NCI Community Oncology Research Program – Kansas City (NCORP-KC)

Study Title for Study Participants: Comparison of Tomosynthesis to Digital Mammography in Breast Cancer Screening

Official Study Title for Internet Search on http://ClinicalTrials.gov:
Tomosynthesis Mammographic Imaging Screening Trial (TMIST)

Version Date: March 12, 2018

Why am I being asked to participate in this study?

You are being asked to take part in this study because you are scheduled to have mammography for your routine breast cancer screening, which makes you eligible to enroll in a clinical trial that will compare two types of screening mammograms, Digital Mammograms and Tomosynthesis Mammograms, for breast cancer screening.

Please take time to make your decision. Participation in this study is voluntary.

What is the usual approach to my breast cancer screening?

The usual approach to breast cancer screening is to have a mammogram every one or two years. This can include a digital mammogram with images of two flat views per breast or a tomosynthesis mammogram, which is a series of image slices through the breasts. The number of images making up a tomosynthesis mammogram is dependent on the tomosynthesis system in use and the preferences of the radiologists at the site.

In some women, the mammogram is also supplemented by other screening tests such as ultrasound or MRI.

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 your care. For example:

- You may choose to have the mammogram for which you were originally scheduled.
- You may choose to take part in a different clinical trial, if one is available.
- You may consult with your doctor about having a digital mammogram or tomosynthesis mammogram supplemented by another test such as ultrasound or MRI.
- You may choose to have a tomosynthesis mammogram outside of a study if it is available.

Why is this study being done?

The main purpose of this clinical trial is to determine whether screening for breast cancer with tomosynthesis mammography is superior to digital mammography. To determine that, we are studying whether women who are screened for breast cancer with tomosynthesis mammography have fewer advanced breast cancers compared with the number of such cancers found when women are screened for breast cancer with digital mammography. This study will also compare whether there is a difference in the number of additional tests recommended after tomosynthesis mammography and digital mammography.

There will be about 164,946 people taking part in this clinical trial in the U.S. and Canada.

What are the study groups?

This clinical trial has two assignment groups: type of screening mammography and screening frequency.

You will be randomly assigned by a computer to a screening mammography group if you consent to participate in the study. If you consent to participate in the study, you are agreeing to have the computer-assigned test for the study period, either tomosynthesis mammography or digital mammography.

You will ALSO be assigned to a screening frequency based on your age, breast density, family history of breast cancer (parent, sibling, or child), presence of known breast cancer genes, use of hormone therapy, and menopausal status. You will have a Digital Mammogram or a Tomosynthesis Mammogram either every year for a total of 5 mammograms or every two years for a total of 3 mammograms. Below are two tables that explain how screening frequency will be determined in this clinical trial. The first one is for women under age 70. The second one is for women ages 70 and over.

Factors determining Frequency of Screening for Women Participating in TMIST, ages 45-69	
Every Year	Every 2 years
You had a period within the last 12 months or you had a hysterectomy but still have your ovaries and are under age 52	None of the factors listed in Column 1 apply to you.
You have dense breasts by mammography	
You take female hormones prescribed by a doctor	
You have a family history of breast cancer (parent, sibling, or child), or have breast cancer risk genes	

Factors determining Frequency of Screening for Women Participating in TMIST, ages 70-74	
Every Year	Every 2 years
You had a period within the last 12 months	None of the factors listed in Column 1 apply to you.
You have dense breasts by mammography	
You take female hormones prescribed by a doctor	

You will be assigned your study screening frequency before your first mammogram if your breast density is known. If your breast density is unknown, a member of the site trial team or clinic staff will inform you of your screening frequency assignment after your mammogram has been interpreted by a radiologist.

Your screening frequency can change from every two years to every year if your breast cancer risk increases because of any of the following factors during the trial: your personal genetic testing, family history of breast cancer (parent, sibling, or child), female hormone use, or breast density.

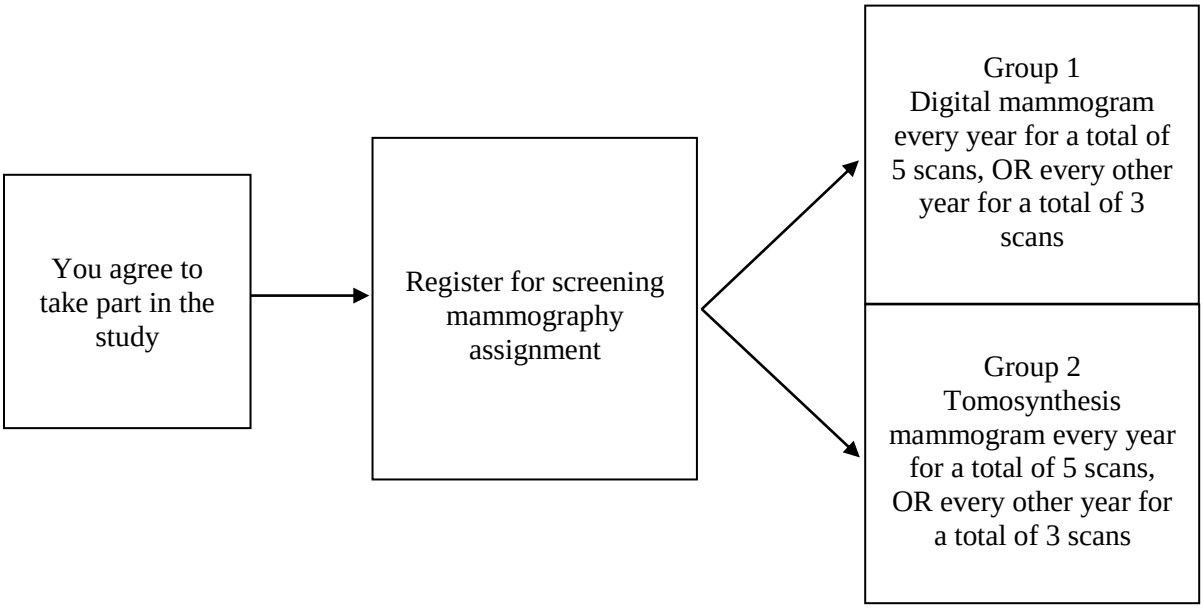
The person who is recruiting you to this study will check the appropriate box below to let you know how frequently you will have screening mammograms.

☐ You will undergo screening mammography every year.

☐ You will undergo screening mammography every 2 years.

☐ You will be assigned to undergo screening mammography either every 1 or 2 years AFTER your first study mammogram.

The chart below explains how you will participate in this clinical trial.



The facility where your TMIST mammogram is being done will notify you of your clinical results, including breast density, through their standard policy. Either your interpreting radiologist or your physician will contact you.

How long will I be in this study?

You are being asked to participate in the study for at least 8 years, as described below.

Screening Period (first 5 years of the study after your study entry)

During the period of screening using digital mammography or tomosynthesis mammography the first 5 years of your enrollment, you will be contacted within two months of the anniversary of your first study screening mammogram by local study personnel to remind you to schedule and have your next study mammogram.

If you do not return as scheduled for a study mammogram, you will be contacted up to three months after the anniversary date of your first study screening mammogram and asked to share the results of whatever breast imaging studies you have undergone at other facilities, and to provide permission to share the reports for your breast imaging that took place at other facilities. In addition, you will be asked questions about your health, including your breast cancer status. There will be a maximum of 6 phone attempts and a single registered mail contact in order to reach you for this purpose.

If you undergo any breast imaging tests or biopsy or are diagnosed with breast cancer at any facility besides the one where you enrolled in TMIST, you are asked to promptly inform personnel at the TMIST site about these incidents and permit access to these tests for use in TMIST. Materials that will be requested include imaging reports and any breast pathology and surgical specimens.

Unless you formally withdraw from the study, you are still considered part of this study, even if you miss scheduled screening mammograms.

Long Term Follow-up (for at least 8 years after your study entry)

After the study screening mammograms end, your subsequent routine breast cancer screening tests will be determined by your personal preferences and the recommendations of your primary care physician

A review of your breast imaging records during the long-term follow-up period will be conducted at your enrolling facility. If you no longer attend routine screening mammography at the facility in which you enrolled in the study, the trial team at your enrolling facility will contact you around the anniversary date of your enrollment into the study and ask you to share the results of whatever breast imaging studies at outside facilities you have had. In addition, you will be asked questions about your health, including your breast cancer status. If your TMIST site personnel lose contact with you during the period of screening or follow-up, TMIST personnel will review your general medical record and state tumor registries for information about your health and breast cancer status.

Since you are giving permission for your medical records to be reviewed, you are considered part of this study even if you are no longer in contact with study personnel.

If you ever desire to formally withdraw from the study for any reason, you should contact study personnel at this mammography facility to inform them of your decision.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual part of breast screenings. However, there are some extra tests that you may have if you take part in this clinical trial.

You will have the following additional studies/tests during the clinical trial:

- Communication with study personnel regarding your health – You will be contacted every year after you have completed the screening portion of this study, for at least eight (8) years from your study entry. You will be contacted via phone, and will be asked to report general information about your health and whether you have been diagnosed with breast cancer or other serious health conditions. These calls are expected to require no more than 30-60 minutes of your time every year.
- As part of this study, the results of any routine clinical breast biopsy (tissue slides and copies of the reports) will be sent to another study pathologist who will provide a second evaluation of the biopsy samples. Also, some of the tissue from the biopsy, if any is available after tests needed to determine your care are completed, will be submitted for genetic analysis in this clinical trial. You will not be given the results of these genetic tests. Both of these uses of the biopsy material, if you have a breast biopsy during your participation in the study are *required* as part of your participation in this study. If you agree, optional blood and cheek cells will also be collected (see Optional Studies Section).

The Table below shows the procedures that you will experience if you participate in TMIST.

TMIST Study Procedures

	At study entry	1 year after entry	2 years after entry	3 years after entry	4 years after entry	4.5 years after entry	Years 5-8 after entry
Screening Examination for those assigned to mammography every 1 year	X	X	X	X	X		
Screening Examination for those assigned to mammography every 2 years	X		X		X		
Questions regarding health						X	X
For those who have breast biopsy: submission of tissue	Tissue will be submitted at the time of biopsy.						
For those who consent to give blood *(OPTIONAL)*	Blood will be collected one time, at the time consent is given, any time during TMIST participation.						
For those who consent to give cheek cells *(OPTIONAL)*	Cheek cells will be collected one time, at the time consent is given, any time during TMIST participation.						

What possible risks can I expect from taking part in this study?

If you choose to take part in this clinical trial, you may be at risk for side effects. Side effects of participating in this clinical trial, if they occur, MUST be reported to study personnel. There also may be other side effects that we cannot predict. Many side effects go away quickly, but in some cases side effects can be serious, long lasting, or permanent.

As with any medical test, you may experience anxiety from having a mammogram. You should talk to your doctor if you experience any increased anxiety.

Questions asked in this study may be upsetting. You can stop answering questions at any time or skip any questions that you are uncomfortable answering.

If you do not join the trial, you will undergo screening mammography as per usual protocols at this clinic.

Possible side effects related to Screening Mammography (These risks are the same for bothTomosynthesis and Digital Mammography):

Likely

- Pain and/or discomfort from breast compression

Less Likely

- Bruising from breast compression
- Tearing of the skin
- Fainting

Radiation Risk:

This clinical trial involves exposure to radiation, regardless of whether you are assigned to tomosynthesis mammography or digital mammography. The radiation dose will be within national guidelines for screening mammography, regardless of whether you undergo digital mammography or tomosynthesis mammography.

All people are exposed to background radiation during their daily life. Common sources of radiation are sunlight and radioactive elements that are commonly found in rocks and soil.

(Institutions will insert one of the next two paragraphs appropriate to the tomosynthesis mammography protocol used at each mammography clinic and delete the other one. Note two of the available array of tomosynthesis systems use the same radiation dose as digital mammography).

[Option 1-digital mammography versus tomosynthesis as 3D plus synthetic 2D, or as 3D MLO plus 2D cc] Regardless of which test you are assigned – digital mammography or tomosynthesis- you will receive the same radiation dose. Every time you have a mammogram in this clinical trial, the amount of radiation will be the amount you ordinarily receive from the environment in approximately 29 days of your ordinary life.

[Option 2- digital mammography versus tomosynthesis as 3D plus 2D tomosynthesis] If you are assigned to undergo digital mammography, every time you have a mammogram in this clinical trial, the amount of radiation that you will receive is the same amount that you ordinarily receive from the environment in approximately one month of your ordinary life. If you are assigned to undergo tomosynthesis mammography, every time you have a mammogram in this clinical trial, the amount of radiation you will receive is doubled compared to digital mammography, or the same radiation dose you would ordinarily receive from the environment in approximately two months of your ordinary life.

Regardless of which test you are assigned, the dose that you yourself receive may vary a bit from these average estimates. A woman who has larger breasts or has increased breast density by mammography will experience more radiation than a woman with smaller breasts or lower breast density.

The risk of harm from this amount of radiation is very low. While most women experience no harmful health effects, there is a very small possible risk of developing a future radiation-induced cancer from receiving radiation from any examination that uses x-rays. However, the benefit of finding cancer from a mammogram outweighs the very small risk of future cancer from the amount of radiation you will receive during a screening mammogram.

If you would like more information about radiation exposure associated with screening mammography, please speak with your study doctor.

Reproductive Considerations

Because possible exposure to radiation can damage an unborn baby, you will need to inform your study doctor if you are pregnant or suspect that you may be pregnant at the time of enrollment and at the time of each study mammography screening visit. You will not be able to enroll in the study if you indicate that you are pregnant or lactating or if you don't know if you are pregnant when you are asked. If you are already enrolled in the study and become pregnant during the trial, you may not be able to undergo a mammogram when you are

scheduled to do so. If that happens, you should let study personnel know why you are not returning for a screening examination. Once you have completed your pregnancy, you can return for the next screening visit. If you are unsure of your pregnancy status at the time of a return visit for a study screening mammography, you should schedule your screening visit after you have had your next period.

What possible benefits can I expect from taking part in this study?

Taking part in this study may or may not benefit you. The results of the mammogram you undergo will be used by your treating physician to screen you for breast cancer.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

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 that may affect your willingness to participate
- If you do not follow the study rules
- If the study is stopped by the sponsor, the Institutional Review Board (IRB) or Food and Drug Administration (FDA).

What are my rights in this study?

Taking part in this clinical trial 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.

For questions about your rights while in this study, call the Central Institutional Review Board at 888-657-3711.

What are the costs of taking part in this study?

You will have tomosynthesis mammography or digital mammography as your routine yearly or every other year screening mammogram. The cost of the screening will be billed according to routine clinical practice and you would be responsible for any co-pays.

The amount that you personally will pay if you are assigned to undergo tomosynthesis mammography in this clinical trial may be higher than the amount you personally pay for digital mammography. The costs to you personally are based on the amount charged by this

clinic for the test you are having as part of this clinical trial after subtracting the amount paid by your specific insurance provider in covering that test at this clinic. Some insurance providers in some states/provinces consider tomosynthesis mammography investigational. *The costs for a digital mammogram or a tomosynthesis mammogram could change during the trial, you should check with your insurance company for the costs you must personally pay prior to each of your future screening mammography visits.*

You should contact your insurance company before enrolling in the study if you have any additional questions regarding potential costs.

Neither you nor your insurance company will be charged for the laboratory research studies performed for this study including the optional collection of cheek cells and blood specimen.

If you have no insurance and qualify for charity care programs at this mammography clinic, the cost of your screening mammograms while on this study may be paid for through existing financial assistance programs used by this mammography clinic or through study specific funds setup to pay for screening mammograms.

You will not be paid for taking part in this clinical trial.

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

If you are injured or hurt as a result of taking part in this clinical trial and need medical treatment, please tell your study doctor. You should seek medical help for any injury. The study sponsors will not pay for medical treatment for injury. Your insurance company may not be willing to pay for clinical trial-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a clinical trial.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. However absolute confidentiality cannot be guaranteed. Your information may be given out if required by law. For example, certain states require doctors to report certain infectious diseases to health boards. However, the researchers will do their best to make sure that any information that is released will not identify you. If the results of this study are presented or published, your name and other personal information will not be used. Some of your health information related to your breast cancer screening exams from this study and information about any associated downstream clinical tests and procedures, and breast biopsies (if you have them), will be kept in a central database for research. No identifying information about you will be put in the database. Your mammography images will be uploaded to a computer. There will be no information that can be used to identify you included with the images.

The ECOG-ACRIN Cancer Research Group is conducting this study. ECOG-ACRIN is a cancer research group that conducts studies for the National Cancer Institute. Your doctor is a member of ECOG-ACRIN or another group that is participating in this study. To help protect your privacy, ECOG-ACRIN has obtained a Confidentiality Certificate from the

Department of Health and Human Services (DHHS). With this Certificate, ECOG-ACRIN cannot be forced (for example, by court subpoena) to disclose information that may identify you in any federal, state or local civil, criminal, administrative, legislative or other proceeding. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The National Cancer Institute in the U.S., and similar ones if other countries are involved in the study.
- Other regulatory agencies and/or their designated representatives
- Central Laboratories who receive your samples for testing or research
- Cancer Trials Support Unit (CTSU). The CTSU is a research group sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials.
- The ECOG-ACRIN Research Group, which is coordinating the study

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on https://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.

Who can answer my questions about this study?

You can talk to the study doctor or their designated study staff about any questions or concerns you have about this study or to report side effects or injuries. Contact the study doctor _____ (insert name of study doctor[s]) at _____ (insert telephone number) or research associate _____ (insert name of research associate[s] at _____ (insert telephone number).

Optional Studies Section:

This section is about optional studies you can choose to take part in.

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading these optional studies hope the results will help other people with cancer in the future.

You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Optional Sample Collections for Biobanking for Possible Future Studies

Researchers are trying to learn more about cancer and other health problems. Much of this research is done using specimens of tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

At this time, we are requesting that you allow us to collect a sample of your blood and cheek cells and to store the samples for future research projects that may be done at a later date. We are also requesting that you allow the storage of leftover samples of your tissue for research projects that may be done at a later date. Storing samples for future research is called "Biobanking." The Biobanks are run by ECOG-ACRIN staff and researchers and are financially supported by the National Cancer Institute.

What is involved if you provide your samples for research?

If you have agreed to participate in the main study including the collection of tissue specimens (only if you have a breast biopsy) and if you agree to the optional blood and/or cheek cell collection, here is what will happen next:

1. Tissue specimens left over after the central review and genetic testing (described above) will be sent to the Biobank.
2. Blood and cheek cells will be collected in coordination with your enrollment visit or during one of your study screening mammography visits.
    a. About two (2) teaspoons of blood will be collected from a vein in your arm in coordination with your enrollment visit or during one of your study screening mammography visits.
    b. Cheek cells will be collected by rinsing your mouth with mouthwash or salt water.
3. Your samples and some related health information will be stored in the Biobank. The information will be kept with specimens and information from other people who took part in this or other research studies.
4. Only qualified researchers can submit a request to use the materials stored in the Biobanks. A committee of experts at ECOG-ACRIN, and/or the National Cancer Institute, will review each request to use the specimens for research. All research projects using these specimens will also be reviewed by an ethics or institutional review board to

ensure that the request is necessary and proper. Researchers who gain approval for use of your specimens stored in the ECOG-ACRIN Biobank will not be given your name or any other information that could directly identify you.

5. Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your specimens.
6. Results from the research may be placed in centralized storage systems called databases. It is possible that some of your genetic information and your health information may be placed in these databases. It is also possible that some of these databases may be public. Your name and other personal identifying information will not be a part of any of these databases.

What are the possible risks in providing your samples for research?

- The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
- There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
- There is a risk that someone could trace the information in a central database back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
- In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

When my samples are used for research, how will information about me be kept private?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1. When your specimens are sent to the researchers, no information identifying you (such as your name) will be sent. Specimens will be identified by a unique code only.
2. The list that links the unique code to your name will be kept separate from your specimen and health information. Any Biobank and ECOG-ACRIN staff with access to the list must sign an agreement to keep your identity confidential.
3. Researchers to whom ECOG-ACRIN sends your specimen from the Biobank will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4. Information that identifies you will not be given to anyone, unless required by law.
5. If research results are published, your name and other personal information will not be used.

What are the Possible Benefits of allowing my samples to be used for research?

You will not benefit from taking part.

The researchers, using the specimens from you and others, might make discoveries that could help people in the future.

Are there any costs or payments associated with providing my samples for research?

There are no costs to you or your insurance for these optional studies. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

What if I change my mind about allowing my samples to be used for research?

Even if you answer "Yes" to allow the collection of the blood and cheek cell samples, you may change your mind to allow the collection of only one or neither sample. Just tell the study team when the samples are being collected that you do not want them collected.

If you decide you no longer want your specimens to be used for research, you can call the study doctor (or research associate), _____, *(insert name of study doctor(name of research associate) for main trial)* at _____ *(insert telephone number of study doctor (or number of research associate) for main trial)* who will let the researchers know. Then, any specimens that remain in the bank will no longer be used and related health information will no longer be collected. Specimens or related information that have already been given to or used by researchers will not be returned.

What if I have more questions?

If you have questions about the use of your specimens for research, contact the study doctor (or research associate), _____, *(insert name of study doctor(or name of research associate) for main trial)*, at _____ *(insert telephone number of study doctor(or number of research associate) for main trial)*.

Please circle your answers to show whether or not you would like to take part in each option:

SAMPLES FOR FUTURE RESEARCH STUDIES:

May we have samples of your blood for future research?

- **I agree to provide additional blood for research.**

YES NO

May we have samples of your cheek cells for future research?

- **I agree to provide cheek cells for research**

YES NO

If a breast biopsy or surgery is performed, may we keep any tissue leftover after the central review and genetic testing for research in the future?

- **My samples and related information may be kept in a Biobank for use in future health research.**

YES **NO**

This is the end of the section about optional studies.

Release

By signing this form you authorize NCORP-KC to access and obtain information that is required for the study. this may include your medical records, labs, radiologic films and reports and pathology specimens. This authorization to disclose your medical records shall not expire, even upon death, unless specifically revoked in writing by you.

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

My signature agreeing to take part in the study

I have read this consent form or had it read to me. I have discussed it with the study doctor or their study staff and my questions have been answered. I will be given a signed copy of this form. I agree to take part in the main study. I also agree to take part in any additional studies where I circled "yes".

Participant _____

Participant's signature_____

Date of signature_____

Person obtaining consent_____

Signature of person obtaining consent_____

Date of signature_____