Department/Section of *Department of Neurology*

A PILOT STUDY USING ULTRASOUND FOR THE DETECTION OF OXALIPLATIN-INDUCED PERIPHERAL NEUROPATHY

Informed Consent Form to Participate in Research
Roy Strowd, MD, Glenn Lesser, MD, Principal Investigators

SUMMARY

You are invited to participate in a research study. The purpose of this research is to find out whether ultrasound can be used to diagnose peripheral neuropathy caused by oxaliplatin. You are invited to be in this study because you have a gastrointestinal cancer, have received oxaliplatin, and have neuropathy. Your participation in this research will involve completing a one time visit where you undergo ultrasound of the nerve, nerve conduction test, skin biopsy, and clinical examination of your nerves. These studies are standard studies performed for patients with neuropathy.

If you participate in this study, you will have one additional visit. During this visit you will undergo a series of tests to see how your nerves are working. This will include a nerve conduction test, nerve ultrasound, skin biopsy, and clinical examination. These tests are performed regularly for patients who have neuropathy. All research studies involve some risks. A risk to this study that you should be aware of is pain, discomfort, or infection from the nerve conduction test or skin biopsy. There is not the possibility that you may benefit from participation in this study.

Your participation in this study is voluntary. You do not have to participate in this study if you do not want to. There may be other choices available to you. Some other choices may include talking with your doctor about treatment of your neuropathy. You will not lose any services, benefits, or rights you would normally have if you choose not to participate.

The remainder of this form contains a more complete description of this study. Please read this description carefully. You can ask any questions if you need help deciding whether to join the study. The person in charge of this study is Roy Strowd, PI. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his/her contact information is: Roy Strowd, MD at 336-716-6777.

If you have any questions, suggestions or concerns about your rights as a volunteer in this research, contact the Institutional Review Board at 336-716-4542 or the Research Subject Advocate at Wake Forest at 336-716-8372.

INTRODUCTION

You are invited to be in a research study. Research studies are designed to gain scientific knowledge that may help other people in the future. You are being asked to take part in this study because you have gastrointestinal cancer, have been or are currently being treated with a chemotherapy drug called a oxaliplatin, and you have symptoms of neuropathy (such as:

numbness, tingling, pain and/or sensitivity in your arms, legs, hands or feet). Your participation is voluntary. Please take your time in making your decision as to whether or not you wish to participate. Ask your study doctor or the study staff to explain any words or information contained in this informed consent document that you do not understand. You may also discuss the study with your friends and family.

WHY IS THIS STUDY BEING DONE?

The purpose of this research study is to find out whether ultrasound can be used to diagnose peripheral neuropathy caused by oxaliplatin. Nerve ultrasound is used regularly to assess other causes of neuropathy. It is not painful and easy for providers to perform and patients to complete. This study will be one of the first to understand whether ultrasound can be used to detect neuropathy in gastrointestinal cancer patients treated with the chemotherapy drug called a oxaliplatin.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

There will be 20 people at one research site that will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

In this study you will have tests done that will help researchers find out if there are better ways to detect neuropathy. If you are eligible for the study and you sign this informed consent, you will be scheduled to have 2 clinic visits.

In the first visit, you will be asked for your medical history to better understand your past and current health and the medicines you have taken or are taking. You will be asked to fill out a questionnaire (survey) about how your neuropathy affects your life. You will also give a little more than 2 teaspoons of blood (12 mLs or 2.43 teaspoons) that will be used for research purposes like looking at molecules in the blood that may be involved in inflammation.

At the second visit, you will have a short physical exam to test your strength and reflexes. Several tests which are routinely done to assess neuropathy will be performed: an ultrasound will be used to look at your nerves, a nerve conduction study will be used to see how your nerves are working, and you will have a skin biopsy from your leg that will to look at the nerves in your skin. Each of these tests is routinely done to look for neuropathy in patients with cancer and other medical problems affecting the nerves. This will be your last visit.

Note:

- All of these activities will take place after signing the consent
- The blood draw and the survey will be given at the same time. It may take 5-10 minutes to complete the survey.

If you take part in this study, you will have the following tests and procedures:

Blood Draws

You will have approximately slightly more than 2 teaspoons (12 mls) of blood withdrawn from a vein once. The total amount of blood withdrawn during the study will be approximately 12 mLs

or slightly more than 2 teaspoons.

Physical Exams
The physical exams will look at height, weight, strength and sensation and is a part of your standard care.

Questionnaires (survey)
A survey will be used so the doctors can determine how your neuropathy is affecting your life. This survey is 19 questions and may take 5-10 minutes to complete. You will fill out this questionnaire one time and is a part of your normal care to assess your neuropathy.

Short Neurological Exam
This exam will test the strength of the tibialis anterior (the muscle on the front part of your lower leg) and gastrocnemius (your calf muscles, on the back part of your lower leg) and deep tendon reflex exam of the Achilles tendon on the limb to be examined with nerve conduction studies and ultrasound. This will be done once and is a part of your normal care to assess your neuropathy.

Ultrasound
This procedure will be done to look at the size of your nerves. It is done as part of the workup for nerve problems. A small amount of jelly will be placed on your skin over a nerve. The ultrasound will then slide along your skin using high frequency sound waves to look at your nerves. Ultrasound is also used to look at babies when they are growing inside their mother. This test is safe and is not painful. This will be done once and is a part of the normal care to assess a neuropathy.

Nerve Conduction Studies
Nerve conduction studies are one way to determine how well your nerves are sending signals. You will have 2 electrodes stuck on the skin (like Band-Aids) along a nerve and the nerve will be stimulated with a mild, brief electric shock. This will be done once and is a part of the normal care to assess a neuropathy.

Skin Biopsy
A skin biopsy will be performed once in this study, typically in your last clinical encounter. A pencil-like biopsy instrument will be used to remove one small, thin cylinder of tissue (4 mm in diameter; smaller than a pencil eraser). The skin biopsy will be removed from the area near the outside, back part of your leg (above your ankle). The biopsy site will be dressed with a bandage or steri-strips which should remain in place for 2-3 days. Prior to the biopsy, you will have a painkiller injection at the spot for the biopsy to numb the area where the biopsy will be taken. This will be done once and is a part of the normal care to assess a neuropathy.

In the future, research on your specimen may involve whole genome sequencing.

Your test results will be made available to your primary cancer doctor. If you do not wish to have any of your medical information sent to your physicians, you can still participate in this research study.

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

[ ] Yes [ ] No _____ Initials

STORAGE OF BIOLOGICAL TISSUE

If you agree to participate in this study, we will draw 12 mLs of the blood and take tissue from your skin to use for future research. This sample will be kept and may be used in future research to learn more about other diseases. Your blood sample will be obtained at the Wake Forest Baptist Comprehensive Cancer Center. Your skin biopsy sample will be obtained at the Departments of Neurology and Dermatology- Dermatopathology at Wake Forest Baptist Medical Center. The sample will be stored in Dr. Yusuke Shiozawa's laboratory and it will be given only to researchers approved by Drs. Roy Strowd or Glenn Lesser. An Institutional Review Board (IRB) must also approve any future research study using your tissue sample. In order to participate in this study, you must be willing to provide this sample for future research.

Your blood/skin samples will be stored with a unique identifier and will not include any identifiable information about you such as your name, address, telephone number, social security number, medical record number or any of the identifiers outlined in the HIPAA Privacy Rule. The unique identifier will be a randomly assigned number and only the principal investigator will have access to the code that links the unique identifier to you. Your name, address, social security number, etc., will never be disclosed to future researchers and neither will the code that links your identifiers to the sample.

The research that may be performed with your blood/skin sample is not designed to help you specifically. There is no personal benefit to you from taking part in this aspect of the research study. It might help people who have diseases at some point in the future, but it is not known if this will happen. The results of the research performed with your blood/skin will not be given to you or your doctor. The results will not be put in your medical record. The research using your blood/skin sample will not affect your care.

Your blood/skin sample will be used only for research and will not be sold. The findings from this research may result in the future development of products that are of commercial value. There are no plans to share any of the profits with you which may occur as a result of the research.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for the length of time needed to perform the clinical procedures and all efforts will be made so that the research activities occur when your normal clinic visits occur. The study may involve up to 2 clinic visits in addition to the visit to sign consent. Depending upon scheduling, it may take up to 4 weeks. You will be followed for an extra 30 days to ensure the spot where the skin biopsies were taken have healed or are healing as they should. This follow-up may take place via telephone or in person.
You can stop participating at any time. If you decide to stop participating in the study we encourage you to talk to the investigators or study staff first. Leaving the study would not affect

your normal care.

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. The main research related risk is from an extra blood draw. All other procedures are a part of your normal care and you would have these procedures done whether you were in the study or not, but the risks are described below. 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 Skin Biopsy
Some risks of the skin biopsy procedure include: some discomfort/pain, bleeding, bruising, pain, scarring, infection or a reaction to the local anesthetic used to numb the area of the biopsy.

Risks of Nerve Conduction Studies
Nerve conduction studies may result in slight discomfort/pain when the electric stimulation of the nerve occurs. There may also be some discomfort from the adhesive used to stick on the electrodes when those electrodes are taken off.

Risks associated with Questionnaires
As part of this study, you will be asked questions about how your neuropathy is affecting your life. These feelings may be heightened when filling out the questionnaires.

Risks Associated with Blood Draws
You may experience discomfort, bruising and/or bleeding where the needle is inserted. 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).

Risks of Ultrasound
Ultrasound is considered to be a safe procedure. However, some risks may be slight warming of the tissue or producing small pockets of gas in the body or tissues.

Risk associated with Providing Confidential or Private Information
There is a slight risk of a breach of confidentiality. We will do our best to protect your confidential information. 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.

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.

REPRODUCTIVE RISKS AND OTHER ISSUES TO PARTICIPATING IN RESEARCH

There are no reproductive risks related to taking part in this research.

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. We hope the information learned from this study will benefit other people in the future.

WHAT OTHER CHOICES ARE THERE?

This is not a treatment study. Your alternative is to not participate in this study.

- Undergo routine diagnostic work-up for your neuropathy without being enrolled on the study (which may also include blood draws, Physical Exams/Quantitative Sensory Testing, questionnaires, neurological exam, nerve conduction studies, or skin biopsy).
- Not have diagnostic work-up for your neuropathy.

WHAT ARE THE COSTS?

Taking part in this study will not lead to added costs to you or your insurance company.

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.

Participant information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

If you choose to participate in this study, your medical record at Wake Forest University Baptist Medical Center will indicate that you are enrolled in a research study. Information about the research and any medications or devices you are being given as a participant may also be included in your medical record. This part of the medical record will only be available to people who have authorized access to your medical record. If you are not a patient at this Medical Center, a medical record will be created for you anyway to ensure that this important information is available to doctors in case of an emergency.

WILL YOU BE PAID FOR PARTICIPATING?

You will receive a $50 gift card to reimburse for travel for the neurodiagnostic and study assessment. To receive payment you must provide your social security number, name and address so that we can comply with IRS (Internal Revenue Service) reporting requirements. When payments are reported to the IRS we do not let them know what the payment is for, only that you have been paid. If you do not wish to provide this information you can still take part in this study but you will not be paid. Parking will be validated for study related visits.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest University Health Science, which is providing money or other support to Wake Forest University Health Sciences to help conduct this study.

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 (336) 716-3467.

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 Roy Strowd, MD and Glenn J. Lesser, MD at 336-716-6777.

WHAT ABOUT MY HEALTH INFORMATION?

In this research study, any new information we collect from you and/or information we get from your medical records or other facilities about your health or behaviors is considered Protected Health Information. The information we will collect for this research study includes**:**

- Medical history including treatments, medications and previous other current diseases;
- Name, address and demographics; and
- Results from clinical tests.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study will be placed in your medical record. 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.

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Your personal health information and information that identifies you ("your health information") may be given to others during and after the study. This is for reasons such as to carry out the study, to determine the results of the study, to make sure the study is being done correctly, to provide required reports and to get approval for new products.

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. Some of the people, agencies and businesses that may receive and use your health information are the Institutional Review Board; representatives of Wake Forest University Health Sciences and North Carolina Baptist Hospital.

Some of these people, agencies and businesses may further disclose your health information. If disclosed by them, your health information may no longer be covered by federal or state privacy regulations. Your health information may be disclosed if required by law. Your health information may be used to create information that does not directly identify you. This information may be used by other researchers. You will not be directly identified in any publication or presentation that may result from this study unless there are photographs or recorded media which are identifiable.

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 for an indeterminate period of time. This authorization does not expire. 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 Roy Strowd, MD or Glenn Lesser, MD 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:

Roy Strowd, MD or Glenn Lesser, MD
Medical Center Blvd
Winston-Salem, NC 27104

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 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 your doctor feels this study would interfere with care for your disease, or if the initial results determined that there was an active problem which necessitated urgent management. Information that identifies you may be removed from the data or specimens that are collected as part of this study and could be used for future research or shared with others without additional consent.

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

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 investigators, Roy Strowd, MD or Glenn Lesser, MD at 336-716-6777.

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 (336) 716-4542.

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

SIGNATURES

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