaluation of functional exercise capacity and is used as a sub-maximal test of aerobic capacity and endurance. The test is self-paced. Participants are allowed to stop and rest during the test; however, the timer does not stop. If a participant is unable to complete the time, the time stopped is noted and reason for stopping prematurely is recorded. Appropriate assistive devices, bracing, and the minimal amount of physical assistance from the physical therapist will be applied.
5. Berg Balance Scale (BBS): The BBS is a 14-item test, scored on a five point ordinal scale. It measures functional balance in a clinical setting and includes static and dynamic tasks (such as sitting, standing, transitioning from sitting to standing, standing on one foot, retrieving an object from the floor), during which participants must maintain their balance.

6. Function in Sitting Test (FIST): The FIST is a 14-item test of sitting balance, scored on a five point ordinal scale. It measures sensory, motor, proactive, reactive, and steady state balance factors.
7. Functional Independence Measure (FIM): The FIM is an 18-item test (13 motor tasks, 5 cognitive tasks) for evaluating level of disability and how much assistance is needed for a participant to perform certain activities of daily living. Each item is scored on a seven point ordinal scale, ranging from total assistance to total independence. Items include eating, grooming, bathing, dressing, toileting, bladder/bowel management, transfers, locomotion, stairs, comprehension, expression, social interaction, problem solving, and memory.
8. Quality Indicators (QI): This is a standardized, evidence-based measure of health care quality used to track clinical performance and outcomes in post-acute care. Items are scored on a six point ordinal scale, ranging from independent to dependent. Items can also be coded as participant refuses, not applicable, environmental limitations, not attempted due to medical condition or safety concerns, or unplanned discharge.
9. Manual Muscle Test (MMT): The MMT is a procedure for evaluating the strength of 16 individual muscles relative to gravity and manual resistance. Instructions are provided to the participant before testing each muscle. A muscle is isolated, and gradual external force is applied at a right angle to the muscle's long axis. Each muscle is scored on a graded scale of "weak" to "strong" based on the participant's ability to resist the external force. The test is first completed for muscles on the unimpaired side to determine normal strength before being repeated on the impaired side. Weaker participants may be tested while lying prone (gravity eliminated).
10. Passive Range of Motion (ROM): The purpose of this test is to evaluate a participant's passive range of motion in the joints of the hips, knees, and ankles.
11. Modified Ashworth Scale (MAS): The MAS is a 6-point ordinal scale used to grade the amount of hypertonicity in individuals with neurological diagnoses. A score of 0 on the scale indicates no increase in tone while a score of 4 indicates rigidity. Tone is scored by passively moving the individual's limb and assessing the amount of resistance to movement felt by the examiner.
12. Step count: The number of steps taken during each session will be measured using ActiGraph GT9X Link activity monitors. These devices are small accelerometers that can be worn on a belt and/or on the ankle to record steps and Kcals during an activity. The therapist leading the intervention session will apply the ActiGraph at the beginning of each intervention session and remove it upon completion.
13. Age-predicted maximum heart rate zone: The target range of 70-85% of age-predicted maximum heart rate will be calculated for each participant utilizing HRmax = 208 − [0.7 × age] as developed by Tanka et al in 2001.[14] It is recommended that clinicians should apply moderate to high-intensity walking training to improve walking speed and endurance individuals poststroke.[1,15] We will record the amount of time participants spend in their pre-calculated target zone during each gait training session utilizing the Polar OH1 Optical Heart Rate Sensor.
14. Borg Rating of Perceived Exertion (RPE): The Borg RPE is a tool to measure the subjective report of effort, exertion, and fatigue during physical work. It consists of a 15-point scale from 6-20, in which 6=no exertion and 20=absolute maximum exertion. It is presented to the participant in written format with descriptors to standardize the report of perceived exertion across tasks.
15. Numerical Rating Pain Scale (NPRS): The NPRS is used to measure the subjective report of pain intensity. It consists of an 11-point scale, 0-10, in which zero indicates no pain and ten indicates the most intense pain imaginable. In this study, therapists will be provided a written format of the NPRS to report their perceived pain following delivery of each intervention session.

DATA COLLECTION AND ANALYSIS
Data from participants will be collected during their hospital stay, including clinical and functional outcomes. The complete medical history of the participants, including physical findings, radiological reports such lesion size, location, type, medications, intervention training parameters and therapist-assessed clinical outcomes may also be collected (See Clinical Assessments section). Participants' records and data will be kept confidential and in compliance with HIPAA requirements. Research data will be de-identified and stored in locked cabinets in the lab with access only to research staff. Electronic data will be de-identified and kept on secure, password protected files, and password protected computers. Analysis will be completed to compare the two intervention groups and draw conclusions on the efficacies of both interventions.

Photographs, audio, and video recordings:
We may photograph, audio, or video record the participants during the study to be used for scientific publications and scholarly presentations only. The photographs will be de-identified, meaning that the face of the participants will not be shown. Participants will be given the choice to accept or decline this optional aspect during the informed consent process. Their choice will not impact their participation in the study.

STUDY TIMELINES
We anticipate it will take each participant up to eight weeks to complete the study protocol. Clinical assessments will be performed at baseline and once weekly for up to eight assessment sessions or until the participant is discharged. The intervention will be delivered three times weekly up to 24 sessions or until the participant is discharged. In total, each individual will participate in 13-34 sessions [Refer to Figure 3]. We anticipate a 12-month period to enroll all inpatient participants.

Type of Session	# of Sessions	Time Required for Each Session
Enrollment/ Baseline Clinical Assessment/ Baseline Measurements	1-2	60-120 minutes
Weekly Clinical Assessments	3-8	60-90 minutes
Training Protocol	9-24	60-90 minutes

Figure 3. Summary of sessions.

INCLUSION AND EXCLUSION CRITERIA
Inclusion Criteria:
- Age 18-80 years old
- Unilateral, supratentorial ischemic or hemorrhagic stroke within the past six months
- Medical clearance from primary medical team (signed Medical Clearance form)
- CPB as determined by a score of >0 on the Scale for Contraversive Pushing
- Adequate cognitive function as determined by the NIH scale: score ≤1 on question 1b and score =0 on question 1c
- Informed consent provided by participant or POA
- English speaking

Exclusion Criteria:

- Severe aphasia limiting ability to express needs or discomfort verbally or nonverbally
- Severe behavioral neglect as determined by a score of ≥ 21 on Catherine Bergego Scale (CBS) via the Kessler Foundation-Neglect Assessment Process (KF-NAP)[16]
- History of prior stroke
- Concurrent neurologic condition (i.e PD, TBI, MS, etc.)
- History of peripheral nerve injury
- Joint contracture or significant spasticity in the lower limbs (Modified Ashworth Scale ≥3)
- Severe knee, hip, or ankle osteoarthritis
- Severe osteoporosis as indicated by physician medical clearance
- Open wounds on surfaces in contact with exoskeleton or harness
- Unstable spine or unhealed fractures
- Weight bearing precautions
- Unresolved deep vein thrombosis (DVT)
- Concurrent participation in other lower limb research studies that according to the PI is likely to affect study outcome or confound results
- Pregnancy

EksoNR Exclusion Criteria[17]:

- Weight >220 lbs (100 kg)
- Height below 60 inches or above 76 inches
- Standing hip width of approximately 18 inches or more
- Joint contractures or range of motion deficits that limit normal range of motion during ambulation
    - Knee flexion contracture greater than 12°
    - Hip flexion contracture greater than 17°
    - Inability to achieve 0° neutral ankle dorsiflexion with knee flexion up to 12°
    - Bilateral hip flexion less than 110°
- Leg length discrepancy
    - Greater than 0.5 in. (1.27 cm) for upper legs
    - Greater than 0.75 in. (1.91 cm) for lower legs
- Active heterotopic ossification
- Significant spasticity in the lower limbs (Modified Ashworth Scale ≥3)
- High anxiety or claustrophobia
- Clostridium difficile or other gastrointestinal isolation precautions
- Colostomy
- Uncontrolled autonomic dysreflexia
- Lower limb prosthesis

VULNERABLE POPULATIONS

We will recruit participants with communication deficits (i.e. aphasia) as a result of their stroke who are deemed safe to consent by their supervising medical and therapy team. For these participants, we will provide the necessary supported communication strategies to ensure the proper understanding of the experimental protocol and consent process prior to obtaining consent.

For those deemed unable to consent by their supervising medical and therapy team as a result of their stroke, we will obtain informed consent from their POA. We will ensure the POA understands the purpose of the study, the procedures, risks and benefits, and the participant's rights before providing informed consent on behalf of the participant.

PARTICIPANT POPULATION(S)

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question
Local	Adults with stroke + CPB	45	30
Study-wide			
Total:		45	30

RECRUITMENT METHODS

This study will involve recruitment of individuals with stroke from the inpatient units at the Shirley Ryan AbilityLab. Clinicians at this location will be informed of the inclusion and exclusion criteria for this study in order to refer appropriate participants to the study coordinators. Information regarding this study will be posted on the Shirley Ryan AbilityLab webpage detailing available research studies. Authorized research personnel will identify and screen potential research participants based on inclusion and exclusion criteria using the Cerner application. After identification of participants based on inclusion and exclusion criteria, a verbal permission from the participant will be obtained to request medical clearance from their physician.

COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES

Participants will not receive compensation for participation in this study.

WITHDRAWAL OF PARTICIPANTS

Participants may be withdrawn from the study without their consent if there are any safety concerns for continued participation. This may be due to a change in medical status or inability to follow the outlined study protocol at any point during the study.

Participants may withdraw from the research study voluntarily at any time. Once the participant has revoked consent, he/she cannot continue to participate in the study. Data collected until point of withdrawal will be maintained. The research team may request reason for withdrawal to monitor study participant attrition.

To revoke consent, the participant must do so in writing to the PI, Dr. Arun Jayaraman. Participants can call the PI at (312)238-6875 if assistance is needed in this process.

RISKS TO PARTICIPANTS

Risk minimization:

Procedures are in place to minimize risk to the human participants. There are minimal risks or side effects associated with using exoskeletons or standard physical therapy care. We will be following hospital/facility safety precautions throughout the study. All clinical assessment and intervention sessions will be under the supervision of a trained researcher and/or physical therapist. Manual assistance or cueing will be provided as necessary for safety and balance. All participants will be permitted to stop physical activity or rest at any time during the study.

EksoNR exoskeleton:
The EksoNR exoskeleton used in this study is commercially available and approved for use by the FDA in this population. The physical therapists operating this device completed formalized training to ensure the proper safety measures are taken to minimize any risk to the participants. Safety procedures include setting range of motion values in the controller, ensuring proper setup within the exoskeleton, monitoring skin tolerance pre/during/post treatment, and knowledge of the emergency protocol when using the EksoNR. Additionally, the EksoNR is equipped with an emergency stop feature to protect the participant during use. The therapists will closely monitor device function throughout the research study.

Muscle soreness or joint pain:
There is a possibility of muscle and/ or joint discomfort as a result of exercise and utilization of the exoskeleton or safety harness. This risk will be minimized through close monitoring of participant feedback by licensed physical therapists throughout all training sessions. In addition, adjustments to the sizing, placement of protective padding, and the amount of therapist assistance can be modified during exoskeleton or harness use. The physical therapists guiding the testing and intervention sessions are trained in how to safely progress the participant to more dynamic and complex activities. Adequate rest periods will be provided per participant request or based on physical therapist judgement.

Fall risk:
Individuals with stroke may be at increased risk for falls when performing functional tasks due to impaired strength, sensation, and balance. It is anticipated that fall risk will not be significantly increased when performing functional tasks in this study. The most appropriate assistive devices and/or bracing will be used to minimize fall risk. In addition, functional tasks will be performed in a harness or with a gait belt with licensed physical therapists closely assisting at all times.

Skin and soft tissue injury:
There may be a risk for skin abrasion, bruising, or discomfort from use of the exoskeleton or safety harness. This risk may be increased for individuals with neurologic conditions due to impaired sensation. Trained personnel will apply and remove the exoskeleton and safety harness to ensure proper alignment. Personnel will also perform skin checks at all areas of contact following each use of the exoskeleton, harness, or standard of care lower extremity bracing (i.e ankle foot orthosis). Participants will be educated to notify personnel immediately of any discomfort during tasks; the tasks will be discontinued and personnel will evaluate the source of discomfort.

Vitals:
Participants in this study are in the inpatient setting following acute stroke diagnoses. As a result, participants may be at risk of fluctuations in cardiovascular response to exercise. We will be checking vital signs including blood pressure, heart rate, and oxygen saturation level throughout each session. If heart rate surpasses 90% of age-predicted heat rate maximum , and/or blood pressure levels surpass 170 systolic and 100 diastolic, a seated rest break will be initiated. If these levels continue to be elevated, the session will be discontinued, and the on-site attending physician will be immediately contacted. Physical therapists administering the intervention protocol have access to nursing and medical staff at all times.

POTENTIAL BENEFITS TO PARTICIPANTS
Research has shown that gait training interventions may lead to significant improvements in mobility and function.[1,15] There is the potential for participants in this study to experience the

same benefits. These outcomes have implications that outweigh the minimal risks (See Risks to Participants section) that are associated with participation.

DATA MANAGEMENT AND CONFIDENTIALITY
All personal information (names, addresses, email, phone numbers, etc.) gathered for this study that can identify participants will be kept secure to protect their privacy and will never be shared with any person or entity at any time. Data collected during the study and shared with others will reference participants only by an alphanumeric code. The “master list” linking personal information to the alphanumeric code will not be shared and will be kept in a secure location.

PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFEY OF PARTICIPANTS
Keeping the confidentiality of all data collected through this study is paramount. As a result, we have devised numerous procedures to ensure the privacy of the participants. Data will be de-identified so information cannot be linked to the participants. Behavioral and functional data collection will take place at the Shirley Ryan AbilityLab. There will be no recordings conducted outside of this institution.

Data storage:
All research data is recorded with a participant code that does not contain personally identifiable information. All personally identifiable information is stored in a locked cabinet within the laboratory and only authorized personnel listed on this IRB will have access to them. There will be no collection of criminal behavior or other potentially sensitive information. Information on the computer will be encrypted and password protected**.** After the study has been completed, we will preserve all study information on a secure and encrypted computer for possible further testing and comparison with future studies. There is no scheduled date on which participant data will be destroyed.

Length of data storage:
De-identified data may be stored indefinitely. Records with identifiable data will be destroyed at the end of the study. Video tapes for educational purposes with the consent of the participant may be kept indefinitely.

Data access:
Only authorized personnel listed on this IRB will have access to the data.

Process for releasing data:
During and after the study, all study records will be assigned a code to protect the confidentiality of the participant’s personal information. The information will be labeled with an unidentifiable code to reduce the risks to participant privacy.

Once research information has been collected, we may share some of it. Any research information shared with people outside of Shirley Ryan AbilityLab/Northwestern (NU) will not contain the participant’s name, address, telephone, or social security number, or any other direct personal identifier unless disclosure of the direct identifier is required by law [except that such information may be viewed by the Study sponsor and its partners or contractors at the Principal Investigator's office]. Research information may be shared with:

- Authorized members of NU and the Shirley Ryan AbilityLab workforce, who may need to see participant information, such as administrative staff members from the Office of Research, and members of the Institutional Review Board (a committee which is responsible for the ethical oversight of the study)

- Other University research centers and University contractors who are also working on the study
- Study monitors and auditors who make sure that the study is being done properly,
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS)

PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS

Steps taken to protect privacy of participants:

The participants will only provide personal information to the study personnel listed on the IRB. All data is obtained specifically and solely for research purposes. The data is made unidentifiable by using anonymous participant codes to minimize the risk to the participants' privacy. Behavioral and functional data will be the only form of research material obtained from individually identifiable living human participants. Human participant personal information (name, contact information) and medical information necessary to the study (age, sex, possible diagnoses, medications) will be taken during recruitment. All recordings are kept in a secure computer, non-accessible to other investigators other than the ones listed on the protocol. All information regarding experimental participants, including consent forms, will be kept in a locked file cabinet. There will not be any type of collection of sensitive data, such as sexual, criminal, or illegal behavior.

Steps taken to ensure participant comfort:

To ensure that participants feel at ease, the purpose of the study in addition to the procedures will be clearly described. At the beginning of each session, the relevant procedures are reviewed with the participant. Throughout the study, there will be open communication between the participant and the research staff, and the study will be stopped should the participant feel uncomfortable with any of the questions or procedures that are part of the protocol.

Research staff permissions:

All study staff are CITI certified and all information and records are in compliance with HIPAA rules.

COMPENSATION FOR RESEARCH-RELATED INJURY

If the participant gets an injury or illness as a result of study, the participant is required to promptly notify the PI or research personnel of the study about the illness or injury. The hospital [Researchers, Shirley Ryan AbilityLab, Northwestern University, and all affiliated clinical sites] will not pay for medical care required because of a bad outcome resulting from participation in this research study. However, this does not keep participant from seeking to be paid back for care required because of a bad outcome.

ECONOMIC BURDEN TO PARTICIPANTS

There is no anticipated economic burden to the participants since they will be inpatients and the study will occur in the same building. Participants will not receive compensation for their participation in this study.

CONSENT PROCESS

Prior to enrollment into the study, the participant will be provided an explanation of the study and the opportunity to review the consent form. Once this is complete and research personnel ensures the participant understands the implications of participating in this study, informed consent will be obtained from the participant with their signature on the IRB-approved consent form. In order to participate in the study, the consent form must be signed and dated by the

participant and the research personnel who completed the consenting discussion. If any changes to the protocol are made, participants will be consented with an updated consent form.

Adults able to consent:
For participants with stroke, informed consent will be obtained by the PI or any trained licensed physical therapist prior to completion of study protocol. We will ensure the participant understands the purpose of the study, the procedures, risks and benefits, and rights as a research participant, and he/she can provide informed consent. Participants able to make their own decisions regarding research participation will be allowed to discuss with other appropriate parties prior to giving informed consent. Participants will not be openly encouraged to participate in the research or told that there is any expected benefit from the experimental interventions during participation. Participants will have access to research staff to assist with any questions or concerns until understanding is achieved to the judgment of the individual asking the question. If a participant refuses participation, no further contact will be made.

Adults able to consent who have communication deficits:
For participants who demonstrate communication deficits (i.e. aphasia) but who are deemed safe to consent by their supervising medical and therapy team, we will provide necessary supportive communication strategies to ensure proper understanding of the consent process prior to obtaining consent.

Adults unable to consent:
For those deemed unable to consent by their supervising medical and therapy team as a result of their stroke, we will obtain informed consent from their POA. We will ensure the POA understands the purpose of the study, the procedures, risks and benefits, and the participant's rights before providing informed consent on behalf of the participant.

Process to document consent in writing:
Informed consent will take place at Shirley Ryan AbilityLab on the inpatient floors with authorized study personnel.

Trained research personnel will guide the participant through consenting process. The participant will be given detailed explanation of the purpose, timeline, commitment, procedures, data handling, privacy, and confidentiality of information pertaining to the study.

For all participants, we will obtain written consent as usual. The signed consent form will be stored in a locked cabinet for the duration of the study. Our consent document has been uploaded to the eIRB folder.

NON-ENGLISH SPEAKING PARTICIPANTS
The study will only recruit participants who are fluent in English because all tests and instructions are administered in English.

PROTECTED HEALTH INFORMATION (PHI AND HIPAA)
Participant records will be kept completely confidential. Every possible precaution will be taken to protect the privacy interests of participants. Participation in this study is completely voluntary. Trained research personnel will explain the purpose of the study, the intended use of a participant's medical information, and the precautions taken to keep the study information and data confidential. Data will be collected and kept confidential and compliant with HIPAA standards.

Participants will be assigned an alphabetical or numerical study identification number. Identifying data will be kept in locked cabinets and password protected servers completely separate from de-identified data. Research data will be de-identified and stored in locked cabinets in the lab accessible only to authorized research personnel. Electronic data will be de-identified and kept on secure, password protected servers at the Shirley Ryan AbilityLab. Only authorized research staff will be able to access any of the formerly mentioned data. De-identified data will be kept indefinitely.

Study documentation will be collected and stored and kept confidential and compliant with HIPAA requirements.

All personal information (names, addresses, email or phone numbers, etc.) gathered for this study that can identify participants will be kept secure to protect their privacy and will never be shared with any person or entity at any time. Data collected during the study and shared with others will reference participants only by an alphanumeric code. The “master list” linking personal information to the alphanumeric code will not be shared and will be kept in a secure location.

QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE
Describe other resources available to conduct the research:
The Shirley Ryan AbilityLab services the stroke poption at a rate of approximately 300 new patients per year. The Shirley Ryan AbilityLab is a research hospital that maintains a research registry (greater than 750 participants). We will recruit inpatients to meet our enrollment goal and perform all research on site at the flagship hospital. The study team members are all employees of the Shirley Ryan AbilityLab. They are familiar with the study site and are experienced with the study population. There will be medical resources including a resident on call and nursing staff available 24 hours a day if needed in case of an emergency.

All study team members will be trained on the study protocol and procedures and have already been trained on how to safely administer all functional outcomes using standardized methods. The research staff consists of clinical researchers and licensed physical therapists trained in the safe use of therapeutic equipment, including the harness system used for locomotor training in the overground gait track and over all treadmills, gait belt use for assessments, and emergency management of the EksoNR exoskeleton. In addition, three therapists within the Legs + Walking team have completed both Part 1 and Part 2 of the EksoNR standardized training program. Experienced physical therapists will lead the assessment and treatment sessions. Finally, all research and therapy staff members have been CITI-certified and have Basic Life Support (BLS) training.

The PI of this study, Arun Jayaraman, PT, PhD, is Director of the Max Nader Center for Rehabilitation Technologies and Outcomes (RT&O Lab), within the Center for Bionic Medicine. Adequate dedicated office space is available for private meetings with potential participants, performing physical evaluations, explaining the study protocol, obtaining study consent, performing data analysis, and writing manuscripts.

Feasibility of recruiting the required number of suitable participants within the agreed recruitment period:
The planned number of participants is relatively small. Therefore, recruitment is not a concern.

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