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EASE Study Protocol Synopsis
Protocol Number: P16-01
NCT #02958553

Sponsor:	Otto Bock HealthCare LP
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Sponsor Protocol Approval Page

StudyTitle:	**E**mPOWERing **A**ctive **S**eniors with **E**nergy
Product:	The study device is the emPOWER Ankle. The emPOWER Ankle is a powered microprocessor-controlled ankle-foot prosthesis. The emPOWER Ankle has been designed and tested to ISO 10328 standards.
Protocol Version:	5.0
Protocol Date:	26 May 2017
Sponsor:	Otto Bock HealthCare LP

As the representative of the study sponsor, the undersigned have read and agree to oversee the conduct of this study according to the requirements outlined in this study protocol.

_____ _____

Andreas Kannenberg, MD, PhD
Executive Medical Director North America
Otto Bock HealthCare LP

Date

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Investigator's Signature Page

STUDY TITLE: **E**mPOWERing **A**ctive **S**eniors with **E**nergy

STUDY SITE: _____
(Print name of study site)

Prior to participation in the study as the research center principal investigator (PI), I understand that I must obtain written approval from my Institutional Review Board (IRB)/Ethics Committee (EC) or the Sponsor will have provided to me a central IRB approval listing me as an investigator. This approval must include my name and a copy must be provided to BionX Medical Technologies, Inc. or designee along with the approved Informed Consent Form prior to the first enrollment of a study subject at my study center.

As the PI, I must also:

1. Conduct the study in accordance with the study protocol, the signed Investigator Agreement, and applicable laws and regulations, as well as ensure that all study personnel are qualified and appropriately trained prior to any study activities.
2. Ensure that the study is not commenced until all necessary approvals have been obtained.
3. Ensure that a written informed consent is obtained from each subject prior to any data collection using the most recent IRB/EC approved subject Informed Consent Form (ICF).
4. Provide all required data and reports, as well as agree to allow source document verification of study data with subject's medical records by a BionX, designee and/or any regulatory authorities.
5. Allow BionX personnel or its designees, as well as regulatory representatives, to inspect and copy any documents pertaining to this clinical investigation according to the federal, state, and institutional data and privacy protection laws.

Investigator Signature

I have read and understand the contents of the study and agree to abide by the requirements set forth in this document.

_____	_____
Investigator Name (print)	Study Center (print)
_____	_____
Investigator Signature	Date

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Protocol Synopsis

EmPOWERing **A**ctive **S**eniors with **E**nergy

Study Population	The study population will include up to ten (10) unilateral transtibial amputees.
Intended Use	The device is intended to replace a missing foot and ankle. The emPOWER Ankle is to be used exclusively for fittings of lower-extremity amputations as prescribed by a healthcare professional.
Control	Subjects serve as their own control with assessments using their prescribed passive lower-extremity prosthesis at Baseline and after 2 weeks of re-accommodation after 3 months of use of emPOWER.
Study Design	This is a pilot, prospective, cross-over, open label observational study. Phase I: Screening through 3 Months Phase II: Long-term follow-up of subjects using the emPOWER Ankle in their daily lives from 3 Months through 12 Months
Primary Objective	The primary objective of this study is to characterize the increase in the distance subjects can walk during a six (6) minute period while wearing the emPOWER Ankle compared to a passive lower-extremity prosthesis.
Primary Effectiveness Endpoint	The primary endpoint of this study will be an improvement in walking distance with the emPOWER Ankle compared to the distance walked with the subject's passive prosthesis as shown by 6 minute Walk Test (6MWT) results at 3 months.
Secondary Endpoints	The secondary endpoints of this study will compare the following assessments on the emPOWER Ankle to the subject's passive prosthesis at Baseline (before wearing the emPOWER, when available) and Crossover: • 12 minute Walk Test (12MWT) • 10 meter Walk Test (10MWT) • L-Test for overall mobility and fall risk • Time and Quality of Ramp Ascent • Time and Quality of Ramp Descent • Activities-specific Balance Confidence (ABC) Scale • Falls Efficacy Scale • Amputee Mobility Predictor (AMP) Assessment • Prosthetic Limb Users Survey of Mobility (PLUS-M) (12 item Short Form) • Patient-specific Functional Scale (PSFS) • Numeric Pain Rating Scale (NPRS) • Activity monitoring over two weeks prior to the assessment session

	with the emPOWER Ankle and the re-assessment session with the previous foot using a Fitbit monitor. • Falls: Diary of reported falls for two weeks • Activity Diary to allow for self-reporting of activities of daily living and unique user experiences with the emPOWER Ankle for two weeks • PROMIS Physical Function (Custom) • PROMIS Global Health Short Form • PROMIS Fatigue Short Form (7a) • PROMIS Pain Intensity Short Form (3a) Long-term follow-up of subjects who agree to continue wearing the emPOWER Ankle at 3, 6 and 12 months with all outcome measures (except the activity monitoring and diaries of steps, activity and falls at 6 & 12 months).
Number of Subjects and Number of Study Sites	Up to ten (10) subjects will be enrolled into this study at one (1) study site.
Study Duration	Overall study enrollment is estimated to take two (2) months. The subject's study participation duration will last approximately four (4) months for the first phase. If the subject elects to continue in the second phase, that will last for an additional 9 months.
Key Inclusion Criteria	I-1. Males and females I-2. 55 years or older I-3. Subjects with transtibial amputations of either leg at least 1-year prior I-4. Suction or elevated vacuum suspension and Socket Comfort Score of at least 6 I-5. Sock fluctuation of ≤ 8 ply per day I-6. K-level rating of 3 or 4 based on the AMP Assessment Tool I-7. Ability to walk at a walking speed of > 0.75 meters per second with the current prosthesis I-8. Unilateral amputees (up to 7 bilateral amputees can be included, 1 per site in addition to the unilateral amputees who will be analyzed as a separate sub group) I-9. Foot size: 25-30 cm I-10. Ability to complete a continuous 6MWT I-11. Ability to provide written, informed consent

	I-12. Ability to complete study visits and study documents I-13. Ability to manage the complexity of a powered device including charging and changing batteries as needed I-14. Ability to read and understand English
Key Exclusion Criteria	E-1. Subjects who have never used a prosthetic device E-2. Less than 55 years of age E-3. Weight <150 lbs. or > 287 lbs. E-4. Transfemoral amputees E-5. Active sores or ulceration on subject's residual limb E-6. Sore on contralateral foot E-7. Cuff-link socket suspension E-8. Socket Comfort Score less than 6 E-9. Sock fluctuation of > 8 per day E-10. K level of 1 or 2 E-11. Amputation clearance < 8.625" E-12. History of stroke or TIA that impairs current walking E-13. Recent history of excessive falling defined as more than 2 falls requiring medical assistance in the prior year E-14. Medications potentially affecting balance E-15. Recent hospitalization (within past 3 months) E-16. Cognitive deficiency that would impact ability to charge and change batteries as needed
Primary Statistical Methods	Subjects will be enrolled to characterize improvements with the emPOWER Ankle compared to the subject's passive prosthesis. Data analysis will be descriptive in nature.
Regulatory Status	This study will be conducted in accordance with the Food and Drug Administration's (FDA) regulations[1] and guidelines. The emPOWER ankle-foot prosthesis is a *Class II exempt* device in accordance with 21 CFR 890.3500, which does not require pre-market notification per section 510(k). [1] 21 CFR 812.2

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Table of Contents

Empowering **A**ctive **S**eniors with **E**nergy

1. Introduction

1.1. *Study Rationale*

Safety and performance of the emPOWER Ankle has been shown in a laboratory setting.

The primary objective of this study is to show increased mobility and improvement in balance and other activities of daily living with the emPOWER Ankle compared to standard carbon fiber prosthetic legs, in active seniors to support marketing and reimbursement needs.

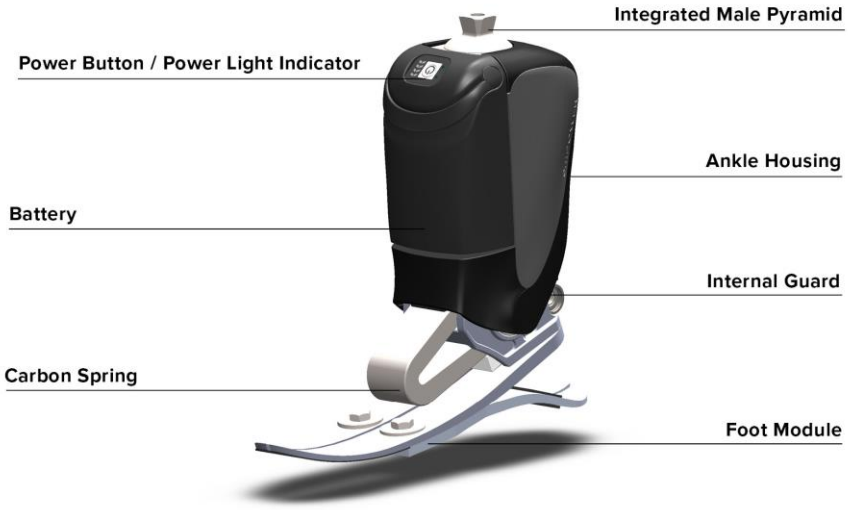
2. Device Information

2.1. *Principle of Operation*

The emPOWER Ankle, a *Class II exempt* device (in accordance with 21 CFR 890.3500, which does not require pre-market notification per section 510(k)), represents the first significant redesign of the BiOM Ankle. The Ankle is a commercially-available prosthetic device that restores ankle power across all walking speeds [1-3]. This emulation is achieved through three technologically-novel functionalities. First, the ankle provides late-stance ***powered assist*** [2-4]. Second, the device provides ***stiffness modulation*** after heel strike, which decelerates the body and thereby reduces impact loads. Finally, the device is adjusted with ***personal bionic tuning***, in which ankle stiffness and power levels are personalized for each user, enabling the user to walk within normal biologic ranges [2, 3].

The ankle optimizes ankle stiffness and power through user-specific settings using a quantitative treatment paradigm in which its dynamic response is adjusted to provide biologically-normal ankle behaviors [2, 3], removing the subjective and qualitative nature of current prosthetic user evaluations and fittings. As shown in Section 2.2, the emPOWER Ankle was designed with both passive and actively powered components in order to emulate biological function throughout the gait cycle. The device continuously modulates ankle stiffness, spring equilibrium and propulsive torque throughout a walking gait cycle [2, 5-11]. Computers and sensors that operate biomimetic control firmware guide the device's performance. The processors are able to adjust the ankle's stiffness, spring equilibria, and propulsive torque 500 times a second. Similar to the muscle-tendons and neural reflex control of the human ankle joint, the device is capable of positive torque feedback. An increase in the sensed prosthetic ankle joint torque triggers an increase in the torque generated by the actuator, resulting in the automatic modulation of ankle power assist with changes in both walking velocity and ground inclination [7,8]. During personal bionic tuning, ankle stiffness and the magnitude and timing of power assist are measured directly from sensors within the prosthesis and then adjusted to match the performance of a biological ankle. Thus, with appropriate tuning of the prosthesis, the walking gait of the user dynamically emulates the walking gait of a non-amputee user across the full range of walking velocities [1-3].

2.2. ***Figure: The emPOWER Ankle***



3. Intended Use

The device is intended to replace a missing foot and ankle. The emPOWER Ankle is to be used exclusively for fittings of lower extremity amputations as prescribed by a healthcare professional.

4. Primary Objective

The primary objective of this study is to characterize the increase in the distance subjects can walk during a 6 minute period while wearing the emPOWER Ankle compared to a passive lower-extremity prosthesis.

5. Study Design

This is a pilot, prospective, cross-over, open label observational study. Study subjects will remain blinded to the results from their testing and questionnaires from their passive device until they have complete the study procedures for the emPOWER.

6. Study Endpoints

6.1. *Primary Endpoint*

The primary endpoint of this study will be an improvement in walking distance with the emPOWER Ankle compared to the distance walked with the subject's passive prosthesis as shown by 6MWT results at 3 months.

6.2. *Secondary Endpoints*

The secondary endpoints of this study will compare the following assessments on the emPOWER Ankle to the subject's passive prosthesis at Baseline (before wearing the emPOWER, when available) and Crossover:

- 12 minute Walk Test (12MWT)
- 10 meter Walk Test (10MWT)
- L-Test for overall mobility and fall risk
- Time and Quality of Ramp Ascent
- Time and Quality of Ramp Descent
- Activities-specific Balance Confidence (ABC) Scale
- Falls Efficacy Scale
- Amputee Mobility Predictor (AMP) Assessment
- Prosthetic Limb Users Survey of Mobility (PLUS-M) (12 item Short Form)
- Patient-specific Functional Scale (PSFS)
- Numeric Pain Rating Scale (NPRS)
- Activity monitoring
- Falls
- Activity Diary
- PROMIS Physical Function (Custom)
- PROMIS Global Health Short Form
- PROMIS Fatigue Short Form (7a)
- PROMIS Pain Intensity Short Form (3a)

Long term follow-up of subjects who agree to continue wearing the emPOWER Ankle at 3, 6 and 12 months with all outcome measures (except the diaries of activity and falls at 6 & 12 months).

7. Study Population

7.1. *Selection Criteria*

Study inclusion and exclusion criteria for the study are included in Table 7.1.1 below. Prior to enrollment in the study, a subject must meet all of the inclusion criteria and none of the exclusion criteria.

Table 7.1.1: Selection Criteria

Selection Criteria

Selection Criteria	
Inclusion Criteria	I-1. Male and Female I-2. 55 years or older I-3. Subjects with transtibial amputations of either leg at least 1-year prior I-4. Suction or elevated vacuum suspension and Socket Comfort Score of at least 6 I-5. Sock fluctuation of ≤ 8 ply per day I-6. K-level rating of 3 or 4 based on the AMP score I-7. Ability to walk at a walking speed of > 0.75 meters per second with the current prosthesis I-8. Unilateral amputees (up to 7 bilateral amputees can be included, 1 per site in addition to the unilateral amputees) I-9. Foot size: 25-30 cm I-10. Ability to complete a continuous 6MWT I-11. Ability to provide written, informed consent I-12. Ability to complete study visits and study documents I-13. Ability to manage the complexity of a powered device including charging and changing batteries as needed I-14. Ability to read and understand English
Exclusion Criteria	E-1. Subjects who have never used a prosthetic device E-2. Less than 55 years of age E-3. Weight <150 lbs. or > 287 lbs E-4. Transfemoral amputees E-5. Active sores or ulceration on subject's residual limb E-6. Sore on contralateral foot E-7. Cuff-link socket suspension E-8. Socket Comfort Score of less than 6 E-9. Sock fluctuation of > 8 per day E-10. K level of 1 or 2 E-11. Amputation clearance < 8.625" E-12. History of stroke or TIA that impairs current walking E-13. Recent history of excessive falling defined as more than 2 falls requiring medical assistance in the prior year

Selection Criteria	
	E-14. Medications potentially affecting balance E-15. Recent hospitalization (within past 3 months) E-16. Cognitive deficiency that would impact ability to charge and change batteries as needed

7.2. *Subject Discontinuation or Withdrawal*

- Subjects may voluntarily withdraw from the study at any time without reason. All information relative to the withdrawal must be fully documented in the subject's chart.
- Subjects withdrawn prior to the study phase where they walk on the emPOWER Ankle will be replaced.

7.3. *Subject Enrollment*

The study will enroll up to ten (10) subjects into Phase I. Subjects will then be invited to participate in Phase II, long-term follow-up. The Study Site will be asked to enroll subjects with a unilateral transtibial amputation (on either the left or right side).

8. Concomitant Medication

All current medications will be recorded at study enrollment and any changes during the study period will be noted.

9. Study Visits

This is a pilot, prospective, cross-over, open label observational study that aims to enroll five (5) subjects at one (1) study site. The study will have two (2) study phases:

Phase I will include all subjects enrolled in the study and followed through emPOWER Follow-up (Visit 3).

Subjects who show benefit from the emPOWER Ankle will be offered the opportunity to continue to use the emPOWER Ankle after the study and participate in Phase II – Long-term follow-up through 12 months.

The schedule of assessments is shown below in Table 9.11.1, and study assessments are detailed in Section 10.

9.1. *Screening*

Subjects presenting to Investigators with transtibial amputations and who are currently using a passive prosthetic device will undergo evaluation for potential participation in the study.

A subject will sign the study-specific informed consent form (ICF) prior to performing any test involved in determining eligibility that goes beyond standard of care.

Each subject must meet the inclusion/exclusion criteria for this study to be eligible for study participation.

9.2. *Moment of Enrollment*

Subjects will be considered "enrolled" in the study once compliance with all inclusion and exclusion criteria has been verified and documented; and the subject has signed the informed consent form. At that point, the subject will enter the baseline phase of the study.

9.3. *Subject Identification*

Each subject will be assigned a unique subject identification number at the time of consent. This subject identification number will be retained throughout the study if the subject is enrolled. Sites will keep a log that notes the subject's name and corresponding subject identification number. All case report forms (CRFs) will be tracked, evaluated, and stored using only the subject ID number and initials. No personal other identifying information will be included on the CRFs.

The ICF will notify subjects that study monitors, auditors, and representatives of government agencies will have access to personal identifying information to ensure that data reported on the CRFs corresponds to the person who signed the ICF and the information contained in the source documentation.

9.4. *Phase I: 1st Visit - Baseline*

For each of the enrolled subjects, characteristics at the time of the procedure including: age, sex, weight, amputation side(s) and amputation type(s), medical history will be recorded. At day of enrollment, subjects will complete:

- Amputee Mobility Predictor (AMP)
- Physical Assessment
- Fitted with a Fitbit® One™ activity tracker
    - The activity tracker will to be used to monitor steps taken on their passive prosthetic device for 14 days. A minimum of twenty-seven hundred (2700) recorded daily steps while using the passive prosthesis will be documented toward ability to perform the study's 6MWT. [12]
- Subjects will be provided a patient diary to track activity, falls and self-reporting of activities of daily living.

9.5. *Phase I: 2nd Visit - Study Procedure*

At the second visit, the subject will complete the following study assessments wearing the passive prosthetic:

- 6MWT
- Ramp Ascent
- Ramp Descent
- ABC Scale
- Falls Efficacy Scale
- Mobility PLUS-M (12 item Short Form)
- PROMIS Questionnaires

At the end of the second visit, subjects will be fitted with the emPOWER Ankle by a qualified clinical prosthetist, trained by BionX personnel. This fitting includes selection of the appropriate size and category carbon fiber foot, alignment, and tuning in accordance with the emPOWER Instructions For Use (IFU). The prosthetist will make a determination that the tuning was successful (within the bounds specified by the IFU) and the Investigator will maintain a copy of the Tuning Record. This initial Tuning Record may also be used to verify that the subject has the ability to walk at a self-selected walking speed (SSWS) > 0.75 meters per second with the current prosthesis and can walk with variable cadence, where variable cadence is defined as three distinguishable walking speeds with a minimum SSWS of 0.75 m/s (one below SSWS, and one above SSWS) on the Tuning record. Distinguishable will be defined as no overlap between the three (3) primary step groupings for each walking speed displayed on the Tuning Record.

At fitting of the emPOWER Ankle, the Investigator will instruct the subject to utilize the device for a 16-day period of time, within the intended and foreseeable range of use (e.g. – ramps, stairs, limited running or jumping, stepping sideways, etc.). In addition, the investigator will take the subject though a series of default operating conditions of the emPOWER Ankle in the clinic setting such as with the power turned off.

Each subject will take the emPOWER Ankle (including batteries and charger) home for 16 days (to ensure 14 full days of step counts) of use in everyday life situations. The subject will not be under the observation of the Investigator during this take home period. During the at home portion of the study, subjects will continue to monitor daily steps with use of a Fitbit® One™ during the time that they are wearing the emPOWER Ankle. Subjects will also maintain an Activities of Daily Living Diary during the take home evaluation portion of the study. This Diary will allow subjects to note specific activity changes due to the emPOWER Ankle and serve as a log for recording any falls.

As a quality check, the steps on the emPOWER Ankle, as recorded in the emPOWER Tuning Records, will also be recorded at baseline and at follow-up.

9.6. *Phase I: 3rd Visit - emPOWER Follow Up*

After the 16-day period of use, the subject will return to the prosthetist. The window for this visit is +1 week.

During this visit, the subject will complete the following study assessments wearing the emPOWER Ankle:

- 6MWT
- Ramp Ascent
- Ramp Descent
- AMP
- ABC Scale
- Falls Efficacy Scale
- Mobility PLUS-M (12 item Short Form)
- PROMIS Questionnaires

In addition, the patient diary will be reviewed for Fitbit steps, falls and daily activity.

The Investigator will maintain a copy of the Tuning Record.

9.7. ***Phase II: 4th Visit – 3 Month Visit***

Subjects will be invited to participate in long-term follow-up. For a minimum of 14 days prior to this visit, the subject should wear the Fitbit and complete the patient diary for steps, fall and daily activity.

Subjects will be seen by the prosthetist after wearing the emPOWER Ankle for 3 months. The window for this visit is -1 week / + 6 weeks.

During this visit, the subject will complete the following study assessments wearing the emPOWER Ankle:

- 12MWT (with distance walked assessed at 6 and 12 minutes)
- 10MWT
- L-Test
- Ramp Ascent
- Ramp Descent
- ABC Scale
- Falls Efficacy Scale
- AMP
- Mobility PLUS-M (12 item Short Form)
- PROMIS Questionnaires
- Patient-specific Functional Scale (PSFS)
- Numeric Pain Rating Scale (NPRS)

In addition, the patient diary will be reviewed for Fitbit steps, falls and daily activity.

At the end of the study visit, subjects will return to wearing their passive prosthetic foot for 2-4 weeks of re-accommodation.

The subjects are reminded to wear the Fitbit activity monitor and complete the patient diaries to track activity, falls and self-reporting of activities of daily living.

9.8. ***Phase II: 5th Visit – Crossover Visit***

Subjects will be seen by the prosthetist after wearing their passive prosthetic foot for 2-4 weeks. The window for this visit is 2-6 weeks after passive device fitting.

For a minimum of 14 days prior to this visit, the subject should wear the Fitbit and complete the patient diary for steps, falls and daily activity.

During this visit, the subject will complete the following study assessments wearing the passive prosthetic:

- 12MWT (with distance walked assessed at 6 and 12 minutes)
- 10MWT
- L-Test
- Ramp Ascent
- Ramp Descent
- ABC Scale
- Falls Efficacy Scale
- AMP
- Mobility PLUS-M (12 item Short Form)
- PROMIS Questionnaires
- PSFS
- NPRS

At the end of the study visit, subjects will return to wearing the emPOWER Ankle for the remainder of the study. If there are any adjustments to the tuning settings different from those previously used for the emPOWER Ankle, the tuning record should be saved.

9.9. ***Phase II: 6th Visit – 6 Month Visit***

Subjects will be seen by the prosthetist. The window for this visit is -4 weeks / + 3 months.

During this visit, the subject will complete the following study assessments wearing the emPOWER Ankle:

- 12MWT (with distance walked assessed at 6 and 12 minutes)
- 10MWT
- L-Test
- Ramp Ascent
- Ramp Descent
- ABC Scale
- Falls Efficacy Scale
- AMP
- Mobility PLUS-M (12 item Short Form)
- PROMIS Questionnaires
- PSFS
- NPRS

If there are any adjustments to the tuning settings for the emPOWER Ankle, the tuning record should be saved.

9.10. ***Phase II: 7th Visit – 12 Month Visit (Final Study Visit)***

Subjects will be seen by the prosthetist. The window for this visit is -3 months / + 3 months. This will be the final study visit.

During this visit, the subject will complete the following study assessments wearing the emPOWER Ankle:

- 12MWT (with distance walked assessed at 6 and 12 minutes)
- 10MWT
- L-Test
- Ramp Ascent
- Ramp Descent
- ABC Scale
- Falls Efficacy Scale
- AMP
- Mobility PLUS-M (12 item Short Form)
- PROMIS Questionnaires
- PSFS
- NPRS

9.11. ***Table 9.11.1: Procedures and Assessments***

The following table summarizes the timing and specific assessments to be conducted in this study:

ASSESSMENT	BASELINE *1ST Visit*	PASSIVE DEVICE ASSESMENT/ ANKLE FITTING *2nd Visit*	emPOWER Follow-Up *3rdVisit*	3 MONTHS *4th Visit*	CROSSOVER *5th Visit*	6 MONTHS *6th Visit*	12 MONTHS *7h Visit*
Visit Window			*16 days after Visit 2 +1 week*	*-1 week / + 6 weeks*	*2-6 weeks after passive device fitting*	*-4 weeks / + 3 months*	*-3 months / + 3 months*
Eligibility Assessment	X						
ICF[a]	X						
Demographics (DOB, Gender)	X						
Physical Assessment (ht, wt, side and type of amputation)	X						
Medical History	X						
AMP	X		X	X	X	X	X
FitBit One™ steps	+	X	X	X	X		
Tuning Record		X**	X		***	***	***
6MWT		X	X				
12MWT *(includes 6 min distance, pain-free walking scale and BORG RPE)*				X	X	X	X
10 MWT				X	X	X	X
L-Test				X	X	X	X
Ramp Test *(Ascent & Descent)*		X	X	X	X	X	X
ABC		X	X	X	X	X	X
Falls Efficacy Scale		X	X	X	X	X	X
PLUS-M		X	X	X	X	X	X
PROMIS Evals		X	X	X	X	X	X
PSFS				X	X	X	X
NPRS				X	X	X	X
EASE Study Activity Diary (Reviewed)	+	X	X	X	X		
Adverse Events & Concomitant Medication	X	X	X		X	X	X

[+] FitBit One™ and diary provided to Subject

[a] If the study ICF is modified during the course of the study, study subjects will be re-consented.

** Confirms walking speeds required for emPOWER Ankle arm

*** Collect the tuning record if adjustments are made to the emPOWER device

10. Study Assessments

10.1. *Amputee Mobility Predictor (AMP)*

The AMP is an instrument designed to measure ambulatory potential of lower-limb amputees [13]. Subjects begin the test seated in a hard chair with arms and are tested for a total of 21 items assessing abilities of increasing level of difficulty. Abilities assessed include sitting balance, transfer from chair to chair, standing balance, gait quality, negotiating obstacles, and the use of assistive devices. The total score range for the AMP is 0 to 47 points. A minimal detectable change of 3.4 points has been reported [14].

10.2. *12-Minute Walk Test (and 6-Minute Walk Test) (12MWT & 6MWT)*

The walking test is a validated performance test used to measure gait speed and aerobic capacity/endurance. The distance that the patient is able to walk in 6 and 12 minutes is recorded. In addition, subjects will be asked to indicate when they experience an onset of pain, if occurring during the test, to determine the pain-free walking distance. Assistive devise may be used, but should be recorded and consistent between tests. Minimally clinically important differences (MCID) have not yet been reported for amputees, but for patients with incomplete spinal cord injury (36 m) [15] and stroke (34.4 m) [16]. Generally in rehabilitation, increases in walking speed of 0.1 m/s or more, which would equal an increase in walking distance of 36 m or more in the 6MWT, are considered clinically meaningful [17-19]. The distance a subject can walk after 6 and 12 minutes while wearing the emPOWER Ankle compared to the subject's passive prosthesis.

The Borg Rating of Perceived Exertion (RPE) score will also be recorded at 6 and 12 minutes and assessment of pain-free walking distance for sound and residual knee and hip, low back pain for subjects that report such pain during the 12minWT. The RPE measures the perceived intensity of physical activities on a visual analogue scale and provides a good estimate of the actual heart rate during physical activity and is correlated with lactate levels, $\%VO_2max$, and breathing rates in athletes [20].

10.3. *10-Meter Walk Test (10MWT)*

The walking test is a validated test used to measure gait speed. When available, data will be collected for the walking tests. Subjects are often allowed the use of walking aids (such as a cane, crutches or hemi-walker) that they normally use in home or community ambulation. In addition to the time to complete the test, the use of walking aids, the distance of the walk test and the use of footwear (e.g. barefoot or with shoes) will be recorded.

10.4. *L-Test*

The L-Test is a timed 20-meter test of basic mobility skills that includes 2 transfers and 4 turns at the subject's usual walking speed. This test is a modified version of the Timed Up and Go Test designed for people with lower limb amputations. The test is measured by the time that it takes a subject to stand from an armless chair, walk 10 meters (in the shape of an L) at the subject's usual walking speed, turn 180 degrees, and return 10 meters (in the shape of an L) back to a seated position in the same chair [21]. The L-test was selected, since it measures overall functional mobility risk and fall and is validated for the amputee population. The time to

perform the L-Test with the emPOWER Ankle will be compared to the time on subject's passive prosthesis.

10.5. *Ramp Tests (Ascent and Descent)*

The ramp ascent test is a timed performance test of walking up a 25-foot ramp with 5 degree incline and an outdoor hill (length and inclination/grade to be determined). The ramp ascent time with the emPOWER Ankle will be compared to the time on the subject's passive prosthesis followed by the Hill Assessment Index. The Hill Assessment Index is an instrument to measure the quality of the subject's gait during ramp ambulation.

The ramp decent test is a timed performance test of walking down a 25-foot ramp with 5 degree incline and an outdoor hill (length and inclination/grade to be determined). The ramp decent time with the emPOWER Ankle will be compared to the time on the subject's passive prosthesis followed by the Hill Assessment Index and questionnaire assessing patient-perceived control of walking speed.

10.6. *Activities-Specific Balance Confidence (ABC) Scale*

The ABC Scale [22] is a self-administered questionnaire that asks the patient to rate his or her confidence in performing various ambulatory activities on a scale from 0% (no confidence) to 100% (complete confidence) without losing balance or becoming unsteady. Scores for each of the 16 items will be collected and an average percentage calculated, with scores <67 indicating an increased risk of falling [23]. The scores on the ABC with the emPOWER Ankle will be compared to the subject's passive prosthesis.

10.7. *Falls Efficacy Scale*

The Falls Efficacy Scale is a validated 10-item self-report questionnaire designed to assess confidence in the ability to perform 10 activities of daily living without falling as an indicator of how one's fear of falling impacts physical performance. Each item is rated from 1 ("very confident") to 10 ("not confident at all"), and the per item ratings are added to generate a summary total score (10 to 100). Lower scores indicate more confidence and higher scores indicate lack of confidence and greater fear of falling. It has been validated for use in the elderly [24] and persons with amputations [25]. Scores ≥70 indicate an increased fear of falling. [24, 25]

10.8. *Prosthetic Limb Users Survey-M (PLUS-M)*

The PLUS-M is a valid and reliable self-reported measure for the mobility of adults with lower limb amputations. PLUS-M asks about the patient's ability to perform simple and complex tasks. This questionnaire is asking about the current timeframe for the patient. High PLUS-M scores correspond with greater mobility [26]. The scores on the PLUS-M with the emPOWER Ankle will be compared to the scores on the subject's passive prosthesis.

10.9. *PROMIS Instruments*

PROMIS item banks and their short forms are a reliable and precise measurements of patient reported outcome measures [27]. For this study, the following instruments will be used: the PROMIS Physical Function (Custom), the PROMIS Global Health Short Form, the PROMIS Fatigue Short Form (7a), and The PROMIS Pain Intensity Short Form (3a). The scores on the

PROMIS instruments with the emPOWER Ankle will be compared to the scores on the subject's passive prosthesis.

10.10. ***Patient Specific Functional Scale (PSFS)***

The PSFS [28] is a self-report measure aimed at identifying functional status limitations that are most relevant to individual patients. The PSFS is a reliable, valid, and efficient measure for detecting clinical change in persons with low back pain and knee dysfunction [29]. Patients will be asked to identify three to five activities that they are having difficulty or are unable to perform because of their injury/condition. For the specified activities, patients will then be asked to rate their ability to perform each activity at that time (0-10 numerical scale) with '0' being unable to perform the activity, and '10' being able to perform the activity at the same level as they could prior to the injury/condition. The scores on the PSFS instruments with the emPOWER Ankle will be compared to the scores on the subject's passive prosthesis.

10.11. ***Numeric Pain Rating Scale (NPRS)***

The NPRS is a valid and reliable measure of pain that may be used across all musculoskeletal injuries/conditions and complements the PSFS [29]. The patient will be asked to rate the pain of their joints, foot, lower back, and if they are using an assistive device any additional affected limbs on average over the last 24 hours on a scale 1-10, with '1' being 'very mild' and '10' being the 'unimaginable unspeakable'. The scores on the NPRS instruments with the emPOWER Ankle will be compared to the scores on the subject's passive prosthesis.

10.12. ***Activity Monitoring***

An activity monitor will be worn to record the number of steps the patient takes with the prosthesis. The patient will return to the site with the activity monitor so that the steps counted can be downloaded from the device. In addition, the patient will be sent home with a prepaid envelope and be instructed to mail back the activity monitor if the next visit will be more than 3 weeks later, to ensure that the data is not lost. The step counts will be downloaded from the device the day the activity monitor is returned to the Investigator. The Investigator will record the date the patient was affixed with the activity monitor, the date they received the returned activity monitor, and the date they synced the monitor.

10.13. ***Subject Diary (Activity Monitoring)***

Subjects will be provided with a 'diary' to record a daily step-count (using the Fitbit provided), falls and daily activity. Subjects will record positive and negative observations about the prosthesis performance while wearing the study devices. These observations will be reviewed together with the Investigator during the study visits. In addition, subjects will also record in the diary any falls and resulting injuries. If any of the diary entries reveal complaints or adverse events, these will be reported on the Adverse Event form.

11. Statistical Methods

The study objective is to characterize the improvement in the 6MWT with the emPOWER Ankle versus the subject's passive lower-limb prosthesis. This is calculated as:

Percent change in 6MWT=100 * (emPOWER Ankle 6MWT – Passive Prosthesis 6MWT) / Passive Prosthesis 6MWT

A positive value for Percent Change in 6MWT represents the percent increase in the 6MWT, and a negative value represents a decrease.

12. Adverse Events

12.1. *Adverse Event Relationship Terms*

All Adverse Events (AEs) occurring in this study will be reported, including characterization by severity, seriousness and relatedness, as described below. Investigators will record characteristics of each adverse event on an Adverse Event CRF. Each adverse event will be judged by the Investigator as to its relationship to the investigational device. In addition, the Investigator will identify the date of onset, severity, seriousness, relatedness and duration of the AE. Severity will be judged using the scale noted in *Table 12.1.1: Definition of event severity for judgment by Investigator.* Seriousness will be judged using the criteria listed in *Table 12.1.2: Definition of serious adverse event, adapted from 21 CFR 803.3*. Device relatedness will be determined by the criteria listed in *Table 12.1.3: Definition of event relatedness.* All adverse events will be monitored until they are adequately resolved, explained or the subject has exited the study.

Table 12.1.1: Definition of event severity for judgment by Investigator.

Definition of event severity for judgment by Investigator.	
Term	**Definition**
Mild	Subject is aware of a sign or symptom, but that sign or symptom does not interfere with normal activity OR symptom is both transient and resolved without treatment
Moderate	Symptoms interfere with the subject's usual activity OR symptoms require treatment
Severe	Symptom(s) cause either severe discomfort OR have a significant impact of the subject's usual activity and symptoms require treatment

Table 12.1.2: Definition of serious adverse event, adapted from 21 CFR 803.3.

Definition of serious adverse event, adapted from 21 CFR 803.3.
An event is considered serious if it: (1) Is life-threatening, (2) Results in permanent impairment of a body function or permanent damage to a body structure, or (3) Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure. Permanent means irreversible impairment or damage to a body structure or

function, excluding trivial impairment or damage.

Table 12.1.3: Definition of event relatedness

Definition of event relatedness	
Term	**Definition**
Definite	Adverse event whose timing is highly plausible for causality and which cannot be explained by other factors
Probable	Adverse event whose timing is reasonable for causality and is unlikely to be explained by other factors
Possible	Adverse event whose timing is reasonable for causality but which could be explained by other factors
Not related	Adverse event whose timing makes causality improbable and which could easily be explained by other factors
Unknown	Adverse event whose plausibility of timing cannot be judged or in which information regarding other factors does not exist

12.2. ***Reporting Requirements***

The communication requirements for Adverse Events reporting, from the beginning of enrollment through procedure completion, to Ottobock are as follows in *Table 12.2.1: Adverse Event Reporting Requirements* below:

Table 12.2.1: Adverse Event Reporting Requirements

Adverse Event Reporting Requirements			
Adverse Event Classification	**Methods of Communicating Events to Ottobock**	**Communication Timeline to Ottobock**	**Source Documentation Requirements**
SAE and/or SADE	Complete AE CRF with all available information. If CRF is unavailable, fax information to the Ottobock Clinical Affairs Department.	Within 24 hours of first becoming aware of the event	Provide copies of all relevant source documents requested by Ottobock or designee as soon as possible after reporting the event.
AE/ADE	Complete AE CRF	Review with Monitor during next monitoring visit	No source documents are required to be submitted to Ottobock.

Table 12.2.2: Sponsor and BionX Reports

Sponsor and BionX Reports			
Responsible Party	**Report**	**Submit to**	**Description**
Sponsor	SADE, Device-related AEs	BionX	All SADEs will be sent to BionX Regulatory Affairs within 24 hours of first becoming aware of the event for review for possible Medical Device Reporting (MDR) in accordance with 21 CFR 803.20. All device-related AEs will be sent to BionX Regulatory Affairs department in a monthly report for MDR assessment.
BionX	Death or serious injury; device malfunction	FDA	Notification within 5 workdays, 10 workdays or 30 calendar days after BionX first learns of the event in accordance with 21 CFR 803.20, depending on the source and action required.

12.3. *Device deficiencies, Device failures, Malfunctions, and Product Nonconformities*

All product deficiencies related to the identity, quality, durability, reliability, safety or performance of the medical device, failures, malfunctions and product nonconformities will be documented on the appropriate CRF and immediately reported to the sponsor (without any delay that cannot be justified and within 24 hours of occurrence). In such cases, the product should either be returned to BionX (an Ottobock company, located at 4 Crosby Drive, Bedford, MA 01730) for analysis or a BionX employee will either inspect or service at the center. Instructions for returning the product will be provided to the centers. Product failures and malfunctions should also be documented in the subject's medical record.

NOTE: Product failures, malfunctions, and product nonconformities are NOT to be reported as adverse events. However, if there is an adverse event that results from an product failure or malfunction, that specific event should be recorded on the AE CRF.

12.4. *Reporting to Regulatory Authorities /IRBs /ECs /Investigators*

Ottobock is responsible for reporting adverse event information to all participating investigators and regulatory authorities as applicable. The Site Principal Investigator is responsible for informing the IRB of SAEs or other events as required by the overseeing IRB. A copy of any reports to IRBs should be sent to the Ottobock Clinical Operations and BionX Regulatory Affairs Department.

13. Risk Benefit Analysis

The emPOWER Ankle prosthesis is designed to provide bionic propulsion, emulating the biological function of an ankle, and attaches to the wearer by a previously fit socket. The benefits of bionic propulsion for the amputee (as compared to conventional prostheses) have been studied and published in peer-reviewed scientific journals, summarized as follows:

a) walk with a more natural gait;

b) reduce musculoskeletal stress believed to be causal of osteoarthritis;
c) use less energy to walk;
d) walk at a normal preferred speed;
e) navigate uneven terrain with less effort and greater speed.

The device's safety and performance profile has been assessed and has been found to add no additional risk to the typical lower-limb prosthetic ankle device.

13.1. *Known and Anticipated Risks*

The emPOWER Ankle is not expected to produce any additional or unique risks as compared to those already associated with existing lower-limb prostheses. The anticipated risks are summarized as:

1. Trip / Fall Hazard: The risk of trips/falls is inherent to the lower-extremity amputee population based on the nature of the condition. The emPOWER Ankle device, by emulating normal biological function of the ankle, is anticipated to exhibit a lower incidence of trips/falls than conventional (non-microprocessor) ankle prostheses.
2. Fire Hazard: The risk of fire from the Li-ion battery which powers the emPOWER Ankle is minimized through design, control circuitry and compliance/testing to international standards.
3. Electrocution Hazard: The battery-powered ankle prosthetic itself does not present a risk of electrocution, however the AC-powered battery charger presents the same risk of electrocution as other 120V AC powered devices.

13.2. *Risk Minimization*

The Sponsor will employ measures throughout the course of this study to minimize risks to subjects choosing to participate. All efforts will be made to minimize potential risks by:

1. Selecting Principal Investigators who are experienced and skilled in fitting and aligning lower limb prostheses.
2. Providing training on the equipment prior to use
3. Defining inclusion/exclusion criteria clearly to ensure only appropriate subjects are enrolled.
4. Ensuring that the treatment of the subject is consistent with current medical practices.

14. Subject Benefit

Subjects who demonstrate improvements using the emPOWER Ankle compared to their passive prosthetic device will be offered the opportunity to continue using the emPOWER Ankle at the end of the study until there is Medicare payment available for the subject to purchase a emPOWER Ankle. The subject will not be told of this prior to study completion to avoid bias. All subjects will receive fair compensation for completion of the study to cover costs of travel to and from the study center and for any potential lost wages due to the study visits.

15. Ethical Considerations

15.1. *Study Conduct*

The Investigator will conduct the study within the regulations and guidelines of the Food and Drug Administration (FDA) and all country/state/local regulations, whichever affords the greater protection to the subject.

15.2. *Institutional Review Board*

A copy of the protocol, proposed ICF, other written subject information and any proposed subject recruitment material must be submitted to the IRB for written approval prior to use. A copy of the written IRB approval of both the protocol and ICF, as well as the IRB's concurrence with the justification for non-significant risk status, must be received by Ottobock before recruitment of subjects into the study and shipment of product.

The Investigator must submit and, where necessary, obtain approval from the IRB for all subsequent protocol amendments and changes to the Informed Consent form. The Investigator must notify the IRB of deviations from the protocol and SAEs occurring at the site and other SAE reports received from Ottobock in accordance with the overseeing IRB's requirements.

The Investigator is responsible for obtaining annual IRB approval and renewal throughout the duration of the study. Copies of the Investigator's reports and the IRB continuance of approval must be sent to Ottobock.

15.3. *Informed Consent Form*

Ottobock will provide a sample ICF to the Investigator to prepare for use at his/her site. The written Informed Consent documents should be prepared in the language(s) of the potential subject population.

Ottobock and the reviewing IRB must approve the ICF before use at that center. The ICF(s) must be in agreement with the 21 CFR Part 50.

15.4. *Obtaining Informed Consent*

The background of the proposed study and the benefits and risks of the procedures and study must be explained to the subject. The subject must sign the consent form prior to enrollment. This form or a modification based on IRB recommendations must be presented to and signed by all enrolled subjects and signed by the principal investigator or designee.

Prior to obtaining informed consent, information should be given in a language and at a level of complexity understandable to the subject in both oral and written form by the investigator or assigned designee. Subjects should not be coerced, persuaded, or unduly influenced to participate or remain in the study. A subject or his/her legal representative must be given ample time and opportunity to inquire about details of the study and all questions about the study should be answered to the satisfaction of the subject or the representative.

Prior to participation in the study, the written informed consent form should be signed and personally dated by the subject or his/her legal representative, and by the person who conducted the informed consent discussion (investigator or designee). If the subject or his/her legal representative is unable to read the consent form, a witness will need to be present during the entire informed consent discussion. After the informed consent form is read to the subject and signed by the subject or his/her legal representative, the witness should also sign the consent form, attesting that informed consent was freely given by the subject. The informed consent process should be documented in each subject's record.

The subject or his/her legal representative must receive a copy of the signed and dated informed consent form.

The consent form should be updated or amended whenever new information becomes available that may be relevant to the subject.

Subjects will be informed that the sponsor and regulatory authorities will have access to personally identifying information for the purposes of monitoring data against source documentation. However, all data stored and presented by the sponsor will be in anonymous form.

15.5. *Amending the Protocol*

This protocol must be followed exactly, and can be altered only by written amendments by the study sponsor.

15.6. *Emergency Actions*

Ottobock accepts the right of the Investigator to deviate from the protocol only in an emergency when necessary to safeguard the life or the physical well-being of a study subject. The Investigator must give notice of any emergency deviations and justification for the deviation to Ottobock and the IRB as quickly as possible after the episode, but in any event no later than 24 hours after the emergency.

15.7. *Protocol Adherence*

Prior to beginning the study, the Investigator must sign the Investigator Agreement and Protocol Signature page documenting his/her agreement to conduct the study in accordance with the protocol. An Investigator must not make any changes or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency. Each deviation from the protocol must be documented with the date and reason for the deviation and reported to Ottobock and to the IRB, per local guidelines and government regulations.

16. Study Logistics

Ottobock and BionX will make necessary efforts to ensure that this study is conducted in compliance with Good Clinical Practices and all applicable regulatory requirements.

All personnel to participate in the conduct of this clinical study will be qualified by training, education and/or experience to perform his or her respective tasks.

16.1. *Data Management*

Subject data will be collected on case report forms (CRFs). The Principal Investigator or Sub-investigator must ensure the accuracy and completeness of the recorded data. Changes to data previously submitted to the sponsor will require the Investigator to acknowledge/approve the changes in writing.

Visual and/or computer data review will be performed to identify possible data discrepancies. queries will be created and will be issued to the center for appropriate response. The site staff will be responsible for resolving all queries.

Data from all study subjects through point of study completion or study withdrawal will be reported.

16.2. *Monitoring and Auditing*

Monitoring visits to the centers will be made periodically during the study, to ensure that all aspects of the current, approved protocol/amendment(s) are followed. Original source documents will be reviewed for verification of data. The Investigator/institution guarantees direct access to original source documents by Ottobock personnel, their designees, and appropriate regulatory authorities. In the event that the original medical records cannot be obtained for a subject that is seen by a non-study physician at a non-study institution, photocopies of the original source documents must be made available for review.

The study may also be subject to a quality assurance audit by Ottobock and/or BionX or its designees, as well as inspection by appropriate regulatory authorities.

It is important that the Investigator and relevant study personnel are available during the monitoring visits and audits and that sufficient time is devoted to the process.

16.3. *Device Accountability*

Device accountability records must be maintained at each center. The quantity of devices received by each center, those returned to the supplier, and those devices used at the center will be recorded in the device accountability record. The Investigator must explain in writing the reasons for any discrepancy noted in device accountability. The centers will return any emPOWER product unwanted by subjects back to BionX. BionX will provide instructions to the centers on the proper method to return the used product.

16.4. *Record Retention*

The Investigator will maintain all essential study documents and source documentation, in original format, that support the data collected on the study subjects. Documents must be retained for at least 2 years after clearance of the marketing application or until at least 2 years

have elapsed since the formal discontinuation of the clinical investigation of the product, whichever is later. When these documents no longer need to be maintained, it is Ottobock's responsibility to inform the Investigator. The Investigator will take measures to ensure that these essential documents are not accidentally damaged or destroyed. If for any reason the Investigator withdraws responsibility for maintaining these essential documents, custody must be transferred to an individual who will assume responsibility. Ottobock must receive written notification of this custodial change.

16.5. *Criteria for Terminating Study*

Ottobock reserves the right to terminate the study but intends only to exercise this right for valid scientific or administrative reasons and reasons related to protection of subjects. Investigators and associated IRBs will be notified in writing in the event of termination.

16.6. *Criteria for Suspending/Terminating a Study Center*

Otto Bock HealthCare LP reserves the right to either suspend or terminate enrollment at a study center at any time after the study initiation if no subjects have been enrolled, if the center has multiple or severe protocol deviations or violations without justification or fails to follow remedial actions.

16.7. *Insurance*

If subjects are injured due to their participation in this study, their physician will provide medical care to treat their injury. Otto Bock HealthCare LPwill maintain appropriate liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a Clinical Study insurance statement/certificate will be provided to the IRB.

16.8. *Publication Policy*

At the conclusion of the study, the aggregate clinical study data may be submitted for publication in a peer- reviewed journal. The order of authorship will be according to the number of subjects enrolled at the site, as well as the level of contribution to the final manuscript. In the event that more investigators participate than allowed by the journal, all Principal investigators will be listed according to the enrollment and sub-investigators will be acknowledged in an acknowledgements section.

This clinical study will be registered on clinicaltrials.gov.

17. References

1. A. Grabowski, S. D'Andrea, H. Herr. "Bionic leg prosthesis emulates biological ankle joint during walking," *Amer. Society of Biomechanics*, 2011.
2. H. Herr, A. Grabowski. "Bionic ankle–foot prosthesis normalizes walking gait for persons with leg amputation," *Proceeding of the Royal society B*, 2011.
3. A.M. Grabowski, S. D'Andrea. "Effects of a powered ankle-foot prosthesis on kinetic loading of the unaffected leg during level-ground walking," *Journal of NeuroEngineering and Rehabilitation* 10: 49, 2013.
4. J. Aldridge, J. Sturdy, J. Wilken. "Stair ascent kinematics and kinetics with a powered lower leg system following transtibial amputation," *Gait & Posture* 36 291–295, 2012.
5. S. Au, J. Weber, E. Martinez-Villapando, H. Herr. "Powered Ankle-Foot Prosthesis for the Improvement of Amputee Ambulation," *IEEE Engineering in Medicine and Biology International Conference*. Lyon, France, pp. 3020-3026, 2007.
6. Au S., Herr H. "On the Design of a Powered Ankle-Foot Prosthesis: The Importance of Series and Parallel Motor Elasticity," Special Issue of the IEEE Robotics & Automation Society IEEE Magazine on Adaptable Compliance for Robotic Applications. September 2008; 52-59.
7. M. Eilenberg, H. Geyer, H. Herr. "Control of a powered ankle-foot prosthesis based on a neuromuscular model," *Neural Systems and Rehabilitation Engineering, IEEE Transactions on* 18, 164-173, 2010.
8. J. Markowitz, P. Krishnaswamy, M. Eilenberg, K. Endo, C. Barnhart, H. Herr. "Speed adaptation in a powered transtibial prosthesis controlled with a neuromuscular model," *Theme Issue of Philosophical Transactions B* 366, 2011.
9. Au S., Weber J., Herr H. "Powered Ankle-foot Prosthesis Improves Walking Metabolic Economy," IEEE Transactions on Robotics. 2009; 25 (1): 51-66.
10. H. Herr, A. Grabowski "Powered ankle-foot prosthesis improves metabolic demand of unilateral transtibial amputees during walking," *Amer. Society of Biomechanics*, 2010.
11. A Grabowski, H Herr "Bionic leg prosthesis normalizes the metabolic cost of walking," *Rocky Mountain Regional Amer. Society of Biomechanics*, 2011.
12. Arch ES, Ero 0, Bortz C, et al. A method to quantify cadence variability of individuals with lower limb amputation. J. Rehabil Res Dev, In Press.
13. Gailey, R. S., Roach, K. E., Applegate, E. B., Cho, B., Cunniffe, B., Licht, S., ... & Nash, M. S. (2002). The amputee mobility predictor: an instrument to assess determinants of the lower-limb amputee's ability to ambulate. *Archives of physical medicine and rehabilitation*, *83*(5), 613-627.
14. Resnik L, Borgia M. (2011). Reliability of outcome measures for people with lower-limb amputations: Distinguishing true change from statistical error. *Phys Ther*, 91(4):555-565.
15. Forrest GF, Hutchinson K, Lorenz DJ, et al. (2014). Are the 10 Meter and 6 Minute Walk Tests Redundant in Patients with Spinal Cord Injury?*PLoS ONE.* 9(5):e94108.
16. Eng JJ, Dawson, AS. (2004). Submaximal exercise in persons with stroke: test-retest reliability and concurrent validity with maximal oxygen consumption. *ArchPhysMedRehabil*, 85(1): 113-118.
17. Perry J, Garrett M, Gronley JK, Mulroy SJ. (1995). Classification of walking handicap in the stroke population. *Stroke,*26(6):982-989.

18. Perrera S, Mody SH, Woodman RC, Studenski SA. (2006). Meaningful change and responsiveness in common physical performance measures in older adults. *J Am Geriatr Sco*, 65(5):743-748.
19. Schmid A, Duncan PW, Studenski S, Lai SM, Richards L, Perera S, Wu SS. (2007). Improvements in speed-based gait classifications are meaningful. *Stroke,* 38(7):2096-2100.
20. Borg G. (1983). A category-ratio perceived exertion scale: relationship to blood and muscle lactates and heart rate. *Med. Sci. Sports Exerc*, 15(6):523-528.
21. Deathe, A. B., & Miller, W. C. (2005). The L test of functional mobility: measurement properties of a modified version of the timed" up & go" test designed for people with lower-limb amputations. *Physical therapy*, *85*(7), 626.
22. Lajoie Y, Gallagher SP. (2004). Predicting falls within the elderly community: comparison of postural sway, reaction time, the Berg balance scale and ABC scale for comparing fallers and non-fallers. *Arch Gerontol Geriatr*, 38(1): 11-26.
23. Miller WC, Deathe AB, Speechley M. (2003). Psychometric properties of the Activities-specific Balance Confidence Scale among individuals with a lower-limb amputation. *Arch Phys Med Rehabil,* 84(5):656-661.
24. Yardley L, Beyer N, Hauer K, Kempen G, Piot-Ziegler C, Todd C. Development and initial validation of the Falls Efficacy Scale International (FES-I). Age Ageing 2005; 34(6):614-619.
25. Miller WC, Deathe AB, Speechley M, Koval J. The influence of falling, fear of falling, and balance confidence on prosthetic mobility and social activitity among individuals with a lower extremity amputation. Arch Phys Med Rehabil 2001;82(8):1238-1244.
26. Hafner BJ, Gaunaurd IA, Morgan SJ, Amtmann D, Salem R, Gailey RS. (2016). Construct validity of the Prosthetic Limb Users Survey of Mobility (PLUS-M) in adults with lower limb amputation. *Arch Phys Med Rehabil* . pii: S0003-9993(16)30902-9. doi: 10.1016/j.apmr.2016.07.026. [Epub ahead of print]
27. Cella, D., et. all. (2005-2008) Initial item banks and first wave testing of the Patient-Reported Outcomes Measurement Information System (PROMIS) network. *Journal of Clinical Epidemiology.* 63(11), 1179-94
28. Stratford, P., Gill.C. et all (1995). Assessing disability and change on individual patients: A report of a patient specific measure. *Physiotherapy Canada.* 47(4):258-262.
29. Chatman, A., Hyams, S., Neel, J., Binkley, J., Stratford, P., Schomberg, A., Stabler, M. (1997). The patient-specific functional scale: measurement properties in patients with knee dysfunction. Phys Ther. 77:820-9.

18. Appendices

18.1. *Abbreviations*

6MWT	Six-Minute Walk Test
10MWT	10 Meter Walk Test
12MWT	12-Minute Walk Test
ABC	Activities-specific Balance Confidence
AE	Adverse Event
ADA	Americans With Disabilities Act
ADE	Adverse Device Effect
AK	Above Knee
AMP	Amputee Mobility Predictor (Score or Assessment Tool)
BK	Below Knee
CFR	Code of Federal Regulations
CRF	Case Report Form
EASE	Empowering Active Seniors with Energy
EC	Ethics Committees
FDA	Food and Drug Administration
ICF	Informed Consent Form
IFU	Instructions for Use
IRB	Institutional Review Board
MCID	Minimally clinically important differences
NPRS	Numeric Pain Rating Scale
PSFS	Patient Specific Functional Scale
PI	Principal Investigator
PLUS-M	Prosthetic Limb Users Survey of Mobility PLUS-M (12 item Short Form)
PROMIS	Patient Reported Outcomes Measurement Information System
RPE	Borg Rating of Perceived Exertion
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SSWS	Self-Selected Walking Speed