Study Protocol and Statistical Analysis Plan

Protocol Title
Precision Gait Retraining for Children with Cerebral Palsy

Sponsor
Altec Inc., Natick, MA 01760

ClinicalTrials.gov Identifier
NCT04717323

Principal Investigator
Paola Contessa

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Note: The text below was extracted from the IRB protocols for this study, which were first approved on 12/27/2019 for testing at Columbia University and on 07/28/2020 for testing at Altec, Inc.

Study Protocol

Background

Cerebral Palsy (CP) is the most common physical disability in the pediatric population, resulting in a variety of gait impairments that present functional deficits such as reduced walking speed, instability, poor endurance, and in some cases limited or no walking ability. Societal impacts are profound and include limited opportunities for socialization, decreased work potential, and a lifetime of greater healthcare costs for corrective surgery, orthotics, spasticity reduction, and therapy. Effective gait rehabilitation has shown to significantly improve gait, but typically requires numerous training sessions with a team of physical therapists and assistants to restore coupling between upper- and lower-body segments while also supporting the patient's weight. To relieve the physical therapist of the need to stabilize the patient while augmenting limb movement, use of robotic rehabilitation devices to support the patient during gait retraining has become increasingly popular and is routinely used in rehabilitation clinics.

Existing robotic rehabilitation devices have two major drawbacks: one is that they constrain the trunk and pelvis range of motion to single-plane motion, impeding natural rotation/ translation of the pelvis and voluntary execution of natural movements that is necessary for effective retraining. The other is that they do not always include the benefits of biofeedback, a technology that is underutilized in this population. There is a need to improve robotic rehabilitation devices with the ability to support the patient weight (through pelvic assistance) while accommodating volitional adaptation of movement and providing biofeedback of trunk and limb movement.

Goal of the Overall Study

Our team of experts in wearable sensor systems and algorithms at Altec, Inc., in collaboration with robotics and rehabilitation experts from the RObotics And Rehabilitation Laboratory (ROAR Lab) of Columbia University, aim to improve current robotic rehabilitation strategies for CP by developing a first-of-its-kind Mobile Pelvic Assist Device (mPAD) for gait retraining. This device will provide adaptable guiding forces directly to the pelvis through cable-operated and robotically controlled mechanisms to provide rotation and translation of the pelvis in as many as 6 degrees-of-freedom. The provisional support and guidance to the pelvis in turn frees the therapist and child to attend to re-establishing normal limb and trunk movements through biofeedback training from advanced wearable sensor technology (surface electromyographic or sEMG and inertial measurement unit or IMU sensors). The proposed combination of pelvic guidance and biofeedback of adjoining trunk and limb segments will provide adaptability to allow the child's remaining volitional control to be active and allow the therapist to tailor the intervention directly to the child's changing status or specific gait anomalies.

This work is a continuation of the efforts from our collaborators at Columbia University who have already succeeded in the design and developments of a Tethered Pelvic Assist Device (TPAD) that is uniquely capable of automating the well-established physiotherapy practice of using the pelvic location near the center of mass as the focal point for proper stabilization and guidance. The study will leverage these successes of a laboratory based TPAD prototype to integrate wearable sensors into the TPAD intervention to facilitate gait retraining.

Study Sites

Data collection will take place in the research laboratories of Altec, Inc. (23 Strathmore Rd. 01760 Natick, MA) under the supervision of the project PI, Dr. Paola Contessa, and the study coordinator, Dr. Serge Roy; and at the CUMC/Harkness Pavilion of Columbia University (180 Fort Washington Avenue, New York, NY) under the supervision of Dr. Sunil Agrawal.

Specific Aims

A series of treadmill and over ground walking experiments will be performed with and without the TPAD device. These experiments will demonstrate that:

1) For testing at Altec, Inc. - Wearable technology for measuring body kinematics is effective at characterizing gait in controls and/or CP individuals and can be used to provide biofeedback during gait.

2) For testing at Columbia University - Sensor-based biofeedback in conjunction with guiding forces applied to the pelvis can be used to facilitate gait retraining in children with CP.

Protocol

For testing at Altec, Inc.: The subjects will first stand on a treadmill during stationary operation and a) stand quietly in place and b) step in place. We will then familiarize the subjects with walking on a moving treadmill at the lowest speed and increase the speed until reaching the most comfortable walking speed for the subjects. We may include trials where the treadmill speed is increased or decreased smoothly in a manner that is comfortable for the subjects, including starting from quiet standing or decreasing speed to quiet standing. The subjects will be notified before each transition. A monitor (computer or tablet) may be placed in front of the subject to display real time biofeedback of body movement or muscle activation from the wearable sensors to inform them on how well they are performing the task in the form of visual cues, acoustic cues, or more interactive videogames. At the end of each trial, subjects will be administered a brief Likert-type questionnaire to survey their perceived level of engagement in the biofeedback. After the treadmill tasks, subjects may be asked to walk a 10-meter distance, turn around, and return to the starting point on level ground within the laboratory.

Each trial will be 1-5 minutes long with frequent rest periods. Trials will be performed first while holding onto the treadmill support bars and again without holding on (only if the subject is comfortable doing so). The subjects will be closely guarded at all times and will be instructed that they can hold onto the bars at any time. For additional safety, both the subject and researcher will have access to an emergency shutoff switch that stops the treadmill belt from moving.

For testing at Columbia University: The subjects will wear a pelvic brace over shorts and walk on a treadmill at a comfortable speed to warm up. Springs and cables will then be attached to the brace to apply a gentle force on subjects' pelvis. The subjects will then be asked to walk on a treadmill at the same speed. The force magnitude will be monitored and maintained using motors. After this period, springs and cables will be detached from the brace and the subject will be asked to walk at the same speed. Overground measures (or over a specialized pressure mat that collects gait parameters) may be repeated while cables are attached to the brace and either no force or a gentle force is applied to the pelvis. The force magnitude will be monitored and maintained using motors.

Subjects may be asked to repeat these procedures in one session or for up to 5 consecutive days. Visual feedback will be provided on a computer screen in front of the patient during the treadmill tasks. The feedback will be given based on each individual subject's gait parameters.

Involvement of Human Subjects

Children and adults (male/female; ≥6 y.o.), including healthy controls and individuals with CP, will be recruited.

Sex considerations: We plan to recruit equal numbers of males and females to assess possible differences between men and women with regards to the expected outcomes of this work.

Age considerations: The proposed work includes children because CP is a congenital disorder that typically results in a progressive gait disorder from childhood into adulthood. Gait intervention is most effective when started young, or at least before a child's motor developmental sequence has fully matured. We will therefore include children ≥6 y.o. (refer to Inclusion/Exclusion criteria for more details). Children younger than 6 will be excluded because they are likely to be unable to follow the instructions and comply with the protocol requirements.

Racial/Ethnic origin considerations: We plan to recruit a subject population that includes equal participation of minorities and is representative of the racial and ethnic diversity of the greater Boston (for testing at Altec, Inc.) and New York regions (for testing at Columbia University).

Recording apparatus: A 16-sensor Trigno Wireless data acquisition system (Delsys Inc., Natick, MA) designed for detecting sEMG and IMU signals from single hybrid wireless sensors (*TrignoIM* sensors) will be used for the gait recording sessions. *TrignoIM* sensors will be located on the body during these experiments to record sEMG and IMU signals as described in the Sensor Locations section below. Passive reflector markers will be located on anatomical bony landmarks for motion capture that will be used to validate sensor-based recordings. Sensor signals from *TrignoIM* sensors will be sampled at 2000 samples/sec using EMGWorks software (Delsys Inc., Natick, MA), and interfaced over USB to a PC workstation for post processing. Recordings from motion capture data will be triggered from the EMGworks software so that biomechanical variables can be compared temporally for accuracy. Footswitch sensors or a pair of shoes with pressure pads may be used to record foot pressure while walking.

Sensor locations: The skin area of each sensor location will be prepared using alcohol wipes to cleanse the skin surface and repeated tape peels to remove possible superficial contaminants (oil; dead skin) so as to improve signal quality. We anticipate placement of no more than 16 sensors at any one time on muscle locations such as: gluteus medius, upper-back (trapezius), elbow flexors (biceps brachii), hip flexors (rectus femoris), knee extensors (vastus lateralis), and ankle dorsiflexors/plantarflexors (tibialis anterior and gastroc-soleus) musculature.

Inclusion/Exclusion Criteria

CEREBRAL PALSY

Inclusion criteria:
- Adults or Children (age≥6 y.o.)
- Male or Female
- Confirmed diagnosis of Cerebral Palsy by a neurologist
- CT or MRI imaging consistent with clinical presentation
- Clinical evidence of preserved cognition as determined by the child's neurologist

- Clinical evidence of Mild to Moderate spastic (pyramidal) diplegia as determined by the child's neurologist
- Gross Motor Function Classification System (GMFS) GMFCS Level II ("walks with limitations. Limitations include walking long distances and balancing, but not as able as Level I to run or jump; may require use of mobility devices when first learning to walk, usually prior to age 4; and may rely on wheeled mobility equipment when outside of home for traveling long distances."
- Spasticity being controlled by pharmaceutical or surgical correction; or has Modified Ashworth scale (MAS) = 0-2 ("More marked increase in muscle tone through most of the ROM but affected part(s) easily moved
- Ambulatory without assistive devices (except for long distances or on uneven terrain)
- No allergies to skin tape such as Band-Aid

Exclusion criteria:
- Inability to follow simple instructions in English, or through a Spanish-speaking translator
- Medical history of other neurological conditions
- Medical history of cardiac or respiratory complications, or disorders that would place the subject at risk for conducting the different motor activities
- Contractures present in lower limb – evaluated based on Tardieu Scale test where joint range of motion is measured during slow velocity movements and where contracture is operationally defined as being present if the angle at the end of range is 5-10 degrees less than full range at ankle; and 5-20 degrees less than full range at hip and knee
- Skin disorders that result in open lesions or hyper-sensitive/fragile skin, preventing the use of medical-grade adhesive tapes to secure the sensors to the skin
- Unable to provide Informed Consent from subject and Assent from parent or guardian using English ICF

CONTROLS

Inclusion Criteria:
- Adults or Children (age≥6 y.o.)
- Male or Female
- Able to walk independently and without assistive devices
- No history of musculoskeletal or neurological disorders
- Able to follow directions in English

Exclusion Criteria:
- Non-English speaker
- Unable to walk independently and without assistive devices
- Medical history of neurological or musculoskeletal conditions (arthritis, spondylosis, etc.)
- Inability to follow simple instructions
- Unable to provide informed consent in English

Recruitment Process

(For testing at Altec, Inc.) Subjects with CP meeting the Inclusion/Exclusion criteria will be recruited primarily through posting and flyers at pediatric and adult rehabilitation centers working with this population in the greater Boston area which will be publicly displayed and

circulated. Control subjects meeting the Inclusion/Exclusion criteria will be recruited primarily through posting and flyers in the immediate area around Altec, Inc. at local cafes, shopping malls, and fitness centers.

(For testing at Columbia University) Research flyers will be placed in outpatient practice offices, and study info will be listed on the RecruitMe website. Further, pediatric individuals with cerebral palsy will be recruited through clinicaltrials.gov listing.

Informed Consent

All subjects will be properly informed of the purpose of the study by the research team at Altec, Inc. or Columbia University. The prospective subjects will have the opportunity to read an IRB-approved informed consent form outlining the experimental procedures, risks, and rights as a human subject and see the actual equipment demonstrated to them. Written consent will be obtained from adults, written parental consent and assent will be obtained from pediatric participants. A signed and dated copy of the consent form will be provided to each subject/parent. All researchers involved in the experimental procedures and analysis of human subject data as outlined in this proposal have training certification on file and are familiar with the appropriate Federal guidelines regarding the use of human subjects for research.

Potential Risk and Protection against Risk

The identifiable risks, which fall into the category of less than minimal physical risks, are described below.

1. The primary medical risk includes possible irritation to the skin caused by securing and removing the sensors from the skin. The risk is comparable to having a Band-Aid on the skin for 2 hours and peeling it off. To mitigate this risk, the skin will be inspected before and following removal of the sensors and wiped using an alcohol swab. An over-the-counter skin moisturizing cream will be available should the subject feel any irritation or dryness at the sensor locations.

2. Some temporary tiredness and muscle fatigue may result from performing the walking activities. This risk is similar to a light exercise session and will be minimized by offering frequent rest periods and breaks for hydration and rest.

3. Risks of falls. Walking on a treadmill can expose an individual to the risk of falling and injuring themselves. This risk is mitigated by constant supervision from a study researcher or physiotherapist, frequent breaks, and choice of comfortable walking speed.

4. The risk of electric shock is highly unlikely and greatly minimized because the sensors used in this study are wireless and designed to completely isolate the subject from sources of electrical current. These circuits ensure subject safety in compliance with United States and European EN60601 safety standards for medical instrumentation. They are in compliance with CE and FDA Medical Device Standards for allowable leakage currents.

5. A subject may feel slight discomfort during walking when wearing the brace. The brace is connected mechanically using springs. Though highly unlikely, a spring could break and stop the treadmill suddenly but the chances of this are slim. Subjects and researchers will have 'Stop' buttons to stop the experiment at any time.

6. The risk of infection from respiratory viruses such as COVID-19 may be increased when spending considerable amount of time in closed spaces, such as offices and laboratory space. To mitigate this risk, precautions following state and CDC guidelines will be followed including: 1) phone and in-person screening of the research participants and any researcher involved in data collection ahead of testing and on the day of testing using the questionnaire attached; 2) temperature check upon arrival; 3) requirement for all individuals involved to maintain at least 6 feet of physical distance as much as possible, and wear a mask at all times; 4) no more than 3 individuals including the research participant involved in the data collection at all times; 5) perform testing in large spaces; 6) require frequent hand-washing and use of gloves when hands-on contact is required; 7) cleaning and disinfecting of all testing equipment and high-contact surfaces using approved disinfectants before and after each data collection.

6. Confidentiality risk: The file linking subjects' name to codes will be in paper form and will be stored in a locked file cabinet along with signed consent forms. All sensor data will be stored on the lab servers for at least 3 years in a password protected folder regarding this project. Access will only be available to those working on the project. For cases where data are shared between Columbia and Altec, Inc. only de-identified, raw data will be shared. This removes risk that a patient's privacy may be compromised. In case the subject gives explicit permission to take photo and video recordings during the experiment these will be stored in the password protected project folder on the lab servers. All digital data will be identified only by subject codes.

Potential Benefits to the Subjects

There are no anticipated benefits for subjects in this study aside from the potential benefits to the population of individuals with CP in need of improved robotic rehabilitation devices for gait retraining if our results lead to a more effective system.

Alternatives to Participation

This study does not involve medical diagnostics or treatments for which alternatives should be offered.

Data & Statistical Analysis Plan

A series of signal acquisition and processing software will be developed to analyze gait temporal metrics and range-of-motion from wearable sensors. We will validate these metrics by comparing them to those derived using concurrent motion capture data – considered a gold-standard. We will adopt a repeated measures design (student's t-test statistic) which will be corrected for possible errors associated with multiple comparisons.

Testing of pelvic guiding forces and biofeedback is not designed for efficacy, but for preliminary prototype studies and early development of concepts. Mixed-design analysis of variance followed by post-hoc analysis will be used to determine the effect of the TPAD and mobile TPAD on walking.