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14. ABSTRACT

The purpose of this project is to study the effects on bone health of exoskeleton-assisted gait in individuals with a complete spinal cord injury. Advanced biomechanical models of human locomotion are utilized to estimate the mechanical effects of the dynamic loading of the bone structures that takes place during exoskeleton-assisted gait. The estimated maximum energy equivalent strain is studied as a potential proxy of bone adaptation and correlated with high-resolution peripheral quantitative computed tomography data and with clinical measures (e.g. biomarkers of inflammation such as C-reactive protein and IL-6) that are collected longitudinally. The work carried out by the research team until now has been focused on the development of advanced biomechanical models. The research team is now scheduling data collections in study volunteers to start the experimental part of the project.

15. SUBJECT TERMS
biomechanical modeling, bone health, exoskeletons, gait, spinal cord injury

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Introduction

Individuals with Spinal cord injury (SCI) are often affected by an accelerated bone loss that occurs primarily at regions below the neurological lesion [1]. The severity of the impairment is directly proportional to the extent of bone loss [2] thus resulting in a greater loss in individuals with motor complete lesions [3]. Furthermore, immobilization after SCI is associated with the development of multiple complications such as decreased pulmonary function, systemic inflammation and loss of muscle mass [4-6].

For these reasons, remobilization is a primary clinical goal for individuals with SCI. The use of exoskeletons (such as the EksoTM system by Ekso Bionics) to achieve remobilization has become increasingly common in the rehabilitation setting [7].

The overall aim of this study was to investigate the motions of and the forces transmitted through the lower extremities during exoskeleton-assisted gait, and determine the specific effects of exoskeleton-assisted gait on bone health, muscle mass, and other clinical functional outcomes. The hypothesis of the study is that exoskeleton-assisted ambulation has skeletal and general health benefits for individuals with SCI that are proportional to the total stimulus delivered. To test this hypothesis, *we quantified the joint kinematics and kinetics and thus we were able to estimate loads on lower limb bones during ambulation using the Ekso™ system by Ekso Bionics. This information, in combination with selected clinical data, was used to develop a model to predict the effects of exoskeleton-assisted gait training on bone health, muscle mass, and functional outcomes.* Fifteen (15) subjects completed the study procedures. The results presented in this final report summarize the findings of the study.

Keywords

Biomechanical modeling, bone health, exoskeletons, gait, spinal cord injury.

Accomplishments

What are the major goals of the project?

The study specific aims, as indicated in the Statement of Work, are the following:
(1) To quantify the motions of and forces transmitted through the lower extremities during exoskeleton-assisted gait;
(2) To explore the development of a model to predict the effects of exoskeleton-assisted gait on bone health, muscle mass, and functional outcomes.

Specific Aim 1 is associated with three major tasks: 1.1) to obtain human subject approval and prepare for the study; 1.2) to contact and screen prospective study participants; and 1.3) to enroll study participants, train them with the exoskeleton and perform gait testing. *Specific Aim 2* is associated with two major tasks: 2.1) to explore ways of modeling the effects of exoskeleton-assisted gait; and 2.2) to perform data analysis.

What was accomplished under these goals?

The table below shows progress on the study according to the above-listed specific aims and tasks.

Specific Aim 1, task #1.1	100% COMPLETED - We accomplished this aim during Year 1 of the study.
Specific Aim 1, task #1.2	100% COMPLETED - We accomplished this aim in January 2018..
Specific Aim 1, task #1.3	100% COMPLETED - 15 subjects completed the study procedures. We accomplished this aim in March 2018.
Specific Aim 2, task #2.1	100% COMPLETED - We developed data collection procedures and models to estimate the loads on the subject's joints during robot-assisted ambulation.
Specific Aim 2, task #2.2	100% COMPLETED - We analyzed the data collected in the study. It is worth noticing that we are still in the process of applying the models developed in Specific Aim 2, subtask #2.1 to the dataset. However, we are marking this task as complete because we believe that the analyses performed so far fulfill the requirement of the study and allow us to draw some preliminary conclusions.

We have described our accomplishments regarding ***Specific Aim 1*** of the project in previous reports. In summary, we leveraged the Spaulding Rehabilitation Hospital SCI Model System to contact prospective study volunteers. We then screened subjects interested in participating in the study and enrolled those who met the study inclusion/exclusion criteria and were willing to comply with the study requirements (i.e. undergo robot-assisted gait training and participate in the evaluation sessions).

Achieving ***Specific Aim 2, task #2.1*** required the development of appropriate data collection procedures and of a biomechanical model to estimate the loads on the subject's joints. The collection of data was carried out using a 10-camera motion capture system (Vicon, Oxford, UK) and two 6-channel force platforms (AMTI, Watertown, MA) embedded in a 12-m walkway that were used to record ground reaction forces. Reflective markers were positioned on the subject and the exoskeleton. Reflective markers on the subject were attached: 1) at pelvis height, directly on the back of the exoskeleton, under the assumption that there was no relative motion between the pelvis and the portion of the exoskeleton attached to it; 2) bilaterally to the thigh, shank, and foot using clusters of three markers. Markers were then placed on the exoskeleton to aid in the estimation of its segment and joint kinematics. Data collection initiated with the calibration of anatomical landmarks which was carried out in a sequence of seated and standing positions. Anatomical landmarks that were calibrated included the tibial tuberosity, head of the fibula, medial and lateral epicondyles, medial and lateral malleoli, first/second/fifth metatarsal heads, heel, anterior superior iliac spines and posterior superior iliac spines. All calibrated landmarks were calibrated at the beginning of the data collection as static trials. This approach is referred to as calibrated anatomical system technique (CAST) [8]. Figure 1 shows an example of the results obtained using this method.

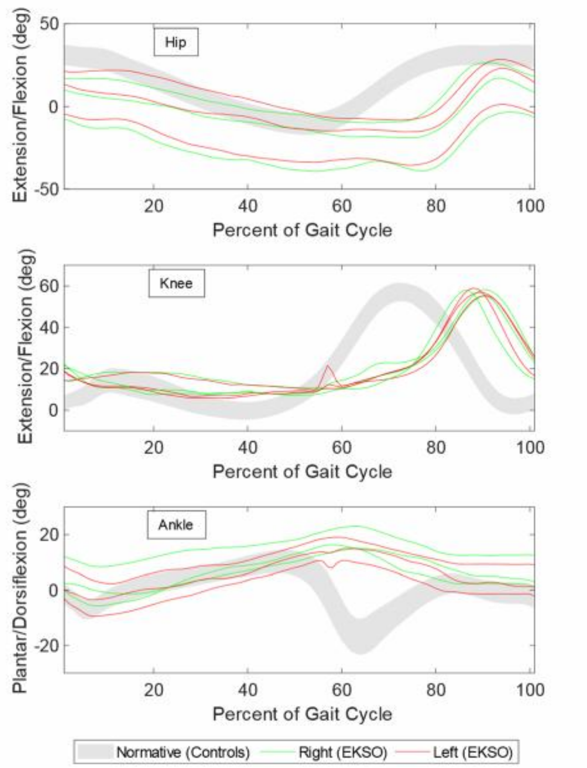

Figure 1 – Comparison of exoskeleton-assisted gait with healthy controls. Gait cycles from a minimum of three trials were averaged together to produce a single representative left and right gait cycle for each subject. Joint angles at the hip, knee, and ankle throughout the gait cycle are shown above.

We recently completed ***Specific Aim 2, task #2.2***. To accomplish this objective, motion capture data, force plate data, and knee and hip actuator torque data obtained directly from the exoskeleton during the walking trials was transferred to Karen Troy's team at the Worcester Polytechnic Institute (WPI). Along with information about the patient and mechanical properties of the Ekso suit, masses and moments of inertia were used to calculate inverse dynamics of the patient+Ekso, henceforth referred to as the "lumped" model. Lumped inverse dynamics outputs consist of net joint reaction forces and net joint moments at the ankle, hip, and knee. The net forces and moments from the lumped model were separated into Ekso and patient forces and moments by subtracting the Ekso-actuator torques and the torques required to move the Ekso through the dynamic motion. The results consisted of: 1) net joint reaction forces, moments, and kinematics *for the patient only*, and 2) actuator torques required to move the patient (applied through the straps and foot-plates). For patients with complete spinal cord injury, we assumed that joint moments generated by the subject arose from one of three possible sources: 1) passive muscle resistance; 2) spasticity; and 3) experimental error. To define user safety parameters, we used a "worst-case" bone loading scenario in which we assumed that subject's joint moments arose from spasticity contractions. We calculated muscle length changes based on patient's kinematics and assigned patterns of activations to muscles crossing the joint from the largest muscle to the smallest, until the calculated net joint moment was achieved. The result consisted of 1) muscle lines of action and activation forces during the gait cycle, and 2) joint *contact* forces at the ankle, knee, and hip. Note that joint contact forces are distinct from joint reaction forces, in that they represent the actual force transmitted from one joint surface to the next (e.g. tibia to femur), and are heavily influenced by muscle loading.

Joint contact forces, muscle forces, and Ekso strap and foot plate forces were looked upon as time-series data. These datasets represented the forces applied to the bones of the lower extremities. Bone stress and strain were calculated using scaled finite element (FE) models. "Generic" FE models of the femur and tibia were scaled such that their material properties reflected average values for an individual with chronic spinal cord injury, based on measured bone mineral content (BMC). Boundary conditions consisted of muscle forces, joint contact forces, and strap forces applied to the bone of interest. The result was an estimate of the maximum energy equivalent strain, a scalar measurement shown to influence bone adaptation.

The development of the above-described techniques allowed us to analyze the data collected from subjects with SCI who participated in the study. Representative knee angle, knee joint reaction forces (JRFs), and internal moments from a subject are shown in Figure 2. A positive knee moment indicating knee extension occurs in the stance phase because constant support is needed to prevent buckling of the knee. Of the four subjects whose data has been fully analyzed so far, user knee moments ranged from 0.67 to 1.02 bodyweight*heights, (mean: 0.90). This result is similar to typical able-bodied walking, in which knee moments are around 0.89. Peak user JRFs at the knee were 82 to 95 percent bodyweight, which is lower than the usual 2 times bodyweight during walking. Our users walked more slowly than able-bodied gait, but the GRF acted with a larger moment arm due to the foot and shank being treated as a single rigid segment. The Ekso also constrained ankle rotation, which could increase the knee moment.

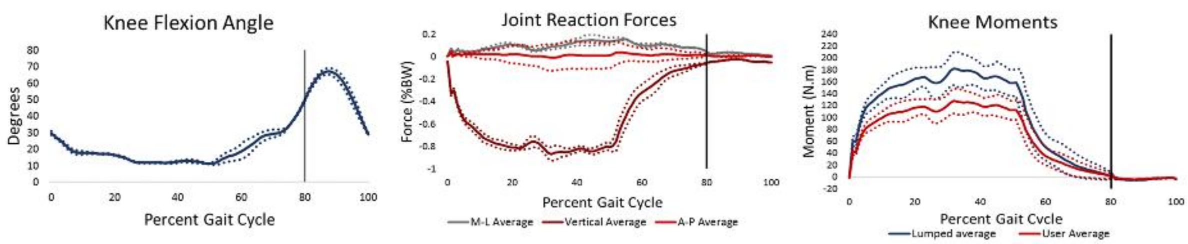

Figure 2 – Single subject Knee Angle, Joint Reaction Forces (JRF), and Knee Moment reported in the anatomical coordinate system. Vertical Line indicates toe-off.

<u>What opportunities for training and professional development has the project provided?</u>

The project was not meant to create training and professional development opportunities.

<u>How were the results disseminated to communities of interest?</u>

We presented the results of the study at the following scientific conferences.

Smith NI, Fabara E, Daneault JF, Adans-Dester CP, O'Brien A, Scarton A, Della Croce U, Bonato P, Troy KL, User Biomechanics during Exoskeleton-Assisted Gait: Theoretical Approach and Case Study, 41st Annual Meeting of the American Society of Biomechanics, Boulder (Colorado), August 8-11, 2017

Fabara E, O'Brien A, Adans-Dester CP, Daneault JF, Della Croce U, Scarton A, Bonato P, Troy K, Biomechanical Evaluation of Exoskeleton-Assisted Gait in Patients with Spinal Cord Injury, 94th Annual Conference of the American Congress of Rehabilitation Medicine, Atlanta (Georgia), October 23 - 28, 2017

Kasen E, Fabara E, Daneault JF, Bonato P, Troy K, User Biomechanics of Exoskeleton-Assisted Gait, BMES Annual Meeting, Atlanta (Georgia), October 17-20, 2018 (to be presented in the fall)

Impact

What was the impact on the development of the principal discipline(s) of the project?

The work achieved in the study has potential for significantly affecting the way exoskeleton-assisted gait is utilized in the clinic. Surprisingly, despite the enthusiasm in the clinical field for the use of robotic exoskeletons to enable gait in individuals with a complete SCI, clinical teams are not provided with appropriate tools to estimate or predict potential health benefits (e.g. bone health) associated with exoskeleton-assisted gait.

What was the impact on other disciplines?

The project that our team carried out was multidisciplinary in nature and hence the results of our studies were bounded to have an impact on multiple disciplines. Specifically, the biomechanical models that we developed have a significant impact on the field of biomedical engineering. The primary impact of the experimental work that we carried out is expected to be clinical in nature. Overall, the combination of technical and experimental developments that took place as part of the project are expected to have a transformative impact on the clinical application of exoskeletons in individuals with a complete SCI.

What was the impact on technology transfer?

Although the project was not meant to generate results or products that would lead to a technology transfer, the methods that we developed to estimate the effects on bone structures of exoskeleton-assisted gait are of clinical interest. Hence, we anticipate that companies will soon demonstrate interest for our work.

What was the impact on society beyond science and technology?

The results of the studies carried out during the project showed the potential benefits of exoskeleton-assisted gait. Hence, the project provided scientific evidence in support of the use of exoskeleton technology in individuals with SCI.

Changes and Problems

Changes in approach and reasons for change

The results achieved in the study showed that the scientific approach that we originally proposed is valid. Hence, there was no need to change the proposed scientific approach so far.

Actual or anticipated problems or delays and actions or plans to resolve them

We experienced significant problems with the remote data logging module of the Ekso system utilized in the study. In May 2017, it came to our attention that remote data logging from the EKSO device had been intermittent starting in mid-March. Technical support was scheduled to attempt local retrieval of stored data affecting one of our data collections, however, further issues with the device prompted us to request a replacement in order to continue with data collections. Despite multiple attempts at data retrieval from the original device, the sessions of interest were lost. We monitored the new device over several weeks of training sessions with no apparent issues. However, towards the end of June, it was noted that remote data logging had become intermittent and eventually ceased completely affecting 2-3 sessions of interest. Technical support replaced the communications components of the device in early August and remote data logging remained stable for a few months. Once data collections were resumed, issues with the data logging were noted and a session of interest lost. In January 2018, the communications components were once again replaced. With the help of the company, we were able to implement a system for verifying the presence of session logs both before and after each session and soliciting verification of data integrity from EKSO for the sessions of interest. We contacted the Partners IRB regarding how to handle the lost data and allow us to re-collect them. We increased our recruitment target of the group 1 from 10 to 20 participants to be able to re-consent participants whom data were lost. All of them (4) agreed to come back for a few training sessions and the gait evaluation. This was made with the amendment number 18, approved by the Partners Ethic Committee on October 14th, 2017. In addition to the repeated subjects, we were able to recruit 4 additional subjects. Two of these completed the study and one full dataset is available. Of the repeats, all the sessions of interest were lost. We are in the process of attempting recovery, in conjunction with EKSO, of training sessions which were available at the time of the study in order to use these as a reference for the device data for the lost sessions of interest. So far, we have been able to recover 1 training session within a few days of a session of interest.

Changes that had a significant impact on expenditures

None.

Other changes

None

Products

Publications, conference papers, and presentations

We presented our work at scientific conferences.

Smith NI, Fabara E, Daneault JF, Adans-Dester CP, O'Brien A, Scarton A, Della Croce U, Bonato P, Troy KL, User Biomechanics during Exoskeleton-Assisted Gait: Theoretical Approach and Case Study, 41st Annual Meeting of the American Society of Biomechanics, Boulder (Colorado), August 8-11, 2017

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Technologies or techniques

We developed software for the implementation of algorithms needed to study the biomechanics of exoskeleton-assisted gait in individuals with a complete SCI.

Participants & Other Collaborating Organizations

The following is the list of individuals who worked on the project.

Name:	Paolo Bonato, PhD
Project Role	Principal Investigator
Institution	Spaulding Rehabilitation Hospital
Contribution to the Project	Dr Bonato contributed to the development and amendment of the study protocol, the development of biomechanical procedures and algorithms for the study of exoskeleton-assisted gait, and the assessment of components of the camera-based motion capture system to evaluate their suitability for the study.

Name:	Leslie Morse, MD
Project Role	Co-Investigator
Institution	Spaulding Rehabilitation Hospital
Nearest Person Month Worked	0
Contribution to the Project	Dr. Morse contributed to the initial phases of the study, including the development and amendment of the study protocol, and the recruitment of subjects in the initial phases of the study.

Name:	Karen Troy, PhD
Project Role	Co-Investigator (site PI)
Institution	Worchester Polytechnic Institute
Contribution to the Project	Dr. Troy contributed to the development and amendment of the study protocol, the development of biomechanical procedures for the study of exoskeleton-assisted gait, the preparatory work to collect data using the scanning techniques at Worchester Polytechnic Institute.

In addition to the PI and Co-Investigators on the study, research project coordinators, a post-doctoral student, two research therapists, a research fellow, and additional personnel with focus on the engineering aspects of the project supported the work coordinated by the PI and Co-Investigators.

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Quad Charts

The attached Quad Chart reflects completion of the project.

Skeletal and Clinical Effects of Exoskeleton-Assisted Gait

Log Number A-18380
Award Number W81XWH-14-1-0611

PI: Paolo Bonato, PhD **Org:** Spaulding Rehabilitation Hospital **Award Amount:** $379,188

Study/Product Aim(s)

- To quantify the motions of and forces transmitted through the lower extremities during exoskeleton-assisted gait.
- To explore the development of a model to predict the effects of regular exoskeleton-assisted gait on bone health, muscle mass, and functional outcomes.

Approach

To achieve the above-stated specific aims, we plan to pursue the following tasks. Task 1.1: to obtain human subject approval and prepare for the study. Task 1.2: to contact and screen prospective study participants. Task 1.3 to enroll study participants and perform gait testing. These tasks are relevant to achieving Aim 1. Task 2.1: to explore modeling the effects of exoskeleton-assisted gait. Task 2.2: to perform data analysis. These tasks are relevant to achieving Aim 2.

Accomplishments: We completed the study in 15 subjects and derived the proposed biomechanical models and thus estimated loads on the lower limbs during exoskeleton-enabled gait.

Timeline and Cost

Activities	14	15	16	17	18
Approval study procedures and set-up					
Screen and enroll study participants					
Modeling effects of Ekso-assisted gait					
Data analysis					
Estimated Budget (~$379K)	**~$60**	**~$220**	**~$80**	**~$20**	

Updated: July 31, 2018

Goals/Milestones (Example)

CY14 Goal – Detailed description of protocols and procedures

☑ Evaluation of the procedures and data collection set-up

CY15 Goals – System validation

☑ Obtain protocol approval

☑ Screen and enroll study volunteers

☑ Complete studies in a subset of subjects

CY16 Goal – Production readiness

☑ Complete studies in all subjects

☑ Perform data analysis

Budget Expenditure to Date

Projected Expenditure: ~$379K

Actual Expenditure: ~$379K