CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Near Infrared Spectroscopy (NIRS) as a method for measuring oxidative capacity of skeletal muscle mitochondria in breast cancer and all gynecological cancer patients

Study to be Conducted at:
Prisma Health Cancer Institute and the University of South Carolina School of Medicine
Greenville Human Performance Laboratory
Greenville Memorial Campus
701 Grove Road
Greenville, SC 29605

Sponsor Name: Prisma Health Cancer Institute

Principal Investigator: Dr. Jennifer Trilk., Associate Professor, Department of Biomedical Sciences

KEY INFORMATION

You are being asked to participate in a research study. Participation in a research study is voluntary. The information in this consent form is meant to better inform you so you may decide whether or not to participate in this research study. Please ask the study doctor to explain anything you do not understand.

The overarching aim of this study is to gain a better understanding of how standard-of-care chemotherapy treatments given to breast cancer and all gynecological cancer patients affects the health of their skeletal muscle throughout their treatment journey. The loss of skeletal muscle during chemotherapy (called cancer cachexia) is well-known and can lead to increased cancer-related fatigue (CRF) and decreased quality of life. By understanding the cellular effects of chemotherapy, and different treatments of chemotherapy, the investigators wish to gain a better understanding on how to slow, stop, and reverse this side effect of chemotherapy through exercise. While chemotherapy is well-known to cause cancer cachexia, exercise is well-known to improve skeletal muscle health, even in cancer patients,

The Institutional Review Board of Prisma Health has reviewed this study for the protection of the rights of human participants in research studies, in accordance with federal and state regulations.

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

PURPOSE

You are being asked to participate in this study because you have breast cancer or gynecological cancer without distant metastasis.

The purpose of this study is to observe whether standard-of-care chemotherapy affects oxygen uptake in the skeletal muscle of cancer patients, as well as to compare the effects of different kinds of chemotherapy treatments on oxygen uptake in skeletal muscle. Oxygen uptake is directly related to skeletal muscle health; therefore, changes in the skeletal muscle's ability to use oxygen can be suggestive of changes in skeletal muscle as well as overall health. Oxygen uptake will be measured using a non-invasive device called near infrared spectroscopy (NIRS) on the quadricep leg muscle while cancer patients are undergoing moderate-intensity stationary cycle exercise. NIRS technology is capable of measuring oxygen uptake in skeletal muscle function non-invasively without the need for more invasive procedures like muscle biopsy. The investigators will also be monitoring fatigue and cognitive function throughout the course of chemotherapy treatment. Patients will perform one exercise session right before each chemotherapy cycle to determine these changes.

Approximately 40 individuals who are being treated with any combination of standard-of-care chemotherapy drugs used for treatment of breast cancer or gynecological cancer will be recruited for this study. If you choose to participate, you will be requested to perform this testing through the duration of your chemotherapy treatments.

HOW THE STUDY WORKS

NIRS is a novel approach because it has never before been used to test the degree to which your muscles can use oxygen in a population of cancer patients. NIRS could provide valuable insight into skeletal muscle health associated with chemotherapy treatment. Additionally, there are few studies focused on the possibility that a decrease in the ability of your muscles to use oxygen could be a root cause for fatigue in cancer patients.

If you choose to participate in this study, you will undergo testing that involves measuring the oxygen levels in one of your quadriceps muscles using the non-invasive NIRS device. This device shines light waves into your leg and uses that light to determine how much oxygen is in your muscle. The NIRS will measure how fast your muscle takes up oxygen during exercise and also how quickly your muscle recovers after exercise.

While you are standing, a non-invasive ultrasound of a large muscle in your thigh will be performed to determine where best to place the NIRS device. The NIRS device will be secured using tape wrapped around your leg (Figure 1). Investigators will confirm that the NIRS is capturing oxygen changes and then

you will proceed with the exercise session. The NIRS will be placed on your dominant leg (unless this leg cannot be tested for medical reasons).

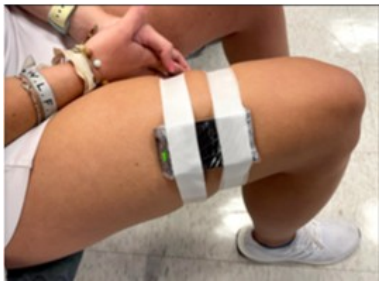

Figure 1. Near Infrared Spectroscopy (NIRS) Device Placed on Leg

The first exercise session (performed one time) will be a graded exercise test to determine what exercise intensity will be used (i.e. Watts) for you to perform throughout your chemotherapy protocol. This exercise session will increase intensity every 3 minutes starting at easy and ending at moderately hard intensity. During the exercise, you will wear a comfortable mask to measure how much air you breathe in and how much oxygen is used by your whole body. Investigators also will perform a finger stick at each stage to determine how much lactate your body is producing during exercise. Lactate is a blood marker that shows how much energy is being used during exercise.

The rest of your exercise sessions will be at moderate intensity in rest/exercise periods. You will perform a 2-minute warm up period on a stationary bike at a very low exercise intensity. After the warm-up, you will begin an exercise period of 2 minutes at a moderate intensity (determined by the test above) followed by a period of rest for 2 minutes. This interval exercise protocol will be repeated three times in total.

The NIRS device will measure the change in the oxygen in your muscles both during exercise and during rest. You will be on the stationary bike for approximately 15 minutes, and the total time for this test will last approximately 30 minutes. You will perform this exercise protocol before you start chemotherapy and one right before each chemotherapy cycle

RESEARCH USE OF BIOSPECIMENS

This study involves the collection of blood specifically for the research that will be drawn during your usual visit to the lab for other blood work. Your blood will be used to look at blood markers of skeletal muscle health to confirm what the NIRS device measures. Your blood may also be used to develop new technologies, treatments, or medications for different diseases.

The biospecimens (blood) collected for this study may be used or distributed for similar research in the future. Your biospecimen will be stored in the Prisma Health Biorepository.

POSSIBLE RISKS

There are no known risks of using the NIRS device.

The exercise that will be performed will include low and moderate-intensity exercise. Participating in exercise carries the possible risks including musculoskeletal injuries such as muscle soreness and muscle pulls, accidental injuries while using the exercise equipment, or shortness of breath. If the participant experiences any pain or discomfort, he/she may stop the testing or training at any time. There is also a slight but possible risk of a cardiovascular event. You will be closely monitored by qualified exercise professionals for any serious events they may arise. If cardiovascular symptoms develop during an exercise session, the Prisma Health Code Response Team will be notified immediately. In addition, all HPL staff have been trained to respond to a medical code via the Clinical Skills Team. A medical code cart is located within 100 feet of the exercise laboratory in the Ambulatory Infusion Center.

This study includes the use of ultrasound in order to identify the location on the muscle with the least amount of subcutaneous adipose tissue for ideal NIRS device placement.

This study includes capillary finger sticks on the first visit only in order to obtain blood lactate levels for point of care testing. Blood will be drawn as part of standard-of-care as ordered by your physician. During the same venipuncture, an additional vial of blood will be drawn for biomarkers related to mitochondrial health for correlative research. If you decide it is too painful, you can have the testing stopped and stop the study at any time. Some people may find the mask or finger sticks uncomfortable, while others do not. Collection of blood samples may cause pain, redness, bleeding, bruising and, rarely, infection at the location where the blood sample is taken.

Some of the questions in the survey are personal and may be upsetting to some participants. The study doctor or staff will be available to discuss these questions should you have a concern or problem. You do not have to answer any questions that you do not want to answer.

The greatest risk is the possible release of your personal health information. Your study records are considered confidential, but absolute confidentiality cannot be guaranteed. This study may result in presentations and publications, but steps will be taken to make sure you are not identified by name.

POSSIBLE BENEFITS

It is not possible to know whether or not you may benefit from participating in this study. The information gained from this study may be useful and may help others.

NEW INFORMATION
Your doctor will tell you about new information that may affect your willingness to participate in this research study. Alternatives, or other choices, concerning your care will be discussed at that time.

There are no plans to share individual research results with you.

COST TO YOU FOR PARTICIPATING IN THIS STUDY
Study funds will pay for all study-related items and services required by the research. We will bill you or your health insurer for items and services that are not part of the research and are part of your routine care. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. You will be responsible for the cost of any care not covered by insurance or study funds.

If you have any questions or are unsure about costs from taking part in the research, please speak with the study doctor or staff.

PAYMENT FOR PARTICIPATION
To You:
You will not be paid for participating in this study.

REIMBURSEMENT FOR TRAVEL EXPENSES
To You:

If you live more than 50 miles from our site at 900 W. Faris Rd Greenville, SC 29605, you may be eligible for reimbursement of your travel expenses. The amount available will be up to $125 per day. This includes gas and/or hotel, as needed to get to your clinical trial appointment. Your travel expenses will be reimbursed to you as a reloadable debit card. Maximum allowed per patient will be determined by the Study Sponsor.

Once we receive your receipts for your travel expenses, you will be asked to complete a W-9 form with your name, address, date of birth, and Social Security number. If you receive $600 or more for study travel in this research study, or a combination of studies at Prisma Health-Upstate in one tax year, Prisma Health-Upstate will send you an IRS Form 1099 for tax purposes.

You will be paid via ClinCard, a reloadable debit card. The ClinCard program is owned by a company called Greenphire. The study team will give Greenphire your name, address, date of birth and Social Security number as part of the payment system. Greenphire will only use this information to make sure you get paid. Greenphire will not use your information for any other purposes, and they will not give or

sell your information to any other company. The study team will provide you more information about the ClinCard program following study enrollment.

I☐ DO or☐ DO NOT live greater than 50 miles from site and will supply receipts as requested prior to receiving reimbursement.

To Institution: Prisma Health Cancer Institute- Center of Integrative Oncology and Survivorship
The Prisma Health- Upstate Cancer Institute is being funded by the sponsor for staff and administrative costs associated with conducting this study.

COMPENSATION FOR INJURY AS A RESULT OF STUDY PARTICIPATION
Prisma Health-Upstate will provide you the care needed to treat any injury, or illness, that directly results from taking part in this research study.

Injuries sometimes happen in research even when no one is at fault. The study sponsor, Prisma Health- Upstate, or the investigators as part of this study have no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the 'Contact for Questions' section of this consent.

VOLUNTARY PARTICIPATION

Participation in this research study is voluntary. You may refuse to participate or withdraw from the study at any time. If you refuse to participate or you withdraw from the study, you will not be penalized or lose any benefits, and your decision will not affect your relationship with your doctor or hospital. If you withdraw from the study, the data collected to that point (including your biospecimens) will still be used unless you specifically request it not be used. We will document your request and remove all data/biospecimen from our collections.

However, if you decide to stop study participation, you are encouraged to talk with your doctor regarding safe removal from the study. Further treatment would be discussed.

You will be required to stop the study before the end if: 1) there is a change in your medical condition, 2) the researchers discover that you have a medical condition that would make it unsafe for you to continue.

If your participation in this research study is stopped, your study doctor will discuss any tests or procedures that might be needed for your health and safety, but you may refuse

any or all of these tests or procedures. Following this discussion with your study doctor, you still have the right to refuse any or all of these tests or procedures.

AUTHORIZATION TO USE AND DISCLOSE (RELEASE) MEDICAL INFORMATION

As part of this research study, the study doctor and his/her research team will keep records of your participation in this study. These study records may be kept on a computer and will include all information collected during the research study, and any health information in your medical records that is related to the research study. The study doctor and his/her research team will use and disclose (release) your health information to conduct this study. This study may result in scientific presentations and publications, but steps will be taken to make sure you are not identified.

Some of the organizations/entities that may receive your information are:

- The study sponsor and any company supporting the study (the sponsor's authorized representatives)
- The Institutional Review Board, which is a group of people who review research with the goal of protecting the people who take part in the study
- The Food and Drug Administration (FDA) and the groups it works with to review research.

Under federal privacy laws, your study records cannot be used or released for research purposes unless you agree. If you sign this consent form, you are agreeing to the use and release of your health information. If you do not agree to this use, you will not be able to participate in this study. Once your health information has been released, federal privacy laws may no longer protect it from further release and use.

The right to use your health information for research purposes does not expire unless you withdraw your agreement. You have the right to withdraw your agreement at any time. You can do this by giving written notice to the study doctor. If you withdraw your agreement, you will not be allowed to continue participation in this research study. However, the information that has already been collected will still be used and released as described above. You have the right to review your health information that is created during your participation in this study. After the study is completed, you may request this information.

If you have any questions about the privacy of your health information, please ask the study doctor.

CONFIDENTIALITY

Your study records are considered confidential (private), but absolute confidentiality cannot be guaranteed. Information may be kept on a computer. All records may be examined and copied by the Institutional Review Board of Prisma Health-Upstate, and other regulatory agencies. This study may result in presentations and publications, but steps will be taken to make sure you are not identified by name.

CONTACT FOR QUESTIONS

For more information concerning this study and research-related risks or injuries, or to give comments or express concerns or complaints, you may contact the principal investigator, whose information is included below.

You may also contact a representative of the Office of Human Research Protection of Prisma Health-Upstate for information regarding your rights as a participant involved in a research study or to give comments or express concerns, complaints or offer input. You may obtain the name and number of this person by calling (864) 455-8997.

Principal Investigator Name: Dr. Jennifer Trilk

Telephone Number: 864-455-9824

CONSENT TO PARTICIPATE

The study doctor, _____, has explained the nature and purpose of this study to me. I have been given the time and place to read and review this consent form and I choose to participate in this study. I have been given the opportunity to ask questions about this study and my questions have been answered to my satisfaction. I have been given the opportunity to review my study doctor's Notice of Privacy Practices. I agree that my health information may be used and disclosed (released) as described in this consent form. After I sign this consent form, I will receive a copy of it for my own records. I do not give up any of my legal rights by signing this consent form.

_____	_____	_____
Printed Name of Participant	Date	Time

_____	_____	_____
Signature of Participant	Date	Time

INVESTIGATOR STATEMENT

I have carefully explained to the participant the nature and purpose of the above study. The participant signing this consent form has (1) been given the time and place to read and review this consent form; (2) been given an opportunity to ask questions regarding the nature, risks and benefits of participation in this research study; and (3) appears to understand the nature and purpose of the study and the demands required of participation. The participant has signed this consent form prior to having any study-related procedures performed.

_____ _____ _____

Signature of Investigator Date Time

Principal Investigator: Dr. Jennifer Trilk Phone: 864-455-9824

Co-Investigators:

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