Clinical Protocol

Study Title: The WISE Trial - Walking Improvement for SCI with Exoskeleton

Protocol Number: 105333

NCT: NCT02943915

Sponsor: Ekso Bionics, Inc.
1414 Harbour Way S Ste 1201
Richmond, CA 94804

Protocol Change Status:

Revision	Date of revision	Reason for amendment
A	10 June, 2016	[redacted]
B	15 July, 2016	Expanded upper age limit, changes to sample size and statistical analysis plan, additional clarifications and corrections
C	30 March, 2017	Additional clarifications, definitions, and rules required after several run-in cases were performed and site feedback obtained; addition of/change in some assessments (see summary table of changes)

Study Acknowledgement and Confidentiality Statement

The information in this document and future information which will be provided to the Principal Investigator and study staff contains information that is confidential to Ekso Bionics, Inc. and may not be disclosed without prior written approval of Ekso Bionics, Inc., unless such disclosure is required by federal or other laws or regulations. Information that is provided to Participants by Ekso Bionics, Inc. may be communicated by Participants to other persons who have a "need to know" the information in order to facilitate and implement the study in which Participants are participating. However, such persons must be informed that the information provided is confidential to Ekso Bionics, Inc and may not be further disclosed by them.

The signature of the investigator below constitutes approval of this protocol and agreement to the confidentiality statement above.

The investigator agrees to supervise all testing of the device and to ensure that requirements for obtaining informed consent are met.

The investigator agrees to:

- conduct the study according to the protocol and approved protocol amendments.
- conduct the study in accordance with the ethical principles stated in the latest version of the Declaration of Helsinki, the applicable guidelines for good clinical practices, and/or the applicable local and international regulations, whichever provide the greater protection of the individual.

Signature of Investigator	Date
Investigator Name (Print)	

Table of Contents

STUDY OUTLINE

Study Title: The WISE Trial - Walking Improvement for SCI with Exoskeleton

Sponsor: Ekso Bionics, Inc.
1414 Harbour Way S Suite 1201
Richmond, CA 94804

Study Description: A randomized, controlled trial comparing exoskeleton gait training with standard gait training or no gait training in community-dwelling participants with chronic incomplete spinal cord injury.

Overall goal: We aim to demonstrate that Ekso exoskeleton training can significantly improve gait speed in stable chronic, community-dwelling incomplete SCI (iSCI) participants.

Rationale: Community dwelling iSCI participants may improve clinical gait function by engaging in a gait training regimen, where robotic exoskeletons can readily deliver a dose and simultaneously reduce the physical stress imposed on therapists who use conventional manually assisted stepping practice. Participants receiving exoskeleton training are predicted to show improved function compared to participants receiving no gait training (daily home care), but not superiority to intensity-matched manual gait training. The rationale to implement exoskeleton robotics as preference in gait training is based on high repetition during overground training and reduced therapist burden.

Hypothesis: Participants undergoing exoskeleton training for 12 weeks /36 sessions will demonstrate equal progress in walking speed as those participants undergoing standard gait training for 12 weeks/36 sessions. Participants in both the exoskeleton group and the standard gait training group will show greater progress after 12 weeks/36 sessions than the participants in the passive control group.

Design: Multi-center, randomized, controlled study.

Participants: Chronic ($\geq$ 1 year after the injury), community-dwelling men and women between the ages of 18 and 75 years, inclusive, diagnosed with motor incomplete spinal cord injury (AIS C and D), with minimal walking function, who may benefit from participating in a 12-week (36-session) outpatient rehabilitation therapy and who fulfill the inclusion/exclusion criteria.

Inclusion criteria:

1. Motor incomplete paraplegia or tetraplegia, chronic ($\geq$ 1 year after the injury). Non-traumatic SCI injuries can be included, given they are neurologically stable conditions for 12 months (e.g. tumor, transverse myelitis, but NOT Guilliane-Barré)
2. NLI C1- approximately T10 (inclusive, for upper motor neuron injuries only), as determined by the International Standards for Neurological Classification of SCI (ISNCSCI)
3. Sufficient diaphragmatic strength such that respiration is not compromised with exercise.
4. 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 4/5)
5. AIS-C SCI & AIS-D SCI, as determined by the International Standards for

Neurological Classification of SCI (ISNCSCI)

6. Ambulates at a self-selected speed of <0.44 meters/second with or without physical assistance and assistance device
7. Able to advance at least one leg forward volitionally with lower extremity muscles (not as a result of trunk movement or spasticity) while using parallel bars, walker or crutches, with or without braces, and with up to 2 people to assist with safety and balance only. Stepping is to be performed by the patient without PT assistance at the lower extremities and no BWS.
8. 18 – 75 yrs old, inclusive
9. No current or history of other neurological conditions
10. Screened and cleared by a physician
11. Involved in standing program or must be able to tolerate at least 15 min upright without signs or symptoms of orthostatic hypotension
12. Weigh 220 pounds (100kg) or less
13. Be able to fit into the Ekso device
14. Between approximately 5'0" and 6'4" tall
15. Standing hip width of approximately 18" or less
16. Have near normal range of motion in hips, knees and ankles

Exclusion criteria:

1. AIS-A SCI or AIS-B SCI
2. Lower motor neuron injuries, as shown by absent reflexes during bilateral quadriceps and Achilles tendon taps
3. < 3 months since previous intensive gait training regimen, FES cycling program, and lower extremity botox injections. The gait training regimen is meant to be formal gait training with feedback for progression of walking (i.e. PT sessions). Participant may have a regular home exercise program and/or a walking exercise program with a companion/ trainer for safety, but not for verbal or tactile cues or feedback regarding gait in the 3 months before initiating the protocol. If participant has a home exercise program and/or a walking exercise program, these programs (except FES cycling) should be continued without changes throughout the protocol. Electrical stimulation devices used regularly for foot drop during ambulation should be considered a brace and should continue to be used as usual throughout the protocol. Upper extremity botox injections are permissible before and during the protocol. One or two PT sessions are allowed to obtain a new brace or progress bracing and check for fit and safety, but no sustained gait training should occur.
4. Already walking at self-selected ambulation speeds of at least 0.44 meter/second with or without assistance
5. Currently involved in another intervention study
6. Concurrent neurological disease
7. Hip flexion contracture greater than ~17°
8. Knee flexion contracture greater than 12°
9. Unable to achieve neutral ankle dorsiflexion with passive stretch (neutral with max 12° knee flexion)
10. Leg length discrepancy
    a. Greater than 0.5" for upper leg
    b. Greater than 0.75" for lower leg
11. Spinal instability
12. Unresolved deep vein thrombosis
13. Uncontrolled autonomic dysreflexia
14. Severe muscular or skeletal pain
15. Spasticity that prevents joint motion (severe stiffness or rigidity,) where both

legs have a MAS score of 3 or higher for half or more of their proximal lower extremity muscles; proximal muscles include hip flexors/ extensors/ adductors and knee flexors/extensors.

16. Open skin ulcerations on buttocks or other body surfaces in contact with exoskeleton or harness
17. Pregnancy
18. Cognitive impairments – unable to follow 2 steps commands and communicate for pain or to stop session
19. Shoulder extension ROM < 50° excludes crutches during sit to stand or vice versa. (Walking with crutches permitted.)
20. Participant requires the assistance of more than one therapist to transfer safely.
21. Uncontrolled or severe orthostatic hypotension that limits standing tolerance; defined as sustained, symptomatic drops in systolic and diastolic blood pressure when moving from sitting to standing
22. Active heterotrophic ossification (HO), hip dysplasia or hip/knee axis abnormalities
23. Colostomy
24. History of long bone fractures since the SCI, secondary to osteoporosis
25. Unable to sustain current medication regimen, specifically those medications that may impact study outcomes (such as spasticity).
26. Any reason the physician may deem as harmful to the participant to enroll or continue in the study

Treatment Groups:	**Run-In Group:** The first 1 to 4 Participants at each site will be assigned to the Run-in Group. The Run-in Group follows the Group 1 assignment described below. After the site has completed the Run-in phase, Participants who meet study entrance criteria will be randomized to one of three groups: **Group 1**: Ekso Intervention - Participants in this group receive Ekso GT robotic gait training 3 times per week for 12 weeks (36 sessions). The goal is a minimum of 300 steps of gait training in the Ekso GT per 45 minute session. Overground walking starts when Participants require only minimal assistance of one therapist and one aide to assist with assistive device, without any BWS, for at least 10 meters. This will be assessed every 3rd session during the 10MWT. At this point, sessions will consist of 30 minutes of gait training in the Ekso, followed by 15 minutes of standard overground gait training without BWS for a total of 45 minutes of walking. See Table I A for the training progression strategy and section 10 – Training Regimen and Rules for details. **Group 2**: Active controls - Participants in this group receive a matched number of sessions of standard gait training. Sessions will consist of 45 minutes of walking 3 times per week for 12 weeks (36 sessions). Standard gait training will be a combination of body-weight supported treadmill training and overground training without BWS, with a goal of a minimum 300 steps during BWSTT per session. Overground walking starts when Participants require only minimal assistance of one therapist and one aide to assist with the assistive device, without any BWS, for at least 10 meters. This will be assessed every 3rd session during the 10MWT. Once the overground criterion is achieved: If the initial 300 steps **are not completed** by the end of the first segment, the middle 15-minute segment must be gait training in BWSTT, and the final 15-minute segment must be OG gait training.If the initial 300 steps **are completed** by the end of the first segment, the middle 15-minute segment can be continued gait training in BWSTT or OG gait training, per PT choice. The final 15-minute segment must be OG gait trainingSee Table 1 B for the training progression strategy and section 10 – Training Regimen and Rules for details. **Group 3**: Passive controls with cross-over option - Participants in this group continue with daily activities as normal over 12 weeks. No new gait training, mobility therapy, nor new medications (including Botox) are commenced during the study period. Participants in this group will come to the study sites for evaluations at baseline, 6 and 12 weeks. After the 12 week evaluation, the participants in this group will have an opportunity to choose to receive either Ekso or standard gait training therapy for 12 weeks.
Sample Size:	Up to 40 Run-In Participants and up to 127 total Randomized Participants; Randomization by groups is 2:2:1.
Blinding:	Outcomes data will be collected by independent, blinded evaluators trained in standard assessment techniques.
Setting/Sites:	Outpatient Rehabilitation Setting involving up to 15 clinical sites. Sites to be chosen based on having Ekso Level 2 training certification, ability to match manual therapy regimen prescribed by this protocol, location, enrollment capabilities, and resources.
Duration:	Each randomized Participant is expected to engage in this study for approximately 6 months. Run-in Participants are expected to be active in the study for approximately 14 weeks. The duration of the study is expected to be approximately 3 years.

Assessment periods:	The study consists of a screening/pre-evaluation period, a 12 week training period (36 sessions) with limited weekly assessments (every 3rd session) for safety/ progression measures, and full evaluations at the end of training weeks 6 (midpoint/following session 18) and 12 (endpoint/following session 36). Randomized Participants are to return 3 months after the last training session (follow up) at which time they will undergo the same full evaluation as training weeks 6 and 12. Assessments are to be performed outside of exoskeleton or any body weight support.
Primary Objective:	To demonstrate that a 12 week robotic gait training regimen can lead to a clinically meaningful improvement in independent gait speed on the 10 Meter Walk Test (10MWT) in community dwelling participants with chronic iSCI.
Secondary Objectives:	To examine the economic factors such as number of physical therapists/staff required during training. To analyze the physical burden on therapists assisting and supervising during training. To study the influence of factors that may modify the gait recovery in the chronic incomplete SCI population (demographic, clinical, functional, psychological, balance, etc.)
Primary End Point:	The primary endpoint is the mean increase in gait speed demonstrated during the 10MWT after 12 weeks/36 sessions of training and compared between groups. Both self-selected and fast speeds will be performed on the 10MWT, with the fast speed taking precedent.
Secondary Endpoints:	Participant outcomes related to physical performance, physiology, quality of life, and safety are to be measured at weeks 6 / following session 18 (midpoint), week 12/ following session 36 (endpoint), and week 24 /3 months after the last sessions (follow-up) (unless otherwise indicated) and compared between groups. By category, these are the following: *PHYSICAL PERFORMANCE OUTCOMES* 10MWT for both self-selected and fast gait speeds Number of participants who achieve the Minimal Clinically Important Difference (MCID) of 0.15 m/s[21] during the 10MWT Number of participants who transition from exercise or household ambulation (defined as a self-selected walking speed of < 0.44 meters/second) to limited community or full community ambulation (≥ 0.44 meter/second) during the self-selected 10MWT[13] Time point of recovery at which participants reach the MCID and/or community ambulation speeds of ≥ 0.44 meters/second[13] 6MWT for endurance TUG for balance during sit-stand, walking, turning, and stand-sit

WISCI-II score for need of assistance and devices.

SCI-FAI for observational gait quality

GAITRite for temporospatial gait parameters and symmetry (if site has access to this device)

SCIM-III, mobility subscale for ability to perform transfers and walking different distances

Berg Balance Scale for measurement of static and dynamic sitting and standing balance

QUALITY OF LIFE/PSYCHOLOGICAL OUTCOMES

International SCI Quality of Life Basic Data Set

Epidemiological Studies Depression Scale (CES-D 10)

NASA Task Load Index for participant self-reported work load

PHYSIOLOGICAL OUTCOMES

ISNCSCI exam between baseline and 12 weeks/36 sessions

Number of participants who convert from AIS C to D per ISNCSCI exam

Body mass index for a general health measure

UEMS and LEMS as measured by the physical therapist for muscle strength

Heart rate and blood pressure before and after 6MWT

Borg Scale for self-reportedmaximal Rate of Perceived Exertion (RPE) during either intervention

SECONDARY COMPLICATIONS

International SCI Pain Basic Data Set

Numeric Pain Rating Scale for Pain upon resting and during gait training

SCATS, Modified Ashworth Scale, patient-report SCI-SET and Numeric Rating Scale for spasticity

Modified International SCI Bowel Function Basic Data Set
Modified International SCI Lower Urinary Tract Basic Data Set

Incidence of urinary tract infections per Participant

Incidence of pressure ulcers per Participant

Incidence of falls per Participant

Incidence of re-hospitalization/unexpected doctor visits per Participant

THERAPIST OUTCOMES

Number of therapists/staff required for each active group (Group 1 and 2), and set-up/donning time for cost effectiveness of the two active therapies

Borg Scale for self-reported maximal RPE during either of the interventions

NASA-Task Load Index for therapists' self-reported work load

Video assessment of training posture for ergonomics

Occupational safety measured by number and severity of therapist reports of orthopedic problems and/or pain

See Appendix A for description of assessments.

List of Abbreviations

6MWT – 6 Minute Walk Test
10MWT – 10 Meter Walk Test
AE - adverse events
AIS - ASIA (American Spinal Injury Association) impairment scale
ASIA - American Spinal Injury Association
BBS - Berg Balance Scale
BMI - body mass index
BP - blood pressure
BWS – Body weight support
BWSTT – Body weight supported treadmill trainingCRF - case report form
DSMB - Data Safety Monitoring Board
EU – European Union
FDA – Food and Drug Administration
GCP - Good Clinical Practice
HR - heart rate
IRB - Institutional Review Board
ISNCSCI – International Standard for Neurological Classification of Spinal Cord Injury
iSCI – incomplete spinal cord injury
LEMS - lower extremity motor scores
LOCF - last observation carried forward
MAS - Modified Ashworth Scale
MCID – minimal clinically important difference
MMT - manual muscle test
NASA – National Aeronautics and Space Administration
NLI - neurological level of injury
NRS – Numeric Rating Scale
PT - physical therapist
QOL - quality of life
RPE - rate of perceived exertion
ROM - range of motion
SAE - serious adverse event
SCATS – Spinal Cord Assessment Tool for Spastic Reflexes
SCI - spinal cord injury
SCI-FAI - Spinal Cord Injury Functional Ambulation Index
SCI-SET – Spinal Cord Injury Spasticity Evaluation Tool
SCIM - Spinal Cord Independence Measure
TUG - Timed Up and Go
UE - upper extremity
UEMS - upper extremity motor score
UL – Underwriters Laboratory
WISCI - Walking Index for Spinal Cord Injury

1. Literature Summary and Study Rationale

The incidence of spinal cord injury (SCI) in the U.S. is approximately 40 cases per million or 12,500 new cases each year. The number of SCI patients living in the U.S. in 2014 has been reported to be roughly 276,000 (range, 240,000 to 337,000).[1] Spinal cord injury usually results in life-long disability with restricted movement. Consequently, many patients remain non-ambulatory and wheelchair-dependent. Life-long inability to stand and walk decreases patient quality of life and may increase the risk of secondary complications, such as skin breakdown, muscle atrophy, osteoporosis and cardiovascular diseases, with resultant psychological depression.[2–4] One of the principle goals for rehabilitation is recovery of walking ability; however, 25% of people with incomplete traumatic SCI fail to become ambulatory.[5–7]

Despite the lack of neuromuscular function in the lower extremities, various interventions have been developed to retrain and improve gait function in these individuals. Manual and robotic-assisted body weight-supported treadmill training (BWSTT) try to optimize sensory inputs relevant to step training, repeated practice, and improvement of neuroplasticity. However, manual BWSTT involves personnel-intensive training with simultaneous physical guidance from up to four staff members, including at least one therapist. Indeed, the major difficulty of BWSTT is the non-ergonomic effort required by the trainers to guide the movements of the individual's legs.[8]

There is increasing evidence that inclusion of variable practice conditions during training enhances motor performance.[9,10] Indeed, early evidence pointed to recovery of basic walking function in those with motor-incomplete SCI after intensive, task-specific training.[11] Gait speed can be evaluated in terms of timed measures, such as the 10-meter walk test (10MWT), and endurance measures, such as the 6-minute walk test (6MWT). Evidence for independent walking indicates that over-ground training is just as effective for AIS C or D individuals than is therapist-assisted BWSTT.[12] Reported velocity requirements for community ambulation suggest a gait speed of 0.44 m/s, and the ideal training would allow for independent ambulation.[13]

Gait training should include outcome measures—such as speed (m/s), walking distance (m), walking index for spinal cord injury (WISCI) scores, functional independent measurement (FIM) and Ashworth scores, and visual analogue scale (VAS) pain scores. These outcomes can be used to assess those walking skills that represent requirements of everyday ambulation.[14] Results from Lam et al's pilot study suggest the value of robotics-based (Lokomat™, Hocoma AG, Switzerland) BWSTT, which incorporates motor learning principles. Likewise, Musselman et al reported on an iSCI case series (n = 4) describing the use of a method (skill training) to retrain walking over-ground, which was intensive, variable, and relevant to daily walking.[15] The authors concluded that retraining walking skills over-ground in challenging situations (over and around obstacles of various sizes) resulted in clinically important changes in walking speed. Median walking speed improved by 0.09 m/s for skilled walkers compared to an improvement of 0.01 m/s for BWSTT walkers.[15]

Mehrholz et al investigated and reviewed the effect of automated electromechanical and robotic-assisted gait training devices on the improvement of walking after stroke.[16] Twenty-three trials involving 999 participants were included. The gait-training devices in combination with physiotherapy significantly increased the odds of participants becoming independent walkers [OR: 2.39; 95% CI: 1.67, 3.43; $p < 0.00001$] but did not significantly increase walking velocity [mean difference = 0.04 m/s; 95% CI: -0.03, 0.11; $p = 0.26$] or walking capacity [6MWT = 3 m; 95% CI: -29, 35; $p = 0.86$]. The results should be interpreted with caution as various devices (some included electrostimulation) were studied over different durations and different frequencies, and some of the trials included participants who could walk ~~at~~ prior to the gait training intervention. The principal finding suggests that people in the acute phase, who are non-ambulatory at intervention onset, may benefit whereas those who are ambulatory may not benefit from this kind of training.

In one randomized controlled trial, the hybrid assistive limb (HAL™) exoskeleton (Cyberdyne, Japan) was compared to conventional BWSTT in terms of gait training in the subacute phase after stroke; 22 participants were randomized equally to the two investigative groups.[17] A significant difference (p = .04) in Functional Ambulation Categories (FAC) was achieved, favoring HAL training. The study was limited by small Participant numbers, differing periods between stroke and training, and lack of blinding by outcome assessments.

The investigational Indego® exoskeleton (Parker Hannifin Corp., USA) was recently studied to evaluate in-device mobility outcomes for individuals with SCI after five 1.5-h gait-training sessions with the device.[18] The average walking speed after the five sessions for those with T9–L1 paraplegia (n = 8) was 0.45 m/s during the 10MWT and the average distance achieved during the 6MWT was 121 meters. Six of the eight study participants were able to walk, while in the device, on a variety of surfaces. The authors concluded that powered exoskeletons can provide individuals with iSCI the ability to ambulate in both indoor and outdoor environments. Interpretation of the study results is limited by the small number of participants; lack of randomization, blinding, and provision of a control group; and no evaluation of independent ambulation.

In a controlled environment, ambulation with the Ekso™ wearable robotic exoskeleton (Ekso Bionics, Inc., USA) was studied to evaluate the feasibility and safety of Ekso to aid ambulation in 8 individuals who had experienced SCI within 2 years of study participation.[19] The lack of consensus regarding the benefit of body weight supported training (BWST) compared to traditional over-ground therapy (TOG) in improving ambulation for those with SCI inspired the study. Results from six weekly sessions with Ekso over increasing session time and with less assistance suggested that the exoskeleton was safe to use in a controlled environment. In 2016, Sale et al. reported gait analysis and clinical outcomes in a prospective pilot study (n = 3) of Ekso. Mean velocity improved statistically from T0 (0.17 ± 0.04 m/s) to T1 (0.23 ± 0.04 m/s) (p = .0188). Improvement over baseline in cadence (steps/min) and step length (m) were also statistically significant.

Locomotor training, whether over-ground or on a treadmill and using partial body weight support, promotes recovery and improvement in mobility in humans with iSCI. Walking repetitively in a natural manner similar to the over-ground gait and with correct proprioceptive and exteroceptive feedback is of critical importance.[20] Sorensen et al conducted a spinal cord injury study in multiple sites across Europe. Fifty-nine participants were divided into four groups. Investigators found that the incomplete spinal cord (n=28) Participants using the Ekso Bionics exoskeleton improved dramatically in 12 weeks (Personal communication.) Complete data on this trial is expected to be presented later in 2016.

2. Study Purpose, Plan, and Objectives

Community dwelling iSCI participants may improve clinical gait function by engaging in a gait training regimen, where robotic exoskeletons can readily deliver a precise dose and simultaneously reduce the physical stress imposed on therapists using conventional manually assisted stepping practice. Exoskeleton training is predicted to improve function in participants receiving usual care, but not superior to intensity-matched manual training. The rationale to implement exoskeleton robotics as preference in gait training is based on precision dosing, over-ground training, and reduced therapist burden for high repetition training.

We aim to demonstrate that Ekso exoskeleton training can significantly improve gait speed in stable chronic, community-dwelling incomplete SCI (iSCI) participants. The objectives of this study are the following:

A. Primary Objective:
   To demonstrate that a 12 week robotic gait training regimen can lead to a clinically meaningful improvement in independent gait speed on the 10 Meter Walk Test (10MWT) in community dwelling

participants with chronic iSCI.

B. Secondary Objectives:
   1. To examine the economic factors such as number of physical therapists/staff required during training.
   2. To analyze the physical burden on therapists assisting and supervising during training.
   3. To study the influence of factors that may modify the gait recovery in the chronic incomplete SCI population (demographic, clinical, functional, psychological, balance, etc.).

3. Study Design

This is a post-market, randomized, prospective, multi-center, blinded, longitudinal, comparative study to evaluate the efficacy of robotic exoskeleton gait training versus standard gait training or usual care. The Run-in phase is designed to 1) to train and carefully supervise the sites prior to starting the randomization 2) test the recruiting ability of the selected sites 3) test the assessment time-points for primary and secondary endpoints, and 4) ensure that the inclusion/exclusion criteria is adequate. Each site is expected to enroll 1-4 Run-in Participants.

4. Study Endpoints

The primary and secondary endpoints are as follows:

The primary endpoint is the mean increase in gait speed demonstrated during the 10MWT after 12 weeks/ 36 sessions of training and compared between groups. Both self-selected and fast speeds will be performed on the 10MWT, with the fast speed taking precedent.

The secondary endpoints of Participant outcomes related to physical performance, physiology, quality of life, and safety are to be measured at week 6/following 18 sessions (midpoint), week 12/following 36 sessions (primary endpoint), and week 24/3 months after the last session (follow-up) (unless otherwise indicated) and compared between groups.

By category, these are the following:

PHYSICAL PERFORMANCE OUTCOMES

10MWT for both self-selected and fast gait speed

Number of participants who achieve the Minimal Clinically Important Difference (MCID) of 0.15 m/s [21] during the 10MWT

Number of participants who transition from exercise or household ambulation (defined as self-selected walking speed of < 0.44 meters/second) to limited community or full community ambulation (≥ 0.44 meter/second) during the self-selected 10MWT[13]

Time point of recovery at which participants reach the MCID and/or community ambulation speeds of ≥ 0.44 meters/second[13]

6MWT for endurance

Timed Up and Go (TUG) for balance during sit-to-stand, walking, turning, and stand-to-sit

WISCI-II score for need of assistance and devices

SCI-FAI for observational gait quality

GAITRite for temporospatial gait parameters and symmetry (if site has access to this device)

SCIM-III, mobility subscale for ability to perform transfers and walking different distances

Berg Balance Scale for measurement of static balance and dynamic sitting and standing balance.

QUALITY OF LIFE/PSYCHOLOGICAL OUTCOMES

International SCI Quality of Life Basic Data Set

Epidemiological Studies Depression Scale (CES-D 10)

NASA Task Load Index for participant self-reported work load

PHYSIOLOGICAL OUTCOMES

ISNCSCI exam between baseline and 12 weeks/36 sessions

Number of participants who convert from AIS C to D per ISNCSCI exam

Body mass index for a general health measure

UEMS and LEMS as measured by the physical therapist for muscle strength

Heart rate and blood pressure before and after 6MWT

Borg Scale for self-reported maximal RPE during either intervention.

SECONDARY COMPLICATIONS

International SCI Pain Basic Data Set

Numeric Pain Rating Scale for self-reported neuropathic pain upon resting and during gait training
SCATS, Modified Ashworth Scale, patient-report SCI-SET, and Numeric Rating Scale for spasticity

Modified International SCI Bowel Function Basic Data Set

Modified International SCI Lower Urinary Tract Basic Data Set

Incidence of urinary tract infections per Participant

Incidence of pressure ulcers per Participant

Incidence of falls per Participant

Incidence of re-hospitalization/unexpected doctor visits per Participant

THERAPIST OUTCOMES

Number of therapists/staff required for each active group (Group 1 and 2), and set-up/donning time for cost effectiveness of the two active therapies

Borg Scale for self-reported maximal RPE during either of the interventions

NASA-Task Load Index for therapists' self-reported work load

Video assessment of training posture for ergonomics

Occupational safety measured by number of therapist reports of orthopedic/neurologic problems and/or pain

See Appendix A for description of assessments.

5. Participant Enrollment

Participants will be identified and recruited from outpatient clinics. Participants will be presented with a study consent form. The point of enrollment is after the patient has met the inclusion/exclusion criteria, and has signed the study consent form. Run-in Participants (the first 1 to 4 recruited) are to be consented using the Run-in consent form. Run-in Participants follow the same assignment as described in Group 1 but are NOT randomized. After the Run-in phase, subsequent Participants are consented using the Randomized Consent Form and then randomized to Group 1, Group 2, or Group 3. This is further detailed in the section on "Screening and Informed Consent."

6. Duration of Participation/Study

Each Run-In participant will be enrolled for approximately 14 weeks. Each randomized Participant will be enrolled for approximately 6 months. The enrollment period for the given target number of Participants is estimated to be 2.5 years and the duration of the study is anticipated to be 3 years following study initiation.

7. Inclusion/Exclusion Criteria

Inclusion criteria:

1. Motor incomplete paraplegia or tetraplegia, chronic (≥ 1 year after the injury). Non-traumatic SCI injuries can be included, given they are neurologically stable conditions for 12 months (e.g. tumor, transverse myelitis, but NOT Guilliane-Barré)

2. NLI C1- approximately T10 (inclusive, for upper motor neuron injuries only), as determined by the International Standards for Neurological Classification of SCI (ISNCSCI)

3. Sufficient diaphragmatic strength such that respiration is not compromised with exercise.

4. 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 4/5)

5.. AIS-C SCI & AIS-D SCI, as determined by the International Standards for Neurological Classification of SCI (ISNCSCI)

6.. Ambulates at a self-selected speed of <0.44 meters/second with or without physical assistance and assistance device

7. Able to advance at least one leg forward (volitionally with lower extremity movement (not as a result of trunk movement or spasticity) while using parallel bars, walker or crutches, with or without braces, and up to 2 people to assist with safety and balance only. Stepping is to be performed by the patient (without PT assistance at the lower extremities and no BWS).

8. 18 – 75 yrs, inclusive

9. No current or history of other neurological conditions

10. Screened and cleared by a physician

11. Involved in standing program or must be able to tolerate at least 15 min upright without signs or symptoms of orthostatic hypotension

12. Weigh 220 pounds (100kg) or less

13. Be able to fit into the Ekso device

14. Between approximately 5'0" and 6'4" tall

15. Standing hip width of approximately 18" or less

16. Have near normal range of motion in hips, knees and ankles

Exclusion criteria:

1. AIS-A SCI or AIS-B SCI

2. Lower motor neuron injuries, as shown by absent reflexes during bilateral quadriceps and Achilles tendon taps

3. < 3 months since previous intensive gait training regimen, FES cycling program, and lower extremity botox injections. The gait training regimen is meant to be formal gait training with feedback for progression of walking (i.e. PT sessions). Participant may have a regular home exercise program and/or a walking exercise program with a companion/ trainer for safety, but not for verbal or tactile cues or feedback regarding gait in the 3 months before initiating the protocol. If participant has a home exercise program and/or a walking exercise program, these programs (except FES cycling) should be continued without changes throughout the protocol. Electrical stimulation devices used regularly for foot drop during ambulation should be considered a brace and should continue to be used as usual throughout the protocol. Upper extremity botox injections are permissible before and during the protocol. One or two PT sessions are allowed to obtain a new brace or progress bracing and check for fit and safety, but no sustained gait training should occur.

4. Already walking at self-selected ambulation speeds of at least 0.44 meter/second with or without assistance

5. Currently involved in another intervention study

6. Concurrent neurological disease

7. Hip flexion contracture greater than ~17°

8. Knee flexion contracture greater than 12°

9. Unable to achieve neutral ankle dorsiflexion with passive stretch (neutral with max 12° knee flexion)

10. Leg length discrepancy

a. Greater than 0.5" for upper leg
b. Greater than 0.75" for lower leg

11. Spinal instability

12. Unresolved deep vein thrombosis

13. Uncontrolled autonomic dysreflexia

14. Severe muscular or skeletal pain

15. Spasticity that prevents joint motion (severe stiffness or rigidity,) where both legs have a MAS score of 3 or higher for half or more of their proximal lower extremity muscles; proximal muscles include hip flexors/extensors/adductors and knee flexors/extensors.

16. Open skin ulcerations on buttocks or other body surfaces in contact with exoskeleton or harness

17. Pregnancy

18. Cognitive impairments – unable to follow 2 steps commands and communicate for pain or to stop session

19. Shoulder extension ROM < 50° excludes crutches during sit to stand or vice versa. (Walking with crutches permitted.)

20. Participant requires the assistance of more than one therapist to transfer safely.

21. Uncontrolled or severe orthostatic hypotension that limits standing tolerance; defined as sustained, symptomatic drops in systolic and diastolic blood pressure when moving from sitting to standing

22. Active heterotrophic ossification (HO), hip dysplasia or hip/knee axis abnormalities

23. Colostomy

24. History of long bone fractures since the SCI, secondary to osteoporosis

25. Unable to sustain current medication regimen

26. Any reason the physician may deem as harmful to the participant to enroll or continue in the study

8. Screening, Enrollment, and Treatment Allocation

8.1 Screening and Informed Consent

Study participants will be recruited after the Institutional Review Board (IRB) has approved the study. The investigator or the investigator's designee will inform all patients who express willingness to enter the study about the purpose of the study, the required testing, procedures, and assessments, the expected duration, and the potential risks and benefits of study participation.

Potential participants are identified by the investigator or the investigator's designee. The investigator or designee will review the patient's history to determine the patient's initial eligibility for study entry. This

may be accomplished first by phone screening. After determining an applicant's initial eligibility status, the applicant may be offered the opportunity to participate in the study and will be given the opportunity to further discuss the available treatments, the risks and benefits, alternative therapies, and study requirements with the investigator or investigator's designee during the consent process. The applicant will be informed by the investigator or investigator's designee that he/she is free to change his/her mind and may withdraw from the study at any time without prejudicing further care. The study investigator or designee will give the applicant an informed consent document to read and time to ask questions and think about his/her decision prior to signing and dating the consent form. **After the Run-in phase has been completed, subsequent applicants must understand that if they qualify for participation in the study, they will be randomized to one of three possible treatments.** Further, the investigator or the investigator's designee will inform the applicant that as a Participant in a study, his or her medical records may be reviewed by the sponsor and representatives of regulatory bodies, and that study information will be used during the analysis of the results of the clinical study, but that the identity of the participant would not be disclosed to any reports emanating from this study. Applicants must sign a consent form before any study-specific evaluations or procedures are performed.

Applicants become enrolled as Participants in the study upon signing the consent form. The original signed consent form will be returned to the investigator and filed in the Participant's study file; the Participant will be given a copy of the signed consent to keep.

8.2 Run-in Participants, Randomization to Treatment Groups, and Treatment Rules

All sites will be allowed to enroll between one and four Run-in Participants. Run-in Participants are necessary for the study staff to demonstrate adequate knowledge and training using the Ekso device and to practice the data collection process that is required for this study. Run-in Participants are *not* randomized; they will be enrolled using a separate consent form. Run-in participants will train in the Ekso device for 12 weeks (36 sessions) and assessments will be done according to the Group 1 schedule except run-in participants will not complete the follow up evaluation visit and assessments (week 24). . It is not required for a site to complete all 12 weeks of training with all Run-in Participants before beginning the screening, enrollment, randomization, and baseline tests of other Participants. All subsequent study Participants are randomized via computer to one of three treatment arms, either Group 1, 2 or 3 defined respectively as Ekso intervention, active control or passive control in a 2:2:1 randomization ratio (respectively). Group 1, 2, or 3 descriptions are as follows:

Group 1: Ekso Intervention - Participants in this group receive Ekso GT robotic gait training 3 times per week for 12 weeks (36 sessions). Sessions will consist of 45 minutes of gait training in Ekso with a goal of a minimum 300 steps per session, and if possible, overground training without BWS. The 45 minutes will exclude set-up/donning/doffing time and include standing/up time, walking time, and seated rest breaks. Standard overground gait training will be included when the Participant requires only minimal assistance of one therapist and one aide to help control the assistive device. This will be assessed weekly during the 10MWT performed every 3rd session. At this point, sessions will consist of 30 minutes of session time gait training in the Ekso, followed by 15 minutes of session time performing standard overground gait training outside the Ekso, for a total of 45 minutes. See Table 1 A for the Ekso training progression strategy. The 15-minute overground gait training may take place at the first session if criterion for assistance is met. During the 15-minute overground gait training, any intervention, device, or bracing may be used EXCEPT Ekso, BWSTT, or any BWS. Stairs may be included during this overground gait training for a maximum of 5 minutes per session when the participant is able to perform them with only minimal assist or less of one PT.

Group 2: Active controls - Participants in this group will receive matched number of sessions of standard gait training 3 times per week for 12 weeks (36 sessions). Sessions will consist of 45 minutes a of body-weight supported treadmill training, and if possible, overground training without BWS. The 45 minutes will exclude set-up/harnessing time and include standing time, walking time, and seated rest breaks.. Sessions will begin with a minimum of 300 steps during BWSTT. Overground gait training will be included when the Participant requires only minimal assistance of one therapist and one aide to help control the assistive device for at least 10 meters. This will be assessed weekly during the 10MWT performed every 3rd session. Once the overground criterion is achieved:

1) If the initial 300 steps **are not completed** by the end of the first segment, the middle 15-minute segment must be gait training in BWSTT, and the final 15-minute segment must be OG gait training.
2) If the initial 300 steps **are completed** by the end of the first segment, the middle 15-minute segment can be continued gait training in BWSTT or OG gait training, per PT choice. The final 15-minute segment must be OG gait trainingSee Table 1 B for the training progression strategy and section 10 – Training Regimen and Rules for details.

See Table 1 B for the BWSTT training progression strategy. The overground gait training may take place at the first session if criterion for assistance is met. During overground gait training, any intervention, device, or bracing may be used, EXCEPT Ekso, BWSTT, or any BWS. Stairs may be included during this overground gait training for a maximum of 5 minutes per session when the participant is able to perform them with only minimal assist or less.

Group 3: Passive controls with cross-over option - Participants in this group continue with daily activities as normal over 12 weeks. No new gait training, mobility therapy, nor new medications (including Botox) are commenced during the study period. Participants in this group will come to the study sites for evaluations at 6 and 12 weeks (midpoint and endpoint). After the 12 week (endpoint) evaluation, the participants in this group will have an opportunity to choose to receive either Ekso or standard gait training therapy for 12 weeks/36 sessions.

9. Ekso Device Description and Safety Features

The Ekso GT is a powered motorized orthosis intended for those experiencing muscular and neurological conditions affecting their lower extremities to perform ambulatory functions including 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 lower legs, thighs, and different hip widths. Typically a physical therapist straps the patient's feet, legs, and torso into the device. When patients become more familiar with the Ekso they may strap themselves in. The straps are designed for the patient to easily get in and out of the device either on their own or with minimal assistance. Softgoods (pads, spacers, straps, and supports) are

available for bracing and adapting to numerous body types. The straps and softgoods 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 Ekso GT in use during gait training of an SCI patient.

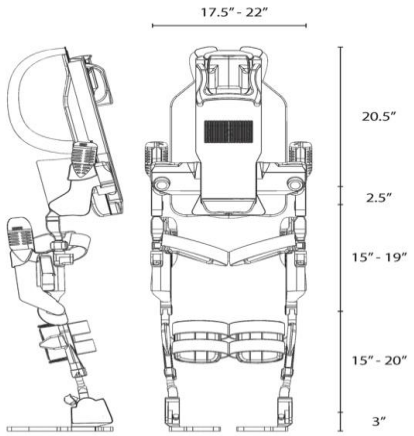

Figure 1 - The Ekso GT structure and general dimensions.

The Ekso GT 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 provided with the device. The physical therapist monitors the patient to ensure balance is maintained and operates the device. 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 Ekso GT has a number of features to ensure patient safety. It is equipped with mechanical hard stops at the limits of healthy subject 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.

The Ekso GT is intended to be used under the supervision of a physical therapist who has successfully completed the level 2 Ekso Bionics training program. This program covers all aspects of device operation and adjustment, including proctored and individual hands-on experience with patients. The program also covers methods of ensuring patient safety and requires participants to demonstrate their knowledge. To date, the Ekso GT has had no adverse events and has not caused any issues of compromised skin integrity.

If a Participant is randomized to Group 1, he/she must meet all criteria related to the Ekso GT per Ekso GT Operating Manual. All Ekso gait training will be conducted using the Ekso GT with SmartAssist base software. The Ekso will be programmed to allow bilateral assist mode with adaptive and fixed swing assist options, as well as unilateral and 2Free modes with neutral, high/low assistance, and high/low resistance options. Weight shifting training will be available as a pre-gait option.

10. Training Regimen and Rules

1. The participants in Groups 1 and 2 will gait train three times per week for 45 minutes per session, ideally over twelve weeks, for a total of 36 sessions.
2. The first patient training session occurs on a separate day from the screening and baseline data collection visit(s).
3. After the 18th and 36th sessions, the evaluations (mid-point and endpoint) are to be performed on a day without a gait training session.
4. It is recommended to schedule ~75 minutes per session not only to allow for set up, adjustments, and donning and doffing time, but also potential participant tardiness and restroom breaks, as well as data collection/testing time, as needed.
5. Donning time excludes all adjustments that can be accomplished prior to patient arrival (such as hardware adjustments and software programing).
6. All 36 sessions must be completed within 15 weeks of beginning training.
7. There should be no more than 4 visits (sessions/evaluation) per week, and no more than 1 session per day.
8. No more than a two week gap in training should occur at any time.
9. Given rules 6, 7, and 8: It is recommended to plan ahead for holidays and participant vacations during the training protocol.
10. Given rules 6, 7, and 8: Evaluations may be able to occur in keeping with a regular schedule (e.g. always MWF, if the participant works) or may be scheduled as a 4th visit for the week. Keep in mind the participant's potential fatigue effects, particularly during evaluation visits, if scheduling 4 visits in a week.
11. Every effort should be made to complete sessions and assessments within the appropriate windows.
12. Total session time is to be 45 minutes, +/- 10 minutes.
13. The 5-minute warm up and 2-minute cool down are counted as part of the walking time.

Table 1A consists of the progression strategy and guidelines for Group 1 (Ekso active group) and Run-in Participants and Table 1B consists of the progression strategy and guidelines for Group 2 (Active control group).

Table 1A Group 1 (Ekso) Progression Strategy

General rules for Ekso Active Group:

1) Sessions are divided into three 15-minute segments. This includes any rest breaks required, as well as a 5-minute warm-up and 2-minute cool down per session required by week 2.
2) Sessions begin with a goal of **a minimum of 300 steps per session in Ekso within trajectory**. Then can do outside of trajectory.
3) All sessions after session #3 must include a 5-minute warmup and end with a 2 minute cool down in Bilateral/Adaptive.
4) All device and assistive device progressions should be done in Bilateral/Adaptive. (Examples: FRW to Crutches; step length increase; step height decrease; target adjustment; turning mode or technique).
5) Each leg may be considered individually when considering reducing Fixed assist level, or choosing high/low assistance/resistance in 2Free. No unilateral trajectory-free stepping is allowed to avoid promoting gait asymmetries.
6) **If the participant is exceeding 750 steps per session, the therapist should increase the challenge to the participant.**
7) Excluding Ekso donning and doffing time, each session will last a total of 45 minutes, which will include standing/up time, walking time, and seated rest breaks.
8) Overground walking will be included when the Participant requires only minimal assistance of one therapist and the assistance of one aide to control the assistive device for at least 10 meters.
9) If participant is not yet performing overground gait training, all 45 minutes of session will be done in Ekso.
10) If participant is performing overground gait training, session will consist of 30 minutes of gait training in the Ekso, followed by 15 minutes performing overground gait training for a total of 45 minutes.
11) Step monitors are to be used during any OG gait training.

Timeline and settings	**Assist**	**Swing Assist**	**Progression and Adjustments**	**Considerations:**
Sessions 1-3	Bilateral	Trajectory Controlled: Adaptive	Pre-gait weight shifting Stance support remains at "Full" Minimize upper extremity loading. Optimize step height; swing time; step length; targets; etc.	Balance and gait progression Consistently hitting >300 steps per session Adjust targets/swing time/step length as appropriate
Anytime Session 3+	Bilateral	Trajectory Controlled: Adaptive	Pre-gait weight shifting when needed. Once participant has consistently managed >300 steps/session, progress to crutches if appropriate and encourage minimal UE loading	Adjust targets/swing time/step length as appropriate Step count with crutches should be at least 80% of step count with walker.
Training Guidelines	Bilateral	Trajectory Controlled: Adaptive->Fixed Trajectory Free: 2Free	PT may progress the participant by lowering the fixed assist for each leg, as tolerated and clinically appropriate. Stance support may be changed from "Full" to "Flex". Once initial 300 steps in trajectory are completed, PT may progress the participant via trajectory free stepping using "2Free". Stance support should begin at appropriate level". As participant improves stance control, support may be reduced as tolerated and clinically appropriate. Swing support should be assessed at "neutral". If a leg is not able to complete a step, "high"/"low assistance" may be provided for more normalized stepping. If a leg is stepping far outside of the general trajectory, "high"/"low resistance" may be provided for more normalized stepping. Progress to more symmetrical gait.	Step count must be at least 300 within trajectory. Must include 5 min warm-up at beginning and 2 min cool down at end in bilateral adaptive. Borg range 12-17 to prevent fatigue early in the session No more than 3 swing completes per minute in Fixed assist. (If so, then increase Fixed swing assist by 10 or reduce swing complete time) No unilateral trajectory free stepping to avoid promoting gait asymmetries.

Progression Guidelines	Bilateral	Trajectory Controlled: Adaptive->Fixed	If initial 300 steps within trajectory is achieved/projected, the therapist may challenge the participant by the following, as tolerated and clinically appropriate: Lower the Fixed assist bilaterally as appropriate Stance support may be changed from "Full" to "Flex".	Step count must be at least 300 within trajectory. Must include 5 min warm-up at beginning and 2 min cool down at end in bilateral adaptive. Borg range 12-17 to prevent fatigue early in the session No more than 3 swing completes per minute in Fixed assist (If so, then increase Fixed swing assist by 10 or reduce swing complete time)
		Trajectory Free: 2Free	Once initial 300 steps in trajectory are completed, set swing support at appropriate assistance/resistance for an appropriate clinical challenge	No unilateral trajectory free stepping to avoid promoting gait asymmetries.

Table 1B Group 2 (Active Controls) Progression Strategy

General rules for Active Controls:

1) Sessions are divided into three 15-minute segments. This includes any rest breaks required, as well as a 5-minute warm-up and 2-minute cool down per session required by week 2.
2) Participants will perform gait training with BWSTT for the full session (all 3 segments) until the OG criterion is met. This gait training must continue for a **minimum of 300 steps** at the beginning of each session.
3) Manual assistance from the physical therapy team to facilitate normal stepping kinematics is permissible.
4) BWS and speed are to be determined by the physical therapist based on appropriate stepping kinematics, level of challenge to the participant, and safety of the participant and trainer(s).
5) Participants will perform gait training with BWSTT for the full session (all 3 segments) until the OG criterion is met. Participants may proceed to overground gait training **without BWS** only when they require minimal physical assistance of the physical therapist, plus assistive device control or supervision of another team member for at least 10 meters.
6) Once the OG criterion is achieved:
   a. If the initial 300 steps **are not completed** by the end of the first segment, the middle 15-minute segment must be gait training in BWSTT, and the final 15-minute segment must be OG gait training.
   b. If the initial 300 steps **are completed** by the end of the first segment, the middle 15-minute segment can be continued gait training in BWSTT or OG gait training, per PT choice. The final 15-minute segment must be OG gait training.
7) Step monitors are to be used during the full 45 minutes of gait training.

	Focus	**Progression and Adjustments as Tolerated****	**Considerations:**
Sessions 1-3	• Determine parameters for best kinematics • Participant familiarization • Posture	Determine comfortable BWS, stepping speed range, amount of physical assistance at each location, and bout length	Educate and engage posture and basic stepping Educate and ensure joint protection
Sessions 4-6	• Posture • Good stepping kinematics • Increase load as tolerated* • Increase speed range as tolerated All sessions should have 5 minute warmup and 2 minute cool-down.	• Decrease BWS if tolerated • Increase/decrease speed • Increase bout lengths	Engage posture and both swing/stance phases of stepping Ensure good posture, stepping kinematics, and joint protection. Borg range 12-17 to prevent fatigue early in the session
Sessions 7-18	• Increase load weekly if tolerated* • Increase speed range as tolerated • Increase independence • Increase endurance All sessions should have 5 minute warmup and 2 minute cool-down.	• Decrease BWS if tolerated • Increase/decrease speed • Decrease physical assistance • Increase bout lengths, decrease rest breaks • Introduce walking sideways, backwards, stepping over obstacles, quick speed changes, quick start/stops if tolerated	Engage hip control and motor control (concentric/eccentric) of stepping, arm-swing Ensure good posture, stepping kinematics, and joint protection. Borg range 12-17 to prevent fatigue early in the session
Sessions 19-36	• Increase load weekly if tolerated* • Increase speed range by as tolerated • Increase independence • Increase endurance • Increase adaptability All sessions should have ~5 minute warmup and ~2 minute cool-down.	• Decrease BWS if tolerated • Increase/decrease range • Decrease physical assistance • Increase bout lengths, decrease rest breaks • Continue or introduce walking sideways, backwards, stepping over obstacles, quick speed changes, quick start/stops	Engage motor control of posture, hips, symmetric stepping, arm swing (when evaluable) Ensure good posture, stepping kinematics, and joint protection. Borg range 12-17 to prevent fatigue early in the session

* Training intensity should be increased first by increasing loading. If amount of loading puts participant or trainers at risk for injury, then increasing speed range or independence can be the focus of increasing intensity.
** PT can adjust one or multiple parameters at a time. PT can adjust parameters for interval training, e.g. lower BWS for 5 minutes.

11. Participant and Therapist Assessments

Phone or in-person limited screening procedures are conducted to assess minimal trial inclusion. Baseline procedures establish a baseline for future comparisons. (Prior to initiating physical or psychological screening evaluations, study personnel must obtain a signed informed consent.) Participant screening can then proceed to ensure the individual meets inclusion/exclusion criteria and baseline data will be collected for comparisons. The screening and baseline procedures can occur over one or two visits.

The following information will be obtained during *screening* and, if Participant passes screening, may be used for baseline.

1. Demographic data including date of birth, gender, date and cause of injury, (self-reported)
2. Past and current medical history (self-reported)
3. List of current medications
4. Weight, height, Body Mass Index (BMI)
5. Blood pressure (sit to stand)
6. Written documentation from the participant's SCI physician verifying the participant is medically stable and cleared for full weight bearing locomotor training and does not have any conditions that would exclude the Participant including: spinal instability, unresolved DVT, decreased standing tolerance due to orthostatic hypotension, two or more spontaneous lower extremity long bone fractures in the last 48 months, hip subluxation, autonomic dysreflexia, known pregnancy (if relevant), colostomy, history of head injury or other central nervous system disorders that may impact motor planning or impulsivity, significant cardiac or pulmonary disease (screening). (see Inclusion/Exclusion criteria)
7. Current practice of standing or walking, level of assistance required, assistive devices and braces used, and any associated adverse events (self-reported)
8. Observation of a level surface wheelchair to mat transfer.
9. Range of motion for hip flexion/extension, knee flexion/extension/ ankle dorsi/plantar flexion
10. Upper extremity MMT to include: shoulder flexion/extension/abduction and elbow extension
11. Spasticity of the hip, knee and ankle muscles as assessed by the Modified Ashworth Scale at screening.
12. Skin check of back, sacrum, shins, and feet (must be done at each visit)
13. Neurological exam will be obtained using the ISNCSCI examination for motor and sensory testing and for designation of AIS and ISNCSCI motor scores of UEMS and LEMS

See Appendix A for description of assessments.

If the participant continues to meet criteria for this study the following data will be collected as *baseline data.* **NOTE: All Participant evaluations are conducted outside of Ekso, BWSTT, or BWS for overground walking**. **Baseline examinations may not occur more than 30 days prior to initiation of the training regimen:**

1. 10 Meter Walk Test (10MWT), at both self-selected and fast speeds
2. GAITRite Pressure Map for Temporospatial Gait Parameters (if site has one)
3. Timed Up and Go (TUG)
4. 6 Minute Walk Test (6MWT)
5. Spinal Cord Injury Functional Ambulation Inventory (SCI-FAI)
6. Walking Index for Spinal Cord Injury (WISCI II)
7. Upper and Lower Extremity Muscle Strength
8. Berg Balance Scale
9. The Spinal Cord Assessment Tool for Spastic Reflexes (SCATS)
10. Spinal Cord Independence Measure III (SCIM-III), Mobility subscale only, by interview
11. Modified Ashworth Scale
12. Spinal Cord Injury Spasticity Evaluation Tool (SCI-SET)

13. Numeric Rating Scale for spasticity
14. International SCI Quality of Life Basic Data Set
15. Epidemiological Studies Depression Scale (CES-D 10)
16. Borg Scale for maximal Rate of Perceived Exertion (collected at baseline 6MWT and at training session 1)
17. International SCI Pain Basic Data Set
18. Modified International SCI Bowel Function Basic Data Set
19. Modified International SCI Lower Urinary Tract Basic Data Set

See Appendix A for description of assessments.

The following data will be collected *per session*:

1. Any adverse events/complications (related to Participant or staff) noted following prior training session and during present session
2. Assessment of skin integrity of the anterior and posterior torso, anterior tibia, sacral area and bilateral feet (before and after training)
3. Walk time*
4. Stand time*
5. Seated rest time
6. Number of steps total and in each mode* or number of steps at each BWS%
7. Time spent in each mode* or time spent at each BWS%
8. Any equipment used for training, including type of assistive device and braces
9. Number of therapists/staff required at each training session to ensure the safety of the Participant and to complete the training session goals
10. Amount of assistance (e.g. min, mod, max) as reported by staff members at each training position (hips, trunk, right LE, left LE, etc.)

* For Group 1 Participants, these data are *automatically collected* by Ekso (in Ekso Pulse) at the end of each training session

The following data will be collected *at every 3rd session* (i.e. session 3, 6, 9, etc.,(refer to Table 2):

1. 10MWT without braces at self-selected speed
2. Borg Scale for maximal RPE during intervention and overground training
3. Numeric Pain Rating Scale of neuropathic pain during rest and during the intervention
4. Numeric Rating Scale for spasticity
5. NASA – Participant Task Load Index
6. Heart rate and blood pressure

Therapist assessments include the following:

1. NASA-Task Load Index
2. Video Assessment of therapist posture during sessions 1 and 36
3. Borg Scale for maximal RPE during intervention and overground training
4. Reports of injuries or pain (includes all treating staff)

Table 2 shows the list of Participant assessments and data collection intervals. Therapist measures are included in Table 3.

Table 2 - Participant Assessments and Data Collection Intervals **Assessment**	**Screening[1] Visit [8]** (may be used for baseline data if done over 1-2 days)	**Baseline[1] Visit[8]** *Week 0* *(Not > 30 days prior to first training session)*	**Session Assessments GROUPS 1 & 2[3] (and Run In•)** *Sessions 1-36*			**Evaluations ALL GROUPS (including Run In)** *After session 18* *Week 6*** *Midpoint* *(+/- 1 week of completing session 18)*	**Evaluations ALL GROUPS (including Run In)** *After session 36* *Week 12*** *Endpoint* *(+/- 1 week of completing session 36)*	**Evaluations GROUPS 1 & 2 only (Not Run-In or Group 3 Participants)** *Week 24*** *Follow-Up,* *3 months following the last training session* *(+/- 3 weeks)*
			B[2]	**D[2]**	**A[2]**			
Physician Clearance		✓						
Demographics ˆ	✓							
Medical History ˆ	✓							
Concomitant Medications[4]	✓	✓	✓			✓	✓	✓
BMI ˆ ‡	✓	✓				✓	✓	✓
Vital Signs ° ˆ	✓°°	✓°°°	✓◌”			✓°°°	✓°°°	✓°°°
ROM: Hip, Knee, Ankle ˆ	✓							
UE MMT[5] ˆ	✓							
Skin Assessment[6]	✓	✓	✓		✓			
Modified Ashworth Scale	✓	✓¤				✓	✓	✓
SCATS		✓				✓	✓	✓
UEMS	✓	✓☆				✓☆		✓☆
LEMS	✓	✓☆				✓☆		✓☆
Full ISNCSCI Exam ˆ	✓						✓	

Assessment	Screening[1] Visit [8] (may be used for baseline data if done over 1-2 days)	Baseline[1] Visit[8] *Week 0 (Not > 30 days prior to first training session)*	Session Assessments GROUPS 1 & 2[3] (and Run-In*) *Sessions 1-36 No braces for 10MWT*			Evaluations ALL GROUPS (including Run-In) *After session 18** (Week 6) Midpoint (+/- 1 week of completing session 18) Braces OK for walking tests*	Evaluations ALL GROUPS (including Run-In) *After session 36** (Week 12)Endpoint (+/- 1 week of completing session 36) Braces OK for walking tests*	Evaluations GROUPS 1 & 2 only (Not Run-In or Group 3 Participants) *3 months following the last training session** (Week 24) Follow-Up, (+/- 3 weeks) Braces OK for walking tests*
			B[2]	D[2]	A[2]			
Berg Balance Scale		✓				✓	✓	✓
10 Meter Walk Test [7] (self-selected and fast)	✓	✓ *(both with and without braces)*	✓[11]			✓ *(baseline + current device/braces)*	✓ *(baseline + current device/braces)*	✓ *(baseline + current device/braces)*
Timed Up & Go (TUG) [10]		✓				✓	✓	✓
6 Minute Walk Test [10]		✓				✓	✓	✓
SCI-FAI		✓				✓	✓	✓
WISCI II[12^]		✓				✓	✓	✓
SCIM-III, Mobility subscale only		✓				✓	✓	✓
SCI-SET		✓				✓	✓	✓
Numeric Rating Scale (for spasticity)		✓ (after 1st session)			✓[11]			
International SCI Quality of Life Basic Data set		✓				✓	✓	✓
Epidemiological Studies Depression Scale (CES-D 10)		✓				✓	✓	✓
Borg - Maximum during training and 6MWT		✓ (during baseline 6MWT and after 1st session)		✓[11]		✓	✓	✓
NASA- Task Load Index		✓ (after 1st session)			✓[11]			
International SCI Pain Basic Data Set		✓				✓	✓	✓
Numeric Pain Scale † (for neuropathic pain)		✓ (after 1st session)	✓[11]	✓[11]				

Assessment	Screening[1] Visit [8] (may be used for baseline data if done over 1-2 days)	Baseline[1] Visit [8] *Week 0* *(Not > 30 days prior to first training session)*	Session Assessments GROUPS 1 & 2[3] (and Run-In•) *Sessions 1-36*			Evaluations ALL GROUPS (including Run-In) *After session 18* *Week 6*** *Midpoint* *(+/- 1 week of completing session 18)*	Evaluations ALL GROUPS (including Run-In) *After session 36* *Week 12*** *Endpoint* *(+/- 1 week of completing session 36)*	Evaluations GROUPS 1 & 2 only (Not Run-In or Group 3 Participants) *Week 24*** *Follow-Up,* *3 months following the last training session* *(+/- 3 weeks)*
			B[2]	D[2]	A[2]			
Modified International SCI Bowel Function Basic Data Set		✓				✓	✓	✓
International SCI Lower Urinary Tract Basic Data Set		✓				✓	✓	✓

Footnotes (Table 2):

‡ Height may be obtained verbally; weight must be measured via scale. ~~Calculate BMI using NIH National Heart Lung and Blood Institute calculator at: http://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm~~

* Skin assessment to be performed before and after training sessions

• Maximum Borg to be done during session 1 then during weekly sessions (every third session) thereafter, and after 6 minute walk test during evaluations

** Assessments to be performed outside of exoskeleton or any body weight support and on a non-training day.

° Vital signs (BP and HR) will be measured as follows:

_ °° Upon relaxation (5 minutes) in sitting position after arrival. After 1 minute of standing (may hold on to something for balance or use standing in frame as needed)

_ °°° Vitals should be taken in sitting before and immediately after 6 minute walk

- ↄ To be taken prior to 10MWT

– ” To be taken prior to each session and needed only if orthostatic hypotension was present at the time of the previous session and/or if symptomatic upon standing at the time of the current session.

♦ Run In will follow Group 1 assessments but will not complete the follow up evaluation visit and assessments

ˆ To be obtained during Screening, and if participant passes screening can be used for Baseline

† Numeric Pain Scale: to be completed before and during session 1 and weekly thereafter

¤ To be done by blinded evaluator for comparison to week 6, 12, 24 (midpoint, endpoint, and follow-up) evaluation visit results.

☆ Done by blinded evaluator for comparison. Testing to be done according to ISNCSCI instructions (supine, using the correct limb positioning and angles for resistance)

[1] May occur over one or two visits

[2] B = before session, D = during session, A = after session

[3] Passive Group 3 will complete all evaluations at Baseline, Week 6 and week 12, the same as Groups 1 and 2, then have the option (per participant decision) to undergo 12 weeks of training using the exoskeleton or standard gait training. The optional 12 week period will consist of training only. No further evaluations will be completed at this time.

[4] Update Concomitant Medication Log accordingly

[5] To include shoulder flexion/extension, abduction/, and triceps

[6] Skin assessment with focus on back, sacrum, shins, and feet to be collected before and after each training session

[7] To be collected outside of the exoskeleton or any body weight support, and prior to any training session; can be used to assess readiness to transition to overground training weekly.

Screening: (10MWT) *1 walk with or without braces at self-selected speed to confirm qualification self-selected speed of <0.44 m/s. A second trial may should be done if first trial is close to 0.44 m/s.*

Baseline: up to *8 trials (total) of 10MWT (2 trials each, with and without braces at both self-selected and fast speeds (to be done by blinded evaluator)*

Every 3rd session: *10MWT (2 trials, without braces at self-selected speed), every 3rd session, if possible. The walk is done without braces (to determine neurological recovery changes). Pt can complete second walk to donn Ekso, or to donn the harness for BWSTT (depending on randomization and tolerance).*

Evaluations at 6, 12, 24 weeks (midpoint, endpoint, and follow-up): *up to 8 trials (total) of 10MWT (2 trials each, with **baseline** device/braces at both self-selected and fast speeds, then 2 trials with **current*** device/braces at self –selected *and fast speeds, performed with whatever assistive devices are needed for safe ambulation (to be done by blinded evaluator)*

[8] The first training in the exoskeleton occurs separately from screening and baseline data collection

[9] Form to be completed at the time of study completion or at any time of early termination

[10] Use baseline assistive device(s) and brace(s) for all TUG and 6 MWT assessments.

[11] Every 3rd session

[12] Score WISCI for current device/braces at self-selected speed

Table 3 - Therapist Assessments, and Data Collection Intervals (to be completed by the lead treating PT). Report of pain/injury to be completed by all participating session staff **Assessment**	**Baseline Visit** After 1st Session	**Session Evaluations GROUPS 1 & 2[3] (and Run-In)** *Sessions 1-36*			**Evaluations ALL GROUPS (including Run-In)** After s*ession 18*** *(Week 6)* *Midpoint* *(+/- 1 week of completing session 18)*	**Evaluations ALL GROUPS (including Run-In)** After s*ession 36*** *(Week 12)* *Endpoint* *(+/- 1 week of completing session 36)*
		B[2]	**D[2]**	**A[2]**		
NASA – Task Load Index, therapist physical load***	✓ (after 1st session)			✓		
Video assessment of posture during training ○	✓ (after 1st session		✓*			
Borg Perceived Exertion (in each training environment) **	✓ (after 1st session		✓			
Therapist/staff report of pain and/or injury ****	✓			✓		

*During first and last sessions only (sessions #1 and #36)

○ Video of session # 36 should be taken at the same general point as session #1 as noted on source document.

** During session 1 and every 3rd session thereafter (starting with session 3)

*** After session 1 and every 3rd session thereafter (starting with session 3)

**** Baseline upon registration for ID in EDC (before first session) and every session thereafter . To be completed by all staff participating in a treatment session.

12. Adverse Events

An adverse event (AE) is any untoward medical event that occurs to a study participant once the individual has signed the informed consent form until the study participant's last study visit.

Examples include:

- Any sign, symptom, or physical examination finding that worsens in nature, severity or frequency compared to baseline

A serious adverse event (SAE) is one that meets any of the following criteria:

- Results in death
- Is life threatening
- Requires inpatient hospitalization or prolongation of an existing hospitalization
- Results in persistent or significant disability/incapacity
- An important medical event that may not result in death, be life-threatening, or require hospitalization, may be considered a serious adverse event when, based upon appropriate medical judgment, it jeopardizes the participant and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.

A life-threatening adverse event is defined as any adverse experience that places the participant, in the view of the Investigator, at immediate risk of death from the event as it occurred, i.e. it does not include an event that, had it occurred in a more severe form, might have caused death. ALL serious adverse events must be reported to the Sponsor within 24 hours of the knowledge of the event and reported to the respective IRB as soon as possible but no later than ten working days after the investigator learns of the event or as required by the IRB. In the event of subject death, a copy of death records, medical records pertaining to the events leading up to the death and an autopsy report (if performed) must be sent to the Sponsor as soon as possible. All subject identifiers other than the subject number and initials must be removed from the documents submitted to the Sponsor.

A pre-existing condition is one that is present prior to or at the start of the study and is to be reported as part of the participant's medical history. It should be reported as an adverse event only if the frequency, intensity, or the character of the condition worsens during study participation.

An unexpected adverse event is one not identified in nature, severity, or frequency in the current protocol.

Adverse events (AE) data collection must begin once the Participant has signed the informed consent document. AEs will continue to be collected each visit during the entire 12 week training period and end at the 6 month visit. In general, AEs should be reported and classified by the investigator using a diagnosis. The diagnosis should be confirmed through specific signs, symptoms, and (if necessary) laboratory tests. Data to be collected will include the description of the event, onset and resolution dates (or whether the event is ongoing), severity, management/treatment, outcome, and determination of the relationship to the device used during training. The relationship of the event to the device used will be further described as related or unrelated to a specific device. If related to a device, the categories will be further described as definitely, probably, or possibly-related using the following definitions:

1. *Definitely device-related*: Any event that is associated with the device by timing and physiology, and was caused or contributed to by the device.
2. *Probably device-related*: Any event that is associated with the device by timing and physiology, and there is a good chance that it may have been caused or contributed to by the device.
3. *Possibly device-related*: Any event that is associated with the device by timing and physiology, and there is a possibility that it may have been caused or contributed to by the device.

Severity of the AE will be coded as to the degree of severity as follows:

A. *Mild***:** Awareness of the event but easily tolerated.

B. *Moderate*: Discomfort enough to cause interference with usual activity.
C. *Severe*: Inability to carry out usual activity (not necessarily the same as a Serious Adverse Event. Subjects may have a severe flu but not require hospitalization.)

Treatment for the AE includes all of the commercially approved products or standard procedures that are to be administered according to standard medical practice. Investigational products or procedures are not to be used as a treatment for an adverse event. All unresolved AEs should be followed by the Investigator until all events are resolved, the event is identified as being a chronic condition, or the participant is lost to follow-up.

The case report form package for this study includes dedicated adverse event and serious adverse event forms.

An independent Data Safety Monitoring Board (DSMB) will assess and adjudicate all SAEs and protocol violations.

13. Participant Termination

Participants will be advised that they may voluntarily withdraw from the study at any time and will be instructed to notify the investigator immediately if they choose to withdraw. Participants may choose to withdraw for any reason and are not obligated to reveal their reason(s) for withdrawal. Should Participants withdraw prior to follow-up completion, they will be asked to complete the final questionnaires if withdrawn prior to the end of the participation period. In addition, Participants may be involuntarily withdrawn by the investigator if the investigator believes it is in the best interests of the Participant (e.g., adverse event that prevents further visits).

If a Participant is lost to follow up, the End of Study CRF must be completed and submitted to the data manager as soon as possible. If a Participant fails to comply with the follow up evaluations, the study site must attempt to contact the Participant at least three times, including once as a registered letter.

In order to minimize loss to follow-up, at the baseline evaluation visit the study coordinator will request that the Participant provide names and contact information of two individuals who have a close relationship with the Participant. The contacts will be utilized in the event that the Participant relocates or cannot be reached by mail or telephone. This information will be treated as confidential and for use by the investigative site only. Every effort will be made to retain Participants for the entire 6 months of follow up.

14. Data Collection and Reporting

Source documents will be used to record demographic and assessment data as well as any adverse events which may occur during the study period. Source document data will be transferred to case report forms that will be submitted to the data manager. The Sponsor reserves the right to use a third-party data manager and/or electronic data capture during this study.

15. Confidentiality of Data

All information and data sent to the Sponsor, Contract Research Organizations, DSMB, or the Data Manager concerning Participants or their participation in this study will be considered confidential. All data used in the analysis and reporting of this evaluation will be used in a manner without identifiable reference to the Participant. The principal investigator consents to visits by the staff of the Sponsor and its authorized representatives or any other local or national governmental body to review the study Participants' medical records including any test or laboratory data that might have been recorded on diagnostic tests media (e.g., X-rays, video, photographs, etc.).

16. Record Retention

The study site is required to retain all study records required by the applicable regulations in a secure and safe facility. The study site must consult with the Sponsor before disposal of any study records, and must notify the Sponsor of any change in the location, disposition or custody of the study files. The study site must take measures to prevent accidental or premature destruction of essential documents, that is, documents that individually and collectively permit evaluation of the conduct of a study and the quality of the data produced, including paper copies of study records (e.g., patient charts) as well as any original source documents that are electronic as required by applicable regulatory requirements. All study records must be retained for at least two years after the study is completed. Participant files and other source data must be kept for the maximum period permitted by the hospital, institution or private practice, but not less than two years. These documents should be retained for a longer period, however, if required by the applicable regulatory requirements. The Sponsor must be notified and will assist with retention should study site be unable to continue maintenance of participant files for the full two years. It is the responsibility of the study site to inform the Sponsor as to when these documents no longer need to be retained.

17. Statistical Methods

17.1 General Principles

The primary analysis for all baseline characteristics and study outcomes will include all available data for all enrolled subjects. Standard summary statistics will be calculated for all study variables. For continuous variables, statistics will include means, standard deviations, medians and ranges. Categorical variables will be summarized in frequency distributions.

Statistical analyses will be conducted according to the principles of intent-to-treat, under which subjects will be evaluated according to their randomized assignment regardless of the treatment actually received. P-values for tests of superiority will be two-sided and for non-inferiority one-sided, with values less than 0.05 deemed statistically significant.

Statistical analyses will be conducted in SAS version 9.3 or above (SAS Institute, Cary, N.C.), R version 3.2 or above (R Foundation for Statistical Computing, Vienna, Austria, http://www.R-project.org) or another validated statistical software package.

17.2 Primary Endpoint

The primary endpoint is change in gait speed (self-selected and fast) demonstrated during the 10MWT after 12 weeks of training, compared to baseline. Two hypotheses are associated with this endpoint; first, that the mean change in the Ekso intervention group will be statistically superior to that in the passive control group, as follows:

$$H_0: \mu_E \leq \mu_P$$
$$H_A: \mu_E > \mu_P,$$

where μ_E and μ_P are the mean change in the Ekso and passive control groups, respectively. The hypothesis will be tested using a two-sample Student's t or Wilcoxon rank-sum depending upon normality of the trial data.

The second hypothesis is that the mean change in the Ekso intervention group will be statistically non-inferior to that in the active control group, as follows:

$$H_0: \mu_E \leq \mu_A - \Delta$$
$$H_A: \mu_E > \mu_A - \Delta,$$

where μ_E and μ_A are the mean change in the Ekso and active control groups, respectively, and Δ is the non-inferiority margin. Δ is selected based upon the principles that it should be substantially less than the expected effect size comparing Ekso to passive control, and that it should represent a clinically acceptable margin of effect when differentiating Ekso from active control.

For this purpose, Δ is therefore defined to be 0.055 m/s, which is one-half of the hypothesized treatment effect of Ekso over passive control as stated below, and one-eighth of the threshold of 0.44 m/s (1.0 mph) commonly used to represent gait speed associated with community ambulation.

17.3 Subgroup analysis

A subgroup analysis of gait quality, including left and right lower extremity single support time, initial double support time, step length, and stride width will be performed in centers using GAITRite equipment and software and compared between randomized groups. The sample available for this sub-analysis is expected to be approximately 30% of the total study population.

17.4 Sample Size

Computations for sample size and power are based on effect sizes derived from internal study data and the relevant clinical literature for the primary endpoint. For the Ekso intervention group, the postulated effect (derived from internal study data) is a mean change from baseline in gait speed of 0.11 m/s, with a corresponding standard deviation of 0.18 m/s. For the active control group, the postulated effect is a mean change from baseline in gait speed of 0.078 m/s (derived from the relevant clinical literature), with a corresponding standard deviation of 0.108 m/s.

The passive control group is postulated to have a mean change of zero with the same standard deviation as active control, or 0.108 m/s. Sample size and power are then computed for both statistical tests cited above: superiority of Ekso to passive control and non-inferiority of Ekso to active control.

Under 2:2:1 randomization with a desired power of 80%, the required sample size for superiority of Ekso intervention to passive control is 38 subjects with evaluable data in the Ekso group and 19 in passive control (incorporating the 2:1 Ekso: passive control randomization). For non-inferiority of Ekso to active control, the groups are of equal size and the required sample size is 37 per group.

Taking the greater of these numbers for each randomized group, total sample size under 2:2:1 randomization is therefore 38 for Ekso intervention, 38 for active control and 19 for passive control, a total of 95. To account for possible attrition as well as potential variance from the postulated effects, up to 127 subjects in the randomized group will be enrolled.

18. Visits and Visit Windows

The following are the planned Participant visits and their associated windows. Missed visits should be made up so that testing can be conducted within the appropriate window of time.

Table 4 – Planned Participant Assessments and Assessment Windows

Time point	Window
Baseline	No more than 30 days prior to start of training
6 Weeks(after 18 session)	No more than 1 week after session 18
12 Weeks (after 36 session)	No more than 1 week after session 36
6 Months	+/- 3 weeks

18.1 Handling of Dropouts, Treatment Rescues and Missing Data

Values for missing data will not be imputed, but exploratory analyses may be performed using the last real assessment for that patient (LOCF).

18.2 Subgroup Definitions

Subgroup factors of interest include age, level of assistance (based on FIM-Scores), non-responders vs. responders, time since injury, spasticity, and other differences among this diverse group.

* Exploratory analyses on these subgroups of Participants will be performed provided that there are a sufficient number of Participants in a given subgroup.

19. Investigative Centers/Minimum and Maximum Enrollment

Up to fifteen centers will participate in the study. Centers are chosen based on experience with the Ekso device and having appropriate personnel to conduct and support research studies. Each center is expected to contribute at least 1 Run-in and 8 Randomized Participants and no center shall contribute more than 4 Run-ins and 37 Randomized Participants (30% of total maximum enrollment for the Randomized group). If very low enrolling centers (<8 Randomized Participants) exist after study close, these may be combined with other centers for analysis purposes assuming that all centers maintained adherence to the protocol and that the data gathering mechanism is the same for all centers.

20. Quality Assurance of the Data

Participant case report forms will be collected and reviewed for completeness and accuracy by the Monitor as well as for any evidence suggesting Participant risk. Where discrepancies are noted, they will be resolved with the investigator and/or an individual designated by the investigator. Where the data are incomplete, attempts will be made to obtain the missing data. The Sponsor reserves the right to use a third-party data manager throughout the study period. The data manager will be required to have quality assurance procedures in place.

21. Study Termination

The Sponsor reserves the right to terminate the study before enrollment has been completed and to report on study results at interim time-points without statistical penalty.

22. Personnel Responsibilities

22.1 Principal investigator responsibilities

a) Permit monitor inspection of facilities and records.
b) Permit inspection of facilities and records by government bodies.
c) Submit protocol and informed consent to IRB and await approval.
d) Submit proposed amendments to protocol and informed consent to IRB and await approval, unless the change reduces the risk to Participants.
e) Obtain informed consent of Participants.
f) Implement study in accordance with protocol.
g) Complete source documents and case report forms.
h) Explain deviations from protocol and report to monitor.
i) Submit annual progress reports, final reports, and adverse effect reports to IRB and sponsor as required by law.
j) Maintain medical histories of Participants.
k) Retain records for two years following study completion.

22.2 Sponsor Responsibilities

Listed below are the Sponsor's responsibilities for this study.

a) Assure IRB approval of protocol and informed consent is obtained
b) Select and train monitors
c) Select investigators
d) Train site personnel in device use (as appropriate)
e) Obtain protocol signature, curriculum vitae and proof of appropriate licensure of investigator and other study staff
f) Investigate device-related adverse events
g) Oversight responsibility for data review and analysis
h) Obtain statement of financial disclosure for publication and presentation purposes

23. Potential Risks to Study Participants and Mitigation of Risks

1) The risk of falling: Having experienced therapists conduct the training sessions will minimize the risk of falling.

2) Risk of exceeding range of motion: This would be caused if any device moves the Participant beyond the normal range of motion, resulting in a strain, sprain or fracture. For the Ekso device, this risk is lessened by mechanical hard stops that prevent the device from exceeding a normal human range of motion even in the event of an electrical or software failure. Software systems are also in place to further reduce range of motion to improve fit and comfort during walking. Participants will be evaluated by clinicians who will eliminate Participants from being included in the study if Participants cannot meet the required range of motion. For all other devices, this risk will be mitigated through proper settings by the physical therapist in charge of Participants treatment.

3) Discomfort, skin pressure/friction, bruising, pain, or unusual swelling caused by any device that contacts the skin. This risk will be minimized by a thorough skin check performed by experienced personnel at each training session. Adjustments to the harness placement and additional padding will be assessed to decrease the risk of skin breakdown as well.

4) Blood pressure instability related to standing or activity. This risk will be reduced by checking blood pressure and heart rate prior to training, and as necessary during training and after.

5) Reflex bowel or bladder activity or autonomic instability during walking. This risk will be minimized by requiring Participants to relieve bowels and bladder prior to walking.

6) Spasms triggered by joint movement in the device. This risk will be reduced through screening prior to enrollment in the study. Participants cannot take part if the Participant's muscles are too stiff.

7) Any device used during this study could malfunction. In the event of device malfunction, Participants will be able to safely transfer out of the device.

8) There is a risk of fractures when participating in a therapy program: this will be minimized by requiring medical clearance if Participants are at risk for severe osteoporosis.

9) Risk from loss of confidentiality. To minimize this risk, Participants will be assigned a unique numeric identifier to be included on test records and test documentation. Research information shared with people outside the study center will not include Participants' name, address, telephone number or any other direct personal identifier unless disclosure of the personal identifier is required by law. Records may be viewed by the study sponsor and Investigators, study monitors and auditors (such as the IRB) who make sure that the study is being done properly.

10) Muscle strains and tendon sprains and swelling due to joint misalignment during stepping. To minimize this risk, therapists and trainers will have undergone training to protect joints. The Ekso minimizes this risk by allowing movement of the hip, knee, and ankle only in the sagittal plane. BWSTT reduces this risk by providing body weight support during stepping.

24. Provisions for Research Related Harm/Injury

Non-Significant Risk
The Ekso GT is a non-significant risk device in the context of the WISE trial. The device is 510(k) cleared by the FDA (K161443) for Individuals with spinal cord injuries at levels T4 to L5 (upper extremity motor function of at least 4/5 in both arms), and individuals with spinal cord injuries at levels of C7 to T3 (ASIA D with upper extremity motor function of at least 4/5 in both arms). Where injuries at a higher level than currently cleared by the FDA are included (C1 to T3), the inclusion criteria is in line with the Ekso GT intended use in the EU per the CE certification (UL as notified body), which has been in effect since 2013 without any serious adverse events. Users must meet functional requirements, including but not limited to sufficient upper body strength to control a walking aid such as a walker, crutches, or a cane. Users must also obtain physician clearance of health status prior to inclusion. Further, the Ekso GT has a number of safeguards to minimize risk to patients and therapists, as outlined below, and is used under the supervision of a physical therapist who has successfully completed the level 2 Ekso Bionics training program.
The Ekso GT is equipped with mechanical hard stops at the limits of healthy subject ranges of motion to prevent powering the joint of the user to a position that the joint cannot reach. The ranges of these joints were selected to provide for necessary functions such as standing, sitting, and walking. 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 an 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 (as in safe mode) 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.

25. Potential Benefits of Participation

Community-dwelling participants often exhaust their medical insurance coverage for physical rehabilitation and retreat from community involvement unless they are presented with an opportunity to participate in a study or are willing to pay out of pocket for training sessions. This study affords those individuals an opportunity to undergo training when they may not have otherwise done so. Participants may also make improvements physiologically, psychologically, as well as in physical performance, specifically walking. This study is set up to benefit all groups though equal benefits cannot be ensured.

26. Monitoring Procedures

Study monitoring will be performed in accordance with sponsor procedures, or those approved by sponsor. The Clinical department will have overall management responsibility for this study. In addition the Clinical department will direct regional monitoring staff, and may serve as clinical study monitors, study administrators, and/or have oversight responsibility for data review and data integrity. Ekso Bionics, Inc. may engage the services of one or more qualified organizations or individuals to perform monitoring and data management functions, and provide participating sites with relevant contact information, as necessary. Study monitors may change periodically over the course of this study. All monitors will be qualified to perform their assigned responsibilities, and participating investigators/site personnel will be notified of any changes as they occur.

On-site monitoring of all participating sites will be frequent enough to assure continued acceptability of the

data by assessing site compliance with the study protocol, adherence to data collection procedures, and maintenance of study records. Scheduled site visits may include, but are not limited to, the following:

- Site initiation visit: An initiation visit will be conducted by clinical personnel to review this study protocol, review the progression strategy for both groups, undergo an evaluation of the site's training status and refresh as required, and discuss source document/ CRF completion and transmittal procedures. Alternatively, a meeting may be conducted for several sites at a common location.
- Interim monitoring site visit: On-site monitoring visits will be conducted at all sites to assess the progress of the study and identify any concerns that result from review of the study records, study management documents, or Participant informed consent documents. To assure the integrity of the data, a representative number of individual Participant records and other supporting source documents will be compared to CRFs completed at the site to determine that:
    - The study protocol is being followed, and only eligible Participants are being enrolled; variances, if they occur, are recorded and reported as appropriate
    - Informed consent is properly documented
    - Adverse Events are being reported appropriately
    - Information recorded on CRFs is complete, accurate and legible
    - Missed follow-up visits and multiple attempts to contact Participant are properly documented
    - Participants failing to complete the clinical study and the reason for failure are properly recorded
- Final monitoring/Close-out site visit: At the close of the study, appropriately trained personnel appointed by the Sponsor will perform a close-out process via the telephone or on-site. The purpose of this visit is to collect all outstanding study data documents, ensure that the investigator's files are accurate and complete, review record retention requirements, provide for appropriate disposition of any remaining supplies, and ensure that all applicable requirements are met for the study. The observations and actions made during this procedure will be documented and communicated to the investigator.

27. Publication

Manuscripts, abstracts, posters, or other informational materials may be presented at scientific meetings, or published in professional journals. The Sponsor reserves the right to publish the results of the run-in group and/or primary endpoint analysis results on the minimum sample size needed in a single publication. Longer-term, qualitative and quantitative analysis may be reported in a separate publication. This study will be listed on clinical trials.gov. Therefore, results will be published per FDA requirements.

28. References

1. https://www.nscsic.uab.edu/Public/Facts%202015.pdf Accessed March 24, 2016.

2. Raab K, Krakow K, Tripp F, Jung M. Effects of training with the ReWalk exoskeleton on quality of life in incomplete spinal cord injury: a single case study. Spinal Cord Series Cases 2016;3:15025 doi:10.1038/scsandc.2015.25

3. Dietz V, Fouad K. Restoration of sensorimotor functions after spinal cord injury. Brain 2014;137:654–67.

4. Post M, Norear L. Quality of life after spinal cord injury. J Neurol Phys Ther 2005;29:139–46.

5. Alcobendas-Maestro M, Esclarin-Ruz A, Casado-Lopez RM, Munoz-Gonzalez A, Perez-Mateos G, Gonzalez-Valdizan E, et al. Lokomat robotic-assisted versus over-ground training within 3 to 6 months of incomplete spinal cord lesion: randomized controlled trial. Neurorehab Neural Repair2012;26(9):1058–63.

6. Wirz M, Zemon DH, Rupp R, Scheel A, Colombo G, Dietz V, et al. Effectiveness of automated locomotor training in patients with chronic incomplete spinal cord injury: a multicenter trial. Arch Phys Med Rehabil 2005;86:672–80.

7. Wirz M, Zemon DH, Rupp R. Response to letter to the editor. Arch Phys Med Rehabil 2005;86:2386–7.

8. Liverman CT, Altevogt BM, Joy JE, Johnson RT. Spinal cord injury: progress, promise and priorities. Washington, DC: The National Academic Press; 2005.

9. Zeigler MD, Zhong H, Roy RR, Edgerton VR. Why variability facilitates learning. J Neurosci 2010;30(32):10720–6.

10. Lee C, Won D, Cantoria MJ, Hamlin M, de Leon RD. Robotic assistance that encourages the generation of stepping rather than fully assisting movements is best for learning to step in spinally contused rats. J Neurophysiol 2011;105(6):2764–71.

11. Barbeau H, Fung J. The role of rehabilitation in the recovery of walking in the neurological population. Curr Opin Neurol 2001;14(6):735–40.

12. Dobkin B, Apple D, Barbeau H, Basso M, Behrman A, Deforge D, et al. Weight-supported treadmill vs over-ground training for walking after acute incomplete SCI. Neurology 2006;66:484–92.

13. van Hedel HJand the EMSCI Study Group. Gait speed in relation to categories of functional ambulationafter spinal cord injury. Neurorehabil Neural Repair 2009 May;23(4):343-50.

14. Lam T, Pauhl K, Ferguson A, Malik RN, Krassioukov A, Eng JJ. Training with robot-applied resistance in people with motor-incomplete spinal cord injury: pilot study. J Rehab Res Dev 2015;52(1):113–29.

15. Musselman KE, Fouad K, Misiaszek JE, Yang JF. Training of walking skills over-ground and on the treadmill: case series on individuals with incomplete spinal cord injury. Phys Ther 2009;89:601–11.

16. Mehrholz J, Elsner B, Werner C, Kugler J, Pohl M. Electromechanical-assisted training for walking after stroke. Cochrane Database Syst Review 2013 doi:10.1002/14651858.CD006185.pub3

17. Watanabe H, Tanaka N, Inuta T, Saitou H, Yanagi H. Locomotion improvement using a hybrid assistive limb in recovery phase stroke patients: a randomized controlled pilot study. Arch Phys Med Rehabil. 2014;95(11):2006–12.

18. Hartigan C, Kandilakis C, Dalley S, Clausen M, Wilson E, Morrison S, et al. Mobility outcomes following five training sessions with a powered exoskeleton. Top Spinal Cord Inj Rehabil. 2015;21(2):93–9.

19. Kolakowsky-Hayner SA, Crew J, Moran S, Shah A. Safety and feasibility of using the EksoTM bionic exoskeleton to aid ambulation after spinal cord injury. Spine. 2013 doi.org/10.4172/2165-7939.S4-003

20. Sale P, Russo EF, Russo M, Masiero S, Piccione F, Calabro RS, et al. Effects on mobility training and de-adaptations in participants with spinal cord injury due to a wearable robot: a preliminary report. BMC Neurology. 2016;16:12. doi 10.1186/s12883-016—0536-0

21. Forrest GF, Hutchinson K, Lorenz DJ, Buehner JJ, Vanheil LR, Sisto SA, Basso DM. Are the 10 meter and 6 minute walk tests redundant in patients with spinal cord injury? PLoS One. 2014 May 1;9(5):e94108. doi: 10.1371/journal.pone.0094108. eCollection 2014.

22. The CES-D Scale A Self-Report Depression Scale for Research in the General Population. Lenore Sawyer Radloff Center for Epidemiologic Studies National Institute of Mental Health. PubMed 1177/014662167700100306 Applied Psychological Measurement June 1977 vol. 1 no. 3 385-401.

23. Charlifue S, Post MW, Biering-Sorensen F, et al. International Spinal Cord Injury Quality Of Life Basic Data Set. Spinal Cord 2012;50(9):672–5. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22450884.

24. Krogh K, Perkash I, Stiens S a, Biering-Sorensen F. International bowel function basic spinal cord injury data set. Spinal Cord. 2009;47(3):230–4. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18725887.

25. Juul T, Bazzocchi G, Coggrave M, et al. Reliability of the international spinal cord injury bowel Function basic and extended data sets. Spinal Cord 2011;49(8):886-91. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21445082.

26. Biering-Sorensen F, Craggs M, Kennelly M, Schick E, Wyndaele J-J. International lower urinary tract function basic spinal cord injury data set. Spinal Cord 2008;46(5):325–30. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18040278.

27. Anon. National Institute of Neurological Disorders and Stroke Common Data Elements. Available at: http://www.comm

28. Poncumhak P, Saengsuwan J, Kamruecha W, Amatachaya S. Reliability and validity of three functional tests in ambulatory patients with spinal cord injury. Spinal Cord 2012;(September):1–4. Available at: http://www.ncbi.nlm.nih.gov/pubmed/23147127.

29. Van Hedel HJ, Wirz M, Dietz V. Assessing walking ability in subjects with spinal cord injury: validity and reliability of 3 walking tests. Arch of Phys Med Rehabil 2005;86(2):190–6. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15706542.

30. Marino RJ, Scivoletto G, Patrick M, et al. Walking index for spinal cord injury version 2 (WISCI---II) with repeatability of the 10-m walk time: Inter-and intrarater reliabilities. Am J Phys Med Rehabil. 2010;89(1):7–15. Available at: http://www.ncbi.nlm.nih.gov/pubmed/20026943.

31. Burns AS, Delparte JJ, Patrick M, Marino RJ, Ditunno JF. The reproducibility and convergent validity of the walking index for spinal cord injury (WISCI) in chronic spinal cord injury. Neurorehabil Neural Repair. 2011;25(2):149–57. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21239706.

32. Benz, E. N., Hornby, T. G., et al. (2005). A physiologically based clinical measure for spastic reflexes in spinal cord injury. Arch Phys Med Rehabil 86(1): 52-59. Available at: http://www.ncbi.nlm.nih.gov/pubmed/15640989

33. Robertson RJ[1], Goss FL, Metz KF. Perception of physical exertion during dynamic exercise: a tribute to Professor Gunnar A. V. Borg. Percept Mot Skills 1998 Feb;86(1):183-91.

34. Steffen T. M.; Hacker T. A.; Mollinger L. (2002). "Age- and Gender-Related Test Performance in Community-Dwelling Elderly People: Six-Minute Walk Test, Berg Balance Scale, Timed Up & Go Test, and Gait Speeds". Journal of Physical Therapy. **82** (2): 128–137.

35. Datta, S., Lorenz, D. J., et al. (2009). "A multivariate examination of temporal changes in Berg Balance Scale items for patients with ASIA Impairment Scale C and D spinal cord injuries." Arch Phys Med Rehabil 90(7): 1208-1217.

36. Donoghue, D. and Stokes, E. K. (2009). "How much change is true change? The minimum detectable change of the Berg Balance Scale in elderly people." J Rehabil Med 41(5): 343-346.

37. Farrar JT et al. Validity, Reliability, and Clinical Importance of Change in a 0–10 Numeric Rating Scale Measure of Spasticity: A Post Hoc Analysis of a Randomized, Double-Blind, Placebo-Controlled Trial. Clin Ther 2008;30(5):974–985.

29. Appendix A – Description of Standardized Measures and Assessments

International SCI Basic Data Sets and Modified Basic Data Sets

The purpose of the International SCI Basic Data Sets is to promote data collection in a uniform manner and documented in a standard format, with precise instructions for each question.[1] The International SCI Basic Data Sets used for the purposes of this study include:

1. Medical History (study specific minor modifications/deletions were made to the exploratory data set) and Demographics (core data set).

2. The International SCI Quality of Life (QOL) Basic Data Set will be used to collect data on quality of life. The International SCI (QOL) Basic data set collects information on three variables: ratings of satisfaction with general quality of life, satisfaction with general quality of life, satisfaction with physical health, and satisfaction with psychological health which are rated on a scale of 1-10.[23]

3. The International SCI Pain Basic Data Set collects information on up to three pain problems, their location, severity, and temporal pattern, as well as impact in daily activities and well-being.

4. Bowel function data will be collected using the Modified International SCI Bowel Function Data Set, which contains 12 items to assess the impact of neurogenic bowel dysfunction ranging from bowel dysfunction unrelated to SCI, surgical procedures related to bowel function, awareness of the need to defecate, defecation method and frequency, incontinence and the use medications impacting bowel function. [24] Reliability has been assessed for this data set. [25]

5. The Modified International SCI Lower Urinary Tract Basic Data Set will be collected to assess lower urinary tract function. [26] The following data will be collected: urinary tract impairment unrelated to spinal cord lesion, awareness of the need to empty the bladder, bladder emptying, average number of voluntary bladder emptyings per day during the last week, incontinence, collecting appliances for urinary incontinence, any drugs for the urinary tract, surgical procedures on the urinary tract and any change in urinary symptoms.

The Medical Research Council Manual Muscle Test (MMT) Scale (as used in the ISNCSCI exam)

The manual muscle test is a standardized assessment to measure muscle strength. Score range 0-5, minimum 0, and maximum 5/5. For the purpose of this study, the Medical Research Council MMT Scale as used in the ISNCSCI exam will be used.[3-4]

Modified Ashworth Scale

As summarized in the National Institute of Neurological Disorders and Stroke Common Data Elements (NINDS CDE) for multiple sclerosis, the Ashworth scale is a widely used method of measuring spasticity, due in a large part to the simplicity and reproducible method[23]. Scores range from 0---5, plus a 1+ scoring category to indicate resistance through less than half of the movement. A score of 0 indicates no resistance and 4 indicates rigidity. Assessment techniques for the MAS must be standardized. Some critics question the validity of the scale and Modified Ashworth Scale in measuring spasticity. It may be a description of resistance to passive movement. Therefore, it measures only one aspect of spasticity, and is not a comprehensive assessment. Administration time is approximately 5 minutes for the six muscle groups tested in this study.

Spinal Cord Assessment Tool for Spastic Reflexes (SCATS)
The Spinal Cord Assessment Tool for Spastic Reflexes (SCATS) assesses three types of spastic motor behaviors in SCI patients - clonus, flexor spasms, and extensor spasms. SCATS Clonus scale uses passive dorsiflexion to assess clonus. SCATS flexor spasm is assessed with a pinprick to the medial arch with the knee and hip fully extended. SCATS extensor spasms are assessed by extending the hip and knee joints from a start position of 90 to110 degrees of hip and knee flexion. Administration time is usually 5 to 10 minutes. [32]

Berg Balance Scale (BBS)
The Berg Balance Scale is a 14-item objective measure designed to assess static and dynamic balance and in adult populations.[34,35,36] Scores range from 0-56, and cut-off scores exist for inferring a participant's categorical fall risk. This test takes an average of 15 minutes to administer. Low-level participants may complete the test in a couple of minutes, if they cannot perform any of the 12 tasks done in standing. However, high-level participants may require up to 30 minutes, because they will be able to attempt all 14 tasks, and may require rest breaks.

International Standards for Neurological Classification of SCI (ISNCSCI)
The International Standards for the Classification of Spinal Cord Injury (ISNCSCI) were developed by the American Spinal Injury Association in 1982 in order to promote common definitions of neurological levels and the extent of complete injuries in patients with SCI and to achieve more consistent and reliable data among centers participating in the National Spinal Cord Injury Database. The Standards have been revised, with the last revision occurring in 2011 with an accompanying article to clarify the changes. The ASIA Standards are the most commonly used neurological examination for classifying patients with SCI for both clinical and research purposes. Since the last publication of a reference manual an electronic on line training program was developed, the International Standards Training e-Learning Program (InSTeP).

The neurological examination consists of both a motor and sensory exam that have been standardized to promote consistency. The ISNCSCI exam consists of the following:

1. Motor examination: 10 key muscles are tested in each half of the body. Each muscle is graded from 0 to 5 and then the total score is calculated, the maximum being 100.
2. Sensory examination: 28 key regions are tested in each half of the body for pinprick and light touch sensations. Each region is given a score of 0 (absent), 1 (impaired), 2 (normal) or NT (not testable). The total score is then calculated with a maximum of 112.

In addition, based on the data collected from the motor and sensory exams, neurological level, completeness of neurological loss, the zone of partial preservation and the ASIA Impairment Scale (AIS) can be determined.

10 Meter Walk Test
The objective of this test is to assess walking speed in meters per second over a short duration. The individual is instructed to walk a distance of 14 meters. The middle 10 meters is timed to allow 2 meters for acceleration at the beginning and deceleration at the end of the walk. The distance covered is divided by the time it took the individual to walk that distance. Data will be collected using both baseline and current braces/devices at both self-selected and fast gait speeds during the 6, 12, and 24 week (midpoint, endpoint, and follow-up) evaluations. Data using current devices and no braces at self-selected speed will be collected every 3rd session as an indicator of incremental neurological recovery.

GAITRite Pressure Map
The GAITRite pressure map is an optional test that may be used during the 10MWT, if the site has access to it, at any 10MWT evaluation timepoint. This pressure map will digitally record the placement and pressure of the participant's footprints as they walk over it during the 10MWT. From this data, it will calculate temporospatial gait parameters, such as swing and stance times, lengths, widths, etc. If used, the GAITRite mat will be placed to begin at the 2 meter mark on the 10MWT pathway. Clear packing tape will be used to tape the ends to the floor to reduce the risk of any walking device being caught in its edges and disrupting the flow of the step pattern. This should also reduce the participant's tendency to slow down or pause at the edge. Because the GAITRite is not placed in the middle of the pathway, each trial of the 10MWT will need to start from the same place.

Timed Up and Go (TUG)
As summarized in the National Institute of Neurological Disorders and Stroke Common Data Elements (NINDS CDE) for multiple sclerosis, the original purpose of this test was to test basic mobility skills of frail elderly patients.[27] The test has been used in other populations, including individuals with SCI.[28,29] The original Get Up and Go Test used an ordinal scoring system based on the observer's assessment of the patient's risk of falling. The participant wears their regular footwear and uses their customary walking aid (none, cane, walker). No physical assistance is given. The subject walks through the test once before being timed in order to become familiar with the test. Either a stopwatch or a wristwatch with a second hand can be used to time the trial. The timed "Up and Go" test measures, in seconds, the time taken by an individual to stand up from a standard arm chair with approximate seat height of 46 cm [18in], arm height 65 cm [25.6 in]), walk a distance of 3 meters (118 inches, approximately 10 feet), turn, walk back to the chair, and sit down. Patients are timed (in seconds) when performing the TUG: from sitting in a chair, stand up, walk 3 meters, turn around, walk back, and sit down. The time taken to complete the task is strongly correlated to level of functional mobility, (i.e. the more time taken, the more dependent in activities of daily living) but will take less than 3 minutes. Psychometric properties for use in SCI have been assessed in multiple publications including but not limited to Ponchumak, et al., and van Hedel, et al. [28. 29.]

6 Minute Walk Test
The objective of the test is to cover as much distance as possible within a six-minute time frame walking laps around 2 cones placed 100 ft apart in a straight path.The level of assistance and assistive devices used during the 6MWT and distance walked will be recorded.

Spinal Cord Injury Functional Ambulatory Index (SCI-FAI)
The SCI-FAI is an observational gait assessment instrument that includes a 2-minute walk test of gait biomechanics and use of assistive device. This SCI ambulatory outcome measure is included as an observational assessment of the quality of the gait pattern. Physical therapists will score the SCI-FAI based on the first 2 minutes of the 6MWT. Video footage should be taken to assist with scoring.

Walking Index for Spinal Cord Injury II
The Walking Index for Spinal Cord Injury II (WISCI II) measures the ability of an individual to complete a locomotor task in a standardized environment. The goal is to rank the severity of the underlying impairment in relation to function. The WISCI II has a total of 21 levels and includes information on the type of gait, bracing and assistive devices utilized and level of assistance walking while walking 10 meters or less. The WISCI II will be scored based on the 10MWT at self-selected speed using the current braces and devices as needed. Reliability of the WISCI II in SCI has been assessed in several publications including but not limited to: Marino et al., Burns et al. [30.31] Completion time is less than 5 minutes.

Spinal Cord Independence Measure (SCIM-III, Mobility subscale)
The SCIM was developed as a comprehensive rating scale specifically for persons with SCI. The instrument assesses independence in all aspects of primary daily activities relevant for patients with SCI; and scores every task or area of function according to its relative weight in the total relevant daily function. SCIM-III consists of 17 items in the following subscales: self-care, respiration and sphincter management, room and toilet mobility and mobility indoors, outdoors and on uneven surfaces. Scores range from 0-100. For the purposes of this study, only the mobility subscale of the SCIM-III will be completed via an interactive interview with the participant. Completion time is approximately 5-10 minutes. The mobility sub-scale consists of 9 items with a maximum score of 40.

Spinal Cord Injury Spasticity Evaluation (SCI-SET)
The SCI-SET is a participant self-report composed of 35 items that assess the degree to which spasticity affects aspects of daily life activities over the past 7 days. Responses are on a 7-point scale that ranges from +3 (extremely helpful) to -3 (extremely problematic).[4] The administration time is 3-9 minutes.

Center for Epidemiologic Studies Short Depression Scale (CES-D 10)
The CES-D is a screening tool measure developed to identify current depressive symptomatology related to major or clinical depression in adults and adolescents. Items include depressed mood, feelings of guilt, worthlessness and helplessness, psychomotor retardation, loss of appetite, and sleep difficulties. There are 10 and 20 item versions of the scale. The most commonly used version of the CES-D is the 10 item version (CES-D 10) which was developed in the 1970's by Lenore Radloff (researcher at National Institute of Mental Health). [22]

Borg Rating of Perceived Exertion
The Borg Rating of Perceived Exertion (RPE) is a way of measuring physical activity intensity level. Perceived exertion is based on the physical sensations a person experiences during physical activity, including increased heart rate, increased respiration or breathing rate, increased sweating, and muscle fatigue. Participants are asked to rate their maximal perception of exertion of physical activity during a session and during the 6MWT. The severity is measured either on the original scale of 6-20 (6 meaning no exertion at all and 20 meaning maximal exertion),. [33]

Numeric Rating Scale (NRS) for spasticity and pain
The Numeric Rating Scale is a participantself-report on a 0-10 scale of overall spasticity or overall pain over the past week. [37] Zero denotes no spasticity/pain, and 10 denotes "worst spasticity/pain imaginable." Completion time for both, inclusive, should be no more than 5 minutes.

NASA Task Load Index for self-reported work load
The NASA Task Load Index is a 6-item, subjective, multidimensional assessment tool that rates perceived workload during a task, or other aspects of performance. The questions include rating physical and mental workloads, as well as psychological/emotional reactions to the workloads. It was developed by NASA Ames Research Center's (ARC) Sandra Hart in the 1980s and has become the gold standard for measuring subjective workload when working with human-machine interface systems. Completion time is no more than 5 minutes.