Study Title: Contrast-Enhanced Ultrasound for Kidney Cancer Subtyping and Staging

NCT Number: NCT04021238

Informed Consent Document

Date of Document: January 11, 2022

University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: January 11, 2022
IRB Study # 19-1851
Title of Study: Contrast-Enhanced Ultrasound for Kidney Cancer Subtyping and Staging.
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The purpose of this research study is to determine if contrast-enhanced ultrasound (CEUS), an experimental imaging test, can predict if a mass found in the kidney is malignant or not. You will undergo an ultrasound of your kidneys, which includes having an intravenous (IV) tube and a microbubble contrast agent called Definity given to you. You will have one visit that will take about 1-2 hours.

There is no direct benefit to you for participating in this study. The greatest risks of this study include the possibility of allergic reaction to the contrast agent, Definity.

If you are interested in learning more about this study, please continue to read below.

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary.
You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

The purpose of this research study is to determine if a special kind of ultrasound, called contrast-enhanced ultrasound (CEUS), an experimental imaging test, can predict whether a mass is malignant or not. The CEUS done in this research study will be compared to the pathology results from your surgery. You are being asked to be in the study because you are scheduled to undergo kidney surgery.

Are there any reasons you should not be in this study?

You should not be in this study if you are less than 18 years of age, unable to give consent, critically ill, experiencing severe, active heart disease, or are pregnant or breastfeeding. You should also not participate in this study if you have any contraindication to ultrasound contrast imaging.

How many people will take part in this study?

A total of approximately 25 people will take part in this study.

How long will your part in this study last?

Your participation in this study will be 1 study visit that lasts approximately 1-2 hours. You may be asked to return for additional imaging sessions. Additional sessions are not required. However, we will review your medical records for results of additional clinical imaging.

What will happen if you take part in the study?

If you decide to participate, you will be escorted to a dressing room, where you will change into a gown. If you are a female of childbearing age and are potentially pregnant, you will be asked to provide a urine sample to confirm you are not pregnant. For the purposes of the CEUS research study, an intravenous (IV) catheter will be placed, and your vital signs will be taken. Then you will be asked to lie on an examination table and positioned. Once you are positioned, gel will be applied to your back or side and an ultrasound will be performed by trained medical personnel.

At the time of imaging, a contrast agent will be administered via IV by a nurse or trained medical personnel. At the conclusion of the ultrasound, the IV will be removed. The total imaging time is anticipated to be less than 30 minutes. The contrast agent used is approved by the FDA for another indication, but we are using this contrast agent outside of its current clinical labeling.

Your ultrasound will be conducted here at UNC, and no UNC physician will review the ultrasound for clinical purposes. Rather, your images will be reviewed by a "blinded reader," physician(s) designated to review all of the images without your name or any identifying information attached.

At the same time as the CEUS imaging, we will perform a B-Mode Ultrasound image. This is a regular, non-investigational procedure that is commonly known as "standard of care" meaning it is what we normally perform for a person with your condition. You may have had these previously.

After you have finished these procedures and the images have been returned, the images will be compared with the results from your pathology results.

New or additional information

You may be asked to return for an additional study visit, which includes contrast administration and imaging. You will also have urine testing before and after imaging as well as be monitored by a medical professional for adverse reactions during imaging.

You will receive a $50 gift card and parking vouchers for the additional study visit.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study.

What are the possible risks or discomforts involved from being in this study?

You will be given a microbubble contrast agent (Definity) for the research images. Definity is an FDA-approved microbubble contrast agent that is administered by an IV catheter. Currently, Definity is approved for use in imaging patients' hearts. Since we will use the contrast agent for ultrasound imaging in the kidney and not the heart, we will be using Definity in a way that was not specifically approved by the FDA, but we do not think that this way of using Definity puts you at any additional risks.

The most common, but still infrequent, side effects of Definity that have been reported are (% of patients experiencing): headache (2.3%), back and renal pain (1.2%), flushing (1.1%) and nausea (1.0%).

The most serious risk of Definity is to the small number of potential patients with undiagnosed allergy to Definity. Post-marketing reports have included allergic reactions and other serious, potentially life-threatening, but to date non-fatal adverse reactions. In order to avoid a potentially fatal event, EpiPen® (epinephrine) injections will be kept near the ultrasound machine for all patients.

In order to administer the contrast, an IV catheter will be inserted into a vein in your arm. You may experience pain or bruising at the site on your arm where the IV was inserted. Localized clotting, irritation, lightheadedness, fainting or infection may rarely occur.

There may be uncommon or previously unknown risks. You should report any problems to the researcher.

Pregnancy tests will be done on all females who might be able to get pregnant at the start of the study. There are no known risks to pregnant women, but since this test has never been conducted in pregnant women, we will not be performing the test in pregnant women. This pregnancy test will be covered by the study.

If you choose not to be in the study, what other treatment options do you have?

You do not have to be in this research study in order to receive treatment. The other procedures

or treatments that are available include having standard imaging (MRI/CT) performed on you.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

Whenever ultrasound is done, there is the chance of finding something unexpected. Unexpected findings can have clinical significance, or no clinical significance. Clinically significant means that the ultrasound shows a problem that may require further follow up or treatment. The imaging studies in this study will be reviewed by a qualified radiologist. You will be informed of any findings of clinical significance that may be discovered during the imaging procedure.

There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as problems with getting insurance or a job or feeling worried about a finding for which no treatment is required or appropriate). The ultrasound we are using in this research study is not the same quality as an ultrasound that you may have as part of your health care. If you believe you are having symptoms that may require clinical imaging, you should contact your primary care physician.

How will information about you be protected?
All your research records will be stored using a case number only. The research records will be kept in a locked office within a locked office suite at UNC. The master file linking your name to your case number will be maintained on a password locked computer at UNC and will only be accessible by the study coordinator and study PI.

Participants will not be identified in any report or publication about this study. We may use de-identified data from this study in future research without additional consent.

Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

By signing this informed consent document, you agree that some of the information generated by participating in this study and/or a copy of the consent form may be included in your medical record and that this information may be viewed by other physicians or caregivers who provide healthcare services to you. This will allow the doctors caring for you to know what study medications or tests you may be receiving as a part of the study and know how to take care of you if you have other health problems or needs during the study. Additionally, the information may be shared with your medical insurance plan if the research services provided are billed to your insurance.

What will happen if you are injured by this research?
All research involves a chance that something bad might happen to you. This may include the

risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. If you think you have been injured from taking part in this study, call Dr. Emily Chang at (919) 445-2621. He/she will let you know what you should do. You do not give up any of your legal rights by signing this form.

What if you want to stop before your part in the study is complete?
You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

Will you receive anything for being in this study?
You will be receiving $50 and a parking voucher for taking part in this study, and an additional $50 and parking vouchers for each additional study visit.

Will it cost you anything to be in this study?
It will not cost you anything to be in this study.

Who is sponsoring this study?
This research is funded by Lantheus Medical Imaging. This means that the research team is being paid by the sponsor for doing the study. In addition, Dr. Emily Chang, the principal investigator on this study, receives money from Lantheus Medical Imaging for work that is not part of this study. These activities may include consulting, service on advisory boards, giving speeches, or writing reports. If you would like more information, please ask the researchers listed in the first page of this form.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

A description of this clinical trial will be available on 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 website at any time.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____ _____

Signature of Research Participant Date

_____

Printed Name of Research Participant

_____ _____

Signature of Research Team Member Obtaining Consent Date

_____

Printed Name of Research Team Member Obtaining Consent