Wake Forest®
School of Medicine

Department of Plastic Surgery

THE USE OF LIPOSOMAL BUPIVACAINE FOR PAIN CONTROL FOLLOWING MASTECTOMY AND BREAST RECONSTRUCTION

Informed Consent Form to Participate in Research

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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 breast cancer requiring reconstruction. 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 determine how well the local anesthetic, liposomal bupivacaine, controls postoperative pain after mastectomy and breast reconstruction. Mastectomy is the surgery that is performed to remove tissue from a breast as a way to treat or prevent breast cancer. At this time, it is common practice to inject the local anesthetic, bupivacaine, into the breast at the time of mastectomy and breast reconstruction to improve post-operative pain. A new formulation of this local anesthetic has been created in order for it to last for a longer period of time. This new formulation is called liposomal bupivacaine and it has been FDA approved for this use in local injection at the surgical site. The goal of this study is to compare the use of bupivacaine to liposomal bupivacaine to determine which medication better controls pain in the postoperative period.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

This study will require 50 patients to be enrolled at Wake Forest Baptist Medical Center. In order to identify the 50 subjects needed, we may need to screen as many as 70 because some people will not qualify to be included in the study.

WHAT IS INVOLVED IN THE STUDY?

You will first be approached to be involved in our study at your pre-operative visit for your mastectomy and breast reconstruction at least 1 week before surgery. During the first visit we will ask you about your medical history, existing pain and any medications that you are taking. We will ask you to complete a pre-op questionnaire throughout the visit in addition to a baseline pain assessment. This should take approximately 30 minutes to complete. When you are asleep in the operating room, you will have either bupivacaine or liposomal bupivacaine injected into the surgical site. After surgery, you will have oral and IV pain medications available to control your pain. During your hospital stay we will rate your pain scales and monitor how much pain medications you need. When you are discharged home we will contact you by phone every 12 hours, for the first 48 hours following discharge to record your pain rating. Also at discharge, we will provide you with a pain medication use diary to record your pain medication use, as well as your pain rating.

You will follow up with our clinic at your regularly scheduled appointment times at 1 week, 3 weeks and 5 weeks postoperatively. At those appointments, we will have you bring in your pain medication diary and fill out a follow-up questionnaire related to your recent surgery. This should take approximately 20 minutes to complete. Your involvement in this study will be complete after the completion of your 5 week follow-up visit.

Once you are enrolled into the study, you will be randomized into the bupivacaine or the liposomal bupivacaine group. 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 any group. Neither you nor the investigator injecting the medication will know which group you are assigned to. This is done so that a fair evaluation of results can be made. This information is available to the researchers if needed in an emergency.

If you take part in this study, you will have the following tests and procedures:
If you are in the bupivacaine local anesthetic group, you will have this medication injected into and around the breast at the end of surgery. This occurs when you are asleep in the operating room. This is a common practice in patients who are undergoing mastectomy who are not enrolled in the study. If you are in the liposomal bupivacaine group, you will have this medication injected into and around the breast. Similarly, this will occur when you are asleep in the operating room.

HOW LONG WILL I BE IN THE STUDY?

You will be in the study for about 2 months. 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. There are no serious health consequences of sudden withdrawal from the study, however we will not be able use your experience in our research.

WHAT ARE THE RISKS OF THE STUDY?

Being in this study involves some risk to you. You should discuss the risk of being in this study with the study staff. Because researchers do not know which drug is better at relieving pain and reducing side effects, there is a chance that you could be assigned to the arm of the study that performs better or worse than the other arm. Risks and side effects related to the liposomal bupivacaine that we are studying include:

More common immediate risks of receiving liposomal bupivacaine may include nausea (2-40%) and vomiting (28%). Uncommon risks include hypotension (low blood pressure) (2-10%), leg swelling (2-10%), insomnia (difficulty falling or staying asleep) (2-10%), itching (3%), anemia (blood has a lower than normal range of red blood cells which can lead to reduced oxygen flow to vital organs)(2-10%), muscle spasm (2-10%). Rare but serious side effects may include central nervous system excitation leading to convulsions or unconsciousness (<2%) and allergic reactions including anaphylaxis (a serious allergic reaction, which in rare cases can be fatal) (<2%). Use of liposomal bupivacaine is contraindicated in pregnancy, but does not pose a long-term reproductive risk to patients. Similar risks are associated with the use of bupivacaine injection. If a high dose is used such that toxicity occurs, this can result in a slow heart rate, cardiac arrest, cessation of breathing and possible death. It should be used in caution with patients with moderate-severe hepatic or renal impairment because of the increased risk of toxicity.

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.

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.

As part of this study, you will be asked questions about long-term quality of life which includes the presence of depression. If we learn that you or someone else is in danger of harm, the study team is required to report that information to the proper authorities. At the end of the consent there is a list of resources you may find helpful.

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 participating in 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. If you are a sexually active woman of childbearing potential and have not been using a reliable method of birth control, two negative pregnancy tests performed 15 days apart are required to check for possible early pregnancy prior to starting treatment.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct benefit to you. We hope the information learned from this study will benefit other people in the future. The benefits of participating in this study may be improved pain control after mastectomy and breast reconstruction with injection of liposomal bupivacaine.

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: undergo your scheduled mastectomy and breast reconstruction.

WHAT ARE THE COSTS?

All study costs, including any study medications and procedures related directly to the study, will be paid for by the study. Costs for your regular medical care, which are not related to this study, will be your own responsibility. Neither you nor your insurance company will be billed for the medication used in this study as it will be funded by the study.

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.

WILL YOU BE PAID FOR PARTICIPATING?

You will receive no payment or other compensation for taking part in this study.

WHO IS SPONSORING THIS STUDY?

This study is being sponsored by Wake Forest Baptist Medical Center, Department of Anesthesia and the Foundation for Anesthesia Education and Research. The researchers do not, however, hold a direct financial interest in the sponsor or the product being studied. There is no potential

conflict of interest between the authors of this study and the sponsors of 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 [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 Christopher Runyan, MD PhD at telephone number: [redacted].

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**:** pain score, use of pain medications, side effects of local anesthetics including nausea and vomiting, length of hospital stay, and quality of life.

If this research study involves the diagnosis or treatment of a medical condition, then Protected Health Information collected from you during this study may 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.

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), the Department of Health and Human Services (DHHS) and similar agencies in other countries.

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 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. 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 Christopher Runyan, MD PhD 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:

Christopher Runyan, MD PhD
[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.

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.

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, you failed to follow instructions, or because the entire study has been stopped.

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 investigator, Christopher Runyan at [redacted]

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 (Printed):_____

Person Obtaining Consent:_____ Date:_____ Time:_____ am pm

Below is a list of resources which may you may find helpful:

Emergencies:
Local Emergency Department
National Suicide Prevention Lifeline: 800-273-TALK (8255)

Non-Emergency:
Wake Forest Psychiatry (medical or counseling): [redacted]
Cancer Patient Support Program (CPSP) :
[redacted]