RESEARCH PARTICIPANT INFORMATION AND CONSENT FORM

Title of Study: "Pre-existing nerve entrapment as a risk factor for Chemotherapy - Induced Peripheral Neuropathy. Could there be a role for physical therapy treatment?**"**

Protocol number: "_____"

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Co-Investigator:	**Dr. Barbara Shay, College of Rehabilitation Sciences. R106-771 McDermot Avenue. Wpg, Mb R3E 0T6. Ph: (204) 977-5636**
Sponsor:	**CancerCare Manitoba (CCMB) Room ON5008 – 675 McDermot Ave. Wpg, Mb R3E 0V9**

You are being asked to participate in a Clinical Trial (a human research study). Please take your time to review this consent form and discuss any questions you may have with the study staff. You may take your time to make your decision about participating in this clinical trial and you may discuss it with your regular doctor, friends and family before you make your decision. This consent form may contain words that you do not understand. Please ask the study doctor or study staff to explain any words or information that you do not clearly understand.

The study team is receiving financial support for the salary of the research coordinator and physiotherapist to conduct this study.

Purpose of Study

This Clinical Trial is being conducted to study Chemotherapy-Induced Peripheral Neuropathy (CIPN). It is a common side effect of chemotherapy treatment causing tingling/numbness, increased sensitivity and shooting/burning pain. It usually starts in the hands and/or feet and can extend up the arms and legs. CIPN is a common reason that cancer patients stop their treatment early. For some people,

the symptoms last beyond their chemotherapy for months or years. You are being asked to take part in this study because you will be completing chemotherapy to treat breast cancer. The chemotherapy drug that you will be taking is known to produce this side effect. A total of 100 participants will participate in this study.

The purpose of this study is to identify risk factors for developing CIPN symptoms and see if physiotherapy treatment may assist with reducing severity of symptoms both during and after chemotherapy.

This research is being done because there is currently no effective treatment to help people manage CIPN symptoms during chemotherapy and we do not know why some people continue to have symptoms after chemotherapy treatment while others do not.

Study procedures

In this study, you will be "randomized" into one of 2 study groups described below. "Randomized" means that you are put into a group by chance, like flipping a coin. You will have an equal chance of being placed in either of the two groups.

Group A is the control group and will have chemotherapy treatment as usual. A total of 6 visits over 9 months are required. On the first visit, the research coordinator (who is also physical therapist experienced in treatment of the upper limb) will assess nerve health before chemotherapy. The next 3 visits will monitor any signs of the chemotherapy-induced peripheral neuropathy (nerve damage with feelings of numbness, tingling, burning, pain and clumsiness) of the arms and hands during chemotherapy. The last 2 visits are at 3 and 6 months post-treatment to measure nerve recovery. On the 6th and final visit your initial measures can be compared to your current measures. This will give you an indication of nerve recovery. If you would like a consultation with the treating physical therapist and a home program to assist with nerve recovery, one visit with no charge will be provided to you. Any follow-up visits after that would not be part of the study and would require private payment or insurance coverage to continue seeing the treating physical therapist that is part of the study. If you do not have the private coverage, physical therapy can still be arranged through a visit to your family doctor. He/she can write a referral to the hospital for physical therapy treatment (covered by Manitoba Health) for exercises to improve nerve health.

Group B is the treatment group and will have the same 6 visits over 9 months. Four additional treatment visits to a physical therapist with training in the treatment of patients with cancer and specializing in treatment of the upper limb will be given prior to chemotherapy. The treatment is to maintain the best possible health of the hand and arm to prior to chemotherapy. We hope that this will diminish symptoms of the chemotherapy-induced peripheral neuropathy both during treatment and recovery after treatment has finished. Treatment will vary for

each person but can include: range of motion exercises, nerve exercises, splints and gloves to reduce swelling and pain and a home exercise program to complete daily. A total of 10 visits are required for the treatment group (Group B).

The research coordinator will not know what group you have been assigned to, but you will. Once the consent form is signed, and the initial assessment is complete, an envelope with your study number will be given to you. The contents will tell you if you are in the control or treatment group. If you are in the treatment group, the contact information for the physical therapist will be included so you can arrange a convenient time to attend the 4 sessions prior to the start of chemotherapy.

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

Attend 6 visits at the rehabilitation hospital (located next to CancerCare) to complete questionnaires and an upper limb nerve assessment. The initial assessment is expected to take 1.5 hours and each re-assessment visit will be scheduled for 1.0 hours. The initial assessment is before the start of chemotherapy. The second visit is after the second round of chemotherapy (6-8 weeks after the initial assessment). The third visit is after the third round of chemotherapy (3 weeks later). The fourth visit is after the fourth round of chemotherapy only if you are scheduled for four rounds (approximately 3 weeks later). The fifth visit is scheduled 3 months after chemotherapy has finished and sixth visit (final appointment) is scheduled six months after chemotherapy has finished.

Nerve assessment testing will include:

1) **Questionnaires on your hand and arm function and current level of pain and type of pain experienced.**
2) **Upper limb tension tests (ULTT's) for nerve sensitivity. These tests require the research coordinator to move your arm into various positions to check for signs and symptoms of nerve irritation.**
3) **Tests for nerve entrapment. Participants will be asked to hold a certain position and determine if any signs and symptoms of nerve irritation are present.**
4) **Testing reflexes with the reflex hammer to measure motor responsiveness of the nerves**
5) **Measuring any hand swelling by submerging the hands into a jug of water a measuring volume displaced**
6) **Grip strength will be measured by grasping a machine called a dynamometer that records the force of the grip.**
7) **Light touch sensation is assessed using small hair-like filaments (called Semmes Weinstein Monofilaments) that have different amounts of force. The smallest one you can sense without looking gives a measure of nerve health in your fingertips.**

8) **Abnormal sensations of pain with normally non-painful touch is assessed by gently brushing over the hand and seeing if a painful response is present or not.**
9) **Pressure-pain thresholds will be measured by using a machine that records maximum pressure until a sensation of pain is felt. The test is stopped and is controlled by the participant depressing the stop switch.**
10) **Temperature and vibration thresholds will be assessed on the fingertips using a Thermal Sensory Analyzer (TSA-II). We will record the point at which each participant can detect cool and warm sensations as well as vibration sensations. Finally, temperature limits for both cold and hot will be measured by increasing or decreasing the temperature until pain is felt. No test pushes through pain. The instructions are always to indicate when pain is felt and then the test stops. All tests are controlled by the participant. There is no risk of tissue damage as the TSA machine can only fluctuate between 0-50 degrees.**

If allocated to the treatment group there will be 4 treatment sessions from a physical therapist (KS) who has additional training in treating cancer and specializes in upper limb assessment and treatment. The office is located at 76 Nature Park Way off of Kenaston and the clinic is called Centric Health Sports Therapy and Wellness Centre. These treatment sessions will be completed as soon as possible after enrolling in the study and prior to the start of chemotherapy. A home program to complete during chemotherapy will also be provided.

Participation in the study will be for approximately 9 months. The researcher may decide to take you off this study if you develop other medical side effects from the chemotherapy that would make completing a home exercise program difficult or if side effects prevent you from using your prescribed splints and gloves. An example would be swelling in the arm and hand (lymphedema) that requires stockings and therapy. In this case, it would be in the participants' best interest to discontinue the study and receive treatment for lymphedema.

To date, no effective treatment exists for CIPN. However, if any medication or therapy becomes available for the treatment of CIPN during the study duration, you will be offered this treatment. We will not remove you from the study but record the treatment given.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the study staff and your regular doctor first. There are no consequences to withdrawing at any time.

Individual results of your nerve health can be provided to you at the 6 month follow-up visit. You can see your data from the initial assessment and compare to the end of treatment. This will give you a measurement of nerve health to see if your symptoms have fully or partially resolved.

Risks and Discomforts

While on the study, you are at minimal additional risk. The physical assessments are safe. Some of tests need to determine at what point you feel pain, but this is when the test stops. There will be no prolonged pain and no risk of skin damage with any tests.

If you are allocated to the treatment group there are safety precautions that must be followed when wearing any glove and/or splint. These precautions will be given to you should you receive a glove and/or splint. These precautions are about proper splint use, watching for areas of redness and skin irritation and changes to the fit of the splint if additional swelling should occur.

Fatigue is a side effect of both the disease and chemotherapy treatment. We will try to coordinate follow-up visits with scheduled oncology follow-ups but this may be tiring as well. We will do our best to meet your needs but all follow-up assessments will occur at the Rehabilitation Hospital (800 Sherbrook Street) between 10am and 2pm.

Your condition may not improve or may worsen while participating in this study.

Benefits

By participating in this study, you will be providing information to the study doctors that will show the effects of physical therapy for the treatment of CIPN as well as identifying additional risk factors for developing symptoms. There may or may not be direct medical benefit to you from participating in this study. We hope the information learned from this study will benefit other participants with all types of cancer receiving similar chemotherapy drugs in the future.

Costs

All clinic and professional fees, splints and gloves which will be performed as part of this study are provided at no cost to you. There will be no cost for the study treatment that you will receive.

Payment for participation

You will be given $70.00 upon completion of the study for your participation in this research study to cover all costs of parking at the Health Sciences Centre.

Alternatives

You do not have to participate in this study to receive treatment for your condition. Please talk to your regular doctor about all your treatment options.

Confidentiality

Information gathered in this research study may be published or presented in public forums, however your name and other identifying information will not be used or revealed. Medical records that contain your identity will be treated as confidential in accordance with the Personal Health Information Act of Manitoba. Despite efforts to keep your personal information confidential, absolute confidentiality cannot be guaranteed. Your personal information may be disclosed if required by law. All study documents related to you will bear only your assigned patient number. The only paper connecting your name to your patient number will

be kept in a locked filing cabinet at all times and destroyed upon completion of the data analysis.

Organizations that may inspect and/or copy your research include the University of Manitoba and CancerCare Manitoba Foundation. Only the study doctors and the study staff will have access to information containing personal health information and all records are kept locked. The treating physical therapist is located at Centric Health at 76 Nature Park Way. Centric Health Sport Wellness Centre has a confidentiality policy and follows the clinic rules and regulations for privacy protection. The treating physical therapist will not have access to any study information.

The University of Manitoba Health Research Ethics Board may review research-related records for quality assurance purposes.

All records will be kept in a locked secure area and only those persons identified will have access to these records. If any of your medical/research records need to be copied to any of the above, your name and all identifying information will be removed. No information revealing any personal information such as your name, address or telephone number will leave the University of Manitoba, Bannatyne Campus. If you are allocated to the treatment group, the contact information of the physical therapist is in your envelope. It will be up to you to contact the physical therapist to arrange the four treatment sessions prior to the start of your chemotherapy. We will not give out your information to the physical therapist. Your physical therapy assessment information will be stored at the Centric Health Sports Therapy and Wellness Clinic. The treating physical therapist will comply with Personal Health and Information Act (PHIA) and protect the privacy of your information according to the regulations of the College of Physical Therapists of Manitoba.

<u>Voluntary Participation/Withdrawal From the Study</u>

Your decision to take part in this study is voluntary. You may refuse to participate or you may withdraw from the study at any time. Your decision not to participate or to withdraw from the study will not affect your other medical care at this site. If your study doctor feels that it is in your best interest to withdraw you from the study, your study doctor will remove you without your consent.

We will tell you about any new information that may affect your health, welfare, or willingness to stay in this study.

<u>Medical Care for Injury Related to the Study</u>

You are not waiving any of your legal rights by signing this consent form nor releasing the investigator(s) or the sponsor(s) from their legal and professional responsibilities.

Questions

You are free to ask any questions that you may have about your treatment and your rights as a research participant. If any questions come up during or after the study or if you have a research-related injury, contact the study doctor and the study staff: Elizabeth Hammond (Research Coordinator) Ph: (204) 451-5702, Dr. Barbara Shay (College of Rehabilitation Sciences) Ph: (204) 977-5636 and Dr. Marshall Pitz (Medical Oncology) Ph: (204)787- 2108

For questions about your rights as a research participant, you may contact The University of Manitoba Health Research Ethics Board at (204) 789-3389

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

Statement of Consent

I have read this consent form. I have had the opportunity to discuss this research study with Dr. Pitz, Dr. Shay or his/her study staff. I have had my questions answered by them in language I understand. The risks and benefits have been explained to me. I believe that I have not been unduly influenced by any study team member to participate in the research study by any statement or implied statements. Any relationship (such as employee, student or family member) I may have with the study team has not affected my decision to participate. I understand that I will be given a copy of this consent form after signing it. I understand that my participation in this clinical trial is voluntary and that I may choose to withdraw at any time. I freely agree to participate in this research study.

I understand that information regarding my personal identity will be kept confidential, but that confidentiality is not guaranteed. I authorize the inspection of my medical records by CancerCare Manitoba Foundation, and The University of Manitoba Health Research Ethics Board.

By signing this consent form, I have not waived any of the legal rights that I have as a participant in a research study.

I agree to being contacted via email in relation to this study in the future.
Yes □ No □

I would like to have the results emailed to me at the end of this study
Yes □ No □

Participant signature_____ Date _____
(day/month/year)

Participant printed name: _____