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A Multicenter Study to Evaluate NEUWAVE Microwave Ablation System Using Ablation Confirmation in Patients with A Soft-Tissue Liver Lesion

Protocol Number: NEU_2017_03

Document	**Effective Date**
Original (version 1.0)	06 Jul 2018
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Sponsor:

NeuWave Medical, Inc.
3529 Anderson Street
Madison, WI 53704

NeuWave Medical Inc. is a subsidiary of:

Ethicon, Inc.
Route 22 West, P.O. Box 151
Somerville, NJ 08876

Name of Finished Product: NEUWAVE Microwave Ablation System with Ablation Confirmation

CONFIDENTIALITY STATEMENT

Sponsor Signature

Protocol Number:	NEU_2017_03
Protocol Title:	A Multicenter Study to Evaluate NEUWAVE Microwave Ablation System Using Ablation Confirmation in Patients with A Soft-Tissue Liver Lesion
Protocol Amendment 2 Date:	26 July 2021

Signature:

Patricia Schleckser
Senior Director, Clinical Research
Ethicon, Inc.

Date

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INVESTIGATOR SIGNATURE

I have read this protocol and agree to conduct this clinical investigation in accordance with the design and specific provisions outlined herein. I understand the protocol, and I understand I am solely responsible to ensure the investigation is conducted in accordance with Good Clinical Practices (GCP), applicable country regulations, the Declaration of Helsinki, the signed clinical study contract with the Sponsor, and with the protocol outlined, herein. I will make reasonable effort to complete the study within the time period designated by the Sponsor.

I will provide copies of the protocol and all pertinent information to all individuals responsible to me who will assist in the conduct of this study. I will discuss this material with them to ensure they are fully informed regarding the device and the conduct of the study.

I will fulfill the requirements of my Institutional Review Board (IRB)/Ethics Committee (EC), or other oversight committee, to ensure complete and continual oversight of this clinical investigation. I will use an Informed Consent Document approved by the Sponsor and my reviewing IRB/EC.

I agree to report all information or data in accordance with the protocol and, in particular, I agree to report any serious adverse events, device related adverse events, or procedure related adverse events as defined in this protocol to the Sponsor, and comply with all adverse event reporting requirements of my reviewing IRB/EC. I agree to permit the Sponsor, its authorized representatives, my reviewing IRB/EC, and any regulatory authority/body access to all records relating to the clinical investigation.

The below signature confirms I have read and understood this protocol and its associated amendments or attachments and will accept respective revisions or amendments provided by the Sponsor.

I agree to comply with all other requirements regarding the obligation of clinical Investigators and all other pertinent requirements of the Sponsor and government agencies.

Principal Investigator Signature	**Date**
[Principal Investigator printed name]	
Name of the site	
Address of the site	
City, State	
Country	

PLEASE RETAIN A COPY FOR YOUR STUDY RECORDS

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1.0 SYNOPSIS

Full Title & Protocol Number	A Multicenter Study to Evaluate NEUWAVE Microwave Ablation System Using Ablation Confirmation in Patients with a Soft-Tissue Liver Lesion (NEU_2017_03)	
Short Title	Ablation Confirmation for soft-tissue liver lesions	
IDE / IND Number	N/A	
Sponsor	NeuWave Medical, Inc.	
Products	NEUWAVE Microwave Ablation System with Ablation Confirmation Software, 120 V, DR-000783 (Product code: NWA1US1N) The NEUWAVE Ablation Probes that may be used in this study include: LK (LK15, LK15XT, LK20, LK20XT), PR (PR15, PR20, PR15XT, PR20XT, PRS15, PRS35); and, SR (NWSR25).	
Indication	Ablation (coagulation) of soft tissue in percutaneous, open surgical, and in conjunction with laparoscopic surgical settings, including the partial or complete ablation of non-resectable liver tumors.	
Study Article Description	Ablation Confirmation (AC) Software is a computed tomography (CT) image processing software package available as an optional feature for use with the NEUWAVE Microwave Ablation System (initially marketed as Certus 140™ 2.45 GHz Ablation System). The NEUWAVE Microwave Ablation System is a general-purpose thermal ablation tool used by physicians to ablate soft-tissue lesions. In this study, the NEUWAVE Microwave Ablation System is used with NEUWAVE Ablation Probes.	
Study Design	This is a prospective, single-arm, multicenter study that will generate clinical data using the NEUWAVE Microwave Ablation System with AC software in patients undergoing microwave ablation (MWA) for soft-tissue liver lesions.	
Sample Size	N = Minimum of 100 patients treated.	
Study Population	Patients $\geq$ 22 years old with at least one soft-tissue liver lesion.	
Geographic Area(s)	US and EMEA	
Study Duration	Enrollment: ~ 1 year	Follow-up: 6 weeks post-ablation

Procedure Description	Patients who meet the eligibility criteria will undergo MWA of at least one soft-tissue liver lesion, in accordance with the study site's standard-of-care (SOC) for MWA. CT will be used throughout the ablation procedure for probe placement and margin assessment. Sites must use the AC software to assess optimal probe placement and to confirm complete ablation with adequate margins. All ablations will be performed percutaneously. The patient will be under general anesthesia or deep conscious sedation, and antibiotics administered, if applicable, per SOC. A patient cannot have more than three lesions ablated during the procedure.
Primary Objective	The primary objective of this study is to examine whether the feedback from the AC software impacts the performing physician's (i.e., the individual performing the ablation procedure) decision making in terms of probe(s) position or number of ablations based on insufficient ablation margins.
Primary Endpoints	• Percentage of repositions informed by AC due to sub-optimal probe placement. • Percentage of re-ablations informed by AC due to insufficient ablation margins.
Secondary Endpoints	• Technical success • Technique efficacy • Hospital resource utilization • Device and procedure safety through the monitoring of adverse events • Device User Experience questionnaire • Patient Quality of Life (QOL) questionnaires • Patient Numeric Pain Rating Scale (NPRS) questionnaire

Inclusion Criteria	1. A patient with at least one soft-tissue liver lesion ≤ 5cm undergoing MWA using the NEUWAVE Microwave Ablation System. Note: A patient cannot have more than three lesions ablated during the procedure. 2. Intent to use Ablation Confirmation software (any AC software version permitted) during the ablation procedure. 3. Written informed consent to voluntarily participate in the study, follow CT scan schedule, and authorize the transfer of his/her data to the Sponsor. 4. Patients ≥ 22 years old. 5. Performance status 0-2 (Eastern Cooperative Oncology Group classification [ECOG]). 6. Class A or B Functional hepatic reserve based on the Child-Pugh score. 7. Lesion must be visualized by non-contrast enhanced CT scan - or- the patient must tolerate contrast and meet institutional guidelines for contrast use based on glomerular filtration rate (GFR).
Exclusion Criteria	1. Active bacterial infection or fungal infection on the day of the ablation. 2. Patients with implantable pacemakers or other electronic implants. 3. Platelet count < 50,000/mm^3. 4. Patients with uncorrectable coagulopathy at the time of ablation. 5. Currently breastfeeding or pregnant (latter confirmed by serum or urine pregnancy test, per site's SOC). 6. Physical or psychological condition which would impair study participation. 7. ASA (American Society of Anesthesiologists) score of ≥ 4. 8. Use of hydrodissection. 9. Systemic chemotherapy or radiation therapy for the liver, within 30 days prior to the study ablation procedure. 10. INR > 1.8. 11. Patient has participated in an investigational clinical study within 30 days of the screening visit for this study. 12. Patient judged unsuitable for study participation by the performing physician for any other reason.
Safety Assessments	Patients will be evaluated for device-related or procedure-related AEs and all SAEs from the time of first probe puncture (Visit 2) through study completion (Visit 3).
Statistical Analysis	Categorical variables will be summarized descriptively by frequencies and associated percentages. Continuous variables will be summarized descriptively by number of patients, mean, standard

	deviation, median, minimum, and maximum. Confidence intervals will also be provided for procedure-related variables. The number and percentage of patients requiring probe repositions based on AC prior to the initial ablation will be summarized and a 95% confidence interval for the percentage will be provided. The number and percentage of patients in whom AC indicates repeat ablation is indicated based on insufficient margins following the initial ablation procedure will be summarized in a similar manner. The number and percentage of patients experiencing device-related or procedure-related AEs and any SAEs will be summarized at the preferred term level.
Interim Analysis	There are no plans for interim analyses whose intent will be to stop the study early or to adapt the study design or planned number of patients.
Schedule of Activities	See Table 1 on the next page.

Table 1: Schedule of Activities

Visit No.	Visit 1:	Visit 2			Visit 3	Unscheduled Visit
Visit	**Screening**[19]	**Ablation Day**			**6 Weeks**	**Unsched.**[18]
Interval Windows	≤ 60 days of Visit 2	Day 0 = ablation of target lesion			(± 3 weeks) post-ablation	NA
Study Activity		pre	during	post[20]		
Informed consent	X					
Demographic information	X					
Medical, surgical, radiation history[1]	X					
BMI	X					
ECOG performance	X	X			X	
Liver tissue assessment[2]	X					
Child-Pugh, ASA scores, BCLC staging	X					
Coagulation tests[3]	X			X	X	
Liver function tests[4]	X			X	X	
Renal function tests[5]	X			X	X	
CBC with differentials[6]	X	X				
Alpha-fetoprotein	X				X	
Carcinoembryonic antigen	X				X	
Pregnancy test[7]	X	X				
Inclusion/exclusion	X	X				
Concomitant medications[8]	X	X	X	X	X	X
QOL questionnaires[9]		X			X	
Numeric Pain Rating Scale		X		X	X	
CT scan, MRI, or Ultrasound	X[10]	X[11]	X[11]	X[11]	X[10]	
Intended ablation treatment plan		X[12]				
Ablation procedure details		X[13]	X[13, 14]	X[14]		
Liver-related concomitant procedures		X	X	X	X	X
Device user experience[15]				X		
Technical success assessment				X		
Technique efficacy assessment					X	
Hospital resource utilization[16]				X		
Follow-up post-ablation treatment[17]					X	X
AEs / SAEs			X	X	X	X

Abbreviations: NA = not applicable; Unsched. = Unscheduled Visit. See Glossary on page following notes, below, for all other acronyms and abbreviations.

Notes:

1. Medical, surgical, and radiation history, including date of diagnosis of soft-tissue lesion under study, hepatitis type and status, smoking status, and biliary manipulation.
2. Liver tissue assessment, if available: categorization of the following; steatosis (mild, moderate, severe); cirrhosis (mild, moderate, severe); microsatellite instability and vascular invasion..
3. INR is required but other tests performed, if applicable, per site SOC: Coagulation tests, including APTT or PTT, PT, and PTA.
4. If applicable, per site SOC: Liver function tests, including ALB, ALK, ALT, AST, T/D bilirubin, GGT, and TP.
5. If applicable, per site SOC: Renal function tests, including BUN, creatinine, and electrolytes (sodium, potassium, chloride, and bicarbonate).
6. Complete blood count (CBC) with differential (RBCs, WBCs, platelets, hemoglobin, hematocrit, neutrophils, etc.).
7. Serum or urine pregnancy test for women of childbearing potential only, per SOC.
8. Record all relevant prior medications taken within 30 days prior to Visit 2 and all relevant concomitant medications (i.e., blood-thinning/coagulation, NSAIDs, steroids, medications used to treat AEs, and medications used to treat hepatitis, if concurrently treating).
9. Quality of Life questionnaires: EORTC QLQ-C30 and the liver-specific QLQ-HCC18. Questionnaires may be administered up to 72 hours prior to the ablation procedure (Day 0) and may be administered over the phone, when needed.
10. Ultrasound or MRI may be used with or without CT for all screening and post-ablation imaging as per site SOC. All scans should be sent to Sponsor.
11. CT must be used for the 'pre, during, and post ablation' imaging. If CT was used with contrast, the physician must record the amount of contrast used. All scans should be sent to Sponsor.
12. Intended ablation treatment plan details include the probe(s) planned to be used, liver segment(s), max power planned, and total ablation time planned.
13. After the patient is sedated under general anesthesia or deep conscious sedation, and administered antibiotics, if applicable, per site SOC, the performing physician will follow the steps outlined in Section 8.2.
14. Ablation procedure details include, but not limited to, the following: date and time of procedure; version of AC software; anatomical location of ablations; liver stiffness near ablation site (if available); number of ablation cycles, including time, maximum temperature and maximum power used for each ablation cycle per probe; guidance method used; number of CT scans performed for probe placement and margin assessment; tissue contraction percentage; number of probe placement attempts per ablation; number and type of probe(s) used; the amount of contrast used (if applicable); type of anesthesia; and duration of procedure (first probe placement to last probe removal). Total radiation exposure will also be captured from the CT scanner and recorded in the clinical database. Some of the above ablation procedure details will be provided to the site via a report generated from NeuWave Medical's Call Home Database. The study site will review the report and enter the procedure details into the clinical database, as applicable.
15. Device user experience, to be completed by the performing physician via the AC User Evaluation Questionnaire: the first half following each ablation procedure, and the second half following approximately every 5 ablations, per treating physician.
16. Hospital resource utilization: length of post-ablation hospital stay and time to perform procedure, which includes 3 measures of time: (1) Overall procedure duration, defined as the time elapsed between loading CT dataset into the AC system and completion of MWA with probe removal; (2) AC imaging duration, defined as the time elapsed between loading CT dataset into AC to plan for the target ablation and last use of AC to plan for the final ablation, and (3) Ablation duration, defined as the time elapsed between first ablation probe puncture and removal of the last probe at the completion of the ablation.
17. Follow-up post-ablation treatment, if applicable, including: If patient has been hospitalized since the initial ablation procedure.
18. Record reason for unscheduled visit, as well as applicable AEs/SAEs updates to the relevant concomitant medications and/or liver-related concomitant procedures, if applicable.
19. When applicable, the Screening Visit may occur on the same day as the Ablation Day (Visit 2).
20. All post-ablation activities should occur prior to subject discharge from the institution.

2.0 GLOSSARY

Table 2. Acronyms/Abbreviations

Acronyms/ Abbreviations	Terms
AC	Ablation Confirmation
AE	Adverse Event
AFP	Alpha-Fetoprotein
ALB	Albumin Concentration
ALBI	Albumin-Bilirubin
ALK	Alkaline Phosphatase
ALT	Alanine Aminotransferase
APTT	Activated Partial Thromboplastin Time
ASA	American Society of Anesthesiologists
AST	Aspartate Aminotransferase
BMI	Body Mass Index
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CEA	Carcinoembryonic Antigen
CFR	Code of Federal Regulations
CT	Computed Tomography
CTC	Common Terminology Criteria
DMC	Data Monitoring Committee
EC	Ethics Committee
ECOG	Eastern Cooperative Oncology Group
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EORTC	European Organization for Research and Treatment of Cancer
GCP	Good Clinical Practices
GFR	Glomerular Filtration Rate
GGT	Gamma-Glutamyl Transpeptidase
HCC	Hepatocellular Carcinoma
HCPs	Healthcare Professionals
HGB/HCT	Hemoglobin/Hematocrit
HIPAA	Health Insurance Portability and Accountability Act of 1996
HPB	Hepatobiliary

Acronyms/ Abbreviations	Terms
ICF	Informed Consent Form
ID	Identification
IFU	Instructions for Use
INR	International Normalized Ratio
IR	Interventional Radiologist
IRB	Institutional Review Board
MDR	Medical Device Problem Report
MDVR	Medical Device Vigilance Report
MedDRA	Medical Dictionary for Regulatory Activities
MRI	Magnetic Resonance Imaging
MWA	Microwave Ablation
NPRS	Numeric Pain Rating Scale
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
PACS	Picture Archiving and Communication Systems
PDM	Power Distribution Module
PI	Principal Investigator
PT	Prothrombin Time
PTA	Plasma Thromboplastin Antecedent
PTT	Partial Prothrombin Time
QLQ	Quality-of-Life Questionnaire
QOL	Quality-of-Life
RBC	Red Blood Cells
RFA	Radiofrequency Ablation
ROW	Rest of World
SAE	Serious Adverse Event
SOC	Standard-of-Care
T/D/I	Total/Direct/Indirect (bilirubin)
TP	Total Protein
US	Ultrasound
VOC	Voice-of-the-Customer
WBC	White Blood Cells

3.0 ETHICS

Institutional Review Board/Ethics Committee

Participating Investigators will ensure that this protocol, Informed Consent Form (ICF), and if applicable, any protocol amendments or other written information provided to the subjects that assist in the decision to participate are reviewed by an Institutional Review Board (IRB) or Ethics Committee (EC) that complies with governmental requirements. The approving IRB/EC will be responsible for the initial and continuing review and approval of this clinical investigation. Participating Investigators will be required to promptly report to the IRB/EC as required by the IRB/EC's policies.

Applicable Regulations

This study will be conducted in compliance with Good Clinical Practice and in accordance with the Declaration of Helsinki, as well as any other applicable local and country regulatory requirements.

Subject Information and Consent

Regulations concerning the protection of subjects require that informed consent be obtained before a subject may participate in any clinical investigation.

An IRB/EC approved informed consent must be sought from each subject and must be appropriately documented in the subject's medical record prior to initiating the study. It is the Investigator's responsibility to obtain written informed consent from the subject, however, the Investigator may delegate this responsibility, if appropriately documented.

The informed consent process involves the following: giving a subject adequate information concerning the study, providing adequate time for the subject to consider all available options, responding to the subject's questions, ensuring that the subject has comprehended this information and finally, obtaining the subject's written consent to participate in this study. All subjects in this study should be completely informed about the purpose, risks, benefits, and other pertinent details of this study. The informed consent process is careful to avoid the perception of any coercion or undue influence on, or inducement of, the subject to participate, and does not waive or appear to waive the subject's legal rights. The ICF is presented in native, non-technical language that is understandable to the subject.

Prior to a subject's participation in this study, an ICF will be signed and dated by the subject and person who conducted the consent discussion. The subject will be provided a copy of the signed ICF. The ICF and any other written materials provided to the subject to assist in the decision to participate must be revised whenever new information becomes available that may be relevant to their willingness to participate or continue participation in this study. Revision to the ICF and other written materials will receive IRB/EC approval before implementation. Each subject will be required to sign any amended ICF (as required by the IRB/EC) and will receive a copy of the signed ICF.

Administrative Requirements

This study is sponsored by NeuWave Medical and will be conducted in approximately 10 study sites in the United States and Europe under a single protocol approved by each participating site's IRB/EC prior to implementation. The Principal Investigator (PI) at each study site must be qualified by education and experience to perform the study procedure and to assume responsibility for the conduct of this study.

The Data Management and Biostatistics groups of NeuWave Medical will be responsible for the analysis of data from this protocol. An electronic data capture (EDC) system will be utilized by study site personnel to transfer study data from source records (the first point of clinical data capture) onto common electronic case report forms (eCRFs). This system is a web-based, secure electronic software application (Medidata® Rave, 350 Hudson Street, 9th Floor, New York, New York, 10014). This system was designed and is developed and maintained by Medidata in a manner that is compliant with national and international Good Clinical Practice (GCP) data protection/data privacy and electronic record/electronic signature (e.g., 21 CFR Part 11) regulatory requirements.

Protocol Modifications

All protocol amendments must be issued by the Sponsor, signed and dated by the Investigator, and should not be implemented without prior IRB/EC approval, except where necessary to eliminate immediate hazards to the subjects or when the change(s) involves only logistical or administrative aspects of the study (e.g., change in monitor, change of telephone number). The Investigator will report the protocol amendments to the IRB/EC as per their local requirements.

4.0 INTRODUCTION

Treatment of liver lesions is challenging, with high complication and recurrence rates. Surgery is the gold standard, but many patients are not surgical candidates because of comorbidities, or the location and nature of the lesions. Thermal ablation has been growing as a treatment option because of its minimally invasive nature, low cost, positive outcomes, and low complication rates. While outcomes are generally good, the rates of successful removal of lesions do not yet approach those of surgical resection and can also be highly variable depending on the experience of the interventional radiologist (IR) and the ablation technology used. Voice-of-the-Customer (VOC) research sponsored by NeuWave Medical indicated that physicians believe that more than half of recurrence in hepatobiliary (HPB) ablation is due to incorrect placement of the probes, inability to determine treatment margins, and other limits of the technology.

NeuWave Medical developed Ablation Confirmation (AC) software to help overcome some of these inherent limitations. Specifically, AC helps the physician:

- Lock the Target: Define / lock the target volume for improved probe placement accuracy and margin analysis.
- Evaluate Probe Placement: See the exact proximity of the probe to the target by viewing combined target and probe placement scans.
- Confirm Technical Success: Verify technical success of the procedure by viewing combined target and ablation margin scans.
- Demonstrate Your Success: Procedure images stored to PACS (picture archiving and communication systems) and can be shared to showcase procedure success.

Ablation Confirmation is a computed tomography (CT) image processing software package available as an optional feature for use with NEUWAVE Microwave Ablation System. The NEUWAVE Microwave Ablation System is a general-purpose thermal ablation tool used by physicians to ablate soft-tissue lesions in a wide variety of tissue and disease states. The NEUWAVE Microwave Ablation System has been cleared by the United States 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, kidney, and lung lesions. Additional, but less common uses have been the ablation of soft-tissue lesions in bone and nerve ablation.

AC is controlled by the user via an independent user interface on a second monitor, which is separate from the Ablation System user interface for the ablation procedure. AC imports images from CT scanners and facility PACS for display and processing during ablation procedures. AC assists physicians in identifying ablation targets, assessing proper ablation probe placement, and confirming the adequacy of the ablation margin, as defined by the performing physician. AC is not intended for diagnosis. AC is an accessory to the NEUWAVE Microwave Ablation System and is not available for sale independently. In this study, the NEUWAVE Microwave Ablation System is used only with NEUWAVE Ablation Probes.

Two types of ablation are primarily used in the liver: radiofrequency ablation (RFA) and MWA. Microwave has many advantages over RFA. For example, it does not use conduction to heat tissue, rather directly heats the diseased tissue leading to more uniform heating while also creating a larger ablation margin around a lesion. MWA also does not use grounding pads, which can cause burns on the areas of attachment. Lastly, MWA has faster heating at higher temperatures, thereby offering improved performance in tumor necrosis.[1]

The NEUWAVE Microwave Ablation System is contraindicated for:

- Use in cardiac procedures.
- 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 microwave power.
- Use on the central nervous system.
- Endometrial applications.

All known hazards associated with the use of the NEUWAVE Microwave Ablation System have been identified and appropriately mitigated. Design considerations were taken to reduce the risks associated with existing MWA systems, including improved system usability and cable management.

The NEUWAVE Microwave Ablation System uses a CO_2 cooling system where all other microwave systems use sterile water. The risks associated with this cooling system do not

differ from the risks inherent in cryogenic ablation systems, which are widely accepted in clinical use. Thus, the NEUWAVE Microwave Ablation System does not introduce new hazards or intended uses.

The information provided by the User Manual and Instructions for Use (IFU) describe the use, risks, and benefits of the devices. The risk/benefit profile of the NEUWAVE Microwave Ablation System is acceptable for the intended use of the ablation/coagulation of soft-tissue relative to other medical alternatives.

The FDA cleared AC for use in 2015. To date, no adverse complications have been reported that were deemed related to AC.

This is a prospective, single-arm, multicenter study that will generate clinical data using the NEUWAVE Microwave Ablation System with Ablation Confirmation in patients undergoing microwave ablation (MWA) of a soft-tissue liver lesion. Although all Investigators in this study have experience using AC, this is the first clinical study assessing how AC impacts the way interventional radiologists perform the ablation.

5.0 STUDY OBJECTIVE

The primary objective of this study is to examine whether the feedback from the AC software impacts the performing physician's (i.e., the individual performing the ablation procedure) decision making in terms of probe(s) position or number of ablations based on insufficient ablation margins.

5.1 Primary Endpoints

The primary endpoints supporting the study objective are, as follows:

- Percentage of repositions informed by AC due to sub-optimal probe placement.
- Percentage of re-ablations informed by AC due to insufficient ablation margins.

5.2 Secondary Endpoints

The secondary endpoints are, as follows:

- Technical success - defined as ablation of the target lesion(s) according to the protocol and covered completely with an adequate margin, as defined by the performing physician (that is, the ablation zone completely overlaps or encompasses the target lesion plus an adequate ablative margin). Technical success will be assessed by the performing physician using AC as a tool immediately following the procedure.
- Technique efficacy - defined as ablation of the target lesion(s) according to the protocol and covered completely, with an adequate margin, as defined by the performing physician (that is, the ablation zone completely overlaps or encompasses the target lesion plus an ablative margin), as assessed by imaging at Visit 3.
- Hospital resource utilization based on:
    - Length of post-ablation hospital stay.
    - Time to perform procedure, which includes 3 measures of time:
        - Overall procedure duration, defined as the time elapsed between loading CT dataset into the AC system and completion of MWA with last probe removal.

- AC imaging duration, defined as the time elapsed between loading CT dataset into AC to plan for the target ablation and last use of AC to plan for the final ablation.
- Ablation duration, defined as the time elapsed between ablation first probe puncture and removal of the last probe at the completion of the ablation.

- Device and procedure safety through the monitoring of adverse events. Patients will be evaluated for all device-related and procedure-related AEs and all SAEs from the time of the first probe puncture (Visit 2) through study completion (Visit 3).
- Device User Experience questionnaire (Appendix 2) will be completed by the performing physician. The first half will be completed following each ablation procedure and the second half will be completed approximately every 5 ablations (per treating physician).
- Patient Quality of Life (QOL) questionnaires as measured by EORTC QLQ-C30 and the liver-specific QLQ-HCC18, at Visit 2 (Pre-Ablation) and at Visit 3 (6 weeks post-ablation).
- Patient Numeric Pain Rating Scale (NPRS) questionnaire at Visit 2 (Pre- and Post-Ablation) and at Visit 3 (6 weeks post-ablation).

5.3 Additional Measurements / Data Collected

- Patient demographics.
- Relevant medical, surgical, and radiation history, including date of diagnosis of soft-tissue lesion under study, hepatitis type and status, smoking status, and biliary manipulation.
- Body mass index (BMI), ECOG performance, Child-Pugh score, and ASA score.
- Length of hospital stay (time of admission to post-ablation observation through discharge).
- Lesion details (size of the lesion, lesion type, location, and shape).
- Ablation procedure details include the following:
    1. Date and time of procedure.
    2. Version of AC software used.
    3. Anatomical location of ablation(s).
    4. Liver stiffness near ablation site, if available.
    5. Number of ablation cycles, including time, and maximum temperature and maximum power used for each ablation cycle per probe.
    6. Guidance method used (ultrasound, CT, or MRI).
    7. Number of CT images performed for probe placement and margin assessment.
    8. Tissue contraction percentage selected.
    9. Number of probe placement attempts per ablation.
    10. Number and type of probe(s) used.

11. Amount of contrast used, if applicable.
12. Type of anesthesia.
13. Duration of procedure (first probe placement to last probe removal).
14. Total radiation exposure from the CT scanner.

Note: Some of the above ablation procedure details will be provided to the site via a report generated from NeuWave Medical's Call Home Database. The study site will review the report and enter the procedure details into the clinical database, as applicable.

6.0 INVESTIGATIONAL PLAN

6.1 Overall Study Design and Plan - Description

This is a prospective, single-arm, multicenter study that will generate clinical data using the NEUWAVE Microwave Ablation System with Ablation Confirmation Software in patients undergoing MWA of at least one soft-tissue liver lesion. Note: A patient cannot have more than three lesions ablated during the procedure.

6.2 Enrollment

A minimum of 100 patients will be enrolled in approximately 10 sites, initially in the United States and later ROW. A patient will be considered enrolled upon signing the ICF.

Enrollment will continue until at least 100 eligible patients have been treated with Neuwave MWA and have used the AC software.

6.3 Inclusion Criteria

Patients satisfying the following criteria will be eligible to participate in this study:

1. A patient with at least one soft-tissue liver lesion ≤ 5cm undergoing MWA using the NEUWAVE Microwave Ablation System. Note: A patient cannot have more than three lesions ablated during the procedure.
2. Intent to use Ablation Confirmation software (any AC software version permitted) during the ablation procedure.
3. Written informed consent to voluntarily participate in the study, follow CT scan schedule, and authorize the transfer of his/her data to the Sponsor.
4. Patients ≥ 22 years old.
5. Performance status 0-2 (Eastern Cooperative Oncology Group classification [ECOG]).
6. Class A or B functional hepatic reserve based on the Child-Pugh score.
7. Lesion must be visualized by non-contrast enhanced CT scan -or- the patient must tolerate contrast and meet institutional guidelines for contrast use based on glomerular filtration rate (GFR).

6.4 Exclusion Criteria

Patients who meet any of the following criteria will not be eligible to participate in this study:

1. Active bacterial infection or fungal infection on the day of the ablation.
2. Patients with implantable pacemakers or other electronic implants.
3. Platelet count < 50,000/mm^3.
4. Patients with uncorrectable coagulopathy at the time of ablation.
5. Currently breastfeeding or pregnant (latter confirmed by serum pregnancy test).
6. Physical or psychological condition which would impair study participation.
7. ASA (American Society of Anesthesiologists) score of ≥ 4.
8. Use of hydrodissection.
9. Systemic chemotherapy or radiation therapy for the liver, within 30 days prior to the study ablation procedure.
10. INR > 1.8.
11. Patient has participated in an investigational clinical study within 30 days of the screening visit for this study.
12. Patient judged unsuitable for study participation by the performing physician for any other reason.

6.5 Prior and Concomitant Therapy

Excluding systemic chemotherapy or radiation therapy for the liver (up to 30 days prior to procedure), patients may continue with their current medical care throughout the duration of the study, including medications. All relevant prior and concomitant medications (i.e., blood-thinning/coagulation, NSAIDs, steroids, medications used to treat AEs, and medications used to treat hepatitis, if concurrently treating) taken within 30 days of Visit 2 through study completion will be recorded on the Concomitant Medication eCRF page.

6.6 Screening Failures

All patients signing consent who do not meet the inclusion and exclusion criteria or who do not have the ablation procedure initiated will be recorded as screen failures and the reason will be captured on the Inclusion/Exclusion Criteria eCRF, if applicable. In addition, the Demographics and Subject Completion/Discontinuation eCRF pages will also be completed for all screen failures.

6.7 Removal of Patients from the Study

In accordance with the current revision of the Declaration of Helsinki and the Code of Federal Regulations, a patient has the right to withdraw from the study at any time for any reason without prejudice to his/her future medical care by the physician or the institution. Should a patient (or patient's legally authorized guardian/representative) decide to withdraw from the study; all efforts will be made to collect any applicable AEs experienced, if applicable, and as defined by this protocol.

Withdrawal of Consent

If a patient chooses to withdraw early from the study, the patient should contact the study site, which will then complete the Subject Completion /Discontinuation eCRF page. When a patient's participation is terminated prior to completing the study, the reason for withdrawal is to be documented on the Subject Completion/Discontinuation eCRF and in the source documentation.

Ablation

The Investigator may withdraw a patient during the ablation procedure for any safety reason, including, but not limited to, the following reasons:

- Inability of Investigator to locate and target the lesion.
- Inability of patient to tolerate the anesthesia or deep conscious sedation.

Note: If a patient experiences a device-related or procedure-related AE or any SAE during probe puncture and is not ablated, this patient should be followed until AE/SAE resolution. If no AE/SAE occurred during probe puncture and the patient could not be ablated, the patient should be discontinued.

Death

When available, the cause of death should be reported via the AE eCRF, per the safety reporting timelines in Section 12.0. The Subject Completion/Discontinuation eCRF also must be completed.

Lost to follow-up

All patients should be encouraged to return for protocol required clinic visits for evaluation during the study follow-up period. If a patient is unable to return for a clinic visit or unable to be contacted by telephone, attempts to contact the patient should be documented in the source documents. Only after failing to contact the patient at the final follow-up visit, the patient will be considered lost to follow-up and the primary reason for early termination will be completed in the Subject Completion/Discontinuation eCRF.

Site Termination or Study Termination:

The Sponsor may terminate a site or the study at any time. When this occurs all patients at the site will be withdrawn and documented as early termination. Reasons for site or study termination may include, but are not limited, to the following:

- Administrative concerns (e.g., inadequate patient enrollment, Investigator/institution non-compliance, change of business strategy, etc.).
- Safety issues, including reaching any of the complication thresholds, including those due to non-compliance, which substantially affect the risk-to-benefit ratio of the study patients at a site or for the study as a whole.
- Regulatory body mandates.

The Investigator also has the right to terminate subject or site participation at any time (e.g., for safety reasons or inability to enroll patients). Should termination of a site be necessary, the Sponsor will provide procedures for termination.

7.0 STUDY PROCEDURES

7.1 Procedure Description(s)

A multi-disciplinary team at the site will determine, with the help of imaging, whether a patient is suitable for ablation of soft-tissue liver lesion. Potential candidates for MWA will undergo tests for complete blood count (CBC) with differential. Test for coagulation, liver function, renal function, and alpha-fetoprotein (AFP), will be collected if applicable, per SOC.

Microwave Ablation Procedure

MWA is a minimally invasive procedure that uses electromagnetic waves to generate tissue necrosis. The ablation will be performed with a single high-powered, gas-cooled microwave system. This NEUWAVE Microwave Ablation System with Ablation Confirmation Software is a CT image processing software package (see Section 7.2 System Overview for a complete description.) Electromagnetic waves will be delivered to the tissue, producing frictional heating to generate tissue necrosis at > 60°C.

In this study, only patients who meet the eligibility criteria will undergo MWA of at least one soft-tissue liver lesion utilizing AC, in accordance with the study site's SOC for MWA. A patient cannot have more than three lesions ablated during the procedure.

To plan the ablation, the performing physician will collect the soft-tissue lesion details: e.g., size, lesion type, location, shape. The patient will be under general anesthesia or deep conscious sedation during the procedure, per the site's SOC. Using CT and, if needed, ultrasound (US) or MRI imaging guidance, the treating physician will insert a small probe percutaneously into the lesion.

CT will be used throughout the ablation procedure for probe placement and margin assessment. Sites must use AC to assess optimal probe placement and confirm complete ablation with adequate margin. AC also provides the ability to capture images from the NEUWAVE monitor via the "snapshot" feature. The physician should use snapshots to document each key step of the procedure as outlined, below, if the Call Home Imaging feature is turned on, though this is not a requirement.

The physician will perform the ablation per the device's Instructions for Use (IFU) and the performing physician's clinical judgment. Duration of procedure and power application will be determined by the performing physician based on manufacturer guidelines, with adjustment for lesion size, proximity to vulnerable structures, and real-time intraprocedural CT scan monitoring. It is suggested that the physician considers using more than one probe for lesions ≥ 2cm.

Steps to Follow During Ablation

The performing physician will follow the steps listed below:

- Use CT, ultrasound, or MRI to collect the lesion details: e.g., lesion type, location, shape, size. If unable to accurately visualize the lesion(s) with non-contrast enhanced CT, ultrasound, or MRI, the patient must tolerate contrast and meet institutional guidelines for contrast used based on glomerular filtration rate (GFR). A CT image is required to define the target with AC. The final visualization of the target lesion should be documented using the AC snapshot feature to capture the contents of the imaging panels.
- Develop a treatment plan to perform the MWA of the patient's liver lesion(s) and

capture the details of the treatment plan (probe(s) planned to be used, liver segment(s), max power planned, and total ablation time planned) in the study database.

- Place probe(s) in target lesion(s).
- Take CT to assess probe placement; repeat as needed. Ultrasound may be used in addition to CT.
- Assess if the probe(s) has been optimally placed based on CT interpretation alone.
- Use AC to validate probe(s) placement. Document the visualization of the probe location(s) using the AC snapshot feature to capture the contents of the imaging panels.
- Reposition, add, or remove probe(s), as needed, based on AC software feedback. Repeat as needed.
- Capture changes made to the placement and sequence of the probe(s) as a result of AC feedback, if any, in the clinical database. Document the visualization of the final probe location(s) using the AC snapshot feature to capture the contents of the imaging panels.
- Once the performing physician is satisfied with the accuracy of the probe(s) placement on the target lesion, ablation of the lesion may begin until deemed to be complete with adequate margins, as defined by the performing physician.
- Take CT following the ablation procedure and assess if ablation has been successfully completed with adequate margins.
- Use AC to confirm complete ablation with adequate margins. Document the visualization of the ablation result using the AC snapshot feature to capture the contents of the imaging panels.
- Take action as per AC software for margin assessment (e.g., ablate for more time, add probe(s), remove probe[s]) if a complete ablation was not achieved.
- Capture actions, if any, taken to achieve complete ablation based on AC software, and enter these actions taken into the clinical database. Document the visualization of the final ablation result using the AC snapshot feature to capture the contents of the imaging panels.
- Use AC software and CT imaging to measure the smallest margin diameter within the ablation zone as well as the smallest diameter of the entire ablation zone.

All recommendations made by the AC software should be captured in the clinical database. If the performing physician does not follow the AC software recommendation, a reason why they did not follow the AC recommendation should be noted. Not following the AC recommendation itself is not a protocol deviation.

Submitting Scans to the Sponsor

AC requires a minimum of 3 CT scans taken on the day of ablation, at least one scan taken at each of the following 3 timepoints: (1) at baseline/pre-ablation; (2) after final probe placement and immediately before ablation; and, (3) after completion of ablation.

The user should also document the AC visualization of procedure steps and decision making as outlined, above.

All required CT scans taken on the day of ablation should be submitted to the Sponsor. The scans will allow the Sponsor to potentially improve the software algorithm.

Total Radiation Exposure

At all follow-up visits, the physician will use CT or MRI scans to collect the lesion details: e.g., size, lesion type, location, shape. The total radiation exposure for each patient will be dependent on the number of CT images taken per patient, as well as many other factors such as the manufacturer of the scanning equipment. The total radiation exposure from the CT scanner on the day of ablation will be captured in the clinical database.

Ablation Success

Ablation success will be classified as:

- Technical success, defined as ablation of the target lesion(s) according to the protocol and covered completely with an adequate margin, as defined by the performing physician (that is, the ablation zone completely overlaps or encompasses the target lesion plus an adequate ablative margin). Technical success will be assessed by the performing physician using AC as a tool, immediately following the procedure.
- Technical failure, defined as ablation of the target lesion(s) with an inadequate margin, as defined by the performing physician (that is, the ablation zone does not completely overlap or encompasses the target lesion plus an adequate ablative margin). This is assessed by the performing physician using AC as a tool, immediately following the procedure.

7.2 System Overview(s)

Ablation Confirmation Software is a CT image processing software package available as an optional feature for use with NEUWAVE Ablation System. NEUWAVE Microwave Ablation System is a general-purpose thermal ablation tool used by physicians to ablate soft-tissue lesions. In this study, the NEUWAVE Microwave Ablation System is used with NEUWAVE Ablation Probes.

AC software is controlled by the user via an independent user interface on a second monitor, which is separate from the user interface for the ablation procedure. AC imports images from CT scanners and facility PACS for display and processing during ablation procedures. AC assists physicians in identifying ablation targets, assessing proper ablation probe placement, and confirming the adequacy of the ablation margin, as defined by the performing physician. AC also provides the ability to capture images from the NEUWAVE monitor via the “snapshot” feature. The physician should use snapshots to document each key step of the procedure.

Refer to the NEUWAVE Microwave Ablation System accompanying documents for a list of Warnings and Cautions.

7.3 Study Article Codes and Storage Conditions

Study product: NEUWAVE Microwave Ablation System with Ablation Confirmation Software:

Product Code(s)	Description
NWA1US1N	NEUWAVE Microwave Ablation System with Ablation Confirmation Software, 120 V, DR-000783
LK15, LK15XT, LK20, LK20XT, PR15, PR20, PR15XT, PR20XT, PRS15, PRS35, and NWSR25	Ablation probes

The NEUWAVE Microwave Ablation System with Ablation Confirmation Software must be stored in conditions according to product labeling and IFU. It is the responsibility of the Principal Investigator to ensure that devices are stored correctly at the site.

8.0 Visits

The Schedule of Activities (Table 1) may be found at the end of the synopsis.

8.1 Visit 1 – Screening

The screening assessments for this visit may occur over several dates, though all should be within 60 days of Visit 2. Note: the Screening Visit may occur on the same day as the Ablation Day (Visit 2). If the Screening Visit and Ablation Day Visit occur on the same day, only complete one set of applicable tests and questionnaires.

Patients with at least one soft-tissue liver lesion will be selected for MWA based on the pre-procedure assessments and the Investigator's interpretation of the clinical picture. Eligible patients will be provided with the study information including the ICF.

The following screening assessments will occur prior to the study procedure:

- Patients must be given ample time to review and sign the ICF.
- Collect demographic information (age, sex, race, ethnicity).
- Review and collect medical and surgical history, including date of diagnosis of soft-tissue lesion under study, radiation history, hepatitis type and status, smoking status, and biliary manipulation.
- Collect height and body weight for body mass index (BMI), and evaluate ECOG performance status.
- Perform a liver tissue assessment, if available, which includes categorization of the following: steatosis (mild, moderate, severe); cirrhosis (mild, moderate, severe); microsatellite instability and vascular invasion.
- Child-Pugh score, to assess the prognosis of chronic liver disease and cirrhosis.
- ASA score.
- Record BCLC staging, if applicable.
- Record all relevant concomitant medications (i.e., blood-thinning/coagulation, NSAIDs, steroids, and medications used to treat hepatitis, if concurrently treating) taken within 30 days prior to Visit 2.
- Review inclusion/exclusion criteria and determine if the patient is eligible to

participate in the study.

- CT, MRI, or Ultrasound may be used for screening. If the scan, based on SOC, was done within 60 days prior to the day of ablation, it does not need to be repeated at the screening visit. Send the scans to the Study Sponsor.
- Laboratory tests: If these tests, based on site SOC, were completed within 60 days of Visit 2, they do not need to be repeated at the screening visit.
    a. Coagulation tests, including activated partial thromboplastin time (APTT) or partial thromboplastin time (PTT), prothrombin time (PT), and plasma thromboplastin antecedent (PTA) may be collected, as applicable, per site SOC, but international normalized ratio (INR) is required.
    b. If applicable, per site SOC, liver function tests, including albumin (ALB), alkaline phosphatase (ALK), alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin (direct and total), gamma-glutamyl transpeptidase (GGT), and total protein (TP).
    c. If applicable, per site SOC, renal function tests include BUN, creatinine, and electrolytes (sodium, potassium, chloride, and bicarbonate).
    d. Complete blood count, with differential (RBCs, WBCs, platelets, hemoglobin, hematocrit, neutrophils, etc.).
    e. Alpha-fetoprotein, which serves as a tumor marker (tumor markers are molecules in the blood that are higher when a person has certain cancers), as per SOC.
    f. Carcinoembryonic antigen (CEA), as per SOC.
    g. Serum or urine pregnancy test, per site SOC, for women of childbearing potential only.

8.2 Visit 2 – Ablation Procedure

The following procedures will be done before the ablation procedure:

- Evaluate ECOG performance status.
- QOL questionnaires: EORTC QLQ-C30 and the liver-specific QLQ-HCC18.
- Pain score, using the Numeric Pain Rating Scale.
- Record any new relevant concomitant medications or changes to existing relevant concomitant medications (i.e., blood-thinning/coagulation, NSAIDs, steroids, and medications used to treat hepatitis, if concurrently treating).
- Record any new liver-related concomitant procedures.
- Confirm that the patient still meets inclusion and exclusion criteria (tests not needed to be repeated).
- Serum urine pregnancy test, per site SOC, for women of childbearing potential only.
- Complete blood count, with differential (RBCs, WBCs, platelets, hemoglobin, hematocrit, neutrophils, etc.).Use CT to collect lesion details: e.g., size of lesion, lesion type, location, shape. If unable to accurately visualize the lesion with non-

contrast enhanced CT, contrast enhanced CT must be used. Note: the Screening Visit CT and Visit 2 CT may occur on the same date if the patient was screened and treated on the same day.

- Use AC to define the target lesion(s). The final visualization of the target lesion should be documented using the AC snapshot feature to capture the contents of the imaging panels.
- Develop a treatment plan to perform the MWA of the patient's liver lesion(s) and capture the details of the treatment plan (probe(s) planned to be used, liver segment(s), max power planned, and total ablation time planned) in the study database. Note: A patient cannot have more than three lesions ablated during the procedure.
- After the patient is sedated under general anesthesia or deep conscious sedation, and administered antibiotics, if applicable, per SOC, the performing physician will place the probe in position without the use of Ablation Confirmation. Probe placement may be performed using either ultrasound or CT scan.

The following procedures will be done during the ablation procedure:

- Take at least 1 CT scan to determine the location and size of the target lesion(s). The scan will be taken after the probe(s) have been positioned and anchored via Tissu-Loc™ (if used). The performing physician will review the probe placement on AC and, if deemed necessary, re-adjust the probe(s) and begin ablation. If CT is used with contrast, the physician must record how much contrast was used. Document the visualization of the probe location(s) using the AC snapshot feature to capture the contents of the imaging panels.
- All recommendations made by the AC software should be captured in the clinical database. If the performing physician does not follow the AC software recommendation, a reason why they did not follow the AC recommendation should be noted.
- Record any potential device-related or procedure-related AEs or any SAEs.
- Record any new relevant concomitant medications or changes to existing relevant concomitant medications (i.e., medications used to treat adverse events).
- Record any new liver-related concomitant procedures.

The following procedures will be done after the ablation procedure:

- Use AC to confirm that the ablation has produced adequate margins, as defined by the performing physician (i.e., assess technical success). Document the visualization of the final ablation result using the AC snapshot feature to capture the contents of the imaging panels. use AC and CT imaging to measure the smallest margin diameter within the ablation zone as well as the smallest diameter of the entire ablation zone. Device user experience: Performing physician evaluates the NEUWAVE Microwave Ablation System with Ablation Confirmation by completing the AC User Evaluation Questionnaire: first half of

the questionnaire following each ablation procedure and the second half following approximately every 5 ablations, per treating physician.

- Laboratory tests, as follows:
  - Coagulation tests, including APTT or PTT PT, and PTA are to be performed, as applicable, per site SOC, but INR is required.
  - As applicable, per site SOC, liver function tests, including ALB, ALK, ALT, AST, T/D/ bilirubin, GGT, and TP.
  - As applicable, per site SOC, renal function tests, including BUN, creatinine, and electrolytes (sodium, potassium, chloride, and bicarbonate).
- Record any new liver-related concomitant procedures.
- Pain score, using the Numeric Pain Rating Scale.
- Record ablation procedure details, including:
  - Date and time of the ablation procedure.
  - Document the version of AC software used.
  - Document the tissue contraction percentage selected.
  - Amount of contrast used, if applicable.
  - Type of anesthesia.
  - Anatomical location of ablations.
  - Liver stiffness near ablation site, if available.
  - Number of ablation cycles, including time, maximum temperature and maximum power used for each ablation cycle per probe.
  - Number of CT scans performed for probe placement and margin assessment.
  - Number of probe placement attempts per ablation.
  - Number and type of probe(s) used.
  - Duration of procedure (first probe placement to last probe removal).
  - Time to perform procedure, which includes 3 measures of time:
    1. Overall procedure duration, defined as the time elapsed between loading the CT dataset into the into AC and completion of MWA with probe removal.
    2. AC imaging duration, defined as the time elapsed between loading CT dataset into the AC software system to plan for the target ablation and last use of AC to plan for the final ablation.
    3. Ablation duration, defined as the time elapsed between ablation probe puncture and removal of the probe at the completion of the ablation.

Note: Some of the above ablation procedure details will be provided to the site via a report generated from NeuWave Medical's Call Home Database, if available. The

study site will review the report and enter the procedure details into the clinical database, as applicable.

- Send all required CT, ultrasound, and MRI scans (taken before, during, and after ablation) to Study Sponsor.
- Length of hospital stay (from the time the patient is taken into observation post the ablation procedure until hospital discharge).
- Capture from the CT scanner, the total radiation exposure.
- Record any potential device-related or procedure-related AEs or any SAEs.
- Record any new relevant concomitant medications or changes to existing relevant concomitant medications (i.e., chemotherapy, blood-thinning/coagulation, NSAIDs, steroids, medications used to treat AEs, and medications used to treat hepatitis, if concurrently treating).

The study site should follow their SOC for discharging patients after the ablation procedure.

8.3 Visit 3: 6 Weeks Follow-up

Six weeks (± 3 weeks) after the ablation procedure, the patient will visit the study site and the following assessments will occur:

- Evaluate ECOG performance status.
- Perform laboratory tests, as follows:
  - Coagulation tests, including APTT or PTT, PT, and PTA are to be performed, as applicable, per site SOC, but INR is required.
  - As applicable, per site SOC, liver function tests, including ALB, ALK, ALT, AST, T/D bilirubin, GGT, and TP.
  - As applicable, per site SOC, renal function tests, including BUN, creatinine, and electrolytes (sodium, potassium, chloride, and bicarbonate).
  - Alpha-fetoprotein, as per site SOC.
  - Carcinoembryonic antigen, as per site SOC.
- Record any new relevant concomitant medications or changes to existing relevant concomitant medications (i.e., chemotherapy, blood-thinning/coagulation, NSAIDs, steroids, medications used to treat AEs, and medications used to treat hepatitis, if concurrently treating).
- QOL questionnaires: EORTC QLQ-C30 and the liver-specific QLQ-HCC18.
- Pain score, using the Numeric Pain Rating Scale.
- Determine soft-tissue lesion(s) details (e.g., size, lesion type, location, shape) via CT or MRI.
  - If CT is used with contrast, record the amount of contrast used.
  - Review soft-tissue lesion(s) details to determine if there is recurrence or progression of the ablated lesion(s). Note: No additional ablation procedures should be performed at this visit as part of this study. If the patient has a progression, they should be treated outside of this study

protocol.

- Record any new, liver-related concomitant procedures.
- Evaluate Technique Efficacy, defined as ablation of the target lesion(s) according to the protocol and covered completely, with an adequate margin, as defined by the performing physician (that is, the ablation zone completely overlaps or encompasses the target lesion plus an ablative margin), as assessed by imaging, at Visit 3.
- Record any potential device-related or procedure-related AEs or any SAEs.
- Record date of study completion (Visit 3, or upon patient's early withdrawal).

8.4 Unscheduled Visits

The following data will be collected during each unscheduled visit:

- Reason for the unscheduled visit.
- Record any potential device-related or procedure-related AEs or any SAEs.
- Any update to relevant concomitant medications and liver-related concomitant procedures.

9.0 DATA MANAGEMENT AND INTEGRITY

9.1 Data Completion and Record Keeping

Source Documents

Source documents are documents on which information regarding patients is first recorded, including printed, optical, or electronic documents. Investigator patient files or hospital records generally are the basis of source document information. This includes but is not limited to, the following: original patient files; certified copies of patient records, hospital/clinic records; original recordings/tracing; digital images from automated instruments (e.g., cameras); radiographs; photographic negatives; and, records kept at the investigation site, at the laboratories, and at other departments involved in the clinical investigation.

In addition to standard clinical study source documents, the Sponsor's NEUWAVE Ablation System has a functionality that electronically collects procedure data and information during the ablation procedure and is transmitted by the NEUWAVE Ablation System to NeuWave Medical, after the conclusion of the ablation procedure; this information is collectively called the "Call Home Database." [redacted]

Relevant ablation procedure details will be provided to the site via a report generated from the Call Home Database, if available. The study site will review the report and enter the procedure details into the clinical database, as applicable. The Investigator must retain reports generated from the Call Home Database, if available, as part of the patient's permanent medical record. The report should be maintained at the site for review, as necessary.

Source documents must be retained by the Investigator as part of the patient's permanent medical record. The information in the source documents is used to complete the eCRFs. All information captured on the eCRFs should be completely and accurately supported in source documentation. Any additional information relevant to the study should be included in the source documents. Particularly, any deviations from the protocol or procedures should be recorded in the source documents. The Investigator will retain originals of all source documents, patient consent forms, and study data.

Electronic Data Capture

An EDC system will be used by site personnel to transfer data from source records (medical records and/or source document worksheets) onto common eCRFs. This system is a web-based, secure electronic software application (Medidata Rave, 350 Hudson Street, 9th Floor, New York, NY 10014 United States; telephone: 212-918-1800; Fax: 212-918-1818; toll-free: 877-511-4200). This system was designed and is developed and maintained by Medidata, Inc. in a manner that is compliant with national and international GCP data protection/data privacy and electronic record/electronic signature (e.g., 21 CFR Part 11) regulatory requirements. The EDC system will be used to facilitate the collection of all data at the site. Designated site personnel will be responsible for entering patient data into the EDC system. [redacted]

Medidata also has an image upload option called Medidata Imaging. Sites are uploading all required images directly to Medidata Imaging.

A 24/7/365 Help Desk Support line (telephone: 973-659-6780; fax: 973-954-5621; toll free: 866-633-4328; Email: helpdesk@mdsol.com) staffed by the outsourced vendor will also be available to respond to site and monitor questions.

Data Collection

Each EDC eCRF will be completed by the Investigator or designee. Every effort should be made to respond to all monitoring and/or data management questions on each eCRF as completion of the data is required by the protocol. A unique ID number will identify each patient. The patient's unique ID number will be visible on each eCRF. At no time, should the patient name appear on the eCRFs.

All data should be recorded accurately and completely. The Investigator is responsible for reviewing and approving each completed eCRF. The Investigator will document assurance of overall review and approval by electronically signing each patient's electronic casebook.

Data Correction

Required data corrections to eCRFs will be prompted via automated electronic edit checks and/or queries manually created by Sponsor reviewers. The change, the person making the change, and the time the change was made to the eCRFs will be automatically captured in the audit trail within Medidata Rave.

Data Privacy

The collection, use, and disclosure of all personal data, including patient health and medical information, are to be maintained in compliance with applicable personal data

protection and security laws and regulations that govern protected health information and the informed consent given by each patient. When collecting and processing such personal data, appropriate measures are to be taken to maintain the confidentiality of patient health and medical information and to prevent access by unauthorized persons.

Record Retention, Inspection, and Custody

The Investigator will allow representatives of the Sponsor, the FDA, or other government regulatory agencies to inspect all study records, eCRFs, and corresponding portions of the patient's office and/or hospital medical records at regular intervals during the study. These inspections are to verify adherence to the protocol, integrity of the data being captured on the eCRFs, and compliance with applicable regulations.

Study reports will not identify patients by name. These reports may be submitted to the FDA and/or regulatory authorities.

If custody of the clinical study records is transferred, notice of such a transfer should be given to the Sponsor no later than 10 working days after the transfer occurs.

9.2 Medical Dictionary Coding

Medical dictionary coding of medical history and verbatim AEs captured on eCRFs will be performed using a coding thesaurus algorithm. The Medical Dictionary for Regulatory Activities (MedDRA) and WHODrug dictionaries will be used after data entry and query resolution, via auto-encoding and interactive coding processes.

9.3 Data Quality Assurance

Steps to be taken to assure the accuracy and reliability of data include the selection of qualified Investigators and appropriate sites, review of protocol procedures with the Investigator and associated personnel prior to the study, and periodic monitoring visits by the Sponsor. The Sponsor will review eCRFs for accuracy and completeness during on-site monitoring visits; any discrepancies will be resolved with the Investigator or designees, as appropriate.

Investigator Training

Prior to screening patients for this study, the PI, sub-Investigators, study coordinators, and other designated staff (as applicable) will be provided information on study execution, data collection, and procedures specific to this clinical protocol.

Monitoring

This study will be monitored by the Sponsor to ensure the following:

- The rights and well-being of the patients are protected.
- The reported data is accurate, complete, and verifiable from source documents where utilized.
- The conduct of the study is in compliance with the currently approved protocol/amendment, applicable GCPs, and with applicable local/regional regulatory requirements.

The extent and nature of monitoring will be predetermined and 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 as characterized in the monitoring plan.

9.4 Protocol Deviations

A protocol deviation is any noncompliance with the protocol, Good Clinical Practice, or protocol-specific requirements. A deviation (any activity conducted outside the parameters established by the protocol) can be identified from a number of sources. Potential sources include but are not limited to: a member of the Investigator's staff, a Sponsor representative during monitoring visits, or a member of the data management or statistical groups when entering or analyzing data. Regardless of the source, it is crucial to document the subject level deviation in the protocol deviation eCRF. The Investigator will report protocol deviations to the IRB/EC as required by the IRB/EC procedures.

Assessments or visits that are not completed because they are not SOC at a site should not be considered protocol deviations if the protocol specifies that the assessment or visit is only to be collected if SOC.

Steps to be taken to assure the accuracy and reliability of data include the selection of qualified Investigators and appropriate sites, review of protocol procedures with the Investigator and associated personnel prior to the study, and periodic monitoring visits by the Sponsor. The Sponsor will review eCRFs for accuracy and completeness during monitoring visits; any discrepancies will be resolved with the Investigator or designees, as appropriate. All deviations to the protocol requirements should be documented in the source as well as the protocol deviation eCRF.

10.0 STATISTICAL METHODS AND DETERMINATION OF SAMPLE SIZE

10.1 Statistical and Analytical Plans

The Sponsor Data Management and Biostatistics groups will be responsible for the analysis of data from this protocol. A comprehensive and detailed Statistical Analysis Plan will be finalized prior to database lock to supplement the statistical design and analysis described in this section.

Categorical variables will be summarized descriptively by frequencies and associated percentages. Continuous variables will be summarized descriptively by number of patients, mean, standard deviation, median, minimum, and maximum. Confidence intervals will also be provided for procedure-related variables.

10.2 Study Design

This is a prospective, single-arm, multicenter clinical study that will generate clinical data using NEUWAVE Microwave Ablation System with Ablation Confirmation Software in patients undergoing MWA of at least one soft-tissue liver lesion as part of the study site's SOC treatment.

10.3 Treatment Assignment

This is a single-arm study where all enrolled patients will be ablated using the NEUWAVE Microwave Ablation System and the AC software tool.

10.4 Interval Windows

Interval windows are provided in Table1: Schedule of Activities, which appears at the end of the Synopsis. No additional interval windows are planned for analysis purposes.

10.5 Primary Endpoint and Associated Hypotheses

The primary objective of this study will be assessed through recording whether feedback from the AC software indicates that the probe should be re-positioned prior to ablation as well as whether feedback from the AC software after the ablation procedure indicates that the margins are insufficient and hence a repeat ablation would be necessary. No hypotheses are specified for either of these endpoints as the study is descriptive in nature and will be used for estimation purposes.

10.6 Levels of Significance

No levels of significance are specified since no hypotheses are planned to be tested.

10.7 Analysis Sets

The primary analysis of safety and effectiveness endpoints will be performed on the Full Analysis Set, defined as all eligible patients who are enrolled in the study and have the AC tool utilized as part of the ablation procedure.

A Per Protocol analysis set will be defined as all patients who had undergone the ablation procedure and have no major protocol deviations. Effectiveness analyses will be repeated for the Per Protocol Set.

10.8 Sample Size Justification

Given that this is an initial experience with the AC system in a general use population, a sample size of a minimum of 100 patients is deemed sufficient for estimating the repositioning rate for appropriate sizing of a subsequent study. With an expected repositioning rate of 15%, a sample size of 100 patients will control the half-width of a 95% confidence interval to less than 7%.

10.9 Analyses to be Conducted

Categorical variables will be summarized descriptively by frequencies and associated percentages. Continuous variables will be summarized descriptively by number of patients, mean, standard deviation, median, minimum, and maximum. Confidence intervals will also be provided for procedure-related variables.

Disposition of Study Patients

Patient disposition will be summarized using counts and percentages. The number and percentage of patients completed and discontinued along with the specific reasons for discontinuation will be tabulated by treatment group and in total.

Demographic and Baseline Characteristics

Summary statistics will be provided for patient demographics and pre-operative ablation characteristics.

Primary and Secondary Endpoint(s) Analyses

The number and percentage of patients requiring probe replacement/changes using the AC software prior to the initial ablation will be summarized and a 95% confidence interval for the percentage will be provided. The number and percentage of patients in whom the AC software indicates repeat ablation is indicated based on insufficient margins following the initial ablation procedure will be summarized in a similar manner.

The number and percentage of patients achieving technical success will be summarized and a 95% confidence interval will be provided. A similar summary will be provided for

technique efficacy.

The number and percentage of patients experiencing device-related and procedure-related AEs and all SAEs from the time of the first probe puncture (Visit 2) through study completion, or, if applicable, the day of early withdrawal, will be summarized by MedDRA preferred term and system organ class. Ninety-five percent confidence intervals may be provided for pre-specified adverse events of interest. The expected side effects related to MWA are as follows:

- Ascites (accumulation of fluid causing abdominal swelling)
- Biloma / bile leak (buildup of the bile within the abdomen / bile leak)
- Bile duct injury
- Bleeding requiring transfusion, embolization, or prolonged hospital stay
- Intrahepatic hematoma
- Pneumothorax or hemothorax
- Organ injury other than the liver (such as gastrointestinal injury/perforation or diaphragmatic injury/hernia)
- Fever
- General feeling of tiredness
- Infection
- Liver dysfunction
- Liver abscess
- Nausea
- Pain
- Pneumonia
- Pleural effusion
- Post-ablation syndrome (body's response to the destroyed lesion appearing as flu-like symptoms, including fever, decreased appetite, and general discomfort occurring most typically 3 to 5 days after the ablation procedure)
- Skin burn
- Thrombosis (local coagulation nor clotting of the blood int eh circulatory system, with or without tube drainage)
- Tumor implantation

QOL questionnaires will be summarized with methodology consistent to the recommendations of the specific survey. Additional endpoints will be summarized with descriptive statistics.

Plans for Interim Analysis

There are no plans for interim analyses whose intent will be to stop the study early or to adapt the study design or planned number of patients.

Ongoing Review

The Sponsor will also review complications periodically, as per the Safety Management Plan.

Analysis of Safety

The analysis of safety is summarized above under Primary and Secondary Endpoint Analyses.

Handling of Dropouts or Missing Data

All analyses will be performed only on patients undergoing ablation with the AC software tool and only observed data will be analyzed. There will be no imputation of missing data for any parameters or for early terminated patients.

Multicenter Studies

No adjustment for center is planned in the statistical analysis. However, center specific analyses may be conducted pending within-center sample size to understand the effect of the performing physician's techniques and the study site's SOC may have on the overall results.

Analysis of Subgroups

No subgroup analyses are currently planned but may be considered pending the distribution of baseline demographic and clinical characteristics. Subgroup analyses, if performed, will be specified in the Statistical Analysis Plan.

11.0 RISKS AND BENEFITS OF THE STUDY

This study may or may not provide any benefits to the patient. However, the Ablation Confirmation software is designed to assist physicians in identifying ablation targets, assessing proper ablation probe placement, and confirming ablation margins.

While there have been no AEs reported that have been associated with the use of the AC software, the AEs that have been reported and associated with the NEUWAVE Microwave Ablation System may be categorized as follows:

1. Mechanical probe breaks due to excessive force applied during probe placement, often through and around boney structures and/or cartilage.
2. Skin burns due to user placing probe improperly close to the patient's skin or delivering power for excess time and power given the probe placement.
3. Known risks associated with thermal ablation not associated with device failure or misuse.

In addition, it is expected but rare to see minimal collection of fluid or blood in the liver, and heat damage to the adjacent areas from the CT scan and other imaging done after the procedure. These events can occur without any other sign and symptom.

No patient complications have been reported related to the AC software to date.

11.1 Comparison with Other Microwave Ablation Systems

Clinical Efficacy

The NEUWAVE Microwave Ablation System has the same intended use as other MWA systems. The power levels of the NEUWAVE Microwave Ablation System provide clinicians with greater flexibility than many of the other systems currently available, including the ability to drive 3 probes, in-phase, at one time as well as having a higher top end power (140 W for a single probe) than most other systems.

However, the total power available does not exceed other microwave systems on the market and thus does not introduce new risks. Multiple ablation probe types are available.

New Hazards or Intended Uses

All hazards associated with the use of the NEUWAVE Microwave Ablation System have been identified and appropriately mitigated. Design considerations were taken to reduce the risks associated with existing MWA systems, including improved system usability and cable management. The NEUWAVE Microwave Ablation System uses a CO_2 cooling system where all other microwave systems use sterile water, but the risks associated with this cooling system do not differ from the risks inherent in cryogenic ablation systems, which are also widely accepted in clinical use. Thus, the NEUWAVE Microwave Ablation System does not introduce new hazards or intended uses.

Clinical Benefit

The NEUWAVE Microwave Ablation System has the same fundamental science and technology as other MWA systems commercially available. MWA has been generally accepted by the clinical community to be safe and effective. Hence, one may conclude that the NEUWAVE Microwave Ablation System is likewise considered safe and effective.

To date, more than 25,000 patients in the United States have had ablations performed using the NEUWAVE Microwave Ablation System.

11.2 Comparison with Radiofrequency Ablation Systems

To date, there is no reported difference in the reported AEs between RFA and MWA. In a meta-analysis by Huo et al,[2] MWA and RFA had similar 1-year to 5-year overall survival, disease-free survival, local recurrence rate, and AEs. In terms of AEs, MWA and RFA have similarly low rates of complications, as identified in the same meta-analysis by Huo et al.

11.2.1 Potential Benefit to Patients

The main benefits to patients from participation in this study are that they will be treated with MWA technology. Poulou et al[1] compared MWA with RFA and found that MWA attains a more predictable ablation zone, permits simultaneous ablation of multiple lesions, and achieves larger coagulation volumes in a shorter procedural time. Nevertheless, Poulou et al stated that there is no compelling evidence for differences in clinical outcomes, including local recurrence rates and survival. The knowledge gained from this clinical study might also help future MWA patients being treated with MWA.

11.3 Comparison of MWA With Liver Resection

Studies comparing MWA and liver resection are lacking. Chong et al [3] conducted a retrospective analysis of patients who received curative liver resection or MWA for hepatocellular carcinoma (HCC) evaluated the survival of patients with HCC treated with liver resection or MWA and the role of Albumin-Bilirubin (ALBI) score in patient selection for treatments. Of the 442 patients who underwent MWA or liver resection for HCC during the study period, 63 patients received MWA and 379 patients received liver resection. Analysis of the results showed that liver resection offered better overall and disease-free survivals in patients with ALBI grade 1. MWA provided a significantly better overall survival ($p = 0.025$) and a trend towards better disease-free survival ($p = 0.39$) in patients with ALBI grade 2 or 3. The authors concluded that liver resection offered superior disease-free survival compared with MWA in patients with HCC. However, the ALBI grade could identify patients with worse liver function who might gain survival advantage from MWA.

Microwave ablation is often used in isolation or succession, and occasionally in combination with resection. Philips et al[4] prospectively reviewed a Hepato-Pancreatico-Biliary database that selected patients with multi-focal bilobar disease who underwent MWA with resection or

only microwave. The multimodality approach has significantly improved outcomes for hepatic malignancies. Potential benefits and pitfalls from combined resection and ablation therapy in patients with complex and extensive bilobar hepatic disease have not been well defined. The study examined the records of 108 patients who were treated with ablation alone or 84 patients who were treated with combined resection and ablation, who were then compared with similar disease-burden patients who underwent resection only. The authors concluded that the use of MWA in addition to surgical resection did not significantly increase the morbidities or short-term outcomes. They also found that the combination with systemic and other local forms of therapy, combined resection and ablation is a safe and effective procedure.

12.0 ADVERSE EVENTS

12.1 Definitions

Adverse Event

For this study, an adverse event is defined as any undesirable clinical occurrence in a patient that is determined to be device-related or procedure-related by the Investigator. All AEs that meet this definition are to be recorded in the eCRF and reported to the Sponsor. All SAEs, regardless of relationship to the study device or procedure, are to be collected.

The Sponsor will review all applicable site-reported AEs and SAEs according to the current Safety Monitoring Plan.

Expected Morbidity/Anticipated Adverse Events

An expected morbidity/procedural complication is defined as an AE that is known to be common or usual in nature, severity, or incidence during ablation of the liver.

Serious Adverse Event

It is the Investigator's responsibility to determine the "seriousness" of an AE using the protocol defined terms below. An SAE is an AE that results in one or more of the following for this study:

- Life-threatening: The patient was at imminent risk of dying at the time of the adverse event.
- Permanent Impairment: An AE that resulted in permanent impairment of a body function or permanent damage to a body structure.
- Necessitated Intervention: An AE that resulted in a condition that necessitated medical or surgical intervention to preclude permanent impairment of a body function or damage to a body structure.
- Required in-patient or prolonged hospitalization.
- A persistent or significant disability or incapacity.
- Resulted in death: An AE that resulted in the patient's death.

Notes:

1. Progression of the disease under study should not be reported as an SAE.
2. "Death" should not be reported as an AE. The cause of death should be reported as an SAE. The only exception is "Sudden Death" when the cause is unknown.
3. Planned hospitalization for a pre-existing condition is not considered an SAE.

Severity of Adverse Events

It is the Investigator's responsibility to assess the severity of an AE. A change in severity of a pre-existing medical condition or of a current AE may constitute a new reportable AE.

In addition, the following guideline may be used to determine the severity of each AE:

- **MILD**: Awareness of signs or symptoms but does not interfere with the patient's usual activity or is a transient event that resolves without treatment and with no sequelae.
- **MODERATE**: A sign or symptom which interferes with the patient's usual activity.
- **SEVERE**: Incapacity with inability to do work or usual activities.

Relationship of Adverse Events

It is the Investigator's responsibility to assess the relationship between all AEs and the study procedure and device. Adverse events deemed to have a possible, probable, or causal relationship to the procedure or device should be captured in source as part of the study and entered into the AE eCRF. AEs deemed to be Not Related to the procedure or device will be noted in source only. The following guidelines should be used in determining the relationship of an adverse event 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.
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
	  ○ The device or procedures are applied to
	  ○ 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.

*Indicates definitions of relationship that qualify to be recorded as part of the study for AEs only. All SAEs, regardless of relationship, will be collected.

12.2 Reporting Adverse Events

All procedure-related and device-related AEs from the time of the first probe puncture (Visit 2) through study completion (Visit 3), or from the time of early withdrawal of the study, must be reported in the AE eCRF.

The Investigator is required to report all applicable non-serious AEs to the Sponsor within 2 weeks of become aware of the adverse events. All SAEs, regardless of relationship to the study device or procedure, are to be reported as soon as possible, but no later than 72 hours after becoming aware of the event, regardless of relationship to the device or study procedure.

The study site will report applicable AEs and all SAEs to the Sponsor by entering the event into the EDC system via the Adverse Event eCRF, which will trigger an automated email to the Sponsor. Additional information, including the Investigator's assessment, may be added to the eCRF later. Any necessary medical management of the event will be recorded in the patient's medical record/source document. If the Sponsor requires

supporting documentation or other information, the Sponsor will contact the study site.

Data related to AEs and SAEs will be collected until event resolution, until the event is considered stable, or until all attempts to determine the resolution of the event are exhausted. All AEs and SAEs that are unresolved at study completion (or early termination) will be recorded as ongoing at study end.

In addition, the following information should be recorded:

- Onset date.
- Resolution date or date of death.
- Severity of the event.
- Action taken.
- Event status (ongoing at study end or resolved).
- Relationship of AE to the ablation device used in the study.
- Relationship of AE to the study procedure.
- Indication of seriousness.
- Was AE anticipated or not.

The report of an AE or SAE by a site does not constitute an admission that study personnel or the user facility (hospital/clinic) caused or contributed to the event. The site is responsible for submitting AEs to the reviewing IRB/EC, per their IRB/EC procedures.

13.0 PRODUCT COMPLAINTS

13.1 Product Complaint Definition

A product complaint is defined as any written, electronic, or oral communication that alleges deficiencies related to the identity, labeling, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution (21CFR 820.3 (b)). A product complaint may or may not be associated with an AE/SAE.

Product complaints may include, but are not limited to:

1. Product contamination;
2. Defective components;
3. Device malfunction (the failure of a device to perform as intended for this study);
4. Poor packaging or product mix-up;
5. Labeling concerns;
6. User errors.

13.2 Reporting Product Complaints

All product complaints related to devices in the procedure shall be documented throughout the clinical investigation.

The study site must report product complaints related to a device manufactured by NeuWave Medical, Inc., in a timely manner after becoming aware of the event.

When any representative of the Sponsor becomes aware of a product complaint, the Sponsor representative must notify the Sponsor's Product Complaint Team With the least practical delay of becoming aware of information (if immediate reporting is not possible).

The Product Complaint Form must be emailed to the Sponsor Customer Complaint team at the following email address: Productcomplaint1@its.jnj.com. One copy of the processed form should be kept on-site, and the device should be retained. Sponsor representatives will organize collection of the device for evaluation, as needed.

The product complaint may also be reported by calling 1-877-ETHICON, Option 5.

14.0 PUBLICATION PLAN

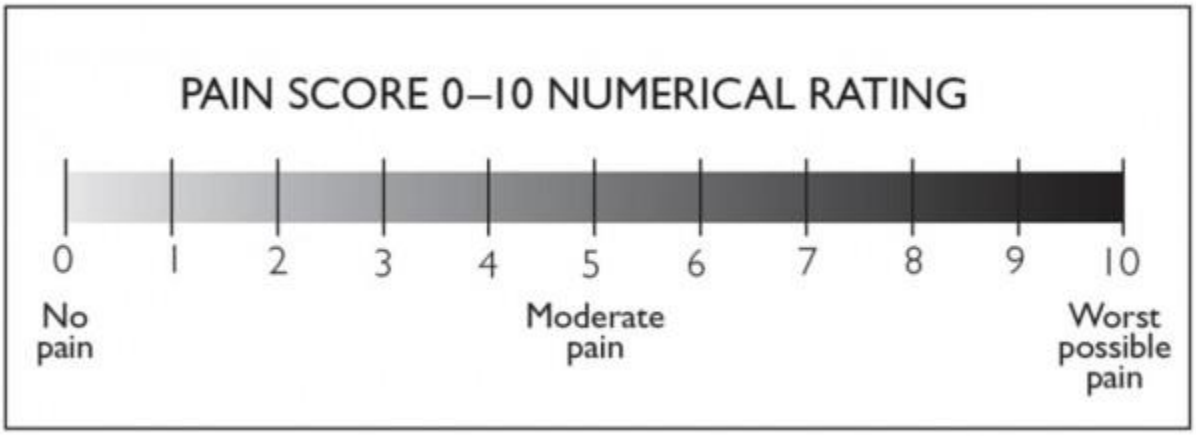
Publication and authorship policies should be determined and aligned with the clinical study agreement executed between operating company and each clinical site. Publication of the results of this study will be governed by J&J publication policies, including current and applicable Medical Device Publication Policy. Any presentation, abstract, or manuscript will be made available for review by the Sponsor prior to submission. Licensing agreements or copyrights applying to tools, work products or intellectual property used during the study should be observed and clearly displayed on study documentation and publications, wherever appropriate.

All manuscripts of data obtained from this clinical study will be reviewed and approved by the Sponsor, and each author, prior to any submission. Current and applicable Medical Device Publication Policy will be followed. The Sponsor will require a written agreement for any external author(s) prior to initiating any publication. All authors must disclose financial or personal affiliations that could be considered a conflict of interest.

15.0 APPENDICES

APPENDIX 1: NUMERIC PAIN RATING SCALE

For the Numeric Pain Rating Scale (NPRS), the patient is asked to indicate the numeric value on the segmented scale that best describes his or her pain intensity.



APPENDIX 2: ABLATION CONFIRMATION USER EVALUATION QUESTIONNAIRE

A Multicenter Study to Evaluate NEUWAVE Microwave Ablation System Using Ablation Confirmation in Patients with A Soft-tissue Liver Lesion

Protocol Number: NEU_2017_03

The Ablation Confirmation User will complete the table below after each ablation:

Please grade, on a scale of 0 to 5 (strongly disagree to strongly agree), how helpful AC was with the following:

Procedure Step	Definition	AC Helped Me (0-5 scale)	Comments
Lesion Visualization	**Marking and tracking the target** (How well the target lesion can be seen in the tissue.)		
Approach Planning	**Planning needle position** (Optimal path selection and ablation coverage optimization.)		
Probe Placement	**Understanding probe position prior to ablation** (The entry and movement traversing until in final position.)		
Ablation Planning	**Determining power and time to deliver to cover target and desired margin** (Probe, time, power, tissue contraction [tissue type])		
Ablation Confirmation	**Evaluating technical success of ablation coverage of target plus margin** (Determination of zone of effective ablation compared to target lesion and desired margin)		

The below is completed after approximately every 5 patients are treated by the performing physician (i.e., 5 patients are ablated with the NeuWave Microwave Ablation System with Ablation Confirmation Software).

Please grade, on a scale of 0 to 5 (Strongly disagree to strongly agree), how helpful AC was with the following:

- AC did not have a significant impact on procedure time or case resources. ____
- I use AC in every case because it increases my confidence in achieving a successful ablation. ____
- Ablation with NeuWave Microwave is more predictable, consistent, and controllable than other thermal ablation technologies. ____
- Ablation with multiple NeuWave probes is faster and more consistent than repeated place and ablate cycles with other thermal ablation technologies. ____
- Ablation with NeuWave Microwave increases my confidence in achieving a successful ablation compared with other thermal ablation technologies. ____

Additional comments not already captured above:

_____
_____
_____

16.0 REFERENCE LIST

[1] Poulou LS, Botsa E, Thanou I, Ziakas PD, Thanos L. Percutaneous microwave ablation *vs* radiofrequency ablation in the treatment of hepatocellular carcinoma. *World Journal of Hepatology*. 2015;7(8):1054-1063. doi:10.4254/wjh.v7.i8.1054.

[2] Huo YR, Eslick GD. Microwave Ablation Compared to Radiofrequency Ablation for Hepatic Lesions: A Meta-Analysis. J Vasc Interv Radiol. 2015 Aug;26(8):1139-1146.e2. doi: 10.1016/j.jvir.2015.04.004. Epub 2015 May 28.

[3] Chong CCN, Lee KF, Chu CM, Chan AWH, et al. Microwave ablation provides better survival than liver resection for hepatocellular carcinoma in patients with borderline liver function: application of ALBI score to patient selection. *HPB (Journal* of *International Hepato-Pancreato-Biliary Association)*. 2018 Jan 15. pii: S1365-182X(17)31182-6. doi: 10.1016/j.hpb.2017.12.001. [Epub ahead of print]

[4] Philips P, Scoggins CR, Rostas JK, McMasters KM, Martin RC. Safety and advantages of combined resection and microwave ablation in patients with bilobar hepatic malignancies. *Int J Hyperthermia*. 2017 Feb; 33:43.