Quantification of myocardial blood flow using dynamic PET/CTA fused imagery to determine the physiological significance of specific coronary lesions.

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You Are Being Asked to Be in a Research Study

What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

Do I Have to Do This?

No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

Emory University
Consent to be a Research Subject / HIPAA Authorization

Title:
Quantification of myocardial blood flow using Dynamic PET/CTA fused imagery to determine physiological significance of specific coronary lesions.

Principal Investigator:
[redacted], PhD

Sponsor:
National Institutes of Health (NIH)

Introduction
You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form, you will not give up any legal rights.

What is the purpose of this study?
The purpose of this study is to develop methodologies ***to assess*** the severity of any given coronary obstruction similarly to what is routinely performed during invasive coronary angiography (ICA), but noninvasively by means of fused dynamic Positron Emission Tomography (PET) and coronary Computed Tomographic Angiography (CCTA) and ***to determine*** whether the lesion requires invasive treatment, i.e. revascularization. In addition to our analysis, the anonymized CCTA images will be shared with an external laboratory for additional measurements obtained with an FDA-approved technique.

What will I be asked to do?
You are eligible for this investigation if you have undergone a nuclear imaging test called cardiac Positron Emission Tomography (PET) and you are asked to participate in a study on assessment of Coronary Artery Disease by agreeing to additional procedures and measurements. All proposed procedures will be performed only by investigators certified to perform these procedures.

You are being considered for the following procedure(s) (with the checked box):

- ❑ **Coronary Computed Tomographic Angiogram (CCTA)**
  If you agree to participate in this study, a noninvasive heart imaging test called coronary Computed Tomographic Angiography will be performed following the clinically used protocols. The procedure requires the intra-venous injection of a contrast media, an inert substance that allows to visualize your arteries. The procedure will last ~30 minutes, 10 for preparation and 20 for the imaging test itself during which you will lay in the CT scanner.

- ❑ **Invasive Measurements in the Cardiac Catheterization Laboratory (ICA-meas)**
  The heart catheterization procedure will be ordered by your doctor and will be performed as part of your regular care due to your clinical needs and not as part of the research. What is part of this research are additional measurements during catheterization as described below.

  Sometimes the doctor may not be able to determine if a blockage is significant by looking at the pictures taken during the intervention. In this case the doctor may want to evaluate the blockage with a special wire to measure the pressure across the narrowing inside your artery. After placing the wire in your heart, a medicine called adenosine is given and the pressure measured. A large pressure change is the indication that the narrowing in the artery needs to be re-opened. This pressure measurement – called Fractional Flow Reserve (FFR) – is required when no other indication exists on the severity of the artery blockage, particularly from previous tests such as the cardiac PET and will be performed as standard of care when your doctor considers it necessary and not as part of the research.

  If you agree to participate in this study, two additional measurements called Coronary Flow Reserve (CFR) and Index of Microvascular Resistance (IMR) that are not commonly measured during catheterization will be obtained. The same wire used to measure FFR will be used, no additional wires will be introduced in your heart. An additional dose of adenosine will be given prior to the measures. The additional measurements will require to extend the procedure for few more minute (~5 minutes on average).

  If no arteries require FFR measurement as a clinically indicated procedure and you agree to join this study, you agree to have the three above-mentioned measurements (FFR, CFR and IMR) performed in one artery for which no previous indication of severity exists (for instance from cardiac PET). All three measures will be performed as part of the research. A single special wire will be introduced in your heart to measure all three indexes, adenosine will be given prior to measurements. The procedure will be extended by few minutes to obtain these measures (~10 minutes).

Who owns my study information?
Emory University owns the study information.

What are the possible risks and discomforts?
There may be side effects from the study procedures that are not known at this time. Precautions will be taken to prevent harmful side effects.
The most common risks and discomforts expected in this study are:

- You will be exposed to radiation exposure during the CCTA scan and, if required by your doctor, Invasive Coronary Angiography (ICA). ICA will be performed as standard of care and the risks of this procedure will be explained to you in detail by your doctor. The ICA is not done as part of research. The CCTA will be performed as part of the research. The estimated radiation dose that you will receive is equal to or less than the annual radiation exposure limit allowed for persons who are occupationally exposed to radiation (for example, x-ray technologist, radiologist). The principal risk associated with a radiation dose is the possibility of developing a radiation-induced cancer later in life. The risk for radiation-induced cancer from this study is minimal. You will receive radiation exposure from the fluoroscope that produces pictures of your internal organs. Your soft tissue and bones will receive a radiation exposure, but the highest radiation exposure will be to your skin. Very high skin exposure can cause reddening of the skin, blistering and even ulceration. Sometimes this will be delayed for weeks or months after exposure. If you should experience skin discomfort in the area that was pictured, report this to your personal physician.
- If ICA performed, inserting a pressure wire for the invasive measurements (FFR, CFR, IMR) is associated with the possibility of the artery constricting for a short time (known as a spasm), tearing the artery wall and blood clot. Tearing and blood clot are very rare (they happen less than 4 times every 1000 procedures). To reduce the risk of temporary spasm, you will be given nitroglycerine. In any case the spasm can be stopped by removing the wire. There is a small risk of temporary low blood pressure with the injection of nitroglycerine. The use of adenosine has a small risk of side effects such as temporary chest pain, shortness of breath, headache, changes in heart rate and blood pressure.

If you are a woman: to protect against possible side effects of the study procedures, women who are pregnant or nursing a child may not take part in this study.

Will I benefit directly from the study?

This study is not designed to benefit you directly. This study is designed to learn more about coronary physiology and to develop novel noninvasive techniques to quantify it in order to properly select a treatment. The study results may be used to help others in the future.

Will I be compensated for my time and effort?

You will get $100.0 for completing the CTA acquisition, to compensate you for your time and effort. The compensation will be given after the study has been acquired. You may be asked to fill out a tax form, including your Social Security or Taxpayer Identification Number, in order to be reimbursed, depending on the amount and method of payment. Some payment methods involve mail coming to your house, which may be seen by others in your household. You can decline payment if you are concerned about confidentiality, or you can talk to the study team to see if there are other payment options.

What are my other options?

You do not have to be in this study to be treated for your heart conditions. Refusal to be part of this research study will have no consequences for the standard of care procedures and treatments you will decide to undertake.

How will you protect my private information that you collect in this study?

Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results. All data collected during the study, as well as all results from analysis, will be stored in the Nuclear Cardiology R&D computer lab (Woodruff Research Building). The room is locked (with coded entry) and access is limited to team members. The lab uses on-site and off-site backup facilities and operates under SOPs, so it can function as a core lab for FDA clinical trials.

Certificate of Confidentiality

There is a Certificate of Confidentiality from the National Institutes of Health for this Study. The Certificate of Confidentiality helps us to keep others from learning that you participated in this study. Emory will rely on the Certificate of Confidentiality to refuse to give out study information that identifies you. For example, if Emory received a subpoena for study records, it would not give out information that identifies you.

The Certificate of Confidentiality does not stop you or someone else, like a member of your family, from giving out information about your participation in this study. For example, if you let your insurance company know that you are in this study, and you agree to give the insurance company research information, then the investigator cannot use the Certificate to withhold this information. This means you and your family also need to protect your own privacy.

The Certificate does not stop Emory from making the following disclosures about you:

- Giving state public health officials information about certain infectious diseases,
- Giving law officials information about abuse of a child, elderly person or disabled person.
- Giving out information to prevent harm to you or others.

Giving the study sponsor or funders information about the study, including information for an audit or evaluation.

Storing and Sharing your Information

De-identified data from this study, may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.
Your data from this study may be useful for other research being done by investigators at Emory or elsewhere. To help further science, we may provide your deidentified data and/or specimens to other researchers. If we do, we will not include any information that could identify you. If your data are labeled with your study ID, we will not allow the other investigators to link that ID to your identifiable information.

Medical Record

If you have been an Emory Healthcare patient before, then you already have an Emory Healthcare medical record. If you have never been an Emory Healthcare patient, you do not have one. An Emory Healthcare medical record will be made for you if an Emory provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory Healthcare medical record you have now or any time during the study.

Emory Healthcare may create study information about you that can help with your care. For example, the results of study tests or procedures. These study results will be put in your Emory Healthcare medical record. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

Tests and procedures done at non-Emory places may not become part of your Emory medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury
If you get ill or are injured from being in the study, Emory will help you to get medical treatment. Emory and the National Institutes of Health have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proved that your injury or illness is directly caused by the negligence of an Emory or sponsor employee. "Negligence" is the failure to follow a standard duty of care.
If you become ill or injured from being in this trial, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. [redacted] at telephone number [redacted]. You should also let any health care provider who treats you know that you are in a research study.

Costs
There will be no costs to you for participating in this study, other than basic expenses like transportation. You will not be charged for any of the research activities. If the study procedures result in any medical complications that would not fall under "injury" as discussed above, the cost of treatment for those complications may be charged to you or your insurance.

Withdrawal from the Study
You have the right to leave a study at any time without penalty.
The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act and regulations (HIPAA). We refer to all of these laws as the "Privacy Rules." Here we let you know how we will use and disclose your PHI for the study.

PHI that Will be Used/Disclosed:
The PHI that we will use or share for the main research study includes:

- Medical information about you including your medical history and present/past medications.
- Radiological Images from multiple sources (PET, ICA, CCTA)
- Results of exams, procedures and tests you have during the study.

Purposes for Which Your PHI Will be Used/Disclosed:
We will use and share your PHI for the conduct and oversight of the research study. We will use and share your PHI to provide you with study related treatment and for payment for such treatment. We will also use and share your PHI to conduct normal business operations. We may share your PHI with other people and places that help us conduct or carry out the study, such as laboratories, data management centers, data monitors, contract research organizations, Institutional Review Boards (IRBs) and other study sites. If you leave the study, we may use your PHI to determine your health, vital status or contact information. We will use and disclose your PHI for the administration and payment of any costs relating to subject injury from the study.

Use and Disclosure of Your Information That is Required by Law:
We will use and disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or abuse of elderly or disabled adults.

Authorization to Use PHI is Required to Participate:
By signing this form, you give us permission to use and share your PHI as described in this document. You do not have to sign this form to authorize the use and disclosure of your PHI. If you do not sign this form, then you may not participate in the research study. You may still receive non-research related treatment.

People Who will Use/Disclose Your PHI:
The following people and groups will use and disclose your PHI in connection with the research study:

- The Principal Investigator and the research staff will use and disclose your PHI to conduct the study.
- Emory may use and disclose your PHI to get payment for study related treatment and to run normal business operations.
- The Principal Investigator and research staff will share your PHI with other people and groups to help conduct the study or to provide oversight for the study.
- The National Institutes of Health is the Sponsor of the study. The Sponsor may use and disclose your PHI to make sure the research is done correctly and to collect and analyze the results of the research. The Sponsor may disclose your PHI to other people and groups like study monitors to help conduct the study or to provide oversight for the study.
- The research team and the Sponsor may use and disclose your PHI, including disclosure to insurance carriers to administer payment for subject injury.
- The following people and groups will use your PHI to make sure the research is done correctly and safely:
  - Emory offices that are part of the Human Research Participant Protection Program and those that are involved in study administration and billing. These include the Emory IRB, the Emory Research and Healthcare Compliance Offices, and the Emory Office for Clinical Research.
  - Other researchers and centers that are a part of this study.
  - Public health agencies.
  - Research monitors and reviewer.
  - Accreditation agencies.
- Sometimes a Principal Investigator or other researcher moves to a different institution. If this happens, your PHI may be shared with that new institution and their oversight offices. PHI will be shared securely and under a legal agreement to ensure it continues to be used under the terms of this consent and HIPAA authorization.

Expiration of Your Authorization
Your PHI will be used until this research study ends.

Revoking Your Authorization
If you sign this form, at any time later you may revoke (take back) your permission to use your information. If you want to do this, you must contact the study team at:

[redacted]

[redacted]

At that point, the researchers would not collect any more of your PHI. But they may use or disclose the information you already gave them so they can follow the law, protect your safety, or make sure that the study was done properly and the data is correct. If you revoke your authorization you will not be able to stay in the study.

Other Items You Should Know about Your Privacy
Not all people and entities are covered by the Privacy Rules. HIPAA only applies to health care providers, health care payers, and health care clearinghouses. If we disclose your information to people who are not covered by the Privacy Rules, including HIPAA, then your information won't be protected by the Privacy Rules. People who do not have to follow the Privacy rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them.

To maintain the integrity of this research study, you generally will not have access to your PHI related to this research until the study is complete. When the study ends, and at your request, you generally will have access to your PHI that we maintain in a designated record set. A designated record set is data that includes medical information or billing records that your health care providers use to make decisions about you. If it is necessary for your health care, your health information will be provided to your doctor.

We may remove identifying information from your PHI. Once we do this, the remaining information will not be subject to the Privacy Rules. Information without identifiers may be used or disclosed with other people or organizations for purposes besides this study.

Contact Information
Contact:

- [redacted]

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Conflict of Interest Disclosure
The following team members have disclosed Conflict of Interest with industry partners. [redacted] and Emory University is/are entitled to royalties derived from Syntermed's sale of products related to the software used in the research described in this paper. Additionally, [redacted] is co-founder and equity holder in Syntermed. [redacted] is entitled to royalties derived from Syntermed's sale of products related to the software used in the research described in this paper.

Additionally, [redacted] serves as a consultant for Synermed and receives compensation for his services. [redacted] [and Emory University] is/are entitled to royalties derived from Syntermed's sale of products related to the software used in the research described in this paper. Additionally, [redacted] is employed with Syntermed and has equity in the company. The terms of these arrangements have been reviewed and approved by Emory University in accordance with its conflict of interest policies.

Consent and Authorization

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in this research study. By signing this consent and authorization form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

Name of Subject

Signature of Subject (18 or older and able to consent) **Date** **Time**

TO BE FILLED OUT BY STUDY TEAM ONLY

Name of Person Conducting Informed Consent Discussion

Signature of Person Conducting Informed Consent Discussion **Date** **Time**