AWARD NUMBER: W81XWH-21-1-0541

TITLE: Chronic Studies of Spinal Cord Stimulation for Restoration of Bladder Function

PRINCIPAL INVESTIGATOR: Warren Grill

CONTRACTING ORGANIZATION: Duke University, Durham, NC

REPORT DATE: October 2023

TYPE OF REPORT: Annual

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
October 2023	Annual	01Sep2022-31Aug2023

4. TITLE AND SUBTITLE

Chronic Studies of Spinal Cord Stimulation for Restoration of Bladder Function

5a. CONTRACT NUMBER
W81XWH-21-1-0541

5b. GRANT NUMBER
SC200190

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Warren Grill, PhD (Prime PI),
Em Abbott, PhD

E-Mail: warren.grill@duke.edu

5d. PROJECT NUMBER
0011611760

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Duke University
2200 W Main St Ste 710
Durham, NC 27708-4677

8. PERFORMING ORGANIZATION REPORT NUMBER

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

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

10. SPONSOR/MONITOR'S ACRONYM(S)

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

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for Public Release; Distribution Unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT
Our objective is to conduct chronic in vivo studies of a novel approach to treat urinary incontinence and poor bladder emptying following spinal cord injury (SCI). We will measure changes in bladder storage and voiding function produced by epidural kilohertz-frequency spinal cord stimulation (KHF SCS) in preclinical experiments in rats. This novel mode of SCS is used successfully to treat chronic pain but has not been developed for treatment of bladder dysfunction. Our acute studies revealed that KFH SCS at four weeks after complete spinal transection reduced the very large bladder capacities that result from SCI, increased voiding efficiency, and reduce non-voiding contractions. While promising, these experiments were limited to terminal acute studies under anesthesia. To advance this novel therapeutic approach, we are conducting chronic studies of the effects of KHF SCS on bladder function in awake, behaving animals following either transection or contusion SCI. These studies take advantage of our established capacity to deliver on-demand electrical stimulation and continuously monitor bladder pressure, external urethral sphincter (EUS) activity, and voiding behavior in awake, behaving animals.

15. SUBJECT TERMS
Spinal cord injury, bladder, electrical stimulation, therapy

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

TABLE OF CONTENTS

1. INTRODUCTION:

Spinal cord injury (SCI) causes bladder dysfunction, specifically urinary incontinence and the inability to empty the bladder voluntarily. Bladder dysfunction after SCI shares pathophysiologies with neuropathic pain. There are commercially available and successful treatments for chronic pain using high frequency electrical stimulation in people, but these therapies have not been developed to treat bladder dysfunction. In this study, we evaluate changes in bladder storage and voiding function produced by epidural kilohertz-frequency spinal cord stimulation (KHF SCS) in preclinical experiments in rats. Our objective is to conduct chronic in vivo studies to advance a novel therapeutic approach that restores bladder function for individuals living with SCI.

2. KEYWORDS:

spinal cord injury, bladder, electrical stimulation, therapy

3. ACCOMPLISHMENTS:

What were the major goals of the project?

Major Goals	Target Date	Completion
Major Task 0: Submit regulatory documents and obtain necessary approvals for study initiation	12/1/2021	100%, 5/10/2021
Milestone(s) Achieved: Duke University IACUC protocol approved, DoD ACURO approval obtained.		
Specific Aim 1: Chronic Evaluation of KHF Spinal Cord Stimulation Following Transection SCI		
Major Task 1.1: Conduct survival surgeries (n=10) to implant telemeter and SCS electrodes.	2/1/2022	30%
Major Task 1.2: Baseline monitoring (2 weeks) of bladder function in metabolic cages (n=10 from MT1.1). (n=10 for no telemeters, n=3 for telemeters)	3/1/2022	30%
Major Task 1.3: Conduct survival surgical procedures (n=10 from MT1.2) to administer transection SCI surgeries & recovery.	5/1/2022	0%
Major Task 1.4: Ongoing weekly assessment of effects of KHF SCS on voiding in metabolic cages (n=10 from MT1.3).	9/1/2022	0%
Major Task 1.5: Conduct data processing and statistical analysis to quantify effects of KHF SCS on voiding behavior.	11/1/2022	0%
Milestone(s) Achieved: During the reporting activity, we have addressed critical roadblocks which include substantial and unanticipated delay in obtaining electrodes, optimizing data transmission through telemeters, and training personnel to provide care of SCI rats. With these accomplishments in training and refinement we are now poised to collect chronic in vivo data of bladder function after SCI.		

What was accomplished under these goals?

In this study, we evaluate changes in bladder storage and voiding function produced by epidural kilohertz-frequency spinal cord stimulation (KHF SCS) in preclinical experiments in rats. To deliver KHF SCS, we surgically implant a paddle electrode into the epidural space of the spinal cord. To measure bladder function, we surgically implant a wireless radio telemeter device in the abdomen of rats. The telemeter implant has electromyography (EMG) leads that measure muscle activity of the external urethral sphincter (EUS) and a pressure gauge that measures detrusor muscle (bladder) activity.

Subtask 0.1: Obtain Duke University IACUC approval for rat experiments
For the use of rats, we secured DUKE IACUC approval for protocol number A079-21-04 on April 20, 2021 entitled “Chronic Studies of Spinal Cord Stimulation for Restoration of Bladder Function.” IACUC approval expires March 31, 2024.

Subtask 0.2: Submit documents for rat experiments to DoD ACURO
We submitted documents to the Animal Care and Use Review Office (ACURO) and received approval on May 10, 2021 for protocol number SC200190.e001.

Subtask 0.3: Review and make modifications as needed to regulatory document, and obtain ACURO approval
We have not modified procedures described in protocol A079-21-04. In the event of any significant changes, we will follow Duke and DoD policies for review and approval.

Major Task 1.1: Conduct survival surgeries to implant telemeter and SCS electrodes.
We made progress toward achieving MT 1.1, notwithstanding significant and unexpected delays in receiving spinal cord stimulation electrodes from our manufacturer, Dyconex, which extended until August 2023 (Problem 1.1a). These delays necessitated significant adjustments to our project timeline. Nevertheless, Dr. Abbott strategically pivoted her efforts. Initially, she dedicated her time to enhancing her proficiency in spinal cord electrode implantation (MT2.1) and spinal cord contusion injury (MT2.2). These skill enhancements significantly bolster our research capabilities throughout the entire project timeline, enabling more precise injuries and improved data collection outcomes. Furthermore, we successfully addressed data transmission issues, achieving nearly a 90% reduction in lost data packets (Problem 1.1b). This resolved issue, which had persisted from the previous reporting period, will substantially enhance the quality of our data.

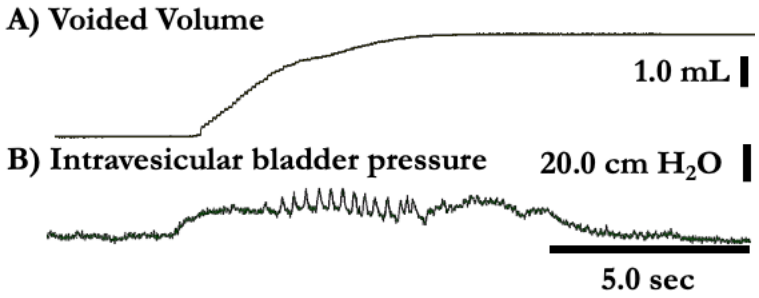


Figure 1.1: Exemplary time-series data of *in vivo* voiding event with <u>resolved data dropout issues (0.33% missed packets during 24hr recording)</u> Key experimental parameters collected by project lead of baseline bladder function were recorded in our metabolic cage of **A)** total weight of urine voided (mL) collected on a scale and **B)** telemeter pressure sensor data (cm H_2O)

Major Task 1.2: Baseline monitoring (2 weeks) of bladder function in metabolic cages (n=10) from MT1.1).
We successfully collected baseline bladder function data from 10 rats without telemeters and from 2 rats with implanted telemeters, all while using the new versions of Stellar Commander software and firmware in the telemeters. The resolution of the data dropout issues has instilled us with the confidence to proceed with the implantation of telemeters in our upcoming research activities.

Major Task 1.3: Conduct survival surgical procedures to administer transection SCI surgeries & recovery.
Recognizing the need for consistent, high-quality care for our spinalized rats, Dr. Abbott facilitated comprehensive training project for undergraduate research assistants. As a result, four undergraduate researchers achieved proficiency in important tasks, including postoperative animal care, sensorimotor behavioral testing (BBB locomotor evaluation), metabolic behavioral data acquisition, and assisting with sterile surgical procedures and anesthesia. This accomplishment ensures that we have a dedicated and skilled team available to support our studies.

Our experience with undergraduate personnel has brought to light two significant challenges. First, we found that we had overestimated their availability (Problem 1.3a), and second, we had underestimated the time required to train undergraduates to reach a level of independence (Problem 1.3b). These challenges created staffing challenge. The positive outcome of these experiences is the development of supporting documentation, such as onboarding task lists, animal care sheets, surgical equipment lists, and extensive beginner-friendly manuals, which have proven instrumental in streamlining the training process for new staff members.

To address these challenges and maintain a strong and capable research team, Dr. Abbott led the recruitment and hiring process for a full-time animal care technician. This role will play a critical part in safeguarding the well-being of our chronic in vivo research animals.

Major Task 1.4: Ongoing weekly assessment of effects of KHF SCS on voiding in metabolic cages
While waiting for plated electrodes from Dyconex, Dr. Abbott trained in electrode implantation and stimulation on acute terminal surgery rats (MT3.6) under the guidance of Dr. Eric Gonzalez. These skills will improve the outcomes of surgery.

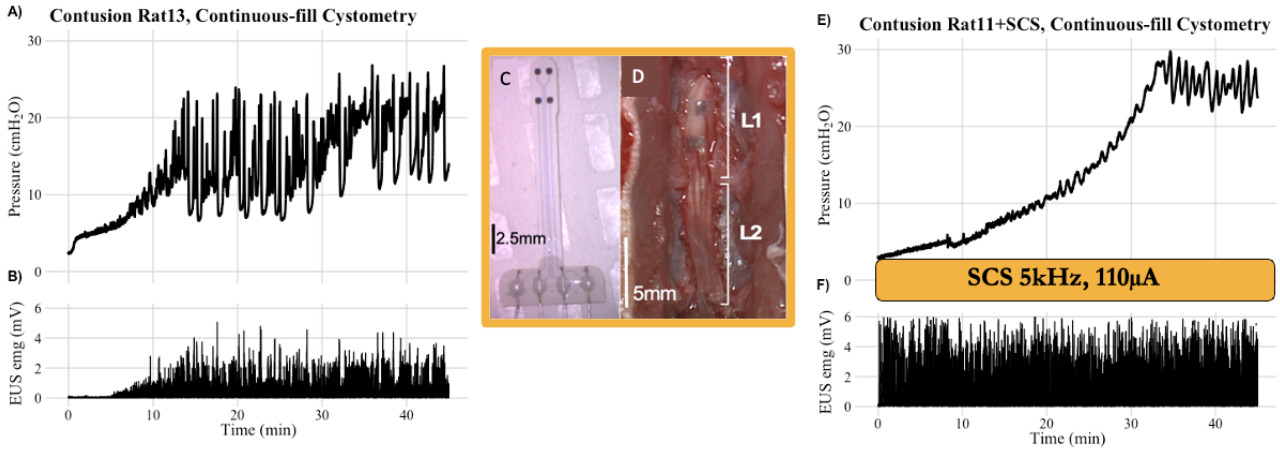


Figure1.4: Successful instrumentation of in-house plated electrode and kilohertz frequency stimulation on S1 spinal cord of urethane anesthetized rats 3 weeks post contusion spinal cord injury.

Major Task 2.3: Conduct survival surgical procedures to administer contusion SCI injuries & recovery

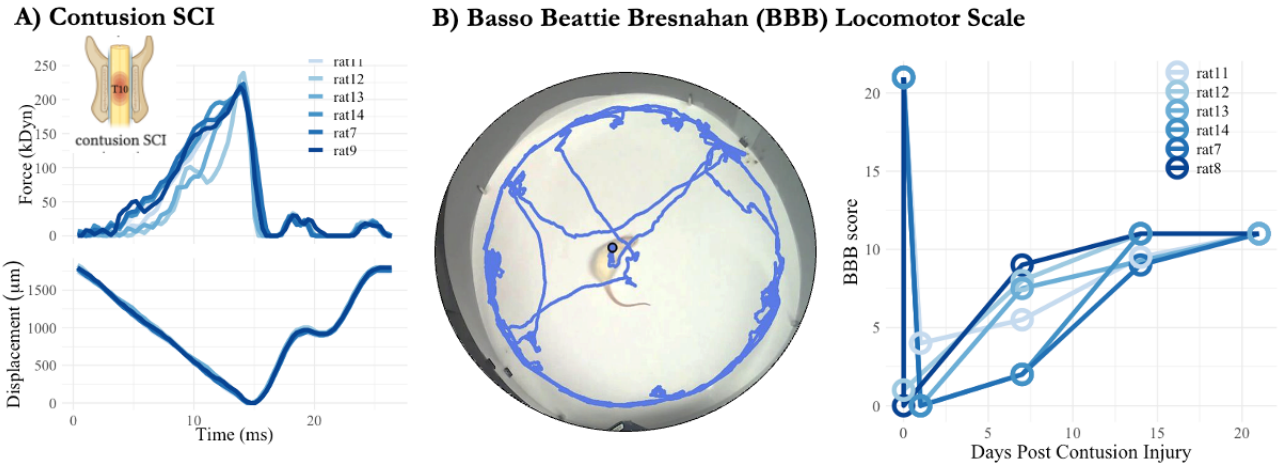


Figure 2.3 A) Surgical training achieved controlled contusion injuries at T9 using the IH-0400 Impactor (Precision Systems and Instrumentation, Lexington, KY). B) Undergraduate researchers achieved proficiency in conducting BBB locomotor tests during recovery period.

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

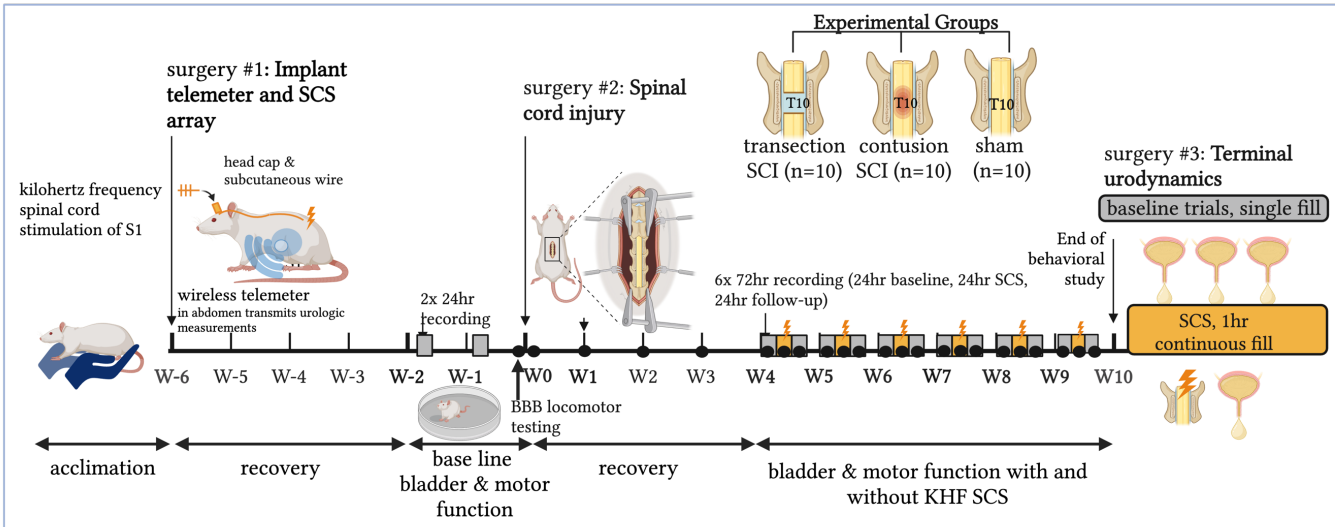
Nothing to Report

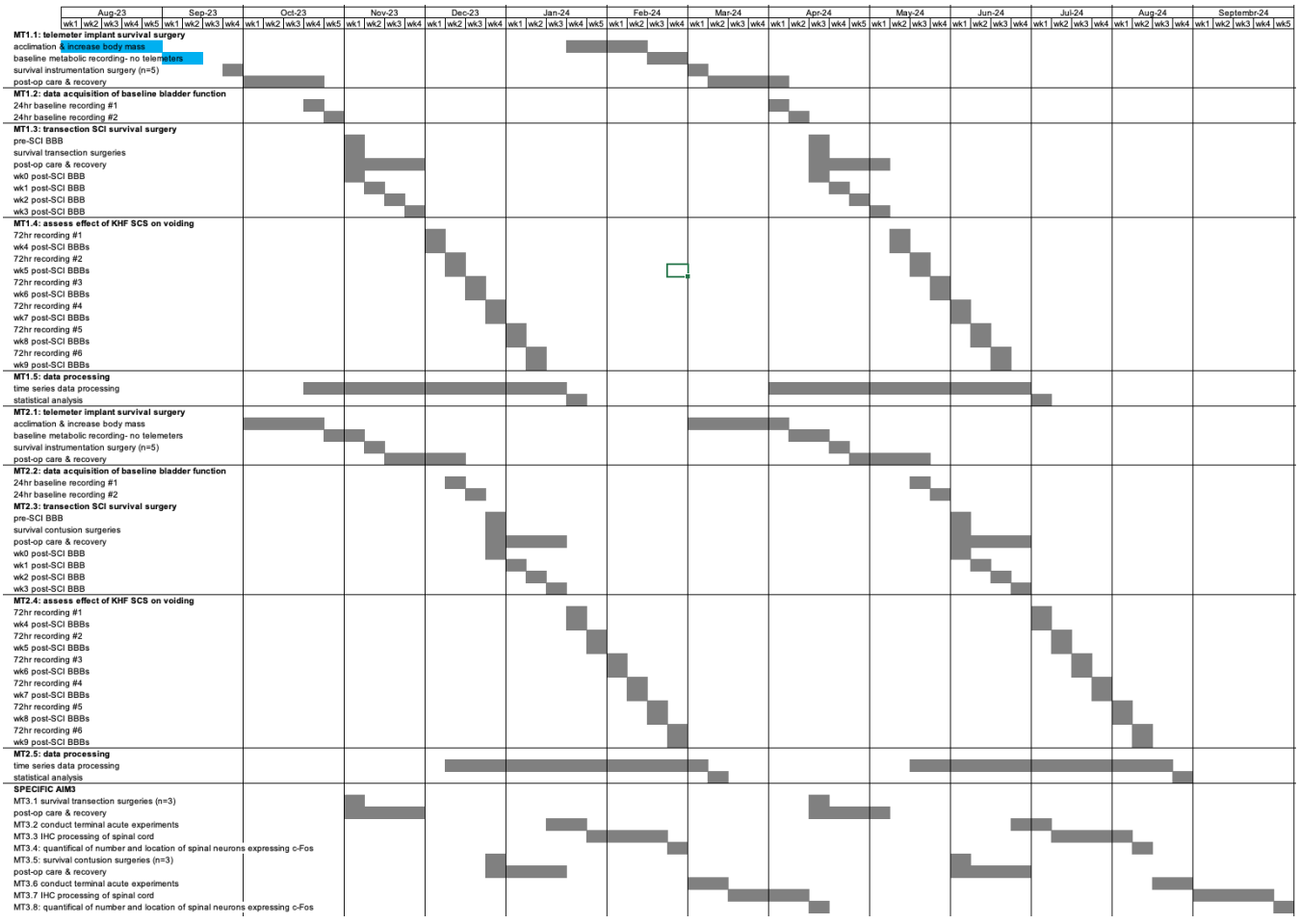
How were the results disseminated to communities of interest?

Nothing to Report. We have yet to initiate publications or conference abstracts to disseminate findings from this project. Dr. Abbott will present findings from the acute terminal SCS used for electrode implant training to the Collaboration for the Advancement of Interdisciplinary Research in Benign Urology (CAIRIBU) 2023 Annual Meeting November 29-Dec 1st (abstract due October 20, 2023)

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

Our trained team is prepared to execute the major tasks specified in Specific Aims 1 and 2 concurrently, utilizing cohorts of telemeter-implanted rats and sham rats (Aim 3).





4. IMPACT:

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

Nothing to Report

What was the impact on other disciplines?

Nothing to Report

What was the impact on technology transfer?

Nothing to Report

What was the impact on society beyond science and technology?

Nothing to Report

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

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

Problem 1.1a: Research timeline postponed by procurement delay and plating requirement of spinal cord stimulation electrodes

During the reporting period, we encountered significant delays and challenges in the procurement and plating of 4-contact paddle electrodes ordered from Dyconex AG, a Micro Systems Technologies company.

- **Procurement Delay:** Our procurement order (Reference #: 4551212030; Invoice 127024603) was initially placed on 09/02/2022. Regrettably, these electrodes were not dispatched until 06/21/2023, as indicated by FedEx tracking#: 610481795490 (Appendix attached).
- **Plating Requirement:** These electrodes, which are essential for in vivo instrumentation, required platinum-black plating to ensure their suitability for stimulation. Unfortunately, Dyconex does not provide these manufacturing services. We sent the electrodes to Epic Medical Inc for plating by Artin Petrossians on 06/27/2023. After plating, we received the electrodes last month on 08/04/2023 (FedEx tracking#: 772887469587).

Resolution attempt 1.1a1: Exploration of alternative electrode sources

Dr. Abbott sought alternative electrodes from regional sources. A quote from Micro-Leads was considered, but it was deemed too expensive, with a cost of $600 per electrode and a non-recurring engineering (NRE) charge of $2500.

Resolution attempt 1.1a2: Skill exchange and reciprocal training

In response to the significant delay in electrode procurement, we sought an approach that would plate copper electrodes and foster a valuable skill exchange and collaboration within our research team. Starting in April 2022, Dr. Abbott commenced training sessions with postdoc and electrical engineer, Dr. Atefeh Ghazavi, focusing on in vivo animal procedures. This comprehensive training included essential surgical and animal handling skills, including isoflurane and urethane anesthesia, surgical preparation, and euthanasia. This collaboration continued until Dr. Ghazavi's departure in January 2023. To reciprocate and further diversify our skill set, Dr. Ghazavi trained Dr. Abbott in the electroplating process, specifically targeting six surplus copper-plated electrodes available in our laboratory. This knowledge exchange was instrumental in equipping Dr. Abbott with a broader range of electrical testing skills such as cyclic voltammetry.

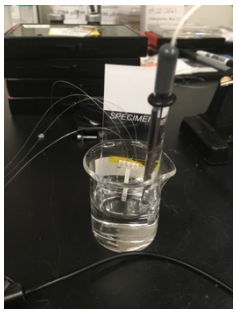


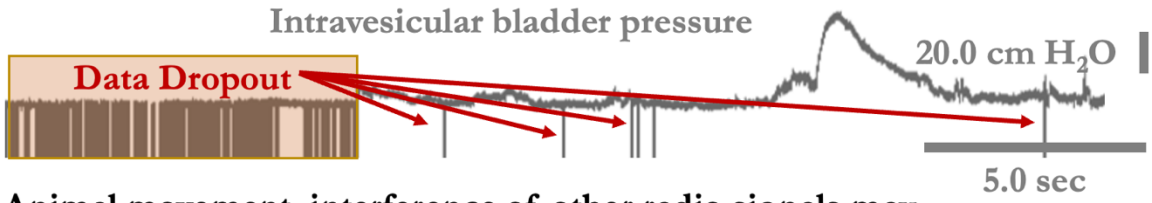
Fig 1.1a2: Electroplating Surplus Copper Electrodes. Dr. Abbott performed a series of electroplating procedures, resulting in the production of a practice SCS electrodes. These electrodes proved invaluable for refining our techniques and procedures. It is important to note that these electrodes exhibited a higher impedance range than ideal for tissue stimulation (6k-30k Ohms); however, they played a vital role in essential training. Notably, Dr. Abbott utilized these electrodes for self-training in the creation of spinal cord stimulation hardware (Fig 1.4), including medical-grade silicone housing and composite head caps, as well as for conducting epidural spinal cord stimulation during terminal acute experiments.

Plan 1.1a: Building upon the valuable experiences gained during our resolution attempts, we are ready to make the most of the electrodes that are currently available as of August 2023. These electrodes, having undergone the necessary plating processes, are now ready for deployment in our research endeavors.

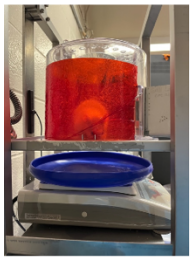
Problem 1.1b: Data dropout issues in all telemeter channels
TSE telemeters are implantable radio transmitters that transmit in vivo data via antennas to a receiver. Each telemeter operates on its own distinct frequency, allowing us to record data simultaneously from multiple implants. However, the proximity of adjacent telemeters and interference from environmental sources, including other equipment, can create challenges in collecting data. Our method of measuring these challenges is by calculating the percentage of missed data packets. In September 2022, we were facing a significant issue, with approximately 53% of data packets being missed during recording.

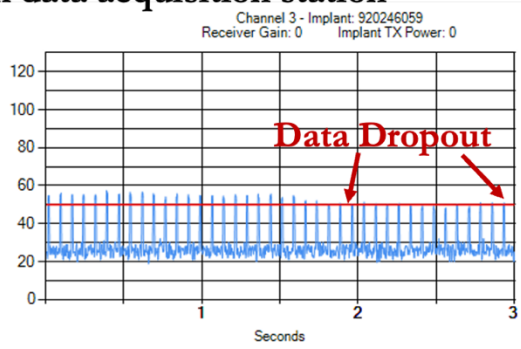
Resolution 1.1b: New Stellar Commander software tools released upon request.
To address this problem, Dr. Abbott met with TSE-System technical support to trouble shoot optimizing the receiver power in relation to the telemeter power through software and firmware updates. TSE generously provided us with their in-house debugging software for the receiver (Stellar Commander v2.0.0.22_DEBUG).

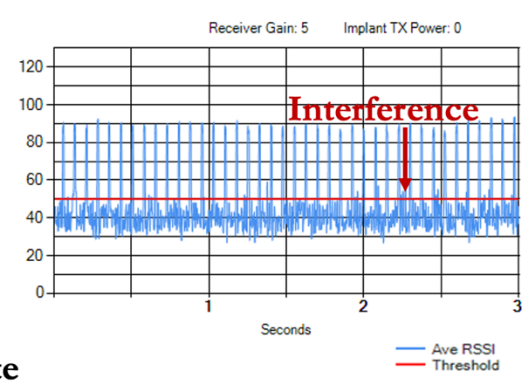
A) Before TSE debugging tools, data dropout difficult to trouble shoot



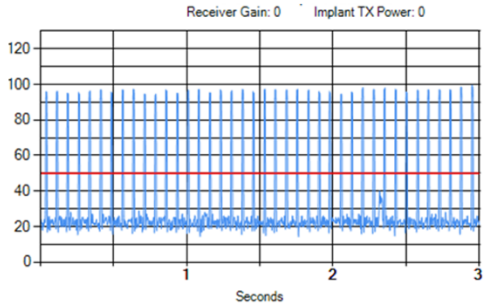
B) Animal movement, interference of other radio signals may vary at each data acquisition station



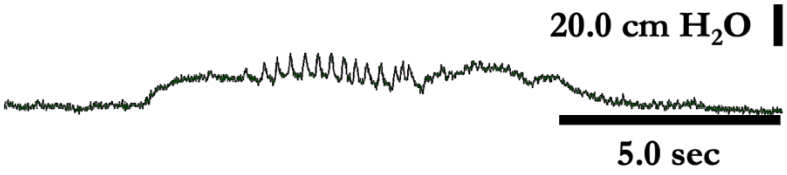




C) TSE firmware and software updates facilitate optimization of receiver and telemeter settings



D) After debugging tools, limited data dropout



Previously, our troubleshooting options were limited to changing cage assignments and implant serial number frequencies. However, the introduction of these new software tools has improved our approach. We can now actively monitor the Received Signal Strength Indicator (RSSI) in real-time and adjust various receiver properties. Specifically, we have the capability to align the RSSI threshold with the baseline radio frequencies and make gain adjustments within the receiver. This substantial improvement has reduced missed data packets from approximately 50% to 5%.

Our goal is to achieve less than 2% missed data packets for each implant, given that we record electromyography software at a high rate of 1000Hz. To mitigate the impact of signal loss in the interim, we activated an option within our data acquisition software (Notocord) that automatically fills data dropouts with the last received value. This minimizes the impact of signal loss on the data analysis but may reduce sensitivity to changes in EUS EMG activity.

Plan 1.1b: We will maintain a close and collaborative partnership with the TSE support technicians, capitalizing on their wealth of expertise and guidance as we work towards achieving our goal of seamless data collection and analysis.

We will explore potential solutions to further enhance our data transmission reliability:

1. **Antenna Frame Adjustment:** One option under consideration is to modify the metal backing of the antenna frame by replacing it with acrylic. This change may potentially reduce interference and enhance signal integrity.
2. **Implant Transmission Power Enhancement:** Another avenue to explore involves increasing the transmission power of the telemeter implant. However, it's worth noting that this adjustment could result in an approximate 8% reduction in battery life. As such, we will reserve this option for further consideration if other measures do not yield the desired improvements.

By maintaining our collaborative spirit with TSE and considering these potential enhancements, we remain committed to resolving these data dropout issues.

Problem 1.1c: Availability and Retention Challenges with Undergraduate Animal Care

Conducting spinal cord injury (SCI) research presents unique demands, especially regarding animal care post-survival SCI. Bladder expression using the Crede method must occur three times daily, with intervals not exceeding 12 hours between expressions. While other labs have bladder expression schedules more aligned with normal work hours (personal discussions, GRC 2023), this schedule was proposed by expert SCI animal care, Chris Langdale, to prevent maladaptations (fibrosis, morphological augmentation) to bladder overload. Since maladaptations would prevent functional recovery of the bladder and the bladder is a primary variable of interest, we will maintain this regimen. This rigorous animal care regimen continues until reflexive voiding is restored, allowing for close urine observation and prevention of bladder ruptures. Unfortunately, animals recovering from transection SCI do not regain reflexive voiding for several weeks, making the care demands often overwhelming for a single staff member.

In September 2022, we introduced undergraduate research assistants as animal care staff. Their intelligence, motivation, and enthusiasm have enriched our research experience. However, we have encountered significant challenges regarding their availability and retention for these vital animal care roles.

Challenges in Undergraduate Staffing:

- *Availability Constraints and Unforeseen Departures:* Most of our undergraduate staff are actively pursuing their education, managing coursework, volunteering, second jobs, and exam pressures. During school holidays, their absence is expected, disrupting the continuity of our animal care efforts. Furthermore, unexpected personal issues, such as family emergencies and health crises, have led to mid-semester departures, necessitating frequent adjustments to our schedules.
- *Covid-19 Impact*- multiple team members contracted the virus, which not only compromised their health but also disrupted our staffing plans. Dealing with illness and the necessary isolation periods not only impacted their ability to contribute to the research but also introduced uncertainty into our workforce scheduling.
- *Transportation and Commute Challenges:* For students residing off-campus, transportation and commute challenges have a significant impact on their attendance and availability. This is especially pertinent when they rely on Duke Bus transportation, which is frequently unavailable on weeknights and holidays, making animal care commitments a logistical challenge. As an additional example, one student encountered a distressing incident while attempting to commute. They sustained an injury while biking through inclement weather to fulfill their work

responsibilities, highlighting the potential risks and hardships associated with transportation for off-campus students.

Collectively, these challenges impacted the effectiveness and continuity of our animal care efforts, prompting the need for a thoughtful approach to address these issues while maintaining our commitment to providing meaningful mentorship to our undergraduate students.

Resolution Attempt 1.1c: Animal Care Exchange and Summer Hiring:

In response to this pressing issue, Dr. Abbott proactively sought solutions to ensure the continuity and quality of animal care for our research program. To address the immediate animal care needs, Dr. Abbott facilitated an exchange of animal care responsibilities with members within the lab. This collaborative effort extended even to holidays like Thanksgiving and Christmas, demonstrating our commitment to maintaining the essential animal care regimen. For the summer of 2023, Dr. Abbott made a strategic move to hire two undergraduates who had previous rodent research experience and access to transportation.

Problem 1.1d: Underestimating Training Time for Undergraduates in Spinal Cord Injury Research:

Another primary challenge we encountered was underestimating the time required to train undergraduates to achieve independence in our spinal cord injury (SCI) research program. This challenge was compounded by several factors:

- *Difficulty Finding Experienced Undergraduates:* In the summer of 2022, finding undergraduates with prior research experience, particularly in animal studies, was an arduous task. The COVID-19 pandemic had disrupted many research programs, making it nearly impossible to locate undergraduates with a rodent research background.
- *Generational Differences:* Supervising and mentoring 19-20 year-olds required bridging significant generational gaps. This included addressing their unfamiliarity with certain technologies and practices integral to our research. Concepts such as external hard drives for data storage, computer folder organization, pagers for on-call veterinarians, and applications beyond web browsers needed additional explanation and guidance. Working with young adults also requires a lot of time discussing how academic research systems work so they can efficiently navigate bureaucracy.
- *Around-the-Clock Care Demands:* In the realm of spinal cord injury (SCI) research, the post-operative care of animals, including the crucial task of bladder expression, demands continuous attention. Placing undergraduates in this intense post-operative care role without experienced supervision would not only jeopardize the well-being of the animals but also pose a risk in handling unexpected emergencies. Dr. Abbott's own 40-minute commute to the research facility underscores the critical importance of having local expertise readily available, especially during emergencies such as immediate euthanasia due to kidney failure.

Resolution Attempt 1.1d: Prioritizing Comprehensive Training and Documentation

Given the critical nature of 12-hour post-injury care windows during the initial 5 days, Dr. Abbott initiated a collaboration with Dr. Tim Faw, who has substantial expertise and experience in SCI. Having both Dr. Abbott and Dr. Faw present was essential to our research's success. Dr. Abbott and Dr. Faw shared supervisory roles with staff, ensuring that their combined guidance not only guaranteed the

highest level of care for our research animals but also equipped staff with the competence to handle unforeseen situations with confidence.

In addition to hands-on training, Dr. Abbott significantly enhanced documentation that improves the efficiency of onboarding new team members. This includes comprehensive care sheets covering various aspects such as animal acclimation, metabolic cage procedures, acute postoperative care, chronic postoperative care for both SCI and telemeters, wellness checks, UTI care, and veterinary consults. Moreover, she facilitated detailed documentation to provide offline support for facilities and equipment location, telemeter optimization, receiver power cycling, and more.

The outcomes of this process have been substantial. Staff are now fully independent in their animal care duties, able to proficiently identify issues such as urinary tract infections (UTIs), abdominal fluid build-up, dehydration, and pain management concerns. Importantly, they have gained confidence in performing bladder expressions, a critical skill in our research. It is worth noting that learning bladder expressions on a separate project allowed undergraduates to develop this skill in rats that do not have telemeter implants in the bladder. This is particularly important because when we plan to perform bladder expressions with 5mm long pressure probes embedded, a task no research team had previously undertaken. Our staff now have a strong understanding of what constitutes normal and abnormal care in spinal cord care with telemeters.

While this decision may have temporarily delayed CDMRP experiments, Dr. Abbott's top priority is to ensure that the individuals under her supervision are well-prepared for the challenging tasks ahead. This approach not only benefits our research team but also upholds our commitment to the welfare of the animals involved in our studies.

Plan 1.1d: Hire a Full-Time Staff Member

Our primary challenge centered on underestimating the time required to train staff to achieve independence while simultaneously overestimating their availability. In response to this pressing issue, Dr. Abbott sought solutions to ensure the continuity and quality of animal care for our research program. We have begun interviewing candidates for full-time research associate specializing in preclinical animal care, with the job posting available [academicjobsonline.org/ajo/jobs/25270]. This addition to our team will not only ensure the continuity of animal care but also yield several benefits for our research efforts.

One significant advantage of incorporating a full-time research associate into our team will be the substantial reduction in the time and effort currently allocated to training undergraduates for animal care roles. Training undergraduates, often involving fundamental instructions on animal care procedures and technologies, necessitates a substantial investment of our postdocs' time and mental capacity.

By introducing a dedicated research associate, we can effectively delegate these training responsibilities, enabling the postdoc to redirect their valuable time and cognitive resources toward core research activities. This shift will empower her to concentrate on conducting experiments, conducting data analysis, and communicating findings to the public, ultimately enhancing the overall productivity of our research program.

Changes that had a significant impact on expenditures

Nothing to Report

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

Nothing to Report

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use or care of vertebrate animals

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. PRODUCTS:

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

Journal publications.

Nothing to Report

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

Nothing to Report

Other publications, conference papers and presentations.

Nothing to Report

- **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:	*Warren M. Grill*
Project Role:	*PI*
Nearest person month worked:	*0.45 Academic and 0.58 Summer months—1.03 total months*
Contribution to project:	Conception and design of the work

Funding Support:	*n/a*

Name:	*Emily Abbott*
Project Role:	*Research Scientist*
Nearest person month worked:	*3.75 months*
Contribution to project:	Surgeries and data collection, training and managing undergraduate animal care assistants, hiring full-time animal technicians.
Funding Support:	*NIH K12 fellowship 75% since 12/1/2022*

Name:	*Danielle Degoski*
Project Role:	*Lab Research Analyst II*
Nearest person month worked:	*2.4 months*
Contribution to project:	Protocol management, purchase orders, on-call animal care
Funding Support:	*n/a*

Name:	*Eric Gonzalez*
Project Role:	*Research Scientist*
Nearest person month worked:	*3 months*

Contribution to project:	Training spinal cord stimulation procedures and protocols to Dr. Abbott. Assistance with post-operative animal care
Funding Support:	*n/a*

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

Changes in Dr. Warren Grill's Other Support:
1OT2OD025430—ended, Boston Scientific "Time Domain.." and "Analysis.." grants—ended, 1UH3NS103468—ended, The Craig H. Neilsen Foundation—ended, Paralyzed Veterans of America—ended, Alfred E. Mann Foundation—ended, Medtronic—ended, Neuromod Prize—new, Boston Scientific "Quantifying SCS..", 1UH3NS129898—new, 1R01NS126376-01A1—new, Coloplast—new. In-kind changes--1F31NS130997-01—new

What other organizations were involved as partners?

Nothing to Report

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS:

QUAD CHARTS:

9. APPENDICES: