Thomas Jefferson University
Informed Consent Document for Human Subjects Research – OHR-8 (v. 7/8/15)

Department: Department of Radiology

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Medical Study Title: 2D and 4D Contrast Enhanced Ultrasound Evaluation of Hepatocellular Carcinoma Chemoembolization

Lay Study Title: A research study to see if ultrasound imaging combined with a contrast agent can determine whether the embolization procedure to treat your liver mass was successful

What Is Informed Consent?

You are being asked to take part in a medical research study. As required by federal regulations, this research study has been reviewed and approved by an Institutional Review Board (IRB), a University committee that reviews, approves and monitors research involving humans. Before a knowledgeable decision about whether to participate in a research study can be made, the possible risks and benefits related to the study should be understood. This process of learning and thinking about a study before deciding to participate is known as *informed consent* and includes:

- Receiving detailed information about this research study;
- Being asked to read, sign and date this consent form once the nature of the study is understood and a decision is made to participate. If there is anything about the study you don't understand or if there are questions, you should ask for explanations before signing this form;
- Being given a copy of the signed and dated consent form to keep for your own records

A patient who joins a research study has a relationship with the study doctor that is different than the relationship with a treating or personal doctor. A treating doctor treats a specific health condition with the goal of improving that condition. A study doctor treats all subjects according to a research plan to obtain information about the experimental drug, device or procedure being studied and with the understanding that there may or may not be benefit from being in the study. The study doctor and study staff can provide more information about research as opposed to treatment.

What is the purpose of this study?

You are being invited to participate in this study because you are scheduled to have a type of treatment for a mass on your liver called transarterial chemoembolization (TACE). TACE involves injecting drugs that treat cancer with small beads or oil directly into a blood vessel that supplies blood to the mass. The beads or oil block the blood flow to the tumor, as well as deliver cancer drugs directly to the mass. Normally, about 1 month after the TACE procedure, you will be scheduled for an MRI or CT to determine whether the TACE procedure successfully treated the liver mass. The MRI or CT involves the use of a dye that can sometimes cause side effects. The purpose of this study is to determine whether another type of imaging test with ultrasound imaging and a contrast agent that does not involve dye can be used to determine whether the TACE procedure treated the liver mass, and if this test can determine the treatment effectiveness earlier. If this is successful, it is possible that people can have this ultrasound imaging exam earlier and rather that the MRI with dye.

This is a Phase 2 study. Phase 2 research studies are done to get further information on safety, dosage, and side effects and to collect preliminary information about how well a drug works (often referred to as efficacy). Phase 2 studies usually have very strict rules about who may and who may not be in the study. Phase 2 studies may compare a new drug to a placebo (inactive substance) or to a known treatment.

You are being asked to participate in this study because you are scheduled for TACE of a liver mass. The purpose of this study is to compare the results of ultrasound imaging with contrast (CEUS) at 1 -2 weeks and 1 month after your TACE with that of the MRI or CT that your doctor has scheduled to receive 1 month after your TACE procedure.

The ultrasound contrast agent being used in this study is Definity. Definity is an ultrasound contrast agent that contains tiny gas bubbles about the same size as red blood cells that reflect ultrasound (sound waves). The microbubbles in Definity stay in areas of blood vessels and reflect sound waves and show where there is blood flow. Definity is FDA-approved in the United States for use with echocardiography (ultrasound of the heart).

For this study, the CEUS imaging will be performed on an FDA-approved ultrasound system, the Logiq E9. To acquire and process the CEUS images, the ultrasound system software has been modified to detect Definity. This only changes the way in which the images are processed by the ultrasound system. It does not change the strength or the composition of the sound waves being transmitted to your body.

How many individuals will participate in the study and how long will the study last?

210 patients will participate nationally. We hope to enroll **up 100** patients at Jefferson. Each participant will be in the study for about 1 month. The entire study will take about 5 years to complete.

What will happen during the study?

Individual participation in this trial will be limited to three 60 minute exams including the CEUS exam and monitoring you after the CEUS. The first examination will be on the morning of your scheduled TACE procedure prior to the procedure, the second will be 1-2 weeks after the TACE procedure, and the third will be on the day you come in for your MR imaging at 1 month after the TACE and will be performed prior to the MR imaging.

For all 3 research visits, you will be asked to review your medical and surgical history, any current medications you are taking, and any known drug allergies or intolerances. If you are a woman of childbearing potential, you will have a urine pregnancy test (the results of which will be made available to you prior to the start of the research study). For the CEUS, an intravenous catheter (small plastic tube) will be placed in a vein in your arm. You will be asked to lay on your back on an examination table. Ultrasound gel, to assist in the ultrasound imaging, will be applied to the area of your abdomen over your liver. An ultrasound probe will be moved across the area over your liver to obtain the ultrasound images.

A standard (without contrast) ultrasound examination of your liver will be performed to locate the liver mass and obtain information about the size, shape and ultrasound characteristics. After the standard exam is complete, you will receive an injection (approximately 1 teaspoon) of Definity through the catheter in your arm, followed by an injection of saline (salt water). You will then have continuous CEUS imaging for 1 minute. If the Definity is not seen on the CEUS, you may receive a second injection of Definity through the catheter in your arm, followed by another injection of saline (salt water). This will be followed by CEUS imaging. The CEUS imaging will not feel any different than the standard imaging.

You will be monitored during the entire procedure and for 30 minutes after the final injection of Definity.

The CEUS findings will be compared to the MRI or CT results at 1 month. Additionally, the CEUS results will be compared to the long term outcome of your TACE treatment.

What are the side effects and other risks or discomforts involved?

There are no risks from the use of diagnostic ultrasound.

The majority of adverse events from Definity are temporary and mild in severity. Of the reported adverse reactions following the use of Definity the most frequently reported were headache (2.3%), back and renal pain (2.1%), sudden increase in blood flow to face (1.1%) and nausea (1.0%). Hypersensitivity reactions (severe allergic reaction that may include abnormal redness of skin, slow heart rate, low blood pressure or, rarely, difficulty breathing) to Definity may occur, although rare.

The company that makes Definity has indicated that there is the potential of serious heart and lung reactions occurring uncommonly during or following administration of Definity. The risk is only in patients with heart and lung problems. You will be screened for any of these conditions and if it is found that you have any of these conditions, you will not be able to participate in this study.

The use of an intravenous needle and the fluids given through the needle may cause minor discomfort, bleeding under the skin (bruise), and possible infection at the site of needle insertion.

The only other risk is the possible breach of confidentiality. The investigators will take every precaution to ensure patient confidentiality will be maintained.

You should tell or call the study doctor as soon as possible at 215-503-5188 if, during the course of this study, you develop any of these side effects or symptoms. The study doctor has told you that if your condition worsens, if side effects become very severe, or if it turns out that being in this study is not in your best interest, you will be taken out of the study. If you have any side effects or symptoms after normal business hours go the nearest emergency room. If questions come up about side effects, ask the study doctor or staff at any time during or after the study.

Are there benefits from being in this study?

There may be no benefit from being in this research, but we hope that what we learn may be helpful to future patients or society in general.

Are there alternatives to being in the study?

Participation in this study is entirely voluntary. The alternative to being in the study is to only have the standard of care 1 month post chemoembolization MRI or CT scan.

How will privacy and confidentiality (identity) be protected?

Federal regulations require that certain information about individuals be kept confidential. This information is called “protected health information” (PHI). PHI includes information that identifies an individual personally such as name, address and social security number, or any medical or mental health record, or test result, that may have this sort of information on it. The laws state that people may see and review their medical records at any time. However, in a research study, people may not see the study results or other data about the study until after the research is completed unless the study doctor decides otherwise.

The following individuals or entities may have access to your PHI and by law must protect it. These include investigators listed on this consent form and other personnel of Thomas Jefferson University, Jefferson University Physicians, Thomas Jefferson University Hospitals, Inc. (add the Rothman Institute if applicable) involved in this specific study, the University's Office of Human Research and the Institutional Review Board (IRB), and your health insurance company (if necessary for billing for standard medical care).

PHI collected during this study may also be shared with the following entities that, while not obligated by law to protect PHI, will protect it to the best of their ability:

- ***NIH*** which is providing funds to Thomas Jefferson University/Jefferson Health to conduct this research
- The Food and Drug Administration (FDA)
- Dr. Robert Den, the medical monitor for the study, who will review medical records if any unexpected side effects occur.
- Research Monitors hired by the sponsor to oversee the study and review medical records to ensure study-related information is correct,
- With any person or agency required by law.

The following information will be provided to the study sponsor and other entities noted above:

Study data for analysis: ***The ultrasound images, MRI or CT images and reports, outcome, pregnancy test (if applicable), and medical/surgical history to determine whether CEUS can access whether TACE was successful and to see whether you meet the eligibility criteria.***

Demographic data: Your race and ethnicity to track enrollment statistics

Other: None

If you develop an illness or injury during the course of participation in this study, other PHI about treating and following the condition may be generated and disclosed as it relates to this study.

PHI collected as part of this research may be used indefinitely.

You may quit the study and revoke permission to use and share PHI at any time by contacting the principal investigator, in writing, at: John Eisenbrey, PhD Thomas Jefferson University, 132 South 10th Street, 7th Floor, Philadelphia, PA 19107. Further collection of PHI will be stopped on those who quit the study, but PHI that has already been collected may still be used.

The results of clinical tests and procedures performed as part of this research may be included in your medical records. The information from this study may be published in scientific journals or presented at scientific meetings but no one will be personally identified in these publications and presentations.

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

What happens in case of injury as a result of being in this study? In the event of a research-related injury, necessary and available medical care (including hospitalization) will be provided. A research-related injury is a physical injury or illness that is directly caused by any procedure or treatment used in this study that is different from the treatment you would receive if not participating in a research study. If physical injury occurs due to any drug/substance or procedure properly given under the plan for this study, medical expenses for treating the injury will be billed to your insurance carrier. You should be aware that some costs may not be covered by insurance and may become your responsibility. There is no plan to provide compensation for loss of wages, lost time from work, personal discomfort, or for injuries or problems related to your underlying medical condition(s).

If you have questions about the sponsor's agreement regarding payment for a research-related injury please discuss with the study doctor.

If a bill related to a research-related injury is received that seems wrong, please discuss it with the study doctor or research coordinator.

Is there payment for being in this study?

There is a payment $100/33.00 per/scan for participating in this study.

Disclosure of Financial Interest

The sponsor of this clinical study, NIH, is paying Thomas Jefferson University to conduct this study.

Are there costs related to being in this study?

Research Procedures

There are no charges to you or your insurance carrier for study visits or tests that are part of this research. The three CEUS exams and the pregnancy test are purely related to the research. Neither you nor your insurance carrier will be charged for this research CEUS imaging.

Standard Testing Procedures

Standard of care procedures and doctor visits will be billed to your health insurance carrier. These are charges that would be billed to insurance whether in a research study or not. It is possible that insurance coverage may be denied. If that happens you may be responsible for some or all of these charges. The study doctor [or study staff] will explain which procedures, tests and doctor visits are considered standard of care.

If a bill is received that you think is wrong, please discuss it with the study doctor or research coordinator.

What if the research results in new findings?

Anything learned during the study, beneficial or not, that may affect your health or willingness to continue in the study, will be explained.

Can I be removed from the study or quit the study?

Your decision to participate in this research study is entirely voluntary. You have been told what being in this study will involve, including the possible risks and benefits.

Your participation in this research project may be terminated by the study doctor or study sponsor without your consent for any reason that he/she feels is appropriate.
You may refuse to participate in this investigation or withdraw consent and quit this study without penalty and without affecting the ability to receive medical care at Thomas Jefferson University/the Rothman Institute.

If you withdraw from this study, you may continue treatment with your Jefferson doctor, or you may seek treatment from another doctor of your choice.

CONTACT INFORMATION

If you are having a medical emergency, call 911 or go directly to an emergency room. You should let emergency personnel or providers know that you are participating in this study.

Telephone number for questions about your rights as a research participant	The Jefferson Institutional Review Board	215-503-8966
For questions, concerns or complaints about the research, or if you suspect a research-related injury	The Principal Investigator, Dr. John Eisenbrey, PhD or any co-investigator listed at the beginning of this form	215-503-5188
If you have difficulty contacting the study staff	Call the Jefferson Office of Human Research	215-503-0203

If you want more information about the Jefferson Institutional Review Board or Jefferson's Human Research Protection Program, please visit our website at http://www.jefferson.edu/human_research/irb/index.cfm.

Subject Communications

Do you wish to communicate with the study staff by e-mail? YES _____ NO _____

If you checked yes, please print your e-mail address on the line below.

_____

RISKS: E-mail correspondence is not always secure and there is a risk of loss of confidentiality. To help protect against loss of confidentiality, all e-mail that originates from Jefferson University or Jefferson Hospital employees using Jefferson University or Jefferson Hospital e-mail addresses is encrypted. That means, unless you have allowed others to have access to your e-mail, only you will see the e-mail.

YOU SHOULD **NEVER** USE E-MAIL TO REPORT A SUSPECTED ADVERSE EVENT OR ANY OTHER MEDICAL PROBLEM. THESE SHOULD BE REPORTED BY TELEPHONE.

Non-Waiver of Legal Rights Statement

- ✓ **By your agreement to participate in this study, and by signing this consent form, you are not waiving any of your legal rights.**
- ✓ **In order to be in this research study, you must sign this consent form.**
- ✓ **You affirm that you have read all pages of this consent form. You have been told that you will receive a copy.**

SIGNATURES

_____	_____	_____
Your Name	Your Signature	Date

_____	_____	_____
Name of **Person Conducting Consent Interview**	Signature of **Person Conducting Consent Interview**	Date

The **investigator's** signature certifies that s/he personally provided the study participant with a description of the study, study procedures, risks, benefits and alternatives to participation.

_____	_____	_____
Name of **Investigator or Co-Investigator**	Signature of **Investigator or Co-Investigator**	Date

☐ **Copy of Signed and Dated Consent Form Given to the Subject/Parent/LAR**

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As Per University Counsel – Do Not Sign
This Consent Form after 3/23/23