

Phase II Clinical Study of Three-Dimensional Printed Coplanar Template Combined with CT-Guided Percutaneous Core Needle Biopsy of Pulmonary Nodules in Elderly Patients

Wangti Xie¹, Yu Wu², Xiaoshan Cheng³, Jianbing Hu¹, Fang Wen¹, Jia Xiao¹, Pan Luo¹, Yuqi Su¹, Xiang Yao¹, Jianlong Fang¹, Grong Dan¹, Xianggan Huang⁴, Dunqian Liu⁵, Jie Weng^{1*}

¹Oncology Department of Yueyang Central Hospital, Yueyang, China

²Radiotherapy Center, Yueyang Central Hospital, Yueyang, China

³Respiratory Department of Yueyang Central Hospital, Yueyang, China

⁴Imaging Department of Yueyang Central Hospital, Yueyang, China

⁵Thoracic Surgery Department of Yueyang Central Hospital, Yueyang, China

Email: *3173720582@qq.com

How to cite this paper: Xie, W.T., Wu, Y., Cheng, X.S., Hu, J.B., Wen, F., Xiao, J., Luo, P., Su, Y.Q., Yao, X., Fang, J.L., Dan, G., Huang, X.G., Liu, D.Q. and Weng, J. (2024) Phase II Clinical Study of Three-Dimensional Printed Coplanar Template Combined with CT-Guided Percutaneous Core Needle Biopsy of Pulmonary Nodules in Elderly Patients. *Journal of Biosciences and Medicines*, 12, 325-336.

<https://doi.org/10.4236/jbm.2024.127030>

Received: June 24, 2024

Accepted: July 28, 2024

Published: July 31, 2024

Copyright © 2024 by author(s) and Scientific Research Publishing Inc.

This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

<http://creativecommons.org/licenses/by/4.0/>

<http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

Background: As the population age structure gradually ages, more and more elderly people were found to have pulmonary nodules during physical examinations. Most elderly people had underlying diseases such as heart, lung, brain and blood vessels and cannot tolerate surgery. Computed tomography (CT)-guided percutaneous core needle biopsy (CNB) was the first choice for pathological diagnosis and subsequent targeted drugs, immune drugs or ablation treatment. CT-guided percutaneous CNB requires clinicians with rich CNB experience to ensure high CNB accuracy, but it was easy to cause complications such as pneumothorax and hemorrhage. Three-dimensional (3D) printing coplanar template (PCT) combined with CT-guided percutaneous pulmonary CNB biopsy has been used in clinical practice, but there was no prospective, randomized controlled study. **Methods:** Elderly patients with lung nodules admitted to the Department of Oncology of our hospital from January 2019 to January 2023 were selected. A total of 225 elderly patients were screened, and 30 patients were included after screening. They were randomly divided into experimental group (Group A: 30 cases) and control group (Group B: 30 cases). Group A was given 3D-PCT combined with CT-guided percutaneous pulmonary CNB biopsy, Group B underwent CT-guided percutaneous pulmonary CNB. The primary outcome measure of this study was the accuracy of diagnostic CNB, and the secondary outcome

measures were CNB time, number of CNB needles, number of pathological tissues and complications. **Results:** The diagnostic accuracy of group A and group B was 96.67% and 76.67%, respectively ($P = 0.026$). There were statistical differences between group A and group B in average CNB time ($P = 0.001$), number of CNB (1 vs more than 1, $P = 0.029$), and pathological tissue obtained by CNB (3 vs 1, $P = 0.040$). There was no statistical difference in the incidence of pneumothorax and hemorrhage between the two groups ($P > 0.05$). **Conclusions:** 3D-PCT combined with CT-guided percutaneous CNB can improve the puncture accuracy of elderly patients, shorten the puncture time, reduce the number of punctures, and increase the amount of puncture pathological tissue, without increasing pneumothorax and hemorrhage complications. We look forward to verifying this in a phase III randomized controlled clinical study.

Keywords

Pulmonary Nodules, Elderly patients, Three-Dimensional (3D), Printed Coplanar Template (PCT), Core Needle Biopsy (CNB), Computed Tomography (CT)

1. Introduction

Lung cancer is the most common malignant tumor in the world, and ranks first in the incidence and mortality of malignant tumors [1]. The active promotion of lung cancer screening programs has significantly increased the detection rate of lung nodules. Pulmonary nodules refer to round or irregular lesions in the lungs with a diameter of ≤ 3 cm. Imaging shows shadows with increased density. They may be single or multiple, with clear or unclear boundaries [2] [3]. When a pulmonary nodule is suspected to be malignant, pathological examination of lung tissue biopsy can provide a basis for the qualitative diagnosis of the pulmonary nodules and the formulation of treatment strategies, There are three feasible methods, including percutaneous biopsy under the guidance of transthoracic computed tomography (CT), endobronchial biopsy and video-assisted thoracoscopic biopsy [4]-[6]. Transthoracic CT-guided biopsy is conducive to the occurrence of peripheral nodules and can prevent the sacrifice of normal lung tissue during liver lobectomy. With the aging of the global population and the continuous extension of life expectancy, some elderly patients with one or more chronic underlying diseases or complex medication conditions are unwilling to undergo surgery or cannot undergo surgery. CT-guided pulmonary nodule core needle biopsy (CNB) is often used to clarify the pathological diagnosis, and then local minimally invasive treatment is performed, which is prone to complications such as hemorrhage and pneumothorax. For such patients, lung nodule biopsy faces great challenges. With the continuous development of medical technology, especially the widespread application of three-dimensional (3D)

printing technology in clinical practice, the current 3D printed coplanar template (PCT) is inexpensive and has been initially used in the diagnosis and treatment of pulmonary nodules. This study aims to explore the accuracy and safety of 3D-PCT combined with CT-guided percutaneous pulmonary nodule CNB technology.

2. Method

2.1. Study Subjects

Elderly patients with lung nodules admitted to the Department of Oncology of our hospital from January 2019 to January 2023 were selected. Inclusion criteria: 1) Pulmonary nodules ≤ 8 mm and ≥ 30 mm in diameter. 2) age ≥ 65 years. 3) All patients underwent positron emission tomography(PET) CT, chest enhanced CT, and artificial intelligence-assisted system diagnosis, and were highly suspected of malignancy. 4) Those who were unwilling or unable to undergo surgery. 5) platelet count $\geq 60 \times 10^9/L$ and coagulation function was basically normal. 6) Karnofsky performance status (KPS score) ≥ 60 points. Exclusion criteria: 1) Patients with aggravated pulmonary infection (pulmonary CT showed pulmonary inflammation, C-reactive protein and procalcitonin were significantly increased). 2) Patients with hemorrhage tendency or receiving anticoagulant treatment, and had a recent history of hemorrhage of more than 2 mL. 3) patients with the following aggravated extrapulmonary diseases [7]: a) Pulmonary artery pressure > 50 mmHg; b) Pro-BNP > 500 pg/mL; c) Any increase in myocardial protein, creatinine, myoglobin, and troponin > 2 items; d) malignant arrhythmia or ventricular rate > 100 beats/min; e) cardiovascular and cerebrovascular stenosis area $> 70\%$; f) status dementia severity score > 3 points; g) systolic blood pressure > 180 mmHg; h) hemoglobin < 60 g/L; i) serum potassium > 5.5 mmol/L; j) D-Dimer > 0.5 mg/L; k) Creatinine > 200 $\mu\text{mol/L}$. 4) Pulmonary artery and deep vein thrombosis. 5) Patients with autoimmune diseases and concurrent anti-immune treatment: rheumatoid arthritis, human immunodeficiency virus/acquired immunodeficiency syndrome, etc. 6) Patients with poorly controlled hypertension and diabetes. A total of 225 elderly patients were screened, according to inclusion and exclusion criteria, and 60 patients were included after screening. They were randomly divided into experimental group (Group A: 30 cases) and control group (Group B: 30 cases) according to the case follow-up system of the oncology department of our hospital.

2.2. Grouping and Methods

This study protocol was registered with the China Clinical Trial Registration Center (ChiCTR1900025625, Registration Date: 20190903) and approved by the Medical Ethics Committee of Yueyang Central Hospital (20190902). According to the Declaration of Helsinki (revised in 2013). All patients were informed of the indications, complications, and emergency measures of pulmonary nodule CNB before treatment and signed informed consent. The biopsy was performed

by four oncologists (Weng Jie with 28 years of experience, Fang Jianlong with 30 years of experience, Xie Wangti with 10 years of experience, and Yao Xiang with 4 years of experience, all had the latest professional certificates). The patients were randomly divided into experimental group A ($n = 30$) and control group B ($n = 30$). The detailed operation process is shown in **Figure 1**. Group A was given 3D-PCT combined with CT-guided percutaneous pulmonary nodule CNB (3D-PCT: Key Laboratory of Lung Cancer Prevention and Treatment, Yueyang, Hunan, China; 17G coaxial CNB needle: C1816B, Bard Medical Devices, USA, 18-gauge core biopsy needle: MN1816, Bard Medical Devices, USA). Group B underwent CT-guided percutaneous pulmonary nodule CNB. If adverse events such as massive hemorrhage and massive pneumothorax occurred, the CNB was stopped immediately and first aid was performed on the spot. Three pathological tissues were obtained from patients in both groups as much as possible. If life-threatening emergencies such as pneumothorax, hemorrhage and shock occurred, one tissue could be obtained. After the operation, the patient was transported back to the ward on a stretcher and lay still for 4 hours.

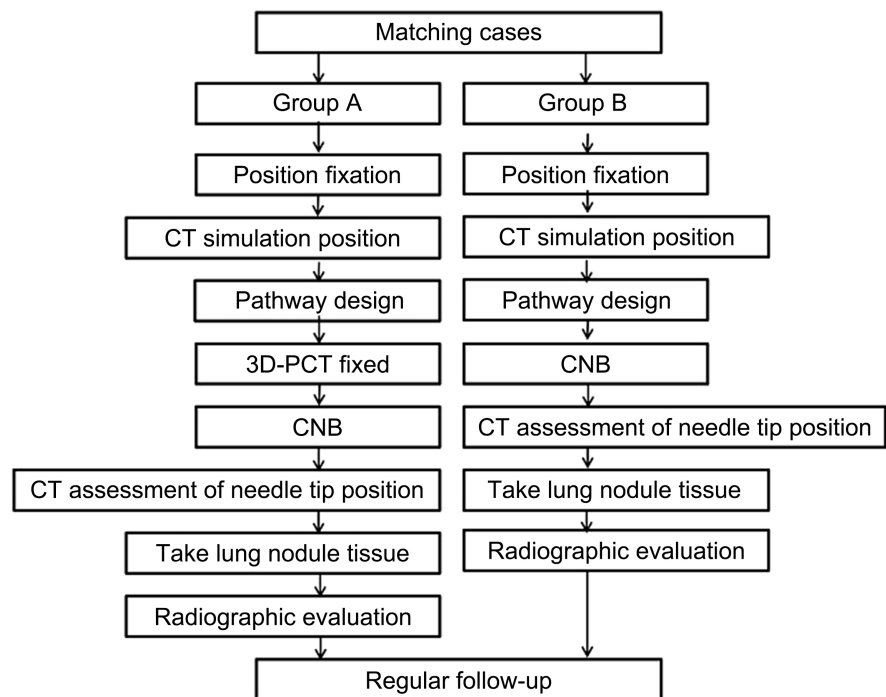


Figure 1. Flow chart of biopsy procedure. Note: Group A used 3D-PCT, Group B used manual puncture.

2.3. Observation Indicators

The primary outcome measure of this study was the accuracy of diagnostic CNB (the success of puncture biopsy depends on pathological examination. The biopsy specimens were double blind diagnosed by two experienced chest pathologists from the pathology department, and histopathological findings reported malignant tumors or non-specific inflammation. Non specific inflammatory

cases showed no significant changes in nodules during follow-up, indicating successful biopsy. The pathological diagnosis report shows that specimens with insufficient tissue or cells are considered undiagnosed cases, suspicious or uncertain cases, and cases that cannot be clearly diagnosed are also considered undiagnosed cases. Therefore, negative biopsy specimens indicate failed puncture biopsy), and the secondary outcome measures were CNB time (it was defined as the time from the CNB needle entering the skin to the successful CNB and removal of the CNB needle), the number of needle insertions (it was defined as the number of times the CNB needle entered the skin), the number of pathological tissues (it was defined as the total number of pathological tissues punctured), and complications. Patient data were collected based on the registration and follow-up system of our department.

2.4. Statistical Analysis

Age, sex, smoking, lung function test results, mean maximum plane diameter, body position, nodule location, needle path length between nodule and skin, CNB time, number of CNB, amount of sampled tissue, postoperative complications (including pneumothorax, hemorrhage, air or pulmonary embolism, anesthesia allergy) and diagnostic accuracy of each group were recorded. The diagnostic accuracy and complications of lesions in the two groups were compared. Biopsy results were considered true positive if the pathological findings were consistent with the patients primary malignancy or if the patients clinical course was consistent with malignancy. Otherwise, a positive biopsy result was considered false positive. A true negative result was considered true negative if the pathological results were benign, a thin-section chest CT scan was repeated 3 months later, and the lesion remained stable or regressed during the year of follow-up. False negative results were considered to be confirmed by further tissue demonstration of malignancy or confirmation of a clearly malignant clinical course. All statistical analyses were performed using SPSS 22.0. Student's t-test or the Mann-Whitney U test was used for continuous data, depending on the distribution of the data. Fisher's exact test or the chi-square test was used for binary data depending on the size of the sample. The significance threshold of the pvalue was set at < 0.05 .

3. Results

The patient characteristics are listed in **Table 1**. The two groups had the same baseline characteristics. The final biopsy results are listed in **Table 2**. Among the patients in Group A, 1 was a false negative, and the remaining 29 were true positive or true negative lesions. The biopsy results of 1 patient showed neutrophils and lymphocytes, and sputum culture and tuberculosis antibodies were negative. After 2 weeks of oral moxifloxacin treatment, the left upper lobe nodule was re-examined without significant changes. After 3 months, the chest CT showed that the nodule had grown, and another biopsy indicated pulmonary tuberculo-

sis. Two patients in group B were false negatives. One of them had lung tissue and neutrophils in the biopsy. After 2 weeks of anti-inflammatory treatment, chest CT scan showed that the nodules in the left lower lobe disappeared, which was considered pulmonary inflammation. Another patient had a biopsy again, which showed lung adenocarcinoma. The diagnostic accuracy of group A (N = 30) and group B (N = 30) was 96.67% and 76.67%, respectively (P = 0.026).

Table 1. Patient characteristics.

	Group A (n = 30)	Group B (n = 30)	P-value
Patient variables			
Age (mean \pm SD)	72.4 \pm 5.9	72.6 \pm 5.5	0.433
Sex			
Male	22	19	0.405
Female	8	11	
Smoking (Y/N)			
Y	13	15	0.605
N	17	15	
Lung function test			
Normal	6	4	0.696
Mild to moderate grade	16	19	
Severe grade	8	7	
Location of the lesions			
Upper/Middle lobes	21	20	0.781
Lower lobes	9	10	
Mean diameter of the target lesion (mm) (mean \pm SD)	16.1 \pm 4.45	22.6 \pm 5.17	0.117

Table 2. Diagnostic accuracy.

Result	Group A (n = 30)	Group B (n = 30)	P-value
True positive	29	23	
True negative	1	7	
False positive	0	0	
False negative	1	2	
Accuracy	96.67%	76.67%	0.026

The complications in the two groups were pneumothorax (6 cases in group A and 10 cases in group B, $P = 0.191$), and no interventional treatment was required. The second most common complication was pulmonary hemorrhage (2 cases in group A and 7 cases in group B, $P = 0.073$). There was one case of hemothorax in group B, which improved after closed drainage, and the rest stopped hemorrhage spontaneously. One patient in group B went into shock after one CNB. After emergency treatment, he recovered and returned to the ward. One week later, a chest wall infusion port was implanted. After lidocaine local anesthesia, he went into shock again. The skin test was positive, and lidocaine allergy was considered likely. No patient had surgery due to needle seeding, air embolism, or death. There were statistical differences between group A and group B in average CNB time ($P = 0.001$), number of CNB (1 vs. more than 1, $P = 0.029$), and pathological tissue obtained by CNB (3 vs 1, $P = 0.040$). There was no statistically significant difference in the CNB needle length and patient position between the two groups ($P > 0.05$) (**Table 3**).

Table 3. Two groups of surgical indicators and complications.

	Group A (n = 30)	Group B (n = 30)	P-value
Distance from subcutaneous (mm) (mean \pm SD)	66.3 \pm 15.2	63.6 \pm 12.8	0.051
Patient positions			
Supine	15	12	0.730
Prone	12	14	
Lateral decubitus	3	4	
CNB time (m) (mean \pm SD)	4.9 \pm 2.5	5.8 \pm 3.5	0.001
Number of sampling			
1	27	20	0.029
>1	3	10	
Number of CNB tissues			
3	28	22	0.040
1	2	8	
Complications			
Pneumothorax	6	10	0.191
Pulmonary hemorrhage	2	7	0.073
Anesthesia accident	0	1	1.000

4. Discussion

With the gradual promotion of early screening for lung cancer, more and more lung nodules have been discovered. Currently, commonly used lung nodule biopsy techniques include CT-guided percutaneous biopsy, endobronchial biopsy [8]-[11] and video-assisted thoracoscopic biopsy [12] [13]. For elderly patients, most of them have underlying diseases such as lung or cardiovascular and cerebrovascular diseases and are difficult to tolerate bronchoscopic ultrasound-guided biopsy and video-assisted thoracoscopic biopsy. CT-guided percutaneous lung nodule biopsy has been used in clinical practice for many years, with a diagnostic accuracy of 76.0% to 93.4% [3] [14]. Despite the high diagnostic accuracy, this technology still has some unavoidable disadvantages. First, the angle of the CNB needle is manually determined under the guidance of CT scans, which depends largely on the experience of the operator and takes a long time to operate. In addition, CT scanning inevitably leads to radiation exposure. In addition, the biopsy needle usually needs to be repeatedly adjusted before accurate insertion, which also increases the operation time and radiation dose. Repeated insertion attempts are also the reason for the high incidence of complications such as pneumothorax and pulmonary hemorrhage [15] [16]. 3D printing technology has been widely used in various fields of medicine [17]. At present, the 3D printed templates used in clinical practice are divided into 3D-PCT and 3D printed navigation template (PNT). Coplanar template can be mass-produced and are inexpensive. Navigation template need to be modeled on a computer through CT images and then transferred to a 3D printer for printing, which is time-consuming and expensive. Our team uses 3D-PCT combined with CT-guided percutaneous lung nodule biopsy. The template bracket is fixed to the edge of the CT bed. CT positioning determines the needle insertion point and needle insertion route. The needle insertion angle can be adjusted at any time and the needle insertion angle is monitored in real time. The CNB needle uses a 19G coaxial needle. We know that the lower lobe lung has a large degree of mobility. For lower lobe lung nodules, take a deep breath and hold your breath during CT positioning. The breathing stage during biopsy is close to the breathing stage during the initial CT scan.

Studies have shown that 3D-PNT have acceptable accuracy and safety for locating peripheral pulmonary nodules [18]-[20], which makes it possible to apply 3D-PNT to percutaneous CNB of pulmonary nodules. Ji *et al.* [21] reported the application of this technology. Since no control group was set up, their results were only compared with previous literature. Wang *et al.* [22] retrospectively analyzed 3D-PCT combined with CT-guided percutaneous pulmonary nodule CNB. The diagnostic accuracy of the 3D-PCT group (95.2%) was significantly higher than that of the control group (87.7%) ($P > 0.05$). There was no significant difference in the incidence of pneumothorax (17.3% vs 18.9%) and pulmonary hemorrhage (7.7% vs 9.4%) between the two groups ($P > 0.05$). There is no difference in the complications between the two groups. Our team has applied for a research and development plan for an artificial intelligence percutaneous

lung puncture surgery navigation system. This study was a prospective, single-center, randomized controlled clinical study. All the patients included were elderly patients, and absolute contraindications to CNB were strictly excluded. The diagnostic accuracy of group A and group B (96.67%) was significantly higher than that of the control group (76.67%) ($P > 0.05$), which was consistent with the conclusion reported by Wang *et al.* [22].

In this study, Group A was superior to Group B in average CNB time ($P = 0.001$), number of CNB (1 vs. more than 1, $P = 0.029$), and pathological tissue obtained by CNB (3 vs. 1, $P = 0.040$). Reducing the CNB time and number of times can reduce the incidence of complications such as pneumothorax and hemorrhage. Obtaining more pathological tissues can provide better support for subsequent genetic testing, PD-L1 testing, etc.

CT-guided percutaneous CNB was a relatively safe method, but it was not without risks [23]-[27]. The mortality rate was 0.01% to 0.15%, and the causes of death include hemorrhage, cardiac arrest, air embolism, etc. Complications include pneumothorax, pulmonary hemorrhage, hemoptysis, and needle tract implantation. Pneumothorax is the most common, with an incidence of 15% - 51.8%, of which 1% - 14.2% require the placement of a closed chest drainage tube. Hemorrhage ranks second, including pulmonary hemorrhage, hemoptysis, and hemothorax, with an incidence of 1% - 27%, of which the incidence of hemoptysis was about 1.25% - 23%, and 17.8% (11.8% - 23.8%) of patients require blood transfusion; hemothorax was 0.20% - 0.92%. Needle tract implantation was very rare, with an incidence of 0.012% - 0.061%. The incidence of air embolism was 0.02% - 1.8%, with a high mortality rate and high disability rate. In this study, there was no difference in the incidence of pneumothorax (20.00% vs 33.33%) and hemorrhage rate (6.67% vs 23.33%) between group A and group B.

5. Conclusion

3D-PCT combined with CT-guided percutaneous CNB can improve the puncture accuracy of elderly patients, shorten the puncture time, reduce the number of punctures, and increase the amount of puncture pathological tissue, without increasing pneumothorax and hemorrhage complications. We look forward to verifying this in a phase III randomized controlled clinical study. Although all operations in this study were performed by 4 experienced oncologists and 1 radiologist, the limitations of our study were the elderly population, single center, and insufficient sample size, which may have led to some defects in the study results. Currently, our unit is conducting a prospective study of 3D-PCT combined with CT-guided percutaneous CNB in cooperation with 5 domestic hospitals, and some questions may be answered in the future.

Acknowledgments

The authors thank the respiratory physicians, radiologists, and pathologists for their assistance with this study and Dr. Jie Weng for her statistical knowledge and help.

Abbreviations

3D, three-dimensional; PCT, printed coplanar template; PNT, printed navigation template; CNB, core needle biopsy; CT, Computed tomography.

Author's Contribution

In 2019, our hospital established a lung nodule MDT with the following members. Xie Wangti is responsible for designing research plans, implementing research, and writing papers; Wu Yu, Cheng Xiaoshan, Hu Jianbing, Weng jie, Wen Fang, Xiao Jia, Dang Rong, Yao Xiang, Huang Xianggan, and Liu Dunqian are responsible for collecting clinical data, proposing research ideas, providing technical guidance, imaging guidance, and revising papers; Su Yuqi and Fang Jianlong are responsible for literature search and data analysis.

Funding

Hunan Clinical Medical Technology Innovation Guidance Project (2021SK52805), Hunan Clinical Medical Technology Innovation Guidance Project (2021SK52806).

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The study was approved by the Medical Ethics Committee of Yueyang Central Hospital (20190902) on 2019/09/02.

Trial Registration

This study was registered with China Clinical Trial Registration Center (<https://www.chictr.org.cn/>, Identifier: ChiCTR1900025625, Registration Date: 20190903).

Conflicts of Interest

This study was independently conducted by the undersigned author in accordance with the following statement of contribution, and no undue position or financial interest was accepted as a result of conducting the study, thereby re-evaluating the independence of the study. Sex and scientificity are guaranteed.

References

- [1] Siegel, R.L., Miller, K.D. and Jemal, A. (2018) Cancer Statistics, 2018. *CA: A Cancer Journal for Clinicians*, **68**, 7-30. <https://doi.org/10.3322/caac.21442>
- [2] Hur, J., Lee, H., Nam, J.E., Kim, Y.J., Kim, T.H., Choe, K.O., *et al.* (2009) Diagnostic Accuracy of CT Fluoroscopy-Guided Needle Aspiration Biopsy of Ground-Glass Opacity Pulmonary Lesions. *American Journal of Roentgenology*, **192**, 629-634. <https://doi.org/10.2214/ajr.08.1366>

- [3] Choi, S.H., Chae, E.J., Kim, J., Kim, E.Y., Oh, S.Y., Hwang, H.J., *et al.* (2013) Percutaneous CT-Guided Aspiration and Core Biopsy of Pulmonary Nodules Smaller than 1 cm: Analysis of Outcomes of 305 Procedures from a Tertiary Referral Center. *American Journal of Roentgenology*, **201**, 964-970. <https://doi.org/10.2214/ajr.12.10156>
- [4] Zhou, Q.H., Fan, Y.G., Wang, Y., *et al.* (2016) Chinese Guidelines for Classification, Diagnosis and Treatment of Pulmonary Nodules (2016 Edition). *Chinese Journal of Lung Cancer*, **19**, 793-798.
- [5] Lung Cancer Group of Respiratory Branch of Chinese Medical Association (2018) Expert Group of China Lung Cancer Prevention and Treatment Alliance Chinese Expert Consensus on Diagnosis and Treatment of Pulmonary Nodules (2018 Edition). *Chin J Tuberc Respir*, **41**, 763-771.
- [6] Bai, C., Choi, C., Chu, C.M., Anantham, D., Chungman Ho, J., Khan, A.Z., *et al.* (2016) Evaluation of Pulmonary Nodules: Clinical Practice Consensus Guidelines for Asia. *Chest*, **150**, 877-893. <https://doi.org/10.1016/j.chest.2016.02.650>
- [7] Wijesundera, D.N., Pearse, R.M., Shulman, M.A., Abbott, T.E.F., Torres, E., Ambosta, A., *et al.* (2018) Assessment of Functional Capacity before Major Non-Cardiac Surgery: An International, Prospective Cohort Study. *The Lancet*, **391**, 2631-2640. [https://doi.org/10.1016/s0140-6736\(18\)31131-0](https://doi.org/10.1016/s0140-6736(18)31131-0)
- [8] Takai, M., Izumo, T., Chavez, C., Tsuchida, T. and Sasada, S. (2014) Transbronchial Needle Aspiration through a Guide Sheath with Endobronchial Ultrasonography (GS-TBNA) for Peripheral Pulmonary Lesions. *Annals of Thoracic and Cardiovascular Surgery*, **20**, 19-25. <https://doi.org/10.5761/atcs.0a.13-00261>
- [9] Oki, M., Saka, H., Ando, M., Asano, F., Kurimoto, N., Morita, K., *et al.* (2015) Ultrathin Bronchoscopy with Multimodal Devices for Peripheral Pulmonary Lesions. A Randomized Trial. *American Journal of Respiratory and Critical Care Medicine*, **192**, 468-476. <https://doi.org/10.1164/rccm.201502-0205oc>
- [10] Asano, F., Shinagawa, N., Ishida, T., Tsuzuku, A., Tachihara, M., Kanazawa, K., *et al.* (2015) Virtual Bronchoscopic Navigation Improves the Diagnostic Yield of Radial-Endobronchial Ultrasound for Peripheral Pulmonary Lesions with Involved Bronchi on CT. *Internal Medicine*, **54**, 1021-1025. <https://doi.org/10.2169/internalmedicine.54.3497>
- [11] Tang, C.L., Luo, W.Z., Zhong, C.H., *et al.* (2016) Diagnostic Value of Radial Ultrasound Combined with Virtual Navigation Guided Lung Biopsy in Peripheral Pulmonary Nodules. *Chin J Tuberc Respir*, **39**, 38-40.
- [12] Moroga, T., Yamashita, S., Tokuishi, K., Miyawaki, M., Anami, K., Yamamoto, S., *et al.* (2012) Thoracoscopic Segmentectomy with Intraoperative Evaluation of Sentinel Nodes for Stage I Non-Small Cell Lung Cancer. *Annals of Thoracic and Cardiovascular Surgery*, **18**, 89-94. <https://doi.org/10.5761/atcs.0a.11.01726>
- [13] Zhao, Z.R., Lau, R.W. and Ng, C.S. (2016) Hybrid Theatre and Alternative Localization Techniques in Conventional and Single-Port Video-Assisted Thoracoscopic Surgery. *Journal of Thoracic Disease*, **8**, S319-S327.
- [14] Laspas, F., Roussakis, A., Efthimiadou, R., Papaioannou, D., Papadopoulos, S. and Andreou, J. (2008) Percutaneous CT-Guided Fine-Needle Aspiration of Pulmonary Lesions: Results and Complications in 409 Patients. *Journal of Medical Imaging and Radiation Oncology*, **52**, 458-462. <https://doi.org/10.1111/j.1440-1673.2008.01990.x>
- [15] Anzidei, M., Sacconi, B., Fraioli, F., Saba, L., Lucatelli, P., Napoli, A., *et al.* (2015) Development of a Prediction Model and Risk Score for Procedure-Related Complications in Patients Undergoing Percutaneous Computed Tomography-Guided Lung Biopsy. *European Journal of Cardio-Thoracic Surgery*, **48**, e1-e6.

- <https://doi.org/10.1093/ejcts/ezv172>
- [16] Heerink, W.J., de Bock, G.H., de Jonge, G.J., Groen, H.J.M., Vliegenthart, R. and Oudkerk, M. (2016) Complication Rates of CT-Guided Transthoracic Lung Biopsy: Meta-Analysis. *European Radiology*, **27**, 138-148. <https://doi.org/10.1007/s00330-016-4357-8>
- [17] Martelli, N., Serrano, C., van den Brink, H., Pineau, J., Prognon, P., Borget, I., *et al.* (2016) Advantages and Disadvantages of 3-Dimensional Printing in Surgery: A Systematic Review. *Surgery*, **159**, 1485-1500. <https://doi.org/10.1016/j.surg.2015.12.017>
- [18] Zhang, L., Wang, L., Kadeer, X., Zeyao, L., Sun, X., Sun, W., *et al.* (2019) Accuracy of a 3-Dimensionally Printed Navigational Template for Localizing Small Pulmonary Nodules: A Noninferiority Randomized Clinical Trial. *JAMA Surgery*, **154**, 295-303. <https://doi.org/10.1001/jamasurg.2018.4872>
- [19] Zhang, L., Li, M., Li, Z., Kedeer, X., Wang, L., Fan, Z., *et al.* (2017) Three-Dimensional Printing of Navigational Template in Localization of Pulmonary Nodule: A Pilot Study. *The Journal of Thoracic and Cardiovascular Surgery*, **154**, 2113-2119.e7. <https://doi.org/10.1016/j.jtcvs.2017.08.065>
- [20] Sun, W., Zhang, L., Wang, L., Ren, Y., She, Y., Su, H., *et al.* (2019) Three-Dimensionally Printed Template for Percutaneous Localization of Multiple Lung Nodules. *The Annals of Thoracic Surgery*, **108**, 883-888. <https://doi.org/10.1016/j.athoracsur.2019.03.060>
- [21] Wang, J., Ji, Z., Wang, G., Chen, B., Zhang, Y., Zhang, L., *et al.* (2018) Clinical Application of Planar Puncture Template-Assisted Computed Tomography-Guided Percutaneous Biopsy for Small Pulmonary Nodules. *Journal of Cancer Research and Therapeutics*, **14**, 1632-1637. https://doi.org/10.4103/jcrt.jcrt_1017_17
- [22] Wang, H., Ren, T., Chen, P., Luo, G., Wei, N., Tang, Y., *et al.* (2022) Application of 3-Dimensionally Printed Coplanar Template Improves Diagnostic Yield of CT-Guided Percutaneous Core Needle Biopsy for Pulmonary Nodules. *Technology in Cancer Research & Treatment*, **21**. <https://doi.org/10.1177/15330338221089940>
- [23] Yang, J., Liu, Y., Mao, Y., Yuan, J., Yu, W., Cheng, R., *et al.* (2014) Meta-Analysis of CT-Guided Transthoracic Needle Biopsy for the Evaluation of the Ground-Glass Opacity Pulmonary Lesions. *The British Journal of Radiology*, **87**, Article ID: 20140276. <https://doi.org/10.1259/bjr.20140276>
- [24] Wu, C.C., Maher, M.M. and Shepard, J.O. (2011) Complications of CT-Guided Percutaneous Needle Biopsy of the Chest: Prevention and Management. *American Journal of Roentgenology*, **196**, W678-W682. <https://doi.org/10.2214/ajr.10.4659>
- [25] Wiener, R.S., Schwartz, L.M., Woloshin, S. and Welch, H.G. (2011) Population-Based Risk for Complications after Transthoracic Needle Lung Biopsy of a Pulmonary Nodule: An Analysis of Discharge Records. *Annals of Internal Medicine*, **155**, 137-144. <https://doi.org/10.7326/0003-4819-155-3-201108020-00003>
- [26] Yoon, S.H., Park, C.M., Lee, K.H., Lim, K.Y., Suh, Y.J., Im, D.J., *et al.* (2019) Analysis of Complications of Percutaneous Transthoracic Needle Biopsy Using CT-Guidance Modalities in a Multicenter Cohort of 10568 Biopsies. *Korean Journal of Radiology*, **20**, 323-331. <https://doi.org/10.3348/kjr.2018.0064>
- [27] Huang, M., Weng, H., Hsu, S., Hsu, L., Lin, W., Chen, C., *et al.* (2019) Accuracy and Complications of CT-Guided Pulmonary Core Biopsy in Small Nodules: A Single-Center Experience. *Cancer Imaging*, **19**, Article No. 51. <https://doi.org/10.1186/s40644-019-0240-6>