Pilot study of Powered Exoskeleton Use for Gait Rehabilitation in Individuals with Multiple Sclerosis

PI: Francois Bethoux
Co-investigators: Matthew Sutliff
Randy Karim
Robert Bermel

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Background

Powered exoskeletons are approved by the FDA to assist in the rehabilitation of persons with spinal cord injury and post-stroke hemiplegia, but not multiple sclerosis (MS). We are aware of only one pilot study of a powered exoskeleton (ReWalk®) in MS. Thirteen persons with MS and EDSS 5.5 to 7.0 were enrolled, and 5 were able to tolerate the device. Skin issues were the most frequent adverse event. Qualitative improvement of sitting, standing, and walking posture was noted in those who used the device consistently. We are not aware of any study of the EksoBionics GT exoskeleton in MS.

Device

The EksoGT is a powered motorized orthosis intended to enable individuals who are experiencing muscular or neurological conditions affecting their lower extremities to perform ambulatory functions such as gait training. (See Figures 1 and 2.) It consists of a fitted metal brace that supports the legs, feet, and torso. It is adjustable to accommodate different length segments and different hip widths. Typically, a physical therapist straps the patient's feet, legs, and torso into the device. Soft goods (pads, spacers, straps, and supports) are available for bracing and adapting to various body types. The straps and soft goods are specifically designed to prevent pressure points or other skin issues. There is also a link (Don-Doff Link) just below each hip joint, which permits abducting the legs while seated to facilitate donning and doffing the device.

Figure 1: The EksoGT in use during gait training of an SCI patient.

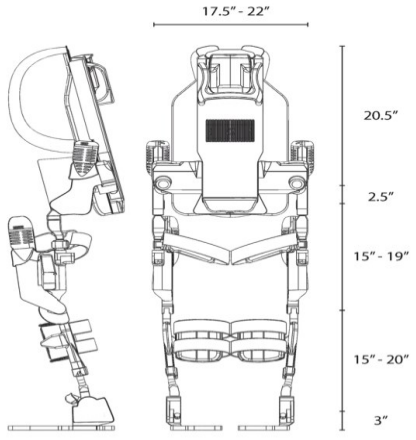


Figure 2: The EksoGT structure and general dimensions.

The EksoGT manipulates the patient's legs and waist to stand up, walk over level ground, and then to sit down. Battery powered motors drive knee and hip joints. The batteries are designed to last for

approximately three hours of normal use. The patient is required to assist with balance and body positioning using a cane, crutches, or walker, which are provided with the device. The physical therapist operates the device and monitors the patient to ensure balance is maintained. The device is operated in various modes. In some modes, steps are triggered with the attached user interface. In other modes, steps are triggered when the machine is in certain target postures. In other modes, the therapist may adjust the level of assistance provided so that, if the patient has some residual strength, the patient performs some of the walking motion with their own muscles.

The EksoGT has a number of features to ensure patient safety. It is equipped with mechanical hard stops at the limits of healthy Participant ranges of motion to prevent powering the joint of the user to a position that the joint cannot reach. The actuated range of motion at the hip is -20° to 135° and the actuated range for the knee is 0° to 120°. Not all of this range of motion is needed in normal walking; however the ranges of these joints were selected to provide for other necessary functions such as standing and sitting. At the ankle the device is passive, with springs to resist sagittal plane motion, and locked in the other degrees of freedom. The range of motion provided at the ankle is from -10° to 20° dorsiflexion with hard stops at the limits of this range to protect the user and a setting to specify the neutral angle.

Redundant position sensing on all of the actuated joints ensures that the motors are always controlled using reliable sensor information. In addition, the device has numerous sensor, motor, and software monitoring systems. If any abnormality is detected (i.e. excess joint speed or force, or if redundant sensors do not agree) the device enters a safe mode, which prevents continued walking and enables the physical therapist to safely remove the patient. The device is also equipped with fail-safe brakes on the actuated knee joints, such that if the device loses power or is shut down for any reason the knees will continue to support the patient. Finally, an emergency disable button is available to instantly shut down the device for any reason. This is implemented via hardware, so it is effective even during a software malfunction.

All study physical therapists will be trained to using the study device by the manufacturer. The training will be conducted at our facility.

Aims

1. To assess the feasibility and safety of using the EksoBionics GT exoskeleton for gait training in patients with relapsing or progressive MS and severe mobility limitations (EDSS 5-5 – 7.5).

2. To collect preliminary efficacy outcomes on gait and walking for the purpose of designing a larger clinical trial of the EksoBionics GT exoskeleton for gait training in patients with MS.

Methods

Design: uncontrolled pre-post intervention study

Participants:

Sample size: up to 15 participants will be enrolled, with the goal of 5 participants completing the study period.

Inclusion/exclusion criteria

Inclusion criteria	Exclusion criteria
• Diagnosis of MS per 2017 revised McDonald criteria • EDSS score 5.5-7.5 (moderate to severe walking disability) • Cleared for gait training with the study device by the study treating physician <u>Device-Specific Criteria</u> • Involved in a standing program or must be able to tolerate at least 15 min upright without signs or symptoms of orthostatic hypotension • Weigh 220 pounds (100kg) or less • Be able to fit into the Ekso device: • Between approximately 5'0" and 6'4" tall (really depends on leg measurements) • Sufficient diaphragmatic strength such that respiration is not compromised with exercise <u>Assessed by physical therapy:</u> • Standing hip width of approximately 18" or less • Have near normal range of motion in hips, knees and ankles • Sufficient upper extremity strength to use a front wheeled walker by manual muscle testing (minimum triceps strength bilaterally of 3/5, shoulder abduction and flexion/extension of 4/5 OR as discussed during demo, 2 normally functioning limbs such as in hemiplegia)	• MS exacerbation, severe acute comorbidity or surgery less than 90 days prior to enrollment • Diagnosed with osteoporosis or history of long bone fractures since diagnosis • Safety concern due to neurologic impairments (e.g. upper extremity weakness, visual loss) or comorbidities (e.g. cardiac, respiratory) • Other neurologic or non-neurologic condition interfering with walking • < 1 month since previous intensive gait training regimen or initiation of treatment that can affect walking (e.g. medication for spasticity) • Planned change in medications that may affect walking during the study period • Uncontrolled or severe orthostatic hypotension that limits standing tolerance • Active heterotrophic ossification (HO), hip dysplasia, or uncontrolled hip/knee axis abnormalities • Score <22 on the Mini-Mental State Examination or deemed to have cognitive impairment precluding safe training with the device during the screening and training process • Colostomy • Pregnancy • Unresolved deep vein thrombosis • Uncontrolled autonomic dysreflexia • Currently involved in another rehabilitation study <u>Assessed by physical therapy:</u> • Severe spasticity that prevents joint motion (severe stiffness or rigidity) in proximal lower extremity muscles, including hip adductors and knee flexors/extensors. • Hip flexion contracture greater than ~17° • Knee flexion contracture greater than 12°

	• Unable to achieve neutral ankle dorsiflexion with passive stretch (achieve neutral with up to 12° knee flexion) • Leg length discrepancy greater than 0.5" for upper leg, greater than 0.75" for lower leg • Spinal instability (TLSO may be worn in device with physician clearance) • Severe muscular or skeletal pain • Open skin ulcerations on buttocks or other body surfaces in contact with exoskeleton or harness • Shoulder extension ROM < 50° excludes using crutches during sit to stand or vice versa. (Walking with crutches permitted, sit <> stand would be done with walker.)

Data collected

Demographic and clinical data: age, sex, duration of MS symptoms in years, MS course (relapsing or progressive), use of assistive device to walk indoors / outdoors (none, unilateral, bilateral), Body Mass Index, concomitant medications

Screening	Expanded Disability Status Scale Mini-Mental State Examination
Safety	Adverse events during or between rehabilitation sessions (particularly falls and musculoskeletal pain) Pain severity on Numeric Pain Rating Scale and pain location
Feasibility	Percentage of patients who complete at least 75% of the training sessions. Percentage of patients who drop out of the study
Acceptability	assistive device subscale of the Quebec User Evaluation of Satisfaction with Assistive Technology questionnaire v.2 (https://www.sralab.org/rehabilitation-measures/quebec-user-evaluation-satisfaction-assistive-technology)
Efficacy (tested without device)	Spasticity (Modified Ashworth Scale) Hip flexor strength (handheld dynamometer) Gait parameters : - GAITRite system (overground gait mat): velocity, cadence, step length, step width, double support time (averaged between left and right when appropriate) - CAREN system (treadmill with harness): gait kinematics

	Timed 25 Foot Walk 2-minute Walk Test MS Walking Scale-12

The **Expanded Disability Status Scale (EDSS)** is a comprehensive, quantitative neurological examination, and is the most widely used measure of MS-related disability for clinical and research purposes. The order of the exam may vary slightly among providers, but generally the patient undergoes a complete neurologic examination, then completes up to a 500 meter walk (with or without an assistive device) which involves walking the length of our 50 meter clinic hallway 10 times. The examiner notes the distance the patient is able to walk, along with the presence of an assistive device, if applicable.

The **Mini Mental State Examination (MMSE)** is an 11-question measure that tests five areas of cognitive function: orientation, registration, attention and calculation, recall, and language. Widely used in clinical practice, the MMSE will be administered in this study to screen for severe cognitive impairment that precludes safe participation.

The **Numeric Pain Rating Scale** evaluates pain by asking the patient to situate the severity of pain experienced on a 0-10 level scale (from no pain to maximal pain). In addition, the patient will be asked to report the location of the pain. A publication from a cross-sectional study using the NRS on 236 MS patients with pain proposed the following cutoff scores: 0-2 : mild, 3-5 : moderate, 6-10 : severe.1 Pain will be assessed as a safety measure.

The **Quebec User Evaluation of Satisfaction with Assistive Technology (QUEST) questionnaire v.2** is a new outcome measurement instrument designed to evaluate a person's satisfaction with his or her assistive technology device. It can be used with adolescents, adults and elderly persons who as a result of a physical or sensory impairment have acquired an assistive technology device. The QUEST 2.0 was created for assistive technology practitioners and researchers. As a clinical tool, the QUEST 2.0 provides practitioners with a means of collecting satisfaction data that can be used to document the real-life benefits of assistive technology and to justify the need for these devices. As a research tool, it can be used to compare satisfaction data with other outcome measures such as clinical results, quality of life, functional status, cost factors and comfort

The **Modified Ashworth Scale (MAS)**: the Ashworth scale, first published in 1964, grades resistance to passive mobilization on a 5-level ordinal scale. The psychometric properties of the Ashworth scale are well documented, and even though this tool has been criticized for its lack of inter-rater reliability, it is still the most widely used measure of spasticity in clinical trials. The modified version of the Ashworth scale, which allows one intermediate grade, will be used for this study. We will evaluate the following muscle groups: hip adductors, knee flexors, and knee extensors. The MAS scores for all muscle groups in both legs will be averaged.

Hip Flexor Strength will be measured bilaterally with a hand-held dynamometer (the Lafayette Manual Muscle Testing System, Lafayette IN). This device provides a digital display of the force generated by active muscle contraction. Two measurements of peak strength will be taken on each side, and the average of the measurements will be calculated. Hand-held dynamometry was found more reproducible and sensitive to change than the manual muscle test grading system.

The **GAITRite electronic walkway** is a computerized gait analysis system consisting of a 30-foot mat with embedded sensors and a data acquisition and processing software. The GAITRite has been used to analyze gait patterns in various neurologic populations, including MS. The spatiotemporal gait parameters analyzed include stride length, double support time, base of support (step width), and the functional ambulation profile (FAP) score.

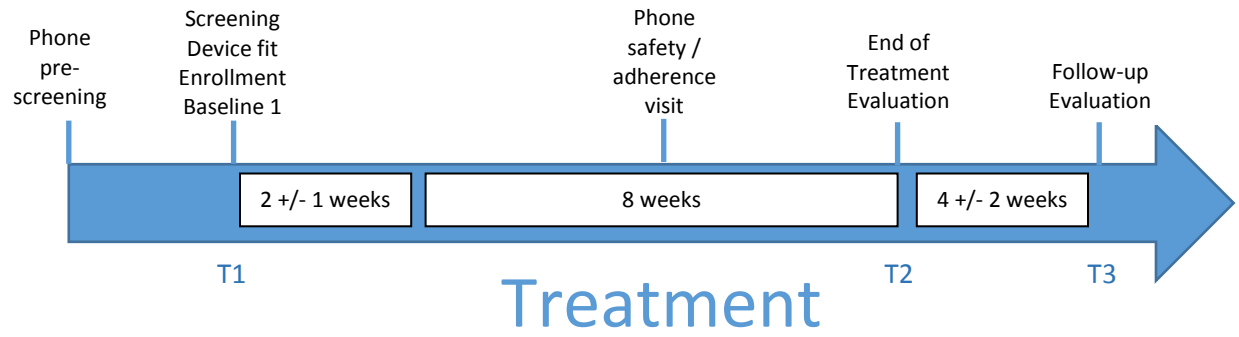
The **Computer Assisted Rehabilitation ENvironment (CAREN)** system is installed in the Mellen Center building and routinely used for patient care and clinical research. The hardware includes: a 6 degrees of freedom motion base on which sits a 3-meter diameter platform with a dual belt instrumented treadmill; a 10-camera real-time motion capture system; a 120-degree cylindrical screen projection system with surround sound; wireless EMG and 3 high-speed cameras. The CAREN system creates an immersive virtual environment with real-time feedback loop, causing the system to respond to subject motion. The software allows to define inputs, perturbations and sensory disturbances, for research and training purposes. Gait data is continuously recorded and analyzed offline using the Gait Off-Line Analysis Tool. The CAREN system is staffed with two trained operators, who are also developers for the system.

The **Timed 25 Foot Walk (T25FW)** is part of the Multiple Sclerosis Functional Composite (MSFC), an outcome measure for MS therapeutic trials. This test has been widely used to measure walking speed in MS. The patient is instructed to walk 25 feet as quickly as possible, but safely. Two trials are conducted, and the average time is calculated.

The **2-Minute Walk (2MW)** has been validated in cardiovascular and respiratory disease, in lower limb amputation, and has been used in neurorehabilitation trials in stroke 6 and multiple sclerosis. The subject is asked to walk as far as possible and as fast as possible (but safely) for 2 minutes in a 50-meter hallway. The timer will not be stopped if the patient takes brief rest periods during the walk. If the test is discontinued before 2 minutes, either by patient request or evaluator decision, the time and reason for stopping will be noted.

The **MS Walking Scale-12** (MSWS-12) is a disease-specific instrument gathering subject-reported information about the impact of MS on their walking ability, designed for use in clinical practice and clinical research. The MSWS-12 contains 12 questions with a recall period of 2 weeks. The psychometric properties of the MSWS-12 have been extensively evaluated in diverse MS populations in both community and hospital settings, with demonstration of internal consistency, high reliability and validity, and good generalizability.

<u>Evaluation schedule</u>



All assessments will be performed at T1, T2, and T3. In addition, a phone visit will be conducted 4 +/- 1 weeks after treatment initiation to review adverse events, adherence to treatment sessions, and any comments / questions the participants may have.

All participants will be invited to participate in the T2 assessment visit, even if they have decided to terminate treatment for various reasons.

Treatment

The rehabilitation treatment will consist of 3 sessions per week for 8 weeks, for a total of 24 sessions. Missed sessions will be made up if possible. Each session will be scheduled for 60 minutes, and will consist of stretching, overground gait training, and gait training with the study device. Rest periods will be provided as necessary during the training visits.

Statistical analysis

Patient characteristics will be summarized using frequencies and percentages for categorical factors and means and standard deviations or medians and quartiles for continuous measures. The percentage of participants meeting established MDC or MCID for any of the outcome measures will also be calculated. Change over time in functional outcomes will be evaluated using linear mixed effect models. In these models, each functional measure will be the outcome and time point will be the predictor. Repeated measures within subject will be models assuming an autoregressive or spatial correlation structure. Estimated changes with 95% confidence intervals will be summarized for each measure. Outcomes measured bilaterally will be averaged for analysis primarily. Incidences and types of adverse events will be summarized overall and by time period. Adherence to training sessions will be summarized descriptively using means and standard deviation and the percentage of patients achieving minimum completion standards will also be described. Analysis will be performed using SAS software (version 9.4, Cary, NC).