Neuromuscular electrical stimulation for physical function maintenance during hematopoietic stem cell transplantation

NCT04364256

September 14, 2023

Consent and Authorization to participate as a Research Subject in:

Muscle Stimulation for Physical Function during Stem Cell Transplant

SUMMARY OF STUDY: This purpose of this study is to test the effect of muscle stimulation on preventing reductions in physical function and worsening of fatigue and quality of life (QOL) after hematologic stem cell transplant (HCT). We will recruit Veterans who are planning autologous HCT. Measurements of physical function, body composition, and QOL will be assessed at Baseline, 1 month after HCT, and 6 months after HCT. The muscle stimulation will occur three times a week, and it will start after the Baseline Visit and end at the 1-Month Visit.

We are inviting you to be in a research study. The purpose of this Consent Form is to give you the information you will need to help you decide whether to be in the study. Please read this form carefully.

You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your rights as a volunteer, and anything else about the research or this form that is not clear.

Your participation in this study is entirely voluntary. Please take as much time as you need to discuss the study with your doctors, family, and friends. The decision to participate or not is yours. If you choose to participate, you have the right to withdraw from the study at any time.

This study is being conducted by the Geriatrics group of VA Puget Sound Health Care System (VA Puget Sound) through a grant from the VA Rehabilitation Research & Development service line.

Principal Investigator:
Lindsey Anderson, PhD

Co-Investigators:
Jose Garcia, MD, PhD
Thomas Chauncey, MD, PhD
Solomon Graf, MD

Study Coordinator:
Lauren Paulsen

Study Title:
Neuromuscular electrical stimulation for physical function maintenance during hematopoietic stem cell transplantation

1. Who can I contact with questions while I am in this study?

During business hours (8:00 a.m. – 4:30 p.m.), please call the Study Coordinator, Lauren Paulsen, at (206) 277-1163 or Principal Investigator at (206) 277-6719. After business hours (nights and weekends), please call 206-762-1010 and ask the operator to page the on-call Marrow Transplant Unit attending physician.

The study researcher(s) listed above must be contacted immediately if:

- You think you may have been harmed or injured as a direct result of this research.
- You have any questions regarding your medical care issues specifically related to the study.

You may also contact the Institutional Review Board (IRB) at (206) 277-1715 if you:

- Would like to speak with a neutral party who is not involved with this study.
- Have questions, concerns, or complaints about the research.
- Would like to verify the validity of the study.
- Have questions about your rights as a research subject.

2. What is the purpose of this research study?

Hematologic stem cell transplantation (HCT) is a common treatment for some blood, bone marrow, and lymphatic cancers but often leads to reduced muscle size and physical function, increased fatigue, and poor quality of life (QOL). These symptoms are often associated with long-term complications such as hospitalization and infection. Despite the impact of these symptoms, there are no approved treatments to prevent/reverse these long-term effects. The cancer itself, side effects of chemotherapy, and reduced physical activity contribute to these effects. And although exercise before and after transplant has helped reduce these effects, it is not consistently recommended to patients, and most patients maintain low activity levels through and after treatment. We are testing an alternative exercise strategy called neuromuscular electrical stimulation (NMES) to maintain physical function and QOL after transplant.

Since we will be comparing the effect of two different types of NMES, which are delivered to the muscle with a device, the term *NMES* will be used to refer to both throughout this Consent Form. The device used to deliver the NMES is approved by the federal Food and Drug Administration for preventing muscle loss related to reduced physical activity. The researchers involved in this study have no conflict of interest with regards to this study.

We will enroll up to 46 patients for this study. If you are interested and would like to participate, you must meet the following criteria:

- You are 18 years old or older;
- You have adequate cognitive and language ability to provide consent; and
- You are a Veteran and enrolled in the Marrow Transplant Unit at VA Puget Sound for planned autologous transplant.

If you are eligible, your participation will be for 6 months, which would include two in-person study visits (3 hours each visit; a portion of one of these two visits may occur at home depending on your schedule) and one remote visit (30 minutes of your time at home; this visit may occur in-person if you are located in the Seattle area at that time). Additional participation will include at-home NMES training sessions (1 hour each) three times a week beginning once you complete a pre-transplant/baseline assessment and continuing until 3 weeks after your transplant.

3. What will I be asked to do in this research study?

This is a randomized study. “Randomization” means you will be put into a group by chance, like the flip of a coin. For this study, you will have an equal (50/50) chance of being assigned to one of the two NMES types. You will be randomized to a group after the Baseline Visit, but you will not know which

group you are assigned to. The study staff assisting you in the weekly training sessions (between the Baseline Visit and the 1-Month Visit) will know your group assignment, but the staff conducting the main study visits (Baseline Visit, 1-Month Visit, and 6-Month Visit) and conducting the analysis will not know which group you are assigned to. This way, the findings from the two groups will be handled in the same way. We will tell you which group you are in if an emergency arises and if knowing this information is relevant for your medical treatment.

You may refuse to answer any question in any test or questionnaire related to the study. You will need to come to some visits in a fasting condition. This means that you cannot eat or drink (this includes nicotine, but water is OK) after 10 p.m. the night before your visit. We will also ask that you refrain from moderate to strenuous physical activity (like high-performance sport or hard labor) other than the NMES training session within 24 hours before the Baseline Visit and the 1-Month Visit. If you did not fast or avoid strenuous activity, your visit will be cancelled for that day and a new test day will be scheduled as soon as possible. You may be exempt from completing some study procedures due to physical inability from disease- or treatment-related symptoms. Determination of these exemptions will be left to the discretion of the study personnel.

You will need to go to VA Puget Sound for all in-person study procedures.

BASELINE VISIT and 1-MONTH VISIT: 3 hours each **VA study visits**

- **MUST ARRIVE FASTING (starting at 10 p.m. the night before)**
- **REFRAIN FROM MODERATE TO STRENUOUS PHYSICAL ACTIVITY FOR 24 HOURS PRIOR TO APPOINTMENT**

During these two visits, the following will be done:

- We will collect a complete **medical history** from you including **height, weight,** and **vital signs** (heart rate, blood pressure, breathing rate, and temperature).

- We will **draw blood** (4 teaspoons) from a vein in your arm to measure muscle, kidney, and liver function; blood counts; and inflammation.

- We will take a measurement of your body composition. To do this, we will perform a **DXA** (dual-energy X-ray absorptiometry) and/or BIA (bioelectrical impedance analysis) scan. Both measurements are painless and do not require injections. The DXA scan is a full-body X-ray which we will use to measure the amount of fat and muscle in your body. Your entire body, from head to toes, will be scanned while you are lying on a table on your back. You will need to keep very still for approximately 3 minutes to reduce the possibility of a blurred image. We can measure BIA by having you step barefoot onto a scale that uses small electrical currents to measure the amount of water, fat, and muscle in your body. You will not be able to feel these electrical currents and the process takes less than one minute.

- We will test your **physical function with multiple tests** including: VO_2 peak test, 6-minute walk test, walking speed, handgrip strength, sit-to-stand test, stair climb, muscle strength, balance, and physical activity level.

    - Using a stationary bike, we will test your exercise capacity by a **VO_2 peak test.** This test measures how much oxygen you use and how much carbon dioxide you produce. You will need to wear a mask with an attached mouthpiece which still allows you to breath normal room air. As you pedal at progressively harder workloads, we will measure your heart rate through a finger monitor. We may also measure your blood pressure with an arm cuff. The test will continue until you become fatigued, decide to stop, or other symptoms that prohibit further exercise. We will instruct you beforehand how to use hand signals to indicate that you need to stop the test. After testing, you will go through a cool-down period. (We are temporarily not completing this test)

    - We will ask you to **walk a short distance at your usual speed** and then **walk for 6 minutes** up and down a corridor as many times as you can. The 6-minute walking test will be measured by study staff. Because you will be repeating this test during the 6-Month Visit at your home, we will have you download a **mobile application** at this time to your cellular phone which measures the 6-minute walk test electronically. You will show study staff or tell them verbally what the result reads on your phone. You will not be asked to send any information from your phone to the study staff or to connect your phone to any other devices. The **usual speed** test and **6-minute** walking test may be performed at your home during the 1-Month Visit if they cannot be performed in-person. If either of these tests will be performed at home, we will give you written instructions and we will call you afterwards to obtain your results.

    - We will test your **handgrip strength** using a handgrip meter and, holding it as instructed, you will need to squeeze as hard as you can for 5 seconds.

    - We will ask you to perform a **sit-to-stand test** where you begin seated, then stand up and sit down 5 times as fast as possible, all while you have your arms crossed across your chest. This test may be performed at your home during the 1-Month Visit if it cannot be performed in-person. If this test will be performed at home, we will give you written instructions and we will call you afterwards to obtain your results.

    - We will test your **stair-climbing power**. You will need to go up a standard flight of stairs as quickly as you can using a handrail, if needed. (We are temporarily not completing this test)

    - We will test your **muscle strength** using equipment similar to that used in a gymnasium by assessing one-repetition maximum tests of the lower body. This is a measure of the maximal weight a person can lift one time.

    - We will test your **balance** to see if you can stand without assistance for 10 seconds with your feet together.

Baseline Visit only

- We will introduce you to the **Actical** (activity monitor), which you will occasionally wear during the study. The Actical is worn at the wrist, like a watch, at all times (even in sleep and showering/bathing). The Actical will track your daily steps and hours of sleep.

- We will give the Actical to you with directions (in person or by mail). You will wear the Actical for *1 week before the Baseline Visit* and *1 week before the 1-Month Visit* and *before the 6-Month Visit*. You will need to return the Actical to study staff at each visit so they can record the readings. You will be given **quality-of-life questionnaires** for fatigue, nausea, pain, and muscle soreness.

At the VA, we will supervise the entire **first NMES session.** NMES involves an electrical signal given to your muscles through sticky pads placed on the skin that are connected to a handheld device that allows you to always be in control of the strength of the signal going to your muscles. During this session, we will instruct you on safety, proper use of the NMES, placement of the sticky pads, and introduce you to the what the signal feels like.

After the Baseline Visit, we will ask you to perform NMES training sessions three times per week, continuing until *3 weeks after your transplant*. These **remaining NMES sessions** will be mostly unsupervised, since you will be given the device to take home. We will call you two-three times a week to remind you to complete the sessions and to see whether you are having any difficulty that we can help with. We will ask you about skin health and skin sensitivity, lab abnormalities that you may be aware of, muscle soreness, involvement in other exercise activities since the previous NMES session, and proper sticky pad placement. You can also complete some sessions with our assistance/supervision if you are already coming to VAPSHCS for any other reason.

Each NMES session will be 1 hour—the first 30 minutes will consist of NMES on the muscles in the back of both of your legs and buttocks; the last 30 minutes will consist of NMES on the muscles in the front of both of your legs. You will perform all sessions while laying down on your back or reclining in a bed or chair with your feet up for safety and comfort. **At the 1-Month Visit only**

At the 1-Month Visit, we will ask you about your **experience using the NMES device**.

6-MONTH VISIT: 30 minutes	**Remote study visit (your home)**
• **REFRAIN FROM MODERATE TO STRENUOUS PHYSICAL ACTIVITY FOR 24 HOURS PRIOR TO APPOINTMENT** 	

During this visit, the following study procedures will occur (and before to prepare for the visit):

- We will mail you **quality-of-life questionnaires** and the **Actical** (activity monitor), which you will wear for 1 week. You will then mail the completed questionnaires and the **Actical** back to study staff with the pre-stamped and pre-addressed envelope that we will provide.

- We will ask you to perform the **6-minute walk test** on your own at home using the mobile application you downloaded on your cellular phone during the Baseline Visit. There will be a place to write down the result on the instructions we send you in the mail. You will then mail your result back to the study staff with the completed questionnaires using the pre-stamped and pre-addressed envelope that we will provide.

4. What are some risks of joining this research study?

The study procedures may involve risks that are currently unknown. We may need to contact you if we learn of a new study risk, even if you have completed the study. If any of the risks included in this Consent Form become significantly updated during this study, we may ask you to sign an updated Consent Form to document that this new information has been explained to you. You will have the right to decide either to continue with the research study or to withdraw.

Below are study-related risks that are known at this time:

NMES: The most common risks associated with NMES are: (1) electrical surge or shock if the device malfunctions; (2) skin irritation, burn, or allergy underneath the sticky pad sites; (3) pain from the signal if the strength is not adjusted slowly; (4) muscle soreness 1-2 days after the session; (5) electrical interference or death when used in a patient with a cardiac pacemaker, implanted defibrillator, or other implanted metallic or electronic device; in addition, (6) long-term effects of NMES are unknown.

DXA scan: Your X-ray will expose you to radiation. The radiation dose you will receive is approximately 1.6 millirem in total. For comparison, the average dose to the U.S. population from natural background radiation sources is 300 millirem per year, and the maximum annual occupational dose limit for radiation workers is 5,000 millirem. The risk of harm from this amount of radiation is low and no harmful health effects are expected; however, your risk of harmful effects may increase if you are exposed to more procedures that involve radiation. Harmful effects could include cancer or genetic changes.

Physical function tests: During these tests, you may experience low or high blood pressure, lightheadedness, heart palpitations, irregular heartbeat, chest pains, feeling unbalanced, or delayed muscle soreness (1-2 days after). In addition, during the VO_2 peak test, you may experience abnormal heartbeat, abnormal blood pressure, muscle cramps, muscle strain and/or joint injury, delayed muscle soreness (1 to 2 days afterwards), light headedness, fatigue, and in rare instances, heart attack. This test will always be monitored by a study doctor.

Actical: There is the risk of discomfort in the area where you are wearing the device, but it is similar to wearing a watch. If your skin becomes red, sore, or unusually itchy under the band, contact your study staff.

Fasting: You may feel hungry or dizzy or have stomach discomfort from not eating before the study visits. If you are a frequent coffee drinker, you may experience discomfort or headache from not

having caffeine. If you normally use nicotine products, you may feel the effects of not having nicotine in your system.

Blood draw: When having blood drawn, you may experience brief pain when the needle punctures the skin. There will also be a risk of soreness or infection.

Questionnaires: The questionnaires include some questions that relate to physical and emotional health. You may feel uncomfortable answering some of these questions. You are free to skip any question if it makes you uncomfortable.

Mobile application: We will have you download a mobile application (a non-VA app), called the iWalkAssess, onto your cellular phone. You will be using this app to perform the 6-minute walk test on your own at home during the 6-Month Visit. (This app is commercially available for free on both android and iOS platforms) Data will be captured by this non-VA entity. This app and its developers do not have any information that can be linked back to you. Only the researchers at the VA will know your "iWalkAssess" score. As "iWalkAssess" is not sponsored by the VA, we recommend that you read their privacy policy and ensure you feel comfortable for data being collected by this app and stored on their servers. The data collected will be accessed only by the study research staff and stored on the VA network.

Confidentiality: There will be a risk of loss of privacy (confidentiality) by participating in this study. We will protect all identifying health care information with great care. We have extensive measures in place to keep this from happening and expect these measures to protect your personal information. For details on the steps we will take to protect your confidentiality, please refer to Section 7.

The autologous transplant that you are scheduled to undergo is not a research procedure. You should review any risks associated with autologous transplant with your regular healthcare providers.

5. What are some benefits of joining this research study?

You may receive no direct personal benefit by participating in the study. However, your participation may contribute to information regarding feasibility and safety of a therapeutic modality aimed at preserving physical function and QOL after a complex cancer treatment in Veterans.

6. Are there other ways I could receive these benefits?

This study is voluntary for research purposes only. Alternatively, you may choose not to participate.

7. Who will see my information and where will it be stored?

Your research information will be kept confidential. However, some data will be shared, communicated, or stored during or after this research study.

If we learn you intend to harm yourself or others, we must report this information to appropriate authorities.

Access to your records, including your medical records, could be either for study-related purposes or to make sure your study record meets all legal, compliance, and administrative requirements. The reviewers will protect your privacy.

We will put information about you from this research study into your medical record. All approved users of the national VA medical records system can have access to your medical record. This may include health insurance companies who are being billed for medical costs. This record will be retained in accordance with the VA records retention policy.

Study code and link

If you agree to participate in our study, we will assign you a study code. We will not include your name or other identifiers (such as your name or social security number) on any of the information or blood specimens that we collect from you. Only your study code will be used. We will keep a master list that links study participants' names to study codes separate from the study data in a secure VA database with restricted access.

Safekeeping / Storage

To protect the confidentiality of the information obtained about you during this research study, we take many preventative measures. Paper study documents we have, receive, or create will be secured in locked file cabinets accessible only to study staff. Electronic study records will be kept in electronic folders on the secure VA network with access to the specific folders restricted to designated study staff.

We will use your de-identified blood samples only for those tests described in this Consent Form and study protocol. You, your family, and your study doctor will not have access to the results of the laboratory testing, except for routine laboratory tests (blood count and blood chemistry). Your blood specimens will be kept until used up or destroyed unless you agree to having it stored in the repository, as described below.

Geriatric Endocrine Repository (optional)

We will ask if you are willing to have your blood samples stored in a biorepository for future research. This is optional. To have your blood samples stored in the biorepository will not involve any extra procedures for you. The samples will be stored indefinitely at VA Puget Sound. We will use the samples for other health research. If you agree, we will have you sign another Consent Form, which will explain the biorepository in detail.

Upon study completion

Once this study is completed, we will not use your data or the study code linking it to you for any additional research. We will keep your data and code in a secure database in accordance with the VA records retention policy (which will be a minimum of 6 years after the study has been completed).

A description of this clinical trial will be available on ClinicalTrials.gov as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

In the future, researchers may write about the information collected from this research study. Any future publications or articles will not include any identifying information about you without your approval in writing. Neither you nor your family will gain financially from discoveries made in the future using the information and/or specimens you provide.

8. What are some other things to think about before I decide to join this research study?

You will not be prevented from consultation for, or participation in, physical therapy as determined by your doctors.

You will not incur any extra costs for participating in this study. The VA requires some Veterans to pay co-payments for medical care and services. You will still have to pay these co-payments as long as they are not related to this research study.

After each study visit, you will receive payment for compensation via Electronic Funds Transfer (EFT). Payments will be determined by you and the study team based on how much you complete at each visit. To comply with Internal Revenue Service (IRS) guidelines, we will collect your social security number. You may receive an IRS Form 1099.

The table below reflects the maximum amount paid for each visit:

Study Visit	Maximum Allowable
Baseline Visit procedures	$50
1-Month Follow-up Visit procedures	$50
6-Month Follow-up Visit procedures	$50
TOTAL POSSIBLE AMOUNT	**$150**

9. What will happen if I decide I don't want to be in this research study later?

You do not have to take part in this study. If you are in this study, you can withdraw at any time. If you decide not to participate or to withdraw, no action will be taken against you; for instance, you will not lose your VA benefits.

The Principal Investigator may decide to stop you from taking part in this study at any time. You could be removed from the study for reasons related only to you (for example, if you move to another city) or because the entire study is stopped.

If you decide to withdraw from the study, no new information will be collected from you; however, the study information, specimens, and data already collected will continue to be part of the analyses unless you request that we destroy your stored specimens or unpublished data related to these samples.

10. What will happen if I am hurt in this research study?

If you are injured as a result of participation in a VA-approved research study, the VA will provide you with the necessary medical treatment. You will not be charged for this treatment. Veterans who are injured because of being in this study may receive payment under Title 38, United States Code, Section 1151. Veterans or non-Veterans who are injured may receive payment under the Federal Tort Claims Act. The VA is not obligated to reimburse medical expenses due to your non-compliance with study procedures as described in this Consent Form or otherwise communicated to you by study personnel.

You do not waive any legal rights by signing this Consent Form.

11. Health Information Portability and Accountability Act (HIPAA)

There are rules to protect your private health information. Federal laws, state laws, and the federal medical law known as the HIPAA Privacy Rule also protect your privacy. By signing this Consent Form, you provide your permission, called your "authorization," for the use and disclosure of information protected by the HIPAA Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this Consent Form. They may also collect other information including your name, address, date of birth, and information from your medical record such as HIV status; drug, alcohol, or sexually transmitted disease treatment; genetic test results; or mental health treatment.

The following list of people or groups may know that you are in this study. They may have access to your research records, which may include your medical records:

- Research team members
- Seattle Institute for Biomedical and Clinical Research (the nonprofit institute that works with VA Puget Sound to conduct research)
- Other federal agencies including, but not limited to, the Food and Drug Administration (FDA), the Office for Human Research Protection (OHRP), the VA Office of Research Oversight (ORO), the VA Office of the Inspector General (OIG), and the Government Accountability Office (GAO)
- The VA committees that oversee research

- The VA Puget Sound Fiscal Department and U.S. Department of the Treasury will be provided with your full name, address, phone number, and social security number in order to authorize payment for your participation in this study
- RS Medical (manufacturer of the NMES device) will receive safety information for reporting to the FDA

Your health information disclosed pursuant to this authorization may no longer be protected by federal laws or regulations and may be subject to re-disclosure by the recipient.

You can revoke this authorization in writing at any time. To revoke your authorization, you must write to the Release of Information Office at this facility or you can ask a member of the research team to give you a form to revoke the authorization. Your request will be valid when the Release of Information Office receives it. If you revoke this authorization, you will not be able to continue to participate in the study. This will not affect your rights as a VHA patient to treatment or benefit outside of the study.

If you revoke this authorization, Dr. Anderson and her research team can continue to use information about you that was collected before receipt of the revocation. The research team will not collect information about you after you revoke the authorization.

Treatment, payment, or enrollment/eligibility for benefits cannot be conditioned on your signing this authorization. This authorization will expire at the end of the research study unless revoked prior to that time.

12. What am I agreeing to by signing this form?

I have read or have had read to me all of the above. The study has been explained to me, including a description of what the study is about and how and why it is being done. All of my questions have been answered. I have been told of the risks and/or discomforts I may encounter in the study, of the possible benefits of the study, and of the other choices of treatment that are available to me.

My rights as a research subject have been explained to me and I voluntarily consent to participate in this study. I will receive a copy of this Consent Form.

I agree to participate in this research study as described in this document.

_____ _____

Subject Signature Date

_____

Print Name of Subject