Could concurrent biopsy and microwave ablation be reliable? Concordance between frozen section examination and final pathology in CT-guided biopsy of lung cancer

Zhigang Wei*, Xia Yangb*, Yan Fengc*, Yongmei Konga*, Zhigang Yaod, Jiwei Ma and Xin Ye

*Department of Oncology, The First Affiliated Hospital of Shandong First Medical University & Shandong Provincial Qianfoshan Hospital, Shandong Key Laboratory of Rheumatic Disease and Translational Medicine, Shandong Lung Cancer Institute, Jinan, Shandong, China; bDepartment of Oncology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong, China; cDepartment of Respiratory Medicine, First Hospital of Jiaxing, Jiaxing, Zhejing, China; dDepartment of Pathology, Shandong Provincial Hospital Affiliated to Shandong First Medical University, Jinan, Shandong, China

**CONTACT**

Xin Ye (xyintaian2020@163.com) Department of Oncology, The First Affiliated Hospital of Shandong First Medical University & Shandong Provincial Qianfoshan Hospital, Shandong Key Laboratory of Rheumatic Disease and Translational Medicine, Shandong Lung Cancer Institute, No. 16766, Jingshi Road, Jinan, 250014, Shandong, China

*These authors contributed equally to this work.

**ARTICLE HISTORY**

Received 11 March 2021
Revised 11 June 2021
Accepted 19 June 2021

**KEYWORDS**

Biopsy; diagnostic techniques and procedures; frozen sections; histopathology; lung cancer

**ABSTRACT**

**Purpose:** Microwave ablation combined with concurrent biopsy has been used for lung cancer. Frozen section (FS) diagnosis is an important supplement for the final pathology (FP). Thus, a retrospective study was conducted to evaluate the concordance between FS examination and FP in the computed tomography (CT)-guided biopsy of lung cancer.  

**Materials and methods:** Patients who underwent percutaneous transthoracic needle lung biopsies and were diagnosed using both intraoperative FS examination and FP were retrospectively enrolled. Concordance between FS findings and FP in the diagnosis of malignant lung cancer and the definitive histology types were recorded.  

**Results:** Overall, 163 patients were enrolled. The concordance rate in the diagnosis of malignant tumors was 96.3%. The definitive histology types were concordant between FS examinations and FP in 112 patients (68.7%). Lung cancers undefined with FS but diagnosed as adenocarcinoma with FP were the most common type, observed in 18 patients. The concordance in the histology type was lower for those requiring immunohistochemistry for FP diagnoses (47.3% vs. 79.6%, p < 0.000). Concordance rates differed for the different histology types diagnosed using FP (adenocarcinoma vs. squamous cell carcinoma vs. small-cell lung cancer vs. others, 76.6% vs. 56.2% vs. 69.2% vs. 0.0%, p < 0.000).  

**Conclusions:** FS was inferior to FP in the diagnosis of definitive histology types, but had a high concordance with FP in the diagnosis of malignant lung cancer.

**Introduction**

Lung cancer (LC) remains the leading cause of cancer-related mortality and morbidity in China [1]. Non-small cell lung cancer (NSCLC), accounting for ~85% of lung cancers, is the predominant histology type. The prognosis of these patients is poor because most patients are diagnosed at an advanced stage [1].  

For advanced non-squamous cell lung cancer, the main treatments included targeted therapy on the epidermal growth factor receptor mutations (EGFR) and anaplastic lymphoma kinase (ALK) fusion, immunotherapy, and chemotherapy [2–6]. For those squamous cell lung cancer, the treatments are restricted to immunotherapy and chemotherapy. So the exact classification of NSCLC types is of significance [6]. Computed tomography (CT)-guided percutaneous lung cancer biopsy is the main method for the diagnosis of peripheral LC [7].

As a local control method, irradiation is used widely for NSCLC. Moreover, microwave ablation (MWA) could also be used for the treatment of NSCLC recently [8–11]. For early-stage NSCLC, MWA could be an alternative regimen for patients with contradictions to surgery [8]. MWA plus EGFR-TKIs or chemotherapy also improved the survival of advanced NSCLC [12–14]. In general, the lung cancer biopsy has been conducted before MWA. However, adverse events, such as pulmonary hemorrhage and pneumothorax induced by biopsy delay the conduction of MWA. MWA could reduce the occurrence of pulmonary hemorrhage especially during the procedure of biopsy. So recently the concurrent biopsy and MWA were explored [15,16]. In the previous two studies, a satisfied treatment effect was achieved and the pathology...
diagnosis rate reached 84.18–89.7% [15,16]. However, only 23 and 85 patients were included in those two studies and nearly 16% of patients failed to make the pathology diagnosis. So there is an urgent need to improve the diagnosis rate during the concurrent biopsy and MWA.

Intraoperative frozen section (FS) examination has been widely applied to guide the surgery regimen. Rapid on-site examination (ROSE) during bronchoscopy has been used as a supplement for diagnosis. However, to date, no frozen section examination during the procedure of CT-guided biopsy has been explored. We speculate that the concordance of intraoperative frozen section examination and final pathology (FP) was verified, the concurrent biopsy and MWA could be more reliable. Hence, we conducted this retrospective study to explore the concordance between FS and FP in patients who underwent CT-guided biopsy.

**Materials and methods**

**Inclusion and exclusion criteria**

Patients who have undergone percutaneous transthoracic needle lung biopsies and were diagnosed with both intraoperative FS examination and FP were retrospectively enrolled. Other inclusion criteria were as follows: (1) FP-verified LC, including both NSCLC and small-cell lung cancer (SCLC); (2) nodules located at the lung periphery; (3) no previous local treatments, such as irradiation, thermal ablation, and immunotherapy. The major exclusion criteria were as follows: (1) mixed LC in FP, for example, NSCLC mixed with SCLC; (2) multiple primary cancers in the past five years; (3) FP failed to verify the definitive histology type; and (4) FP verified the diagnosis of benign lesions. The study was approved by the ethics committee of Shandong Provincial Hospital Affiliated to Shandong First Medical University and the First Affiliated Hospital of Shandong First Medical University. Written informed consent was obtained from all enrolled patients.

**Biopsy procedure**

CT-guided percutaneous transthoracic needle lung biopsies is conducted as per the protocol published in our previous report [17]. A 16-gauge or 18-gauge biopsy core needle (PRECISA fine core needle; H.S. Hospital Service S.P.A, Aprilia, Italy) was inserted into the center of the tumor through a coaxial cannula. A biopsy was conducted to obtain four to six specimens from one core needle. One or two tissue samples were used for FS diagnosis. Others were preserved in 10% formalin and cut into 4-μm-thick slices for FP diagnosis.

**Procedure of FS and FP examination**

FS examination was conducted as per the protocol described below:

1. The core lesion area of the specimen was collected. An OCT-embedding agent was used to seal the tissue on the frozen tray with the temperature-controlled between −18 and −30°C. The specimen was cut at a thickness of a single slice (between 4 and 6μm). The flat tissue sheet was attached to the slide and fixed with 95% alcohol immediately. Hematoxylin and eosin (HE) staining was performed before the slice was sealed with neutral gum. In our hospital, the FS IHC is not used for clinical practice. Thereafter, the specimens were observed by the pathologists.

2. FP was performed for pathological diagnosis as follows: The tissues were fixed with 10% formaldehyde solution, followed by gradient alcohol solution for dehydration. The alcohol concentrations used were 70, 85, 95, 100, and 100%, in this order, and the dehydration procedure was maintained for 1–2 h. The tissues were made transparent with xylene thereafter, and the volume of xylene was 5–10 times that of the tissues. Wax immersion was followed, and the temperature of the wax was maintained at 45–50°C for 2 h and 56–58°C for 1 h. Subsequently, the tissue was embedded to make sure it was flat. Following that, an automatic slicing machine was used to slice, and the thickness of the slices was 3–5μm. The wax slices were placed on the slides, and excess water was sucked dry with the filter paper. The slides were then baked-dried on the incubator to remove the wax, and the temperature was controlled at 60–65°C. Finally, HE staining was performed before the pathologist made the diagnosis. Two pathologists participate in the diagnosis of both FS and FP separately.

**Statistical analysis**

The SPSS version 19.0 software (SPSS, Chicago, IL, USA) was used for statistical analyses. The Pearson chi-square test was used to compare the frequencies for categorical variables. Paired independent-sample t-test or one-way analysis of variance was used to compare continuous variables. All tests were two-sided, and a p-value <0.05 was considered significant.

**Results**

**Baseline characteristics**

From 1 June 2018 to 30 May 2019, 163 FP-verified LC patients were retrospectively enrolled. All patients underwent FS examination simultaneously.

The mean age was 66.6 years, ranging from 32 to 90 years. There were 115 (70.6%) male patients, and 102 (62.6%) smokers were enrolled. All patients had an Eastern Cooperative Oncology Group performance score of 0–1. Only five patients with a weight loss ≥5% during the past six months were included.

Overall, 116 (63.0%) tumors were located in the right lung and 129 (70.1%) in the upper and middle lobes. The mean tumor size was 3.9 cm (range 1.0–12.0 cm). The tumor sizes in 166 (90.2%), 116 (63.0%), and 64 (34.8%) patients were
2.0, 3.0, and ≥4.0 cm, respectively. Furthermore, among 23 patients with previous lung diseases, the most common was a chronic obstructive pulmonary disease, followed by pulmonary tuberculosis and interstitial lung disease. The baseline characteristics of the enrolled patients are shown in Table 1.

### Table 1. The baseline characteristics of enrolled patients.

| Characteristic                  | Final pathology number (%) |
|---------------------------------|-----------------------------|
| Gender                          |                             |
| Male                            | 115 (70.6)                  |
| Female                          | 48 (29.4)                   |
| Age                             |                             |
| Mean (range)                    | 66.6 (32–90)                |
| ≥65                             | 99 (60.7)                   |
| <65                             | 64 (39.3)                   |
| Smoking history                 |                             |
| Non-smokers                     | 61 (37.4)                   |
| Smokers                         | 102 (62.6)                  |
| Weight loss                     |                             |
| <5%                             | 158 (96.9)                  |
| ≥5%                             | 5 (3.1)                     |
| ECOG                            |                             |
| 0                               | 5 (3.1)                     |
| 1                               | 158 (96.9)                  |
| Baseline pulmonary disease      |                             |
| No                              | 143 (87.7)                  |
| Yes                             | 20 (12.3)                   |
| Final pathology                 |                             |
| Adenocarcinoma                  | 117 (71.8)                  |
| Squamous cell carcinoma         | 14 (8.6)                    |
| Others                          | 32 (19.6)                   |
| Immunohistochemistry assistance |                             |
| No                              | 29 (52.7)                   |
| Yes                             | 22 (20.4)                   |
| Tumor location                  |                             |
| Right lung                      | 102 (62.6)                  |
| Left lung                       | 61 (37.4)                   |
| Tumor location                  |                             |
| Upper and middle lobe           | 113 (69.3)                  |
| Lower lobe                      | 50 (30.7)                   |
| Tumor size                      |                             |
| Mean (range)                    | 3.9 (1–12)                  |
| <2 cm                           | 17 (10.4)                   |
| ≥2 cm                           | 146 (89.6)                  |
| <3 cm                           | 62 (38.0)                   |
| ≥3 cm                           | 101 (62.0)                  |
| <4 cm                           | 106 (65.0)                  |
| ≥4 cm                           | 57 (35.0)                   |
| Tumor characteristics           |                             |
| Circular shape                  | 57 (35.0)                   |
| Non-circular shape              | 106 (65.0)                  |
| Tumor characteristics           |                             |
| Spicule sign                    | 79 (48.5)                   |
| Non-spicule sign                | 84 (51.5)                   |
| Tumor characteristics—pneumonia |                             |
| Yes                             | 20 (12.3)                   |
| No                              | 143 (87.7)                  |
| Tumor characteristics—vessel adjacent |             |
| Yes                             | 4 (2.5)                     |
| No                              | 159 (97.5)                  |
| Tumor characteristics—inner necrosis |                |
| Yes                             | 7 (4.3)                     |
| No                              | 156 (95.7)                  |

*Others included SCLC and other LC.

### Diagnostic accuracy of frozen section

#### Malignant lung cancer

In total, 158 of 163 patients in the FS group were diagnosed with LC, indicating that the total concordance between FS examination and FP in the diagnosis of malignant LC was 96.3%. FS examination in the other five patients revealed normal pulmonary tissue, while LC was verified using FP examination.

#### Definitive histology type

Regarding the exact pathological diagnosis, adenocarcinoma (ADC), squamous cell carcinoma (SCC), SCLC, others, and benign pulmonary lesions were identified in 92, 19, 14, 33, and 5 patients, respectively, according to the FS examination. The corresponding diagnosis using FP in these patients is shown in Table 2. Diagnosis with FS examination and FP was concordant in 112 patients (68.7%), while the diagnosis was discordant in 51 patients.

The accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of ADC, SCC, SCLC, LC undefined, and normal pulmonary tissue with FS are shown in Table 3. Patients with a diagnosis of ADC in FS examination had the highest sensitivity and PPV. The diagnosis of SCC using FS had the highest specificity, followed by the diagnosis of SCLC. The diagnosis of SCLC had the highest accuracy and NPV.

There were 51 patients with discordance in the diagnosis of the definitive histology type between FS examination and FP. LC which was undefined in FS but was diagnosed as ADC in FP was the most common type, which was observed in 18 patients. LC which was undefined in FS but was diagnosed as SCC in FP was the second most common type, which was observed in 19 patients.

### Table 2. Comparison between frozen section and final pathology.

| Frozen section diagnosis | Benign lesion (n = 0) | ADC | SCC | SCLC | Other | Total (n = 163) |
|--------------------------|-----------------------|-----|-----|------|-------|----------------|
| Benign lesion            | No 0                  | 5 100 | 0 0 | 0 0 | 0 0 | 5 |
| ADC                      | 0 0                  | 85 92.4 | 4 4.3 | 2 2.2 | 1 1.1 | 92 |
| SCC                      | 0 0                  | 1 5.3 | 16 84.2 | 1 5.3 | 1 5.3 | 19 |
| SCLC                     | 0 0                  | 2 14.3 | 1 7.1 | 2 14.3 | 9 64.3 | 14 |
| Other                    | 0 0                  | 18 54.5 | 11 33.3 | 2 6.1 | 2 6.1 | 33 |

ADC: adenocarcinoma; SCC: squamous cell carcinoma; SCLC: small cell lung cancer.

### Table 3. Accuracy of the diagnosis of frozen section.

| Category                  | Accuracy (%) | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|---------------------------|--------------|-----------------|-----------------|---------|---------|
| ADC                       | 79.8         | 76.6            | 86.5            | 92.4    | 63.4    |
| SCC                       | 88.3         | 50.0            | 97.7            | 84.2    | 88.9    |
| SCLC                      | 93.9         | 69.2            | 96.7            | 64.3    | 93.7    |
| Other                     | 76.7         | 22.2            | 79.9            | 6.1     | 94.6    |

PPV: positive predict value; NPV: negative predict value; ADC: adenocarcinoma; SCC: squamous cell carcinoma; SCLC: small cell lung cancer; Other included other LC types and benign lesions.
found in 11 patients. The types of discordance between FS examination and FP are clarified in Supplementary Table 1.

Factors influencing the concordance between FS examination and FP

We further explored the factors that influence the concordance between FS examination and FP. Immunohistochemistry (IHC) in FP was the only factor that affected the concordance between FS examination and FP (benign or malignant). The concordance was lower for cases requiring IHC for the FP diagnoses (47.3 vs. 79.6%, \( p < 0.000 \)). Different histology types in FP also had different concordance rates (ADC vs. SCC vs. SCLC vs. other, 76.6 vs. 56.2 vs. 69.2 vs. 0.0%, \( p < 0.000 \)). Tumors with the characteristic spicule sign tended to have discordance (61.9 vs. 75.9%, \( p = 0.053 \); Table 4).

Adverse events of biopsy

As for the adverse events, pulmonary hemorrhage, pneu-mothorax, intrathoracic bleeding, and pleural effusion were observed in 48 (29.4%), 24 (14.7%), 3 (1.8%), and 1 (0.6%) patient(s), respectively. Chest tube insertions were required in 0, 11, 1, and 1 patient(s), respectively. All patients recovered after the intervention, and no treatment-associated death was identified.

Discussion

To the best of our knowledge, this is the first study to evaluate the concordance between FS examination and FP in the CT-guided biopsy of LC. The concordance in the diagnosis of the malignant pulmonary disease reached as high as 96.3%; however, the consistency in definitive histology was only 68.7%, indicating that FS could be an alternative method for diagnosing malignant LC but not in diagnosing the definitive histology type. The discrepancy was primarily observed in patients who required IHC for diagnostic assistance. Different histology types in FP also predict the discrepancy.

CT-guided biopsy has been used for diagnosis and treatment-associated biomarker selection, especially in advanced stage LC. FS has been widely used during surgery to define the surgical procedure. It is estimated that the concordance rates between FS examination and FP in patients treated with surgery ranged from 87.9 to 100% [17–25]. For those with ground-glass opacity (GGO) or small tumor size, the concordance reduced to 67–89% [26]. Other studies explored concurrent CT-guided biopsy and thermal ablation [15,16]. All these associated studies were similar to our study. Our study showed that the concordance between FS examination and FP in the definitive pathology type was lower than that of surgery mainly because the tumor tissues were small. However, the study verified that in the diagnosis of malignant lung cancer, the FS examination and FP had high concordance, which reached as high as 96.3%, indicating that once the FS examination confirms the malignant tumors, the

| Table 4: The correlation between concordance of frozen section and final pathology and baseline characteristics. |
|---|
| Concordance \((n = 112)\) | Discordance \((n = 51)\) | \( p \)-Value |
| Gender | | | 0.136 |
| Male | 75 (65.2) | 40 (34.8) | |
| Female | 37 (77.1) | 11 (22.9) | 0.723 |
| Age | | | |
| <65 | 45 (70.3) | 19 (29.7) | 0.281 |
| ≥65 | 67 (67.7) | 32 (32.3) | |
| Smoking history | | | 1.000 |
| Non-smokers | 45 (73.8) | 16 (26.2) | |
| Smokers | 67 (65.7) | 35 (34.3) | |
| Weight loss | | | 0.000 |
| ≤5% | 103 (68.7) | 47 (31.3) | 1.000 |
| >5% | 9 (69.2) | 4 (30.8) | |
| ECOG | | | |
| 0 | 3 (60.0) | 2 (40.0) | 0.370 |
| 1 | 109 (69.0) | 49 (31.0) | |
| Baseline pulmonary disease | | | |
| No | 100 (69.9) | 43 (30.1) | |
| Yes | 12 (60.0) | 8 (40.0) | |
| Final pathology | | | <0.001 |
| ADC | 85 (76.6) | 26 (23.4) | |
| SCC | 18 (56.2) | 14 (43.8) | |
| SCLC | 9 (69.2) | 4 (30.8) | |
| Other | 0 (0) | 7 (100.0) | |
| Immunohistochemistry assistance | | | <0.001 |
| No | 86 (79.6) | 22 (20.4) | |
| Yes | 26 (47.3) | 29 (52.7) | |
| Tumor location | | | 0.171 |
| Right lung | 66 (64.1) | 37 (35.9) | |
| Left lung | 8 (88.9) | 1 (11.1) | |
| Tumor location | | | 0.171 |
| Upper and middle lobe | 74 (65.5) | 39 (34.5) | |
| Lower lobe | 38 (76.0) | 12 (24.0) | |
| Tumor size | Mean ± SD | 3.9 ± 2.1 | 3.9 ± 1.7 | 0.903 |
| <2 cm | 12 (70.6) | 5 (29.4) | 0.860 |
| ≥2 cm | 100 (68.5) | 46 (31.5) | |
| <3 cm | 46 (74.2) | 16 (25.8) | 0.237 |
| ≥3 cm | 66 (65.3) | 35 (34.7) | |
| <4 cm | 73 (68.9) | 33 (31.1) | 0.953 |
| ≥4 cm | 39 (68.4) | 18 (31.6) | |
| Tumor characteristics-circular shape | Yes | 38 (66.7) | 19 (33.3) | 0.680 |
| No | 74 (69.8) | 32 (30.2) | |
| Tumor characteristics-spicule sign | Yes | 52 (61.9) | 32 (38.1) | 0.053 |
| No | 60 (75.9) | 19 (24.1) | |
| Tumor characteristics—pneumonia | Yes | 15 (75.0) | 5 (25.0) | 0.517 |
| No | 97 (67.8) | 46 (32.2) | |
| Tumor characteristics—vessel adjacent | Yes | 2 (50.0) | 2 (50.0) | 0.590 |
| No | 110 (69.2) | 49 (30.8) | |
| Tumor characteristics—inner necrosis | Yes | 6 (85.7) | 1 (14.3) | 0.436 |
| No | 106 (67.9) | 50 (32.1) | |

FP would make the definitive pathology type diagnosis undoubtedly. Although concurrent FS biopsy lacks the diagnostic accuracy of FP concerning the histology typing of malignant lung cancers, this capability might less critical when malignant lung cancer is being treated with ablative technology.

Regarding the concordance between FS examination and FP for the exact histology type, SCLC showed the highest concordance, followed by SCC and ADC. Most previous studies explored the correlation between FS findings and FP in patients with small pulmonary lesions or peripheral GGO. It was shown that patients with invasive ADC showed the
highest concordance between FS examination and FP. Patients with microinvasive ADC and ADC in situ often had FS deferrals and FS errors [27].

IHC plays an important role in distinguishing ADC compared with its role in distinguishing other histology types, especially SCLC and SCC. In this study, we confirmed that IHC addition and histology types in FP were the factors contributing to the discordance between FS examination and FP. According to previous studies, several factors also led to the discordance between FS examination and FP [27]. The presence or absence of histologic patterns also induces a discrepancy. The highest accuracy rate was for the acinar pattern (89%), followed by solid (84%), lepidic (80%), papillary (72%), and micropapillary (67%). Sampling error plus interpretation error also affected the discrepancy [25,26].

The addition of FS did not influence adverse events. Pulmonary hemorrhage, pneumothorax, intrathoracic bleeding, and pleural effusion were observed in 48, 24, 3, and 1 patient(s), respectively. However, only 13 patients (8.0%) needed chest tumor insertion, and no biopsy-associated death was identified, indicating that the addition of FS examination did not influence the complications.

Although FS was inferior to FP in the diagnosis of the definitive histology types, FS and FP had a high concordance in the diagnosis of malignant LC. FS could be used as a guide for immediate ablation during the procedure of concurrent biopsy and MWA.

Acknowledgments

The institutional review board of The First Affiliated Hospital of Shandong First Medical University and Shandong Provincial Hospital Affiliated to Shandong First Medical University has approved this study. Informed consent was obtained from all individuals included in the study. The work has not been published elsewhere. All the authors listed have seen and approved the manuscript that is enclosed, contributed significantly to the work.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

The study was funded by the National Natural Science Foundation of China (Nos. 81901851 and 82072028).

References

[1] Chen W, Zheng R, Baade PD, et al. Cancer statistics in China. CA Cancer J Clin. 2016;66(2):115–132.
[2] Hsu WH, Yang JC, Mok TS, et al. Overview of current systemic management of EGFR-mutant NSCLC. Ann Oncol. 2018;29(Suppl_1):i3–i9.
[3] Tan CS, Kumarakulasinghe NB, Huang YQ, et al. Third generation EGFR TKIs: current data and future directions. Mol Cancer. 2018;17(1):29.
[4] Recondo G, Facchinetti F, Olaussen KA, et al. Making the first move in EGFR-driven or ALK-driven NSCLC: first-generation or next-generation TKI? Nat Rev Clin Oncol. 2018;15(11):694–708.
[5] Arbour KC, Riely GJ. Systemic therapy for locally advanced and metastatic non-small cell lung cancer: a review. JAMA. 2019;322(8):764–774.
[6] Akinleye A, Rasool Z. Immune checkpoint inhibitors of PD-L1 as cancer therapeutics. J Hematol Oncol. 2019;12(1):92.
[7] Stamatis G. Staging of lung cancer: the role of noninvasive, minimally invasive and invasive techniques. Eur Respir J. 2015;46(2):521–531.
[8] Quirk MT, Lee S, Murali N, et al. Alternatives to surgery for early-stage non-small cell lung cancer: thermal ablation. Clin Chest Med. 2020;41(2):197–210.
[9] Stone J, Hartley-Blossom Z, Healey T. The emerging role of percutaneous thermal ablation in the treatment of thoracic malignancies: a review. Surg Technol Int. 2020;36:257–264.
[10] Tafuri BA, Geshta S, Suh R, et al. Lung ablation: indications and techniques. Semin Intervent Radiol. 2019;36(3):163–175.
[11] Moussa AM, Ziv E, Solomon SB, et al. Microwave ablation in primary lung malignancies. Semin Intervent Radiol. 2019;36(4):326–333.
[12] Ni Y, Ye X, Yang X, et al. Microwave ablation for non-small cell lung cancer with synchronous solitary extracranial metastasis. J Cancer Res Clin Oncol. 2020;146(5):1361–1367.
[13] Wei Z, Ye X, Yang X, et al. Efficacy and safety of microwave ablation in the treatment of patients with oligometastatic non-small-cell lung cancer: a retrospective study. Int J Hyperthermia. 2019;36(1):827–834.
[14] Wei Z, Yang X, Ye X, et al. Microwave ablation plus chemotherapy in advanced non-small cell lung cancer: a multicenter, randomized, controlled, phase III clinical trial. Eur Radiol. 2020;30(5):2692–2702.
[15] Liu J, Huang W, Wu Z, et al. The application of computed tomography-guided percutaneous coaxial biopsy combined with microwave ablation for pulmonary tumors. J Cancer Res Ther. 2019;15(4):760–765.
[16] Li W, He XF, Wei YT, et al. [Clinical application of CT-guided radiofrequency ablation combined with biopsy synchronously to multiple small nodules of lung metastatic tumors]. Zhonghua Yi Xue Za Zhi. 2018;98(27):2189–2193.
[17] Yoshida J, Nagai K, Yokose T, et al. Limited resection trial for pulmonary ground-glass opacity nodules: fifty-case experience. J Thorac Cardiovasc Surg. 2005;129(5):991–996.
[18] Yamato Y, Tsuchida M, Watanabe T, et al. Early results of a prospective study of limited resection for bronchioalveolar adenocarcinoma of the lung. Ann Thorac Surg. 2001;71(3):971–974.
[19] Kondo D, Yamada K, Kitayama Y, et al. Peripheral lung adenocarcinomas: 10 mm or less in diameter. Ann Thorac Surg. 2003;76(2):350–355.
[20] Gupta R, McKenna R Jr., Marchevsky AM. Lessons learned from mistakes and deferrals in the frozen section diagnosis of bronchioalveolar carcinoma and well-differentiated pulmonary adenocarcinoma: an evidence-based pathology approach. Am J Clin Pathol. 2008;130(1):11–20.
[21] Watanabe T, Okada A, Imakiire T, et al. Intentional limited resection for small peripheral lung cancer based on intraoperative pathologic exploration. Jpn J Thorac Cardiovasc Surg. 2005;53(1):29–35.
[22] Yamada S, Kohn T. Video-assisted thoracic surgery for pure ground-glass opacities 2 cm or less in diameter. Ann Thorac Surg. 2004;77(6):1911–1915.
[23] Koike T, Togashi K, Shirato T, et al. Limited resection for noninvasive bronchioloalveolar carcinoma diagnosed by intraoperative pathologic examination. Ann Thorac Surg. 2009;88(4):1106–1111.

[24] Xu X, Chung JH, Jheon S, et al. The accuracy of frozen section diagnosis of pulmonary nodules: evaluation of inflation method during intraoperative pathology consultation with cryosection. J Thorac Oncol. 2010;5(1):39–44.

[25] Walts AE, Marchevsky AM. Root cause analysis of problems in the frozen section diagnosis of in situ, minimally invasive, and invasive adenocarcinoma of the lung. Arch Pathol Lab Med. 2012;136(12):1515–1521.

[26] Yeh YC, Nitadori J, Kadota K, et al. Using frozen section to identify histological patterns in stage I lung adenocarcinoma of ≤3 cm: accuracy and interobserver agreement. Histopathology. 2015;66(7):922–938.

[27] Liu S, Wang R, Zhang Y, et al. Precise diagnosis of intraoperative frozen section is an effective method to guide resection strategy for peripheral small-sized lung adenocarcinoma. J Clin Oncol. 2016;34(4):307–313.