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The clinical performance of robotic assisted navigation system versus conventional freehand technique for percutaneous transthoracic needle biopsy

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This study aimed to assess the feasibility and safety of robotic-assisted navigation system for percutaneous transthoracic needle biopsy (PTNB), compare it with conventional freehand technique, and evaluate its generalizability across operators with varying experience levels. After excluding 5 patients in whom robotic-assisted PTNB could not be performed due to technical problems, a total of 50 patients with robotic-assisted PTNB and 200 patients who performed freehand puncture were included. Using propensity score matching (PSM) to match two groups of patients and simulate a randomized controlled scenario. The results showed that robotic-assisted PTNB significantly reduced the number of punctures, CT scans, and total procedure time ($P < 0.05$). These reductions were accompanied by a significantly lower rate of pneumothorax ($P = 0.05$), a common complication in PTNB procedures. While the overall adverse event rates remained similar between the two groups, the robotic-assisted technique demonstrated a more favorable safety profile, particularly with regard to reduced pneumothorax and hemorrhage rates. Additionally, there were no significant differences in the number of punctures, CT scans, total procedure time, and radiation dose administered to patients during robotic-assisted PTNB, irrespective of the operator. This suggests that operator experience does not significantly influence the outcomes of robotic-assisted PTNB, further highlighting the potential of the robotic system to minimize the impact of operator variability. Thus, we think robotic-assisted PTNB is feasible, safe, and less dependent on operator experience, suggesting its potential for clinical promote.

Keywords Robotic-assisted, Navigation system, Percutaneous transthoracic needle biopsy (PTNB), Interventional radiology, Lung cancer

Recently, statistics from relevant organizations show that as of 2022, the incidence of lung cancer has once again surpassed that of breast cancer to become the cancer with the highest incidence and mortality rate in the world[1]. For lung cancer patients, early and accurate diagnosis is the key to treatment. In recent years, with the popularization and development of low-dose computed tomography (CT), lung cancer screening by low-dose CT in high-risk populations and even in routine clinical practice has become a worldwide consensus[2]. Because of this, more suspicious lung lesions have been detected in clinical practice.

Currently, lung biopsy can be used to determine the benignity or malignancy of the lesion and subsequent genetic testing can be used to determine the patient's treatment plan. The three commonly used methods are transbronchoscopic biopsy, percutaneous transthoracic needle biopsy (PTNB), and surgery. Surgery is more invasive, costly, and complex than the other two methods. For central lesions, transbronchoscopic biopsy possesses more advantages, whereas for peripheral lesions, it is less diagnostic and more limited[3,4]. Therefore, with the development of minimally invasive fields such as interventional radiology, PTNB has gradually become a widely accepted maneuver in clinical practice, especially for peripheral lesions[5–7]. The biggest advantage of lung

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puncture biopsy is the ability to accurately puncture the lesion under the guidance of CT. Compared with the traditional surgical operation, image-guided interventions therapy are inexpensive, less invasive and have fewer complications. However, the traditional method of PTNB is mainly freehand puncture, which is dependent on the experience of the operator. During the procedure, the operator needs to adjust the direction of the needle several times, and multiple CT scans are required to assess the needle tip position, which greatly elevates the risk of radiation injury to the patient as well as potential complications.

In order to improve the accuracy of puncture and reduce the complication rate, many robotic navigation-assisted puncture systems for CT-guided percutaneous puncture have been created[8,9]. Previous studies have shown that robotic navigation systems are feasible, safe, and effective for assisted puncture of phantom, swine livers and kidneys models compared to manual puncture[10–12]. Based on these previous studies, in order to compare the accuracy and safety of robotic navigation system-assisted puncture with freehand puncture in thoracic and abdominal lesions, a clinical trial was conducted at our center, enrolling a total of 60 patients, which demonstrated that robotic navigation system-assisted CT-guided thoracic and abdominal lesion puncture improves the accuracy and safety of the punctures[13]. However, the small sample size of our previous study resulted in the inclusion of fewer patients with PTNB. The presence of respiratory motion in the lungs makes the process of freehand puncture procedure complex and difficult[14]. In this study, we aim to evaluate the clinical performance of this robot-assisted navigation system in assisting PTNB compared to conventional freehand puncture.

Methods
Study procedures
This study was conducted in accordance with the Declaration of Helsinki. This study was approved by the institutional review board (JD-LK-2022-163-01), and written informed consent was obtained from all patients. Procedures were performed at a single institution (The second affiliated hospital of Soochow University) between January 2022 and June 2024. Fifty-five consecutive patients undergoing robotic assisted PTNB formed a "robotic group" where data were collected prospectively. Patients who underwent freehand puncture from January 2022 to June 2024 were retrospectively collected and matched 1:1 with the robotic group using propensity matching analysis method (PSM) to derive the freehand group.

Study participants
The inclusion and exclusion criteria were the same for both groups. Inclusion criteria were (i) patients requiring PTNB after multidisciplinary consultation (ii) age > 18 years (iii) ECOG (physical status) score ≤ 1. Exclusion criteria were (i) patients who had not discontinued anticoagulant and(or) antiplatelet medications 5 days prior to procedures (ii) ECOG Score > 3 (iii) poor patient compliance (iv) patient age < 18 years (v) pregnancy.

Procedures
All patients received local infiltration anesthesia, and all underwent PTNB guided by 16-row helical CT. All biopsies were performed with a core needle in a coaxial cutting needle system using an 18 G puncture needle (OptiMed 1399-1210, 18 G-100/150 mm). For robotic group, we utilized a commercially available robotic-assisted navigation system (TH-S1) obtained from TrueHealth Medical Technology Co. Ltd. in Hengqin, China. This system holds approval from the National Medical Products Administration (NMPA) as a class III medical device. The system comprises a photoelectric navigation system, a surgical planning system, and a robotic arm positioning and puncture system (Fig. 1), specifically designed for interventional procedures. The operational principle of the robotic-assisted navigation system for preoperative lung nodule localization is as follows:

(I) The patient's preoperative CT scan is imported into the surgical planning system, enabling the reconstruction of a comprehensive 3D model encompassing the pulmonary nodules, vessels, bronchi, bone structures, and skin.
(II) The 3D model is automatically registered with the patient's position information obtained through the photoelectric navigation system, ensuring accurate alignment.
(III) Based on the location of the lesion in the 3D model, the simulated puncture path is generated after selecting the entry point and target location.
(IV) The robotic arm positioning and puncture system precisely positions the puncture path, including the puncture site, needle direction, and depth, within the surgical space.
(V) A puncture needle is then inserted manually, and biopsy sampling is performed after CT scanning to verify the needle tip position.

In the traditional manual CT-guided percutaneous puncture procedure, an experienced operator determines the needle insertion trajectory based on the initial CT image. The entry point is determined using the CT scan frame laser line to indicate the axial position. Since the operator chooses the needle angle based on their experience, they must repeatedly adjust the needle's direction and depth based on multiple CT scans to ensure a safe and accurate puncture.

Outcome measures
Feasibility
Number of CT scans: The number of CT scans required for the needle tip to reach the position that meets feasibility criteria.

Procedure timing (PT): The time elapsed from the initial CT scan used to localize the image to the time of the post-biopsy scanning of the CT to verify complications.

Fig. 1. The robotic-assisted navigation system. (**A**) The photoelectric navigation system used to track the position of the robotic arm and the patient; (**B**) the surgical planning system employed for the precise planning of the needle insertion path; (**C**) the robotic arm positioning and puncture system responsible for accurate positioning of the needle holder and assisting with needle insertion.

Number of punctures: The number of puncture times required for the needle tip to reach the position that meets the feasibility criteria. In the robotic group, if the needle tip position is not considered to be capable of performing biopsy after the first needle tip insertion, the operator could adjust the position by planning a new path. After the second failed adjustment, the procedure is considered unsuccessful and converted to freehand puncture.

Generalizability

Generalizability is defined as the clinical performance of PTNB using robotic-assisted navigation system by different interventional radiologists.

Safety

Safety was evaluated as the number of major adverse events attributable to the needle insertion. The method of evaluation was based on a common surgical grading of complications[15].

Grade I: Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions.
Grade II: Requiring pharmacological treatment with drugs other than such allowed for grade I complications. Blood transfusions and total parenteral nutrition are also included.
Grade III: Requiring surgical, endoscopic or radiological intervention.
Grade IV: Life-threatening complication requiring IC/ICU management.

Statistical analysis

Data were analyzed using GraphPad Prism 9.5.0 (GraphPad, San Diego, Calif). Measurements are expressed as mean ± standard deviation ($\bar{X} \pm s$). All data were checked for normality using the Shapiro–Wilk test. For data that conformed to normal distribution, paired *t*-tests were used for comparisons between two groups, one-way ANOVA was used for comparisons between multiple groups, and Wilcoxon signed rank-sum tests were used for data that did not conform to normal distribution. Count data were expressed as rates or component ratios, and comparisons between groups were made using the chi-square test. $P < 0.05$ was considered to be statistically significant.

Propensity score matching (PSM)

The PSM process was implemented using the PSM extension program for SPSS: with whether or not a robotic-assisted navigation system aid was used to assist PTNB as a dependent variable, age, sex, BMI, lesion location, lesion size, and lesion edge-to-skin distance as covariates, matching was performed using a 1:1 nearest neighbor matching method, in which each robotic group was matched to 1 freehand group with the most similar scoring values. The process ensures the excellence of the matching results by defining the caliper values, after which the standardized differences of the covariates between the groups are changed before and after the matching is compared; the closer the standardized differences are to 0 after the matching, the more satisfactory the matching results are. When the absolute value of the standardized difference is less than 0.1 (10%), the balance of variables between groups is considered to be better.

Results

Baseline characteristics of the two groups of patients before and after matching

After excluding 5 patients who were unable to proceed to the next step due to technical errors during puncture, a total of 50 patients were included in the robotic group as the test group. A total of 200 patients who underwent freehand puncture at our center from January 2022 to June 2024 were included, and a total of 170 patients were included as the control group after excluding patients with incomplete corresponding data. Baseline characteristics (age, sex, BMI, lesion location, lesion size, and lesion edge-to-skin distance) were compared between the two groups, and the results showed no significant differences in baseline characteristics between the two groups. However, in order to simulate the randomization scenario as much as possible, we chose to use PSM with 1:1 nearest-neighbor matching method and a caliper value of 0.15, which finally resulted in 50 patients who were most closely matched to the robotic group. The equalization of the covariates was also significantly improved from before by PSM. The baseline characteristics of patients before and after matching is shown in Table 1.

Main results

A summary of results comparing technical outcomes between robotic versus freehand procedures is shown in Table 2.

Technical success

Technical success was achieved in all procedures in both groups. The needle tip reached the edge of the lesion to obtain the tissue and the final definitive pathologic tissue results were obtained. And no cases in the robotic group were converted to freehand puncture. Example images from a typical robotic assisted PTNB procedure are provided in Fig. 2.

Feasibility

The robotic group required fewer puncture times in place (1.4 ± 0.8 vs. 2.3 ± 1.5), $P < 0.05$, had a shorter procedure time (15.33 ± 5.47 vs. 20.43 ± 9.78), $P < 0.05$, and the patients underwent fewer CT scan times (3.80 ± 1.22 vs. 5.75 ± 2.12) compared with the freehand group, $P < 0.05$ (Fig. 3).

Generalizability

The test group involved three interventional radiologists with different experiences, including an attending with 20 years of experience, an attending with 10 years of experience, and a resident with 5 years of experience. The number of puncture times made during the procedure, the procedure time, the number of CT scans and the radiation dose received by the patient were collected for each interventional radiologist. The statistical analysis showed no significant differences between the interventional radiologists (Table 3).

Safety

Six adverse events in the robotic group were pneumothorax of which four were managed conservatively (grade I) and 2 were managed with chest drain insertion (grade III). Two adverse events in the robotic group were

Variable	Before PSM				After PSM			
	Total (*n* = 220)	Robotic (*n* = 50)	Freehand (*n* = 170)	*P*	Total (*n* = 100)	Robotic (*n* = 50)	Freehand (*n* = 50)	*P*
Age, M (Q_1, Q_3)	69.00 (60.00, 76.00)	67.50 (60.75, 75.25)	69.00 (60.00, 76.00)	0.985	68.50 (60.00, 75.25)	67.50 (60.75, 75.25)	69.00 (59.75, 74.75)	0.962
BMI, M (Q_1, Q_3)	22.41 (20.06, 24.76)	22.99 (21.12, 25.57)	22.25 (19.98, 24.24)	0.095	22.73 (20.28, 25.14)	22.99 (21.12, 25.57)	22.47 (19.65, 24.63)	0.209
Size, M (Q_1, Q_3)	35.24 (24.00, 50.80)	31.75 (24.75, 42.25)	36.14 (23.77, 54.46)	0.131	31.25 (23.64, 43.25)	31.75 (24.75, 42.25)	30.30 (22.95, 45.46)	0.954
Distance, M (Q_1, Q_3)	51.01 (39.56, 63.82)	54.30 (39.41, 72.01)	50.34 (40.00, 62.36)	0.231	52.80 (40.78, 70.13)	54.30 (39.41, 72.01)	52.12 (41.63, 64.60)	0.683
Gender, n (%)				0.173				0.361
Male	135 (64.29)	22 (55.00)	113 (66.47)		48 (60)	22 (55.00)	26 (65.00)	
Female	75 (35.71)	18 (45.00)	57 (33.53)		32 (40)	18 (45.00)	14 (35.00)	
Positions, n (%)				0.458				0.891
LUL	34 (16.19)	9 (22.50)	25 (14.71)		18 (22.5)	9 (22.50)	9 (22.50)	
LLL	63 (30)	10 (25.00)	53 (31.18)		23 (28.75)	10 (25.00)	13 (32.50)	
RUL	59 (28.1)	13 (32.50)	46 (27.06)		24 (30)	13 (32.50)	11 (27.50)	
RLL	54 (25.71)	8 (20.00)	46 (27.06)		15 (18.75)	8 (20.00)	7 (17.50)	

Table 1. Baseline characteristics before and after matching. *LUL* left upper lobe, *LLL* left lower lobe, *RUL* right upper lobe, *RLL* right lower lobe.

Outcome	Robotic group	Freehand group	*P* value
Technical success-n (%)	50 (100)	50 (100)	> 0.99
Number of puncture times	1.4 ± 0.8	2.3 ± 1.5	< 0.05
Number of CT scan times	3.80 ± 1.22	5.75 ± 2.12	< 0.05
Procedure timing (min)	15.33 ± 5.47	20.43 ± 9.78	< 0.05
Overall adverse events-n (%)	8 (16)	15 (30)	0.095
Grade I-n (%)	6 (12)	10 (20)	0.274
Grade II-n (%)	0 (0)	0 (0)	
Grade III-n (%)	2 (4)	4 (8)	0.209
Grade IV-n (%)	0 (0)	1 (2)	0.461
Pneumothorax	6 (12)	14 (28)	0.05
Chest drain insertion	2 (4)	4 (8)	0.209
Pathology-n (%)			
Adenocarcinoma	24 (48)	27 (54)	
Mesothelioma	5 (10)	4 (8)	
Small cell lung cancer	1 (2)	1 (2)	
Metastatic carcinoma	10 (20)	6 (12)	
Neuroendocrine cancer	0 (0)	2 (4)	

Table 2. Outcomes of robotic versus freehand procedures.

slight postoperative pain. There were fifteen adverse events in the freehand group, of which fourteen were pneumothoraxes, ten were treated conservatively (grade I), 4 required chest drain insertion (grade III), and 1 hemorrhage required emergency resuscitation (grade IV). The results after statistical analysis showed that there was no statistical difference between the two groups in terms of the overall number of adverse events ($P > 0.05$), but according to the sub-stratum analysis of pneumothorax showed a statistical difference ($P = 0.05$) (Fig. 4).

Discussion

PTNB is widely used for early diagnosis of suspected malignant tumors due to its simplicity and effectiveness[16]. However, inaccurate localization may lead to repeated scanning and puncture attempts, resulting in potential radiation exposure as well as the risk of complications to the patient[17]. To tackle this problem, a novel robotic-assisted navigation system was developed with the aim of improving the accuracy of puncture, shortening the procedure time, reducing the complication rate, and decreasing the radiation exposure to the patient. In this study, we aim to evaluate the clinical performance of this robot-assisted navigation system in assisting PTNB compared to conventional freehand puncture. Our study included a larger sample size than previous reports on robotic navigation system[18,19]. In a previous study by Erica S. Alexander et al. on robotic navigation-assisted lung biopsy[20], the baseline of lesion size was not standardized between the two groups; in this study, we used PSM to ensure the consistency of the baseline of lesion size and the distance from the lesion edges to the skin, which yielded a pleasing experimental result.

The traditional approach to CT-guided PTNB is mainly freehand puncture with stepwise needle entry. This method leads to longer procedure times and increased radiation exposure for the patient, as it requires multiple CT scans to determine the needle tip position during the procedure. In this study, the robotic group required shorter procedure time when the needle gain an acceptable position compared with the freehand group, and the patients underwent fewer CT scan times. The traditional puncture approach, which relies heavily on the operator's experience, uses a stepwise needle advancement method that requires repeated intraoperative adjustments of the needle angle. This method can lead to the creation of multiple puncture passages, seriously increasing the risk of potential complications. A retrospective study of 10,568 cases of percutaneous lung biopsy showed that the occurrence of pneumothorax in two puncture channels was significantly higher than in 1 ($P < 0.001$), and the frequency of pneumothorax (requiring catheter drainage) was significantly increased in three puncture channels ($P < 0.001$)[21]. A retrospective study of serious complications such as pneumothorax and/or parenchymal hemorrhage after CT-guided transthoracic biopsy shows that the most important risk factor for the development of pneumothorax is the number of needle insertion times, with the higher the number of needle insertion times being associated with a higher risk of pneumothorax[22]. In this study, the robotic group had a statistically significant reduction in the number of puncture attempts needed to achieve an acceptable co-axial needle position before biopsy, compared to the freehand group. There was also a reduction in the number of adverse events (8 vs. 15), but the difference was not statistically significant. Among the complications related to PTNB, pneumothorax was the most common, as reported in related studies[23]. Therefore, we conducted a sub-stratum analysis specifically for the complication of pneumothorax. The results indicated that the number of pneumothoraxes in the robotic group was significantly reduced compared with the Freehand group, which was statistically significant and superior to the results reported in previous related studies[24,25].

Several studies have shown that accuracy decreases when novice operators perform freehand PTNB[26,27]. One of the major advantages of robotic-assisted navigation system is that it can reduce the negative consequences of lack of operating experience, but until now, there is a lack of relevant studies on this topic. Therefore, in this

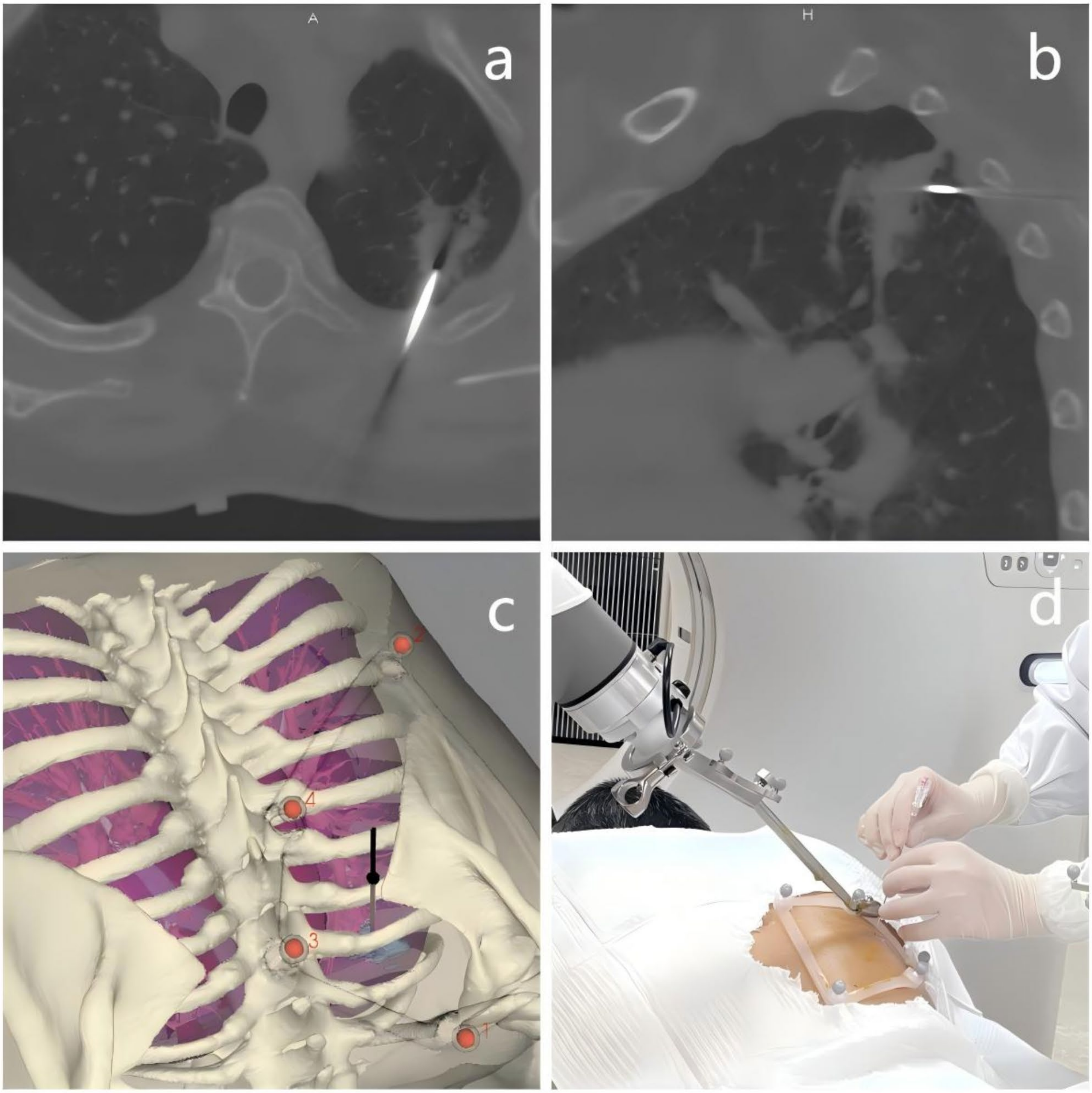

Fig. 2. Example out-of-plane robotic assisted PTNB in a 61-year-old woman with a 14 mm solitary left upper lobe lesion. (**a**) Unenhanced axial CT image showing the out-of-plane puncture to the edge of the lesion. (**b**) Reconstructed sagittal CT image of the puncture in place. (**c**) 3D reconstruction of the thoracic structure and 3D verification of the puncture site. (**d**) photograph demonstrating the out-of-plane approach taken by the needle system.

study, we included for the first time three interventional radiologists with varying levels of experience in robot-assisted percutaneous needle biopsy (PTNB): one attending with 20 years of experience, another with 10 years, and a resident with 5 years of experience. Statistical analysis of the results showed that there were no significant differences in the number of needle puncture times required to reach the target position, the procedure time, the number of CT scan times required, and the radiation dose to the patient between operators with different levels of experience when using robot-assisted PTNB. This further confirms that robot-assisted PTNB reduces the impact of operator experience.

Simultaneously, in this study, contrary to conventional practice, we allowed the patients to breathe freely and quietly during the procedure. There were two reasons why it is not necessary to hold their breath: firstly, the reproducibility of the diaphragm position between breath holds is not good, and secondly, the deep breaths that follow may result in a pinprick laceration of the pleura[28]. At the same time, relevant study pointed out that the performance as well as complications of PTNB performed under calm breathing were acceptable[29]. Furthermore,

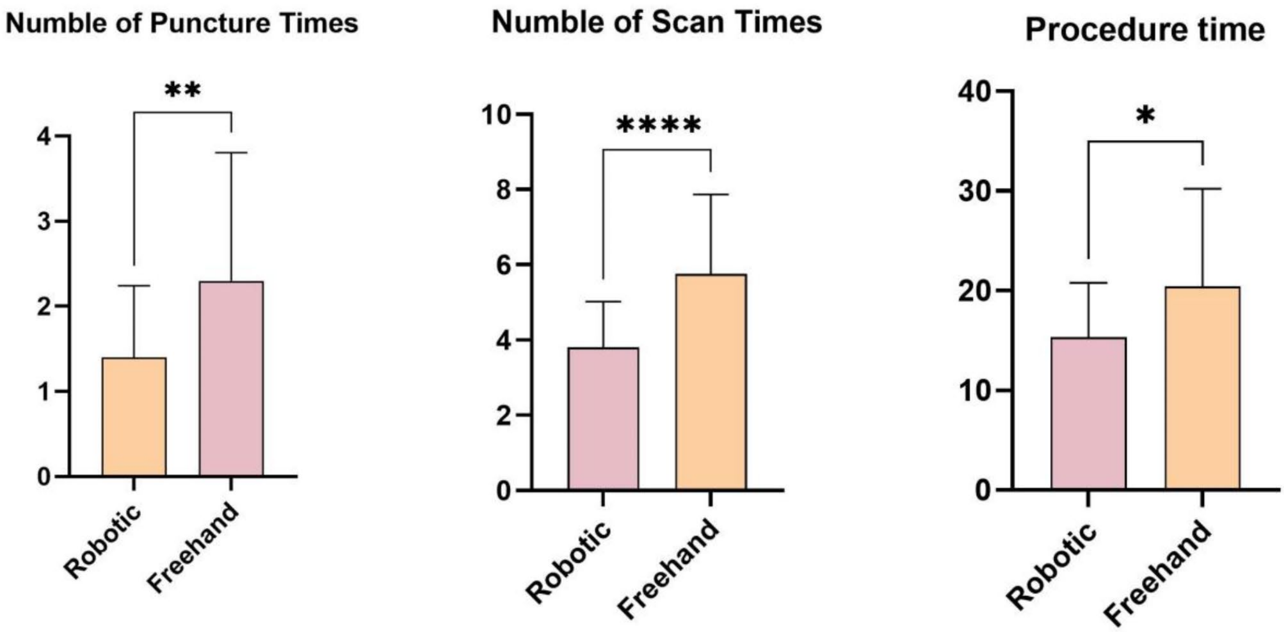

Fig. 3. Procedure time, number of puncture times and scan times required to gain an acceptable position of the co-axial needle prior to biopsy in the robotic and freehand group.

	Interventional radiologist 1	Interventional radiologist 2	Interventional radiologist 3	*P* value
Per patient-n (%)	20 (40)	15 (30)	15 (30)	
Number of puncture times	1.32 ± 0.85	1.78 ± 0.97	1.17 ± 0.4	0.293
Procedure timing (mins)	14.6 ± 5.42	18.9 ± 5.62	13.0 ± 3.03	0.065
Number of CT scan times	3.76 ± 1.23	4.33 ± 1.41	3.17 ± 0.41	0.140
Radiation dose (mGy)	29.07 ± 14.41	34.28 ± 12.93	28.87 ± 13.85	0.190

Table 3. Clinical performance of PTNB using robotic-assisted navigation system by different interventional radiologists.

asking the patient to breathe steadily and regularly while being comfortable can increase the patient's cooperation, reduce the patient's nervousness, improve puncture efficiency and reduce the complications due to poor patient cooperation[30].

Presently, the main robotic-assisted navigation systems that exist on the market are divided into two main categories: electromagnetic navigation systems and optical navigation systems[31]. Electromagnetic navigation systems operate based on electromagnetic principles, utilizing sensors to detect the position and orientation of medical instruments (such as puncture needles or guide needles). An example is the CorPath® system[32]. These systems do not rely on external visual guidance, allowing for precise positioning even in deep body tissues. But electromagnetic navigation systems may be susceptible to performance interference from metals or other magnetic sources, which can easily lead to technical malfunctions during the puncture process, rendering the procedure unfeasible, especially in a CT environment. In a previous study, out of 26 patients who required electromagnetic navigation-assisted puncture, 8 experienced technical malfunctions during the procedure[33]. Optical navigation systems, on the other hand, use optical sensors (such as cameras, lasers, or infrared devices) to track the position of the target. An example is the OpticNav® system[34]. These systems offer high precision, clear real-time feedback, and intuitive operation. They are suitable for surface-visible areas and do not rely on complex sensor equipment. In this study, we utilized an optical navigation system, which, despite being compatible with the CT environment, has a significant drawback: the camera and optical markers must not be obstructed. Among the 55 patients who required optical navigation system-assisted PTNB, 5 experienced technical malfunctions that prevented the machine arm from reaching the preset position, necessitating replanning or conversion to a freehand puncture. The results, while clearly superior to electromagnetic navigation, are poorer in terms of system usability than previous studies related to optical navigation[18,35]. Upon analyzing the reasons, in 2 of the patients, the robot experienced calibration and control errors during the operation. This is mainly due to a flaw in the design of the system, which is not expected to occur subsequently as the technology is updated. In the other 3 cases, we attributed the issues to the patient's respiratory amplitude and the navigation system's inability to recognize the optical markers, leading to planning failures. Upon further analysis, it was observed that all three patients were female, and their predisposition to chest breathing contributed to pronounced chest surface

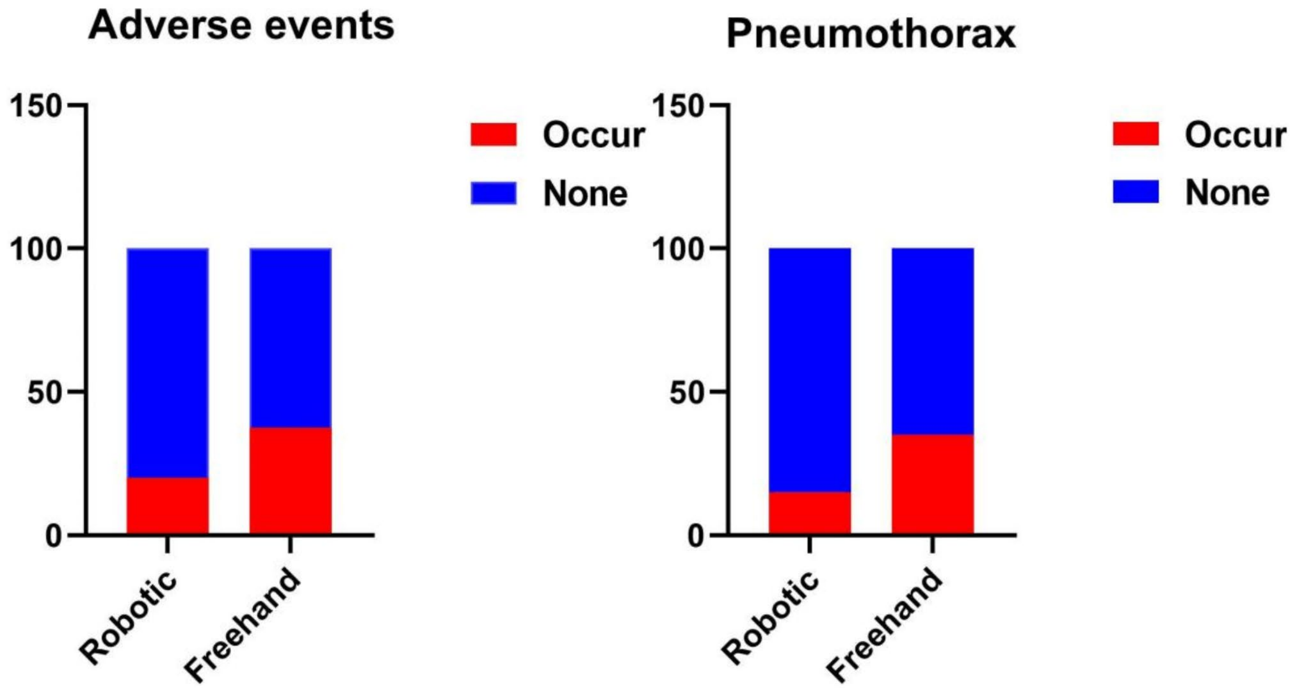

Fig. 4. Number of total adverse events and number of pneumothoraxes with acceptable coaxial needle position obtained before biopsy in the robotic and freehand groups.

motion during respiration. The increased respiratory amplitude caused significant fluctuations, hindering the navigation system's ability to accurately detect the markers. Unlike rigid and static organs such as the brain and bones, robot-assisted navigation systems may make errors in lung puncture[30]. Preoperative image data cannot be aligned in real time with the patient's lung anatomical data because respiratory motion changes the position of the lung lesion, which makes the widespread use of navigation techniques in lung puncture challenging. We will conduct a further study to investigate the patterns of respiratory displacement and respiratory motion in various regions of the lung to update the respiratory gating technique for puncture navigation.

The limitation of this study is the retrospective data collection of the freehand puncture group, which led to the lack of some important information, such as the CT scan parameters, which resulted in the unmeasurable radiation dose to the patients during the operation, even though the study showed a significant reduction in the number of CT scan times in the robotic group compared with the freehand group. Additionally, in this study, we utilized PSM to control for confounding factors and ensure that baseline characteristics, such as lesion size and puncture path distance, were similar between the two groups. While this approach closely simulates a randomized controlled scenario[36], it still has limitations and shortcomings compared to a randomized control trial.

Conclusion
This study is a real-world clinical study which confirms that robotic-assisted PTNB is feasible and safe in the clinic. Compared to the conventional freehand technique, the robot-assisted navigation system can reduce the number of puncture times, the number of CT scan times, and the rate of adverse events such as pneumothorax. Additionally, its accuracy is comparable to that of the conventional freehand technique. At the same time, the robot-assisted navigation system can also reduce the influence of operator experience on PTNB, which can be widely promoted in the clinic.

Data and code availability
Any additional information required to reanalyze the data reported in this paper is available from the lead contact, Xuming Bai (2005baixuming@163.com).

Materials availability
This study did not generate new unique reagents.

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Conceptualization, Xuming Bai and Yong Jin; methodology, Yifan Jing and Xuming Bai; Investigation, Yifan Jing, Jian Jing, Jiayi Liu and Jian Zhang; writing—original draft, Yifan Jing and Jiayi Liu; writing—review and editing, Yifan Jing, Yong Jin and Xuming Bai; funding acquisition, Xuming Bai and Yong Jin; resources, Yifan Jing and Xuming Bai; supervision, Xuming Bai and Yong Jin.

Declarations

Competing interests
The authors declare no competing interests.

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