PROTOCOL TITLE: Are Two Needles Really Better than One? A Time, Economic, and Environmental Evaluation of EBUS-TBNA.

PRINCIPAL INVESTIGATOR:
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STUDY SUMMARY:

Investigational Agent(s) (Drugs or Devices)	N/A
IND / IDE / HDE #	
Indicate Special Population(s)	☐ Children ☐ Children who are wards of the state ☐ Adults Unable to Consent ☐ Cognitively Impaired Adults ☐ Neonates of Uncertain Viability ☐ Pregnant Women ☐ Prisoners (or other detained/paroled individuals) ☐ Students/Employees
Sample Size	138 patients across all study sites
Funding Source	Northwestern University
Indicate the type of consent to be obtained	☒ Written ☐ Verbal/Waiver of Documentation of Informed Consent ☐ Waiver of HIPAA Authorization ☐ Waiver/Alteration of Consent Process
Site	☐ Lead Site (For A Multiple Site Research Study) ☐ Data Coordinating Center (DCC)
Research Related Radiation Exposure	☐ Yes ☒ No
DSMB / DMC / IDMC	☐ Yes ☒ No

FEDERAL FUNDING: N/A

OBJECTIVES:
Primary: To compare the time difference (in minutes and seconds) of using one Endobronchial Ultrasound (EBUS) needle to using two EBUS needles.

Secondary:

- To evaluate the economic impact of using one versus two needles (endoscopy suite time cost, anesthesia service cost, needles cost)
- To evaluate the environmental impact of using one versus two EBUS needles and time added or saved in endoscopy. This will be reported by calculating scope 3 CO2e per device inclusive of packaging and user manuals included within each disposable device.

BACKGROUND:
Endobronchial Ultrasound (EBUS) is a mainstay of diagnostic bronchoscopy, as it is performed for mediastinal and hilar lymph node sampling for cancer staging, diagnosis of sarcoidosis, lymphoma, infection, and other disease processes. It is a procedure that is commonplace in all bronchoscopy suites across the world.

In our bronchoscopy suite, our current practice varies based on the bronchoscopist and number of lymph nodes requiring sampling in a procedure (can range from 1-5) as to whether one or two needles are utilized. The bronchoscopist may use two needles to save time when multiple lymph nodes must be biopsied or if an individual node needs to be biopsied several times to obtain more tissue for pathologic study.

EBUS needles are single use and there is one randomized trial (n=20 patients) that showed a decreased time of procedure in patients where two needles were used versus one (Khan et al., 2013). However, no data exist evaluating the economic impact (cost of needle versus endoscopy dollars saved) or environmental impact of using one versus two needles. This study will examine these factors to determine the optimal way to perform this procedure in the future, considering the procedure and anesthesia time, economic costs, and environmental costs.

STUDY ENDPOINTS:
Primary:
Time in seconds and minutes from first needle stick into lymph node (T0) until 5 passes have been completed.
Timing:
- T0: Opening of needle when the physician performing the EBUS decides to biopsy a lymph node station
- TF: Last needle rinse of needle into the specimen cup at end of 5th pass (if more passes are taken, they will not be included in this analysis)

In patients who have multiple lymph nodes biopsied, the time will reset with each node.

Secondary:
1. Cost of endoscopy time per procedure
2. Cost of disposable needles being used
3. Environmental Cost of Endoscopy Time Used
4. Environmental Cost of Needles Used

STUDY INTERVENTION(S) / INVESTIGATIONAL AGENT(S): N/A

PROCEDURES INVOLVED:
Participants enrolled in this study at each study site (will include Northwestern University, Duke University, and UC Davis)will undergo the linear endobronchial ultrasound procedure as part of their

standard of care and will be randomized to one of two groups: Group 1 will have the procedure using one needle and Group 2 will have the procedure using two needles. Participants will have an equal chance of being randomized into each group. Participants will be told their randomization group. Both arms of the study are standard of care for linear EBUS. During the procedure, a member of the study team will be using a stopwatch to time the seconds and minutes spent at each lymph node station, which will be recorded in a secure REDCap database. The procedure will then be finished and the study visit completed for the patient.

The research team will also collect demographic data from the EMR, procedural characteristics, and pathologic outcomes. Collected data will include lymph node characteristics, procedural characteristics including time at each lymph node station, pathologic diagnosis, and adverse events as follows:

- Demographics: Age, sex, race/ethnicity
- Dates: Date of birth, date of procedure, etc.
- Lymph Node characteristics: Size of the lymph node and other characteristics may be documented in the REDCap form.
- Procedural Characteristics: Information collected will include the number of needle passes (standardization of 5 at each station unless ROSE deems inadequate and the provider needs to continue collecting samples for the procedure. If this occurs, only the first five needle passes will be timed). Total procedure time will also be collected.
- Final Pathologic Diagnosis: Collected to ensure there is no difference between the two groups (one versus two needles)
- Adverse Events: Any AEs that occur during the procedure will be recorded and assessed by the PI or Sub-Is regarding their relationship to the study procedures.

DATA AND SPECIMEN BANKING

Data will be stored in a secure REDCap database hosted on the Northwestern website with password protection only accessible to study personnel. All identifiers (Patient Name, DOB, MRN, contact information) will be stored in StudyTracker for Northwestern participants or in a similar site-specific database at Duke and UC Davis and will not be shared across institutions. Once the study is closed, identifiers stored in StudyTracker or similar database will no longer be accessed, ensuring that the data retained is deidentified. Data sharing agreements will be executed for Duke and UC Davis and only the limited dataset (to include dates such as date of consent, date of procedure, etc., but no other identifiers) will be shared between the groups.

SHARING RESULTS WITH PARTICIPANTS

Results from the study will not be shared with participants.

STUDY TIMELINES

Patients will be enrolled before or on the day of their standard of care EBUS bronchoscopy procedure and the standard of care EBUS bronchoscopy visit will be the only required study visit. We anticipate completing enrollment over the course of the next year.

INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria:

1. Subject is undergoing a linear EBUS for diagnosis of mediastinal or hilar adenopathy as defined by a mediastinal lymph node >1 cm in short axis or a normal sized lymph node with uptake on FDG-PET (fluorodeoxyglucose positron emission tomography) scan that is higher than background PET activity

2. Subject is 18 years old or older
3. Subject is willing and able to provide informed consent

Exclusion Criteria:

1. Subject does not undergo a biopsy during the EBUS bronchoscopy for various reasons (procedure aborted, lymph nodes not large enough to warrant biopsy, etc.)

VULNERABLE POPULATIONS
Will not be recruited for this study.

PARTICIPANT POPULATION(S)

Accrual Number:	Category/Group: (Adults/Children Special/Vulnerable Populations)	Consented: Maximum Number to be Consented or Reviewed/Collected/Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question
~~Local~~Study-wide (competitive enrollment)	Group 1 (One needle)	69	63
	Group 2 (Two needles)	69	63
Total:		138	126

RECRUITMENT METHODS
Patients who are scheduled for a standard of care EBUS bronchoscopy at Northwestern will be screened by the study team. All patients undergoing a bronchoscopy with linear EBUS for enlarged mediastinal/hilar lymph nodes who meet the inclusion criteria may be approached for participation. Patients may be approached before or on the day of the planned standard of care EBUS procedure by one of the study team members to provide informed consent. Patients may be approached in person during their standard of care clinic or bronchoscopy visit, or one of the study team members may contact the patient by phone and/or email. If the patient is contacted by phone or email, and are interested in hearing more about the study, the study team will send the consent form by email to the patient and arrange a time to discuss the study over the phone or video call. If the patient agrees to participate, the study team will send the consent form for signature via DocuSign and will send a final signed copy by email back to the study participant. The study team will document that the consent process took place remotely in StudyTracker.

Any patients not wishing to participate in the study will still have the standard of care procedure completed at the assigned time.

COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES
None

WITHDRAWAL OF PARTICIPANTS

Subjects who provide informed consent but are determined to be ineligible will be considered screen failures. The reason for screen failure will be documented and the procedure will continue as per standard of care.

RISKS TO PARTICIPANTS

There is no expected physical risk related to whether one or two needles are used for the procedure. The bronchoscopy procedure only allows for the use of one needle at a time in the working channel of the bronchoscope. The use of a second needle allows for the biopsy to occur while the sample is being processed from the other needle, whereas if only one needle is used, no biopsy occurs while the sample is being processed. The biopsy procedure is the same for both groups.

We have equipoise with respect to anesthesia time and the impact of using one versus two needles. There are no studies in bronchoscopy to date to suggest that limiting procedure time by a few minutes impacts anesthesia outcomes. Both one and two needles are used for standard of care bronchoscopies at Northwestern and we have observed no differences related to anesthesia outcomes. Further, it is not known if using two needles will significantly decrease the procedure time as this has not been prospectively studied in randomized fashion.

There is the risk of loss of confidentiality of health information. To minimize this risk, all coded clinical data collected and used as part of this project will be stored in a secure REDCap database or on a password-protected spreadsheet stored securely by the PI/Co-Is. Only elements of dates will be included in the REDCap database (date of consent, date of procedure, etc.). The key linking the code to identifying information (name, DOB, MRN, contact information) will be stored securely in StudyTracker.

POTENTIAL BENEFITS TO PARTICIPANTS

There is no direct benefit to participants. This research may help us determine the optimal way to perform this procedure, potentially saving environmental costs or time under anesthesia in the future.

DATA MANAGEMENT AND CONFIDENTIALITY

To protect confidentiality, all data will be coded with a study code. Data will be password-protected and stored securely by the PI/Co-Is on their computers, on FSMResFILES or NM SharePoint, and on a REDCap database. Coded data will be stored on REDCap until at least 3 years after study closure. Coded data may be shared with other investigators conducting IRB approved projects that reference the use of these data, upon permission from the PI. Codes will be linked to identifying information (name, DOB, MRN, contact information) via StudyTracker.

Sample size justification: Up to 69 patients will be enrolled in each group across all study sites. Using anticipated means in the two needle group (10 minutes with a standard deviation of 4 minutes) and one needle group (12 minutes) based on timing our procedure in the bronchoscopy suite at Northwestern, using an alpha of 0.05 and a statistical power of 80%, we would need to recruit 63 patients in each arm to have adequate power. We will plan to enroll 126 patients +10% (12 patients) assuming a low drop out rate given this is only a single study visit. This brings the total to 138 patients enrolled across all study sites.

PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS

Consenting done in person will be conducted in a private location at the clinic or bronchoscopy suite. All participants will be informed that participation in this study is optional and will not affect their medical care. All personal health information will be coded at the time of collection. Only the authorized

research personnel for this study will have access to the key linking the code to the participant's name and other identifying information. Identifying information may be used to obtain health information from the electronic medical record (Epic) for this research study. The key to the code will be kept in confidential files with standard security precautions and will never leave Northwestern University.

ECONOMIC BURDEN TO PARTICIPANTS
There are no costs to the participant for being in this study. The EBUS bronchoscopy procedure is performed for standard of care and will be billed to the patient and/or to the patient's insurance company in the usual way. Insurance dictates procedural cost and reimbursement and is not based on the equipment used (e.g., one vs two needles).

CONSENT PROCESS
Written informed consent will be obtained from each participant by the PI, Co-Is, or their study coordinators, either at the time of an in-person visit or remotely. If consent if obtained remotely, the research coordinator will contact the patient by phone or email to arrange a time to review the consent form. The research coordinator will send the ICF by email ahead of time to the patient and will arrange to speak with the participant via phone or video call for the consent review. If the patient is interested in participating, the coordinator will send the ICF for signature via DocuSign and will send a final copy by email back to the participant. The coordinator will also document that the ICF process took place virtually in StudyTracker. The physicians and study coordinators will verbally explain the study in detail and ensure that any questions are answered before prospective participants sign the consent form. They will reinforce that participation in the study is voluntary and they can withdraw their consent at any time.

Consent may be obtained on the day of the procedure. Consent will not follow any stressful situation (ie, patient being informed he/she may have cancer) and will not be conducted if the patient has received any mind-altering medications or anesthesia. Patients will be assessed for their capacity to consent by the ability to show comprehension of the research, ask appropriate questions, and appear properly oriented. A signed copy of the consent form will be offered to participants.

NON-ENGLISH SPEAKING PARTICIPANTS
We will utilize the short form consent with the assistance of a translator for non-English speaking participants. Once the same short form has been used for two participants or the English main ICF has undergone revision, we will translate the main ICF.

WAIVER OR ALTERATION OF CONSENT PROCESS: N/A

PROTECTED HEALTH INFORMATION (PHI AND HIPAA)
A HIPAA Authorization will be obtained as part of the consent form for the use of Protected Health Information (PHI). Health information that we may collect and use for this research includes:

- Names
- Dates: All elements of dates directly related to an individual, including birth date, date of procedure, etc.
- Contact information (Address, telephone number, email address)
- Medical record number
- Demographic information (Age, sex, race/ethnicity)
- Information related to the EBUS bronchoscopy (such as procedural characteristics including time at each lymph node station)

- EBUS bronchoscopy results (such as lymph node characteristics, pathologic diagnosis)

WAIVER OF HIPAA AUTHORIZATION: N/A

QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE
All physicians performing the EBUS procedures for this research are study investigators. The PI and Co-Is have extensive experience in clinical research and the Division of Pulmonary and Critical Care Medicine has experienced research managers and coordinator who will assist with this study, including consenting patients, creating a REDCap database for data collection, and obtaining and entering clinical data.

The PI/Co-Is perform 7-10 EBUS bronchoscopy procedures per week, so have sufficient volume of patients to conduct this study. The needles that are used in this study (22G Olympus EBUS Needle (ViziShot 2)) are standard of care and FDA approved.

MULTI-SITE RESEARCH: This research will be performed at Northwestern University as the host site, with Duke University and University of California – Davis potentially contributing data from their patients. Although this is a multi-site study, Northwestern University IRB will serve as the IRB of record only for the Northwestern study site. All other sites will obtain local IRB approval for this study.~~N/A – This research will only be performed at Northwestern University.~~

REFERENCES:

1. Khan W, Bailey S, Najib M. M12 EBUS- are two needles better than one? Thorax 2013;68:A200.