Informed Consent Form Of the The Study for Diagnostic Value and Safety of Transbronchial Mediastinal Cryobiopsy Combined with EBUS-TBNA in Mediastinal Lesions

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Principal Investigator: Ye Fan
Dear participant,

Thank you sincerely for participating in the project, Transbronchial Mediastinal Cryobiopsy Combined With EBUS-TBNA in the Diagnosis of Mediastinal Lesions. It was a clinical trial rather than routine therapy. This trial was launched by the Department of Respiratory in the second affiliated hospital of the Army Medical University and has been approved by medical ethnic committee. It is estimated that it would last for 12 months and about 190 participants would be involved in.

1. Background

Mediastinal and hilar lesions can present in both malignant diseases as well as benign disorders as the acquisition of a biopsy specimen qualified for pathological assessments is essential for accurate diagnosis. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) biopsy is a well-established technique and has been widely used for mediastinum lesion sampling. However, the insufficiency of obtained intact tissues still restricted its diagnostic yields and utilities on lung cancer staging and identification of uncommon mediastinal neoplasms and benign diseases. We have previously shown that EBUS-guided mediastinal cryobiopsy could provide larger amounts of intact mediastinal tissue.

2. Study Protocol

The included patients are randomized into two groups (EBUS-TBNA or EBUS-TBNA + transbronchial mediastinal cryobiopsy (EBUS-TBMCB)) through computerized randomization. Those receive additional transbronchial mediastinal cryobiopsy will receive TBMCB after the completion of TBNA. Outcome measures include diagnostic utility, feasibility and safety. Diagnostic utility is evaluated by diagnostic sensitivity, accuracy and sample size. Feasibility is evaluated by consumed time and operators’ score of each procedure. Safety is evaluated by the prevalence of adverse events.

3. Protocol of the operation procedure
After local anesthesia is achieved, vital signs and pulse blood oxygen saturation are continuously monitored. An EBUS bronchoscope is inserted into the trachea through the nose (if the nose is too narrow for the EBUS bronchoscope to pass through or there are other contradictions, the oral way could be the alternative option). Mediastinal lesions located at group 2, 4, 7, 10, 11, 12 are sequentially detected by the EBUS bronchoscope. For each lesion, the blood supply is identified by the Doppler Ultrasound and the size is measured. After the target is localized, EBUS-TBNA and EBUS-TBMCB are performed according to the randomized group.

All the specimens obtained from patients are then sent to the Department of Pathology for assessment.

After operation, you are supposed to tell the doctor whether there is any discomfort and Chest X-ray or other imaging examinations are required within 24 hours to detect whether there is emphysema or hematoma in mediastinum.

4. Interruption of the procedure accordingly in the following situations

4.1 the ultrasound fails to detect the lesion;
4.2 The blood supply is so abundant in the lesion that is considered inappropriate to continue biopsy due to the high bleeding risk;
4.3 The ultrasound identifies it is a cyst;
4.4 Severe adverse events occur during operation such as severe bleeding.

5. Voluntary principle for subjects to participate in the study

Before you sign this informed consent form, please read this informed consent form carefully and make a careful decision on whether or not to participate in this study. You can ask your research doctor anything you don't understand and ask him or her to explain it to you until you fully understand. Before you make a decision to participate in this study, you can discuss it with your family and friends and give it full consideration. You have the right to refuse to participate in this study and to withdraw from this study at any time. You will not be subject to any punishment or damage to other rights and interests as a result.
6. Rights and responsibilities of subjects

If you are participating in another clinical study or trial, be sure to inform your research doctor or other researchers. By signing this informed consent form, you agree to comply with the arrangements made by the researchers based on the specific requirements of the research scheme. This study is a randomized controlled trial. You and the research doctor will not be able to choose or decide which diagnostic method you want.

By signing this informed consent form, you also agree with the research team to make direct use of the remaining biological samples after your medical records and/or routine medical use in our hospital. Of course, the above circumstances do not limit your right to withdraw from the study at any time. You have the right to refuse that the biological samples provided this time will be used for other clinical studies, and you have the right to refuse that the biological samples provided this time will be stored by the research group after this study, and inform the research group to destroy them. If you need to know about the rights and interests of the subjects, you can contact Deng Fan, Secretary of the Office of the Medical Ethics Committee of our hospital at 68755422. You have the right to your own data. If you need know more research information, please contact researcher Guo Jieru (name) at 18883923067.

7. Duties of the research doctors

The researcher doctor who performs the EBUS-TBNA and EBUS-TBMCB is not the doctor who is in charge of the patient during the hospitalization.

The pathology department of our hospital is responsible for the diagnosis and preservation of biopsy samples, and the pathological diagnosis required by medical treatment has been carried out. The medical records and/or biological samples that the subjects explicitly refused to be used for the second time were not used for a second study. Biological samples are not used as commercial products.

Research-related injuries of the subjects would be dealt with duly.

If we get any information that may affect the performance of the study, you or your legal agent will be informed in timely.

8. Risks and benefits

Similar to the combined application of EBUS-TBNA and EUS-FNA recommended in the guidelines, bleeding may occur during EBUS-TBNA and
EBUS-TBMCB. In most situations, it requires no intervention. Other adverse events include pneumothorax, infection, hematoma or air leak in mediastinum, of which are much less possible to occur. The doctors will try their best to operate carefully to avoid damage to blood vessels and other important tissues. You are required to reexamine Chest X-ray or other imaging examinations within 24 hours to detect whether there is emphysema or hematoma in mediastinum. Timely detection and treatment of complications can generally avoid serious adverse events.

Compared with the routine application of EBUS-TBNA alone in our hospital, the operation time may be prolonged by 10-30 minutes, which may increase the discomfort of patients. During the operation, local anesthesia and continuous ECG monitoring should be used to minimize the discomfort of patients and ensure the safety of the subjects.

Compared with the conventional operation scheme, the operation scheme of the experimental group helps to obtain more intact tissues and improve diagnostic utilities and avoid more invasive examinations or even unnecessary surgeries.

8. Measures to deal with research-related damage

If subjects participating in this clinical study suffer from research-related damage, Fan Ye, the principal investigator of the study is available through 13983815728. There is also a legal guarantee for you to obtain compensation in our country when research-related damage occurs. If the study-related damage has not been satisfactorily dealt with, the subjects can contact Deng Fan, secretary of the office of the Medical Ethics Committee of our hospital at 68755422.

9. Other alternative treatments that may be available

If you refuse to participate in this study, you have alternative treatments. They include EBUS-TBNA, EBUS-TFB (Endobronchial ultrasound-guided transbronchial forceps biopsy), mediastinoscopy, percutaneous biopsy and so on.

10. Research-related expenses and the economic compensation to the subjects

There is no difference in the cost between different groups. Compared with simply applying EBUS-TBNA in our hospital, the combined application of the two methods does not increase the cost. There is no additional compensation as all the cost,
time and complications are within the range of normal diagnosis and treatment.

The research team does not provide any financial compensation or subsidy to the subjects, and the related examination and other treatment expenses involved in this study shall be borne by the subjects themselves.

11. Privacy and personal information protection

1. The research group hereby promises to protect the privacy and personal information of the subjects, the security measures to protect the privacy and confidentiality of personal information include hiding information that can identify the subjects during data reports, restricting access to using such information, data anonymity, and so on.

2. Legally, there are exceptions for researchers to protect the privacy and personal information of subjects when inspections are required by administrative authorities, sponsor inspectors or inspectors, ethics committee, etc.

3. If genetics is involved, the researcher guarantees that the results of diagnostic genetics research will not be made public to a third party (including your relatives) without your consent.
As a participant, I have read the Information Sheet and have had the details of the study explained to me. My questions have been answered to my satisfaction, and I understand that I may ask further questions at any time. I understand I have the right to withdraw from the study at any time. I agree to give my consent freely. I will keep this original informed consent form.

Participant/Guardian signature: ___________________ Date: ________________
Contact number: ___________________

As a member of the research team, I have got a medical certificate and have the appropriate qualifications to obtain the informed consent from the participants and perform the duty of signing the informed consent form.

Investigator signature: ___________________ Date: ________________
Contact number: ___________________