

LCCC 1405: Comparison of the sensitivity and specificity of acoustic angiography (Micro-tumor detection by quantifying tumor-induced vascular abnormalities) to the sensitivity and specificity of conventional ultrasound

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

Consent Form Version Date: **May 1, 2018**
IRB Study # **14-0161**

Title of Study: Comparison of the specificity of acoustic angiography (Micro-tumor detection by quantifying tumor-induced vascular abnormalities) to the specificity of conventional ultrasound

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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 refuse to join, 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 evaluate the clinical application of acoustic angiography with traditional b-mode ultrasound in order to improve physicians' ability to assess cancer risk.

Acoustic angiography is a new type of ultrasound imaging which enables the physician to visualize blood vessels which might be associated with cancer. Pre-clinical research has shown that specific blood vessel characteristics are related to certain cancer types. Acoustic angiography uses sound waves, similar to traditional ultrasound imaging. For example, physicians may be able to use acoustic angiography to view the vessel shape and other features, which may show the presence of cancer in the breast(s). These structures may also be useful in seeing the progression of cancer. Increasing the ability to diagnose using imaging in high risk patients could provide substantial clinical benefit by improving diagnosis, preventing over-treatment, and reducing healthcare costs.

You are being asked to be in the study because you are a female that has recently been scheduled to undergo a breast core needle biopsy or surgical biopsy of at least one breast lesion.

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

You should not be in this study if you are: male, less than 18 years of age, unable to give consent, an institutionalized subject (prisoner or nursing home patient), pregnant or breastfeeding. You should also not participate in this study if you have any contraindication for contrast imaging.

How many people will take part in this study?

There will be approximately 75 people in this research study.

How long will your part in this study last?

You will have an acoustic angiography in coordination with your clinical imaging. It will take roughly 45-60 minutes to complete the study, including consent time.

What will happen if you take part in the study?

If you decide to participate, you will be escorted by the research coordinator to a dressing room, where you will change into a gown. Then, you will receive acoustic angiography ultrasound exam in conjunction with the standard diagnostic imaging, including b-mode ultrasound. We may also do another FDA approved ultrasound with the acoustic angiography imaging. Acoustic angiography imaging will be performed by a trained medical personnel using mild compression to eliminate motion, similar to when you received your breast ultrasound. The total imaging time is estimated to be less than 15 minutes.

At the time of imaging, FDA-approved lipid-shell microbubble contrast agent (Definity®) will be administered intravenously by a nurse or trained medical personnel. This contrast agent is generally used for cardiac (heart) imaging and is being used off label and with a higher dose, double the conventional single administration dose. The purpose of the contrast agent is to enhance the visualization of blood vessels in the breast. The usage of this contrast agent has been reviewed by the FDA specifically for this study. The total imaging time is anticipated to be

less than 15 minutes. You will be imaged with a new type of ultrasound system for the acoustic angiography procedure. This system is a research system and has not been approved for clinical use. The amount of ultrasound energy that is deposited by the system is calibrated to be equivalent to or less than a conventional ultrasound imaging study, and within the energy levels ('mechanical index') that is indicated for use in patients with the contrast agent Definity.

You will be monitored by medical professionals for 30 minutes after the contrast is administered. Once these images are collected, they will be deidentified for interpretation and analysis.

After the acoustic angiography for this study, you will undergo the biopsy that your physician ordered. The acoustic angiography images that we collect are for study purposes, and will not be used to guide your biopsy or future care. At a later date, we will review your pathology report in order to compare the results of your biopsy with the images that we collect.

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?

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

You will be given a contrast agent (Definity) for the research images. Definity (perflutren lipid) is an FDA-approved lipid-shell microbubble contrast agent that may be administered by an intravenous (IV) bolus or infusion. Currently, this contrast agent is approved for use in patients with echocardiograms that are difficult for physicians to see the specific features of the heart so that they can see them better. Since we will use the contrast agent for acoustic angiography in the breast 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 will put you at any additional risks. We have also submitted this study to the FDA for review.

The most common 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%). There were no differences in the overall incidence based on age, gender, or route of administration.

The real risk of Definity in our study is to the small number of potential patients with undiagnosed allergy to Definity. Post-marketing reports have included allergic reactions and other serious but non-fatal adverse reactions, typically within 30 minutes of drug administration. In order to avoid a potentially fatal event, EpiPen® (epinephrine) injections will be kept near the ultrasound machine for all patients.

Since we will be using a dose that is more than what the FDA has approved (double) for other types of ultrasounds, there could be other unknown risks that we are not aware of. You should tell your study team about any changes to how you feel or other problems that arise at any time during the course of this study.

In order to administer the contrast an intravenous catheter (IV) 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.

The ultrasound system that we are utilizing is a system that has been approved for use in animal imaging, but not specifically approved for human imaging. It utilizes a transducer which was designed for research and has also not been specifically approved for human imaging. However, the system performs within similar energy and frequency levels as an FDA approved ultrasound imaging systems and thus we do not anticipate any significant risk from the use of the system.

What are the risks to a pregnancy or to a nursing child?

If you are pregnant or are planning to get pregnant, you will not be allowed to participate in this study. If you are of childbearing age, you will be required to undergo a pregnancy test at no charge to you. You will not need a pregnancy test if you are surgically sterile or if you are post-menopausal (no menstrual cycle for one year). If later you learn that you were pregnant during the study, you are asked to contact the study doctor immediately for further instructions. By signing this consent form, you confirm to the best of your knowledge that you are not pregnant now.

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. If you choose not to participate, you will receive all your previously planned clinical imaging and biopsy.

What if we learn about new findings or information during the study?

The acoustic angiographs will NOT be interpreted prior to your biopsy, and therefore will not influence clinical decision making concerning the biopsy. Your images will be de-identified and read once all patients have been completed their imaging.

How will information about you be protected?

All of your research records will be stored using your initials and a case number only. The research records will be kept in a locked cabinet 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.

Participants will not be identified in any report or publication about this study. 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.

Certificate of Confidentiality

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

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. 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 parking vouchers for taking part in this study. You will only be compensated at the completion of the study visit. This compensation is in exchange for your time required for participating in the study.

Will it cost you anything to be in this study?

It will not cost you anything in addition to what you will be billed for your routine medical care to be in this study. All tests, visits or procedures other than what is done for this study (the acoustic angiography imaging and a pregnancy test, if needed) will be related to medical care that is part of the usual care for your condition and would be suggested even if you decided not to be in the research study.

If a concerning area is detected with this experimental device, you and your referring doctor will be notified and you will be recommended for further standard of care work-up that may include: mammogram pictures, ultrasound, MRI, and possible biopsy. This extra work-up will not be paid for by this study. You and your insurance company would be responsible for any additional costs.

Who is sponsoring this study?

This research is funded by a grant from the National Institutes of Health (NIH). This means that the research team is being paid by the sponsor, the NIH, for doing the study. In addition, SonoVol, Llc. is a company involved in this research because it owns or makes a technology that is being used in this study.

Dr. Paul Dayton, the scientist whose NIH grant is funding this study, is an inventor on the patent for the technology; he is also currently part-owner of SonoVol. The University of North Carolina at Chapel Hill also has a small ownership interest in the SonoVol company. If the technology or approach is successful at some point in the future, UNC-Chapel Hill and Dr. Dayton may receive financial benefits.

A committee at the University of North Carolina at Chapel Hill has reviewed these arrangements. They concluded that the possible benefit to the University or the company listed above is not likely to affect your safety or the scientific quality of the study. If you would like more information, please ask the researchers or the study coordinator listed on 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 _____