NEU_2020_02

A Single-Arm, Prospective, Multicenter Study to Evaluate the Effectiveness and Safety of the NeuWave Certus Microwave Ablation System in Chinese Patients with Primary or Secondary Tumors in the Lung

Name of Investigational Medical Device	NeuWave Certus Microwave Ablation System and Accessories
Model Specification	See Appendix
Management Category of Investigational Medical Device	Class III medical device requiring clinical trial approval Yes□ No√ Predicate Product in China Yes √ No□
Protocol Version Number	V2.0
Protocol Version Date	September 15, 2021
Clinical Trial Leading Institution	Beijing Hospital
Leading Investigator	Dr. Li, Xiaoguang
Sponsor	NeuWave Medical, Inc.
Agent	Johnson & Johnson Medical (Shanghai) Ltd.

Protocol Approval Form

Protocol Number:	NEU_2020_02
Protocol Title:	A Single-Arm, Prospective, Multicenter Study to Evaluate the Effectiveness and Safety of the NeuWave Certus Microwave Ablation System in Chinese Patients with Primary or Secondary Tumors in the Lung
Protocol Date:	September 15, 2021

	Name	Signature	Date
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COMPLIANCE STATEMENT

This study will be conducted in compliance with the Declaration of Helsinki as well as all applicable local regulations.

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LIST OF ABBREVIATIONS

Abbreviations	Description of Abbreviations
2D	Two Dimensional
3D	Three Dimensional
ALT	Alanine Aminotransferase
AST	Aspartate Aminotransferase
APTT	Activated Partial Thromboplastin Time
AE	Adverse Event
CHU	Complaint Handling Unit
CT	Computed Tomography
CRF/e-CRF	Case Report Form / Electronic Case Report Form
EC	Ethics Committee
ECOG	Eastern Cooperative Oncology Group
EDC	Electronic Data Capture
EORTC QLQ	European Organization for Research and Treatment of Cancer Quality of Life Questionnaire
FAS	Full Analysis Set
FDA	Food and Drug Administration
GCP	Good Clinical Practices
ICF	Informed Consent Form
IFU	Instructions for Use
INR	International Normalized Ratio
IRB	Institutional Review Board
IRC	Independent Review Committee
ITT	Intention to Treat
MW	Microwave
NSAID	Nonsteroidal Anti-inflammatory Drug
NMPA	National Medical Products Administration
NPRS	Numeric Pain Rating Scale
NSCLC	Non-Small Cell Lung Cancer
OS	Overall Survival
PP	Per Protocol
PI	Principle Investigator
PDM	Power Distribution Module
PLT	Platelet Count
PT	Prothrombin Time
QOL	Quality of Life Questionnaire
RF	Radiofrequency

SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SIR	Society of Interventional Radiology
SCLC	Small Cell Lung Cancer
SOC	Standard of Care
SOP	Standard Operation Procedure
US	United States
USV	Unscheduled Visit

SYNOPSIS

Study Title	A Single-Arm, Prospective, Multicenter Study to Evaluate the Effectiveness and Safety of the NeuWave Certus Microwave Ablation System in Chinese Patients with Primary or Secondary Tumors in the Lung
Protocol No.	NEU_2020_02
Sponsor	NeuWave Medical, Inc.
Study Objectives	To evaluate the effectiveness and safety of the NeuWave Certus Microwave Ablation System and Accessories in the percutaneous microwave ablation of primary or secondary lung tumor.
Study Devices	NeuWave Certus Microwave Ablation System and Probes
Study Design	This study is a single-arm, prospective, multicenter clinical trial with a performance goal (PG). The study population includes patients with non-small cell lung cancer (NSCLC) or oligometastatic lung tumor who plan to receive percutaneous microwave ablation. Individuals who have lung tumor(s) meeting the eligibility criteria of the study and sign the Informed Consent Form will be enrolled into this study. Each enrolled patient will have his or her eligible lung tumor(s) ablated using the NeuWave Certus Microwave Ablation System (in conjunction with the NeuWave Certus Microwave Ablation Probes) in a single surgery. Subjects will be followed at 1, 3, 6, and 12 months after the initial microwave ablation procedure to evaluate the effectiveness and safety of percutaneous microwave ablation with the study device.

	To provide study sites with an opportunity to get equal experience in the use of the Certus system, each study site will have 2 subjects treated as part of a run-in phase. These subjects will only be included in the safety analysis set.	
Sample Size	N=120 plus run in subjects (each site will enroll 2 run-in subjects)	
Study Population	Adult patients with NSCLC or oligometastatic lung tumor(s)	
Study Duration	Enrollment: Approximately 18 months	Follow-Up: 1 year
Procedures Description	All the NSCLC and oligometastatic lung tumor microwave ablation procedures of this study will be performed percutaneously by doctors who are experienced in lung tumor ablation in the study site using the NeuWave Certus Ablation System (in conjunction with NeuWave Certus Microwave Ablation Probes). During the ablation, subjects will be under anesthesia as per the institution's standard of care (SOC). CT scan will be used to guide the probe to the tumor, confirm accurate placement of the probe prior to emitting the microwaves and confirm final ablation zone.	
Primary Endpoint and Follow-up Interval	Technical Efficacy Rate: Percentage of tumors that are completely covered by the ablation zone with no sign of pathological enhancement according to the lung contract-enhanced CT assessment at Visit 3 (30 days ± 7 days after the initial ablation procedure).	
Secondary Endpoints and Follow-up Interval	**Secondary Effectiveness Endpoints:** • Technical Success Rate: Percentage of tumors that achieve A0 or A1 ablation classification determinations (i.e., complete tumor ablation with a surrounding margin)	

	in the lung CT immediately following the initial ablation procedure. • A0 Ablation Rate: Percentage of tumors that achieve A0 ablation (i.e., the ablation zone covers the tumor completely and has a margin of at least 5mm for secondary lung tumors and at least 10mm for primary lung tumors) in the lung CT immediately following the initial ablation procedure. • Re-Ablation Technical Success Rate: Percentage of tumors that achieve Technical Success in the lung CT immediately following the repeat ablation with the study device during the study. • Local Tumor Progression: Local tumor progression and time to local tumor progression of any original-ablated tumor(s). • Progression-Free Survival: Length of the time the patient is still alive after the original ablation procedure and with no evidence of any tumor progression (local, regional, or distant). • Overall Survival: Length of time that the patient is still alive after the original ablation procedure within the study duration. **Safety Endpoints:** • All AEs from the start of any ablation procedure (from the probe puncture on skin) to 30 days post-ablation or early discontinuation . • All SAEs from the start of ablation procedure through the end of the study or early discontinuation. • All device-related AEs, procedure-related AEs, device-related SAEs, procedure-related SAEs from the start of ablation procedure through the end of the study or early discontinuation.

Exploratory Endpoints	**Patient Report Outcomes:** • Ablation-Procedure Related Pain: Compare the 1 day post-ablation, 3 day post-ablation, 1 month post-ablation versus pre-ablation patient-reported pain levels using the Numeric Pain Rating Scale. • Quality of Life: Compare the patient's 1 month post-ablation, 6 months post-ablation, and 12 months post-ablation to the pre-ablation Quality of Life scores using EORTC QLQ-C30 and Lung-specific QLQ-LC13. **ECOG Performance Status:** Patient functionality as measured by distribution of Eastern Cooperative Oncology Group (ECOG) classification scores over time. **Ablation Procedure Related Indicators:** Number and types of probes used, number of ablation cycles, ablation power and time. **Length of Hospital Stay:** The duration from the patient's completion of ablation procedure to discharge. **Re-Admission Rate:** Percentage of unplanned hospital admission or re-admission due to an adverse event occurring within 30 days after any ablation procedure using the study device (i.e. the original ablation or a repeat ablation).
Inclusion Criteria	**Subjects will be included if ALL of the following inclusion criteria are met:** 1. Signed the informed consent form and willing to fulfill the study-related assessments and procedure schedule. 2. Lung tumor patients ≥ 18 years of age who are ineligible for/decline surgery and who plan to receive microwave ablation therapy. 3. ECOG performance status score of 0-2. 4. Patients with stages IA1-IA2 NSCLC with

	documented results from a biopsy or patients with clinically diagnosed oligometastatic lung tumor(s). 5. Tumor(s) to be ablated in a single surgery should be a maximum of one NSCLC tumor or a maximum of three ipsilateral oligometastatic lung tumors. 6. Tumor(s) to be ablated in a single surgery should be ≤ 2cm, locate in the outer two-thirds of a lung, not closer than 1cm from the hilum of lung, great vessels, principal bronchus, trachea or esophagus, and not contiguous with the pleura.
Exclusion Criteria	**Subjects will be excluded if ANY of the following exclusion criteria is met:** 1. Pregnant or breast-feeding. 2. Patients with implantable pacemakers or other electronic implants. 3. Oligometastatic tumors patients whose primary lesion cannot be controlled or have widely metastases, in the opinion of the investigator and/or treating oncologist. 4. Any planned concurrent procedure at the time of ablation. 5. Planned treatment for other tumors in the same side lung during the study period. 6. With a skin infection or ulceration at the site to be punctured by probe(s). 7. Clinical or imaging findings consistent with an active pulmonary infection. 8. Patients with severe pulmonary fibrosis in the area intended to ablate, especially drug-induced pulmonary fibrosis. 9. Patients with prior radiotherapy in the area intended

	to ablate. 10. Patients with uncontrolled malignant pleural effusion at the lung side with tumor to ablate. 11. Tumors where the anticipated zone of ablation would encompass significant (in the opinion of the treating physician) emphysematous or bullous disease. 12. The investigator anticipates that the ablation zone of the multiple tumor(s) to be ablated may have overlapping ablation zones. 13. Patients who have received lung ablation or surgical resection therapy within 30 days prior to the ablation procedure under study and those who plan to receive lung tumor ablation or surgical resection therapy or radiation therapy on the ablated lung side before completing the primary efficacy endpoint assessment approximately 30 days after the ablation procedure. 14. Patients who received systemic therapy such as chemotherapy, targeted drug therapy, or immunotherapy within 7 days prior to the ablation procedure under study, and patients who had a systemic treatment plan such as chemotherapy, targeted drug therapy, immunotherapy, etc. before completing the primary efficacy endpoint assessment approximately 30 days after the ablation procedure. 15. Patients with uncorrectable coagulopathy based on investigator judgment. 16. Patients with a platelet count $\leq 50 \times 10^9$/L. 17. Patients who cannot discontinue antiplatelet medication (e.g., aspirin, clopidogrel, prasugrel, ticagrelor) at least **5 days** before the ablation procedure through **24 hours** post-procedure.

	18. Patients who cannot discontinue anticoagulant medication (e.g., rivaroxaban, apixaban, dabigatran, edoxaban) at least **3 days** before the ablation procedure through **24 hours** post-procedure. 19. Patients who cannot discontinue warfarin before at least **5 days** before the ablation procedure of the study or have an INR > 1.5. 20. As judged by the investigator, the patient has hypertension that cannot be effectively controlled by pharmacological treatments. 21. Severe hepatic, renal, cardiac, pulmonary or cerebral insufficiency, severe anemia, dehydration, and severe nutrition and metabolism disorders, which cannot be corrected or improved within a short term; or serious systemic infection; or severe neuromuscular diseases. 22. Expected survival less than 6 months. 23. Participation in any other interventional clinical study within 30 days before screening. 24. Physical or psychological condition which would impair study participation. 25. Patient is judged unsuitable for study participation by the investigator for any other reason. Intra-Ablation Exclusion Criteria: 26. Before ablation probe puncture on the skin, patient is judged unsuitable for study participation due to intolerance to anesthesia. 27. Before ablation probe puncture on the skin, patient is judged unsuitable for study participation due to presenting any other condition.
Safety Assessments	From the time of signing the informed consent form until approximately 30 days (Visit 3) after ablation (including

	primary and repeat ablation) or early discontinuation, all adverse events will be recorded. During this period, all adverse events from the start of ablation (i.e., probe puncture on the skin) will be reported. After approximately 30 days (Visit 3) post ablation, adverse events considered by the investigator as related to the study device or/and study procedures and all serious adverse events will be recorded and reported till the end of the study or early discontinuation.
Statistical Analysis	**Sample Size Calculation:** A systematic review and meta-analysis was performed and resulted in selecting a performance goal (PG) of 80%. A sample size of 120 subjects is necessary to achieve at least 80% power for demonstrating that the Technical Efficacy rate of the NeuWave Certus Microwave Ablation System is > 80% when the expected performance is 90%, and a one-sided significance level of 0.025 is used with the Normal Approximation to the Binomial distribution, with adjustment for 10% dropout. Each site will enroll 2 subjects first in the run-in phase besides the 120 subjects. In view of the lack of available clinical data for evaluating the performance of the study product in percutaneous lung tumor ablation procedure, the sample size will be re-estimated adopting a self-adaptive method after approximately 50% of the initial planned sample size are enrolled. **Statistical analysis of study endpoints:** The number and percentage of tumors achieving Technical Efficacy will be summarized and corresponding 95% confidence intervals will be estimated. If the lower limit of the 95% CI of the Technical Efficacy Rate is higher than the predefined PG value, primary endpoint success will be concluded. The Technical Success Rate, A0 Ablation Rate, Re-Ablation Technical Success Rate will be summarized in a similar way.

	The Local Tumor Progression, Progression-Free Survival, and Overall Survival will be calculated using the Kaplan-Meier method, and corresponding 95% confidence intervals will be provided. The number and percentage of subjects experiencing any adverse event (AE) and serious adverse event (SAE) will be summarized at the preferred term level of MedDRA. Study device-related AEs, ablation procedure-related AEs, device-related SAEs, and ablation procedure-related SAEs will be summarized in a similar way. The incidence of specified AEs of interest will be summarized and reported. In addition, descriptive statistics of all other endpoints defined in the protocol will be provided. Three analyses are planned. The first analysis will occur after 50% of the target enrolled subjects complete the Visit 3, aiming to inspect the assumptions used for calculation of sample size and determine if the sample size should be increased. The second analysis will occur after all enrolled subjects complete the 1-month visit, aiming to evaluate the Technical Efficacy Rate, peri-procedural endpoints, and safety in the period from the ablation procedure to 1 month post-procedure, and if the primary endpoint success is deemed, the study report will be submitted to the National Medical Products Administration (NMPA) for the registration application of lung ablation indication. The third analysis will occur after all subjects complete the study.

TABLE 1: SCHEDULE OF ACTIVITIES

Visit number	Visit 1	Visit 2A	Visit 2B	Visit 3	Visit 4	Visit 5	Visit 6	USV[25]
Visits	Screening	Ablation	Discharge	Follow-up	Follow-up	Follow-up	Follow-up	
Interval Window	Within 30 d prior to ablation	Ablation Day	Post-ablation	30 days (±7 d)	3 months (±14 d)	6 months (±30 d)	12 months (±30 d)	
Informed consent	X							
Assess Inclusion / Exclusion Criteria	X	X[1]						
Collection of demographic information and body height, body weight	X							
Blood or urine pregnancy test [2]	X							
Laboratory tests [3]	X							
Medical/surgical history/radiation history [4]	X							
ECOG performance status score[5]	X		X	X	X	X	X	
Biopsy	X[6,7]							
Contrast-enhanced CT of the lungs	X[8]			X[9]	X[9]	X[9]	X[9]	
Plain CT scan or X-ray of the lungs		X[10]	X[11]					
Pre-procedure classification of lung tumor(s) to be ablated [12]	X							
Pre-procedure assessment of lung tumor [13]	X	X						
Recording ablation procedure details [14]		X						
Numeric Pain Rating Scale		X[15]	X[15]	X				
QOL Quality of Life Questionnaires [16]	X			X		X	X	
Length of stay [17]			X					
Re-admission assessment [18]				X				

Visit number	Visit 1	Visit 2A	Visit 2B	Visit 3	Visit 4	Visit 5	Visit 6	USV[25]
Visits	Screening	Ablation	Discharge	Follow-up	Follow-up	Follow-up	Follow-up	
Interval Window	Within 30 d prior to ablation	Ablation Day	Post-ablation	30 days (±7 d)	3 months (±14 d)	6 months (±30 d)	12 months (±30 d)	
Technical Success evaluation (investigator and IRC) [19]		X						
Technical Efficacy evaluation (investigator and IRC) [20]				X				
Local Tumor Progression evaluation (investigator and IRC) [21]					X	X	X	
Progression-Free Survival evaluation [21]				X	X	X	X	
AEs/SAEs [22]	X	X	X	X	X	X	X	X
Concomitant meds[23]	X	X	X	X	X	X	X	X
Concomitant procedures [24]	X	X	X	X	X	X	X	X

Notes:

1. On the day of ablation and before the ablation procedure is performed, the inclusion and exclusion criteria will be reviewed again to make sure all subjects continue to meet all criteria.
2. The blood or urine pregnancy test must be performed within **7 days** prior to ablation (Visit 2A); otherwise the test must be repeated and available prior to ablation. Applicable to women of childbearing potential only.
3. All laboratory tests must be performed within **7 days** prior to ablation (Visit 2A), otherwise the test(s) must be repeated and available prior to ablation. Laboratory tests include complete blood count (including differential count) and coagulation test (APTT, PT, and INR).

4. The relevant medical/surgical/radiation history should at least include previous diagnosis of systemic tumors and pathological results (if any), history of other non-tumor lung diseases, history of chronic diseases, history of lung and/or oncologic-related mediation/surgery/procedure/radiation history and smoking status.
5. ECOG performance status score.
6. If the investigator assesses a patient's lung tumor(s) to be ablated as primary, the patient can be enrolled only if the lesion to be ablated is biopsy-proven as NSCLC before the ablation.
7. The investigator should not perform concurrent biopsy on tumors during the ablation procedure. Biopsy results should be collected before the ablation procedure.
8. Subjects must receive at least one contrast-enhanced CT scan of the lungs in the study site within 30 days prior to ablation (Visit 2A).
9. Lung contrast-enhanced CT scan will be performed at Visits 3-6 to follow up the lungs, and these CT results will be used to evaluate the Technical Efficacy and lung tumor progression profile.
10. During the ablation procedure, lung CT will be used to guide the microwave ablation probe to the lung tumor at a minimum of 3-4 time points: (1) Before probe insertion; (2) Before ablation: use CT to confirm the probe is in the expected position at the moment before ablation. If not in the expected position, reposition the probe and perform another scan. The doctor should repeat this process until the probe is placed in the expected position; (3) During ablation (optional); (4) After ablation: After completion of the ablation, use CT to confirm the ablation procedure has been completed and assess how the tumor is covered by the ablation zone.
11. As clinically necessary, the investigator can schedule a lung X-ray and/or lung CT scan as needed post-procedure within visit 2B for a patient to assess the occurrence of post-ablation lung complications. This is optional based on investigator's determination.
12. The investigator should classify the lung tumor(s) to be ablated before the ablation procedure: (1) Stage 1A1-1A2 NSCLC: Staging assessment should be based on images within 6 weeks before the ablation. The images should minimally include: "Chest CT + head MRI or CT + neck and supraclavicular lymph node ultrasound or CT + upper abdominal ultrasound or CT + bone scan" as recommended by 2019 edition of Chinese Medical Association Guidelines for Clinical Diagnosis and Treatment of Lung Cancer; "PET/CT from skull base to mid-thigh" can also be used (if available by SOC); "Mediastinal staging" is nice to have (if available by SOC). (2) Oligometastatic lung tumor: Images required should minimally cover

the primary lesion, abdomen and chest; brain MRI or CT is nice to have if investigator considers the patient with suspected brain metastases (if available by SOC). Besides, investigator should also assess if the tumor(s) to be ablated is a GGO (classification: pure GGO, partial-solid GGO, pure solid tumor).

13. During screening and enrollment, the investigator should identify the lung tumor(s) to be ablated through the pre-procedure lung CT imaging, assess and document the baseline profile of the lung tumor(s), including the number, size, location of the tumor(s) to be ablated, and the number, size and location of the other intrapulmonary tumors not to be ablated in the same study surgery. The size of the tumor(s) to be ablated must be measured with three-dimensional (3D) imaging in the lung window. For lung tumors not to be ablated in the same surgery, only need measuring size on 2D imaging together with the location and number. On the day of ablation, the investigator must re-assess the baseline profile of the lung tumor(s) based on the lung CT scan performed before the ablation procedure to make sure that all tumors to be ablated still meet the entry criteria.
14. The ablation procedure details must be recorded, including: date and time of procedure, mode of anesthesia, guidance method used, anatomical location of ablated tumors, number and types of probes used, number of ablation cycles, ablation power and time. For re-ablation procedures performed using the study device during the course of the study, the above ablation procedure details should also be recorded.
15. Pain assessment at the Visit 2A should be conducted before the ablation, and at the Visit 2B it should be conducted at **1 day** and **3 days** post ablation.
16. The QOL questionnaires include EORTC QLQ-C30 and lung-specific QLQ-LC13.
17. Length of stay (LOS): The duration from completion of ablation to discharge.
18. Any unplanned hospitalization in any hospital for any reason within 30 days post-ablation will be recorded, and the investigator will assess the reason for re-admission and record it in the study database.
19. Evaluation of Technical Success: Both the investigators and IRC will measure and record the post-procedure maximum and minimum diameters of ablation zone, and minimum ablation margin on CT taken approximately 10 minutes after the ablation and evaluate the Technical Success or not based on the measurements.
20. Evaluation of Technical Efficacy: The assessment should be based on contrast enhanced CT performed in visit 3 and both investigators and IRC's evaluations will be recorded.
21. (1) Evaluation of Local Tumor Progression: Contrast-enhanced CT scans during follow up visits will be used to evaluate

local malignant tumor lesion(s) at the ablation site. Both investigators' and IRC's evaluations will be recorded. (2) Evaluation of Progression-free survival: It will be based on investigator and/or the subject's treating oncologist. If there is a progression, the study physician should specify if the progression is of the original target tumor, a new lung malignant tumor or a distant metastasis.

22. From the time of signing the informed consent form until approximately 30 days (Visit 3) after ablation (including primary and repeat ablation) or early discontinuation, all adverse events should be recorded. After approximately 30 days (Visit 3) post ablation, adverse events considered by the investigator as related to the study device or/and study procedures and all serious adverse events will be recorded through the end of the study or early discontinuation.
23. All relevant prior concomitant medications used within 30 days prior to Visit 1 and all relevant concomitant medications used throughout the study period will be recorded.
24. All concomitant procedures that are performed from 30 days before Visit 1 to the entire study period will be recorded with procedure name, time, location and purpose (including but not limited to paracentesis, radiotherapy, ablation therapy, surgical resection therapy, etc.).
25. The reason for unscheduled visit will be recorded, as well as all SAEs and AEs (if applicable), all relevant concomitant medications and all concomitant procedure, or any other study assessments, per SOC.

1. SPONSOR INFORMATION

Name and Address of Sponsor

NeuWave Medical, Inc.

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Sponsor's Contact Information

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Related Qualification Documents of Sponsor

Related qualification documents of Sponsor include: ISO 13485 etc., see relevant appendix.

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Relevant qualification documents of the agent include: business license etc., see relevant appendix.

2. LIST OF ALL THE CLINICAL TESTING FACILITIES AND INVESTIGATORS PARTICIPATING IN THE CLINICAL TRIAL

See relevant appendix

3. OBJECTIVE AND CONTENTS OF CLINICAL TRIAL

3.1. Objective of Clinical Trial

The primary objective of this study is to evaluate the efficacy and safety of NeuWave Certus Microwave Ablation System and accessories for percutaneous microwave ablation of non-small cell lung cancer and oligometastatic lung tumor.

3.2. Contents of Clinical Trial

This study employs single-arm, prospective and multi-center design with single-arm performance goal comparing study device performance indexes with the predetermined performance goal, in order to evaluate study device efficacy and safety. Approximately 120 plus run-in subjects (each site will enroll 2 run-in subjects) of Chinese patients with non-small cell lung cancer or oligometastatic lung tumor scheduled for microwave ablation will be recruited. After the informed consent is signed, lung cancer patients according to the inclusion and exclusion criteria will be included in this study. All qualified subjects at the study sites will receive the same procedure: microwave ablation using only the NeuWave Certus Microwave Ablation System and accessories. Subjects in this study will come to their study site for the ablation procedure. After the ablation procedure, the patient will be observed according to medical routine, and afterwards may return home. If the Study Doctor decides it is warranted for patient safety, the patient will remain in the hospital longer. All subjects will be required to return to their study site for at least 4 follow-up visits over a period of 12 months to assess the efficacy and safety of ablation.

Computerized tomography (CT) is used to evaluate the efficacy to verify whether patient's lung tumor is completely ablated. CT scan will be carried out approximately 10 minutes after the ablation to assess Technical Success Rate and A0 Ablation Rate. Enhanced CT scan will be completed within 30 days (±7 days) after the ablation to evaluate Technical Efficacy Rate. During the subsequent visits in Months 3, 6, and 12 after the ablation, subjects will receive at least one enhanced CT scan each time at the study site to observe whether there are imaging manifestations of tumor progression inside the ablation zone and at its margin. These enhanced CT scans will serve as the basis for determining the Local Tumor Progression. Progression-Free Survival including local, regional, or distant progression will also be determined according to the study physician and/or the patient's treating oncologist. Another valuable endpoint during the 12-month follow-up period will be overall survival.

Within 30 days after the ablation (initial or repeated), all adverse events (AE) and serious adverse events (SAE) experienced by the patient will be evaluated; from 30 days after the ablation to the

ending of this study, SAE and study device/procedure-related AE determined by investigators will be evaluated.

Device efficacy evaluation is based on the hypothesis test of Technical Efficacy at visit 3 and the predetermined performance goal (PG). This efficacy result together with peri-procedural endpoints and the safety evaluation result within 30 days after the ablation will be submitted to National Medical Products Administration (NMPA) for the application of lung ablation indication.

4. BACKGROUND INFORMATION OF CLINICAL TRIAL

4.1. Introduction to the Condition

4.1.1. Explanation for the Condition

Lung cancer is the most common type of cancer in the world, its morbidity and mortality rank the first among all malignant tumors, there are approximately 1,800,000 new cases and 1,600,000 deaths each year[1]. In China, lung cancer also ranks the first among all malignancies in terms of morbidity and mortality, the new cases account for about 1/5 of all malignant tumors, there are about 780,000 new cases of lung cancer annually with an incidence of 57.26/100,000. Every year, the death toll of lung cancer is approximately 631,000 and the mortality rate is 45.87/100,000[2]. The incidence of lung cancer is higher in men than in women, and the risk of disease onset increases with age.

Based on cell types, primary lung cancer is divided into two major categories, namely non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC). Among which, NSCLC has three main subtypes, namely squamous cell carcinoma, adenocarcinoma and large cell carcinoma, accounting for about 80% of all primary lung cancers, when compared with SCLC, its metastasis and spreading occur relatively late due to slower growth and division of the cancer cells[3]. The most important cause of primary lung cancer is smoking, because benzopyrene, nitrosamines, nicotine and other compounds in the smoke all have carcinogenic effects. When compared with non-smokers, the risk for developing lung cancer is 4-10 times higher in smokers, and the smoking amount has an apparent dose-effect relationship with lung cancer[4]. Other causes of disease include air pollution (e.g., benzopyrene, arsenious oxide and radioactive substances that are released from indoor cooking fume and present in serious outdoor air pollution), occupational exposure (e.g., asbestos, arsenic, chromium, nickel, Ionizing radiation), and previous chronic lung infections (e.g., tuberculosis, bronchiectasis)[5]. In addition, genetic factors also play an important role in the onset of lung cancer, multi-step accumulation of genetic changes is considered to be related to all histological types of lung cancer[4,6].

Secondary lung cancer refers to a malignant tumor at any site that has metastasized to the lungs through various metastatic routes, including blood dissemination, lymph node metastasis or direct invasion from adjacent organs, among which blood metastasis is the most common route. Lungs are the organ with the highest incidence of systemically metastatic tumors, the main reason is that

the lungs not only have a dual blood supply of pulmonary artery and bronchial artery but also are the only way that the systemic circulation must pass. In the meantime, the pulmonary circulation is a low-pressure system, the slow blood flow makes tumor cells easy to stagnate[7]. In the autopsy of all malignancy-related deaths, approximately 30% have lung metastases[8]. Primary cancers outside the lungs that most commonly cause lung metastases are breast cancer (16.92%), followed by colorectal cancer (15.86%), thyroid cancer (7.68%), liver cancer (7.48%), lymphoma (6.61%), kidney cancer (6.39%), esophageal cancers (6.085%), and uterine cancers (5.41%). Among secondary lung cancers, 80%-90% are multiple, and 10%-20% are solitary.

4.1.2. Selection of Diagnosis and Treatment Method and Disease Prognosis

The treatment of primary lung cancer includes surgical resection, radiotherapy, chemotherapy, thermal ablation or a combination of these methods. Among them, SCLC is usually inoperable and cannot be treated with local methods, because this type of lung cancer has already metastasized at the time of diagnosis. For advanced NSCLC, a systemic comprehensive treatment strategy is generally selected. For early stage NSCLC, surgical operation is the standard treatment method and can obtain the best prognosis. Following operation, the 5-year survival rate is 60%-80% for stage I NSCLC, and 40%-50% for stage II NSCLC[9]. Although earlier stage NSCLC benefits the most from surgical resection, about 1/3 of lung cancer patients cannot tolerate resection due to poor lung function, complications and other reasons[10]. For patients with primary lung cancer who cannot tolerate surgical operations, thermal ablation therapy has been recommended as one of the alternative treatments for lung cancer by various regional guidelines and consensus for the diagnosis and treatment of lung cancer[11,12]. Besides, thermal ablation therapy has also been proven to be effective in treating secondary lung cancer[13,14].

In 2017, Chinese experts published an expert consensus on thermal ablation of primary and secondary lung cancers. In this consensus, thermal ablation is recommended as a curative method for the treatment of small primary lung cancers and small intrapulmonary metastases with good prognosis as shown by the biological characteristics (e.g., sarcoma, kidney cancer, colorectal cancer, breast cancer, melanoma and hepatocellular carcinoma) in patients who cannot tolerate surgical operations. In addition, it can also be combined with traditional radiotherapy and chemotherapy in patients with advanced large lung cancers to minimize tumor burden, relieve symptoms caused by tumors, and improve patient's Quality of Life[12].

In terms of the clinical results of thermal ablation therapy for primary lung cancers, two large multicenter, prospective and observational studies in patients with stage IA NSCLC found that the results of thermal ablation in clinically inoperable patients are similar to the results reported in previous stereotactic radiotherapy, the OS of thermal ablation therapy was ~86% in 1 year and ~69% in 2 years[15,16]. Two large national cancer database studies found no significant difference in OS between thermal ablation and stereotactic radiotherapy for early NSCLC[17,18]. In advanced NSCLC, thermal ablation is proven to be an effective treatment for local recurrence after radiotherapy.

Therefore, thermal ablation is considered as a palliative treatment option for advanced NSCLC[12,19].

There are increasingly more literatures on the clinical results of thermal ablation for the treatment of secondary lung cancers, especially lung metastasis from colorectal cancer, but it is mainly based on observational studies. A large systematic review included 8 observational studies involving a total of 903 patients with colorectal cancer lung metastases. The 1-year, 3-year, and 5-year survival was 89%, 44%, and 19.9%, respectively, while the tumor-free survival was 60.5%, 14.4% and 7% respectively[20]. Another prospective observational study found that, for small secondary lung cancer, repeated thermal ablation can achieve similar survival benefits as surgical resection. This study included 566 patients with a total of 1037 secondary lung cancers, through repeated thermal ablation therapy and control of lung cancers in this population during the follow-up period, the median OS was 62 months, the 5-year survival was 51.5%, and the 4-year local treatment efficacy was 89%[21].

Previous study reports on thermal ablation of lung cancer mainly focused on radiofrequency ablation, the number of studies on microwave ablation of lung cancer was relatively small. From the perspective of technical principles, however, microwave ablation has unique advantages besides the benefits of radiofrequency ablation: the operation time is shorter, the "heat sink effect" is reduced, it is less affected by the impedance, and no grounding device is needed[22]. As shown by two currently published comparative meta-analyses of microwave ablation versus radiofrequency ablation, both had similar effects in local tumor control, but the meta-analysis pointed out that the level of evidence based on the original research was low, the amount of data was insufficient for sub-group analysis to evaluate whether microwave ablation had a greater advantage in tumors of specific size or location[23,24]. Some research has already found better local tumor control for lung cancer in microwave ablation than in radiofrequency ablation[25]. With wider application of microwave ablation technology in the future, the availability of more high-level evidence data is expected to help evaluate the respective advantages of microwave ablation and radiofrequency ablation in different types of lung cancers.

4.2. Application of Investigational Product

Brace et al[26] first reported the clinical efficacy and safety of investigational product Certus Microwave Ablation System and accessories for lung cancer ablation. Five patients received percutaneous microwave ablation to treat lung cancer and were followed up for 18 months, all ablation procedures were technically successful without local tumor recurrence or serious complications during follow up.

Kurilova et al[27] reported the results of percutaneous microwave ablation for the treatment of 0.3-3.2 cm colorectal cancer lung metastases, the median follow-up time was 25.6 months. Among the 90 lung cancer lesions of a total of 50 patients, Certus Microwave Ablation System and accessories was used in 91% of the lesions. The total Technical Success rate was 99%, the Technical Efficacy was 90% for the first treatment and 92% for the second treatment. During the follow-up period, 10%

of the tumors showed local progression, and the median OS was 58.6 months. The incidence of complications requiring intervention in hospital was 10%.

4.3. Product Registration Profile and Reason for Conducting the Registration Clinical Trial in China

The Certus Microwave Ablation System and Accessories have been cleared by the United States (US, country of origin) Food and Drug Administration (FDA) and has been in clinical use since 2011 in the United States. The most common applications by clinicians have been the ablation of liver, lung, and kidney lesions. In addition, it is also used for the ablation of bone tumors.

Certus Microwave Ablation System and accessories have been approved by National Medical Products Administration (NMPA) and can be used for ablation of liver tumors from January 8th, 2020. However, there is no data on the use of this device for lung tissue ablation in the Chinese population. Therefore, this clinical study aims to support the registration of this device for lung cancer ablation indication in China.

5. FEATURES, STRUCTURAL COMPOSITION, OPERATION PRINCIPLE, MECHANISM OF ACTION, AND STUDY POPULATION

5.1.Features

5.1.1. Design Features of Investigational Product

This investigational product consists of Certus Microwave Ablation System equipped with software version 3.0.X, and NeuWave Certus PR, NeuWave Certus LK and NeuWave Certus LN microwave ablation probes. Several accessories are designed to allow mechanical interfacing of the power distribution module (PDM) with CT (computed tomography) from different vendors. These accessories are convenient to use without affecting the clinical functions of this system, therefore, they will not be described in detail.

Certus Microwave Ablation System uses a single 2.45GHz signal generator and 3 independent power amplifiers, each of which can generate up to 140W of power. Under ablation mode, the maximum output power is 65W when a single PR probe is connected, and 140W when a single LK or LN probe is connected, the power output time range is 1-10 minutes per transmission.

The PDM of Certus Microwave Ablation System is designed to minimize the user's setup time, improve the safety of operators and patients, and improve energy release efficiency at the same time. With the support of PDM interface, the users can connect with power source, electrical signal and cooling line of Certus energy release accessories in just one step. In percutaneous applications, PDM can be directly mounted on CT bed so that it can move with the CT bed during imaging. The probe and cable will also move synchronously with the patient, this can greatly reduce the risk of patient injuries due to accidental movement of the probe and cable. In open surgery applications, PDM can be directly mounted on Certus mainframe or on the operating table. In addition, PDM

uses wider and highly efficient cables to connect with the power amplifier. Since a wider cable can increase energy transfer efficiency, it is able to transfer more energy to the energy release accessory.

Certus Microwave Ablation System uses CO_2 cooling system to ensure that non-radiation part of the probe does not exceed the temperature requirements, while all other microwave ablation systems use sterile water for cooling purpose, but there is no difference between risks related to this air cooling system and inherent risks of water-cooled cryoablation systems widely accepted in clinical practice. Thus, the Certus system does not introduce new hazards.

The ablation probes include 3 general types, namely Certus LK, LN and PR. Certus LK and LN probes are specifically used to achieve higher energy transfer efficiency in the tissues in order to cover a larger ablation area. Certus LK probe can be used in lung ablation. Certus LN probe is specially designed for lung tissue properties and limited to the use in lung tissues to optimize energy transfer efficiency of the probe in lung tissues. Certus PR probe is specifically designed to limit the length of ablation, for example, when a small ablation zone is needed, it can realize the ablation effect by quickly wrapping the antenna and limiting the anterior ablation length. When compared with other Certus probes, Certus PR probe can not only provide doctors with a smaller ablation area but also limit necrosis of the anterior distal tissues.

5.1.2. Material Features of Investigational Product

Material properties of disposable microwave ablation probes of this investigational product

Code No.	Component	Material properties
1	Ablation probe	Titanium (except for PR ablation probe); titanium, aluminum coating (PR ablation probe)
2	Radiation area	Zirconia, FEP heat shrink tubing (whole body, except for antenna)
3	Tissue loc zone	Stainless steel, FEP heat shrink tubing (whole body, except for antenna)
4	Insertion depth mark	Stainless steel, FEP heat shrink tubing (whole body, except for antenna)
5	Cauterize stop mark	Stainless steel, FEP heat shrink tubing (whole body, except for antenna)
6	Ablation probe shaft	Stainless steel, FEP heat shrink tubing (whole body, except for antenna)
7	Handle, LED light	ABS resin
8	Protective sheath	Polypropylene

5.2.Structural Composition, Operation Principle, Mechanism of Action

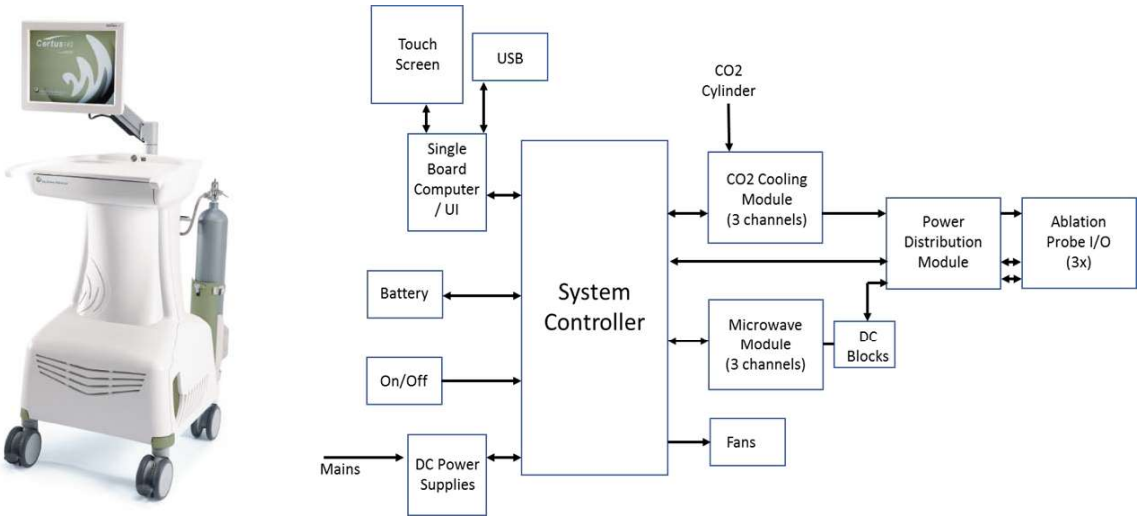
5.2.1. Composition of Investigational Product

This investigational product consists of Certus Microwave Ablation System and microwave ablation probes (Certus PR, Certus LK and Certus LN) made by NeuWave Medical. The system consists of a generator, an energy module PDM (probe interface unit, connected to ablation probe of the system), a temperature measurement system, a cooling system using CO_2 cylinder (the cylinder is not included in the registration device), software and CT brackets.

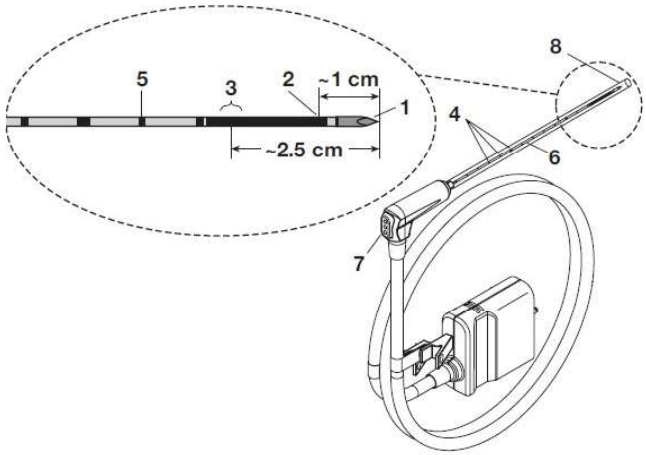
The Certus microwave ablation probe consists of a handle (with LED indicator), coaxial connector, cable, ablation probe shaft, microwave radiation ablation antenna tip, 3 temperature sensors and a CO_2 circulation loop.

Schematic diagrams of the system and ablation probe product are as follows:

NeuWave Certus Microwave Ablation System



Schematic diagram of Certus Microwave Ablation Probes and components (Taking PR probe for example)



Note: 1-cannula, 2-radiation point, 3-Tissue-loc area, 4-insertion depth mark, 5-cautertize stop mark, 6-shaft axis, 7-handle/LED, 8-protective sleeve.

5.2.2. Operation Principle and Mechanism of Action of Investigational Product

In this investigational product, the mainframe of Certus Microwave Ablation System generates 2450MHz microwave energy through microwave source, power amplifiers and DC module. Microwave energy is transmitted to the ablation probe through connected cable, and then delivered to the tumor site waiting for treatment through the ablation probe. Under the action of microwave magnetic field, water, protein and other polar molecules in tumor tissues vibrate in high speed to cause collision and friction between these molecules. As a result, a high temperature up to 60°C-150°C is generated within a short time, leading to coagulative necrosis of the cells and subsequent necrosis of tumor tissues. This system is controlled by an easy-to-use touch screen user interface. Each power amplifier can generate up to 140W of microwave. Generator power is limited by the selected probe type. Up to 3 microwave ablation probes can be connected each time to receive energy transmission. If Certus system is malfunctioning, the system will automatically stop emitting microwave energy. The Certus Microwave Ablation System and Accessories are general purpose thermal ablation tools used by physicians to ablate soft tissue lesions in a wide variety of tissue and disease states (including lung tumors) in the United States.

The PDM is designed to improve system utility by reducing device complexity and minimizing wiring from the probe to the generator. In addition, PDM also helps use wider and lower loss cables between microwave generator and PDM. Wider cables in combination with PDM can safely deliver more energy to the ablation probe without incurring risks due to heated probe cable or handle.

The principle of CO_2 cooling system is to deliver high-pressure CO_2 to gas circulation loop within the ablation probe. When the pressure drops rapidly, the resulted Joule-Thomson effect will cool

the ablation probe. The system uses two CO_2 cylinders to supply gas to the cooling system. When the gas cylinder becomes empty, the system will automatically switch to another gas cylinder and notify the user to replace empty cylinder. CO_2 temperature and pressure can be monitored and automatically adjusted by the system to maintain CO_2 cooling effect. This cooling system can ensure that non-radiation parts of the probe will not exceed the temperature requirement. In addition, a Tissue-loc effect can be formed to help adhere ablation probe to the tissues during pre-ablation imaging period and initial ablation stage, thereby reducing displacement risk of the ablation probe placed in tissues.

Microwave ablation probe is a sterile device, and each probe is for one-time use only for patients. The probe adopts a three-dimensional antenna design, the principle is to let a coaxial unipolar antenna pass through a hollow needle. The probe constitutes a three-dimensional structure, and the antenna is located besides the unipolar base-the distance is about 1/4 of the wavelength. This position improves antenna efficiency and reduces microwave field reflux of the coaxial outer conductor. Subsequently, more energy can accumulate within the tissues.

5.3.Study Population

This study will enroll at least 120 plus run-in subjects (each site will enroll 2 run-in subjects) of Chinese patients with NSCLC or oligometastatic lung tumor who are scheduled to be hospitalized for microwave ablation. For each patient, tumor(s) to be ablated in a single procedure should be a maximum of one ipsilateral biopsy proven NSCLC tumor with documented results or a maximum of three ipsilateral oligometastatic lung tumors with a clinical diagnosis. Each tumor to be ablated should be $\leqslant$ 2cm and locates in outer two-thirds of a lung.

6. PRODUCT INDICATIONS AND CONTRAINDICATIONS, PRECAUTIONS

[Indications]

The Certus Microwave Ablation System and Accessories are intended to ablate/coagulate soft tissues. The Certus Microwave Ablation System and Accessories are general purpose thermal ablation tools used by physicians to ablate soft tissue lesions in a wide variety of tissue and disease states. The most common applications by clinicians have been the ablation of liver, kidney and lung lesions. Additional, but less common uses have been the ablation of soft tissue lesions in bone and nerve ablation.

[Contraindications]

The Certus Microwave Ablation System and Accessories are contraindicated for:

- Cardiac operation
- Pregnant patients, potential risks to patient and/or fetus have not been established.
- Patients with implantable pacemakers or other electronic implants. Implanted electronic devices may be adversely affected by MW power.

- Central nervous system ablation

[Precautions]

All hazards associated with the use of the Certus system have been identified and appropriately mitigated. Design considerations were taken to reduce the risks associated with existing MW ablation systems, including improved system usability and cable management.

- Probe temperatures are highly dependent on tissue variables such as perfusion and vasculature. Probe temperatures are likely to vary from procedure to procedure based on these tissue variables. These temperature variations do not, by themselves, indicate a malfunctioning probe or system.
- Electrosurgical/electrocautery devices may interfere with the Certus system and cause system errors. Ensure that all Certus probes are removed from the patient prior to using electrosurgical/electrocautery devices.
- Use only Certus Ablation Probes from NeuWave Medical with the Certus Ablation System. Probes from other manufacturers may cause patient injury or make the product function improperly.
- The Certus system uses a CO_2 cooling system where all other MW systems use sterile water, but the risks associated with this cooling system do not differ from the risks inherent in cryogenic ablation systems, also widely accepted in clinical use. Thus, the Certus system does not introduce new hazards.
- This product should only be used by clinicians and staff properly trained in the use of the technology and its associated warnings and cautions.
- Refer to the Certus Microwave Ablation System and Accessories accompanying documents for a complete and comprehensive list of Warnings and Cautions.

7. OVERALL DESIGN

7.1. Trial Design

7.1.1. Trial Objective

The primary objective of this study is to evaluate the effectiveness and safety of the NeuWave Certus Microwave Ablation System and Accessories in the percutaneous microwave ablation of NSCLC or oligometastatic lung tumor.

7.1.2. Trial Method Selection and Its Rationale

This is a prospective multicenter study with single-arm performance goal. The prospective study design can reduce bias and provides better data accuracy without any needs for recall. A single-arm design with performance goal is adopted. Due to the lack of published objective performance criteria (OPC), the performance goal (PG) is constructed as the target value. The statistical considerations are to calculate point estimate of the primary study endpoint and its corresponding

95% confidence interval. This 95% confidence interval will be compared with clinically significant PG predefined in the protocol to determine whether this investigational product has reached the minimum standards recognized in the professional field. Based on the scientific hypothesis that the primary endpoint is superior to PG, and the permissible type I and type II errors, the correspondingly required sample size will be estimated to ensure statistical significance of the results.

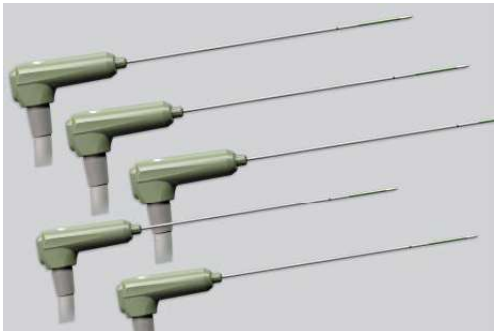
7.1.3. Measures to Reduce and Avoid Bias

This study adopts a prospective design to avoid possible bias of retrospective study. The Independent Review Committee (IRC) will be set up for the determination of key endpoints in order to standardize and unify the evaluation methods, and to avoid potential bias caused by surgeon's judgment.

This study collects data on objective indexes, and all relevant study data will be recorded in the original medical records for inspection and verification during the monitoring process. All investigators will receive proper training to ensure that they are familiar with this study device before their study sites are initiated, and to ensure scientific attitude of the study personnel. In addition, each study site will set a run-in period to include the first 2 subjects treated at this site, but these subjects will be included in the safety set only. This is intended to reduce operational bias due to learning curve.

The investigator should have more communication with the subjects to improve subject compliance. This will help reduce the informational bias.

7.1.4. Investigational Medical Device

	Study Device Composition 1 Certus Microwave Ablation System	**Study Device Composition 2 Certus microwave ablation probe**
Figure		
Entering global market (year)	Global: 2011	Global: 2011

<table>
<tr><th></th><th>Study Device Composition 1
Certus Microwave Ablation System</th><th>Study Device Composition 2
Certus microwave ablation probe</th></tr>
<tr><td>Indications</td><td>Certus Microwave Ablation System and accessories are applicable for soft tissue ablation (coagulation) in percutaneous, open surgery and laparoscopic surgery.</td><td>Certus disposable microwave ablation probe is a dedicated accessory of Certus Microwave Ablation System, and applicable for soft tissue ablation (coagulation) in percutaneous, open surgery and laparoscopic surgery.</td></tr>
<tr><td>Components</td><td>It consists of a generator, a PDM (probe interface unit, connected to ablation antenna of the system), a temperature measurement system, a cooling system using CO_2 gas cylinder (the cylinder is not included in the registration device), software and CT brackets.</td><td>It consists of a handle (with LED indicator), coaxial connector, cable, ablation probe shaft, microwave radiation tip, 3 temperature sensors, and a CO_2 circulation loop.</td></tr>
<tr><td>Dimension</td><td>Width: 23" (58.4 cm)
Depth: 28" (71.1 cm)
Height (including display): 52" (132 cm) (minimum), 59" (150 cm) (maximum)
Weight: ~250 pounds (113 kg)</td><td>Certus PR and Certus LK models use 17 gauge and 15-gauge probes.
Certus LN model uses a 17-gauge probe.
All models of probes have 15 cm and 20 cm in length.</td></tr>
<tr><td>Material</td><td>NA</td><td><table>
<tr><td>Ablation probe</td><td>Titanium (except for PR ablation probe); titanium, aluminum coating (PR ablation probe)</td></tr>
<tr><td>Ablation probe shaft, radiation zone, tissue loc area, insertion depth mark, cauterize stop mark</td><td>Zirconia, FEP heat shrink tubing (whole body, except for antenna)</td></tr>
<tr><td>Handle, LED light</td><td>ABS resin</td></tr>
<tr><td>Protective sheath</td><td>Polypropylene</td></tr>
</table></td></tr>
</table>

7.1.5. Selection of Subjects:

1) Inclusion criteria

Subjects will be included if ALL of the following inclusion criteria are met:

1. Signed the informed consent form and willing to fulfill the study-related assessments and procedure schedule.
2. Lung tumor patients ≥ 18 years of age who are ineligible for/decline surgery and who plan to receive microwave ablation therapy.
3. ECOG performance status score of 0-2.
4. Patients with stages IA1-IA2 NSCLC with documented results from a biopsy or patients with clinically diagnosed oligometastatic lung tumor.
5. Tumor(s) to be ablated in a single surgery should be a maximum of one NSCLC tumor or a maximum of three ipsilateral oligometastatic lung tumors.
6. Tumor(s) to be ablated in a single surgery should be ≤ 2cm, locate in the outer two-thirds of a lung, not closer than 1cm from the hilum of lung, great vessels, principal bronchus, trachea or esophagus, and not contiguous with the pleura.

2) Exclusion Criteria

Subjects who meet ANY of the following exclusion criteria will be excluded:

1. Pregnant or breast-feeding.
2. Patients with implantable pacemakers or other electronic implants.
3. Oligometastatic tumors patients whose primary lesion cannot be controlled or have widely metastases, in the opinion of the investigator and/or treating oncologist.
4. Any planned concurrent procedure at the time of ablation.
5. Planned treatment for other tumors in the same side lung during the study period.
6. With a skin infection or ulceration at the site to be punctured by probe(s).
7. Clinical or imaging findings consistent with an active pulmonary infection.
8. Patients with severe pulmonary fibrosis in the area intended to ablate, especially drug-induced pulmonary fibrosis.
9. Patients with prior radiotherapy in the area intended to ablate.
10. Patients with uncontrolled malignant pleural effusion at the lung side with tumor to ablate.
11. Tumors where the anticipated zone of ablation would encompass significant (in the opinion of the treating physician) emphysematous or bullous disease.
12. The investigator anticipates that the ablation zone of the multiple tumor(s) to be ablated

may have overlapping ablation zones.

13. Patients who have received lung ablation or surgical resection therapy within 30 days prior to the ablation procedure under study and those who plan to receive lung tumor ablation or surgical resection therapy or radiation therapy on the ablated lung side before completing the primary efficacy endpoint assessment approximately 30 days after the ablation procedure.
14. Patients who received systemic therapy such as chemotherapy, targeted drug therapy, or immunotherapy within 7 days prior to the ablation procedure under study, and patients who had a systemic treatment plan such as chemotherapy, targeted drug therapy, immunotherapy, etc. before completing the primary efficacy endpoint assessment approximately 30 days after the ablation procedure.
15. Patients with uncorrectable coagulopathy based on investigator judgment.
16. Patients with a platelet count $\leq 50 \times 10^9$/L.
17. Patients who cannot discontinue antiplatelet medication (e.g., aspirin, clopidogrel, prasugrel, ticagrelor) at least **5 days** before the ablation procedure through **24 hours** post-procedure.
18. Patients who cannot discontinue anticoagulant medication (e.g., rivaroxaban, apixaban, dabigatran, edoxaban) at least **3 days** before the ablation procedure through **24 hours** post-procedure.
19. Patients who cannot discontinue warfarin before at least **5 days** before the ablation procedure of the study or have an INR > 1.5.
20. As judged by the investigator, the patient has hypertension that cannot be effectively controlled by pharmacological treatments.
21. Severe hepatic, renal, cardiac, pulmonary or cerebral insufficiency, severe anemia, dehydration, and severe nutrition and metabolism disorders, which cannot be corrected or improved within a short term; or serious systemic infection; or severe neuromuscular diseases.
22. Expected survival less than 6 months.
23. Participation in any other interventional clinical study within 30 days before screening.
24. Physical or psychological condition which would impair study participation.
25. Patient is judged unsuitable for study participation by the investigator for any other reason.

Intra-Ablation Exclusion Criteria:

26. Before ablation probe puncture on the skin, patient is judged unsuitable for study participation due to intolerance to anesthesia.

27. Before ablation probe puncture on the skin, patient is judged unsuitable for study participation due to presenting any other condition.

3) Criteria of and procedure of Study Discontinuation

The criteria for Subject's Discontinuation from Study include, but are not limited to:

1. Subject withdraws the informed consent: Subject decides to withdraw from the study. This decision must be an "independent decision" and should be recorded in the subject's study files;
2. Investigator's decision: According to reasonable medical determination, the investigator can decide that allowing the subject to withdraw from this study serves the subject's best interests (including subject's discontinuation from the study due to the procedure being stopped before the ablation began);
3. Adverse events (AE)/serious adverse events (SAE): AE/SAE may not cause the subject to terminate this study. If the investigator decides to terminate a subject from the study, this subject must be followed up, until the AE/SAE is resolved or until the stable clinical endpoint is reached or until the event is adequately explained.;
4. Subject died;
5. Lost to follow-up: all subjects should provide corresponding contact information and agree to participate in all planned clinical follow-ups. If the subject cannot return to complete the required clinical visit, then 3 telephone contacts should be attempted and ask the subject to return for the scheduled clinical visit. Each contact attempt should be recorded in the original medical record. If the subject does not respond to any of the 3 phone calls, the investigator must send the subject a registered letter or an express mail (EMS) that can record the sending and receiving information. If the subject does not respond to the registered letter or EMS, and no further contact is made, this subject should be regarded as having missed the scheduled visit. If the above contact attempts still fail in 1 month after the ending of last scheduled visit, then this subject will be regarded as lost to follow-up; at this time, the electronic case report form (e-CRF) at the end of study must be filled in;
6. The sponsor discontinues the study;
7. The health authorities request study termination.

Procedure for subject's discontinuation from the trial:

If the subject discontinues the study, the reasons for termination will be documented in the source document and site files and submitted via the eCRF.

For a subject that discontinues the study due to procedure stop before ablation power emitting and

after probe puncture on the skin, there will be a new subject enrolled as a replacement. No replacement plan for other discontinued subjects.

Criteria of Sponsor's Discontinuation of the Trial:

Sponsor has the rights to temporarily suspend/discontinue or prematurely terminate studies of a single site, multiple sites or all sites for reasons including but not limited to: safety issues, ethical issues, administrative issues, inaccurate or incomplete data records, non-compliance, the quality or quantity of recruited subjects is not satisfactory.

Flow of Sponsor's Discontinuation of the Trial:

If the sponsor decides to suspend or terminate the clinical trial, it shall notify the medical device clinical trial management departments of all the clinical trial institutions according to regulatory requirements and provide reasons in writing. The departments shall promptly notify corresponding investigators and ethics committees. Suspended clinical trials shall not be resumed without the approval of the ethics committees.

4) Time of enrollment

Subjects are considered as being enrolled when they have completed the followings:

- Completion of the informed consent process;
- The investigator determines that the subject has met all the inclusion criteria without meeting any exclusion criteria.

Before the informed consent is signed, no study-related operating procedures can be implemented.

5) Expected overall duration of clinical trial and reasons for determination

The expected overall duration is approximately 40 months, including ethics committee meeting, agreement signing, subject enrollment and follow-up, data management, statistical analysis, writing final clinical report, etc.

6) Expected duration of participation of each subject

According to the Schedule of Activities specified in the protocol, the duration of each subject's participation in the study will be 13 months (about 1 month for Screening and 12 months for follow-up). The follow-up schedule will be based on the original ablation procedure date. A re-ablation for any reason will not change or extend the follow-up visit schedule.

7) Number of subjects required for clinical trial

This study plans to enroll 120 subjects plus run-in subjects (each site will enroll 2 run-in subjects) . Because this is a single-arm study, there will be no randomization of subjects. See Section 8 "Sample size calculation" for this sample size selection basis

7.1.6. Efficacy Evaluation Method

1) Description of efficacy parameters

The primary efficacy endpoint:

- Technical Efficacy Rate, defined as the percentage of tumor that is completely covered by the ablation area without signs of pathological enhancement as assessed by lung enhanced CT at Visit 3 (i.e., 30 days±7 days after the first ablation).

Secondary efficacy endpoints: Including Technical Success Rate, A0 Ablation Rate, Re-ablation Technical Success Rate, Local Tumor Progression, Progression-Free Survival, and Overall Survival. The respective definitions are as follows:

1. Technical Success Rate: Percentage of tumors that achieve A0 or A1 ablation (i.e., the ablation zone covers the tumor completely and has a surrounding margin) in the lung CT immediately following the initial ablation procedure.
2. A0 Ablation Rate: Percentage of tumors that achieve A0 ablation (i.e., the ablation zone covers the tumor completely and has a margin of at least 5 mm for secondary lung tumors and at least 10 mm for primary lung tumors) in the lung CT immediately following the initial ablation procedure.
3. Re-Ablation Technical Success Rate: Percentage of tumors that achieve Technical Success in the lung CT immediately following the repeat ablation with the study device during the study.
4. Local Tumor Progression: Local tumor progression and time to local tumor progression of any original-ablated tumor(s).
5. Progression-Free Survival: Length of the time the patient is still alive after the original ablation procedure and with no evidence of any tumor progression (Local, regional, or distant).
6. Overall Survival: Length of time that the patient is still alive after the original ablation procedure within the study duration.

2) Selection of method and time to evaluate, record and analyze the efficacy parameters

For efficacy parameters including Technical Efficacy, Technical Success, A0 Ablation, Re-Ablation Technical Success and Local Tumor Progression, IRC will be used to evaluate the CT images in order to achieve standardization and consistency defined in the protocol and to reduce biases in surgeon's judgment. Investigator’s evaluation results will also be recorded. Both results will be recorded in the e-CRF. The composition of IRC and endpoint definition details will be described thoroughly in a separate imaging chapter, which will be finalized before the first patient is enrolled. Primary statistical analysis and hypothesis testing for the primary effectiveness endpoint will be based on IRC’s evaluation results.

For effectiveness endpoints Progression-Free Survival and Overall Survival, they will be based on reports by study physician and/or subject's treating oncologist. The evaluation results will be recorded in the e-CRF and reported in the final clinical study report.

- Primary efficacy endpoint:
  - Technical Efficacy Rate will be determined according to lung enhanced CT at Visit 3 (30 days±7 days after surgery).
- Secondary efficacy endpoints:
  - Technical Success Rate, A0 Ablation Rate, and Re-ablation Technical Success Rate: determined according to the maximum diameter, minimum diameter and minimal ablative margin of the ablated lesions as measured by lung CT approximately 10 minutes after ablation.
  - Local Tumor Progression: determined by lung enhanced CT after initial ablation.
  - Progression-Free Survival will be determined by study physician and/ or be reported by the patient's oncologist after initial ablation.
  - Overall Survival will be determined based on investigator recorded ablation time and death time.

See Section 8 for analytical methods of the above endpoints.

7.1.7. Exploratory Parameters Evaluation Method

1） Description of exploratory parameters

Exploratory parameters include:

1. Patient-reported outcomes:
   - Ablation-Procedure Related Pain: Compare the 1 day, 3 days, 1-month post-ablation versus pre-ablation patient-reported pain levels using the Numeric Pain Rating Scale.
   - Quality of Life: Compare the patient's 1 month post-ablation, 6 months post-ablation, 12 months post-ablation to the pre-ablation Quality of Life scores using EORTC QLQ-C30 and Lung-specific QLQ-LC13.

2. ECOG Performance Status: Patient functionality as measured by distribution of Eastern Cooperative Oncology Group (ECOG) classification scores over time.

3. Ablation Procedure Related Indicators: Number and types of probes used, number of ablation cycles, ablation power and time.

4. Length of hospital stay: The duration from the patient's completion of ablation procedure to discharge.

5. Re-Admission Rate: Percentage of subjects with unplanned hospital admission or re-admission due to adverse event occurring within 30 days after any ablation procedure using the study device

(i.e. the original ablation or a repeat ablation).

2） Selection of method and time to evaluate, record, and analyze the exploratory parameters

Ablation Procedure-Related Pain and Quality of Life will be based on patient report digital pain rating scale results at Visits 2B, and 3 and EORTC QLQ-C30 and lung-specific QLQ-LC13 at Visits 3, 5, and 6. The results will be recorded in the e-CRF.

The following exploratory endpoints evaluated by investigators will be recorded in the e-CRF:

- ECOG Performance Status is based on performance score at Visit 1, Visit 2B, Visit 3-6.
- Ablation Procedure Related Indicators are based on investigator's assessment of the ablation procedures at Visit 2A or any other Visits using study device for re-ablation.
- Length of Hospital Stay is based on ablation and discharge time recorded by the investigator during Visit 2A and Visit 2B.
- Re-Admission Rate is based on the investigator recorded readmissions.

See Section 8 for analytical methods of the exploratory parameters.

7.1.8. Safety Evaluation Method

1) Description of safety parameters

Safety parameters include:

- All AEs from the start of any ablation procedure (from the probe puncture on skin) to 30 days post-ablation or early discontinuation.
- All SAEs from the start of ablation procedure through the end of the study or early discontinuation.
- All device-related AEs, procedure-related AEs, device-related SAEs and procedure-related SAEs from the start of ablation procedure through the end of the study or early discontinuation.

The incidence of the prespecified AEs below will also be summarized and reported:

1. Pneumothorax (all and those requiring chest tube drainage)
2. Hemorrhage (all and those requiring treatment)
3. Post-ablation syndrome
4. Chest wall pain
5. Pleural effusion (all and those requiring chest tube drainage)
6. Pneumonia
7. Lung or chest abscess
8. Other infections
9. Bronchopleural fistula

2) Selection of method and time to evaluate, record, and analyze the safety parameters

From the time of signing the informed consent form until approximately 30 days (Visit 3) after ablation (including primary and repeat ablation) or early discontinuation, all adverse events will be recorded. During this period, all adverse events from the start of ablation (i.e., probe puncture on the skin) will be reported.

After approximately 30 days (Visit 3) post ablation, adverse events considered by the investigator as related to the study device or/and study procedures and all serious adverse events will be recorded and reported till the end of the study or early discontinuation.

For subjects who stop ablation and withdraw from the study without ablation power emission while the needle has punctured the skin during the ablation procedure, the subject will be followed up for safety events up to 30 days after the procedure. If the discontinued subject reports a serious adverse event, the subject will be followed until event resolution, stabilization, or until the event is adequately explained.

The safety parameters will be recorded on the e-CRF according to the investigator's record, medical record, and all other related source documents collected at each follow-up visit.

See Section 8 for safety endpoint analysis methods.

7.2. Trial Flow

7.2.1. Trial Flow Chart

Refer to Table 1: Schedule of Activities, which may be found at the end of the Protocol Synopsis.

7.2.2. Specification for Device Use

According to Instructions For Use (IFU) and technical manual of the product, the requirements for the use of study product are as follows:

Indications/scope of application

Study Product: Certus Microwave Ablation System and Accessories, intended to ablate/coagulate soft tissues. The Certus Microwave Ablation System and Accessories are general purpose thermal ablation tools used by physicians to ablate soft tissue lesions in a wide variety of tissue and disease states. The most common applications by clinicians have been the ablation of liver, kidney and lung lesions. Additional, but less common uses have been the ablation of soft tissue lesions in bone and nerve ablation.

Recommended operation mode

Physicians who are experienced with tumor ablation will do all ablations percutaneously using only the NeuWave Certus Ablation System. During the ablation, subjects will be under an anesthesia as per the institution's SOC. In this study, microwave ablation is a minimally invasive procedure that uses electromagnetic waves to generate tissue necrosis in the lung tissues. Using CT scan guidance,

a probe is inserted percutaneously into the lesion.

The ablation will be performed with a single high-powered, gas-cooled, multiple antenna-capable MW system (NeuWave Medical's Certus Ablation System and Accessories) with single-probe antenna for single tumor, according to the IFU and the performing physician's clinical judgment. Electromagnetic waves are delivered to the tissue, producing frictional heating to generate tissue necrosis at > 60°C. Duration of the ablation and power application will be determined by the performing physician based on manufacturer guidelines, with adjustment for tumor size, proximity to vulnerable structures, and real-time intraprocedural monitoring. Single or multiple ablation sessions may be done in one procedure.

The Certus Ablation System rests on a cart that contains the MW power amplifiers and cooling system. The user interface for the Certus Ablation System is a system display to access all controls and settings. When ready to begin the procedure, the display will be used to select the organ locations in which probes will be inserted during the procedure.

Target ablation involves placing a probe into a substantial target and then ablating for up to several minutes until the target tissue is necrotic. This can be done by percutaneous surgery. In Ablation Mode, power delivery times can be set from 1 to 10 minutes per delivery. The efficiency at which different types of soft tissue receive MW energy differ based on the electrical properties of the tissue. For lung tissue ablation, the investigator should select the probe type based on the size, location, etc. of the tumor and the patient ' s underlying condition, and use the device for ablation in the study according to the Instructions for Use (IFU).

Ablation time and power will also be controlled via the system display, which has buttons to control for Time and Power. Pressing the buttons next to the Time box adds or subtracts from the Target Time in 1-minute increments. The buttons next to the Power box add or subtract from the Power in 5-Watt increments.

Each connected probe must successfully pass a functional test before Tissu-Loc, Ablate, or Cauterize buttons are activated. The functional test must be conducted and passed before a probe may be used for ablation or surgical functions. Once a probe passes test, the functional controls become active.

Pressing the Ablation Tissu-Loc button starts the CO_2 cooling system to cool the Tissu- Loc zone in the probe to between 0 and -15°C. Once the Tissu-Loc Zone temperature reaches -5°C, the button turns gray, a green check mark appears on the button, and the button text reads 'Stop Tissu-Loc'.

The Probe Temperature is displayed below the probe image. A green highlighted outline appears around the Time box to indicate that power is being delivered. The Time display begins to count down from the target Time or count up to the target Time. An audible tone sounds continuously to indicate that power is being delivered. If more than one probe is delivering power, the audible tone changes pitch.

When the Stop Ablate button or Stop All Ablation Bar is pressed, energy delivery is stopped, and

the Ablation Time is displayed below the Time Box. This indicates the total time that power has been delivered via that probe. The probe temperature remains on the display.

A cauterizing feature is available to cauterize the insertion track when removing the probe from the patient. This feature is to cauterize the insertion track only. It should not be used to ablate or cauterize target tissue. Only one probe can be used in Cauterize mode at a time. No other probes may be delivering energy when cauterizing with a probe.

After the probe is removed from the patient, the Certus Ablation System cart may be wheeled to the side to allow the doctor to clean and bandage the probe insertion site.

Warnings and precautions

All hazards associated with the use of the Certus have been identified and appropriately mitigated. Design considerations were taken to reduce the risks associated with existing MW ablation systems, including improved system usability and cable management.

Important: Probe temperatures are highly dependent on tissue variables such as perfusion and vasculature. Probe temperatures are likely to vary from procedure to procedure based on these tissue variables. These temperature variations do not, by themselves, indicate a malfunctioning probe or system.

Electrosurgical/electrocautery devices may interfere with the Certus system and cause system errors. Ensure that all Certus probes are removed from the patient prior to using electrosurgical/electrocautery devices.

Use only Certus Ablation Probes from NeuWave Medical with the Certus Ablation System. Probes from other manufacturers may cause patient injury or fail to function properly.

The Certus system uses a CO_2 cooling system where all other MW systems use sterile water, but the risks associated with this cooling system do not differ from the risks inherent in cryogenic ablation systems, also widely accepted in clinical use. Thus, the Certus system does not introduce new hazards or intended uses.

This product should only be used by clinicians and staff properly trained in the use of the technology and its associated warnings and cautions.

Refer to the Certus Microwave Ablation System and Accessories accompanying documents for a complete and comprehensive list of Warnings and Cautions.

7.2.3. Study Procedure

1) Visit 1 - Baseline/Screening Visit

The following screening procedures should be performed before the study procedure, and all screening procedures should be completed within 30 days before ablation:

- The patient must be given ample time to review and sign the ICF.
- Collect demographic information (year and month of birth, sex, race, ethnicity), body height and body weight.
- Blood or urine pregnancy test shall be performed for women of childbearing potential and should be performed within 7 days prior to the ablation; otherwise the test must be repeated and available prior to ablation.
- Laboratory tests: including complete blood count (including differential count), coagulation test (APTT, PT and INR) should be performed within 7 days prior to the ablation; otherwise the test must be repeated and available prior to ablation.
- Collection of relevant medical/surgical/radiation history： at least include previous diagnosis of systemic tumors and pathological results (if any), history of other non-tumor lung diseases, history of chronic diseases, history of oncologic-related mediation/surgery/procedure/radiation history and smoking status.
- ECOG performance status score.
- Subjects must receive at least one contrast-enhanced CT scan of the lungs in the study site within 30 days prior to ablation (Visit 2A).
- The investigator should record the baseline information of all lung tumors observed on the pulmonary enhanced CT before ablation, including:
  - The number, location, size of the tumor to be ablated. The size of the tumor to be ablated must be measured using three-dimensional (3D) imaging on the lung window.
  - Whether the tumor to be ablated has been examined by biopsy before ablation, and the biopsy time and results should be recorded.
  - The number, location and size of other non-ablated tumors in the lung. For tumors not to be ablated, only need measuring size on 2D imaging.
- The investigator shall classify and determine the tumors to be ablated according to preoperative lung CT images as follows:
  - Classify the lung tumors to be ablated into: ① Stage 1A1-1A2 NSCLC; ② Oligometastatic lung tumor;
    - NSCLC should be diagnosed based on biopsy results. NSCLC staging assessment should be based on images within 6 weeks before the ablation. The images requirements are：
      - Minimally include: “Chest CT + head MRI or CT + neck and supraclavicular lymph node ultrasound or CT + upper abdominal ultrasound or CT + bone scan” as recommended by the 2019 edition

of Chinese Medical Association Guidelines for Clinical Diagnosis and Treatment of Lung Cancer;

- Acceptable if available by SOC: “PET/CT from skull base to mid-thigh”;
- Nice to have if available by SOC: “Mediastinal staging”.

- The images requirements for oligometastatic lung tumor diagnosis are：
  - Minimally cover the primary lesion, abdomen and chest;
  - Nice to have if available by SOC: brain MRI or CT if the investigator considers the patient having suspected brain metastases.

- The determination of whether the lung tumor to be ablated is GGO will be made by the investigator and classified as: pure GGO, partial solid GGO, and pure solid tumor.

- Quality of Life assessment: including EORTC QLQ-C30 and lung-specific QLQ-LC13.
- All relevant prior medications taken within 30 days of visit 1will be recorded, including blood-thinning/anticoagulants, chemotherapy/targeted therapy/immunotherapy and other anti-neoplastic agents, steroids, anti-inflammatory drugs, NSAIDs, antibiotics, and drugs used to treat relevant medical history.
- For all anti-tumor agents used prior to ablation, the pre-ablation withdrawal time should also be recorded.
- The name, time, location and purpose of all concomitant procedures within 30 days before visit 1 (including but not limited to puncture, radiotherapy, ablation therapy, surgical resection, etc.) will be recorded.
- Review inclusion/exclusion criteria and determine whether the patient meets the participation criteria.
- Record AEs and SAEs from signing the ICF.

Pre-Ablation Screening

Subjects will be consented prior to any actual study-specific screening procedures being conducted. Subjects will be considered enrolled into the study upon satisfaction of the following criteria:

- Completion of the informed consent process and signing the Informed Consent Form (ICF).
- Verification of the eligibility criteria by the Principal Investigator (PI) and/or authorized investigators. The verification must be conducted by the PI and/or authorized investigators prior to performing any study-related procedure or completing any form associated with this study.

Pre-Ablation Screening Failures

Subjects who have signed the informed consent form but are not included in the study after pre ablation screening will be considered screening failures. For subjects who are deemed as screening failure during the pre-ablation screening, only the following data will be recorded on the eCRF:

- Informed consent date.
- Demographic information (age, race, gender, and ethnicity).
- Reason for screening failure.

2) Visit 2 - Ablation (till discharge)

The ablation procedure (Visit 2A), followed by post ablation observation and discharge (Visit 2B)

1) Visit 2A- Ablation

The study is performed using the NeuWave Certus microwave ablation system in combination with the NeuWave Certus microwave ablation probe by a physician experienced in tumor ablation at the study site during the same procedure. During the ablation, subjects will be under an anesthesia as per the institution's SOC.

- The inclusion and exclusion criteria should be confirmed again to ensure that the patient continued to meet all criteria. Otherwise the patient will be a screen failure case.
- Pain assessment (prior to ablation): using the Numeric Pain Rating Scale (NPRS).
- On the day of ablation, the size of tumor to be ablated should be measured and recorded (3D) according to the CT image on that day again.
- CT-guided ablation procedure: during the ablation procedure, the microwave ablation probe is guided to the lung tumor by the lung CT guide, and CT will be used at least at 3 time points:

  (1) Before probe insertion: before inserting the probe into the tumor, the tumor to be ablated and surrounding structures are confirmed by CT. The investigator should record whether there are important normal anatomical structures or pathological structural changes around the tumor that affect the ablation range or/and safety, and if any, measure the shortest distance from this structure to the ablated tumor.

  (2) Before ablation: immediately prior to ablation, confirm that the probe is in the desired location using CT. If not in the expected position, reposition the probe and perform another scan. The physician should repeat the ablation process until the intended location is reached;

  (3) During ablation: Using CT to monitor the ablation probe and adjust the ablation time and power (this is an optional CT);

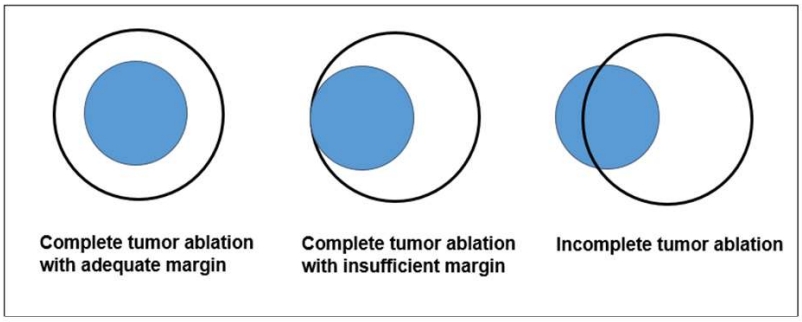
  (4) Post-ablation: After the ablation is completed, confirm the ablation procedure is completed using CT taken approximately 10 minutes after the ablation is completed and

determine whether the ablation lesion covers the tumor. If the ablation margin is not sufficient (i.e. Did not reach at least 5mm of safety margin for oligometastatic lung tumor or at least 1cm safety margin for NSCLC), the study physician should repeat the ablation to achieve an adequate ablation margin if the situation permits.

- Record ablation procedure details, including but not limited to the following:
  - Procedure date and time
  - Mode of anesthesia
  - Guidance method used
  - Anatomic location of ablated tumor
  - Number of ablation cycles
  - Ablation power and time
- Device count: all probe types and amounts.
- Intra-ablation Screening: For patients who meet the intra ablation exclusion criteria, they will be considered an intra-ablation screening failure, and will record:
  - Informed consent date
  - Demographic information (age, race, gender, and ethnicity)
  - Reason for screening failure
- Intra-ablation Stopping Criteria and Procedure:
  - During the ablation procedure, if the investigator should stop the procedure after probe puncture but before any microwave power emission to the subject's lung tumor, due to adverse events like severe bleeding/pneumothorax, or due to any other presenting conditions, the patient will be withdrawn from the study, recording the reason, and receive a follow-up period of 30 days after the procedure from the safety evaluation perspective. If the withdrawn subject reports a SAE, the subject will be followed until resolution of the event, a stable endpoint is reached, or until the event is appropriately explained.
  - For subjects with multiple tumors identified to be ablated during screening, if not all of the identified tumors receive ablation, the reason(s) for not ablating any of the identified tumors will be recorded. The subject will not be withdrawn from study. Further treatment on the non-ablated tumors will be based on sites' SOC (i.e., not using the study devices).
- The tumors that have been identified to be ablated during screening and receive ablation power during the initial ablation procedure will be regarded as "Target Tumor(s)". Only the "Target Tumor(s)" will undergo tumor level effectiveness evaluations (i.e., Technical

Success, Technical Efficacy, and Local Tumor Progression).

- The investigator should measure and record the maximum diameter and minimum diameter of each ablation lesion, as well as the minimum ablation margin (i.e., the distance from the edge of ablation lesion to the tumor edge).
- Document the investigator's classification for tumor ablation result evaluation:
  - A0 = Completed ablation procedure protocol with the ablation zone fully covering the tumor with an adequate safety margin (i.e., minimum safety margin of at least 5mm for secondary lung tumors and at least 10mm for primary lung tumors) as assessed by approximately 10 minutes post-ablation lung CT
  - A1= Completed ablation procedure protocol with the ablation zone fully covering the tumor but with insufficient safety margin (i.e., minimum safety margin less than 5mm for secondary lung tumors or less than 10mm for primary lung tumors) as assessed by approximately 10 minutes post-ablation lung CT
  - A2= Failure to complete the ablation procedure according to the ablation plan, and the ablation zone does not completely cover the tumor as assessed by approximately 10 minutes post-ablation lung CT



NOTE: While Technical Success will be defined as either an A0 or A1 ablation, the goal is to achieve A0 ablation, and this will be a pre-specified secondary analysis. For all A1 and A2 ablation classifications, the investigator will document the reason(s) why a margin of 5mm for secondary lung cancer or a margin of 1cm for NSCLC was not attainable on the applicable eCRF.

NOTE: If ablation procedure could not be completed after microwave power has started emitting, this case will be regarded as A2 ablation.

- All AEs and SAEs.
- Relevant concomitant medication: including blood thinning/anticoagulants, antineoplastic agents such as chemotherapy/ targeted therapy/ immunotherapy, steroids, anti-inflammatories, NSAIDs, antibiotics and medications used to treat relevant medical history and adverse events. There is no need to record the anesthetics used during the

ablation procedure.

- Concomitant procedure: the name, time, site and purpose of the concomitant procedure (**NOTE:** There should be no planned concomitant procedure at the time of the ablation according to exclusion criteria).

The basic tumor information(not include assessment results of investigator) will be jointly provided with the CTs to IRC, which includes enhanced CT before ablation, CT before probe insertion, CT before ablation, CT during ablation (optional) and CT after ablation, for ablation size measurement, ablation margin measurement, determination of immediate ablation results (A0, A1, A2), and determination of Technical Success Rate, A0 Ablation Rate.

2) Visit 2B

The following data will be collected after ablation till discharge:

- ECOG performance status score at day 1 after the ablation.
- Pain assessment: using the Numeric Pain Rating Scale (NPRS) at day 1 and day 3 after the ablation, this can be done by phone as needed.
- As clinically necessary, the study doctor can schedule a lung X-ray and/or lung CT scan as needed as an optional imaging test (e.g. at 1-3 days post-procedure) for a patient to assess the occurrence of post-ablation lung complications.
- Length of stay (LOS): the time from ablation completion to discharge is recorded.
- Relevant concomitant medication: including blood thinning/anticoagulants, antineoplastic agents such as chemotherapy/ targeted therapy/ immunotherapy, steroids, anti-inflammatories, NSAIDs, antibiotics and medications used to treat relevant medical history and adverse events.
- Concomitant procedure: the name, time, site and purpose of the concomitant operation (including but not limited to puncture, radiotherapy, ablation therapy and surgical resection).
- All AEs and SAEs.

NOTE: Between post-ablation and Visit 3, if the investigator considers it in the best interest of the patient to restart systemic therapy before completing the primary efficacy endpoint assessment approximately 30 days after the initial ablation, the investigator should contact the Sponsor medical monitor for discussion.

3) Visit 3

One month following the ablation procedure (30 days ± 7 days post procedure), subjects will return to the study site for the following evaluations:

- ECOG performance status score.

- Pain assessment: using numeric pain rating scale, this can be done by phone as needed.
- Quality of Life assessments: the QOL questionnaires include the EORTC QLQ-C30 and the lung-specific QLQ-LC13.
- Enhanced CT scan of the lung.
- Document the investigator's determination of Technical Efficacy evaluation.
- Submit the CT images to the IRC for determination of Technical Efficacy evaluation.
- Progression at other site to be evaluated by a study physician or may be reported by a patient's primary treating oncologist. If there is a progression, the study physician should specify if the progression is a new lung malignant tumor, or a distant metastasis.
- Any unplanned hospitalization in any hospital for any reason within 30 days post-ablation will be recorded, and the investigator will assess the reason for re-admission and record it in the study database.
- Relevant concomitant medication: including blood thinning/anticoagulants, antineoplastic agents such as chemotherapy/ targeted therapy/ immunotherapy, steroids, anti-inflammatories, NSAIDs, antibiotics and medications used to treat relevant medical history and adverse events.
- Concomitant procedure: the name, time, site and purpose of the concomitant procedure (including but not limited to puncture, radiotherapy, ablation therapy and surgical resection).
- All AEs and SAEs.

Note: Within the study, re-ablations on the initially ablated target tumor(s) should not be performed before the Visit 3 assessment for Technical Efficacy has been completed. If investigators assess it is medically indicated/necessary to re-ablate before the Visit 3 Technical Efficacy assessment, the re-ablated tumor's Technical Efficacy assessment will be counted as failure. The re-ablation will not change or extend the subject's follow-up schedule.

4) Visit 4 to visit 6 (end of study)

Visit 4 will occur at 3 months (± 14 days), Visit 5 will occur at 6 months (± 1 month), and Visit 6 will occur at 12 months (± 1 month) after surgery during which subjects will return to the study site for the following assessments:

- ECOG performance status score.
- Quality of Life questionnaire: the QOL questionnaires include the EORTC QLQ-C30 and the lung-specific QLQ-LC13 (Visits 5 and 6 only).
- Enhanced CT scan of the lung.
- Document the investigator's determination of Local Tumor Progression.

- Submit the CT images to the IRC for determination of whether Local Tumor Progression has occurred or not.
- Progression at other site to be evaluated by a study physician or may be reported by a patient's primary treating oncologist. If there is a progression, the study physician should specify if the progression is a new lung malignant tumor, or a distant metastasis.
- Relevant concomitant medication: including antineoplastic agents such as chemotherapy/targeted therapy/immunotherapy and drugs related to the recorded adverse events.
- Concomitant procedure: the name, time, site and purpose of the concomitant operation (including but not limited to puncture, radiotherapy, ablation therapy and surgical resection).
- All AEs considered by the investigator as related to the study device or/and study procedures and all SAEs.

5) Unscheduled Visits

The following data will be collected at all unscheduled visits:

- Reason for the unscheduled visit.
- Relevant concomitant medication: Including antineoplastic agents such as chemotherapy/targeted therapy/immunotherapy and drugs related to the recorded adverse events.
- Concomitant procedure: the name, time, site and purpose of the concomitant operation (including but not limited to puncture, radiotherapy, ablation therapy and surgical resection).
- All AEs and SAEs.
- Any other study assessments, per SOC.

Notes: Re-ablations on the target tumor(s) in the study should only be conducted after finishing Visit 3 evaluation.

Re-ablations using the microwave ablation system and ablation probe provided in this study can only be performed when there is local progression of lung tumor after initial ablation, or residual tumor or insufficient margin during initial ablation of tumor (if considered medically indicated/ necessary by the investigator so as to obtain sufficient ablation margin of tumor). The study device provided by this study cannot be used for the ablation of other lesion foci.

For each re-ablation using the study device within this study, the following information will be captured:

- Reason for the re-ablation.

- Record ablation procedure details, including but not limited to the following:
  - Procedure date and time
  - Mode of anesthesia
  - Guidance method used
  - Anatomic location of ablated tumor
  - Number of ablation cycles
  - Ablation power and time
- Device count: all probe types and amounts.
- Document the investigator's re-ablation result evaluation.
- Submit the CT to IRC for re-ablation result evaluation.
- All AEs and SAEs.

7.3. Monitoring Plan

This study is conducted in compliance with Good Clinical Practice for Medical Devices and relevant international laws, regulations and guidelines, such as ISO 14155.

The sponsor shall undertake monitoring responsibility for the clinical trial, select qualified monitors to perform relevant duties, and make sure:

1. The rights and well-being of the subjects are protected;
2. Reported study data is accurate, complete, and verifiable from source documents;
3. The conduct of the study is in compliance with the currently approved protocol/amendment(s), applicable GCPs for medical devices, and applicable regulatory requirements.

Steps to be taken to ensure the accuracy and reliability of data include the selection of qualified investigators and appropriate study centers, review of protocol procedures with the Investigator and associated personnel prior to the study, and periodic monitoring visits by the Sponsor. The Sponsor will verify the authenticity, accuracy, completeness and legibility of the source documents and source data as well as the completeness of each subject’s source documents, and review the eCRFs for accuracy and completeness during on-site monitoring visits and after their return to the Sponsor; any discrepancies will be resolved with the Investigator or designees, as appropriate. The data will be entered into the clinical study database and verified for accuracy.

The extent and nature of monitoring will be predetermined and based on considerations such as the objective, design, complexity, and endpoints of the study and mutually agreed to by the Sponsor and investigators. Monitors will comply with established written standard operating procedures as well as procedures (i.e., monitoring plan) specified by the Sponsor for monitoring this study.

This study may be subject to inspection by the sponsor or inspection by health authorities. The investigator shall agree to and cooperate with the Sponsor or its designated representative and regulatory authorities in on-site review and inspection of all study-related documents and subject records. By signing the signature page for this protocol, the investigator agrees to allow the sponsor or its designated representative and regulatory authorities to monitor all project-related study documents on site.

See the attached monitoring plan for details.

8. STATISTICAL CONSIDERATIONS

8.1. Statistical Design, Method and Analysis Procedure

This study is a single-arm, prospective, multi-center clinical study with performance goals.

Categorical variables will be summarized descriptively by frequencies and associated percentages. Continuous variables will be summarized descriptively by number of subjects, mean, standard deviation, median, quartile, minimum, and maximum.

All endpoint analyses at the tumor level will be conducted on "Target Tumors" (i.e. tumors identified to be ablated during screening and receive ablation power during the initial ablation procedure).

The data analysis plan will be documented in detail in the Statistical Analysis Plan (SAP).

- **Primary Effectiveness Endpoint-Technical Efficacy Rate**

The analysis of the primary effectiveness endpoint is to demonstrate the technical effectiveness of the NeuWave Certus microwave ablation system and accessories in the ablation of Chinese patients with NSCLC or secondary lung cancer. This endpoint will be based on the scan obtained at Visit 3 and will count as successes when tumors with completely covered ablation zone without pathological enhancement as assessed by enhanced CT scan at Visit 3 (i.e., 30 days ± 7 days after the first ablation procedure). Additionally, if an initial ablated tumor had re-ablation before the Visit 3 Technical Efficacy assessment, the re-ablated tumor will be considered a failure.

The primary endpoint will be assessed based on an independent review committee (IRC)'s evaluation results using the following methods:

The hypothesis test for Technical Efficacy Rate is null hypothesis (H0): $P \leq P0$ (80%) vs. alternative hypothesis (H1): $P > 80\%$. Wherein, P represents the true technical efficiency for the NeuWave Certus Microwave Ablation System and 80% is the Performance Goal (PG). If the lower limit of the 95% CI of the Technical Efficacy rate based on the Normal Approximation to the Binomial distribution (Z-test that uses S(P0) to estimate the standard deviation) is higher than the predefined PG value, primary endpoint success is considered.

PG is determined based on the results of the meta-analysis on the existing literature of similar techniques. The Technical Efficacy rate at 1 month after microwave ablation was extracted from

existing literature, and then the point estimate and corresponding 95% confidence interval were estimated by meta-analysis using random effects. The meta-analysis results showed that, prior studies based on a variety of populations have a mean Technical Efficacy rate of 87% (95%CI: 79%-92%) after MWA of lung cancer at 1 month. Considering that PG is the minimum threshold of the acceptable performance, new product-related study curve, clinically significant Technical Efficacy rate, and lower limit of the above 95% confidence interval, the PG of the study is set as 80%. The primary analysis of Technical Efficacy will be performed at the Target Tumor level and at the subject level on the Full Analysis Set. For multi-target-tumor subjects, the largest Target Tumor, determined by the maximum three dimensions of each target tumor, will be used for the subject-level analysis. This will be repeated for the Per Protocol Set.

An additional analysis will be conducted based on the investigators evaluation of Technical Efficacy Rate.

- **Secondary endpoints:**

  1. The number and percentage of tumors with Technical Success Rate, A0 Ablation Rate, and Re-ablation Technical Success Rate will be summarized and 95% confidence interval will be estimated based on the Normal Approximation to the Binomial distribution.
     - Technical Success Rate and A0 Ablation Rate will be based on ablation zone tumor coverage and the ablation margin achieved after the first ablation and prior to any repeat ablations.
     - Re-Ablation Technical Success Rate will be based on ablation zone tumor coverage and ablation margin achieved after re-ablation.
  2. Local Tumor Progression will be estimated using Kaplan-Meier method and 95% confidence interval will be provided.
  3. Progression-Free Survival and Overall Survival will be estimated based on patient level using Kaplan-Meier method and 95% confidence interval will be provided.
  4. The summary description of pain scores, ECOG scores and Quality of Life scores will be reported based on patient level according to the standard recommended method.
  5. The length of stay as well as the number and percentage of readmissions will be described based on the patient level, and the reasons for readmission will be counted and percentage will be calculated.
  6. Ablation Procedure Related Indicators will be reported descriptively.
  7. The number and percentage of subjects who complete and do not complete the study and the specific reasons for not completing the study will be counted and calculated based on the patient level.

Note: Primary and secondary efficacy endpoints related to efficacy that are assessed by both the study physician (i.e., PI) and Independent Central Imaging Committee (IRC) as described in

Section 7.1, including Technical Efficacy Rate, Technical Success Rate, A0 Ablation Rate, Re-ablation Technical Success Rate, and Local Tumor Progression will be recorded.

- **Safety endpoints:**

The safety endpoints will be summarized in the safety set, where the safety data of subjects in the run-in period can be summarized separately from the rest of subjects. The number and percentage of subjects experiencing any adverse event (AE) and serious adverse event (SAE) will be summarized at the preferred term level of MedDRA. The severity of AEs and SAEs will be summarized. The AEs and SAEs will also be summarized according to the Society of Interventional Radiology (SIR) classification. Study device-related AEs, ablation procedure-related AEs, all SAEs, device-related SAEs, and ablation procedure-related SAEs will be summarized in a similar way. Besides, the incidence of the predefined AEs below will also be summarized and reported:

1. Pneumothorax (all and those requiring chest tube drainage)
2. Hemorrhages (all and those requiring treatment)
3. Post-ablation syndrome
4. Chest wall pain
5. Pleural Effusion (all and those requiring chest tube drainage)
6. Pneumonia
7. Pulmonary or pleural abscess
8. Other infections
9. Bronchopleural fistula

- **Three analyses in total are planned.**

1. The first analysis will occur after 50% of the target enrolled subjects complete the 1-month visit, aiming to inspect the assumption used for calculation of sample size and determine if the sample size should be increased. In view of the lack of available clinical data for evaluating the performance of the study product in percutaneous lung tumor ablation procedure, the sample size will be re-estimated adopting a self-adaptive method after approximately 50% of the initial planned sample size are enrolled. The sample size will be re-estimated based on the assessment of conditional power, so as to increase the sample size to the predefined maximum value of 200 subjects or more or maintain the originally planned sample size of 120 subjects plus run-in subjects (each site will enroll 2 run-in subjects). Enrollment in the trial will continue while this interim analysis is being conducted. Complete details of the methodology will be provided in the SAP.
2. The second analysis will occur after all enrolled subjects finish the 1-month visit, aiming to evaluate the Technical Efficacy, periprocedural endpoints and safety of lung tumor ablation, and if the primary endpoint success is deemed, the study report will be submitted

to NMPA for the registration application of lung ablation indication.

3. The third analysis will occur after all subjects complete the study.

8.2. Calculation of Sample Size

8.2.1. Total Sample Size

It plans to enroll 120 subjects plus run-in subjects (each site will enroll 2 run-in subjects) in this clinical study. The sample size calculation is justified as follows:

The study sample size is determined by hypothesis testing for the comparison of the primary endpoint versus the performance goal (PG). PG is determined based on the results of the meta-analysis on the existing literature of similar techniques. The Technical Efficacy rate at 1 month after microwave ablation was extracted from existing literature, and then the point estimate and corresponding 95% confidence interval were estimated by meta-analysis using random effects. The meta-analysis results showed that, prior studies based on a variety of hypotheses have a mean Technical Efficacy rate of 87% (95%CI 79%-92%) at 1 month. Considering that PG is the minimum threshold of the acceptable performance, new product-related study learning curve, clinically significant Technical Efficacy rate, and lower limit of the above 95% confidence interval, the PG of the study is set as 80%.

The Technical Efficacy hypothesis test of the primary endpoint is: H0: $P \leq P0$ (80%) vs. H1: $P >$ 80%, where P is the actual Technical Efficacy rate of the NeuWave Certus Microwave Ablation System. A sample size of 120 subjects is necessary to achieve at least 80% power for demonstrating that the Technical Efficacy rate of the NeuWave Certus Microwave Ablation System is > 80% when the expected performance is 90% and a one-sided significance level of 0.025 is used with the Normal Approximation to the Binomial distribution (Z-test that uses S(P0) to estimate the standard deviation), with adjustment for up to 10% dropout. Besides, each site will enroll 2 subjects first in the run-in phase. So the total sample size will be 120 subjects plus run-in subjects (each site will enroll 2 run-in subjects).

In addition, given the lack of available clinical data for the evaluation of the performance of the investigational product in pulmonary tumor ablation procedures, an adaptive approach will be used to re-estimate the sample size after enrolling approximately 50% of the originally planned sample size. The sample size will be re-estimated based on the assessment of conditional power, so as to increase the sample size (the predefined maximum value is 200 subjects) or maintain the originally planned sample size of 120 subjects plus run-in subjects(each site will enroll 2 run-in subjects).

8.2.2. Number of Clinical Trials Subjects for Each Disease and Reasons for Determination

Each site should at least enroll 2 run-in subjects. No disease type (NSCLC or oligometastatic lung tumor) requirement for the run-in phase subjects. Of the 120 non run in sample, the number of cases for each disease type is limited at up to 75% (i.e. in the 120 non run in sample, up to 90 subjects

could be NSCLC or oligometastatic lung tumor).

8.2.3. Significance Level and Power of Clinical Trial

In this study, the statistical power is set as 80% for the sample size calculation of primary effectiveness endpoint test, and the significance level of hypothesis test is set as one-sided 0.025.

8.2.4. Expected Dropout Rate

The expected drop-out rate for this clinical study is 10% at Visit 3.

8.3. Acceptance/Nonacceptance Criteria of Clinical Trial Results

If the lower limit of the 95% confidence interval of the technical response rate of the primary endpoint in this study is greater than the pre-specified PG of 80%, the null hypothesis is rejected and the alternative hypothesis is accepted, and the clinical trial succeeded.

If the lower limit of the 95% CI of the technical response rate of the study primary endpoint is ≤ 80% of the pre-set PG, it is considered that the clinical trial failed.

8.4. Criteria and Reason for Terminating the Trial Based on the Statistical Results

There is no planned termination of the trial due to statistical reasons.

8.5. Statistical Method of All Data, together with the Handling Method of Missing, Unused and Error Data (including Termination and Withdrawal Halfway) and Unreasonable Data

All effectiveness endpoint analyses will be performed only on subjects undergoing ablation with the NeuWave Microwave Ablation System and observed data will be analyzed.

1) In the primary analysis of the primary effectiveness endpoint:

- A new subject will be recruited to replace any subject who discontinues the ablation procedure after the ablation probe punctures the skin and before the microwave energy is released.
- If an initial ablated tumor had re-ablation before the Visit 3 Technical Efficacy assessment, the re-ablated tumor will be considered as failure.
- Other subjects with missing parameters or other early discontinuations will not have data imputation.

2) A sensitivity analyses will also be performed for the primary effectiveness endpoint after missing data are imputed according to the following methods:

- A new subject will be recruited to replace any subject who discontinues the ablation procedure after the ablation needle punctures the skin and before the microwave energy is released.
- If an initial ablated tumor had re-ablation before the Visit 3 Technical Efficacy assessment, the re-ablated tumor will be considered as failure.
- As a conservative surrogate endpoint, if the subject does not have Visit 3, then chest enhanced

CT at Visit 4 will be sent to the IRC for local tumor progression assessment, and if local tumor progression occurs, the primary effectiveness endpoint at Visit 3 will be imputed as a failure. If there is no local tumor progression at Visit 4, the primary effectiveness endpoint at Visit 3 will be imputed as successful. If a subject does not have both Visit 3 and Visit 4, the subject will be excluded from the analysis of the primary effectiveness endpoint.

For secondary endpoint missing value, there will be no imputation. The handling methods for missing values and outliers are detailed in the Statistical Analysis Plan (SAP).

8.6. Procedures for Reporting Deviations from the Original Statistical Plan

Any major changes to the SAP should be described and justified in an amendment to the SAP and/or in the final report.

8.7. Selection Criteria and Rationale for Subjects Included in the Analysis

All subjects who met the inclusion and exclusion criteria are considered to meet the recruitment requirements.

The primary analysis of safety and effectiveness endpoints will be performed on the Full Analysis Set. Primary Effectiveness endpoint analyses will be repeated for the Per Protocol Set. The Safety Set will only be used for summarization of safety endpoints. Safety and effectiveness data collected on patients participating in the run-in phase may be summarized separately from the remaining patients.

Subgroup analysis will be conducted as needed and will be described in the SAP.

The analysis sets in this study are defined as follows:

8.7.1. Full Analysis Set

The full analysis set (FAS) set is defined as all patients that are included in the study, do not enter the run-in period and received ablation power.

8.7.2. Per-Protocol Set

The per protocol (PP) set is defined as patients in the full analysis (FAS) set without major protocol deviations that have great impact on the primary effectiveness endpoint.

8.7.3. Safety Set

Safety set (SAF) includes all subjects who provide informed consent and have microwave ablation attempted with the NeuWave system and includes the run-in phase patients.

9. DATA MANAGEMENT

The individual patient data collected during the period of this trial will be recorded in the corresponding study database. The captured data will be reviewed by the data management team and other applicable Sponsor study team members. Any unexpected or missing data points will generate a query for the site to assess and resolve. Sponsor provided monitors will be available for

questions and follow-up with the sites, as needed.

When all subjects complete all follow-up evaluations and the corresponding data is entered, this study will be closed. Data analysis will be performed following database lock.

10. FEASIBILITY ANALYSIS

10.1. Analysis on the Possibility of Success

Pre-clinical and clinical data has shown that MW ablation is safe and effective in small lung tumors with low complication rates, high rates of Technical Success, low rates of Local Tumor Progression. In terms of clinical results of thermal ablation therapy for primary lung cancer, the OS of thermal ablation therapy is approximately 86% at 1 year and 69% at 2 years[15,16]. Regarding the use of thermal ablation for the treatment of secondary lung cancer, a prospective observational study found that for small secondary lung cancers, reuse of thermal ablation resulted in a survival benefit similar to surgical resection. This includes 566 patients with a total of 1037 secondary lung tumors. By controlling the lung tumors with repeated thermal ablation during the follow-up period, the OS of this population is 62 months, the 5-year survival rate is 51.5%, and the 4-year local treatment effectiveness is 89%[21].

The Certus Microwave Ablation System and Accessories have been cleared by the United States (US) Food and Drug Administration (FDA) and has been in clinical use since 2011 in the United States. The growing popularity of the Certus Microwave Ablation System in lung cancer ablation therapy result from its low risks of complications and high effectiveness in ablating lesions of the lung. The published clinical data on Certus lung ablation is limited. But from previous data, there is a high likelihood of meeting the protocol Technical Efficacy goal and previous major complications rate was low, which is unlikely to cause discontinuing of the study due to safety concerns.

The study device is provided free of charge and does not increase the burden on subjects, so the recruiting and screening of subjects will not be fairly difficult. Patients need to return to their study site for continued follow-up, a total of 4 times, lasting for 1 year, which is in line with the frequency of clinical routine visits after lung cancer ablation. So it will not be too difficult to obtain the results of the visits required for the study.

10.2. Feasibility analysis of Failure

As mentioned earlier, although the investigational product is a mature ablation product for lung tumors, the amount of relevant clinical literature published is small, and there may be some unidentified problems, resulting in some unanticipated problems in this study.

Because this study limits the inclusion and exclusion criteria for the included lung cancer lesions, there is a risk that 120 patients could not be completed within the planned time of the study.

In addition, the study requires that subjects return to the hospital for visits at 4 follow-up points within 1 year after the completion of ablation and discharge, which may cause some subjects to be

lost to follow-up. Although with full informed consent, this situation may not be completely avoided. The total sample size has considered a 10% drop-out rate at postoperative 1 month.

11. QUALITY CONTROL OF CLINICAL TRIAL

During the clinical study, the sponsor and investigators shall fulfill their respective responsibilities in accordance with the Good Clinical Practice for Medical Devices (No. 25) and applicable Chinese and international regulations, and strictly follow the clinical trial protocol to ensure the quality of clinical trials.

The sponsor should, in accordance with the requirements of the clinical trial protocol, organize the training on the clinical trial protocol and the use and maintenance of the investigational product for all the investigators participating in the trial to ensure the consistency in the implementation of the clinical trial protocol and the use of the investigational product.

During the implementation of the study, the sponsor is responsible for monitoring each phase of the clinical trial. The clinical research associate designated by the sponsor or the designated representative should follow the relevant SOP and clinical trial protocol formulated by the sponsor to monitor the clinical trial so as to ensure that the data are complete, accurate, true and reliable.

In order to ensure the quality of the study, the sponsor may entrust a qualified quality control or auditor to audit the clinical trial as needed. After receiving the notice, the investigator shall allow the auditor to view the original data and documents related to the study.

When administration departments send the inspection personnel to carry out the inspection, the clinical trial institution and Investigator should cooperate and immediately notify the Sponsor.

12. ETHICAL ISSUES AND INFORMED CONSENT OF CLINICAL TRIAL

12.1. Ethical Considerations

Comply with Chinese laws and regulations, Helsinki Declaration and other international consensus to protect the rights, safety and health of subjects, including:

1) Ensure that the subjects are fully informed and agree to voluntarily participate in this study;
2) Respect and protect the privacy of the subjects, and keep confidential the information that may identify the subjects;
3) The production of investigational medical devices shall meet the relevant requirements of the applicable medical device quality management system; the use of test medical devices and control products shall comply with the requirements of instructions, schemes and relevant operating guidelines;
4) Select qualified clinical sites and investigators;
5) The subject has the right to withdraw from the study at any time and for any reason without prejudice to the future medical care provided to them by the physician or the

institution;

6) Protocol and amendments, ICF and amendments and other applicable documents related to the study should not be implemented before obtaining the written approval from the Ethics Committee.

12.2. Review and Approval of Trial Protocol

The trial protocol should be internally approved and filed according to the company's SOP prior to submitting to the external agency (including but not limited to the government regulatory agencies, Ethics Committee).

The clinical trial protocol should not be implemented until the written approval is obtained from the Ethics Committee according to the relevant requirements of laws and regulations.

12.3. Process of Informed Consent and Text of Informed Consent Form

12.3.1. Process of Informed Consent

The informed consent of all potential patients must be obtained prior to performing any study tests/procedures that are not SOC. Once the investigator determines that the patients are suitable for participating in this study, the investigator must explain the background of the study presented and the benefits and risks of surgery and study to the patients and answer the questions raised by patients. Only the patient who signs the informed consent form that is approved by the EC prior to participating in the study is eligible to participate in this study.

Each patient (or legally authorized representative) must sign and date the informed consent form that is approved by the EC (and other documents as per local regulations) prior to implementing any study-related items or operations not belonging to the SOC and after the nature of this study is fully explained.

The process of obtaining the written informed consent needs to prove that the subjects volunteer to participate in this study. All aspects of this study must be clarified to the subjects prior to signing the informed consent form. The process of obtaining the informed consent must be clearly documented by the investigator and/or designated person in the original clinical trial documents of subjects. The investigator has responsibilities to ensure the process of obtaining the informed consent is implemented according to the Good Clinical Practice for Medical Device Trials and related regulations, such as ISO 14155, the Declaration of Helsinki.

12.3.2. Text of Informed Consent Form

See the attached ICF.

13. DEVICE MANAGEMENT

In this study, the sponsor will supply all study products. All devices clearly labeled as "For Study Only" on the packaging must be stored according to the product labeling and IFU conditions. It is the responsibility of the Principal Investigator to ensure that devices are stored correctly at the sites.

The Principal Investigator or responsible person designated by the Principal Investigator must account for all study devices throughout and, at the end of, the clinical study. During the entire course of the study, the study ablation probes must be stored in a locked or secure access location. An inventory record must be maintained of all devices received, used or returned during the clinical trial. Details of the product code and lot numbers must be documented in the CRF as well as the patient's hospital notes. The Principal Investigator must allow the Monitor access to the secure facility where the study devices are stored during the clinical trial to check inventory. At the end of the clinical trial all machine and all unused probes must be returned to Johnson & Johnson Medical (Shanghai) Ltd. with the appropriate study device return form.

13.1. Packaging and Labeling of Study Device

All study devices provided by the sponsor in this study will be prepared, packaged, and labeled under the responsibility of qualified personnel or sponsor's designee in accordance with the company's SOPs, Good Manufacturing Practice (GMP) guidelines, and applicable local laws/regulations.

Each device is labeled in accordance with regulatory agency guidelines, GMPs, local laws and regulations, and company SOPs to identify investigational product for clinical trial use only.

13.2. Shipping of Study Device

The sponsor or sponsor's designee will ship the device to the study site under the device shipping conditions specified in the device's instructions.

13.3. Management of Study Device

The sponsor will be responsible for supplying qualified study products to the site. Each site will designate study personnel to be responsible for the management of the study device. During the entire course of the study, the study ablation probes must be stored in a locked or secure access location. The investigator should ensure that all investigational medical devices are only used for the subjects of the clinical trial. Details of the product code and lot numbers must be documented in the CRF as well as the patient's hospital record.

Records related to the receipt, distribution, use, recovery and disposal of investigational products shall be maintained in accordance with GCP requirements. Upon receipt of the investigational product at the site, the investigational product must be reconciled and packaged in the correct quantity and under the appropriate shipping conditions. During the study, a designated person will be responsible for recording and counting the use of the study product.

The Principal Investigator must allow the Monitor access to the secure facility where the study devices are stored during the clinical trial to check inventory. The responsible monitor will review the investigational device accountability as applicable. At the end of the clinical trial all machine and all unused study devices must be returned to Johnson & Johnson Medical (Shanghai) Ltd. with the appropriate study device return form.

13.4. Return and Destruction of Study Device

All machine, unused, opened, unused, damaged, mislabeled, or malfunctioning study devices will be returned to the Sponsor's designated address. Complete the appropriate form to properly return the device to the sponsor's specified address.

14. REGULATIONS OF ADVERSE EVENT AND DEVICE COMPLAINT REPORTING

14.1. Adverse events

An adverse event refers to any detrimental medical events in the course of a clinical trial, whether or not related to the investigational medical device.

From the time of signing the informed consent form until approximately 30 days (Visit 3) after ablation (including primary and repeat ablation) or early discontinuation, all adverse events will be recorded. During this period, all adverse events from the start of ablation (i.e., probe puncture on the skin) will be reported.

After approximately 30 days (Visit 3) post ablation, adverse events considered by the investigator as related to the study device or/and study procedures and all serious adverse events will be recorded and reported till the end of the study or early discontinuation.

The investigator will determine whether AEs have occurred and determine the relationship of these events to the study device or ablation procedure at each evaluation for subjects enrolled in the clinical study.

All AEs must be recorded in the original records and entered in the e-CRF. All AEs need to be recorded in the Electronic Data Capture (EDC) system (also called study database) within 2 weeks of site awareness.

The following guideline should be used to determine the severity of each AE:

AE severity grading criteria:

Mild	Awareness of sign or symptom that does not interfere with the subject’s usual activity or is transient, resolved without treatment and with no sequelae
Moderate	Interferes, but does not hinder, the subject’s usual activity and may require treatment
Severe	Symptoms causing severe discomfort, substantial impact on subject's usual activities, treatment or intervention required

The AEs should be classified according to the SIR classifications:

Category	Definitions
Mild complications	

A	No intervention, no adverse consequences
B	Nominal treatment, no adverse consequences; including stay for observation
Severe complications	
C	Treatment required, short-term hospitalization (< 48 hours)
D	Severe treatment required, increased need for care level, prolonged hospitalization (> 48 hours)
E	Permanent adverse sequelae
F	Dead

It is the investigator's responsibility to assess the relationship between all AEs and the study procedure. The following guidelines should be used in determining the relationship of an AE to a device, study procedure, or other causality:

Not Related:	Relationship to the procedure or device can be excluded when: • The event is not a known side effect of the product category the device belongs to or of similar device and procedures; • The event has no temporal relationship with the use of the device or the procedures; • The event does not follow a known response pattern to the device (if the response pattern is previously known) and is biologically implausible; • The discontinuation of the device application or the reduction of the level activation/exposure (when clinically feasible) and reintroduction of its use (or increase of the level of activation/exposure), does not impact on the event; • The event involves a body-site or an organ not expected to be affected by the device or the procedure; • The event can be attributed to another cause (e.g. an underlying or concurrent illness/clinical condition, an effect of another device, drug, treatment, or other risk factors); • Harms to the subject are not clearly due to use error; or

	• To establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedure and the event.
Unlikely	The relationship with the use of the device seems not relevant and/or the event can be reasonably explained by another cause, but additional information may be obtained.
Possible	The relationship with the use of the device is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/condition and/or an effect of another device, drug, or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.
Probable	The relationship with the use of the device seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.
Causal Relationship	The event is associated with the device or with procedures beyond reasonable doubt when: • The event is a known side effect of the product category the device belongs to or of similar device and procedure; • The event has a temporal relationship with the device uses/application or procedures • The event involves a body-site or organ that: o The device or procedures are applied to o The device or procedures have an effect on • The event follows a known response pattern to the medical device (if the response pattern is previously known)

	• The discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the event (when clinically feasible) • Other possible causes (e.g. an underlying or concurrent illness/clinical condition and/or an effect of another device, drug, or treatment) have been adequately ruled out; • Harm to the subject is due to error in use • To establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedure and the event.

14.2. Serious Adverse Event

It is the investigator's responsibility to determine the "seriousness" of an AE using the protocol defined terms below. All SAEs need to be recorded in the Electronic Data Capture (EDC) system (also called study database) within 24 hours of site awareness. An SAE is an AE that results in one or more of the following for this study:

- Resulted in death: An AE that resulted in the patient's death.
- Life-threatening illness or injury: The patient is at imminent risk of dying at the time of the AE.
- Permanent Impairment: An AE that resulted in permanent impairment of a body function or permanent damage to a body structure.
- Required in-patient or prolonged hospitalization. Note: If a patient has prolonged hospitalization due to having an additional ablative procedure and with no other adverse event, this should not be considered an SAE.
- Resulted in medical or surgical intervention to prevent life threatening illness or injury or permanent impairment to a body or body function.
- Led to fetal distress, fetal death or congenital abnormality or birth defects.
- A persistent or significant disability or incapacity.

Notes:

1. Progression of the disease under investigation should not be reported as an SAE.
2. "Death" should not be reported as an SAE. The cause of death, however, should be reported as an SAE, except for progressive disease.
3. Planned hospitalization for a pre-existing condition, but without serious deterioration in

health, is not considered a serious adverse event.

4. A procedure required by the protocol is not considered an SAE unless the patient experiences a serious deterioration in health or hospitalization is prolonged.

14.3. Device Complaints

A device complaint is any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a product after it is released for distribution. Any device complaint must be notified to the monitor by the study site and tracked and reported according to the procedures specified by the sponsor. The monitor will track and report in time according to the methods specified by the sponsor and Chinese regulations and return relevant products (as required) to the quality department of JJMS/Johnson & Johnson Medical (China) Ltd. (JJMC) according to the sponsor's requirements.

14.4. Device Deficiencies

Device defects refer to unreasonable risks that may endanger human health and life safety during medical use in the process of clinical trials, such as label errors, quality issues, and malfunction.

For equipment defects that may result in SAE, the sponsor shall report to the food and drug regulatory authority for registration and the health and family planning department at the same level within 5 working days after the knowledge. Meanwhile, it shall notify other clinical trial institutions and investigators participating in the trial and promptly advise the ethics committees of relevant clinical trial institutions via its medical device clinical trial management department. The investigator should record all AEs occurring and device deficiencies found in the process of clinical trial, work with the Sponsor to analyze the causes of the events, generate the written analysis report, present the comments on the continuation, discontinuation or termination of the trial, and report to the Ethics Committee by the administrative department for clinical trial of medical device of clinical trial institution for review.

14.5. Reporting Procedure, Contact Person Information

The investigator should provide the sufficient treatment for any AE of any subjects, including the laboratory detection value with clinical significance whether or not it is related to this study.

From signing the ICF, all AEs related to the patient’s participation in this study should be followed up until the event is resolved, or if the event causes the permanent damage, it should be followed up until the event is stable and the clinical outcome is determined. If the event is not resolved or stable at the end of study, the medical monitor in this clinical study will decide whether it is necessary to collect further follow-up information.

All AEs and SAEs that occur within the period from Visit 2A (day of ablation) to Visit 3 (about one month after ablation) will be reported; from Visit 3 to through the end of the study, all SAEs, and AEs assessed as related to the study device/ablation procedure by the investigator will be reported. All AEs should be followed up, until the AE is resolved, stable or the study is completed.

The investigator should record the nature, severity, treatment and outcome of an SAE, and determine whether it is related to the study device or ablation procedure. The investigator will report all AEs to the Sponsor via the study database EDC.

The investigator must submit any SAEs that occurred in the study and the device deficiencies that may cause an SAE, to the Sponsor and National Medical Products Administration (NMPA) (or designated person) immediately after being informed of the event. If required by the Sponsor, the further information should be provided.

The investigator and Sponsor should report the SAEs which occurred in the study, and the device deficiencies that may cause an SAE, to the regulatory authorities at every level according to the requirements of laws and regulations.

For all SAEs and device deficiencies that may cause SAEs, the Sponsor should report to the Food and Drug Administration where the clinical study was filed and the competent department of health and Family Planning Commission within 5 workdays after awareness. The Sponsor should also inform other clinical trial institutions/sites and investigators that participate in the trial and inform the Ethics Committees by their medical device clinical trial management departments in a timely manner.

The study device with a device complaint should be returned to the Sponsor according to the instructions given in Section 13 of this study protocol. Once a device complaint is found, the site should inform the Sponsor as soon as possible, and report the device related information on the relevant CRF.

Refer to Section 14.3 for details of the device complaint report process. The contacts to report SAEs and device complaints are as follows:

Adverse events

China AE reporting: China_CT_Safety@its.jnj.com

Global AE reporting: ETHMedAlerts@its.jnj.com

Medical device complaints

Local CHU reporting: ChinaCustomerQuality-CS@its.jnj.com

Global CHU reporting: Productcomplaint1@its.jnj.com

15. REGULATIONS ON CLINICAL TRIAL PROTOCOL DEVIATIONS AND CLINICAL TRIAL PROTOCOL AMENDMENT

Study protocol deviation refers to a case where the requirements of the Clinical Trial Protocol are not followed intentionally or unintentionally.

All protocol deviations should be reported to the sponsor as protocol deviations, and all protocol deviations should be reported in the protocol deviation form and monitoring report, including the date and reason of protocol deviation. The investigator should also report the protocol deviation to

the hospital's medical device clinical trial management department according to the hospital's procedures and regulations, and report to EC through the department.

If a protocol amendment occurs, the Sponsor or designated person should submit a summary of changes of the study protocol to the Investigator, regulatory authority, and the Ethics Committee, etc. according to the relevant laws and regulations. All significant amendments must be approved by the EC and regulatory authorities (if required) prior to implementation of any changes to study procedures.

An amendment is regarded substantial when they are likely to have a significant impact on:

- The safety or physical or mental integrity of the subjects;
- Scientific value of trial;
- Conduct or management of the trial;
- Quality or safety of investigational medical device specified in the trial.

16. DIRECT ACCESS TO SOURCE DATA AND DOCUMENTS

Source data refers to the original records of clinical findings, observations and other activities during clinical trials, as well as all information in their approved copies, which can be used for clinical trial redesign and evaluation. A source document is a printed, paper or electronic file containing source data, among others.

The investigator should maintain and retain information in the subject's medical records and other study-related documents (source documents). The Investigator should allow the monitors and auditors/inspectors to review the following information, including but not limited to:

- Confirm the medical history/physical condition of the study subject who meets the inclusion criteria of the study protocol before participating in this study;
- Medical record documenting the informed consent process;
- Description of operation of investigational product;
- All inspection results and follow-up;
- Dated and signed inspection printouts or reports;
- Description of AE and follow-up of AE (event description, severity, onset date, duration, correlation with the study device, study procedures, outcome and treatment of AE, concomitant medication/procedure when AE occurs);
- Description of the device defects
- Conditions of study subjects when they complete the study or withdraw from the study.

Appropriate source documents must be available for reviewing during the monitoring visit. The Sponsor expects that the study coordinator and/or investigator will also be available for questions during monitoring visits.

17. FINANCES AND INSURANCE

See the relevant study contract and insurance documents.

18. CONTENTS TO BE COVERED IN THE CLINICAL TRIAL PROTOCOL

According to regulatory requirements, the clinical trial report will include the following contents:

The clinical trial report shall be consistent with the protocol, mainly including:

1) General Information;
2) SYNOPSIS;
3) Introduction;
4) Objective of Clinical Trial；
5) Clinical Trial Method;
6) Contents of Clinical Trial;
7) General Data of Clinical Trial;
8) Diagnosis and treatment methods of investigational medical devices;
9) Statistical analysis methods and evaluation methods adopted;
10) Clinical Evaluation Criteria;
11) The organizational structure of clinical trial;
12) Ethical description;
13) Results of the clinical trial;
14) Adverse events found in clinical trial and corresponding treatment;
15) Analysis and discussion of clinical trial results, especially indications, scope of application, contraindications and precautions;
16) Clinical trial conclusion;
17) Problems in existence and suggestions for improvement;
18) List of study personnel;
19) Other Situations to be Explained;
20) Clinical trial summary of each sub-site.

19. PRINCIPLES OF CONFIDENTIALITY

The personal data of subjects participating in the trial shall be kept confidential. However, the Ethics Committee, the sponsor, the health regulatory authorities and their authorized representatives may review the personal data of subjects participating in the trial according to the specified procedures.

Subject confidentiality will be maintained throughout the clinical study in a way that ensures the information can always be tracked back to the source data. For this purpose, a unique subject identification code (site number and subject number) will be used to identify all data reported for each subject. So long as the data is kept strictly confidential and that the privacy of the subject is ensured to be protected, the data related to this study may be available to third parties (for example, under the audit of regulatory authority).

20. CONVENTION ON PUBLICATION OF TRIAL RESULTS

At the end of the study, a multicenter clinical trial manuscript will be prepared and published in a reputable scientific journal as needed. The publication of the principal results from any single-site experience within the study is not allowed until the preparation and publication of the multi-center trial results. Exceptions, such as pre-specified and non-pre-specified analyses of other endpoints, or such secondary analyses and proposed additional investigational studies, require prior approval by the sponsor. For purposes of timely abstract presentation and publication, secondary publications will be delegated to the appropriate principal authors, and final analyses and manuscript review for all multi-center trial data will require the approval of the sponsor.

21. RESPONSIBILITIES UNDERTAKEN BY DIFFERENT PARTIES

21.1. Responsibilities of the Sponsor

1) The Sponsor is responsible for the initiation, application, organization and monitoring of clinical trial.

2) The Sponsor is responsible for the organization to establish and modify the investigator's brochure, clinical trial protocol, informed consent form, Case Report Form, relevant standard operating procedure and other relevant documents, carry out the training required for the clinical trial, and provide these documents to the investigators before the study starts.

3) The Sponsor should select the qualified trial institution and investigators.

4) The Sponsor should sign a written agreement with the clinical trial institution and the investigator regarding the clinical trial.

5) The Sponsor should provide qualified study product according to the regulatory requirements. The Sponsor should be responsible for the safety of investigational medical device in the clinical trial. The AE, SAE, and the device complaint that may cause an SAE should be collected and reported in accordance with the provisions.

6) The Sponsor should inform the regulatory authority at every level when the Sponsor decides to suspend or terminate the clinical trial or at the end of the study.

7) The Sponsor should ensure the investigator conducts the study strictly in compliance with the clinical trial protocol, corrects the protocol deviations in a timely way, and reserves the rights to

report, to the regulatory authority, any of issues related to this.

8) The Sponsor should bear the treatment cost and relevant economic compensation for the clinical trial-related injury or death of subjects, except for damages due to the fault of medical institution and medical staff in the diagnosis and treatment.

9) The Sponsor should select qualified monitors for monitoring and organizing any inspections, as appropriate.

21.2. Responsibilities of Clinical Trial Institution and Investigator

1) The clinical trial institution should evaluate the relevant resources according to the features of investigational medical device prior to the clinical trial, to decide whether to participate in this clinical trial.

2) The clinical trial institution should properly keep the records and documents of clinical trial according to the agreement with the Sponsor.

3) Make sure that the investigators responsible for the clinical trial have the qualification in accordance with the requirements of related laws and regulations.

4) The administrative department of the clinical trial institution conducting the medical device clinical trial should cooperate with the Sponsor to apply to the Ethics Committee and submit the relevant documents prior to the clinical trial according to requirements.

5) The investigator should ensure that the relevant workers participating in the trial have the enough resources and proper training and keep the training related documents.

6) The investigator should ensure to use the investigational medical device only for the subjects of this clinical trial.

7) The investigator may not charge subjects any fees for participating in the study.

8) The investigator should strictly follow the clinical trial protocol, with the exception of emergency circumstances when the patient faces the direct risk and needs immediate clinical measures, which can be reported later in a written form.

9) The investigator is responsible for recruiting the subjects, communicating with the patient or its legal representative before signing the informed consent.

10) The investigator should protect the rights, safety and health of the subjects.

11) In case of an AE occurring in the clinical trial, the investigator should protect the safety of the subjects and timely report the event to the regulatory authority.

12) The investigator should record all AEs occurring and device deficiencies found in the process of clinical trial, work with the Sponsor to analyze the causes of the events, generate the written analysis report, present the comments on the continuation, discontinuation or termination of the trial, and report to the Ethics Committee by the administrative department for clinical trial of

medical device of clinical trial institution for review.

13) The investigator should make sure that the clinical trial data is accurately, completely, clearly and timely recorded in the Case Report Form.

14) The clinical trial institution and investigator should make sure that the data, documents and records generated in the clinical trial are timely, true, accurate, clear, and attributable.

15) The clinical trial institution and investigator should accept and cooperate with the monitoring and audit of the Sponsor, the supervision of the Ethics Committee, and the inspection of the Food and Drug Administration, competent department of health and family planning, etc., and provide all required records related to the trial.

16) If the clinical trial needs to be suspended or terminated, the subjects should be informed accordingly. It should be ensured that the subjects receive the proper care and follow-up. The clinical trial institution and investigator should also report this in accordance with the regulations and provide a detailed written explanation. The relevant report should be submitted to the local Food and Drug Administration at the provincial, autonomous regional and municipal level, if necessary.

17) The clinical trial institution and investigator reserve the rights to report to the regulatory authority at every level when the Sponsor violates relevant laws and regulations.

18) The investigator should complete all records and reports at the end of clinical trial. The investigator should also ensure that the received investigational medical devices are properly handled and recorded according to the requirements.

21.3. Responsibilities of Other Interested Parties

See the study related contract, which is available as a separate attachment.

STATEMENT OF INVESTIGATOR

I agree to:

1. Conduct this clinical trial in strict accordance with the requirements of the Declaration of Helsinki, China's current laws and regulations and trial protocol.
2. Record all required data correctly in the study EDC database and input, review, and approve the clinical trial report on schedule.
3. Use the investigational medical device only for this clinical trial, accurately and completely record the investigational medical device receipt and use condition during the clinical trial and keep these records for review.
4. Allow the monitor and inspectors authorized and dispatched by the Sponsor and regulatory authority to monitor, inspect and audit this clinical trial.
5. Strictly implement the terms in the clinical trial contract/protocol signed by all parties.

I have read thoroughly the clinical trial protocol, including the above statements, and I agree to all the above contents

Comments of Sponsor Signature (stamp) Day Month Year

Comments of investigator Signature Day Month Year

Comments of clinical trial institution of medical device Signature (stamp) Day Month Year

APPENDIX 1: STUDY DEVICES CODE LIST

Investigation Product

Model	Description
NWC2CN1N	NeuWave Certus™ Microwave Ablation System
CTBKT1	CT Bed Rail PDM Mounting Bracket, Standard (Applicable to GE, Philips)
CTBKT2	CT Bed Rail PDM Mounting Bracket, D68 X W585 Standard (Applicable to Siemens)
CTBKT3	CT Bed Rail PDM Mounting Bracket, D48 X W656 Standard (Applicable to Toshiba)
CTBKT4	CT Bed Rail PDM Mounting Bracket, D88 X W645 (Siemens Alt)
CTBKT5	CT Bed Rail Mount, Flat
LN15CN	NEUWAVE CERTUS LN Probe 15CM 17ga
LN20CN	NEUWAVE CERTUS LN Probe 20CM 17ga
LK15CN	NEUWAVE CERTUS LK Probe 15CM 17ga
LK20CN	NEUWAVE CERTUS LK Probe 20CM 17ga
LK15XTCN	NEUWAVE CERTUS LK XT Probe 15CM 15ga
LK20XTCN	NEUWAVE CERTUS LK XT Probe 20CM 15ga
PR15CN	NEUWAVE CERTUS PR Probe 15CM 17ga
PR20CN	NEUWAVE CERTUS PR Probe 20CM 17ga
PR15XTCN	NEUWAVE CERTUS PR XT Probe 15CM 15ga
PR20XTCN	NEUWAVE CERTUS PR XT Probe 20CM 15ga

NOTE: These are collectively described as "study devices."

APPENDIX 2: REFERENCES

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