Synchronous core-needle biopsy and microwave ablation for highly suspicious malignant pulmonary nodule via a coaxial cannula

ABSTRACT

Aims: This study aimed to evaluate the safety and feasibility of computed tomography (CT)-guided synchronous percutaneous core-needle biopsy and microwave ablation (MWA) for highly suspicious malignant pulmonary nodules.

Materials and Methods: This retrospective study evaluated medical records of 54 consecutive patients (mean age, 65.5 ± 11.2 years) with 62 highly suspicious malignant pulmonary nodules who synchronously underwent percutaneous core-needle biopsy and MWA via a coaxial cannula (Group A) or sequentially underwent these procedures (Group B) from September 2016 to November 2017. All patients were followed up for at least 6 months after MWA. The safety and feasibility of synchronous core-needle biopsy and MWA were analyzed by comparing clinical data, technical success rate, complication, and curative effect per nodule with those of sequential procedures.

Results: Technical success rates were 100% in both groups. The pneumothorax rate was 29.6% (8/27) in Group A and 57.1% (20/35) in Group B, which was statistically different (P = 0.031). In Group A, hemothorax and pleural effusion rates were 22.2% (6/27), and in Group B, the corresponding rates were 28.6% (10/35) and 20.0% (7/35), respectively. No postprocedural pulmonary artery pseudoaneurysm, bronchopleural fistula, or needle-tract tumor seeding developed in both groups. After 6 months' follow-up, the effective rates (complete + partial response) in both groups were 100%.

Conclusions: Synchronous core-needle biopsy and MWA via a coaxial cannula is technically safe and feasible in the management of highly suspicious malignant pulmonary nodules, and this procedure has lesser complications and similar effects (both 100% effective treatment) compared with sequential procedures.

KEY WORDS: Coaxial cannula, lung biopsy, microwave ablation, pulmonary nodule

INTRODUCTION

With the frequent application of low-dose computed tomography (CT) in lung cancer screening, pulmonary nodules are incidentally detected.[1] Nodules presenting with irregular margins, complex density, and spiculate or lobular outline are highly suspicious for malignancy.[2] However, benign nodules, such as tuberculosis or inflammatory pseudotumor, might demonstrate similar signs.[3,4] CT-guided core-needle biopsy is usually safe and frequently performed to obtain specimens for pathologic diagnosis.[5] However, biopsy confers a risk of pneumothorax, air embolism, hemorrhage, and death. Surgical resection is also an option to provide pathologic diagnosis and local cure. Due to factors of old age, poor cardiopulmonary function, or existence of comorbidities, many patients are ineligible for or refuse to accept surgical resection, even for nodules highly suspected or confirmed to be malignant.[6] Thermal ablation, such as radiofrequency ablation (RFA) or microwave ablation (MWA), is already proven to be safe and effective for non-small cell lung cancers (NSCLCs) and lung metastases,[7,8] especially for tumors <3 cm in size or oligometastases. Although thermal ablation for lung tumors is usually safe, it still carries similar risks and common complications.
such as pneumothorax and hemorrhage with core-needle biopsy. In an attempt to reduce the risk and complications of lung biopsy and MWA, we synchronously combined the two procedures via a coaxial cannula. Therefore, we performed this retrospective comparative study to further evaluate the safety, feasibility, and efficacy of the combined procedure (synchronous core-needle biopsy and MWA) for highly suspicious malignant pulmonary nodules.

**MATERIALS AND METHODS**

This retrospective study was approved by the Ethics Committee of our institution. From September 2016 to November 2017, patients undergoing biopsy and MWA after multidisciplinary discussions were included in this study. The inclusion criteria were ≤3 highly suspicious pulmonary nodules, absence of mediastinal or hilar lymphadenopathy, and both core-needle biopsy and MWA performed either synchronously or sequentially. In patients with a history of malignancy, the inclusion criteria also included removal of primary tumor and absence of extrapulmonary metastases. The patients had normal coagulation parameters before the procedures (international normalized ratio <1.5 and platelet count >50,000/µl). Written informed consent was obtained from all patients. In general, patients underwent synchronous or sequential procedures randomly, but for nodules rich in blood supply or adjacent to large blood vessels, which may carry a high risk of bleeding, synchronous procedures are advised. Patients who underwent synchronous procedures were classified as Group A, and those who received sequential procedures were classified as Group B.

**Technical procedures**

The main steps of the synchronous procedure were as follows: First, patients were positioned for optimal access to the lesion. Second, local CT images were obtained using 5-mm section thickness, and the nodule was reconstructed using 2.5-mm thickness. Then, the selected entry site was marked and prepared in a sterile fashion. Patients received analgesia (morphine 10 mg subcutaneous injection) and sedation (promethazine hydrochloride 25 mg intramuscular injection). After local anesthesia with 1% lidocaine (6–10 mL), a 15G coaxial introducer needle (Argon Medical Devices, Inc 1445 Flat Creek Road, Athens, Texas 75751, USA) was advanced into the nodule along a designed path. Then, another CT was performed to confirm the position of the needle tip. Subsequently, the stylet was replaced by a 16G full-core biopsy needle (Argon Medical Services, USA) through the cannula. Biopsy was performed and was repeated until adequate specimens were obtained for pathologic examinations. Consequently, a 17G microwave antenna (MTC-3C MWA instrument SFDA 20163251059; Nanjing Vision Medical Equipment Co. Jiangsu, China) was advanced into the nodule through the cannula [Figure 1]. The assembly consisted of a 15G cannula and a 17G microwave antenna, which were previously tested to ensure that they fit each other and the active portion of the antenna protruded adequately beyond the cannula tip using a rubber securing device [Figure 2]. In our experience, the optimal length ranged from 3 to 4 cm, and the generator using 60-W output power could maximally achieve nearly 3.5 cm × 4.0-cm ablative zone in 5 min. One more CT was performed to confirm that the active part was precisely placed into the target lesion and the estimated ablating sphere was covering the nodule. Sometimes, the antenna was adjusted into different parts of the irregular nodule to achieve sufficient ablation area by shifting the direction of the cannula. The emission frequency of the antenna was 2450 ± 50 Mz, and the output energy ranged from 30 to 60 W. After MWA, thoracic CT was performed to estimate the ablated area and detect possible complications. After 48 h, the patients were monitored in a ward for vital signs and potential complications, including pain, hemoptysis, shortness of breath, and chest tightness. At our institution, patients with nodules at high risk of bleeding were treated with synchronous biopsy and ablation to decrease the risk of severe hemoptysis.

In Group B, the patients who were diagnosed with NSCLC or metastases after biopsy sequentially underwent percutaneous MWA after 3–14 days when the preceding complication due to biopsy was controlled. The technical aspects of biopsy and MWA were similar to those of the synchronous procedure, except that the size of the biopsy instrument was smaller, which was 17G for the coaxial cannula and 18G for the cutting needle. In the processes of synchronous and sequential procedures, the step-by-step needle method was used by the same physician with at least 10 years’ experience in CT-guided percutaneous lung biopsy and thermal ablation to accurately puncture the nodules.

**Complications and efficacy**

After MWA, unenhanced thoracic CT was immediately performed to detect possible complications and estimate the ablation margin. A 0.5–1.0-cm surrounding ground-glass opacity occurring in the adjacent normal pulmonary parenchyma was defined as an adequate ablation margin.[9,10] Complications that resulted from cumulative data of each complete procedure, including biopsy or MWA, were recorded. The degree of hemoptysis was classified as severe (>100 mL), moderate (10–100 mL), and mild (≤10 mL). The degree of
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pneumothorax was classified as severe (lung compression >50%), moderate (lung compression ≤50% and >20%), and mild (lung compression ≤20%). Technical success referred to completion of the procedures.

Follow-up observation items included pathologic results, efficacy, and delayed complications, such as infection, pleural effusion, bronchopleural fistula, pulmonary artery pseudoaneurysm, and tumor seeding. The therapeutic response was classified as “complete response (CR),” “partial response (PR),” “stable disease (SD),” and “progression disease (PD)” based on nodule’s characteristics shown on enhanced thoracic CT, which was performed at the 1st, 3rd, and 6th months after MWA. Characteristics of the ablated nodule on the 1st-month thoracic CT were considered as baseline data for follow-up comparison. CR and PR indicated effective treatment.

Statistical analysis

Demographic data of the enrolled patients, characteristics of pulmonary nodules, and complication and efficacy rates per nodule were retrieved for statistical analysis. Different characteristics between the synchronous and sequential procedures were analyzed by Pearson’s Chi-squared test for categorical values. P < 0.05 was considered statistically significant. All analyses were performed using SPSS software version 19.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Twenty-one patients with 27 highly suspicious malignant pulmonary nodules (2.08 ± 0.68 cm, 0.8–3.0 cm) who underwent synchronous core-needle biopsy and MWA via a coaxial introducer were enrolled in Group A, including 16 patients with a single nodule, 4 patients with 2 nodules each, and 1 patient with 3 nodules. Thirty-three patients with 35 pathologically proven NSCLC or metastases by core-needle biopsy who sequentially underwent MWA, including 31 patients with a single nodule and 2 patients with 2 nodules each, were enrolled in Group B. There were 10 (47.6%) and 13 (39.4%) patients with chronic obstructive pulmonary disease (COPD) in Group A and Group B, respectively. Twelve and 18 patients had a history of tobacco smoking in Group A and Group B, respectively. There were 12 (57.1%) and 11 (33.3%) patients with a history of malignant tumor in Groups A and B, respectively. The mean nodular size was 2.08 ± 0.68 cm in Group A and 2.2 ± 0.52 cm in Group B. The basic clinical data were not statistically significant [Table 1].

Table 1: Basic clinical data of patients

| Demographics                     | Group A | Group B | χ²   | P     |
|----------------------------------|---------|---------|------|-------|
| COPD (%)                         | 47.6    | 39.4    | 0.355| 0.584 |
| Yes                              | 10      | 13      |      |       |
| No                               | 11      | 20      |      |       |
| History of tobacco smoking (%)   | 57.1    | 54.3    | 0.035| 0.851 |
| Never smoker                     | 9       | 15      |      |       |
| Former smoker                    | 10      | 14      |      |       |
| Active smoker                    | 2       | 4       |      |       |
| History of malignant tumors (%)  | 57.1    | 33.3    | 2.97 | 0.099 |
| Yes                              | 12      | 11      |      |       |
| No                               | 9       | 22      |      |       |
| Sex                              |         |         | 0.023| 0.544 |
| Male                             | 8       | 17      |      |       |
| Female                           | 13      | 16      |      |       |
| Mean age±SD (years)              | 65.9±9.3| 65.4±11.8| 0.958| 0.332 |
| Number of patients               | 21      | 33      |      |       |
| Number of nodules                | 27      | 35      |      |       |
| Number of nodules per patient    |         |         |      |       |
| 1                                | 16      | 31      |      |       |
| 2                                | 4       | 2       |      |       |
| 3                                | 1       | 0       |      |       |
| Nodule size (cm)                 | 2.08±0.68| 2.2±0.52 | 1.669| 0.201 |
| ≥0.8, ≤1.0                       | 4       | 3       |      |       |
| >1.0, ≤2.0                       | 9       | 15      |      |       |
| >2.0, ≤3.0                       | 14      | 17      |      |       |

COPD=Chronic obstructive pulmonary disease, SD=Standard deviation

Figure 2: Synchronous procedure. (a) Computed tomography image showing a single peripheral nodule (arrow), 15 mm × 10 mm, in the posterior segment of the left upper lobe with inhomogeneous density, irregular margin, and pleural tail sign. (b) Computed tomography scan showing a coaxial introducer needle (arrow) which was placed abutting the lesion. (c) An ablative antenna (short arrow) was placed through the coaxial cannula (long arrow) into the nodule after biopsy. (d) In the thoracic computed tomography scan immediately after ablation, the ablated nodule presented with a circular ground-glass opacity (arrows).
hemoptysis, and seven patients developed pleural effusion. The incidence rate of pneumothorax had statistically significant difference ($P = 0.036$), but there was no statistically significant difference in the incidence rates of hemoptysis or pleural effusion between the two groups. Rare complications, such as air embolization, bronchopleural fistula, pulmonary artery pseudoaneurysm, and tumor needle seeding, were not detected within the 6 months’ follow-up (6–15 months, mean 9.5 months) (Table 2).

Patients with moderate-to-severe pneumothorax (three patients in Group A and five patients in Group B) or pleural effusion (two patients in Group A and two patients in Group B) were treated with chest tube placement, whereas those with mild pneumothorax or pleural effusion recovered spontaneously after conservative management. Patients who suddenly developed hemoptysis during biopsy were encouraged to slightly cough and spit the blood out. In patients with mild hemoptysis (three patients in Group A and eight patients in Group B), careful observation and intravenous administration of hemostatic medications, such as etamsylate, were performed. In Group A, in those with moderate (one patient) or severe hemoptysis (two patients), more active therapies were initiated as follows: first, the MWA antenna was immediately placed into the lesion through the cannula that had been already inserted for biopsy; then, MWA was started, and during this course, the extravasated blood was also coagulated. If hemoptysis was severe, the patient was placed in a lateral position with the punctured side down and was encouraged to slightly cough and spit out the extravasated blood, and negative-pressure ventilation and oxygen inhalation were simultaneously applied to avoid asphyxia. In Group B, two patients with moderate hemoptysis were encouraged to spit out the extravasated blood, and intravenous administration of hemostatic medications and oxygen inhalation were performed. If the hemoptysis due to core-needle biopsy did not promptly resolve, MWA was performed under the provisional decision of the operator, and written permission was obtained from the patient’s guardian or relative. In our study, all patients with hemoptysis completely recovered, and no patient died.

Pathologic results
By analyzing the 62 nodules of 54 patients, 55 nodules were diagnosed as malignant. In Group A, two nodules were diagnosed as benign, including an inflammatory hyperplasia nodule and atypical adenomatoid hyperplasia. One biopsy result was nondiagnostic because of inadequate samples and necrosis. The remaining nodules were malignant on pathologic analysis, and the types of malignancy are detailed in Table 3.

Efficacy analysis
The follow-up duration was at least 6 months (6–15 months; mean, 9.5 months), and all patients underwent contrast-enhanced thoracic CT at the 1st, 3rd, and 6th months after MWA. The total effective rate (CR + PR) was 100.0% (62/62). Images of

### Table 2: Complication of procedures

| Complications                  | Group A (%) | Group B (%) | $\chi^2$ | $P$ |
|-------------------------------|-------------|-------------|---------|-----|
| Pneumothorax (%)              | 29.6        | 57.1        | 4.659   | 0.031 |
| Mild                          | 5           | 15          |         |     |
| Moderate                      | 2           | 3           |         |     |
| Severe                        | 1           | 2           |         |     |
| Chest tube                    | 3           | 5           |         |     |
| Pleural effusion (%)          | 22.2        | 20.0        | 0.045   | 0.831 |
| Mild                          | 4           | 5           |         |     |
| Moderate                      | 2           | 2           |         |     |
| Severe                        | 0           | 0           |         |     |
| Chest tube                    | 2           | 2           |         |     |
| Hemoptysis (%)                | 22.2        | 28.6        | 1.032   | 0.571 |
| Mild                          | 3           | 8           |         |     |
| Moderate                      | 1           | 2           |         |     |
| Severe                        | 2           | 0           |         |     |
| Bronchopleural fistula        | 0           | 0           |         |     |
| Pulmonary artery pseudoaneurysm | 0         | 0           |         |     |
| Needle-tract tumor seeding     | 0           | 0           |         |     |

### Table 3: Detailed types of malignancy

| Pathologic result                      | Group A | Group B |
|----------------------------------------|---------|---------|
| Adenocarcinoma                          | 5       | 13      |
| Squamous cell carcinoma                 | 2       | 3       |
| Adenosquamous carcinoma                 | 1       | 4       |
| SCLC                                    | 1       | 0       |
| Metastasis                              | 15      | 13      |
| Large cell neuroendocrine carcinoma    | 0       | 2       |

42 lesions (67.5%) did not demonstrate any enhancement (CR), and twenty lesions (32.5%) presented with slightly irregular rim-like enhancement (PR). No lesion presented with nodular enhancement (maximum diameter $\geq$ 5 mm). The curative effect was remarkable, similar to that reported in literature. No procedure- or tumor-related death occurred during the follow-up. Effective rates of synchronous and sequential procedures were not statistically different.

**DISCUSSION**

With increased application of low-dose thoracic CT and programs in lung cancer screening, the detection sensitivity of pulmonary nodules is increasing. Obtaining pathologic result of highly suspicious malignant pulmonary nodules is greatly important in planning for reasonable management. Surgical resection is a traditional and preferred method to remove lung nodules and obtain specimen for pathologic diagnosis. However, some patients are ineligible for or reluctant to accept surgical resection due to old age or comorbidities. Under these situations, CT-guided percutaneous biopsy is generally performed. RFA or MWA is a preferred alternative treatment for malignant nodules with advantages of minimal invasiveness, less complications, wider range of indications, quick recovery, repeatable application, and similar results as those of surgical resection.

Pneumothorax is the most common complication of either percutaneous biopsy or MWA, and a higher number of pleural effusions was reported more frequently in MWA than percutaneous biopsy.
punctures increase the risk of pneumothorax. Hemoptysis is usually the second most common complication of lung biopsy but less common with MWA due to its coagulative effect. Some physicians simultaneously apply a biopsy instrument and MWA antenna in a tandem fashion with the intent to reduce the incidence of severe bleeding. Repeat pleural punctures increase the risk of patient discomfort and risk of pneumothorax. Repeat punctures may also increase the technical difficulty of the procedure. Therefore, the procedures were combined together via a coaxial cannula to synchronously obtain specimen and ablate the nodule to inactivate tumor cells and reduce complications and patients’ discomfort. In the present study, the incidence rate of pneumothorax in synchronous procedures was significantly lower than that in sequential procedures. The biopsy needle used in the synchronous group was larger than that in the sequential group. Theoretically, the incidence of complications in the synchronous group might be higher than that in the sequential group. However, it has been reported that there is no significant correlation between the occurrence of pulmonary complications and the different diameters of commonly used needles. In the course of synchronous and sequential treatment, accurate puncture of nodules was performed by doctors with more than 10 years of experience in CT-guided percutaneous lung biopsies and thermal ablation. Simultaneous surgery required one pleural puncture, and sequential surgery required at least two pleural punctures. By analyzing risk factors for pneumothorax, one-time puncture through the pleura via a coaxial cannula did really reduce the incidence of pneumothorax. It was slightly higher in the present study than that reported in literature. This might be due to the fact that most patients were of old age or had COPD. The difference between Groups A and B in terms of chest tube requirement for pneumothorax was not statistically different. Patients with severe pneumothorax need chest tube drainage. The main factors of severe pneumothorax caused by pleural puncture are emphysema, pulmonary bullae, and interstitial lung disease. The complication rate of COPD in Group A (47.6%) was higher than that in Group B (39.4%). Therefore, although there may be statistically significant differences in the incidence of pneumothorax, there is no statistically significant difference in chest tube requirement. Lung nodules with rich blood supply or those adjacent to rich blood vessels and pulmonary arterial hypertension are risk factors for severe hemoptysis during biopsy. Severe hemoptysis during biopsy may be life threatening due to the risk of asphyxiation. Besides the administration of hemostatic medications, urgent bronchial artery embolization or surgery might be performed to control severe hemoptysis due to biopsy injury. However, these procedures are not always effective and readily unavailable in the CT room. MWA may be considered as a method to control bleeding by coagulating the extravasated blood and cautering small injured vessels within several minutes. The pathologic cause of hemoptysis is pulmonary vascular injury, which is mainly caused by cutting tissues. Both procedures do not lead to more risk factors for cutting tissues. Therefore, the incidence rates of hemoptysis in both groups were not statistically significantly different.

Three nodules were not pathologically diagnosed as malignant lesion. Although MWA was possibly unnecessary, core-needle biopsy was still needed for this patient, and malignancy could not be fully excluded due to the possibility of a false-negative result. The synchronous MWA not only inactivated the potential malignant cells but also relieved the patients’ anxiety. All the three patients were recommended to be followed up every 6 months in the 1st year postoperatively so as not to delay further treatment due to possible false-negative results. One nodule diagnosed as small cell lung cancer (SCLC) was ablated. According to the NSCLC (NCCN) guidelines, the recommended treatment for SCLC is chemotherapy, but Maxwell et al. retrospectively evaluated ten SCLCs in nine consecutive patients managed by RFA without adjuvant therapy. It was suggested that the median and 1-year overall survival rates were better in patients with local SCLCs compared with those with disseminated disease. Song et al. concluded that RFA improved the prognosis of SCLC and should be considered for its treatment.

There was no statistically significant difference in the effective rate. Similar to those in sequential procedures, one single antenna’s ablative scope can completely cover a regular nodule, and it is usually unnecessary to adjust the antenna’s position. Even if adjustment is necessary for an irregular nodule during the synchronous procedure, it is quite easy to perform by adjusting the direction of the coaxial cannula. In the present study, the front edge of the antenna protruding 3–4 cm out of the coaxial cannula provided adequate space for the active part. Therefore, the synchronous procedure did not reduce the ability of sufficient ablation.

Therefore, our study demonstrates that synchronously performing biopsy and MWA via a coaxial cannula significantly reduces the incidence rate of pneumothorax compared to sequentially performing these procedures, although there is no difference in chest tube requirement. While bleeding complications were similar between the two groups, patients at high risk of bleeding were selected to undergo the synchronous procedure, which likely affects these results. Randomized studies would be beneficial in further evaluating our results.

CONCLUSIONS

Synchronous core-needle biopsy and MWA via a coaxial cannula is technically safe and feasible in the management of highly suspicious malignant pulmonary nodules, and this procedure has lesser complications and similar effects compared with sequential procedures.

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Conflicts of interest
There are no conflicts of interest.

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