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Consent Form

Osteoporosis in people with Neurofibromatosis (NF1)

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Sponsor: none

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INTRODUCTION
We are inviting you to take part in this research study because your are an adult with neurofibromatosis (NF1.)

PARTICIPATION IS VOLUNTARY
Your participation is entirely voluntary. This consent form tells you about the study. Please take the time to read it and discuss it before you decide whether or not you wish to participate. If other questions come to mind, please feel free to call us.

If you wish to participate, please sign this form. If you do not wish to participate, you do not have to give any reason for your decision, and your decision will not affect the medical care you receive.

WHO IS CONDUCTING THE STUDY?
The study is being conducted doctors Linlea Armstrong, J.M. Friedman, and Dr. David Kendler.

BACKGROUND

Bone problems such as scoliosis and pseudarthrosis (bending and breaking of the long bones) are fairly common in people with NF1. There is increasing evidence that adults with NF1 have a much higher risk of osteoporosis, a condition of decreased bone density that can lead to fragile bones and bone breakage.

Recently, some studies in mice have shown that neurofibromin, the protein that the NF1 gene makes, is involved in bone metabolism. Studies have not yet been done in people but NF1 causes reduced neurofibromin production because of the non-functional NF1 gene. It therefore makes sense that the bones of people who have NF1 might be affected in a general way and might be at higher risk for generalized bone problems like osteoporosis.

Putting all these facts together, we wonder if people with NF1 may have a generalized problem with low bone mineral density. If this is true, then there are various ways that low bone mineral density can be treated.

WHAT IS THE PURPOSE OF THE STUDY?

The purpose of this study is to survey bone health and measure bone metabolism (that is, the way that bone is created and broken down). This is a small study (sometimes called a pilot study) that will lead to a larger study based on what is learned in this study.

WHO CAN PARTICIPATE IN THE STUDY?

We are looking for 20 adults to participate in our study. Participants must be:

- Men with NF1 who are over the age of 49 years
  or
- Women with NF1 who are post menopausal or over the age of 49
  or
- Women with NF1 who are over age 49 and who had a hysterectomy

WHO SHOULD NOT PARTICIPATE IN THE STUDY?

If you do not fit in any of the above categories or do not want to come to Vancouver for the testing, then don't participate.

WHAT DOES THE STUDY INVOLVE?

There are various parts to the study. All but one will take place in Vancouver in the lab of Dr. David Kendler. His lab is at 41st Avenue and Willow Street. We will help to arrange your travel.

The entire study will take about four hours.

The procedures for the study are described below:

- First, you will have a brief physical examination performed by Dr. Linlea Armstrong. This is to confirm that you have NF1 and to document its severity.

- Next you will have a blood test. This will be performed by the technologists in the lab of Dr. David Kendler, or by Patricia Birch RN. The amount of blood required is about one tablespoon. The blood is to test for various factors that measure bone metabolism. These tests are: vitamin D, parathyroid, alkaline phosphatase and total calcium levels.

- You will need to give us two urine specimens. These should be the first urination of the morning on the day of your appointment and on the previous day. Depending on where you live and the time of your appointment with us, it might be easier for you if we mail a specimen container for you to use at home. We will discuss this with you before the appointment.

- We will complete a questionnaire related to bone health with you. If we or you are short on time, this can be done later, over the phone. The questionnaire is called the CaMOS questionnaire and has been used in many studies to measure factors that may relate to bone health.

- You will have a bone mineral density (BMD) assessment (sometimes called DEXA, or DXA) in the lab of Dr. David Kendler. This is a type of very low radiation x-ray that assesses the density of your hip, spine, and wrist bones. This density can be compared to Canadian data to determine if your BMD is normal or low.

- Finally, you will have an x-ray of the lower spine to assess existing bone shape. This will be done near by in a commercial radiography lab. This is a recommended part of the study but is optional. The spine x-ray will look for collapsed or unusually shaped spines that can give false readings of BMD. This is the one part of the study that is optional. However, if you do not want to have this x-ray, the BMD measurement may not be 100% reliable.

WHAT ARE THE POSSIBLE HARMS AND SIDE EFFECTS OF PARTICIPATING?

Blood test: You may experience brief pain or possible bruising from the blood test.

<u>BMD test and Spinal x-ray</u>: All medical procedures attempt to minimize the amount of radiation people are exposed to, particularly for research procedures. The radiation dosage for a lumbar spinal radiograph is about 70 mrem (mrem is an estimated measure of absorbed radiation) and that from a bone mineral density scan is about 6 mrem. For comparison, the annual background radiation exposure from the earth and atmosphere in an average person is roughly 300 mrem.

All radiation can damage the cells in our body. The day-to-day background radiation we receive is considered to be low-level and our cells usually repair the damage it causes. An exposure such as the 70mrem from a spinal x-ray can also damage cells and some cells may die. Usually, these cells are replaced by the body. Sometimes, instead of dying, the cells are changed permanently and may go on to produce abnormal cells, like cancer cells, when they divide. The risk for cancer from a spinal x-ray is low but we cannot say exactly what it is. The Health Physics Society states that the risks for health effects of exposures under 5,000 to10,000mrem are either non-existent or too small to be measured (http://hps.org/documents/radiationrisk.pdf).

However, all these calculations are based on the general population. We do not know what the risks are for people with neurofibromatosis, a condition that causes benign (non-cancerous) tumours as a result of a mutation in the *NF1* gene, which is a tumour suppressor gene. If you have concerns about this, please fee free to discuss it with us or with your doctor.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

It is likely that some of the participants in this study will be diagnosed with low bone mineral density and osteoporosis. This may be of benefit to them because this is a treatable condition. Others, who may be diagnosed with borderline low bone mineral density, will also benefit in that they may be able to prevent or slow the development of osteoporosis. Other people may receive reassurance about their BMD, and may use the scan as a baseline for the future.

If you are diagnosed with low bone mineral density or osteoporosis, you will be given the option of having their results sent to you family doctor so that you may be offered a referral to a specialist for treatment and advice. We can make a direct referral for any individuals with no family doctor.

You will be given a copy of your individual results for your own records.

WHAT HAPPENS IF I DECIDE TO WITHDRAW MY CONSENT TO PARTICIPATE?

Your participation in this research is entirely voluntary and you may withdraw from the study at any time. If you decide to enter the study but withdraw at any time in the future, there will be no penalty or loss of benefits to which you are otherwise entitled. Your future medical care will not be affected.

If you enter the study and then withdraw at a later time, all data collected during enrolment in the study will be retained for analysis. By law, these data cannot be destroyed.

WHAT HAPPENS IF SOMETHING GOES WRONG?

You do not waive any of your legal rights by signing this consent form.

AFTER THE STUDY IS FINISHED
Your identifying information will be removed from the blood and urine samples but the samples will be kept in the lab for one year in case it is necessary to check the findings. Should you wish to obtain general results about the study as a whole, they will be available in summarized form from the Principal Investigator approximately two years from now. As mentioned above, specific results relating to you will be given to you immediately.

WHAT WILL THE STUDY COST ME?
All participants will receive $40 to partially compensate them for their time, parking expenses, and gas. People from outside the lower mainland will also be partially compensated for travel. For example, people coming from Victoria will be offered reimbursement for the equivalent of the Pacific Coast Line fare, which is $67.50 return ($45.00 for BC seniors). People coming from the Okanagan will be offered the equivalent of the Greyhound bus fare between Kelowna and Vancouver, which is $64.00 return (advanced purchase). People from others locations will be compensated in a similar manner. We will discuss this with you in advance of your appointment and will let you know in writing what the travel compensation will be. Payment will be mailed to you after you participate.

WILL MY TAKING PART IN THIS STUDY BE KEPT CONFIDENTIAL?
Your confidentiality will be respected. No information that discloses ayour identity will be released or published without your specific consent to the disclosure. However, research records and medical records identifying you may be inspected in the presence of the Investigator or his designate by representatives of the UBC Research Ethics Board for the purpose of monitoring the research. However, no records which identify your name or initials will be allowed to leave the Investigators' offices.

WHO DO I CONTACT IF I HAVE QUESTIONS ABOUT THE STUDY
If you have any questions or desire further information about this study before, during, or after participation, you can contact the Principal Investigator, Dr. Linlea Armstrong or Patricia Birch (research assistant) at 604-875-2000 ext 5622, or you may email Patricia Birch at: birch@interchange.ubc.ca.

WHO DO I CONTACT IF I HAVE ANY QUESTIONS OR CONCERNS ABOUT MY RIGHTS AS A SUBJECT DURING THE STUDY?
If you have any concerns about your rights as a research subject and/or your experiences while participating in this study, contact the “Research Subject Information Line” in the University of British Columbia Office of Research Services' at 604-822-8598.

SUBJECT'S CONSENT TO PARTICIPATE

By signing this form, you are consenting to participate.

Please review the following Check List before signing:

☐ I have read and understood the subject information and consent form.

☐ I understand that my participation in this study is voluntary and that I can refuse to participate or to withdraw from this study at any time without influencing the medical care I receive

☐ I understand that I am not waiving any of my legal rights by signing this consent form.

☐ I understand that the information collected for this study will be kept confidential and will only be used for scientific objectives.

☐ I have been told that I will receive a dated and signed copy of this form.

☐ I have read this form and freely consent to participate in this study.

SIGNATURES

_____	_____	_____
Printed name of subject	Signature	Date
_____	_____	_____
Printed name of witness	Signature	Date
_____	_____	_____
Printed name of principal investigator/ designated representative	Signature	Date