Study Title:	A Multicenter Randomized Trial of EBUS-TBNA versus EBUS-TBNA plus Transbronchial Mediastinal Cryobiopsy for Adequacy of Next Generation Sequencing
Version Date:	8/23/2023 NCT06105801
Study PI:	Fabien Maldonado, MD

Name of participant: _____ Age: _____

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

Key Information:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Key information about this study:

You are being asked to participate in this research study because you are undergoing a bronchoscopy with a biopsy of a spot in your lungs suspicious of cancer. As per usual care, if we find cancer, we do a procedure known as an endobronchial ultrasound with transbronchial needle aspiration (EBUS-TBNA) to take samples of your lymph nodes to evaluate for cancer spread. If you have suspected cancer in your lymph nodes, we take multiple samples for molecular testing to help guide treatment decisions. It requires a certain amount of tissue to send for these molecular markers, which can be achieved with EBUS-TBNA about 70% of the time.

This research is being done to evaluate the utility of adding a biopsy tool currently used in usual care, known as a cryoprobe, on its ability to acquire more tissue for molecular analysis. This cryoprobe uses a freezing technique to biopsy and can potentially gather larger and higher quality tissue samples than the standard methods. It has been studied in several randomized control trials for diagnosis and shows an excellent safety profile. Our goal with this study is to see if this tool following EBUS-TBNA can increase the ability to acquire this tissue needed for molecular analysis up to 85%.

By consenting to this study, you will not be automatically included in this study. We will only include you in this study if your biopsy suggests cancer. If you are included, we will collect data during the study and monitor for safety events within 24 hours following the procedure.

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The rest of this document includes detailed information about this study (in addition to the information listed above).

the mediastinum is EBUS-TBNA. The small sample size or poor quality can make it challenging to meet the criteria needed for a pathologist to send the sample to the companies evaluating for molecular mutations. This could result in the patient having to return for another procedure.

Cryoprobes are another device that has been proven safe and effective for transbronchial mediastinal biopsies. The ERBE (Tubingen, Germany), a 1 mm flexible, single-use cryoprobe, is used through the bronchoscope's working channel and can be used in the tract that was initially created from the EBUS-TBAN needle. The FDA has approved this novel sheath cryoprobe as at least as safe and effective as other currently available devices. They have been shown to gather larger samples of higher quality than EBUS-TBNA.

After your biopsy confirms the suspicion of malignancy by our in-room cytopathologists, you will undergo randomization that will result in either continuing with EBUS-TBNA for sample acquisition, or switching to a cryoprobe, determined by the choice of the randomization algorithm. If we cannot obtain cryoprobe samples, we will change back to an EBUS-TBNA needle.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study. Your medical record will contain a note saying you are in a research study and may collect some information about you. Anyone you authorize to receive your medical record will also get this information.

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Side effects and risks that you can expect if you take part in this study:

Bronchoscopy:

Common (>10%): cough, sore throat, temporary hoarseness

Uncommon (< 10%): lung collapse (also known as a pneumothorax)

Rare (< 1%): bleeding, respiratory distress, infection, trauma to the airway or perforation, adverse reaction to medications used during the procedure, and extremely rarely (1/100,000) death.

EBUS-TBNA

Rare (< 1%): lung collapse (also known as a pneumothorax), bleeding, infection, trauma to the airway or perforation, escalation in the level of care[30]

Transbronchial Mediastinal Cryobiopsy Using ERBE 1.1mm Flexible Single-Use Cryoprobe

We estimate the risk of transbronchial mediastinal Cryobiopsy based on clinical experience and a recent randomized controlled trial showing an excellent safety profile.

Common (> 10%): Minor bleeding not requiring intervention

Uncommon (< 10%): Moderate to severe bleeding requiring intervention

Rare (< 1%): lung collapse (also known as a pneumothorax), infection, trauma to the airway or perforation, escalation in the level of care

Risks that are not known:
There may be side effects and discomforts that are not yet known.

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Good effects that might result from this study:

You may or may not benefit from being in this study. It is possible that you will not receive any benefits from the transbronchial mediastinal cryobiopsy. You may benefit from optimized medical management of your condition or disease. Potential benefits of the procedure may be increased tissue size that yields improved molecular analysis that will affect downstream management and treatment.

Procedures to be followed:

You will only be included in this study if cancer is suspected within your mediastinum on rapid onsite evaluation (ROSE). If you are included, we will randomize you to continue with EBUS-TBNA to obtain a cell block for molecular analysis or switch to a cryoprobe with a 1.1m probe.

The following is a more detailed description of the study procedure that you will (or could) undergo as indicated by and at the discretion of your physician: After informed consent is obtained, the anesthesiologist will sedate you as a part of the standard of care. When sufficient sedation has been given, an artificial airway (endotracheal tube, laryngeal mask airway, or tracheostomy) will be put in place. The bronchoscope will then be inserted, and a complete examination of the airways will take place. The proceduralist may use advanced navigation and robotic techniques to biopsy a lung nodule or mass concerning cancer. If the area of concern is within the mediastinum (lymph node or mass), the proceduralist may start with EBUS for biopsies.

Other Standard of Care Testing Procedures: The physician may perform different standard-of-care testing procedures to evaluate the target airway/site for your condition. Such procedures may include but are not limited to fluoroscopy, radial endobronchial ultrasound, and electromagnetic navigation.

Post-Procedure: After your bronchoscopy and biopsy are complete, you will be sent to recovery and monitored according to the standard of care. The physician may order a post-procedure chest x-ray, which you will be expected to complete after being discharged from recovery.

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Imaging and Pathology Reports: Before the bronchoscopic biopsy, study doctors and staff will evaluate and collect information from your imaging reports (CT scans, PET scans, and/or x-rays). After the procedure, study doctors and staff will collect data from your pathology reports in addition to your imaging (CT scans, PET scans, and/or x-rays).

Follow-Up Data: Patients enrolled in this study will have data collected by research staff for up to 30 days after the bronchoscopic biopsy procedure is performed. This 30-day follow-up period is the standard of care following bronchoscopic biopsy procedures. Data collected will come from your patient chart and may include radiologic and pathology findings and any significant symptoms or side effects related to using the study device. If information cannot be accessed through your patient chart, research staff may contact you over the phone.

Any data or reports shared with other sites or staff outside of Vanderbilt University Medical Center will have all personal identifying information removed

Payments for your time spent taking part in this study or expenses:
If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

Costs to you if you take part in this study:
You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator with that an injury occurred, then you and/or your insurance may be billed for the cost of medical care provided at Vanderbilt to treat

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the injury. You will be responsible for any copayments or deductibles associated with treating that injury. There are no plans for Vanderbilt to pay for the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:
If you have any questions about this research study or feel you have been hurt by being a part of this study, please feel free to contact [redacted]

For additional information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the VUMC Institutional Review Board Office at (615) 322-2918 or toll-free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:
You may be taken out of the investigation if:

- Staying in the study would be harmful
- The study doctor believes you should be out of the study
- You do not follow directions and requirements for the study
- You become pregnant
- The study is canceled
- You have a new injury or illness
- There may be other reasons to take you out of the study that we do not know at this time

What will happen if you decide to stop being in this study?
If you decide to stop being part of the study, you should tell your study doctor. Deciding not to be part of the study will not change your regular medical care.

Clinical Trials Registry:
This clinical trial will be described on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will consist of a summary of the results. You can search this Web site at any time.

Confidentiality:
All efforts, within reason, will be made to keep your personal information in your research record confidential, but total confidentiality cannot be guaranteed. Your information will be stored on password-protected Vanderbilt computers and protected databases. Your data will be coded, so they do not contain your name.

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The Vanderbilt University Office of Research will be a central data processing and management location. REDCap (Research Electronic Data Capture) is a secure, web-based application that is the database. REDCap servers are housed in a local data center at Vanderbilt, and all web-based information transmission is encrypted. REDCap was developed specifically around HIPAA-Security guidelines. Only those involved with this study will have access to your information. Any information that is shared or published will not include identifiable information. Your information will be kept indefinitely. Vanderbilt may share your information, without identifiers, with others or use it for other research projects not listed in this form. Vanderbilt, Dr. Maldonado, and his staff will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

Privacy:
Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You will not receive any benefit from the tests done on your samples. These tests may help us, or other researchers, learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Study Results:
This study involves research tests that may produce information that could be useful for your clinical care. We will share this information with you.

Your treating physician will share the results of your bronchoscopic biopsy with you according to the standard institutional procedure. If a diagnosis is not obtained after the procedure, further recommendations regarding treatment will be made by the treating physician (e.g., follow-up CT chest, surgery, or further diagnostic testing).

HIPPA Authorization
All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is your health information that is, or has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, Vanderbilt University Medical Center may share the results of your study and/or non-study linked *including, pathological slides and specimens* as well as parts of your medical record, to the groups named below. These groups may include people from the Federal

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Government Office for Human Research Protections, the VUMC Institutional Review Board, Vanderbilt University, *CROs, IBC, SRC, INSURANCE COMPANIES FOR BILLING PURPOSES, ETC.* Federal privacy rules may not apply to these groups; they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact [redacted]
At that time, we will stop getting any more data about you. But, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT BY PERSON AGREEING TO BE IN THIS STUDY

I have read this authorization form and this has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in the associated study.

_____ _____
Date Signature of patient/volunteer

Consent obtained by:

_____ _____
Date Signature

_____
Printed Name and Title

Time: _____

VUMC Institutional Review Board
Informed Consent Document for Research

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