Clinical Investigational Plan (CIP) Information	
Protocol Title	**The EMPrint™ Ablate and RESect Study in Patients with Metastatic Lung Tumors (EMPRESS)**
CIP Number	COVEMPR0437
Version Date	05 March 2018
Revision	Version 3.0
Sponsor Representative	Amanda Cafaro RN, BSN Director Clinical Research

Summary of Changes to CIP			
Rev.	**Section**	**Description of Change**	**Reason for Change**
2.0	3.2.2 Procedure Planning Application	Change from investigational device to FDA cleared device with specific indications for use	FDA cleared the procedure planning application
	5.3.1 Histological Analysis	Change number and type of samples read at core lab; change from 2 to 3 categories to evaluate complete ablation: 1) Complete Ablation, 2) Delayed Necrosis, 3) Incomplete Ablation	Consistent with final Histology Charter; add subgroup for delayed necrosis
	5.5.1 Inclusion Criteria	Add inclusion of primary LC; reduce tumor-free parenchyma requirement between the pleura and tumor from ≥ 2cm to ≥ 1cm	Investigator feedback
	5.5.2 Pre-procedure Exclusion Criteria	Exclude only GOLD Stage IV instead of GOLD Stage III and IV; delete specific test parameters for uncontrollable	Inclusion of primary LC population more likely to have GOLD Stage III disease and be surgical

		coagulopathy	candidates; investigator feedback
	5.7.5 Microwave Ablation Planning and Procedure	Addition of 4th CT after antenna is removed	Capture acute pneumothorax and/or bleeding events attributed to ablation procedure
	5.7.6 Planned Surgical Resection	Change acceptable time delay until surgical procedure definition from "day after ablation" to 36 hours after ablation. Change definition of protocol deviation to surgery performed beyond 36 hours after ablation,	Clarify definition for protocol deviation
	5.7.8 Sample Preparation for Histological Analysis	Addition of dye and fixation methods	Consistent with final Histology Charter
	7.2 Risks associated with Additional Radiation Exposure from Study-related CT imaging	Updated dose of radiation exposure	Addition of 4th CT
	8.10 Adverse Event Recording and Reporting	Specify which adverse events will be collected	Consistent with final Safety Plan
	11.1 Statement of Compliance	Statement following ISO GCP	clarity
	13.0 Monitoring	Statement following ISO GCP	clarity
3.0	CIP Information	Removed Sponsor Representative Location	Redaction of personal and proprietary information for CT.gov Results Posting to comply with Final Rule
	3.1 Background/Justification of Investigation	Removed internal background information	Redaction of personal and proprietary information for CT.gov Results Posting to comply with Final Rule
	3.2 Report of Prior Investigations	Removed internal and proprietary information; Removed Infernally referenced documents	Redaction of personal and proprietary information for CT.gov Results Posting to comply with Final Rule

Principal Investigator Signature Page

Protocol Title: **The EMPrint™ Ablate and RESect Study in Patients with Metastatic Lung Tumors (EMPRESS)**

Protocol Number: **COVEMPR0437**

Revision: **3.0**

I, the undersigned, have read and understood the protocol specified above and agree on its content. I agree to perform and conduct the study as described in the protocol and in accordance with the relevant laws/regulations and standards outlined in the Clinical Trial Agreement.

Name	Signature	Date

1.0 Table of Contents

2.0 Acronyms and Definitions

Term	Definition
ADE	Adverse Device Effect; Adverse event related to the use of an investigational medical device, including adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device, as well as any event resulting from use error or from intentional misuse of the investigational medical device.
AE	Adverse event; Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational device. This includes events related to the investigational device or the comparator and procedures involved.
ASADE	Anticipated serious adverse device effect; an effect which by its nature, incidence, severity, or outcome has been identified in the risk analysis report (R0042262).
CIP	clinical investigational plan
CRF	Case report form
CT	computed tomography
Device deficiency	Inadequacy of a medical device related to its identity, quality, durability, reliability, safety, or performance, such as malfunction, misuse or use error and inadequate labeling.
EC	Ethics committee (see IEC)
eCRF	Electronic case report form
H&E	Hematoxylin and eosin stain routinely used to evaluate the structural integrity of cells
IEC	Institutional ethics committee (see EC)
IFU	Instructions for Use; a manual or document accompanying a technical device that describes the directions by which the device should be used, applied, etc.
Investigative Site	An approved, participating study center/institution
Investigator	Either a principal, coordinating or sub-investigator, unless otherwise specified
IRB	Institutional Review Board
ITT	Intention to treat
MITT	Modified intention to treat
MWA	microwave ablation
NADH	β-nicotinamide adenine dinucleotide, reduced; assay used to determine cell viability

OR	Operating Room

RDC	Remote data capture; internet-based data entry system used to enter and store study data points
RTP	remote temperature probe
SADE	Serious adverse device effect; adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event
SAE	Serious adverse event; an adverse event that a) led to death, b) led to serious deterioration in the health of the subject, that either resulted in 1) a life-threatening illness or injury, or 2) a permanent impairment of a body structure or a body function, or 3) in-patient or prolonged hospitalization, or 4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function, c) led to fetal distress, fetal death or a congenital abnormality or birth defect NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered a serious adverse event.
TEAE	Treatment-emergent adverse event; any event not present prior to the initiation of the treatments or any event already present that worsens in either intensity or frequency following exposure to the treatments.
USADE	Unanticipated serious adverse device effect; serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report.

3.1 Introduction

3.2 Background/Justification of Investigation

Following CT-guided ablation of the tumor, a CT image will be performed to evaluate dose response. The ablation zone will then be resected as part of the standard surgical procedure and the tissue specimen will be examined using histology to determine the completeness of tumor ablation.

3.3 Report of Prior Investigations

The Covidien Emprint™ Ablation System under study in the current clinical investigational plan (CIP) was cleared by the U.S. FDA (K133821) in April 2014 and CE Mark was obtained in March 2014.

4.0 Identification and Description of Devices

4.1 Device Description

Devices that will be used in this study are the Emprint™ Ablation System and Accessories (K133821). Refer to the Emprint™ System IFU's and User's Guide for component descriptions. Additionally, the Emprint™ Procedure Planning Application, version 1.1 will be used to plan ablation dosing. Refer to the Emprint™ Procedure Planning Application, version 1.1 User's Guide for a description of the device.

Please reference the Instructions for Use for the Emprint™ Ablation System and Accessories. The Emprint™ Ablation Generator, the Reusable Cable, the Pump, and the Cart are provided non- sterile and are not used in the sterile field. These four components are reusable. Cleaning instructions for these components are provided in the Emprint™ Ablation System User's Guide, Reusable Cable Instructions for Use, and the Emprint™ Cart Instructions for Use.

The Emprint™ Percutaneous Antenna is provided sterile, is single use, and is intended to be used within the sterile field.

4.2 Indications

The Emprint™ Ablation System is intended for use in percutaneous, laparoscopic, and intraoperative coagulation (ablation) of soft tissue, including partial or complete ablation of non-resectable liver tumors. The System is not intended for use in cardiac procedures.

The Emprint™ Procedure Planning Application is a stand-alone software product that allows physicians to visualize and compare CT image data. The display, annotation, and volume rendering of medical images aids in the intervention planning for video-assisted thoracoscopic surgery (VATS) and ablation procedures using the Emprint™ Ablation System. The software is not intended for diagnosis.

4.3 Warnings

The following uses of MWA have not been studied:

- Pregnant patients: Microwave ablation procedures are not recommended for pregnant patients. Potential risks to the patient and/or fetus have not been established.
- Patients with implantable pacemakers and other electronic implants. Microwave ablation procedures are not recommended for patients with cardiac pacemakers or other implanted electronic devices. Potential risks have not been evaluated.

4.4 Identification and Dosage

Once all internal Covidien requirements are met, the Emprint™ Ablation System, the Emprint™ Percutaneous antennas, the reusable cable, ablation pump, and ablation cart and isolation transformer, will be shipped to each site. Additionally, a laptop loaded with the Emprint™

Procedure Planning Application, version 1.1, will be sent to each site prior to the study. Each site will document the quantity, lot number and/or serial number of each piece of equipment upon receipt.

5.1 Study Design

5.2 Overview

This will be a post market prospective, non-randomized, single-arm, multicenter study, designed to demonstrate dose response of the Emprint™ Ablation System using a percutaneous approach in patients with metastatic or primary lung tumors.

Up to 30 subjects who are scheduled for resection of metastatic or primary lung tumor(s) will be enrolled. Ablations will be carried out using a percutaneous approach at a dose (power and time setting) selected during procedure planning. NOTE: The procedure planning application will be used as an adjunct planning tool. While the physician prescribes the dose, the Emprint™ Procedure Planning Application overlays the 3-dimensional predicted ablation zone on the patient CT images, facilitating visualization of the predicted ablation zone relative to the target tumor. Once the ablation procedure is complete, the scheduled surgical tumor resection will be performed. Up to 10 study sites in the United States and Europe will participate in this trial.

5.3 Primary Effectiveness Endpoint: Dose Response

The primary endpoint of this study is dose response. Dose response will be assessed by comparing actual ablation zone size and volume to predicted ablation zone size and volume prescribed by the physician using the Emprint™ Procedure Planning Application, version 1.1. Dose response will be measured for each ablation zone using CT imaging immediately post ablation and prior to the surgical resection.

All measurements used to determine dose response will be measured and reported by an independent core imaging lab. To assess dose response, the following measurements will be taken:

Predicted Ablation Zone:

5.2.1 Predicted Ablation Zone Size

- The width (X), height (Y), and depth (Z) of the ablation zone, as depicted in the planning application annotation (via snapshot) will be measured and reported. All measurements will be taken from the planes depicted in **Figure 3.1**.
- Ablation zone volume as calculated by the planning application, captured in the snapshot.
- Volume is calculated using the ellipsoidal approximation where A is $\bar{}$width and is assumed to be axially symmetric, and B is height.

5.2.2 Predicted Ablation Zone Shape

Ablation zone shape will be reported as a ratio of width (X) to height (Y) (Figure 3.1). A more spherical shape will be indicated by a ratio close to one.

Actual ablation zone:

5.2.3 Actual Ablation Zone Size

- The width (X), height (Y), and depth (Z) of the ablation zone will be measured and reported, based on the planes depicted in **Figure 3.1**. In instances where the ablation zone width is not fully circular, the shortest diameter for X will be measured.
- Ablation zone volume will be measured using immediate post-procedure CT imaging and volumetric software package.

5.2.4 Actual Ablation Zone Shape

Ablation zone shape will be reported as a ratio of width (X) to height (Y) (**Figure 3.1**). A more spherical shape will be indicated by a ratio close to one.

5.2.5 Confirmation of Dose Response: Ablation Zone Size

Confirmation of dose response will be assessed by comparing the following measurements:

- Predicted ablation size (width (X), height (Y), depth (Z)) *vs.* actual ablation zone size (width (X), height (Y), depth (Z))
- Predicted ablation zone volume as determined by the Procedure Planning Application *vs.* actual ablation zone volume

5.3 Secondary Endpoint

Complete tumor ablation immediately post-procedure will be measured for each target tumor using histologic analysis to evaluate complete ablation at the cellular level.

5.3.1 Histological Analysis

All histology samples will be evaluated by a core laboratory. Both vital staining (Nicotinamide adenine dinucleotide (NADH) assay) and structural staining (hematoxylin and eosin; H&E) techniques will be used to evaluate cellular integrity within the ablation zone. Additionally, pixel enumeration techniques will be used to evaluate histologic ablation (coagulation zone and hyperemic zone). Once the samples have been received from the study site, the frozen sample will be serially sectioned into 8-10 micron increments, maintaining the axis along the previously inked black plane of division and continuing into the tissue beyond the ablation zone. Three distinct regions of the ablation zone will be evaluated. Four tissue sections from each region will be performed. The first, third and fourth will be used for NADH staining. The second section will be post-fixed in 10% buffered formalin in preparation for H&E staining. With binary staining characteristics, NADH staining assays will be used to assess viability in regions deemed equivocal on H&E stained samples. Positive staining is indicative of mitochondrial enzymatic activity and hence tissue viability, while a lack of staining is consistent with cellular death. Once the slides are processed and stained, the slides will be scanned into the Aperio™ digital image analyzer (Aperio ScanScope™). The ScanScope is a high throughput automated slide scanner which scans the entire slide and stores the digital images in a tiff format, allowing viewing and digital analysis of the slides with the ImageScope™ viewer. The Aperio ScanScope™ technology determines percent cell viability based on pixel quantification, where 0% color pixels indicates 100% non-viable cells, ≤10% color pixels indicates ≥ 90% non-viable cells and >10% color pixels indicates <90% non-viable cells. Complete tumor ablation using pixel quantification software will be defined as follows:

	Oncologic Characteristic	Histological Findings
Complete Ablation	Negative Margin	100% non-viable tumor cells
Delayed Necrosis	Weakly Positive Margin	≥90% non-viable tumor cells
Incomplete Ablation	Positive Margin	<90% non-viable tumor cells or tumor extends to the edge of the sample

Samples will be taken from three distinct regions of the ablation specimen and will be analyzed. Percent cell viability will be averaged over the entirety of the transition zone from each region and will be recorded.

5.4 Selection of Investigators and Training

Board-certified thoracic surgeons and interventional radiologists, in accordance with United States and European Union and hospital guidelines, will be considered for participation as

investigators in this study. Physicians in training (residents, fellows) and Physician Assistants may assist the Study Investigator in any aspect of the procedure as per standard procedures and practices at his/her institution with the following exception:

- Antenna placement

Sites must have imaging available to ablate percutaneously, including either computed tomography (CT) equipment in the operating room or the ability to transport patients from the interventional radiology suite to the operating room.

In addition, either a thoracic surgeon who will perform both the ablation and surgical procedure, or functional teams including both an interventional radiologist and a thoracic surgeon must be available at each site to participate in the study. If the ablation procedure is carried out by a thoracic surgeon, a thoracic surgeon investigator(s) must be available to carry out both the ablation and the subsequent scheduled resection.

Each Investigator and laboratory participating in the clinical trial and the associated clinical study staff will receive training on the clinical protocol, use of the Emprint™ Ablation System and Procedure Planning Application, as well as study-related methods for tissue sample preparation and CT image processing. Additionally, investigators will be trained on the device characteristics, device application and removal instructions, device dosage, device use and warnings associated with the technology per the IFU's and User's Guides.

5.5 Subject Selection and Enrollment

After being informed of the nature of the study, the subject will provide written informed consent that has been approved by the appropriate IRB or EC of the respective clinical site. A total of up to 30 subjects will be enrolled in the study at up to 10 clinical sites in the United States and Europe. Subjects' participation in the study may last 60-90 days after informed consent has been provided and eligibility has been confirmed. Subject enrollment will begin the day of the ablation procedure when the administration of the anesthesia for the ablation procedure begins and conclude after completion of the first standard of care post-operative follow-up visit. Prior to the administration of anesthesia, study eligibility will be confirmed the day of the ablation procedure.

The surgical procedure will be performed per the institution's standard practice. Patients scheduled for a pulmonary resection will be considered for study enrollment if they meet specific preoperative and intraoperative inclusion/exclusion criteria. The criteria for enrollment must be followed explicitly. If a subject does not meet all enrollment criteria and is inadvertently enrolled, the severity of the deviation will be reviewed by the Sponsor and assessments will be made to determine if the subject should remain in the study and if the site should continue to be allowed to enroll further subjects.

5.5.1 Inclusion Criteria

- Subject or authorized representative has provided informed consent
- Subject is ≥18 years of age

- At least one pulmonary metastasis ≤ 3.0 cm in maximum diameter resulting from distant primary cancers or one primary lung cancer ≤ 3.0 cm in maximum diameter
- Subject has been confirmed by a thoracic surgeon to be a surgical candidate for resection of the tumor targeted for ablation
- Subject is willing and able to comply with all aspects of the treatment and evaluation schedule
- ≥ 1 cm of tumor-free lung parenchyma between target tumor and pleura or fissure

5.5.2 Pre-procedure Exclusion Criteria

- Contraindicated for surgery
- Prolonged chest infection, defined as lung consolidation that requires hospitalization and greater than 10 days of antibiotics 30 days prior to surgery
- Tumor abutting main stem bronchus, main pulmonary artery branches, esophagus and/or trachea
- Tumor with pleural contact
- Tumors located < 3 cm of staple lines or other metal objects
- Patients diagnosed with GOLD Stage IV Emphysema
- Uncontrollable coagulopathy
- Patients unable to tolerate discontinued use of anti-coagulants prior to and during the ablation procedure
- Subject is pregnant (documented by a positive pregnancy test according to hospital standard practices) or is actively breast-feeding
- Subject has participated in an investigational drug or device research study within 30 days of enrollment that would interfere with this study
- The investigator determines that participation in the study may jeopardize the safety or welfare of the subject
- Patients with implantable pacemakers and other electronic implants, in accordance with IFU

5.5.3 Intraprocedural Exclusion Criteria

- Incidental finding that the subject no longer meets the study eligibility criteria

5.6 Withdrawal of Subjects

The reason for study exit will be documented on the applicable eCRF. In the event the subject withdraws consent during the study, the date of withdrawal will be documented. If the Study Investigator removes a subject from further study participation, supporting documentation must be in place for the rationale and date of removal.

5.7 Study Procedures

5.7.1 Study Assessments Table

	Patient Screening (within 30 days prior to surgery)	Procedure Day(s)	Post-operative Follow-up Visit	Imaging Analysis by Core Lab	Histology / Pathology Core Lab
Informed consent	X				
Preoperative eligibility criteria	X				
Demographics	X				
Medical / surgical history	X				
Height and weight	X				
Physical exam	X				
Primary cancer	X				
Pregnancy test[a]	X	X			
Study Start		X			
Ablation Planning		X			
Ablation start / stop times		X			
Ablation Procedure start / stop times		X			
Ablation dose		X			
Acute hemorrhage/hemoptysis rate		X			
Thermal injury rate		X			
Acute pneumothorax incidence		X			
Ablation-specific complications		X			
Device malfunctions		X			
Adverse events		X	X		
Study exit			X		
Hematoxylin and eosin staining					X
Vital staining					X
Tumor Size analysis	X			X	

	Patient Screening (within 30 days prior to surgery)	Procedure Day(s)	Post-operative Follow-up Visit	Imaging Analysis by Core Lab	Histology / Pathology Core Lab
Ablation volume / completeness				X	X
Ablation zone Size				X	

a. Pregnancy test to be administered to females of reproductive age who have not undergone previous sterilization or hysterectomy procedures. Should be administered only during the pre-procedure screening visit unless surgery is scheduled greater than 14 days from screening visit, in which case a pregnancy test should be administered prior to surgery.

5.7.2 Informed Consent and Screening

Subjects will be approached to obtain written informed consent prior to any study specific procedures being performed. The purpose of the study and the benefits and risks of the procedures will be explained to the subject. Subjects who agree to study participation must sign an IRB- or EC-approved informed consent form. Subjects will be informed that their participation in this study is voluntary and they may refuse to participate or discontinue from the study at any time. Subjects will be given the opportunity to ask the investigator questions so that they are adequately informed about the research. A copy of the signed informed consent will be offered to the subject and the informed consent process will be documented in source documents.

If new information becomes available that may affect a subject's decision to continue to take part in the study, this information will be discussed with the subject by the investigator.

5.7.3 Screening / Baseline Visit

A screening/baseline visit will be performed within 30 days prior to the scheduled procedure to assess preoperative eligibility. The following assessments will be performed and the results recorded on the appropriate subject eCRFs:

- Demographics
  - Age
  - Gender
  - Height
  - Weight
  - Body Mass Index
  - Race
  - Ethnicity
- Laboratory tests
- Pre-op Physical examination
- Medical history
- Location of primary cancer
- History of prior thoracic surgery (if applicable)
- Concomitant medications

- Comorbidities
- Pregnancy test (if applicable)
- Verification of preoperative eligibility criteria
- Verification of surgical candidacy
- Axial diameter of target pulmonary tumor along longest axis as determined through pre-operative CT imaging
- Pulmonary tumor volume as determined through pre-operative CT imaging

5.7.4 Screen Failures

Subjects will be considered enrolled into the study after written informed consent has been provided and the ablation procedure is initiated (defined as the time point when the patient is administered anesthesia in preparation for the ablation procedure). Subjects who provide study consent, but then are determined to be ineligible prior to the administration of anesthesia in preparation for the ablation procedure, will be considered screening failures. The reason for the screening failure will be clearly delineated on the applicable CRFs.

5.7.5 Microwave Ablation

In accordance with inclusion criteria, target tumors ≤3.0 cm in maximum axial diameter resulting from either distant primary cancers or primary lung cancers are eligible to be considered target tumors for the study analysis. Ablation dosing will be dependent on physician prescription based on target tumor size plus a minimum of a 0.5 cm margin, established during the ablation planning phase.

Ablation Planning and Procedure

If the pre-operative CT was taken greater than 30 days prior to the date of the procedure, a low-dose CT image will be taken prior to initiating the ablation procedure to confirm the tumor size and location prior to ablation planning. The interventional radiologist or thoracic surgeon will use the pre-procedure CT in the Emprint™ Procedure Planning Application to initiate ablation planning. Investigators will first launch the lung ablation planning application on the planning application laptop. They will next import the baseline CT from a USB drive onto the planning laptop and verify the quality of the CT image as assessed by the planning application. Once the investigator has located the tumor, he or she will add a virtual target to the target tumor and take a snapshot of the final target annotation. The investigator will then add an ablation zone that encompasses the target tumor with a minimum margin of 0.5 cm. They will select the appropriate antenna length from the dropdown menu, adjust the antenna trajectory to reflect desired insertion vector and mark the antenna insertion depth. The investigator will then view the planned ablation zone and antenna trajectory in all available planes for three dimensional confirmation of placement, and make any necessary adjustments to the ablation zone and/or antenna trajectory to ensure a safe and effective planned ablation. Finally, the investigator will take a snapshot of the final plan to capture predicted ablation zone measurements and calculated predicted ablation volume.

Patients will be positioned on the CT table (*e.g.,* supine, prone, or lateral) according to the location of the tumor, to achieve the shortest accessible path to the tumor in the position most tolerable to the patient. The microwave antenna will be applied percutaneously through a skin nick and will be advanced under CT guidance. Once final placement of the antenna has been achieved, a CT image will be taken to verify final placement.

Once antenna placement has been verified, the Emprint™ generator will be set by clinician to deliver the prescribed dose based on target tumor size plus a 0.5 cm margin and physician experience. Once the generator settings have been verified, the ablation will be initiated either by the investigator, using a foot switch, or radiology technician / scrub nurse, using the user interface on the generator.

Once the ablation is complete, the antenna will remain in place and the third CT image will be taken to evaluate the characteristics of the resulting ablation zone. The antenna will then be removed and the final CT image will be taken and will be used to identify adverse events that may have occurred during the ablation procedure.

Once the final CT image has been acquired, the ablation zone will be resected as scheduled, by the thoracic surgeon per standard surgical practice. The resected tissue will then be sent to the on-site pathology laboratory for sample preparation. The prepared samples will be sent to a core laboratory for histologic analyses.

If complications arise due to the microwave ablation, termination of the session will be determined at the discretion of the investigator according to the severity of the event and the extent of the intervention required.

CT imaging using a multidetector row helical CT scanner (minimum 8 detector) will be employed four times during the patients' enrollment in the study. The first three scans will be higher resolution to accurately measure target tumor size, antenna placement, and the ablation zone. The final CT will be a low dose scan to assess the presence of bleeding or pneumothorax that occurred during the ablation. Scan parameters for the first three scans will be as follows:

- Detector collimation – 1.5 mm or less
- Pitch < 1
- 120kVp
- Reference 100-140 mA (dependent upon body habitus). Auto mA may be left on, but all other dose reduction should be turned off.
- Scans will be performed with a breath hold at end inspiration with arms elevated over head if possible.
- No IV contrast.
- Images for 3D processing will be reconstructed at 1.5 mm with a 20% overlap using a standard kernel.

Scan parameters for the fourth low dose scan will be as follows:

- Detector collimation – 2.5 mm or less
- 120kVp

- Reference 40-80 mA (dependent upon body habitus)
- Scans will be performed with a breath hold at end inspiration with arms elevated over head if possible.
- No IV contrast.

1. Pre-procedure Scan

A Pre-procedure CT scan is only required on the day of the procedure if the standard of care CT scan was performed more than 30 days prior to the procedure date.

Scan volume should extend from the clavicles through the lung bases.

CT imaging either acquired the day of the procedure or up to 30 days prior will be used by Intrinsic, to confirm the location of the target tumor. More specifically, all tumors will be measured in three dimensions (maximum dimension, maximum perpendicular dimension, and third perpendicular dimension) on pre-procedure CT images by the imaging core laboratory. Tumor volume will also be directly measured with volumetric post-processing. Maximum transverse axial and perpendicular axial measurements will also be obtained to allow for comparison of tumor sizes with tumor sizes as recorded in most standard oncology trials.

These images and required reconstructions must be sent to Intrinsic Imaging.

2. Intra-procedural Scan

When the antenna is in its final location prior to commencing ablation, the intra-procedural CT will be obtained. Scan volume should extend from 5cm above the superior margin of the tumor to 5cm below the inferior margin of the tumor to help minimize unnecessary imaging of tissue outside the area of immediate procedural concern.

Intrinsic Imaging will use the image(s) of final placement of the antenna to evaluate technical accuracy, which is defined as correct positioning of antenna within the tumor. These data will specifically be used to evaluate any occurrence of incomplete ablation.

These images and required reconstructions must be sent to Intrinsic Imaging.

3. Post Procedure Scan (Antenna in Place)

Scan volume should extend from the clavicles through the lung bases. This CT scan will be obtained once the ablation is complete but with the antenna still in place. This Post-procedural imaging will be used to assess dose response.

These images and required reconstructions must be sent to Intrinsic Imaging.

4. Post Procedure Scan (Antenna Removed)

Scan volume should extend from the clavicles through the lung bases.

This CT scan will be obtained to identify and evaluate acute adverse events that may have occurred during the ablation procedure.

Anesthesia

Anesthesia use will be determined by each site per standard of care and will be administered after ablation planning has occurred.

Ablation Procedure

An appropriate length Emprint™ percutaneous antenna (15 cm or 20 cm) will be placed into the target tumor under CT image guidance. An ablation zone will then be generated using a single application of a prescribed dose based on target tumor size. Following completion of the prescribed dose, a post ablation CT image will be taken. The antenna will then be removed and the planned surgical resection will be conducted as scheduled.

In addition, the following ablation-specific variables will be collected at the time of procedure:

- Date
- Ablation zone diameter of longest axis as determined through post-procedure CT imaging
- Ablation zone volume as determined through post-procedure CT imaging
- Ablation start and stop times
- Total ablation time
- Overall ablation procedure time from beginning of antenna placement to completion of the ablation.
- Antenna size
- Dose used
- Adverse events
- Device Deficiencies
- Procedural failures (e.g., failure of microwave application, patient factors that prematurely stop procedure, etc.)

5.7.6 Planned Surgical Resection

Surgical resection and postoperative management will occur per standard local practice. The entirety of each target tumor and the microwave ablation zone should be resected. Every attempt will be made by each site to perform the surgical resection immediately after or the same day of the ablation procedure. However, if an unforeseen event occurs resulting in an OR scheduling conflict, surgical resection performed up to 36 hours after the ablation procedure is acceptable.

However, surgical resection of the ablation zone performed beyond 36 hours will be considered a protocol deviation.

The following procedural variables will be collected:

- Device and/or ablation procedure related adverse events as defined in section 6.6.2.

5.7.7 Postoperative Evaluation / End of Study Visit

The study subject will complete the study at the conclusion of the first post-operative visit, conducted per standard local practice, but occurring no later than 30 days after the scheduled resection.

5.7.8 Sample Preparation for Histological Analyses

Each study site will be supplied with a kit for sample preparation and shipment. All samples and kits will be de-identified by labeling with an assigned study identification number. Once the ablation zone is resected, the sample will be taken to the pathology lab on site. The resection will be examined to identify the antenna track. Once identified, the tissue will be transected down the plane of the antenna track. A digital photograph will be taken of each ablation cross section. Half of the sample will then be kept by the onsite pathology lab for future analysis. The plane of resection of the remaining half will be dyed with black India ink to maintain orientation for histologic examination. The India ink is fixed with Bouin's solution to prevent tracking of ink. The research half of the sphere is then sliced perpendicular to the initial cross section (quartered) to provide two samples. One new cut section is inked green, fixed with Bouin's, submitted in formalin; the other cut section is inked blue, fixed with Bouin's and flash frozen. Both samples will be shipped overnight to the Core Histology Laboratory for analysis. Standard H&E and NADH technique will be performed on the tissue samples.

6.1 Statistical Analysis

6.2 General

A detailed statistical analysis plan will be finalized prior to performing any analyses to expand upon the statistical methods presented below. Summary tables will summarize data for all subjects together.

6.3 Sample Size Determination

No pre-specified sample size calculations were performed for this post-market, prospective, non-randomized, single-arm, multicenter study.

6.4 Analysis Populations

Intent-To-Treat (ITT): subjects enrolled into the study.

Modified ITT (MITT): ITT subjects who underwent the ablation procedure.

6.5 Demographics and Other Subject Characteristics

Subject demographics and pre-treatment characteristics will be summarized for the ITT population.

6.6 Effectiveness Analysis

Effectiveness analyses will be done for the MITT population.

6.5.1 Primary Endpoint

The primary endpoint is dose response immediately post-procedure (for each target tumor) and is defined as the percentage change from the predicted outcome to the actual outcome. The percentage change (calculated as 100*(A-P)/P) will be calculated for each target tumor, where P=predicted and A=actual. The percentage change will be calculated for each tumor for the following measurements:

- Ablation zone width (X)
- Ablation zone height (Y)
- Ablation zone depth (Z)
- Ablation zone volume
- Ablation zone shape

For each of the above measurements, the percentage change for all tumors will be summarized. Summary will also be done by tumor type.

The predicted values will come from the Procedure Planning Application and the actual values will come from the CT imaging.

6.5.2 Secondary Endpoints

The number and percentage of tumors which achieve complete tumor ablation, incomplete tumor ablation (delayed necrosis) and incomplete tumor ablation (positive margin) (both overall and according to tumor type) will be presented. Ablation will be assessed using histology. A 95% exact binomial confidence interval will be calculated for each response.

6.6 Safety Analysis

Safety analyses will be done for the MITT population.

6.6.1 Exposure

The dosing information (time, power) will be listed by subject.

6.6.2 Adverse Events & Complications

Tables to summarize the incidence rates will be created for each of the following groups:

- Adverse events
- Serious adverse events
- Adverse events leading to premature discontinuation
- Adverse device effects (ADE)
- Serious adverse device effects (SADE)
- Unanticipated serious adverse device effects (USADE)
- Adverse events by intensity
- Adverse events by relationship to study product administration

Adverse events that led to premature discontinuation from the study will be listed. Serious adverse events, SADE and USADE will also be listed.

6.7 Interim Analyses

An interim analysis will be conducted once the first 15 tumors are ablated (preferably representative samples from each site).

6.8 Handling of Missing Data

Missing data rules will be specified in the detailed statistical analysis plan.

7.1 Risk/Benefit Analysis

The purpose of this study is to create and evaluate an ablation zone created in patients already scheduled for surgical resection of metastatic or primary lung disease per standard practice. The ablation procedure is not intended to treat the target tumor.

Since the Emprint™ Ablation system is similar in technology and indication to the existing MWA systems currently marketed in the U.S., EU and ROW, the potential harms associated with the Emprint™ Ablation System are the same as those presented in the literature and reported complaints. More specifically, the current hazard analysis for the Emprint™ Ablation system identified the following lung specific potential harms related to use of the Emprint™ Ablation System:

- Pneumothorax
- Skin Burn
- Unintended Parenchymal Ablation, defined as lung parenchymal ablation extended > 1 cm beyond predetermined volume of ablation safety margins
- Tissue Tear
- Microwave/Thermal Burn causing damage to extrapulmonary structure (*e.g.,* pleural burn, Diaphragmatic Paresis or perforation, Vessel Thrombosis, Mediastinal burn)
- Bleeding (*e.g.,* Hemorrhage, Hemothorax, Hematoma, Hemoptysis)
- Infection (*e.g.,* Abscess, Pneumopathy)
- Procedural Delay (*e.g.* delayed or canceled surgery)
- Foreign Object in Body

The risk analysis assumes the system is operated by quality, properly trained personnel. The overall residual risk after design risk mitigation strategies and/or design control was deemed acceptable in the Risk Management Report for the Emprint™ Ablation System.

7.2 Anticipated Risks Associated with Lung Tumor Ablation Reported in Literature and by Investigators

Based on the evidence summarized in Section 3.2, potential risks associated with lung tumor ablation with the Emprint™ Ablation System include but are not limited to:

- Pneumothorax (9,10,12)
    - Mild severity (reported incidence: 4.6% - 27%)
    - Moderate or severe severity (reported incidence: 3.9% -12%)
- Pleural Effusion
- Skin burns (reported incidence: 0.8 % - 4.3%) (9,10,16)
- Acute respiratory distress (reported incidence: 2%) (9)
- Self-limiting hemoptysis (reported incidence: 4.6% – 7.25%) (9,10,12,14)
- Hemorrhage requiring additional intervention treatment (reported incidence: 1-2%) (investigator experience)
- Empyema development (reported incidence: <5%) (17)
- Post-ablation syndrome, defined as productive cough with or without minor hemoptysis, residual soreness in the treated area, and fever occurring several days post-ablation (reported incidence: 2%) (9)
- Post-procedural pain (reported incidence: 2%) (9)
- Slight risk of bleeding from placement of the microwave ablation antenna
- Insufficient coagulation (single report in MAUDE database)
- Nerve Injury (*e.g.,* stallate ganglion, intercostal and phrenic nerves)

Oncologic and surgical principles should not be compromised by the addition of tumor ablation to the surgical resection procedure. The tumor will be completely excised and the single-use antenna will not be used again in any living tissue. Thus, this study protocol does not impart any risk of spreading tumor cells.

Reproductive and developmental toxicology studies in animals to evaluate the potential for AEs on reproductive ability and effects on the embryo/fetus have not been conducted. Subjects who are pregnant (documented by a positive pregnancy test) or are actively breast-feeding are excluded per study protocol.

7.3 Risks Associated with Additional Radiation Exposure for Study-Related CT Imaging

There are risks associated with the use of CT. The main risks are those associated with the increased possibility of cancer induction from x-ray radiation exposure. Normally, an individual may be exposed to approximately 3 millisieverts of radiation each year just from background environmental radiation, such as radon and cosmic rays. In higher elevation areas an individual's background exposure can be as high as 10 millisieverts per year. The expected additional exposure due to the CT procedures in this study would be in the range of 12 to 30 millisieverts.

The probability for absorbed x-rays to induce cancer or heritable mutations leading to genetically associated diseases in offspring is thought to be very small for radiation doses of the magnitude that are associated with CT procedures and for any one person the risk of radiation-induced cancer is much smaller than the natural risk of cancer. However, an individual's risk of harmful effects may increase if they are exposed to additional procedures that involve radiation such as x-rays or if additional CT scans are required for care.

7.4 Risks Associated with Study Procedure

There is a potential for longer procedure time; however, because other aspects of the planned surgical resection procedure can be conducted during the ablation, the addition of ablation to the procedure is unlikely to cause a significant increase in procedure time.

Additionally, there is a risk that based on the length and execution of the ablation procedure, the standard of care surgical resection may need to be rescheduled to the day after the ablation procedure, resulting in an overnight hospital stay for the study subject. This is a small risk, however, if this occurs, all costs related to the additional overnight hospital stay will be incurred by the Sponsor.

7.5 Potential Benefits to the Subject

Because this study will be conducted in patients already scheduled for surgical resection of metastatic or primary lung tumors, the study protocol will not impart significant benefits beyond the benefit of lung resection alone.

If the results of this study are favorable, further studies may be justified to evaluate the potential for improved standard of care using microwave ablation technology in inoperable lung tumors and patients.

8.1 Adverse Events, Complications, and Product Complaints

Since this product is a legally marketed product, all SAE's regardless of cause, device and/or ablation procedure related AEs or complications and product complaints will be reported to Covidien Post Market Vigilance for documentation and investigation according to CI-007D.

8.2 Adverse Event (AE)

An Adverse Event is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the medical device.

Adverse events will be collected starting from the initial administration of anesthesia to the patient until conclusion of the first post-operative follow-up visit. All enrolled subjects will be evaluated for Adverse Events regardless of whether or not the subject received the planned ablation and resection.

It should be noted the risks identified above are similar to those noted for standard lung resection. In some cases, it will be impossible to differentiate surgery induced AE's from ablation induced AEs, specifically for AE's that occur after surgery. This should be noted as a limitation in quantifying device and/or ablation procedure related AEs .

8.3 Serious Adverse Event (SAE)

A Serious Adverse Event is an adverse event that has

a) led to death,

b) led to serious deterioration in the health of the subject, that either resulted in

1) a life-threatening illness or injury, or

2) a permanent impairment of a body structure or a body function, or

3) in-patient or prolonged hospitalization, or

4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,

NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered a serious adverse event.

8.4 Adverse Device Effect (ADE)

An Adverse Device Effect is an adverse event related to the use of a medical device.

This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, installation, or operation, or any malfunction of the medical device.

This definition includes any event resulting from use error or from intentional misuse of the medical device.

8.5 Serious Adverse Device Effect (SADE)

A Serious Adverse Device Effect is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

8.6 Unanticipated Serious Adverse Device Effect (USADE)

An Unanticipated Serious Adverse Device Effect is a serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current version of the risk analysis report.

8.7 Definitions of Specific Adverse Events

This list is not meant to be all inclusive but representative of specific adverse events relevant to the ablation procedure and/or outcome.

- Pneumothorax, defined as clinically significant: expanding and requiring a chest tube insertion or non-clinically significant: radiologically apparent in a non-symptomatic patient
    - The incidence of non-clinically significant pneumothoraxes will be collected as a safety endpoint only and will be used to determine trends for follow on studies. Clinically significant pneumothoraxes will be reported as AE's if a chest tube is needed prior to the surgical intervention.
- Pleural Effusion, defined as the accumulation of excess fluid in the pleural cavity after the ablation procedure and prior to the initiation of the surgical procedure
- Bleeding – an outcome of the failure to achieve or maintain hemostasis that results in
    - Hematoma
    - Hemorrhage (includes parenchymal pulmonary hemorrhage, hemothorax, and hemoptysis), defined by a change in vital signs sometimes requiring resuscitation

Bleeding will be assessed after the ablation procedure and prior to initiation of the surgical resection and will be evaluated based on the following CTCAEv.4 definitions:

HEMORRHAGE/BLEEDING						Page 1 of 4
		Grade				
Adverse Event	Short Name	1	2	3	4	5
Hematoma	Hematoma	Minimal symptoms, invasive intervention not indicated	Minimally invasive evacuation or aspiration indicated	Transfusion, interventional radiology, or operative intervention indicated	Life-threatening consequences; major urgent intervention indicated	Death
REMARK: Hematoma refers to extravasation at wound or operative site or secondary to other intervention. Transfusion implies pRBC. ALSO CONSIDER: Fibrinogen; INR (International Normalized Ratio of prothrombin time); Platelets; PTT (Partial Thromboplastin Time).						
Hemorrhage/bleeding associated with surgery, intra-operative or postoperative	Hemorrhage with surgery	—	—	Requiring transfusion of 2 units non-autologous (10 cc/kg for pediatrics) pRBCs beyond protocol specification; postoperative interventional radiology, endoscopic, or operative intervention indicated	Life-threatening consequences	Death
REMARK: Postoperative period is defined as ≤72 hours after surgery. Verify protocol-specific acceptable guidelines regarding pRBC transfusion. ALSO CONSIDER: Fibrinogen; INR (International Normalized Ratio of prothrombin time); Platelets; PTT (Partial Thromboplastin Time).						
Hemorrhage, CNS	CNS hemorrhage	Asymptomatic, radiographic findings only	Medical intervention indicated	Ventriculostomy, ICP monitoring, intraventricular thrombolysis, or operative intervention indicated	Life-threatening consequences; neurologic deficit or disability	Death
ALSO CONSIDER: Fibrinogen; INR (International Normalized Ratio of prothrombin time); Platelets; PTT (Partial Thromboplastin Time).						

- Device Deficiencies including but not limited to:
    - Device components left inside the subject – any part of the antenna breaking and dislodging in the patient
    - Generator malfunction leading to premature termination of ablation cycle
- Unintended Parenchymal Ablation, defined as lung parenchymal ablation extended > 1 cm beyond predetermined volume of ablation safety margins
- Microwave/Thermal Burn causing damage to extrapulmonary structures (*e.g.,* pleural burn, Diaphragmatic Paresis or perforation, Vessel Thrombosis, Mediastinal burn)
    - Grade 1: minimal symptoms, no intervention
    - Grade 2: medical intervention, debridement
    - Grade 3: moderate/major debridement, reconstruction
- Nerve Injury (*e.g.* stallate ganglion, intercostal and phrenic nerves), defined as one of the following:
    - Neuropathic pain or dysesthia in the distribution of an intercostal nerve adjacent to the ablation zone
    - Horner's Syndrome (proptosis, meiosis and anhydrosis of the ipsilateral eye) related to thermal injury of a high upper lobe tumor situated medially abutting the paraspinal region
    - New paralysis of the ipsilateral hemidiaphragm related to thermal injury of the phrenic nerve
- Musculoskeletal Fracture- if immobilization needed or operative intervention is required
- Soft Tissue Tear resulting in partial resection of injured area
- Allergic/Toxic Reaction

8.8 Adverse Event Severity Classification

Severity will be defined according to the following CTCAEv.4 criteria:

Grade 1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
Grade 2	Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL.
Grade 3	Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL**
Grade 4	Life-threatening consequences; urgent intervention indicated.
Grade 5	Death related to AE

8.9 Adverse Event Relationship Classification

Relationship to study product administration will be determined as follows:

- *No Relationship*: No relationship between the AE and the administration of study treatment and a known relationship to other etiologies such as concomitant medications, surgical procedure, or subject's clinical state.
- *Possible Relationship:* An AE that follows a reasonable temporal sequence from administration of the study treatment and follows a known response pattern to the study treatment but could have been produced by the participant's clinical state or by other therapies.
- *Probable Relationship:* An AE that follows a reasonable temporal sequence from administration of the study treatment; follows a known response pattern to the study treatment; and cannot be reasonably explained by the known characteristics of the participant's clinical state or by other therapies.
- *Definite Relationship:* An AE that follows a plausible temporal sequence from administration of the study treatment and follows a known response pattern to the study treatment. The reaction cannot be reasonably explained by the known characteristics of the subject's clinical state or other modes of therapy administered to the subject.
- *Unknown/Impossible to Determine:* Given the information available, sequence and timing of events, it is unknown or impossible to determine the relationship of the AE with the study treatment.

8.10 Adverse Event Outcome Classification

Outcome of the event will be defined according to the following:

- *Resolved:* The event has fully resolved at the end of the study.
- *Resolved with sequelae*: The event has resolved, but retained pathological conditions resulting from the prior disease or injury.
- *Continuing:* The event is ongoing at the end of the study.
- *Death:* This event is determined to be the cause of death.

8.11 Adverse Event Recording and Reporting

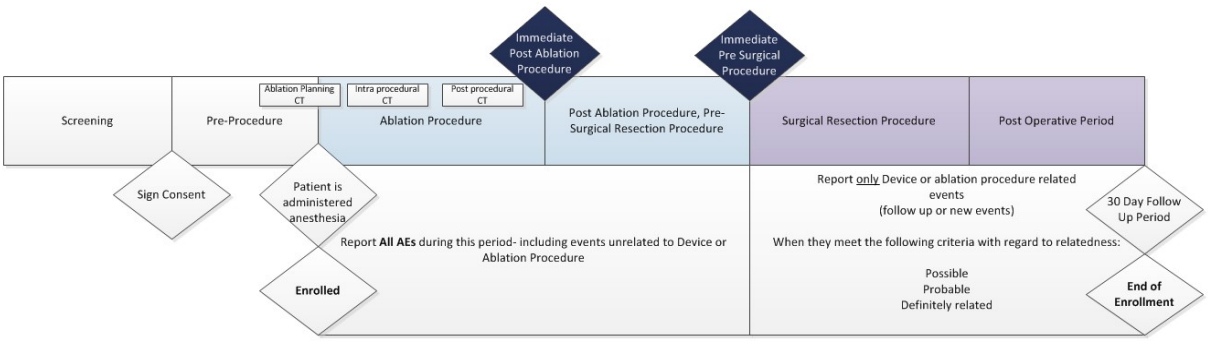
In addition to the adverse event reporting required for post market device reporting, adverse events occurring during the ablation procedure and/or attributed to the ablation procedure will be recorded in an AE CRF and reported in clinical study reports.

Assessment of the occurrence of an AE will be based on changes in the subject's physical examination, laboratory results and/or signs and symptoms. Adverse events will be monitored until conclusion of the first post-operative follow-up visit unless the Investigator determines the event is related to the device or ablation procedure, in which case they will be monitored until resolution if possible. Medical care will be provided, as defined in the informed consent, for any device or ablation procedure related AEduring study participation. Adverse events will be collected on an AE eCRF and applicable source documentation. To the extent possible, the event to be recorded and reported is the event diagnosis as opposed to event symptoms (e.g., fever, chills, nausea and vomiting in the presence of a clinically diagnosed infection is to be reported as infection only). For the purposes of this protocol, only those AEs occurring after initial administration of anesthesia will be recorded.

The following should not be considered an AE:

- A condition requiring a preplanned procedure unless the condition worsened since screening
- A preexisting condition found as a result of screening, unless the condition has worsened since the screening visit, and is noted on the day of the procedure

All AEs observed during the ablation procedure for this study, regardless of severity or relationship to the device will be recorded on the appropriate CRF and reported in clinical study reports. Only device and/or ablation procedure related AE's deemed possible, probable, or definitely related will be reported during the surgical resection. To ensure reported events can be attributed to the device and/or ablation procedure, it is strongly recommended that a safety evaluation be performed immediate post-ablation procedure to capture acute events and again prior to the scheduled surgical resection.



8.12 Notification to Authorities

The following events are generally considered reportable during the course of this study and should be reported to the sponsor within 24 hours of the time the Site learns of the event:

- any ADE, SADE, SAE, or USADE
- any Investigational Medical Device Deficiency that might have led to an SADE if
  - a) suitable action had not been taken or
  - b) intervention had not been made or
  - c) if circumstances had been less fortunate
- new findings/updates in relation to already reported events.

Events will be reviewed by Covidien or designee and will be reported to comply with local standards and mandatory reporting practices.

9.0 Device Deficiencies

A Device deficiency is an inadequacy of a medical device related to its identity, quality, durability, reliability, safety, or performance, such as malfunction, misuse or use error and inadequate labeling.

All Emprint™ Ablation System device deficiencies will be documented on the appropriate Device deficiency eCRF and the device should be returned to Covidien for analysis, if possible. Instructions for returning the device will be provided. Device deficiencies should also be documented in the subject's medical record.

Device deficiencies are NOT to be reported as AEs. However, if there is an AE that results from a device deficiency, that specific event would be recorded on the appropriate eCRF.

10.0 Safety Committees

The sponsor will employ a comprehensive safety plan for this study comprised of the following components:

10.1 Independent Medical Monitor

The Sponsor will utilize an Independent Medical Monitor to provide an independent medical review and adjudication of pre-specified adverse events in support of protocol defined endpoint data. The Independent Medical Monitor is a qualified, board-certified Interventional Radiologist.

Refer to the Independent Medical Monitor charter for additional details.

11.0 Steering Committee

The Steering Committee will consist of the Principal Investigator at each clinical site as well as appropriate members of Covidien Clinical and Medical Affairs. The role of the steering committee is to make recommendations on the design and conduct of the study, the analysis of data, and the communication of results in alignment with the Covidien Publication and Authorship Policy.

12.0 Compliance

12.1 Statement of Compliance

This clinical investigation will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, Clinical investigation of medical devices for human subjects — ISO 14155:2011 Good Clinical Practice, and any regional or national regulations, as appropriate.

The clinical investigation will not begin until all necessary approvals/favorable opinions are obtained from the appropriate IRB or IEC or regulatory authority, as appropriate. Should an IRB or IEC or regulatory authority impose any additional requirements, they will be followed.

Information regarding the study and study data will be made available via publication on clintrials.gov. Additionally, the results of this study will be offered for publication at the conclusion of the study, if participating investigators believe the data warrants publication in an appropriate journal.

12.2 Protocol Compliance

No changes to the protocol will be permitted without the written approval from Covidien and the IRB/EC. The investigator must notify Covidien and the reviewing IRB/EC of any deviation from the Investigational Plan when specific to the protection of the life or physical well-being of a subject in an emergency. Such notice must be given as soon as possible, but in no event later than 5 working days after the emergency has occurred. Except in such an emergency, prior written approval by Covidien is required for changes in or deviations from the Plan. If these changes or deviations affect the scientific soundness of the Plan or the rights, safety, or welfare of human subjects the IRB/EC will also be notified. All other deviations will be reported per the site's IRB/EC deviation policy. Should any deviations from the Investigational Plan occur, these

will be reviewed by Covidien for their clinical significance. If the event is performed without written approval from all parties, the investigator may be terminated from the study.

13.1 Monitoring Procedures

Site visits will be conducted by an authorized Covidien representative to inspect study data, subjects' medical records, and eCRFs in accordance with ISO 14155:2011 Good Clinical Practices and the respective local and national government regulations and guidelines (if applicable).The Study Investigator and the investigating site will permit authorized clinical research personnel and clinical monitors from Covidien and/or designee(s) employed by Covidien to review completed eCRFs, IEC or IRB decisions, and Investigator, clinical site records, and facilities relevant to this study at regular intervals throughout the study per the monitoring plan. Additionally, subject charts and clinical records will be requested and reviewed so that protocol adherence and source documentation can be verified. The accuracy and quality of the data obtained from the investigator and maintained by Covidien will be confirmed through a structured program of clinical field auditing and internal review detailed in the monitoring plan. In instances where data protection regulations prohibit the direct examination of hospital records by the study Sponsor or designee(s), the Investigator will cooperate in a system of source data verification with the Sponsor. Monitoring may be performed with in person visits or remotely, when applicable.

To ensure the rights, safety, and welfare of study subjects are being maintained, the monitor will review training records to ensure all study staff are trained on the study protocol and use of the study devices. If the monitor discovers that an investigator is not complying with the signed Investigator Agreement, the investigational plan, applicable laws, or any conditions of approval imposed by the reviewing IEC or IRB the monitor will report to the Sponsor and take such steps necessary to promptly secure compliance. If compliance cannot be secured, device shipments to the investigator may be discontinued and the investigator's participation in the investigation terminated. The monitor shall also require such an investigator to dispose of or return the device, unless this action would jeopardize the rights, safety, or welfare of a subject.

13.2 Data Collection and Processing

This study will utilize an electronic database and eCRF. In order to accurately collect all information, subject worksheets will be provided for study specific data (specific operative data points, etc.) not found in the medical records and will be considered the source document. All data requested on the eCRF are considered required. Data points not collected and/or recorded will be considered deviations unless otherwise specified. The Principal Investigator must ensure the accuracy and completeness of the recorded data and then provide his/her electronic signature on the appropriate eCRFs. The Investigator's electronic signature for specific eCRFs will be documented in compliance with local regulations. Changes to data previously submitted to the sponsor will require a new electronic signature by the Investigator to acknowledge/approve the changes.

Visual and/or computer data review will be performed to identify possible data discrepancies. Manual and/or automatic queries will be created in LiveTrial (RDC) system and will be issued to

the site for appropriate response. The site staff will be responsible for resolving all queries in the database.

14.0 Study Supplies and Device Accountability

14.1 Emprint™ Ablation System

The Emprint™ Ablation System will be provided to each site upon Sponsor collection and approval of all required regulatory documentation. The device will be labeled "Exclusively for Clinical Investigations" and should be stored in a secure (locked) area under the appropriate storage conditions. Access should be limited to designated study staff only. Device accountability logs will be provided to the site. It is the site's responsibility to document the receipt (maintain shipping logs), disposition of the product (per subject use, including amount used, amount remaining, etc.), transfer (if applicable) and return of all unopened study devices.

14.2 Planning Laptop

A laptop loaded with the ablation planning application software will be provided prior to the start of the study. It is the site's responsibility to record the serial number of the laptop upon receipt. Access to and use of the planning laptop should be limited to designated study staff only. Once the study has concluded, the planning laptop will be returned to Covidien.

15.1 General Information

15.2 Study Contact Information

Questions regarding safety or medical procedures should be directed to Medical Affairs. All other questions should be directed to Clinical Affairs.

Amanda Cafaro, RN, BSN Director Clinical Research	Jaime Kean, Ph.D. Program Manager, Clinical Affairs

15.3 Retention of Records

The investigator will maintain the records of the study including all pertinent correspondence, the study protocol with any/all amendments, all correspondence with and approval from the IEC, the clinical trial agreement, the Investigator Agreement, investigational device accountability records, individual subject records, and signed informed consent forms. Subject files and other source data must be kept for a period of not less than 2 years after the date on which this investigation is terminated or completed. Records may need to be maintained by the Principal Investigator for a longer duration if national regulations require or if agreed to in writing with Covidien. All data and documents should be made available if requested by relevant authorities.

15.4 Study Completion/Termination of Study

Covidien reserves the right to discontinue the study at any stage, with suitable written notice to all investigators, all reviewing IRBs or IECs, and FDA or Competent Authorities. Similarly, investigators may withdraw from the study at any time, subject to providing written notification to Covidien 30 days prior to the date they intend to withdraw. However, Covidien and investigators will be bound by their obligation to complete the follow-up of subjects already participating in the study. The subjects must be followed according to the clinical protocol, and information obtained during subject follow-up shall be reported to Covidien on the appropriate eCRF.

16.0 Appendices

There are no appendices to this protocol.