STUDY PROPTOCOL

Generative AI–Powered Navigation System for Precision Puncture: A Multicenter Randomized Controlled Trial Evaluating Efficacy and Safety

Co-Principal Investigators: Bo Du, Huangxuan Zhao

Data: 17 June 2025

Principal Investigators	**Bo Du, PhD** School of Computer Science, Wuhan University. Location: Wuhan, Hubei Province, China. Email: dubo@whu.edu.cn. **Huangxuan Zhao, PhD** School of Computer Science, Wuhan University/ Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. Location: Wuhan, Hubei Province, China. Location: Wuhan, Hubei Province, China. Email: zhao_huangxuan@sina.com
Other Investigators	**Lei Chen, MD** Department of Radiology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. Location: Wuhan, Hubei Province, China. Email: chan0812@126.com.
Version	V 2.0

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Project Proposal Signature Page

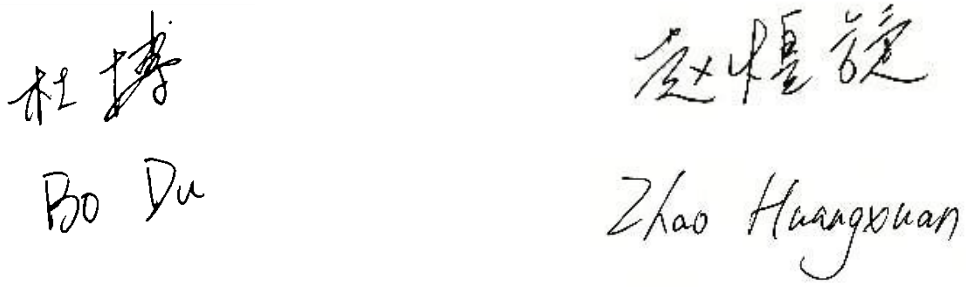
Project Title: Generative AI–Powered Navigation System for Precision Puncture: A Multicenter Randomized Controlled Trial Evaluating Efficacy and Safety

Version Number / V2.0

I have read and understood this research proposal and confirm that it includes the necessary content for conducting the study, clearly outlining the responsibilities of researchers involved in this project. As the Principal Investigator, I will provide all participating researchers with a copy of this proposal and all relevant materials. I will discuss these materials with them to ensure they fully understand the implementation of this research proposal. I agree to strictly adhere to all applicable laws and regulations, the Declaration of Helsinki, Good Clinical Practice guidelines, and this research proposal in fulfilling my responsibilities.

Principal Investigator (Print): Bo Du; Zhao Huangxuan

Principal Investigator Signature:



Clinical Research Institution:

Union Hospital, Tongji Medical College, Huazhong University of Science and Technology

1 Introduction and rationale

Lung nodules are highly prevalent in the population, and percutaneous lung puncture (PLP) is one of the gold standards for the qualitative diagnosis of lung nodules[1,2]. Cone-beam CT (CBCT) plays a critical role in guiding percutaneous lung puncture[3-5]. However, the poor quality of CBCT imaging can complicate the procedure, especially in certain patient populations. Improving the quality of CBCT images may increase the success rate of CBCT-guided lung nodule puncture procedures, reduce radiation exposure, and minimize the number of punctures. Although several previous studies have used generative deep learning methods to improve CBCT image quality[6-8], no prospective clinical trials have yet validated the practical application of these models. In this study, a Generative AI-Powered Puncture Surgery Navigation System for lung punctures (GPS-Lung) systems constructed based on the synthesis CT (sCT) images and intraoperative guidance system, and a prospective cohort is used to validate its efficacy in clinical practice.

2 Objectives

- To construct a GPS-Lung system to improve CBCT imaging quality in clinical practice and evaluate the integration of GPS-Lung system to guide lung puncture surgery, with the goal of improving puncture surgery efficiency, reducing radiation exposure, and minimizing procedural complications.

3 Study design

This study used a prospective randomized controlled study design. Participants scheduled to undergo percutaneous lung puncture were included and randomly assigned in a 1:1 ratio to either the GPS-Lung system guided puncture group or the CBCT-guided puncture group.

Study type: Prospective randomized controlled trial.

Study schedule: January 2025-May 2025 (5 months total).

Study location: Three Level 3A hospitals in China (Wuhan Union Hospital, Wuhan Union West Hospital, and Wuhan Union Jinyinhu Hospital).

4 Study population

4.1 Study population

Participants scheduled to undergo CBCT-guided lung puncture.

4.2 Inclusion criteria

- Participants require CBCT-guided PLP and meet the indications for the procedure.
- Participants have pre-operation CT images.
- Participant's physical condition is suitable for PLP.

4.3 Exclusion criteria

- Participants have a history of allergy or serious adverse reaction to iodine contrast media or other related drugs.
- Participants are pregnant or breastfeeding.
- Participants are unwilling or unable to provide informed consent.

5 Study process

Group: A Web-based platform was used to randomize patients into experimental group or control group.

Experimental group: Percutaneous lung puncture procedure using GPS-Lung system guidance.

Control group: Percutaneous lung puncture procedure using CBCT guidance.

Observation indicators: The number of puncture needles, radiation dose, puncture time and intraoperative and postoperative complications within 7 days.

6 Randomization and binding

6.1 Randomization

Randomization was performed using a Web-based system (https://www.randomizer.org/#randomize) that employed computer-generated, permuted-block sequences, with stratification by center. Notably, the Web-based central randomization service ensured concealment of trial-group assignments.

6.2 Binding

This study conducted a double-blind design to ensure that neither participants nor researchers were aware of the group assignments throughout the study. Participants, researchers, data collectors, and outcome assessors were blinded to the group allocation. Statisticians and authors were unaware of the subgroups during data analysis. Doctors, technicians and trial nurses were aware of the subgroups but were not involved in data collection or analysis.

For image quality and lesion quality scoring, we will give a mixture of CBCT, sCT, and CT images to the scorers, and they unaware of the images type.

7 Observation outcomes

7.1 Primary outcome

Puncture times of participants for GPS-Lung system and CBCT-guided lung puncture procedures. Puncture times was defined as the number of punctures performed throughout the PLP procedure.

7.2 Secondary outcomes

Radiation dose, duration of surgery and intraoperative and postoperative complications

within 7 days of participants for GPS-Lung system and CBCT-guided lung puncture procedures.

7.3 Other outcomes

Algorithmic performance for image quality enhancement and doctors' scoring of image and lesion quality.

8 Complications

Potential complications are listed below:
Pneumothorax: Air may enter the pleural cavity after a lung puncture, causing the lung atrophy.
Bleeding: Puncture of lung tissue may result in bleeding within the lung or chest cavity.
Pneumonia: The puncture procedure may trigger an infection, which can result in pneumonia.
Atelectasis: Airway obstruction or atrophy of lung tissue may cause partial atelectasis.
Intercostal neuralgia: The puncture procedure may irritate the intercostal nerves, resulting in postoperative pain.
Lung abscess: Both intraoperative and postoperative infections may lead to localized abscess formation.
Air embolism: Intraoperative entry of puncture gas into the vessel resulting in air embolism.

9 Sample size estimation

The sample size calculation in this study was estimated based on the number of intraoperative lung punctures. A total of 38 participants received CBCT-guided PLP from retrospective cohort were included from Wuhan Union Hospital. The mean (SD) puncture times of these patients were 2.3±2.2. We used a 2.5% one-sided significance

level with 90% efficacy for sample allocation on a 1:1 basis. The sample size was calculated based on the following formula:

$$n = \frac{2(Z_{\alpha/2} + Z_{\beta/2})^2 * \sigma^2}{\Delta^2}$$

n represents the sample size of each group. $Z_{\alpha/2}$ represents the critical value of the significance level (α), and the α=0.025 in the study. $Z_{\beta/2}$ represents the critical value of efficacy (1 - β), and the β=0.9 in the study. σ^2 represents the within-group variance. In the current, σ was substituted by the standard deviation of puncture times from 38 participants. Δ represents the smallest difference between the means of the two groups. In the current, the Δ was considered as 1. Therefore, the sample size to be included in this study for each group is 103. We will included 220 participants (each group 110 participants).

10 Data analysis program

The baseline comparisons between the two groups, appropriate statistical tests will be employed based on the type of data (parametric or non-parametric). Categorical variables will be analyzed using the Chi-squared test or Fisher's exact test, while continuous variables will be analyzed using the *t*-test or the Mann-Whitney U test. Paired *t*-tests will be used to compare the means of the scores for overall image quality and lesion visualization between paired groups. The weighted kappa coefficient (κ) or kendall coefficient of concordance (W) or intra-class correlation coefficient (ICC) will be used to assess the agreement of the image quality of all samples and the lesions score of sCT among different readers.

11 Data management and monitoring

Data management: All data will be anonymized and stored in a secure, specialized database (Picture Archiving and Communication Systems, PACS) to ensure data integrity and confidentiality. Researchers can access it in PACS. Data will be kept for a

period of 15 years. Imaging data is evaluated independently by an imaging assessment team.

Data monitoring: An independent Data Safety Monitoring Committee (DMC) will be established to regularly review the progress, safety, and overall quality of the trial.

12 Ethical considerations

12.1 Ethical approved

The study will be registered with the Clinical Trial Registry. This study has been approved by the ethics committees of the Wuhan Union Hospital (Reference number: UHCT-IEC-SOP-016-03-01).

12.2 Informed consent

All participants will be requested to sign an informed consent form prior to participation in the trial. The consent form will provide the participants with a clear explanation of the purpose of the study, potential risks, and possible benefits. Participants have the right to withdraw from the study at any time, without any impact on their subsequent treatment.

13 Schedule of the trial

January-March 2025: Trial initiated, ethical approval granted, and patient recruitment initiated. Data collection for participant recruitment and scanning completed.

April-May 2025: Data analysis and summary report.

14 Discussion

In this study, the efficacy of the GPS-Lung system in guiding percutaneous lung

puncture procedures was comprehensively evaluated through a prospective randomized controlled trial. The expected results will provide strong evidence for the clinical application of GPS-Lung system to improve the success rate of percutaneous lung puncture procedures, while reducing the radiation exposure and minimize complications for patients.

15 References

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