Study Protocol

Project Title (English): Comparative Study of Rotational Cryobiopsy Needle and Automated Biopsy Needle in Transthoracic Needle Biopsy for the Diagnosis of Peripheral Pulmonary Lesions

Version Number: V 1.2
Version Date: 2026-01-15

I. Research Background

Global cancer statistics indicate that lung cancer is currently the second most prevalent cancer worldwide. According to data released by the National Cancer Center in 2022, the overall incidence of cancer in China continues to rise, with lung cancer ranking first in both incidence and mortality rates (1). With the rapid development and widespread adoption of imaging technologies, chest CT scans have been progressively introduced and utilized in secondary and even primary healthcare institutions, enabling the earlier detection of small pulmonary nodules. Among these nodules, malignant and benign pulmonary nodules may exhibit similar radiographic features in their early stages; therefore, a rapid and accurate diagnosis directly determines the treatment strategy and prognosis, which holds significant importance for the clinical management of pulmonary nodules. However, relying solely on the patient's clinical and imaging data often makes it difficult to establish a definitive diagnosis. In such cases, invasive lung nodule biopsy is recommended to provide sufficient specimens for pathological evaluation and further molecular analysis.

According to existing literature, percutaneous needle biopsy is one of the primary methods for diagnosing pulmonary nodules; however, its diagnostic accuracy and risk of complications largely depend on the size of the lesion and the biopsy technique and instrument employed. For lesions smaller than 1.5 cm in diameter, the diagnostic accuracy decreases to approximately 70% (2, 3), which may be attributed to insufficient tissue sampling or necrosis. The choice of biopsy instrument is also particularly critical: when assisted by a coaxial needle, the

displacement during the sampling process can be minimized, thereby elevating the diagnostic rate to 85–90% (4). Currently, traditional automated needle biopsy devices are widely used in clinical practice, yet they still exhibit certain limitations. Studies have shown that when using conventional biopsy needles for ground-glass opacities, the cells within the lesion often exhibit a adherent growth pattern, while the alveolar architecture remains intact; consequently, this may compromise the accuracy of the pathological diagnosis due to inadequate tissue acquisition or poor specimen quality (5). Rapid on-site evaluation can assist in determining whether the specimen is sufficient and reduce instances of inadequate sampling (6). Regarding complications, the incidence of pneumothorax and hemorrhage associated with percutaneous biopsy techniques is relatively high; studies have reported that the incidence of pneumothorax with conventional biopsy needles ranges from 15% to 25% (7–13), the incidence of hemorrhage is 20% (14), and the incidence of hemothorax ranges from 0.1% to 0.2% (10,14,15).

In recent years, the percutaneous rotational cryobiopsy needle technique (CassiII rotational core biopsy) has demonstrated significant advantages as an emerging diagnostic approach. This technique utilizes a cryoprobe to precisely reach the target site with millimeter-level accuracy; leveraging the principle of cryogenic freezing, it "adheres" the pathological tissue to the needle tip, thereby preventing displacement during sampling and enables simultaneous rotational cutting of the lesion, allowing for the acquisition of larger and more complete tissue specimens. Currently, this technique is being applied in China across various anatomical sites,

including the breast, thyroid, lymph nodes, and lungs. Compared with traditional biopsy needles, the unique advantages of the CassiII rotational core biopsy technique lie in the fact that the obtained tissue specimens not only exhibit larger (averaging 2–4 times those obtained via conventional biopsy) but also maintain superior structural integrity. This preservation of tissue integrity is of paramount importance for subsequent pathological diagnosis, particularly for molecular testing. However, there is currently a lack of high-level evidence-based medical data directly comparing the safety and efficacy of these two biopsy techniques in the diagnosis of pulmonary nodules. Existing studies have primarily consisted of retrospective analyses of breast cancer cases (16), while validation studies involving pulmonary lesions have lacked prospective randomized controlled designs. Therefore, this study aims to systematically compare the diagnostic efficacy, specimen quality, and complication rates of the cryobiopsy needle technique（CassiII rotational core biopsy）versus the automated biopsy technique in the biopsy of pulmonary nodules, thereby providing a reliable evidentiary basis for clinical practice.

II. Research Objectives

This single-center, prospective, randomized controlled study aims to compare the diagnostic yield and safety of CassiII rotational core biopsy versus traditional automatic biopsy for the diagnosis of peripheral pulmonary nodules, thereby providing a basis for future clinical practice.

III. Research Methods and Technical Approach

3.1 Research Design

This study employed a prospective, randomized, single-blind, parallel-group, single-center trial design, enrolling consecutive patients with peripheral pulmonary nodules of unknown etiology. The subjects were randomly assigned (1:1) to either the CassiII rotational core biopsy group (experimental group) or the automated biopsy needle group (control group). The study compared diagnostic accuracy, the incidence of procedure-related complications, as well as the size and quality of the obtained tissue specimens.

3.2 Study Subjects

3.2.1 Study Population

This study cohort comprised hospitalized patients who visited Beijing Chaoyang Hospital (single-center) between 2026 and 2027, for whom chest CT scans indicated peripheral pulmonary nodules and who were scheduled for lung puncture biopsy.

3.2.2 Inclusion Criteria

Subjects enrolled in this study must meet all of the following criteria:

① Age: 18–90 years; gender: unrestricted;

② If a chest CT scan reveals pulmonary nodules with an unknown nature, a biopsy is required for definitive diagnosis; if the chest CT shows multiple pulmonary nodules, one of these nodules should be selected as the target lesion;

③ Axial chest CT imaging demonstrates peripheral pulmonary nodules located in the pulmonary region, with diameters ranging from 8 mm to 30 mm;

④ Voluntarily undergo CT-guided lung puncture biopsy and meet all preoperative

requirements;

⑤ Participants demonstrate good compliance, are able to cooperate with the study observations, are fully informed about the study's objectives and methods, acknowledge the potential risks, agree to participate in the study, and sign the informed consent form.

3.2.3 Exclusion Criteria

Individuals meeting any of the following criteria will be excluded from this study:

① Severe cardiopulmonary dysfunction;

② Irreversible coagulation disorders;

③ Suspected vascular lesions or arteriovenous malformations (assessed by contrast-enhanced CT), or presence of bronchial artery penetration at the planned biopsy site, or suspected pulmonary metastasis from renal cell carcinoma, indicating a high risk of hemorrhage;

④ PET-CT findings indicate a malignant pulmonary nodule; surgical evaluation may prioritize surgical intervention for the patient;

⑤ Pregnant or lactating women;

⑥ Patients with psychiatric disorders or those unable to cooperate during the puncture procedure;

⑦ Presence of anesthesia contraindications; allergy to anesthetic agents; or a history of multiple severe allergies or hereditary allergies;

⑧ If the participant has participated in other studies within the past three months without withdrawing or completing those studies, this will affect the observation of

the present study;

⑨ Refusal to participate in this study, unwillingness to accept the follow-up protocol, or other circumstances in which the investigator deems the participant unsuitable for participation in this study.

3.2.3 Mid-term withdrawal criteria

Patients who meet the inclusion criteria but did not complete the study for any reason, including subjects who withdrew voluntarily and investigators.

There are two circumstances under which withdrawal is decided.

① Subjects have the right to withdraw from the trial at any time without requiring any reason, and will be arranged for appropriate follow-up or recommended to receive other suitable treatments.

② Withdrawal from the trial at the discretion of the investigators: If any of the following circumstances occurs, after clinical relevance has been assessed,

If the investigator determines that the subject is unable to continue with this clinical trial, the subject may withdraw from the trial ahead of schedule:

When a specific medical condition arises, and the investigators determine that continuing participation may pose a risk to the subject's safety;

Other management-related reasons.

3.3 Research Steps and Research Endpoints

3.3.1 Intervention Steps

① Patients with peripheral pulmonary nodules who meet the inclusion and exclusion criteria were continuously enrolled; after signing informed consent, they were

included in the study.

② Collect preoperative patient data, including chest CT scans and other laboratory test results.

③ Based on pre-prepared random envelopes, subjects will be randomly assigned to either CassiII rotational core biopsy group (experimental group) or the automated biopsy needle group (control group) (1:1).

④ Optimize preoperative preparation: all patients shall fast for 6 hours and abstain from water for 2 hours prior to surgery. A contrast-enhanced preoperative CT scan is performed to determine the location, size, and relationship of the nodule with surrounding blood vessels. The surgeon will plan the optimal puncture trajectory, ensuring it avoids major blood vessels and bronchi. During the procedure, local infiltration anesthesia or nerve block anesthesia is administered.

a) CassiII rotational core biopsy group: Under CT guidance, a percutaneous puncture is performed using a coaxial needle; upon reaching the target lesion, the CassiII rotational core biopsy needle is inserted along the coaxial needle for biopsy. At the same lesion site, ⩾1 biopsy is performed; depending on sample adequacy, the maximum number of biopsies shall not exceed 3, with at least 1 tissue specimen obtained from each biopsy. Subsequently, the CassiII rotational core biopsy needle and the coaxial needle are withdrawn sequentially. After resting for 5–10 minutes, a repeat CT scan is performed to assess for any complications such as hemorrhage or pneumothorax.

b) Automated biopsy needle group: Under CT guidance, a coaxial needle is

percutaneously inserted; upon reaching the target lesion, an automated biopsy needle is advanced along the coaxial needle and activated. Biopsy is performed at least once at the same lesion site; depending on sample adequacy, the procedure may be repeated up to a maximum of 3 times, with at least one tissue specimen obtained from each attempt. Subsequently, the automated biopsy needle and the coaxial needle are withdrawn sequentially. After resting for 5–10 minutes, a repeat CT scan is performed to assess for any complications such as hemorrhage or pneumothorax.

c) For specimens obtained from both groups, an Artificial Intelligence-assisted Rapid On-Site Evaluation was performed; subsequently, the tissue samples were placed in formalin-fixed specimen containers for pathological examination. The pathological diagnosis was independently reviewed by two pathologists using a back-to-back review approach; if the results agreed, a definitive diagnosis was established. In cases where the results differed, a third pathologist conducted a final review, and the final diagnosis was determined through consensus among all three experts.

⑤ Postoperative management: The patient should remain in a supine position for 4 hours postoperatively, with close monitoring of vital signs, oxygen saturation levels, and for any signs of complications. A chest imaging study should be performed within 24 hours postoperatively to exclude asymptomatic pneumothorax or hemorrhage. If no complications are observed, the patient may be discharged after 24 hours, with follow-up scheduled accordingly.

⑥ Data collection: Clinical data include medical history, physical signs, laboratory results, pulmonary function tests, and imaging studies; record these findings.

Record the number and size of biopsy specimens; report surgical-related complications such as hemorrhage, pneumothorax, or infection (including those occurring within 7 days postoperatively).

⑦ Follow-up: Follow-up visits will be conducted at 1 month, 3 months, 6 months, 12 months, and 24 months postoperatively. For pathological-negative subjects, a repeat chest CT scan will be performed to evaluate their final diagnosis based on changes in pulmonary nodules and results from surgical biopsies.

3.3.2 Study Endpoints

Gold Standard – Pathological Examination: The pathological specimens shall be classified into the following categories: normal lung tissue, specific inflammation/non-specific inflammation, atypical tumor-like hyperplasia, carcinoma in situ, and invasive carcinoma.

A positive pathological diagnosis indicates that a diagnostic conclusion has been reached based on the obtained biopsy specimen; all conditions—including specific inflammation, granuloma, atypical tumor-like hyperplasia, carcinoma in situ, and invasive carcinoma—are defined as pathologically positive.

A negative pathological diagnosis indicates that the obtained biopsy specimen did not yield a definitive diagnosis—for example, in cases of normal lung tissue or nonspecific inflammation. If the pathological diagnosis is negative, further surgical biopsy should be performed until a definitive diagnosis can be established.

A "positive" result for pathological diagnosis of the lung biopsy specimen obtained via CassiII rotational core biopsy needle that is positive; a "true negative" result refers

to a pathological diagnosis of the lung biopsy specimen obtained via CassiII rotational core biopsy needle that is negative, yet the pathological diagnosis of the surgical lung biopsy specimen is also negative; a "false negative" result refers to a pathological diagnosis of the lung biopsy specimen obtained via CassiII rotational core biopsy needle that is negative, whereas the pathological diagnosis of the surgical lung biopsy specimen is positive.

1）Primary endpoint:

Diagnostic yield of the two biopsy methods

Using pathology as the gold standard, we calculated the diagnostic accuracy rates and their 95% confidence intervals for both methods and conducted a comparison between them. The calculation formulas are as follows:

Diagnostic yield = (Number of pathologically positive cases / Total number of enrolled cases) × 100%

$$confidence\ interval\ = [\overline{\mathrm{X}} \pm \frac{\sigma}{\sqrt{n}} z_{\frac{\alpha}{2}}]$$

Furthermore, ROC (Receiver-operating characteristic) curve analysis was performed on the test data to calculate the area under the ROC curve, thereby providing a comprehensive evaluation of the diagnostic value of different biopsy techniques.

2) Secondary endpoints

① Specimen indicators:

- Specimen size (long diameter, short diameter)
- Specimen integrity score (1–3 points: 1 = completely fragmented; 2 = incomplete

cord-like structure; 3 = intact cord-like structure)

• Pathological evaluable parameters, including effective tissue/cell availability and molecular diagnostic aspects, shall be assessed by a pathologist (satisfactory/acceptable/unsatisfactory).

• AI-assisted ROSE enables rapid on-site assessment and demonstrates comparable accuracy to the gold standard.

② Operational performance indicators:

• Total procedure time (from positioning to biopsy completion)

• Number of punctures and number of obtained tissue samples

③ Safety indicators:

• Complications: Incidence (including pneumothorax, hemorrhage, respiratory failure, infection, and severe complications requiring endotracheal intubation and mechanical ventilation to be transferred to the Intensive Care Unit), severity levels, and corresponding management measures.

④ Clinical efficacy endpoints:

• Total hospital stay duration

• Postoperative recovery time

For comparisons of intergroup incidence rates of adverse reactions, the chi-square test or Fisher's exact probability test was employed; for comparisons of intergroup operative times, the t-test or non-parametric tests were used.

3.4 Observation of Adverse Events/Complications

3.4.1 Occurrence and Management of Adverse Events/Complications

Percutaneous lung puncture may be associated with various intraoperative and postoperative complications, including but not limited to: hemorrhage, pneumothorax, mediastinal emphysema, subcutaneous emphysema, pleural reaction, pleural effusion, pulmonary inflammation, air embolism, anaphylaxis to anesthetic agents, radiation exposure during fluoroscopic imaging, cerebrovascular or cardiovascular events, respiratory arrest, and even mortality. In response to these potential intraoperative and postoperative complications, once any complication occurs — regardless of its relevance to the study — close monitoring and follow-up will be conducted; appropriate management/treatment measures will be promptly implemented for the patient based on the investigator's assessment and adherence to established clinical diagnostic and therapeutic guidelines. The recommended management/treatment measures for the most likely complications are as follows:

① Pneumothorax: An intraoperative or delayed pneumothorax may occur; a small amount of pneumothorax may not require intervention; for moderate to large pneumothorax, thoracentesis for air evacuation or placement of a closed thoracic drainage device may be performed; if a tension pneumothorax develops, the biopsy procedure must be stopped immediately.

② Hemorrhage: Minor intraoperative bleeding may be managed with observation; moderate hemorrhage can be controlled using hemostatic agents; in cases of significant hemorrhage, the biopsy procedure should be immediately terminated, and the patient should be transferred to the intensive care unit (ICU) for further management; if necessary, interventional embolization or surgical hemostasis may be

performed.

③ Pulmonary infection: Confirmation should be obtained via chest plain radiography or chest CT scan; antibiotics should be adjusted based on the results of sputum, blood, or pus cultures; if the chest X-ray or chest CT scan indicates the presence of a pulmonary or pleural abscess, catheter drainage should be performed.

④ Pleural effusion: Generally, observation or conservative management is sufficient. However, if moderate to large amounts of pleural effusion occur, thoracentesis or closed thoracic drainage should be performed.

⑤ Other: Implement appropriate therapeutic measures in a timely manner based on the investigator's assessment and established clinical practice guidelines.

3.4.2 Assessment of the severity of adverse events/comorbidities

Pneumothorax：

Grade 1: Mild; pulmonary compression <30%; no specific treatment required; observation and follow-up are sufficient.

Grade 2: Moderate; 30% ≥ pulmonary compression <50%; or presence of chest pain or dyspnea.

Grade 3: Severe; lung compression ≥50%; presents with markedly pronounced chest pain and dyspnea; requires immediate implementation of closed thoracic drainage for air evacuation or other invasive interventional measures.

Haemorrhage ：

Grade 0: No bleeding.

Grade 1: Ground-glass opacities or consolidation appear within a ≤2 cm radius

around the puncture needle; mild local hemorrhage is observed, which typically resolves spontaneously and does not require intervention.

Grade 2: The area of hemorrhage is> 2 cm and is confined to the pulmonary segment; this represents moderate hemorrhage, which may require sputum suctioning or temporary pharmacological hemostatic measures.

Grade 3: Hemorrhage involving at least one lung lobe or a larger area; severe hemorrhage, often requiring pharmacological hemostasis or intensive care unit (ICU) management.

Grade 4: Hemorrhage accompanied by hemothorax; severe complications requiring thoracic drainage or surgical intervention.

Other complications:

Grade 1: Mild; asymptomatic or mild; only detectable clinically or on diagnostic imaging; no treatment is required.

Level 2: Moderate; requires small-scale, localized, or non-invasive treatment; involves performing instrumental activities of daily living at an age-appropriate level. Mobility is restricted.

Grade 3: Severe or medically significant but not immediately life-threatening; leads to hospitalization or prolongs hospital stay; causes

Residual; self-care activities are limited.

Level 4: Life-threatening: requires emergency treatment.

Grade 5: Death associated with adverse events.

Instrumental activities of daily living refer to tasks such as cooking, purchasing

clothing, using a telephone, and managing finances.

Self-care activities in daily life refer to tasks such as bathing, dressing and undressing, eating, washing hands, and taking medication; these activities do not require the individual to remain bedridden.

3.4.3 Recording and Reporting of Adverse Events

During the treatment period, clinical adverse events may occur in the subjects; should any adverse event (including serious adverse events) occur

For adverse events, the time of occurrence, clinical manifestations, and management measures should be recorded in detail on the case report form.

The relationship between these parameters and the duration of the condition, clinical outcomes, and the intervention method; patients who exhibit abnormal laboratory findings must undergo follow-up monitoring.

The patient's condition may return to normal test results, revert to pre-intervention levels, or be determined to be unrelated to the intervention method; severe adverse events may also occur.

For serious adverse events, the Serious Adverse Event Report Form must be completed, and the event must be reported to the sponsor and the Ethics Committee within 24 hours.

CFDA, regulatory authorities, and health administrative departments.

3.5 Sample Size Calculation

Based on previous analyses of studies involving peripheral pulmonary nodules, we assumed that the diagnostic yield of conventional automated biopsy needles is 85%,

while the diagnostic yield of CassiII rotational core biopsy needles is 95%. According to clinical practice, we set α = 0.05 (two-sided), β = 0.20 (power of 80%), and a loss-to-follow-up rate of 10%; using the PASS 21.0 software, we performed a sample size calculation. The results indicated that 154 subjects were required per group, totaling 308 subjects. We ultimately plan to enroll 308 subjects.

Tests for Two Proportions

Numeric Results for Testing Two Proportions using the Z-Test with Unpooled Variance
Hypotheses: H0: P1 - P2 = 0 vs. H1: P1 - P2 ≠ 0

Target Power	Actual Power*	N1	N2	N	P1	P2	Diff D1	Alpha
0.8	0.80183	138	138	276	0.95	0.85	0.1	0.05

* Power was computed using the normal approximation method.

Summary Statements
Group sample sizes of 138 in group 1 and 138 in group 2 achieve 80.183% power to detect a difference between the group proportions of 0.1. The proportion in group 1 (the treatment group) is assumed to be 0.85 under the null hypothesis and 0.95 under the alternative hypothesis. The proportion in group 2 (the control group) is 0.85. The test statistic used is the two-sided Z-Test with unpooled variance. The significance level of the test is 0.05.

Dropout-Inflated Sample Size

	Sample Size			Dropout-Inflated Enrollment Sample Size			Expected Number of Dropouts		
Dropout Rate	N1	N2	N	N1'	N2'	N'	D1	D2	D
10%	138	138	276	154	154	308	16	16	32

Procedure Input Settings
Autosave Inactive

Design Tab

Solve For:	Sample Size
Power Calculation Method:	Normal Approximation
Alternative Hypothesis:	Two-Sided
Test Type:	Z-Test (Unpooled)
Power:	0.8
Alpha:	0.05
Group Allocation:	Equal (N1 = N2)
Input Type:	Proportions
P1 (Group 1 Proportion|H1):	0.95
P2 (Group 2 Proportion):	0.85

3.6 Randomization and Blinding

Computer-generated random numbers are prepared by a statistician who is not involved in the study implementation. The random sequence is sealed within an opaque envelope; once patients meet all inclusion criteria, the study coordinator sequentially opens the envelopes to determine the group assignment scheme. While the surgeon cannot be blinded, the pathologist employs a blinded approach when assessing specimen quality, and the patients remain blinded regarding their group assignment.

3.7 Data Collection and Management

3.7.1 Data Collection

① Baseline data: demographic information, medical history, symptoms and signs, physical examination, hematological tests, imaging studies

Such as examining imaging characteristics (lesion location, relationship between the lesion and adjacent bronchi, nature of the lesion);

② Operational documentation: operating time, sample quantity, etc.;

③ Pathological data: histopathological results, tissue sample quality, molecular testing results, AI-ROSE results, etc.;

④ Safety evaluation data: type of complications, management approach, length of hospital stay, etc.;

⑤ Postoperative follow-up: Follow-up will be conducted at 24 months; for patients with pathological negative results, the nature of the nodule will be determined based on either an imaging evaluation (where a reduction in nodule size of at least 20% is considered indicative of a benign lesion) or whether a surgical biopsy was performed.

Data will be collected using a Case Report Form (CRF). All data will undergo regular review by an independent Data Monitoring Committee to ensure data quality and completeness. Investigators will conduct follow-up visits at 1 week, 1 month, 3 months, 6 months, 12 months, and 24 months after patient enrollment to confirm the final diagnosis and long-term complications.

Research Workflow Diagram

	Preoperative	During surgery	Postoperative follow-up					
Visit Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**
Number of days since enrollment	**D-30~D-1**	**D0**	**D1-7**	**1 month postoperatively**	**3 months postoperatively**	**6 months postoperatively**	**12 months postoperatively**	**24 months postoperatively**
Visit Window (Number of Days)	**/**	**/**	**/**	**±7**	**±15**	**±15**	**±15**	**±15**
Sign the informed consent form	×							
Inclusion and Exclusion Criteria	×							
Demographic Information Collection	×							
history-taking	×							
Concomitant Medication Collection	×	×	×					
vital sign	×	×	×					

chest CT	×			×	×	×	×	×
pulmonary function test	×							
laboratory examination	×							
needle biopsy of lung		×						
Chest X-ray/CT scan			×					
Pathological diagnostic data			×					
Clinical diagnostic results								×
Adverse Event Collection		×	×					

3.7.2 Statistical Analysis

Statistical analysis was performed using SPSS 31.0 software. Measurement data were expressed as mean ± standard deviation or median (interquartile range), with intergroup comparisons conducted using the t-test or Mann–Whitney U test; categorical data were presented as frequencies (percentage), with intergroup comparisons performed using the χ^2 test or Fisher's exact test. The area under the ROC curve (AUC) was used to evaluate diagnostic performance. Comparisons of diagnostic accuracy were carried out using the McNemar test. Logistic regression analysis was employed to identify independent factors associated with diagnostic accuracy. A P value <0.05 was considered statistically significant.

3.8 Quality Control Measures

① All procedures shall be performed by physicians with at least 5 years of experience in interventional radiology; prior to the commencement of the study, each physician must complete training in the respective techniques and pass the corresponding assessment. The percutaneous lung puncture procedure shall be strictly adhered to; all intraoperative procedures shall be performed by the same operator to minimize variability between operators.

② The pathological diagnosis results shall be reviewed independently by two pathologists; if the results are consistent, a definitive diagnosis is established; if the results are inconsistent, a third pathologist shall conduct a review, and the final diagnosis shall be determined through discussion among all three experts.

③ All participating researchers must undergo unified training, as well as follow standardized recording methods and evaluation criteria. Researchers shall complete the Case Report Form in accordance with the filling requirements, recording all items on the form truthfully, comprehensively, and meticulously, to ensure that the content of the subject's Case Report Form is complete, authentic, and reliable.

④ Perform regular equipment calibration and data verification to ensure data integrity.

⑤ Quality Assurance (QA) is managed by an independent Data Safety Monitoring Board (DSMB), which regularly reviews the progress of the study and adverse events, and recommends the early termination of the study when necessary.

IV. Research-related Ethics

4.1 Ethics Committee Review

This study was conducted in compliance with relevant laws and regulations, including the "Regulations on the Supervision and Administration of Medical Devices (2014)", the "Good Clinical Practice for Medical Devices (2016)", the "Helsinki Declaration", as well as the requirements outlined in the clinical trial protocol. Prior to the initiation of the trial, the principal investigator is responsible for submitting the trial protocol, informed consent forms, and all other relevant research documents to the Ethics Committee for review and obtaining its approval prior to proceeding with the clinical trial. The sponsor shall promptly report any serious adverse events occurring during the course of the study, including risks to the subjects and other related issues. Any modification to the trial protocol must first obtain the approval of the Ethics

Committee and be duly filed with the Ethics Committee.

4.2 Informed Consent

All subjects may only be enrolled in this study after receiving an oral and written explanation of the details of the clinical trial and signing the informed consent form. The signed informed consent form shall be prepared in duplicate: one copy shall be retained by the investigator for inclusion in the designated clinical trial management file, and the other copy shall be retained by the subject.

4.3 Risk-Benefit Analysis

Percutaneous needle biopsy is a traumatic medical procedure that entails certain medical risks; during or after the procedure, unexpected events and complications may occur. The primary risks associated with percutaneous lung biopsy include pneumothorax, hemorrhage, infection, and air embolism. The techniques employed in this study are all clinically established methods, and their associated risks are relatively manageable. Patients may benefit from more accurate diagnoses and fewer complications. Patients can receive standardized diagnostic and therapeutic recommendations, as well as follow-up care and disease management, under current clinical conditions. Furthermore, the findings of this study will provide evidence for developing optimal diagnostic strategies for patients with pulmonary nodules, thereby contributing significantly to societal benefits.

V. Confidentiality Measures

The findings from this project may be published in medical journals; however, we will strictly adhere to legal requirements to ensure the confidentiality of patient

information, and personal patient data will not be disclosed unless required by applicable laws. When necessary, government regulatory authorities, hospital ethics committees, and their authorized personnel may access patient records in accordance with established regulations.

VI. Data Management and Security

6.1 Data Entry and Verification

Patient screening numbers are assigned using an S followed by three Arabic numerals, e.g., S001; enrollment numbers are assigned using three Arabic numerals, e.g., 001; patient Case Report Forms (CRFs) are collected and entered into the Electronic Data Capture (EDC) system; a computer-aided verification system is then used to re-check the entered data to ensure its completeness and accuracy.

6.2 Data Management

The principal investigator is responsible for managing the data, which shall be stored in both paper and electronic formats, except for personnel within the research team. Researchers may view the data; however, personnel outside the research group shall not have access to this information.

This study employs a rigorous prospective randomized controlled design to systematically compare the value and efficacy of the percutaneous puncture cryosuction needle versus the automated puncture biopsy needle in the diagnosis of pulmonary nodules; the results will provide high-quality evidence-based medical data for the precise diagnosis of pulmonary nodules and hold significant importance for

guiding clinical practice.

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