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Research Subject Informed Consent Form

Title of Study:	Pulmonary Embolism – Thrombus Removal With Catheter-Directed Therapy **(PE-TRACT)** S22-01272
Principal Investigator:	Name of the Principal Investigator Department of Principal Investigator Address Phone Numbers
Emergency Contact:	Insert Emergency Contact Insert Phone Number/Pager, etc.

INTRODUCTION

You are being invited to take part in this research study because you have blood clots in your lungs (called pulmonary embolism). Pulmonary embolism is a serious problem, especially when clots are large. There are several treatments that doctors typically use, but it is not clear which works best, especially with regard to longer-term outcomes such as exercise tolerance. This study will help answer that question.

You are an appropriate candidate for this study, but it is your choice whether to be in this study. If you decide not to be in the study, your care will not be compromised in any way. If you decide to be in the study, you can stop participating at any time. This form tells you about the study. Please ask questions about anything that you do not understand.

WHAT IS THE STUDY ABOUT?

The study is designed to identify the best way to treat pulmonary embolism, specifically when there is a large amount of clot but the patient's blood pressure is stable. While this condition is sometimes life-threatening, either of the treatments in this study work well to help people survive. Less is known about which treatment helps people do better in terms of breathing, heart function, and ability to exercise over time.

All patients with pulmonary embolism are treated with blood thinner medicines (anticoagulation). Sometimes, doctors will additionally do a procedure using a catheter to either remove the clot or give clot-dissolving medicines (catheter-directed therapy). It is not clear whether doing these procedures help patients who have a large amount of clot but who are more stable and at lower risk. This study, called PE-TRACT, compares blood thinners alone to blood thinners plus catheter-directed therapy in order to answer these questions and be able to provide patients with the most effective treatment. This is a national multi-site clinical trial and NYU Langone Health (NYULH) is the central coordinating center for the study.

Both treatment approaches are considered standard care and commonly used for patients with pulmonary embolism who are stable but who have large amounts of clot. The clot-dissolving medicine and devices used in catheter-directed therapy are cleared by the FDA for treatment of pulmonary embolism.

HOW IS THIS DIFFERENT FROM WHAT WILL BE DONE NORMALLY?

Normally, the doctor on call decides which treatment approach to recommend and use. These decisions vary from doctor to doctor, and doctors don't know which one is best. Both treatment approaches are accepted as standard practice but there is not enough data to determine which treatment is better for you. Therefore, in this study, treatment will be determined by a computer, at random, in order to learn what treatment works best. There are also some follow-up activities and tests that will help to answer that question.

HOW IS IT DECIDED WHICH TREATMENT GROUP I WILL GO IN?

You will receive treatment for pulmonary embolism no matter which treatment group you are in. In the study, we will use a computer to assign you randomly to 1 of the 2 treatment groups. You will have a 50/50 (equal) chance of being in either treatment group.

WHAT IS INVOLVED IN THE RESEARCH STUDY?

If you agree to participate, you will be randomly assigned to one treatment group or the other.

Group A will be treated with standard blood thinners and will have catheter-directed therapy to deliver a blood clot-dissolving medicine directly into the blood clot and/or suck out the blood clot. The procedure is done by inserting a thin plastic tube (catheter) into a vein, typically in the groin, or neck. The catheter is guided toward the blood clots in the lungs using x-ray. Then, a clot-dissolving medicine is used or a vacuum can be used to suck out the blood clot. Exactly how this is performed will be determined by the study doctor doing the procedure. If you are assigned to this group, your study doctor will tell you more details about the procedure (such as information about sedation used) during the standard consent process for the procedure.

Group B will be treated with standard blood thinners alone. Patients in Group B will not have catheter-directed therapy. However, if you are in Group B and your condition worsens significantly, you will have additional procedures if your doctor thinks they are needed.

Regardless of treatment group, you will be evaluated by the study team before leaving the hospital. You will also have a computed tomography angiography (CTA) scan of your lungs (for research purposes) to see how much clot remains.

After you leave the hospital, we will contact you at 1 month to see how you are doing and ask some quality of life questionnaires. We will also ask you to return at 3 months and 12 months from when you entered the study for an exercise test. There will also be several phone calls to see how you are doing and some quality of life questionnaires.

OPTIONAL COLLECTION OF BIOSPECIMENS AND/OR STORAGE OF LEFTOVER SAMPLES FOR FUTURE RESEARCH

If you opt-in to collect the optional research specimens, there will be 2 blood samples, each up to approximately 3 tablespoons that will be collected for future research purposes. You may withdraw your participation at any time. If you decide to participate in this optional future research, your samples will be labeled with a unique code that does not contain identifiable information and stored at NYU Center for Biospecimen Research and Development (CBRD), which is the central repository for this multi-site study. In addition, part of your samples will be stored at the NIH Biorepository. Please refer to FUTURE RESEARCH AND STORAGE OF DATA/SAMPLES AT NIH section below.

Only your study doctor and their team will be able to link your coded samples back to your identifiable information. If you decide to allow us to store your samples and later change your mind, you can ask your study doctor to destroy any remaining samples. We won't be able to take back any data generated from tests performed on your samples prior to your request, but will make sure any remaining samples are destroyed after all study analyses are completed so that they are not used for future research.

Your samples will not be used for research to benefit you. The biorepository will serve for future analysis, and we anticipate opportunities for ancillary studies and sharing of resources with other investigators both within the scope of this study and outside of the scope of this study.

We may also perform a whole genome analysis on your DNA sample. Usually, researchers study just a few areas of your genetic code that are linked to a disease or condition. In whole genome studies, all or most of your genes are analyzed and will be used by researchers to study links to blood clots.

Genetic testing can also generate information about your personal health risks and can cause or increase anxiety, damage family relationships, and/or compromise insurability, employability and can even lead to discrimination. Very rarely health or genetic information could be misused by employers, insurance companies, and others. For example, it could make it harder for you to get or keep a job or insurance, or life insurance companies may charge a higher rate based on this information. We believe the chance these things will happen is very small, but we cannot make guarantees.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans and most employers to discriminate against you based on your genetic information. GINA also limits the organizations from sharing your genetic information.

This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that the sponsor will get from this research.

- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that the sponsor will get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans and all employers with 15 or more people must follow this law.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance or long-term care insurance.

Please mark your initials next to one of the options below:

_____I consent to the collection of my samples as described above.

_____I DO NOT consent to the collection of my samples as described above. Choosing this option does not affect your participation in the overall study.

If we complete all study related tests on your blood samples and there is leftover blood, we would like your permission to store this leftover blood indefinitely for future research that may or may not be related to this study. This is optional, meaning you can choose not to have your leftover blood stored for future research and still be in this study.

Please mark your initials next to one of the options below:

_____I consent to the storage of my samples for future research as described above.

_____I DO NOT consent to the storage of my samples for future research as described above. Choosing this option does not affect your participation in the overall study.

FUTURE RESEARCH AND STORAGE OF DATA/SAMPLES AT NIH

In order to allow researchers to share research results, the National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that analyze data and collect the results of whole genome studies. Often, data sharing is required as a condition of funding or for publishing study results. It also is needed to allow other researchers to test study findings and to come up with new ideas. Therefore, we will store your data, biological specimens such as blood draws, genetic information that may be obtained from those

specimens, and imaging with NIH. Sharing data is part of research and may increase what we can learn from this study. These researchers may be at other research centers or institutions, for-profit companies, sponsors, government agencies, and other research partners. Because science constantly advances, we do not yet know what future use of research data may include. These studies may provide additional information that will be helpful in understanding pulmonary embolisms or other diseases or conditions, including research to develop investigational tests, treatments, drugs or devices that are not yet approved by the FDA. It is unlikely that what we learn from these studies will have a direct benefit to you. There are no plans to provide financial compensation to you should this occur.

We do not think that there will be further risks to your privacy and confidentiality by sharing your samples and whole genome information with these banks. However, we cannot predict how genetic information will be used in the future. All of the shared data or samples will be labeled by code only and all personal identifiers will be removed before sharing. The other way we protect data is by limiting the uses of the information and the type of information that is shared, especially your personal information. This may occur through data sharing agreements and review by oversight groups within NIH. The use and sharing of your data with NIH is required for participation in this research study. If you are not comfortable with the use and sharing of your data in future research, you should not participate in this study.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THE STUDY?

It is possible that one treatment approach helps patients more than the other. For example, if catheter-directed therapy improves how patients do in the hospital or their exercise capacity long-term, you may benefit from having this treatment. If it does not turn out to be helpful, you may benefit from not having had this treatment. We do not know which group will do better, and you may not benefit personally from being in this study. We hope that future patients will benefit because the study will help doctors understand which treatment is better.

WHAT ARE THE POSSIBLE RISKS OF TAKING PART IN THE STUDY?

Since the methods used in this study are considered standard of care, the risks of being in this study are no different than the risks associated with clinical care, which are:

Risks of Blood Thinners (All participants)

The primary risk with blood thinner treatment is bleeding. This can be minor (bruising) or more serious, especially if the bleeding is inside the brain or if a large amount of blood is lost. All patients with pulmonary embolism are treated with blood thinners.

Risks of Catheter-Directed Therapy (for patients assigned to Group A)

The most important risks of catheter-directed therapy are the following:

- Pain, bleeding, or infection at the site where the catheter is inserted.
- Damage to the vessel where the catheter is inserted or to vessels inside of the lung, which could be life-threatening.

- Internal bleeding from clot-dissolving medicines; the most serious bleeding is in the brain, also known as a stroke. A stroke can cause lasting brain damage, long-term disability, or even death.
- Risks associated with sedation and use of X-ray for procedures.

If you are assigned to Group A, your doctor will go through a standard consent process with additional information about the procedure before starting it.

Risks of Additional Study Activities (All participants)

All patients, regardless of treatment group, will have the same follow-up activities. The risks of these activities are minor but include:

- Minor bruising, bleeding, or discomfort from blood draws
- Radiation exposure from the follow-up CT scan, which is done for research purposes. The risk from this amount of radiation is less than the risk from everyday exposure to the sun. If you are pregnant, you will not have this CT scan done, and women must have a negative pregnancy test before the CT scan and before entering the study.
- Low risks associated with exercise during exercise tests in a monitored setting.

Risks Associated with Personal Data

Information and samples from this study will be used in future research studies. Identifying information will be removed and standard precautions will be taken to protect data. There is a slight risk in any research study that personal information could be accidentally released to people who are not supposed to have it.

Group Risks Associated with Whole Genome Sequencing (Only if participating in optional collection of biospecimens)

Although we will not give researchers your name, we will give them basic information such as your race, ethnic group, and sex. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes, stigmatize, or discriminate against members of a socially defined group such as race or ethnicity; which could impact employability as well as marital, adoption, and child-custody opportunities.

INCIDENTAL FINDINGS ASSOCIATED WITH WHOLE GENOME SEQUENCING (Only if participating in optional collection of biospecimens)

There are currently no plans to return genetic research results to you or your personal physician. However, during whole genome sequencing, we may incidentally find something on a part of your genome that's known to be associated with a certain disease or condition. There's no guarantee that all incidental findings will be discovered in this research study. We do not plan to share the results with you because they will be anonymized (unable to be linked back to you) once collected and sent to the laboratory. The information will not be used for any clinical purposes, only for the advancement of generalized knowledge in research.

CAN I BE IN THE STUDY IF I AM PREGNANT OR BREAST-FEEDING?

If you are currently pregnant, you will not be able participate in the study. Breast-feeding does not impact your ability to be in the study. If you become pregnant during the study period, you must notify the study team as you will have to be withdrawn from the study.

HOW LONG WILL THE STUDY LAST?

The PE-TRACT study is expected to include about 500 patients and will last for approximately 6 years.

This study is expected to end after all participants have completed all visits, and all information has been collected. Your role in the study will end after one year from entering the study. This study may also be stopped or your participation may be ended at any time by your study doctor or the study sponsor without your consent because:

- The Principal Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The study sponsor, the Principal Investigator, or other body responsible for monitoring the safety of the study has decided to stop the study.

You are free to leave the study at any time. Leaving the study will not interfere with your future care, payment for your health care or your eligibility for health care benefits.

WHAT CAN I EXPECT FROM THE RESEARCHERS?

If the researchers find out about unexpected risks or dangers to you or others in the study, they will inform you and may remove you from the study, in accordance with standard practice.

During the course of this study, the researchers may find information that could be important to you. This includes information that might cause you to change your mind about being in the study. They will notify you as soon as possible if such information becomes available. The researchers will honor any decision you make to leave the study at any time.

WHAT IS THE ALTERNATIVE TO BEING IN THE STUDY?

Should you choose not to participate, you will have standard treatment for pulmonary embolism. Your doctor may choose to use the same medical devices, procedures, and blood thinners in your medical care. All options can be discussed with your personal physician at any time.

WHAT HAPPENS IF I AM HARMED BY BEING IN THE STUDY?

For medical emergencies contact 911. If you think you have been injured as a result of taking part in this research study, tell the Principal Investigator as soon as possible. The Principal Investigator's name and phone number are listed at the top of page 1 of this consent form.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. NYULH and/or the study site <<Fill in your Site Name>> cannot provide compensation for any injuries you may have. We may bill your insurance company or other third parties, if

appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them. If you have questions about this, someone from the study team can help to answer them.

This study does not provide financial help for medical or other injury-related costs. You do not give up any rights to seek payment via the legal system for personal injury by signing this form.

WHAT ARE MY COSTS TO BE IN THIS STUDY?

Some costs of your care that relate to this study will be billed to your insurance, since both treatments are standard care, just like other parts of your care. If your insurance does not cover these costs or you do not have insurance, these costs will be your responsibility, as they would be if you were not in the study. Based on your overall health and recovery, your doctors will judge how long you should stay in the hospital. You may or may not have a longer hospital stay if you are in the study. If you do have a longer hospital stay, your insurance company may incur additional costs, and you may as well.

If you have questions about what your insurance will and will not pay for, or if you do not have insurance, please ask the study team.

Other costs, such as the optional biospecimen collections, the computed tomography angiography (CTA) done after you enter the study and the cardiopulmonary exercise test (CPET) at 3 months, will be covered by the research study, because they are done for study purposes. If your exercise test at 12 months (the 6-minute walk distance) is part of normal clinical care at your institution, it may be billed to your insurance company. If it is not a part of normal clinical care, it will be covered by the research study.

WILL I BE PAID FOR BEING IN THE STUDY?

You will receive compensation for travel (e.g. taxi, tolls, parking) to attend follow-up visits up to $225. Travel will be reimbursed by the study team after the completion of each visit upon the presentation of receipts. You will also receive up to $150 compensation for the completion of questionnaires over the course of the study ($100 at Month 3 follow-up visit and $50 at Month 12 follow-up visit).

WILL MY INFORMATION BE KEPT PRIVATE?

<<Fill in your Site Name>> will keep your information private and follow all research regulations. We will use a code rather than your name to label your information, and we will not identify you in research reports. Your records may be reviewed by study sponsors, as allowed by research regulations.

Your medical information is protected health information, or “PHI”, and is protected by federal and state laws, such as the Health Insurance Portability and Accountability Act, or HIPAA. This includes information in your research record as well as information in your medical record at <<Fill in your Site Name>>. In compliance with NYULH and <<Fill in your Site Name>> policies and procedures and with HIPAA, only those individuals with a job purpose related to this study can access this information. Except as required by law, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier outside of this study.

Medical information created by this research study may become part of your medical record. We may include your research information in your medical record for several reasons, including for the billing of services provided in connection with the study, to securely document any medical services you receive, and so that other members of the <<Fill in your Site Name>> community who may treat you have access to important information about your health.

You have a right to access information in your medical record. In some cases, when necessary to protect the integrity of the research, you will not be allowed to see or copy certain information relating to the study while the study is in progress, but you will have the right to see and copy the information once the study is over in accordance with <<Fill in your Site Name>> policies and applicable law.

Certificate of Confidentiality

To help us further protect your confidentiality, this research is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH). The NIH has issued a Certificate of Confidentiality for this research. This adds special protection for the research information (data, documents, or biospecimens) that may identify you.

Research information protected by this Certificate of Confidentiality cannot be disclosed to anyone else who is not connected with the research without your consent. With this Certificate of Confidentiality, the researchers may not disclose or use research information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, without your consent. However, disclosure, without your consent, is still necessary if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases).

The Certificate of Confidentiality cannot be used to refuse a request for information from appropriate government agencies responsible for project oversight.
The Certificate of Confidentiality does not prevent you from releasing information about yourself and your involvement in this research, including for your medical treatment. Federal regulations may also allow for the use or sharing of information for other scientific research.

By agreeing to be in this research and signing below, you are giving your consent to share research information with others at <<Fill in your Site Name>>. This means that your research information may be included in your <<Fill in your Site Name>> electronic medical record.

HIPAA Authorization

As noted in the Confidentiality section above, federal law requires us, and our affiliated researchers, 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. We are asking for your permission (authorization) to use and share your health information with others in connection with this study - in other words, for purposes of this research, including conducting and overseeing the study.

Your treatment outside of this study, payment for your health care, and your health care benefits will not be affected even if you do not authorize the use and disclosure of your information for this study.

What information may be used or shared with others in connection with this study?
All information in your research record for this study may be used and shared with those individuals listed in this section. Additionally, information in your medical record that the research team believes may be important to the study may be accessed by those listed here. This includes, for example, results from your physical examinations, laboratory tests, procedures, questionnaires, and diaries.
As part of this study, you may be asked to sign a Medical Billing Release form. This form will be used by the PE-TRACT Economic Core Lab to collect hospital bills from the patient accounting department at any hospital to which you are admitted, from the time of enrollment in the study through the study follow-up period. This information will be kept strictly confidential and be used solely to assess the medical expenses that occur during the course of this study.

Who may use and share information in connection with this study?
The following individuals associated with the following may use, share, or receive your information for this research study:

- The research team, including the Principal Investigator, study coordinators, and personnel responsible for the support or oversight of the study
- The study sponsor: National Heart, Lung, and Blood Institute (NHLBI)/National Institutes of Health (NIH)
- A group that oversees the data (study information) and safety of this research including monitoring of the data by an outside agency
- The IRB that oversees the research and the research quality improvement programs
- People from organizations that provide independent accreditation and oversight of hospitals and research
- People or groups that we hire to do work for us, such as data storage companies, insurers, and lawyers
- Governmental agencies responsible for research oversight
- Health care providers, including your doctors and others who provide services to you in connection with this study, and laboratories or other individuals who analyze your health information in connection with this study
- Other study sites involved in the research
- Other persons/entities as applicable, for example:
  - Central research laboratories
  - Study related committees/boards/centers (Data & Safety Monitoring Board, Endpoint Committees, Clinical or Data Coordination Centers, etc.)

Your information may be re-disclosed or used for other purposes if the person who receives your information is not required by law to protect the privacy of the information.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your health information.

The results of this research study may be published in a medical book or journal or used to teach others. However, your name or other identifying information will not be used for these purposes without your specific permission.

What if I do not want to give permission to use and share my information for this study?
Participating in this study involves giving permission to use and share your information. It is your choice if you want to participate in this study. But you must agree to give us permission to use and share your information in order to participate in the study.

Can I change my mind and withdraw permission to use or share my information?
Yes, you may withdraw or take back your permission to use and share your health information at any time for this research study. If you withdraw your permission, we will not be able to take back information that has already been used or shared with others. To withdraw your permission, send a written notice to the principal investigator for the study noted at the top of page 1 of this form. If you withdraw your permission, you will not be able to stay in this study.

How long may my information be used or shared?
Your permission ~~to~~ granting authorized individuals to use or share your personal health information for this study will never expire unless you withdraw it.

The Institutional Review Board (IRB) and how it protects you

The IRB reviews all human research studies – including this study. The IRB follows Federal Government rules and guidelines designed to protect the rights and welfare of the people taking part in the research studies. The IRB also reviews research to make sure the risks for all studies are as small as possible. This study utilizes a central single IRB at NYULH for all sites. The NYULH IRB Office number is 212-263-4110. The NYULH IRB is made up of:

- Doctors, nurses, non-scientists, and people from the Community

WHOM CAN I CONTACT IF I HAVE QUESTIONS OR CONCERNS?

If you have questions, concerns, or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on top of the page 1 of this consent form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the IRB at (212) 263-4110.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website site at any time.

When you sign this form, you are agreeing to take part in this research study as described to you. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer.

Name of Subject (Print)	Signature of Subject	Date

Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date

Witness to Consent Process for Non-English-Speaking Subjects (using a translated consent form OR "Short Form" in Subject's Spoken Language)

Statement of Witness
As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

Name of Witness (Print)	Signature of Witness	Date

Witness to Consent of a Subject Who Cannot Read or Write

Statement of Witness
I represent that the consent form was presented orally to the subject in the subject's own language, that the subject was given the opportunity to ask questions, and that the subject has indicated his/her consent and authorization for participation by (check box that applies).

- ☐ Subject making his/her own "X" above in the subject signature line
- ☐ Subject showed approval for participation in another way; describe:

Name of Witness (Print)	Signature of Witness	Date