Informed Consent Form

Single-Institution Trial Investigating the Effectiveness of Transcutaneous Electrical nerve stimulation (TENS) in Taxane Induced Peripheral Neuropathy (CIPN) in Patients with Early Stage Breast Cancer

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EMORY | WINSHIP CANCER INSTITUTE
National Cancer Institute-Designated Comprehensive Cancer Center

You Are Being Asked to Be in a Research Study

Concise presentation of key concepts

You are being asked to be in a research study. A research study is designed to answer a scientific question. If you agree to be in the study you will be one of 27 who are being studied at Emory.

Why is this study being done?

This study is being done to answer the question: does transcutaneous electrical nerve stimulation (TENS) improve symptoms of chemotherapy induced peripheral neuropathy (CIPN) while on chemotherapy? You are being asked to be in this research study because you have been identified by your doctor as having new CIPN symptoms like pain, numbness or tingling in your hands or feet since starting chemotherapy for breast cancer. Given that current CIPN treatments are often ineffective there is currently a critical need to identify new therapies, as worsening CIPN symptoms reduce quality of life and in severe cases can cause interruption of chemotherapy.

Do you have to be in the study?

It is your choice to join this research study. You do not have to be in it. Your choice will not affect your access to medical care for your condition. Before you choose, take time to learn about the study.

What do you have to do if you choose to join this study?

If you qualify and choose to join the study, you will participate for 6 weeks which will include 3 clinic visits. The researchers will ask you to do the following: you will be asked some questions about your CIPN symptoms and have a baseline test to measure the degree of nerve damage (monofilament testing), use the portable TENS unit for 1-hour each day for 2 weeks, and keep a diary each day to help us know how TENS is working for your CIPN symptoms. The first TENS treatment will take place at the initial clinic visit. The subsequent 13 treatments will take place at home. If you feel that TENS benefited you during the first 2 weeks you will have the option to continue using TENS for the remaining 4 weeks of the study. Some of these procedures will be paid for by the study.

How is this study going to help you?
If you are in the study, you will be helping the researchers answer the study question. As we are not sure whether TENS works for CIPN symptoms, this study may not benefit you directly.

What are the risks or discomforts you should know about before deciding?
The study will take time. The device that is being tested may not work any better than regular care and may even cause harm. All studies have some risks. Some risks are relatively small, like being bored or losing time. Some are more serious. Risks for this study include:

- risks of the device, some of which include rash at the site of electrode pad placement, as well as worsening pain, numbness, or tingling after starting TENS
- loss of privacy
- breach of confidentiality

You can find a full list of expected risks, their frequency and severity in the section titled “What are the possible risks and discomforts?”

Alternatives to Joining This Study
If you decide not to enroll in this study you would discuss with your medical oncologist other options to treat your CIPN symptoms including starting new medications or other treatments.

Costs
The study will pay for certain items and services that you may receive if you take part in this study. Specifically, the study will pay for the cost of the TENS unit, as well as the monofilaments used for neuropathy testing at each visit. You will have to pay for the items or services for which the study does not pay. The study will not pay for your regular medical care.

There is more information in the “Costs” section further below.

What Should You Do Next?
Read this form, or have it read to you. Make sure the study doctor or study staff explains the study to you. Ask questions such as how much time you will have to spend on the study, any words you do not understand and more details about study procedures. Make sure you understand which parts of the study are research and which are standard care that you would have even if you did not join the study. Take time to think about this and talk about it with your family and friends.

Emory University and Saint Joseph's Hospital
Consent to be a Research Subject / HIPAA Authorization

Title: Single-Institution trial investigating the effectiveness of transcutaneous electrical nerve stimulation in taxane induced peripheral neuropathy in patients with early stage breast cancer

IRB #: STUDY00003705

Principal Investigator: Manali Bhave, MD

Introduction

You are being asked to be in a medical research study. This form tells you what you need to think about before you choose if you want to join the study. **It is your choice. If you choose to join, you can change your mind later and leave the study.** Your choice will not cause you to lose any medical benefits. If you choose not to join this study, your doctor will still treat you.

Before you decide:

- Read this form or have it read to you
- Listen to the study doctor or study staff explain the study to you
- Ask questions about anything that is not clear

You will get a copy of this form. Take your time to think about joining the study. You may wish to discuss it with family or friends. Do not sign this form if you still have questions or something does not make sense to you. By signing this form, you will not give up any legal rights.

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.

What is the purpose of this study?

The purpose of this study is to determine if transcutaneous electrical nerve stimulation (TENS) is feasible and effective for chemotherapy induced peripheral neuropathy (CIPN) symptoms that develop while on chemotherapy.

What will you be asked to do?

If you would like to be part of this study, you will be asked to use the portable TENS unit for 1-hour each day while at home for a total of 14 days. All patients enrolled on the trial will receive TENS, there will be no "placebo" group. The TENS unit is battery powered and consists of 4 electrode pads. These electrodes deliver electrical impulses to the skin. There is evidence in previous studies that normal nerve signals are disrupted in CIPN and that the electrical impulses from the TENS unit may counteract these disordered signals. Two pads will be placed on each extremity (either the lower legs if the CIPN symptoms are mostly in the feet/toes or on the forearms if symptoms are mostly in your hands/fingers). At the first visit the clinical trial staff will measure the extent of your CIPN by having you complete a few questionnaires. They will also conduct monofilament testing, a simple test to determine the extent of nerve damage in your feet. A monofilament consists of a pointed tip that is

placed on the skin and measures touch perception. At every assessment each end of a two-sided monofilament will be placed on 10 touch points located throughout both feet. At each touch point you will be asked if you feel the monofilament (yes or no response). A score will be recorded at every visit. A doctor will review the TENS operating instructions with you, including the recommended TENS settings and the optimal placement of the electrode pads based on your symptoms. You will complete the 1st of 14 one-hour TENS treatments during this initial visit to make sure that you understand how to use the TENS unit and place the pads correctly on your skin. You will complete the subsequent 13 daily treatments at home. Each day that you complete TENS you will fill out a diary that includes the following: the start and end times of the treatment, a daily symptom scale, and space to record any issues or adverse events with TENS. On Day 3, a member of the trial staff will call you to review the operating procedure and to answer any questions that you may have. On day 14 you will return for a follow-up visit to review your diary and repeat the questionnaires and monofilament testing, which will help us measure whether TENS is working. If you found TENS helpful during the initial treatment period you will be able to continue using TENS as you did for the first two weeks for the remainder of the trial (weeks 3-6) while completing weekly diary entries. Whether or not you use TENS during weeks 3-6 there will be a final follow up at end of week 6, where the same questionnaires and monofilament testing will be repeated. You will be able to keep the TENS unit at the conclusion of the trial.

Who owns your study data?

If you join this study, you will be donating your data. You will not be paid if your data are used to make a new product. If you leave the study, the data that was already collected may be still be used for this study. If you withdrawal from the study early we may continue to use the data we collected from you while you were enrolled on the study. There will be no tissue or blood samples collected from you as part of this study.

What are the possible risks and discomforts?

There may be side effects from the study device or procedures that are not known at this time. No serious adverse events attributed to TENS occurred in two previous studies (total of 68 participants) of TENS in chronic CIPN.

The most common risks and discomforts expected in this study are:
Worsening pain, cramping, or tingling in 10% of patients (7 out of 68 patients reported this in two previous studies)

The less common risks and discomforts expected in this study are:
Skin rash at the site of the electrode pad placement in 4% of patients (3 out of 68 patients reported this is two previous studies)

Rare but possible risks include:
Burns have not been reported in previous trials, but this is a possible risk as TENS utilizes electricity. Another risk due to electrical current includes electrocution. TENS should not be used near water, while operating machinery or placed in sensitive areas like the throat/neck, head, eyes, chest, or genitals, given the possible risk for electrocution or involuntary muscle contraction. Patients with an implanted electronic device like a cardiac pacemaker, defibrillator or pain pump should not enroll in this trial as TENS could interfere with their function and cause harm.

If you are a woman: to protect against possible side effects of the study device, women who are pregnant may not take part in this study. If you become pregnant, there may be risks to you, the embryo, or fetus. These risks are not yet known. If you are a woman of childbearing ability, you and the study doctor must agree on a method of birth control to use throughout the study. If you think that you have gotten pregnant during the study, you must tell the study doctor immediately. Pregnant women will be taken out of the study.

While using the TENS device at home, keep it out of the reach of children or anyone else who may not be able to read or understand the label. Do not let anyone else use the TENS unit besides you.

Researchers may learn something new during the study that may affect your choice to be in the study. If this happens, they will tell you about it. Then you can choose if you want to stay in this study. You may be asked to sign a new form if you choose to stay in the study.

Will you benefit from the study?
This study is not designed to benefit you directly. As it is not known whether TENS helps CIPN symptoms while patients are on chemotherapy your symptoms may improve while you are on this study but they may not, and in rare cases may even get worse. This study is designed to learn more about the feasibility of a home-based TENS regimen and to look for signs that TENS may be beneficial for CIPN. The study results may be used to help others in the future.

Will you be paid for your time and effort?
You will not be compensated for being in this study.

What are your other options?
If you choose not to join this study, you can get care outside of this study. Other treatments for CIPN outside of a study that you could receive from your treating medical oncologist or anesthesia-pain physician include neuropathic mediations like duloxetine, gabapentin, pregabalin or amitriptyline, which may or may not help your symptoms. The study doctor will discuss these with you. You do not have to be in this study to be treated for CIPN.

How will your private information be protected?
Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Storing and Sharing your Information
We will store all the data that you provide using a code. We need this code so that we can keep track of your data over time. This code will not include information that can identify you (identifiers). Specifically, it will not include your name, initials, date of birth, or medical record number. We will keep a file that links this code to your identifiers in a secure location separate from the data.

We will not allow your name and any other fact that might point to you to appear when we present or publish the results of this study.

Your data may be useful for other research being done by investigators at Emory or elsewhere. We may share the data, linked by the study code, with other researchers at Emory, or with researchers at other institutions that maintain at least the same level of data security that we maintain at Emory. We will not share the link between the study code and your identity.

We may also place data in public databases accessible to researchers who agree to maintain data confidentiality, if we remove the study code and make sure the data are anonymized to a level that we believe that it is highly unlikely that anyone could identify you. Despite these measures, we cannot guarantee anonymity of your personal data.

We will use your data only for research. We will not sell them. However, the results of this research might someday lead to the development of products (such as a commercial cell line, a medical or genetic test, a drug, or other commercial product) that could be sold by a company. You will not receive money from the sale of any such product.

Medical Record

If you have been an Emory and Emory Saint Joseph's Hospital patient before, then you already have an Emory and Emory Saint Joseph's Hospital medical record. If you have never been an Emory and Emory Saint Joseph's Hospital patient, you do not have one. An Emory and Emory Saint Joseph's Hospital medical record will be made for you if an Emory Atlanta and Emory Saint Joseph's Hospital provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory and Emory Saint Joseph's Hospital medical record you have now or any time during the study.

Emory and Emory Saint Joseph's Hospital may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory and Emory Saint Joseph's Hospital medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

Tests and procedures done at non-Emory and Emory Saint Joseph's Hospital places may not become part of your Emory and Emory Saint Joseph's Hospital medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

If you believe you have become ill or injured from this research, you should contact Dr. Manali Bhave at telephone number [redacted] You should also let any health care provider who treats you know that you are in a research study.

If you get ill or injured from being in the study, Emory and Emory Saint Joseph's Hospital will help you to get medical treatment. Neither Emory and Emory Saint Joseph's Hospital have set aside money to pay for this medical treatment. Your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurance does not pay, then you will have to pay these costs.

For Emory and Emory Saint Joseph's Hospital, the only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory employee. "Negligence" is the failure to follow a standard duty of care. You do not give up any legal rights you may have by being in this study, including any right to bring a claim for negligence.

Costs

The study will pay for certain items and services that you may receive if you take part in this study. Specifically, the study will pay for the TENS unit for each participant and will cover the cost of items needed to operate the TENS unit (e.g. batteries or extra electrode pads). Additionally, the study will pay for the monofilaments that will be used for neuropathy testing at each visit.

You will have to pay for the items or services for which the study does not pay. The study will not pay for your regular medical care. If you have insurance, Emory and Emory Saint Joseph's Hospital will submit claims to your insurance for items and services that the study does not cover. Emory and Emory Saint Joseph's Hospital will send in only those claims for items and services that it reasonably believes your insurance will pay and that the study has not paid. Participation in this study requires three clinic visits (Day 1, 15, 42 +/- 7). These visits are part of your regular medical care (not dedicated research visits) so they will be billed to your insurance as such. We will gather the study-specific data while you are at these appointments. The Day 1 assessment will take place at your initial referral visit for CIPN with the cancer pain physician. Day 15 will be at your medical oncology appointment and Day 42 will take place at a follow up appointment with the cancer pain physician.

The actual amount that you have to pay depends on whether or not you have health insurance and whether or not that insurance will pay for any research study costs. Generally, insurance companies will not pay for items and services that are required just for a research study. Some insurance companies will not pay for regular medical treatment or treatment for complications if you are in a study. How much you will have to pay for any co-payments, deductibles or co-insurance depends on your plan. Emory and Emory Saint Joseph's Hospital will not pay for these costs.

It is a good idea to contact your insurance provider and tell them you want to be in this research study. Ask them what they will pay for and what they will not pay for. You can also ask the study team for help in figuring out what you will have to pay.

If you do not have insurance, Emory and Emory Saint Joseph's Hospital will review your case as part of its program for low-income patient care. The standard policies of that program will apply. The program will figure out if you have to pay any costs for taking part in the study and what those costs will be.

Withdrawal from the Study

You have the right to leave a study at any time without penalty.

For your safety, however, you should consider the study doctor's advice about how to go off the study treatment. If you leave the study before the last planned study visit, the researchers may ask you to complete some of the final steps such as lab work or imaging as applicable.

The researchers also have the right to take you out of the study without your consent for any reason. They may do this if they believe it is in your best interest or if you do not agree to changes that may be made in the study.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the study.

PHI that Will be Used/Disclosed:
The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Results of exams, procedures and tests you have before and during the study.
- Laboratory test results.

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults. We will also comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form. If you do not sign this form, you may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study.

- Emory and Emory Saint Joseph's Hospital may use and disclose your PHI to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
    - Emory and Emory Saint Joseph's Hospital offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
    - Government agencies that regulate the research including: Food and Drug Administration.
    - Public health agencies.
    - Research monitors and reviewer.
    - Accreditation agencies.
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

Manali Bhave, MD
Winship Cancer Institute, Emory University
1365-C Clifton Road NE
Atlanta, GA 30322

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information

If you have questions about the study procedures, appointments, research-related injuries or bad reactions, or other questions or concerns about the research or your part in it, contact Dr. Manali Bhave at [redacted]

This study has been reviewed by an ethics committee to ensure the protection of research participants. If you have questions about your **rights as a research participant**, or if you have **complaints** about the research or an issue you would rather discuss with someone outside the research team, contact the Emory Institutional Review Board at [redacted]

To tell the IRB about your experience as a research participant, fill out the Research Participant Survey at **https://tinyurl.com/ycewgkke**.

Consent and Authorization

TO BE FILLED OUT BY SUBJECT ONLY

Print your name, **sign**, and **date** below if you choose to be in this research study. You will not give up any of your legal rights by signing this form. We will give you a copy of the signed form to keep.

_____
Name of Subject

_____ _____ ___:___ am / pm
Signature of Subject (18 or older and able to consent) **Date** **Time (please circle)**

TO BE FILLED OUT BY STUDY TEAM ONLY

_____
Name of Person Conducting Informed Consent Discussion

_____ _____ ___:___ am / pm
Signature of Person Conducting Informed Consent Discussion **Date** **Time (please circle)**