Can Sensory Feedback Training Improve the Biomechanical and Metabolic Effects of Using Passive or Powered Lower Limb Prostheses During Walking for Veterans With Transtibial Amputations?

NCT03974945

September 14, 2021

Protocol #: 19-0971
Project Title: Can Sensory Feedback Training Improve the Biomechanical and Metabolic Effects of Using Passive or Powered Lower Limb Prostheses During Walking for Veterans with Transtibial Amputations?
Principal Investigator: Alena Grabowski
Version Date: 9/14/21

I. Hypotheses and Specific Aims:

The purpose of the research study is to determine the effects of real-time visual feedback training of peak propulsive ground reaction force on walking performance while people with transtibial amputations (TTAs) use passive and powered prostheses. Thus, the proposed research is highly relevant to the rehabilitation of Veterans with TTAs. Previous studies suggest that use of passive-elastic and/or powered ankle-foot prostheses do not optimize the function of Veterans with TTAs during walking. Targeted, real-time visual feedback of peak propulsive force has improved walking biomechanics in non-amputees with impaired ankle function. Thus, such feedback presents a promising rehabilitation strategy for Veterans with TTAs. With real-time visual feedback of peak propulsive force, Veterans with TTAs using passive-elastic or powered prostheses could improve functional ability, increase physical activity, and reduce pain and the risk of comorbidities. We aim to determine the underlying metabolic costs, biomechanics, stability, and muscle activity resulting from targeted real-time visual feedback of peak propulsive force to identify how Veterans with TTAs benefit from more effective use of a passive-elastic and/or a battery-powered ankle-foot prosthesis and if the additional mechanical power provided by a battery-powered prosthesis further enhances the function of Veterans with TTAs.

Specific Aim 1. Determine the biomechanics and metabolic costs of level-ground walking for 30 Veterans with unilateral TTAs using their own passive-elastic prosthesis both with and without visual feedback training. Each subject will walk at 1.25 m/s on a dual-belt force-measuring treadmill while they use their own passive-elastic prosthetic foot: 1) with no visual feedback, and then with real-time visual feedback targets of: 2) peak propulsive force from the "no feedback" condition, 3) +20% greater peak propulsive force, and 4) +40% greater peak propulsive force. During these visual feedback trials (2-4), we will ask subjects to match the peak propulsive force displayed on a computer monitor (Fig. 1) with their affected leg (AL). We will also ask subjects to: 5) match symmetric visual feedback of the peak propulsive force from both legs. **Hypothesis 1a:** Because passive-elastic prosthetic feet cannot generate power *de novo*, Veterans with TTAs using such prostheses will adopt compensatory biomechanics in their AL and/or unaffected leg (UL) to match the +20% and +40% greater peak propulsive force conditions with their AL and symmetric peak propulsive forces in both legs when using visual feedback during walking, which will increase asymmetry in other values between legs and worsen dynamic stability. Examples of compensatory biomechanics include greater positive joint work and peak joint power in the AL hip joint and/or UL ankle, knee, and hip joints. **Hypothesis 1b:** Due to the negative relation between peak propulsive force and metabolic cost, the metabolic cost of walking when using a passive-elastic prosthesis will be lowest when subjects use visual feedback of +40% peak propulsive force compared to all other conditions. **Hypothesis 1c:** After a 5-min rest period, subjects using their own passive-elastic prosthetic foot will not retain the biomechanics resulting from the prior visual feedback conditions due to compromised stability.

Specific Aim 2. Determine the biomechanics and metabolic costs of level-ground walking for 30 Veterans with unilateral TTAs using a battery-powered ankle-foot prosthesis both with and without visual feedback training. Each subject will walk at 1.25 m/s on a dual-belt force-measuring treadmill while they use a battery-powered ankle-foot prosthesis (emPOWER, BiONX, Ottobock):

1) with no visual feedback, and then with real-time visual feedback targets of: 2) peak propulsive force from the “no feedback” condition, 3) +20% greater peak propulsive force, and 4) +40% greater peak propulsive force. During these visual feedback trials (2-4), we will ask subjects to match the peak propulsive force displayed on a computer monitor (Fig. 1) with their AL. We will also ask subjects to: 5) match symmetric visual feedback of the peak propulsive force from both legs. **Hypothesis 2a:** Because the emPOWER generates stance-phase prosthetic ankle joint power and net positive work, Veterans with TTAs using the battery-powered prosthesis will be able to match the +20% and +40% greater peak propulsive force conditions with their AL and symmetric peak propulsive forces in both legs without requiring compensatory biomechanics when using visual feedback during walking, which will improve symmetry between legs and dynamic stability. **Hypothesis 2b:** Due to the negative relation between peak propulsive force and metabolic cost, the metabolic cost of walking when using a powered ankle-foot prosthesis will be lowest when subjects use visual feedback of +40% peak propulsive force compared to all other conditions. **H2c:** After a 5-min rest period, subjects will retain the biomechanics resulting from the visual feedback conditions due to improvements in symmetry, metabolic costs, and stability. **Hypothesis 2d:** Veterans with TTAs will have more symmetric biomechanics, lower metabolic costs, and improved dynamic stability when using powered compared to passive-elastic prostheses across all conditions.

II. **Background and Significance**:

Healthcare costs in the United States (US) now exceed $3.2 trillion per year and many of the healthcare conditions associated with these costs, such as diabetes and obesity, are preventable by engaging people in basic physical activity such as walking. Due in part to the increased prevalence of diabetes, as well as previous military conflicts, there are over one million people in the US who have a TTA [1] and this number continues to grow appreciably. In the US, 87-90% of extremity amputations result from vascular disease [1], which is most often associated with diabetes. Nearly one million Veterans (1 in 5 patients) have diabetes, an incidence substantially higher than that of the general population [2]. It is projected that by 2050 the number of Americans with diabetes who are living with limb loss will nearly triple and the prevalence of limb loss will more than double, to 3.7 million people [1, 3]. In addition, over 25% (1 in 4) of US Veterans who have had an amputation due to vascular disease/diabetes will need an additional amputation [4]. Though there is no established cure for Type 2 diabetes, enhancing function through optimized biomechanics and increasing the physical activity of Veterans with TTAs could reduce the risk of this chronic healthcare condition [5]. Morrato et al. [6] determined the prevalence of physical activity among adults with and at risk for diabetes. They found that 58% of adults without a diabetes diagnosis were physically active compared to only 39% of adults with diabetes, and the strongest underlying clinical factors that constrained physical activity included limitations in physical function and severe obesity. People with diabetes walk less than people without diabetes and the perceived effort required to exercise may also be a barrier to participation in physical activity. Using ratings of perceived exertion, Huebschmann et al. [7] found that women with Type 2 diabetes felt that exercise required a higher effort than women without diabetes. Further, Huebschmann et al. [8] found that people with diabetes report that fear of injury is a barrier to physical activity compared to people without diabetes. Thus, decreasing perceived effort and reducing the fear of injury by providing feedback that optimizes the biomechanics and metabolic costs associated with use of a prosthesis by a person with a TTA would likely lead to increased physical activity. Specifically, increases in physical activity could ensue from lower metabolic costs and enhancements in function could result from symmetric walking biomechanics in Veterans with a TTA.

Rates of combat-related orthopaedic injuries in US military personnel, specifically war-related amputations, are at least twice those suffered in previous wars. Recent military conflicts such as Operation Iraqi Freedom, Operation Enduring Freedom, Operation New Dawn, and other unaffiliated conflicts have accounted for more than 1800 major limb amputations [9]. Service members in this cohort and those who have sustained a traumatic amputation are typically young and healthy, and wish to return to a healthy, vigorous lifestyle and full physical function. However, these Veterans typically suffer from severe back pain that impairs their ability to engage in physical activity. Therefore, understanding the biomechanical and metabolic effects of using visual feedback training and the resulting enhancements in function when using a passive-elastic or battery-powered prosthesis could be used to develop rehabilitation strategies that decrease the asymmetric biomechanics that contribute to back pain, and enhance the cardiovascular health of Veterans with TTAs, which would reduce healthcare costs, expedite return to work/duty, and enhance quality of life.

Due in part to the increased prevalence of lower limb amputations in Veterans and Service members, the VA and Department of Defense (DoD) Rehabilitation Directive has put forth an initiative that aims to improve and restore function in wounded Service members so that they have the choice to return to active duty and/or productive civilian employment. Thus, use of visual feedback training that optimizes the utilization of a prosthesis and enables Veterans with TTAs to regain normative function, including vigorous physical activity, without incurring excessive metabolic costs, asymmetrical loading, or discomfort would be extremely valuable. The use of a prosthesis that does not allow optimal or normative function is a critical barrier to facilitating physical activity in Veterans with TTAs. By determining the effects of targeted real-time visual feedback training while using a passive-elastic prosthesis and a battery-powered ankle-foot prosthesis, we aim to eliminate this barrier, enhance function and improve the quality of life of Veterans and Service members with TTAs.

III. Preliminary Studies/Progress Report:

Our previous research examined how use of the BiOM battery-powered ankle-foot prosthesis affects the metabolic cost and biomechanics of people with TTAs (n=13) compared to using their own passive-elastic prosthetic foot to walk on level-ground and a range of uphill and downhill slopes (1.25 m/s at 0°, ±3°, ±6°, and ±9°) and to non-amputees (n=20) [10]. For the studies assessing the use of the BiOM, we "tuned" the battery-powered prosthesis for each slope using motion capture and GRF data. We adjusted the tuning parameters until each subject's prosthetic ankle data matched biological ankle data within two SD. Then, we calculated net metabolic power, individual leg mechanical step-to-step transition work, and individual leg net mechanical work symmetry while subjects used their own passive-elastic prosthesis and the BiOM with the established tuning parameters for each slope. Net metabolic power was 5% lower (better) during walking on uphill slopes of +3° and +6° when subjects used the BiOM compared to their own passive-elastic prosthetic foot ($p<0.05$). Use of the BiOM battery-powered ankle-foot prosthesis did not affect individual leg mechanical step-to-step transition work ($p>0.05$) compared to a passive-elastic prosthetic foot but did improve individual leg net mechanical work symmetry on uphill slopes of +6° and +9° ($p<0.01$). Thus, use of a battery-powered ankle-foot prosthesis reduced metabolic costs and improved biomechanical symmetry during walking on uphill slopes for people with TTAs. It is likely that by using visual feedback of peak propulsive force from the emPOWER, people with TTAs will further improve their biomechanics and metabolic costs during walking.

We also investigated how use of a passive-elastic prosthetic foot and the BiOM battery-powered ankle-foot prosthesis affect leg joint biomechanics during level-ground and sloped walking. We calculated affected leg (AL) and unaffected leg (UL) prosthetic, ankle, knee, hip, and individual leg positive, negative, and net mechanical work. Use of the BiOM compared to a passive-elastic prosthesis resulted in greater AL prosthetic and individual leg net mechanical work on uphill and downhill slopes. Over a stride, AL prosthetic positive work was 23-30% greater ($p<0.05$) on uphill slopes of +6°, and +9°, prosthetic net mechanical work was 1 to 10 times greater (more positive) ($p\leq0.005$) on all uphill and downhill slopes, and individual leg net mechanical work was 146% and 82% more positive ($p<0.05$) on uphill slopes of +6° and +9°, respectively, with the use of the BiOM compared to a passive-elastic prosthetic foot. Greater prosthetic positive and net mechanical work through the use of a battery-powered ankle-foot prosthesis during level ground [11], uphill, and downhill walking would presumably improve functional mobility in people with TTAs. Within our protocol, we iteratively tuned the BiOM to match average biological ankle sagittal plane range of motion, peak moment, peak power, and net mechanical work from twenty non-amputees at each slope [10]. Then, subjects completed three days of metabolic testing, and a final test session where we measured kinematics and kinetics while subjects used the BiOM. Though subjects used the exact tuning parameters, prosthetic components, and alignment established in the tuning/acclimation sessions for all experimental sessions, they modified the way they walked while using the BiOM during the final experimental session compared to the tuning/acclimation sessions. It is possible that after acclimation to walking while using the battery-powered ankle-foot prosthesis, the tuning parameters of the BiOM could be further adjusted and/or the user should be provided with appropriate feedback so that they could more effectively use the battery-powered prosthesis. Based on the measured prosthetic ankle joint mechanics data, subjects were able to match the BiOM prosthetic ankle net mechanical work to within two SD of average biological ankle values during tuning and on the final day of our protocol, though prosthetic ankle net mechanical work was an average of 37% numerically lower on all slopes except -3°. It is unclear why subjects did not utilize the BiOM in the same way on Day 1 vs. the final day. Thus, the proposed research is needed to better understand the interaction of the user and the prosthesis, and the effects of targeted real-time visual feedback on walking biomechanics, metabolic costs, and stability.

Whole body angular momentum (*H*) is indicative of dynamic stability/balance, strongly influences fall risk, is highly regulated, and is primarily controlled by muscle force generation during walking. Previous studies found that people with TTAs using passive-elastic prostheses have greater frontal and sagittal plane *H* ranges during level-ground walking compared with non-amputees [10], which may explain the increased risk of falling in this population [12], particularly during the AL stance phase [13]. Approximately 52% of people with a TTA incur at least one fall per year and 49% report a fear of falling [12]. Thus, we conducted a study that assessed *H* for eight people with and without a TTA while they walked using their own passive-elastic prosthesis and the BiOM powered ankle-foot prosthesis over level ground at 0.75, 1.0, 1.25, 1.5, and 1.75 m/s [14]. We found that use of a passive-elastic prosthesis resulted in 32-59% greater (worse) sagittal plane *H* ranges during the AL stance phase compared to non-amputees at 1.0-1.75 m/s and resulted in 5% and 9% greater sagittal plane *H* ranges compared to use of the BiOM at 1.25 and 1.5 m/s, respectively. Use of a passive-elastic prosthesis resulted in 29% and 17% greater frontal *H* ranges at 0.75 and 1.5 m/s, respectively, compared with non-amputees. Use of the BiOM resulted in 26-50% greater sagittal *H* ranges during the AL stance phase compared with non-amputees at 1.0-1.75 m/s and in 26% greater frontal *H* range compared with non-amputees at 0.75 m/s. These results suggest that use of a powered prosthesis allows better regulation of *H* compared to use of a passive-elastic prosthesis, but the greater ranges of *H* for both prostheses suggest that people with a TTA have a higher fall risk compared to non-amputees. It is likely that providing feedback to the user that allows him/her to better utilize his/her prosthesis could improve balance and stability in Veterans with a TTA.

Though previous research has analyzed the metabolic and biomechanical effects of using passive-elastic prosthetic feet and battery-powered ankle-foot prostheses for walking in people with TTAs, no published studies have comprehensively and systematically analyzed the effects of targeted real-time visual feedback training while people with unilateral TTAs use a passive-elastic prosthetic foot and a battery-powered ankle-foot prosthesis. BionX Medical Technologies has recently developed the emPOWER prosthesis, which has a longer battery run time, weather protection, and new and presumably more effective state-space control compared to the BiOM battery-powered ankle-foot prosthesis. Thus, we will use the emPOWER in our proposed project due to the enhanced control of the prosthesis. By systematically determining the effects of varying targeted peak forces, the results of our proposed research will optimize biomechanics and metabolic costs, which will enhance rehabilitation and prosthetic technology, and subsequently improve the function and of Veterans with TTAs. The results of our research would also provide evidence-based research to prosthetists, which could improve rehabilitation and potentially reduce the need to re-prescribe Veterans with TTAs with multiple prostheses. Improvements in rehabilitation could restore biomechanics, decrease overuse injuries, improve cardiovascular health, and increase participation in physical activity, thus improving function and reducing disability in Veterans with TTAs.

IV. Research Methods

The proposed study will be a repeated-measures within-subjects design. This is a multi-site study, and the VA Eastern Colorado Healthcare System and University of Colorado Boulder will be participating.

A. Outcome Measure(s):

Metabolic Cost. Each metabolic trial will be five minutes long and at least five minutes of rest will be enforced between trials. We will measure rates of oxygen consumption and carbon dioxide production using indirect calorimetry (ParvoMedics TrueOne 2400, Sandy, UT) and will calculate average steady-state metabolic power (W) from minutes 3-5 of each trial using a standard equation [15]. We will subtract the metabolic power required for standing from the metabolic power required for walking to determine net metabolic power (W/kg). A trial length of five minutes is typically more than adequate for participants to reach steady state metabolic rates. To ensure that we measure metabolic rates during steady-state activity, we will verify all data, and if needed, the trial length will be adjusted. We will minimize day-to-day variability by asking subjects to fast and drink nothing but water at least two hours prior to their experimental session, scheduling sessions at the same time of day, and scheduling sessions that are separated by at least 22 hours and no more than two weeks.

Kinematics and Kinetics. We will measure the movements of the body and body/prosthetic segments dynamically. Prior to data collection, we will place reflective markers on the following anatomical landmarks of each leg: anterior superior iliac spines, posterior superior iliac spines, iliac crests, greater trochanters, medial and lateral knee joint centers, medial and lateral ankle joint centers, 1st and 5th metatarsal heads, base of the 5th metatarsals, posterior calcanei, and clusters of at least 3 markers along the thigh and shank segments. For the AL, we will place markers at the same levels and approximately same positions as those on the contralateral UL. Then using a 10-camera 3D motion analysis system (Vicon Motion Systems, Centennial, CO), and 3D force-measuring treadmill (Bertec, Columbus, OH), we will simultaneously measure GRF at 1000 Hz and lower body kinematics at 100 Hz throughout each five-minute trial to facilitate real-time feedback of peak propulsive force. The reflective marker positions will be digitized using motion tracking software (Nexus 2 Vicon Motion Systems, Centennial, CO), and filtered with a 6-Hz Butterworth low-pass filter. Then, we will calculate joint segment velocities and accelerations, and joint angles, angular velocities, and angular accelerations using inverse dynamics within Visual 3D software (C-Motion, Germantown, MD). We will apply a fourth-order zero lag 30 Hz Butterworth low-pass digital filter on kinetic data using a custom software program (Matlab, Mathworks, Natick, MA) and combine these data with the kinematic data to derive joint torques using inverse dynamics techniques. Then, we will calculate the dot product of the joint torque and angular velocity to compute joint power and integrate joint power with respect to time to compute joint work using Matlab. Because a passive-elastic prosthetic foot does not have a functional ankle joint or similar mass distribution compared to a biological foot and ankle, we will use custom segment masses and moments of inertia within the inverse dynamics analyses to determine the prosthesis' contribution to movement during walking. The emPOWER prosthesis has similar mass and moment of inertia compared to a biological foot and partial shank and thus we will use conventional segments for modelling the battery-powered ankle-foot prosthesis.

Unified deformable (UD) segment analysis. We will use a UD segment analysis to determine the mechanical power derived from the prosthesis plus the residual shank due to elastic energy storage and return [16]. We will develop a model of each prosthesis as a UD segment to characterize the limb-to-ground interaction during walking. The UD segment power analysis is a mathematical algorithm that synthesizes force and displacement in a shank-based reference frame to quantify the rate of prosthetic energy stored and returned. This analysis does not require an 'ankle' joint to be defined, and thus is well-suited to quantify passive-elastic prosthetic foot mechanics. The UD analysis will allow precise measurement of how changes to the use of passive-elastic or battery-powered ankle-foot prostheses affect overall prosthetic function; in particular, the magnitude of prosthetic energy storage and return during walking. These analyses will help identify causal relationships between prosthetic mechanics and overall walking performance for Veterans with TTAs [16].

Symmetry Index (SI). We will calculate the absolute value of the symmetry index [17-19], which is expressed as a percentage, to establish the magnitude of asymmetry between the AL and UL for each biomechanical variable (var): $\mathrm{SI} = \left|\frac{\mathrm{var_{UL}} - \mathrm{var_{AL}}}{0.5(\mathrm{var_{UL}} + \mathrm{var_{AL}})}\right| \times 100$. These variables will include 3D joint range of motion, peak moment, peak power, net mechanical work, stiffness, and UD power, as well as peak and stance-average GRFs, individual leg mechanical work, and kinematic timing for each leg.

Dynamic Stability. We will determine 3D angular momentum (*H*) as a measure of dynamic stability [14]. We will calculate *H* for the frontal, transverse, and sagittal planes in the same manner as in D'Andrea et al. [14]. We will use the digitized reflective marker positions and filter these data with a 6-Hz Butterworth low-pass filter using a custom Matlab code. Then, we will use an eight segment model to determine segmental kinematics from marker data and to calculate *H* using custom software (Visual 3D, C-Motion Inc., Germantown, MD, USA). Our model will include the feet (or prosthesis), shanks, thighs, pelvis, and trunk/abdomen. The mass and inertial properties of the body segments will be based on Dempster and Aitkens [20] and/or on the prosthetic properties. Using a custom Matlab code, we will calculate *H* from the model as described by Herr and Popovic [21], where the vector of whole-body angular momentum equals the sum of the orbital and spin components:

$$\vec{H} = \sum_{i=1}^{8} [(\vec{r} - \vec{r}_{com})\ x\ m_i\ (\vec{v} - \vec{v}_{com}) + I^i\ \vec{\omega}^i$$

where *i* is the segment, $\vec{r}$ is the position vector in the global coordinate frame, *com* is the model center of mass; m_i is the segment mass, $\vec{v}$ is the linear velocity vector in the global coordinate frame, I^i is the segment moment of inertia matrix, and $\vec{\omega}^i$ is the angular velocity vector of segment *i*. We will time-normalize *H* to a percentage of a stride beginning with the AL heel strike through the subsequent heel strike with the same leg. Then we will divide *H* by velocity (1.25 m/s), body mass (kg), and height (m) to calculate *H* in dimensionless units. We will calculate the average *H* range, defined as the peak-to-peak value of *H* in each plane of motion for all trials of each subject. We will also calculate sagittal plane *H* ranges for the first and second portions of a stride because there is a clear biphasic pattern in sagittal *H* that corresponds to the contact phases of the AL and UL, respectively [14].

Muscle Activity. We will measure muscle activity patterns and activation magnitudes throughout the walking gait cycle using surface electromyography (sEMG) (Noraxon, Scottsdale, AZ). We will measure sEMG from five major muscles of each leg, the biceps femoris (long head), rectus femoris, vastus lateralis, gluteus maximus, and gluteus medius, and three additional muscles of the UL, the soleus, lateral gastrocnemius, and tibialis anterior. Before the experimental sessions, we will prepare the skin over each muscle by shaving, using a mild abrasive, and applying rubbing alcohol. Then, surface electrodes, with a 2cm inter-electrode distance, will be placed on the skin over the muscle belly according to [22]. During each trial, we will record sEMG at 1000 Hz simultaneously with the kinematic and kinetic data. We will process and analyze the raw sEMG data using a band-pass filter (10-500 Hz) and rectify the signal. Then, we will normalize the processed sEMG signals to the peak signal during walking at 1.25 m/s without visual feedback while subjects use their own passive-elastic prosthetic foot to compare each individual to themselves and to minimize individual differences and variability. We will integrate the processed sEMG during the stance and swing phases using trapezoidal integration with a custom software program (Matlab, Mathworks, Natick, MA). Then we will average data across subjects. The processed and integrated sEMG will allow us to compare muscle activity burst magnitude and duration patterns across conditions.

Description of Population to be Enrolled:

We will enroll up to 40 Veterans with unilateral TTAs who are at or above a K3 Medicare functional classification level (MFCL), and who are 18-67 years old and at least 6-mpnths post-amputation from the VA Jewell Clinic, locally, and nationally. Subjects will give informed consent prior to participation. A K3 MFCL means that a person has the ability or potential for ambulation with variable cadence. A person at K3 MFCL is a typical community ambulator who has the ability to traverse most environmental barriers and may have vocational, therapeutic or exercise activity that demands prosthetic use beyond simple locomotion. Subjects will have no known neurological disease or disorder, and will have no musculoskeletal injuries beyond an amputation. These inclusion/exclusion criteria will minimize any potential confounding variables, thereby increasing the internal validity of the proposed studies. Any person matching the inclusion criteria of the study, regardless of race or gender, will be recruited to participate.

Women and/or minorities will be included in the proposed study. Anyone matching the inclusion criteria of the study, regardless of race, sex, or ethnicity will be recruited to participate.

B. Study Design and Research Methods

Before participants are enrolled in each study, we will complete a pre-screening form and each participant will be asked to give informed written consent. We will ensure that all participants understand the consent form and protocol prior to participation.

Subjects will be asked to complete an acclimation session and three experimental sessions at the VA ECHCS/University of Colorado Applied Biomechanics Lab. The experimental sessions will be on a separate day at the same time of day, and each session will require approximately 2 hours of time. On each day, we will measure subject's height, weight, and limb segment lengths. Then, we will place reflective markers on their legs and torso using double-sided tape. These markers will allow us to track their body position using our motion capture system. We will also record the forces that they exert on the ground using a force-measuring treadmill. Further, on days 2-4 we will measure their leg muscle activity using wireless electrodes that will be placed over their muscles using double-sided tape and their metabolic rates from the air that they breathe out into a mouthpiece. On days 2-4, we will ask subjects to perform a 30-60 sec walking trial at 1.25 m/s using their own prosthesis.

Day 1 – Acclimation Session. We will determine the strength of subject's lower limb muscles using an isokinetic dynamometer (Biodex Medical Systems, Shirley, NY). Then, our prosthetist will align the emPOWER (BiONX, Ottobock, Duderstadt, Germany) battery-powered ankle-foot prosthesis to each subject. We will attach reflective motion capture markers to their legs and pelvis using double-sided tape and Velcro straps, and tune the emPOWER prosthesis by having them walk on a force-measuring treadmill at 1.25 m/s for a series of ~45 sec trials. Then, we will give them additional time to walk using the emPOWER prosthesis.

Days 2, 3 and 4 – Experimental Sessions. We will ask subjects to fast and drink nothing but water for at least 2 hours prior to each experimental session. On each day, we will attach reflective motion capture markers to their legs and pelvis using double-sided tape and Velcro straps, and surface electrodes over their leg muscles using double-sided tape and elastic wraps. We will mark the locations of each electrode with "permanent" marker on their skin. Then, we will ask subjects to walk for 30-60 sec at 1.25 m/s (2.8 mph) using their own prosthesis.

On Days 2, 3, or 4, we will ask subjects to walk at 1.25 m/s on a dual-belt force-measuring treadmill while we measure their metabolic rates, biomechanics, and muscle activity using their own passive-elastic prosthetic foot for:
1) 5 min with no visual feedback
2) 5 min with real-time visual feedback of affected leg (AL) peak propulsive force from the "no feedback" condition, and 5 min with no visual feedback
3) 5 min with real-time visual feedback of +20% greater AL peak propulsive force than the "no feedback" condition, and 5 min with no visual feedback
4) 5 min with real-time visual feedback of +40% greater AL peak propulsive force than the "no feedback" condition, and 5 min with no visual feedback
5) 5 min with real-time visual feedback of AL peak propulsive force and unaffected leg (UL) peak propulsive force, and 5 min with no visual feedback

On Days 2, 3, or 4, we will ask subjects to walk at 1.25 m/s on a dual-belt force-measuring treadmill while we measure their metabolic rates, biomechanics, and muscle activity using the emPOWER battery-powered ankle-foot prosthesis for:
1) 5 min with no visual feedback

2) 5 min with real-time visual feedback of AL peak propulsive force from the "no feedback" condition, and 5 min with no visual feedback
3) 5 min with real-time visual feedback of +20% greater AL peak propulsive force than the "no feedback" condition, and 5 min with no visual feedback
4) 5 min with real-time visual feedback of +40% greater AL peak propulsive force than the "no feedback" condition, and 5 min with no visual feedback
5) 5 min with real-time visual feedback of AL peak propulsive force and UL peak propulsive force, and 5 min with no visual feedback

We will enforce 5 minutes of rest between trials. During the real-time visual feedback trials, we will ask subjects to match the power magnitude displayed on a computer screen placed in front of them with their AL and/or UL for those 5 minutes. Subjects will be asked to perform a maximum of 35 minutes of walking per day and each experimental session will require ~2 hours of time. The total time commitment for this study is approximately 8 hours; 2 hours per day over 4 days.

D. Description, Risks and Justification of Procedures and Data Collection Tools:

We propose to study healthy people who are familiar with using a prosthesis because this choice minimizes any potential confounding factors associated with novel prosthetic use. Walking requires low exercise intensity, yet poses no more than minimal cardiac risk for this population. We will restrict our patient age range to comply with the American College of Sports Medicine guidelines. The American College of Sports Medicine (ACSM) Guidelines for Exercise Testing and Prescription (Ninth edition, 2014) classify individuals of any age as having low or moderate risk to participate in an exercise program if they present no more than two of the following risk factors: males age ≥ 45 yrs, females age ≥ 55 yrs, first degree family history of coronary artery disease, cigarette smoking, sedentary lifestyle, obesity, hypertension, dyslipidemia (high cholesterol), and pre-diabetes. These guidelines further recommend that a medical exam and diagnostic exercise testing are not warranted prior to beginning a moderate exercise program for individuals at low to moderate risk. We are being conservative by including patients under 67 years of age (i.e. before their 67th birthday) who do not have any of the other risk factors listed above.

We will comply with Good Clinical Practices (GCPs) by upholding standards for the design, conduct, performance, monitoring, auditing, recording, analysis and reporting of our clinical studies, and by protecting the rights, safety, and well-being of human subjects. We will assure the quality, reliability, and integrity of data collected. We will maintain and monitor GCPs by obtaining Institutional Review Board (IRB)-approval, requiring informed consent, having a data-monitoring plan, reporting Adverse or Serious Adverse Events, having proper documentation, and validating our data collection and reporting procedures.

<u>Foreseeable risks:</u>

1. There is a small risk of falling during the experimental trials.
2. There is a potential risk of physical discomfort from wearing any type of prosthesis.
3. The adhesive used for motion capture and muscle activity measurements may produce slight discomfort or irritation.
4. The metabolic analysis mouthpiece may produce slight discomfort or irritation.
5. Confidential information will be collected as part of this study; therefore, there is a risk of disclosure.

<u>Risk management (corresponds directly to the Foreseeable risks listed above):</u>

1. Subjects will have access to parallel bars on the treadmill and an overhead safety harness in case they need to catch them self in the unlikely event of a fall.
2. If subjects become fatigued, they may ask to rest or stop the study at any time.
3. Before participating, subjects will be asked if they have any adhesive allergies and if they do, we will use tight-fitting clothing to attach the motion capture markers and hypoallergenic tape to attach surface electrodes.
4. Subjects may ask to remove the mouthpiece, rest or stop at any time.

5. Significant efforts will be made to guard against the disclosure of confidential information. All data collected will be de-identified so that each subject's identity is protected; however, the data collected poses no apparent risk to their privacy. We will implement a data and safety-monitoring plan to ensure their privacy. To de-identify subject's data, they will be given a unique code, and only the research team will have access to the key (linking the code to participant identifiers), which will be kept in a locked cabinet in a locked office. The key will be destroyed upon study completion.

E. Potential Scientific Problems:

We have a few potential limitations that could affect the proposed project. Previous studies have found that peak propulsive force is 23-36% lower in the AL when people with a TTA use a passive-elastic prosthesis and is 15-28% lower in the AL when people with a TTA use a powered ankle-foot prosthesis compared to non-amputees [14]. Though it's unlikely, it is conceivable that a subject could elicit more symmetric peak propulsive GRFs. If we find that a subject has a symmetry index for peak propulsive force that is less than 5% during the initial "no feedback" walking trial, we will provide visual feedback of peak propulsive GRFs from both legs at +20% and +40% compared to "no feedback" and will compare the results from these subjects with the overall results from all subjects. It is possible that we will not find significant differences in biomechanics, metabolic costs, or muscle activity with use of targeted visual feedback training of peak propulsive force. However, peak propulsive force has a strong influence on step-to-step transition work and the metabolic cost of walking; therefore, we believe that there will be a significant beneficial effect of real-time visual feedback training. It is also possible that there would be no significant differences between use of passive-elastic versus battery-powered ankle-foot prostheses, but this seems highly unlikely based on previous studies that have compared the use of passive-elastic prosthetic feet to battery-powered ankle-foot prostheses and found significant differences in metabolic cost of transport, step-to-step transition work, and preferred walking speed [11, 14, 23, 24]. Further, though there may be small differences between walking on a treadmill and over-ground walking, we chose to have participants perform experimental trials on a treadmill, which will allow us to control speed while we measure multiple consecutive strides and steady-state metabolic rates, while providing targeted real-time visual feedback. We will then use the results from a treadmill and computer monitor to inform future prosthetic designs that could use a different type of feedback, such as vibration or sound, to provide feedback in a real-world setting. No procedures, situations, or materials are considered to be hazardous to personnel. In addition to improving prosthetic rehabilitation and function, our results could inform the design and control of lower limb prostheses.

F. Data Analysis Plan:

Table 1. Statistical Power for variables reported by previous studies from 0.75-1.75 m/s.

Variable	Statistical Power
SI 1st peak vertical GRF	0.689-1.0 [14]
SI 2nd peak vertical GRF	0.249-1.0 [14]
SI Peak horizontal braking GRF	0.996-1.0 [14]
SI Peak horizontal propulsive GRF	0.717-1.0 [14]
SI Sagittal Plane *H* range	0.115-0.95 [14]
UL Leading/AL Trailing Leg Mechanical Work	1.0 [11]
Metabolic Cost (0.75-1.75 m/s)	0.655-1.0 [11]

We developed our research protocol to ensure an adequate sample size for statistical analyses. We used previous data to calculate statistical power for biomechanical and metabolic variables using G*Power statistical software [25]. We set $\alpha = 0.05$, had a sample size of 30, and used a paired t-test design. We used data from D'Andrea et al. [14] who compared peak vertical GRFs, peak horizontal GRFs, and sagittal plane *H* range during walking at 0.75-1.75 m/s for eight participants with unilateral TTAs using a passive-elastic prosthesis compared to a powered ankle-foot prosthesis. We calculated symmetry indices (SI) for these biomechanical variables and found strong statistical power (>0.689) for detecting differences in the first peak vertical GRF and strong statistical power (>0.717) for detecting differences in the peak horizontal braking and propulsive GRF in subjects using their own passive-elastic prosthesis compared to the BiOM battery-powered ankle-foot prosthesis (Table 1). The second peak vertical GRF and sagittal plane *H* had strong statistical power (1.0) at 1.75 m/s, but moderate to low power at the other walking speeds. Further we used data from Herr & Grabowski [11] to determine the statistical power for UL leading leg and AL trailing leg mechanical work and metabolic cost between subjects using their own passive-elastic prosthesis compared to the BiOM battery-powered ankle-foot prosthesis across five walking speeds (0.75-1.75 m/s). We found strong statistical power (1.0) to detect differences in mechanical work and metabolic cost at 1.0-1.75 m/s (Table 1).

G. Summarize Knowledge to be Gained:

With the knowledge gained from the proposed research, people with transtibial amputations could eventually improve their function and ambulatory ability. The data from the proposed research will be used to improve rehabilitation outcomes through more effective training and prosthetic design. The risks to subjects are minimal, reasonable, and no more than typical risks experienced during activities of daily living, such as walking on a sidewalk, going to the gym, etc.

H. References:

1. Adams, P., G. Hendershot, and M. Marano, *Current estimates from the National Health Interview Survey.* Vital Health Stat 1999, 1996. **10**: p. 1-203.
2. US Department of Veterans Affairs, *Fact Sheet. VA Achievements in Diabetes Care, February, 2006*, 2006, http://www1.va.gov/opa/fact/diabtsfs.asp.
3. Ziegler-Graham, K., et al., *Estimating the prevalence of limb loss in the United States: 2005 to 2050.* Archives of Physical Medicine and Rehabilitation, 2008. **89**(3): p. 422-429.
4. Sambamoorthi, U., et al., *Initial nontraumatic lower-extremity amputations among veterans with diabetes.* Medical Care, 2006. **44**(8): p. 779-787.
5. Ghosh, S., et al., *Selecting exercise regimens and strains to modify obesity and diabetes in rodents: an overview.* Clinical Science, 2010. **119**(1-2): p. 57-74.
6. Morrato, E.H., et al., *Physical activity in US adults with diabetes and at risk for developing diabetes, 2003.* Diabetes Care, 2007. **30**(2): p. 203-209.
7. Huebschmann, A.G., et al., *Women with type 2 diabetes perceive harder effort during exercise than nondiabetic women.* Applied Physiology Nutrition and Metabolism-Physiologie Appliquee Nutrition Et Metabolisme, 2009. **34**(5): p. 851-857.
8. Huebschmann, A.G., et al., *Fear of Injury With Physical Activity Is Greater in Adults With Diabetes Than in Adults Without Diabetes.* Diabetes Care, 2011. **34**(8): p. 1717-1722.
9. Fischer, H., *U.S. Military Casualty Statistics: Operation New Dawn, Operation Iraqi Freedom, and Operation Enduring Freedom*, 2010, http://www.fas.org/sgp/crs/natsec/RS22452.pdf Congressional Research Service.
10. Jeffers, J.R., A.G. Auyang, and A.M. Grabowski, *The correlation between metabolic and individual leg mechanical power during walking at different slopes and velocities.* Journal of Biomechanics, 2015(0).
11. Herr, H.M. and A.M. Grabowski, *Bionic ankle-foot prosthesis normalizes walking gait for persons with leg amputation.* Proceedings of the Royal Society B-Biological Sciences, 2012. **279**(1728): p. 457-464.
12. Miller, W.C., M. Speechley, and B. Deathe, *The prevalence and risk factors of falling and fear of falling among lower extremity amputees.* Archives of Physical Medicine and Rehabilitation, 2001. **82**(8): p. 1031-1037.
13. Kulkarni, J., et al., *Falls in patients with lower limb amputations: prevalence and contributing factors.* Physiotherapy, 1996. **82**: p. 130-6.
14. D'Andrea, S., et al., *Does Use of a Powered Ankle-foot Prosthesis Restore Whole-body Angular Momentum During Walking at Different Speeds?* Clinical Orthopaedics and Related Research, 2014. **472**(10): p. 3044-3054.
15. Brockway, J.M., *Derivation of formulae used to calculate energy expenditure in man.* Human Nutrition - Clinical Nutrition, 1987. **41**(6): p. 463-71.
16. Takahashi, K.Z., T.M. Kepple, and S.J. Stanhope, *A unified deformable (UD) segment model for quantifying total power of anatomical and prosthetic below-knee structures during stance in gait.* J Biomech, 2012. **45**(15): p. 2662-2667.
17. Herzog, W., et al., *Asymmetries in Ground Reaction Force Patterns in Normal Human Gait.* Medicine and Science in Sports and Exercise, 1989. **21**(1): p. 110-114.

18. Robinson, R.O., W. Herzog, and B.M. Nigg, *Use of Force Platform Variables to Quantify the Effects of Chiropractic Manipulation on Gait Symmetry.* Journal of Manipulative and Physiological Therapeutics, 1987. **10**(4): p. 172-176.
19. Wilson, J.R., et al., *A new methodology to measure the running biomechanics of amputees.* Prosthetics and Orthotics International, 2009. **33**(3): p. 218-229.
20. Dempster, P. and S. Aitkens, *A New Air Displacement Method for the Determination of Human-Body Composition.* Medicine and Science in Sports and Exercise, 1995. **27**(12): p. 1692-1697.
21. Herr, H. and M. Popovic, *Angular momentum in human walking.* Journal of Experimental Biology, 2008. **211**(4): p. 467-481.
22. Rainoldi, A., G. Melchiorri, and I. Caruso, *A method for positioning electrodes during surface EMG recordings in lower limb muscles.* Journal of Neuroscience Methods, 2004. **134**(1): p. 37-43.
23. Grabowski, A.M. and 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, 2013. **10**.
24. Pickle, N.T., et al., *The Functional Roles of Muscles, Passive Prostheses, and Powered Prostheses During Sloped Walking in People With a Transtibial Amputation.* Journal of Biomechanical Engineering-Transactions of the Asme, 2017. **139**(11).
25. Faul, F., et al., *G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences.* Behavior Research Methods, 2007. **39**(2): p. 175-191.