Limb Health and Socket Pressure in Response to Powered Ankle Prostheses
IRB # 12143

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1.0 Background & Rationale

Some estimates suggest that by 2050, as many as 3.6 million people in the United States will be living with limb loss, and if historical trends continue, at least 60% of them will have had at least a foot removed [1]. For military personnel, combat-related amputations remain one of the most common major disabling war-related injuries from modern armed conflict. The return-to-duty (RTD) status of these Service members following amputation depends on the severity of injury, treatments rendered, and regenerative rehabilitation. Adequate rehabilitation post-amputation enables our nation's heroes to reach their maximum functional recovery and independence [3].

Technological advancements in active prosthetic devices for individuals with transtibial amputation offer the potential for superior function in key areas that could lead to higher rates of RTD and improved quality of life. Currently intended primarily for individuals with a K-level of 3 or 4, (This means the person can walk most environmental barriers possibly with variable cadence and some could have more than basic walking ability that could include the ability to do athletic activities) active transtibial prostheses that provide controlled plantar/dorsiflexion in either swing (microprocessor-controlled prostheses) or late stance (prostheses with powered propulsion) are likely to become the gold standard in the future as technology continues to improve [4]. Indeed, users of these types of prostheses have higher mobility than those using any of the other four categories of prosthetic ankle-foot mechanisms for unlimited community ambulators [5].

The PROPRIO FOOT® by Ossur is a microprocessor-controlled prosthesis that regulates the angle of ankle dorsiflexion during the swing phase. This added ankle control reduces the risk of falls by increasing toe clearance [6, 7], supports more natural standing posture on slopes [8, 9], and improves stair and slope ascent/descent capability by adapting to the change in terrain. These improvements also contributed to higher interlimb symmetry [12, 14, 15], reduced energetic cost of slope ascent [16], and higher Amputee Mobility Predictor with a Prosthesis (AMPPRO) scores [17].

The Empower ankle by Ottobock is a powered prosthesis that provides active propulsion in late stance to mimic the positive work performed by the ankle plantar-flexors in push-off. The Empower has been shown to improve affected leg kinematics (increased ankle range of motion and reduced knee flexion) on smooth flat ground [18], ramp ascent [19], and gravel [20]. The kinetic properties of Empower translate into increased affected ankle and whole leg work [23] and can produce higher self-selected walking speeds by increasing both step length and cadence [18, 24, 25]. However, the impact on interlimb symmetry is somewhat mixed, with peak ground reaction force [26,27] and leg work [28] asymmetries improving, while others remain [18, 22]. Overall, the relationship between the power setting of the device and performance characteristics can vary considerably with subject [29].

Interlimb symmetry is a focus because individuals with transtibial amputation who have used a prosthesis for several years experience a higher incidence of osteoarthritis in the intact leg [30],

osteoporosis in the affected leg [31], and other musculoskeletal problems. Residual limb tissues were not designed to tolerate the loads associated with supporting an individual's weight, so elevated socket loading can result in skin problems such as pressure sores [33, 34] and abrasions [35, 36]. The patellar tendon and the distal end of the fibula are known to be the most and least load-tolerant regions, respectively [37, 38]. In general, dissatisfaction with prosthesis comfort remains high [32, 39] due to the prevalence of skin sores or irritation within the socket [40].

The most common quantitative measure of prosthetic fit is pressure inside the socket during locomotion activities, and a wide range of measurement techniques have been pursued [41, 42]. Results show that mediolateral pressures tend to be less than anterior and posterior pressures, with anterior pressures typically being the highest [43]. Walking on slopes and stairs is of particular interest since internal stresses are known to be elevated in these cases [44] and pressure in level-ground walking is a poor predictor of that in these more challenging circumstances [45]. In stair ascent, the highest pressures are located in the proximal region of the anterior surface [46, 47], whereas they shift to the distal region with stair descent [47]. Gait and Motion Analysis is of particular interest to understand how a participant's gait can affect the amount of pressure that they place on their residual and intact limb. Beyond these activity-specific results, socket pressure has also been shown to be influenced by the type of suspension [43, 46], the type of foot [48, 49], and the alignment of the prosthesis [50–54].

Measuring fit via socket pressure, though, remains one step removed from limb health, the actual quantityof interest. More direct measures of limb health include transepidermal water loss (TEWL) for quantifying the functional integrity of the skin and laser speckle imaging (LSI) for quantifying skin perfusion. The PI's prior work has shown that, like socket pressure, TEWL is affected by the type of suspension (Fig. 3), but perfusion is not necessarily (Fig. 4) [62]. No studies to date have examined the effects of active lower-limb prostheses, neither micro-controlled nor powered, on these direct measures of limb health.

Active prostheses like the PROPRIO FOOT® and Empower ankle offer great potential to more completely restore the locomotor capabilities of individuals with transtibial amputation, perhaps enhancing RTD for military personnel. As with all prosthetic components, though, these active devices are of little use if they induce pain and/or injury at the residual limb to the degree that the user will simply not wear them. Overall, this project seeks to understand and quantify the effects of powered transtibial prostheses on socket loading and direct measures of residual limb health so as to inform the optimization of prosthesis fit.

2.0 Objective(s)

2.1 Primary Objective

Use of the powered Empower ankle prosthesis to determine differences in socket pressures compared to both the microprocessor-controlled PROPRIO FOOT® and a user's standard passive prosthesis for level-ground walking, stair ascent, and ramp ascent.

2.2 Secondary Objective

Obtaining quantitative measures of limb health, transepidermal water loss (TEWL) and skin perfusion, to identify differences among the use of the Empower ankle, the PROPRIO FOOT®, and an individual's standard passive prosthesis.

3.0 Outcome Measures/Endpoints

3.1 Primary Outcome Measures

Determine the effects of a powered transtibial prosthesis on the socket pressure for level-ground walking, stair ascent/descent, and ramp ascent/descent in comparison to a microprocessor-controlled prosthesis and a passive prosthesis at 4 weeks.

3.2 Secondary Outcome Measures

Determine the relative impact on residual limb health of the use of a powered prosthesis, a microprocessor-controlled prosthesis, and a passive prosthesis for individuals with transtibial amputation at 4 weeks.

- Transepidermal water loss (TEWL) measurements at 4 weeks
- Skin perfusion measurements and analysis at 4 weeks
- PEQ , CLASS and Comfort Score responses at 4 weeks

4.0 Eligibility Criteria

4.1 Inclusion Criteria

- Ages 18 and above
- Weight ≤ 280 lb
- Ambulate at a K3 level or higher-level determined from patient EHR (Electronic Health Record)
- At least 3 months post-amputation per physician discretion
- Residual limb length greater than 4.5 inches
- Use of a passive prosthesis
- Unilateral transtibial amputees
- Must be able to ambulate without any assistive devices
- Subjects must be able to follow directions and give informed consent on their own

4.2 Exclusion Criteria

- Conditions and/or co-morbidities that would prevent wearing a prosthetic socket, affect gait, or influence function of the contralateral limb
- Amputees other than Unilateral transtibial

- Cognitive deficits or mental health problems that would limit ability to consent and participate fully in the study protocol
- Women who are pregnant or who plan to become pregnant in the near future
- Individuals undergoing dialysis and/or those with significant persistent fluctuations in residual limb volume
- Participants unwilling to wear a cloth face covering for the duration of each visit
- Must not have an active wound or scarring

5.0 Study Design

Participants will have the option to choose to attend 4 or 6 study visits. The number of visits participants decide to choose is based on subject preference depending on preferred time allocation. If opting for 4 study visits, visit 3 and 4 will be combined, as well as visit 5 and 6. The total time per participant to complete all visits will remain the same despite which option is chosen.

Randomization: Upon completion of study visit 1/ evaluation the subject will be randomized to initially receive either the PROPRIO FOOT® or the Empower ankle. A licensed prosthetist will fit the subject with the designated device at study visit 2 and establish the control settings per manufacturer recommendations and complete an alignment. The alternate device will be fitted at study visit 4.

Study Visit 1/Evaluation: This initial visit will take place at IU Health Methodist Hospital. Subjects will need to be evaluated to see if they are candidates for a prosthetic foot. They will need to undergo a clinical evaluation prior to determining eligibility, examining limb length and MPT-to-floor measurements. Additionally, for women participants of childbearing potential, attestation is required stating participant is not currently pregnant, nor planning to become pregnant and the date of their last menstrual period. Once subject is deemed to be a candidate, the following research activities will take place.

- Informed consent and HIPAA (if not previously completed)
- Research personnel will administer Socket Comfort Score questionnaire and PEQ-13 survey and CLASS survey
- Body weight recorded.
- Non-invasive limb health measurements performed (TEWL and Laser Speckle Imaging (LSI))
- Randomization
- Licensed prosthetist will perform pre-fitting and adjustments on the patient, ensuring the research foot (Foot A) will be ready to deliver during participant's next visit

Study Visit 2/Baseline: The subject's second visit will take place at the Noyes Pavilion of IU Health Methodist Hospital (Noyes). Study Visit 2 will occur within a week after Visit 1 with a window of 0-7 days. Participants will be asked to wear fitting shorts/athletic wear for visits held at Noyes prior to attending this visit. Study team members will offer specific guidance on style if necessary. The following procedures will be performed during this visit:

- Digital shape capture
- Administer pressure sensors inside participant's standard-of-care socket and initiate recording
- Body weight recorded.
- Multiple ambulation trials will be performed including level-ground walking tasks, stair ascent/descent tasks, and ramp ascent/descent trials
- 3D motion capture using the motion capture system will be conducted with the use of an electronic device that measures and reports a body's specific force, angular rate, and sometimes the orientation of the body, which are placed on subjects clothing to capture movement
  Walking tasks and ascending/descending tasks on stairs and ramps will be completed with the use of force-sensing pads
- Timed get up and go test will be performed: subject will stand from seated position and walk 3 meters and then return and sit down
- Prosthetist will fit the participant with the research foot that was randomized to them
  - 15-30 minutes of usage of the prosthetic foot will be provided for acclimation
- Subject will repeat the level-ground, stair, and ramp trials with the new prosthetic foot (Foot A)
- Prosthetist will remove pressure sensors from the socket after ambulation and recording will be terminated

Upon completion of baseline, the subject will wear the research device (Foot A) for 4 weeks to become accustomed to the new technology through its exclusive use in place of their standard-of-care prosthetic foot.

Study Visit 3: After the four-week acclimation period, the subject will return for Visit 3 at IUH Methodist Hospital. A window of +/- 7 days will be implemented, ensuring the duration to complete Visit 3 remains consistent among all participants. The following activities will take place during Visit 3:

- Participant's weight will be captured
- Research personnel will administer surveys (Socket Comfort Score, CLASS and PEQ-13)
- Non-invasive limb health measurements performed (TEWL and Laser Speckle Imaging (LSI))

- Licensed prosthetist will perform pre-fitting and adjustments on the patient, ensuring the other research foot (Foot B) will be ready to deliver during participant's next visit

Study Visit 4 (Study Visit 3 if opted for 4 Study Visits): Study Visit 4 will occur within a week after Visit 3 with a window of 0-7 days. This visit will take place at Noyes. The following activities will take place:

- Digital shape capture will be performed
- Administer pressure sensors on participant's research socket and recording will be initiated using Foot A
- Body weight recorded.
- 3D motion capture using the motion capture system will be conducted with the use of an electronic device that measures and reports a body's specific force, angular rate, and sometimes the orientation of the body, which are reflective markers placed on subjects to capture movement
    - Level-ground, stair ascent/descent, and ramp ascent/descent trials will be completed with the device under the control settings established during Visit 1 (battery on)
    - Repetition of level-ground, stair ascent/descent, and ramp ascent/descent trials with the device's battery off
- Prosthetist will remove research foot (Foot A) from participant and fit with the other research foot (Foot B)
    - 15-30 minutes of usage of the prosthetic foot will be provided for acclimation
- Subject will repeat the level-ground, stair, and ramp trials with the new prosthetic foot (Foot B) with battery on
  Prosthetist will remove pressure sensors from the socket after ambulation and recording will be terminated.
- Timed get up and go test will be performed: subject will stand from seated position and walk 3 meters and then return and sit down

Upon completion of study Visit 4, the subject will wear the research device (Foot B) for 4-weeks to become accustomed to the new technology through its exclusive use in place of their standard-of-care prosthetic foot.

Study Visit 5 (Final Visit if opted for 4 Study Visits): Study Visit 5 will occur at IUH Methodist Hospital, Comprehensive Wound Center Innovation Suite. A window of +/- 7 days will be implemented, ensuring the duration to complete Visit 3 remains fairly consistent among all participants. The following activities will take place during Visit 5:

- Participant's weight will be captured
- Research personnel will administer surveys (Socket Comfort Score, CLASS and PEQ-13)

- Non-invasive limb health measurements performed (TEWL and Laser Speckle Imaging (LSI))

Study Visit 6: Study Visit 6 will be the final visit which will occur within a week after Visit 5 with a window of 0-7 days. This visit will take place at Noyes. The following activities will take place:

- Digital shape capture will be performed
- Administer pressure sensors on participant's research foot (Foot B) and recording will be initiated
- Participant's weight will be captured
- 3D motion capture using the motion capture system will be conducted with the use of an electronic device that measures and reports a body's specific force, angular rate, and sometimes the orientation of the body, which are reflective markers placed on subjects to capture movement
    - Level-ground, stair ascent/descent, and ramp ascent/descent trials will be completed with the device under the control settings established during Visit 3 (battery on)
    - Repetition of level-ground, stair ascent/descent, and ramp ascent/descent trials with the device's battery off
    - Timed get up and go test will be performed: subject will stand from seated position and walk 3 meters and then return and sit down

Prosthetist will remove research foot (Foot B) from participant and recording will be terminated. At this point, the subject's participation in the study is complete, and the prosthetist will remove the pressure sensors from the socket, refit the subject's original standard of care prosthetic foot, evaluate alignment, and verify comfort for return to pre-study standard of care.

6.0 Enrollment/Randomization

Upon completion of Study Visit 1/Evaluation, the subject will be randomized to initially receive either the PROPRIO FOOT® or the Empower ankle. At study visit 4, the subject will switch to the alternate device.

7.0 Study Procedures

Socket Comfort Score survey: a subjective measure on an 11-point scale of how comfortable the individual feels in the socket. ("On a 0 to 10 scale, if 0 represents the most uncomfortable socket fit you can imagine, and 10 represents the most comfortable socket fit, how would you score the comfort of the socket fit of your artificial limb at the moment?").

PEQ-13 survey: a 13-question subset of the Prosthesis Evaluation Questionnaire that focuses on the perceived potential for mobility, ambulation, and transfers while using a prosthetic device.

The PEQ-13 uses a 100-point formatted visual analog scale with a scoring range of 0 to 130 in which a higher score indicates high functioning.

CLASS Survey (Comprehensive Lower Limb Amputee Socket Survey): this survey is a self report measure of socket fit that asks the subject to rate stability, comfort, appearance and suspension for their prosthetic socket.

Pressure Sensors (Tekscan F-Socket System): pressure sensors will be placed inside the socket to quantify the amount of force that the participant puts on their residual limb. The sensors will be trimmed to fit the curvature of the socket interface so that reliable measurements can be made in the distal, medial, and proximal regions on the anterior and posterior surfaces of the socket, as well as the fibular head.

Shape Capture: The experimenter will conduct a 3D scan of the residual limb to capture its shape using an optical tracking CAD/CAM system.

K3 Activity Level: Has the ability or potential for ambulation with variable cadence, typical of the community ambulator who has the ability to transverse most environmental barriers and may have vocational, therapeutic, or exercise activity that demands prosthetic utilization beyond simple locomotion.

TEWL: Transepidermal water loss quantifies the functional integrity of the skin. A breach in the physical integrity of the skin (i.e. ulceration) is preceded by breach of functional integrity of the skin, which is indicated by elevated TEWL measurements. This instrument is a non-invasive probe that is placed on the skin that measures water loss coming from the skin. The PI's prior work has shown that, like socket pressure, TEWL is affected by the type of suspension.

Weight: We will obtain weight at all study visits

Laser Speckle Imaging (LSI): A non-invasive device that measures blood flow, referring to the rate of blood flow through the vessels serving the skin.

Timed Up and Go test: The subject will stand from a seated position and walk approximately 3 meters and then return to a seated position. This activity will be timed by research staff.

Motion Capture and Gait Analysis: Reflective markers will be placed on the subject with the goal of recording the movement of the subject during ambulation. Upon completion of the activities, motion analysis will be interpreted and will provide a clear and detailed picture of how a participant moves in space. Gait and Motion Analysis is of particular interest to understand how a participant's gait can affect the amount of pressure that they place on their residual and intact limbs.

8.0 Study Calendar

	Week 0	Study Visit 1: Evaluation (CWC) Week 1	Study Visit 2: Baseline (Goodman Hall) Week 2 (+ 7 days)	Study Visit 3 (CWC) Week 6 (+/- 7 days)	Study Visit 4 (Goodman Hall) Week 7 (+/- 7 days)	Study Visit 5 (CWC) Week 11 (+/- 7 days)	Study Visit 6 (Goodman Hall) Week 12 (+/- 7 days)
Device randomized		X					
Informed consent[1]	X	X					
Enrollment		X					
Socket Comfort Score		X		X		X	
CLASS Survey		X		X		X	
PEQ-13		X		X		X	
Weight recorded		X	X	X	X	X	X
TEWL measurement		X		X		X	
Laser Speckle Imaging (LSI)		X		X		X	
Pre-fitting and adjustments		X		X		X	
Digital shape capture			X		X		X
Administer pressure sensors			X		X		X
Ambulation trials (level-ground, stairs, and ramps)			X		X		X
3D motion capture			X		X		X
Timed Up and Go			X		X		X
Fitting of research device			X		X		
Adverse event review			X	X	X	X	X

Footnote: [1] consent could be at either week 0 or study visit 1, at the convenience of the subject

9.0 Reportable Events

Protocol deviations and Unanticipated Problems involving risks to subjects or others, Adverse Events, and Other Problems will be reported to Indiana University per IU IRB reporting requirements.

Unanticipated problems can occur in any type of research (medical or non-medial) and may include occurrences such as adverse events, subject complaints, protocol deviations, and other untoward events involving risk. Events requiring prompt reporting by investigators and research staff may involve physical, psychological, social, legal, or economic harms.

Event reports and accompanying information will be screened for completeness by research staff members, additional clarifications will be requested from the investigator, as necessary. Research staff members and the principal investigator will make an initial determination about whether the event represents a possible unanticipated problem involving risks to subjects or others and/or potential noncompliance. Reports of events determined during screening to represent possible unanticipated problems involving risks to subjects or others and/or serious/continuing noncompliance will be forwarded to the IRB for convened review. Reports of events that do not meet the requirements for prompt reporting may be reported at time of study renewal.

10.0 Payment to Participants

Participants will be compensated for their time and effort as follows with a study payment card that can be used like a debit or credit card, all payments will generally be available within 24 hours of the study visit.

- Study Visit 1: $50
- Study Visit 2: $50
- Study Visit 3: $100 (Payment of $150 will be compensated if opted for 4 study visits)
- Study Visit 4: $50
- Study Visit 5: $50 (Payment of $150 will be compensated if opted for 4 study visits)
- Study Visit 6: $100

Since the visits are going to be long, lunches will be provided. Lunches will be catered, and no reimbursements or vouchers will need to be administered. The participant will not be charged for their lunch.

11.0 Safety Monitoring Plan

A physician who is a member of the study team and the study coordinator will meet at the following timepoints to review the study data and any adverse events to ensure continued subject safety: prior to initiation of the study, after the 5th subject is enrolled, after the 10th subject is enrolled, and 60 days following the conclusion of study procedures for all subjects.

12.0 Study Withdrawal/Discontinuation

Patients will be informed during the informed consent process (in writing and verbally) that they are free to withdraw from the trial at any time. The investigator may exercise his medical judgement to terminate a patient's participation in the trial due to clinically relevant changes in any clinical or laboratory parameter. The Sponsor-Investigator also reserves the right to discontinue/terminate the trial at any time.

Discontinuation criteria for individual subjects include: (1) Non-compliance with the inclusion/exclusion criteria, (2) treatment non-compliance, such as use of another ankle

prosthesis, (3) withdrawal from the study due to reasons not related to the treatment, (4) prosthetic socket becomes uncomfortable.

13.0 Statistical Considerations

This longitudinal study will compare the effects of the three prostheses on the various measured quantities for each subject. Motion capture data will be filtered with an 8 Hz Butterworth low-pass filter, and ground reaction forces will be filtered with a 50 Hz critically damped filter. These data will be collected and analyzed primarily to interpret how differences in kinematics and kinetics associated with the prostheses contribute to corresponding differences in socket pressure and limb health measures. All pressure measurements will be normalized with respect to body weight as measured during the session of data collection. Mean peak pressure within and pressure-time integrals across each gait cycle will be calculated for each sensor location. The peak pressure provides an indication of the maximum loading at any location, while the pressure-time integral combines both the magnitude and duration of loading since both arerelevant for limb health.

The 3D scans of the residual limb will be compared between Visits 2 and 4 and between Visits 4 and 6 as a means of interpreting whether significant changes in socket pressure are due to corresponding changes in residual limb volume and/or shape. Both TEWL and skin perfusion, i.e., laser speckle imaging, will be measured or quantified into continuous scales from a three-period, baseline, 30 min post-fitting and 4 weeks post-fitting. The values will be normalized using the values collected from the corresponding reference site [62].

Mean peak socket pressure will serve as the primary outcome measure, with particular emphasis on the proximal region of the anterior surface. Pressure-time integrals will serve as the secondary outcome measure, again emphasizing the same region. TEWL values will be used as the primary outcome measure of overall limb health, while skin perfusion will be the secondary outcome measure. For each measure, comparisons among the three prostheses will be made via a repeated measures ANOVA with Bonferroni correction. For both aims, the survey responses will provide a means of evaluating whether subject impressions aligned with quantitative measures of socket pressure and limb health.

14.0 Statistical Data Management

14.1 CLINICAL DATA: Will be recorded in RedCap (research electronic data capture (HIPAA compliant) as clinical research database. Prior to being given access to the data, HIPAA and human subjects certified “study staff” will be trained in the collection of patient-reported outcomes. Study data will be collected using standardized case report forms (CRFs), with clear, uniform instructions for study staff. Researcher’s access to files will be governed by institutional secure data access policies. The RedCap platform is developed and operated by IU clinical research IT team.

14.2 DATA QUALITY AND SECURITY. The study team will review all CRFs. All incoming data will be monitored, with particular attention to: 1) enrollment and follow-up reports as entered into the database; 2) potential adverse events, and 3) missing data or extreme values. The clinical database administrator will generate reports of enrollment progress and data quality control results, to be distributed to the study team bi-monthly and ad hoc as needed, as well as to the safety committee.

15.0 Privacy/Confidentiality Issues

15.1 PRIVACY/CONFIDENTIALITY ISSUES. Records of the participation in this study will be held confidential so far as permitted by law. Any information about participants will be obtained from this study will be kept confidential. The sponsor's delegates, IRB, and the United States Food and Drug Administration (FDA) have access to and may copy the medical records applicable for this study therefore absolute confidentiality cannot be guaranteed.

15.2 CLINICAL TRIALS.GOV. A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. law. This web site will not include information that can identify the participants. At most, the web site will include a summary of the results. The research study coordinator will have access to subject identity. All samples that will undergo analysis will only be identified by a subject code which can only be linked with protected health information (PHI) database by persons who have access to the study database (i.e., research nurses, investigators) via a password. This procedure satisfies HIPAA and is standard for clinical studies run at IU, and as overseen by the IU-CTSA.

16.0 Follow-up and Record Retention

Study results, data, and documentation will be stored for a minimum of 6 years.