NewGait: A Low-Cost Rehabilitation System to Improve Post-Stroke Gait (Biomechanical Adaptations)

NCT06269367

Date of IRB Approval: February 5, 2024

Background

Post-stroke gait recovery is a significant rehabilitation challenge. Stroke is the leading cause of long-term adult disability worldwide.[1] By 2030, nearly 4% of the US population is expected to have had a stroke, leading to an estimated cost burden of ~$184B.[2] Even after completion of therapy, up to 80% of stroke survivors experience significant gait impairment.[3-5] Several gait therapies (e.g., treadmill training, split-belt training, robotic training) have been established;[6-18] however, recovery after these interventions is modest at best, and results vary from significant to minimal improvement.[19] Therefore, there is a critical need for rigorous science-based approaches to effectively address post-stroke gait deficits.

Metric	NewGait	ReWalk ReStore	Theratogs Full Body System	Therasuit
Power source not required	✅	❌	✅	✅
Targets multiple joints	✅	❌	✅	✅
Design based on biomechanical modeling	✅	✅	❌	❌
Specifically designed for post stroke adults	✅	✅	❌	❌
Can provide both assistance and resistance	✅	❌	✅	✅
Plantarflexion assistance	✅	❌	❌	❌
Modular Design	✅	❌	✅	❌
Can be worn under clothing	✅	❌	❌	❌
Retail cost	$500	$28,900	$1,449	$2,600

Fig. 1 Chart comparing NewGait to existing devices.

Current comparable solutions are limited to a single joint, expensive, and/or ineffective: Consumers can choose a variety of devices for post-stroke gait training, but many barriers to adoption exist, especially for those that are economically disadvantaged. While there is a wide range of gait devices, from ankle foot orthoses (AFOs) to powered exoskeletons, the focus of our comparison will be on other lightweight and "low-cost" devices (Fig. 1). Regular AFOs, though simple and cost-effective, may lead to disuse atrophy[20,21] and reduce gait efficiency by decreasing Achilles tendon excursion and propulsive forces during walking.[22,23] Further, they only target the ankle joint, whereas the hip, knee, and trunk play an important role in gait and balance. TheraTogs (Fig. 2a) and TheraSuit (Fig. 2b) closely resemble our current technology (NewGait). However, these devices primarily target the pediatric market (although adult versions exist) and evidence for these devices is of low quality.[24] Both devices fit like close-fitting clothing, which increases donning and doffing time. They are also 3-5x more expensive than typical Medicare reimbursement rates for conventional AFOs,[25] which reduces the likelihood of insurance coverage and affordability. ReWalk ReStore is a powered, soft robotic exosuit for ankle plantarflexion and dorsiflexion assistance[24] (Fig. 2c). Though effective in improving gait speed, it is a relatively large and expensive device (~$30K) and only *assists* the ankle joint. Thus, there is a significant unmet need for an effective, affordable, and portable, gait mobility/rehabilitation device for stroke survivors.

Fig. 2 Comparable devices.

Prior research suggests that rehab interventions need to be intense,[26,27] highly repetitive,[27-29] and task-oriented[30] to induce neuroplasticity[31,32] – a key element for long-lasting gait recovery. Yet, an average stroke patient spends only ~20% of their physical therapy time on gait-oriented activities.[33] The dosage of therapy could be increased substantially if therapy can be transferred outside the clinic; however, most therapeutic solutions are only assistive (thus, not intense) and

too costly for use in a patient's home. Moreover, most low-cost commercial solutions are not designed based on end-user feedback and biomechanical data, which limits usability and optimal patient outcomes. Hence, many current approaches show clinically small and unsustainable improvements in gait and mobility after the stroke.[34,35] Given that repetitive and intensive treatments that challenge the central nervous system are crucial for inducing neuroplasticity and promoting gait recovery after stroke,[35] a therapeutic solution that caters to user needs and is widely adapted is needed to create a paradigm shift in post-stroke rehabilitation.

Our solution. We will leverage the existing wearable, gait system (**NewGait**) and refine it for post-stroke gait rehabilitation based on end-user feedback and biomechanical modeling. The current device (costs $520; Fig. 3) is highly preferred by clinicians and used in patient populations suffering from a wide range of neurological conditions, including stroke, multiple sclerosis, and Parkinson's disease. Our preliminary data show that NewGait induces biomechanical gait adaptations and improves gait and balance in stroke survivors. However, feedback from clinicians has indicated the need for design improvements. Further, it is currently unknown how our device performs against our immediate competitors (such as TheraTogs, TheraSuit, TripleFlex, or other similar devices). Hence, in this STTR Phase-I, we propose to perform biomechanical experiments, and compare the short-term adaptations and usability with other comparable devices. Successful completion of this project will provide much-needed data for improving customer experience, boosting sales, acquiring new markets, and more.

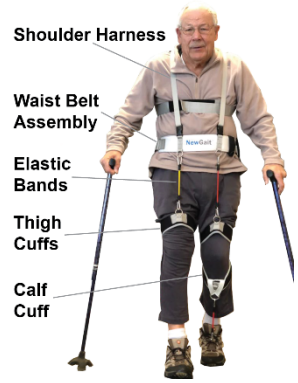

Fig. 3 The NewGait system

Study Aims

Significance. Restoration of gait function is a major goal in post-stroke rehabilitation, yet most stroke survivors experience significant gait deficits when discharged from physical therapy. Current evidence suggests that intense, highly repetitive, and task-oriented rehabilitation interventions are essential to promote optimal neuroplasticity—a critical factor for long-lasting gait recovery. Accordingly, several therapeutic solutions involving specialized treadmills, robotic devices, and exosuits have been designed to induce neuroplasticity and post-stroke gait recovery. However, these gait training devices are typically expensive and bulky, making them less accessible to most clinics and patients. As a result, stroke survivors do not receive adequate dosage of gait therapy to achieve meaningful clinical improvements, creating a significant clinical need for new and efficient strategies to increase therapy dosage. While some lightweight and "low-cost" commercial devices exist (e.g., TheraSuit, TheraTogs, TripleFlex, or other similar devices), they are not often designed based on multi-user feedback and robust biomechanical data and their clinical utility have not been tested in stroke survivors, thereby limiting usability and effectiveness. All these limitations create barriers to access for effective gait training, particularly for economically disadvantaged and rural populations. Thus, there is a significant unmet need for an

effective, affordable, and portable gait mobility/rehabilitation device that permits evidence-based gait training accessible to most stroke survivors.

Innovation. We will develop an optimized wearable system based on an innovative human-centered design approach (design sprints and think aloud technique) and biomechanical simulations and test its clinical utility for post-stroke rehabilitation. The device is non-powered, lightweight, low-cost, and built to be more accessible to the general stroke population. Our modular design will promote adoption by allowing users to change configurations based on patient needs.

Phase I Goals. Our interdisciplinary team will (1) identify the optimal biomechanical design with improved usability based on end-user feedback and musculoskeletal modeling, (2) refine the current NewGait prototype to meet stroke-specific needs, and (3) perform a comparative clinical feasibility study to establish the clinical potential of the NewGait device in comparison with other comparable devices.

Aim 1: Identify an optimal NewGait design based on end-user feedback and musculoskeletal modeling. *Aim 1a*. We will obtain end-user preferences and requirements through a series of human-centered design sprints with stroke survivors and their caregivers, and physical therapists, to inform potential design changes. ***Aim 1b*.** We will simulate subject-specific NewGait training for walking using a rigorously vetted musculoskeletal modeling software (OpenSim) to identify the effect of various design configurations on post-stroke gait mechanics. We will also investigate the effects of pertinent geometric and material parameters on lower-extremity joint moments and powers using inverse dynamics. Muscle activation effects will be quantified using computed muscle control. ***Milestones*:** 1) Determine end-user preferences and requirements for a stroke-specific NewGait design; and 2) using musculoskeletal modeling, produce a look-up table to provide changes in joint moments, powers, and muscle activations as a function of length, stiffness, and attachment points of the elastic bands.

Aim 2: Refine the current prototype and perform benchtop testing to validate durability. We will refine the current NewGait prototype to meet stroke-specific needs and validate its mechanical behavior during repeated cyclical loading via extensive benchtop testing of the interfaces between the straps, anchor points, and elastic bands. We will also perform fatigue analysis to evaluate durability. ***Milestones:*** Produce a light-weight, durable prototype that satisfies end-user preferences and modeling results.

Aim 3: Examine short-term gait adaptations and clinical feasibility in stroke survivors. We will conduct a pilot randomized, crossover study comparing NewGait with comparable devices based on short-term biomechanical adaptations, clinical feasibility, and adoption potential for day-to-day activities in chronic stroke survivors. Outcomes will be evaluated at three levels: 1) biomechanical (gait mechanics); 2) neurophysiological (muscle activation, and coordination); and 3) clinical (walking speed), which will help establish the mechanistic underpinnings of training-related adaptations. We will gather end-users' feedback on the usability, comfort, and satisfaction between devices. ***Milestones:*** Obtain and compare (a) gait mechanics, muscle activation, and gait

speed data between NewGait and competitors' devices, and (b) participant feedback on usability, comfort, and satisfaction for the NewGait and competitive devices.

Phase-I Impact. This Phase-I STTR project will improve the current device based on end-user feedback and musculoskeletal modeling and demonstrate the clinical potential of NewGait for restoring gait function in stroke survivors against its comparable, competitive devices. The results will also provide insights into the mechanistic basis for gait adaptations following NewGait training. The resulting data will support an STTR phase II grant, where the long-term effects of the NewGait will be assessed in a large-scale randomized control trial.

Note that Aim 1a is exempt project and we have a separate exempt 3 IRB approval (HUM00221923). Aim 2 is not a human subjects study. Aim 3 is a clinical trial based on NIH definition of a clinical trial. All devices that are used in the training are considered to be class 1 510(K) exempt devices.

This study will not meet the Food and Drug Administration Amendments Act (FDAAA) of 2007 (FDAAA 801) definition of an "applicable clinical trial" as the studied devices are not subject to section 510(k), 515, or 520(m) of the FDC act.

We note that the devices used in this study will fall into a generic category of Class I 510(k) exempt devices as defined by 21 CFR Parts 862-892 and would not require FDA review. These devices would come under one of the following categories: (1) Limb Orthosis (regulation no. 890.3405) and (2) Truncal Orthosis (regulation no. 890.3490), (3) Nonmeasuring exercise equipment (regulation no. 890.5370), (4) Daily Activity Assist Device (regulation no. 890.5050). Many of the commercial robotic devices (Lokomat, Armeopower, Armeospring, etc.) that are powered and actuated using motors are also 510(k) exempt under regulation no. 890.1925 (Isokinetic testing and evaluation system).

Methods

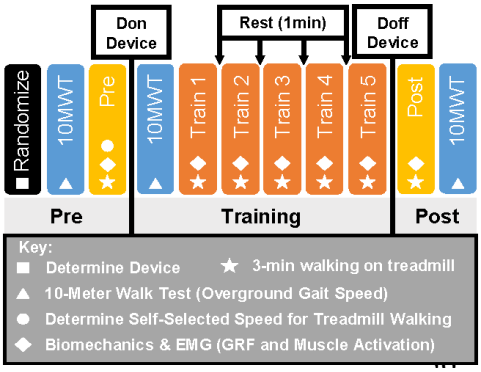

Fig. 4 A schematic of the testing protocol. GRF = ground reaction forces

The acute effects of NewGait training will be studied using a pre-post randomized crossover study design in individuals with chronic stroke (Fig. 4). Participants will serve as their own control and undergo training with NewGait, and other comparable control devices on the same or different days. The training session order will be randomized. Outcomes will be evaluated at three levels: 1) *biomechanical* (gait mechanics); 2) *neurophysiological* (changes in EMG activity and muscle coordination using synergy analysis); 3) *clinical* (changes in gait speed). Our primary outcomes are changes in a) gait speed and b) ankle muscle activation. Our secondary outcome measure is changes in paretic leg propulsive force. Our other outcome measures are

muscle coordination, other lower extremity muscle activation, and paretic leg loading. Finally, we will conduct brief in-person interviews at the end of each session to collect feedback on usability, comfort, satisfaction, and the potential for adoption of the device in their day-to-day activities.

Subjects and Recruitment: We anticipate that about 18 subjects will be needed to meet the primary endpoint. We will recruit 30 participants who are diagnosed with stroke to participate in this study to account for screening failure and drop-outs. Subjects will be recruited via face-to-face contact, email, public advertisements, posting on UMClinicalStudies.org website/social media, or through a stroke registry (IRB: HUM00099109). Additionally, subjects may be recruited from subject pools created through existing IRBs (HUM00073356, and HUM00087962). Subjects may be pre-screened to ensure their eligibility before coming to the lab.

Inclusion Criteria

1. Aged between 40 to 75 years
2. Unilateral cortical or subcortical stroke
3. Chronic stroke (≥ 6 months) At least 6 months following their stroke
4. Able to walk independently with/without assistive devices for 5-10 mins (~150m)
5. No significant cognitive deficits as determined by the Mini Mental State Examination (MMSE) score (score ≥ 22)

Exclusion Criteria

A subject is not eligible for inclusion if any of the following criteria apply:

1. Cerebellar stroke
2. Traumatic brain injury
3. History of unstable heart condition, uncontrolled diabetes or hypertension
4. History of a recent lower-extremity trauma or fracture
5. History of significant orthopedic or neurological conditions that could limit walking ability (e.g., multiple sclerosis, total knee replacement)
6. History of significant spatial neglect
7. Joint contractures or significant spasticity in the lower-extremity
8. History of a recent Botulinum Toxin (Botox) injection to the lower-extremity muscles (≤ 3 months)
9. Pregnant or actively planning to become pregnant (self-reported)
10. Inability to communicate or unable to consent

We do not plan to exclude subjects based on stroke severity/impairment or stroke location as a post-hoc analysis would inform us on appropriate patient population selection for future interventional studies. We note that the risks of participating in the study do not change based on the severity or location of the stroke,[36,37] There are no imaging requirements for the study subjects and interpretation (performed using chart reviews, medical records, or by the stroke physician) of the images (if available through medical records) will be used only to characterize the lesion location, severity, and type of injury for publication purposes.

Experimental Procedures

The experiment may consist of about 4 successful sessions/visits depending on subject's availability. Each session will last approximately 2-3 hours in duration. Participants may be required to undergo additional visits in the event of inability to complete a session for any reason (e.g., technical difficulty, equipment issues). Different conditions may happen on the same day or different, depending on the participant's ability and availability.

Screening, Orientation, and Informed Consent Visit: Subject will meet an authorized research personnel in the Neuromuscular and Rehabilitation Robotics Laboratory (NeuRRo Lab). During this visit, the participant will be provided with detailed information about the study, the risks and benefits of participation, and the nature of study procedures, including orientation to various testing devices used in this study. A study member will screen the subjects for the eligibility criteria using screening questionnaires and health related assessments including chart reviews. The screening process may be completed prior to coming to the lab through online questionnaire (e.g., RedCap) or phone calls. During the screening/orientation session, we will also orient the participant to the study procedures. We may also measure their muscle strength of various joints by having them perform maximal contractions against manual resistance or instrumented dynamometers. We may also have them walk on a treadmill to test their ability to walk and to perform a biomechanical evaluation. We may also measure their movement ability using standardized test procedures. These tests include 10-meter walk test, 6-minute walk test, clinical assessments like Fugl-Meyer evaluation, and balance assessments.

Experimental Paradigm

Once screening has been completed, we will begin recording baseline measurements of the subject's biomechanics and physiology.

Beginning of the Session

Using the methods and equipment noted above, we will measure the subject's spatiotemporal gait parameters. We will apply surface electromyography (EMG) sensors to many of the key muscles used in gait [e.g., vastus medialis (VM), rectus femoris (RF), medial hamstring (MH), lateral hamstring (LH), tibialis anterior (TA), medial gastrocnemius (MG), soleus (SO), and gluteus medius (GM)]. Typically, electrodes will be secured to the skin using self-adhesive tapes and cohesive flexible bandages. Electrode placement will be carried out according to the

guidelines established by the international SENIAM initiative (www.seniam.org). Should electrode positions be occluded by the device, electrodes will be placed over non-occluded but similar synergist muscles. The quality of the EMG signals will be visually inspected to ensure that the electrodes were appropriately placed. We will then apply reflective markers that can track their movements during walking.

Treadmill Walking

First, subjects will walk for about 10 meters overground so walking speed can be determined. Then, they will walk for a few minutes on the treadmill so that we can measure their normal biomechanics with or without feedback. A body-weight supporting harness may be used as an additional support in case the participant has substantial motor impairments or feels unsecure without the provision of supporting harness. Next, intervention or control device will be put on the participants based on a random selection. Because the mobility device is passive (i.e., does not add energy to the subject's movement, as a motor would) it is of minimal risk to the subject. Afterwards, another approximately 10 meter overground walk will be performed to determine walking speed. Then, about 5 trials will be recorded during which the participant will walk on the treadmill for a few minutes while biomechanics (e.g., kinematics and kinetics) and EMG activity and spatiotemporal gait parameters are being recorded. We may also provide feedback of their muscle activation or biomechanics (*e.g.,* kinematics, kinetics) during the trials to improve their engagement during the experiment. Afterwards, the device will be taken off and another approximately 3-minute walk on the treadmill will be recorded for post training measurements. At the end, the participant will walk overground for about 10-meters to determine gait speed.

End of the Session

After completion of data collection, participants will provide end-user feedback regarding the device. Subjects will be tested for their subsequent condition (*e.g.,* control condition) or asked to return to the lab for the subsequent sessions.

Paradigms and Assessments

The following tools may be used to quantify the biomechanical and neurophysiological effects of walking with assistive devices. <u>All assessment tools are noninvasive and are of minimal risk to the subject and have been previously approved by the IRB.</u>

1. <u>Muscle Activation and Coordination:</u> The magnitude of muscle activation and co-contraction of the antagonist muscles during testing will be measured using Electromyography (EMG) by means of noninvasive surface electrodes. Brands used in our lab include: (Trigno Wireless EMG, Delsys, Inc., Natick, MA, USA) and (Model MA-311, Motion Labs Systems, Inc., Baton Rouge, LA, USA). Previously accepted for use on human subjects in IRBs (HUM00081480, HUM00073356, HUM00130845, HUM00087962, and HUM00080244).

2. Kinematics and Kinetics: The subject's movement patterns, ground reaction forces, and joint moments during the experiment will be evaluated using instrumented treadmill and motion capture camera system or similar instruments (i.e., angle encoders or goniometers) and monitored over time to see how the subject walks with and without assistive devices. We will compare the subjects gait kinematics and kinetics for various assistive devices. Previously accepted for use on human subjects in IRB (HUM00073356, HUM00087962, and HUM00133860).
3. Spatiotemporal Gait Parameters: Mobility lab (APDM Inc.) – which measures temporal-spatial events and limb accelerations, or instrumented walkway/treadmill will be used to measure the subject's spatiotemporal gait parameters (e.g., gait speed, cadence, stride length, stride duration, etc.) before, during, and after assisted walking. Previously accepted for use on human subjects in IRB (HUM00087962).

Data Analyses

Gait Mechanics Testing. Ground reaction forces (GRFs) during walking will be collected on both legs using an instrumented treadmill. Surface EMG signals from the lower-extremity muscles will also be collected according to SENIAM guidelines. All evaluations will be performed at their self-selected walking speed.[38] Speed may be adjusted if the participant has difficulty in walking at their seif-selected speed. All biomechanical data (including EMG) will be time normalized to stance and swing phase of the gait cycle.[39-40] We will examine the changes (from baseline) in vertical and antero-posterior propulsive forces recorded during walking (with paretic-leg propulsive forces being the primary focus) and compared across conditions. Where feasible, we may also collect kinematic (e.g., joint angles) and kinetic (e.g., joint moment and power) data to evaluate training effects during walking.

Muscle Activation and Coordination during Gait. The mean EMG activity during walking will be evaluated to quantify the changes in lower-extremity muscle excitation due to the training. Apart from the amplitude-related EMG evaluation, muscle coordination will be studied using nonnegative matrix factorization (NMF)[41] as we have done previously.[42-44] Lower-extremity EMG data will be collected using standard protocols.[16,43,44] The raw EMG data will be band-pass filtered (20-500 Hz), rectified, and smoothed with a zero-phase low-pass Butterworth filter (2nd order, 6 Hz).[43,44] EMG data for each stride will be time/amplitude normalized and concatenated together. The similarity between the synergies will be computed by calculating the angle between the synergies and the independence of neural control signals (i.e., the ability to selectively activate muscles during gait) will be characterized by studying the number of muscle modes required to account for muscle activation during walking.

Clinical Measure: The 10-Meter Walk Test (10-MWT) will be performed using standardized clinical assessment procedures to evaluate changes in walking speed with training.[45,46] The individual will be instructed to walk at their self-selected pace on a 12-meter straight walkway,

while a stopwatch will be used to time the intermediate 10-meter walk (participants will be given one meter to accelerate and decelerate).

End-User Evaluation of Devices: End-user insights are extremely critical when designing novel rehab devices [47,48] however, there is very limited literature addressing common usability concerns for gait re/training or exoskeleton devices.[49] In this study, in addition to the assessment of gait mechanics, muscle activation, and walking speed, we will complement the clinical measures by assessing usability factors for each device, such as ease of use, comfort, satisfaction, perceived effectiveness, and potential for adoption in day-to-day activities. To collect these data, first we will observe the patient interacting with the device during the session and record time needed to don/doff the device, ability to follow instructions to use the device, questions they asked about the device or its use, any difficulties using the device, and device malfunctions. Following the treadmill walking with the device, we will interview the stroke survivor and caregiver about their experience with the device using a semi-structured interview format and Likert-scales. To design the interview guide and Likert scales, we will build on what we learn from design sprints and think aloud sessions during prototyping to ensure that we evaluate factors that end-users find most relevant for uptake and adoption of gait devices.

Statistical Analyses

Outcomes will be evaluated at three levels: 1) *biomechanical* (gait mechanics); 2) *neurophysiological* (changes in EMG activity and muscle coordination using synergy analysis); 3) *clinical* (changes in gait speed). Our primary outcomes are changes in a) gait speed and b) ankle muscle activation. Our secondary outcome measure is changes in paretic leg propulsive force. Our other outcome measures are muscle coordination, other lower extremity muscle activation, and paretic leg loading. Finally, we will conduct brief in-person interviews at the end of each session to collect feedback on usability, comfort, satisfaction, and the potential for adoption of the device in their day-to-day activities.

Linear mixed models (or other similar analysis) will be used to compare the primary, secondary, and other outcomes between NewGait and control/comparative devices/conditions. Participant's demographics (e.g., sex) may be used as a covariate. Exploratory linear regression analysis may be used to determine the association between changes in biomechanical and neurophysiological variables and changes in gait speed. For data collected on the end-user experience of each device, we will use complementary methods of analyzing qualitative and quantitative data.

This is a pilot study; hence, sample size is based on feasibility considerations. Using a two-sided test with a conservatively corrected α of 0.0167, 18 subjects will provide >80% power to detect significant differences with an effect size of 'f' of 0.40 (partial $\eta^2 = 0.14$) (GPower3.1).

Safety Considerations

The study procedures for this experiment are considered to be no greater than minimal risk. All procedures are noninvasive, the resistance methods are passive, and there are no children or vulnerable groups involved in this study. Almost all of the experimental testing procedures have been approved previously for use on human subjects (as a minimal risk procedure) in our other IRBs (HUM00133860, HUM00081480, HUM00073356, HUM00080244, HUM00130845, and HUM00087962). The potential risks for this study are described below:

Potential Risks

Surface EMG Related:

- *Allergic Reaction (infrequent):* Subjects may experience allergic reactions from the application of electrode paste and adhesive tapes necessary for surface EMG recordings. We will use hypoallergenic tapes to minimize allergic reactions. If redness or excessive itching occurs, the area will be monitored closely by study staff and testing will be ended at their discretion or in accordance with the subject's wishes.

Walking Related:

- *Spasms (Infrequent):* If subjects suffer from spasticity, the initial movement while walking with resistance may trigger muscle spasms. This will gradually settle down with time. The resistance will be adjusted if this occurs to ease the spasms.

- *Skin irritation (Infrequent):* Subjects may experience some skin irritation from the cuffs due to bracing attached to the limbs. If subjects experience irritation, adequate padding (coban or foam pads) will be provided between their skin and the cuffs to reduce the amount of irritation.

- *Tripping/Fall (Infrequent):* Subjects may trip if walking with resistance/assistance, especially if the subject has weak muscles. To minimize risk, subjects will be able to hold handrails, which increases stability while walking. We will also provide them with an option of wearing a body weight supporting harness to improve the feeling of safety during some activities. However, in our experience many people do not prefer wearing a harness, as the harness may produce some amount of discomfort while walking (a feeling of tight compression). Subjects may also experience tripping or falling during functional evaluation. However, these risks are no more than what they would encounter in their day-to-day activities. For safety purposes, the subject will always be under close supervision of a researcher while undergoing functional evaluation.

- *Muscle or joint pain (Infrequent):* During or following the experiment, subjects may feel temporary or persistent muscle aching or joint pain, or general fatigue. Any discomfort may be improved by adjusting the resistance, providing appropriate rest breaks at any time during the experiment, or using over-the-counter pain reliever.

- *Risk of fatigue (Likely):* There is a risk that subjects can become fatigued from walking with resistance for prolonged periods of time. Subjects will be allowed to rest and can also choose to end the test at their own will at any time. As with any research study, there may be additional risks that are unknown or unexpected. As described above, these risks will be minimized by allowing subjects to rest as needed and withdraw from the study voluntarily at any time. A research assistant will stand near subjects during the tests and will actively observe the subject for any distress. All devices will be built to eliminate risks of irritation or severe discomfort.

- *Muscle Fatigue or Soreness (Infrequent):* During measurement of muscle strength, subjects may experience temporary muscle fatigue and soreness. Although this soreness may persist for a period of several days following testing, this level of soreness is not greater than they would experience following a regular exercise session.

- Loss of privacy (Rare): A loss of privacy may occur from participating in this study. The seriousness of a breach of this information is minimal. All data and medical information collected from participants will be considered privileged and held in confidence; participants will be assigned confidential codes and no identifying personal data will be stored with study data. RedCap™ (Research Data Capture) system may be utilized for the storage of patient demographic information, clinical assessment scores, and all processed data via encrypted university computers. The raw/unprocessed data will be coded with a unique patient identifier and stored offline on a password protected laboratory computer.

- Unforeseeable Risks (Rare): As with any research study, there may be additional risks that are unknown or unexpected.

References:

1. GBD 2016 Stroke Collaborators. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol.* 2019;18(5):439-458.
2. Ovbiagele B, Goldstein LB, Higashida RT, et al. Forecasting the future of stroke in the United States: a policy statement from the American Heart Association and American Stroke Association. *Stroke.* 2013;44(8):2361-2375.
3. Duncan PW, Zorowitz R, Bates B, et al. Management of Adult Stroke Rehabilitation Care: a clinical practice guideline. *Stroke.* 2005;36(9):e100-143.
4. Li S, Francisco GE, Zhou P. Post-stroke Hemiplegic Gait: New Perspective and Insights. *Front Physiol.* 2018;9:1021.
5. Wade DT, Wood VA, Heller A, Maggs J, Langton Hewer R. Walking after stroke. Measurement and recovery over the first 3 months. *Scand J Rehabil Med.* 1987;19(1):25-30.
6. Duncan PW, Sullivan KJ, Behrman AL, et al. Body-weight-supported treadmill rehabilitation after stroke. *N Engl J Med.* 2011;364(21):2026-2036.
7. Jayaraman A, O'Brien MK, Madhavan S, et al. Stride management assist exoskeleton vs functional gait training in stroke: A randomized trial. *Neurology.* 2019;92(3):e263-e273.
8. Kesar TM, Reisman DS, Perumal R, et al. Combined effects of fast treadmill walking and functional electrical stimulation on post-stroke gait. *Gait Posture.* 2011;33(2):309-313.
9. Lewek MD, Braun CH, Wutzke C, Giuliani C. The role of movement errors in modifying spatiotemporal gait asymmetry post stroke: a randomized controlled trial. *Clin Rehabil.* 2018;32(2):161-172.
10. Madhavan S, Cleland BT, Sivaramakrishnan A, et al. Cortical priming strategies for gait training after stroke: a controlled, stratified trial. *J Neuroeng Rehabil.* 2020;17(1):111.
11. Nadeau SE, Wu SS, Dobkin BH, et al. Effects of task-specific and impairment-based training compared with usual care on functional walking ability after inpatient stroke rehabilitation: LEAPS Trial. *Neurorehabil Neural Repair.* 2013;27(4):370-380.
12. Reisman DS, McLean H, Keller J, Danks KA, Bastian AJ. Repeated split-belt treadmill training improves poststroke step length asymmetry. *Neurorehabil Neural Repair.* 2013;27(5):460-468.
13. Wade E, Winstein CJ. Virtual reality and robotics for stroke rehabilitation: where do we go from here? *Top Stroke Rehabil.* 2011;18(6):685-700.
14. Wu M, Hsu CJ, Kim J. Forced use of paretic leg induced by constraining the non-paretic leg leads to motor learning in individuals post-stroke. *Exp Brain Res.* 2019;237(10):2691-2703.
15. Wu M, Landry JM, Kim J, Schmit BD, Yen SC, Macdonald J. Robotic resistance/assistance training improves locomotor function in individuals poststroke: a randomized controlled study. *Arch Phys Med Rehabil.* 2014;95(5):799-806.

16. Washabaugh EP, Claflin ES, Gillespie RB, Krishnan C. A Novel Application of Eddy Current Braking for Functional Strength Training During Gait. *Ann Biomed Eng.* 2016;44(9):2760-2773.
17. Washabaugh EP, Krishnan C. A wearable resistive robot facilitates locomotor adaptations during gait. *Restor Neurol Neurosci.* 2018;36(2):215-223.
18. Krishnan C, Ranganathan R, Kantak SS, Dhaher YY, Rymer WZ. Active robotic training improves locomotor function in a stroke survivor. *J Neuroeng Rehabil.* 2012;9:57.
19. Teasell RW, Bhogal SK, Foley NC, Speechley MR. Gait retraining post stroke. *Top Stroke Rehabil.* 2003;10(2):34-65.
20. Hesse S, Werner C, Matthias K, Stephen K, Berteanu M. Non-velocity-related effects of a rigid double-stopped ankle-foot orthosis on gait and lower limb muscle activity of hemiparetic subjects with an equinovarus deformity. *Stroke.* 1999;30(9):1855-1861.
21. Lam WK, Leong JC, Li YH, Hu Y, Lu WW. Biomechanical and electromyographic evaluation of ankle foot orthosis and dynamic ankle foot orthosis in spastic cerebral palsy. *Gait Posture.* 2005;22(3):189-197.
22. Choi H, Bjornson K, Fatone S, Steele KM. Using musculoskeletal modeling to evaluate the effect of ankle foot orthosis tuning on musculotendon dynamics: a case study. *Disabil Rehabil Assist Technol.* 2016;11(7):613-618.
23. Yamamoto M, Shimatani K, Hasegawa M, Kurita Y. Effects of Varying Plantarflexion Stiffness of Ankle-Foot Orthosis on Achilles Tendon and Propulsion Force During Gait. *IEEE Trans Neural Syst Rehabil Eng.* 2020;28(10):2194-2202.
24. Almeida KM, Fonseca ST, Figueiredo PRP, Aquino AA, Mancini MC. Effects of interventions with therapeutic suits (clothing) on impairments and functional limitations of children with cerebral palsy: a systematic review. *Braz J Phys Ther.* 2017;21(5):307-320.
25. DMEPOS Fee Schedule. https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/DMEPOSFeeSched/DMEPOS-Fee-Schedule. Published 2021. Accessed.
26. Nelles G. Cortical reorganization--effects of intensive therapy. *Restor Neurol Neurosci.* 2004;22(3-5):239-244.
27. Hornby TG, Henderson CE, Holleran CL, Lovell L, Roth EJ, Jang JH. Stepwise Regression and Latent Profile Analyses of Locomotor Outcomes Poststroke. *Stroke.* 2020;51(10):3074-3082.
28. Butefisch C, Hummelsheim H, Denzler P, Mauritz KH. Repetitive training of isolated movements improves the outcome of motor rehabilitation of the centrally paretic hand. *J Neurol Sci.* 1995;130(1):59-68.
29. Cha J, Heng C, Reinkensmeyer DJ, Roy RR, Edgerton VR, De Leon RD. Locomotor ability in spinal rats is dependent on the amount of activity imposed on the hindlimbs during treadmill training. *J Neurotrauma.* 2007;24(6):1000-1012.
30. Bayona NA, Bitensky J, Salter K, Teasell R. The role of task-specific training in rehabilitation therapies. *Top Stroke Rehabil.* 2005;12(3):58-65.

31. Kleim JA, Jones TA. Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. *J Speech Lang Hear Res.* 2008;51(1):S225-239.
32. Reinkensmeyer DJ, Burdet E, Casadio M, et al. Computational neurorehabilitation: modeling plasticity and learning to predict recovery. *J Neuroeng Rehabil.* 2016;13(1):42.
33. Kuys SS, Ada L, Paratz J, Brauer SG. Steps, duration and intensity of usual walking practice during subacute rehabilitation after stroke: an observational study. *Braz J Phys Ther.* 2019;23(1):56-61.
34. Green J, Forster A, Bogle S, Young J. Physiotherapy for patients with mobility problems more than 1 year after stroke: a randomised controlled trial. *Lancet.* 2002;359(9302):199-203.
35. Cirstea CM. Gait Rehabilitation After Stroke: Should We Re-Evaluate Our Practice? *Stroke.* 2020;51(10):2892-2894.
36. Demirtas-Tatlidede A, Alonso-Alonso M, Shetty RP, Ronen I, Pascual-Leone A, Fregni F. Long-term effects of contralesional rTMS in severe stroke: Safety, cortical excitability, and relationship with transcallosal motor fibers. *NeuroRehabilitation*. 2015;36(1):51-59. doi:10.3233/NRE-141191.
37. Kirton A, deVeber G, Gunraj C, Chen R. Cortical excitability and interhemispheric inhibition after subcortical pediatric stroke: Plastic organization and effects of rTMS. *Clin Neurophysiol*. 2010;121(11):1922-1929. doi:10.1016/j.clinph.2010.04.021.
38. Bejek Z, Paroczai R, Illyes A, Kiss RM. The influence of walking speed on gait parameters in healthy people and in patients with osteoarthritis. *Knee Surg Sports Traumatol Arthrosc.* 2006;14(7):612-622.
39. Lepley AS, Gribble PA, Thomas AC, Tevald MA, Sohn DH, Pietrosimone BG. Longitudinal Evaluation of Stair Walking Biomechanics in Patients with ACL Injury. *Med Sci Sports Exerc.* 2016;48(1):7-15.
40. McLean SG, Fellin RE, Suedekum N, Calabrese G, Passerallo A, Joy S. Impact of fatigue on gender-based high-risk landing strategies. *Med Sci Sports Exerc.* 2007;39(3):502-514.
41. Tresch MC, Cheung VC, d'Avella A. Matrix factorization algorithms for the identification of muscle synergies: evaluation on simulated and experimental data sets. *J Neurophysiol.* 2006;95(4):2199-2212.
42. Augenstein TE, Washabaugh EP, Remy CD, Krishnan C. Motor Modules are Impacted by the Number of Reaching Directions Included in the Analysis. *IEEE Trans Neural Syst Rehabil Eng.* 2020;28(9):2025-2034.
43. Ranganathan R, Krishnan C, Dhaher YY, Rymer WZ. Learning new gait patterns: Exploratory muscle activity during motor learning is not predicted by motor modules. *J Biomech.* 2016;49(5):718-725.
44. Ranganathan R, Krishnan C. Extracting synergies in gait: using EMG variability to evaluate control strategies. *J Neurophysiol.* 2012;108(5):1537-1544.
45. Rehabilitation Measures Database. https://www.sralab.org/rehabilitation-measures. Published 2021. Accessed July 24, 2021.

46. Washabaugh EP, Kalyanaraman T, Adamczyk PG, Claflin ES, Krishnan C. Validity and repeatability of inertial measurement units for measuring gait parameters. *Gait Posture.* 2017;55:87-93.
47. Bonato P. Clinical applications of wearable technology. *Annu Int Conf IEEE Eng Med Biol Soc.* 2009;2009:6580-6583.
48. Olatunji S, Oron-Gilad T, Sarne-Fleischmann V, Edan Y. User-centered feedback design in person-following robots for older adults. *Paladyn, Journal of Behavioral Robotics.* 2020;11(1):86-103.
49. Bae J, Rossi SMMD, Donnell KO, et al. A soft exosuit for patients with stroke: Feasibility study with a mobile off-board actuation unit. Paper presented at: 2015 IEEE International Conference on Rehabilitation Robotics (ICORR); 11-14 Aug. 2015, 2015.
.