EVALUATE THE SAFETY AND INITIAL RESULTS OF APPLYING THE TECHNIQUE OF TREATING LUNG CANCER BY MICROWAVE ABLATION UNDER THE GUIDANCE OF COMPUTED TOMOGRAPHY

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ABSTRACT: *A retrospective, cross-sectional study to evaluate the safety and initial results of applying the technique of treating lung cancer by microwave ablation under the guidance of computed tomography in 30 patients with non-small cells primary lung cancer, at the National Lung Hospital, from June, 2018 to August, 2020.*

Results: *The average age of patients was 61.9 ± 6.5 years; male/female ratio was 14/1; 56.7% of patients had a history of multimodality therapy. The features on computed tomography film: the average tumor size was 37.94 mm; most of the lung tumors have peripheral locations (84.0%), solid tumors (93.5%), have mediastinal lymph nodes (50.0%). The proportion of patients treated with microwave ablation under the guidance of computed tomography: 1 time (60.0%), 2 times (33.3%), and 3 times (6.7%). The average burning time for lung tumors was 13.67 ± 5.3 minutes. Damage response after performing microwave ablation under the guidance of computed tomography: 15/23 patients (65.2%) had complete tumor necrosis and 8/23 patients (34.8%) had necrosis, not a complete tumor. 36.7% of patients had complications and 36.7% of patients had unwanted reactions. The average hospital stay after performing microwave ablation under the guidance of computed tomography was 11.2 ± 4.6 days. The rate of local recurrence was 18.2%, the rate of new metastasis was 22.7%.*

Keywords: Microwave ablation of lung tumors, lung cancer.

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1. INTRODUCTION.

Lung cancer is a malignant tumor that develops from bronchial epithelial cells, terminal bronchioles - alveoli, or from bronchial glands [1]. Lung cancer is the most common cancer and is the leading cause of death among all cancers. According to GLOBOCAN 2018, there are an estimated 2 million new cases of lung cancer, accounting for 11.6% of all cancers, with a corresponding mortality rate of 18.4% [14]. In Vietnam, the incidence of lung cancer ranks second (after liver cancer) and the mortality rate is high (because 80% of the cases are detected at a late stage (IIIB and IV) [2]).

According to the classification of the World Health Organization (WHO), lung cancer consists of two main groups (based on histopathological characteristics): non-small cell tumors (accounting for 80-85%) and small cell tumors (accounting for from 10-15%). In general, the disease has a poor prognosis, the 5-year survival rate is still low (less than 25%) [3]. Treatment of lung cancer depends on the stage of the disease, usually it requires a combination of treatment methods, such as surgery, chemotherapy, targeted therapy, radiation therapy…

For early-stage of non-small cell lung cancer, surgery is considered the optimal method to completely remove the tumor. However, about 20% of patients are not eligible for surgery due to impaired cardiopulmonary function, poor physical condition [5]. These cases will be treated with chemotherapy, radiation therapy... to improve symptoms, reduce mortality rate, but not worth mentioning. Currently, the method of treating lung tumors using Microwave ablation (MWA) under the guidance of computed tomography has been applied in many countries.

National Lung Hospital is the first unit in the country and Southeast Asia to implemented MWA equipment to treat patients with lung cancer. Here, the technique of treating lung cancer by percutaneous (through chest wall) MWA under the guidance of computed tomography was studied and applied. Contributing to confirming and improving the quality of the technique, we carried out this study to evaluate the safety and initial results of applying the technique of treating cancer with MWA under the guidance of computed tomography at the National Lung Hospital.

2. SUBJECTS, METHODS OF THE STUDY.

2.1. Subjects of the study:

30 patients with a definite diagnosis of primary non-small cell lung cancer, treated with MWA under the guidance of computed tomography, at the National Lung Hospital, from June 2018 to August 2020.

- Selective criteria: the patients with indications for radical treatment (such as having surgery but not responding to surgery; patients refusing surgery; recurrent lesions after treatment with other methods; patients who have isolated metastatic lesions after surgery or radiation therapy; multiple primary lung tumors (tumor count ≤ 3 for one lung or ≤ 5 for two lungs), tumor diameter ≤ 30 mm, no distant metastasis or indicated for palliative treatment (relieves symptoms caused by the tumor, improved quality of life in patients unable to respond to radical treatment conditions; appropriate expansion of treatment with tumor counts > 3 for one lung or > 5 for two lungs, tumor diameter > 30 mm performed multiple times and at multiple sites in one session or combination with other methods); patient and family agreed to participate in the study.

- Exclude patients with contraindications to thermal ablation (such as puncture site infection; severe pulmonary fibrosis; risk of major bleeding); patients with poorly controlled malignant pleural effusion on the affected side; patients with dysfunction of the severe liver, kidney, heart, lung, and brain; patients with anemia and severe dehydration, nutritional metabolism disorders cannot be corrected or improved; patients with severe systemic infection and fever (> 38.5°C); patients with extensive extrapulmonary metastases, with an expected survival time of fewer than 3 months; patient has ECOG score > 3.

2.2. Methods of the study:

- Study design: retrospective, cross-sectional description.

- Diagnosis of non-small cell Lung cancer according to the Guidelines for the diagnosis and treatment of non-small cell Lung cancer of the Ministry of Health in 2018 [1].

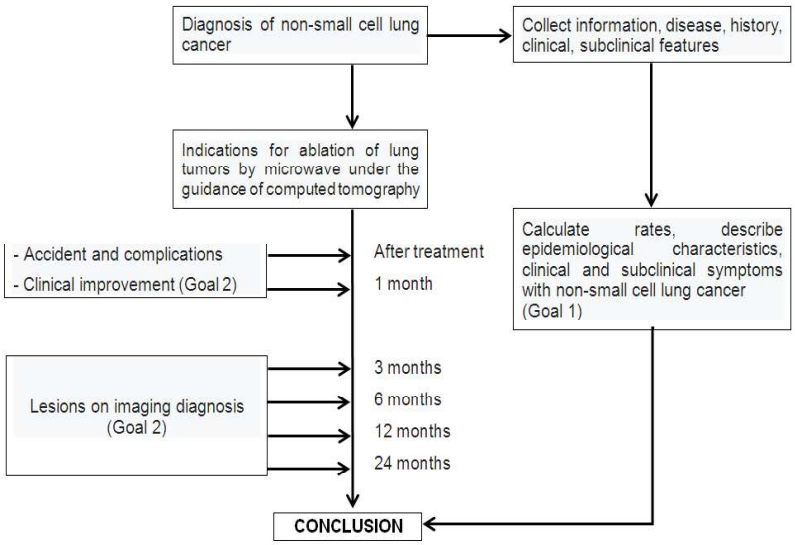
- Select sample: select the whole sample, convenient.

- Steps to carry out the study according to the diagram:

- Research criteria: the characteristics of research patients; characteristics of computed tomography of the chest; evaluation of initial results and safety of lung tumor ablation technique by MWA: evaluation of treatment results at 1, 3, 6, 12 and 24 months of technique implementation. The accidents were encountered immediately after performing the technique.

- Data processing: by SPSS 20.0 software.

STUDY DIAGRAM



3. RESULTS OF THE STUDY.

3.1. The characteristics of the patients:

- Age (n = 30):

+ Under 51 years old: 2 patients (6.7%).

+ From 51-60 years old: 9 patients (30.0%).

+ From 61-70 years old: 17 patients (56.7%).

+ Over 70 years old: 2 patients (6.7%).

+ Average: 61.9 ± 6.5 years old.

- Gender (n = 30):

+ Male: 28 patients (93.0%).

+ Female: 2 patients (7.0%).

- Combined disease (n = 30):

+ Chronic obstructive pulmonary disease: 7 patients (23.3%).

+ Old pulmonary tuberculosis: 1 patient (3.3%).

+ Chest trauma: 1 patient (3.3%).

+ Hypertension: 3 patients (10.0%).

+ Diabetes: 2 patients (6.7%).

+ Renal failure: 1 patient (3.3%).

+ Other diseases: 4 patients (13.3%).

- History of treatment (n = 30):

+ Surgery: 1 patient (6.0%).

+ Surgery and chemotherapy: 2 patients (11.7%).

+ Chemotherapy: 4 patients (23.5%).

+ Chemotherapy and radiotherapy: 5 patients (29.4%).

+ Targeted treatment: 2 patients (11.7%).

+ Chemotherapy and targeted therapy: 2 patients (11.7%).

+ Cryotherapy of the tumor: 1 patient (6.0%).

- Diagnosis of disease stage (n = 30):

+ Stage IA: 1 patient (3.3%).

+ Stage IIIA: 9 patients (30.0%).

+ Stage IIIB: 4 patients (13.4%).

+ Stage IIIC: 1 patient (3.3%).

+ Stage IVA: 13 patients (43.3%).

+ Stage IVB: 2 patients (6.7%).

3.2. Features of thoracic computed tomography scan:

- Tumor size on thoracic computed tomography (maximum transverse diameter): the lung tumor size from 17-77 mm, mean 37.94 ± 16.6 mm, with median value of 32.

- The characteristics of lesions on thoracic computed tomography film (n = 30):

+ Nodules/solid mass: 29 patients (93.5%).

+ Mass with cave: 2 patients (6.5%).

+ Mediastinal lymph nodes: 15 patients (50.0%).

+ Lung hilar lymph nodes: 7 patients (23.3%).

+ Atelectasis around the block: 2 patients (6.7%).

+ Thickening of the lung pleura: 6 patients (20.0%).

- Tumor location on thoracic computed tomography film (n = 30):

+ Peripheral: 26 patients (84%).

+ Central: 5 patients (16%).

- Number of lung tumors per patient (n = 30):

+ 1 tumor: 29 patients (96.7%).

+ 2 tumors: 1 patient (3,3%).

3.3. Evaluation of initial results and safety of MWA technique:

Table 1. The number of burning time for lung tumors with MWA (n = 30).

Parameter		Number of patients	Rate %
Number of burning time	1 time	18	60.0
	2 time	10	33.3
	3 time	2	6.7
Burning intensity		100W	
Burning time		13.67 ± 5.3 minutes (from 6-25 minutes)	

- Response to treatment:

- Surgical complications:

Table 2. Change of lesion area after treatment.

Tumor size	Nodules/ tumor (n = 23)	Degree of necrosis				p
		Completely		Not completely		
		Number of lung tumors	Rate %	Number of lung tumors	Rate %	
Total	23	15	65.2	8	34.8	
≤ 30 mm	11	10	90.9	1	9.1	0.027
> 30 mm	12	5	41.7	7	58.3	

Table 3. Complications after surgery (n = 30).

Complications		Number of patients	Rate %
Side-effects	With side-effects	11	36.7
	Fever	4	13.3
	Chest pain	10	33.3
Accidents	Had accidents	11	36.7
	Pneumothorax	6	20.0
	Hydrothorax	3	10.0
	Hemoptysis	4	13.3
	Chest wall inflammation	1	3.3
	Death in 30 days	0	0

- Combined treatment after burning of lung tumors with MWA:

Table 4. Combined treatment after tumor burning (n = 30).

Combined methods	Number of patients	Rate %
Chemotherapy alone	13	43.3
Chemotherapy + radiotherapy	5	16.7
Targeted treatment	2	6.7
Chemotherapy + targeted therapy	3	10.0
Immunotherapy	1	3.3

- Observation time:

Table 5. Observation time after surgery

Time	Min	Max	± SD
Hospital stay after surgery (day)	3	22	11.2 ± 4.6
Observation time (month)	3	24	13 ± 5.7

- Monitoring recurrence, metastasis after performing the technique:

Table 6. The rate of recurrence, metastasis after performing the technique (n = 22).

Characteristics	Number of patients	Rate %
Local recurrence	4	18.2
Time of recurrence	5 ± 2.7 months (3-9 months)	
Metastasis	5	22.7
Time of metastasis	7 ± 2.9 months (3-10 months)	

4. DISCUSSION.

Compared with the previous lung tumor technology of radiofrequency ablation (RFA), the MWA technique has more advantages, such as being able to generate high temperature in the tumor quickly, reducing the heat dissipation effect compared to RFA, thereby less affecting the surrounding healthy tissues, especially large blood vessels, pericardium, trachea, and main bronchus. On the other hand, the environment around the tumor is usually a gaseous environment, with poor thermal conductivity, which increases the concentration of heat at the tumor and protects the surrounding healthy tissues. When the thermal effect is high, the solid lesion near the blood vessel is destroyed, while the flow effect helps to dissipate heat quickly, without damaging the vessel wall structure.

In this study, the majority of patients were male (93.0%). The mean age of the patients was 61.9 ± 6.5 years. Mainly the patients with comorbidities, such as chronic obstructive pulmonary disease, chest trauma, diabetes, hypertension..., leading to impaired body function, inability to have surgery; Some patients after internal treatment (chemotherapy, radiation therapy, targeted therapy or a combination of measures...), the recurrent disease. This result was consistent with the epidemiological and clinical studies of Lung cancer by domestic and international authors.

30 study patients had a total of 31 lung tumors (one patient had 2 tumors), with lung tumor diameter from 17-77 mm, the mean diameter was 37.94 ± 16.6 mm, the median value was 32 mm. Of which, 14 lung tumors (45.2%) had tumor size ≤ 30 mm and 17 lung tumors (54.8%) had tumor size > 30 mm. This result was equivalent to the study of Claudio Pusceddu in 2019 (the mean tumor size was 50 mm [7]); Xia Yang (the mean tumor size was 30 mm [9]); Lou Zhong in 2017 (the mean tumor size was 31 mm [5]).

A concerning problem for the MWA technique when treating patients with central lung tumors (near the anatomical structures, such as blood vessels, trachea, main bronchus, esophagus, pericardium, etc.). This was a location that can cause thermal damage to adjacent structures when performing MWA techniques. The results of this study showed that all five patients (16.0%) with central lung tumors treated with the MWA technique had no serious complications during and after treatment; different from the study of Claudio Pusceddu (24.6% of patients had central lung tumors [7]).

Most patients with lung cancer of stage III, IV cancer (96.7%), of which stage IVA accounted for the most proportion (43.3%). This study mainly dealt with the role of the MWA technique in the treatment of late-stage non-small cell Lung cancer without surgical indication. The study found that two patients had indications for surgery but the patient refused; one patient was diagnosed with lung cancer with stage IA, combined with laryngeal cancer being treated. 17 patients (56.7%) with lung cancer had a history of treatment with other methods before the lung tumor ablation with MWA. Of which, chemotherapy was the most used method (13/17 patients, accounting for 43.3%). The study showed that the technique of lung tumors ablation with MWA was a lifesaving treatment for patients who have progressed after traditional treatments, such as surgery, radiation therapy, chemotherapy, or patients with a poor response after the first step of treatment. This advantage was also proved through the studies of Xia Yang [9] and Claudio Pusceddu [7].

The time of lung tumors ablation with the MWA technique was from 6-25 minutes, the average was 13.67 ± 5.3 minutes. The time of Lung tumors ablation depended on tumor size. This is also a decisive factor in the ability to completely remove the tumor. Some studies showed that one of the advantages of the lung tumor ablation method was that it can use multiple antennas at the same time to treat large tumors, or repeat the technique at different times after [7, 12]. The technique was performed once for tumors with

a diameter of ≤ 30 mm, performed several times for tumors > 30 mm in diameter [15]. In this study, the number of patients who performed ablation of their lung tumors with MWA technique one, two, and three times accounted for 60.0%, 33.3%, and 6.7%, respectively. The patients performed ablation of lung tumors many times to completely remove the tumors. Results: 23/30 patients (76.7%) changed the area of lung tumor lesions after treatment. Of which, 15/23 patients (65.2%) had complete tumor necrosis (ten patients with tumor < 30 mm, five patients with tumor > 30 mm) and 8/23 patients (34.8%) with tumor necrosis. incompletely (one patient with tumor < 30 mm, seven patients with tumor > 30 mm).

This rate was higher than the study results of Claudio Pusceddu (only 44.6% [7]) but lower than the results of Henry Zhao (the rate of complete necrosis was 76.5% [8]). This difference may be due to the larger tumor size in Claudio Pusceddu's study (50 mm) and Henry Zhao's study (26 mm) being smaller than in this study (37.94 mm). It can be seen that tumor size was a factor affecting the resection efficiency of the technique. To clarify this point, we divided the tumor size into two groups to compare the degree of necrosis: the tumor group had a diameter of ≤ 30 mm, the rate of complete necrosis was 90.9%; The tumor group with diameter > 30 mm, the rate of necrosis was 41.7%, the difference was statistically significant with $p < 0.05$. This rate was also consistent with the research results of Fei Cao et al in 2019 (tumor group ≤ 30 mm, the rate of complete necrosis was 90.22%; tumor group > 30 mm, the rate of complete necrosis was 55.6% [12]).

The accidents and complications after performing the technique: 11/30 patients (36.7%) had complications after performing the technique. Of which, 6/30 patients (20.0%) had a pneumothorax (two patients had to put a needle for air drainage), 4/13 patients (13.3%) with hemoptysis mild, 3/30 patients (10.0%) had pleural effusion, 1/30 patients (3.3%) had chest wall inflammation, no need for intervention, not any case of death. All patients were on stable internal treatment. About unwanted reactions: we encountered in 11/30 patients (36.7%); of which, 33.3% of patients with chest pain were treated with the strongest painkiller, a second-line opioid (tramadol, codeine), 13.3% of patients had a fever. The study by Claudio Pusceddu (2019) found that the rate of complications was 27.7%, of which 18.4% of patients with pneumothorax (1 patient had to undergo surgery to treat pneumothorax), 3.1% of patients with hydrothorax (one case of bronchial fistula), the mortality rate 0% [7].

Research by Lou Zhong 2017 found side effects: fever, nausea: 27.4%, pneumothorax: 10.6%, hydrothorax: 8.0%, hemoptysis: 9.7%, pneumonia: 7.1%; All patients were effectively treated with antibiotic therapy and were stable, had no deaths [6]. A systematic literature study by Binghu Jiang (2018) found the complication rate was 22.5% [12]. Compared with other studies, our study had a higher accident rate. It may be because this study sample has up to 23.3% of patients with Lung cancer who have a chronic obstructive pulmonary disease (among patients with chronic obstructive pulmonary disease, there were 43.5% of patients with obstructive ventilation disorder).

The hospital stay after performing the MWA technique ranged from 3-22 days, with an average of 11.2 days. Some patients were hospitalized for a long time due to the indications for chemotherapy in the course of treatment that was not related to complications after the procedure. The follow-up time of patients after the technique was from 3-24 months, the average was 13 months. Due to the newly developed technique, the follow-up time was not long enough to fully evaluate the effectiveness of the technique, especially the overall survival time.

Evaluation of relapse after treatment found that four patients (18.2%) had local recurrence, the time to detect recurrence was 3-9 months, the average time was 5 ± 2.7 months; 5 patients with distant metastases (22.7%), time to detect distant metastases from 3-10 months, the average was 7 ± 2.9 months. Metastatic locations were the adrenal gland, bone, brain, mediastinal ganglia. This result was different from the study results of Lou Zhong (the relapse rate was 15.9% [6]), Claudio Pusceddu (the relapse rate was 35.8% [7]), and Henry Zhao (the relapse rate was 29% [8]). A systematic literature study by Binghu Jiang (2018) showed that the recurrence rate was 10.9% [12].

As observed, in studies with high recurrence rates, the mean tumor diameter was also high. In fact, as larger the tumor, as the lower the rate of complete necrosis, so the risk of local recurrence was high. There were many reasons to explain this phenomenon, such as the tumor size was being too large and the irregular shape will lead to the ablation antenna could not destroying all the tumor cells and the rest of the tumor cells. Furthermore, there were more and more large blood vessels in tumors and it was the blood vessel itself that

causes the heat dissipation effect. Therefore, for large tumors, it was advisable to combine other treatment methods, such as radiation therapy, chemotherapy... The relapse cases in our study were local radiation therapy combined with systemic treatments methods. Besides, re-implementation of tumor ablation technique with MWA was also a treatment method for the group of patients with relapse [6, 7, 8].

5. CONCLUSION.

A study of 30 patients with primary non-small cell lung cancer, treated with MWA under the guidance of computed tomography, at the Central Lung Hospital, from June 2018 to August 2020, concluded:

- The average age of patients was 61.9 ± 6.5 years; male/female ratio was 14/1; 56.7% of patients received multimodality treatment.

- The characteristics of computed tomography film: the average tumor size was 37.94 mm. Most of the lung tumors had peripheral locations (84.0%), solid tumors (93.5%), and mediastinal lymph nodes (50.0%).

- The number of times to lung tumors ablation by MWA technique: one time (60.0%), two times (33.3%), and three times (6.7%). The average time for lung tumors ablation was 13.67 ± 5.3 minutes. The injury response after performing lung tumor ablation by MWA: 15/23 patients (65.2%) had complete tumor necrosis (ten patients with tumor < 30 mm, five patients with tumor > 30 mm) and 8/23 patients (34.8%) with incomplete necrosis (one patient with tumor < 30 mm, seven patients with tumor > 30 mm). 36.7% of patients had complications and 36.7% of patients had side effects. The average hospital stay after the technique was 11.2 ± 4.6 days. The rate of local recurrence was 18.2%, the rate of new metastasis was 22.7%.

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