Official Title: Improving Exercise Capacity With a Tailored Physical Activity Intervention in Lymphoma and Breast Cancer Patients Undergoing Treatment - An Addendum to NIH R01CA167821 "Early Imaging Detection of Cardiovascular Injury After Cancer
IRB-Approved Date: 4/27/22
NCT01719562

Department/ Section of Internal Medicine, Cardiovascular Medicine

Improving Exercise Capacity with a Tailored Physical Activity Intervention in Lymphoma and Breast Cancer Patients Undergoing Treatment – An addendum to NIH R01CA167821 "Early Imaging Detection of CV Injury after Cancer"

Informed Consent Form to Participate in Research
W. Gregory Hundley, M.D., Principal Investigator

INTRODUCTION

You are being asked to participate in a supplemental research study to an existing protocol entitled "Early Imaging Detection of CV Injury after Cancer". In this supplemental study for patients with non and Hodgkin lymphoma or stage I-IV breast cancer, we will test whether participating in either a physical activity intervention or a series of educational classes will help to preserve exercise capability, heart function, brain-based activities (like memory), and your quality of life.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

There will be a total of 21 subjects enrolled in this study at this site. These subjects will be oncology lymphoma or stage I-IV breast cancer patients that expect to receive chemotherapy

WHAT IS INVOLVED IN THE STUDY?

If you agree to participate in the study, you will be met by a study team member who will verify your medical history, current medications, identify any illness or injury that would prevent MRI or exercise testing, and answer any questions you may have about the study**.**

You will then be randomized into one of two pathways. Randomization is the process in which you would be put into a group by chance. In this study, you have a 2: 1 chance to be in the second pathway versus the first pathway. In the first pathway, you will participate in organized health workshops. These workshops are intended to provide information on topics such as proper nutrition, management of stress, sleep practices, and emphasis on an active lifestyle that may help you as you continue through your cancer treatment. This pathway will also test whether stretching exercises may help you as you proceed through cancer treatment. In the other (second) pathway of the study, you will participate in some unsupervised and potentially some supervised moderate activity sessions per week throughout your cancer treatment. The workshops and unsupervised activity sessions are designed to take place either remotely or in-

person, depending on the availability of facilities at the time the visits are scheduled. The supervised sessions will be offered intermittently, as testing centers can accommodate and as appropriate for research participants.

You may not be able to participate in the in-person aspects of this study if you have been recently affected by COVID-19 or if you have been in close contact with a person affected by COVID-19. Prior to each visit, you may be asked to undergo screening questions and tests for COVID-19 as per standard protocol at the testing facility, which may include answering questions about your health, measuring your temperature, or having a nasopharyngeal test performed to detect the presence of SARS-CoV2 virus. During your visit you may be asked to wear a mask depending on the requirements in place at the testing facility.

Whether you participate in the first or second pathway, you may also undergo a series of

1. tests that include MRI scans, blood draws and a cardiopulmonary exercise test performed in an MRI scanning facility. This will depend on the ability of the testing facility to accommodate in-person testing at the time of your scheduled visit. If in-person testing is restricted, some or all of these tests will not be performed.
2. questions that ask you about your quality of life, and
3. questions that test your cognitive or brain function for things like memory, recognition of numbers, etc.

MRI and Exercise testing:

In-person testing:

For the cardiopulmonary exercise test in the MRI facility, please wear loose clothes and comfortable walking shoes.

You will first lie down in the MRI scanner, in which images of your heart will be taken. For the MRI portion of the study, you will need to go to the MRI scanning facility. After arrival at the MRI suite, you will be asked to fill out an MRI Participant Screening Form, which the MRI technologist will review with you prior to your MRI examination.

- A locker with a lock will be assigned to you where you can place your belongings while you are in the scanner.
- Afterwards you will be escorted to the MRI suite where you will be positioned on the MRI table.
- You will then be advanced into the MRI scanner for scanning. You will hear the normal "knocking" sound of the magnet during each scan and will be given a headset or earplugs to reduce the noise. Some people become anxious when advanced into the closed space of the scanner. If this happens to you, we will remove you from the scanner immediately.

Once we begin the scanning process, we ask that you remain as still as possible. On occasion, you may be asked to hold your breath for periods of time lasting 10-30 seconds.
You will then be escorted to a treadmill outside of the MRI room. You will walk on a motor-driven treadmill with the amount of effort increasing gradually. The speed and grade of the treadmill will increase every two minutes and you will continue until symptoms such as fatigue, shortness of breath, or chest discomfort may appear, at which point the test will be terminated. We would like for you to exercise as long as possible. Staff present will remain in constant communication with you to determine when you feel that you are in your final 30 seconds of exercise. At this point, the staff will transfer you back to the MRI scanner.

During the performance of the test, a physician and other trained observer will monitor you and would stop the test if abnormal responses occur. Oxygen consumption (i.e. how much oxygen

your body uses) will be measured through a mouthpiece during the test to measure your exercise capacity.

Certain changes may occur during these tests. These changes include abnormal blood pressure, fainting, disorders of heart beat (too rapid, too slow, or ineffective), and, in very rare instances, heart attack and death. The mouthpiece may cause slight mouth dryness but no other complication. Every effort will be made to minimize such changes through the preliminary examination and observations during testing. Emergency equipment and trained personnel will be available to deal with unusual situations that may arise.

At the completion of the exercise test, you will leave the treadmill and return to the MRI examining table within 1 minute after ceasing exercise to capture further images. This test will be performed during your first study visit and then, in identical fashion, at the 3 and 6 month study visits.

Home-based physical testing:
All participants will complete some home-based testing in addition to the in-person physical testing described above (if availability allows). Participants will receive by mail or delivery by the study team a sanitized box containing the following:

1. A detailed instruction packet for completing the test battery which is comprised of:
    a. Balance test: Using an app on a study provided phone, answer a few questions and hold different positions, like feet side by side, semi-tandem stance, tandem stance, and standing on one foot.
    b. Grip strength test: Involves squeezing the handle of a device that will measure the amount of strength you can generate
    c. 4-meter walk test: Involves measuring the time it takes to walk 4 meters at a normal pace
    d. 6-minute walk test: Involves measuring the distance a participant can walk in 6 minutes
    e. Chair stand test: Involves measuring the amount of time it takes to stand from a seated position and how many times it can be completed in 30 seconds.
2. A smartphone that is not connected to the internet or cellular service, but which contains software for administering a balance assessment.
3. A grip strength dynamometer for measuring upper body strength
4. An actigraph if not already in possession of one from previous visits
5. A 15-meter length of rope and 2 weighted markers to mark out the course for a 6-minute walk test and 4-meter walk test
6. A return shipping label to use to return the exercise kit to the research team after completion of home based testing

The instruction packet with details regarding the various tests is included as an addendum to this consent form. Please review and ask questions prior to signing this consent form. Once testing is complete we ask that you to send back the locked container using the pre-addressed shipping label. This can be picked up by a shipper if you do not feel safe dropping it off at the shipping facility.

We can send copies of your test results to you and to your personal physician. Even if you do not wish to have any of your medical information sent to you and to your physician, you can still participate in this research study.

Do you request that we send important medical findings from your study tests/exams to you and to your personal physician?

[ ] Yes [ ] No _____Initials

Blood Draw:

During each of your research visits, you will have approximately 5 teaspoons of blood withdrawn from either a vein in your arm or a currently placed central line port-a-cath. A portion of your blood from each visit will be used to collect information about your blood cell count and kidney function.

After your blood is drawn, a portion of your blood sample will be saved from each visit for future testing to detect markers of inflammation and evidence of heart injury and stored within the Wake Forest facility. This saved portion will be given only to researchers approved by Dr. W. Gregory Hundley. The total amount of blood withdrawn during your participation in this study will be approximately 3 ounces.

Questionnaires:

Also at each visit, you will be asked to complete several questionnaires that will measure your fatigue, general health, cognitive function (tasks that assess memory, ability to count, etc.) and physical activity. The questionnaires will take 15-40 minutes to complete. You will be given the option to complete these questionnaires electronically at your convenience prior to your research visits or if you will not be participating in in-person visits, using a link to a secure web application named REDCap.

Pathway 1 – Healthy Living Instruction (HLI):

Individuals in this pathway will either come to a centralized meeting location, or will log in to an online meeting space to participate in organized health workshops. Each session will last 60 minutes. Session attendance: 2 sessions offered per month on Reynolda Campus or online and remaining sessions over the telephone over the 6 months. Make up sessions either in person or over the telephone will be offered for those participants who have to miss a group session.

Session Content: Introduction and Review past material (10 mins); Interactive Healthy Living Presentation (30 mins); Short instructor-led program of upper body stretching exercises (10 mins); Wrap-Up, Questions and Promotion of next Workshop (10 mins).

The Healthy Living presentations will be interactive and will provide useful information on such topics as proper nutrition, management of stress, and sleep practices. Experts across a broad range of relevant topics will be brought in to give guest lectures over the course of the 6 months. Participants will be asked to complete homework assignments, review past topics, and engage in small group discussions as a means to increase active involvement in this study arm. The final component of the workshop, the upper body stretching component, will be performed at each visit.

The daily and weekly physical activity will be self-monitored by the participant and validated by the healthy living instruction staff from the objective data obtained by the wrist-worn Actigraph activity monitor. An Actigraph monitor is a small, wrist-sized device that continuously measures activity or movement.

All participants in the HLI group will participate in qualitative assessments of the healthy living instruction using our QPRO program which includes audio-recordings that will be transcribed by an institutionally-approved service, Landmark Associates Inc.

Pathway 2 –Physical activity intervention (PAI):

Patient PAI will be performed either independently or at the Health and Exercise Science Clinical Research Center near the Reynolda Campus of Wake Forest University or other Cardiovascular Rehabilitation Facilities in your community with supervision of clinical exercise physiologist. Center-based Patient PAI sessions will be offered when facilities are available . Participants will have the ability to participate in two to four training sessions per week. Each Patient PAI session will consist of a slow (15min) aerobic warm-up; 20 minutes of strength training; 15 minutes of progressive intensity aerobic exercise (AE); followed by 10 minutes cool-down by stretching/toning with elastic bands similar to those recommended by the American Cancer Society.

The mode of activity for the center-based AE sessions will be over-ground walking and/or stationary cycling. This approach adheres to the principle of progressive intensity and is designed to increase exercise capacity outcomes (peak VO2 peak and 6min walk distance), yet also permit individual "tailoring" based on each participant's daily perceived level of fatigue and disease/treatment related symptoms. Each session is progressively modified with regard to the intensity and duration along with appropriate rest and recovery sessions.

Intermittently, average of every two weeks, there will be the possibility of introducing a single session will be dedicated to short bouts of high levels of activity separated in time by periods of low levels of activity. The advantage of these once every two weeks training sessions is that the duration of the AE session can be decreased and yet the physiological stimulus can increase to produce greater physiological adaptations.

Home based activities will be offered if you are unable to travel to the exercise center. The exercises will be constructed similarly to the center-based exercise and tailored to your access to equipment and symptoms. The study interventionist will work with you to create an exercise session and find creative ways to complete different types of exercises. Exercises could include, but not limited to, over ground walking, body weight exercises, or use of resistance bands.

In addition, participants will be encouraged to accumulate 150 minutes (~30 minutes day) of moderate-light intensity physical activity per week outside the program facility. This can be achieved through a variety of domestic and recreational activities performed at home. The daily and weekly targets for physical activity will be self-monitored by the participant and validated weekly by the intervention staff from the objective data obtained by the wrist-worn Fitbit and Actigraph activity monitors. An Actigraph monitor is a small, wrist-sized device that continuously measures activity or movement.

All participants in the PAI group will participate in qualitative assessments of the physical activity intervention using our QPRO program which includes audio-recordings that will be transcribed by an institutionally-approved service, Landmark Associates Inc.

To enhance safety, each subject will be instructed to participate at an individually prescribed level of exertion, report any symptoms or problems they might encounter during physical activity, and to rest as needed. The interventionist will take time to communicate with participants during the center-based AE sessions in order to determine whether physical activity prescriptions are appropriate, to ask how participants are feeling, and to answer questions regarding the physical activity prescription.

How Long Will I Be in the Study?

Approximately a 6-month period.

What Are the Risks of the Study?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Risks and side effects related to the procedures we are studying include:

Risks of COVID-19 testing

A COVID-19 (coronavirus) nasopharyngeal test can be an uncomfortable procedure. This test typically involves the use of a nasal swab. Determining whether you have been exposed to and

carry the COVID-19 virus is important for your own safety and that of other patients and study staff.

Risks of Exercise Test
A small chance exists that the exercise test could lead to symptoms of heart disease or injury. About 1 in every 10,000 patients with heart disease dies during an exercise test, and serious complications such as heart attack, prolonged chest pain or serious heart rhythm problems can happen in approximately 4 of every 10,000 participants. During the exercise test, there is a chance you could lose your balance, trip, or fall. To minimize this risk, trained staff will ensure that the treadmill is free from obstruction and remain nearby. As well, the exercise test could result in findings that might be helpful (for example, early detection of a particular condition) or troublesome (for example, causing you worry, involving additional and perhaps costly testing that may or may not benefit your health).

Home-based physical activities and testing:
There are slight risks of participating in the home-based physical testing including injury due to a loss of balance or a fall, muscle discomfort or strain due to strength tests (grip and chair stand). However, the use of balance screening tests and the measurement of resting ECG and blood pressure are designed to limit these risks as much as possible and we do not expect the risks to outweigh those associated with participating in routine activities of daily living.

Risks of MRI Scans
MRI scans are not associated with any known side effects. Some subjects experience discomfort associated with enclosed spaces during MRI scanning. All standards of care used to monitor for any potential side effects that are used for clinical MRI facility today will be implemented and the exercise test will be carefully monitored by a cardiologist and exercise physiologist.

Risks of Blood Draws
You may experience discomfort, bruising and/or bleeding where the needle is inserted during the blood draw. Occasionally some people become dizzy, lightheaded or feel faint. Infection may occur on rare occasions. Frequent donation of blood can result in low iron in your blood (iron deficient anemia). You should not donate blood more than 2 times per week and no more than approximately one pint (about 500 ml) of blood in an eight week period.

Risks of Surveys and Questionnaires
In this study you will fill out questionnaires. These questionnaires will ask about how you are feeling. These feelings may become more intense when you fill out these questionnaires.

Risks of Providing Confidential Information
In addition, there is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. Taking part in this research study may involve providing information that you consider confidential or private. Efforts, such as coding research records, keeping research records secure and allowing only authorized people to have access to research records, will be made to keep your information safe.

There also may be other side effects that we cannot predict. You should tell the research staff about all the medications, vitamins and supplements you take and any medical conditions you have. This may help avoid side effects, interactions and other risks.

Pregnant women are excluded from participation in this study.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

You are not expected to receive any direct benefit from taking part in this research study. Results from this study could provide additional information about your cardiovascular health that could be accessed by your primary care physician to better manage your care. Occasionally, these new findings provoke anxiety until they are resolved. The study team will assist the participant in referrals so that any new findings will be taken care of immediately. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

Your alternative is not to participate, or you may want to ask local facilities if they have such a program for cancer patients.

What About My Health Information?

In this research study, any new information we collect from you and/or about your health or behaviors is considered Protected Health Information. The information we will collect for this research study may include**:** Name, date of birth, height, weight, medical record number, address, contact information, oncology and cardiac related health and treatment information, research generated data/information, serum hematocrit measures, MRI measures, and exercise capacity measures.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may be placed in your medical record, and may be used to help treat you, arrange payment for your care, or assist with Medical Center operations.

We will make every effort to keep your Protected Health Information private. We will store records of your Protected Health Information in a cabinet in a locked office or on a password protected computer. Only the following people or organizations will be granted access to your Protected Health Information:

1) The study investigator and his/her staff, or others at Wake Forest University Health Sciences who oversee research

2) Other people or laboratories providing services for this research project on behalf of Wake Forest University Health Sciences and Wake Forest University Baptist Medical Center

3) Wake Forest University Health and Exercise Sciences

4) Some of the people, agencies and businesses that may receive and use your health information are the research sponsor; representatives of the sponsor assisting with the research; investigators at other sites who are assisting with the research; central laboratories, reading centers or analysis centers; the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital; representatives from government agencies such as the Food and Drug Administration (FDA) or the Office of Human Research Protections (OHRP), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

If required by law or court order, we might also have to share your Protected Health Information with a judge, law enforcement officer, government agencies, or others. If your Protected Health

Information is shared with any of these groups it may no longer be protected by federal or state privacy rules.

Any Protected Health Information collected from you in this study that is maintained in the research records will be kept an indeterminate period of time. This authorization does not expire and any research information entered into your medical record will be kept for as long as your

medical record is kept by the Medical Center. You will not be able to obtain a copy of your Protected Health Information in the research records until all activities in the study are completely finished.

You can tell Dr. Gregory Hundley that you want to take away your permission to use and share your Protected Health Information at any time by sending a letter to this address:

Gregory Hundley
[redacted]

However, if you take away permission to use your Protected Health Information you will not be able to be in the study any longer. We will stop collecting any more information about you, but any information we have already collected can still be used for the purposes of the research study.

By signing this form you give us permission to use your Protected Health Information for this study.

Laboratory test results and other medical reports created as a result of your participation in the research study may be entered into the computer systems of Wake Forest University Health Sciences and North Carolina Baptist Hospital. These will be kept secure, with access to this information limited to individuals with proper authority, but who may not be directly involved with this research study.

A North Carolina Baptist Hospital (NCBH) medical record will be created for all study

participants. Information about your participation in the study will be placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WHAT ARE THE COSTS?

There are no costs to you for taking part in this study. All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Participants who are randomized into the "Participants Pathway 1" will be provided an Actigraph at no charge to use during their participation in the study. Participants who are randomized into the "Participants Pathway 2" will be provided a Fitbit and Actigraph at no charge to use during their participation in the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility.

WILL YOUR RESEARCH RECORDS BE CONFIDENTIAL?

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed unless it is authorized by you, required by law, or necessary to protect the safety of yourself or others. There is always some risk that even de-identified information might be re-identified.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institutes of Health (NIH) which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal,

state, or local law of the results from the following research activities of this study: Exercise tests, MRI exams, blood draws, surveys and questionnaires.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document to a) allow important medical findings from your study tests/exams be sent to your personal physician and b) regarding information about your participation in the study being placed in the NCBH medical record, along with any routine medical test results that were obtained at NCBH as part of this study.

WILL YOU BE PAID FOR PARTICIPATING?

Parking validation will be provided for all study-related visits. Also, we will provide bi-monthly participant stipends of $30 for continuing through the study.

WHO IS SPONSORING THIS STUDY?

This study is being co-sponsored by the Comprehensive Cancer Center of Wake Forest University Health Science and the National Institutes of Health (NIH). The NIH sponsor is providing money or other support to Wake Forest University Health Sciences to help conduct this study. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied.

WHAT HAPPENS IF YOU EXPERIENCE AN INJURY OR ILLNESS AS A RESULT OF PARTICIPATING IN THIS STUDY?

Should you experience a physical injury or illness as a direct result of your participation in this study, Wake Forest University School of Medicine maintains limited research insurance coverage for the usual and customary medical fees for reasonable and necessary treatment of such injuries or illnesses. To the extent research insurance coverage is available under this policy the reasonable costs of these necessary medical services will be paid, up to a maximum of $25,000. Wake Forest University Baptist Medical Center holds the insurance policy for this coverage. It provides a maximum of $25,000 coverage for each claim and is limited to a total of $250,000 for all claims in any one year. The Wake Forest University School of Medicine, and the North Carolina Baptist Hospitals, Incorporated do not assume responsibility to pay for these medical services or to provide any other compensation for such injury or illness. Additional information may be obtained from the Medical Center's Director of Risk and Insurance Management, at [redacted]

If you are injured, the insurer may require information such as your name, social security number, and date of birth in order to pay for your care. This is because the insurer is required by law to report any payments made to cover the care of any persons who are members of a government insurance plan to the Department of Health and Human Services.
You do not give up any legal rights as a research participant by signing this consent form. For more information on medical treatment for research related injuries or to report a study related illness, adverse event, or injury you should call Gregory Hundley at [redacted]

WHAT ARE MY RIGHTS AS A RESEARCH STUDY PARTICIPANT?

Taking part in this study is voluntary. You may choose not to take part or you may leave the study at any time. Refusing to participate or leaving the study will not result in any penalty or loss of benefits to which you are entitled. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first to learn about any potential health or safety consequences. The investigators also have the right to stop your participation in the study at any time. This could be because it is in your best medical interest, your condition worsened, new information becomes available, you had an unexpected reaction, you failed to follow instructions, or because the entire study has been stopped.

You will be given any new information we become aware of that would affect your willingness to continue to participate in the study.

Other Choices

It is not known if any of the activities in Pathways 1 or 2 will be of benefit to you. Your alternative is not to participate.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or in the event of a research-related injury, contact the study investigator, Dr. Gregory Hundley at [redacted]

The Institutional Review Board (IRB) is a group of people who review the research to protect your rights. If you have a question about your rights as a research participant, or you would like to discuss problems or concerns, have questions or want to offer input, or you want to obtain additional information, you should contact the Chairman of the IRB at [redacted].

You will be given a copy of this signed consent form.

I agree to take part in this study. I authorize the use and disclosure of my health information as described in this consent and authorization form. If I have not already received a copy of the Privacy Notice, I may request one or one will be made available to me. I have had a chance to ask questions about being in this study and have those questions answered. By signing this consent and authorization form, I am not releasing or agreeing to release the investigator, the sponsor, the institution or its agents from liability for negligence.

Subject Name (Printed):_____

Subject Signature:_____Date:_____Time:_____am pm

Person obtaining consent (Printed):_____

Person Obtaining Consent:_____Date:_____Time:_____am pm