TUFTS MEDICAL CENTER
TUFTS UNIVERSITY
Emergency Department

INFORMED CONSENT TO PARTICIPATE IN RESEARCH

Rule Out Myocardial Ischemia/Infarction Using Computer Assisted Tomography (*ROMICAT II)*

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INTRODUCTION

You are being invited to take part in a research study to find out if a test called "cardiac computed tomography angiography (CTA)" can help doctors in the emergency department (ED) safely and rapidly detect whether your current symptoms are related to disease in the blood vessels of your heart. This test can be used to assess the function of your heart and the oxygen supply to your heart muscle as well as to see the arteries supplying blood to your heart ("coronary arteries").

Taking part in this research study is completely your choice. You can decide to stop taking part in this research study at any time for any reason. If you stop being in this research study, it will not affect how you are treated at Tufts Medical Center/Tufts University.

Please read all of the following information carefully. Ask Dr. Weiner, or his representative, to explain any words, terms, or sections that are unclear to you. Ask any questions that you have about this research study. Do not sign this consent form unless you understand the information in it and have had your questions answered to your satisfaction.

If you decide to take part in this research study, you will be asked to sign this form. You will be given a copy of the signed form. You should keep your copy for your records. It has information, including important names and telephone numbers, to which you may wish to refer in the future.

New things might be learned during this study that you should know about. The investigators will tell you about new information that may affect your willingness to stay in this study.

If you are eligible to participate and agree to be in the study, the Principal Investigator may still choose to stop your participation in this study if he thinks it is in your best medical interest.

If you have question about your rights as a research study subject, call the Tufts Medical Center and Tufts University Health Sciences Institutional Review Board (IRB) at (617) 636-7512. The Institutional Review Board is a group of doctors, nurses, and non-medical people who review human research studies for safety and protection of people who take part in the studies. Federal law requires the Institutional Review Board to review and approve any research study involving humans. This must be done before the study can begin. The study is also reviewed on a regular basis while it is in progress.

This research study has been reviewed and approved by the IRB of Tufts Medical Center and Tufts University Health Sciences.

PURPOSE OF STUDY

The purpose of this study is to find out if a test called "cardiac computed tomography angiography (CTA)" can help doctors in the emergency department (ED) safely and rapidly detect whether your current symptoms are related to disease in the blood vessels of your heart. This test can be used to assess the function of your heart and the oxygen supply to your heart muscle as well as to see the arteries supplying blood to your heart ("coronary arteries").

People who agree to take part in this study will be randomly selected either to undergo routine care for chest pain or to receive a CT scan in addition to routine care. Study doctors want to see if the CT scan can safely provide enough information to Emergency Department doctors to send people at low risk for heart disease home without having to stay overnight in the hospital.

The results of this test - both good and bad - will be compared to those which are routinely used in the standard hospital procedure - measurement of blood markers (chemicals whose increase can indicate an injury of your heart muscle), electrocardiogram (ECG - a recording of your heart's electrical activity) or heart perfusion imaging (a procedure that can visualize your heart muscle's blood supply). For research purposes, the medical records of your current hospital admission will be reviewed. This study will compare the effects - good and bad - of 2 different ways of diagnosing heart disease in the ED.

We are inviting you to take part in this study because you have come to the ED for care and you may have a heart condition. The doctor who is taking care of you in the emergency department believes you might have acute coronary syndrome, a heart condition that can cause chest pain and other symptoms because the heart is not getting enough blood. Acute coronary syndrome is caused by the build-up of plaque in the arteries that supply blood to the heart. This plaque can cause the pathways to become narrow or blocked, and reduce the amount of blood reaching your heart muscle. Heart attacks, also called myocardial infarction or MI, can also be caused by acute coronary syndrome.

About 1000 people will take part in this research study across 9 sites in the United States. We anticipate 200 people at Tufts Medical Center will participate in the study. This study is being sponsored by the National Institute of Health (NIH).

PROCEDURES TO BE FOLLOWED

It will take about 1 month to complete this research study. Most of the study will take place while you are in the emergency department. In addition, one of the study team members will call you 1 time (at 1 month) after your hospital visit ends to ask about any tests or treatment for heart problems, you may have experienced, after leaving the ED. In addition, if you were discharged directly from the ED, a study member will call you after 48-72 hours to ask about your symptoms.

What will happen in this research study?

If you agree to take part in this study, and sign this consent form, you will be assigned randomly or by chance (like the flip of a coin) to one of 2 study groups. You will have an equal chance of being in each group. Neither you nor the study doctor can choose your group assignment.

- **Standard of Care Group** -- The subjects in this group may have any or all of the standard functional tests that doctors in the ED or Observation Floor use to find the cause of a subject's chest discomfort, including exercise treadmill test, nuclear stress test or stress ECHO. The ED doctors will decide exactly which of these tests is most appropriate. One half the subjects in this study will be assigned to this group.
- **Standard of Care + CT Scan Group** -- The subjects in this group will have a cardiac CT scan as part of their initial evaluation and in addition to the standard functional tests that are routinely performed on subjects.. One half the subjects taking part in this study will be assigned to this group.

All subjects in both groups will have a complete evaluation by a doctor. This will include a health history, physical examination, blood tests and an EKG. During the health history, you **may** be asked questions regarding sensitive information about drug use. Please know that this information **may** be subpoenaed by a court of law. If you are assigned to the Cardiac CT Group, we will perform the scan as soon as possible, most often, while you are still in the Emergency Department. In all cases, your health is the major concern of the medical staff and study doctors, and if necessary, we will stop you from further participation, if it is not in your best interest to continue.

At any point, you may change your mind about taking part in this study. This is perfectly acceptable, and you will continue to receive your standard, routine care.

Group A - Standard Care
If you are assigned to this group (the control group), you will receive all the standard care as determined by your study and treating doctor, which includes a blood test and ECG. In this control group, your treating doctors may determine that no additional testing is needed, per standard of care; or, the doctor may deem it best to perform additional tests on your heart, including exercise treadmill test, nuclear stress test or stress ECHO.

The study doctors will look at your medical records to understand the medical care you received and the decision to admit or discharge you from the hospital.

Group B - Standard care + CT Scan Group
If you are selected to be in Group B you will receive standard of care as determined by your study and treating doctor, which includes a blood test and ECG. After the results of you first blood test, you will receive a CT scan of your chest/heart, most likely, during your stay in the ED.

The CT involves taking "highlighted" pictures of the blood vessels of your heart. If you do not have an "IV catheter" in your arm at this time, a study doctor or nurse will place one for administering the contrast dye during the scan.

Then we will take you to the CT scan room. A study doctor will go with you and monitor your heart rate and how you are feeling. You will lie on a table in front of the CT scanner. The scanner is a short tube that has an opening in the middle a little wider than your body. Before the scan begins, we will put four stickers with wires on your chest that attach to a heart monitor, so that we can watch your heart rate at all times during the scan. The study doctor will tell you what to expect during the scanning process.

Next, the study doctor will check your blood pressure and how fast your heart is beating, to see if it is okay to begin the scan. We can make the best pictures when your heart is beating less than 65 times per minute. Depending on how fast your heart is beating, the study doctor may give you a drug called metoprolol through your IV to lower your heart rate. Metoprolol is a commonly prescribed blood pressure medicine. This will be administered for research purposes as part of being in Group B (Standard Care + CT Scan Group). You should not receive this drug if you are currently suffering from asthma. If you have had an asthma attack in the last two days, you must tell your study doctor.

Before the scan begins, the study doctor may also give you a nitroglycerine tablet to place under your tongue to dissolve. Nitroglycerin helps relax the blood vessels so they are easier to see on the scan. This will be administered for research purposes as part of being in Group B (Standard Care + CT Scan Group). If you have taken drugs such as sildenafil (Viagra), tadalafil (Cialis), or vardenafil (Levitra) within 72 hours of the scan, please let the physician know and we will not administer nitroglycerin to you. The combination of any of these drugs with nitroglycerine may cause drops in blood pressure greater than those occurring with nitroglycerin alone.

During the cardiac CT, we will take 3 sets of pictures of your heart. The first set of pictures takes about 5 seconds, while the next two sets of pictures take 10 to 15 seconds. You will need to hold your breath while all 3 sets of pictures are being taken. The study doctor will review these instructions with you. During the second and third sets of pictures, we will inject a small amount of fluid into your IV catheter. This fluid is called "contrast" or "IV dye." The contrast fluid allows us to see the arteries in your heart better. The IV contrast is commonly used for CT scans of other parts of the body, as well as for special X-rays of the heart. Some subjects say that the contrast fluid makes them feel warm or even hot when it is injected. This is a normal reaction to the dye. This feeling usually goes away within a few minutes after the scan is over. If you have diabetes mellitus and are taking metformin, you will have to stop this medication for 2 days after the scan, so your kidneys are not harmed.

After the study doctor finishes your scan, s/he will make sure that you are feeling well and will measure your blood pressure and heart rate again. You will stay for about 15 minutes after the scan, so the CT staff and the study doctor can watch to make sure you are all right after the scan. You will then return to the ED. A study doctor will go with you and watch your heart rate and how you are feeling at all times. When you return to the ED, the study doctor will review the results of the CT scan with the doctors caring for you there. The ED doctors will then decide whether it would be best for you to be admitted to the hospital or to be discharged home.

If the results of your CT scan come back negative, your treating doctor(s) may determine that you are not at high risk for a cardiac event (such as a heart attack) and might send you home from the ED that same day.

If the results of your CT scan come back positive, then you will be admitted to the hospital and your treating doctors will decide what is best for you. Clinical information about your symptoms and condition while in the hospital will be recorded. This information will be recorded on our data sheets.

Both Groups

Regardless of which group you are in, your study and treating doctors will want to gather information about your heart health, including what tests and treatments you have had and whether you have returned to the hospital after you leave the ED. We will ask you to provide your contact information, including your mailing address, and the name of another person or doctor(s) we can contact, who know about your

health should you be unavailable to provide any information. We may need to access your medical records at facilities outside this one.

We will call you after about 28 days, after your hospital visit to ask you if you had any chest pain since you left the hospital or if you returned to the hospital. The phone calls will take between 5 and 10 minutes. If you did have chest pain or return to the hospital, we will check your medical records to see if your symptoms or hospitalization was related to your chest pain in the ED. This information will help us find out if cardiac CT is a useful tool to find the cause for your chest pain.
In addition, if you were were discharged directly from the ED, we will call you once more after 48-72 hours of your discharge, to ask if you had any further symptoms or returned to the hospital in the meantime.

RISKS

Overall, the risks of the study procedure and the standard procedures are relatively equal. Inclusion and exclusion criteria have been designed to enroll only subjects who are at low to intermediate risk for ACS and who have normal vital signs, and without any medical condition that would knowingly predispose them to harm by their participation (e.g., pregnancy, renal insufficiency, or known allergy to iodinated contrast agents).

Radiation Risks:
Both the standard of care group and the cardiac CT scan group will undergo diagnostic tests involving ionizing radiation with their involvement in this study. The standard group may have standard x-rays or CT x-ray exams and treadmill nuclear stress tests, which are routinely performed on subjects presenting in an emergency room with cardiac problems. The cardiac CT group will receive a series of CT x-ray exams with and without contrast agents, the diagnostic method being evaluated in this study. Any participant in either group may receive more or less radiation than a specific participant in the other group, depending on the difficulty of diagnosing each participant's condition and the number of tests necessary. However, it is unlikely that any participant in either group will receive more radiation exposure than the maximum dose a radiation worker is allowed to receive in one year under existing radiation control regulations in the United States.

Risks with CT Angiography:
Some people may develop discomfort from lying still on the enclosed scanning table. Although the tube through which the table moves is open at both ends, some people may develop claustrophobia.

If you have an electronic medical device implanted, such as a pacemaker or a drug pump, please make sure that you tell your study doctors and research staff. It was recently reported by the FDA that the CT scan may cause the malfunction of electronic medical devices.
Since the CT angiogram provides your study and treating doctors with a picture of your chest, there may be a possibility that other conditions, unrelated to the present illness, could be discovered.

Risks during pregnancy:

Since X-ray exposure can be harmful to an unborn baby, pregnant women and those who are breastfeeding will not be able to be part of this research study. If you are a woman who can become pregnant, we will do a urine pregnancy test to be sure you can take part in this study.

Risks of the CT scan contrast (dye) material:
When you receive the contrast during the CT scan for research purposes, you may experience a warm or hot sensation and/or a metallic taste in your mouth. These are normal reactions and are not dangerous. You cannot be in this study if you have a history of allergic reactions to contrast or if you have kidney problems. A study doctor will ask you if you are allergic to any medicine. The study doctor will review the results of your blood exams to see if you have kidney problems.

Since your kidneys must be healthy for you to be in this study, there is only a very minor risk that the injection of contrast will result in any damage to your kidneys. This can happen in subjects with weak or damaged kidneys from certain medical conditions.

The kidneys remove metformin (a drug used to treat diabetes mellitus). Contrast medium can greatly increase the level of metformin in the blood because damaged kidneys are not as effective at removing metformin from the body. High levels of metformin in the blood increase the risk of lactic acidosis. Because lactic acidosis is so dangerous, metformin should be temporarily stopped for procedures involving contrast medium.

There is a very small possibility that you are allergic to the dye, if you have not received it before. In nearly all subjects, the allergic reaction consists of developing temporary shortness of breath or itching on the skin. If this happens, the study doctor will stop the scan immediately and treat you for the allergic reaction.

You cannot be in this study if you have a history of allergic reactions to contrast or if you have kidney problems. In addition, you must be willing to stop metformin for 2 days after the scan if you have diabetes and are taking that drug.

Risks with an IV line or catheter:
Sometimes an IV line may cause pain, a bruise, swelling, and/or bleeding at the needle site. Contrast material could also leak out of your IV and collect under the skin of your arm. Rarely, an infection may develop. If infection does occur, we will treat it.

Risks with metoprolol:
As mentioned, you may receive a medicine to reduce your heart rate called metoprolol. The doctor caring for you in the Emergency Department will decide this. Most people do not feel anything from this medicine, but sometimes subjects feel a bit tired for a few hours after they take it. In addition, since this medicine may also reduce the blood pressure, you could feel dizzy. We will check your blood pressure several times during the scan to watch for this side effect. If you do not feel well, we will treat you.

Metoprolol can cause narrowing of the breathing tubes in people with acute asthma. If you have experienced an attack of asthma in the last 2 days, please let the physician know, and we will not administer metoprolol to you.

Risks with nitroglycerin:
You may also receive nitroglycerin under your tongue. Some times, subjects develop a headache after receiving nitroglycerin. This will typically go away within 1-2 hours. You can take medicines that you normally take for a headache to help with this side effect, such as aspirin or Tylenol. Some times, nitroglycerin may also reduce blood pressure. This could cause you to feel dizzy. We will check your blood pressure several times during the test to monitor for this.

If you do not feel well, we will provide treatment for you.

If you have taken drugs such as sildenafil (Viagra), tadalafil (Cialis), or vardenafil (Levitra) within 72 hours of the scan, please let the physician know and we will not administer nitroglycerin to you. The combination of any of these drugs with nitroglycerine may cause drops in blood pressure greater than those occurring with nitroglycerin alone.

There may be other risks and side effects that are not known at this time.

BENEFITS

Taking part in this study may or may not directly benefit you. Subjects in this study who undergo cardiac CT scans may be discharged directly from the ED within a few hours and thus avoid hospital admission, depending on what the cardiac CT shows. Subjects undergoing CT will also receive information about the heart, including whether it is healthy or diseased. This information may permit your doctors to better assess your risk for future cardiovascular events. The cardiac CT scan may decrease time and money for you and other subjects with similar issues. We hope that the information learned from this study will benefit other subjects with potential heart problems in the future.

ALTERNATIVES

You may choose not take part in this study. If you do not take part in this study, you will still receive standard testing in the Emergency Department to find out the cause of your chest pain. This may include further laboratory tests, further EKGs, and a stress test.

WHOM TO CONTACT

If you ever have questions about this study or in case of research-related injuries, you should contact Scott Weiner, MD, the Principal Investigator, as soon as possible at Tufts Medical Center at 617-636-8060. During non-business hours and holidays, please contact the page operator at 617-636-5114.

You may also contact any of the following study investigators through the page operator day or evening at Tufts Medical Center: James Udelson (page # 1465), Neal Halin (page# 1443), Martin Maron (page# 4081), E. Kent Yucel (page# 0315), Brien Barnewolt (page# 2134).

If you have questions about your rights as a research subject, you can call the Institutional Review Board at 617-636-7512.

RESEARCH RELATED INJURY

Emergency medical treatment will be given to you if you are hurt or get sick as a direct result of being in this research study. You or your insurance carrier are to pay for any such medical care. Any needed medical care is available at the usual cost. All needed facilities, emergency treatment, and professional services are available to you, just as they are to the general public. There are no plans to pay for your treatment if you get hurt or sick as part of this study. The institution has not set aside any money to pay for a research-related injury or illness.

COSTS

There are no costs associated with this study.

PAYMENT

There are no payments associated with this study.

PRIVACY AND CONFIDENTIALITY

If you agree to take part in this research study, your personal information will not be given to anyone unless we get your permission in writing. It will only be given if the law requires it. It will also only be given for regular hospital treatment, payment, and hospital management activities. We will do our best to make sure that your personal information will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by the law. Records of your participation in this study, your progress and images submitted (CT Angiography) while you are in the study, will be kept in a confidential form here at Tufts Medical Center and in a computer file at the headquarters or ROMICAT. All data sent over the Internet will be coded so that other people cannot read it. All personal identifiers are removed and replaced with a unique identifying number.

You further understand and agree that authorized representatives of NIH, Massachusetts General Hospital (MGH), the Institutional Review Board (IRB) at Tufts Medical Center and other groups or organizations that have a role in this study may, without obtaining additional consent from you, have access to and the ability to copy information from your medical and research records that is relevant to this research study, including the results of your participation in this study. This access is necessary to ensure the accuracy of the findings, the completion of the study, and your safety and welfare. If any publication or presentations result from this study, you will not be identified by name. Results will be reported in a summarized manner in which you cannot be identified.

Your research records and images will be kept permanently on file at MGH and may be used for future research. All personal identifiers will be removed and replaced with a unique identifying number to protect your identity. You can review your medical records at any time, however you may only be able to access your research records upon completion of the study.

PARTICIPANT'S STATEMENT

I have read this consent form and have discussed with Dr. Weiner or his representative the procedures described above. I have been given the opportunity to ask questions, which have been answered to my satisfaction. I understand that any questions that I might have will be answered verbally or, if I prefer, with a written statement.

I understand that I will be informed of any new findings developed during the course of this research study that may affect my willingness to stay in this research study.

I understand that my participation is voluntary. I understand that I may refuse to participate in this study. I also understand that if, for any reason, I wish to discontinue participation in this study at any time, I will be free to do so, and this will have no effect on my future care or treatment by my physicians or this hospital.

I understand that in the event I become ill or am injured as a result of participating in this research study, medical care will be provided to me. However, such medical care will not be provided free of charge, even if the injury or illness is a direct result of this research study. I understand that no funds to provide financial compensation for research-related injury or illness are available.

If I have any questions concerning my rights as a research subject in this study, I may contact the Institutional Review Board at (617) 636-7512.

I have been fully informed of the above-described study with its risks and benefits, and I hereby consent to the procedures set forth above.

I understand that as a participant in this study my identity and my medical records and data relating to this research study will be kept confidential, except as required by law, and except for inspections by the U.S. Food and Drug Administration which regulates investigational drug/device studies, and the study sponsor.

_____ _____

Date Participant's Signature

I have fully explained to _____ the nature and purpose of the above-described study and the risks that are involved in its performance. I have answered all questions to the best of my ability.

_____ _____

Date Principal Investigator or Representative's Signature