Chapter 13
The Application Value of Virtual Reality Navigation Combined with Rapid On-Site Evaluation in CT-Guided Lung Biopsy

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Abstract The purpose is to evaluate the value of Virtual Reality (VR) navigation system-assisted CT-guided percutaneous aspiration biopsy combined with Rapid on-site Evaluation (ROSE) in the accurate diagnosis of pulmonary nodules and pulmonary infections. This study retrospectively analyzed the medical records of CT-guided percutaneous transthoracic needle biopsy (CT-PTNB) patients at the Second Hospital of Qiqihar Medical College from March 2018 to December 2021. The 158 eligible patients who underwent lung aspiration biopsy were divided into an experimental group (81 patients) and a control group (77 patients). In the experimental group, a VR navigation system was used to assist CT-guided percutaneous aspiration biopsy combined with ROSE, and in the control group, patients underwent plain CT-guided pulmonary aspiration biopsy. Basic clinical information including gender, age, lesion location, and puncture length was recorded for all patients. The occurrence of intraoperative complications of lung puncture biopsy and secondary postoperative biopsies between the two groups of patients were also compared. There was no statistically significant difference between the two groups of patients in terms of clinical base information (all $P > 0.05$). Meanwhile, the incidence of bleeding [13.58% (11/81) vs. 27.27% (21/77), $\chi 2 = 4.582$, $P = 0.032$] and pneumothorax [6.17% (5/81) vs. 15.58% (12/77), $\chi 2 = 4.916$, $P = 0.027$] were significantly lower in the experimental group than in the control patients. In contrast, there was no statistically significant difference in the rate of secondary biopsy between the two groups [0.00%

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(0/81) vs. 3.90% (3/77), $\chi 2 = 3.217$, $P = 0.073$]. VR navigation system-assisted CT-guided pulmonary aspiration biopsy combined with rapid on-site evaluation (ROSE) is significantly better than conventional CT-guided pulmonary aspiration biopsy in terms of safety and reduction of secondary biopsy rate in patients and has high clinical application value.

13.1 Introduction

In recent years, with the development of society, due to the decline of air quality or some bad habits of people, lung diseases are increasing year by year, and the incidence and death rate of lung cancer tops the list [1]. CT-PTNB is a relatively simple, minimally invasive procedure in which the location of the lesion is determined by a CT scan, and aspiration or biopsy is performed under CT guidance to obtain a pathologic diagnosis [2]. However, conventional CT-guided needle biopsy (CTNB) is highly susceptible to factors such as the experience and skill level of the patient, resulting in the patient obtaining additional puncture injury, radiation damage, and even elevating the complication rate of the puncture procedure.

For this reason, many experimental studies have been conducted to improve the accuracy and safety of puncture operations by applying various methods for positioning and navigating the puncture needle, such as optical navigation systems, electromagnetic navigation systems, virtual reality (VR) navigation systems, and robotic navigation systems. Cheng et al. [3] showed that the application of electromagnetic navigation system to CT-PTNB in pulmonary nodule surgery could reduce complications, reduce patient turnaround, and save total time. Wang et al. [4] showed that optical positioning technology assisted puncture could improve puncture accuracy and shorten puncture procedure time within a certain range. VR navigation systems can assist in intraoperative positioning and real-time tracking of the puncture needle tip to provide precise, objective, and real-time interactive guidance for lung puncture biopsy during surgical operations to reduce injury to the organs. However, the application of VR navigation has hardly been reported.

Rapid on-site evaluation (ROSE) is a rapid cytology interpretation technique that accompanies the sampling process in real-time. When the target site is sampled, a portion of the sampled material is blotted onto a slide with essentially no loss of tissue specimen to make a cytological film base that is rapidly stained and immediately interpreted with a special microscope synthesizing clinical information. ROSE is more frequently used in bronchoscope biopsies to reduce the insufficiency of bronchoscope biopsy pathology specimens, and Izumo et al. [5] showed that ROSE can reduce the number of EBUS (Endobronchial Ultrasonography) punctures and improve the accuracy of pathology results. In contrast, few reports have applied ROSE to CT-PTNB.

VR navigation systems can not only reduce the risk of lung biopsy but also improve medical safety, diagnosis and treatment effects. ROSE not only ensures sufficient materials but also improves the accuracy of diagnosis and significantly reduces the rate of the second biopsy. At present, there are few reports on the application of VR navigation system-assisted CT-guided percutaneous biopsy combined with ROSE in the accurate diagnosis of pulmonary nodules and lung infections. Therefore, this study evaluates its application value.

13.2 Materials and Methods

13.2.1 Study Population

This study was authorized by the Ethics Committee of Qiqihar Medical College (Qiqihar, China; protocol number: 2021–193). All the data showed in this study were anonymous, therefore, informed consent was waived for this study in compliance with the Declaration of Helsinki. This study retrospectively analyzed the patients' medical records who have PTNB in the Second Affiliated Hospital of Qiqihar Medical College from March 2018 to December 2021. Inclusion criteria: patients who underwent PTNB and were able to provide images and reports. Exclusion criteria: lesions located in non-pulmonary parenchyma such as pleura and mediastinum. A total of 158 patients (age 18–86 years; 83 males and 75 females) were involved; patients were partitioned into two groups by random number table (Fig. 13.1). There were 81 patients in the experimental group (VR navigation combined with ROSE), 42 males and 39 females; 77 patients in the control group (traditional CT-PTNB), 41 males and 36 females; the gender, age, lesion location, comparison of the size of the body part affected by the diseases (measured by the long diameter of the mediastinal window lesion) and puncture length (the length of the coaxial needle entering the body during puncture). They all have no statistical significance ($P > 0.05$), as shown in Table 13.1.

13.2.2 Operation Steps

All patients signed an informed consent form for PTNB before the procedure. Patients did not receive aspirin for more than 7 days and their blood counts and coagulation were within interventional radiology guidelines [6]. Guided by 64 rows of spiral CT scans, an 18G semi-automatic biopsy needle and a 17G coaxial needle were used. During the operation, the VR navigation system was used to assist CT-guided positioning, and the patient breathed calmly for CT scanning, and the scanned data was transmitted to the navigation system synchronously to identify the marked points of the CT image and determine the target area. After correcting the image, the fused image showed a real-time VR fusion navigation mode (Fig. 13.2), and then the best needle route was determined to avoid the interlobar pleura, nerves, blood vessels, and pulmonary vesicles. Under 3D guidance, a 17G coaxial needle was inserted into

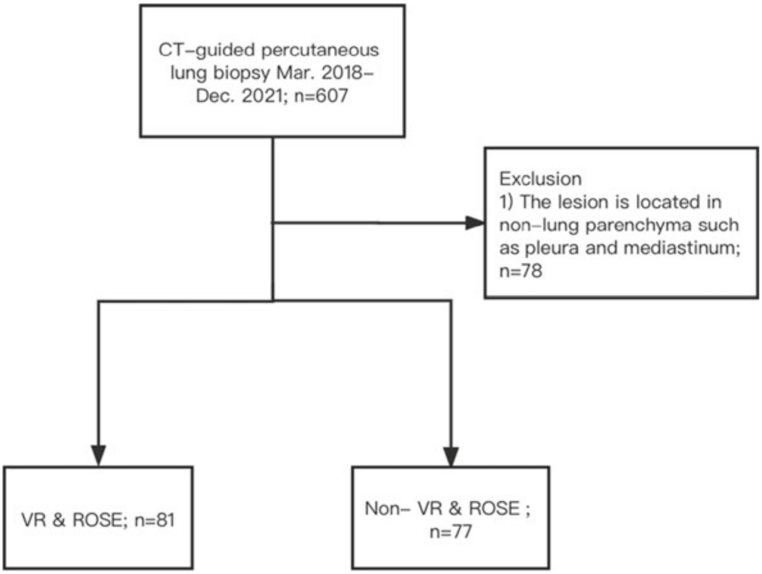


Fig. 13.1 Flow chart of patients enrolled in the present study. (n, number of samples participating in the experiment. VR, virtual reality navigation systems. ROSE, rapid on-site evaluation)

Table 13.1 Demographics and baseline values of the two groups

	Sex, male/female	Age[a] (years)	Nodule distribution		Nodule size[a] (cm)	Distance from nodule to pleura[a] (cm)
			Upper lung	*Lower lung*		
VR & ROSE	41/36	62.71 ± 10.83	43	34	31.10 ± 18.44	18.59 ± 9.93
Non-VR & ROSE	42/39	63.67 ± 10.56	53	28	32.19 ± 16.95	17.31 ± 10.41
χ2- or t-value	0.031[b]	−0.559[c]	4.476[b]		−0.400[c]	0.795[c]
P-value	0.816	0.577	0.345		0.690	0.428

a. Data are expressed as the mean ± standard deviation; b. t-value; c. χ2-value

the border of the lesion, and the 18G semi-automatic biopsy needle was replaced for biopsy. On the premise of no loss of tissue specimens, part of the imprints was applied on the glass sheet, fixed in 95% ethanol solution, and stained with rapid hematoxylin–eosin (Hematoxylin–eosin, HE). If the nuclear heterogeneous cells are observed under the microscope (Fig. 13.3), stop the operation, otherwise re-biopsy through the coaxial needle, until qualified, the comprehensive clinical information will be read immediately. The tissue was put into a formalin-fixed solution and sent to the pathology department for pathological diagnosis.

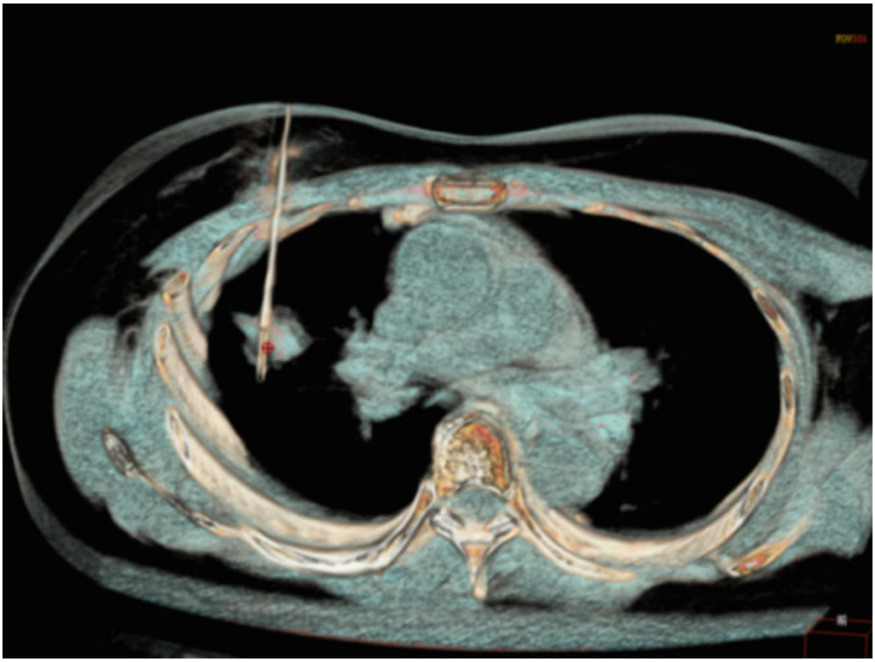
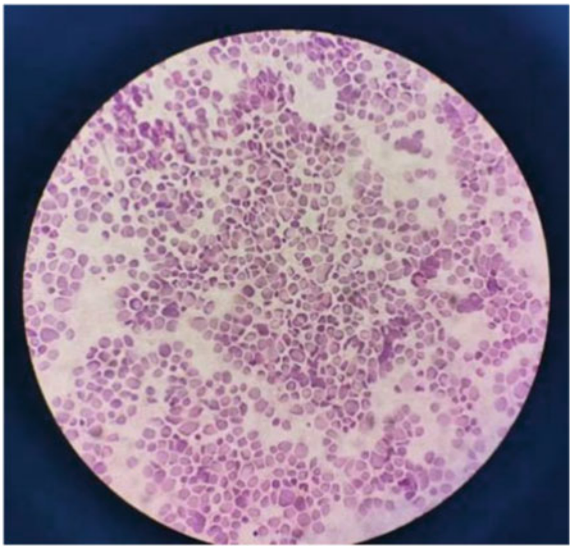


Fig. 13.2 VR navigation system assists in real-time puncture image, and the red dot is the target marking position

Fig. 13.3 Microscopic observation of nuclear heterogeneous cells



13.2.3 Statistical Methods

The measurement data of normal distribution are processed by SPSS25.0 statistical software, and the mean ± standard deviation ($\overline{x} \pm s$) table is used. The counting data is expressed in the number of examples. The age, lesion diameter (upper and middle lobe of the upper lung, the lower lobe of the lower lung), and puncture length between groups were compared by independent sample t-test. The sex, location of focus, and incidence of complications between the two groups were compared by chi-square test, $P < 0.05$ was regarded as a statistically significant difference.

13.3 Results

In this study, there were no major complications in both groups, including bleeding in control group'21 patients and 11 in the experimental group, pneumothorax in 12 participants in the control group, and 5 patients in the magnetic conductivity group. The incidence of bleeding [13.58% (11/81) vs. 27.27% (21/77), $\chi2 = 4.582$, $P = 0.032$] and pneumothorax [6.17% (5/81) vs. 15.58% (12/77), $\chi2 = 4.916$, $P = 0.027$] was significantly reduced in all patients in the experimental group in comparison with the control group, as shown in Table 13.2. At the same time, the bleeding in both groups can be stopped and pneumothorax can be absorbed by itself, and there are no follow-up hospitalized patients due to puncture complications.

In this study, there were no serious symptoms like air embolism. In this study, 3 patients in the control group needed secondary biopsies, while no patients in the experimental group underwent secondary biopsies. The secondary biopsy rate of the control group was 3.90% (3/77), and that of the experimental group was 0% (0/81). There were no statistical differences in the second biopsy between the two groups ($\chi2 = 3.217$, $P = 0.073$), as shown in Table 13.2.

Table 13.2 Comparison of complications and the rate of secondary biopsy between the two groups of patients

	Complications		The rate of secondary biopsy
	Hemoptysis	Pneumothorax	
VR & ROSE	21 (27.27)	12 (15.58)	3 (3.90)
Non-VR & ROSE	11 (13.58)	5 (6.17)	0
$\chi2$-value	4.582	4.916	3.217
P-value	0.032	0.027	0.073

VR, virtual reality navigation systems. ROSE, rapid on-site evaluation

13.4 Discussion

CT-guided percutaneous lung aspiration biopsy has been widely applied in clinical diagnosis of lung diseases, however, as a blinded operation, CTNB has many drawbacks. The smaller the lesion, the deeper the location, and the more complex the anatomy, all result in more frequent needle tract adjustments. However, repeated lung punctures can lead to various complications, and there is also a certain probability that a second biopsy will be required due to insufficient samples obtained from the puncture, causing extra injury to the patient. To reduce the adverse effects of blind puncture, the image navigation-assisted positioning puncture system comes into being, which mainly composed of spatial positioning systems, computing and corresponding data processing, and image processing software [7]. Puncture surgery navigation systems are mainly used in fields like head, neurosurgery, orthopedics, and more. Because the thoracic surgery navigation technology is still in the early research stage with electromagnetic navigation, it has technical shortcomings such as the puncture needle end wire affecting the operation, a bit long preparation time, and may be subject to magnetic interference. Electromagnetic navigation still cannot provide accurate depth and real-time monitoring of the lung puncture path information, nor can it send feedback on the margin of error caused by the needle tip entering the lung tissue and cannot resolve the margin of error when puncturing on account of patient's respiratory motion [7]. The key to accurate lung puncture lies in quickly tracking organ displacement, and deformation during lung puncture and finding the best time to puncture.

Virtual Reality (VR) is an advanced computer human–computer interface that has been developed in recent years and is characterized by conceptualization, interactivity and immersion. VR technology has been widely used in the modern biomedical field and has had a huge and far-reaching impact on the development of medical care. With the combination of VR technology and recently developed surgical technologies (imaging, navigation, etc.), VR technology is playing an increasingly important role in disease diagnosis, surgery, and medical teaching. In this study, VR navigation technology was used to monitor the puncture procedure in real-time, combined with spatial positioning, to accurately grasp the spatial alignment between the surgical site and the puncture needle, to determine its anatomical structure, and to adjust the depth and angle of the needle based on the patient's respiratory motion, to facilitate the precise operation of the lung lesion. This approach not only ensures a high degree of accuracy, but also avoids electromagnetic interference and can be used in all areas of biopsy guidance.

The VR navigation system includes 2 main key functional modules: (1) image acquisition and reconstruction: image acquisition and multi-directional reconstruction according to the standard scanning method, forming a three-dimensional data field, which is used as a data source to simulate the implementation of the navigation interface in the CT surgical navigation system during surgery. In addition, the original acquisition image and the 3D image can be used to plan the puncture according to the surgical plan and mark the target area to ensure the efficacy and safety of the surgery. (2) location: the system is used to monitor the position of the surgical tool relative to the human body, including the direction and depth of puncturing, and to match the actual coordinate system of the patient with the spatial scale of the preoperative scan image, and to guide the doctor's puncture operation through the virtual 3D VR image. The VR technology inputs the patient's preoperative imaging data (e.g., CT, MRI) into the working system for processing, analyzing, and integrating to form objective and detailed 3D simulated images, and the fitted 3D images can be highly compatible with the actual anatomical position during surgery or even completely overlapped [8]. In summary, CT scan is performed during the surgery when the patient is breathing calmly, and the acquired scan trapped image data is input into VR navigation computer system to reconstruct and form 3D visualized images, which can outline the tumor shape and size, and observe the spatial location relationship between the tumor and adjacent important structures such as nerves, blood vessels, intestinal tubes, etc., design the surgical planning and needle route according to the images, pay attention to the puncture route to avoid important tissues. Design the surgical planning and needle route according to the image, pay attention to the puncture route to avoid the important tissues, identify the marker points of CT image, determine the target area, and fuse the image after correction to appear the real-time VR fusion navigation.

With the help of a VR real-time accurate lung puncture navigation system, we can plan the accurate and safe puncture path, calculate the position error caused by the patient's breathing in real-time, predict the puncture risk of lung biopsy, and accurately simulate the needle tip position on the image in real-time during the puncture process, effectively improve the accuracy of the puncture needle to reach the target point of the lesion, thus to avoid important blood vessels and organs, and to reduce the occurrence of surgical complications. It also greatly shortens the puncture time, reduces the radiation dose suffered by patients and doctors, and improves the efficiency of imaging equipment use.

CTNB being an invasive operation, obtaining a qualified and enough histological specimen is essential to puncture biopsy. In general, the more specimens, the higher the positive rate. But complications may also increase, so quality assessment after obtaining the specimen is especially important. ROSE is an immediate diagnostic pathology procedure that allows a rapid evaluation of the adequacy and accuracy of material obtained during bronchoscopy within 2–3 min using rapid staining of smears, studies written by Wang et al. [9] show that in pulmonary nodule punctures $\leq$2 cm in diameter, the application of ROSE can reduce both the drawbacks due to the inadequacy of biopsy pathology specimens and the number of puncture biopsies. Meanwhile, the accuracy of the pathology results will be improved.

Because percutaneous lung aspiration biopsy is an invasive procedure, postoperative complications are inevitable. According to studies, hemorrhage and pneumothorax are the most frequent complications of percutaneous lung biopsy, but the reports on its incidence are inconsistent, ranging from 7 to 30% for bleeding [10] and about 20% for pneumothorax [11]. In this study, the puncture was successful in both groups, and the incidence of hemorrhage and pneumothorax in the VR navigation group was significantly lower than that in the control group, and there were no severe complications such as air embolism. However, further analysis showed that most of these symptoms such as bleeding or pneumothorax were mild, and only in rare cases did they require further special treatment such as thoracentesis and drainage, and in most cases, no special treatment was needed after surgery until the patient coughed up the bleeding mass or absorbed it on his own. Therefore, although there is a significant difference in the overall complication rate between the two, the impact of the difference in clinical practice is limited. There was no need for a second biopsy in the VR group, and 3 patients in the control group had a second biopsy following the first puncture because the specimen was too small to be diagnosed. However, there was no significant difference in the secondary puncture rate between the two groups, which may be due to the small total sample size in this study.

There are some limitations in this study. First, this is a retrospective study, and some data might not be complete. Secondly, there is insufficient sample size, and it is necessary to conduct multi-dose clinical studies with large samples in the event of a bias.

In conclusion, VR navigation system-assisted CT-guided puncture biopsy combined with ROSE is significantly better than conventional CT-guided lung puncture biopsy in terms of safety and the degree of harm to patients by reducing the incidence of complications, improving the diagnostic rate, some reduction in secondary biopsy rate, lessening the number of CT scans while cutting down the cost and the harm caused to patients by radiation. With the update and diversification of VR technology, its use will become more convenient and accessible. Therefore, as a new technology, VR navigation has a vast prospect for lung nodule localization, biopsy, and minimally invasive interventional procedures.

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