Clinical Protocol

Study Title: Exoskeleton Treatment of Deconditioning Due to Limited Ambulation Caused by Illness or Injury

Protocol Number: 107159

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

Protocol Change Status

Revision	Date of Revision	Reason for Amendment
A	**27 July, 2017**	[redacted]

Study Acknowledgement and Confidentiality Statement

The information in this document and future information that 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 by 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" for 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.

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Signature of Investigator Date

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Investigator Name (Print)

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Title of Investigator (Print)

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Institution (Print)

Study Outline

Study Title: Exoskeleton Treatment of Deconditioning Due to Limited Ambulation Caused by Illness or Injury

Sponsor: Ekso Bionics, Inc.
1414 Harbour Way S Ste 1201
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Study Description: A safety and feasibility study of robotic exoskeleton training in deconditioned patients residing in a healthcare facility.

Overall goal: We aim to demonstrate that EksoGT™ robotic exoskeleton training can be performed safely with patients who have been hospitalized and are at risk of experiencing a further decline in their physical condition.

Rationale: Patients who are hospitalized for several weeks or months are at a higher risk of decline in physical condition and are also at a higher risk of rehospitalization within 30 days of discharge. A program incorporating robotic exoskeleton training may provide sufficient physical support and challenge for patients to maintain a higher level of physical condition than if they did not undergo exoskeleton training.

Hypothesis: Robotic exoskeleton training during hospitalization is safe and feasible.

Design: Single-arm safety and feasibility study.

Participants: Patients who fulfill the inclusion/exclusion criteria.

Inclusion criteria:

1. A diagnosis of "deconditioned", defined as the loss of muscle tone and endurance due to chronic disease, immobility, or loss of function.
2. Adults 18 years and older (or as specified by state law).
3. Admitted into a hospital, long-term care facility, skilled nursing facility, or similar.
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. Screened and cleared by a physician for full weight-bearing exercise training.
6. Weigh 220 pounds (100kg) or less.
7. Between approximately 5'0" and 6'4" tall.
8. Standing hip width of approximately 18" or less.
9. Have near normal range of motion in hips, knees and ankles.

Exclusion criteria:

1. Currently involved in another intervention study.
2. Transferred to the intensive care unit or isolation-room stay.
3. Currently on a ventilator or extracorporeal membrane oxygenation

(ECMO) machine.
4. Currently have a ventricular assist device (VAD) or an automatic implantable cardioverter-defibrillator (AICD).
5. Advanced heart failure - ejection fraction of < 20%.
6. Documented cardiovascular risk from exercise.
7. Resting heart rate <50 bpm or >120 bpm.
8. Uncontrolled or new (within 24 hours) arrythmias.
9. Resting blood pressure below 90/70 or above 160/100.
10. Oxygen saturation (O_2 sat) < 90% during rest.
11. Uncontrolled or severe orthostatic hypotension that limits standing tolerance.
12. Cardiac ischemia within 24 hours.
13. Unresolved or new (within 24 hours) deep vein thrombosis.
14. Concurrent severe neurological pathology/disease or stroke within 72 hours.
15. Open skin ulcerations on any body surfaces in contact with exoskeleton.
16. Acute fracture
17. Osteoporosis
18. Active heterotrophic ossification (HO) of the lower extremity, hip dysplasia, or hip/knee axis abnormalities.
19. Current chemotherapy
20. Inability to speak or understand the English language.
21. Inability to cooperate in tests/exercises.
22. Hip flexion contracture greater than ~17°.
23. Knee flexion contracture greater than 12°.
24. Unable to achieve neutral ankle dorsiflexion with passive stretch (neutral with max 12° knee flexion).
25. Cognitive impairments - unable to follow 2 step commands or to communicate pain or to stop session.
26. Pregnancy
27. Any reason the physician may deem as harmful to the participant to enroll or continue in the study.

Sample Size: Forty (40) Participants who meet the inclusion and exclusion criteria will be enrolled.

Blinding: Blinding will not be implemented during this study.

Setting/Sites: Hospital, long-term care facilities, or skilled nursing facilities (up to 5 clinical sites). Sites are to be chosen based on having Ekso Level 2 training certification, location, enrollment capabilities, and resources.

Duration: Each enrolled Participant is expected to engage in this study for up to 2 weeks. The duration of the study is expected to be approximately 6 months.

Assessment periods: The study consists of a screening period and up to 5 training sessions with assessments for safety.

Primary Objective: To demonstrate that a multi-day robotic gait training regimen is safe and feasible for deconditioned patients who have been admitted to a healthcare facility.

Primary End Point: The primary endpoint is safety defined as the number of device-related serious adverse events per Participant and overall during the study period.

List of Abbreviations

- AE – adverse events
- BMI – body mass index
- BP – blood pressure
- BWS – body weight support
- CRF – case report form
- DSMB – Data Safety Monitoring Board
- FDA – Food and Drug Administration
- GCP – Good Clinical Practice
- IRB – Institutional Review Board
- LE – lower extremity
- PT – physical therapist
- ROM – range of motion
- SAE – serious adverse event
- UE – upper extremity

1. Literature Summary and Study Rationale

Multiple factors can lead to a general decline in the physical condition of adults at any age. Medical challenges posed by illness or injury often result in sedentary behavior followed by a general loss of muscle mass, decreased balance, and increased risk of falling. The Center for Disease Control and Prevention (CDC) states, "As an older adult, regular physical activity is one of the most important things you can do for your health. It can prevent many of the health problems that seem to come with age."[1] Despite our best efforts, illness and injuries occur and often lead to sedentary behavior and a general deconditioning of adults of all ages. Deconditioning is defined as "the loss of muscle tone and endurance due to chronic disease, immobility, or loss of function."[2] Falvey et al[3] studied one group of adults that experienced "hospital-associated deconditioning" or HAD, defined as "marked deficits in physical function secondary to an acute hospitalization" and stated that "68% of patients are discharged from post-acute care settings below their prehospitalization level of function." Further, hospitalized older adults are 61 times more likely to develop disability in activities of daily living (ADLs) than those who are not hospitalized.[4] In fact, older adults who are discharged with poor physical function have 3 times the odds of being rehospitalized within 30 days than older adults with medically complex conditions and high physical function.[4] This decline in function during acute hospitalization is considered to be partially avoidable.[5]

Injury and illness leading to confinement and general inactivity does not occur solely in acutely hospitalized patients. Long-term care facilities and skilled nursing facilities admit adults with a variety of conditions that limit daily ambulation. This pilot study aims to enroll a small group of adults that have experienced a loss of physical strength due to limited ambulation during convalescence and to offer a short exercise program using a robotic exoskeleton that provides support and physical challenge during ambulation.

2. Study Objectives

The primary objective is to demonstrate that a multi-day robotic rehabiliation regimen is safe and feasible in deconditioned patients who have been admitted to a facility.

3. Study Design

This is a single-arm, short term, safety and feasibility study.

4. Study Endpoints

The primary endpoint is safety defined as the number of device-related serious adverse events per Participant and overall during the study period.

5. Participant Enrollment

Participants are inpatients that are identified and recruited from participating facilities. Eligible patients 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.

6. Duration of Participation/Study

Each Participant will be enrolled for up to 2 weeks or until the Participant elects to terminate participation, is discharged from the facility, or a physician removes the Participant from the study.

7. Inclusion/Exclusion Criteria

Inclusion criteria:

1. A diagnosis of "deconditioned", defined as the loss of muscle tone and endurance due to chronic disease, immobility, or loss of function.
2. Adults 18 years and older (or as specified by state law).
3. Admitted into hospital, long term care facility, skilled nursing facility, or similar.
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. Screened and cleared by a physician for full weight-bearing exercise training.
6. Weigh 220 pounds (100kg) or less.
7. Between approximately 5'0" and 6'4" tall.
8. Standing hip width of approximately 18" or less.
9. Have near normal range of motion in hips, knees, and ankles.

Exclusion criteria[6,7]:

1. Currently involved in another intervention study.
2. Transferred to the intensive care unit or isolation-room stay.
3. Currently on a ventilator or extracorporeal membrane oxygenation (ECMO) machine.
4. Currently have a ventricular assist device (VAD) or an automatic implantable cardioverter-defibrillator (AICD).
5. Advanced heart failure - ejection fraction of < 20%.
6. Documented cardiovascular risk from exercise.
7. Resting heart rate <50 bpm or >120 bpm.
8. Uncontrolled or new (within 24 hours) arrythmias.
9. Resting blood pressure below 90/70 or above 160/100.
10. Oxygen saturation (O_2 sat) < 90% during rest.
11. Uncontrolled or severe orthostatic hypotension that limits standing tolerance.
12. Cardiac ischemia within 24 hours.
13. Unresolved or new (within 24 hours) deep vein thrombosis.
14. Concurrent severe neurological pathology/disease or stroke within 72 hours.
15. Open skin ulcerations on any body surfaces in contact with exoskeleton.
16. Acute fracture
17. Osteoporosis
18. Active heterotrophic ossification (HO) of the lower extremity, hip dysplasia, or hip/knee axis abnormalities.
19. Current chemotherapy
20. Inability to speak or understand the English language.
21. Inability to cooperate in tests/exercises.
22. Hip flexion contracture greater than ~17°.
23. Knee flexion contracture greater than 12°.
24. Unable to achieve neutral ankle dorsiflexion with passive stretch (neutral with max 12° knee flexion).
25. Cognitive impairments - unable to follow 2 step commands or to communicate pain or to stop session.
26. Pregnancy
27. Any reason the physician may deem as harmful to the participant to enroll or continue in the study.

8. Screening, Enrollment, and Treatment

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. 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. Further, the investigator or the investigator's designee will inform the applicant that as a Participant in a study, his/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.

Treatment will consist of exercise using the EksoGT described below. Dosage (daily or weekly) and progression of settings (challenge) will be highly individualized due to the heterogeneous population to be enrolled in this study. No participant is expected to exceed 5 sessions in the exoskeleton.

9. Ekso Device Description and Safety Features

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

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

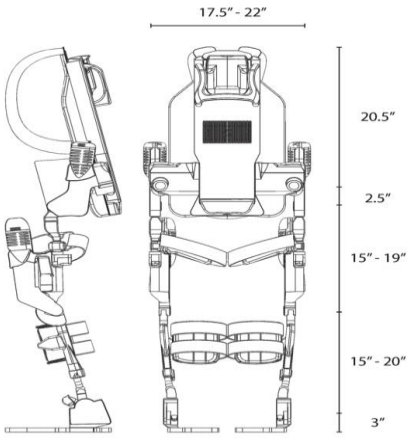

Figure 2: The EksoGT structure and general dimensions.

The EksoGT manipulates the patient's legs and waist to stand up, walk over level ground, and then to sit down. Battery powered motors drive knee and hip joints. The batteries are designed to last for approximately three hours of normal use. The patient is required to assist with balance and body positioning using a cane, crutches, or walker, which are provided with the device. The physical therapist operates the device and monitors the patient to ensure balance is maintained. The device is operated in various modes. In some modes, steps are triggered with the attached user interface. In other modes, steps are triggered when the machine is in certain target postures. In other modes, the therapist may adjust the level of assistance provided so that, if the patient has some residual strength, the patient performs some of the walking motion with their own muscles.

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

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

The EksoGT 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.

Participants must meet all criteria related to the EksoGT per EksoGT Operating Manual. All Ekso training will be conducted using the EksoGT with SmartAssist™ 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. All pre-gait features will be available during this study.

There is no comparator device in this single -arm study.

Inventory control is not applicable in this trial since sites will use their commercially acquired devices for this study of a new indication for use.

10. General Rules for Training Sessions

1. The goal is to have Participants train in the EksoGT daily for 30-45 minutes per session, or as tolerated, ideally over the entire time of admission, but for no greater than 5 sessions.
2. It is recommended to schedule Ekso during a 45-60 minute session.
3. Patients should achieve at least 5 minutes of stable blood pressure during standing in the EksoGT prior to walking in the device.
4. Participants may use the PreGait function to perform activities in the EksoGT and walk in EksoGT both inside and outside of the trajectory, at the therapist's discretion.

To challenge Participant:

1. In Fixed Assist, lower the swing assist for each leg as appropriate.
2. In Fixed Assist, stance support may be changed from "Full" to "Flex" as appropriate.
3. In FreeGait, stance support should begin at an appropriate level. As Participant improves stance control, support may be reduced as tolerated and clinically appropriate.
4. In FreeGait, swing assist 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 a more symmetrical gait.
5. In FreeGait, set swing support at lower assistace or higher resistance for an appropriate clinical challenge.

11. Participant Assessments

In-person limited screening procedures are conducted to assess minimal trial inclusion. 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.

The following information will be obtained during *screening*:

1. Demographic data including date of birth, gender, date of illness (self-reported).
2. Past and current medical history (from medical records).
3. Reason for admission to the facility (from medical records).
4. List of current medications (from medical records).
5. Weight and height (from medical records).
6. Vital signs (HR, BP, O_2 sat from medical records).

7. Written documentation from the patient's physician verifying the patient is medically stable and cleared for full weight bearing locomotor training and does not have any conditions that would exclude the Participant (see Inclusion/Exclusion criteria).
8. Current practice of standing or walking, level of assistance required, assistive devices and braces used, and any associated adverse events (self-reported).
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. Skin check of back, sacrum, shins, and feet (must be done at each visit).

The following data will be collected *per session*:

1. Any adverse events/complications noted following prior to 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. Vital signs (HR, BP, O_2 sat collected daily).
4. Walk time.
5. Stand/Uptime.
6. Estimated seated rest time.
7. Estimated regular overground walking time (outside of EksoGT).
8. Number of steps total and in each mode of EksoGT.
9. Time spent in each EksoGT mode.

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 Participant 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 Participant identifiers other than the Participant 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 unanticipated 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. Participants 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 study completion, they will be asked to complete the final evaluations. 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).

When the Participant is discharged from the facility, the End of Study CRF must be completed and submitted to the data manager as soon as possible.

14. Data Collection, Management, and Reporting

Source documents will be used to record demographic and assessment data as well as any adverse events that may occur during the study period. Source document data will be transferred to case report forms that will be submitted to the data manager. Reports will be generated by the data manager periodically. Ekso Bionics reserves the right to use a third-party data manager.

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 the 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

This is an observational, feasibility study; therefore, statistical methods will not be employed. Data will be reported as a number (n) of adverse events and categories of patient conditions will be assembled.

18. Investigative Centers/Minimum and Maximum Enrollment

Up to five centers will participate in the study. Centers are chosen based on experience with the EksoGT device and having appropriate personnel to conduct and support research studies. Each center is expected to contribute at least 8 Participants (20%) and no more than 20 Participants (50% of total).

19. 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 set is 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.

20. 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.

21. Personnel Responsibilities

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 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.

Sponsor Responsibilities

a. Listed below are the Sponsor's responsibilities for this study.
b. Assure IRB approval of protocol and informed consent is obtained
c. Select and train monitors
d. Select investigators
e. Train site personnel in device use (as appropriate)
f. Obtain protocol signature, curriculum vitae and proof of appropriate licensure of investigator and other study staff
g. Investigate device-related adverse events
h. Oversight responsibility for data review and analysis

i. Obtain statement of financial disclosure for publication and presentation purposes

22. 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 or heart arrhythmias 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.

23. Provisions for Research Related Harm/Injury

If medical resources are required, each site will be responsible for seeking assistance and for reporting the injury to the Sponsor. The Sponsor carries clinical trial insurance in the event that insurance coverage for the subject is unavailable.

24. Non-Significant Risk Determination.

The EksoGT is a non-significant risk device in the context of this trial. The device is 510(k) cleared by the FDA (K161443) for individuals with stroke or spinal cord injuries, and it is expected that this population of hospitalized Participants will be less severely disabled than those for whom the device is currently intended. 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 EksoGT 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 EksoGT is equipped with mechanical hard stops at the limits of healthy Participant ranges of motion to prevent powering the joint of the user to a position that the joint cannot reach. The 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) then the device will enter 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

This study affords individuals an opportunity to undergo physical training when they may not have otherwise done so. Participants may also make improvements physiologically, psychologically, as well as in physical performance, specifically walking.

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 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 on a smaller sample size. This study will be listed on clinical trials.gov. Therefore, results will be published per FDA requirements.

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