AWARD NUMBER: W81XWH-21-1-0922

TITLE: Dosing of Overground Robotic Gait Training with Functional Outcomes and Neuroplasticity After Spinal Cord Injury (DOOR SCI)

PRINCIPAL INVESTIGATOR: Chad Swank, PT, PhD

CONTRACTING ORGANIZATION: Baylor Scott & White Research Institute
3434 Live Oak St Ste 501
Dallas, TX 75204

REPORT DATE: OCTOBER 2022

TYPE OF REPORT: Annual Technical Report

PREPARED FOR: U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED *(From - ~~To~~)*
OCTOBER 2022	Annual Technical Report	9/15/2021 - 9/14/2022

4. TITLE AND SUBTITLE

Dosing of Overground Robotic Gait Training with Functional Outcomes and Neuroplasticity After Spinal Cord Injury (DOOR SCI)

5a. CONTRACT NUMBER

5b. GRANT NUMBER
W81XWH-21-1-0922

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Chad Swank, PT, PhD
Christa Ochoa, MPH
Faith Meza, MPH

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Baylor Scott & White Research Institute
909 N. Washington Ave., Suite 232
Dallas, TX 75246

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)

U.S. Army Medical Research and Development Command
Fort Detrick, Maryland 21702-5012

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution is unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The goals of this project are 1) to conduct a randomized controlled trial to prospectively examine whether the dosing frequency [24 sessions delivered as high, moderate, or low frequency, defined by number days/ week (4, 3, or 2 days/week over 6, 8, 12 weeks)] of robotic gait training (RGT) therapy provided during the acute/subacute recovery phase after incomplete SCI impacts outcomes compared to usual care only; 2) investigate the difference over 9 months of the neuroplastic effect of RGT dosing as measured by single pulse TMS; and 3) evaluate the safety, tolerability, and feasibility of delivering different dosing frequency levels of RGT from inpatient to outpatient rehabilitation settings. Over year 1 of the project, we achieved all IRB and HRPO approvals, initiated our advisory board and DSMB meetings, completed study team trainings and began participant recruitment and data collection. By grant year 1 end, we had enrolled 7 participants.

15. SUBJECT TERMS

spinal cord injury; robotic gait training; exoskeleton; transcranial magnetic stimulation

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER *(include area code)*
U	U	U	UU	24	

Standard Form 298 (Rev. 8-98)
Prescribed by ANSI Std. Z39.18

TABLE OF CONTENTS

1. INTRODUCTION:

Emerging evidence indicates that robotic exoskeleton use results in positive outcomes for those with chronic SCI, yet limited evidence exists for the acute setting. The potential benefit of robotic gait training (RGT) initiated during inpatient rehabilitation when recovery is greatest is unknown yet appears promising due to established principles of neuroplasticity and the fact that RGT incorporates the critical components of gait training. As a result of the lack of evidence, no clinical practice guidelines exist that delineate which gait retraining approach or dose during early phases of recovery results in the best outcomes for people with motor incomplete SCI. This project will be the first to (1) generate efficacy data concerning the dose of RGT initiated during early phases of recovery in people with SCI, (2) provide mechanistic data of neuroplasticity based on RGT dose, and (3) confirm that the intervention is safe, tolerable, and feasible to administer across inpatient and outpatient rehabilitation settings. Findings will directly impact rehabilitation clinical practice and patient outcomes for people with motor incomplete SCI.

2. KEYWORDS:

spinal cord injury; robotic gait training; exoskeleton; transcranial magnetic stimulation

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Study Specific Aims:

Aim 1: Using a randomized controlled trial, prospectively examine whether the dosing frequency [24 sessions delivered as high, moderate, or low frequency, defined by number days/week (4, 3, or 2 days/week over 6, 8, 12 weeks)] of RGT therapy provided during the acute/subacute recovery phase after incomplete SCI impacts outcomes compared to usual care only.

Aim 2: Investigate the difference over 9 months of the neuroplastic effect of RGT dosing as measured by single pulse TMS.

Aim 3: Evaluate the safety, tolerability, and feasibility of delivering different dosing frequency levels of RGT from inpatient to outpatient rehabilitation settings.

	Timeline [Year(Quarter)]	**Status (Percent complete)**
Major Task 1: Achieve IRB Approval		
Coordinate with Sites for clinical trial agreements (CTAs) submission	Y1(Q1)	Complete (100%)
Coordinate with Sites for nondisclosure agreements (NDAs).	Y1(Q1)	Complete (100%)
Refine eligibility criteria, exclusion criteria, screening protocol	Y1(Q1)	Complete (100%)

Finalize consent form & human subjects protocol	Y1(Q1)	Complete (100%)
Coordinate with Sites for IRB protocol submission	Y1(Q1)	Complete (100%)
Obtain HRPO approval	Y1(Q2)	Complete (100%)
Submit amendments, adverse events and protocol deviations	As Needed	Complete (100%)
Coordinate with Sites for annual IRB report for continuing review	Annually	In progress (25%)
Milestone Achieved: Local IRB approval at BSW and TWU	Y1(Q1)	Complete (100%)
Milestone Achieved: IRB approval at HARPO	Y1(Q2)	Complete (100%)
Major Task 2: Train and Coordinate Study Staff for Clinical Trial		
Training of Study Staff		
Coordinate with Sites for training staff until 100% concordance with study protocol and site-specific demands	Y1-Y4(Q1)	Complete (100%)
Milestone Achieved: Research staff trained	Y1(Q1)	Complete (100%)
Major Task 3: Patient Recruitment and Enrollment		
Subtask 1: Recruitment of 144 patients admitted to BSW for inpatient rehabilitation	Y1(Q2)-Y4(Q1)	In progress (~5%)
Milestone Achieved: Maintained ongoing recruitment procedure throughout duration of clinical trial	Y1(Q2)-Y4(Q1)	In progress: 2 of 11 quarters completed (~18%)
Subtask 2: Enrollment of 144 patients into study		
Patients complete assigned dosing group intervention during inpatient and outpatient rehabilitation. High frequency group: 4 sessions/week x 6 weeks (n=36) Moderate frequency group: 3 sessions/week x 8 weeks (n=36) Low frequency group: 2 sessions/week x 12 weeks (n=36) Control group: usual care only, no RGT sessions (n=36)	Y1(Q3)-Y4(Q1)	In progress (~3%)
Patients complete clinical assessments including but not limited to WISCI-II, 10MWT, and SCIM.	Y1(Q3)-Y4(Q3)	In progress (0%)

Assessments for the RGT groups will be conducted on 5 occasions: (1) admit to and (2) discharge from inpatient rehabilitation, (3) completion of 24 sessions, (4) 1-month post RGT, and (5) 9-months post-SCI. The control would complete assessments at 5 timepoints corresponding to the RGT groups [(1) inpatient admit (2) inpatient discharge, (3) 1-month post inpatient discharge, 4) 2-months post inpatient rehabilitation discharge, and (5) 9-months post-injury].		
Patients complete research self-report assessments, including but not limited to NPRS, FSS, PSFS, PHQ-9, and LiSAT9. Assessments will be conducted on 5 occasions: (1) admit to and (2) discharge from inpatient rehabilitation, (3) completion of 24 sessions, (4) 1-month post RGT, and (5) 9-months post-SCI.	Y1(Q3)-Y4(Q3)	In progress (0%)
Patients complete transcranial magnetic stimulation (TMS) assessments during inpatient and outpatient rehabilitation	Y1(Q3)-Y4(Q3)	In progress (0%)
Milestone Achieved: Report quarterly patients enrolled and findings from patients completing study	Y1(Q3)-Y4(Q3)	In progress (0%)
Major Task 4: Data Analysis		
Subtask 1: Amalgamate site specific assessments for data analysis		
Coordinate TMS data sharing from TMS assessments	Y1(Q3)-Y4(Q4)	In progress (25%)
Build database consistent with outcomes	Y1(Q3)	Completed (100%)
Clean and manage data for analysis	Y1-4(Q4)	In progress (25%)
Subtask 2: Conduct data analysis using methodologies including but not limited to general linear mixed effects models to assess the differences between groups and over time, as well as the time by group interaction.	Y1-4(Q4)	Pending (0%)
Milestone Achieved: Report findings from Outcomes assessments	Y1-4(Q4)	Pending (0%)
Major Task 5: Dissemination		
Subtask 1: Scientific & Peer Reviewed Efforts		
Generate presentation(s) for national conferences	Y1-4(Q4)	In progress (25%)

Generate manuscript(s) for submission to peer reviewed journals	Y1-4(Q4)	Pending (0%)
Generate plain language summaries for consumers/policymakers	Y1-4(Q4)	Pending (0%)
Subtask 2: Non-Refereed Activities		
Conduct Consumer Seminar	Y3(Q4)	Pending (0%)
Conduct VA Educational Meeting	Y3(Q4)	Pending (0%)
Conduct VA Educational Meeting	Y3(Q4)	Pending (0%)
Conduct Clinician-Researcher workshops	Y4(Q4)	Pending (0%)
Milestone Achieved: Report findings (agendas, meeting summaries/notes/minutes) from non-refereed activities	Y3-4(Q4)	Pending (0%)

What was accomplished under these goals?

Over the past year, we have achieved the following:

1. Obtained IRB approval (Major Task 1)
    a. Baylor Scott & White (BSW) IRB approval on 9/16/2021
    b. Texas Woman's University (TWU) IRB approval via inter-institutional agreement on 10/8/2021.
    c. HRPO approval on 11/29/2021.
2. Convened our Advisory Board including individuals with SCI Lived Experience on 10/19/2021 and 5/10/2022 (Major Task 2).
    a. The purpose of these meetings is to review the project goals, protocol, and progress with the stakeholders in addition to obtaining their feedback related to potential recruitment and retention issues.
3. Identified the three members, determined the chair of our DSMB and held the initial DSMB meeting to review study aims and projected outcomes on 1/19/2022.
4. Held our study team kick-off meeting on 2/25/2022.
5. Initiated conversations with the VA North Texas Health Care System to explore partnership to develop educational meetings and workshops activities for study years 3 and 4 (Major Task 5).
    a. We established a monthly standing meeting to make steady progress towards this deliverable.
6. Completed staff training on study procedures, study protocol, TMS and SCI transfers.
7. Completed database development and have initiated quarterly data and source document checks.
8. Compiled Standard Operating Procedures and Data Management Plan.
9. Submitted a Protocol Revision with revised statement of work to the Business Office in December 2021 and received approval by HRPO.
    a. The Protocol Revision was for the addition of a control group who will not receive robotic gait training.
10. Initiated Patient Recruitment & Enrollment (Major Task 3).
    a. As of 9/15/2022:
        i. Screened 88 admits for study eligibility (Major Task 3).
        ii. Of the 14 eligible patients, we enrolled 7 participants into the study and began data collection (Major Task 3).
11. Coordinated TMS data sharing between BSW and TWU.
12. Presented the DOOR SCI study protocol at the American Spinal Injury Association (ASIA) Conference 2022 (Major Task 5).
13. Drafted a manuscript detailing the study protocol to the journal *Spinal Cord* (under review).
14. Obtained Continuing Review approval
    a. Baylor Scott & White (BSW) IRB approval on 7/21/2022

What opportunities for training and professional development has the project provided?

Members of the study team attended the following conferences:

2022 American Spinal Injury Association Conference in New Orleans, LA :

- Chad Swank, PT, PhD (PI)
    - Presented "A Retrospective Analysis of the Utilization of Robotic Exoskeleton Gait Training in Spinal Cord Injury during Inpatient Rehabilitation."
- Rita Hamilton, DO (Co-I)
- Seema Sikka, MD (Co-I)
- Alexandria Holden, MPH (Lead Coordinator)
    - Presented "Dosing Overground Robotic Gait Training after Spinal Cord Injury: Department of Defense Protocol"

2022 Academy of Spinal Cord Injury Professionals Conference in Kansas City, MO:

- Chad Swank, PT, PhD (PI)
    - Presented "Metabolic testing for exercise intensity during overground robotic exoskeleton gait training in two persons with complete tetraplegia."
- Rita Hamilton, DO (Co-I)
- Seema Sikka, MD (Co-I)
- Jaime Gillespie, PT, DPT (Study Therapist)
- Dannae Arnold, PT, DPT (Study Therapist)
    - Presented "Clinical delivery of overground exoskeleton gait training in persons with spinal cord injury across the continuum of care: a retrospective analysis"
- Lindsey Wynne, PT, DPT (Inpatient Physical Therapist)
    - Presented "Dynamic variable exoskeleton gait training following spinal cord injury in inpatient rehabilitation: A case series."

How were the results disseminated to communities of interest?

Presentations (oral and poster) at scientific meetings.

What do you plan to do during the next reporting period to accomplish the goals?

We intend to continue to screen and enroll participants into the study while conducting data collection across all assessment periods (Major Task 3). Additionally, we will continue to develop the educational workshops in collaboration with the VA (Major Task 5). We will also engage in dissemination efforts including publication of the study protocol manuscript which is currently under review (Major Task 5).

4. IMPACT:

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

This study is on track to provide the first evidence-based guidelines for RGT dosing (including outcomes related to walking function, neuroplasticity and feasibility) during inpatient and outpatient rehabilitation during the subacute phase of recovery after SCI. The principal discipline to benefit from the findings of this study is physical therapy. To date, physical therapists within BSW and those engaged in our Advisory Board and DSMB meetings have reported considerable interest in our study topic and findings. Additionally, physical therapy colleagues at ASIA2022 and ASCIP2022 during and following our scientific presentations indicate interest in our pending study findings.

What was the impact on other disciplines?

Rehabilitation is a team sport and this study takes place within inpatient and outpatient rehabilitation settings. The allied health providers (physician, nursing, occupational therapy, speech therapy) within BSW have collectively supported this study by helping identify interested patients and sharing IRB approved study flyers with patients.

Beyond the walls of BSW, conversations with colleagues at the VA North Texas Health Care System to develop educational workshops indicate interest in our pending study findings. Additionally, allied health colleagues at ASIA2022 and ASCIP2022 during and following our scientific presentations indicate interest in our pending study findings. Overall, the study has been well-received by our colleagues in the scientific community.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

We have engaged in initial conversations with robotic exoskeleton industry provider Ekso Bionics to strengthen our developing relationship. The goal of these conversations with the robotic exoskeleton industry whereby study findings can inform the 'next generation' of robotic exoskeleton technology. We hope to leverage this relationship with industry to facilitate 'next generation' of robotic exoskeletons to maximize outcomes for people after SCI.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Our original randomized control trial lacked a true (no RGT) control group. Based upon the recommendation of the Reviewers, our Advisory Board of individuals with SCI lived experience, and the DSMB, our study team met with our biostatistician Dr. Monica Bennett to explore the inclusion of a true control group as a fourth group. As a team, we arrived at consensus for the

following proposed amendments to the study protocol. This change to the protocol was approved in a revised Statement of Work and by HRPO, in addition to our local IRB.

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

As planned, we initiated recruitment and enrollment during Y1Q3. During the Y1Q3-Q4, recruitment has been slower than initially anticipated (n=13 patients/quarter). This slower recruitment rate is partially explained by not initiating recruitment until the second month of Y1Q3 as we awaited IRB approval for the addition of the control arm to the study. A second potential reason for the slower recruitment has been the complexion of patients admitted to our inpatient rehabilitation facility. Of those screened (n=88), a majority have not been eligible to participate in the study. Common reasons for exclusion include:

- Not motor incomplete (AIS level C or D) (n=61)
- Patient lives >90 miles away from the rehabilitation facility (n=18)
- Not within the acute/subacute recovery period (i.e. greater than 6-months post-injury) (n=17)
- Patient did not meet Ekso manufacturer device requirements (n=19)

As of 9/15/2022, 14 patients met the eligibility criteria and were approached to participate in the study. However, 7 patients declined to participate. Commonly expressed reasons for declined to participate were 1) having no interest in study participation, 2) feeling overwhelmed, 3) not wanting to risk being randomized to the control group), 4) concerns over access to transportation (for post-inpatient rehabilitation RGT sessions and assessments), 5) unease over additional caregiver burden, and 6) desire to prioritize other activities.

We are undertaking the following action steps to identify solutions to increase enrollment:

- We are examining our internal screening and recruitment processes,
- We are engaging with our stakeholders with SCI Lived Experience,
- We are engaging with our DSMB.

Changes that had a significant impact on expenditures

None to report.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

None to report.

Significant changes in use or care of vertebrate animals

N/A.

Significant changes in use of biohazards and/or select agents

None to report.

6. PRODUCTS:

- **Publications, conference papers, and presentations**

Journal publications.

Holden, A, Ochoa, C, Hamilton, R, Sikka, S, Goh, H-T, Driver, S, & Swank, C. (September 2022) Dosing Overground Robotic Gait Training after Spinal Cord Injury: A Randomized Clinical Trial Protocol. Submitted to Spinal Cord (under review).

Books or other non-periodical, one-time publications.

Nothing to report.

Other publications, conference papers and presentations.

Conference Presentations:

Gillespie, J, Holden, A, Callender, L, Bennett, M, Driver, S, Sikka, S & Swank, C. (May 2022) A Retrospective Analysis of the Utilization of Robotic Exoskeleton Gait Training in Spinal Cord Injury during Inpatient Rehabilitation. American Spinal Injury Association 2022 Annual Scientific Meeting. New Orleans, LA.

Holden, A, Hamilton, R, Sikka, S, Goh, H-T, Driver, S, & Swank, C. (May 2022) Dosing Overground Robotic Gait Training after Spinal Cord Injury: Department of Defense Protocol. Presented at the ASIA 2022 Annual Scientific Meeting held in New Orleans, LA.

Wynne, L, Arnold, D, Gillespie, J, Trammell, M, & Swank, C. (September 2022) Dynamic variable exoskeleton gait training following spinal cord injury in inpatient rehabilitation: A case series. Academy of Spinal Cord Injury Professionals. Kansas City, MO.

Arnold, D, Gillespie, J, Trammell, M, Stevens, C, Bennett, M, Callender, L, Sikka, S, & Swank, C. (September 2022) Clinical delivery of overground exoskeleton gait training in persons with spinal cord injury across the continuum of care: a retrospective analysis. Academy of Spinal Cord Injury Professionals. Kansas City, MO. (oral presentation).

Brown, K, Trammell, M, Moore, A, Weeks, A, Wynne, L, Gilliland, T, Reynolds, M, McShan, E, Driver, S, Sikka, S, Hamilton, R, & Swank, C. (September 2022) Metabolic testing for exercise intensity during overground robotic exoskeleton gait training in two persons with complete tetraplegia. Academy of Spinal Cord Injury Professionals. Kansas City, MO.

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Nothing to report.

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Name: Chad Swank, PT, PhD
Project Role: Principal Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0002-7865-179X
Nearest person month worked: 3.0
Contribution to Project: Dr. Swank oversees all aspects of the project including scientific oversight and management of day-to-day issues that arise (e.g., leading weekly meeting, budget, IRB, recruitment), attends weekly meetings, provides training and supervision on assessments of functional measures (10-meter walk test, WISCI-II), and oversees recruitment strategies, Consumer Advocates, data collection, results, and dissemination activities.

Name: Simon Driver, PhD
Project Role: Co- Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0003-2356-432X
Nearest person month worked: 1.2
Contribution to Project: Dr. Driver attends weekly meetings, supports Dr. Swank with study administration including actigraphy, assists with recruitment strategies, protocol for treatment fidelity, data collection, results, and dissemination activities.

Name: Rita Hamilton, DO
Project Role: Co- Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0002-8893-2739
Nearest person month worked: 1.2
Contribution to Project: Dr. Hamilton attends weekly meetings, provides medical oversight, rehabilitation hospital administrative assistance, and assists with screening, recruitment, results, and dissemination activities.

Name: Seema Sikka, MD
Project Role: Co- Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0003-4918-4480
Nearest person month worked: 1.2
Contribution to Project: Dr. Sikka attends weekly meetings, provides medical oversight, and assists with screening, recruitment, results, and dissemination activities.

Name: Hui-Ting Goh, PT, PhD
Project Role: Co- Investigator
Researcher Identifier (e.g. ORCID ID): 0000-0001-9460-9869
Nearest person month worked: 3.0
Contribution to Project: Dr. Goh oversees the TWU subaward, attend weekly meetings, administers TMS assessments, processes and analyzes TMS data, trains staff for assisting with TMS assessments, and assists with results and dissemination activities.

Name: Hui-Ting Shih, PhD
Project Role: Postdoctoral Researcher
Researcher Identifier (e.g. ORCID ID): 0000-0002-1757-9691
Nearest person month worked: 6.0
Contribution to Project: Dr. Shih started her post-doctoral fellowship 09/01/2022 under the mentorship of Drs. Swank (PI) and Driver (Co-I). She has completed training on the study protocol including with Dr. Goh to collect TMS data and troubleshoot issues. Dr. Shih attends weekly meetings, assists with recruitment strategies, protocol for treatment fidelity, data collection, results, and dissemination activities.

Name: Alexandria Holden
Project Role: Lead Project Coordinator
Researcher Identifier (e.g. ORCID ID): 0000-0001-9533-9872
Nearest person month worked: 12.0
Contribution to Project: Ms. Holden serves as the project coordinator and is responsible for recruitment and project management.

Name: Christa Ochoa
Project Role: Project Coordinator
Researcher Identifier (e.g. ORCID ID): 0000-0002-9252-5247
Nearest person month worked: 7.2

Contribution to Project: Ms. Ochoa has provided data management/quality assurance and database maintenance during the study-startup phase and initial recruitment/enrollment period. She has also handled all IRB and DoD correspondence.

Name: Librada Callender
Project Role: Project Manager
Researcher Identifier (e.g. ORCID ID): 0000-0002-8655-6952
Nearest person month worked: 0.6
Contribution to Project: Ms. Callender has worked with coordinators and Dr. Swank to ensure progress of the project towards the quarterly goals has been achieved.

Name: Faith Meza
Project Role: Project Coordinator
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 3.0
Contribution to Project: Ms. Meza has assisted with study screening, enrollment, and recruitment. She is also currently working on scheduling, data collection, data entry, and planning for the Years 3 and 4 workshops.

Name: Dannae Arnold
Project Role: Research Physical Therapist
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 3.0
Contribution to Project: Ms. Arnold has completed study-related training and assisted with study recruitment, assessments, and intervention delivery.

Name: Jaime Gillespie
Project Role: Research Physical Therapist
Researcher Identifier (e.g. ORCID ID): N/A
Nearest person month worked: 3.0
Contribution to Project: Ms. Gillespie has completed study-related training and assisted with study recruitment, assessments, and intervention delivery.

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report.

What other organizations were involved as partners?

Organization Name: Texas Woman's University

Location of Organization: Dallas, Texas
Partner's contribution to the project: Collaboration with Dr. Hui-Ting Goh

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: Not applicable.

QUAD CHARTS: See attachments.

9. APPENDICES:

APPENDIX I.

ASIA 2022 Conference Abstracts, presented May 2022:

Title: Dosing Overground Robotic Gait Training after Spinal Cord Injury: Department of Defense Protocol

Authors: Alexandria Holden, Rita Hamilton, Seema Sikka, Hui-Ting Goh, Simon Driver, Chad Swank,

Abstract/Course Body Background: Robotic exoskeletons have changed rehabilitation care available to people after spinal cord injury (SCI). Our pilot data suggest that using overground robotic gait training (RGT) can be feasibly integrated into acute clinical practice, yield greater improvements in gait than usual care, and enable a dose of 140% more minutes walking than usual care. Yet, the current evidence base is insufficient to identify the optimal dose and neurophysiological mechanism of RGT as an effective rehabilitation approach. We will 1) examine whether the frequency of RGT after motor incomplete SCI impact's function and health outcomes, 2) analyze the difference of the neuroplastic effect of RGT dose as measured by transcranial magnetic stimulation (TMS), 3) evaluate the safety (rate of adverse events), tolerability (visual analog scale), and feasibility (treatment completion rate) of delivering different RGT dose. Study Design: We will randomize 138 patients with motor incomplete SCI into 1 of 3 RGT frequency groups (high, moderate, or low) based on injury severity and level. Patients will complete assessments at 5 time points: inpatient admission and discharge, after completing 24 RGT sessions, 1-month post-RGT, and 9-months post-SCI. RGT sessions will use the Ekso robotic exoskeleton [class II medical device (United States FDA)]. Our primary outcome is WISCI-II. Secondary outcomes are gait speed, Spinal Cord Independence Measure, Numeric Pain Rating Scale, Fatigue Severity Scale, Penn Spasm Frequency Scale, Patient Health Questionnaire-9, Life Satisfaction Questionnaire-9, and physical activity. Neurophysiological measures will include MEP amplitudes obtained using TMS. Dosing effects of RGT will be evaluated using general linear mixed effects models to analyze differences between groups, settings, and the interaction. Clinical Impact: Our study tackles critical questions of dosing gait training interventions for people with SCI during subacute rehabilitation and links dose with neurophysiological markers of neuroplasticity with delivery across rehabilitation care settings. Support: DOD, W81XWH-21-1-0922 The contents of this abstract were developed under a grant from the Department of Defense office of the Congressionally Directed Medical Research Programs (grant number W81XWH2110922). Opinions, interpretations, conclusions, and recommendations are those of the author(s) and are not necessarily endorsed by the Department of Defense.

Learning Objectives: Discuss robotic gait training as a rehabilitation tool and potential impact on neuroplasticity, function, and health outcomes.

Title: A Retrospective Analysis of the Utilization of Robotic Exoskeleton Gait Training in Spinal Cord Injury during Inpatient Rehabilitation

Authors: Jaime Gillespie[1], Alexandria Holden[2], Librada Callender[1,2], Monica Bennett[2], Simon Driver[1,2], Seema Sikka[1,3] & Chad Swank[1,2]

[1]Baylor Scott & White Institute for Rehabilitation; [2]Baylor Scott & White Research Institute; [3]Baylor Scott & White University Medical Center

Purpose: Technological advancements in rehabilitation enable overground robotic exoskeleton gait training (RGT) in patients with spinal cord injury (SCI). Yet, routine utilization of RGT in inpatient rehabilitation is minimal even within SCI Model Systems centers. Integration of RGT into clinical practice during inpatient rehabilitation is feasible and well-tolerated by patients although session details concerning the use of RGT are poorly characterized. Our purpose was to describe RGT session details with patients with SCI during inpatient rehabilitation.

Participants: Patients admitted to a large, urban inpatient rehabilitation facility between September 2016 to August 2021 with SCI who completed at least one RGT session during inpatient rehabilitation. Eligibility for RGT included meeting robotic exoskeleton manufacturer and clinical criteria.

Methods: Retrospective review of medical records over five years. RGT session data included frequency, dose, and device assistance details. Functional data was analyzed and comprised initially of Functional Independence Measure (FIM) scores and transitioned to Continuity Assessment and Record Evaluation (CARE) scores as mandated by the Center for Medicare and Medicate Services.

Results: Of 1,203 SCI admissions, 73 patients (6.1%) met our criteria and were included in the analysis. Patients averaged 46.8 ± 17.3 years and were primarily male (68.5%), white (68.5%), tetraplegic (49.3%), non-traumatic (34.2%) and variable severity [ASIA Impairment Scale A (11.0%), B (13.7%), C (21.9%), D (19.2%)]. Patients completed an average of 6.2±4 sessions (ranging = 1 to 19) during inpatient rehabilitation (median length of stay = 43 days). On average, up time (16:20 to 23:49 minutes), walk time (9:48 to 20:17 minutes), and step count (286.1 to 692.2) increased while exoskeleton device swing assistance (left: 92.7 to 73.2, right: 93.1 to 77.7) decreased. The most common exoskeleton device assistance mode utilized was “bilateral adapt” (>95% of sessions) indicating lower extremities were provided with variable assistance during swing phase of gait. Mid-session assist mode changes were rare (4 total sessions) but were made to allow the patient more independent with stepping. Functional changes were observed for both FIM motor (29.9±15.2 points) and CARE Self-Care/Mobility-Walk (33.9±19 points) scores.

Conclusion: Patients with SCI demonstrated improved walking parameters and reduced device assistance over time during RGT sessions. Therapists consistently selected variable assistance mode with RGT regardless of injury level or severity.

Clinical Relevance: Robotic exoskeletons may be a useful tool for progressing walking interventions for patients with incomplete SCI during inpatient rehabilitation. Future studies should explore the association of RGT session details with mobility and health outcomes.

Learning Objectives:
Discuss robotic exoskeleton gait training session details with patients with SCI during inpatient rehabilitation.

References
Swank, C., Sikka, S., Driver, S., Bennett, M., & Callender, L. (2020). Feasibility of integrating robotic exoskeleton gait training in inpatient rehabilitation. *Disability and Rehabilitation: Assistive Technology*, *15*(4), 409-417.

Heinemann, A. W., Jayaraman, A., Mummidisetty, C. K., Spraggins, J., Pinto, D., Charlifue, S., ... & Field-Fote, E. C. (2018). Experience of robotic exoskeleton use at four spinal cord injury model systems centers. *Journal of Neurologic Physical Therapy*, *42*(4), 256-267.

Bach Baunsgaard, C., Vig Nissen, U., Katrin Brust, A., Frotzler, A., Ribeill, C., Kalke, Y. B., León, N., Gómez, B., Samuelsson, K., Antepohl, W., Holmström, U., Marklund, N., Glott, T., Opheim, A., Benito, J., Murillo, N., Nachtegaal, J., Faber, W., & Biering-Sørensen, F. (2018). Gait training after spinal cord injury: safety, feasibility and gait function following 8 weeks of training with the exoskeletons from Ekso Bionics. Spinal cord, 56(2), 106–116. https://doi.org/10.1038/s41393-017-0013-7

Mekki, M., Delgado, A. D., Fry, A., Putrino, D., & Huang, V. (2018). Robotic Rehabilitation and Spinal Cord Injury: a Narrative Review. Neurotherapeutics : the journal of the American Society for Experimental NeuroTherapeutics, 15(3), 604–617. https://doi.org/10.1007/s13311-018-0642-3

Brazg, G., Fahey, M., Holleran, C. L., Connolly, M., Woodward, J., Hennessy, P. W., ... & Hornby, T. G. (2017). Effects of training intensity on locomotor performance in individuals with chronic spinal cord injury: a randomized crossover study. *Neurorehabilitation and neural repair*, *31*(10-11), 944-954.

APPENDIX II.

ASCIP 2022 Conference Abstracts, presented September 2022:

Title: Exoskeleton gait training across the continuum of care following spinal cord injury: a retrospective analysis.

Authors: Dannae Arnold, PT, DPT, ATP[1, 2]; Jaime Gillespie PT, DPT[1, 2]; Molly Trammell, PT[1]; Christi Stevens, PT[1]; Monica Bennett, PhD[2]; Librada Callender, MPH[1,2]; Seema Sikka, MD[1,3]; Chad Swank, PT, PhD, NCS[1,2]

[1]Baylor Scott & White Institute for Rehabilitation; [2]Baylor Scott & White Research Institute; [3]Baylor Scott & White University Medical Center

Background: After spinal cord injury (SCI), rehabilitation begins during inpatient (IP) and continues through outpatient (OP) settings. Overground exoskeleton gait training (OEGT) is feasible in both settings, yet no guidelines exist for its use across the continuum.

Objective: To describe the clinical use of OEGT initiated during IP and continued through OP.

Design: Retrospective review of medical records from 2018-2021 of patients with SCI who completed at least one OEGT session during IP and OP.

Methods: Demographic data, clinical outcomes, and OEGT session details [frequency, "walk" time , "up" time, step count, and device assistance settings] were extracted from the medical record.

Results: Eighteen patients met criteria: male (83%), white (61%), aged 37.4±15 years, tetraplegic (53%), ASIA Impairment Scale A (22%), B (28%), C (39%), D (11%). OEGT sessions (IP=8.8±5.3; OP=11.5±8.9) were completed over 17.7±7.3 weeks. Across sessions, "walk" time (11:49±7:06 minutes to 26:43±13:36), "up" time (16:39±6:12 minutes to 31:34±15:46), and step count (361.7±249.6 to 792.4±466.5) increased while assistance for left (78.4±7.3 to 70.1±10.5) and right (79.4±8.1 to 67.6±11.7) step decreased. Initially, the most common exoskeleton software setting was "Bilateral Adapt", indicating device assistance provided as needed for limb swing. As sessions continued, mid-session setting changes became more frequent to encourage reduced device assistance. Session details were communicated from IP to OP allowing uninterrupted progression of OEGT.

Conclusions: OEGT was integrated into clinical practice following SCI across IP and OP, though more sessions were completed during OP. Coordinated communication between IP and OP contributed to seamless session progression.

Keywords: Neurological Rehabilitation; Exoskeleton Device; Spinal Cord Injury; Physical Therapy; Walking.

Learning Objectives:

1. Describe the use of overground exoskeleton gait training across inpatient and outpatient rehabilitation settings.
2. Examine the clinical results associated with overground exoskeleton gait training following spinal cord injury.
3. Discuss progression of gait training using an exoskeleton device across the continuum of care.

References:

1. Delgado AD, Escalon MX, Bryce TN, Weinrauch W, Suarez SJ, Kozlowski AJ. Safety and feasibility of exoskeleton-assisted walking during acute/sub-acute SCI in an inpatient rehabilitation facility: A single-group preliminary study. *The journal of spinal cord medicine*. 2020;43(5):657-666.
2. Esquenazi A, Talaty M, Jayaraman A. Powered exoskeletons for walking assistance in persons with central nervous system injuries: a narrative review. *PM&R*. 2017;9(1):46-62.
3. Heinemann AW, Jayaraman A, Mummidisetty CK, et al. Experience of robotic exoskeleton use at four spinal cord injury model systems centers. Journal of Neurologic Physical Therapy. 2018;42(4):256-267.
4. Kaiser A, Chan K, Pakosh M, Musselman KE. Characteristics of activity-based therapy interventions for people living with spinal cord injury or disease across the continuum of care: a scoping review protocol. BMJ open. 2020;10(7):e040014.
5. Manns PJ, Hurd C, Yang JF. Perspectives of people with spinal cord injury learning to walk using a powered exoskeleton. Journal of neuroengineering and rehabilitation. 2019;16(1):1-10.
6. Miller LE, Zimmermann AK, Herbert WG. Clinical effectiveness and safety of powered exoskeleton-assisted walking in patients with spinal cord injury: systematic review with meta-analysis. Medical devices (Auckland, NZ). 2016;9:455.
7. Swank C, Sikka S, Driver S, Bennett M, Callender L. Feasibility of integrating robotic exoskeleton gait training in inpatient rehabilitation. Disability and Rehabilitation: Assistive Technology. 2020;15(4):409-417.
8. Wallace MA, Kendall MB. Transitional rehabilitation goals for people with spinal cord injury: looking beyond the hospital walls. Disability and rehabilitation. 2014;36(8):642-650.

Title: Dynamic variable exoskeleton gait training following spinal cord injury in inpatient rehabilitation: A case series.

Authors: Lindsey Wynne, PT, DPT, NCS; Dannae Arnold, PT, DPT, ATP; Jaime Gillespie, PT, DPT; Molly Trammell, PT; Seema Sikka, MD; Faith Meza, MPH; Angelo Abis, SPT; Chad Swank, PT, PhD, NCS

[1]Baylor Institute for Rehabilitation, Dallas, Texas, [2]Baylor Scott & White Research Institute, Dallas, Texas

Context: Promoting gait adaptability is critical for improving gait following spinal cord injury (SCI). Recent advances in exoskeleton technology allow for dynamic stepping tasks (e.g. multidirectional stepping, challenging stability by reducing device assistance, adding resistance to step trajectory) during overground exoskeleton gait training (OEGT). This case series describes incorporating dynamic stepping tasks during OEGT for three individuals with incomplete SCI during inpatient rehabilitation. Outcomes included OEGT session metrics [step count and walk duration], walking measures [Walking Index for Spinal Cord Injury-revised (WISCI-II) and 10-meter walk test (10mWT)], and cardiovascular intensity [heart rate (HR), rate of perceived exhaustion (RPE)].

Findings: Patients [males, aged 29 to 51 years, with tetraplegia, ASIA Impairment Scale D (AIS D)] completed OEGT [sessions Patient A=2, Patient B=4, Patient C=3; walk duration (average minutes) A=21:03, B=18:24, C=21:40; step count A=1290, B=835, C=664] during inpatient rehabilitation. Positive changes were observed in WISCI-II (A=12 levels, B=20, C=20 and gait speed (A=3.16m/s, B=2.12m/s, C=1.26 m/s). Moderate HR intensity (A=34% of OEGT session, B=75%, C=36%) and high HR intensity (A=1%, B=2.5%, C=22%) were observed during OEGT sessions. Patients generally perceived attaining moderate intensity (RPE: A=2, B=6, C=5).

Clinical Relevance: Contemporary exoskeleton devices allow for dynamic stepping tasks beyond active assistance gait training. Dynamic stepping tasks were incorporated during OEGT for 3 patients with AIS D tetraplegia SCI to maximize gait training progression during inpatient rehabilitation. Physiologic and patient-report indicators of cardiovascular intensity suggest dynamic stepping tasks during OEGT were tolerated without undue burden.

Learning Objectives:

1. Explore dynamic step training within an OEGT for patients with incomplete SCI.
2. Describe methods to increase variability within gait interventions for patients with incomplete SCI.
3. Identify improvements in overground ambulation outcome measures after performing OEGT intervention.

Source of Funding: Baylor Research Institute in collaboration with National Institute on Disability, Independent Living, and Rehabilitation Research

Keywords: spinal cord injury; exoskeleton device; gait; heart rate

References:

1. Swank C, Sikka S, Driver S, Bennett M, Callender L. Feasibility of integrating robotic exoskeleton gait training in inpatient rehabilitation. *Disability and Rehabilitation: Assistive Technology*. 2020; 15(4):409-417.
2. Bach Baunsgaard C, Vig Nissen U, Katrin Brust A, Frotzler A, Ribeill C, Kalke YB, León N, Gómez B, Samuelsson K, Antepohl W, Holmström U, Marklund N, Glott T, Opheim A, Benito J, Murillo N, Nachtegaal J, Faber W, Biering-Sørensen F. Gait training after spinal cord injury: Safety, feasibility and gait function following 8 weeks of training with the exoskeletons from Ekso Bionics. *Spinal Cord*. 2018; 56(2):106–116.
3. Brazg G, Fahey M, Holleran CL, Connolly M, Woodward J, Hennessy PW, Hornby T. Effects of training intensity on locomotor performance in individuals with chronic spinal cord injury: A randomized crossover study. *Neurorehabilitation and Neural Repair*. 2017; 31(10-11):944-954.
4. Leech K, Kinnaird C, Holleran C, Kahn J, Hornby T. Effects of locomotor exercise intensity on gait performance in individuals with incomplete spinal cord injury. *Physical Therapy Journal.* 2016; 96-(12):1919-1929.
5. Sohn WJ, Tan AQ, Hayes HB, Pochiraju S, Deffeyes J, Trumbower RD. Variability of leg kinematics during overground walking in persons with chronic incomplete spinal cord injury. *J Neurotrauma*. 2018;35(21):2519-2529.

Title: Metabolic testing for exercise intensity during overground robotic exoskeleton gait training in two persons with complete tetraplegia.

Authors: Katelyn Brown[1,3], MS, Molly Trammell[2], PT, DPT, Ashlyn Moore[2], PT, DPT, Ariana Weeks[2], PT, DPT, Lindsey Wynne[2], PT, DPT, NCS, Taylor Gilliland[1,3], MS, Chol Ho James Kim[1,3], BS, BA, Megan Reynolds[1,3], MS, Evan McShan[1,3], MS, Simon Driver[1,2, 3]PhD, Seema Sikka[2], MD, Rita Hamilton[2], DO, Chad Swank[2, 3], PT, PhD

Affiliations: [1]Baylor Scott & White Sports Therapy & Research Center, Frisco, TX, USA, [2]Baylor Scott & White Institute for Rehabilitation, Dallas, TX, USA, [3]Baylor Scott & White Research Institute, Dallas, TX, USA.

Context
Participation in moderate-to-vigorous intensity physical activity (MVPA) is recommended to reduce chronic disease risk in individuals following spinal cord injury (SCI). Assessing exercise intensity using traditional methods (e.g., heart rate, rate of perceived exertion) may be inaccurate in patients with tetraplegia due to neuromuscular and autonomic dysfunction. Direct gas analysis may be more accurate. Overground robotic exoskeleton gait training (OEGT) can be physiologically demanding. Yet, its utility in facilitating MVPA in patients with chronic and acute complete tetraplegia has not been explored. We present the results of two participants who completed one OEGT session with intensity assessed using a portable metabolic system and expressed in metabolic equivalents (METs).

Findings
METs were calculated using a rolling 30-second average with 1 MET defined as 2.7 mL/kg/min and MVPA defined as MET ≥3.0. Participant A (28-year-old male, BMI 16.7) with a chronic (>10 yrs) SCI (C5-C6, AIS A) completed 37.39 min of OEGT (28.9 min walking) achieving 1,047 steps. Peak METs were 2.9 (average 2.3). Participant B (21-year-old male, BMI 17.3) with an acute (<3 months) SCI (C4, AIS A) completed 42.33 min of OEGT (40.5 min walking) achieving 1,023 steps. Peak METs were 3.3 (average 2.5) with 12% of walk time spent in MVPA. Both participants tolerated activity well without observed adverse responses to activity.

Clinical Relevance
OEGT may be an effective training modality to attain moderate intensity exercise patients with acute tetraplegia. However, chronicity of SCI may play a role in exercise intensity achieved.

Keywords: Ekso, spinal cord injury, metabolic testing, oxygen consumption, rehabilitation