Principal Investigator

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NAU NORTHERN ARIZONA UNIVERSITY

Office of Research Compliance

Project Narrative for Prospective Research

Project Title:	Ankle assistance and resistance in older adults
Investigator:	Zachary Lerner, PhD

Project Abstract

Background

Preventing walking disability in our aging population is an enormous public health challenge. Mobility impairment is pervasive among older adults; 17, 28, and 47% of people in the United States aged 65–74, 75–84, and 85þ years, respectively, reported that difficulty in walking interferes with their daily activities (Greenberg and Fowles, 2011). Fundamental to their loss of independent mobility is that older adults walk more slowly, with shorter steps, and have higher metabolic energy costs than young adults—factors that have a severe negative impact on quality of life (Daly et al., 2013). These walking impairments are governed in large part by reduced force-generating capacity and functional output from muscle-tendon units spanning the ankle, resulting in reduced ankle power output via the plantar flexor (i.e., calf) muscles the during the propulsive "push-off " phase of walking (Franz, 2016; Boyer et al., 2017).

Age-associated deficits in ankle push-off during walking are highly resistant to conventional intervention; interventions designed solely to strengthen the plantar flexor muscles have generally failed to improve push-off power or walking economy. Isolated strengthening interventions seem to be unable to facilitate transfer between improved muscle force-generating capacity and more enhanced ankle push-off, and therefore do not change global measures of gait performance (Berg and Lapp, 1998; Beijersbergen et al., 2013, 2017). We suspect that these disappointing translational outcomes from isolated muscle strengthening arise from poor task-specificity in the context of walking. There appears to be a neuromuscular disconnect between newfound strength gains and functional utilization of muscle during walking, which motivates the need for new, yet accessible interventions capable of training improved plantar flexor utilization during walking in the elderly.

Purpose:

The overarching goal of this study is to improve mobility in older adults through advances in wearable assistance (i.e. powered orthoses). This goal will be accomplished by focusing on two specific research aims.

Aim 1: To study if targeted ankle resistance gait training improves walking performance in older individuals.

Aim 2: To evaluate the potential of wearable assistance at the ankle, knee, and/or hip joints to increase walking performance in older individuals.

Lay Summary:

Many older individuals have impaired walking ability that limit quality of life and lead to long-term health consequences. Reduced physical activity from age-related decline in gait dysfunction can lead to a downward spiral that results in a deterioration of walking ability with age, ultimately leading to a loss of ambulation in a large portion of the affected population.

The goal of this research protocol is to improve mobility in older individuals through advances in wearable assistive devices by focusing on two specific aims. The first aim is to study if targeted ankle resistance gait training improves walking performance in older individuals. The second aim is to evaluate the potential of wearable assistance at the ankle, knee, and/or hip joints to increase walking performance in older individuals.

Resources:
This study will take place in the Biomechatronics Lab let by PI Assoc. Prof. Zach Lerner. Post-docs, graduate student researchers and undergraduate student researchers will be assisting with data collection and processing.

Population & Recruitment

- Maximum number of participants to be enrolled in the study: 30

- Please check all the categories of participants that will be included in the research:

☐Children (1-17 yrs old)- **Complete Appendix A**	☒Adults
☐Prisoners- **Complete Appendix C**	☐Refugees
☐Native Americans - **See the** Tribal Consultation Policy	☐NAU Staff/Faculty
☐Pregnant Woman/ Neonates – **Complete Appendix B**	☐NAU Students
☐Cognitively Impaired Subjects	☐Other- Explain Below

- What are the inclusion and exclusion criteria for study participation?

Subject population will include:

- 30 older individuals with age-related walking deficits. We will recruit 33 individuals anticipating a 10% withdrawal rate to obtain the target sample size.

Inclusion criteria:

- Age between 65 and 85 years old, inclusive.
- Must be able to understand and follow simple directions based on parent report and clinical observation during the history and physical examination.
- Able to provide verbal assent, if appropriate. If the participant is non-verbal, parental interpretation of gesticulation for assent will be used.
- The ability to read and understand English.
- Able to walk at least 30 feet with or without a walking aid
- Able to safely fit into a device configuration and tolerate assistance without knee

hyperextension while walking

Exclusion criteria:

- Any neurological, musculoskeletal or cardiorespiratory injury, health condition (including pregnancy), or diagnosis that would affect the ability to walk as directed for short periods of time. Note: For elderly participants, a history of joint replacement or joint degeneration that does not impair their ability to walk safely is allowable.
- Participant or parent report that the perspective participant's physician has recommended that they not engage in moderate intensity walking exercise.

Note: No exclusions will be made on the basis of race, gender or ethnic background and efforts will be made to recruit underrepresented minorities.

- Indicate age range, gender and ethnicity of your research population:
  There will be no restriction on sex, gender, ethnicity, or race.
  Age between 65-85 years old.

- Will there be any individuals working on the research project (consenting, collecting data, analyzing identifiable data) who are not affiliated with NAU? ☒No ☐ Yes- Please complete **Appendix E: Multi-site Research** for each unique site if the site will not obtain their own IRB approval.

- Will any documents be translated into another language? ☒ No ☐ Yes- Please explain below
  Explain: Click or tap here to enter text.

- Please select the methods that will be used to recruit individuals. **Provide copies of documents, as applicable.**

☐ Email	☐ Social Media
☒ Flyers	☐ Online Advertisements
☐ TV, Radio, Print	☐ Phone Calls
☐ In Person Presentations	☐ Screening of the Electronic Medical Record (EMR)
☒ Face to Face	☐ SONA
	☐ Other- Please explain below

Explain: We will use an email, phone, and face to face script for participant recruiting

- When will recruitment occur? Please provide time frame with dates if applicable: 1/1/2024-1/1/2027

- Please explain the recruitment process (who is recruiting, how and where will recruitment take place?): The PI, staff, and students assigned to the project will recruit by placing flyers in the community.

- Will 1,000 or more NAU members (prospective, current, or former students, or faculty, staff, or alumni) be solicited/recruited (e.g., NAU Listservs, etc.) to be surveyed?
  ☒ No ☐ Yes **See the** Conducting University Surveys Policy.

Informed Consent

1. Please indicate the informed consent process(es) and/or document(s) to be used in the study. Check all that apply. **Provide copies of documents, as applicable.**

☒ Informed Consent (ICF)– written form	☐ Informed Consent – oral script/online/unsigned*
☐ Assent (participants under 18) – written form	☐ Assent – oral script/online/unsigned**
☐ Parental Permission – written form	☐ Parental Permission – oral script/online/unsigned**
☐ Translated Consent/Assent – written form(s)	☐ Translated Consent/ Assent- oral script/online/unsigned
☐ Combined ICF/PHI Authorization- form	☐ Waivers of consent or waiver or alteration of PHI*
☐ Broad Consent for future research	☐ Short Consent Form- written from
☐ Debriefing Script	☐ Protected Health Information (PHI) Authorization- written form
	☐ Other – please explain below

* Complete and submit **Appendix D: Alteration/Waiver of Consent, or Alteration/Waiver of PHI.**
** Complete and submit **Appendix A: Children**.

2. **Describe in detail the consent processes checked above:**
   Study team members will contact potential participants to determine interest. If a potential participant is interested, study team members will follow-up to answer questions, describe the study, go through the consent form, determine eligibility, and schedule research visits as appropriate. Email and text communication will be utilized when possible.

Data Collection Procedures

1. Please select the methods of data collection that will be employed in this study (select all that apply):

☒ Audio/Video recording	☐ Use of radiation (e.g., DXA, x-ray)
☒ Benign Interventions	☒ Anthropometric measures (e.g., height, weight, waist circumference, etc.)
☐ Biological Specimens- Blood Draws	☐ Biological Specimens (urine/feces, tissue, saliva, skin, hair, nails, nasal swab)
☐ Deception	☐ Biological Specimens- Clinical discarded of blood or specimens

☐ Interviews- Focus groups	☐ Cognitive or behavioral measures, including daily diaries (Note- if surveys will also be administered, please select the appropriate option)
☐ Interviews- In person	☐ Data previously collected for research purposes
☐ Interviews- Online	☐ Data collected using other communication/electronic devices (e.g., cell phones, pagers and texting devices)
☐ Interviews - Telephone	☐ Non- invasive instruments(e.g. external sensors applied to the body)
☐ Participant Observation	☐ Self-health monitoring (e.g., pedometers, food diaries, etc.)
☐ Surveys- Paper	☐ Surveys- Internet (including online and email based data collection)
☐ Surveys- Telephone	☐ Randomization with Control and Experimental Groups
☐ Records- Educational	☐ Records- Lab, pathology and/or radiology results
☐ Records- Employee	☐ Records- Mental Health
☐ Records- Medical Review	☐ Records- Substance Abuse
☐ Records- Physician/Clinical	☐ Use of Social Networking Sites
☐ Use of recombinant DNA	☐ Other activities or interventions- Describe below

2. Please provide details of the research procedures and include the study population who will be completing them:

COVID-19 Mitigation Statement

In an effort to mitigate exposure to COVID-19, the study team will follow all CDC and NAU required COVID precautions, such as screening all individuals before they enter the facility, minimizing the number of individuals present at visit, enforce social distancing and universal masking/face covering and cleaning and sanitizing heavily used areas.

Non-significant risk device information. Wearable assistance will be provided from powered and unpowered orthoses (e.g. Fig. 1). The devices provide a small amount of motorized assistance that is intended to augment existing muscle activity to elicit function changes at the ankle, knee, and hip joints. This and other similar investigational devices have been classified by the Food and Drug Administration as a *nonsignificant risk device* because they do not meet the definition of significant risk under 812.3(m) of the investigational device exemption (IDE) regulation (21 CFR 812 and outlined in HRP-418 Checklist: Non-Significant Risk Device). In other words, the devices:

- are not an implant;
- are not supporting or sustaining life;
- are not used for diagnosing/curing/mitigating/treating disease; and
- do not present the potential for serious risk to health or safety.

Following 21 CFR 812.2 (as outlined in HRP-307 Worksheet: Medical Devices), our devices fit within the *abbreviated IDE requirements* as:

- our activities are testing the safety and efficacy of the research devices;
- they are nonsignificant risk devices;
- they are not banned from use by the FDA; and
- informed consent and documentation of informed consent will be obtained from all participants.

Further, following the requirements for an abbreviated IDE, the investigator will follow regulations and reporting requirements as appropriate (21 CFR 812.150).

Figure 1. Picture of the powered orthoses used in our research.

Experimental conditions: Several powered orthosis conditions will be tested during several modes of walking or running and balance throughout the course of the study. Trials will take place over-ground and/or on a treadmill. Balance trials will take place on a treadmill. Participants will walk for up to 40 minutes. Frequent breaks will be provided between trials and conditions to avoid fatigue; a maximum of 15 minutes of continuous walking will take place between breaks.

1) Level walking over ground
2) Level walking on a treadmill
3) Walking at a mild incline/decline (0°-15°) on the treadmill
4) "Walking" on a stepmill machine
5) Walking on stairs
6) Balance on a treadmill
7) All terrain walking over ground
8) Mobility analysis
9) At-home walking and/or running, and usability testing

<u>Orthosis Conditions:</u>

1) *Walking or running without assistance/resistance*: We will obtain the normal/representative walking pattern of each participant. This condition will be used to compare the effectiveness of the assistive conditions.
2) *Walking with basic powered orthosis assistance/resistance*: We will provide on/off assistance/resistance during walking, depending on the individual's specific gait deficits.
3) *Walking with adaptable powered orthosis assistance/resistance*: We will provide assistance/*resistance* that changes magnitude based on measures of gait performance.

4) *Walking with powered assistance/resistance and biofeedback*: We will combine assistance with real-time feedback of walking performance. Individually tuned performance measures will be identified for each participant, and used to identify walking goals. Participants will be instructed to try to meet and maintain their goals.
5) *Walking with passive (unpowered) orthosis assistance*: We will evaluate the ankle neutral angle and AFO stiffness that more beneficial for each participant.

In Laboratory Mobility analysis:

To assess mobility, participants will undergo the following tests, with or without a powered orthosis, under direct supervision by a research team member, who will be available to spot for safety (heart rate and metabolic cost may be collected):

1) Timed up and go: participants will walk as quickly as possible in a safe and controller manner to a cone 3 meters away, turn around, walk back to the chair and sit down; 3 – 6 trials will be collected.
2) 6 minute walk test: participants will walk as quickly as possible in a safe and controlled manner for 6 minutes to test walking endurance; 1 – 3 trials will be collected.

All terrain walking over ground:

Participants will be monitored and accompanied at all times by the trained safety advocate and study staff during indoor or outdoor all terrain walking or running trials that may take place on or off campus. Trials will include ambulation with and without wearable assistance. On-campus locations will include the Engineering, Business, and Learning resource Center buildings, the north and south quads, and campus walkways and urban trails. Off-campus locations will include Buffalo Park and surrounding Elden trails.

Data Collection: Experimental data collection will include motion capture (movement and force gait analysis), measurement of muscle activity (electromyography, EMG), measurement of reflexes (H-Reflex), measurement of muscle architecture (Ultrasound), measurement of oxygen consumption/c02 production (metabolic rate), and brain activity (electroencephalography, EEG).

Physical activity questionnaire: We will ask questions to understand the physical activity levels of older adults.

Description of laboratory visits for ankle resistance training:

Pre-visit phone call: Optional phone call prior to first in-person visit (but after consent) to collect relevant medical history and physical activity questionnaire.

Visit 1: Participants will undergo consent (if not done over the phone), history/physical/activity questionnaire, and orthotic device fitting. Following device fitting, the participants will undergo a pre-assessment baseline gait and mobility analysis, and then practice walking with powered resistance. The expected duration is 3-4 hours.

Visits 2 through 13: On each visit, participants will complete 20-30 minutes of ankle resistance training. This will involve walking on a treadmill with stance phase ankle resistance and biofeedback.

Final visit: On the post-assessment visit participants will complete a follow-up gait and mobility analysis. The expected duration is 2 – 3 hours.

Timeline: The participants will be asked to complete 1-4 visits per week for 3-12 weeks. To accommodate illness, travel, and scheduling conflicts, the maximum time that a participant can be enrolled in the study is 16 weeks.

Description of laboratory visits for walking with assistance:

Pre-visit phone call: Optional phone call prior to first in-person visit (but after consent) to collect relevant medical history.

Visit 1: Participants will undergo consent (if not done over the phone), history/physical/activity questionnaire, and orthotic device fitting. Following device fitting, the participants will undergo a pre-assessment baseline gait and mobility analysis with and/or without assistance. The expected duration is 3-4 hours.

Visits 2 through a maximum of 17: On each visit, participants will complete 20-40 minutes of walking with powered or passive assistance at the ankle, knee, or hip joints.

Final visit: On the post-assessment visit participants will complete a follow-up gait and mobility analysis with and/or without assistance. The expected duration is 2 – 3 hours.

Timeline: The participants will be asked to complete 1-4 visits per week for 3-12 weeks. To accommodate illness, travel, and scheduling conflicts, the maximum time that a participant can be enrolled in the study is 16 weeks.

Recruitment: We will recruit people from our network of individuals/families of a child with CP and from PT clinics and hospitals across the state of Arizona.

Management of Project Personnel: Dr. Lerner will be responsible for managing project research personnel (graduate students, staff, etc.), including their CITI Training.

3. Please state the estimated time commitment for subject participation: The estimated time commitment to complete the assigned study tasks is 1-18 sessions, each lasting up to 1-4 hours.

4. Does this project involve investigating a Drug, Device or Biologic? ☐ No ☒ Yes- Complete **Appendix F: Drugs and Devices**

5. Is this project a Clinical Trial? ☐ **No** ☒ **Yes** **See** **clinical trial guidance**

*A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Compensation & Costs

(See Compensation of Subjects Guidance)

1. Provide the amount of compensation (monetary and/or non-monetary) subjects may receive:

   Subjects will receive monetary compensation for their participation in the study.

   All participants with gait deficits will be compensated $30 per hour for lab visits; payment will be made to the parents/legal guardians of minor participants. The minimum compensation for each visit is $30, should the participant or investigator choose to stop the study within the first hour, and the maximum is $120. For those with gait deficits who complete all visits, the maximum possible compensation would be $2160 if they complete all data collection and the visit durations all last 4 hours.

2. Describe the process for distribution to subjects, including how the compensation will be prorated, as applicable: Click or tap here to enter text.

   Participants will receive a check in the mail at the completion of the study or when requested.

3. Indicate the source of compensation: NSF and NAU Foundation

☐ Personal funds	☒ Funds outlined in the NAU Research Application

4. Describe any costs, monetary and non-monetary, that subjects may incur:

   Extraneous travel expenses to the lab.

5. Describe the provisions for medical care and available compensation in the event of research related injury, as applicable. If the Human Research has a clinical trial agreement, this language should reflect what is stated in the agreement: None proposed, the activities pose no greater than minimal risk.

Benefits & Risks

1. Describe the anticipated benefits of this study to society, academic knowledge or both: Click or tap here to enter text.
   Achieving and maintaining independent mobility for the estimated 17 million individuals with walking disabilities in the US is an essential rehabilitation challenge. The proposed studies have the potential

to improve gait rehabilitation outcomes and meet the increasing demand for therapy from our aging population.

2. Describe any benefits that individuals may reasonably expect from participation: Click or tap here to enter text.

   Walking can be challenging for the target population. Properly implemented wearable assistance has a strong potential to improve their ambulatory ability and balance. These studies will determine if wearable assistance is a viable treatment strategy for each of our participants, which can be used to guide future treatment and therapy.

3. Please describe all physical, psychological, social, legal, and/or economic risks you feel are associated with participation in this research. NOTE: Risks not directly related to the research need not be included in this section: Click or tap here to enter text.

   There may be a small risk of physical discomfort due to the device or injury due to falling during walking or running. There may be a risk of skin irritation due to muscle activity and motion capture marker adhesive. There is minimal risk associated with heart-rate monitoring or open-circuit respirometer recording; a facemask covering the nose and mouth that is connected to a respirometer will capture breath inhalation/exhalation.

4. Discuss what steps have been taken to minimize risk to subjects/data: Click or tap here to enter text.

   We will use an overhead safety tether while participants walk on the treadmill if they appear unstable. Safety measures are integrated within the control algorithms of the powered devices such that it automatically deactivates during gait disturbances.

Privacy and Confidentiality

Follow NAU's data security policy. Please make sure to look at the *Data Security* guidance.

1. What records will the research team be accessing during the research?

☐ Educational ☐ Medical ☐ Employee ☐ Substance Abuse ☒ NA

2. What platform is being used to store the data?

☐ Password Protected Drive	☐ Encrypted Drive
☐ External Drive (USB, Flash Drive)	☐ Departmental Drive
☒ Cloud Server	☒ Departmental Office
	☐ Other- Please explain below

Explain: Click or tap here to enter text.

3. For each of the platforms checked above (both hard copy and electronic information), discuss the type of data to be stored in each platform (including if the data is identifiable), who may have access to the platform, and how long the information will be stored: Click or tap here to enter text.

   De-identifiable experimental data and an excel file with participant demographic information may be stored on our lab's Google Drive account; this information will be stored indefinitely. Everyone in the Biomechatronics Lab will have access to these data. Identifiable information (e.g., consent form) will be stored in hard copy form in the PI's locked drawer in his locked office; this info will be stored for 5 years after study completion.

4. Discuss how, when and why subjects/data may be removed from the study. If abrupt withdrawal is necessary, discuss how subjects will be withdrawn so that they are not put at increased risk. Discuss what happens if a subject is withdrawn from one part of the study but asked to continue with other parts, such as ongoing follow-up: Click or tap here to enter text.

   Withdrawal Circumstances:

   Participants will be withdrawn if they are later identified as not meeting the inclusion criteria (e.g., identified as eligible in error), if they miss more than 2-3 research visits in a given experiment, or if they decide to stop participating in the study.

   Withdrawal Procedures:

   If a participant consents to the study but elects to stop participating after data collection has started, any data that was collected will be retained unless the participant asks otherwise.

   Participants must alert the study team in writing of their request to be withdrawn from the study.

   Termination Procedures:

   Data collected and completed up to the point of withdrawal or termination will still be included in the study unless the participant asks otherwise.

5. Describe steps, if any, to protect the privacy of the subjects throughout their participation in the Human Research (e.g. during the recruitment process, consent process, and/or research procedures): Click or tap here to enter text.

   Study team members are trained on appropriate data use and storage, and every reasonable effort is made to minimize risk associated with loss of privacy and confidentiality.

6. Will you be transmitting/receiving any subject data to/from an outside group?
   ☒ No ☐ Yes- Please complete below:

a. Describe the data to be transmitted/received, name of outside party institution and how the data will be transmitted/received (e.g., secure file transfer, encrypted email). Click or tap here to enter text.

7. Describe when and how will the data be destroyed: See the Data Security guidance.
Click or tap here to enter text.
When the study is complete, hard copy documents will be stored following standard regulatory practices on and offsite. When that period has expired, hard copy forms will be destroyed following standard institutional practices.

Use of Data/ Specimens

1. Please check which of the following formats the data will be kept in:
☒ Identifiable- Complete 1a below ☒ Coded ☒ De-identified- Complete 1b below

a. Please list the identifiers that will be kept: Click or tap here to enter text.

A study ID will be assigned to participants as they are enrolled. This will be linked to the identified data. Identifiers will remain on the data until all data analyses are complete and the study is closed with the IRB, at which time the key will be destroyed following institutional practices. After the study is complete, research records will be stored long-term following institutional practices, and de-identified information will be retained and preserved indefinitely. If required, de-identified data may be saved or shared in a publicly accessible manner.

b. Is there the possibility that the data could be re-identified? ☒ No ☐ Yes- Please explain:
Click or tap here to enter text.

2. What security controls are in place to make sure data/specimens are secure, please explain:
Click or tap here to enter text.

All research data and analyses will be stored on password protected computers and cloud storage accounts.

3. Will data/ specimens be kept for future research, including unspecified future research, genetics and/or whole genome sequencing? ☒ No ☐ Yes- Complete below:

a. Will subjects receive results for any future research? ☒ No ☐ Yes- Explain what results individuals will receive: Click or tap here to enter text.

4. Will the data /specimens be kept in a repository? ☒ No ☐ Yes- Complete below:
a. Please list what repository: Click or tap here to enter text.

5. Will the data/specimens be shared with collaborating entities? ☒ No ☐ Yes- Complete below:
    a. Explain where the data/specimens will be going: Click or tap here to enter text.

6. Will the data/specimens be sold to pharmaceutical companies? ☒ No ☐ Yes- Complete below:
    a. Explain where the data/specimens will be going: Click or tap here to enter text.