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Protocol Title:

Contrast Enhanced Spectral Mammography vs. MRI for Breast Cancer Screening

DF/HCC Principal Research Doctor / Institution:

Olga Brook, MD / Beth Israel Deaconess Medical Center

A. INTRODUCTION

You are invited to take part in a clinical trial, a type of research study, because you have been diagnosed with an area in your breast that needs to be biopsied. This research study is evaluating whether contrast enhanced mammography can be used as an alternative to breast Magnetic Resonance Imaging (MRI) for cancer screening. MRI uses magnets to create a detailed image of the tissues and bones inside of the body.

The name of the study device involved in this study is:

- Contrast enhanced mammography

For purposes of this research, you will be referred to as a “participant”.

It is expected that about 82 people will take part in this research study.

GE Healthcare, an industry company, is supporting this research study by providing funding for the contrast mammograms and breast MRI exams.

This research consent form explains why this research study is being done, what is involved in participating in the research study, the possible risks and benefits of participation, alternatives to participation, and your rights as a research participant. The decision to participate is yours. If you decide to participate, please sign and date at the end of this form. We will give you a copy so that you can refer to it while you are involved in this research study. If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future.

B. WHY IS THIS RESEARCH STUDY BEING DONE?

This research study is the first time investigators are examining contrast enhanced mammograms for breast cancer screening. Mammography is the main way to help find breast cancers early so they can be treated. Unfortunately, mammography does not work as well in women who have dense breast tissue. In these women, breast MRI is also used to help find breast cancers.

Contrast enhanced mammography is a new type of mammogram. It uses contrast material combined with the mammogram to highlight areas that might be breast cancer and that could be missed on the mammogram alone. This is similar to breast MRI with contrast. However, the contrast used in contrast enhanced mammography is different than the contrast used with breast MRIs. Contrast mammography uses iodinated contrast, while MRI uses gadolinium based contrast.

For the study, you will have a contrast enhanced mammogram and a breast MRI before your biopsy. We will then include your contrast enhanced mammogram and breast MRI images within a large collection of images. Radiologists will compare the images to see if the contrast enhanced mammograms and the breast MRI find the same number of breast cancers. If we find they perform similarly, then contrast mammography may be used to aid in breast cancer screening in the future.

C. WHAT OTHER OPTIONS ARE THERE?

Taking part in this research study is voluntary. Instead of being in this research study, you have other options which may include the following:

- Receive standard treatment.
- Take part in another research study.

Please talk to the research doctor about your options before you decide whether you will take part in this research study.

D. WHAT IS INVOLVED IN THE RESEARCH STUDY?

Before the research starts (screening):
After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- **A medical history,** which includes questions about your health, current medications, and any allergies.
- **Blood test** to check your kidney function. About less than one half of a teaspoon of blood will be drawn.
- **Urine test** to see if you are pregnant.

If these tests show that you are eligible to participate in the research study, you may begin the study treatment. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

After the screening procedures confirm that you are eligible to participate in the research study, you can choose to have the breast MRI and contrast mammogram performed on the same day or on different days. The images can also be done right before your biopsy.

If they happen on the same day, you will first have an intravenous (IV) line inserted into a vein in your arm. You will then have a breast MRI performed which should take about 30 minutes. Following the breast MRI, you will have the contrast enhanced mammogram which will take about 10 minutes. You will then be asked to take a brief anonymous survey about your contrast mammogram experience and how it compared to scans you have had in the past. You will then have your biopsy.

If the contrast enhanced mammogram and the breast MRI are performed on different days, then you will undergo the IV procedure described above before both exams. You may also need to redo some of the eligibility tests. You will be asked to take the brief survey described above once both the contrast enhanced mammogram and the breast MRI have been completed. Your biopsy will then be performed.

If the images find any other concerning areas in either breast, more imaging may be recommended. This may include mammography or an ultrasound exam. This may happen before or after your biopsy. The radiologist will let your doctors know the final results of the imaging test.

Research Study Plan:

	Visit 1a,b
	Screening & exam
Informed Consent	X
Medical History	X
Urine pregnancy Test	X[c]
Blood Test	X[d]
Contrast Mammogram	X[e]
Breast MRI with contrast	X[e]
Patient Experience Survey	X[f]
Breast Biopsy	X

[a] If abnormal findings are detected on the contrast mammogram or breast MRI, there is the potential that additional standard of care tests and procedures will need to be performed. These may occur on the same day or at a later date.

[b] The contrast mammogram and the breast MRI may be performed on the same day or on different days. They may also be performed on the same day or a separate day from the breast biopsy.

[c] For patients who are of child-bearing potential, and having both MRI and CESM performed on the same day, you will receive a single pregnancy test immediately before the imaging tests are performed. If the studies are not performed on the same day, then you will have a pregnancy test before each of the imaging tests on the day of the imaging exams.

[d] For patients having both MRI and CESM performed on the same day, you may need to get blood work testing how your kidneys work. This will happen once immediately before the imaging tests, on the day of the imaging exams. If the

MRI and CESM are performed on different days, you may need blood work before each imaging test.

[e] If either the contrast mammogram or the breast MRI are performed as part of standard of care, then they will be billed to insurance. If they are performed for research purposes only, then they will be billed to the grant.

[f] The patient experience survey will only be given once after the second of the two imaging tests has been performed.

MRI Procedures:
The basic procedure includes a standard MRI scan. MRI is a method of taking pictures of the breast using a large magnet and radio signals Prior to the procedure, you will change into a hospital gown. You will then lie on the scanning table and your breasts will be placed in a specialized "coil" or radio antenna to allow imaging of that area. During the scan, you will be asked to lie still on your stomach for about 20 to 30 minutes. You will hear a loud knocking or hammering noise while the MRI is taking pictures, but the process itself will be painless. You will be given disposable earplugs to use to help make the noise less noticeable and a pneumatic squeeze ball that triggers an alert at the scanner console when squeezed. During the procedure, you will be in constant contact with the MRI technologist through an intercom. If at any time during the scan you feel too uncomfortable to continue, no matter what the reason, the procedure will be immediately stopped and you will be removed from the MRI scanner.

Planned Follow-up:
If we see a problem on your contrast mammogram or MRI that we did not detect on your standard mammogram, we will either schedule additional imaging on the same day or at a later date. This imaging may include standard mammography, ultrasound, additional contrast mammograms, or breast MRI. We will let you and your doctor know of all recommendations.

E. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

You will be in this research study for up to 2 years. Your participation will require one day with possible additional days depending on when you want to get the contrast mammogram and breast MRI, or if additional imaging procedures are recommended. Although this is the extent of personal involvement in this study, your deidentified imaging may be used for future undefined research.

You may be taken off the research study for many reasons including if:

- It is considered to be in your best interest
- You are a female and become pregnant or plan to become pregnant
- A decision is made to close the study
- Or for other unforeseen reasons that make it necessary to stop your participation in the research study

If you are removed from the research study, the research doctor will explain to you why you were removed. In addition, you can stop participating in the research study at any time, however, the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study. If you decide to stop participating in this research study, we encourage you to talk to the research doctor and your primary doctor first.

F. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

Risks Associated with Mammograms:
While you are in this research study contrast mammograms will be used. The frequency of these exams is greater than what you would receive as standard care. There is thought to be a low but increased risk of cancers associated with radiation in the long term over many years.

Risks Associated with MRI Scans:
When having an MRI (Magnetic Resonance Imaging) scan, you will lie still on a table that slides into a tunnel slightly wider than your body. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. If you feel uncomfortable in confined spaces, please tell your research doctor. Your doctor may give you a medication to make you feel more comfortable. As images are taken, a loud banging noise will be produced. Earplugs or headphones will be available if needed. The MRI can be stopped at any time at your request, but the scan may not be complete.

Abnormal Findings on Contrast Mammogram or MRI:
There is a chance of having an abnormal contrast mammogram or MRI. This could require further testing with more mammogram or MRI imaging, breast biopsy, and possible other tests. If you have an abnormal mammogram or MRI, this could result in your needing a breast biopsy you would not otherwise get. An

abnormal mammogram or MRI may cause you to feel upset, worried, or depressed. If you are upset, you may speak with the research doctor or ask to be referred for additional emotional support.

Risks Associated with Contrast Agents Used During Scans:
There is a small risk with using a contrast agent that is injected into a vein during the MRI and contrast mammogram. The contrast agent is a special dye that highlights organs, blood vessels or tissue to make them more visible. Depending on the type of contrast agent that is used, it may cause decreased kidney function or worsen kidney function in people who already have decreased kidney function. Gadolinium-based contrast agents (GBCAs) for MRI have been known to cause a severe skin disease in people who already have some degree of kidney failure. This is known as Nephrogenic Systemic Fibrosis (NSF). It can cause a widespread stiffening of the tissues in the body. While the precise cause of this disorder remains a mystery, it generally occurs in patients whose kidney function is so limited that they require dialysis. Therefore, we will check your kidney function before you get the exam. If your kidney function is abnormal, then you will not be eligible for this study.

Uncommonly, some people have allergic reactions (such as hives and itching) to the contrast agent. Serious reactions (for example, drop in blood pressure, difficulty breathing or severe allergic reaction and death) are rare.

Contrast agents can also leak out of the vein into the surrounding tissue when it is given. This is called extravasation. During the contrast injection, you will be carefully monitored for signs of extravasation. Evidence of extravasation includes swelling or tightness at the injection site, and/or stinging or burning pain. The area also may get red and painful. The vast majority of patients in whom extravasations occur recover without significant sequelae. More severe reactions include compartment syndrome, a serious condition that occurs when there is a large amount of pressure inside a muscle compartment, and skin ulceration, but this is uncommon.

The United States Food and Drug Administration (FDA) issued a warning about the risk of brain deposits following repeated intravenous use of GBCAs for MRI. After being administered intravenously, GBCAs are mostly eliminated from the body by the kidneys. Trace amounts of gadolinium, however, may stay in the body long-term and are known to be deposited in the skin, bone, and brain.

Recent studies conducted in people and animals have confirmed that gadolinium can remain in the brain after intravenous administration, even in individuals with normal kidney function. Available information at this time does not show any adverse health effects related to the deposits in the brain.

G. WHAT ARE THE BENEFITS OF THE RESEARCH STUDY?

We do not know if taking part in this study will help you. This study may help researchers learn information that could help women have access to contrast mammography for breast cancer screening.

H. CAN I STOP BEING IN THE RESEARCH STUDY AND WHAT ARE MY RIGHTS?

You have the right to choose not to sign this form. If you decide not to sign this form, you cannot participate in this research study.

You can stop being in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop. Leaving the research study will not affect your medical care outside of the research study.

If you choose not to participate, are not eligible to participate, or withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

I. WILL I BE PAID TO TAKE PART IN THIS RESEARCH STUDY?

You will not be paid for participating in this study. However, the study team will cover parking related costs for the duration of your study visit.

J. WHAT ARE THE COSTS?

Taking part in this research study might lead to added costs to you or your insurance company.

You will not be charged for the contrast enhanced mammogram or breast MRI unless they are recommended as part of standard of care.

You or your insurance company may be charged if follow-up imaging including mammography, ultrasound, or MRI is necessary based on the contrast enhanced mammogram or breast MRI. You may be responsible for co-payments and deductibles that are typical for your insurance coverage.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services are:

- Beth Israel Deaconess Medical Center: (617) 667-5661

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

www.cancer.gov or 1-800-4-CANCER (1-800-422-6237)

K. WHAT HAPPENS IF I AM INJURED OR BECOME SICK BECAUSE I TOOK PART IN THIS RESEARCH STUDY?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.

The treating hospital will offer you the care needed to treat injuries directly resulting from taking part in this research. These treatments will be billed to your insurance company. You will be responsible for deductibles and co-payments. There are no plans to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

We will need to collect certain personal information about you for insurance or payment reporting purposes, such as your name, date of birth, gender, social security number or Medicare identification number and information related to this research study. We may be required to report this information to the Centers for Medicare & Medicaid Services. We will not use this information for any other purpose.

L. WHAT ABOUT CONFIDENTIALITY?

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information and imaging created by this research study, including the contrast mammogram and MRI, will become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file. It may also become part of a DF/HCC research database.

The results of this research study may be published. You will not be identified in publications without your permission.

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.

M. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact the research doctor or study staff as listed below:

Beth Israel Deaconess Medical Center

- Olga Brook, MD: 617-754-3379

24-hour contact: BIDMC: Olga Brook, MD at 617-754-3379 or page at 90861

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at Dana-Farber Cancer Institute (617) 632-3029. This can include questions about your participation in the study, concerns about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

N. FUTURE USE OF DATA

Your personal information collected during this study will be stored in a database for research. The information in this database may be used for future research. If so, any personal identifiers will be removed so that the information cannot be linked back to you. As a result, we will no longer be able to identify and destroy them.

Investigators, including investigators from collaborating institutions, can request this data for new research. Data may also be shared with outside non-profit

academic investigators as well as with for-profit pharmaceutical investigators or commercial entities, with whom we collaborate.

You will not be asked to provide additional informed consent for the use of your de-identified information in future research.

O. PRIVACY OF PROTECTED HEALTH INFORMATION

Federal law requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions ("protected health information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements;
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug(s) used in the study and for the purpose of this or other research relating the study drug(s) and their use in cancer;
- To better understand the diseases being studied and to improve the design of future studies; and,

- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- Other research doctors and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes. A qualified representative of the FDA and the National Cancer Institute may review your medical records.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"
- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"

P. DOCUMENTATION OF CONSENT

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

_____ _____

Signature of Participant or Legally Authorized Representative

Date

_____

Relationship of Legally Authorized Representative to Participant

To be completed by person obtaining consent:

Adult Participant

The consent discussion was initiated on_____(date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

☐ A copy of this signed consent form will be given to the participant or legally authorized representative.

☐ 1) The participant is an adult and provided consent to participate.

☐ 1a) Participant (or legally authorized representative) is a non-English speaker and signed the translated Short Form in lieu of English consent document:

As someone who understands both English and the language spoken by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.

Signature of Interpreter/Witness: _____

Printed Name of Interpreter/Witness: _____

Date: _____

☐ 1b) Participant is physically unable to sign the consent form because:

☐ The participant is illiterate.

☐ The participant has a physical disability.

☐ Other (please describe): _____

The consent form was presented to the participant who was given the opportunity to ask questions and who communicated agreement to participate in the research.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

☐ 2) The participant is an adult who lacks capacity to provide consent and his/her legally authorized representative:

- ☐ 2a) gave permission for the adult participant to participate
- ☐ 2b) did not give permission for the adult participant to participate