Official Title: A Prospective Randomized Phase II Study of 1 vs 2 Fractions of Palliative Radiation Therapy for Patients with Symptomatic Bone Metastasis
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Department/Section of *Department of Radiation Oncology*

# A PROSPECTIVE RANDOMIZED PHASE II STUDY OF 1 VS 2 FRACTIONS OF PALLIATIVE RADIATION THERAPY FOR PATIENTS WITH BONE METASTASIS.

Informed Consent Form to Participate in Research
Doris Brown, M.D., Principal Investigator

## 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 cancer that has spread to the bone causing pain. 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?

Patients who receive a single fraction (dose) of radiation therapy to treat bone metastasis get effective control of pain. However, some patients require a second treatment at some point in the future. The purpose of this research study is to find out what effects (good and bad) immediate treatment with a second fraction (dose) of radiation therapy has on you and your condition.

## HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

102 people will take part in this study. This study is only being done at the Comprehensive Cancer Center of Wake Forest University (CCCWFU).

## WHAT IS INVOLVED IN THE STUDY?

As part of this study, you'll receive radiation therapy that is standard treatment for palliation of cancer that has spread to the bone causing pain. You will be randomized into one of the study groups described below. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in either group. Both groups will receive one fraction of radiation therapy, but one of the groups will receive a second fraction 3-7 days later.

**You will be "randomized" into one of the study groups described below.** Randomization means that you are put into a group by chance. A computer program will place you in one of the study groups. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being in either group.

**If you are in group 1,** you will receive one fraction of radiation therapy. Before receiving a treatment, you will have a treatment planning session. A computer-assisted treatment will be designed and a radiation dose will be worked out for you. The session will last about 60 minutes. Within a few days following your treatment planning session, you will receive one radiation treatment to the bone causing pain. This treatment will last about 30 minutes. Your doctor may give you pain medication before the planning session and/or the radiation treatment to decrease any discomfort you may have due to the time spent in each session. Your doctor also may give you medicine to decrease any anxiety you may feel. If the pain persists or recurs, the second fraction of treatment can be used at some point in the future.

**If you are in group 2,** you will receive second radiation treatment, just like the first. This treatment will occur within 3-7 days of the first treatment.

**Before you begin the study** you will need to have the following to find out if you can be in the study. Some of these exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Physical examination, including a neurologic examination (an examination to test the brain and nervous system)
- Radiologic imaging (X-ray, CT, or MRI) to check your bones for fractures.
- If you are female, you will have a blood (serum) pregnancy test done.
- Evaluation of your ability to carry out your daily activities
- Optional: You will have 2 tablespoons of blood taken from a vein in your arm for research purposes.
- You will be asked to complete surveys that evaluate your quality of life and other outcomes.
- You will be asked to identify how much pain you are having by choosing a number from 0 (no pain) to 10 (the worst pain imaginable). This could also be done over the phone.
- You will be asked what other medicines including pain medicines, if any, you are taking and what dose and how often you take the medicine.

**At each of your treatment visits** we will only collect your vital signs, changes in your weight, changes to your medications, and ask about any unusual symptoms you may be having.

**At one and two months after you finish treatment**, we will call you on the phone and ask you to identify how much pain you are having by choosing a number from 0 (no pain) to 10 (the worst pain imaginable). We will also ask you to tell us about changes to your medications and any unusual or adverse symptoms you may be experiencing.

**In the follow-up visits (3 and 6 months after treatment)** you will receive the following tests/questions/procedures to see how you and your cancer were affected by the treatment you received. Some of these tests and procedures are part of regular cancer care.

- Physical and neurological examinations

 You may receive radiologic imaging (X-ray, CT, or MRI) to check your bones for fractures, if your doctor feels this is appropriate.
 If you agreed to the optional blood draw at study entry: You will have 2 tablespoons of blood taken from a vein in your arm for research purposes (3 month follow-up only.)
 Evaluation of any side effects you may be experiencing
 You also will be asked about any unusual symptoms you may be experiencing
 You will be asked to identify how much pain you are having by choosing a number from 0 (no pain) to 10 (the worst pain imaginable).
 You will be asked what other medicines including pain medicines, if any, you are taking and what dose and how often you take the medicine
 You will be asked to complete surveys that evaluate your quality of life and other outcomes.

If you are undergoing any other cancer treatments during your time on this study, this 3-6 month follow up visit can be done by your treating physician as standard of care. The study coordinator or nurse may call you on the phone to ask you about your pain level, adverse symptoms, and the quality-of-life questionnaires within 5 days of this visit.

## Storage of Biological Tissue

If you agree to participate in this study, we will have 2 tablespoons of blood withdrawn from a vein before treatment and again 3 months later to use for future research. This is optional and not a requirement to participate in the study. The total amount of blood withdrawn during the study will be approximately 4 tablespoons. This sample will be kept and may be used in future research to learn more about other diseases.

The future research may include studying your genetic information. At some point in the future, we may be required to share genetic data with federal repositories. The National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that collect the results of genetic studies, especially when the research looks at all or large sections of individual's genetic code. This is often called whole genome sequencing. Genomic information relates to the structure and function of all of the genetic material in the body. These central banks will store your genetic information and give them to other qualified and approved researchers to do more studies. The data that we share with federal repositories will be coded in such a way that you would not be able to be identified. We will not share your name, birth date, or any other information that could directly identify you. The link to the code would be kept securely at the Wake Forest Baptist Health. Even so, there is a possibility that when your genomic information is combined with other information available to researchers, either now or in the future, they may be able to identify a group you belong to (like an ethnic group or a disease population) or, less likely, you personally. NIH prohibits people from trying to identify individuals whose genomic information is in an NIH-designated repository.

We do not think that there will be further risks to your privacy and confidentiality by sharing your genetic information with these banks. However, we cannot predict how genetic information will be used in the future. The genetic data could be used to study a wide variety of diseases.

Your sample will be obtained in the CCCWFU. The sample will be stored in the CCCWFU and it will be given only to researchers approved by Dr. Doris Brown. An Institutional Review Board (IRB) must also approve any future research study using your tissue sample.

____YES I would agree to have blood drawn and stored for future research.
____NO I do not want to have blood drawn.

Your *blood* sample 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.

In the future, people who do research may need to know more about your health. While the study investigator may give reports about your health, he/she will NOT be given your name, address, phone number, or any other identifying information about who you are, unless you agree to be contacted in the future.

____YES you many contact for future research studies
____NO I do not want to be contacted regarding future research studies.

## How Long Will I Be in the Study?

You will be in the study for about 6 months, or until the study has completed recruiting patients.

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 to learn about any potential health or safety consequences.

## What Are the Risks of the Study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, researchers don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after the radiation treatment. In some cases, side effects can be serious, long lasting, or may never go away.

**You should talk to your study doctor about any side effects that you have while taking part in the study.**

Common Side Effects, Some Maybe Serious

- Hair loss in the treated area
- Skin in treatment area may become reddened, irritated, and/or dry

The following risks are likely if you have treatment to the bones of the spine in the neck:

- Inflammation of the lining of the mouth and esophagus (passageway from mouth to stomach), which can result in difficulty swallowing, and if you cannot swallow water, dehydration can occur (your body does not have as much water and fluids as it should)
- Inflammation of the back of the throat, which can result in difficulty swallowing, and if you cannot swallow water, dehydration can occur
- Inflammation of the part of the airway that includes the vocal cords, which can result in hoarseness or loss of voice

Occasion Side Effects, Some Maybe Serious

- Tiredness
- Low blood counts, which could lead to an increased risk of infection, weakness, and/or in bleeding and bruising easily
- If you have treatment to the abdominal area, it may result in nausea and/or vomiting, loose bowel movements, or increased frequency of urination

Rare and Serious Side effects

- Esophageal fistula (abnormal opening in the passageway from mouth to stomach)
- Scarring of the small or large bowel, which can result in a blockage in the bowel that would require treatment
- Fracture of the bone
  - Fractures may require surgical treatment to prevent permanent disability
- Temporary or permanent damage to the spinal cord, which can result in:
  - Skin sensations, such as burning, prickling, itching, or tingling
  - Muscle weakness causing inability to walk (paralysis)
  - Decreased ability or loss of ability to move a body part or to hold urine or control a bowel movement

In addition, 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.

If you participate in this study, you will be exposed to amounts of radiation above what you would normally receive in daily life. To be sure that you do not receive an unhealthy amount of radiation from your participation in this study, you should let your study doctor know if you have had, or are going to have, any other scans or x-rays as part of your medical or dental care. It is very important that you let your study doctor know if you already are participating in, or plan to participate in, any other research study that involves radiation exposure.

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.

If you agree to participate in the voluntary donation of blood, 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).

## Reproductive Risks and other Issues to Participating in Research

Due to unknown risks and potential harm to the unborn fetus, sexually active women of childbearing potential must use a reliable method of birth control while being treated on this study. Reliable methods of birth control are: abstinence (not having sex), oral contraceptives, intrauterine device (IUD), DepoProvera, tubal ligation, or vasectomy of the partner (with confirmed negative sperm counts) in a monogamous relationship (same partner). An acceptable, although less reliable, method involves the careful use of condoms and spermicidal foam or gel and/or a cervical cap or sponge. We encourage you to discuss this issue further with your physicians if you have any questions.

Pregnant women are excluded from participation in this study. Because some methods of birth control are not 100% reliable, a pregnancy test is required at least 10 days from your last normal menstrual period, if you are a sexually active woman of childbearing potential.

## ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

Taking part in this study may or may not make your health better. While researchers hope that a second fraction of radiation therapy will rapidly relieves your pain and for a longer time than standard radiation therapy, there is no proof of this yet. We do know that the information from this study will help researchers learn more about the effects of radiation therapy for the treatment of cancer that has spread to the bone. This information could help future cancer patients.

## WHAT OTHER CHOICES ARE THERE?

You do not have to be in this study to receive treatment. You should talk to your doctor about all the choices you have. Instead of being in this study, you have these options:

- Getting radiation treatments without being in a study
- Taking part in another study
- Getting no treatment

## 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: disease status, medical conditions, demographics, pain, medications, radiation history, chemotherapy history, quality of life, social support, performance status, and other information.

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, 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

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 at least six years after the study is finished. At that time any research information not already in your medical record will either be destroyed or it will be de-identified. 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 Doris Brown, M.D. 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:

**Doris Brown, M.D.**
[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.

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 clinical trial. 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.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

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.

## WHAT ARE THE COSTS?

Taking part in this study may lead to added costs to you or your insurance company. We will give you an estimate of what the added cost may be based on your particular situation and insurance coverage.

## WILL YOU BE PAID FOR PARTICIPATING?

Parking validation will be provided for all study-related visits.

You will receive no payment or other compensation aside from parking validation for taking part in this study.

The findings from this research may result in the future development of products that are of commercial value. There are no plans to provide you with financial compensation or for you to share in any profits if this should occur.

## WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest University Health Science.

## 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 Doris Brown, M.D. at [redacted] (after hours number).

## 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.

## 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, Doris Brown, M.D. at [redacted] after hours).

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.

## 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:_____ Date:_____ Time:_____ am pm