Principle Investigator

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NAU NORTHERN ARIZONA UNIVERSITY

Office of Research Compliance

Project Narrative for Prospective Research

Project Title:	Adjustable ankle orthosis STTR
Investigator:	Zachary Lerner, PhD

Project Abstract

Background

CP is the most common cause of pediatric physical disability in the U.S. and worldwide [1]. Imagine a child who is unable to keep up with her friends at school and is physically and socially isolated with a level of habitual activity well below guidelines [2]. As a young adult, she develops metabolic dysfunction, cardiovascular disease, fatigue, weakness, osteoporosis, chronic pain, depression, and anxiety [3], [4]. This is the reality for many of the 500,000 children in the U.S. with cerebral palsy (CP), and the likely fate for many of the 10,000 children diagnosed with CP in the U.S. every year [5]. Current treatment does not fully address long-term gait deficits from CP [6]. Neuromuscular dysfunction caused by CP often results in pathological walking patterns [7], such as crouch gait [8]. Surgery [9], [10], anti-spastic injections [11], and physical therapy [12], can reduce severity of gait impairments, but long-term deficits typically remain [13], [14] (Fig. 1). AFOs are often prescribed as a standard of care for the majority of ambulatory children with cerebral palsy. However, current AFOs restrict undesired movements, such as plantarflexion to assist toe-clearance, but also interfere with desired movements like stance-phase plantarflexion required for push-off propulsion, often leading to toe-walking and reduced ankle power [15]. AFOs make it difficult or impossible to safely navigate graded terrain, like stairs [16].

The design of the most commonly prescribed AFOs for children with CP is ripe for change. Solid Ankle-Foot Orthoses, stiff boot-like structures that encase the foot and lower leg to prevent ankle movement, are the most commonly-prescribed AFO for CP [15]. Posterior Leaf Spring Ankle-Foot Orthoses AFOs have an ability to return energy during the gait cycle, and are often made from carbon fiber leaf springs located behind the limb. These AFOs allow for a custom stiffnesses by modifying the lever arm or the leaf spring thickness, but the stiffness is set (static) from the time of fabrication [17]. Most recently, spring-like dorsal leaf spring AFOs with differential stiffness have demonstrated an improved ability to preserve positive ankle power [18], and improve efficiency as compared to AFOs provided in usual care.

Why do we need quickly adjustable AFO stiffness? Improving mobility in the community requires adjustable ankle stiffness. Ankle joint stiffness varies considerably across different speeds and terrains, which suggests the same for optimal AFO stiffness. Unfortunately, commonly prescribed AFOs are unable to easily or quickly vary the joint stiffness; most are not able to vary stiffness at all. The result, at best, is a single AFO stiffness that is only optimized for ambulating in a single condition at a single speed. AFOs are typically too stiff for slower speeds, often even prevent children from getting off the ground, and yet also unsuitable for stair climbing, ramp ascent or descent, and running. Research has demonstrated that individually tuned stiffness is critical for maximizing improvements in walking performance in CP [19]. There is a need to create an AFO where children can change the stiffness themselves “on the fly.”

Why do we need differential AFO stiffness? There may be long-term danger of locking the ankle and preventing plantarflexion during walking [20]. AFOs typically resist ankle plantar flexion by the same amount that they resist ankle dorsiflexion, resulting in a dramatic reduction in active neuromuscular engagement of the plantar flexor muscles, reduced range of motion, and minimal ankle push-off power [20]. One paper demonstrated that spring like differential stiffness preserves ankle power and work in CP, whereas a rigid configuration did not [18]. There is a need to create an AFO that allows users to maintain some ability to plantarflex at the ankle.

Why do we need a modular design? A design that allows the calf cuffs and footplates to be customized and interchanged based on changing needs or growth has several benefits. First, it reduces waste for expensive and hard to recycle composite materials (e.g., carbon fiber). Second, it reduces the need for custom molding sessions. Third, it may allow us to reduce fabrication costs by benefiting from economies of scale when manufacturing common sizes and form factors. There is a need to create an AFO that grows with the child and adapts to their needs.

Purpose:
Our long-term goal is to establish effective therapies that restore function and improve mobility to enable increased levels of habitual physical activity for improved quality of life and longitudinal health outcomes in individuals with CP. The primary goal of this study is to validate the benefits of, and customer need for, differential and adjustable stiffness AFO features.

Our first aim is to confirm that the differential and adjustable stiffness (DAS) AFO improves plantarflexor push-off power and range of motion compared to standard (physician prescribed) AFOs during walking in CP.
Our second aim is to confirm that the differential and adjustable stiffness (DAS) AFO improves plantarflexor muscle activity while maintaining improved posture compared to standard AFOs during walking in CP.
Our third aim is to validate the need and usability of real-time stiffness adjustment during play and school activities; obtain feedback from the children, their parents, and orthotists to design the MVP.

Lay Summary:
This study seeks to determine how an adjustable stiffness ankle braces affects walking performance and biomechanics in cerebral palsy.

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: 11

- 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?
  Inclusion Criteria:
  - Age between 8-45 years old, inclusive
  - Diagnosis of cerebral palsy (CP)
  - Gross motor functional classification score level I, II, or III
  - Physician-prescribed AFOs of common design (i.e., rigid molded thermoplastic)

  Exclusion Criteria:
  - Excessive knee flexion during walking caused by CP
  - Ability to walk for 6 minutes on a treadmill
  - At least 20° of passive plantar-flexion range of motion
  - No concurrent treatment other than those assigned during the study
  - No condition other than CP that would affect safe participation
  - No surgery within 6 months of participation.

- Indicate age range, gender and ethnicity of your research population:
  There will be no restriction on sex, gender, ethnicity, or race.
  Age between 8-45 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 wil use an email, phone, and face to face script for participant recruiting

- When will recruitment occur? Please provide time frame with dates if applicable: 1/1/2024-1/1/2025

- 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 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:

Informed Consent:

The consent process will take place in person or over the phone in a private room by a member of the research team. Consent will be obtained before any study procedures are done. If eligibility criteria are met, the participant, legally authorized individual (LAR), or a legal guardian in the case of minors will be verbally taken through and be provided an electronic (if phone consenting) or hard copy of the combined consent form and assent form to review. For the case of a subject being represented by a LAR, both the subject and the LAR will be present while the consent process. If the subject indicates a willingness to participate via verbal or gesticulated assent, the LAR will sign the consent form on their behalf. Any questions will be answered. The consent form will be provided in English. Once consent and assent are obtained in writing and prior to undergoing any research assessments, all enrolled patients will have their relevant medical history recorded and physical examination completed ("history and physical"). The medical history may be recorded over the phone as well if the participant or guardian is willing to share that information over the phone. The physical will be performed by a licensed physical therapist or trained research team member and relevant medical information such as having a seizure disorder, other current medications, presence of any communicable diseases and allergy history will be documented. Each participant will be screened for any cardiorespiratory, neurological or musculoskeletal contraindications to short exercise bouts of walking or moving lower limbs. Minor assent will be obtained after parental consent has been provided.

COVID-19 Mitigation Statement

In an effort to mitigate exposure to COVID-19, the study team will follow all CDC, NAU, and Gillette 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. The passive ankle brace help support the use. 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 braces:

- 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).

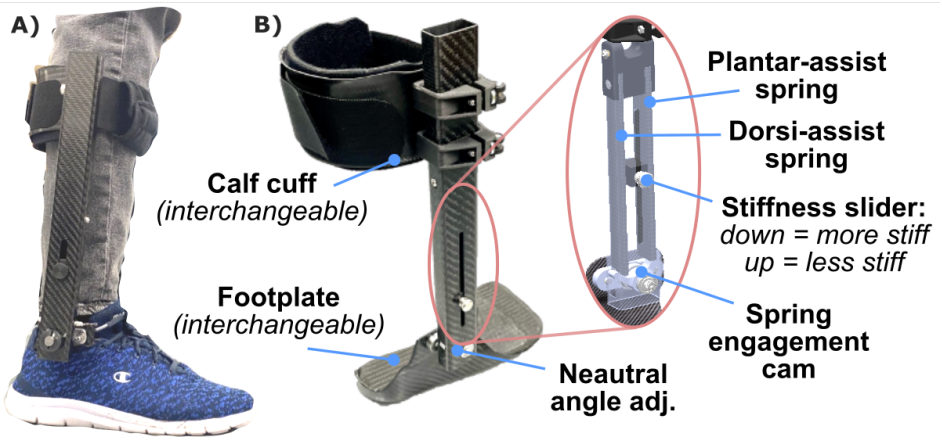

Figure 1. Functional prototypes of the Differential and Adjustable Stiffness AFO (DAS-AFO) with internalized springs.

Overview: We have developed a differential and adjustable stiffness AFO (DAS-AFO): Differential stiffnesses allows for customizing the stiffness in the plantarflexor and dorsal directions separately to maximize neuromuscular engagement and positive biological ankle power during push-off; A "real-time" stiffness adjusting slider allows for rapid and easy adjustment for different ambulatory conditions (e.g., walking, stairs, running). The primary goal of this study is to validate the benefits of, and need for, differential and adjustable stiffness AFO features. Our first aim is to confirm that the differential and adjustable stiffness AFO improves plantarflexor push-off power and range of motion compared to standard (physician prescribed) AFOs during walking in cerebral palsy (CP). Our second aim is to confirm that the differential and adjustable stiffness AFO improves plantarflexor muscle activity while maintaining improved posture compared to standard AFOs during walking in CP. Our third aim is to validate the need and usability for real-time stiffness adjustment during play and school activities; obtain feedback from the children and their parents.

Experimental Protocol for Aim 1 and 2: Participants will complete two 30-minute practice sessions, and a final assessment. On the final assessment, participants will walk on an instrumented treadmill for 6 minutes with their normal AFOs and with the DAS-AFO tuned to provide just enough dorsiflexor assistance to address drop foot (if present). Testing order will be block randomized. Treadmill speed will be set to each participant's preference, as will the stance phase plantarflexor stiffness for the DAS-AFO.

Experimental Protocol for Aim 3: Participants will complete a series of play and school activities using the DAS-AFO and their normal AFOs; order will be block randomized. During the DAS-AFO condition, participants will be instructed to adjust stiffness using the simple slider as desired. Activities will include a series of floor-seated, chair-seated, standing, walking, and running (if applicable) tasks to capture the breadth of possible movements encountered during a typical school day. We will use video recording to observe and characterize interactions. These sessions will be followed by dedicated discussion time and validated product evaluation/usability questionnaires.

Outcome Measures: The following experimental data may be collected under each experimental protocol:

- Electromyography
- Ground reaction forces
- Motion capture marker trajectories
- Metabolic cost of transport
- Pictorial pediatric exertion scale
- System Usability Scale questionnaire
- Video recordings

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 2-3 sessions, each lasting up to 3-4 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:

Participants will receive $30 per hour. If participants voluntarily withdraw, they will not receive the compensation. Participants may receive $10 of travel compensation for every 25 miles traveled to the facility where the study will take place, with a maximum of $60 per visit. Participants may be reimbursed up to $120/night of hotel or Airbnb accommodations if an overnight stay is necessary for participation.

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: NIH STTR Grant

☐ 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.
   This study will advance our knowledge on the design of better ankle braces for children with CP.

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

   There are no anticipated benefits for participants beyond their compensation and perhaps contributing to their personal interest or knowledge in wearable devices.

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. We will use a overhead safety tether while participants walk on the treadmill if they appear unstable.

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

We will use a overhead safety tether while participants walk on the treadmill if they appear unstable.

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 (i.e., walking ability, GMFCS Score, height, weight, age) 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.