Project Title: *Role of Magnetic Resonance Fingerprinting and Quantitative MR Imaging in Assessment of Response to Neo-Adjuvant Chemotherapy in Breast Cancer*

Sponsor: Investigator Initiated

Principal Investigator(s): Holly Marshall, MD

Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (Case CCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio. This study is being offered at University Hospitals (UH).

What is the usual approach to my breast cancer?
Your physician will order a clinical MRI scan prior to starting treatment. In some cases, an MRI is ordered again at the end of treatment or before surgery.

What are my other choices if I do not take part in this study?
If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available

Why is this study being done?
The purpose of this study is to determine if new methods of MRI imaging can better measure your response to chemotherapy treatment. There will be a total of 124 subjects enrolled in this study.

How long will I be in this study?
Visit 1: MRI research images will be added to the clinical MRI scan before start of chemotherapy. If you have already had a clinical MRI, we will contact you for a research-only MRI before start of chemotherapy. Getting the additional research images will take less than 20 minutes.

Visit 2: You will be contacted by a member of the study team to schedule a research only non-contrast MRI research scan 7- 10 days after the first cycle of chemotherapy. It will take approximately 30 minutes to get these images.

Visit 3: If the treating physician orders a clinical MRI scan within 1 month of end of chemotherapy treatment, we will add MRI research images to the clinical scan. Getting the additional research images will take less than 20 minutes. .

If you are not scheduled for a clinical scan within 1 month of end of chemotherapy treatment, a member of the study team will contact you to schedule a research only MRI scan. Breast cancer is hard to see on MRI after treatment, so it is helpful to give a contrast agent or dye called gadolinium through an IV into a vein for research purposes. At this visit, you will be given the option of doing the research MRI with or without contrast and another consent will be obtained at that time. If you do not want contrast for the after treatment scan, we will do a non-contrast

scan. It will take 45-60 minutes to get these images.

What extra tests and procedures will I have if I take part in this study?
Most of the exams and tests you will have are part of the usual care for your cancer. However, there will be some extra MRI scans that you will need to have if you take part in this study.

What possible risks can I expect from taking part in this study?
If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss

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Potential Risk or Discomfort from Research Procedures

IV

The insertion of a needle for an IV is painful; however, the discomfort is usually brief. For most people, needle punctures for an IV do not cause any serious problems; however, they may cause bleeding, bruising, discomfort, infections, dizziness, or fainting.

Magnetic Resonance Imaging (MRI)

If you take part in this research, you will have an MRI (magnetic resonance imaging and/or magnetic resonance spectroscopy). MRI uses a magnet and radio waves to make images (pictures) of the inside of the head and/or body. There have been no ill effects reported from exposure to the magnetism or radio waves used for these studies; however, it is possible that harmful effects could be recognized in the future. A known risk is that the magnet could attract certain kinds of metal that may cause injury to you. We will ask you about metal within your body (this includes certain dyes used in tattoos and body piercings). If there is any question about potentially hazardous metal within your body, you will not be able to participate in this research study. We will also keep the MRI room locked so that no one carrying metal objects enters the room while you are having this scan performed. In addition, the MRI scanner makes a loud buzzing noise that could affect hearing ability. You will be provided with earplugs and assistance in their use in order to protect your hearing. You will be able to communicate with the scanner technologist using an intercom and/or signaling device. The technologist will try to help you feel as comfortable as possible in the scanner. You can ask to stop the scan and be removed from the scanner at any time by using the intercom or signaling device.

There is a very slight risk of an allergic reaction if contrast material is injected. Such reactions usually are mild and easily controlled by medication. If you experience allergic symptoms, a radiologist or other physician will be available for immediate assistance.

Over 300 million doses of Gadolinium based contrast agents (GBCAs) have been administered since the introduction of these medications in the mid 1980s. The known and proven adverse effects of these drugs are the possibility of allergic reactions (rare and idiosyncratic), and the development of the extremely rare disease Nephrogenic Systemic Fibrosis (NSF) with the administration of contrast agents in patients with severe renal dysfunction. NSF has been virtually eliminated upon not administering GBCAs in patients with end stage renal disease. Additional precautions such as minimizing use of GBCAs associated with NSF, and elimination of simultaneous administration of double/triple doses of agents, have also contributed. While all GBCAs are known to deposit in neural and other tissues, no harmful effect of this deposition has been documented. No guidelines exist to guide how many times a GBCA may be administered to the same subject for research purposes.

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Confidentiality
Finally, there is a risk of that your private information could be revealed to people outside of the study team. To lower this risk, information will be de-identified by a study team member trained in protecting PHI (Protected Health Information). A unique study code will be assigned to every study subject. This code will be used instead of identifiable information to describe which study subject is which when cases are discussed among study team members.

What possible benefits can I expect from taking part in this study?
There may be no direct health benefits for participation in this study. Participation in this study will help the investigators determine whether these MRI techniques are useful, and may provide benefit to patients undergoing MRI examinations in the future.

Can I stop taking part in this study?
Yes. You can decide to stop at any time.

The study doctor may take you out of the study:
- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study requirements
- If the study is stopped by the sponsor, Institutional Review Board (IRB) or FDA.

What are my rights in this study?
Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

What are the costs of taking part in this study?
The study will pay for all procedures that are directly associated with this research study.
You/your insurance will not be charged for the research-only MRIs.
Procedures or drugs that are considered standard of care will be the responsibility of the patient and their insurance company.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://www.cancer.gov/clinicaltrials/learningabout.

Compensation:
Visit 1: You will receive $100 for the research scan

Visit 2: You will receive $150 for the non-contrast research scan
Visit 3: You will receive $50 for the non-contrast research scan or $100 for the contrast research scan

What happens if I am injured or hurt because I took part in this study?

If injury occurs as a result of your involvement in this research, medical treatment is available from University Hospitals, Cleveland Clinic or another medical facility but you/your medical insurance will be responsible for the cost of this treatment. A research injury is an injury that happens as a result of taking part in this research study. If you are injured by a medical treatment or procedure that you would have received even if you weren't in the study, that is not considered a "research injury". There are no plans for payment of medical expenses or other payments, including lost wages, for any research related injury. To help avoid injury, it is very important to follow all study directions.

Further information about research-related injuries is available by contacting the University Hospitals Cleveland Medical Center's Research Subject Rights phone line at (216) 983-4979.

Student/Employee Rights
Choosing not to participate or withdrawing from this study will not affect your employment or class standing, nor will the results be shared with your supervisor.

HIPAA AUTHORIZATION
Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to Holly Marshall, MD, and the study team members at University Hospitals for the purposes of this research and to Case Western Reserve University for administration.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth, Social Security number, information from your medical record, lab tests, or certain information relating to your health or condition.

Some of the tests and procedures done solely for this research study may also be placed in your medical record so other doctors know you are in this study. Upon completion of the study, you may have access to the research information that is contained in your medical record.

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In addition to the investigators and study team members listed above, your PHI may be looked at by other groups involved with the study such as the University Hospitals Institutional Review Board and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed to:

- Case Comprehensive Cancer Center members and collaborators
- The Food and Drug Administration;
- The Department of Health and Human Services;
- The National Cancer Institute (NCI);
- Other Institutional Review Boards;
- Data Safety and Monitoring Boards;

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to:

Holly Marshall, MD
Case Comprehensive Cancer Center
University Hospitals Cleveland Medical Center
11100 Euclid Ave.
Cleveland, OH 44106

Your participation in the research will stop, but any information already recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, information already disclosed outside University Hospitals cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

University Hospitals will not use your information collected in this study for another research purpose without your written permission; unless the University Hospitals Institutional Review Board assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

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By signing this informed consent form, you are allowing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This consent does not have an expiration date.

Voluntary Participation
Your participation in this research study is voluntary. Choosing not to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

Questions about the Research
If you have any questions, you can ask the Principal Investigator and/or research staff at [redacted]

Emergency or after-hours contact information
If you are a University Hospitals patient, and you need to contact study staff outside normal business hours, you may contact [redacted] and you will be transferred to the answering service, which can put you in contact with Dr. Marshall.

Where Can I Get More Information?
If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about: concerns regarding the study, research participant's rights; research-related injury; or other human subjects issues, you may contact the Institutional Review Board (IRB) at University Hospitals Cleveland Medical Center's Research Subjects Rights Phone line at 216-983-4979.

You may call the National Cancer Institute's Cancer Information Service at:
1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at http://cancer.gov/

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

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You will get a copy of this form. If you want more information about this study, ask your study doctor.

US National Institutes of Health (NIH) Clinical Trial Database:
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, if applicable, 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.

Disclosure
Some of the technology developed under this study at University Hospitals and Case Western Reserve University has been licensed to Siemens Healthineers by the institutions and the investigators. University Hospitals, CWRU, and some of the investigators on this study receive royalties from Siemens Healthineers, and a research grant from Siemens Healthineers partially funds this research.

This disclosure is made so that you can decide if this relationship will affect your willingness to participate in this study

Signature
Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

Signature of Participant	Date	Printed Name of Participant
Signature of Witness (if applicable)	Date	Printed Name of Witness

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I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____	_____	_____
Signature of Person Obtaining Consent	Date	Printed Name of Person Obtaining Consent