UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study (this "Research Study")?

Fibrinolytic Therapy versus Medical Thoracoscopy for Treatment of Severe Pleural Infection: A Randomized Clinical Trial

3. Whom do you call if you have questions about this Research Study (the "Study Team")?

Principal Investigator: Hiren Mehta, M.D.
(352) 273-8737 (business hours)
(352) 265-0111 (24 hour)

Other research staff: Erin Silverman, Ph.D.
(352) 273-5870 (business hours)

4. Who is paying for this Research Study?

The sponsor of this study is the University of Florida, Gatorade Fund

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits

to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research, how long will you be involved?

The purpose of this research study is to compare two currently accepted standard-of-care adjuvant treatment strategies for the management of severe infections of the space surrounding the lungs. We will compare two standard of care procedures:

Procedure 1: Medical thoracoscopy, and

Procedure 2: Fibrinolytic therapy

These procedures are described later. This study will help us determine if one procedure is superior to the other for treating severe infection of the areas surrounding the lungs. Specifically:

- Comparing the length of hospital stay for patients who receive Procedure 1, with those of patients who receive Procedure 2.
- Comparing the need for later, more invasive procedures to treat pleural infections for patients who receive Procedure 1, with those of patients who receive Procedure 2.
- Comparing the number of days of chest tube drainage following Procedure 1 versus the Procedure 2.

You are being asked to be in this research study because you have been diagnosed with a severe infection of the areas surrounding the lungs. This is called a *pleural infection*. The pleura is thin tissue covered by a layer of cells (mesothelial cells). This tissue surrounds the lungs and lines the inside of the chest wall. The pleural space is the area between the lungs and the chest wall. This space helps keep the lungs inflated by allowing them to “stick” to the chest wall. It also contains a small amount of liquid, which helps lubricate the surface of the lungs, helping them slide along the inner chest wall during breathing. Sometimes, fluid, air, or particles can move into the pleural space from other areas of the body. When this happens, the liquid in the plural space can become infected and lead to severe compromises in health, including death if left untreated. In addition, infections within the pleural space may result in an unwanted compression of the lung, resulting in shortness of breath and difficulty performing normal day-to-day physical activities.

A description of this clinical trial is available on www.ClinicalTrials.gov as required by U.S. law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time. The ClinicalTrials.gov number for this study is NCT03213834.

b) **What is involved with your participation, and what are the procedures to be followed in the research?** All participants will have a complete medical evaluation and chest tube placement. Depending on which group you are assigned to, you may undergo medical thoracoscopy or fibrinolytic therapy.

c) **What are the likely risks or discomforts to you?** Potential risks include pain during chest tube placement, bleeding, collapsed lung, anesthesia-related drowsiness or depressed breathing, heart problems, air leak from the lungs, low oxygen levels, infections, and death.

d) **What are the likely benefits to you or to others from the research?** Medical thoracoscopy or fibrinolytic therapy are both acceptable options for treatment of pleural infection. We do not know whether one treatment is superior to another. It is not possible to predict whether you will benefit directly from participation in this study. Your participation may help others in the future as a result of knowledge gained from the research that might help other people with lung infections.

e) **What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?** If you do not want to be in this study, you may choose to have a medical thoracoscopy, or fibrinolytic therapy, as part of your normal clinical care.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this Research Study)?

This study compares two standard-of-care procedures for treating severe infection in the areas surrounding the lungs. As part of your normal clinical care, you will undergo either Procedure 1 (Medical thoracoscopy) or Procedure 2 (Fibrinolytic therapy) as treatment for this infection. The decision to undergo, or not undergo, treatment for your infection is one you make with your doctor, just as with normal clinical care.

7. What will be done only because you are in this Research Study?

If you choose to participate in this study you will be randomly assigned (much like the flip of a coin) to receive either Procedure 1 or Procedure 2 as treatment for your infection. You will not be able to choose which procedure you have, and your doctor will not be able to choose the procedure for you either. Rather, your treatment will be determined by chance. In a “randomized” study, you procedures you will receive. From that point forward your treatment will proceed just as it would during normal clinical care.

If you choose to participate in this study we will also take a small amount of fluid from the pleural space to test for various biomarkers that give us information about the body's responses to infection. This fluid will be sampled when performing procedure 1 or procedure 2 as a part of which procedure you get randomized to.

We will also make measurements of how much fluid is in the area around your lungs, both before and after treatment. This measure will be made by looking at the images are produced when you receive your standard-of-care CT scan once treatment ends.

You will meet with the principal investigator, Dr. Hiren Mehta, M.D./ Dr Michael Jantz, MD (Co-PI) throughout the course of this study. They will evaluate the results of your tests before scheduling the study procedure. Dr. Hiren Mehta and/or Dr Michael Jantz will perform the procedure and will monitor your health until you are discharged, and for all follow-up visits.

Baseline Procedures (these are measures that will be collected before you receive get randomized to one of the procedures for your infection):

We will obtain a medical history from you, as well as from your medical chart. You will have a general physical examination. This will include measuring your height, weight, heart rate, blood pressure, respiratory rate, and how much oxygen is contained in your blood.

Examination of your lung function

You will undergo an ultrasound examination of the pleural space to measure how much pleural fluid there is and find the best location for the doctor to take a sample of this fluid via needle. An ultrasound is a non-invasive test that makes pictures with sound waves. During the ultrasound examination, the medical team will check your pleural cavity (the thin fluid-filled space between the two pulmonary pleurae (visceral and parietal) of each lung) to look for the pleural fluid and localize a safe pocket to insert a small needle for fluid sampling.

Thoracentesis involves placing a thin needle or tube into the pleural space to remove some of the fluid. The needle or tube is inserted through the skin, between the ribs and into the chest. This procedure is done to remove fluid for testing. The needle or tube is removed when the procedure is completed.

If you meet criteria for inclusion in the study, you will complete informed consent which involves reading, discussing, and signing this document. During informed consent all your questions about this study and all study-related procedures will be answered.

Randomization Procedures

Once you consent to participate in this study, and meet all of the eligibility criteria you will be randomly assigned to receive either Procedure 1 (Medical thoracoscopy) or Procedure 2 (Fibrinolytic therapy). This assignment will be completed using a computer-generated spreadsheet. You have a 1 in 2 (50%) chance of being assigned to Procedure 1 and a 1 in 2 (50%) chance of being assigned to Procedure 2. You will not be able to choose which procedure you receive.

Procedures

If you qualify to take part in this research study, you will undergo these procedures:

<u>If you are assigned to receive Procedure 1 (Medical thoracoscopy) the following will be completed.</u>

Before and during the medical thoracoscopy:

- You will report to the bronchoscopy suite and sign a separate (standard of care) consent form in order to undergo thoracoscopy. This procedure will occur in the bronchoscopy suite.
- A sedative drug may be injected into your vein to relax you. Sometimes you will not remember having the procedure because of the sedative.
- The doctor will make a small incision with a scalpel and will then insert a telescopic device through the hollow tube. The doctor will use this instrument to look around the pleural space.
- The doctor will clean the pleural space and may break any existing adhesions to help your lung expand.
- The doctor will then place chest tube, commonly referred to as “putting in a chest tube.” This is a procedure that is done to drain fluid, blood, or air from the space around the lungs.

Monitoring after the medical thoracoscopy:

- You will be transferred to an observation area after the study procedure
- You should gradually become more alert as the sedation/ anesthesia wears off
- You will remain in the hospital until infection is improved and your chest tube is removed
- At discharge, you will be given instructions for your medications and follow-up appointments by your treating team.

<u>If you are assigned to receive Procedure 2 (Fibrinolytic therapy), the following will be completed:</u>

Before and during fibrinolytic therapy:

- You will report to the bronchoscopy suite and sign a separate (standard of care) consent form in order to undergo fibrinolytic therapy. This procedure will occurin the bronchoscopy suite.
- A sedative drug may be injected into your vein to relax you. Sometimes you will not remember having the procedure because of the sedative. The skin will be thoroughly cleaned and you will be given an injection of local anesthetic into the skin and then into the muscle between your ribs.
- The doctor will use a scalpel to make a cut, from ¾ inch to 1½ inches long, between the ribs (the exact location depends on what is being drained and its location in the lungs). Then the doctor will guide the tube into the chest. The tube is usually a little thinner than a pinky finger, although there are different sizes that can be used. The doctor will collect 10 mL of fluid from the placed

drain, in order to check for substances that are produced, by the body, in response to infection

- It will be stitched into place to prevent it from slipping out. A sterile dressing bandage is placed over the insertion site. The doctor will use an ultrasound, a non-invasive device that makes pictures out of sound waves, to help guide the placement of the chest tube.
- The doctor will inject medicines through the chest tube and into the pleural space up to 6 times. These medicines will thin the fluid that is in the area surrounding your lungs, helping the fluid to drain and the infection to be removed. This may take one to two days, to a week or more depending on the severity of your infection.

Monitoring after fibrinolytic therapy:

- You will be transferred to an observation area after the study procedure
- You should gradually become more alert as the sedation/ anesthesia wears off
- You will be asked to rate your pain using a simple pain measurement scale
- You will remain in the hospital until infection is improved and your chest tube is removed. This can be anywhere from a day or two to a week, depending on how severe the infection.
- You will have a standard-of-care CT scan to determine if your infection is resolved.
- At discharge, your treating team will give you instructions for your medications and follow-up appointments.

Patients in both groups will participate in routine follow-up clinic visits at approximately 6 and 12 weeks after discharge from the hospital.

Table 1 summarizes the tests and procedures.

Table 1. Summary of tests and procedures

	Medical thoracoscopy group	Fibrinolytic therapy group
Evaluation	X	X
Medical thoracoscopy	X	
Fibrinolytic therapy		X
Chest tube	X	X

Once this research study is completed, any information that could identify you **might** be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during this Research Study, please contact one of the Research Team members listed on the front page of this form.

8. What identifiable health information will be collected about you and how will it be used?

The Research Team will collect:

- Medical and research records
- Hospital cost and billing records
- Records about your study visits
- Records of physical exams
- Laboratory, X-ray, and other test results
- Questionnaires
- Records about any study

The Research Team may collect this information from other healthcare providers, such as laboratories, which are a part of this research, as well as healthcare providers that are not part of this research (other doctors, hospitals or clinics). Other professionals at the University of Florida or Shands Hospital who provide study-related care, and the University of Florida Institutional Review Board (IRB), may also collect your health information.

The Research Team listed in question 3 above will use or share your health information as described below to carry out this research study.

9. With whom will this health information be shared?

This health information may be shared with:

- the study sponsor (listed in Question 4 of this form);
- United States governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections;
- Government agencies which are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments.
- Hospital and Clinical Research Accrediting Agencies
- Data and Safety Monitoring boards that oversee this study
- The IRB that reviewed this Research Study and ensures your rights as a Study Subject are protected

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

10. How long will you be in this Research Study?

You will be in this research study for up to 12 weeks after getting discharged from the hospital.

This Authorization to use and share your health information expires at the end of the study, unless you revoke it (take it back) sooner.

11. How many people are expected to take part in this Research Study?

At least 60 patients are expected to take part in this study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

12. What are the possible discomforts and risks from taking part in this Research Study?

As a result of your participation in this study, you are at risk for possible complications listed in this section. You should discuss these with the investigator and with your regular doctor if you choose.

Thoracentesis:

You will sign a separate consent form for the thoracentesis. The thoracentesis consent form will also include possible complications.

- Pain during placement—Discomfort can result from the needle at the time it is inserted. Doctors try to lessen any pain or discomfort by giving a local numbing medicine (topical anesthetic). The discomfort is usually mild and goes away once the needle or tube is removed.
- Bleeding—During insertion of the needle, a blood vessel in the skin or chest wall may be accidentally nicked. Bleeding is usually minor and stops on its own. Sometimes, bleeding can cause a bruise on the chest wall. Rarely, bleeding can occur into or around the lung and may require a chest tube or surgery.
- Collapsed lung—When the needle is being placed, it may puncture the lung. This hole may seal quickly on its own. If the hole does not seal over, air can leak out and build up around the lung. This build-up of air can cause part or all of the lung on that side to collapse (pneumothorax). If this happens, the doctor can place a chest tube between the ribs into the chest to remove the air that is leaking from the lung

Moderate sedation may cause these risks/possible complications:

- Drowsiness, slurred speech, tremor, fatigue, and low blood pressure, increase carbon dioxide in your blood, slowing of the heart rate, anxiety, confusion, dizziness and shivering.
- Respiratory depression. Trained medical professionals with extensive experience and expertise will administer these medications and will be responsible for you care during the course of the procedure.

Thoracoscopy:

You will sign a separate consent form for the thoracoscopy. The thoracoscopy consent form will also include possible complications.

- Chest pain (5%). The nerves between the ribs are bruised after the procedure, which can cause some persistent pain.
- Air leak from lung (1-5%). A small hole develops in the lung. This means the chest tube has to stay in longer.
- Bleeding (< 1%). Usually it is minor and settles quickly. Bleeding is more common if you have been taking blood-thinning drugs.
- Heart problems (< 1%). A brief minor strain may be put on the heart. This can cause abnormal beating of the heart, fluid to accumulate in the lungs, a heart attack, or the heart may stop beating.
- Low oxygen levels (< 1%). You will be given oxygen.
- Death(< 1%) as a result of this procedure is uncommon.

Chest tube:

You will sign a separate consent form for the chest tube. The chest tube consent form will also include possible complications.

- Pain during placement—Discomfort often occurs as the chest tube is inserted. Doctors try to lessen any pain or discomfort by giving a local numbing medicine. The discomfort usually decreases once the tube is in place.
- Bleeding (<5%) — During insertion of the tube, a blood vessel in the skin or chest wall may be accidently nicked. Bleeding is usually minor and stops on its own. Rarely, bleeding can occur into or around the lung and may require surgery. Usually bleeding can just be watched with the chest tube in place.
- Infection (< 5%)—Bacteria can enter around the tube and cause an infection around the lung. The longer the chest tube stays in the chest, the greater the risk for infection. The risk of infection is decreased by special care in bandaging the skin at the point where the tube goes into the chest.

Fibrinolytic Therapy:

The fibrinolytic therapy includes possible complications.

- Pain (15%)-While the medications are in the pleural space, you might feel some discomfort. Usually such pain can be relieved by analgesics.
- Bleeding (5%)-While medications are in the pleural space, you might experience bleeding inside the pleural space. Usually, it resolves with stopping medications. Rarely, blood transfusion might be need or require surgery.

Reproductive Risks:

If you are pregnant, you will not be able to participate in this study. Females who have the potential to become pregnant will require a negative urine pregnancy test prior to starting study procedures.

Privacy:

The data collected both written and electronic will be held securely in a locked cabinet and secure server behind the UF Health firewall respectively. Only the study individual will be contacted and the questionaries' administered in the privacy of a secluded clinic room. The data collected will be restricted to only the minimum amount necessary to accomplish the aim of the study.

Psychological Stress:

You may refuse to answer any of the questions and you may take a break at any time during the study. You may stop your participation in the study at any time.

Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release could upset or embarrass you, or possibly affect your insurability or employability. Questions 17-21 in this form discuss what information about you will be collected, used, protected, and shared.

This Research Study may also include risks that are unknown at this time.

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by University policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question 3 in this form.

13a. What are the potential benefits to you for taking part in this Research Study?

So far medical thoracoscopy or fibrinolytic therapy are both acceptable options for treatment of pleural infection. We do not know whether one treatment is superior to another. It is not possible to predict whether you will benefit directly from participation in this study.

13b. How could others possibly benefit from this Research Study?

Your participation may help others in the future as a result of knowledge gained from the research that could help other people with similar disease.

13c. How could the Research Team members benefit from this Research Study?

In general, presenting research results helps the career of a researcher. Therefore, the Research Team listed in question 3 of this form may benefit if the results of this Research Study are presented at scientific meetings or in scientific journals.

14. What other choices do you have if you do not want to be in this study?

Taking part in this study is voluntary. Instead of being in this study, you have the following options:

- Choose to have medical thoracoscopy or fibrinolytic therapy without being involved on the study

This research study is not meant to diagnose or treat medical problems. Participation in this research study does not take the place of routine physical examinations or visits to your regular doctor. We recommend that you discuss these and other options with the investigator and your regular doctor so that you can make a well-informed decision about participating in this study.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

15a. Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the Research Team listed in question 3 of this form. They will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 3 of this form to let them know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with a member of the Research Team listed in question #3.

15b. Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

- The study doctor thinks it necessary for your health or safety
- You have not followed study instructions
- Administrative reasons require your withdrawal

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

16. If you choose to take part in this Research Study, will it cost you anything?

Study Services

The Sponsor will pay for or provide the following study-required services/activities at no cost to you:

- Study questionnaires
- Lab analysis of pleural fluid for study purposes only

If you receive a bill for these services, please contact Hiren Mehta at 352-273-8737

Items/Services Not Paid for by the Sponsor

Any other medical services you receive would have been provided to you even if you were not in this study. These services will be billed to you or your insurance company in the usual manner. You will be responsible for paying any deductible, co-insurance, co-payments, for those services, and for any non-covered or out-of-network services. Some insurance companies may not cover costs associated with studies. Please contact your insurance company for additional information.

17. Will you be paid for taking part in this Research Study?

You will not receive any payment for taking part in this study.

18. What if you are injured while in this Research Study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or

research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is routinely offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact one of the Research Team members listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this Research Study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this Research Study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization	Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing	Date